RICERCA BIBLIOGRAFICA COVID 19

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FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE

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AUTORE/RIVISTA	TITOLO	OUTCOME PRINCIPALE	ABSTRACT
Uzcategui EM Nature https://www.nature.com/articles/d41586-020-03166-8	What Pfizer's landmark COVID vaccine results mean for the pandemic	Significato del comunicato stampa diramato da Pfizer in merito al vaccino a mRNA attualmente in fase III di sperimentazione, che sarebbe efficace nel contrastare l'infezione nel 90% dei casi. Rimangono aperte alcune questioni, ad esempio la gravità delle infezioni scongiurate, la durata dell'immunità conferita, l'efficacia su sottopopolazioni vulnerabili (come anziani, afroamericani).	Scientists welcome the first compelling evidence that a vaccine can prevent COVID-19. But questions remain about how much protection it offers, to whom and for how long.

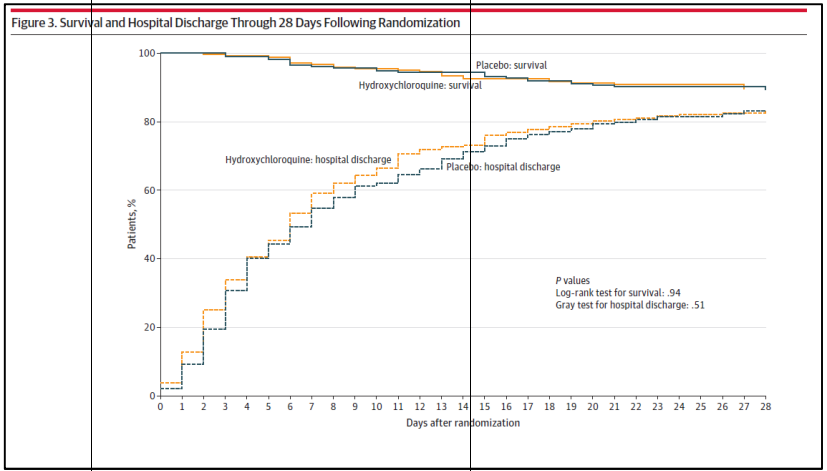
Miller B JAMA https://jamanetwork.com/journals/jama/fullarticle/2772693	Science Denial and COVID Conspiracy Theories Potential Neurological Mechanisms and Possible Responses	Il negazionismo nei confronti della scienza, esploso durante la pandemia da COVID-19, può essere ricondotto a un meccanismo neurofisiopatologico ? Analogie tra le fallacie logiche dei negazionisti e quelle dei pazienti affetti da demenza.	The US public health response to coronavirus disease 2019 (COVID-19) has been dismal, characterized by antimask behavior, antivaccine beliefs, conspiracy theories about the origins of COVID-19, and vocal support by elected officials for unproven therapies. Less than half of the people in the US heed health recommendations to wear a mask when out in public.1 Antiscience rhetoric has consequences. While only 4% of the world's population resides in the US, the US has accounted for 20% of the world's deaths related to COVID-19 and has performed less well than several other wealthy nations.2 Low science literacy contributes to denial of science. The relationship between antiscience viewpoints and low science literacy underscores new findings regarding the brain mechanisms that form and maintain false beliefs.
Wu Z et al European Journal of Medical Research https://doi.org/10.1186/s40001-020-00454-x	A meta-analysis of the impact of COVID-19 on liver dysfunction.	Metanalisi dell'impatto di SARS-CoV-2 sul fegato : il danno epatico (in particolare i livelli di AST) è associato alla mortalità per COVID-19.	BACKGROUND: The novel coronavirus disease 2019 (COVID-19), which is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is leading to a worldwide pandemic. Except representative manifestation of pneumonia and acute respiratory symptoms, COVID-19 patients have also shown different levels of liver injury or liver dysfunction. The aim of our study was to explore the probable clinical severity and mortality of COVID-19 patients and their liver dysfunction. METHOD: A combination of computer and manual retrieval was used to search in Medline through PubMed, EMBASE and Web of Science. Review Manager 5.3 software was used to examine the heterogeneity among the studies and to calculate the combined effect value (OR, 95CI). Subgroup analysis, sensitivity analysis, and publication bias test were also performed. RESULTS: We found a significant connection between liver dysfunction and mortality of COVID-19 patients with a pooled OR of 1.98 (95% CI 1.39-2.82; P = 0.0002). There was a significant association between AST and severity of COVID-19 with a

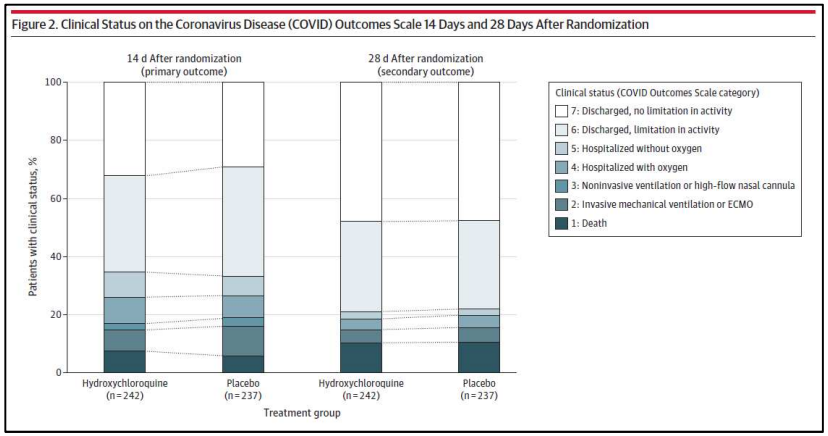
			pooled OR of 4.48 (95% CI 3.24-7.21; P < 0.001), and a pooled WMD of 3.35 (95% CI, 2.07 to 4.64; P < 0.001). In addition, there was a significant difference between TBIL and severity of COVID-19, with a pooled OR of 1.91 (95% CI 1.40-2.60; P < 0.001), and with a pooled WMD of 1.18 (95% CI, 0.78 to 1.58; P < 0.001). CONCLUSION: The mortality and severity of COVID-19 patients are significantly associated with liver dysfunction. The non-survivors and severe COVID-19 patients have elevated serum AST levels than the survivors and non-severe COVID-19 patients. The results of this study form a basis for better clinical liver management of patients with COVID-19.
Azzi Y et al Transplantation https://doi.org/10.1097/TP.0000000000003523	Covid-19 and Solid Organ Transplantation: A Review Article.	Revisione degli aspetti del trapianto d'organo solido legati alla pandemia da COVID-19.	The coronavirus pandemic has significantly impacted solid organ transplantation (SOT). Early in the outbreak period, transplant societies recommended suspending living kidney transplant programs in communities with widespread transmission to avoid exposing recipients to increased risk of immunosuppression, while recommendations were made to reserve deceased-donor kidney transplantation for likely life-saving indications. SOT recipients may be at high risk from COVID-19 disease due to chronic immunosuppressive treatment and other medical comorbidities. Mortality rates reported between 13 to over 30% in SOT recipients. In addition to high rates of complications and mortality attributable to COVID-19 infections, the pandemic has also led to additional complexities in transplantation including new questions regarding screening of donors and recipients, decision making to accept a patient for kidney transplant or wait after pandemic. The clinical implications of COVID-19 infection may also differ depending on the type of the transplanted organ and recipient comorbidities which further impacts decisions on continuing transplantation during the pandemic. Transplant activity during a pandemic should be tailored

			with careful selection of both donors and recipients. Furthermore, while tremendous strides have been made in treatment strategies and vaccinations, the impact of these in transplant recipients may be attenuated in the setting of their immunosuppression. In this review, we aim to summarize several aspects of COVID-19 in transplantation, including the immune response to SARS-CoV-2, SARS-CoV-2 diagnostics, clinical outcomes in SOT recipients and end stage kidney disease patients, transplant activity during the pandemic and treatment options for COVID-19 disease.
Vishwanath W et al JAMA https://jamanetwork.com/channels/health-forum/fullarticle/2772795	Reimagining Cardiac Rehabilitation in the Era of Coronavirus Disease 2019	L'epidemia da COVID-19 ha favorito l'affermarsi della riabilitazione cardiologica domiciliare, che assicurerebbe gli stessi risultati di quella ospedaliera secondo recenti studi.	The coronavirus pandemic has spurred significant growth in home-based cardiology care, facilitated by delivery and financing innovations. Since February 2020, the Centers for Medicare & Medicaid Services have issued 190 ambulatory care waivers, including allowing virtual cardiology visits. As a result, 25% to 34% of Medicare beneficiaries have received telehealth care during the pandemic, compared with less than 1% in 2016.1 On October 14, in an unprecedented move, the Centers for Medicare and Medicaid Services initiated reimbursements for virtual cardiac rehabilitation. Lessons learned from virtual delivery during the pandemic should inform delivery and payment reform for cardiac rehabilitation going forward.
Wesley HS et al JAMA https://pubmed.ncbi.nlm.nih.gov/33165621/	Effect of Hydroxychloroquine on Clinical Status at 14 Days in Hospitalized Patients With COVID-19 : A Randomized Clinical Trial	Tral clinico multicentrico che ha incluso 479 pazienti ospedalizzati per COVID-19 ed è stato interrotto per futilità del trattamento in studio : il trattamento con idrossiclorochina non determina miglioramento	IMPORTANCE Data on the efficacy of hydroxychloroquine for the treatment of coronavirus disease 2019 (COVID-19) are needed. OBJECTIVE To determine whether hydroxychloroquine is an Efficacious treatment for adults hospitalized with COVID-19. DESIGN, SETTING, AND PARTICIPANTS This was a multicenter, blinded, placebo-controlled randomized trial conducted at 34 hospitals in the US. Adults hospitalized with respiratory symptoms from severe acute respiratory syndrome coronavirus 2 infection

