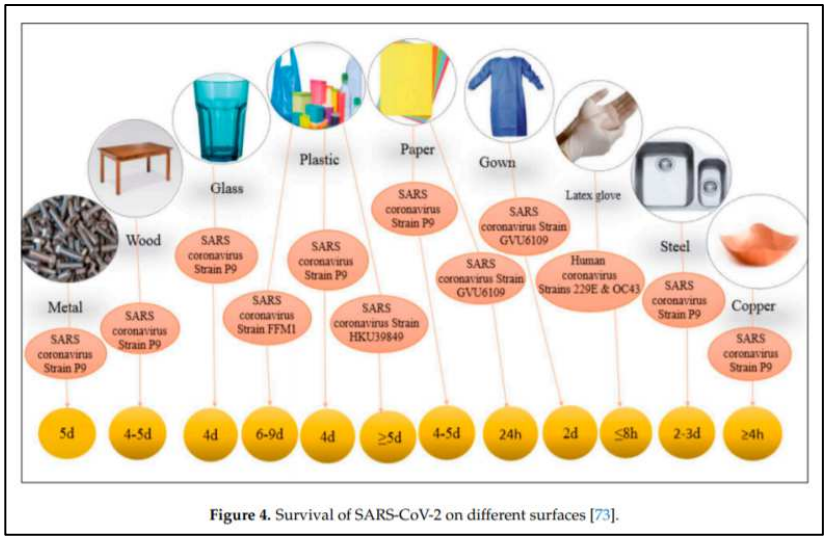
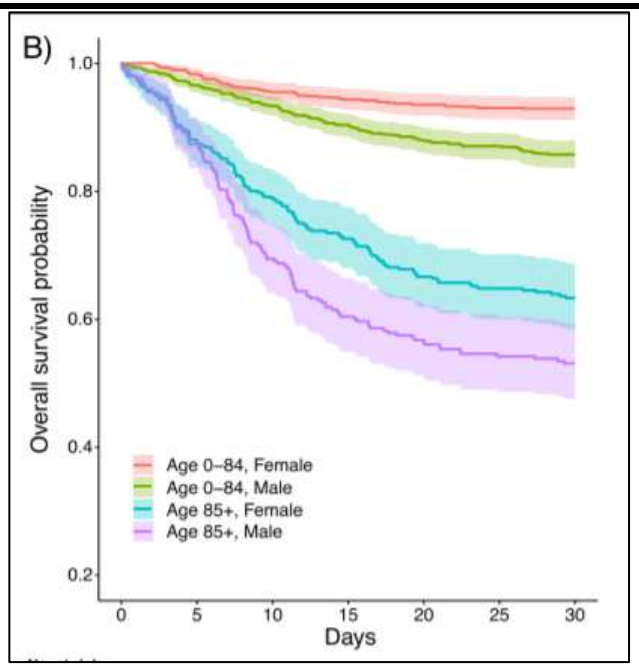
RICERCA BIBLIOGRAFICA COVID 19 SETTIMANA 11-17.01.2021 FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE DOTT.SSA ELEONORA TADDEI			
AUTORE/RIVISTA	**TITOLO**	**OUTCOME PRINCIPALE**	**ABSTRACT**
Deng F et al Medicina Clinica https://doi.org/10.1016/j.medcli.2020.11.030	Increased levels of ferritin on admission predicts intensive care unit mortality in patients with COVID-19.	Studio retrospettivo su 100 pazienti ricoverati in rianimazione in Cina, per i quali si dimostra una associazione fra ferritinemia al ricovero e gravità del decorso. La ferritinemia è inoltre predittore indipendente di mortalità intraospedaliera.	BACKGROUND: The aim of this study was to evaluate hyperferritinemia could be a predicting factor of mortality in hospitalized patients with coronavirus disease-2019 (COVID-19). METHODS: A total of 100 hospitalized patients with COVID-19 in intensive care unit (ICU) were enrolled and classified into moderate (n=17), severe (n=40) and critical groups (n=43). Clinical information and laboratory results were collected and the concentrations of ferritin were compared among different groups. The association between ferritin and mortality was evaluated by logistic regression analysis. Moreover, the efficiency of the predicting value was assessed using receiver operating characteristic (ROC) curve. RESULTS: The amount of ferritin was significantly higher in critical group compared with moderate and severe groups. The median of ferritin concentration was about three times higher in death group than survival group (1722.25mug/L vs. 501.90mug/L, p<0.01). The concentration of ferritin was positively correlated with other

			inflammatory cytokines, such as interleukin (IL)-8, IL-10, C-reactive protein (CRP) and tumor necrosis factor (TNF)-alpha. Logistic regression analysis demonstrated that ferritin was an independent predictor of in-hospital mortality. Especially, high-ferritin group was associated with higher incidence of mortality, with adjusted odds ratio of 104.97 [95% confidence interval (CI) 2.63-4185.89; p=0.013]. Moreover, ferritin had an advantage of discriminative capacity with the area under ROC (AUC) of 0.822 (95% CI 0.737-0.907) higher than procalcitonin and CRP. CONCLUSION: The ferritin measured at admission may serve as an independent factor for predicting in-hospital mortality in patients with COVID-19 in ICU.
Delikhoon M et al International Journal fo Environmental Research and Public Health https://doi.org/10.3390/ijerph18020395	Modes of Transmission of Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2) and Factors Influencing on the Airborne Transmission: A Review.	Revisione sistematica delle vie di trasmissione di SARS-CoV-2	The multiple modes of SARS-CoV-2 transmission including airborne, droplet, contact, and fecal-oral transmissions that cause coronavirus disease 2019 (COVID-19) contribute to a public threat to the lives of people worldwide. Herein, different databases are reviewed to evaluate modes of transmission of SARS-CoV-2 and study the effects of negative pressure ventilation, air conditioning system, and related protection approaches of this virus. Droplet transmission was commonly reported to occur in particles with diameter >5 microm that can quickly settle gravitationally on surfaces (1-2 m). Instead, fine and ultrafine particles (airborne transmission) can stay suspended for an extended period of time (>/=2 h) and be transported further, e.g., up to 8 m through simple diffusion and convection mechanisms. Droplet and airborne transmission of SARS-CoV-2 can be limited indoors with adequate ventilation of rooms, by routine disinfection of toilets, using negative pressure rooms, using face masks, and maintaining social distancing. Other preventive measures recommended include increasing the number of screening tests of suspected carriers of SARS-CoV-2, reducing the number of persons in a room to minimize

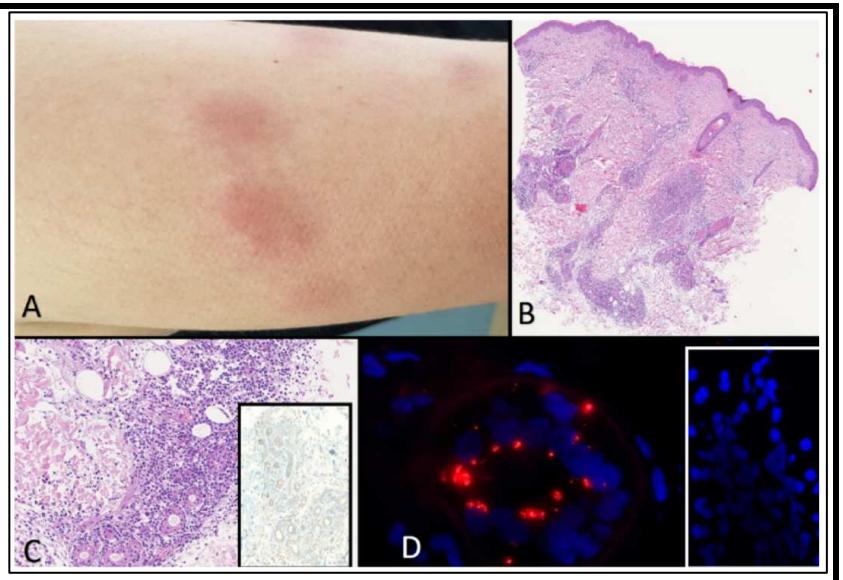
			sharing indoor air, and monitoring people's temperature before accessing a building. The work reviews a body of literature supporting the transmission of SARS-CoV-2 through air, causing COVID-19 disease, which requires coordinated worldwide strategies.  **Figure 4.** Survival of SARS-CoV-2 on different surfaces [73].
Holler JG et al BMC Infectious Diseases https://doi.org/10.1186/s12879-020-05717-w	First wave of COVID-19 hospital admissions in Denmark: a Nationwide population-based cohort study.	Studio di coorte nazionale sui pazienti ospedalizzati nella prima ondata di COVID-19 in Danimarca : 2431 persone tra febbraio e luglio, di cui si individuano i fattori associati alla mortalità.	BACKGROUND: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its associated disease coronavirus disease 2019 (COVID-19), is a worldwide emergency. Demographic, comorbidity and laboratory determinants of death and of ICU admission were explored in all Danish hospitalised patients. METHODS: National health registries were used to identify all hospitalized patients with a COVID-19 diagnosis. We obtained demographics, Charlson Comorbidity Index (CCI), and laboratory results on admission and explored prognostic factors for death using multivariate Cox proportional hazard regression and competing risk survival analysis. RESULTS: Among 2431 hospitalised patients with COVID-19

