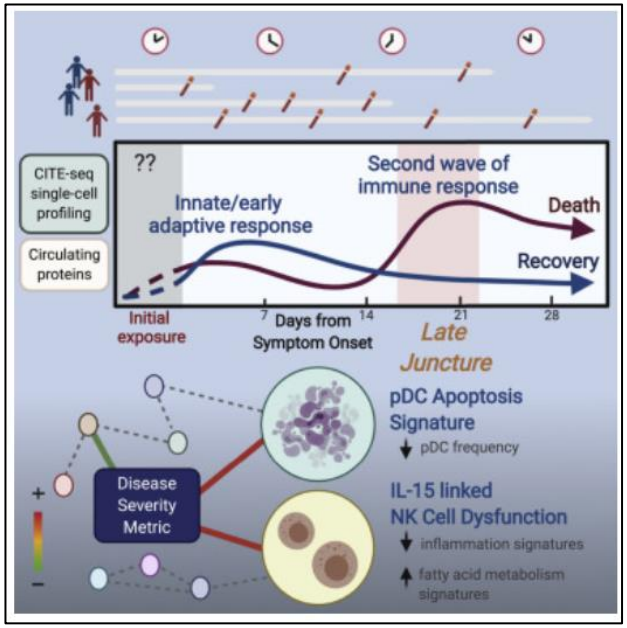
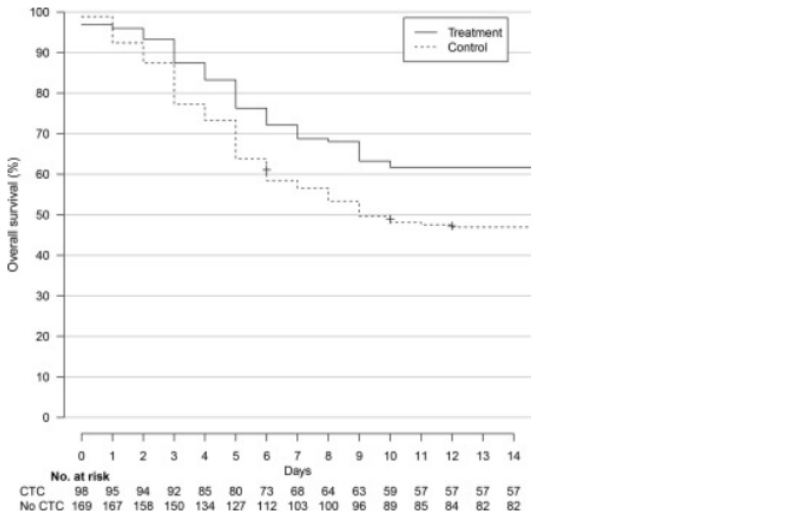
RICERCA BIBLIOGRAFICA COVID 19 SETTIMANA 5.04 – 11.04.2021 FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE DOTT.SSA ELEONORA TADDEI			
AUTORE/RIVISTA	**TITOLO**	**OUTCOME PRINCIPALE**	**ABSTRACT**
Liu C et al Cell https://www.cell.com/cell/fulltext/S0092-8674(21)00168-9	Time-resolved systems immunology reveals a late juncture linked to fatal COVID-19	Tentativo di stratificare i pazienti con COVID-19 sulla base del trascrittoma delle cellule mononucleate, delle loro proteine di superficie, della struttura dei recettori T e B cellulari e dei livelli di citochine circolanti, al fine di individuare le caratteristiche di chi ha un decorso peggiore : l'apoptosi delle cellule dendritiche si associa a maggiore gravità all'esordio, così come la scarsa attivazione delle cellule Natural Killer (« esaurite ») ; inoltre, nei	COVID-19 exhibits extensive patient-to-patient heterogeneity. To link immune response variation to disease severity and outcome over time, we longitudinally assessed circulating proteins as well as 188 surface protein markers, transcriptome, and T cell receptor sequence simultaneously in single peripheral immune cells from COVID-19 patients. Conditional-independence network analysis revealed primary correlates of disease severity, including gene expression signatures of apoptosis in plasmacytoid dendritic cells and attenuated inflammation but increased fatty acid metabolism in CD56dimCD16hi NK cells linked positively to circulating interleukin (IL)-15. CD8+ T cell activation was apparent without signs of exhaustion. Although cellular inflammation was depressed in severe patients early after hospitalization, it became elevated by days 17–23 post symptom onset, suggestive of a late wave of inflammatory responses. Furthermore, circulating protein trajectories at this time were divergent between and predictive of recovery versus fatal

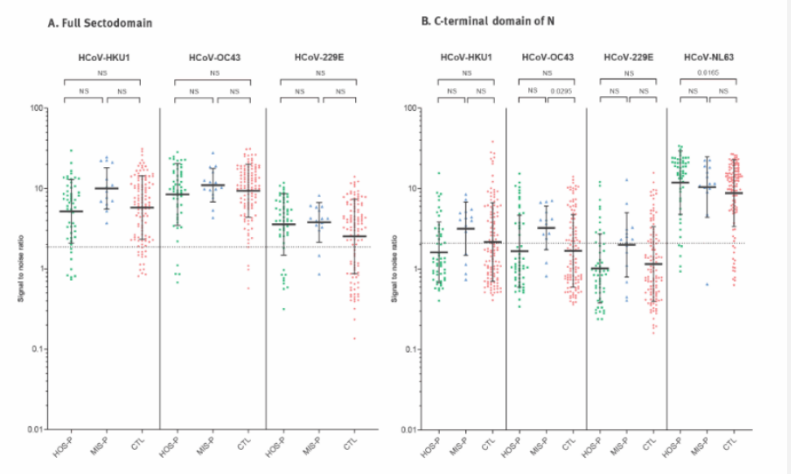
		giorni 17-23 dall'esordio si osserva una differente espressione di marcatori di danno cellulare ed endoteliale che caratterizzano i pazienti con esito infausto rispetto a chi ha un decorso migliore. Correlare queste osservazioni alla gestione clinica e alla scelta della terapia appropriata appare ancora molto difficile.	outcomes. Our findings stress the importance of timing in the analysis, clinical monitoring, and therapeutic intervention of COVID-19. 
Wiley Z et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab290/6209403?searchresult=1	Racial and Ethnic Differences and Clinical Outcomes of COVID-19 Patients Presenting to the Emergency Department	Studio di coorte su 94683 pazienti che hanno effettuato accesso in Pronto Soccorso negli USA e ricevuto diagnosi di infezione da SARS-CoV-2, stratificati per etnia : gli afroamericani e gli ispanici hanno rischio di morte intraospedaliera maggiore dei bianchi.	Background : Since the introduction of remdesivir and dexamethasone for severe COVID-19 treatment, few large multi-hospital system US studies have described clinical characteristics and outcomes of minority COVID-19 patients who present to the emergency department (ED). Methods : This cohort study from the Cerner Real World Database (87 US health systems) from December 1, 2019 to September 30, 2020 included PCR-confirmed COVID-19 patients who self-identified as non-Hispanic Black (Black), Hispanic White (Hispanic), or non-Hispanic White (White). The main outcome was hospitalization among ED patients. Secondary outcomes included mechanical

			ventilation, intensive care unit care, and in-hospital mortality. Descriptive statistics and Poisson regression compared sociodemographics, comorbidities, receipt of remdesivir, receipt of dexamethasone, and outcomes by racial/ethnic groups and geographic region. Results : 94,683 COVID-19 patients presented to the ED. Blacks comprised 26.7% and Hispanics 33.6%. Nearly half (45.1%) of ED patients presented to hospitals in the South. 31.4% (n=29,687) were hospitalized. Lower proportions of Blacks were prescribed dexamethasone (29.4%; n=7,426) compared to Hispanics (40.9%; n=13,021) and Whites (37.5%; n=14,088). Hospitalization risks, compared to Whites, were similar in Blacks (Risk Ratio (RR)=0.94; 95% CI:0.82, 1.08; p=0.4)) and Hispanics RR=0.99 (95% CI:0.81, 1.21; p=0.91), but risk of in-hospital mortality was higher in Blacks, RR=1.18 (95% CI:1.06, 1.31; p=0.002) and Hispanics, RR=1.28 (95% CI: 1.13, 1.44; p < 0.001). Conclusions : Minority patients were overrepresented among COVID-19 ED patients, and while they had similar risks of hospitalization as Whites, in-hospital mortality risk was higher. Interventions targeting upstream social determinants of health are needed to reduce racial/ethnic disparities in COVID-19.
Gallay L et al Clinical Microbiology and Infection https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00156-7/fulltext	14-Day survival among older adults with severe SARS-Cov2 infection treated with corticosteroid: a cohort study	Studio retrospettivo su 267 pazienti anziani (età mediana 86 anni) ricoverati per COVID-19 con insufficienza respiratoria e trattati o meno con steroidi : la mortalità a 14 giorni si riduce significativamente nel gruppo trattato.	Objective : To assess the effectiveness of corticosteroids among older adults with COVID-19 pneumonia requiring oxygen. Methods : We used routine care data from 36 hospitals in France and Luxembourg to assess the effectiveness of corticosteroids at 0.4 mg/kg/day eq. prednisone (treatment group) versus standard of care (control group) among adults ≥ 80 years old with PCR-confirmed SARS-CoV-2 infection or CT-scan images typical of COVID-19 pneumonia, requiring oxygen ≥ 3 L/min, and with an inflammatory syndrome (C-reactive protein ≥ 40 mg/L). The primary

			outcome was overall survival at day 14. In our main analysis, characteristics of patients at baseline (i.e., time when patients met all inclusion criteria) were balanced by using propensity-score inverse probability of treatment weighting. Results : Among the 267 patients included in the analysis, 98 were assigned to the treatment group. Their median age was 86 years (interquartile range 83 to 90), and 95% had a SARS-CoV-2 PCR-confirmed diagnosis. In total, 43/98 (43.9%) patients in the treatment group and 84/166 (50.6%) in the control group died before day 14 (weighted hazard ratio [wHR] 0.67, 95% CI 0.46 to 0.99). The treatment and control groups did not differ significantly for the proportion of patients discharged to home/rehabilitation at day 14 (wRR 1.12, 95% CI 0.68 to 1.82). Twenty-two (16.7%) patients receiving corticosteroids developed adverse events, but only 11 (6.4%) from the control group. Conclusions : Corticosteroids were associated with a significant increase in the overall survival at day 14 of patients aged 80 years and older hospitalised for severe COVID-19.

			 Figure 1 Kaplan Meier curves for survival in the inverse probability of treatment (IPT) sample.
Roubinian NH et al JAMA https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2778371	Incidence of 30-Day Venous Thromboembolism in Adults Tested for SARS-CoV-2 Infection in an Integrated Health Care System in Northern California	Studio degli eventi tromboembolici su oltre 220000 pazienti testati per SARS-CoV-2 in California : a 30 giorni dal primo test, la trombosi venosa profonda è significativamente più frequente negli infetti da SARS-CoV-2 (0.8% contro 0.5%), ma in particolare lo è nei pazienti ospedalizzati, mentre non c'è differenza fra negativi e positivi a domicilio. Gli autori sono dunque contrari alla profilassi antitrombotica per	Hospitalization for COVID-19 is associated with high rates of venous thromboembolism (VTE).1 Whether SARS-CoV-2 infection affects the risk of VTE outside of the hospital setting remains poorly understood. We report on the 30-day incidence of outpatient and hospital-associated VTE following SARS-CoV-2 testing among adult members of the Kaiser Permanente Northern California health plan. Table 2. Incidence of 30-Day Venous Thromboembolism (VTE) Among Participants (n=220 588) by Diagnosis Location and SARS-CoV-2 Status Table 2. Incidence of 30-Day Venous Thromboembolism (VTE) Among Participants (n = 220 588) by Diagnosis Location and SARS-CoV-2 Status No. (rate per 1000 participants) Location / SARS-CoV-2 positive (n = 26 104) / SARS-CoV-2 negative (n = 194 484) / P value[a] All VTE events[b] / 198 (7.6) / 1008 (5.2) / <.001 Outpatient VTE / 47 (1.8) / 434 (2.2) / .16 Hospital-associated VTE / 151 (5.8) / 574 (3.0) / <.001 Inpatient / 125 (4.8) / 352 (1.8) / <.001 Posthospitalization / 26 (1.0) / 222 (1.1) / .51 Viral testing Outpatient / 117 of 24 746 (4.7) / 297 of 182 074 (1.6) / <.001 Inpatient / 81 of 1358 (59.6) / 711 of 12 410 (57.3) / .72 Abbreviation: IQR, interquartile range. [a] χ^2 test. [b] Outpatient, occurring in outpatient or emergency department settings; hospital-associated VTE, occurring during or after hospitalization.

		i pazienti con COVID-19 a domicilio.	
Sermet-Gaudelus I et al Eurosurveillance https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.13.2001782	Prior infection by seasonal coronaviruses, as assessed by serology, does not prevent SARS-CoV-2 infection and disease in children, France, April to June 2020	In uno studio su bambini ospedalizzati per COVID-19 e per altre cause in Francia, la presenza di anticorpi contro i Coronavirus endemici non differisce fra bambini con e senza infezione da SARS-CoV-2 ed eventualmente sindrome infiammatoria multisistemica, il che suggerisce che la pregressa infezione da altri Coronavirus non interferisca con quella da SARS-CoV-2.	Background : Children have a low rate of COVID-19 and secondary severe multisystem inflammatory syndrome (MIS) but present a high prevalence of symptomatic seasonal coronavirus infections. Aim : We tested if prior infections by seasonal coronaviruses (HCoV) NL63, HKU1, 229E or OC43 as assessed by serology, provide cross-protective immunity against SARS-CoV-2 infection. Methods : We set a cross-sectional observational multicentric study in pauci- or asymptomatic children hospitalised in Paris during the first wave for reasons other than COVID (hospitalised children (HOS), n = 739) plus children presenting with MIS (n = 36). SARS-CoV-2 antibodies directed against the nucleoprotein (N) and S1 and S2 domains of the spike (S) proteins were monitored by an in-house luciferase immunoprecipitation system assay. We randomly selected 69 SARS-CoV-2-seropositive patients (including 15 with MIS) and 115 matched SARS-CoV-2-seronegative patients (controls (CTL)). We measured antibodies against SARS-CoV-2 and HCoV as evidence for prior corresponding infections and assessed if SARS-CoV-2 prevalence of infection and levels of antibody responses were shaped by prior seasonal coronavirus infections. Results : Prevalence of HCoV infections were similar in HOS, MIS and CTL groups. Antibody levels against HCoV were not significantly different in the three groups and were not related to the level of SARS-CoV-2 antibodies in the HOS and MIS groups. SARS-CoV-2 antibody profiles were different between HOS and MIS children.

