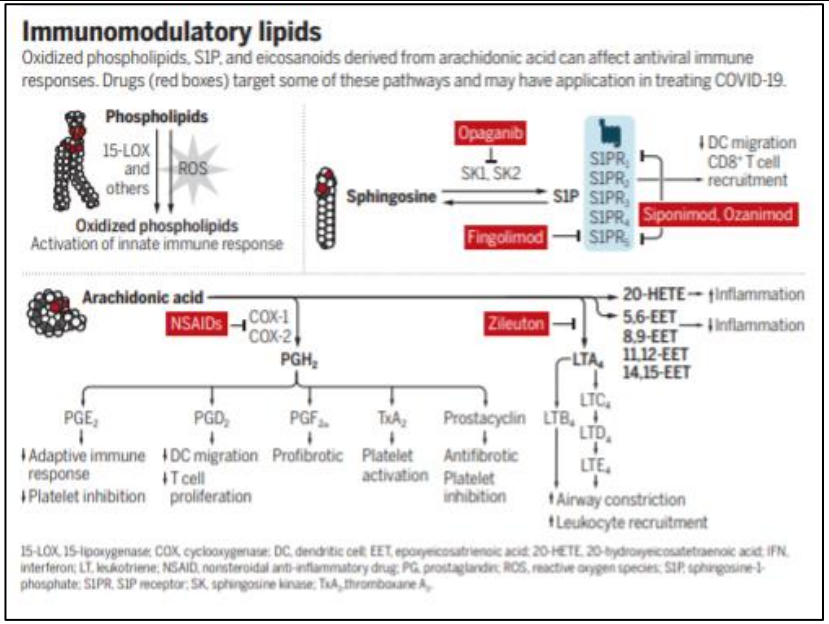
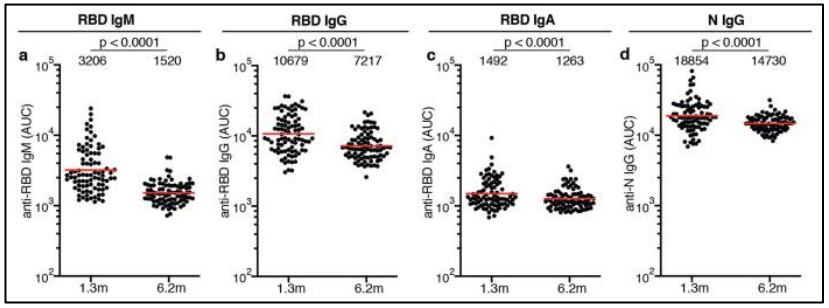
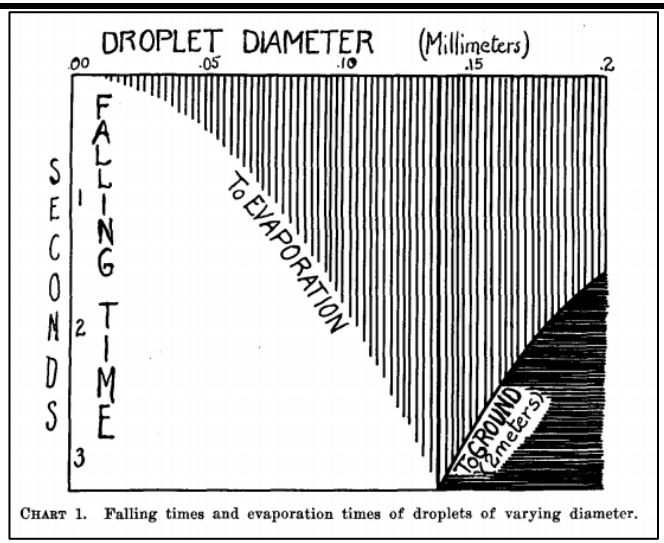
RICERCA BIBLIOGRAFICA COVID 19 SETTIMANA 18 - 24.01.2021 FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE DOTT.SSA ELEONORA TADDEI			
AUTORE/RIVISTA	**TITOLO**	**OUTCOME PRINCIPALE**	**ABSTRACT**
Theken KN et al Science https://science.sciencemag.org/content/371/6526/237	Bioactive lipids in antiviral immunity	Ruolo dei lipidi – in particolare gli eicosanoidi - e possibili target terapeutici per il trattamento dell'infezione da SARS-CoV-2.	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has brought focus to attempts to limit viral replication and manage the immunological response to infection. Lipids modulate host receptor binding, facilitate viral fusion, and fuel viral replication; thus, modulation of viral-host lipid interactions may have therapeutic utility (1). Indeed, the spike (S) glycoprotein on the surface of SARS-CoV-2 tightly binds the free fatty acid linoleic acid, stabilizing it and reducing its interaction with the host angiotensin-converting enzyme 2 (ACE2) receptor that facilitates viral cell entry (2). However, in the case of many viral infections, including COVID-19, it is the overexuberant host immune response that results in life-threatening consequences of infection. Therefore, therapies that modulate bioactive lipids that regulate the host immune response to respiratory viral infections may be beneficial.

			
Gaebler C et al Nature https://www.nature.com/articles/s41586-021-03207-w	Evolution of antibody immunity to SARS-CoV-2	Studio di coorte su 87 persone con storia di infezione da SARS-CoV-2 che dimostra la persistenza di cellule B della memoria fino a 6 mesi di distanza dall'infezione. Nelle biopsie intestinali di alcuni pazienti persistono antigeni virali, forse alla base della maturazione della risposta anticorpale nei centri germinativi e del mantenimento dei livelli di	Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has infected 78 million individuals and is responsible for over 1.7 million deaths to date. Infection is associated with development of variable levels of antibodies with neutralizing activity that can protect against infection in animal models. Antibody levels decrease with time, but the nature and quality of the memory B cells that would be called upon to produce antibodies upon re-infection has not been examined. Here we report on the humoral memory response in a cohort of 87 individuals assessed at 1.3 and 6.2 months after infection. We find that IgM, and IgG anti-SARS-CoV-2 spike protein receptor binding domain (RBD) antibody titres decrease significantly with IgA being less affected. Concurrently, neutralizing activity in plasma decreases by fivefold in pseudotype virus assays. In contrast, the number of RBD-specific memory B cells is unchanged. Memory

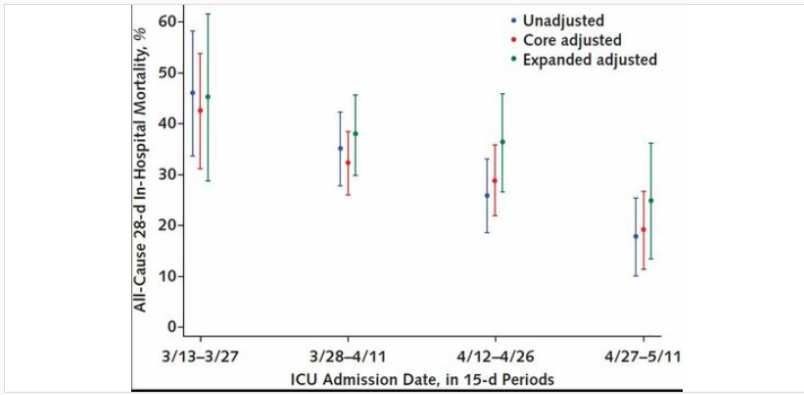
		IgA, pure osservato in questo lavoro.	B cells display clonal turnover after 6.2 months, and the antibodies they express have greater somatic hypermutation, increased potency and resistance to RBD mutations, indicative of continued evolution of the humoral response. Analysis of intestinal biopsies obtained from asymptomatic individuals 4 months after the onset of coronavirus disease-2019 (COVID-19), using immunofluorescence, or polymerase chain reaction, revealed persistence of SARS-CoV-2 nucleic acids and immunoreactivity in the small bowel of 7 out of 14 volunteers. We conclude that the memory B cell response to SARS-CoV-2 evolves between 1.3 and 6.2 months after infection in a manner that is consistent with antigen persistence. 
Samet JM et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab039/6103221	Airborne Transmission of SARS-CoV-2: What We Know	Quattro domande sulla trasmissione di SARS-CoV-2, con un richiamo ai fondamentali studi di Wells, 1934 (https://academic.oup.com/aje/article-abstract/20/3/611/280025?redirectedFrom=fulltext)	We examine airborne transmission of SARS-CoV-2 potential using a source-to-dose framework beginning with generation of virus-containing droplets and aerosols and ending with virus deposition in the respiratory tract of susceptible individuals. By addressing four critical questions, we identify both gaps in addressing four critical questions with answers having policy implications.

			 CHART 1. Falling times and evaporation times of droplets of varying diameter.
Servick K Science https://science.sciencemag.org/content/371/6526/224	COVID-19 measures also suppress flu—for now	La diffusione dell'influenza nell'emisfero boreale si mantiene a livelli « inter-stagionali », probabilmente per effetto delle misure di contenimento di SARS-CoV-2. Questo fatto non è completamente positivo: sarà più difficile selezionare i ceppi per il vaccino dell'anno prossimo, che d'altra parte è fondamentale dato che una maggiore proporzione di popolazione sarà suscettibile dopo questa stagione anomala.	Influenza forecasters are a cautious bunch. Flu cases can spike in late winter after months of low infection rates, making experts reluctant to predict a mild season too soon. But many are ready to declare that COVID-19 control measures have dramatically tamped down the flu and other respiratory viruses that would normally be ripping through the Northern Hemisphere.

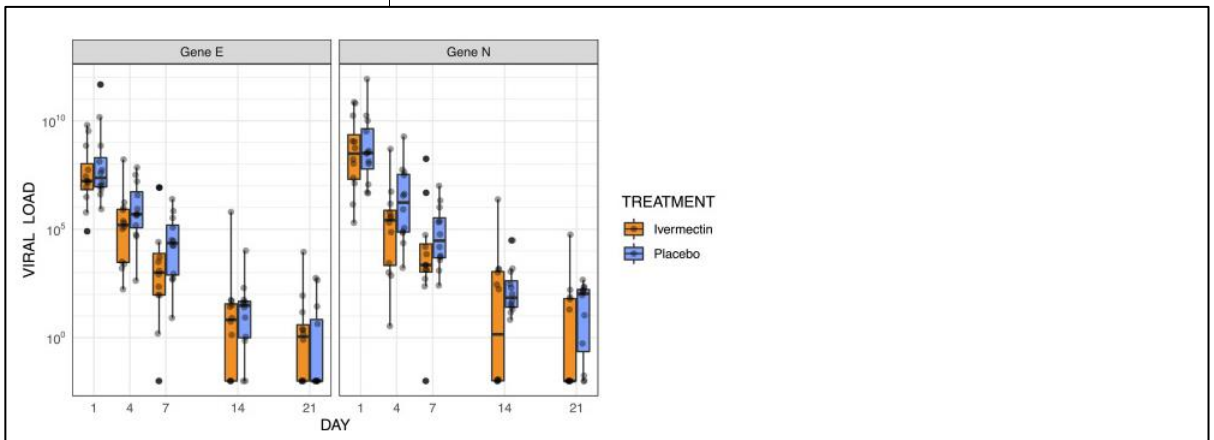
Sax PE NEJM https://www.nejm.org/covid-vaccine	Covid-19 Vaccine Resource Center	Risposte ad alcune domande sui vaccini contro SARS-CoV-2, con riferimento a quelli approvati negli USA, dall'infettivologo Paul Sax della Harvard Medical School.	Paul Sax, M.D., a Professor of Medicine at Harvard Medical School and an infectious disease specialist, provides concise and engaging answers to clinicians' questions about Covid-19 vaccination and to the questions and concerns patients will raise.
Wang H et al Emerging Infectious Diseases https://wwwnc.cdc.gov/eid/article/27/1/20-3379_article	Performance of Nucleic Acid Amplification Tests for Detection of Severe Acute Respiratory Syndrome Coronavirus 2 in Prospectively Pooled Specimens	Il pooling dei campioni testati per SARS-CoV-2 può essere utile per risparmiare risorse, in particolare nello screening : si unisce un certo numero di campioni, ciascuno dei quali risulterà diluito nel pool finale, e solo in caso di positività del pool si ritestano i singoli componenti per trovare il positivo. In questo studio su 1648 campioni sottoposti a pooling si osserva come il numero di positivi, la carica virale e la sensibilità del test utilizzato influenzino la concordanza fra risultato del pool e dei singoli test.	Pooled nucleic acid amplification tests for severe acute respiratory syndrome coronavirus 2 could increase availability of testing at decreased cost. However, the effect of dilution on analytical sensitivity through sample pooling has not been well characterized. We tested 1,648 prospectively pooled specimens by using 3 nucleic acid amplification tests for severe acute respiratory syndrome coronavirus 2: a laboratory-developed real-time reverse transcription PCR targeting the envelope gene, and 2 commercially available Panther System assays targeting open reading frame 1ab. Positive percent agreement (PPA) of pooled versus individual testing ranged from 71.7% to 82.6% for pools of 8 and from 82.9% to 100.0% for pools of 4. We developed and validated an independent stochastic simulation model to estimate effects of dilution on PPA and efficiency of a 2-stage pooled real-time reverse transcription PCR testing algorithm. PPA was dependent on the proportion of tests with positive results, cycle threshold distribution, and assay limit of detection.