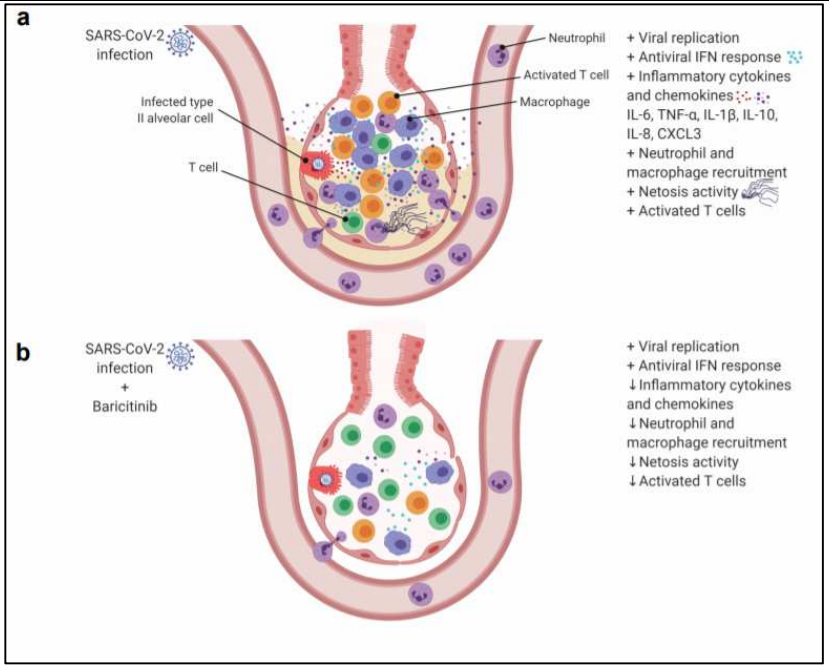
		clinico a 14 giorni dalla randomizzazione,	were enrolled between April 2 and June 19, 2020, with the last outcome assessment on July 17, 2020. The planned sample size was 510 patients, with interim analyses planned after every 102 patients were enrolled. The trial was stopped at the fourth interim analysis for futility with a sample size of 479 patients. INTERVENTIONS Patients were randomly assigned to hydroxychloroquine (400mg twice daily for 2 doses, then 200mg twice daily for 8 doses) (n = 242) or placebo (n = 237). MAIN OUTCOMES AND MEASURES The primary outcomewas clinical status 14 days after randomization as assessed with a 7-category ordinal scale ranging from 1 (death) to 7 (discharged from the hospital and able to perform normal Activities). The primary outcome was analyzed with a multivariable proportional odds model, with an adjusted odds ratio (aOR) greater than 1.0 indicating more favorable outcomes with hydroxychloroquine than placebo. The trial included 12 secondary outcomes, including 28-day mortality. RESULTS Among 479 patients who were randomized (median age, 57 years; 44.3%female; 37.2%Hispanic/Latinx; 23.4%Black; 20.1%in the intensive care unit; 46.8%receiving supplemental oxygen without positive pressure; 11.5%receiving noninvasive ventilation or nasal high-flow oxygen; and 6.7%receiving invasive mechanical ventilation or extracorporeal membrane oxygenation), 433 (90.4%) completed the primary outcome assessment at 14 days and the remainder had clinical status imputed. The median duration of symptoms prior to randomization was 5 days (interquartile range [IQR], 3 to 7 days). Clinical status on the ordinal outcome scale at 14 days did not significantly differ between the hydroxychloroquine and placebo groups (median [IQR] score, 6 [4-7] vs 6 [4-7]; aOR, 1.02 [95%CI, 0.73 to 1.42]).

			None of the 12 secondary outcomes were significantly different between groups. At 28 days after randomization, 25 of 241 patients (10.4%) in the hydroxychloroquine group and 25 of 236 (10.6%) in the placebo group had died (absolute difference, −0.2%[95%CI, -5.7%to 5.3%]; aOR, 1.07 [95%CI, 0.54 to 2.09]). CONCLUSIONS AND RELEVANCE Among adults hospitalized with respiratory illness from COVID-19, treatment with hydroxychloroquine, compared with placebo, did not significantly improve clinical status at day 14. These findings do not support the use of hydroxychloroquine for treatment of COVID-19 among hospitalized adults.
Saag MS JAMA	Misguided Use of Hydroxychloroquine for COVID-19: The Infusion of Politics Into Science	La parabola dell'idrossiclorochina fra dubbie evidenze, supporter illustri e sincere speranze dell'intera comunità medica	How did medicine get to the point where so many studies were conducted assessing the possible benefit of hydroxychloroquine, that led to nearly identical findings, and have been published in major journals?

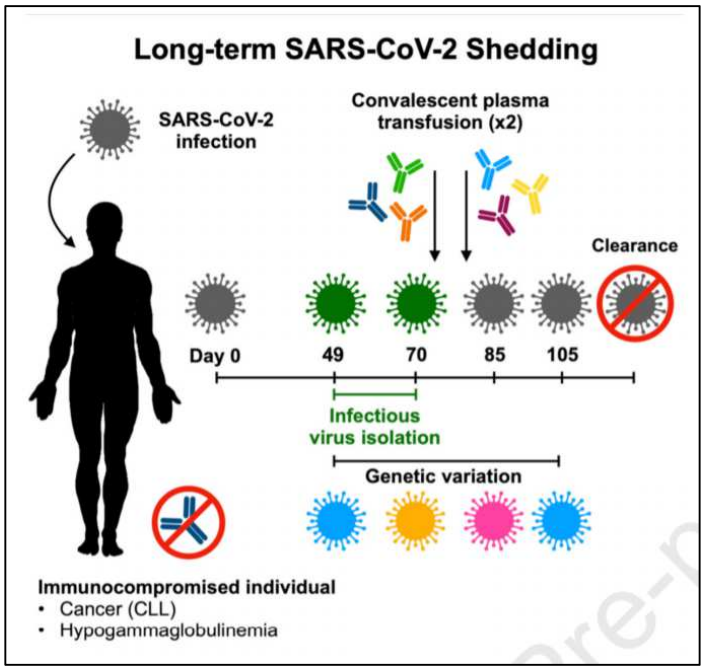




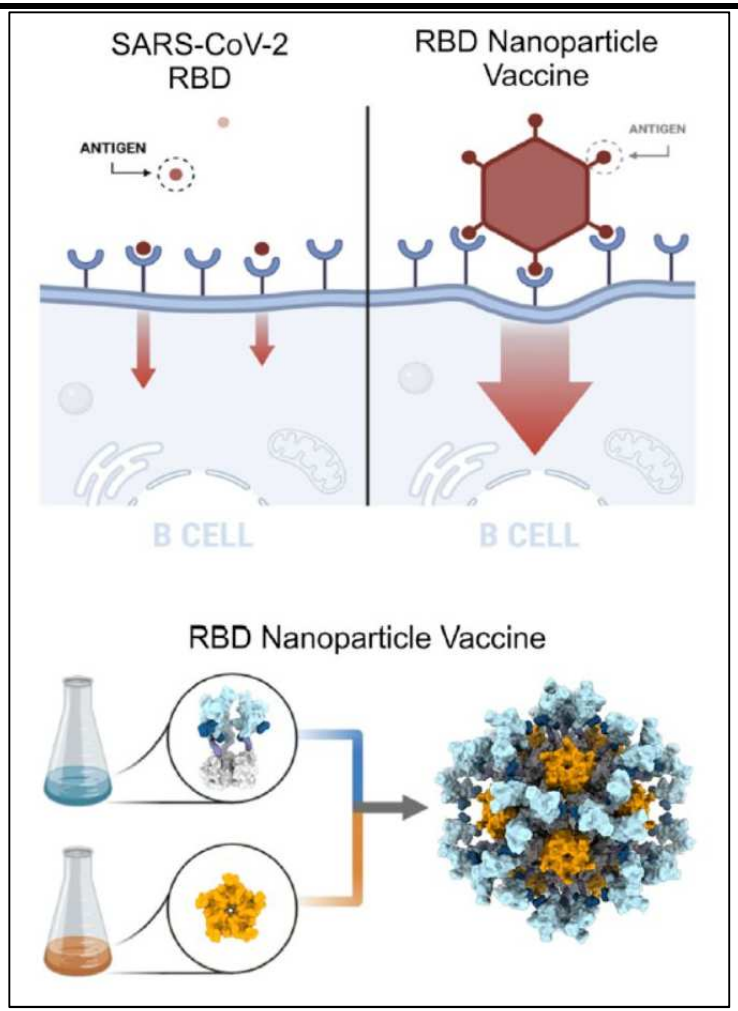
https://pubmed.ncbi.nlm.nih.gov/33165507/		alle prese con la pandemia da COVID-19.	
Hoang TN et al Cell https://www.cell.com/cell/fulltext/S0092-8674(20)31466-5	Baricitinib treatment resolves lower airway macrophage inflammation and neutrophil recruitment in SARS-CoV-2-infected rhesus macaques	L'inibitore di JAK1/2 baricitinib riduce la produzione di citochine da parte dei macrofagi alveolari di scimmie *Macaca mulatta* modello di infezione da SARS-CoV-2 : supporto all'utilizzo del farmaco per l'infezione umana, attualmente in studio in trial clinici.	SARS-CoV-2 induced hypercytokinemia and inflammation are critically associated with COVID-19 disease severity. Baricitinib, a clinically approved JAK1/2 inhibitor, is currently being investigated in COVID-19 clinical trials. Here, we investigated the immunologic and virologic efficacy of baricitinib in a rhesus macaque model of SARS-CoV-2 infection. Viral shedding measured from nasal and throat swabs, bronchoalveolar lavages and tissues was not reduced with baricitinib. Type-I IFN antiviral responses and SARS-CoV-2-specific T-cell responses remained similar between the two groups. Animals treated with baricitinib showed reduced inflammation, decreased lung infiltration of inflammatory cells, reduced NETosis activity, and more limited lung pathology. Importantly, baricitinib treated animals had a rapid and remarkably potent suppression of lung macrophages production of cytokines and chemokines responsible for inflammation and neutrophil recruitment. These data support a beneficial role for, and elucidate the immunological mechanisms underlying, the use of baricitinib as a frontline treatment for inflammation induced by SARS-CoV-2 infection.