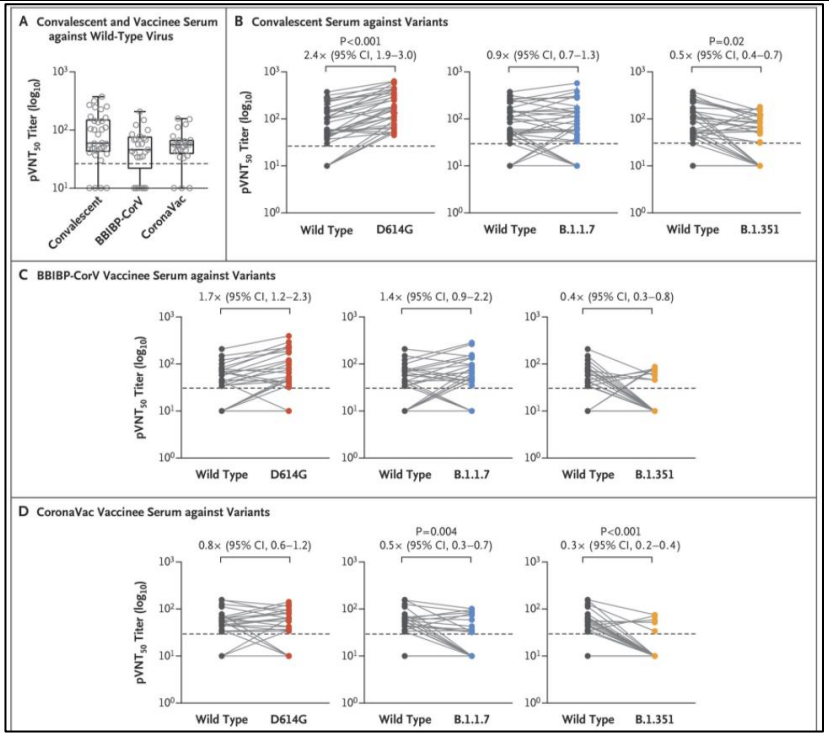
			Conclusion : Prior infection by seasonal coronaviruses, as assessed by serology, does not interfere with SARS-CoV-2 infection and related MIS in children. **Figure 2.** Antibody responses against seasonal HCoV in HOS-P, MIS-P and CTL children, France, April–June 2020 (n=184)  Click to view CTL: SARS-CoV-2-seronegative control group; HCoV: human coronavirus; HOS-P: SARS-CoV-2-seropositive hospitalised patients who did not develop an MIS; MIS-P: SARS-CoV-2-seropositive patients with multisystemic inflammatory syndrome; N: nucleoprotein; NS: non-significant; S: spike. Green: HOS-P; blue: MIS-P; pink: CTL. Antibodies directed against full S ectodomain and N domain are described for each group of patients. The Kruskal-Wallis ANOVA and Dunn's multiple comparisons tests were performed for each antigen considered to compare the level of antibody response between the three groups.
Jentsch PC et al The Lancet https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00057-8/fulltext	Prioritising COVID-19 vaccination in changing social and epidemiological landscapes: a mathematical modelling study	Modello matematico che stima l'effetto di diverse strategie di vaccinazione contro SARS-CoV-2 : prima gli anziani, prima i ragazzi, tutte le fasce d'età oppure sulla base del contact tracing (ovvero vaccinando prima le classi di età che emergono come	Background : During the COVID-19 pandemic, authorities must decide which groups to prioritise for vaccination in a shifting social–epidemiological landscape in which the success of large-scale non-pharmaceutical interventions requires broad social acceptance. We aimed to compare projected COVID-19 mortality under four different strategies for the prioritisation of SARS-CoV-2 vaccines. Methods : We developed a coupled social–epidemiological model of SARS-CoV-2 transmission in which social and epidemiological dynamics interact with one another. We modelled how population

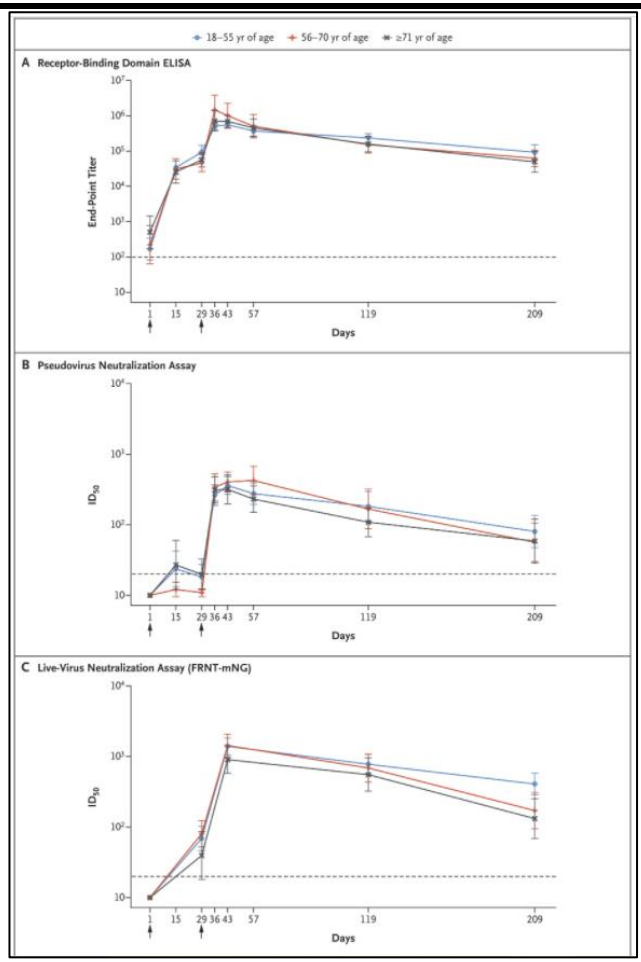
		maggiormente responsabili della trasmissione in base ai dati di contact tracing). L'ultimo modello sembra in grado di impedire un maggior numero di decessi se la vaccinazione inizia tardi nel corso della pandemia, quando questa ha già avuto diverse ondate e non tutta la popolazione è uniformemente suscettibile (come adesso).	adherence to non-pharmaceutical interventions responds to case incidence. In the model, schools and workplaces are also closed and reopened on the basis of reported cases. The model was parameterised with data on COVID-19 cases and mortality, SARS-CoV-2 seroprevalence, population mobility, and demography from Ontario, Canada (population 14·5 million). Disease progression parameters came from the SARS-CoV-2 epidemiological literature. We assumed a vaccine with 75% efficacy against disease and transmissibility. We compared vaccinating those aged 60 years and older first (oldest-first strategy), vaccinating those younger than 20 years first (youngest-first strategy), vaccinating uniformly by age (uniform strategy), and a novel contact-based strategy. The latter three strategies interrupt transmission, whereas the first targets a vulnerable group to reduce disease. Vaccination rates ranged from 0·5% to 5% of the population per week, beginning on either Jan 1 or Sept 1, 2021. Findings : Case notifications, non-pharmaceutical intervention adherence, and lockdown undergo successive waves that interact with the timing of the vaccine programme to determine the relative effectiveness of the four strategies. Transmission-interrupting strategies become relatively more effective with time as herd immunity builds. The model predicts that, in the absence of vaccination, 72 000 deaths (95% credible interval 40 000–122 000) would occur in Ontario from Jan 1, 2021, to March 14, 2025, and at a vaccination rate of 1·5% of the population per week, the oldest-first strategy would reduce COVID-19 mortality by 90·8% on average (followed by 89·5% in the uniform, 88·9% in the contact-based, and 88·2% in the youngest-first strategies). 60 000 deaths (31 000–108 000) would occur from Sept 1, 2021, to March 14, 2025, in the absence of vaccination, and the contact-based strategy would

			reduce COVID-19 mortality by 92·6% on average (followed by 92·1% in the uniform, 91·0% in the oldest-first, and 88·3% in the youngest-first strategies) at a vaccination rate of 1·5% of the population per week. Interpretation : The most effective vaccination strategy for reducing mortality due to COVID-19 depends on the time course of the pandemic in the population. For later vaccination start dates, use of SARS-CoV-2 vaccines to interrupt transmission might prevent more deaths than prioritising vulnerable age groups.
Wadman M Science https://science.sciencemag.org/content/372/6537/13	Pandemic scientists fight burnout	La pandemia di COVID-19 nell'esperienza di medici e accademici, fra sofferto burnout e volontà di continuare a dare il proprio contributo.	From academic research centers to intensive care units (ICUs) to scientific journals to government agencies, scientists fighting the pandemic say they are hitting a wall, 15 months after the first report of a cluster of cases of pneumonia in Wuhan, China, introduced the virus that would upend their lives. "The pace that led to the incredible generation of knowledge on SARS-CoV-2 and COVID-19 has put enormous demands on the people who are expected to generate that knowledge," says David O'Connor, a viral sequencing expert at the University of Wisconsin, Madison, who has been tracking the spread of the virus, doing Zoom Q&A sessions with the vaccine hesitant, and helping neighborhood schools set up diagnostic testing. "This is a terrible time and we should all do what we can to help. But is it going to be sustainable?"
The Lancet Microbe Editorial Board The Lancet	Vaccine certificates: does the end justify the means?	Ancora riflessioni sull'opportunità di introdurre passaporti vaccinali per COVID-19.	As COVID-19 vaccination programmes proceed in many countries, governments worldwide are considering issuing so-called vaccine certificates to facilitate the re-opening of their stumped economies by easing some restrictions for individuals who have been vaccinated against SARS-CoV-2. But are such certificates justified? Are they likely to be useful? And, most importantly, are they fair?

https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(21)00067-7/fulltext			
Schuit M et al The Journal of Infectious Diseases https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiab171/6209391?searchresult=1	The stability of an isolate of the SARS-CoV-2 B.1.1.7 lineage in aerosols is similar to three earlier isolates	La stabilità di isolati di SARS-CoV-2 in aerosol non differisce significativamente fra variante B.1.1.7 (« inglese ») e varianti più antiche, per cui la maggiore trasmissibilità della prima non deriverebbe dalla resistenza agli agenti atmosferici.	Background : Our laboratory previously examined the influence of environmental conditions on the stability of an early isolate of SARS-CoV-2 (hCoV-19/USA/WA-1/2020) in aerosols generated from culture medium or simulated saliva. However, genetic differences have emerged among SARS-CoV-2 lineages, and it is possible that these differences may affect environmental stability and the potential for aerosol transmission. Methods : The influence of temperature, relative humidity, and simulated sunlight on the decay of four SARS-CoV-2 isolates in aerosols, including one belonging to the recently emerged B.1.1.7 lineage, were compared in a rotating drum chamber. Aerosols were generated from simulated respiratory tract lining fluid to represent aerosols originating from the deep lung. Results : No differences in the stability of the isolates were observed in the absence of simulated sunlight at either 20°C or 40°C. However, a small but statistically significant difference in the stability was observed between some isolates in simulated sunlight at 20°C and 20% relative humidity. . Conclusions : The stability of SARS-CoV-2 in aerosols does not vary greatly among currently circulating lineages, including B.1.1.7, suggesting that the increased transmissibility associated with recent SARS-CoV-2 lineages is not due to enhanced survival in the environment.