Vasques Nonaka CK et al Preprint - not peer reviewed preprints202101.0132.v1.pdf	Genomic evidence of a SARS-CoV-2 reinfection case with E484K spike mutation in Brazil	Caso di reinfezione da parte di SARS-CoV-2 del ceppo « brasiliano » B.1.1.248, portatore della mutazione E484K già associata a escape da siero immune e ridotta affinità con anticorpi neutralizzanti.	To date, uncertainty remains about how long the protective immune responses against SARSCoV-2 persists and the first reports of suspected reinfection began to be described in recovered patients months after the first episode. Viral evolution may favor reinfections, and the recently described spike mutations, particularly in the receptor binding domain (RBD) in SARS-CoV2 lineages circulating in the UK, South Africa, and most recently in Brazil, have raised concern on their potential impact in infectivity and immune escape. We report the first case of reinfection from genetically distinct SARS-CoV-2 lineage presenting the E484K spike mutation in Brazil, a variant associated with escape from neutralizing antibodies.
Anesi GL et al Annals of Internal Medicine https://www.acpjournals.org/doi/10.7326/M20-5327	Characteristics, Outcomes, and Trends of Patients With COVID-19–Related Critical Illness at a Learning Health System in the United States	Studio di coorte retrospettivo su 468 pazienti critici ricoverati con COVID-19 (68.2% ventilati, 25.9% trattati con vasopressori) tra marzo e maggio 2020: si osserva una riduzione della mortalità tra i primi e gli ultimi 15 giorni del periodo studiato, a fronte di caratteristiche di base invariate.	Background: The coronavirus disease 2019 (COVID-19) pandemic continues to surge in the United States and globally. Objective: To describe the epidemiology of COVID-19–related critical illness, including trends in outcomes and care delivery. Design: Single–health system, multihospital retrospective cohort study. Setting: 5 hospitals within the University of Pennsylvania Health System. Patients: Adults with COVID-19–related critical illness who were admitted to an intensive care unit (ICU) with acute respiratory failure or shock during the initial surge of the pandemic. Measurements: The primary exposure for outcomes and care delivery trend analyses was longitudinal time during the pandemic. The primary outcome was all-cause 28-day in-hospital mortality. Secondary outcomes were all-cause death at any time, receipt of mechanical ventilation (MV), and readmissions. Results: Among 468 patients with COVID-19–related critical illness, 319 (68.2%) were treated with MV and 121 (25.9%) with

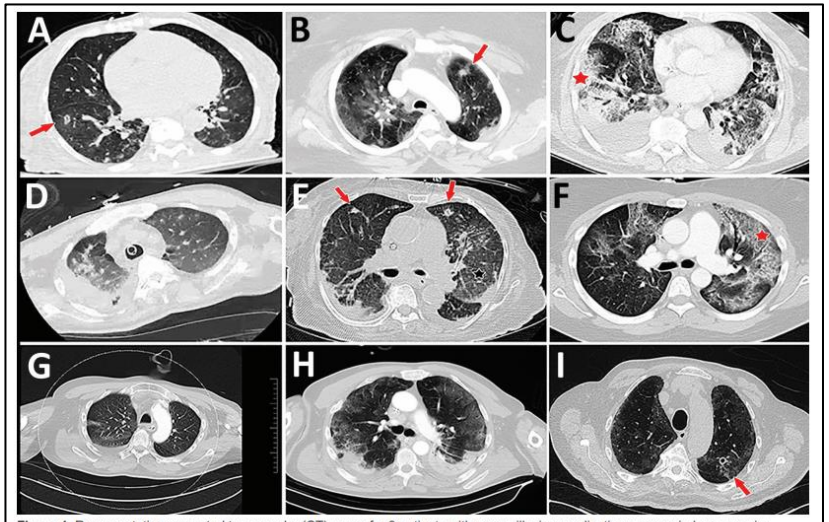
			vasopressors. Outcomes were notable for an all-cause 28-day in-hospital mortality rate of 29.9%, a median ICU stay of 8 days (interquartile range [IQR], 3 to 17 days), a median hospital stay of 13 days (IQR, 7 to 25 days), and an all-cause 30-day readmission rate (among nonhospice survivors) of 10.8%. Mortality decreased over time, from 43.5% (95% CI, 31.3% to 53.8%) to 19.2% (CI, 11.6% to 26.7%) between the first and last 15-day periods in the core adjusted model, whereas patient acuity and other factors did not change. Limitation: Single–health system study; use of, or highly dynamic trends in, other clinical interventions were not evaluated, nor were complications. Conclusion: Among patients with COVID-19–related critical illness admitted to ICUs of a learning health system in the United States, mortality seemed to decrease over time despite stable patient characteristics. Further studies are necessary to confirm this result and to investigate causal mechanisms.

			 Figure 1. All-cause 28-day in-hospital mortality over time. All-cause 28-day in-hospital mortality decreased over ICU admission dates in 15-day periods in the unadjusted (observed), core adjusted, and expanded adjusted models. The core adjusted model includes age, Charlson Comorbidity Index score, SOFA score, and hospital; the expanded adjusted model also includes body mass index, Glasgow Coma Score, oxygen saturation, respiratory rate, platelet count, and Pao2–FIo2 ratio. ICU = intensive care unit; SOFA = Sequential Organ Failure Assessment.
Chaccour C et al EClinicalMedicine https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30464-8/fulltext	The effect of early treatment with ivermectin on viral load, symptoms and humoral response in patients with non-severe COVID-19: A pilot, double-blind, placebo-controlled, randomized clinical trial	Trial pilota sulla terapia con una singola dose di ivermectina in 12 pazienti con COVID-19 lieve, contro 12 trattati con placebo : si osserva un apparente effetto di precoce scomparsa dei sintomi e una tendenza alla minore carica virale (non statisticamente significativa) al tampone di controllo dopo 7 giorni nei trattati. Poiché l'ivermectina è attiva in vitro contro la replicazione di SARS-CoV-2, gli autori suggeriscono ulteriori studi.	Background : Ivermectin inhibits the replication of SARS-CoV-2 in vitro at concentrations not readily achievable with currently approved doses. There is limited evidence to support its clinical use in COVID-19 patients. We conducted a Pilot, randomized, double-blind, placebo-controlled trial to evaluate the efficacy of a single dose of ivermectin reduce the transmission of SARS-CoV-2 when administered early after disease onset. Methods : Consecutive patients with non-severe COVID-19 and no risk factors for complicated disease attending the emergency room of the Clínica Universidad de Navarra between July 31, 2020 and September 11, 2020 were enrolled. All enrollments occurred within 72 h of onset of fever or cough. Patients were randomized 1:1 to receive ivermectin, 400 mcg/kg, single dose (n = 12) or placebo (n = 12). The primary outcome measure was the proportion of patients with detectable SARS-CoV-2 RNA by PCR from nasopharyngeal swab at day 7 post-treatment. The primary outcome was supported by

			determination of the viral load and infectivity of each sample. The differences between ivermectin and placebo were calculated using Fisher's exact test and presented as a relative risk ratio. This study is registered at ClinicalTrials.gov: NCT04390022. Findings : All patients recruited completed the trial (median age, 26 [IQR 19–36 in the ivermectin and 21–44 in the controls] years; 12 [50%] women; 100% had symptoms at recruitment, 70% reported headache, 62% reported fever, 50% reported general malaise and 25% reported cough). At day 7, there was no difference in the proportion of PCR positive patients (RR 0·92, 95% CI: 0·77–1·09, p = 1·0). The ivermectin group had non-statistically significant lower viral loads at day 4 (p = 0·24 for gene E; p = 0·18 for gene N) and day 7 (p = 0·16 for gene E; p = 0·18 for gene N) post treatment as well as lower IgG titers at day 21 post treatment (p = 0·24). Patients in the ivermectin group recovered earlier from hyposmia/anosmia (76 vs 158 patient-days; p < 0.001). Interpretation : Among patients with non-severe COVID-19 and no risk factors for severe disease receiving a single 400 mcg/kg dose of ivermectin within 72 h of fever or cough onset there was no difference in the proportion of PCR positives. There was however a marked reduction of self-reported anosmia/hyposmia, a reduction of cough and a tendency to lower viral loads and lower IgG titers which warrants assessment in larger trials.

		 Fig. 2 Viral load evolution by study arm. Viral load values were log-transformed. The boxes show the interquartile range. Dots represent each individual value.	
Smit M et al Clinical Microbiology and Infection https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00040-9/fulltext	Prophylaxis for COVID-19: a systematic review	Revisione sistematica sulla profilassi pre- e post-esposizione contro COVID-19 : l'idrossiclorochina sembra aver ormai fallito nei trial clinici, rimangono da studiare eventuali nuove molecole.	Background : While the landscape of vaccine and treatment candidates against the novel coronavirus (COVID-19) has been reviewed systematically, prophylactic candidates remain unexplored. Objectives : Map pre- and post-exposure prophylactic (PrEP and PEP) candidate for COVID-19. Data sources : PubMed/Medline, Embase, International Committee of Medical Journal Editors and International Clinical Trials Registry Platform clinical trial registries and MedRxiv. Study eligibility criteria and Participants : All studies in humans or animals and randomized clinical trials (RCTs) in humans reporting primary data on prophylactic candidates against COVID-19, excluding studies focused on key populations. Interventions : PrEP and PEP candidate for COVID-19. Methods : Systematic review (SR) and qualitative synthesis of COVID-19 PrEP and PEP studies and RCTs complemented by search

			of MedRxiv and PubMed and Embase for studies reporting RCTs outcomes since SR search completion. Results : We identified 13 studies (out of 2,119 database records) and 117 RCTs (out of 5565 RCTs in the registries) meeting inclusion criteria. Non-RCT studies reported on cross-sectional studies using hydroxychloroquine (HCQ) in humans (n=2) or reported on animal studies (n=7) most of which used antibodies. All five completed RCTs focused on the use of HCQ as either PrEP or PEP and these and the cross-sectional studies reported no prophylactic effect. The majority of ongoing RCTs evaluated HCQ or other existing candidates including non-SARS-CoV-2 vaccines, anti(retro) virals, or use of vitamins and supplements. Conclusions : The key message from completed studies and RCTs seems to be that HCQ does not work, there is little evidence regarding other compounds with all RCTs using candidates other than HCQ still ongoing. It remains to be seen if the portfolio of existing molecules being evaluated in RCTs will identify successful prophylaxis against COVID-19 or if there is a need for the development of new candidates.
Marr KA et al Emerging Infectious Diseases https://wwwnc.cdc.gov/eid/article/27/1/20-2896_article	Aspergillosis Complicating Severe Coronavirus Disease	Venti casi di aspergillosi polmonare associata a COVID-19 (CAPA) e disamina della letteratura.	Aspergillosis complicating severe influenza infection has been increasingly detected worldwide. Recently, coronavirus disease–associated pulmonary aspergillosis (CAPA) has been detected through rapid reports, primarily from centers in Europe. We provide a case series of CAPA, adding 20 cases to the literature, with review of pathophysiology, diagnosis, and outcomes. The syndromes of pulmonary aspergillosis complicating severe viral infections are distinct from classic invasive aspergillosis, which is recognized most frequently in persons with neutropenia and in other immunocompromised persons. Combined with severe viral infection, aspergillosis comprises a constellation of airway-invasive

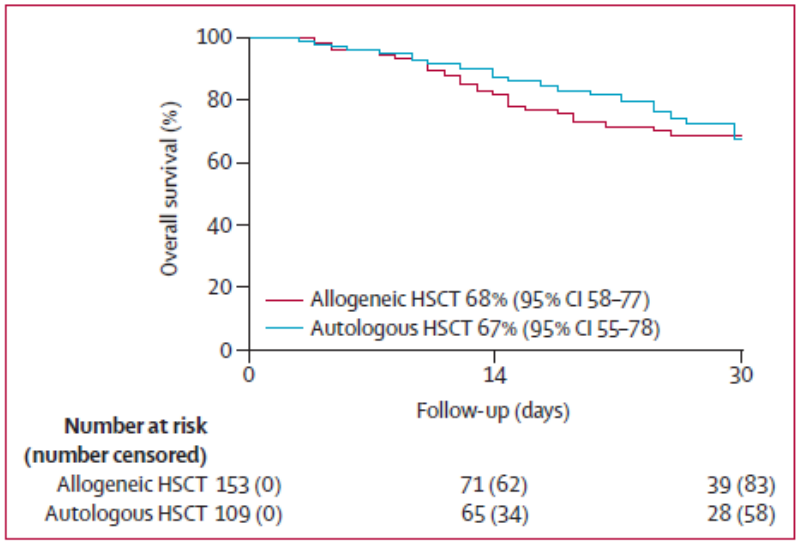
			and angio-invasive disease and results in risks associated with poor airway fungus clearance and killing, including virus- or inflammation-associated epithelial damage, systemic immunosuppression, and underlying lung disease. Radiologic abnormalities can vary, reflecting different pathologies. Prospective studies reporting poor outcomes in CAPA patients underscore the urgent need for strategies to improve diagnosis, prevention, and therapy.  **Figure 1.** Representative computed tomography (CT) scans for 9 patients with aspergillosis complicating severe viral pneumonia in patients with coronavirus disease. Scans were obtained at or around diagnosis of coronavirus disease–associated pulmonary aspergillosis in this series of patients, described in the Table (https://wwwnc.cdc.gov/EID/article/27/1/20-2896-T1.htm). Corresponding case-patients are indicated with lettered superscripts in the radiology column of Table 1. Examples of nodules and cavitating nodules are indicated by red arrows, and prominent airway thickening and bronchiectasis in ground glass opacities are indicated by red stars.
Li F et al The Lancet https://www.thelancet.com/journals/laninf/article/	Household transmission of SARS-CoV-2 and risk factors for susceptibility and infectivity in Wuhan: a retrospective observational study.	Studio retrospettivo su 57 581 contatti domestici di 29 578 casi di COVID-19 (sintomatici e asintomatici) segnalati a Wuhan tra dicembre 2019 e aprile	Background : Wuhan was the first epicentre of COVID-19 in the world, accounting for 80% of cases in China during the first wave. We aimed to assess household transmissibility of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and risk factors associated with infectivity and susceptibility to infection in Wuhan.