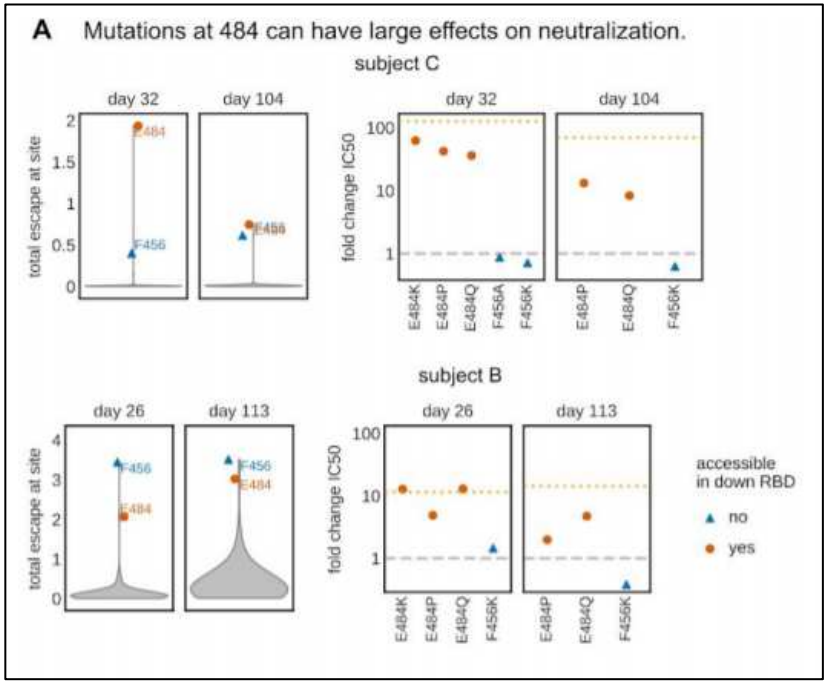
			between February 27 and July 8 (median age 69 years [IQR 53-80], 54.1% males), 359 (14.8%) needed admission to an intensive care unit (ICU) and 455 (18.7%) died within 30 days of follow-up. The seven-day cumulative incidence of ICU admission was lower for females (7.9%) than for males (16.7%), ($p < 0.001$). Age, high CCI, elevated C-reactive protein (CRP), ferritin, D-dimer, lactate dehydrogenase (LDH), urea, creatinine, lymphopenia, neutrophilia and thrombocytopenia within +/-24-h of admission were independently associated with death within the first week in the multivariate analysis. Conditional upon surviving the first week, male sex, age, high CCI, elevated CRP, LDH, creatinine, urea and neutrophil count were independently associated with death within 30 days. Males presented with more pronounced laboratory abnormalities on admission. CONCLUSIONS: Advanced age, male sex, comorbidity, higher levels of systemic inflammation and cell-turnover were independent factors for mortality. Age was the strongest predictor for death, moderate to high level of comorbidity were associated with a nearly two-fold increase in mortality. Mortality was significantly higher in males after surviving the first week.

			
Huang C et al The Lancet https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32656-8/fulltext	6-month consequences of COVID-19 in patients discharged from hospital: a cohort study	Follow up a 6 mesi di una coorte di 1733 pazienti dimessi da un ospedale della città di Wuhan dopo ricovero per COVID-19 : nei guariti persistono sintomi a lungo termine e alterazioni della funzionalità polmonare.	Background : The long-term health consequences of COVID-19 remain largely unclear. The aim of this study was to describe the long-term health consequences of patients with COVID-19 who have been discharged from hospital and investigate the associated risk factors, in particular disease severity. Methods : We did an ambidirectional cohort study of patients with confirmed COVID-19 who had been discharged from Jin Yin-tan Hospital (Wuhan, China) between Jan 7, 2020, and May 29, 2020. Patients who died before follow-up, patients for whom follow-up would be difficult because of psychotic disorders, dementia, or re-admission to hospital, those who were unable to move freely due to concomitant osteoarthropathy or immobile before or after discharge due to diseases such as stroke or pulmonary embolism, those who declined to participate, those who could not be

			contacted, and those living outside of Wuhan or in nursing or welfare homes were all excluded. All patients were interviewed with a series of questionnaires for evaluation of symptoms and health-related quality of life, underwent physical examinations and a 6-min walking test, and received blood tests. A stratified sampling procedure was used to sample patients according to their highest seven-category scale during their hospital stay as 3, 4, and 5–6, to receive pulmonary function test, high resolution CT of the chest, and ultrasonography. Enrolled patients who had participated in the Lopinavir Trial for Suppression of SARS-CoV-2 in China received severe acute respiratory syndrome coronavirus 2 antibody tests. Multivariable adjusted linear or logistic regression models were used to evaluate the association between disease severity and long-term health consequences. Findings : In total, 1733 of 2469 discharged patients with COVID-19 were enrolled after 736 were excluded. Patients had a median age of 57·0 (IQR 47·0–65·0) years and 897 (52%) were men. The follow-up study was done from June 16, to Sept 3, 2020, and the median follow-up time after symptom onset was 186·0 (175·0–199·0) days. Fatigue or muscle weakness (63%, 1038 of 1655) and sleep difficulties (26%, 437 of 1655) were the most common symptoms. Anxiety or depression was reported among 23% (367 of 1617) of patients. The proportions of median 6-min walking distance less than the lower limit of the normal range were 24% for those at severity scale 3, 22% for severity scale 4, and 29% for severity scale 5–6. The corresponding proportions of patients with diffusion impairment were 22% for severity scale 3, 29% for scale 4, and 56% for scale 5–6, and median CT scores were 3·0 (IQR 2·0–5·0) for severity scale 3, 4·0 (3·0–5·0) for scale 4, and 5·0 (4·0–6·0) for scale 5–6. After multivariable adjustment, patients showed an odds ratio

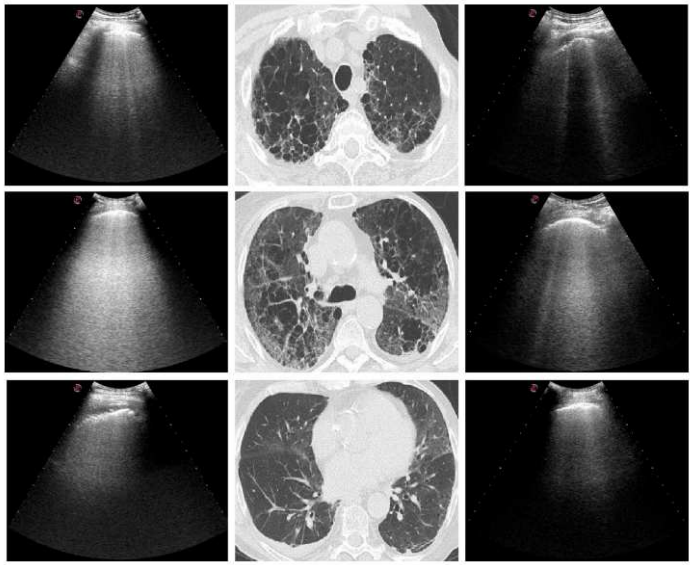
			(OR) 1·61 (95% CI 0·80–3·25) for scale 4 versus scale 3 and 4·60 (1·85–11·48) for scale 5–6 versus scale 3 for diffusion impairment; OR 0·88 (0·66–1·17) for scale 4 versus scale 3 and OR 1·77 (1·05–2·97) for scale 5–6 versus scale 3 for anxiety or depression, and OR 0·74 (0·58–0·96) for scale 4 versus scale 3 and 2·69 (1·46–4·96) for scale 5–6 versus scale 3 for fatigue or muscle weakness. Of 94 patients with blood antibodies tested at follow-up, the seropositivity (96·2% vs 58·5%) and median titres (19·0 vs 10·0) of the neutralising antibodies were significantly lower compared with at the acute phase. 107 of 822 participants without acute kidney injury and with estimated glomerular filtration rate (eGFR) 90 mL/min per 1·73 m2 or more at acute phase had eGFR less than 90 mL/min per 1·73 m2 at follow-up. Interpretation : At 6 months after acute infection, COVID-19 survivors were mainly troubled with fatigue or muscle weakness, sleep difficulties, and anxiety or depression. Patients who were more severely ill during their hospital stay had more severe impaired pulmonary diffusion capacities and abnormal chest imaging manifestations, and are the main target population for intervention of long-term recovery.
Gianotti R et al British Journal of Dermatology	COVID-19 related dermatosis in November 2019. Could this case be Italy's patient zero?	L'individuazione di SARS-CoV-2 tramite ibridazione in situ fluorescente (FISH) in una biopsia cutanea eseguita a Milano in novembre 2020 su una paziente con sierologia in seguito dimostrata positiva viene proposta come la prova del caso più antico	Milan, the largest city in northern Italy, was one of the first European metropolitan areas to be affected by the COVID-19 pandemic. We analyzed skin biopsies of patients from Milan with dermatoses and positive PCR swabs for SARS-CoV-2 at different stages of the infection. The results were compared to skin biopsies of 20 COVID-19 non-diagnosed patients with dermatoses, who were at high-risk of COVID-19 infection.

https://onlinelibrary.wiley.com/doi/10.1111/bjd.19804		finora dimostrato di COVID-19 nel nostro Paese.	
Greaney AJ et al bioRXiv https://www.biorxiv.org/content/10.1101/2020.12.31.425021v1	Comprehensive mapping of mutations to the SARS-CoV-2 receptor-binding domain that affect recognition by polyclonal human serum antibodies	Effetto delle mutazioni conosciute a carico della porzione legante il recettore (RBD) della proteina spike di SARS-CoV-2 sull'affinità con il siero di soggetti guariti : poche mutazioni sono responsabili degli effetti più notevoli, in particolare quella a carico del sito E484 può ridurre di più di 10 volte l'affinità di alcuni sieri (ma non di tutti) ; la mutazione N501Y della « variante inglese » - che come è noto conferisce maggiore affinità per ACE2 - non influenza	The evolution of SARS-CoV-2 could impair recognition of the virus by human antibody-mediated immunity. To facilitate prospective surveillance for such evolution, we map how convalescent serum antibodies are impacted by all mutations to the spike's receptor-binding domain (RBD), the main target of serum neutralizing activity. Binding by polyclonal serum antibodies is affected by mutations in three main epitopes in the RBD, but there is substantial variation in the impact of mutations both among individuals and within the same individual over time. Despite this inter- and intra-person heterogeneity, the mutations that most reduce antibody binding usually occur at just a few sites in the RBD's receptor binding motif. The most important site is E484, where neutralization by some sera is reduced >10-fold by several mutations, including one in emerging viral lineages in South Africa

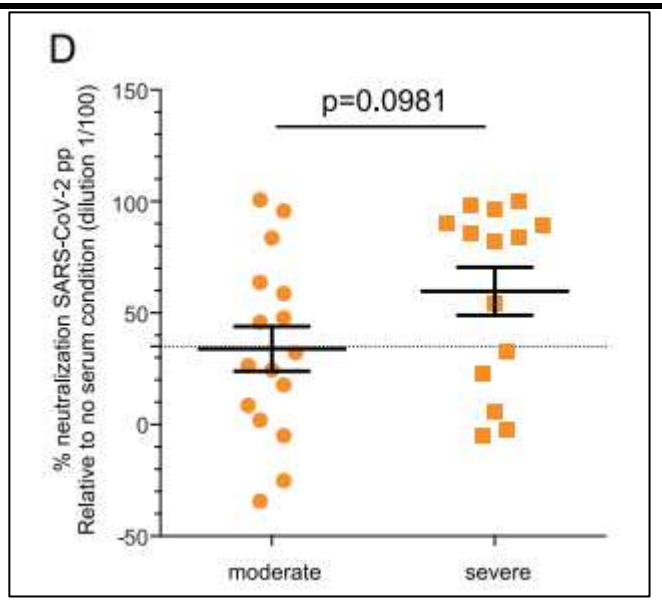
		l'affinità con i sieri policlonali studiati; le quattro mutazioni più frequentemente descritte della proteina ugualmente non influenzano l'affinità con i sieri.	and Brazil. Going forward, these serum escape maps can inform surveillance of SARS-CoV-2 evolution. 
Harrington D et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab014/6076528?searchresult=1	Confirmed Reinfection with SARS-CoV-2 Variant VOC-202012/01	Reinfezione da ceppo B.1.1.7 (« variante inglese ») di SARS-CoV-2, a distanza di 8 mesi dal primo episodio e con decorso più grave, in un paziente dializzato di 78 anni nel Regno Unito. Non si può escludere l'escape virale alla risposta immunitaria; una maggiore gravità della reinfezione da	We have detected a confirmed case of reinfection with SARS-CoV-2 with the second episode due to the 'new variant' VOC-202012/01 of lineage B.1.1.7. The initial infection occurred in the first wave of the pandemic in the UK and was a mild illness. 8 months later, during the second wave of the pandemic in the UK reinfection with the 'new variant' VOC-202012/01 was confirmed and caused a critical illness.