Wang L et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMc2103022?query=featured_home	Susceptibility of Circulating SARS-CoV-2 Variants to Neutralization	La variante « sudafricana » di SARS-CoV-2 mostra resistenza alla neutralizzazione da parte del siero di soggetti guariti e vaccinati con i vaccini Sinopharm e Corovac sviluppati in Cina rispetto alla variante « inglese » e al virus wild-type.	Our findings suggest that B.1.1.7 showed little resistance to the neutralizing activity of convalescent or vaccinee serum, whereas B.1.351 showed more resistance to the neutralization of both convalescent serum (by a factor of 2) and vaccinee serum (by a factor of 2.5 to 3.3) than the wild-type virus. Most of the vaccinee serum samples that were tested lost neutralizing activity, a finding that was consistent with the results of other recent studies of neutralization by convalescent serum or serum obtained from recipients of messenger RNA or BBIBP-CorV vaccines. Our findings also highlight the importance of sustained viral monitoring and evaluation of the protective efficacy of vaccines in areas where variants are circulating.

			
Doria-Rose N et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMc2103916?query=featured_home	Antibody Persistence through 6 Months after the Second Dose of mRNA-1273 Vaccine for Covid-19	Gli anticorpi contro SARS-CoV-2 stimolati dal vaccino MODERNA persistono a 6 mesi in una coorte di 33 pazienti. I livelli effettivamente associati a una protezione contro l'infezione non sono noti.	We describe mRNA1273-elicited binding and neutralizing antibodies in 33 healthy adult participants in an ongoing phase 1 trial, stratified according to age, at 180 days after the second dose of 100 µg (day 209). Antibody activity remained high in all age groups at day 209.

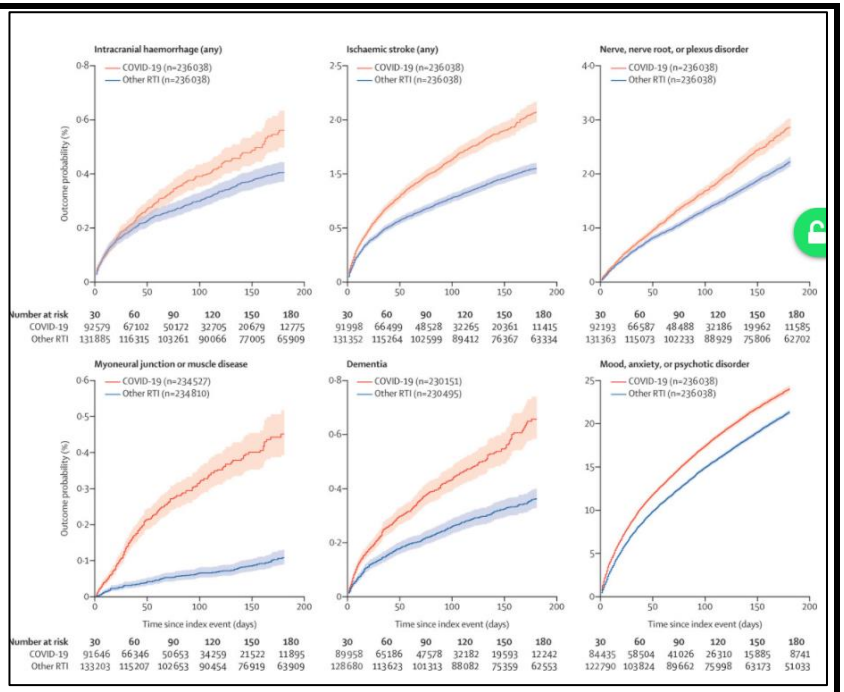
			
Santhosh L et al Chest	“How I Do It: Rapid Design & Implementation of Post-COVID Clinics”	Struttura delle cliniche post-COVID19 della Johns Hopkins e dell’Università della California – San Francisco.	Survivors of COVID-19 are a vulnerable population, with complex needs owing to lingering symptoms and complications across multiple organ systems. Those who required hospitalization or intensive care are also at risk for post-hospital syndrome and post-ICU syndromes, with attendant cognitive, psychological, and physical impairments, and high levels of healthcare utilization.

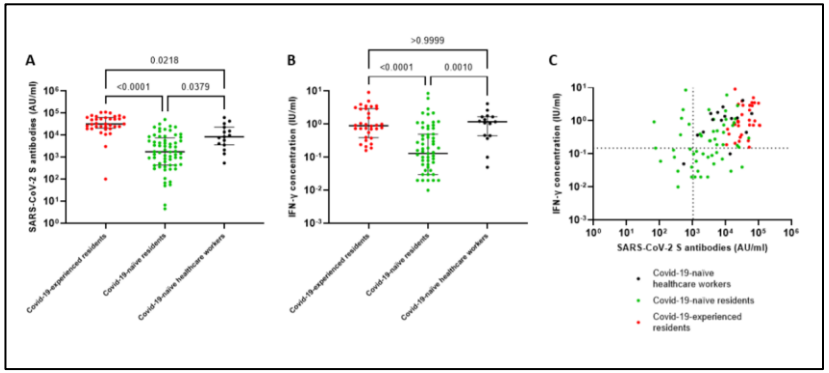
https://journal.chestnet.org/article/S0012-3692(21)00655-3/fulltext			Effective ambulatory care for COVID-19 survivors requires coordination across multiple subspecialties, which can be burdensome if not well-coordinated. With growing recognition of these needs, post-COVID-19 clinics are being created across the country. We describe the design and implementation of multidisciplinary post-COVID-19 clinics at two academic health systems, Johns Hopkins and the University of California-San Francisco. We highlight components of the model which should be replicated across sites, while acknowledging opportunities to tailor offerings to the local institutional context. Our goal is to provide a replicable framework for others to create these much-needed care delivery models for survivors of COVID-19.
European Medicines Agency https://www.ema.europa.eu/en/news/astrazenecas-covid-19-vaccine-ema-finds-possible-link-very-rare-cases-unusual-blood-clots-low-blood	AstraZeneca's COVID-19 vaccine: EMA finds possible link to very rare cases of unusual blood clots with low blood platelets	A seguito della revisione di 62 casi di trombocitopenia con trombosi venosa cerebrale e 24 di trombosi venosa splancnica verificatisi entro 2 settimane dalla somministrazione del vaccino Vaxzevria (Astrazeneca) contro SARS-CoV-2, l'EMA conclude che sia possibile un nesso di causalità fra vaccino e trombosi ma si tratti di un evento avverso così raro (somministrate oltre 25 milioni di dosi tra Unione Europea e Regno Unito) da non superare i benefici della vaccinazione. Inoltre, non vi	EMA's safety committee (PRAC) has concluded today that unusual blood clots with low blood platelets should be listed as very rare side effects of Vaxzevria (formerly COVID-19 Vaccine AstraZeneca). In reaching its conclusion, the committee took into consideration all currently available evidence, including the advice from an ad hoc expert group. EMA is reminding healthcare professionals and people receiving the vaccine to remain aware of the possibility of very rare cases of blood clots combined with low levels of blood platelets occurring within 2 weeks of vaccination. So far, most of the cases reported have occurred in women under 60 years of age within 2 weeks of vaccination. Based on the currently available evidence, specific risk factors have not been confirmed.

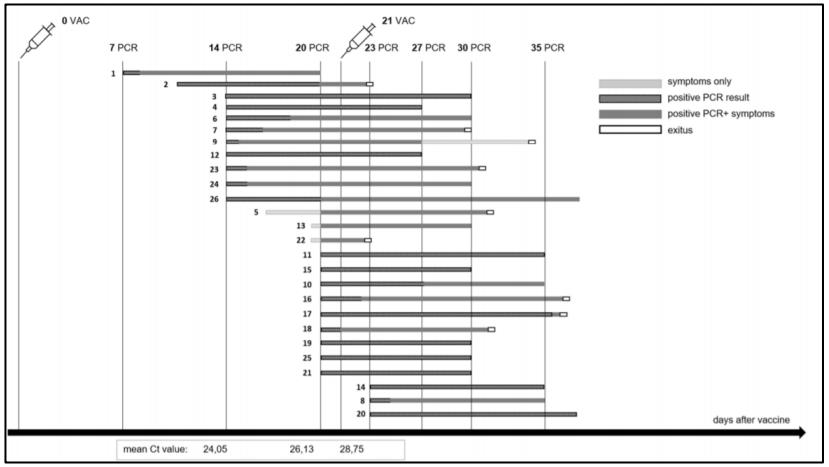
		sono dati sufficienti per controindicare il vaccino in alcune fasce d'età, anche se la trombosi si è verificata prevalentemente in donne di età inferiore a 60 anni.	
Taquet M et al The Lancet https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(21)00084-5/fulltext	6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records	Circa un terzo di oltre 200.000 pazienti con storia di COVID-19 riporta una sequela neurologica o psichiatrica a 6 mesi dalla diagnosi.	Background : Neurological and psychiatric sequelae of COVID-19 have been reported, but more data are needed to adequately assess the effects of COVID-19 on brain health. We aimed to provide robust estimates of incidence rates and relative risks of neurological and psychiatric diagnoses in patients in the 6 months following a COVID-19 diagnosis. Methods : For this retrospective cohort study and time-to-event analysis, we used data obtained from the TriNetX electronic health records network (with over 81 million patients). Our primary cohort comprised patients who had a COVID-19 diagnosis; one matched control cohort included patients diagnosed with influenza, and the other matched control cohort included patients diagnosed with any respiratory tract infection including influenza in the same period. Patients with a diagnosis of COVID-19 or a positive test for SARS-CoV-2 were excluded from the control cohorts. All cohorts included patients older than 10 years who had an index event on or after Jan 20, 2020, and who were still alive on Dec 13, 2020. We estimated the incidence of 14 neurological and psychiatric outcomes in the 6 months after a confirmed diagnosis of COVID-19: intracranial haemorrhage; ischaemic stroke; parkinsonism; Guillain-Barré syndrome; nerve, nerve root, and plexus disorders; myoneural junction and muscle disease; encephalitis; dementia; psychotic, mood, and anxiety disorders (grouped and separately); substance use disorder; and insomnia. Using a Cox model, we compared incidences with those in propensity score-matched cohorts of

			patients with influenza or other respiratory tract infections. We investigated how these estimates were affected by COVID-19 severity, as proxied by hospitalisation, intensive therapy unit (ITU) admission, and encephalopathy (delirium and related disorders). We assessed the robustness of the differences in outcomes between cohorts by repeating the analysis in different scenarios. To provide benchmarking for the incidence and risk of neurological and psychiatric sequelae, we compared our primary cohort with four cohorts of patients diagnosed in the same period with additional index events: skin infection, urolithiasis, fracture of a large bone, and pulmonary embolism. Findings : Among 236 379 patients diagnosed with COVID-19, the estimated incidence of a neurological or psychiatric diagnosis in the following 6 months was 33·62% (95% CI 33·17–34·07), with 12·84% (12·36–13·33) receiving their first such diagnosis. For patients who had been admitted to an ITU, the estimated incidence of a diagnosis was 46·42% (44·78–48·09) and for a first diagnosis was 25·79% (23·50–28·25). Regarding individual diagnoses of the study outcomes, the whole COVID-19 cohort had estimated incidences of 0·56% (0·50–0·63) for intracranial haemorrhage, 2·10% (1·97–2·23) for ischaemic stroke, 0·11% (0·08–0·14) for parkinsonism, 0·67% (0·59–0·75) for dementia, 17·39% (17·04–17·74) for anxiety disorder, and 1·40% (1·30–1·51) for psychotic disorder, among others. In the group with ITU admission, estimated incidences were 2·66% (2·24–3·16) for intracranial haemorrhage, 6·92% (6·17–7·76) for ischaemic stroke, 0·26% (0·15–0·45) for parkinsonism, 1·74% (1·31–2·30) for dementia, 19·15% (17·90–20·48) for anxiety disorder, and 2·77% (2·31–3·33) for psychotic disorder. Most diagnostic categories were more common in patients who had COVID-19 than in those who had influenza (hazard ratio [HR] 1·44,

			95% CI 1·40–1·47, for any diagnosis; 1·78, 1·68–1·89, for any first diagnosis) and those who had other respiratory tract infections (1·16, 1·14–1·17, for any diagnosis; 1·32, 1·27–1·36, for any first diagnosis). As with incidences, HRs were higher in patients who had more severe COVID-19 (eg, those admitted to ITU compared with those who were not: 1·58, 1·50–1·67, for any diagnosis; 2·87, 2·45–3·35, for any first diagnosis). Results were robust to various sensitivity analyses and benchmarking against the four additional index health events. Interpretation : Our study provides evidence for substantial neurological and psychiatric morbidity in the 6 months after COVID-19 infection. Risks were greatest in, but not limited to, patients who had severe COVID-19. This information could help in service planning and identification of research priorities. Complementary study designs, including prospective cohorts, are needed to corroborate and explain these findings.