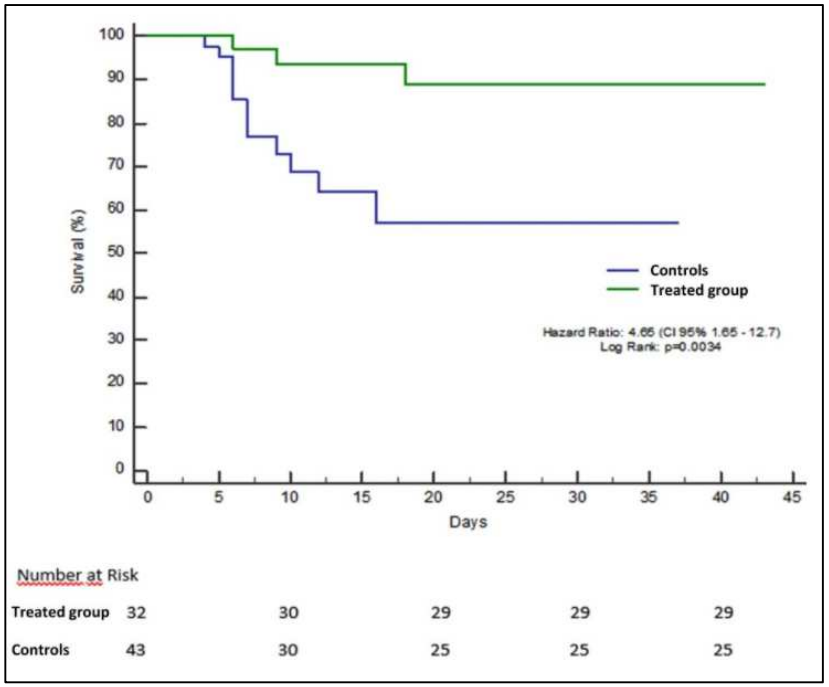
			
Taccone FS et al Critical Care Medicine https://journals.lww.com/ccmjournal/Fulltext/2020/11000/Higher_Intensity_Thromboprophylaxis_Regimens_and.36.aspx	Higher Intensity Thromboprophylaxis Regimens and Pulmonary Embolism in Critically Ill Coronavirus Disease 2019 Patients	Studio retrospettivo su dati raccolti prospetticamente su 49 pazienti sottoposti a ventilazione meccanica per COVID-19 : il 33% ha embolia polmonare, meno frequente in chi è trattato con profilassi anticoagulante aumentata (4000 UI ogni 12 ore) rispetto alla profilassi standard.	Objectives: To assess the role of thromboprophylaxis regimens on the occurrence of pulmonary embolism in coronavirus disease 2019 patients. Design: Retrospective analysis of prospectively collected data on coronavirus disease 2019 patients, included between March 10, and April 30, 2020. Setting: ICU of an University Hospital in Belgium. Patients and Interventions: Critically ill adult mechanically ventilated coronavirus disease 2019 patients were eligible if they underwent a CT pulmonary angiography, as part of the routine management in case of persistent hypoxemia or respiratory deterioration. The primary endpoint of this study was the occurrence of pulmonary embolism according to the use of

			standard thromboprophylaxis (i.e. subcutaneous enoxaparin 4,000 international units once daily) or high regimen thromboprophylaxis (i.e. subcutaneous enoxaparin 4,000 international units bid or therapeutic unfractioned heparin). Measurements and Main Results: Of 49 mechanically ventilated coronavirus disease 2019, 40 underwent CT pulmonary angiography after a median of 7 days (4–8 d) since ICU admission and 12 days (9–16 d) days since the onset of symptoms. Thirteen patients (33%) were diagnosed of pulmonary embolism, which was bilateral in six patients and localized in the right lung in seven patients. D-dimers on the day of CT pulmonary angiography had a predictive accuracy of 0.90 (95% CIs: 0.78–1.00) for pulmonary embolism. The use of high-regimen thromboprophylaxis was associated with a lower occurrence of pulmonary embolism (2/18; 11%) than standard regimen (11/22, 50%—odds ratio 0.13 [0.02–0.69]; p = 0.02); this difference remained significant even after adjustment for confounders. Six patients with pulmonary embolism (46%) and 14 patients without pulmonary embolism (52%) died at ICU discharge (odds ratio 0.79 [0.24–3.26]; p = 0.99). Conclusions: In this study, one third of coronavirus disease 2019 mechanically ventilated patients have a pulmonary embolism visible on CT pulmonary angiography. High regimen thromboprophylaxis may decrease the occurrence of such complication.
Avanzato VA et al Cell https://www.cell.com/cell/fulltext/S0092-8674(20)31456-	Case Study: Prolonged infectious SARS-CoV-2 shedding from an asymptomatic immunocompromised cancer patient.	Caso clinico di una paziente neoplastica con COVID-19 che ha presentato emissione di SARS-CoV-2 infettivo (come dimostrato da crescita in coltura cellulare) fino a 70 giorni dalla diagnosi e la	Long-term SARS-CoV-2 shedding was observed from the upper respiratory tract of a female immunocompromised patient with chronic lymphocytic leukemia and acquired hypogammaglobulinemia. Shedding of infectious SARS-CoV-2 was observed up to 70 days, and genomic and subgenomic RNA up to 105 days past initial diagnosis. The infection was not cleared after a first treatment with convalescent plasma, suggesting limited impact

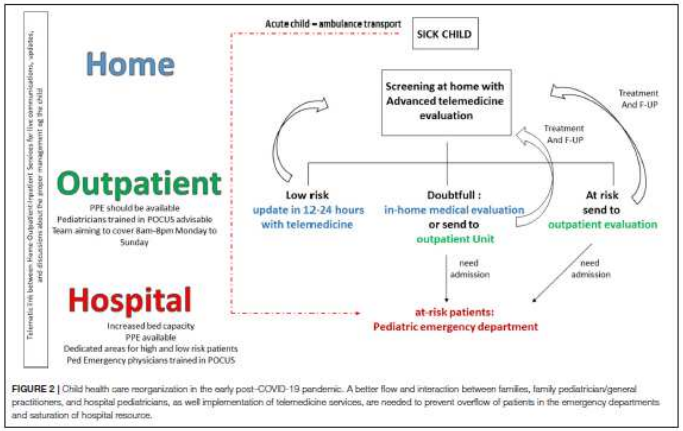
2?utm_medium=homepage		persistenza di tampone molecolare positivo fino a 105 giorni. Inoltre, il sequenziamento del virus isolato nel corso della malattia dimostra una evoluzione di esso all'interno dell'ospite.	on SARS-CoV-2 in the upper respiratory tract within this patient. Several weeks after a second convalescent plasma transfusion, SARS-CoV-2 RNA was no longer detected. We observed marked within-host genomic evolution of SARS-CoV-2, with continuous turnover of dominant viral variants. However, replication kinetics in Vero E6 cells and primary human alveolar epithelial tissues were not affected. Our data indicate that certain immunocompromised patients may shed infectious virus for longer durations than previously recognized. Detection of subgenomic RNA is recommended in persistently SARS-CoV-2 positive individuals as a proxy for shedding of infectious virus. 

