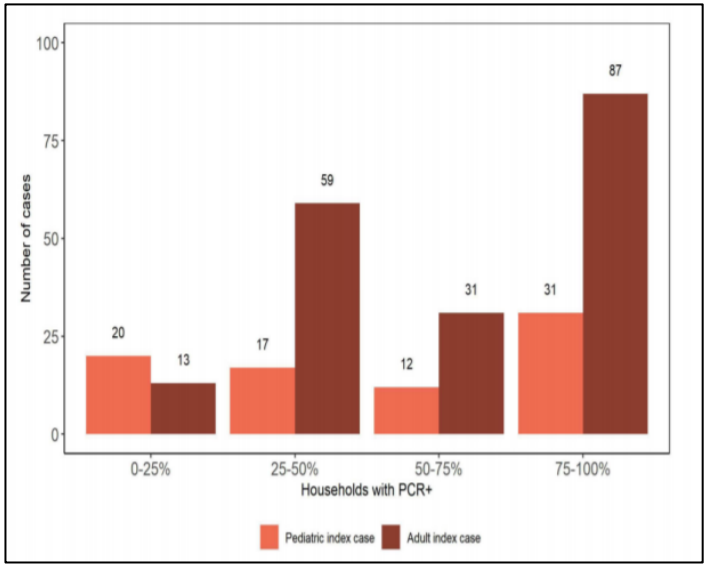
RICERCA BIBLIOGRAFICA COVID 19 SETTIMANA 15.03 – 21.03.2021 FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE DOTT.SSA ELEONORA TADDEI			
AUTORE/RIVISTA	**TITOLO**	**OUTCOME PRINCIPALE**	**ABSTRACT**
Bauer G et al International Journal of Infectious Diseaeses https://doi.org/10.1016/j.ijid.2021.01.061	The potential significance of high avidity IgG for protective immunity towards SARS-CoV-2.	Proposta di introduzione dei test di avidità (forza di legame tra antigene e anticorpo) per gli anticorpi anti-SARS-CoV-2 per definire la qualità della risposta ai vaccini.	BACKGROUND: Avidity is defined as the strength of binding between IgG and its specific target epitope. IgG of high avidity is established during affinity maturation. A failure to achieve high avidity IgG may result in the lack of protective immunity towards infection and disease. It is known that the interaction between SARS-CoV-2 spike protein and its cellular receptor is driven by high affinity. Therefore it is predictable that protective antibodies towards SARS-CoV-2 should show high affinity/avidity. AVIDITY AFTER SARS-COV-2 INFECTION: Recent findings by several groups demonstrate that the serological response towards infection with SARS-CoV-2 as well as with seasonal coronaviruses is characterized by incomplete avidity maturation, followed by a decline of the serological response. This might facilitate reinfection, prevent herd immunity and potentially allow repeated cycles of infection. CONSEQUENCES FOR VACCINATION TOWARDS SARS-COV-2: Therefore, the sole focus on antibody titers reached after

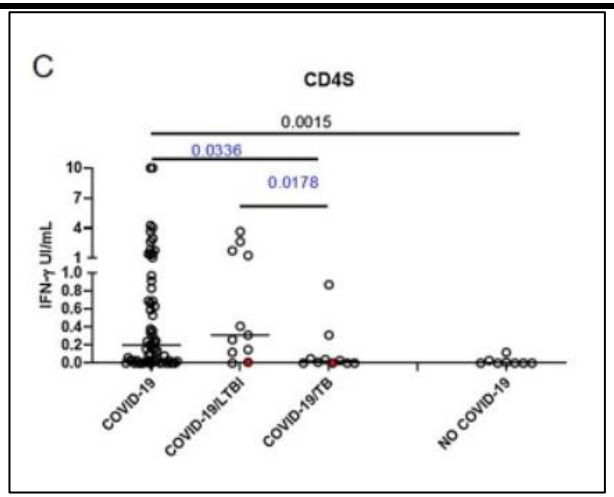
			vaccination towards SARS-CoV-2 might not be sufficient to evaluate the degree of achieved protection. Rather, it is suggested to include avidity determination into the optimization of vaccination protocols and to try to achieve high avidity IgG directed towards SARS-CoV-2 through vaccination. Avidity determination also might be useful to control for truly protective immunity towards SARS-CoV-2 in individual cases.
Soriano – Arandes A et al Clinical Infectious Diseases https://doi.org/10.1093/cid/ciab228	Household SARS-CoV-2 transmission and children: a network prospective study.	Studio osservazionale su 1040 bambini e ragazzi con COVID-19 e sui loro contatti familiari: circa la metà è asintomatico e solo il 7.7% dei bambini viene considerato caso indice della propria famiglia (sulla base della datazione riferita dei sintomi), per cui gli autori concludono che i bambini non siano una significativa fonte di cluster.	BACKGROUND: The role of children in household transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) remains uncertain. Here, we describe the epidemiological and clinical characteristics of children with COVID-19 in Catalonia (Spain) and investigate the dynamics of household transmission. METHODS: Prospective, observational, multicenter study performed during summer and school periods (1 July-31 October, 2020), in which epidemiological and clinical features, and viral transmission dynamics were analyzed in COVID-19 patients <16 years. A pediatric index case was established when a child was the first individual infected within a household. Secondary cases were defined when another household member tested positive for SARS-CoV-2 before the child. The secondary attack rate (SAR) was calculated, and logistic regression was used to assess associations between transmission risk factors and SARS-CoV-2 infections. RESULTS: The study included 1040 COVID-19 patients <16 years. Almost half (47.2%) were asymptomatic, 10.8% had comorbidities, and 2.6% required hospitalization. No deaths were reported. Viral transmission was common among household members (62.3%). More than 70% (756/1040) of pediatric cases were secondary to an adult, whereas 7.7% (80/1040) were index cases. The SAR was significantly lower in households with COVID-19 pediatric index cases during the school period relative to summer (p=0.02), and