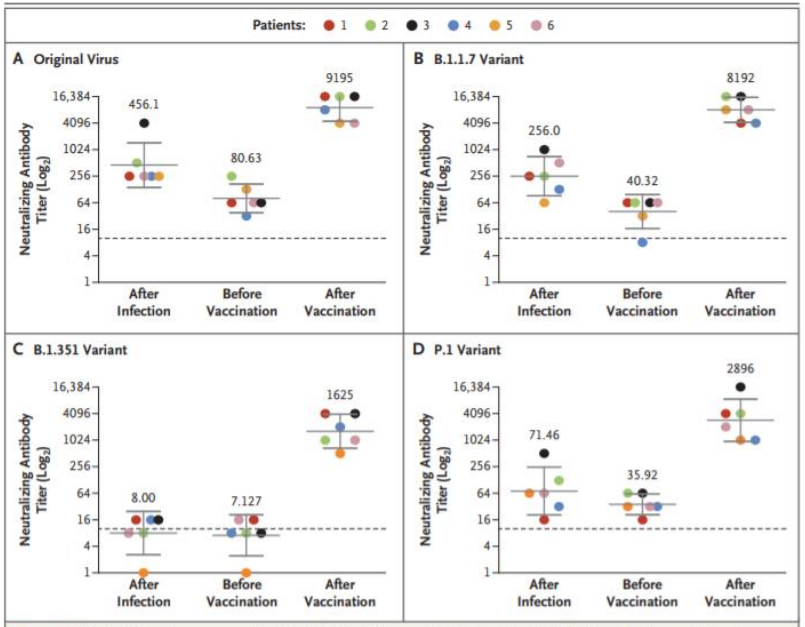
			
Van Praet JT et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab300/6213866?searchresult=1	Humoral and cellular immunogenicity of the BNT162b2 mRNA Covid-19 Vaccine in nursing home residents	Risposta anticorpale e celluare subottimale in 46 anziani residenti in strutture in Belgio e senza storia precedente di COVID-19 a confronto con 15 operatori sanitari, a distanza di quattro settimane dalla prima dose di vaccino Pfizer contro SARS-CoV-2.	One-hundred consecutive residents from 2 Belgian long-term care facilities were studied after vaccination with 2 doses, administered with a 3-week interval. This study was approved by the local institutional review board, and written informed consent was obtained. We determined both humoral (antibodies against the receptor binding domain of S1 subunit of the spike protein, CMIA on Architect-I System from Abbott) and cellular (QuantiFERON SARS-CoV-2 Antigen 2, Qiagen) responses, as current evidence indicates that the immunological correlate of protective immunity requires a balance between neutralizing anti-S antibodies and Th1 responses. COVID-19-experienced and COVID-19-naïve residents were segregated by presence (n=64) or absence (n=46) of antibodies against SARS-CoV-2 nucleocapsid (CMIA on Architect-I System from Abbott), based on the observations by Capetti et al. Fifteen

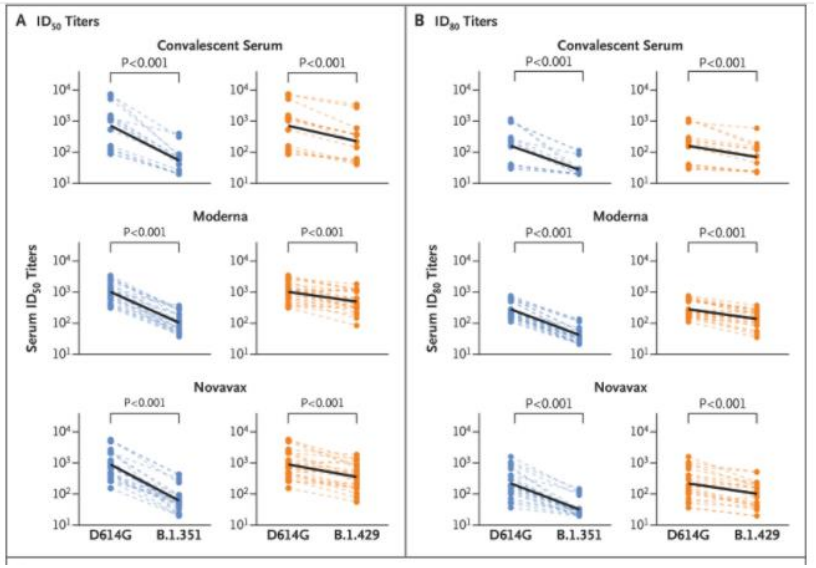
			consecutive healthcare workers without spike antibodies before vaccination were used as controls. 
Westholter D et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab299/6213878?searchresult=1	SARS-CoV-2 outbreak in a long-term care facility after vaccination with BNT162b2	Dopo la prima dose di vaccino Pfizer, un cluster di infezioni da SARS-CoV-2 si è verificato in una casa di riposo per anziani, con casi diagnosticati fino a 23 giorni dal vaccino, a suggerire una scarsa protezione conferita dalla singola dose. Le infezioni hanno avuto esito fatale nel 35% dei casi e il ciclo-soglia medio delle PCR positive è risultato basso, a suggerire un decorso « classico » delle infezioni e non attenuato dal vaccino.	In early January 2021 73/76 (96%) residents and about 90% of the employees received a first dose of BNT162b2. SARS-CoV-2 rapid antigen tests were all negative among residents and participating employees the day before. However, a member of the mobile vaccination team as well as an employee reported respiratory symptoms one and four days after vaccination, respectively and tested positive for SARS-CoV-2 by PCR. Thereupon, local health authorities ordered serial PCR testings of all residents 7, 14, 20, 23, 27, 30 and 35 days after the first vaccination and imposed intensified quarantine measures. A boosting dose of BNT162b2 was offered to all asymptomatic residents 21 days after the first vaccination. The median age of all residents was 88 years and 61/76 (80%) were female. The vaccination itself was not associated with any serious adverse events in this cohort. Serial PCR testings identified SARS-CoV-2 infections in 26/76 (34%) residents. Positive cases were detected 7 days (1), 14 days (10), 20 days (12) and 23 days (3) after the first vaccination. Only 3/26 (12%) residents were symptomatic at the time of diagnosis while 12/26 (46%) positively

			tested residents developed symptoms in the further course. Overall case fatality rate was 9/26 (35%). Of note, 5 of the 9 patients with fatal outcome were diagnosed on day 20 after vaccination. 
Glover RE et al BMJ https://www.bmj.com/content/372/bmj.n120	Vaccinating against covid-19 in people who report allergies	Editoriale sulla vaccinazione contro SARS-CoV-2 in persone con storia di allergie a farmaci : le componenti degne di nota sono il polietilenglicole 2000 nel vaccino Pfizer e il polisorbato 80 in quello AstraZeneca/Vaxzevria, mentre le allergie ad altri farmaci o alimenti non costituiscono una controindicazione.	Importantly, history of severe allergy does not preclude vaccination unless that allergy is to the vaccine or its components. Only one of the excipients in the Pfizer-BioNTech vaccine is a known potential allergen, polyethylene glycol (PEG 2000), and this is an inactive ingredient in over 1000 medications. The Oxford-AstraZeneca vaccine does not contain PEG 2000 so remains an alternative for people with a history of allergy to this ingredient. However, there is some cross-reactivity between PEG and polysorbate 80, an ingredient in the Oxford-AstraZeneca vaccine, so evaluation by an allergy specialist may be advisable before vaccination in anyone with a suspected PEG allergy history.Allergy is antigen specific, although people with one drug allergy may be more susceptible to other drug allergies than the general population.

Eguiluz-Gracia I et al Allergy https://doi.org/10.1111/all.14831	Real-life impact of COVID-19 pandemic lockdown on the management of pediatric and adult asthma: a survey by the EAACI Asthma Section.	Durante la pandemia di COVID-19 il follow-up dei pazienti con asma ha subito una riduzione in termini di visite di persona ed esami strumentali.	BACKGROUND: The restrictions imposed by the COVID-19 pandemic impact heavily the management of chronic diseases like asthma. This study aimed to evaluate the management of adults and children with asthma during COVID-19-related lockdown. METHODS: A survey was launched by the European Academy of Allergy and Clinical Immunology (EAACI) via e-mail, website and social media to EAACI members and members of peer societies. RESULTS: The survey was completed by 339 healthcare professionals from 52 countries. 79% of follow-up consultations were replaced by phone calls, whereas 49% of newly referred patients attended the clinic. 62%, 76%, 66%, 76% and 87% of responders did not conduct spirometry, impulse oscillometry, bronchodilator test, FeNO or methacholine provocation, respectively, for asthma diagnosis in adults. The numbers were similar for children. 73% of responders based the initial asthma diagnosis andthe prescription of inhaled therapy on clinical parameters only. Lung function tests were used in 29% of cases to monitor asthma worsening and only 56% of participantsrecommendedto their patients ambulatory peak expiratory flow (PEF) measurements. Using a 1 (not at all) to 5 (very much) scale, the responders considered that the quality of health care provided and the patients' asthma status had deteriorated during the lockdown with 3.2 points and 2.8 points, respectively. CONCLUSION: Collectively, these results suggest that all necessary resources should be allocated to ensure the performance of lung function tests for initial diagnosis, whereas digital remote monitoring should be reinforced for the follow-up of children and adults with asthma.

Lustig Y et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMc2104036?query=featured_home	Neutralizing Response against Variants after SARS-CoV-2 Infection and One Dose of BNT162b2	A 6 operatrici sanitarie con storia di COVID-19 è stato prelevato siero per eseguire saggi di neutralizzazione anticorpale contro SARS-CoV-2 (varianti « inglese », « sudafriacana » e « brasiliana ») in tre momenti : entro tre mesi dall'infezione, prima del vaccino ed entro due settimane dalla prima dose di vaccino Pfizer. Nell'ultima determinazione, dopo il vaccino, si osserva un significativo aumento dell'attività neutralizzante.	Samples obtained at the first time point had neutralizing activity against the original virus and the B.1.1.7 and P.1 variants, with geometric mean titers of 456, 256, and 71, respectively, but had little or no neutralizing activity against the B.1.351 variant, with a geometric mean titer of 8. At the second time point, geometric mean titers were 81, 40, 36, and 7 for the original virus and the B.1.1.7, P.1, and B.1.351 variants, respectively. Of note, at the third time point, geometric mean titers were 9195, 8192, 2896, and 1625 for the original virus and the B.1.1.7, P.1, and B.1.351 variants, respectively — that is, the titers after vaccination were 114, 203, 81, and 228 times as high as the titers immediately before vaccination (Figure 1 and Table S2).

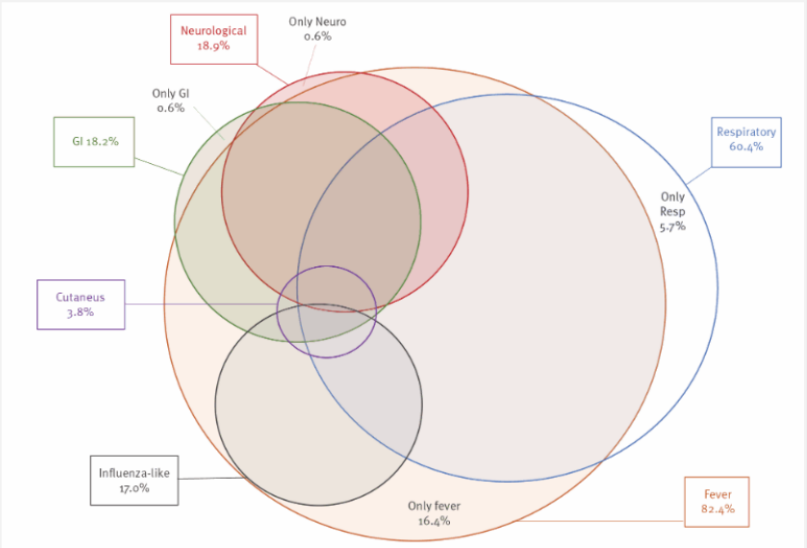
			 **Figure 1. Neutralizing Response against the Original Virus and Variants after SARS-CoV-2 Infection and One Dose of the BNT162b2 Vaccine.** Serum samples from six patients previously infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), obtained 1 to 12 weeks after natural infection, immediately before receiving one dose of the BNT162b2 vaccine, and 1 to 2 weeks after vaccination, were tested with a microneutralization assay for the neutralizing response against sublineage B.1 of the original virus (Panel A), the B.1.1.7 variant first identified in the United Kingdom (Panel B), the B.1.351 variant first identified in South Africa (Panel C), and the P.1 variant first identified in Brazil (Panel D). Dashed lines indicate the cutoff titer. Solid lines and numbers indicate the geometric mean titer, and I bars show the 95% confidence interval.
Shen X et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMc210	Neutralization of SARS-CoV-2 Variants B.1.429 and B.1.351	La variante « californiana » di SARS-CoV-2 viene neutralizzata con piccola riduzione dell'attività da parte del siero di soggetti guariti e vaccinati con vaccini Moderna e Novavax, mentre la « sudafricana » lo	The neutralizing activity of all serum samples was tested against the B.1.429 variant and a variant of concern that first emerged in South Africa (B.1.351, also called 20H/501Y.V2). We compared this neutralizing activity to the activity the serum samples exhibited against the prototypical D614G variant. As compared with the D614G variant, we found that B.1.429 was approximately 2 to 3 times less sensitive to neutralization by convalescent serum and by