Walls AC et al Cell https://doi.org/10.1016/j.cell.2020.10.043	Elicitation of Potent Neutralizing Antibody Responses by Designed Protein Nanoparticle Vaccines for SARS-CoV-2.	Potenzialità di un vaccino a nanoparticelle contro la proteina S di SARS-CoV-2, da studiare in prossimi trial clinici.	A safe, effective, and scalable vaccine is needed to halt the ongoing SARS-CoV-2 pandemic. We describe the structure-based design of self-assembling protein nanoparticle immunogens that elicit potent and protective antibody responses against SARS-CoV-2 in mice. The nanoparticle vaccines display 60 SARS-CoV-2 spike receptor-binding domains (RBDs) in a highly immunogenic array and induce neutralizing antibody titers 10-fold higher than the prefusion-stabilized spike despite a 5-fold lower dose. Antibodies elicited by the RBD nanoparticles target multiple distinct epitopes, suggesting they may not be easily susceptible to escape mutations, and exhibit a lower binding:neutralizing ratio than convalescent human sera, which may minimize the risk of vaccine-associated enhanced respiratory disease. The high yield and stability of the assembled nanoparticles suggest that manufacture of the nanoparticle vaccines will be highly scalable. These results highlight the utility of robust antigen display platforms and have launched cGMP manufacturing efforts to advance the SARS-CoV-2-RBD nanoparticle vaccine into the clinic.

			
D'Alessio A et al Leukemia	Low-dose ruxolitinib plus steroid in severe SARS-CoV-2 pneumonia	Effetto favorevole dell'inibitore di JAK1/2 ruxolitinib sulla mortalità da COVID-19 in un piccolo	SARS-CoV-2 is a biphasic illness characterized by a first flu-like phase, followed by a pulmonary and systemic disease, in which a dysregulated cytokine storm may lead to acute respiratory distress (ARDS) and death. JAK-STAT inhibitors block the common pathway of cytokine activation, may reduce the over-exuberant

https://doi.org/10.1038/s41375-020-01087-z		studio clinico non randomizzato.	inflammatory reaction and decrease mortality. Ruxolitinib is a JAK 1 and 2 (Janus Kinase) inhibitor used in the treatment of myelofibrosis, policytemia vera and hemophagocytic lymphohistiocytosis, which is characterized by a cytokine derangement similar to what observed in SARS-CO-V2 infection. 
Letizia AG et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa20	SARS-CoV-2 Transmission among Marine Recruits during Quarantine	Diffusione di SARS-CoV-2 fra 1848 reclute dei Marines negli USA, sottoposti a un periodo di quaratena a casa e quindi due settimane di ritiro in caserma con misure di distanziamento sociale :	BACKGROUND : The efficacy of public health measures to control the transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has not been well studied in young adults. METHODS : We investigated SARS-CoV-2 infections among U.S. Marine Corps recruits who underwent a 2-week quarantine at home followed by a second supervised 2-week quarantine at a closed college campus that involved mask wearing, social distancing, and

29717?query=featured_coronavirus		2% di positivi a 14 giorni di quarantena in caserma.	daily temperature and symptom monitoring. Study volunteers were tested for SARS-CoV-2 by means of quantitative polymerase-chain-reaction (qPCR) assay of nares swab specimens obtained between the time of arrival and the second day of supervised quarantine and on days 7 and 14. Recruits who did not volunteer for the study underwent qPCR testing only on day 14, at the end of the quarantine period. We performed phylogenetic analysis of viral genomes obtained from infected study volunteers to identify clusters and to assess the epidemiologic features of infections. RESULTS : A total of 1848 recruits volunteered to participate in the study; within 2 days after arrival on campus, 16 (0.9%) tested positive for SARS-CoV-2, 15 of whom were asymptomatic. An additional 35 participants (1.9%) tested positive on day 7 or on day 14. Five of the 51 participants (9.8%) who tested positive at any time had symptoms in the week before a positive qPCR test. Of the recruits who declined to participate in the study, 26 (1.7%) of the 1554 recruits with available qPCR results tested positive on day 14. No SARS-CoV-2 infections were identified through clinical qPCR testing performed as a result of daily symptom monitoring. Analysis of 36 SARS-CoV-2 genomes obtained from 32 participants revealed six transmission clusters among 18 participants. Epidemiologic analysis supported multiple local transmission events, including transmission between roommates and among recruits within the same platoon. CONCLUSIONS : Among Marine Corps recruits, approximately 2% who had previously had negative results for SARS-CoV-2 at the beginning of supervised quarantine, and less than 2% of recruits with unknown previous status, tested positive by day 14. Most recruits who tested positive were asymptomatic, and no infections

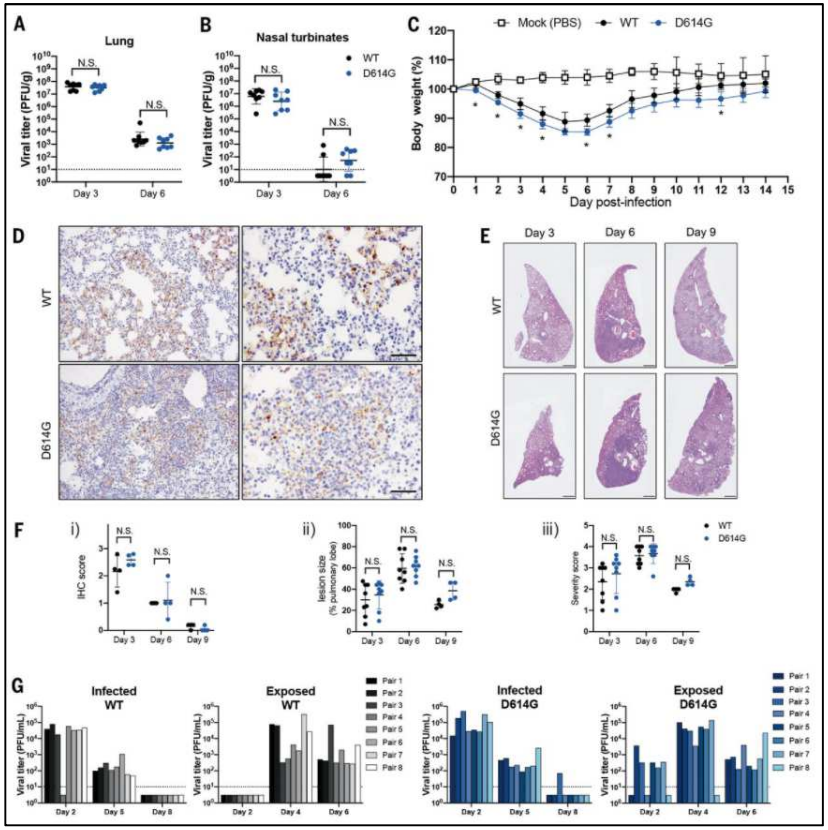
			were detected through daily symptom monitoring. Transmission clusters occurred within platoons.
Buonsenso D et al Frontiers in Pediatrics https://doi.org/10.3389/fped.2020.582798	A Pediatric Strategy for the Next Phase of the SARS-CoV-2 Pandemic.	Proposte per affrontare in modo efficace una seconda ondata di pandemia da SARS-CoV-2 nella popolazione pediatrica.	Although the first wave of the SARS-CoV-2 pandemic relatively spared children, the next winter season will put a strain on health systems including pediatric services. Clinical staff managing children will need to deal not only with suspected cases of COVID-19, but also with the classic infectious agents that involve children during cold seasons. It will be necessary for physicians, institutions, policy makers, and families to prepare themselves for difficulties of this phase of the pandemic. Otherwise, the same problems experienced during the first wave of SARS-CoV-2, including shortages of human resources, personal protective equipment, and uncertainty, will be exacerbated by significant issues in hospital capacity. Here we highlight the potential role of improved vaccination services, school reorganization, home-outpatient-inpatients flows and telemedicine services in order to face the coming winter season.  FIGURE 2	Child health care reorganization in the early post-COVID-19 pandemic. A better flow and interaction between families, family pediatrician/general practitioners, and hospital pediatricians, as well implementation of telemedicine services, are needed to prevent overflow of patients in the emergency departments and saturation of hospital resource.