			when compared to adults (p=0.006). No individual or environmental risk factors associated with the SAR were identified. CONCLUSIONS: Children are unlikely to cause household COVID-19 clusters or be major drivers of the pandemic even if attending school. Interventions aimed at children are expected to have a small impact on reducing SARS-CoV-2 transmission. 
Jordan I et al Clinical Infectious Diseases https://doi.org/10.1093/cid/ciab227	Transmission of SARS-CoV-2 infection among children in summer schools applying stringent control measures in Barcelona, Spain.	I casi secondari agli individui contagiati da COVID-19 in una scuola estiva di Barcellona sono inferiori rispetto all'atteso nella popolazione generale della stessa area, grazie alle misure di screening e contenimento applicate. Gli autori concludono che con le adeguate precauzioni le	BACKGROUND: Understanding the role of children in SARS-CoV-2 transmission is critical to guide decision-making for schools in the pandemic. We aimed to describe the transmission of SARS-CoV-2 among children and adult staff in summer schools. METHODS: During July 2020 we prospectively recruited children and adult staff attending summer schools in Barcelona who had SARS-CoV-2 infection. Primary SARS-CoV-2 infections were identified through: (1) surveillance program in 22 summer schools' of 1905 participants, involving weekly saliva sampling for SARS-CoV-2 RT-PCR during 2-5 weeks; (2)cases identified through the Catalonian

		scuole possano funzionare senza rischi aggiuntivi per la comunità.	Health Surveillance System of children diagnosed with SARS-CoV-2 infection by nasopharyngeal RT-PCR. All centres followed prevention protocols: bubble groups, hand washing, facemasks and conducting activities mostly outdoors. Contacts of a primary case within the same bubble were evaluated by nasopharyngeal RT-PCR. Secondary attack rates and effective reproduction number in summer schools(R*) were calculated. RESULTS: Among the over 2000 repeatedly screened participants, 30children and 9adults were identified as primary cases. A total of 253 close contacts of these primary cases were studied (median 9 (IQR 5-10) for each primary case), among which twelve new cases (4.7%) were positive for SARS-CoV-2. The R* was 0.3, whereas the contemporary rate in the general population from the same areas in Barcelona was 1.9. CONCLUSIONS: The transmission rate of SARS-CoV-2 infection among children attending school-like facilities under strict prevention measures was lower than that reported for the general population. This suggests that under preventive measures schools are unlikely amplifiers of SARS-CoV-2 transmission and supports current recommendations for school opening.
Jimenez-Soto R et al Thrombosis Research https://www.thrombosisresearch.com/article/S004	The impact of different prophylactic anticoagulation doses on the outcomes of patients with COVID-19	Studio osservazionale retrospettivo su 321 pazienti ricoverati per COVID-19 e trattati con eparina a basso peso molecolare a dosaggio profilattico, profilattico aumentato (0.5 mg/Kg bid o 4000 UI bid) oppure terapeutico (1 mg/Kg bid) : gli eventi emorragici, anche	We conducted a study to determine if intermediate and formal anticoagulation were associated with a lower risk of death. From March 12th to July 15th, 2020 we collected information on clinical, biochemical and imaging variables from patients admitted at the ABC Medical Center, a private hospital in Mexico City, as part of the ARMII cohort. We included patients who were 18 years or older and had a diagnosis of COVID-19, defined as a positive PCR for SARS-CoV2 and/or a chest CT scan with characteristic findings and who received thromboprophylaxis with enoxaparin since admission. We excluded patients receiving anticoagulation prior to admission and

9-3848(21)00086-4/fulltext		se molto rari, sono più frequenti in caso di dosaggio terapeutico, mentre non si riesce a dimostrare un beneficio su embolia polmonare o mortalità.	those who received other anticoagulants. The study was approved by local scientific and ethics committees.
Gallastegui N et al Clinical and Applied Thrombosis and Hemostasis https://journals.sagepub.com/doi/10.1177/1076029621996471	Pulmonary Embolism Does Not Have an Unusually High Incidence Among Hospitalized COVID19 Patients.	Revisione sistematica della letteratura in merito all'incidenza di embolia polmonare nei pazienti ricoverati per COVID-19, in cui si osserva una percentuale di casi inferiore rispetto ai primi report di inizio pandemia. Gli autori ritengono che le stime iniziali, su piccole casistiche, fossero alterate in eccesso.	INTRODUCTION: Acute respiratory illnesses from COVID19 infection are increasing globally. Reports from earlier in the pandemic suggested that patients hospitalized for COVID19 are at particularly high risk for pulmonary embolism (PE). To estimate the incidences of PE during hospitalization for COVID19, we performed a rigorous systematic review of published literature. METHODS: We searched for case series, cohort studies and clinical trials from December 1, 2019 to July 13, 2020 that reported the incidence of PE among consecutive patients who were hospitalized for COVID19 in ICUs and in non-ICU hospital wards. To reflect the general population of hospitalized COVID19 patients, we excluded studies in which subject enrollment was linked to the clinical suspicion for venous thromboembolism (VTE). RESULTS: Fifty-seven studies were included in the analysis. The combined random effects estimate of PE incidence among all hospitalized COVID19 patients was 7.1% (95% CI: 5.2%, 9.1%). Studies with larger sample sizes reported significantly lower PE incidences than smaller studies (r(2) = 0.161, p = 0.036). The PE incidence among studies that included 400 or more patients was 3.0% (95% CI: 1.7%, 4.6%). Among COVID19 patients admitted to ICUs, the combined estimated PE incidence was 13.7% (95% CI: 8.0%, 20.6%). The incidence of ICU-related PE also decreased as the study sample sizes increased. The single largest COVID19 ICU study (n = 2215) disclosed a PE incidence of 2.3% (95% CI: 1.7%, 3.0%).