3740?query=featured_home		è in misura significativamente minore.	serum samples obtained from vaccinated persons, whereas B.1.351 was approximately 9 to 14 times less sensitive to neutralization. 
Anderson JL et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2778155?resultClick=1	Association of Sociodemographic Factors and Blood Group Type With Risk of COVID-19 in a US Population	Il gruppo AB0 non è associato alla suscettibilità all'infezione da SARS-CoV-2 né alla gravità dell'infezione stessa in questo ampio studio caso-controllo, in contrasto con risultati precedenti (da studi più piccoli).	The observed variability in susceptibility to SARS-CoV-2 and severity of the ensuing COVID-19 have raised intense interest in their environmental and genetic risk factors. An early report from China1 suggested that blood group A was associated with increased susceptibility and blood group O was associated with reduced susceptibility to SARS-CoV-2 infection. These reports motivated widespread interest in examining ABO blood groups as potential COVID-19 risk factors. Subsequent studies from Italy and Spain2 reported that blood group A was associated with an increased risk of severe COVID-19 and blood group O was associated with a reduced risk. In contrast, a large Danish study3 implicated disease susceptibility but not severity. However, observations from Boston, Massachussets,4 and New York, New York,5 did not confirm any

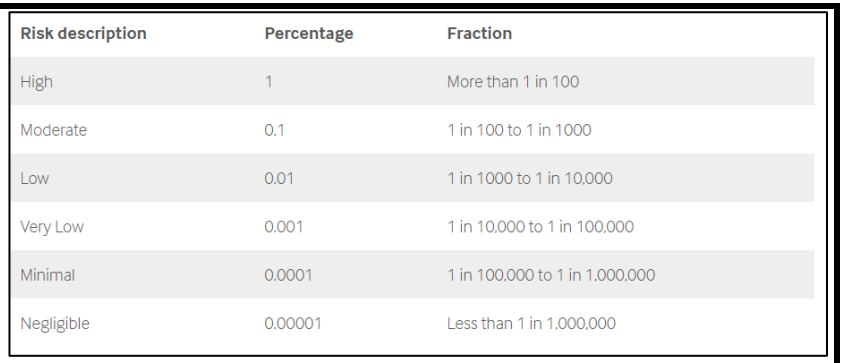
			specific associations between ABO blood group and disease. The controversy raised by these contrasting reports led to this case-control study. **Table 2. Risk of Positive SARS-CoV-2 Test Results, Hospitalization Among Individuals With Positive SARS-CoV-2 Test Results, and ICU Admission Among Patients Hospitalized With COVID-19 by Blood Type[a]** Table 2. Risk of Positive SARS-CoV-2 Test Results, Hospitalization Among Individuals With Positive SARS-CoV-2 Test Results, and ICU Admission Among Patients Hospitalized With COVID-19 by Blood Type[a] | Outcome | Type A vs Type O, OR (95% CI) | *P* value | Type B vs Type O, OR (95% CI) | *P* value | Type AB vs Type O, OR (95% CI) | *P* value | |---|---|---|---|---|---|---| | All individuals | | | | | | | | Positive test results | 0.97 (0.93-1.01) | .11 | 0.96 (0.89-1.03) | .25 | 0.96 (0.86-1.07) | .48 | | Hospitalized | 0.89 (0.80-0.99) | .03 | 0.91 (0.75-1.09) | .30 | 1.02 (0.77-1.35) | .91 | | ICU admission | 0.84 (0.69-1.02) | .08 | 0.89 (0.64-1.23) | .47 | 0.69 (0.40-1.18) | .17 | | White individuals only | | | | | | | | Positive test results | 0.97 (0.93-1.01) | .17 | 0.94 (0.87-1.01) | .10 | 0.94 (0.83-1.07) | .34 | | Hospitalized | 0.88 (0.78-0.99) | .04 | 0.92 (0.74-1.13) | .42 | 0.92 (0.66-1.28) | .63 | | ICU admission | 0.89 (0.71-1.11) | .30 | 0.94 (0.64-1.39) | .76 | 0.81 (0.43-1.53) | .51 | Abbreviations: ICU, intensive care unit; OR, odds ratio. [a] Models were adjusted for age, sex, and Rh factor. Given that each set underwent 9 comparisons, significance for individual comparisons was set at *P* = .006.
Havervall S et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2778528	Symptoms and Functional Impairment Assessed 8 Months After Mild COVID-19 Among Health Care Workers	Persistenza di sintomi a lungo termine dopo infezione lieve da SARS-CoV-2. Gli operatori sanitari sono una popolazione soggetta a « recall bias ».	Approximately 80% of hospitalized patients with COVID-19 report persistent symptoms several months after infection onset.1,2 However, knowledge of long-term outcomes among individuals with mild COVID-19 is scarce, and prevalence data are hampered by selection bias and suboptimal control groups.3,4 This cohort study investigated COVID-19–related long-term symptoms in health care professionals.Symptoms and Functional Impairment Assessed 8 Months After Mild COVID-19 Among Health Care Workers
Park M et al Eurosurveillance https://www.eurosurveillance.org/content/10.2807/1560-	Determining the communicable period of SARS-CoV-2: A rapid review of the literature, March to September 2020	Revisione della letteratura in merito al periodo di contagiosità di individui con COVID-19 :	Introduction : Standard testing for infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is based on RT-PCR tests, but detection of viral genetic material alone does not indicate ongoing infectious potential. The ability to isolate whole virus represents a better proxy for infectivity. Aim : The objective of this study was to gain an understanding of the current literature and compare the reported periods of positive

7917.ES.2021.26.14.2001506			SARS-CoV-2 detection from studies that conducted RT-PCR testing in addition to experiments isolating whole virus. Methods : Using a rapid review approach, studies reporting empirical data on the duration of positive RT-PCR results and/or successful viral isolation following SARS-CoV-2 infection in humans were identified through searches of peer-reviewed and pre-print health sciences literature. Articles were screened for relevance, then data were extracted, analysed, and synthesised. Results : Of the 160 studies included for qualitative analysis, 84% (n = 135) investigated duration of positive RT-PCR tests only, 5% (n = 8) investigated duration of successful viral isolations, while 11% (n = 17) included measurements on both. There was significant heterogeneity in reported data. There was a prolonged time to viral clearance when deduced from RT-PCR tests compared with viral isolations (median: 26 vs 9 days). Discussion : Findings from this review support a minimum 10-day period of isolation but certain cases where virus was isolated after 10 days were identified. Given the extended time to viral clearance from RT-PCR tests, future research should ensure standard reporting of RT-PCR protocols and results to help inform testing policies aimed at clearance from isolation.
Lazzerini M et al Eurosurveillance https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.14.2001248	Characteristics and risk factors for SARS-CoV-2 in children tested in the early phase of the pandemic: a cross-sectional study, Italy, 23 February to 24 May 2020	Erano fattori associati a positività di tampone nasofaringeo per SARS-CoV-2 in bambini e ragazzi fino a 18 anni in Italia nel periodo febbraio-maggio 2020: storia di esposizione a un positivo, febbre, anosmia e ageusia.	Background : Very few studies describe factors associated with COVID-19 diagnosis in children. Aim : We here describe characteristics and risk factors for COVID-19 diagnosis in children tested in 20 paediatric centres across Italy. Methods : We included cases aged 0–18 years tested between 23 February and 24 May 2020. Our primary analysis focused on children tested because of symptoms/signs suggestive of COVID-19. Results : Among 2,494 children tested, 2,148 (86.1%) had symptoms suggestive of COVID-19. Clinical presentation of confirmed COVID-

			19 cases included besides fever (82.4%) and respiratory signs or symptoms (60.4%) also gastrointestinal (18.2%), neurological (18.9%), cutaneous (3.8%) and other unspecific influenza-like presentations (17.8%). In multivariate analysis, factors significantly associated with SARS-CoV-2 positivity were: exposure history (adjusted odds ratio (AOR): 39.83; 95% confidence interval (CI): 17.52–90.55; p < 0.0001), cardiac disease (AOR: 3.10; 95% CI: 1.19–5.02; p < 0.0001), fever (AOR: 3.05%; 95% CI: 1.67–5.58; p = 0.0003) and anosmia/ageusia (AOR: 4.08; 95% CI: 1.69–9.84; p = 0.002). Among 190 (7.6%) children positive for SARS-CoV-2, only four (2.1%) required respiratory support and two (1.1%) were admitted to intensive care; all recovered. Conclusion : Recommendations for SARS-CoV-2 testing in children should consider the evidence of broader clinical features. Exposure history, fever and anosmia/ageusia are strong risk factors in children for positive SARS-CoV-2 testing, while other symptoms did not help discriminate positive from negative individuals. This study confirms that COVID-19 was a mild disease in the general paediatric population in Italy. Further studies are needed to understand risk, clinical spectrum and outcomes of COVID-19 in children with pre-existing conditions.

			Figure 2. Clinical presentation of SARS-CoV-2-positive children, Italy, 23 February–24 May 2020 (n =159)  Click to view GI: gastrointestinal; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.
Agenzia Italiana del Farmaco https://www.aifa.gov.it/-/vaccino-covid-19-astrazeneca-ema-trova-un-possibile-collegamento-con-casi-molto-rari-di-trombi-inusuali-associati-a-bassi-livelli-di-piastrine	Vaccino COVID-19 AstraZeneca: EMA trova un possibile collegamento con casi molto rari di trombi inusuali associati a bassi livelli di piastrine	Comunicato stampa AIFA sul pronunciamento dell'EMA in merito alla associazione fra vaccino Vaxzevria/AstraZeneca contro SARS-CoV-2 e casi di trombosi con trombocitopenia.	L'EMA richiama l'attenzione degli operatori sanitari e delle persone vaccinate affinché siano consapevoli della possibilità che entro 2 settimane dalla vaccinazione si verifichino casi molto rari di trombi associati a bassi livelli di piastrine nel sangue. Finora, la maggior parte dei casi segnalati si è verificata entro 2 settimane dalla vaccinazione in donne di età inferiore a 60 anni. Sulla base delle prove attualmente disponibili, non sono stati confermati i fattori di rischio predisponenti. Le persone vaccinate devono cercare immediata assistenza medica se avvertono sintomi indicativi di problemi di coagulazione e piastrine basse (vedere sezione Informazioni per il pubblico).

Agenzia Italiana del Farmaco https://www.aifa.gov.it/-/covid-19-studio-tsunami-il-plasma-non-riduce-il-rischio-di-peggioramento-respiratorio-o-morte	COVID-19: Studio Tsunami, il plasma non riduce il rischio di peggioramento respiratorio o morte	Comunicato stampa AIFA che anticipa l'esito del trial clinico TSUNAMI sull'utilizzo di plasma di convalescenti per la terapia di COVID-19 : nessun vantaggio in termini di peggioramento respiratorio o mortalità a 30 giorni.	Si è conclusa l'analisi dei dati dello studio clinico randomizzato e controllato chiamato TSUNAMI, promosso da ISS e AIFA e coordinato da ISS, sul ruolo terapeutico del plasma convalescente nei pazienti che hanno sviluppato malattia COVID-19. Lo studio ha confrontato l'effetto del plasma convalescente ad alto titolo di anticorpi neutralizzanti (^{3}1:160), associato alla terapia standard, rispetto alla sola terapia standard in pazienti con COVID-19 e polmonite con compromissione ventilatoria da lieve a moderata (definita da un rapporto PaO2/FiO2 tra 350 e 200). Hanno partecipato allo studio 27 centri clinici distribuiti in tutto il territorio nazionale che hanno arruolato 487 pazienti (di cui 324 in Toscana, 77 in Umbria, 66 in Lombardia e 20 da altre regioni). Le caratteristiche demografiche, le comorbidità esistenti e le terapie concomitanti sono risultate simili nei due gruppi di pazienti, 241 assegnati al trattamento con plasma e terapia standard (231 valutabili), e 246 alla sola terapia standard (239 valutabili). Non è stata osservata una differenza statisticamente significativa nell'end-point primario ("necessità di ventilazione meccanica invasiva, definita da un rapporto tra PaO2/FiO2 < 150, o decesso entro trenta giorni dalla data di randomizzazione") tra il gruppo trattato con plasma e quello trattato con terapia standard.
Elwyn G BMJ Best Practice https://bestpractice.bmj.com/info/toolkit/practise-ebm/understanding-risk/	What is a risk?	Materiale per i pazienti sul significato di rischio relativo e assoluto, con esempi di rischio di eventi della vita quotidiana. Pensiamo tutti al rischio di trombosi con vaccino Vaxzevria/AstraZeneca, che si colloca fra « minimal » e	A risk is the chance that something will happen. For example, if you smoke a packet of cigarettes a day for 30 years, research suggests you have a 10 percent risk of dying from lung cancer.

		« negligible » a seconda delle casistiche.	