Liotti FM et al JAMA https://jamanetwork.com/journals/jama/fullarticle/10.1001/jamainternmed.2020.7570?utm_campaig%20n=articlePDF%26utm_medium=articlePDFlink%26utm_source=articlePDF%26utm_content=jamaintern%20med.2020.7570	Assessment of SARS-CoV-2 RNA Test Results Among Patients Who Recovered From COVID-19 With Prior Negative Results	Caratteristiche di 32/176 (18%) pazienti guariti da COVID-19 con doppio tampone negativo, che hanno presentato nuovamente tampone nasofaringeo positivo per SARS-CoV-2 al follow up.	Some patients who have recovered from coronavirus disease 2019 (COVID-19) with documented negative real-time polymerase chain reaction (RT-PCR) results at the time of recovery have had subsequent positive RT-PCR test results for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the absence of any symptoms suggestive of new infection. It is unknown whether such patients are infectious and whether they should be quarantined. Real-time PCR is not a viral culture and does not allow determination of whether the virus is viable and transmissible. We investigated RT-PCR retested positive nasal/oropharyngeal swab (NOS) samples from recovered patients with COVID-19 with prior negative results for the presence of replicative SARS-CoV-2 RNA.
Kim PS et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2773058	Therapy for Early COVID-19 A Critical Need	Una terapia per i casi lievi di COVID-19, gestiti fuori dall'ospedale, non è disponibile mentre sarebbe molto utile anche al fine di alleggerire la pressione sui sistemi sanitari.	While coronavirus disease 2019 (COVID-19) is predominantly self-limited, up to 20%of symptomatic individuals will progress to severe or critical disease with clinical manifestations including pneumonia, acute respiratory distress syndrome, multiorgan system dysfunction, hypercoagulation, and hyperinflammatory manifestations. There have been more than 47 million cases of COVID-19 globally resulting in more than 1.2 million deaths. Additionally, a growing body of data suggests thatsomepatients withCOVID-19, including individuals with mild symptoms, will have a variably prolonged course of recovery including fatigue, cognitive impairment, and cardiopulmonary dysfunction. While treatment options for patients with severe disease requiring hospitalization are now available, with corticosteroids emerging as the treatment of choice for critically ill patients, interventions that can be administered early during the course of infection to prevent

			disease progression and longer-term complications are urgently needed.
Lum BX et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1722/5974991?searchresult=1	Establishing a New Normal for Hospital Care: A Whole of Hospital Approach to COVID-19	Come è stata affrontata la pandemia da COVID-19, dal primo caso fino alla creazione di una « nuova normalità » nella routine ospedaliera, in un policlinico universitario a Singapore.	Singapore's hospitals had prepared operations to receive patients (potentially) infected with SARS-CoV-2, planning various scenarios and levels of surge with a policy of isolating all confirmed cases as inpatients. The National University Hospital, adopted a whole of hospital approach to COVID-19 with three primary goals: zero hospital-acquired COVID-19, all patients receive timely necessary care, and maintenance of staff morale. These goals to date have been met. A large influx of COVID-19 cases emerged requiring a significant transformation of clinical and operational processes. Isolation room numbers almost tripled and dedicated COVID-19 cohort wards were established, elective care was postponed and Intensive Care Units were augmented with equipment and manpower. In the wake of the surge establishing a new normal for hospital care requires a considered balance of maintaining vigilance to detect endemic COVID-19, establishing contingency plans to ramp up in case of another surge, while returning to business as usual.
Sharma O et al Frontiers in Immunology https://doi.org/10.3389/fimmu.2020.585354	A Review of the Progress and Challenges of Developing a Vaccine for COVID-19.	Candidati vaccini in via di sperimentazione, oltre alla molecola Pfizer recentemente annunciata.	A novel coronavirus, which has been designated as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first detected in December 2019 in Wuhan China and causes the highly infectious disease referred to as COVID-19. COVID-19 has now spread worldwide to become a global pandemic affecting over 24 million people as of August 26th, 2020 and claimed the life of more than 800,000 people worldwide. COVID-19 is asymptomatic for some individuals and for others it can cause symptoms ranging from

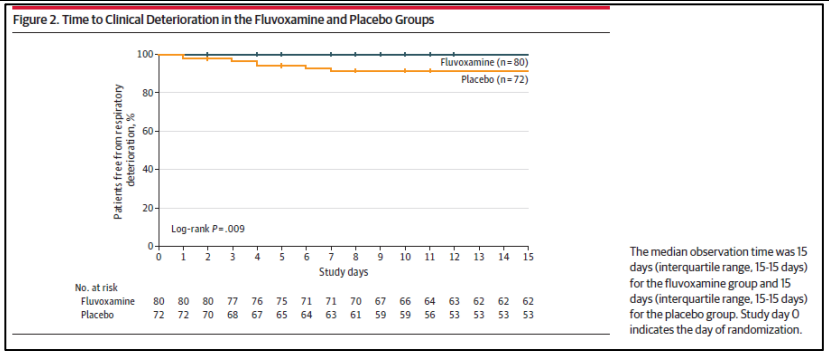
			flu-like to acute respiratory distress syndrome (ARDS), pneumonia and death. Although it is anticipated that an effective vaccine will be available to protect against COVID-19, at present the world is relying on social distancing and hygiene measures and repurposed drugs. There is a worldwide effort to develop an effective vaccine against SARS-CoV-2 and, as of late August 2020, there are 30 vaccines in clinical trials with over 200 in various stages of development. This review will focus on the eight vaccine candidates that entered Phase 1 clinical trials in mid-May, including AstraZeneca/Oxford's AZD1222, Moderna's mRNA-1273 and Sinovac's CoronaVac vaccines, which are currently in advanced stages of vaccine development. In addition to reviewing the different stages of vaccine development, vaccine platforms and vaccine candidates, this review also discusses the biological and immunological basis required of a SARS-CoV-2 vaccine, the importance of a collaborative international effort, the ethical implications of vaccine development, the efficacy needed for an immunogenic vaccine, vaccine coverage, the potential limitations and challenges of vaccine development. Although the demand for a vaccine far surpasses the production capacity, it will be beneficial to have a limited number of vaccines available for the more vulnerable population by the end of 2020 and for the rest of the global population by the end of 2021.
Boushra M et al American Journal of Emergency Medicine https://doi.org/10.1016/j.ajem.2020.10.055	COVID-19 in pregnancy and the puerperium: A review for emergency physicians.	Effetti di SARS-CoV-2 durante la gravidanza e aspetti complessi della gestione della paziente gravida con infezione severa.	BACKGROUND: Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is a novel virus responsible for causing the novel coronavirus disease of 2019 (COVID-19). OBJECTIVE: This article discusses the clinical manifestations of COVID-19 in pregnant patients, the effects of pregnancy on the course of COVID-19 disease, and the impact of COVID-19 on pregnancy outcomes. DISCUSSION: The physiological and mechanical changes associated

			with pregnancy increase maternal susceptibility to infections and complicate intubation and mechanical ventilation. The most common symptoms of COVID-19 in pregnant patients are cough and fever, although many infected individuals are asymptomatic. The majority of pregnant women diagnosed with COVID-19 disease have a mild course of illness and will recover without needing to deliver, but the risks of critical illness and need for mechanical ventilation are increased compared to the general population. Risk factors for death and severe disease include obesity, diabetes, and maternal age > 40 years. Women in their third trimester have the highest risk for critical illness, intensive care unit admission, and need for mechanical ventilation. Adverse fetal outcomes of maternal COVID-19 infection include increased risk of miscarriage, prematurity, and fetal growth restriction. Vertical transmission of SARS-CoV-2 is possible but has not been conclusively proven. CONCLUSIONS: COVID-19 is a potentially deadly infection, but data are limited concerning the pregnant population. Pregnant patients appear to present similarly to the general population, with fever and cough being the most reported symptoms in studies. Knowledge of these presentations and outcomes can assist clinicians caring for these patients.
Yixuan JH et al Science https://science.sciencemag.org/content/early/2020/11/11/science.abe8499	SARS-CoV-2 D614G variant exhibits efficient replication ex vivo and transmission in vivo	La variante di SARS-CoV-2 con sostituzione D614G a carico della proteina spike mostra maggiore infettività, fitness e trasmissibilità rispetto al virus wild-type, il che spiega la sua diffusione.	The spike D614G substitution is prevalent in global SARS-CoV-2 strains, but its effects on viral pathogenesis and transmissibility remain unclear. We engineered a SARS-CoV-2 variant containing this substitution. The variant exhibits more efficient infection, replication, and competitive fitness in primary human airway epithelial cells, but maintains similar morphology and in vitro neutralization properties, compared with the ancestral wild-type virus. Infection of human angiotensin-converting enzyme 2 (ACE2) transgenic mice and Syrian hamsters with both viruses resulted in

			similar viral titers in respiratory tissues and pulmonary disease. However, the D614G variant transmits significantly faster and displayed increased competitive fitness than the wild-type virus in hamsters. These data show that the D614G substitution enhances SARS-CoV-2 infectivity, competitive fitness, and transmission in primary human cells and animal models. 