			CONCLUSION: PE incidences among hospitalized COVID19 patients are much lower than has been previously postulated based on smaller, often biased study reports. The incidence of "microthrombosis," leading to occlusion of microscopic blood vessels, remains unknown.
Petrone L et al International Journal of Infectious Diseases https://doi.org/10.1016/j.ijid.2021.02.090	Coinfection of tuberculosis and COVID-19 limits the ability to in vitro respond to SARS-CoV-2.	I pazienti con tubercolosi sia attiva che latente e contemporanea infezione da SARS-CoV-2 mostrano minore produzione di IFN-gamma in vitro in risposta alla stimolazione con peptidi estratti da SARS-CoV-2 (preparato CD4-S) rispetto ai pazienti senza infezione tubercolare.	OBJECTIVES: The interaction of COVID-19 and tuberculosis (TB) are still poor characterized. Here we evaluated the immune response specific for M. tuberculosis (Mtb) and SARS-CoV-2 using a whole-blood-based assay-platform in COVID-19 patients either with TB or latent TB infection (LTBI). METHODS: We evaluated IFN-gamma level in plasma from whole-blood stimulated with Mtb antigens in the Quantiferon-Plus format or with peptides derived from SARS-CoV-2 spike protein, Wuhan-Hu-1 isolate (CD4-S). RESULTS: We consecutively enrolled 63 COVID-19, 10 TB-COVID-19 and 11 LTBI-COVID-19 patients. IFN-gamma response to Mtb-antigens was significantly associated to TB status and therefore it was higher in TB-COVID-19 and LTBI-COVID-19 patients compared to COVID-19 patients (p </= 0.0007). Positive responses against CD4-S were found in 35/63 COVID-19 patients, 7/11 LTBI-COVID-19 and only 2/10 TB-COVID-19 patients. Interestingly, the responders in the TB-COVID-19 group were less compared to COVID-19 and LTBI-COVID-19 groups (p = 0.037 and 0.044, respectively). Moreover, TB-COVID-19 patients showed the lowest quantitative IFN-gamma response to CD4-S compared to COVID-19-patients (p = 0.0336) and LTBI-COVID-19 patients (p = 0.0178). CONCLUSIONS: Our data demonstrate that COVID-19 patients either TB or LTBI have a low ability to build an immune response to SARS-CoV-2 while retaining the ability to respond to Mtb-specific antigens.

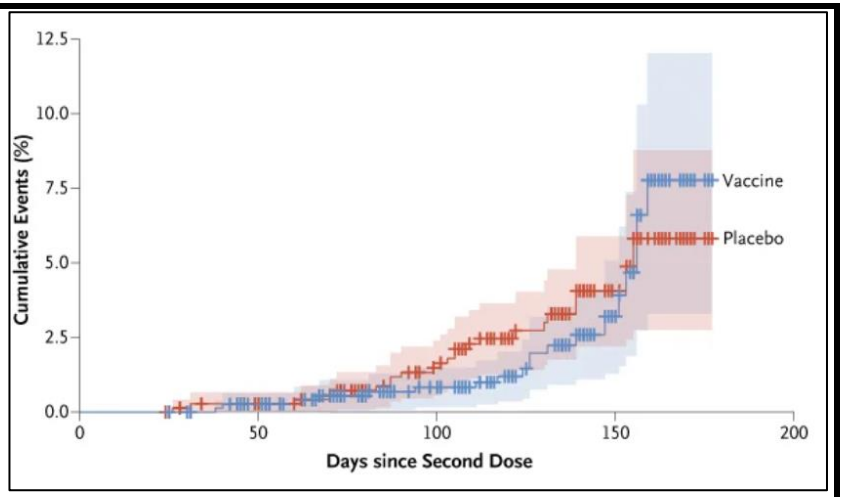
			
Pranata R et al Archives in Gerontology and Geriatrics https://doi.org/10.1016/j.archger.2021.104388	Delirium and Mortality in Coronavirus Disease 2019 (COVID-19) - A Systematic Review and Meta-analysis.	Metanalisi che mostra come il delirium dell'anziano sia indipendentemente associato a maggiore mortalità durante infezione da SARS-CoV-2.	INTRODUCTION: Older adults are indisputably struck hard by the coronavirus disease 2019 (COVID-19) pandemic. The main objective of this meta-analysis is to establish the association between delirium and mortality in older adults with COVID-19. METHODS: Systematic literature searches of PubMed, Embase, and Scopus databases were performed up until 28 November 2020. The exposure in this study was the diagnosis of delirium using clinically validated criteria. Delirium might be in-hospital, at admission, or both. The main outcome was mortality defined as clinically validated non-survivor/death. The effect estimates were reported as odds ratios (ORs) and adjusted odds ratios (aORs). RESULTS: A total of 3,868 patients from 9 studies were included in this systematic review and meta-analysis. The percentage of patients with delirium was 27% [20%, 34%]. Every 1 mg/L increase in CRP was significantly associated with 1% increased delirium risk (OR 1.01 [1.00. 1.02], p=0.033). Delirium was associated with mortality (OR 2.39 [1.64, 3.49], p<0.001; I(2): 82.88%). Subgroup analysis on delirium assessed at admission indicate independent association