Risk description	Percentage	Fraction
High	1	More than 1 in 100
Moderate	0.1	1 in 100 to 1 in 1000
Low	0.01	1 in 1000 to 1 in 10,000
Very Low	0.001	1 in 10,000 to 1 in 100,000
Minimal	0.0001	1 in 100,000 to 1 in 1,000,000
Negligible	0.00001	Less than 1 in 1,000,000

Greinacher A et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2104840?query=featured_home	Thrombotic Thrombocytopenia after ChAdOx1 nCov-19 Vaccination	Versione finale (sul NEJM !) del pre-print già condiviso su una casistica di 11 persone (9 donne, età media 36 anni) con storia di trombosi e trombocitopenia a distanza di 5-16 giorni dal vaccino Vaxzevria/Astrazeneca contro SARS-CoV-2, eventi di cui si ipotizza una genesi simile alla trombocitopenia indotta da eparina (HIT), in questo caso detta « vaccine-induced immune thrombotic thrombocytopenia (VITT) ».	BACKGROUND : Several cases of unusual thrombotic events and thrombocytopenia have developed after vaccination with the recombinant adenoviral vector encoding the spike protein antigen of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (ChAdOx1 nCov-19, AstraZeneca). More data were needed on the pathogenesis of this unusual clotting disorder. METHODS : We assessed the clinical and laboratory features of 11 patients in Germany and Austria in whom thrombosis or thrombocytopenia had developed after vaccination with ChAdOx1 nCov-19. We used a standard enzyme-linked immunosorbent assay to detect platelet factor 4 (PF4)–heparin antibodies and a modified (PF4-enhanced) platelet-activation test to detect platelet-activating antibodies under various reaction conditions. Included in this testing were samples from patients who had blood samples referred for investigation of vaccine-associated thrombotic events, with 28 testing positive on a screening PF4–heparin immunoassay. RESULTS : Of the 11 original patients, 9 were women, with a median age of 36 years (range, 22 to 49). Beginning 5 to 16 days after vaccination, the patients presented with one or more thrombotic events, with the exception of 1 patient, who presented with fatal intracranial hemorrhage. Of the patients with one or more thrombotic events, 9 had cerebral venous thrombosis, 3 had

			splanchnic-vein thrombosis, 3 had pulmonary embolism, and 4 had other thromboses; of these patients, 6 died. Five patients had disseminated intravascular coagulation. None of the patients had received heparin before symptom onset. All 28 patients who tested positive for antibodies against PF4–heparin tested positive on the platelet-activation assay in the presence of PF4 independent of heparin. Platelet activation was inhibited by high levels of heparin, Fc receptor–blocking monoclonal antibody, and immune globulin (10 mg per milliliter). Additional studies with PF4 or PF4–heparin affinity purified antibodies in 2 patients confirmed PF4-dependent platelet activation. CONCLUSIONS : Vaccination with ChAdOx1 nCov-19 can result in the rare development of immune thrombotic thrombocytopenia mediated by platelet-activating antibodies against PF4, which clinically mimics autoimmune heparin-induced thrombocytopenia. **Table 2. Clinical and Laboratory Summary of 11 Patients with Available Clinical Information.*** **Variable** / **Patient Number** 1 2 3 4 5 6 7 8 9 10 11 Platelet nadir (per mm³) 13,000 107,000 60,000 9,000 23,000 75,000 29,000 16,000 13,000 8,000 NA because of death CVT Yes No Yes Yes Yes Yes Yes Yes Yes Yes Pending† Splanchnic-vein thrombosis‡ Yes No No No Yes No No No No Yes No Pulmonary embolism Yes Yes No No Yes No No No No No No Other thrombosis Aortoiliac No No No Right intraventricular, iliofemoral vein, IVC No No Widespread microvascular (brain, lungs, kidneys)§ Multiple organ thrombi§ No Cerebral hemorrhage† Symptom onset (no. of days after vaccination) 5 6 9 7 13 7 8 8 16 11 12¶ INR peak 1.40 1.12 NA 1.66 1.25 1.05 1.34 NA 1.70 NA NA PTT peak (sec) 41.6 29.0 NA 46.6 64.8 23.0 45.0 NA 46.1 NA NA D-dimer peak (mg/liter) 142.0 1.8 13.0 NA NA 2.6 >33.0 NA 21.0 >35.0 NA Fibrinogen nadir (mg/dl) 78 568 NA NA 173 NA 210 NA 40 80 NA PF4–heparin ELISA (optical density) 3.16 3.08 3.50 3.40 1.20 NA NA 2.02 3.51 2.35 2.16 PF4-dependent platelet-activation assay Pos Pos‖ Pos Pos Pos NA NA Pos Pos Pos Pos Heparin treatment Yes LMWH** Unknown Yes Yes Unknown Yes No No No No Other medical condition No No No CND VWD-I; FVL ACL-Abs No No No No No Unknown Outcome Fatal Recovering Unknown Fatal Recovering Recovering Recovering Fatal Fatal Fatal Fatal
Schultz NH et al NEJM	Thrombosis and Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination	Cinque casi clinici di persone (4 donne, età 32-54 anni) vaccinate con Vaxzevria/AstraZeneca contro SARS-CoV-2 che	We report findings in five patients who presented with venous thrombosis and thrombocytopenia 7 to 10 days after receiving the first dose of the ChAdOx1 nCoV-19 adenoviral vector vaccine against coronavirus disease 2019 (Covid-19). The patients were

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<td>hanno sviluppato trombosi venosa cerebrale o splancnica, con riscontro di meccanismo tipo VITT. Tre donne assumevano terapie ormonali estroprogestiniche.</td>
<td>health care workers who were 32 to 54 years of age. All the patients had high levels of antibodies to platelet factor 4–polyanion complexes; however, they had had no previous exposure to heparin. Because the five cases occurred in a population of more than 130,000 vaccinated persons, we propose that they represent a rare vaccine-related variant of spontaneous heparin-induced thrombocytopenia that we refer to as vaccine-induced immune thrombotic thrombocytopenia.

Table 1. Characteristics of the Patients.*

Characteristic	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age — yr	37	42	32	39	54
Sex	Female	Female	Male	Female	Female
Preexisting conditions	Pollen allergy	Pollen allergy	Asthma	None	Hypertension
Medication on admission	Contraceptive pill	Contraceptive vaginal ring	None	None	Hormone-replacement therapy, antihypertensive agents
Time from vaccination to admission — days	8	10	7	10	7
Symptoms	Fever, headaches, visual disturbances	Headaches, drowsiness	Back pain	Headaches, abdominal pain	Headaches, hemiparesis
Location of thrombosis	Cortical veins, left transverse sinus, and sigmoid left sinus	Cortical veins, left transverse sinus, and left sigmoid sinus	Portal vein, left hepatic vein, splenic vein, azygos vein, hemiazygos vein, and several basivertebral veins	Inferior sagittal sinus, vein of Galen, straight sinus, right transverse sinus, and right sigmoid sinus	Cortical veins, superior sagittal sinus, both transverse sinuses, and left sigmoid sinus
Platelet count nadir — per mm^3	22,000	14,000	10,000	70,000	19,000
D-dimer peak — mg/liter	>35	>35	>35	13	>35
INR peak	1.2	1.0	1.1	1.3	1.1
aPTT peak — sec	25	31	25	25	29
Fibrinogen nadir — g/liter†	2.1	0.8	2.3	1.2	1.2
SARS-CoV-2 antibody test results					
Nucleocapsid protein	Negative	Negative	Negative	Negative	Negative
Spike protein	Positive	Positive	Positive	Positive	Positive
Anticoagulation treatment	Initial low dose of LMWH	Reduced dose of LMWH	Reduced dose of LMWH	Reduced dose of LMWH	Heparin (5000 IU)
No. of platelet units transfused	7	19	2	0	2
Other treatment	None	Methylprednisolone (1 mg/kg), IVIG (1 g/kg)	Prednisolone (1 mg/kg), IVIG (1 g/kg)	Prednisolone (1 mg/kg), IVIG (1 g/kg)	Methylprednisolone (1 mg/kg), IVIG (1 g/kg)
Outcome	Fatal	Fatal	Full recovery	Full recovery	Fatal

* The abbreviation aPTT denotes activated partial thromboplastin time, INR international normalized ratio, IVIG intravenous immune globulin, LMWH low-molecular-weight heparin, and SARS-CoV-2 severe acute respiratory syndrome coronavirus 2.
† The reference range used for fibrinogen at Oslo University Hospital is 1.9 to 4.0 g per liter.</td>
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<td>Finelli L et al

JAMA

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2778237?resultClick=1</td>
<td>Mortality Among US Patients Hospitalized With SARS-CoV-2 Infection in 2020</td>
<td>Studio di coorte su oltre 500.000 pazienti ricoverati negli USA per COVID-19 fra marzo e novembre 2020 : si osserva un trend di mortalità in riduzione- Secondo gli autori ciò è solo in parte attribuibile all’età progressivamente più</td>
<td>Importance : Mortality is an important measure of the severity of a pandemic. This study aimed to understand how mortality by age of hospitalized patients who were tested for SARS-CoV-2 has changed over time.
Objective : To evaluate trends in in-hospital mortality among patients who tested positive for SARS-CoV-2.
Design, Setting, and Participants This retrospective cohort study included patients who were hospitalized for at least 1 day at 1 of 209 US acute care hospitals of variable size, in urban and rural</td>
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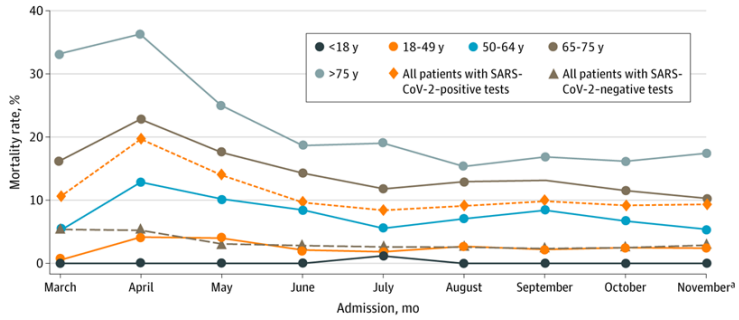
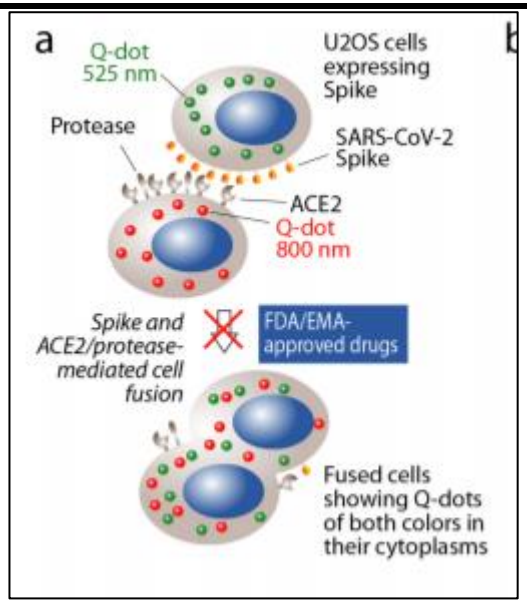
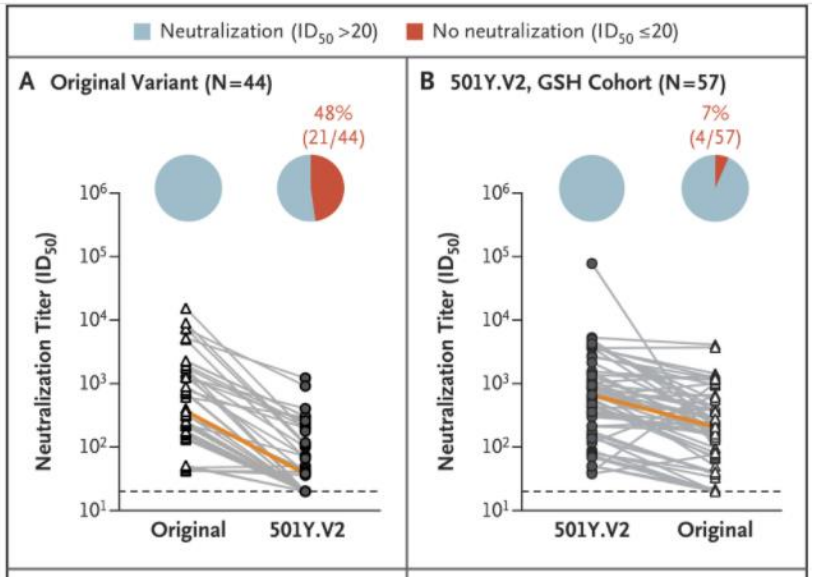
		giovanile delle persone infettate, mentre potrebbero avere un ruolo l'introduzione degli steroidi e la maggiore esperienza nella gestione dell'insufficienza respiratoria da COVID-19.	areas, between March 1 and November 21, 2020. Eligible patients had a SARS-CoV-2 polymerase chain reaction (PCR) or antigen test within 7 days of admission or during hospitalization, and a record of discharge or in-hospital death. Exposure : SARS-CoV-2 positivity. Main Outcomes and Measures : SARS-CoV-2 infection was defined as a positive SARS-CoV-2 PCR or antigen test within 7 days before admission or during hospitalization. Mortality was extracted from electronically available data. Results Among 503 409 admitted patients, 42 604 (8.5%) had SARS-CoV-2–positive tests. Of those with SARS-CoV-2–positive tests, 21 592 (50.7%) were male patients. Hospital admissions among patients with SARS-CoV-2–positive tests were highest in the group aged 65 years or older (19 929 [46.8%]), followed by those aged 50 to 64 years (11 602 [27.2%]) and 18 to 49 years (10 619 [24.9%]). Hospital admissions among patients 18 to 49 years of age increased from 1099 of 5319 (20.7%) in April to 1266 of 4184 (30.3%) in June and 2156 of 7280 (29.6%) in July, briefly exceeding those in the group 50 to 64 years of age (June: 1194 of 4184 [28.5%]; 2039 of 7280 [28.0%]). Patients with SARS-CoV-2–positive tests had higher in-hospital mortality than patients with SARS-CoV-2–negative tests (4705 [11.0%] vs 11 707 of 460 805 [2.5%]; P < .001). In-hospital mortality rates increased with increasing age for both patients with SARS-CoV-2–negative tests and SARS-CoV-2–positive tests. In patients with SARS-CoV-2–negative tests, mortality increased from 45 of 11 255 (0.4%) in those younger than 18 years to 4812 of 107 394 (4.5%) in those older than 75 years. In patients with SARS-CoV-2–positive tests, mortality increased from 1 of 454 (0.2%) of those younger than 18 years to 2149 of 10 287 (20.9%) in those older than 75 years. In-hospital mortality rates among patients with