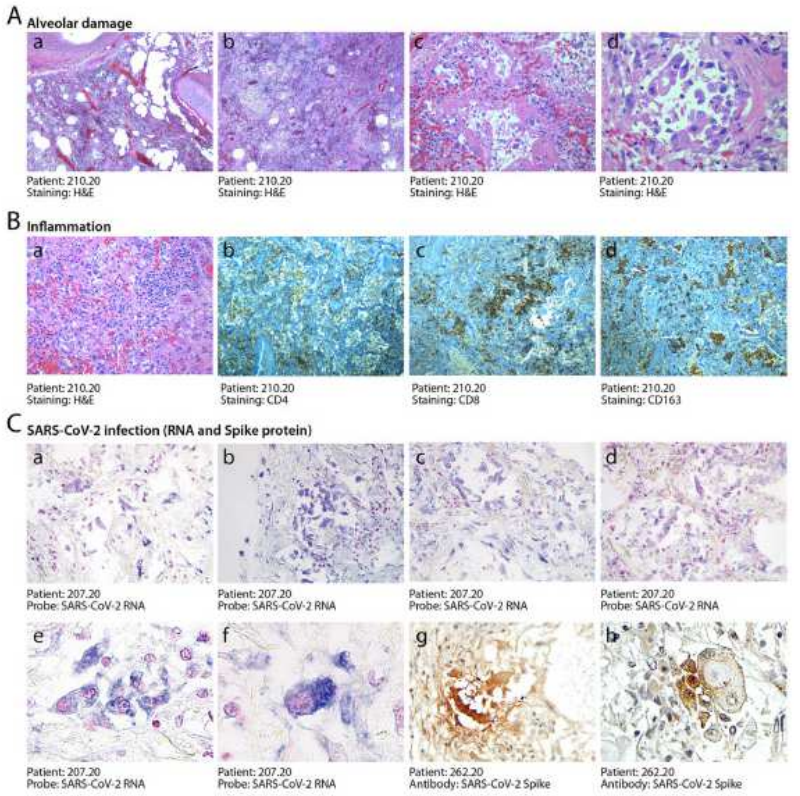
Richterman A et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2773128	Hospital-Acquired SARS-CoV-2 Infection Lessons for Public Health	L'utilizzo universale delle mascherine negli ospedali ha ridotto significativamente la trasmissione nosocomiale di SARS-CoV-2, ma appare necessario lavorare sulle situazioni di rischio misconosciute, come la promiscuità del personale nei momenti di pausa in ambienti non adeguati a consentire il distanziamento.	From the outset of the coronavirus disease 2019 (COVID-19) pandemic, it was clear that hospitals were an important setting for viral transmission. A review of 2 early case series in China estimated that 44% of 179 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections were hospital acquired. An illustrative example of the devastating potential for health care transmission of SARS-CoV-2 came from St Augustine's Hospital in Durban, South Africa, a facility with 469 beds, including 18 wards, 6 intensive care units, and 735 clinical staff. Through a detailed epidemiologic study supplemented by phylogenetic analyses, investigators documented how a single unsuspected case of SARS-CoV-2 led to 6 major clusters involving 5 hospital wards and an outside nursing home and dialysis unit, with infection ultimately confirmed among 80 staff members and 39 patients, 15 of whom died.
Lenze EJ et al JAMA https://jamanetwork.com/article.aspx?doi=10.1001/jama.2020.22760	Fluvoxamine vs Placebo and Clinical Deterioration in Outpatients With Symptomatic COVID-19 A Randomized Clinical Trial	Trial clinico randomizzato in doppio cieco che confronta la terapia con l'antidepressivo fluvoxamina (classe SSRI) con un placebo per 105 pazienti con infezione da SARS-CoV-2 sintomatica senza necessità di ricovero ospedaliero : i trattati con fluvoxamina vanno incontro meno frequentemente a peggioramento clinico. La base di questa osservazione sarebbe l'effetto modulatore del farmaco	Importance Coronavirus disease 2019 (COVID-19) may lead to serious illness as a result of an excessive immune response. Fluvoxamine may prevent clinical deterioration by stimulating the σ-1 receptor, which regulates cytokine production. Objective To determine whether fluvoxamine, given during mild COVID-19 illness, prevents clinical deterioration and decreases the severity of disease. Design, Setting, and Participants Double-blind, randomized, fully remote (contactless) clinical trial of fluvoxamine vs placebo. Participants were community-living, nonhospitalized adults with confirmed severe acute respiratory syndrome coronavirus 2 infection, with COVID-19 symptom onset within 7 days and oxygen saturation of 92% or greater. One hundred fifty-two participants were enrolled from the St Louis metropolitan area (Missouri and Illinois) from April 10, 2020, to August 5, 2020. The final date of follow-up was September 19, 2020.

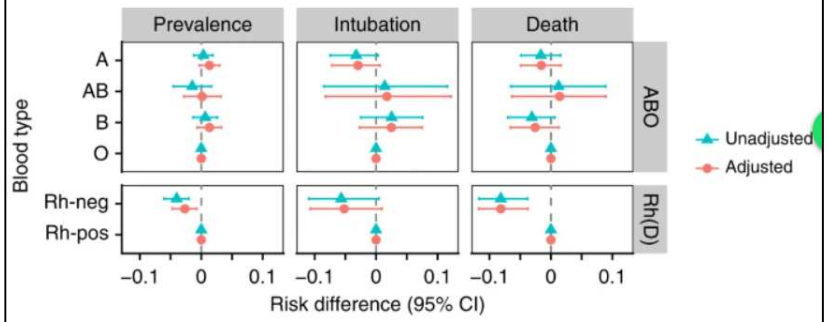
		sulla produzione di citochine infiammatorie.	Interventions Participants were randomly assigned to receive 100 mg of fluvoxamine (n = 80) or placebo (n = 72) 3 times daily for 15 days. Main Outcomes and Measures The primary outcome was clinical deterioration within 15 days of randomization defined by meeting both criteria of (1) shortness of breath or hospitalization for shortness of breath or pneumonia and (2) oxygen saturation less than 92% on room air or need for supplemental oxygen to achieve oxygen saturation of 92% or greater. Results Of 152 patients who were randomized (mean [SD] age, 46 [13] years; 109 [72%] women), 115 (76%) completed the trial. Clinical deterioration occurred in 0 of 80 patients in the fluvoxamine group and in 6 of 72 patients in the placebo group (absolute difference, 8.7% [95% CI, 1.8%-16.4%] from survival analysis; log-rank P = .009). The fluvoxamine group had 1 serious adverse event and 11 other adverse events, whereas the placebo group had 6 serious adverse events and 12 other adverse events. Conclusions and Relevance In this preliminary study of adult outpatients with symptomatic COVID-19, patients treated with fluvoxamine, compared with placebo, had a lower likelihood of clinical deterioration over 15 days. However, the study is limited by a small sample size and short follow-up duration, and determination of clinical efficacy would require larger randomized trials with more definitive outcome measures.

			
Seymour WC et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2773107	COVID-19 Infection—Preventing Clinical Deterioration	Commento allo studio di Lenze et al che sottolinea l'importanza di un approccio terapeutico definito per i pazienti con COVID-19 non ospedalizzati e non gravi.	But what about treatments for patients with COVID-19 who are neither hospitalized nor severely ill? The pilot study by Lenze and colleagues addresses a critically important question during the pandemic of how to prevent individuals who acquire COVID-19 from deteriorating to serious illness. If an effective treatment is found for this key gap in treatment, it will affect the health of millions of people worldwide. This study has important limitations, and the findings should be interpreted as only hypothesis generating; they should not be used as the basis for current treatment decisions. Despite this representing preliminary evidence, there were 2 reasons the editors decided to publish it in JAMA.
Meppiel E et al Clinical Microbiology and Infection https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30698-4/fulltext	Neurological manifestations associated with COVID-19: a multicentric registry	Studio retrospettivo multicentrico condotto in Francia con lo scopo di descrivere le manifestazioni neurologiche associate a COVID-19 : descritti 222 pazienti con differenti sindromi cliniche, verosimilmente legate a meccanismi fisiopatologici vari.	Objective : This study aims to provide an overview of the spectrum, characteristics and outcomes of neurological manifestations associated with SARS-CoV-2 infection. Methods : We conducted a multicentric, retrospective study during the French COVID-19 epidemic in March-April 2020. All COVID-19 patients with de novo neurological manifestations were eligible. Results : We included 222 COVID-19 patients with neurological manifestations from 46 centers in France. Median age was 65 years (IQR 53-72), and 136 patients (61.3%) were male. COVID-19 was severe or critical in 102 patients (45.2%). The most common

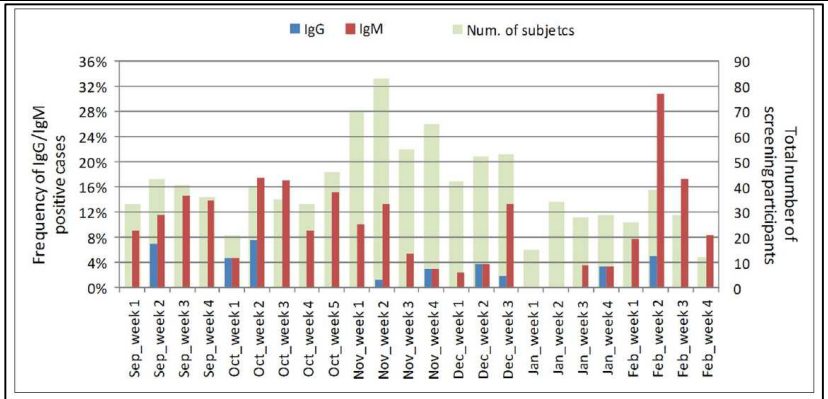
			neurological diseases were COVID-19 associated encephalopathy (67/222, 30.2%), acute ischemic cerebrovascular syndrome (57/222, 25.7%), encephalitis (21/222, 9.5%), and Guillain-Barré Syndrome (15/222, 6.8%). Neurological manifestations appeared after first COVID-19 symptoms with a median (IQR) delay of 6 (3-8) days in COVID-19 associated encephalopathy, 7 (5-10) days in encephalitis, 12 (7-18) days in acute ischemic cerebrovascular syndrome and 18 (15-28) days in Guillain-Barré Syndrome. Brain imaging was performed in 192 patients (86.5%), including 157 MRI (70.7%). Among patients with acute ischemic cerebrovascular syndrome, 13/57 (22.8%) had multi territory ischemic strokes, with large vessel thrombosis in 16/57 (28.1%). Brain MRI of encephalitis patients showed heterogeneous acute non vascular lesion in 14/21 patients (66.7%). Cerebrospinal fluid was analyzed in 97 patients (43.7%), with pleocytosis in 18 patients (18.6%) and a positive SARS-CoV-2 PCR in 2 patients with encephalitis. The median (IQR) follow-up was 24 (17-34) days with a high short-term mortality rate (28/222, 12.6%). Conclusion : Clinical spectrum and outcomes of neurological manifestations associated with SARS-CoV-2 infection were broad and heterogeneous, suggesting different underlying pathogenic processes.
Bussani R et al EClinical Medicine - The Lancet https://www.thelancet.com/journals/ebiom/article	Persistence of viral RNA, pneumocyte syncytia and thrombosis are hallmarks of advanced COVID-19 pathology	Sulla base delle autopsie eseguite su 41 persone decedute per COVID-19, si conclude che il danno polmonare associato alla malattia è costituito da danno alveolare diffuso e formazione di sincizi di pneumociti, microtrombosi	Background : COVID-19 is a deadly pulmonary disease with peculiar characteristics, which include variable clinical course and thrombophilia. A thorough understanding of the pathological correlates of the disease is still missing. Methods : Here we report the systematic analysis of 41 consecutive post-mortem samples from individuals who died of COVID-19. Histological analysis is complemented by immunohistochemistry for