		SARS-CoV-2 era già stata riportata in altri casi.	
Meyerowitz EA et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab016/6089186?searchresult=1	A defense of the classical model of transmission of respiratory pathogens	La dicotomia droplet-aerosol non appare più così netta dopo un anno di pandemia di COVID-19, ma non dovrebbe essere del tutto abbandonata, per via dei suoi utili effetti pratici, secondo gli Autori di questa lettera.	We fully agree that an important lesson from the ongoing COVID-19 pandemic has been that the aerosol-droplet dichotomy for transmission of respiratory pathogens is oversimplified.However, it is remarkable that this model has held up surprisingly well in informing effective public health strategies to minimize spread. The overwhelming evidence suggests that respiratory transmission is dominant and that, despite the flaws of the aerosol-droplet model, classical droplet (and in particular the infection control practices implied by it) is more important than aerosol transmission for SARSCoV-2. There are several points to consider.
Kessler T et al Frontiers in Cardiovascular Medicine https://doi.org/10.3389/fcvm.2020.599299	SARS-CoV-2 Infection in Asymptomatic Patients Hospitalized for Cardiac Emergencies: Implications for Patient Management.	Studio retrospettivo su 710 pazienti con emergenze cardiologiche in atto ricoverati in un centro di riferimento : tutti asintomatici per COVID-19 e tutti con tampone di screening coerentemente negativo, a suggerire che l'attesa del tampone negativo prima di eseguire una procedura urgente potrebbe non essere giustificata (almeno in una regione a bassa prevalenza di infezione come era la Baviera quando è stato	Background: The coronavirus disease (COVID-19) pandemic imposed diverse challenges on the health care system. Morbidity and mortality of non-COVID-19 emergencies might also have changed because hospitals may not be able to provide optimal care due to restructured resources and uncertainties how to deal with potentially infected patients. It has been recommended to stratify treatment of cardiovascular emergencies according to cardiovascular risk. However, data on the prevalence of asymptomatic SARS-CoV-2 infection in patients presenting with cardiac emergencies remain scarce. Methods: We retrospectively analyzed patients' data from a tertiary cardiology department between April 15 and May 31, 2020. All patients were screened on admission for COVID-19 symptoms using a questionnaire and body temperature measurements. All hospitalized patients were routinely screened using nasopharyngeal swab testing. Results: In total, we counted 710 urgent and emergency admissions.

		svolto lo studio). Probabile che la dispnea rimanga un sintomo molto difficile da interpretare a fini di screening.	Nasopharyngeal swab tests were available in 689 (97%) patients, 409 and 280 of which presented as urgent and emergency admissions, respectively. Among 280 emergency admissions, none tested positive for SARS-CoV-2. Conclusion: In cardiac emergency patients which were screened negative for COVID-19 symptoms, the prevalence of SARS-CoV-2 infection in regions with a modest overall prevalence is low. This finding might be helpful to better determine timing of emergency procedures and reasonable usage of protective equipment during the COVID-19 crisis and the future.
Dacrema A et al Internal and Emergency Medicine https://doi.org/10.1007/s11739-020-02596-6	A simple lung ultrasound protocol for the screening of COVID-19 pneumonia in the emergency department.	Proposta di uno score ecografico polmonare per lo screening della polmonite da SARS-CoV-2 e il rapido isolamento dei pazienti in pronto soccorso.	The most relevant manifestation of coronavirus disease 2019 (COVID-19) is interstitial pneumonia. Several lung ultrasound (US) protocols for pneumonia diagnosis are used in clinical practice, but none has been proposed for COVID-19 patients' screening in the emergency department. We adopted a simplified 6-scan lung US protocol for COVID-19 pneumonia diagnosis (LUSCOP) and compared its sensitivity with high resolution computed tomography (HRCT) in patients suspected for COVID-19, presenting to one Emergency Department from February 21st to March 15th, 2020, during the outbreak burst in northern Italy. Patients were retrospectively enrolled if both LUSCOP protocol and HRCT were performed in the Emergency Department. The sensitivity of LUSCOP protocol and HRCT were compared. COVID-19 pneumonia's final diagnosis was based on real-time reverse-transcription polymerase chain reaction from nasal-pharyngeal swab and on clinical data. Out of 150 suspected COVID-19 patients, 131 were included in the study, and 130 had a final diagnosis of COVID-19 pneumonia. The most frequent lung ultrasonographic features were: bilateral B-pattern in 101 patients (77%), B-pattern with subpleural consolidations in 26 (19.8%) and lung consolidations in 2 (1.5%). LUSCOP Protocol was consistent with HRCT in correctly screening

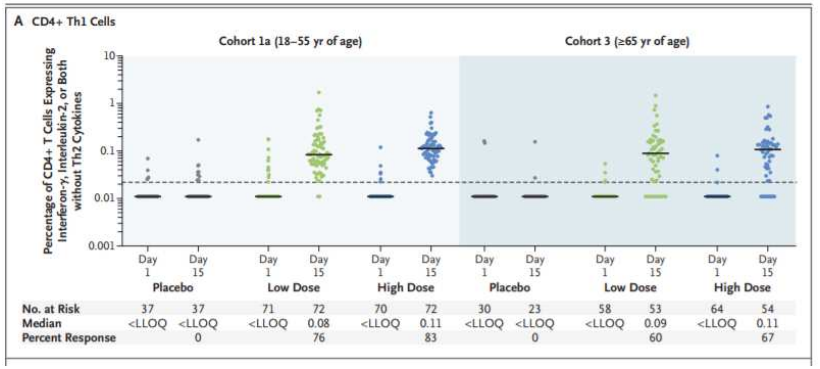
			130 out of the 131 COVID-19 pneumonia cases (99.2%). In one case COVID-19 pneumonia was excluded by both HRCT and lung US. LUSCOP protocol showed optimal sensitivity and can be proposed as a simple screening tool for COVID-19 pneumonia diagnosis in the context of outbreak burst areas where prompt isolation of suspected patients is crucial for patients' and operators' safety.  **Fig. 3** Comparison between HRCT and lung US according to LUSCOP protocol. From top to bottom: upper, medium, and lower fields are shown both in HRCT slices and in the corresponding right and left lung US. HRCT shows diffuse pulmonary emphysema mostly in upper and medium fields, associated with COVID-19 bilateral dorsal, subpleural ground-glass opacities, and consolidations. In the upper fields, B-lines at the lung US correspond to areas of mild interstitial involvement. In the middle fields, lung ultrasound shows confluent B-lines with pleural thickening. In the lower fields, pleural effusion is detected by lung US in the right side, associated with pleural thickening and irregularity; the left lung US shows a predominantly A-pattern corresponding to relatively spared parenchyma.
Legros V et al	A longitudinal study of SARS-CoV-2-infected patients reveals a high correlation between neutralizing	In questa coorte di 140 pazienti con COVID-19 di varia gravità, il titolo degli anticorpi neutralizzanti (siero in grado di « proteggere » una coltura	Understanding the immune responses elicited by SARS-CoV-2 infection is critical in terms of protection against reinfection and, thus, for public health policy and vaccine development for COVID-19. In this study, using either live SARS-CoV-2 particles or retroviruses pseudotyped with the SARS-CoV-2 S viral surface

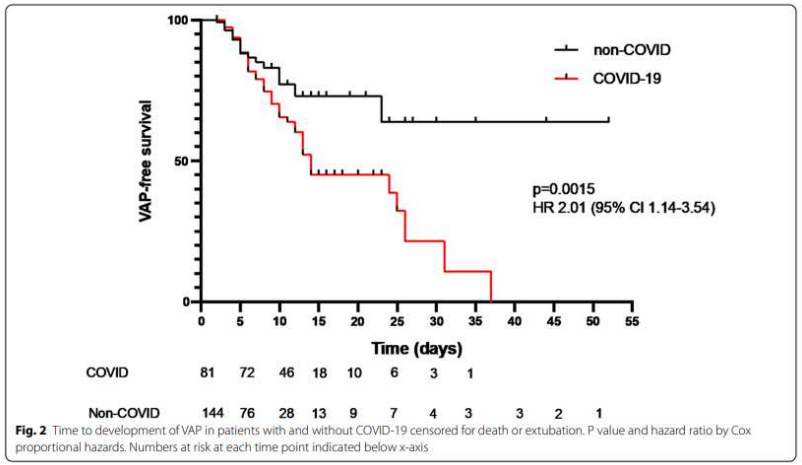
Nature – Cellular and Molecular Immunology https://www.nature.com/articles/s41423-020-00588-2	antibodies and COVID-19 severity	cellulare dall'effetto citopatico di SARS-CoV-2 introdotto nella coltura) è correlato con la gravità di malattia e con la quantità di IgG anti-proteina S presenti.	protein (Spike), we studied the neutralizing antibody (nAb) response in serum samples from a cohort of 140 SARS-CoV-2 qPCR-confirmed infections, including patients with mild symptoms and also more severe forms, including those that required intensive care. We show that nAb titers correlated strongly with disease severity and with anti-spike IgG levels. Indeed, patients from intensive care units exhibited high nAb titers; conversely, patients with milder disease symptoms had heterogeneous nAb titers, and asymptomatic or exclusive outpatient-care patients had no or low nAbs. We found that nAb activity in SARS-CoV-2-infected patients displayed a relatively rapid decline after recovery compared to individuals infected with other coronaviruses. Moreover, we found an absence of cross-neutralization between endemic coronaviruses and SARS-CoV-2, indicating that previous infection by human coronaviruses may not generate protective nAbs against SARS-CoV-2. Finally, we found that the D614G mutation in the spike protein, which has recently been identified as the current major variant in Europe, does not allow neutralization escape. Altogether, our results contribute to our understanding of the immune correlates of SARS-CoV-2-induced disease, and rapid evaluation of the role of the humoral response in the pathogenesis of SARS-CoV-2 is warranted.