			(OR 2.12 [1.39, 3.25], p<0.001; I(2): 82.67%). Pooled adjusted analysis indicated that delirium was independently associated with mortality (aOR 1.50 [1.16, 1.94], p=0.002; I(2): 31.02%). Subgroup analysis on delirium assessed at admission indicate independent association (OR 1.40 [1.03, 1.90], p=0.030; I(2): 31.19%). Meta-regression indicates that the association between delirium and mortality were not significantly influenced by study-level variations in age, sex [reference: male], hypertension, diabetes, and dementia. CONCLUSION: The presence of delirium is associated with increased risk of mortality in hospitalized older adults with COVID-19.
The Lancet Infectious Diseases Editorial Board https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00080-3/fulltext	The COVID-19 exit strategy—why we need to aim low	Strategie possibili per limitare la circolazione di SARS-CoV-2, non solo basate sui vaccini.	As we find ourselves in the second year of a global pandemic, the question on everyone's mind is: when will this end? Much of the narrative around the pandemic last year was that all hopes for a return to normal hinged on development of an effective vaccine. This rhetoric was deaf to the concerns of vaccine and public health experts, and for many a SARS-CoV-2 vaccine has become the magic bullet to deliver us from endless cycles of lockdown and economic decline. Against all precedent, going into 2021, the world had several vaccines with demonstrated efficacy against symptomatic COVID-19 in its armamentarium. Yet a magic bullet they are not.
Baumann M et al Preprint – not peer reviewed https://www.researchgate.net/publication/348659574_A_proactive_approa	A proactive approach to fight SARS-CoV-2 in Germany and Europe	Una proposta tedesca per fermare la pandemia di COVID-19 : raggiungere un basso numero di contagi tramite restrizioni nazionali, quindi consentire – sulla scorta dell'esperienza di Paesi quali la Nuova Zelanda, la circolazione di persone solo all'interno di aree « free » senza	This paper develops a sustainable way to deal with the Covid-19 pandemic. The strategy presented here aims to avoid new infections, deaths and more nationwide lockdowns. It consists of three core elements: First, a rapid reduction in the number of infections to zero. Second, the avoidance of transmissions/reintroduction of the virus into virus-free green zones through local travel restrictions, tests and quarantines. Third, rigorous outbreak management if new cases occur sporadically. In June/July of last year, Germany and many other European countries reached a situation of low incidence after a major struggle but failed to maintain it in the long run. In order to succeed

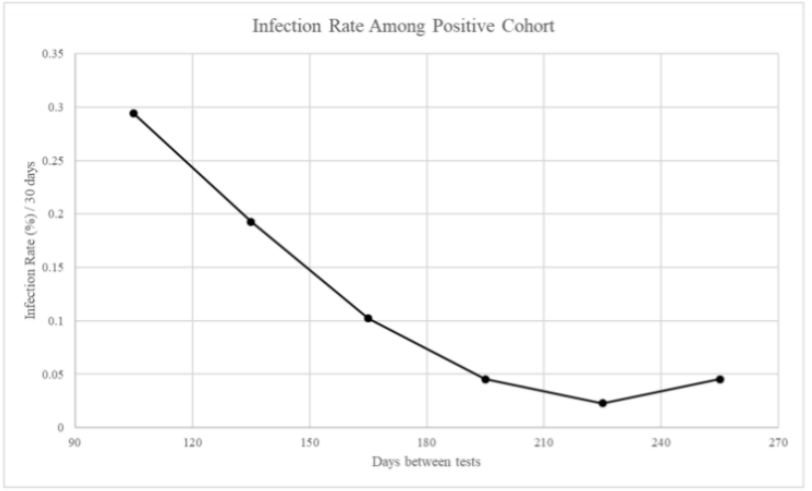
ch_to_fight_SARS-CoV-2_in_Germany_and_Europe		permettere la reintroduzione del virus dall'esterno.	this time, our countries need a concrete and uniform overall goal as well as a consistent strategy for reopening and the time thereafter. The NO-COVID target and the Green Zone strategy, for which we advocate, have already been applied successfully in several countries, thereby enabling their populations to return to a nearly normal life situation. For the Federal Republic of Germany and other European countries this path is both possible and optimal.
Agenzia Italiana del Farmaco https://www.aifa.gov.it/-/aifa-sospensione-precauzionale-del-vaccino-astrazeneca	AIFA: sospensione precauzionale del vaccino AstraZeneca	A 24 ore dalla nota precedente, AIFA si allinea con altri Paesi europei e sospende precauzionalmente la somministrazione del vaccino AstraZeneca contro SARS-CoV-2.	L'AIFA ha deciso di estendere in via del tutto precauzionale e temporanea, in attesa dei pronunciamenti dell'EMA, il divieto di utilizzo del vaccino AstraZeneca Covid19 su tutto il territorio nazionale. Tale decisione è stata assunta in linea con analoghi provvedimenti adottati da altri Paese europei Ulteriori approfondimenti sono attualmente in corso. L'AIFA, in coordinamento con EMA e gli altri Paesi europei, valuterà congiuntamente tutti gli eventi che sono stati segnalati a seguito della vaccinazione.
European Medicines Agency https://www.ema.europa.eu/en/news/investigation-covid-19-vaccine-astrazeneca-thromboembolic-events-continues	Investigation of COVID-19 Vaccine AstraZeneca and thromboembolic events continues Share	L'EMA aggiorna sulla prosecuzione delle ricerche in merito ai casi di tromboembolia venosa riportati in concomitanza temporale con la somministrazione di vaccino AstraZeneca contro SARS-CoV-2.	EMA's safety committee (PRAC) made further progress today, Tuesday 16 March, in its detailed evaluation of cases of blood clots, some with unusual features such as low numbers of platelets, in recipients of COVID-19 Vaccine AstraZeneca. As previously stated, while its investigation is ongoing, EMA currently remains of the view that the benefits of the AstraZeneca vaccine in preventing COVID-19, with its associated risk of hospitalisation and death, outweigh the risks of side effects.