PIIS1473-3099(20)30981-6/fulltext		2020 : si stima un tasso d'attacco del 15%, con differente suscettibilità all'infezione nelle diverse classi di età ed evidenza di una minore contagiosità degli asintomatici rispetto ai sintomatici.	Methods : This retrospective cohort study included the households of all laboratory-confirmed or clinically confirmed COVID-19 cases and laboratory-confirmed asymptomatic SARS-CoV-2 infections identified by the Wuhan Center for Disease Control and Prevention between Dec 2, 2019, and April 18, 2020. We defined households as groups of family members and close relatives who did not necessarily live at the same address and considered households that shared common contacts as epidemiologically linked. We used a statistical transmission model to estimate household secondary attack rates and to quantify risk factors associated with infectivity and susceptibility to infection, accounting for individual-level exposure history. We assessed how intervention policies affected the household reproductive number, defined as the mean number of household contacts a case can infect. Findings : 27 101 households with 29 578 primary cases and 57 581 household contacts were identified. The secondary attack rate estimated with the transmission model was 15·6% (95% CI 15·2–16·0), assuming a mean incubation period of 5 days and a maximum infectious period of 22 days. Individuals aged 60 years or older were at a higher risk of infection with SARS-CoV-2 than all other age groups. Infants aged 0–1 years were significantly more likely to be infected than children aged 2–5 years (odds ratio [OR] 2·20, 95% CI 1·40–3·44) and children aged 6–12 years (1·53, 1·01–2·34). Given the same exposure time, children and adolescents younger than 20 years of age were more likely to infect others than were adults aged 60 years or older (1·58, 1·28–1·95). Asymptomatic individuals were much less likely to infect others than were symptomatic cases (0·21, 0·14–0·31). Symptomatic cases were more likely to infect others before symptom onset than after (1·42, 1·30–1·55). After mass isolation of cases, quarantine of household contacts, and restriction

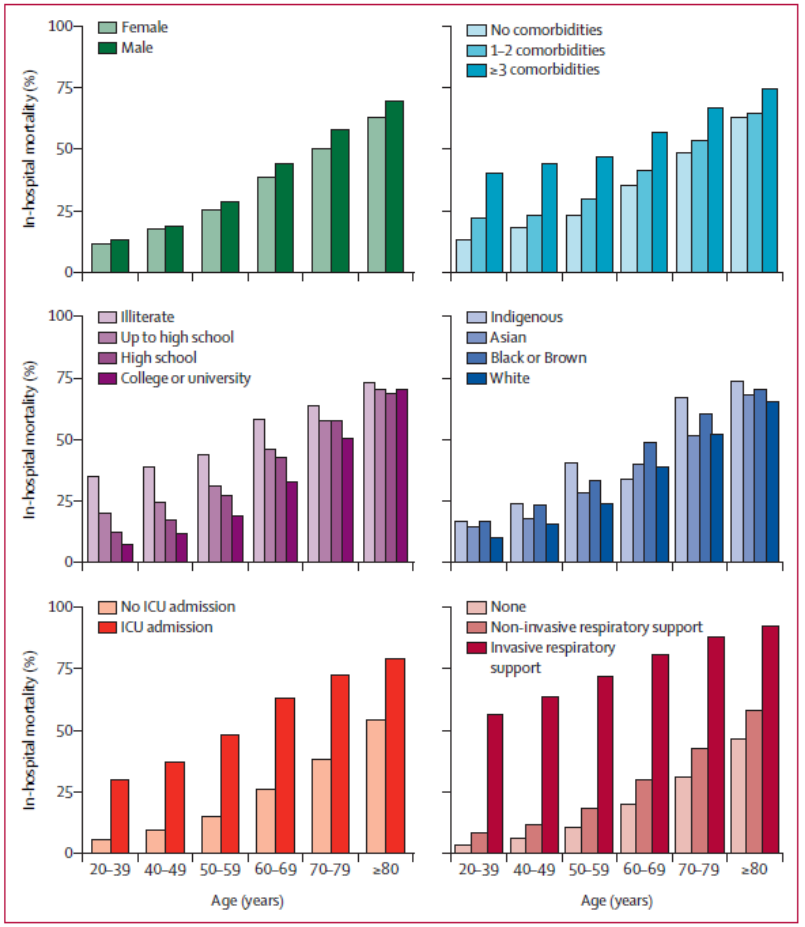
			of movement policies were implemented, household reproductive numbers declined by 52% among primary cases (from 0·25 [95% CI 0·24–0·26] to 0·12 [0·10–0·13]) and by 63% among secondary cases (from 0·17 [0·16–0·18] to 0·063 [0·057–0·070]). Interpretation : Within households, children and adolescents were less susceptible to SARS-CoV-2 infection but were more infectious than older individuals. Presymptomatic cases were more infectious and individuals with asymptomatic infection less infectious than symptomatic cases. These findings have implications for devising interventions for blocking household transmission of SARS-CoV-2, such as timely vaccination of eligible children once resources become available.
Mahase E BMJ https://www.bmj.com/content/372/bmj.n158	Covid-19: What new variants are emerging and how are they being investigated?	Domande e risposte sulle varianti conosciute di SARS-CoV-2 : in particolare, si ritiene che i vaccini approvati finora debbano continuare ad essere efficaci poiché la proteina spike è molto grande e singole mutazioni non dovrebbero compromettere l'immunità ottenuta.	The new, more transmissible variant of SARS-CoV-2 found in England is just one of many variations of the virus being detected around the world. Elisabeth Mahase looks at what we know so far
Connors M et al Annals of Internal Medicine	SARS-CoV-2 Vaccines: Much Accomplished, Much to Learn	Cosa sappiamo e cosa rimane da capire nell'ambito dei vaccini contro SARS-CoV-2 in una lettera di Anthony Fauci e collaboratori.	Over the next weeks and months, physicians will face questions regarding the science, safety, and efficacy of the first wave of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) vaccines to be authorized and distributed. In most cases these vaccine platforms will be new technologies that have not previously been administered other than through clinical trials. Although the initial data on efficacy and safety are extraordinarily encouraging, many questions remain regarding who should receive these vaccines and

https://www.acpjournals.org/doi/10.7326/M21-0111			the immediate, intermediate, and long-term impact of the vaccination program on the pandemic.
Sharma A et al The Lancet https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(20)30429-4/fulltext	Clinical characteristics and outcomes of COVID-19 in haematopoietic stem-cell transplantation recipients: an observational cohort study	Studio di coorte osservazionale su 318 persone sottoposte a trapianto di cellule staminali ematopoietiche che hanno contratto l'infezione da SARS-CoV-2 (intervallo mediano 17 mesi dal trapianto allogenico e 23 dal trapianto autologo) : sopravvivenza a 30 giorni del 68% per il trapianto allogenico e 67% per quello autologo, un dato che mette in luce la fragilità di questi pazienti.	Background : Haematopoietic stem-cell transplantation (HSCT) recipients are considered at high risk of poor outcomes after COVID-19 on the basis of their immunosuppressed status, but data from large studies in HSCT recipients are lacking. This study describes the characteristics and outcomes of HSCT recipients after developing COVID-19. Methods : In response to the pandemic, the Center for International Blood and Marrow Transplant Research (CIBMTR) implemented a special form for COVID-19-related data capture on March 27, 2020. All patients—irrespective of age, diagnosis, donor type, graft source, or conditioning regimens—were included in the analysis with data cutoff of Aug 12, 2020. The main outcome was overall survival 30 days after a COVID-19 diagnosis. Overall survival probabilities were calculated using Kaplan-Meier estimator. Factors associated with mortality after COVID-19 diagnosis were examined using Cox proportional hazard models. Findings : 318 HSCT recipients diagnosed with COVID-19 were reported to the CIBMTR. The median time from HSCT to COVID-19 diagnosis was 17 months (IQR 8–46) for allogeneic HSCT recipients and 23 months (8–51) for autologous HSCT recipients. The median follow-up of survivors was 21 days (IQR 8–41) for allogeneic HSCT recipients and 25 days (12–35) for autologous HSCT recipients. 34 (18%) of 184 allogeneic HSCT recipients were receiving immunosuppression within 6 months of COVID-19 diagnosis. Disease severity was mild in 155 (49%) of 318 patients, while severe disease requiring mechanical ventilation occurred in 45 (14%) of

			318 patients—ie, 28 (15%) of 184 allogeneic HSCT recipients and 17 (13%) of 134 autologous HSCT recipients. At 30 days after the diagnosis of COVID-19, overall survival was 68% (95% CI 58–77) for recipients of allogeneic HSCT and 67% (55–78) for recipients of autologous HSCT. Age 50 years or older (hazard ratio 2·53, 95% CI 1·16–5·52; p=0·020); male sex (3·53; 1·44–8·67; p=0·006), and development of COVID-19 within 12 months of transplantation (2·67, 1·33–5·36; p=0·005) were associated with a higher risk of mortality among allogeneic HSCT recipients, and a disease indication of lymphoma was associated with a higher risk of mortality compared with plasma cell disorder or myeloma (2·41, [1·08–5·38]; p=0·033) in autologous HSCT recipients. Interpretation : Recipients of autologous and allogeneic HSCT who develop COVID-19 have poor overall survival. These data emphasise the need for stringent surveillance and aggressive treatment measures in HSCT recipients who develop COVID-19.

			 ***Figure:*** **Overall survival after COVID-19 diagnosis**
Ranzani OT et al The Lancet https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30560-9/fulltext	Characterisation of the first 250 000 hospital admissions for COVID-19 in Brazil: a retrospective analysis of nationwide data	Analisi retrospettiva delle caratteristiche dei primi 250.000 pazienti adulti ricoverati per COVID-19 in Brasile.	Background : Most low-income and middle-income countries (LMICs) have little or no data integrated into a national surveillance system to identify characteristics or outcomes of COVID-19 hospital admissions and the impact of the COVID-19 pandemic on their national health systems. We aimed to analyse characteristics of patients admitted to hospital with COVID-19 in Brazil, and to examine the impact of COVID-19 on health-care resources and in-hospital mortality. Methods : We did a retrospective analysis of all patients aged 20 years or older with quantitative RT-PCR (RT-qPCR)-confirmed COVID-19 who were admitted to hospital and registered in SIVEP-Gripe, a nationwide surveillance database in Brazil, between Feb 16 and Aug 15, 2020 (epidemiological weeks 8–33). We also examined the progression of the COVID-19 pandemic across three 4-week periods within this timeframe (epidemiological weeks 8–12, 19–22,

			and 27–30). The primary outcome was in-hospital mortality. We compared the regional burden of hospital admissions stratified by age, intensive care unit (ICU) admission, and respiratory support. We analysed data from the whole country and its five regions: North, Northeast, Central-West, Southeast, and South. Findings : Between Feb 16 and Aug 15, 2020, 254 288 patients with RT-qPCR-confirmed COVID-19 were admitted to hospital and registered in SIVEP-Gripe. The mean age of patients was 60 (SD 17) years, 119 657 (47%) of 254 288 were aged younger than 60 years, 143 521 (56%) of 254 243 were male, and 14 979 (16%) of 90 829 had no comorbidities. Case numbers increased across the three 4-week periods studied: by epidemiological weeks 19–22, cases were concentrated in the North, Northeast, and Southeast; by weeks 27–30, cases had spread to the Central-West and South regions. 232 036 (91%) of 254 288 patients had a defined hospital outcome when the data were exported; in-hospital mortality was 38% (87 515 of 232 036 patients) overall, 59% (47 002 of 79 687) among patients admitted to the ICU, and 80% (36 046 of 45 205) among those who were mechanically ventilated. The overall burden of ICU admissions per ICU beds was more pronounced in the North, Southeast, and Northeast, than in the Central-West and South. In the Northeast, 1545 (16%) of 9960 patients received invasive mechanical ventilation outside the ICU compared with 431 (8%) of 5388 in the South. In-hospital mortality among patients younger than 60 years was 31% (4204 of 13 468) in the Northeast versus 15% (1694 of 11 196) in the South. Interpretation : We observed a widespread distribution of COVID-19 across all regions in Brazil, resulting in a high overall disease burden. In-hospital mortality was high, even in patients younger than 60 years, and worsened by existing regional disparities within the

			health system. The COVID-19 pandemic highlights the need to improve access to high-quality care for critically ill patients admitted to hospital with COVID-19, particularly in LMICs.  ***Figure 3:*** **In-hospital mortality stratified by age, sex, comorbidities, level of education, self-reported race, ICU admission, and invasive mechanical ventilation for patients with COVID-19 admitted to hospital in Brazil** Data are from patients with a defined hospital outcome; proportions of patients were calculated on the basis of complete case data for sex, comorbidities, level of education, self-reported race, ICU admission, and invasive ventilation variables. Data on race were collected as self-reported race or skin colour, classified as *Branco* (White), *Preto* (Black), *Pardo* (Brown), *Amarelo* (Asian), or *Indígena* (Indigenous). ICU=intensive care unit.