			
Joyner MJ et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2031893?query=featured_home	Convalescent Plasma Antibody Levels and the Risk of Death from Covid-19	Studio retrospettivo su 3082 pazienti trattati con plasma per COVID-19 : nei trasfusi con plasma a basso titolo (in base a un saggio qualitativo a chemioluminescenza che misura le IgG presenti) anticorpale la mortalità è maggiore rispetto a quelli che hanno ricevuto plasma ad alto titolo. La differenza si osserva solo nei non ventilati.	BACKGROUND : Convalescent plasma has been widely used to treat coronavirus disease 2019 (Covid-19) under the presumption that such plasma contains potentially therapeutic antibodies to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that can be passively transferred to the plasma recipient. Whether convalescent plasma with high antibody levels rather than low antibody levels is associated with a lower risk of death is unknown. METHODS : In a retrospective study based on a U.S. national registry, we determined the anti–SARS-CoV-2 IgG antibody levels in convalescent plasma used to treat hospitalized adults with Covid-19. The primary outcome was death within 30 days after plasma transfusion. Patients who were enrolled through July 4, 2020, and for whom data on anti–SARS-CoV-2 antibody levels in plasma transfusions and on 30-day mortality were available were included in the analysis.

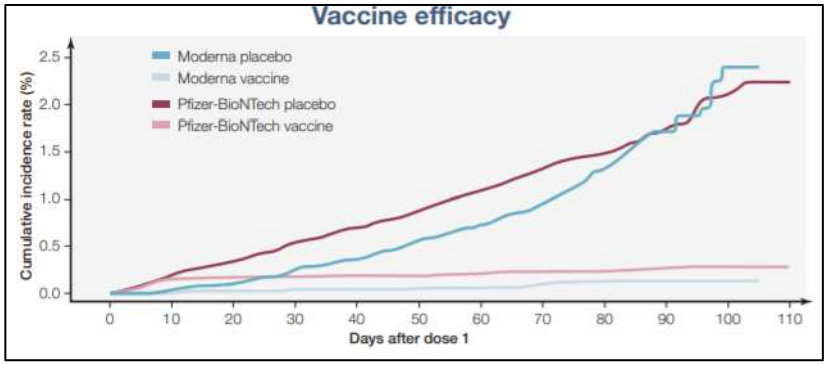
			RESULTS : Of the 3082 patients included in this analysis, death within 30 days after plasma transfusion occurred in 115 of 515 patients (22.3%) in the high-titer group, 549 of 2006 patients (27.4%) in the medium-titer group, and 166 of 561 patients (29.6%) in the low-titer group. The association of anti–SARS-CoV-2 antibody levels with the risk of death from Covid-19 was moderated by mechanical ventilation status. A lower risk of death within 30 days in the high-titer group than in the low-titer group was observed among patients who had not received mechanical ventilation before transfusion (relative risk, 0.66; 95% confidence interval [CI], 0.48 to 0.91), and no effect on the risk of death was observed among patients who had received mechanical ventilation (relative risk, 1.02; 95% CI, 0.78 to 1.32). CONCLUSIONS : Among patients hospitalized with Covid-19 who were not receiving mechanical ventilation, transfusion of plasma with higher anti–SARS-CoV-2 IgG antibody levels was associated with a lower risk of death than transfusion of plasma with lower antibody levels.
Sadoff J et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2034201?query=featured_home	Interim Results of a Phase 1–2a Trial of Ad26.COV2.S Covid-19 Vaccine	Analisi ad interim dei risultati dello studio di fase 1-2 su immunogenicità e sicurezza del vaccino a vettore adenovirale Ad26.COV2.S contro SARS-CoV-2, testato su adulti di età anche superiore a 65 anni.	BACKGROUND : Efficacious vaccines are urgently needed to contain the ongoing coronavirus disease 2019 (Covid-19) pandemic of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). A candidate vaccine, Ad26.COV2.S, is a recombinant, replication-incompetent adenovirus serotype 26 (Ad26) vector encoding a full-length and stabilized SARS-CoV-2 spike protein. METHODS : In this multicenter, placebo-controlled, phase 1–2a trial, we randomly assigned healthy adults between the ages of 18 and 55 years (cohort 1) and those 65 years of age or older (cohort 3) to receive the Ad26.COV2.S vaccine at a dose of 5×1010 viral particles (low dose) or 1×1011 viral particles (high dose) per milliliter or placebo in a single-dose or two-dose schedule. Longer-term data

			comparing a single-dose regimen with a two-dose regimen are being collected in cohort 2; those results are not reported here. The primary end points were the safety and reactogenicity of each dose schedule. RESULTS : After the administration of the first vaccine dose in 805 participants in cohorts 1 and 3 and after the second dose in cohort 1, the most frequent solicited adverse events were fatigue, headache, myalgia, and injection-site pain. The most frequent systemic adverse event was fever. Systemic adverse events were less common in cohort 3 than in cohort 1 and in those who received the low vaccine dose than in those who received the high dose. Reactogenicity was lower after the second dose. Neutralizing-antibody titers against wild-type virus were detected in 90% or more of all participants on day 29 after the first vaccine dose (geometric mean titer [GMT], 224 to 354) and reached 100% by day 57 with a further increase in titers (GMT, 288 to 488), regardless of vaccine dose or age group. Titers remained stable until at least day 71. A second dose provided an increase in the titer by a factor of 2.6 to 2.9 (GMT, 827 to 1266). Spike-binding antibody responses were similar to neutralizing-antibody responses. On day 14, CD4+ T-cell responses were detected in 76 to 83% of the participants in cohort 1 and in 60 to 67% of those in cohort 3, with a clear skewing toward type 1 helper T cells. CD8+ T-cell responses were robust overall but lower in cohort 3. CONCLUSIONS : The safety and immunogenicity profiles of Ad26.COV2.S support further development of this vaccine candidate.

			
Maes M et al Critical Care https://doi.org/10.1186/s13054-021-03460-5	Ventilator-associated pneumonia in critically ill patients with COVID-19.	Studio osservazionale retrospettivo su 81 pazienti ventilati per polmonite in COVID-19 a confronto con 144 non COVID : i primi hanno maggiore incidenza di VAP, mentre i microrganismi responsabili sono analoghi fra i due gruppi.	BACKGROUND: Pandemic COVID-19 caused by the coronavirus SARS-CoV-2 has a high incidence of patients with severe acute respiratory syndrome (SARS). Many of these patients require admission to an intensive care unit (ICU) for invasive ventilation and are at significant risk of developing a secondary, ventilator-associated pneumonia (VAP). OBJECTIVES: To study the incidence of VAP and bacterial lung microbiome composition of ventilated COVID-19 and non-COVID-19 patients. METHODS: In this retrospective observational study, we compared the incidence of VAP and secondary infections using a combination of microbial culture and a TaqMan multi-pathogen array. In addition, we determined the lung microbiome composition using 16S RNA analysis in a subset of samples. The study involved 81 COVID-19 and 144 non-COVID-19 patients receiving invasive ventilation in a single University teaching hospital between March 15th 2020 and August 30th 2020. RESULTS: COVID-19 patients were significantly more likely to develop VAP than patients without COVID (Cox proportional hazard ratio 2.01 95% CI 1.14-3.54, p = 0.0015) with an incidence density of 28/1000 ventilator days versus 13/1000 for patients without COVID (p = 0.009). Although the distribution of organisms causing VAP was similar between the two groups, and

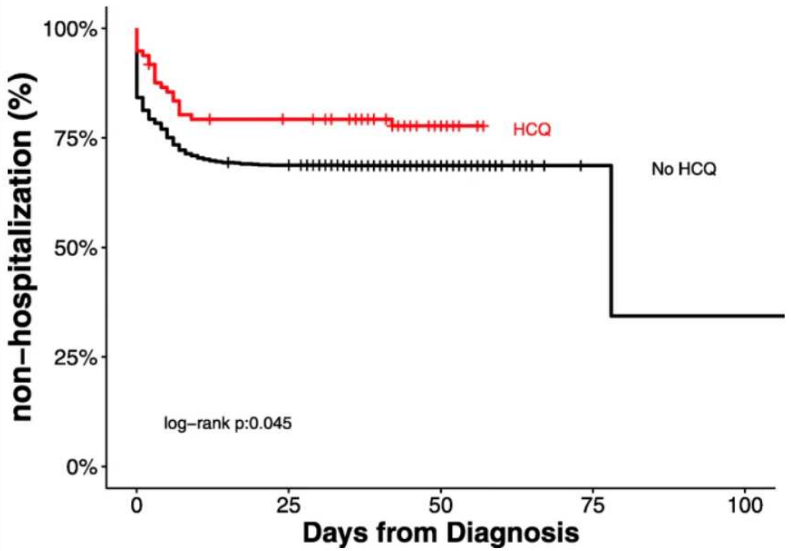
			the pulmonary microbiome was similar, we identified 3 cases of invasive aspergillosis amongst the patients with COVID-19 but none in the non-COVID-19 cohort. Herpesvirade activation was also numerically more frequent amongst patients with COVID-19. CONCLUSION: COVID-19 is associated with an increased risk of VAP, which is not fully explained by the prolonged duration of ventilation. The pulmonary dysbiosis caused by COVID-19, and the causative organisms of secondary pneumonia observed are similar to that seen in critically ill patients ventilated for other reasons.  **Fig. 2** Time to development of VAP in patients with and without COVID-19 censored for death or extubation. P value and hazard ratio by Cox proportional hazards. Numbers at risk at each time point indicated below x-axis
Jones A et al Morbidity and Mortality Weekly Report	Assessment of day-7 postexposure testing of asymptomatic contacts of COVID-19 patients to evaluate early release from quarantine	Su un campione di 8798 contatti di casi di COVID-19, quelli asintomatici e con test negativo a 7 giorni dall'esposizione, se ritestati nei giorni 8-14 avevano sempre tampone negativo, il che può giustificare una	On May 8, 2020, the Vermont Department of Health (VDH) issued a Health Update* recommending shortening the duration of quarantine for persons exposed to SARS-CoV-2, the virus that causes coronavirus disease 2019 (COVID-19). Exposed persons who were in quarantine could be tested by polymerase chain reaction (PCR) on or after quarantine day 7. Those who had remained