Medicines & Healthcare products Regulatory Agency – United Kingdom https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting	Coronavirus vaccine - weekly summary of Yellow Card reporting	Report, rassicurante, dell'agenzia di sorveglianza farmaceutica del Regno Unito sugli effetti avversi registrati in seguito all'utilizzo di vaccini contro SARS-CoV-2.	This safety update report is based on detailed analysis of data up to 28 February 2021. At this date, an estimated 10.7 million first doses of the Pfizer/BioNTech vaccine and 9.7 million doses of the Oxford University/AstraZeneca vaccine had been administered, and around 0.8 million second doses, mostly the Pfizer/BioNTech vaccine, had been administered. This represents an increase of 2.8 million on the previous week. Conclusions : • The increases in number of ADR reports reflects the increase in vaccine deployment as new vaccination centres have opened across the UK. • The number and nature of suspected adverse reactions reported so far are not unusual in comparison to other types of routinely used vaccines. • The overall safety experience with both vaccines is so far as expected from the clinical trials. • Based on current experience, the expected benefits of both COVID-19 vaccines in preventing COVID-19 and its serious complications far outweigh any known side effects. • As with all vaccines and medicines, the safety of COVID-19 vaccines is being continuously monitored.
Madhi SA et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2102214?query=featured_home	Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant	Trial clinico sull'efficacia del vaccino AstraZeneca contro SARS-CoV-2 in Sudafrica : si dimostra un'efficacia scarsa, del 21.9% nel ridurre l'infezione sintomatica lieve-moderata (nessuna ospedalizzazione nello studio, età mediana dei pazienti 30 anni); l'efficacia	BACKGROUND : Assessment of the safety and efficacy of vaccines against the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in different populations is essential, as is investigation of the efficacy of the vaccines against emerging SARS-CoV-2 variants of concern, including the B.1.351 (501Y.V2) variant first identified in South Africa. METHODS : We conducted a multicenter, double-blind, randomized, controlled trial to assess the safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) in people not infected with the human immunodeficiency virus (HIV) in South Africa. Participants 18 to less

		contro la variante B.1.351 si riduce a 10.4%.	than 65 years of age were assigned in a 1:1 ratio to receive two doses of vaccine containing 5×1010 viral particles or placebo (0.9% sodium chloride solution) 21 to 35 days apart. Serum samples obtained from 25 participants after the second dose were tested by pseudovirus and live-virus neutralization assays against the original D614G virus and the B.1.351 variant. The primary end points were safety and efficacy of the vaccine against laboratory-confirmed symptomatic coronavirus 2019 illness (Covid-19) more than 14 days after the second dose. RESULTS : Between June 24 and November 9, 2020, we enrolled 2026 HIV-negative adults (median age, 30 years); 1010 and 1011 participants received at least one dose of placebo or vaccine, respectively. Both the pseudovirus and the live-virus neutralization assays showed greater resistance to the B.1.351 variant in serum samples obtained from vaccine recipients than in samples from placebo recipients. In the primary end-point analysis, mild-to-moderate Covid-19 developed in 23 of 717 placebo recipients (3.2%) and in 19 of 750 vaccine recipients (2.5%), for an efficacy of 21.9% (95% confidence interval [CI], −49.9 to 59.8). Among the 42 participants with Covid-19, 39 cases (92.9%) were caused by the B.1.351 variant; vaccine efficacy against this variant, analyzed as a secondary end point, was 10.4% (95% CI, −76.8 to 54.8). The incidence of serious adverse events was balanced between the vaccine and placebo groups. CONCLUSIONS : A two-dose regimen of the ChAdOx1 nCoV-19 vaccine did not show protection against mild-to-moderate Covid-19 due to the B.1.351 variant.

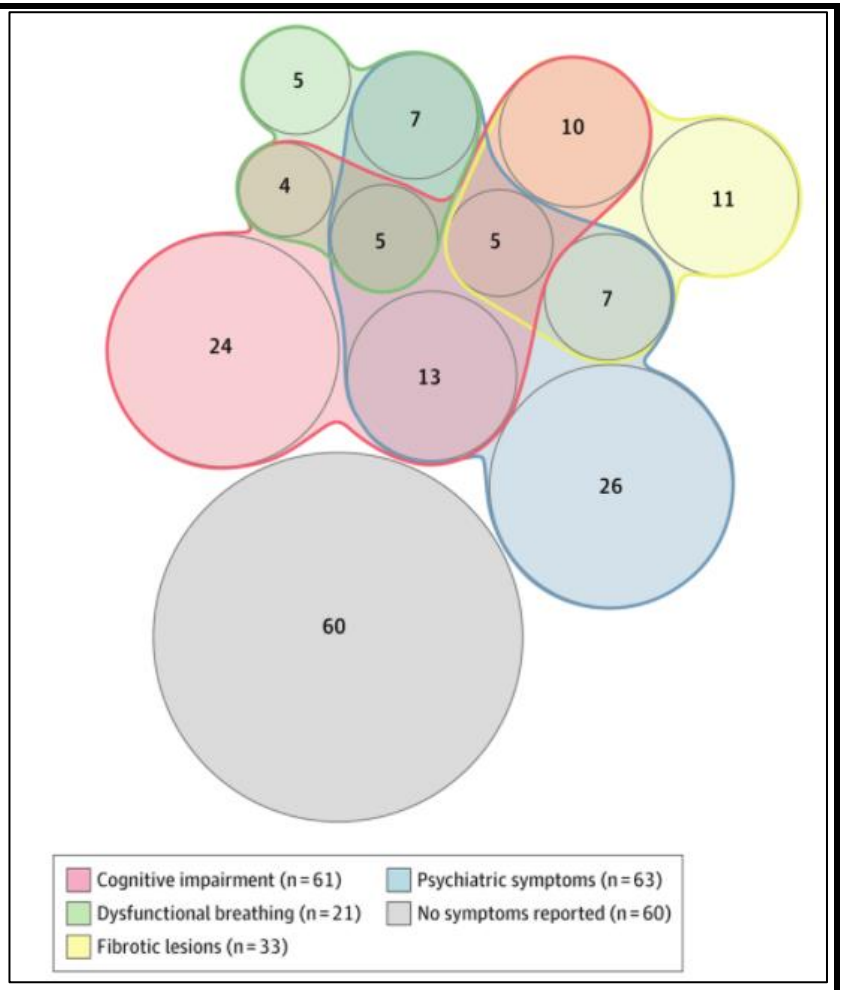
			
Boyarsky BJ et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2777685?resultClick=1	Immunogenicity of a Single Dose of SARS-CoV-2 Messenger RNA Vaccine in Solid Organ Transplant Recipients	Studio sulla risposta anticorpale a 20 giorni dalla prima dose di vaccino a mRNA contro SARS-CoV-2 su 436 trapiantati d'organo : solo il 17% ha un titolo anti-spike.	Immunocompromised individuals have been excluded from studies of SARS-CoV-2 messenger RNA (mRNA) vaccines. In such patients, the immune response to vaccination may be blunted. To better understand the immunogenicity of mRNA vaccines in immunocompromised individuals, we quantified the humoral response to the first dose in solid organ transplant recipients.
Krutikov M et al NEJM	Spread of a Variant SARS-CoV-2 in Long-Term Care Facilities in England	A metà dicembre 2020, oltre il 60% dei tamponi positivi per SARS-CoV-2 nelle case di riposo in Inghilterra lo è per la variante « inglese » B.1.1.7	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections and hospital admissions for coronavirus disease 2019 (Covid-19) increased rapidly in the South East region of England in November and December 2020, despite lockdown measures.1,2 More than half of these infections were associated with a distinct phylogenetic cluster that is estimated to be 40 to 70% more transmissible than previous variants and is driving the growth of infections across England.3 Given the excess deaths seen in long-