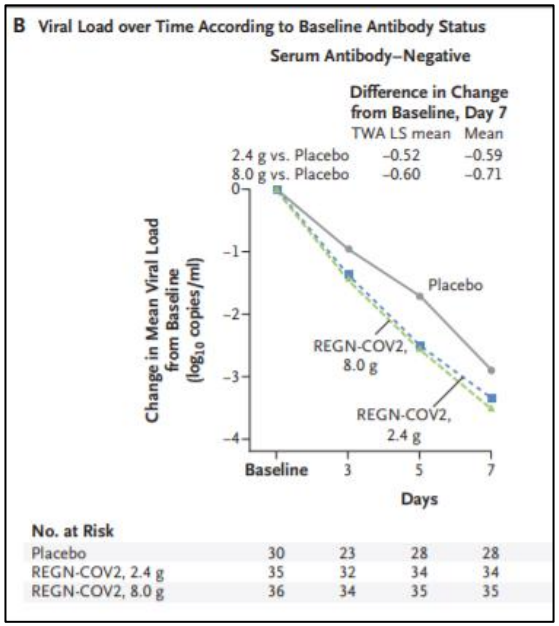
Goyal R et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab037/6104139?searchresult=1	Evaluation of SARS-CoV-2 transmission mitigation strategies on a university campus using an agent-based network model	Modello virtuale di mitigazione della diffusione di SARS-CoV-2 in una università, basato sulle caratteristiche della University of California San Diego.	Universities are faced with decisions on how to resume campus activities while mitigating SARS-CoV-2 risk. To provide guidance for these decisions, we developed an agent-based network model of SARS-CoV-2 transmission to assess the potential impact of strategies to reduce outbreaks. The model incorporates important features related to risk at the University of California San Diego. We found that structural interventions for housing (singles only) and instructional changes (from in-person to hybrid with class size caps) can substantially reduce R0, but masking and social distancing are required to reduce this to at or below 1. Within a risk mitigation scenario, increased frequency of asymptomatic testing from monthly to twice weekly has minimal impact on average outbreak size (1.1-1.9), but substantially reduces the maximum outbreak size and cumulative number of cases. We conclude that an interdependent approach incorporating risk mitigation, viral detection, and public health intervention is required to mitigate risk.
Schjorring OL et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2032510?query=featured_home	Lower or Higher Oxygenation Targets for Acute Hypoxemic Respiratory Failure	Trial clinico multicentrico che confronta l'effetto sulla sopravvivenza dell'utilizzo di diversi target di ossigenazione nel paziente critico con insufficienza respiratoria ipossica acuta : randomizzando 2928 pazienti fra i target di paO2 60 mmHg o 90 mmHg non si riesce a dimostrare una differenza di mortalità o di giorni senza supporto	BACKGROUND : Patients with acute hypoxemic respiratory failure in the intensive care unit (ICU) are treated with supplemental oxygen, but the benefits and harms of different oxygenation targets are unclear. We hypothesized that using a lower target for partial pressure of arterial oxygen (Pao2) would result in lower mortality than using a higher target. METHODS : In this multicenter trial, we randomly assigned 2928 adult patients who had recently been admitted to the ICU (≤12 hours before randomization) and who were receiving at least 10 liters of oxygen per minute in an open system or had a fraction of inspired oxygen of at least 0.50 in a closed system to receive oxygen therapy targeting a Pao2 of either 60 mm Hg (lower-oxygenation

		intensivo a 90 giorni.	group) or 90 mm Hg (higher-oxygenation group) for a maximum of 90 days. The primary outcome was death within 90 days. RESULTS : At 90 days, 618 of 1441 patients (42.9%) in the lower-oxygenation group and 613 of 1447 patients (42.4%) in the higher-oxygenation group had died (adjusted risk ratio, 1.02; 95% confidence interval, 0.94 to 1.11; P=0.64). At 90 days, there was no significant between-group difference in the percentage of days that patients were alive without life support or in the percentage of days they were alive after hospital discharge. The percentages of patients who had new episodes of shock, myocardial ischemia, ischemic stroke, or intestinal ischemia were similar in the two groups (P=0.24). CONCLUSIONS : Among adult patients with acute hypoxemic respiratory failure in the ICU, a lower oxygenation target did not result in lower mortality than a higher target at 90 days.

Table 2. Primary and Secondary Outcomes.

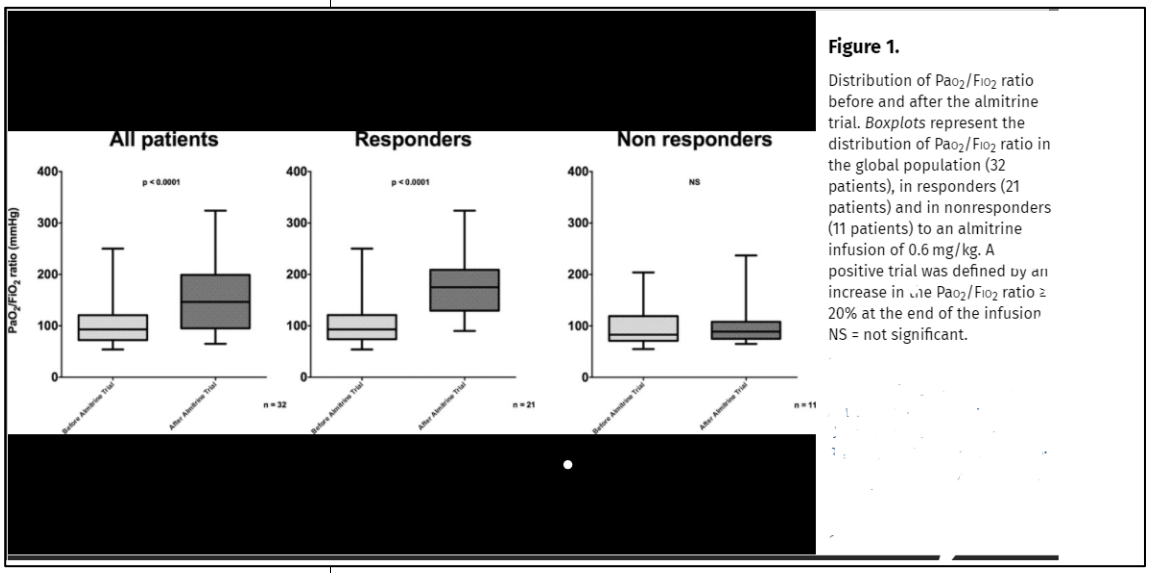
Outcome	Lower-Oxygenation Group	Higher-Oxygenation Group	Risk Ratio (95% CI)*	Risk Difference (95% CI)*	Adjusted Odds Ratio (95% CI)	P Value
Primary outcome†						
Death by day 90 — no./total no. (%)	618/1441 (42.9)	613/1447 (42.4)				
Adjusted for stratification variables‡			1.02 (0.94 to 1.11)	0.63 (−2.92 to 4.17)		0.64
Adjusted for stratification and baseline variables§					1.06 (0.90 to 1.24)	0.50
Secondary outcomes¶						
Median percentage of days alive without life support (IQR)	87.8 (0.0–96.7)	84.4 (0.0–96.0)				0.10
Median percentage of days alive after hospital discharge (IQR)	55.6 (0.0–85.6)	50.0 (0.0–84.4)				0.67
Serious adverse events — no./total no. (%)	525/1453 (36.1)	555/1457 (38.1)	0.95 (0.84 to 1.07)	−1.6 (−6.0 to 2.8)		0.24
Shock	492/1453 (33.9)	521/1457 (35.8)				
Myocardial ischemia	14/1453 (1.0)	8/1457 (0.5)				
Ischemic stroke	19/1453 (1.3)	23/1457 (1.6)				
Intestinal ischemia	32/1453 (2.2)	29/1457 (2.0)				

Weinreich DM et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2035002?query=featured_home	REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with Covid-19	Analisi ad interim dei risultati di un trial clinico su 275 pazienti con infezione da SARS-CoV-2, non ospedalizzati, trattati con un cocktail di due anticorpi monoclonali diretti contro la proteina spike a due diversi dosaggi o con placebo: riduzione della carica virale a 7 giorni dall'esordio nei trattati.	BACKGROUND : Recent data suggest that complications and death from coronavirus disease 2019 (Covid-19) may be related to high viral loads. METHODS : In this ongoing, double-blind, phase 1–3 trial involving nonhospitalized patients with Covid-19, we investigated two fully human, neutralizing monoclonal antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein, used in a combined cocktail (REGN-COV2) to reduce the risk of the emergence of treatment-resistant mutant virus. Patients were randomly assigned (1:1:1) to receive placebo, 2.4 g of REGN-COV2, or 8.0 g of REGN-COV2 and were prospectively characterized at baseline for endogenous immune response against SARS-CoV-2 (serum antibody–positive or serum antibody–negative). Key end points included the time-weighted average change in viral load from baseline (day 1) through day 7 and the percentage of patients with at least one Covid-19–related medically attended visit through day 29. Safety was assessed in all patients. RESULTS : Data from 275 patients are reported. The least-squares mean difference (combined REGN-COV2 dose groups vs. placebo group) in the time-weighted average change in viral load from day 1 through day 7 was −0.56 log10 copies per milliliter (95% confidence interval [CI], −1.02 to −0.11) among patients who were serum antibody–negative at baseline and −0.41 log10 copies per milliliter (95% CI, −0.71 to −0.10) in the overall trial population. In the overall trial population, 6% of the patients in the placebo group and 3% of the patients in the combined REGN-COV2 dose groups reported at least one medically attended visit; among patients who were serum antibody–negative at baseline, the corresponding percentages were 15% and 6% (difference, −9 percentage points; 95% CI, −29 to 11). The percentages of patients with hypersensitivity reactions,

			infusion-related reactions, and other adverse events were similar in the combined REGN-COV2 dose groups and the placebo group. CONCLUSIONS : In this interim analysis, the REGN-COV2 antibody cocktail reduced viral load, with a greater effect in patients whose immune response had not yet been initiated or who had a high viral load at baseline. Safety outcomes were similar in the combined REGN-COV2 dose groups and the placebo group. (Funded by Regeneron Pharmaceuticals and the Biomedical and Advanced Research and Development Authority of the Department of Health and Human Services; ClinicalTrials.gov number, NCT04425629. opens in new tab.) 
Klass P et al NEJM	Vaccinating Children against Covid-19 — The Lessons of Measles	Perché è importante ottenere dati sui vaccini contro SARS-CoV-2 nei bambini e quali sfide	Imagine a highly contagious virus circulating in the community. Many infected children have fever and some general misery but recover without incident. Rarely, devastating complications occur, leading to hospitalization, severe illness, and occasional deaths.

https://www.nejm.org/doi/full/10.1056/NEJMp2034765?query=featured_coronavirus		dovranno essere affrontate per la vaccinazione pediatrica.	Susceptible adults fare worse, with higher rates of poor outcomes. Would you want your child vaccinated against this disease? You guessed we were talking about measles, right?
Alteri C et al Nature https://www.nature.com/articles/s41467-020-20688-x	Genomic epidemiology of SARS-CoV-2 reveals multiple lineages and early spread of SARS-CoV-2 infections in Lombardy, Italy	Analisi genomica di 346 virus provenienti da casi di COVID-19 registrati in Lombardia nel periodo febbraio-aprile 2020.	From February to April 2020, Lombardy (Italy) reported the highest numbers of SARS-CoV-2 cases worldwide. By analyzing 346 whole SARS-CoV-2 genomes, we demonstrate the presence of seven viral lineages in Lombardy, frequently sustained by local transmission chains and at least two likely to have originated in Italy. Six single nucleotide polymorphisms (five of them non-synonymous) characterized the SARS-CoV-2 sequences, none of them affecting N-glycosylation sites. The seven lineages, and the presence of local transmission clusters within three of them, revealed that sustained community transmission was underway before the first COVID-19 case had been detected in Lombardy.
Morgan C et al Critical Care Medicine https://journals.lww.com/ccmjournal/Fulltext/2021/02000/Almitrine_Infusion_in_Severe_Acute_Respiratory.38.aspx?context=FeaturedArticles&collectionId=3	Almitrine Infusion in Severe Acute Respiratory Syndrome Coronavirus 2-Induced Acute Respiratory Distress Syndrome: A Single-Center Observational Study	Studio retrospettivo su 169 pazienti con infezione da SARS-CoV-2 ricoverati in rianimazione per ARDS, di cui 33 trattati con il vasocostrittore almitrina (e nel 75% dei casi con ossido nitrico per via inalatoria) allo scopo di ripristinare il meccanismo di vasocostrizione ipossica : nei responders c'è un vantaggio in sopravvivenza.	Objectives: Treating acute respiratory failure in patients with coronavirus disease 2019 is challenging due to the lack of knowledge of the underlying pathophysiology. Hypoxemia may be explained in part by the loss of hypoxic pulmonary vasoconstriction. The present study assessed the effect of almitrine, a selective pulmonary vasoconstrictor, on arterial oxygenation in severe acute respiratory syndrome coronavirus 2-induced acute respiratory distress syndrome. Design: Single-center retrospective observational study. Setting: ICU of Lille Teaching Hospital, France, from February 27, 2020, to April 14, 2020. Patients: Patients with coronavirus disease 2019 pneumonia confirmed by positive reverse transcriptase-polymerase chain reaction for severe acute respiratory syndrome-coronavirus 2 and acute respiratory distress syndrome according to Berlin definition.