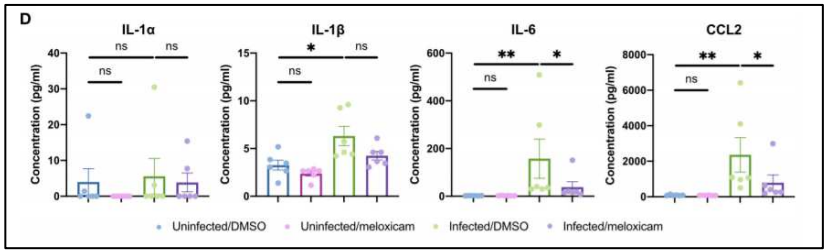
https://www.cdc.gov/mmwr/volumes/70/wr/mm7001a3.htm?s_cid=mm7001a3_w		riduzione della quarantena nei contatti.	asymptomatic throughout quarantine and who received a negative SARS-CoV-2 PCR test result on or after day 7 could end quarantine.
Salman D et al BMJ https://www.bmj.com/content/372/bmj.m4721	Returning to physical activity after covid-19	Indicazioni su come guidare i pazienti nel ritorno all'attività fisica dopo l'infezione da SARS-CoV-2.	What you need to know Risk stratify patients before recommending a return to physical activity in people who have had covid-19. Patients with ongoing symptoms or who had severe covid-19 or a history suggestive of cardiac involvement need further clinical assessment Only return to exercise after at least seven days free of symptoms, and begin with at least two weeks of minimal exertion Use daily self monitoring to track progress, including when to seek further help
Mahase E BMJ https://www.bmj.com/content/372/bmj.n124.full	Covid-19: Past infection provides 83% protection for five months but may not stop transmission, study finds	In un articolo non ancora pubblicato, due coorti di operatori sanitari rispettivamente con e senza storia di infezione da SARS-CoV-2 sono state seguite per 6 mesi, osservando 44 casi di potenziale reinfezione su 6614 casi.	People who have previously been infected with covid-19 are likely to be protected against reinfection for several months, but could still carry the virus in their nose and throat and transmit it to others, according to a study which regularly tested thousands of healthcare workers.
Fiorentini S et al The Lancet https://www.thelancet.com/journals/laninf/article/	First detection of SARS-CoV-2 spike protein N501 mutation in Italy in August, 2020	Nel tampone di un paziente con infezione da SARS-CoV-2 da agosto 2020 in Italia si osserva la mutazione N501T nella sequenza della proteina spike, nello stesso sito della mutazione caratteristiche della	A new variant of SARS-CoV-2, known as VOC-202012/01, is spreading in the UK and is rapidly becoming a global threat. VOC-202012/01 is characterised by multiple mutations in the spike protein. Among them, N501Y is of major concern because it involves one of the six key amino acid residues determining a tight interaction of the SARS-CoV-2 receptor-binding domain (RBD) with its cellular receptor angiotensin-converting enzyme 2 (ACE2).

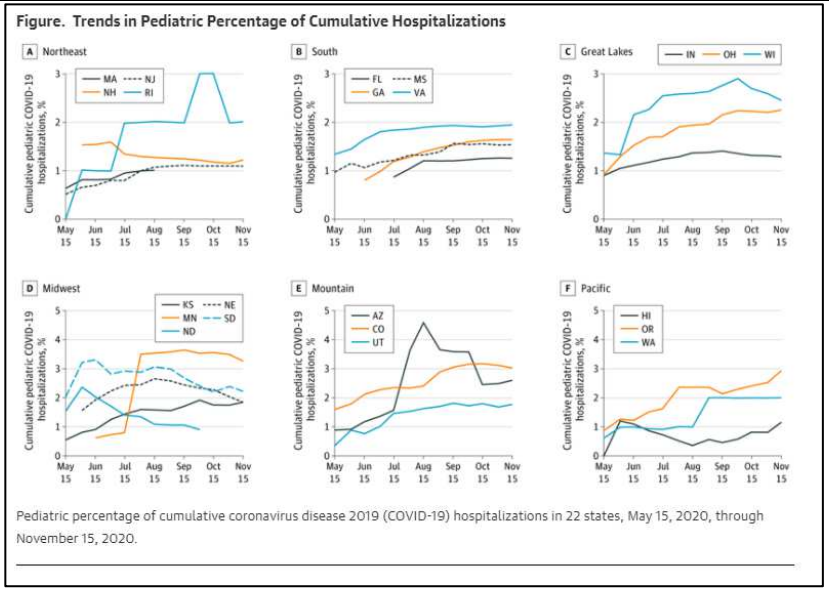
PIIS1473-3099(21)00007-4/fulltext		« variante inglese » (N501Y) che dunque potrebbe essere già stata presente nel nostro Paese da allora.	On Nov 10, 2020, a 59-year-old man with a history of SARS-CoV-2 infection persistence presented for molecular testing. Infection was laboratory confirmed; therefore, genetic characterisation of viruses detected in the sample collected in November (MB61-Nov) and in a previous sample collected in August (MB61-Aug) was done by metagenomic sequencing.
Pollard A et al BMJ https://www.bmj.com/content/372/bmj.n86	How the Oxford-AstraZeneca covid-19 vaccine was made	Domande e risposte sul vaccino Oxford-AstraZeneca (basato su vettore adenovirale) col vaccinologo Andrew Pollard.	Andrew Pollard has been leading the Oxford vaccine clinical trials in the UK, Brazil, and South Africa. He tells Elisabeth Mahase how the Oxford vaccine came to be, how dosing was worked out, and whether it will stand up to the new variants
Topol EJ et al Cell https://www.cell.com/action/showPdf?pii=S0092-8674%2820%2931761-X	Messenger RNA vaccines against SARS-CoV-2	Breve sinossi dell'attività dei due vaccini a mRNA contro SARS-CoV-2 approvati finora : Pfizer e Moderna.	The first two vaccines proven to be effective for inhibiting COVID-19 illness were both mRNA, achieving 95% efficacy (and safety) among 74,000 participants (half receiving placebo) after intramuscular delivery of two shots, 3–4 weeks apart. 

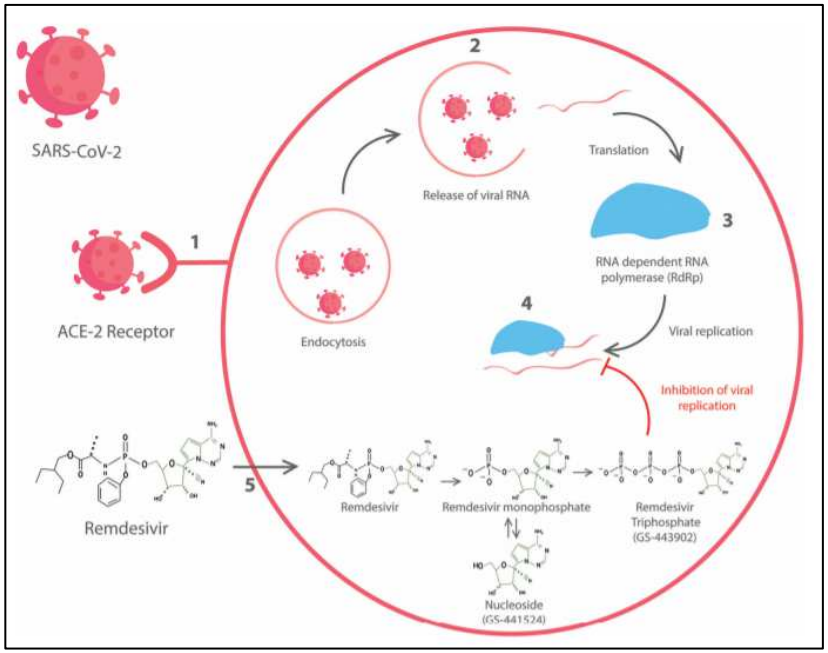
Downar J et al The Lancet https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00025-4/fulltext	Improving family access to dying patients during the COVID-19 pandemic	Proposte per affrontare il problema della separazione tra pazienti morenti ricoverati in diversi contesti e familiari durante la pandemia di COVID-19.	In response to the COVID-19 pandemic, most health-care organisations have implemented policies to restrict visitor access. Although there are exceptions to some of these policies, including limited visiting for patients nearing the end of life, they still have profound effects on the dying and their family members. We are still in the midst of the pandemic, but there are compelling reasons to expand access of family members to their loved ones as they near the end of life, despite the risk of infection.
Newlove-Delgato T et al The Lancet https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(20)30570-8/fulltext	Child mental health in England before and during the COVID-19 lockdown	Esiti di un sondaggio condotto nel Regno Unito sulla salute mentale di bambini e ragazzi di 5-16 anni a seguito della diffusione di SARS-CoV-2.	Although evidence has emerged of the effect of COVID-19 on adult mental health, few studies around the world cover children. Given the importance of probability sampling and similar prepandemic baseline measures, the follow-up of England's Mental Health of Children and Young People (MHCYP) survey provides a rare resource on what the pandemic has meant for children.We consider the clinical and policy implications of the initial study results.
Ip A et al BMC Infectious Diseases https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-021-05773-w	Hydroxychloroquine in the treatment of outpatients with mildly symptomatic COVID-19: a multi-center observational study	Studio osservazionale retrospettivo su 1274 pazienti con infezione da SARS-CoV-2 non ospedalizzati : i trattati con idrossiclorochina (7.6% del totale, 97 persone) hanno minore tasso di	Background : Hydroxychloroquine has not been associated with improved survival among hospitalized COVID-19 patients in the majority of observational studies and similarly was not identified as an effective prophylaxis following exposure in a prospective randomized trial. We aimed to explore the role of hydroxychloroquine therapy in mildly symptomatic patients diagnosed in the outpatient setting.