https://www.nejm.org/doi/full/10.1056/NEJMc2035906?query=featured_home			term care facilities during the pandemic, preventing further spread of this variant, known as B.1.1.7, to long-term care facilities is a public health priority.
Sheehan MM et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab234/6170939	Reinfection Rates among Patients who Previously Tested Positive for COVID-19: a Retrospective Cohort Study	Studio di coorte retrospettivo su oltre 150000 pazienti ricoverati tra marzo e agosto 2020, di cui 5.9% positivi per infezione da SARS-CoV-2 : una storia di infezione conferisce protezione dell' 84.5% contro la reinfezione sintomatica da SARS-CoV-2 (follow up fino a febbraio 2021). Gli autori suggeriscono che questo dovrebbe portare a ritardare la vaccinazione di chi è stato positivo, a favore delle categorie più a rischio.	Protection afforded from prior disease among patients with coronavirus disease 2019 (COVID-19) infection is unknown. If infection provides substantial long-lasting immunity, it may be appropriate to reconsider vaccination distribution plans. Methods : This retrospective cohort study of one multi-hospital health system included 150,325 patients tested for COVID-19 infection via PCR from March 12, 2020 to August 30, 2020. Testing performed up to February 24, 2021 in these patients was included for analysis. The main outcome was reinfection, defined as infection ≥ 90 days after initial testing. Secondary outcomes were symptomatic infection and protection of prior infection against reinfection. Results : Of 150,325 patients, 8,845 (5.9%) tested positive and 141,480 (94.1%) tested negative prior to August 30. 1,278 (14.4%) of the positive patients were retested after 90 days, and 62 had possible reinfection. Of those, 31 (50%) were symptomatic. Of those with initial negative testing, 5,449 (3.9%) were subsequently positive and 3,191 of those (58.5%) were symptomatic. Protection offered from prior infection was 81.8% (95% confidence interval 76.6 to 85.8), and against symptomatic infection was 84.5% (95% confidence interval 77.9 to 89.1). This protection increased over time. Conclusions : Prior infection in patients with COVID-19 was highly protective against reinfection and symptomatic disease. This protection increased over time, suggesting that viral shedding or ongoing immune response may persist beyond 90 days and may not represent true reinfection. As vaccine supply is limited, patients with

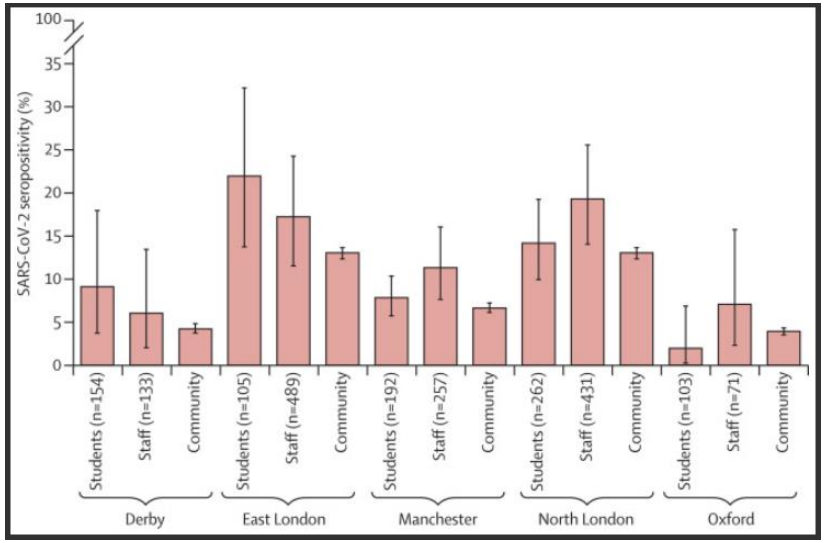
			known history of COVID-19 could delay early vaccination to allow for the most vulnerable to access the vaccine and slow transmission. 
Luchsinger LL et al Science https://science.sciencemag.org/content/371/6534/1116.1	Vaccine efficacy probable against COVID-19 variants	Un invito a interpretare con cautela il dato di riduzione del titolo anticorpale neutralizzante riportato da numerosi studi sull'efficacia dei vaccini anti-SARS-CoV-2 rispetto alle varianti del virus: l'unico dato significativo sarebbe invece il numero di infezioni in soggetti vaccinati.	The U.S. Food and Drug Administration (FDA) emergency use authorization of three vaccines, all of which have shown greater than 85% effectiveness against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has provided the public with the hope of ending the global COVID-19 pandemic. However, recent outbreaks of more transmissible variant SARS-CoV-2 strains that harbor mutations in the spike protein—the critical viral target of immune responses produced by the vaccines —has invited a dour outlook on the vaccines' continued efficacy. The trepidation is based on the prompt compilation of in vitro data that demonstrate as much as 10-fold reduction in neutralization antibody (NAb) activity in vaccinated samples against mutant spike protein pseudovirus, which is thought to be an important metric of acquired immunity. Although reports of NAb reduction are alarming in magnitude, the proof of vaccine effectiveness can only be measured definitively by challenging vaccinated subjects with infection.