			Data focused on clinicobiological features, ventilator settings, therapeutics, outcomes, and almitrine-related adverse events. Interventions: Almitrine was considered in patients with severe hypoxemia (Pao2/Fio2 ratio < 150 mm Hg) in addition to the recommended therapies, at an hourly IV delivery of 10 µg/kg/min. Comparative blood gases were done before starting almitrine trial and immediately after the end of the infusion. A positive response to almitrine was defined by an increase of Pao2/Fio2 ratio greater than or equal to 20% at the end of the infusion. Measurements and Main Results: A total of 169 patients were enrolled. Thirty-two patients with acute respiratory distress syndrome received an almitrine infusion trial. In most cases, almitrine was infused in combination with inhaled nitric oxide (75%). Twenty-one patients (66%) were responders. The median Pao2/Fio2 ratio improvement was 39% (9–93%) and differs significantly between the responders and nonresponders (67% [39–131%] vs 6% [9–16%], respectively; $p < 0.0001$). The 28-day mortality rates were 47.6% and 63.6% ($p = 0.39$) for the responders and nonresponders, respectively. Hemodynamic parameters remained similar before and after the trial, not suggesting acute cor pulmonale. Conclusions: Almitrine infusion improved oxygenation in severe acute respiratory syndrome coronavirus 2-induced acute respiratory distress syndrome without adverse effects. In a multistep clinical approach to manage severe hypoxemia in this population, almitrine could be an interesting therapeutic option to counteract the loss of hypoxic pulmonary vasoconstriction and redistribute blood flow away from shunting zones.

			 **Figure 1.** Distribution of Pao_2/Fio_2 ratio before and after the almitrine trial. *Boxplots* represent the distribution of Pao_2/Fio_2 ratio in the global population (32 patients), in responders (21 patients) and in nonresponders (11 patients) to an almitrine infusion of 0.6 mg/kg. A positive trial was defined by an increase in the Pao_2/Fio_2 ratio ≥ 20% at the end of the infusion NS = not significant.
Shah P et al Critical Care Medicine https://journals.lww.com/ccmjournal/Fulltext/2021/02000/Is_Cardiopulmonary_Resuscitation_Futile_in.4.aspx	Is Cardiopulmonary Resuscitation Futile in Coronavirus Disease 2019 Patients Experiencing In-Hospital Cardiac Arrest?	Studio di coorte retrospettivo sulle caratteristiche e l'outcome di 63 pazienti ricoverati per COVID-19 che hanno subito un arresto cardiaco intraospedaliero e sono stati sottoposti a rianimazione cardiopolmonare: mortalità 100% indipendentemente dalle condizioni di base, 8% presentava ritmo defribillabile e l'insufficienza respiratoria era la causa più frequente.	Objectives: There is limited data regarding outcomes after in-hospital cardiac arrest among coronavirus disease 2019 patients. None of the studies have reported the outcomes of in-hospital cardiac arrest in coronavirus disease 2019 patients in the United States. We describe the characteristics and outcomes of in-hospital cardiac arrest in coronavirus disease 2019 patients in rural Southwest Georgia. Design: Retrospective cohort study. Setting: Single-center, multihospital. PATIENTS: Consecutive coronavirus disease 2019 patients who experienced in-hospital cardiac arrest with attempted resuscitation. Interventions: Attempted resuscitation with advanced cardiac life support. Measurement and Main Results: Out of 1,094 patients hospitalized for coronavirus disease 2019 during the study period, 63 patients

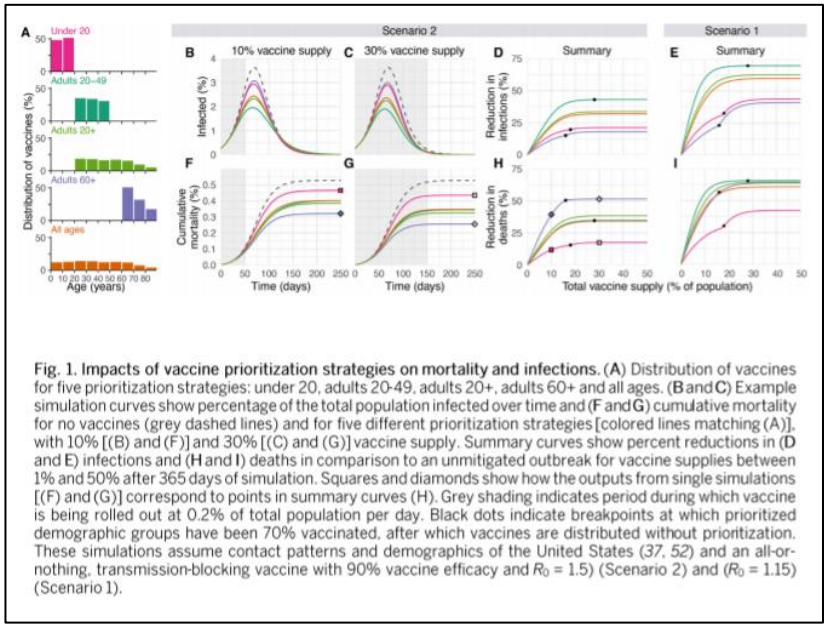
			suffered from in-hospital cardiac arrest with attempted resuscitation and were included in this study. The median age was 66 years, and 49.2% were males. The majority of patients were African Americans (90.5%). The most common comorbidities were hypertension (88.9%), obesity (69.8%), diabetes (60.3%), and chronic kidney disease (33.3%). Eighteen patients (28.9%) had a Charlson Comorbidity Index of 0–2. The most common presenting symptoms were shortness of breath (63.5%), fever (52.4%), and cough (46%). The median duration of symptoms prior to admission was 14 days. During hospital course, 66.7% patients developed septic shock, and 84.1% had acute respiratory distress syndrome. Prior to in-hospital cardiac arrest, 81% were on ventilator, 60.3% were on vasopressors, and 39.7% were on dialysis. The majority of in-hospital cardiac arrest (84.1%) occurred in the ICU. Time to initiation of advanced cardiac life support protocol was less than 1 minute for all in-hospital cardiac arrest in the ICU and less than 2 minutes for the remaining patients. The most common initial rhythms were pulseless electrical activity (58.7%) and asystole (33.3%). Although return of spontaneous circulation was achieved in 29% patients, it was brief in all of them. The in-hospital mortality was 100%. Conclusions: In our study, coronavirus disease 2019 patients suffering from in-hospital cardiac arrest had 100% in-hospital mortality regardless of the baseline comorbidities, presenting illness severity, and location of arrest.
Irving AT et al Nature	Lessons from the host defences of bats, a unique viral reservoir	Interessanti caratteristiche dei pipistrelli, in particolare nel bilanciamento tra risposta immunitaria effettrice e immunoregolazione, che li	There have been several major outbreaks of emerging viral diseases, including Hendra, Nipah, Marburg and Ebola virus diseases, severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS)—as well as the current pandemic of coronavirus disease 2019 (COVID-19). Notably, all of these

https://www.nature.com/articles/s41586-020-03128-0		rendono reservoir virali ideali.	outbreaks have been linked to suspected zoonotic transmission of bat-borne viruses. Bats—the only flying mammal—display several additional features that are unique among mammals, such as a long lifespan relative to body size, a low rate of tumorigenesis and an exceptional ability to host viruses without presenting clinical disease. Here we discuss the mechanisms that underpin the host defence system and immune tolerance of bats, and their ramifications for human health and disease. Recent studies suggest that 64 million years of adaptive evolution have shaped the host defence system of bats to balance defence and tolerance, which has resulted in a unique ability to act as an ideal reservoir host for viruses. Lessons from the effective host defence of bats would help us to better understand viral evolution and to better predict, prevent and control future viral spillovers. Studying the mechanisms of immune tolerance in bats could lead to new approaches to improving human health. We strongly believe that it is time to focus on bats in research for the benefit of both bats and humankind. **Fig. 2: The unique balance between host defence and immune tolerance in bats.**  Bats show an excellent balance between enhanced host defence responses and immune tolerance through several mechanisms. Examples of enhanced host defences include constitutive expression of IFNs and interferon-stimulated genes (ISGs), increased expression of heat-shock proteins (HSPs), a higher base level expression of the efflux pump ABCB1 and enhanced autophagy. On the other hand, dampened STING and suppressed inflammasome pathways—such as dampened NLRP3, loss of PYHIN and downstream IL-1β—contribute to immune tolerance in bats.

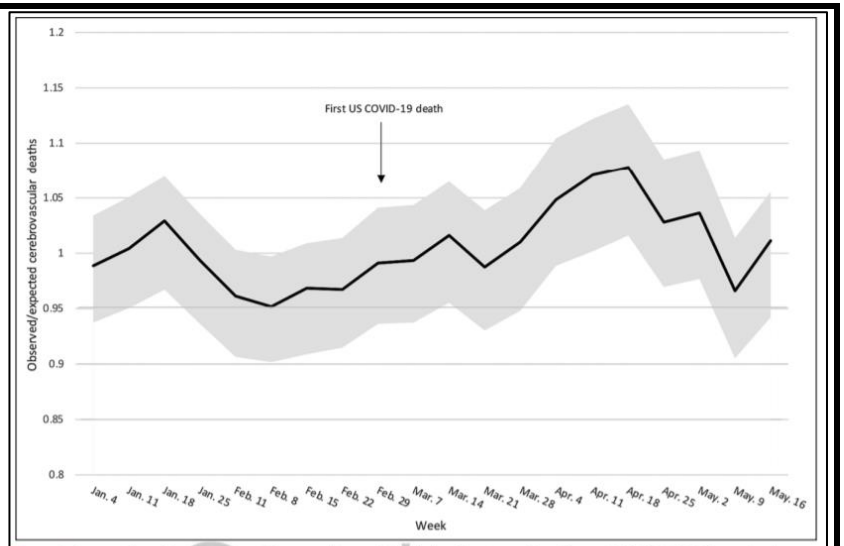
Del Borrello G et al Journal Thrombosis and Haemostasis https://onlinelibrary.wiley.com/doi/10.1111/jth.15216	SARS-COV-2–associated coagulopathy and thromboembolism prophylaxis in children: A single-center observational study	Studio osservazionale prospettico su 35 bambini ricoverati con COVID-19 ed esperienza in merito all'utilizzo di profilassi antitrombotica.	Background : Multiple investigators have described an increased incidence of thromboembolic events in SARS-CoV-2–infected individuals. Data concerning hemostatic complications in children hospitalized for COVID-19/multisystem inflammatory syndrome in children (MIS-C) are scant. Objectives : To share our experience in managing SARS-CoV-2–associated pro-coagulant state in hospitalized children. Methods : D-dimer values were recorded at diagnosis in children hospitalized for SARS-CoV-2–related manifestations. In moderately to critically ill patients and MIS-C cases, coagulation and inflammatory markers were checked at multiple time points and median results were compared. Pro-thrombotic risk factors were appraised for each child and thromboprophylaxis was started in selected cases. Results : Thirty-five patients were prospectively enrolled. D-dimer values did not discriminate COVID-19 of differing severity, whereas were markedly different between the COVID-19 and the MIS-C cohorts. In both cohorts, D-dimer and C-reactive protein levels increased upon clinical worsening but were not accompanied by decreased fibrinogen or platelet values, with all parameters returning to normal upon disease resolution. Six patients had multiple thrombotic risk factors and were started on pharmacological thromboprophylaxis. No deaths or thrombotic or bleeding complications occurred. Conclusions : COVID-19 pediatric patients show mildly altered coagulation and inflammatory parameters; on the other hand, MIS-C cases showed laboratory signs of an inflammatory driven pro-coagulant status. Universal anticoagulant prophylaxis in hospitalized children with SARS-CoV-2–related manifestations is not warranted,