/PIIS2352-3964(20)30480-1/fulltext		dei vasi polmonari, con presenza di RNA virale negli pneumociti ed endoteliociti.	cellular and viral antigens and the detection of viral genomes by in situ RNA hybridization. Findings : COVID-19 is characterized by extensive alveolar damage (41/41 of patients) and thrombosis of the lung micro- and macro-vasculature (29/41, 71%). Thrombi were in different stages of organization, consistent with their local origin. Pneumocytes and endothelial cells contained viral RNA even at the later stages of the disease. An additional feature was the common presence of a large number of dysmorphic pneumocytes, often forming syncytial elements (36/41, 87%). Despite occasional detection of virus-positive cells, no overt signs of viral infection were detected in other organs, which showed non-specific alterations. Interpretation : COVID-19 is a unique disease characterized by extensive lung thrombosis, long-term persistence of viral RNA in pneumocytes and endothelial cells, along with the presence of infected cell syncytia. Several of COVID-19 features might be consequent to the persistence of virus-infected cells for the duration of the disease.

			
Choi B et al NEJM https://www.nejm.org/doi/10.1056/NEJMc2031364	Persistence and Evolution of SARS-CoV-2 in an Immunocompromised Host	Caso clinico di un paziente immunocompromesso con infezione da SARS-CoV-2, andato incontro a persistenza dell'infezione (confermata da analisi filogenetica) per circa 4 mesi e deceduto per shock settico.	A 45-year-old man with severe antiphospholipid syndrome complicated by diffuse alveolar hemorrhage, who was receiving anticoagulation therapy, glucocorticoids, cyclophosphamide, and intermittent rituximab and eculizumab, was admitted to the hospital with fever (Fig. S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org). On day 0, Covid-19 was diagnosed by SARS-CoV-2 reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assay of a nasopharyngeal swab specimen, and the patient received a 5-day course of remdesivir (Fig. S2). Glucocorticoid doses were increased because of

			suspected diffuse alveolar hemorrhage. He was discharged on day 5 without a need for supplemental oxygen.
Zietz M et al Nature https://www.nature.com/articles/s41467-020-19623-x	Associations between blood type and COVID-19 infection, intubation, and death	Studio osservazionale condotto a New York che evidenzia l'associazione fra gruppo sanguigno e rischio di infezione/outcome di infezione da SARS-CoV-2 : come già proposto in altri lavori, i gruppi sanguigni si distinguono e in particolare il gruppo 0 ha una prevalenza di infezione lievemente minore rispetto agli altri gruppi, l'intubazione è più frequente nei gruppi AB, B, 0 e A in questo ordine e infine il gruppo AB è associato a maggiore mortalità.	The rapid global spread of the novel coronavirus SARS-CoV-2 has strained healthcare and testing resources, making the identification and prioritization of individuals most at-risk a critical challenge. Recent evidence suggests blood type may affect risk of severe COVID-19. Here, we use observational healthcare data on 14,112 individuals tested for SARS-CoV-2 with known blood type in the New York Presbyterian (NYP) hospital system to assess the association between ABO and Rh blood types and infection, intubation, and death. We find slightly increased infection prevalence among non-O types. Risk of intubation was decreased among A and increased among AB and B types, compared with type O, while risk of death was increased for type AB and decreased for types A and B. We estimate Rh-negative blood type to have a protective effect for all three outcomes. Our results add to the growing body of evidence suggesting blood type may play a role in COVID-19. **Fig. 1: Estimated risk differences for blood types during the period from March 10 to August 1, 2020.** 

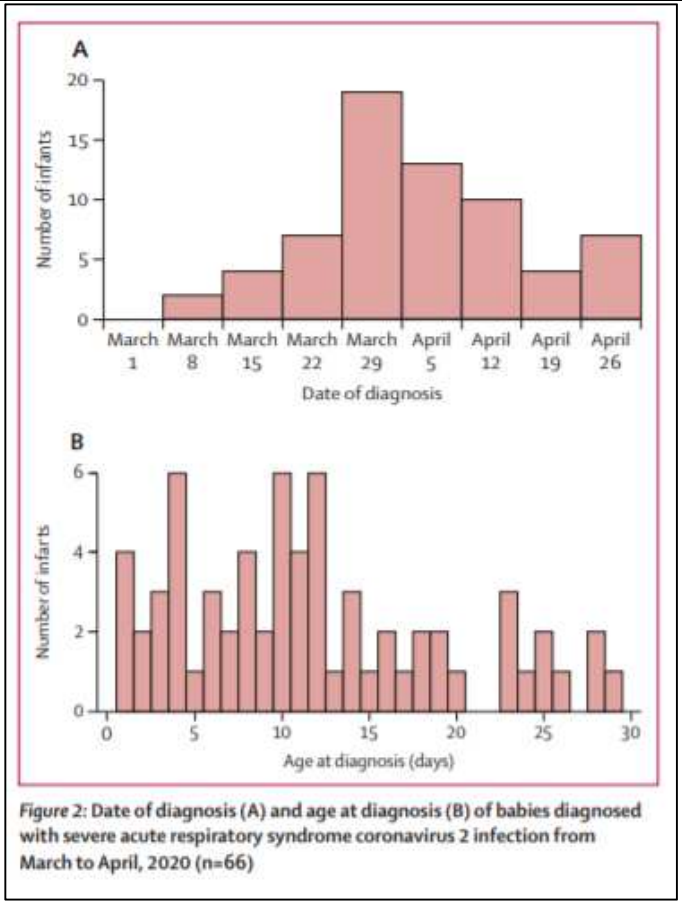
Tao J et al Sexually Transmitted Diseases https://doi.org/10.1097/OLQ.0000000000001306	Impact of the COVID-19 pandemic on sexually transmitted infection clinic visits.	Una riduzione nel ricorso alle cure mediche, già osservata in altri settori, si è verificata anche per le malattie sessualmente trasmesse : ecco una conseguenza della pandemia da affrontare per evitare danni collaterali.	Coronavirus disease (COVID-19) is responsible for a global pandemic and has impacted health care accessibility and delivery. Clinic data was reviewed for a sexually transmitted infection (STI) clinic from September, 2019 to May, 2020. A significant decrease in rates of STIs visits and treatments during the COVID-19 pandemic was observed.
Apolone G et al Tumori Journal https://journals.sagepub.com/doi/10.1177/0300891620974755?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub++0pubmed&	Unexpected detection of SARS-CoV-2 antibodies in the prepandemic period in Italy	Analizzando retrospettivamente i campioni ematici di 959 persone asintomatiche arruolate in uno screening del tumore del polmone in Italia a partire da Settembre 2019, gli Autori di questo studio hanno rinvenuto anticorpi anti-SARS-CoV-2 in 111 casi (11.6%) : il virus circolava già nel nostro Paese, inosservato.	There are no robust data on the real onset of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and spread in the prepandemic period worldwide. We investigated the presence of SARS-CoV-2 receptor-binding domain (RBD)–specific antibodies in blood samples of 959 asymptomatic individuals enrolled in a prospective lung cancer screening trial between September 2019 and March 2020 to track the date of onset, frequency, and temporal and geographic variations across the Italian regions. SARS-CoV-2 RBD-specific antibodies were detected in 111 of 959 (11.6%) individuals, starting from September 2019 (14%), with a cluster of positive cases (>30%) in the second week of February 2020 and the highest number (53.2%) in Lombardy. This study shows an unexpected very early circulation of SARS-CoV-2 among asymptomatic individuals in Italy several months before the first patient was identified, and clarifies the onset and spread of the coronavirus disease 2019 (COVID-19) pandemic. Finding SARS-CoV-2 antibodies in asymptomatic people before the COVID-19 outbreak in Italy may reshape the history of pandemic.