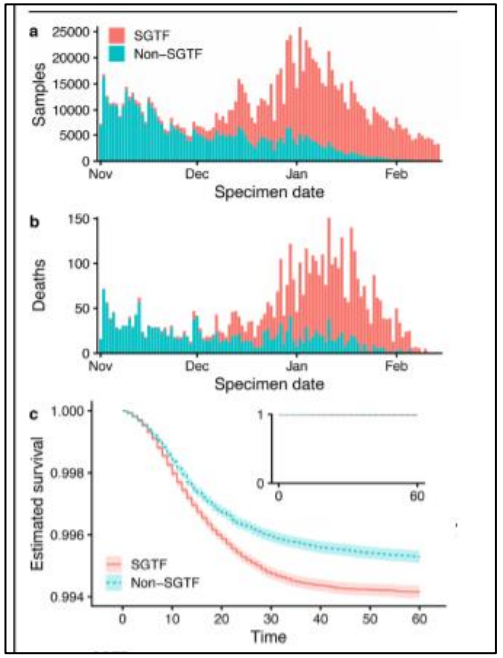
The Writing Committee for the COMEBAC Study Group JAMA https://jamanetwork.com/journals/jama/fullarticle/2777787	Four-Month Clinical Status of a Cohort of Patients After Hospitalization for COVID-19	Studio di coorte prospettico che ha seguito dopo la dimissione per 4 mesi 478 pazienti ospedalizzati per COVID-19 in Francia.	Importance Little is known about long-term sequelae of COVID-19. Objective To describe the consequences at 4 months in patients hospitalized for COVID-19. Design, Setting, and Participants In a prospective uncontrolled cohort study, survivors of COVID-19 who had been hospitalized in a university hospital in France between March 1 and May 29, 2020, underwent a telephone assessment 4 months after discharge, between July 15 and September 18, 2020. Patients with relevant symptoms and all patients hospitalized in an intensive care unit (ICU) were invited for further assessment at an ambulatory care visit. Exposures Survival of hospitalization for COVID-19. Main Outcomes and Measures Respiratory, cognitive, and functional symptoms were assessed by telephone with the Q3PC cognitive screening questionnaire and a checklist of symptoms. At the ambulatory care visit, patients underwent pulmonary function tests, lung computed tomographic scan, psychometric and cognitive tests (including the 36-Item Short-Form Health Survey and 20-item Multidimensional Fatigue Inventory), and, for patients who had been hospitalized in the ICU or reported ongoing symptoms, echocardiography. Results Among 834 eligible patients, 478 were evaluated by telephone (mean age, 61 years [SD, 16 years]; 201 men, 277 women). During the telephone interview, 244 patients (51%) declared at least 1 symptom that did not exist before COVID-19: fatigue in 31%, cognitive symptoms in 21%, and new-onset dyspnea in 16%. There was further evaluation in 177 patients (37%), including 97 of 142 former ICU patients. The median 20-item Multidimensional Fatigue Inventory score (n = 130) was 4.5 (interquartile range, 3.0-5.0) for reduced motivation and 3.7 (interquartile range, 3.0-4.5) for mental fatigue (possible range, 1 [best] to 5 [worst]). The median 36-Item

			Short-Form Health Survey score (n = 145) was 25 (interquartile range, 25.0-75.0) for the subscale “role limited owing to physical problems” (possible range, 0 [best] to 100 [worst]). Computed tomographic lung-scan abnormalities were found in 108 of 171 patients (63%), mainly subtle ground-glass opacities. Fibrotic lesions were observed in 33 of 171 patients (19%), involving less than 25% of parenchyma in all but 1 patient. Fibrotic lesions were observed in 19 of 49 survivors (39%) with acute respiratory distress syndrome. Among 94 former ICU patients, anxiety, depression, and posttraumatic symptoms were observed in 23%, 18%, and 7%, respectively. The left ventricular ejection fraction was less than 50% in 8 of 83 ICU patients (10%). New-onset chronic kidney disease was observed in 2 ICU patients. Serology was positive in 172 of 177 outpatients (97%). Conclusions and Relevance Four months after hospitalization for COVID-19, a cohort of patients frequently reported symptoms not previously present, and lung-scan abnormalities were common among those who were tested. These findings are limited by the absence of a control group and of pre-COVID assessments in this cohort. Further research is needed to understand longer-term outcomes and whether these findings reflect associations with the disease.

			
Ladhani SN et al The Lancet https://www.thelancet.com/journals/lanchi/article/	SARS-CoV-2 infection and transmission in primary schools in England in June–December, 2020 (sKIDs): an active, prospective surveillance study	Esito di uno studio di sorveglianza delle nuove infezioni da SARS-CoV-2 negli alunni e nel personale delle scuole primarie inglesi, in cui si osserva una bassa incidenza.	Background : Little is known about the risk of SARS-CoV-2 infection and transmission in educational settings. Public Health England initiated a study, COVID-19 Surveillance in School KIDs (sKIDs), in primary schools when they partially reopened from June 1, 2020, after the first national lockdown in England to estimate the incidence