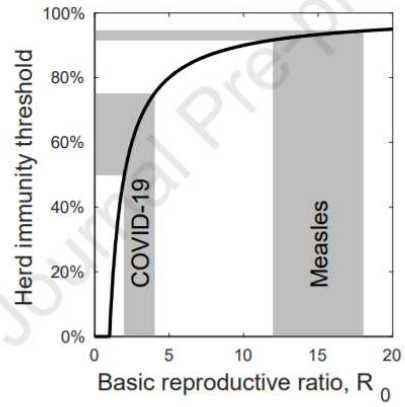
		ospedalizzazione rispetto a una coorte propensity-matched di non trattati.	Methods : We examined the association between outpatient hydroxychloroquine exposure and the subsequent progression of disease among mildly symptomatic non-hospitalized patients with documented SARS-CoV-2 infection. The primary outcome assessed was requirement of hospitalization. Data was obtained from a retrospective review of electronic health records within a New Jersey USA multi-hospital network. We compared outcomes in patients who received hydroxychloroquine with those who did not applying a multivariable logistic model with propensity matching. Results : Among 1274 outpatients with documented SARS-CoV-2 infection 7.6% were prescribed hydroxychloroquine. In a 1067 patient propensity matched cohort, 21.6% with outpatient exposure to hydroxychloroquine were hospitalized, and 31.4% without exposure were hospitalized. In the primary multivariable logistic regression analysis with propensity matching there was an association between exposure to hydroxychloroquine and a decreased rate of hospitalization from COVID-19 (OR 0.53; 95% CI, 0.29, 0.95). Sensitivity analyses revealed similar associations. QTc prolongation events occurred in 2% of patients prescribed hydroxychloroquine with no reported arrhythmia events among those with data available. Conclusions : In this retrospective observational study of SARS-CoV-2 infected non-hospitalized patients hydroxychloroquine exposure was associated with a decreased rate of subsequent hospitalization. Additional exploration of hydroxychloroquine in this mildly symptomatic outpatient population is warranted.

			Fig. 2  Hospitalization according to Hydroxychloroquine Exposure from Date of Confirmed SARS-CoV-2 Infection. Cumulative prevalence of hospitalization among mildly symptomatic COVID-19 patients according to outpatient exposure to hydroxychloroquine from date of polymerase chain reaction confirmed infection with SARS-CoV-2 in propensity matched cohort. HCQ = hydroxychloroquine
Chen JS et al Journal of Virology https://jvi.asm.org/content/early/2021/01/12/JVI.00014-21	Non-steroidal anti-inflammatory drugs dampen the cytokine and antibody response to SARS-CoV-2 infection	L'inibizione delle ciclossigenasi da parte dei FANS potrebbe interferire in molti modi con l'infezione da SARS-CoV-2, ad esempio riducendo la produzione di citochine proinfiammatorie e la risposta anticorpale, come si dimostra nel topo secondo questo studio. La presenza di tali effetti nell'uomo e la loro eventuale valenza positiva o	Identifying drugs that regulate severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and its symptoms has been a pressing area of investigation during the coronavirus disease 2019 (COVID-19) pandemic. Nonsteroidal anti-inflammatory drugs (NSAIDs), which are frequently used for the relief of pain and inflammation, could modulate both SARS-CoV-2 infection and the host response to the virus. NSAIDs inhibit the enzymes cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2), which mediate the production of prostaglandins (PGs). As PGs play diverse biological roles in homeostasis and inflammatory responses, inhibiting PG production with NSAIDs could affect COVID-19 pathogenesis in multiple ways, including: (1) altering susceptibility

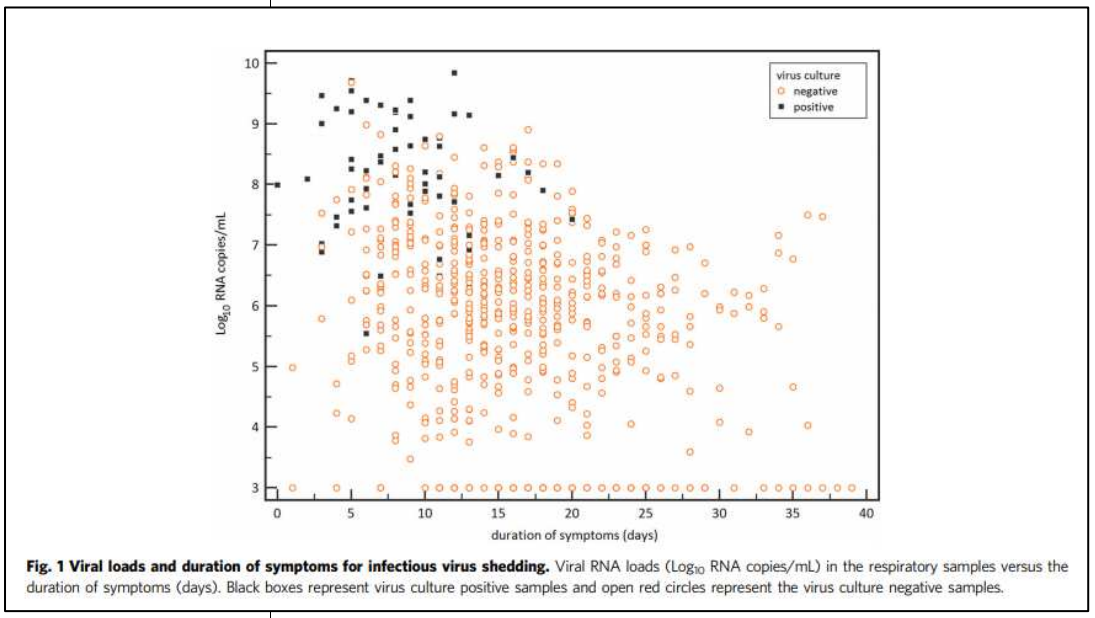
		negativa rimangono da investigare [in figura, DMSO = controllo].	to infection by modifying expression of angiotensin-converting enzyme 2 (ACE2), the cell entry receptor for SARS-CoV-2; (2) regulating replication of SARS-CoV-2 in host cells; and (3) modulating the immune response to SARS-CoV-2. Here, we investigate these potential roles. We demonstrate that SARS-CoV-2 infection upregulates COX-2 in diverse human cell culture and mouse systems. However, suppression of COX-2 by two commonly used NSAIDs, ibuprofen and meloxicam, had no effect on ACE2 expression, viral entry, or viral replication. In contrast, in a mouse model of SARS-CoV-2 infection, NSAID treatment reduced production of pro-inflammatory cytokines and impaired the humoral immune response to SARS-CoV-2 as demonstrated by reduced neutralizing antibody titers. Our findings indicate that NSAID treatment may influence COVID-19 outcomes by dampening the inflammatory response and production of protective antibodies rather than modifying susceptibility to infection or viral replication. 
Levin Z et al JAMA	Trends in Pediatric Hospitalizations for Coronavirus Disease 2019	Incremento delle ospedalizzazioni pediatriche per COVID-19 in 22 stati degli USA dall'inizio della pandemia; un problema da tenere presente con la	While early evidence and experience with coronavirus disease 2019 (COVID-19) suggests that children are less susceptible to infection and have a lower risk for symptomatic and severe disease, pediatric patients are not immune from the virus. We examined pediatric COVID-19 hospitalization trends in 22 states for indications of both severity among this population and spread of the virus.

https://jamanetwork.com/journals/jamapediatrics/fullarticle/2775008		progressiva riapertura delle scuole.	
Muneerah MA et al Antimicrobials Agents and Chemotherapy https://aac.asm.org/content/aac/65/1/e01814-20.full.pdf	New Perspectives on Antimicrobial Agents: Remdesivir Treatment for COVID-19	Revisione delle caratteristiche e dei benefici finora dimostrati del remdesivir nell'infezione da SARS-CoV-2.	ABSTRACT Remdesivir was recently approved by the Food and Drug Administration for the treatment of hospitalized patients with coronavirus disease 2019 (COVID-19). Remdesivir is the prodrug of an adenosine analogue that inhibits viral replication of several RNA virus families, including Coronaviridae. Preclinical data in animal models of coronavirus diseases, including COVID-19, have demonstrated that early treatment with remdesivir leads to improved survival, decreased lung injury, and decreased levels of viral RNA. Recent clinical data have demonstrated the clinical activity of remdesivir in terms of faster time to recovery in patients with severe COVID-19 and higher odds of improved clinical status in patients with moderate COVID-19. Here, clinical trials published to date are presented and appraised. Remdesivir's potential benefits and its favorable adverse-event profile make it an option

			for the treatment of COVID-19. This article examines the available literature describing remdesivir's pharmacology, pharmacokinetics, and preclinical and clinical data. 
Ashby B et al Current Biology https://www.cell.com/current-biology/pdf/S0960-9822(21)00039-7.pdf?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%	Herd immunity	Definizione e implicazioni della « immunità di gregge ».	Herd immunity is an important yet often misunderstood concept in epidemiology. As immunity accumulates in a population — naturally during the course of an epidemic or through vaccination — the spread of infectious disease is limited by the depletion of susceptible hosts. If a sufficient proportion of the population is immune — above the 'herd immunity threshold' — then transmission generally cannot be sustained. Maintaining herd immunity is therefore critical to long-term disease control. In this primer, we discuss the concept of herd immunity from first principles, clarify common misconceptions, and consider the implications for disease control.