			SARS-CoV-2–negative tests were similar for male and female patients (6273 of 209 086 [3.0%] vs 5538 of 251 719 [2.2%]) but higher mortality was observed among male patients with SARS-CoV-2–positive tests (2700 of 21 592 [12.5%]) compared with female patients with SARS-CoV-2–positive tests (2016 of 21 012 [9.60%]). Overall, in-hospital mortality increased from March to April (63 of 597 [10.6%] to 1047 of 5319 [19.7%]), then decreased significantly to November (499 of 5350 [9.3%]; P = .04), with significant decreases in the oldest age groups (50-64 years: 197 of 1542 [12.8%] to 73 of 1341 [5.4%]; P = .02; 65-75 years: 269 of 1182 [22.8%] to 137 of 1332 [10.3%]; P = .006; >75 years: 535 of 1479 [36.2%] to 262 of 1505 [17.4%]; P = .03). Conclusions and Relevance : This nationally representative study supported the findings of smaller, regional studies and found that in-hospital mortality declined across all age groups during the period evaluated. Reductions were unlikely because of a higher proportion of younger patients with lower in-hospital mortality in the later period. **Figure 3. In-Hospital Mortality Rates by Month of Admission Among Patients With SARS-CoV-2-Positive and SARS-CoV-2-Negative Tests**  The assessment period was from March 1 to November 21, 2020, and included data from 42 604 patients cared for in 209 hospitals. [a]The November time period extended from November 1 to November 21, 2020.

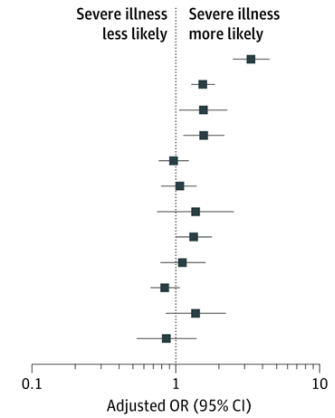
Braga L et al Nature https://www.nature.com/articles/s41586-021-03491-6	Drugs that inhibit TMEM16 proteins block SARS-CoV-2 Spike-induced syncytia	Nei polmoni di 90 pazienti deceduti per COVID-19 si osservano sincizi cellulari di pneumociti ; essi si formerebbero per azione della proteina spike di SARS-CoV-2, con un meccanismo che coinvolge i canali del calcio TMEM16F. Da un punto di vista fisiopatologico, farmaci che blocchino tali canali come la niclosamide, utilizzata nelle infezioni da cestodi, potrebbero contrastare il danno da SARS-CoV-2.	COVID-19 is a disease with unique characteristics including lung thrombosis, frequent diarrhoea, abnormal activation of the inflammatory response and rapid deterioration of lung function consistent with alveolar oedema. The pathological substrate for these findings remains elusive. Here we show that the lungs of patients with COVID-19 contain infected pneumocytes with abnormal morphology and frequent multinucleation. Generation of these syncytia results from activation of the SARS-CoV-2 Spike protein at the cell plasma membrane level. Based on these observations, we performed two high-content microscopy-based screenings with over 3000 approved drugs to search for inhibitors of Spike-driven syncytia. We converged on the identification of 83 drugs that inhibited Spike-mediated cell fusion, several of which belonged to defined pharmacological classes. We focussed our attention on effective drugs that also protected against virus replication and associated cytopathicity. One of the most effective molecules was Niclosamide, which markedly blunted calcium oscillations and membrane conductances in Spike-expressing cells by suppressing the activity of TMEM16F/Anoctamin6, a calcium-activated ion channel and scramblase responsible for phosphatidylserine exposure on the cell surface. These findings suggest a potential mechanism for COVID-19 disease pathogenesis and support the repurposing of Niclosamide for therapy.

			
Moyo-Gwete T et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMc2104192?query=featured_home	Cross-Reactive Neutralizing Antibody Responses Elicited by SARS-CoV-2 501Y.V2 (B.1.351)	La risposta anticorpale di individui con infezione da SARS-CoV-2 variante « sudafricana » neutralizza anche la « brasiliana » e i ceppi più antichi. Dunque un vaccino diretto contro la prima dovrebbe proteggere anche contro le altre.	We characterized the SARS-CoV-2 infections in a cohort of patients with coronavirus disease 2019 (Covid-19) who were hospitalized in the Groote Schuur Hospital, Cape Town (Table S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org), after the emergence and dominance of 501Y.V2 in South Africa. Blood samples were obtained from 89 patients between December 31, 2020, and January 15, 2021; of these patients, 28 (31%) were randomly selected for SARS-CoV-2 sequencing, all of whom were shown by phylogenetic analysis to be infected with 501Y.V2. Furthermore, at this time, the epidemic in Cape Town and in South Africa as a whole was dominated by 501Y.V2, which accounted for more than 90% of infections. No patient in our study reported previous SARS-CoV-2 infection.

			
Siggins MK et al Trends in Microbiology https://www.cell.com/trends/microbiology/fulltext/S0966-842X(21)00092-5	Durability of immunity to SARS-CoV-2 and other respiratory viruses	Una revisione sull'immunità contro SARS-CoV-2, in analogia con quella contro altre infezioni respiratorie.	Even in non-pandemic times, respiratory viruses account for a vast global burden of disease. They remain a major cause of illness and death and pose a perpetual threat of breaking out into epidemics and pandemics. Many of these respiratory viruses infect repeatedly and appear to induce only narrow transient immunity, but the situation varies from one virus to another. In the absence of effective specific treatments, understanding the role of immunity in protection, disease and resolution is of paramount importance. These problems have been brought into sharp focus by the coronavirus COVID-19 pandemic. Here, we summarise what is now known about adaptive immunity to SARS-CoV-2 and draw comparisons with immunity to other respiratory viruses, focusing on the longevity of protective responses.

Hossain MM et al Helyon https://www.cell.com/heliyon/fulltext/S2405-8440(21)00780-5	Prevalence of anxiety and depression in South Asia during COVID-19: A systematic review and meta-analysis	Revisione di studi cross-sectional sulla prevalenza di ansia e depressione nella popolazione dell'Asia meridionale a seguito della pandemia di COVID-19. A questo si aggiunga il sentimento anti-asiatico riportato nello stesso periodo nel mondo occidentale.	Introduction : The COVID-19 pandemic has impacted biopsychosocial health and wellbeing globally. Pre-pandemic studies suggest a high prevalence of common mental disorders, including anxiety and depression in South Asian countries, which may aggravate during this pandemic. This systematic meta-analytic review was conducted to estimate the pooled prevalence of anxiety and depression in South Asian countries during the COVID-19 pandemic. Method : We systematically searched for cross-sectional studies on eight major bibliographic databases and additional sources up to October 12, 2020, that reported the prevalence of anxiety or depression in any of the eight South Asian countries. A random-effects model was used to calculate the pooled proportion of anxiety and depression. Results : A total of 35 studies representing 41,402 participants were included in this review. The pooled prevalence of anxiety in 31 studies with a pooled sample of 28,877 was 41.3% (95% confidence interval [CI]: 34.7–48.1, I2 = 99.18%). Moreover, the pooled prevalence of depression was 34.1% (95% CI: 28.9–39.4, I2 = 99%) among 37,437 participants in 28 studies. Among the South Asian countries, India had a higher number of studies, whereas Bangladesh and Pakistan had a higher pooled prevalence of anxiety and depression. No studies were identified from Afghanistan, Bhutan, and Maldives. Studies in this review had high heterogeneity, high publication bias confirmed by Egger's test, and varying prevalence rates across sub-groups. Conclusion : South Asian countries have high prevalence rates of anxiety and depression, suggesting a heavy psychosocial burden during this pandemic. Clinical and public mental health interventions should be prioritized alongside improving the social

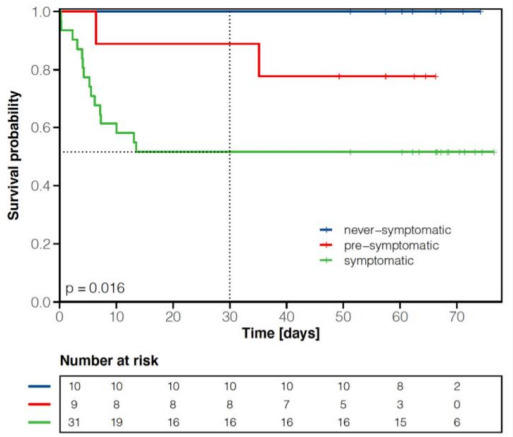
			determinants of mental health in these countries. Lastly, a low number of studies with high heterogeneity requires further research exploring the psychosocial epidemiology during COVID-19, which may inform better mental health policymaking and practice in South Asia.
Preston LE et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2778347	Characteristics and Disease Severity of US Children and Adolescents Diagnosed With COVID-19	Studio di coorte condotto negli USA sulle caratteristiche di oltre 20000 bambini e ragazzi con COVID-19, di cui 2430 ricoverati ; risultano più a rischio di malattia grave i bambini con almeno una condizione cronica, di età inferiore a 11 anni e maschi.	Among 20 714 pediatric patients with COVID-19, 10 950 (52.9%) were girls, 11 153 (53.8%) were aged 12 to 18 years, 8148 (39.3%) were Hispanic or Latino individuals, 5054 (24.4%) were non-Hispanic Black individuals. Among these patients with COVID-19, 6047 (29.2%) had 1 or more chronic conditions. Among the cohort of 2430 pediatric patients (11.7%) who were hospitalized with COVID-19, 756 (31.1%) experienced severe COVID-19. An increased association of severe COVID-19 was observed among patients with 1 or more chronic conditions vs those with none (AOR, 3.27; 95% CI, 2.44-4.37); in children aged 2 through 5 years or 6 through 11 years vs those aged 12 through 18 years (AORs, 1.53; 95% CI, 1.11-2.13 and 1.53; 95% CI, 1.04-2.23, respectively); and in male vs female patients (AOR, 1.52; 95% CI, 1.26-1.83). There was no statistically significant association between race/ethnicity or insurance type and severe COVID-19.

			Figure. Adjusted Odds Ratios (ORs) of Severe COVID-19 Among Hospitalized Patients 18 Years or Younger  An increased association of severe COVID-19 was observed in patients with 1 or more chronic conditions vs those with none, in male vs female patients, and in children aged 2 through 5 years or 6 through 11 years vs children aged 12 through 18 years. An increased association was also found in male vs female patients. Non-Hispanic Black and Hispanic or Latino children with COVID-19 were overrepresented compared with all pediatric patients in the Premier Healthcare Database Special COVID-19 Release. [a]The reference group is patients aged 12 to 18 years.
Langford BJ et al Clinical Microbiology and Infection https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30778-3/fulltext?dgcid=raven_jbs_etoc_email	Antibiotic prescribing in patients with COVID-19: rapid review and meta-analysis	In questa revisione sistematica di 154 studi, oltre il 74% dei pazienti con COVID-19 ha ricevuto almeno un antibiotico nel corso della malattia, mentre la prevalenza di co-infezioni batteriche sarebbe dell'8%.	Background : The proportion of patients infected with SARS-CoV-2 that are prescribed antibiotics is uncertain, and may contribute to patient harm and global antibiotic resistance. Objective : The aim was to estimate the prevalence and associated factors of antibiotic prescribing in patients with COVID-19. Data Sources : We searched MEDLINE, OVID Epub and EMBASE for published literature on human subjects in English up to June 9 2020. Study Eligibility Criteria We included randomized controlled trials; cohort studies; case series with ≥10 patients; and experimental or observational design that evaluated antibiotic prescribing. Participants : The study participants were patients with laboratory-confirmed SARS-CoV-2 infection, across all healthcare settings (hospital and community) and age groups (paediatric and adult). Methods : The main outcome of interest was proportion of COVID-19 patients prescribed an antibiotic, stratified by geographical