			but may be offered to patients with other pro-thrombotic risk factors in the context of a multi-modal therapeutic approach.
Koenig PA et al Science https://science.sciencemag.org/content/early/2021/01/11/science.abe6230	Structure-guided multivalent nanobodies block SARS-CoV-2 infection and suppress mutational escape	Messa a punto di nanoparticelle neutralizzanti, con la stessa funzione di anticorpi monoclonali ma più vantaggiose da produrre, dirette contro la proteina spike di SARS-CoV-2.	The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic continues to spread with devastating consequences. For passive immunization efforts, nanobodies have size and cost advantages over conventional antibodies. Here, we generated four neutralizing nanobodies that target the receptor-binding domain of the SARS-CoV-2 spike protein. We defined two distinct binding epitopes using x-ray crystallography and cryo-electron microscopy. Based on the structures, we engineered multivalent nanobodies with more than 100-fold improved neutralizing activity than monovalent nanobodies. Biparatopic nanobody fusions suppressed the emergence of escape mutants. Several nanobody constructs neutralized through receptor-binding competition, while other monovalent and biparatopic nanobodies triggered aberrant activation of the spike fusion machinery. These premature conformational changes in the spike protein forestalled productive fusion, and rendered the virions non-infectious.
Somekh I et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab035/6103916	Reopening Schools and the Dynamics of SARS-CoV-2 Infections in Israel: A Nationwide Study.	Analisi dei casi e dei ricoveri per COVID-19 in Israele dopo la riapertura delle scuole a livello nazionale : non si riesce a dimostrare una associazione e gli autorni suggeriscono un ruolo non déterminante della scuola nella diffusione di SARS-CoV-2.	Background : The benefits of school reopening must be weighed against the morbidity and mortality risks and the impact of enhancing spread of COVID-19. We investigated the effects of school reopening and easing of social distancing restrictions on the dynamics of SARS-CoV-2 infections in Israel, between March-July 2020. Methods : We examined the nationwide agewise weekly incidence, prevalence, SARS-CoV-2 PCR tests, their positivity, COVID-19 hospitalizations and associated mortality. Temporal differences in these parameters following school reopening, school ending, and

			following easing of restrictions such as permission of large scale gatherings, were examined. Results : The incidence of SARS-CoV-2 infections gradually increased following school reopening in all age groups, with a significantly higher increase in adults compared to children. Higher relative ratios (RRs) of sample positivity rates 21-27 days following school reopening relative to positivity rates prior to openings were found for the age groups 40-59 (RR: 4.72, 95% CI: 3.26 - 6.83) and 20-39 years (RR: 3.37 [2.51 - 4.53]), but not for children aged 0-9 (RR: 1.46 [0.85 - 2.51]) and 10-19 years (RR: 0.93 [0.65 - 1.34]). No increase was observed in COVID-19 associated hospitalizations and deaths following school reopening. In contrast, permission of large-scale gatherings was accompanied by increases in incidence and positivity rates of samples for all age groups, and increased hospitalizations and mortality. Conclusions: This analysis does not support a major role of school reopening in the resurgence of the COVID-19 curve in Israel. Easing restrictions on large scale gatherings was the major influence on this resurgence.
Bubar KM et al Science https://science.sciencemag.org/content/early/2021/01/21/science.abe6959	Model-informed COVID-19 vaccine prioritization strategies by age and serostatus	Modello matematico per confrontare diverse strategie di allocazione dei vaccini per fasce d'età : la minore perdita di anni di vita si ottiene dando priorità agli over 60.	Limited initial supply of SARS-CoV-2 vaccine raises the question of how to prioritize available doses. Here, we used a mathematical model to compare five age-stratified prioritization strategies. A highly effective transmission-blocking vaccine prioritized to adults ages 20-49 years minimized cumulative incidence, but mortality and years of life lost were minimized in most scenarios when the vaccine was prioritized to adults over 60 years old. Use of individual-level serological tests to redirect doses to seronegative individuals improved the marginal impact of each dose while potentially reducing existing inequities in COVID-19 impact. While maximum impact prioritization strategies were broadly consistent across

			countries, transmission rates, vaccination rollout speeds, and estimates of naturally acquired immunity, this framework can be used to compare impacts of prioritization strategies across contexts.  Fig. 1. Impacts of vaccine prioritization strategies on mortality and infections. (A) Distribution of vaccines for five prioritization strategies: under 20, adults 20-49, adults 20+, adults 60+ and all ages. (B and C) Example simulation curves show percentage of the total population infected over time and (F and G) cumulative mortality for no vaccines (grey dashed lines) and for five different prioritization strategies [colored lines matching (A)], with 10% [(B) and (F)] and 30% [(C) and (G)] vaccine supply. Summary curves show percent reductions in (D and E) infections and (H and I) deaths in comparison to an unmitigated outbreak for vaccine supplies between 1% and 50% after 365 days of simulation. Squares and diamonds show how the outputs from single simulations [(F) and (G)] correspond to points in summary curves (H). Grey shading indicates period during which vaccine is being rolled out at 0.2% of total population per day. Black dots indicate breakpoints at which prioritized demographic groups have been 70% vaccinated, after which vaccines are distributed without prioritization. These simulations assume contact patterns and demographics of the United States (*37*, *52*) and an all-or-nothing, transmission-blocking vaccine with 90% vaccine efficacy and R_0 = 1.5) (Scenario 2) and (R_0 = 1.15) (Scenario 1).
European Medicines Agency https://www.ema.europa.eu/en/medicines/human/EPAR/covid-19-vaccine-moderna	COVID-19 Vaccine Moderna	Report finale della valutazione del vaccino Moderna contro SARS-CoV-2, autorizzato per l'uso in Europa dall'EMA.	COVID-19 Vaccine Moderna is a vaccine for preventing coronavirus disease 2019 (COVID-19) in people aged 18 years and older. COVID-19 Vaccine Moderna contains a molecule called messenger RNA (mRNA) with instructions for producing a protein from SARS-CoV-2, the virus that causes COVID-19. COVID-19 Vaccine Moderna does not contain the virus itself and cannot cause COVID-19.
Sharma R et al Stroke	Excess Cerebrovascular Mortality in the United States During the COVID-19 Pandemic	Aumento della mortalità e riduzione degli accessi ospedalieri per ictus nel periodo gennaio-maggio	Background and Purpose: The magnitude and drivers of excess cerebrovascular-specific mortality during the coronavirus disease 2019 (COVID-19) pandemic are unknown. We aim to quantify excess stroke-related deaths and characterize its association with social distancing behavior and COVID-19–related vascular pathology.

https://www.ahajournals.org/doi/10.1161/STROKEAHA.120.031975		2020 in 40 stati americani e New York.	Methods: United States and state-level excess cerebrovascular deaths from January to May 2020 were quantified using National Center for Health Statistic data and Poisson regression models. Excess cerebrovascular deaths were analyzed as a function of time-varying stroke-related emergency medical service (EMS) calls and cumulative COVID-19 deaths using linear regression. A state-level regression analysis was performed to determine the association between excess cerebrovascular deaths and time spent in residences, measured by Google Community Mobility Reports, during the height of the pandemic after the first COVID-19 death (February 29). Results: Forty states and New York City were included. Excess cerebrovascular mortality occurred nationally from the weeks ending March 28 to May 2, 2020, up to a 7.8% increase above expected levels during the week of April 18. Decreased stroke-related EMS calls were associated with excess stroke deaths one (70 deaths per 1000 fewer EMS calls [95% CI, 20–118]) and 2 weeks (85 deaths per 1000 fewer EMS calls [95% CI, 37–133]) later. Twenty-three states and New York City experienced excess cerebrovascular mortality during the pandemic height. A 10% increase in time spent at home was associated with a 4.3% increase in stroke deaths (incidence rate ratio, 1.043 [95% CI, 1.001–1.085]) after adjusting for COVID-19 deaths. Conclusions: Excess US cerebrovascular deaths during the COVID-19 pandemic were observed and associated with decreases in stroke-related EMS calls nationally and mobility at the state level. Public health measures are needed to identify and counter the reticence to seeking medical care for acute stroke during the COVID-19 pandemic.

			 **Figure 2. Increase in national excess cerebrovascular mortality during the coronavirus disease 2019 (COVID-19) pandemic.** Observed divided by expected counts for each week in the study period±95% prediction interval.
Horby P et al NERVTAG_paper_on_variant_of_concern__VOC__B.1.1.7.pdf	NERVTAG note on B.1.1.7 severity	Il Nen and Emerging Respiratory Virus Threats Advisory Group (NERVTAG) del Regno Unito ha diffuso un articolo in cui comunica che alcuni dati, in via di revisione e pubblicazione, suggerirebbero una maggiore mortalità legata a infezione da SARS-CoV-2 ceppo B.1.1.7 rispetto a ceppi diversi.	1.The variant of concern (VOC) B.1.1.7 appears to have substantially increased transmissibility compared to other variants and has grown quickly to become the dominant variant in much of the UK. 2. Initial assessment by PHE of disease severity through a matched case-control study reported no significant difference in the risk of hospitalisation or death in people infected with confirmed B.1.1.7 infection versus infection with other variants. 3. Several new analyses are however consistent in reporting increased disease severity in people infected with VOC B.1.1.7 compared to people infected with non-VOC virus variants. 4. There have been several independent analyses of SGTF and non-SGTF cases identified through Pillar 2 testing linked to the PHE COVID-19 deaths line list: a. LSHTM: reported that the relative hazard of death within 28 days of test for VOC-infected individuals compared to non-VOC was 1.35 (95%CI 1.08-1.68).

			b. Imperial College London: mean ratio of CFR for VOC-infected individuals compared to non-VOC was 1.36 (95%CI 1.18-1.56) by a case-control weighting method, 1.29 (95%CI 1.07-1.54) by a standardised CFR method. c. University of Exeter: mortality hazard ratio for VOC-infected individuals compared to non-VOC was 1.91 (1.35 - 2.71). d. These analyses were all adjusted in various ways for age, location, time and other variables. 5. An updated PHE matched cohort analysis has reported a death risk ratio for VOC infected individuals compared to non-VOC of 1.65 (95%CI 1.21-2.25). 6. There are several limitations to these datasets including representativeness of death data (<10% of all deaths are included in some datasets), power, potential biases in case ascertainment and transmission setting. 7. Based on these analyses, there is a realistic possibility that infection with VOC B.1.1.7 is associated with an increased risk of death compared to infection with non-VOC viruses. 8. It should be noted that the absolute risk of death per infection remains low. 9. An analysis of CO-CIN data has not identified an increased risk of death in hospitalised VOC B.1.1.7 cases. However, increased severity may not necessarily be reflected by increased in-hospital death risk. 10. Since the time lag from infection to hospitalisation and death is relatively long, data will accrue in coming weeks, at which time the analyses will become more definitive.

Raches E et al The Lancet https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30942-7/fulltext	Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBV152: a double-blind, randomised, phase 1 trial	Esito del trial di fase I su efficacia e sicurezza del vaccino a virione inattivato BBV152 : 375 partecipanti randomizzati fra placebo e bracci di trattamento con diversi adiuvanti, con riscontro di eventi avversi lievi e sieroconversione in tutte le formulazioni del vaccino, che verrano testate in fase II.	Background : To mitigate the effects of COVID-19, a vaccine is urgently needed. BBV152 is a whole-virion inactivated SARS-CoV-2 vaccine formulated with a toll-like receptor 7/8 agonist molecule adsorbed to alum (Algel-IMDG) or alum (Algel). Methods : We did a double-blind, multicentre, randomised, controlled phase 1 trial to assess the safety and immunogenicity of BBV152 at 11 hospitals across India. Healthy adults aged 18–55 years who were deemed healthy by the investigator were eligible. Individuals with positive SARS-CoV-2 nucleic acid and/or serology tests were excluded. Participants were randomly assigned to receive either one of three vaccine formulations (3 µg with Algel-IMDG, 6 µg with Algel-IMDG, or 6 µg with Algel) or an Algel only control vaccine group. Block randomisation was done with a web response platform. Participants and investigators were masked to treatment group allocation. Two intramuscular doses of vaccines were administered on day 0 (the day of randomisation) and day 14. Primary outcomes were solicited local and systemic reactogenicity events at 2 h and 7 days after vaccination and throughout the full study duration, including serious adverse events. Secondary outcome was seroconversion (at least four-fold increase from baseline) based on wild-type virus neutralisation. Cell-mediated responses were evaluated by intracellular staining and ELISpot. The trial is registered at ClinicalTrials.gov (NCT04471519). Findings : Between July 13 and 30, 2020, 827 participants were screened, of whom 375 were enrolled. Among the enrolled participants, 100 each were randomly assigned to the three vaccine groups, and 75 were randomly assigned to the control group (Algel only). After both doses, solicited local and systemic adverse reactions were reported by 17 (17%; 95% CI 10·5–26·1) participants in the 3 µg with Algel-IMDG group, 21 (21%; 13·8–30·5) in the 6 µg

			with Algel-IMDG group, 14 (14%; 8·1–22·7) in the 6 µg with Algel group, and ten (10%; 6·9–23·6) in the Algel-only group. The most common solicited adverse events were injection site pain (17 [5%] of 375 participants), headache (13 [3%]), fatigue (11 [3%]), fever (nine [2%]), and nausea or vomiting (seven [2%]). All solicited adverse events were mild (43 [69%] of 62) or moderate (19 [31%]) and were more frequent after the first dose. One serious adverse event of viral pneumonitis was reported in the 6 µg with Algel group, unrelated to the vaccine. Seroconversion rates (%) were 87·9, 91·9, and 82·8 in the 3 µg with Algel-IMDG, 6 µg with Algel-IMDG, and 6 µg with Algel groups, respectively. CD4+ and CD8+ T-cell responses were detected in a subset of 16 participants from both Algel-IMDG groups. Interpretation : BBV152 led to tolerable safety outcomes and enhanced immune responses. Both Algel-IMDG formulations were selected for phase 2 immunogenicity trials. Further efficacy trials are warranted.