2Fpii%2FS0960982221000397%3Fshowall%3Dtrue			 **Figure 3. Relationship between the basic reproduction number, R_0 and the herd immunity threshold.** In a randomly mixing, homogeneous population, the herd immunity threshold is equal to $1 - 1/R_0$. The herd immunity threshold therefore initially increases rapidly for small values of R_0 but then slows down for larger values. Shaded regions illustrate estimated herd immunity thresholds for COVID-19 (with $2 < R_0 < 4$) and measles (with $12 < R_0 < 18$).
National Institute for Health and Care Excellence (NICE) https://www.nice.org.uk/guidance/NG188	COVID-19 rapid guideline: managing the long-term effects of COVID-19 NICE guideline [NG188]	Linee guida NICE sulla gestione dei sintomi a lungo termine di COVID-19 (cosiddetto « long COVID»).	This guideline covers identifying, assessing and managing the long-term effects of COVID-19, often described as 'long COVID'. It makes recommendations about care in all healthcare settings for adults, children and young people who have new or ongoing symptoms 4 weeks or more after the start of acute COVID-19. It also includes advice on organising services for long COVID.
Back A et al Annals of Internal Medicine	Communication Skills in the Age of COVID-19	Un articolo di alcuni mesi fa che rimanda a una piattaforma sempre aggiornata (VITAL talk,	In a new, cruel way, the coronavirus 2019 (COVID-19) pandemic has revealed limitations in medical capacity that amplify the challenges that clinicians already face in communicating with patients about serious illness.

https://www.acpjournals.org/doi/10.7326/M20-1376		https://www.vitaltalk.org/topics/covid-videos/) che suggerisce strategie evidence-based per migliorare la comunicazione medica, con focus sull'epidemia di COVID-19.	
van Kampen JJA Nature https://www.nature.com/articles/s41467-020-20568-4	Duration and key determinants of infectious virus shedding in hospitalized patients with coronavirus disease-2019 (COVID-19)	Su un campione di 129 pazienti ricoverati per COVID-19 (69% ICU, 8.5% immunocompromissione grave) si osserva una durata mediana di shedding di virus infettante (= osservabile in coltura cellulare) di 8 giorni dall'esordio dei sintomi; a 15 giorni dall'esordio, meno del 5% dei campioni è ancora infettante. Campioni con più di 10^7 copie/ml sono indipendentemente associati a presenza di virus infettante, al contrario un titolo anticorpale neutralizzante superiore a 1:20 è associato allo shedding di virus non infettante.	Key questions in COVID-19 are the duration and determinants of infectious virus shedding. Here, we report that infectious virus shedding is detected by virus cultures in 23 of the 129 patients (17.8%) hospitalized with COVID-19. The median duration of shedding infectious virus is 8 days post onset of symptoms (IQR 5–11) and drops below 5% after 15.2 days post onset of symptoms (95% confidence interval (CI) 13.4–17.2). Multivariate analyses identify viral loads above 7 log10 RNA copies/mL (odds ratio [OR] of 14.7 (CI 3.57-58.1; $p < 0.001$) as independently associated with isolation of infectious SARS-CoV-2 from the respiratory tract. A serum neutralizing antibody titre of at least 1:20 (OR of 0.01 (CI 0.003-0.08; $p < 0.001$) is independently associated with non-infectious SARS-CoV-2. We conclude that quantitative viral RNA load assays and serological assays could be used in test-based strategies to discontinue or de-escalate infection prevention and control precautions.

		 **Fig. 1 Viral loads and duration of symptoms for infectious virus shedding.** Viral RNA loads (Log_{10} RNA copies/mL) in the respiratory samples versus the duration of symptoms (days). Black boxes represent virus culture positive samples and open red circles represent the virus culture negative samples.	
Butler-Laporte G et al JAMA https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2775397	Comparison of Saliva and Nasopharyngeal Swab Nucleic Acid Amplification Testing for Detection of SARS-CoV-2	Revisione sistematica e metanalisi dei lavori che confrontano l'accuratezza della ricerca molecolare di SARS-CoV-2 su tampone nasofaringeo e su saliva: sulla base di 16 studi selezionati, che includono perlopiù pazienti ambulatoriali non gravi, la sensibilità e specificità dei due test appaiono comparabili, incoraggiando l'introduzione del test salivare su più larga scala.	Importance: Nasopharyngeal swab nucleic acid amplification testing (NAAT) is the noninvasive criterion standard for diagnosis of coronavirus disease 2019 (COVID-19). However, it requires trained personnel, limiting its availability. Saliva NAAT represents an attractive alternative, but its diagnostic performance is unclear. Objective: To assess the diagnostic accuracy of saliva NAAT for COVID-19. Data Sources: In this systematic review, a search of the MEDLINE and medRxiv databases was conducted on August 29, 2020, to find studies of diagnostic test accuracy. The final meta-analysis was performed on November 17, 2020. Study Selection: Studies needed to provide enough data to measure salivary NAAT sensitivity and specificity compared with imperfect nasopharyngeal swab NAAT as a reference test. An imperfect

			reference test does not perfectly reflect the truth (ie, it can give false results). Studies were excluded if the sample contained fewer than 20 participants or was neither random nor consecutive. The Quality Assessment of Diagnostic Accuracy Studies 2 tool was used to assess the risk of bias. Data Extraction and Synthesis: Preferred Reporting Items for Systematic Reviews and Meta-analyses reporting guideline was followed for the systematic review, with multiple authors involved at each stage of the review. To account for the imperfect reference test sensitivity, we used a bayesian latent class bivariate model for the meta-analysis. Main Outcomes and Measures :The primary outcome was pooled sensitivity and specificity. Two secondary analyses were performed: one restricted to peer-reviewed studies, and a post hoc analysis limited to ambulatory settings. Results: The search strategy yielded 385 references, and 16 unique studies were identified for quantitative synthesis. Eight peer-reviewed studies and 8 preprints were included in the meta-analyses (5922 unique patients). There was significant variability in patient selection, study design, and stage of illness at which patients were enrolled. Fifteen studies included ambulatory patients, and 9 exclusively enrolled from an outpatient population with mild or no symptoms. In the primary analysis, the saliva NAAT pooled sensitivity was 83.2% (95% credible interval [CrI], 74.7%-91.4%) and the pooled specificity was 99.2% (95% CrI, 98.2%-99.8%). The nasopharyngeal swab NAAT had a sensitivity of 84.8% (95% CrI, 76.8%-92.4%) and a specificity of 98.9% (95% CrI, 97.4%-99.8%). Results were similar in secondary analyses. Conclusions and Relevance: These results suggest that saliva NAAT diagnostic accuracy is similar to that of nasopharyngeal swab NAAT,

especially in the ambulatory setting. These findings support larger-scale research on the use of saliva NAAT as an alternative to nasopharyngeal swabs.

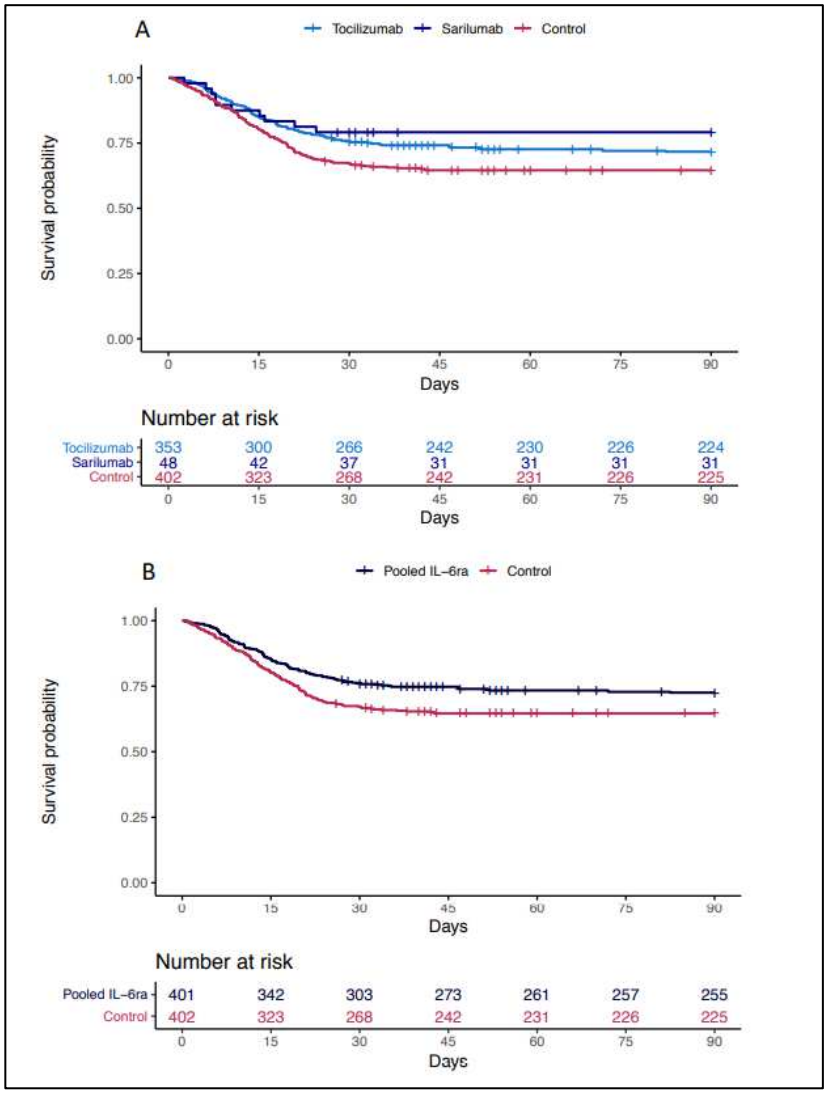
Figure 3. Primary Meta-analysis Results for the Detection of Severe Acute Respiratory Syndrome Coronavirus 2 in Saliva Samples

Source	Test finding, No. TP	FP	FN	TN	Sensitivity (95% CrI), %	Specificity (95% CrI), %
Akgun et al[14]	30	5	25	38	60.6 (46.3-77.0)	98.8 (95.4-99.9)
Becker et al[15]	11	2	10	62	65.4 (44.3-89.8)	99.0 (96.5-99.9)
Byrne et al[16]	12	0	2	96	82.2 (64.8-95.5)	99.3 (98.0-99.9)
Caulley et al[22]	34	14	22	1869	79.5 (56.8-95.8)	99.3 (98.3-99.9)
Cheuk et al[25]	104	37	18	70	84.5 (72.4-92.0)	99.1 (97.3-99.9)
Iwasaki et al[26]	8	1	1	66	83.8 (65.8-96.1)	99.2 (97.5-99.9)
Hanson et al[23]	75	6	5	268	87.3 (74.1-96.5)	99.2 (97.7-99.9)
Kojima et al[17]	20	6	3	16	84.6 (69.9-95.0)	99.1 (97.2-99.9)
Landry et al[27]	28	2	5	89	81.8 (66.8-93.9)	99.2 (97.6-99.9)
McCormick-Baw et al[29]	47	1	2	105	86.0 (71.1-96.0)	99.2 (97.8-99.9)
Miller et al[21]	33	1	1	56	86.7 (73.1-96.6)	99.2 (97.6-99.9)
Pasomsub et al[3]	16	2	3	179	83.3 (66.1-96.0)	99.2 (97.8-99.9)
Teo et al[18]	139	70	11	116	89.4 (77.1-96.3)	99.1 (97.1-99.9)
Vogels et al[19]	32	3	2	30	86.4 (72.1-96.1)	99.1 (97.2-99.9)
Williams et al[28]	33	1	6	49	79.9 (65.0-91.6)	99.1 (97.5-99.9)
Yokata et al[20]	42	6	4	1872	85.9 (71.0-96.6)	99.2 (98.2-99.8)
Pooled	**664**	**157**	**120**	**4981**	**83.2 (74.7-91.4)**	**99.2 (98.2-99.8)**

Sensitivity and specificity estimates (with their 95% credible intervals [CrI]) are obtained from the latent class bivariate bayesian model. The true-positive (TP), false-positive (FP), false-negative (FN), and true-negative (TN) counts in the sensitivity graph are with respect to the nasopharyngeal swab nucleic acid amplification testing. Note the y-axis scale difference between the 2 forest plots. Diamond indicates pooled data.