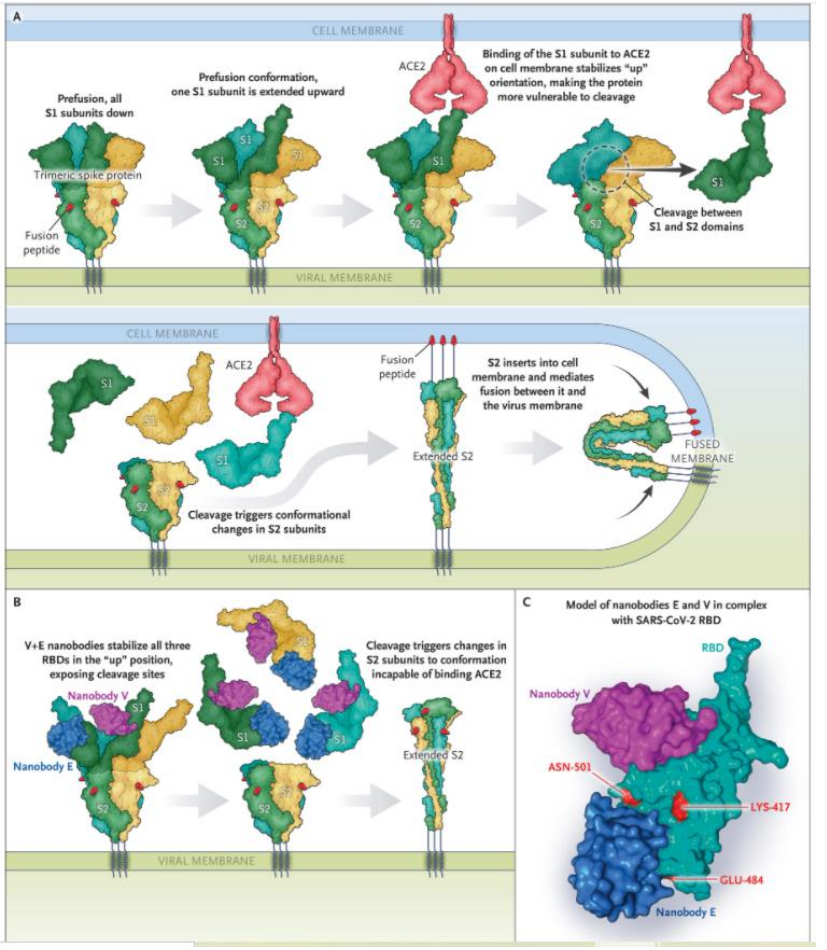
			region, severity of illness and age. We pooled proportion data using random effects meta-analysis. Results : We screened 7469 studies, from which 154 were included in the final analysis. Antibiotic data were available from 30 623 patients. The prevalence of antibiotic prescribing was 74.6% (95% CI 68.3–80.0%). On univariable meta-regression, antibiotic prescribing was lower in children (prescribing prevalence odds ratio (OR) 0.10, 95% CI 0.03–0.33) compared with adults. Antibiotic prescribing was higher with increasing patient age (OR 1.45 per 10 year increase, 95% CI 1.18–1.77) and higher with increasing proportion of patients requiring mechanical ventilation (OR 1.33 per 10% increase, 95% CI 1.15–1.54). Estimated bacterial co-infection was 8.6% (95% CI 4.7–15.2%) from 31 studies. Conclusions : Three-quarters of patients with COVID-19 receive antibiotics, prescribing is significantly higher than the estimated prevalence of bacterial co-infection. Unnecessary antibiotic use is likely to be high in patients with COVID-19.
Fauci AS et al Science https://science.sciencemag.org/content/372/6538/109	The story behind COVID-19 vaccines	La storia dei vaccini contro SARS-CoV-2 raccontata da Tony Fauci, che lancia un monito sull'importanza della ricerca scientifica : non si sa mai quando una scoperta possa tornare utile.	SARS-CoV-2 vaccines based on the new immunogen rapidly moved to clinical trials. Several of these vaccines were tested in phase 3 efficacy trials at a time when the level of community spread of SARS-CoV-2 was extremely high, allowing vaccine efficacy endpoints of greater than 90% to be reached in a timely fashion. The speed and efficiency with which these highly efficacious vaccines were developed and their potential for saving millions of lives are due to an extraordinary multidisciplinary effort involving basic, preclinical, and clinical science that had been under way—out of the spotlight—for decades before the unfolding of the COVID-19 pandemic. When the stories and recounting of this pandemic are written, it is important that this history not be forgotten, as we are

			reminded once again of the societal value of a sustained and robust support of our scientific enterprise.
Sami S et al Morbidity and Mortality Weekly Report https://doi.org/10.15585/mmwr.mm7014e3	Community Transmission of SARS-CoV-2 Associated with a Local Bar Opening Event - Illinois, February 2021.	L'inaugurazione di un bar al chiuso in Illinois (41–42 infezioni da SARS-CoV-2 per 100,000 persone al momento dei fatti) è stata collegata a un cluster di 46 casi di COVID-19 : i casi indice sarebbero state 4 persone sintomatiche che hanno partecipato all'evento. L'isolamento preventivo e responsabile dei sintomatici e l'applicazione dei dispositivi di protezione sono ancora necessari nelle comunità in cui il virus circola.	During February 2021, an opening event was held indoors at a rural Illinois bar that accommodates approximately 100 persons. The Illinois Department of Public Health (IDPH) and local health department staff members investigated a COVID-19 outbreak associated with this opening event. Overall, 46 COVID-19 cases were linked to the event, including cases in 26 patrons and three staff members who attended the opening event and 17 secondary cases. Four persons with cases had COVID-19-like symptoms on the same day they attended the event. Secondary cases included 12 cases in eight households with children, two on a school sports team, and three in a long-term care facility (LTCF). Transmission associated with the opening event resulted in one school closure affecting 650 children (9,100 lost person-days of school) and hospitalization of one LTCF resident with COVID-19. These findings demonstrate that opening up settings such as bars, where mask wearing and physical distancing are challenging, can increase the risk for community transmission of SARS-CoV-2, the virus that causes COVID-19. As community businesses begin to reopen, a multicomponent approach should be emphasized in settings such as bars to prevent transmission. This includes enforcing consistent and correct mask use, maintaining >/=6 ft of physical distance between persons, reducing indoor bar occupancy, prioritizing outdoor seating, improving building ventilation, and promoting behaviors such as staying at home when ill, as well as implementing contact tracing in combination with isolation and quarantine when COVID-19 cases are diagnosed.

Huemer F et al Geroscience https://www.ncbi.nlm.nih.gov/research/coronaviruses/publication/33837912	Results of a hospitalization policy of asymptomatic and pre-symptomatic COVID-19-positive long-term care facility residents in the province of Salzburg-a report from the AGMT COVID-19 Registry.	Studio osservazionale su 50 persone provenienti da casa di riposo e ospedalizzate alla diagnosi di infezione da SARS-CoV-2, indipendentemente dai sintomi (poi dimesse con due tamponi consecutivi negativi) : la mortalità e significativamente maggiore fra coloro che erano sintomatici al momento del ricovero, rispetto agli asintomatici e ai pre-sintomatici (che hanno sviluppato sintomi durante la degenza) ; per questo motivo non sarebbe vantaggioso ricoverare gli anziani in assenza di sintomi.	COVID-19-associated case fatality rates up to 48% were reported among nursing facility residents. During the first wave of the COVID-19 pandemic, routine SARS-CoV-2 testing in long-term care facilities in the Province of Salzburg and centralized hospitalization in the COVID-19 unit of the Paracelsus Medical University Salzburg (Austria) irrespective of symptoms was implemented. Baseline characteristics and the course of COVID-19 disease were assessed among hospitalized long-term care facility residents within the COVID-19 Registry of the Austrian Group Medical Tumor Therapy (AGMT; NCT04351529). Between the 24(th) of March and the 20(th) of April 2020, 50 COVID-19-positive residents were hospitalized. The median age was 84.5 years (range: 79-88) and the median number of comorbidities and baseline medication classes was 6 (IQR: 4-7) and 5 (IQR: 3-6), respectively. At admission, 31 residents (62%) were symptomatic, nine residents (18%) pre-symptomatic whereas ten residents (20%) remained asymptomatic. The 30-day mortality rate from hospitalization was 32% and significantly higher in symptomatic residents at admission when compared to asymptomatic residents including pre-symptomatic residents (48% [95% CI: 27-63%] versus 5% [95% CI: 0-15%], p=0.006). The Early Warning Score (EWS) at admission was associated with 30-day mortality: high risk: 100%, intermediate risk: 50% (95% CI: 0-78%), and low risk: 21% (95% CI: 7-32%) (p<0.001). In light of comparably low mortality rates between asymptomatic and pre-symptomatic hospitalized COVID-19-positive residents, we suggest the supply of comparable intensity and quality of monitoring and care in long-term care facilities as an alternative to immediate hospitalization upon a positive COVID-19 test in asymptomatic residents.

			Fig. 5 Overall survival according to COVID-19 symptoms during the course of disease among 50 long-term care facility residents. *y*-axis: survival probability, *x*-axis: time in days from admission. Tick marks on the curves represent censored patients; dashed vertical line depicts 30-day cut-off 
Ming Z et al Nature Communications https://doi.org/10.1038/s41467-021-22297-8	GCG inhibits SARS-CoV-2 replication by disrupting the liquid phase condensation of its nucleocapsid protein.	L'assemblaggio della proteina N (nucleocapside) dei Coronavirus, fra cui SARS-CoV-2, con l'RNA virale dipende dal processo detto di « separazione di fase liquido-liquido » : inibitori di questo processo, come l'antiossidante allocatechina gallato, hanno una teorica attività di contrasto alla replicazione virale.	Lack of detailed knowledge of SARS-CoV-2 infection has been hampering the development of treatments for coronavirus disease 2019 (COVID-19). Here, we report that RNA triggers the liquid-liquid phase separation (LLPS) of the SARS-CoV-2 nucleocapsid protein, N. By analyzing all 29 proteins of SARS-CoV-2, we find that only N is predicted as an LLPS protein. We further confirm the LLPS of N during SARS-CoV-2 infection. Among the 100,849 genome variants of SARS-CoV-2 in the GISAID database, we identify that ~37% (36,941) of the genomes contain a specific trio-nucleotide polymorphism (GGG-to-AAC) in the coding sequence of N, which leads to the amino acid substitutions, R203K/G204R. Interestingly, N(R203K/G204R) exhibits a higher propensity to undergo LLPS and a greater effect on IFN inhibition. By screening the chemicals known to interfere with N-RNA binding in other viruses, we find that (-)-gallocatechin gallate (GCG), a polyphenol from green tea, disrupts the LLPS of N and inhibits SARS-CoV-2 replication. Thus, our study reveals that targeting N-RNA condensation with GCG could be a potential treatment for COVID-19.

Sasisekharan R NEJM https://www.nejm.org/doi/full/10.1056/NEJMcibr2101205?query=featured_home	Preparing for the Future — Nanobodies for Covid-19?	Commento a un lavoro già presentato (Koenig et al, Science https://pubmed.ncbi.nlm.nih.gov/33436526/)sull'utilizzo di nanoparticelle in grado di modificare la conformazione della proteina spike di SARS-CoV-2 rendendola incapace di legare il recettore cellulare ACE-2 : si tratterebbe di farmaci più facili da produrre e adattare alle varianti del virus rispetto agli anticorpi monoclonali.	Although nanobodies are under clinical investigation for use in a wide range of diseases from cancer to infectious diseases, it was the approval of caplacizumab (an anti–von Willebrand factor bivalent nanobody) by the European Medicines Agency and the FDA for the treatment of thrombotic thrombocytopenic purpura and thrombosis that marked the foray of nanobodies into clinical medicine. The format of the biparatopic nanobody V+E engineered by Koenig et al., although distinct from that of a conventional nanobody, is similar to that of the FDA-approved single-chain, variable fragment–based bispecific antibody blinatumomab (Figure 2). All things considered, the available structural and clinical data suggest that the biparatopic antibody could potentially offer a better alternative to conventional monoclonal antibodies for the treatment of Covid-19.

			
MCMahon DE et al Journal of the American Academy of Dermatology https://doi.org/10.1016/j.jaad.2021.03.092	Cutaneous Reactions Reported after Moderna and Pfizer COVID-19 Vaccination: A Registry-Based Study of 414 Cases.	Registo di 414 reazioni avverse cutanee ai vaccini a mRNA contro SARS-CoV-2, di cui meno della metà ricorrenti dopo la prim dose: importante conoscerle per rassicurare i pazienti.	BACKGROUND: Cutaneous reactions after mRNA-based COVID-19 vaccines have been reported but are not well characterized. OBJECTIVE: To evaluate morphology and timing of cutaneous reactions after mRNA COVID-19 vaccines. METHODS: A provider-facing registry-based study collected cases of cutaneous manifestations after COVID-19 vaccination.

			RESULTS: From December 2020-February 2021, we recorded 414 cutaneous reactions to mRNA COVID-19 vaccines from Moderna (83%) and Pfizer (17%). Delayed large local reactions were most common, followed by local injection site reactions, urticarial eruptions, and morbilliform eruptions. Forty-three percent of patients with first dose reactions experienced second dose recurrence. LIMITATIONS: Registry analysis does not measure incidence. Morphologic misclassification is possible. CONCLUSION: We report a spectrum of cutaneous reactions after COVID-19 mRNA vaccines. Most patients with first dose reactions did not develop a second dose reaction, and no patients in the registry developed serious adverse events after the first or second dose. These data provide reassurance to patients and providers.