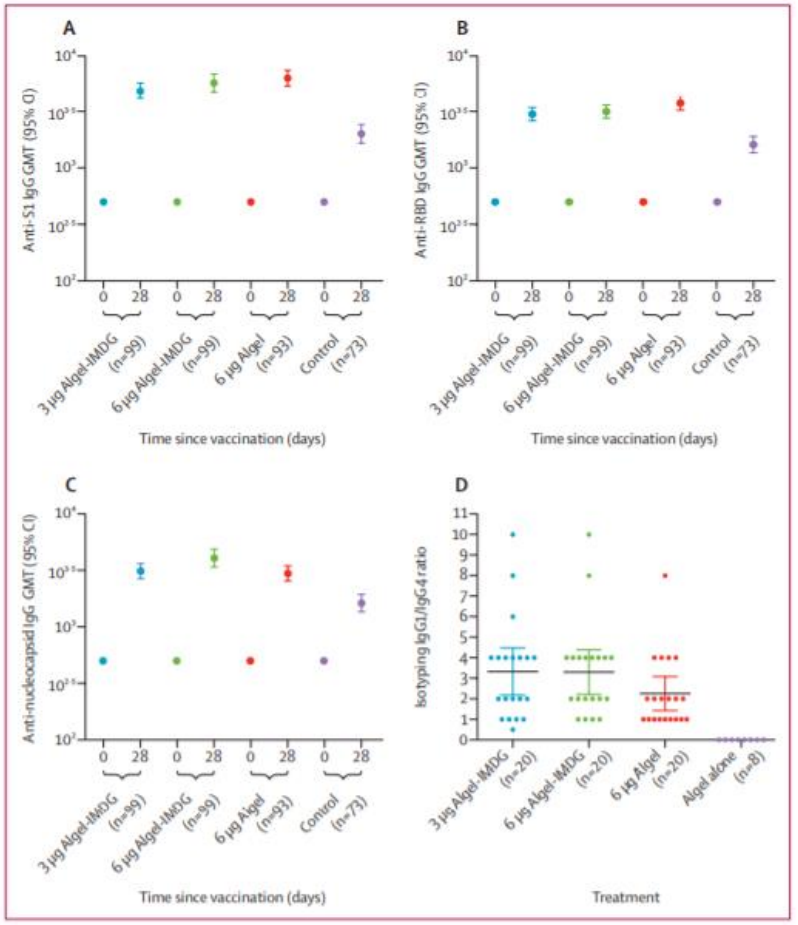


Figure 2: **SARS-CoV-2 IgG titres against anti-spike protein (A), receptor-binding domain (B), and nucleocapsid IgG (C) and anti-spike protein IgG1/IgG4 ratio (D)**

ELISA results at baseline (day 0) and 2 weeks after the second vaccination (day 28). In A–C, error bars show 95% CIs. The cutoff for detectable antibodies was 1/500. Some samples were positive for SARS-CoV-2 in the control group, as evident by the antibody titres on day 28. Endpoint titre dilution for day 28 sera samples was established with baseline (day 0), interpolated from the absorbance of the corresponding day 0 sample. Cutoff (mean ± 3 SD) for day 0 was calculated considering the absorbance of all sera dilutions (1/500 to 1/32000) tested, except the lowest dilution (1/500). ELISA titres (endpoint titres) on day 14 were not analysed. In D, the isotyping ratio was calculated (in a randomly selected subset) as IgG1/IgG4; dots show the individual datapoints and horizontal bars show means with error bars for 95% CIs. Endpoint titre=the highest sera dilution at which the absorbance was above the cutoff. GMT=geometric mean titre. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

Rostad CA et al The Lancet https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30988-9/fulltext	Optimism and caution for an inactivated COVID-19 vaccine	Commento all'articolo precedente che solleva le potenziali criticità di un vaccino a virus inattivato : la produzione anche di anticorpi non neutralizzanti che potrebbero determinare un peggioramento della sindrome clinica in caso di infezione e il fenomeno dell' antibody-dependent enhancement (ADE).	Although the COVID-19 pandemic has caused substantial morbidity, mortality, and social upheaval worldwide, the final months of 2020 heralded the high efficacy and safety results of three phase 3 clinical trials of SARS-CoV-2 vaccines.1, 2, 3, 4 The first COVID-19 vaccine to be approved in the western world, BNT162b2 (Pfizer),1 was closely followed by mRNA-1273 (Moderna),2 and the chimpanzee-adenovirus vectored AZD1222 (AstraZeneca–Oxford).3 Unfortunately, cold-chain requirements, finite global manufacturing capacity, and insufficient supply are likely to disproportionately affect low-income and middle-income countries (LMICs). Although multilateral agreements have been made to purchase vaccines for LMICs through the COVID-19 Vaccine Global Access Facility, a global collaboration established to provide equitable access to COVID-19 vaccines, only enough doses to vaccinate 250 million people have been purchased to date. Mathematical models indicate there will not be an adequate supply of vaccines available to cover the global population until 2023,5 further exacerbating health and other disparities in LMICs.
The CORIMUNO-19 Collaborative group The Lancet https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30556-7/fulltext#%20	Effect of anakinra versus usual care in adults in hospital with COVID-19 and mild-to-moderate pneumonia (CORIMUNO-ANA-1): a randomised controlled trial	Trial clinico sull'effetto dell'aggiunta dell'inibitore del recettore di IL-1 anakinra a standard of care in 116 pazienti con COVID-19 di gravità lieve-moderata : non si dimostra un vantaggio in termini di ventilazione invasiva o non invasiva e sopravvivenza.	Background : Patients with COVID-19 pneumonia have an excess of inflammation and increased concentrations of cytokines including interleukin-1 (IL-1). We aimed to determine whether anakinra, a recombinant human IL-1 receptor antagonist, could improve outcomes in patients in hospital with mild-to-moderate COVID-19 pneumonia. Methods : In this multicentre, open-label, Bayesian randomised clinical trial (CORIMUNO-ANA-1), nested within the CORIMUNO-19 cohort, we recruited patients from 16 University hospitals in France with mild-to-moderate COVID-19 pneumonia, severe acute respiratory syndrome coronavirus 2 infection confirmed by real-time RT-PCR, requiring at least 3 L/min of oxygen by mask or nasal

			cannula but without ventilation assistance, a score of 5 on the WHO Clinical Progression Scale (WHO-CPS), and a C-reactive protein serum concentration of more than 25 mg/L not requiring admission to the intensive care unit at admission to hospital. Eligible patients were randomly assigned (1:1) using a web-based secure centralised system, stratified by centre and blocked with varying block sizes (randomly of size two or four), to either usual care plus anakinra (200 mg twice a day on days 1–3, 100 mg twice on day 4, 100 mg once on day 5) or usual care alone. Usual care was provided at the discretion of the site clinicians. The two coprimary outcomes were the proportion of patients who had died or needed non-invasive or mechanical ventilation by day 4 (ie, a score of >5 on the WHO-CPS) and survival without need for mechanical or non-invasive ventilation (including high-flow oxygen) at day 14. All analyses were done on an intention-to-treat basis. The trial is registered with ClinicalTrials.gov, NCT04341584, and is now closed to accrual. Findings : Between April 8 and April 26, 2020, we screened 153 patients. The study was stopped early following the recommendation of the data and safety monitoring board, after the recruitment of 116 patients: 59 were assigned to the anakinra group, and 57 were assigned to the usual care group. Two patients in the usual care group withdrew consent and were not analysed. In the analysable population, the median age was 66 years (IQR 59 to 76) and 80 (70%) participants were men. In the anakinra group, 21 (36%) of 59 patients had a WHO-CPS score of more than 5 at day 4 versus 21 (38%) of 55 in the usual care group (median posterior absolute risk difference [ARD] −2·5%, 90% credible interval [CrI] −17·1 to 12·0), with a posterior probability of ARD of less than 0 (ie, anakinra better than usual care) of 61·2%. At day 14, 28 (47%; 95% CI 33 to 59) patients in the anakinra group and 28 (51%; 95% CI 36

			to 62) in the usual care group needed ventilation or died, with a posterior probability of any efficacy of anakinra (hazard ratio [HR] being less than 1) of 54·5% (median posterior HR 0·97; 90% CrI 0·62 to 1·52). At day 90, 16 (27%) patients in the anakinra group and 15 (27%) in the usual care group had died. Serious adverse events occurred in 27 (46%) patients in the anakinra group and 21 (38%) in the usual care group (p=0·45). Interpretation : Anakinra did not improve outcomes in patients with mild-to-moderate COVID-19 pneumonia. Further studies are needed to assess the efficacy of anakinra in other selected groups of patients with more severe COVID-19.

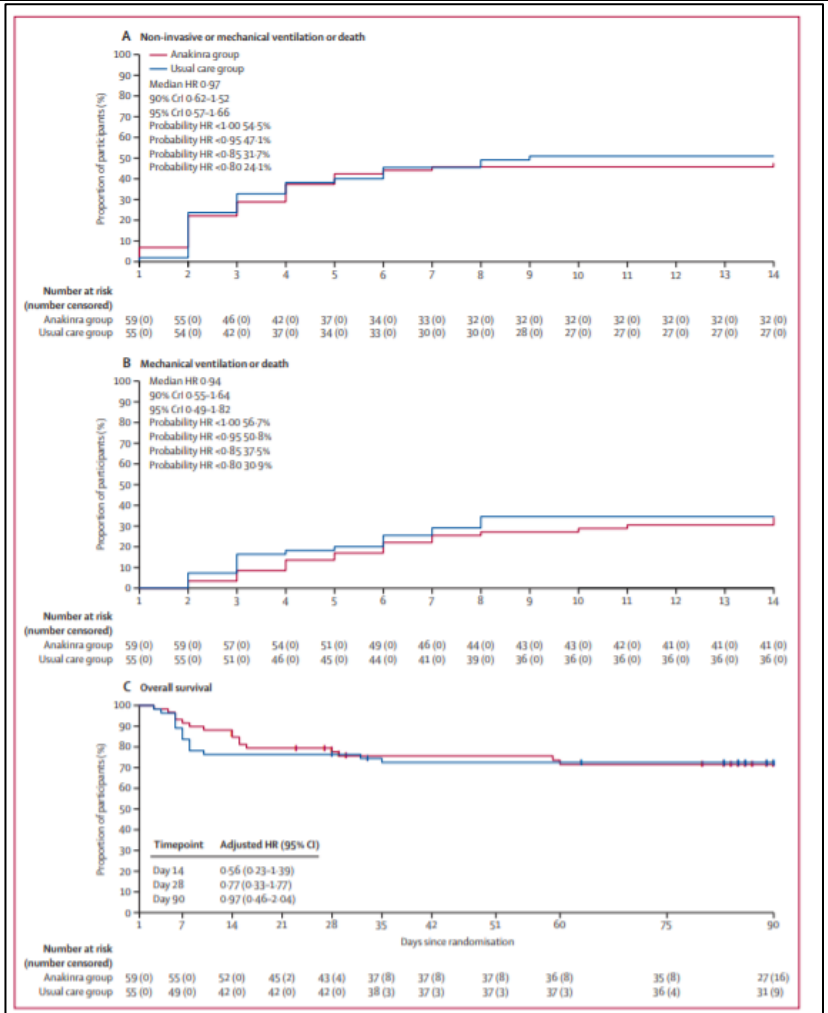
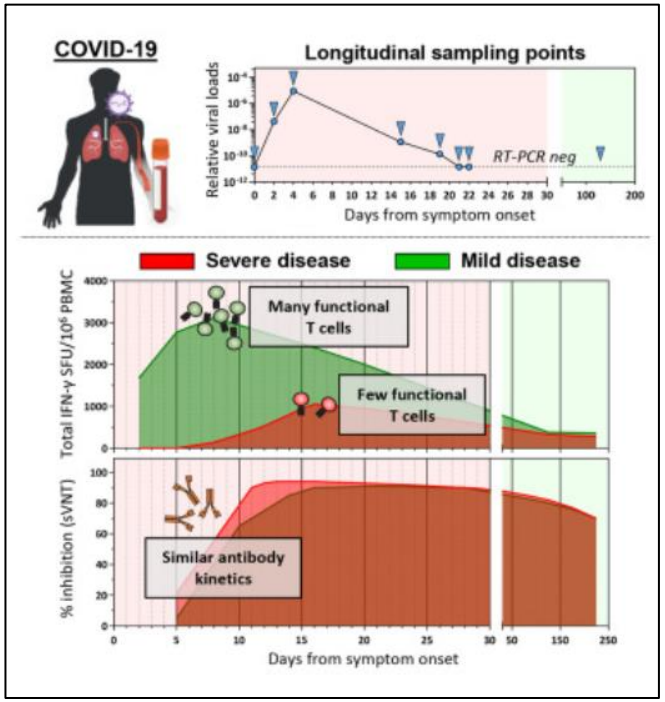
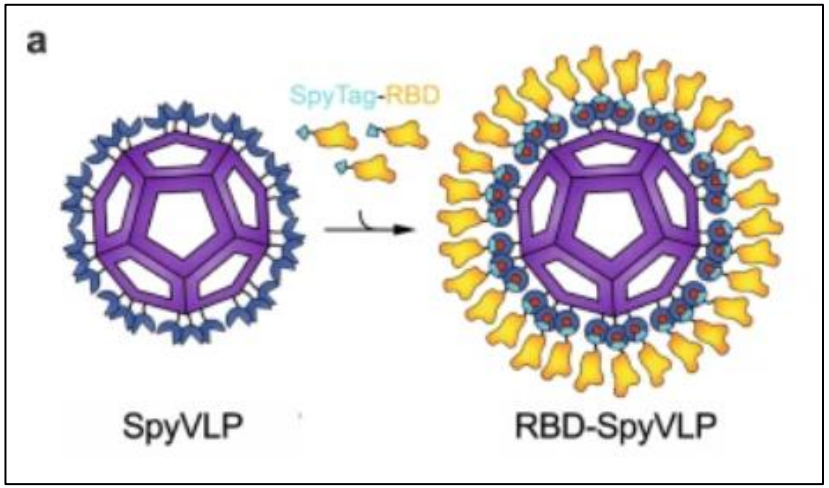