			 **Figure 1.** Frequency of immunoglobulin M (red columns) and immunoglobulin G (blue columns) receptor-binding domain (RBD)–positive cases in respect to the total number of screening participants (green columns) throughout the 24 weeks from September 2019 to February 2020.
Krsak M et al Viral Immunology https://doi.org/10.1089/vim.2020.0246	COVID-19: Way Forward With Serosurveillance Without Overemphasizing Neutralizing Antibodies.	Gli Autori di questa lettera propongono l'utilizzo della sierologia per SARS-CoV-2 – senza approfondimento alla ricerca di anticorpi neutralizzanti – accompagnata alla risoluzione dei sintomi come indice di guarigione e non contagiosità (per un determinato periodo di tempo da definire), che consentirebbe di rimuovere più agevolmente l'indicazione all'isolamento senza ricorrere ai tamponi molecolari.	Serosurveillance of coronavirus disease 2019 (COVID-19) is lagging due to concerns regarding testing performance and interpretation of what represents protective immunity. The scientific community has pointed out concerns related to suboptimal performance of certain tests, although a selection of tests with sensitivity and specificity of >99% is available. Neutralizing antibodies represent a generally accepted surrogate marker of immunological protection against viral infections. In COVID-19, we argue that focusing only on neutralizing antibodies may not be necessary and that evidence of spontaneous clearance of COVID-19 may be a reliable surrogate marker of individuals' immune competency toward future reinfections (regardless of its mechanism) for a period of time. Furthermore, current polymerase chain reaction testing lacks the ability to determine the duration of transmissibility, thus alternatives for direct testing of replicating virus are needed. Broadly applied viable virus testing together with serosurveillance will help reopen the economy with more precision and speed, and help guide isolation, quarantine, and cohorting protocols in

			conglomerate settings such as correctional facilities, nursing facilities, schools, and long-distance travel.
Von Cube M et al Critical Care Med https://journals.lww.com/ccmjournal/Abstract/9000/Harmonizing_Heterogeneous_Endpoints_in_Coronavirus.95443.aspx	Harmonizing Heterogeneous Endpoints in Coronavirus Disease 2019 Trials Without Loss of Information	Un articolo di metodo che propone di omogeneizzare la presentazione dei risultati dei trial clinici riguardanti COVID-19: utile includere uno stacked probability plot che riporti in modo chiaro l'effetto dei trattamenti in esame su pochi outcome fondamentali (dimissione, ventilazione meccanica, morte) su tempo di ospedalizzazione.	OBJECTIVES: Many trials investigate potential effects of treatments for coronavirus disease 2019. To provide sufficient information for all involved decision-makers (clinicians, public health authorities, and drug regulatory agencies), a multiplicity of endpoints must be considered. The objectives are to provide hands-on statistical guidelines for harmonizing heterogeneous endpoints in coronavirus disease 2019 clinical trials. DESIGN: Randomized controlled trials for patients infected with coronavirus disease 2019. SETTING: General methods that apply to any randomized controlled trial for patients infected with coronavirus disease 2019. PATIENTS: Coronavirus disease 2019 positive individuals. INTERVENTIONS: None. MEASUREMENTS AND MAIN RESULTS: We develop a multistate model that is based on hospitalization, mechanical ventilation, death, and discharge. These events are both categories of the ordinal endpoint recommended by the World Health Organization and also within the core outcome set of the Core Outcome Measures in Effectiveness Trials initiative for coronavirus disease 2019 trials. To support our choice of states in the multistate model, we also perform a brief review of registered coronavirus disease 2019 clinical trials. Based on the multistate model, we give recommendation for compact, informative illustration of time-dynamic treatment effects and explorative statistical analysis. A majority of coronavirus disease 2019 clinical trials collect information on mechanical ventilation, hospitalization, and death.

			Using reconstructed and real data of coronavirus disease 2019 trials, we show how a stacked probability plot provides a detailed understanding of treatment effects on the patients' course of hospital stay. It contributes to harmonizing multiple endpoints and differing lengths of follow-up both within and between trials. Conclusions: All ongoing clinical trials should include a stacked probability plot in their statistical analysis plan as descriptive analysis. While primary analysis should be on an early endpoint with appropriate capability to be a surrogate (parameter), our multistate model provides additional detailed descriptive information and links results within and between coronavirus disease 2019 trials.
Gale C et al The Lancet https://doi.org/10.1016/S2352-4642(20)30342-4	Characteristics and outcomes of neonatal SARS-CoV-2 infection in the UK: a prospective national cohort study using active surveillance.	Studio di coorte prospettico condotto nel Regno unito che descrive le caratteristiche di 66 neonati (< 28 giorni di vita) con infezione da SARS-COV-2.	BACKGROUND: Babies differ from older children with regard to their exposure to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). However, data describing the effect of SARS-CoV-2 in this group are scarce, and guidance is variable. We aimed to describe the incidence, characteristics, transmission, and outcomes of SARS-CoV-2 infection in neonates who received inpatient hospital care in the UK. METHODS: We carried out a prospective UK population-based cohort study of babies with confirmed SARS-CoV-2 infection in the first 28 days of life who received inpatient care between March 1 and April 30, 2020. Infected babies were identified through active national surveillance via the British Paediatric Surveillance Unit, with linkage to national testing, paediatric intensive care audit, and obstetric surveillance data. Outcomes included incidence (per 10 000 livebirths) of confirmed SARS-CoV-2 infection and severe disease, proportions of babies with suspected vertically and nosocomially acquired infection, and clinical outcomes. FINDINGS: We identified 66 babies with confirmed SARS-CoV-2 infection (incidence 5.6 [95% CI 4.3-7.1] per 10 000 livebirths), of whom 28 (42%) had severe neonatal SARS-

			CoV-2 infection (incidence 2.4 [1.6-3.4] per 10 000 livebirths). 16 (24%) of these babies were born preterm. 36 (55%) babies were from white ethnic groups (SARS-CoV-2 infection incidence 4.6 [3.2-6.4] per 10 000 livebirths), 14 (21%) were from Asian ethnic groups (15.2 [8.3-25.5] per 10 000 livebirths), eight (12%) were from Black ethnic groups (18.0 [7.8-35.5] per 10 000 livebirths), and seven (11%) were from mixed or other ethnic groups (5.6 [2.2-11.5] per 10 000 livebirths). 17 (26%) babies with confirmed infection were born to mothers with known perinatal SARS-CoV-2 infection, two (3%) were considered to have possible vertically acquired infection (SARS-CoV-2-positive sample within 12 h of birth where the mother was also positive). Eight (12%) babies had suspected nosocomially acquired infection. As of July 28, 2020, 58 (88%) babies had been discharged home, seven (11%) were still admitted, and one (2%) had died of a cause unrelated to SARS-CoV-2 infection. INTERPRETATION: Neonatal SARS-CoV-2 infection is uncommon in babies admitted to hospital. Infection with neonatal admission following birth to a mother with perinatal SARS-CoV-2 infection was unlikely, and possible vertical transmission rare, supporting international guidance to avoid separation of mother and baby. The high proportion of babies from Black, Asian, or minority ethnic groups requires investigation. FUNDING: UK National Institute for Health Research Policy Research Programme.

			 *Figure 2*: Date of diagnosis (A) and age at diagnosis (B) of babies diagnosed with severe acute respiratory syndrome coronavirus 2 infection from March to April, 2020 (n=66)
Kasper MR et al NEJM https://doi.org/10.1056/NEJMoa2019375	An Outbreak of Covid-19 on an Aircraft Carrier.	Descrizione di un focolaio di infezione da SARS-CoV-2 a bordo di una portaerei dell'esercito americano, con 1271/4779 membri dell'equipaggio contagiati e il 50% circa di questi asintomatico per tutto il corso dell'infezione.	BACKGROUND: An outbreak of coronavirus disease 2019 (Covid-19) occurred on the U.S.S. Theodore Roosevelt, a nuclear-powered aircraft carrier with a crew of 4779 personnel. METHODS: We obtained clinical and demographic data for all crew members, including results of testing by real-time reverse-transcriptase polymerase chain reaction (rRT-PCR). All crew members were followed up for a minimum of 10 weeks, regardless of test results or the absence of symptoms. RESULTS: The crew was predominantly

			young (mean age, 27 years) and was in general good health, meeting U.S. Navy standards for sea duty. Over the course of the outbreak, 1271 crew members (26.6% of the crew) tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection by rRT-PCR testing, and more than 1000 infections were identified within 5 weeks after the first laboratory-confirmed infection. An additional 60 crew members had suspected Covid-19 (i.e., illness that met Council of State and Territorial Epidemiologists clinical criteria for Covid-19 without a positive test result). Among the crew members with laboratory-confirmed infection, 76.9% (978 of 1271) had no symptoms at the time that they tested positive and 55.0% had symptoms develop at any time during the clinical course. Among the 1331 crew members with suspected or confirmed Covid-19, 23 (1.7%) were hospitalized, 4 (0.3%) received intensive care, and 1 died. Crew members who worked in confined spaces appeared more likely to become infected. CONCLUSIONS: SARS-CoV-2 spread quickly among the crew of the U.S.S. Theodore Roosevelt. Transmission was facilitated by close-quarters conditions and by asymptomatic and presymptomatic infected crew members. Nearly half of those who tested positive for the virus never had symptoms.