Jering KS et al JAMA https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2775396	Clinical Characteristics and Outcomes of Hospitalized Women Giving Birth With and Without COVID-19	Caratteristiche ed ouctome clinici delle donne con infezione da SARS-CoV-2 ricoverate per partorire tra aprile e novembre 2020, a confronto con le non infette.	Physiologic adaptations and changes in immune regulation may increase the risk of morbidity and mortality in pregnant women with respiratory infections. The effects of coronavirus disease 2019 (COVID-19) in pregnancy have not been fully delineated. We compared the clinical characteristics and outcomes of hospitalized women who gave birth with and without COVID-19.
Weigand M The Centers for Disease Control and Prevention https://www.cdc.gov/amd/pdf/slidesets/ToolkitModule_1.3.pdf	How to read a phylogenetic tree	Breve presentazione dal sito dei CDC per una introduzione alla lettura degli alberi filogenetici, con specifico riferimento alle varianti di SARS-CoV-2.	Viruses mutate as they spread, providing a “fingerprint” that can be used to infer ancestral relationships among sampled individuals. Using phylogenetics, those relationships can be visualized as a “tree” that is always an approximation of the true network. Strains that are phylogenetically closer are more likely to share an epidemiological association.
Koheler P et al The Lancet https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30847-1/fulltext	Defining and managing COVID-19-associated pulmonary aspergillosis: the 2020 ECMM/ISHAM consensus criteria for research and clinical guidance	Consensus su diagnosi e trattamento dell’aspergillosi invasiva associata a COVID-19 (CAPA).	Severe acute respiratory syndrome coronavirus 2 causes direct damage to the airway epithelium, enabling aspergillus invasion. Reports of COVID-19-associated pulmonary aspergillosis have raised concerns about it worsening the disease course of COVID-19 and increasing mortality. Additionally, the first cases of COVID-19-associated pulmonary aspergillosis caused by azole-resistant aspergillus have been reported. This article constitutes a consensus statement on defining and managing COVID-19-associated pulmonary aspergillosis, prepared by experts and endorsed by medical mycology societies. COVID-19-associated pulmonary aspergillosis is proposed to be defined as possible, probable, or proven on the basis of sample validity and thus diagnostic certainty. Recommended first-line therapy is either voriconazole or isavuconazole. If azole resistance is a concern, then liposomal

			amphotericin B is the drug of choice. Our aim is to provide definitions for clinical research and up-to-date recommendations for clinical management of the diagnosis and treatment of COVID-19-associated pulmonary aspergillosis.
Gordon CA et al medRXiv Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19 – Preliminary report | medRxiv	Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19 – Preliminary report	Analisi ad interim dei dati del trial REMAP-CAP su pazienti critici con COVID-19: il trattamento con tocilizumab EV o sarilumab EV rispetto allo standard of care conferisce in entrambi i casi un vantaggio in giorni senza supporto intensivo e in sopravvivenza.	Background The efficacy of interleukin-6 receptor antagonists in critically ill patients with coronavirus disease 2019 (Covid-19) is unclear. Methods We evaluated tocilizumab and sarilumab in an ongoing international, multifactorial, adaptive platform trial. Adult patients with Covid-19, within 24 hours of commencing organ support in an intensive care unit, were randomized to receive either tocilizumab (8mg/kg) or sarilumab (400mg) or standard care (control). The primary outcome was an ordinal scale combining in-hospital mortality (assigned −1) and days free of organ support to day 21. The trial uses a Bayesian statistical model with pre-defined triggers to declare superiority, efficacy, equivalence or futility. Results Tocilizumab and sarilumab both met the pre-defined triggers for efficacy. At the time of full analysis 353 patients had been assigned to tocilizumab, 48 to sarilumab and 402 to control. Median organ support-free days were 10 (interquartile range [IQR] −1, 16), 11 (IQR 0, 16) and 0 (IQR −1, 15) for tocilizumab, sarilumab and control, respectively. Relative to control, median adjusted odds ratios were 1.64 (95% credible intervals [CrI] 1.25, 2.14) for tocilizumab and 1.76 (95%CrI 1.17, 2.91) for sarilumab, yielding >99.9% and 99.5% posterior probabilities of superiority compared with control. Hospital mortality was 28.0% (98/350) for tocilizumab, 22.2% (10/45) for sarilumab and 35.8% (142/397) for control. All secondary outcomes and analyses supported efficacy of these IL-6 receptor antagonists.

			Conclusions In critically ill patients with Covid-19 receiving organ support in intensive care, treatment with the IL-6 receptor antagonists, tocilizumab and sarilumab, improved outcome, including survival. (ClinicalTrials.gov number: NCT02735707) 

Cruz AF et al Clinical Infecitous Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa865/5862696	The right time for steroids in COVID-19.	Tenere conto dell'esordio dei sintomi e non del giorno di ricovero per scandire temporalmente l'infezione da SARS-CoV-2 e valutare il momento di inizio della terapia steroidea: ragionevole.	However, we would like to make a point on what we consider "early" treatment. From a physiopathological standpoint, we assume that during the first days after the infection by SARS-CoV-2, clinical manifestations are due to direct viral damage, whereas in a second phase, lung damage is driven by a hyperinflammatory response. With the limitations of current knowledge, it could be considered that anti-inflammatory therapy administered too early in the course of the disease could be deleterious, whereas given at the right time it would hamper inflammation, with a positive effect in oxygenation and therefore in survival.
Jia-Tsrong J et al PNAS https://www.pnas.org/content/118/5/e2021579118	Identification of existing pharmaceuticals and herbal medicines as inhibitors of SARS-CoV-2 infection	Metodo di individuazione di potenziali antivirali contro SARS-CoV-2 tra molecole già utilizzate per altri scopi, la base del "drug repurposing".	The outbreak of COVID-19 caused by SARS-CoV-2 has resulted in more than 50 million confirmed cases and over 1 million deaths worldwide as of November 2020. Currently, there are no effective antivirals approved by the Food and Drug Administration to contain this pandemic except the antiviral agent remdesivir. In addition, the trimeric spike protein on the viral surface is highly glycosylated and almost 200,000 variants with mutations at more than 1,000 positions in its 1,273 amino acid sequence were reported, posing a major challenge in the development of antibodies and vaccines. It is therefore urgently needed to have alternative and timely treatments for the disease. In this study, we used a cell-based infection assay to screen more than 3,000 agents used in humans and animals, including 2,855 small molecules and 190 traditional herbal medicines, and identified 15 active small molecules in concentrations ranging from 0.1 nM to 50 μM. Two enzymatic assays, along with molecular modeling, were then developed to confirm those targeting the virus 3CL protease and the RNA-dependent RNA polymerase. Several water extracts of herbal medicines were active in the cell-based assay and could be further developed as plant-derived anti–SARS-CoV-2 agents. Some of the

			active compounds identified in the screen were further tested in vivo, and it was found that mefloquine, nelfinavir, and extracts of Ganoderma lucidum (RF3), Perilla frutescens, and Mentha haplocalyx were effective in a challenge study using hamsters as disease model.
Lavine JS et al Science https://science.sciencemag.org/content/early/2021/01/11/science.abe6522	Immunological characteristics govern the transition of COVID-19 to endemicity	Quando COVID-19 sarà una malattia endemica, ci si infetterà da bambini: la gravità della malattia in questa fascia d'età determinerà la necessità o meno di proseguire con la vaccinazione nell'infanzia.	We are currently faced with the question of how the CoV-2 severity may change in the years ahead. Our analysis of immunological and epidemiological data on endemic human coronaviruses (HCoVs) shows that infection-blocking immunity wanes rapidly, but disease-reducing immunity is long-lived. Our model, incorporating these components of immunity, recapitulates both the current severity of CoV-2 and the benign nature of HCoVs, suggesting that once the endemic phase is reached and primary exposure is in childhood, CoV-2 may be no more virulent than the common cold. We predict a different outcome for an emergent coronavirus that causes severe disease in children. These results reinforce the importance of behavioral containment during pandemic vaccine rollout, while prompting us to evaluate scenarios for continuing vaccination in the endemic phase.
Buss LF et al Science https://science.sciencemag.org/content/371/6526/288?ijkey=346f967e4b650c46124ce0f04c69574c3a1ea048&keytype2=tf_ipsecsha	Three-quarters attack rate of SARS-CoV-2 in the Brazilian Amazon during a largely unmitigated epidemic	Sieroprevalenza di SARS-CoV-2 a Manaus, città brasiliana duramente colpita dalla pandemia di COVID-19: 44-66% entro luglio 2020, molto vicino alla soglia teorica di immunità "di gregge" per SARS-CoV-2. Tuttavia, il virus ha continuato a circolare, possibilmente in conseguenza di fattori come perdita	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spread rapidly in Manaus, the capital of Amazonas state in northern Brazil. The attack rate there is an estimate of the final size of the largely unmitigated epidemic that occurred in Manaus. We use a convenience sample of blood donors to show that by June 2020, 1 month after the epidemic peak in Manaus, 44% of the population had detectable immunoglobulin G (IgG) antibodies. Correcting for cases without a detectable antibody response and for antibody waning, we estimate a 66% attack rate in June, rising to 76% in October. This is higher than in São Paulo, in southeastern Brazil, where the estimated attack rate in October was 29%. These results

		dell'immunità e casi di importazione.	confirm that when poorly controlled, COVID-19 can infect a large proportion of the population, causing high mortality.
Sridhar D et al Science https://science.sciencemag.org/content/371/6526/230	Herd immunity by infection is not an option	Commento all'articolo precedente, che vuole sancire il fallimento del tentativo di raggiungere l'immunità "di gregge" tramite la diffusione incontrollata di SARS-CoV-2.	Herd immunity is expected to arise when a virus cannot spread readily, because it encounters a population that has a level of immunity that reduces the number of individuals susceptible to infection. On page 288 of this issue, Buss et al. describe the extent of the largely uncontrolled severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) epidemic in Manaus, the capital of Amazonas state in Brazil. Their data show the impact on mortality rates of a largely unmitigated outbreak where even with an estimated 76% of the population being infected, herd immunity was not achieved. Manaus provides a cautionary example of unmitigated spread across a population, showing that herd immunity is likely not achieved even at high levels of infection and that it comes with unacceptably high costs.