Figure 2: **Kaplan-Meier estimates of probability of mechanical or non-invasive ventilation or death (A), mechanical ventilation or death (B), and overall survival (C) during follow-up, for the anakinra group versus usual care group**

In panel A, events occurring on day 1 occurred on the same day as but after randomisation. For the outcomes of death or ventilation support and death or mechanical ventilation, data are analysed in a Bayesian framework, and median posterior HRs and 90% CrIs are presented, together with posterior probabilities of achieving specified outcomes. Overall survival was analysed in a frequentist framework, and so posterior probabilities are not relevant and not calculated. In part C, HRs are adjusted for age and centre. CrI=credible interval. HR=hazard ratio.

Callaway E et al Nature https://www.nature.com/articles/d41586-021-00121-z	Fast-spreading COVID variant can elude immune responses	La variante Sudafricana di SARS-CoV-2 potrebbe eludere l'immunità acquisita tramite l'infezione o i vaccini : riassunto discorsivo delle evidenze a riguardo.	Evidence is growing that some coronavirus variants could evade immune responses triggered by vaccines and previous infections. Researchers are trying to make sense of a tsunami of lab studies released this week that raise concerns about some emerging variants and mutations.
Shimabukuru et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2775646	Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine	Revisione di 21 casi di anafilassi verificatisi dopo la somminstrazione di 1 893 360 prime dosi di vaccino Pfizer contro SARS-CoV-2 (circa 11.1 casi per milione di dosi).	On December 11, 2020, the US Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for the Pfizer-BioNTech coronavirus disease 2019 (COVID-19) vaccine, administered as 2 doses separated by 21 days. Shortly after, the Advisory Committee on Immunization Practices (ACIP) issued an interim recommendation for its use. Following implementation of vaccination, reports of anaphylaxis after the first dose of the Pfizer-BioNTech COVID-19 vaccine emerged. Anaphylaxis is a life-threatening allergic reaction that occurs rarely after vaccination, with onset typically within minutes to hours.
Tan AT et al Cell Reports https://www.cell.com/cell-reports/fulltext/S2211-1247(21)00041-3	Early induction of functional SARS-CoV-2 specific T cells associates with rapid viral clearance and mild disease in COVID-19 patients	I pazienti con decorso più benigno di COVID-19 hanno livelli più elevati di Interferone-gamma prodotto dai linfociti T in questa piccola casistica.	Virus-specific humoral and cellular immunity act synergistically to protect the host from viral infection. We interrogate the dynamic changes of virological and immunological parameters in 12 patients with symptomatic acute SARS-CoV-2 infection from disease onset to convalescence or death. We quantify SARS-CoV-2 viral RNA in the respiratory tract in parallel with antibodies and circulating T cells specific for various structural (NP, M, ORF3a and spike) and non-structural proteins (ORF7/8, NSP7 and NSP13). While rapid induction and quantity of humoral responses associates with an increase in disease severity, early induction of IFN-γ secreting SARS-CoV-2 specific T cells is present in patients with mild disease and accelerated viral clearance. These findings provide support for the

			prognostic value of early functional SARS-CoV-2 specific T cells with important implications in vaccine design and immune monitoring. 
Tan TK et al Nature https://www.nature.com/articles/s41467-020-20654-7	A COVID-19 vaccine candidate using SpyCatcher multimerization of the SARS-CoV-2 spike protein receptor-binding domain induces potent neutralising antibody responses	Vaccino a nanoparticelle contro SARS-COV-2 prodotto con tecnologia SpyTag/SpyCatcher, che consiste nella formazione di un legame irreversibile fra un piccolo peptide (in questo caso RBD della proteina S) e una proteina (il « catcher ») dopo la loro sintesi: si dimostra una risposta anticorpale	There is need for effective and affordable vaccines against SARS-CoV-2 to tackle the ongoing pandemic. In this study, we describe a protein nanoparticle vaccine against SARS-CoV-2. The vaccine is based on the display of coronavirus spike glycoprotein receptor-binding domain (RBD) on a synthetic virus-like particle (VLP) platform, SpyCatcher003-mi3, using SpyTag/SpyCatcher technology. Low doses of RBD-SpyVLP in a prime-boost regimen induce a strong neutralising antibody response in mice and pigs that is superior to convalescent human sera. We evaluate antibody quality using ACE2 blocking and neutralisation of cell infection by pseudovirus or wild-type SARS-CoV-2. Using competition assays with a monoclonal

		policlonale nel topo e nel maiale, superiore a quella dosabile nel siero umano post-infezione.	antibody panel, we show that RBD-SpyVLP induces a polyclonal antibody response that recognises key epitopes on the RBD, reducing the likelihood of selecting neutralisation-escape mutants. Moreover, RBD-SpyVLP is thermostable and can be lyophilised without losing immunogenicity, to facilitate global distribution and reduce cold-chain dependence. The data suggests that RBD-SpyVLP provides strong potential to address clinical and logistic challenges of the COVID-19 pandemic. 
Gottlieb RL et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2775647	Effect of Bamlanivimab as Monotherapy or in Combination With Etesevimab on Viral Load in Patients With Mild to Moderate COVID-19	Il trattamento con la combinazione dei due anticorpi monoclonali bamlanivimab e etesevimab contro SARS-CoV-2 nei casi di COVID-19 lieve-moderato riduce significativamente la carica virale nel tampone nasofaringeo dei trattati. Restano da indagare gli outcome clinici e, piuù in	Importance Coronavirus disease 2019 (COVID-19) continues to spread rapidly worldwide. Neutralizing antibodies are a potential treatment for COVID-19. Objective To determine the effect of bamlanivimab monotherapy and combination therapy with bamlanivimab and etesevimab on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral load in mild to moderate COVID-19. Design, Setting, and Participants The BLAZE-1 study is a randomized phase 2/3 trial at 49 US centers including ambulatory patients (N = 613) who tested positive for SARS-CoV-2 infection and had 1 or

		generale, resta da capire che ruolo abbiano gli anticorpi monoclonali in un mondo in cui si diffondono i vaccini contro SARS-CoV-2.	more mild to moderate symptoms. Patients who received bamlanivimab monotherapy or placebo were enrolled first (June 17-August 21, 2020) followed by patients who received bamlanivimab and etesevimab or placebo (August 22-September 3). These are the final analyses and represent findings through October 6, 2020. Interventions Patients were randomized to receive a single infusion of bamlanivimab (700 mg [n = 101], 2800 mg [n = 107], or 7000 mg [n = 101]), the combination treatment (2800 mg of bamlanivimab and 2800 mg of etesevimab [n = 112]), or placebo (n = 156). Main Outcomes and Measures The primary end point was change in SARS-CoV-2 log viral load at day 11 (±4 days). Nine prespecified secondary outcome measures were evaluated with comparisons between each treatment group and placebo, and included 3 other measures of viral load, 5 on symptoms, and 1 measure of clinical outcome (the proportion of patients with a COVID-19–related hospitalization, an emergency department [ED] visit, or death at day 29). Results Among the 577 patients who were randomized and received an infusion (mean age, 44.7 [SD, 15.7] years; 315 [54.6%] women), 533 (92.4%) completed the efficacy evaluation period (day 29). The change in log viral load from baseline at day 11 was –3.72 for 700 mg, –4.08 for 2800 mg, –3.49 for 7000 mg, –4.37 for combination treatment, and –3.80 for placebo. Compared with placebo, the differences in the change in log viral load at day 11 were 0.09 (95% CI, –0.35 to 0.52; P = .69) for 700 mg, –0.27 (95% CI, –0.71 to 0.16; P = .21) for 2800 mg, 0.31 (95% CI, –0.13 to 0.76; P = .16) for 7000 mg, and –0.57 (95% CI, –1.00 to –0.14; P = .01) for combination treatment. Among the secondary outcome measures, differences between each treatment group vs the placebo group were statistically significant for 10 of 84 end points. The proportion

			of patients with COVID-19–related hospitalizations or ED visits was 5.8% (9 events) for placebo, 1.0% (1 event) for 700 mg, 1.9% (2 events) for 2800 mg, 2.0% (2 events) for 7000 mg, and 0.9% (1 event) for combination treatment. Immediate hypersensitivity reactions were reported in 9 patients (6 bamlanivimab, 2 combination treatment, and 1 placebo). No deaths occurred during the study treatment. Conclusions and Relevance Among nonhospitalized patients with mild to moderate COVID-19 illness, treatment with bamlanivimab and etesevimab, compared with placebo, was associated with a statistically significant reduction in SARS-CoV-2 viral load at day 11; no significant difference in viral load reduction was observed for bamlanivimab monotherapy. Further ongoing clinical trials will focus on assessing the clinical benefit of antispike neutralizing antibodies in patients with COVID-19 as a primary end point.
Hanson KE et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab048/6106562?searchresult=1	The Infectious Diseases Society of America Guidelines on the Diagnosis of COVID-19: Molecular Diagnostic Testing	Linee guida della Società Americana di Malattie Infettive (IDSA) sulla diagnostica molecolare di SARS-CoV-2.	Background : Accurate molecular diagnostic tests are necessary for confirming a diagnosis of coronavirus disease 2019 (COVID-19). Direct detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleic acids in respiratory tract specimens informs patient, healthcare institution and public health level decision-making. The numbers of available SARS-CoV-2 nucleic acid detection tests are rapidly increasing, as is the COVID-19 diagnostic literature. Thus, the Infectious Diseases Society of America (IDSA) recognized a significant need for frequently updated systematic reviews of the literature to inform evidence-based best practice guidance. Objective : The IDSA's goal was to develop an evidence-based diagnostic guideline to assist clinicians, clinical laboratorians, patients and policymakers in decisions related to the optimal use of SARS-CoV-2 nucleic acid amplification tests. In addition, we provide a conceptual framework for understanding molecular diagnostic

			test performance, discuss the nuance of test result interpretation in a variety of practice settings and highlight important unmet research needs in the COVID-19 diagnostic testing space. Methods : IDSA convened a multidisciplinary panel of infectious diseases clinicians, clinical microbiologists, and experts in systematic literature review to identify and prioritize clinical questions and outcomes related to the use of SARS-CoV-2 molecular diagnostics. Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology was used to assess the certainty of evidence and make testing recommendations. Results : The panel agreed on 17 diagnostic recommendations. Conclusions : Universal access to accurate SARS-CoV-2 nucleic acid testing is critical for patient care, hospital infection prevention and the public response to the COVID-19 pandemic. Information on the clinical performance of available tests is rapidly emerging, but the quality of evidence of the current literature is considered moderate to very low. Recognizing these limitations, the IDSA panel weighed available diagnostic evidence and recommends nucleic acid testing for all symptomatic individuals suspected of having COVID-19. In addition, testing is recommended for asymptomatic individuals with known or suspected contact with a COVID-19 case. Testing asymptomatic individuals without known exposure is suggested when the results will impact isolation/quarantine/personal protective equipment (PPE) usage decisions, dictate eligibility for surgery, or inform solid organ or hematopoietic stem cell transplantation timing. Ultimately, prioritization of testing will depend on institutional-specific resources and the needs of different patient populations.

Mele D et al Internal and Emergency Medicine https://link.springer.com/article/10.1007/s11739-021-02635-w	Myocarditis in COVID-19 patients: current problems	Revisione sul problema della miocardite come complicanza di COVID-19.	Myocarditis has been reported as a possible clinical presentation or complication in patients with coronavirus disease (COVID)-19 due to SARS-CoV-2. Despite the alarm that this possibility generated among physicians, there is paucity of information about mechanisms, prevalence, prognosis, diagnosis and therapy of myocarditis in the context of COVID-19. This brief review has the goal to revise and summarize current knowledge on myocarditis in COVID-19 patients and underline problems especially related to diagnosis and treatment.