PIIS2352-4642(21)00061-4/fulltext			of symptomatic and asymptomatic SARS-CoV-2 infection, seroprevalence, and seroconversion in staff and students. Methods : sKIDs, an active, prospective, surveillance study, included two groups: the weekly swabbing group and the blood sampling group. The swabbing group underwent weekly nasal swabs for at least 4 weeks after partial school reopening during the summer half-term (June to mid-July, 2020). The blood sampling group additionally underwent blood sampling for serum SARS-CoV-2 antibodies to measure previous infection at the beginning (June 1–19, 2020) and end (July 3–23, 2020) of the summer half-term, and, after full reopening in September, 2020, and at the end of the autumn term (Nov 23–Dec 18, 2020). We tested for predictors of SARS-CoV-2 antibody positivity using logistic regression. We calculated antibody seroconversion rates for participants who were seronegative in the first round and were tested in at least two rounds. Findings : During the summer half-term, 11 966 participants (6727 students, 4628 staff, and 611 with unknown staff or student status) in 131 schools had 40 501 swabs taken. Weekly SARS-CoV-2 infection rates were 4·1 (one of 24 463; 95% CI 0·1–21·8) per 100 000 students and 12·5 (two of 16 038; 1·5–45·0) per 100 000 staff. At recruitment, in 45 schools, 91 (11·2%; 95% CI 7·9–15·1) of 816 students and 209 (15·1%; 11·9–18·9) of 1381 staff members were positive for SARS-CoV-2 antibodies, similar to local community seroprevalence. Seropositivity was not associated with school attendance during lockdown (p=0·13 for students and p=0·20 for staff) or staff contact with students (p=0·37). At the end of the summer half-term, 603 (73·9%) of 816 students and 1015 (73·5%) of 1381 staff members were still participating in the surveillance, and five (four students, one staff member) seroconverted. By December, 2020, 55 (5·1%; 95% CI 3·8–6·5) of 1085 participants who were seronegative at

			recruitment (in June, 2020) had seroconverted, including 19 (5·6%; 3·4–8·6) of 340 students and 36 (4·8%; 3·4–6·6) of 745 staff members (p=0·60). Interpretation : In England, SARS-CoV-2 infection rates were low in primary schools following their partial and full reopening in June and September, 2020. 
Davies NG et al Nature https://www.nature.com/articles/s41586-021-03426-1	Increased mortality in community-tested cases of SARS-CoV-2 lineage B.1.1.7	Versione definitiva di uno studio già circolato come pre-print che riporta un aumento del rischio di morte (da 0.6% a 0.9% per un maschio di età 55-69 anni) a seguito di infezione da SARS-CoV-2 variante « inglese » (identificata come non replicazione del gene S alla PCR – ovvero	SARS-CoV-2 lineage B.1.1.7, a variant first detected in the UK in September 20201, has spread to multiple countries worldwide. Several studies have established that B.1.1.7 is more transmissible than preexisting variants, but have not identified whether it leads to any change in disease severity2. Here we analyse a dataset linking 2,245,263 positive SARS-CoV-2 community tests and 17,452 COVID-19 deaths in England from 1 September 2020 to 14 February 2021. For 1,146,534 (51%) of these tests, the presence or absence of B.1.1.7 can be identified because of mutations in this lineage preventing PCR amplification of the spike gene target (S gene target failure, SGTF). Based on 4,945 deaths with known SGTF status, we

		SGTF) rispetto alle varianti preesistenti.	estimate that the hazard of death associated with SGTF is 55% (95% CI 39–72%) higher after adjustment for age, sex, ethnicity, deprivation, care home residence, local authority of residence and test date. This corresponds to the absolute risk of death for a 55–69-year-old male increasing from 0.6% to 0.9% (95% CI 0.8–1.0%) within 28 days after a positive test in the community. Correcting for misclassification of SGTF and missingness in SGTF status, we estimate a 61% (42–82%) higher hazard of death associated with B.1.1.7. Our analysis suggests that B.1.1.7 is not only more transmissible than preexisting SARS-CoV-2 variants, but may also cause more severe illness. 

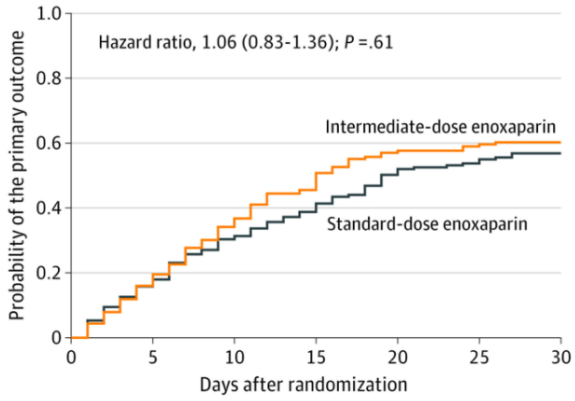
Yuan S et al Nature https://www.nature.com/articles/s41586-021-03431-4	Clofazimine broadly inhibits coronaviruses including SARS-CoV-2	La clofazimina, farmaco utilizzato nella terapia della lebbra, è attiva in vitro e su modello animale contro i Coronavirus e mostra sinergia con remdesivir.	COVID-19 pandemic is the third zoonotic coronavirus (CoV) outbreak of the century after severe acute respiratory syndrome (SARS) in 2003 and Middle East respiratory syndrome (MERS) since 2012. Treatment options for CoVs are largely lacking. Here we show that clofazimine, an anti-leprosy drug with a favourable safety profile, possesses pan-coronaviral inhibitory activity, and can antagonize SARS-CoV-2 and MERS-CoV replication in multiple in vitro systems. The FDA-approved molecule was found to inhibit viral spike-mediated cell fusion and viral helicase activity. In a hamster model of SARS-CoV-2 pathogenesis, prophylactic or therapeutic administration of clofazimine significantly reduced viral load in the lung and faecal viral shedding, and also mitigated inflammation associated with viral infection. Combinatorial application of clofazimine and remdesivir exhibited antiviral synergy in vitro and in vivo, and restricted upper respiratory tract viral shedding. Since clofazimine is orally bioavailable and has a comparatively low manufacturing cost, it is an attractive clinical candidate for outpatient treatment and remdesivir-based combinatorial therapy for hospitalized COVID-19 patients, particularly in developing countries. Taken together, our data provide evidence that clofazimine may have a role in the control of the current pandemic SARS-CoV-2, and, possibly most importantly, emerging CoVs of the future.
Walensky RP et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2777786	Experts Discuss COVID-19—Vaccine Questions, School Openings, and More	Domande e risposte su COVID-19 da parte di esperti internazionali.	JAMA Live Highlights features comments from livestream interviews by JAMA Network Editor in Chief Howard Bauchner, MD. His discussions with experts in clinical care, public health, and health policy focus on critical issues related to the COVID-19 pandemic. Comments have been edited for clarity.

European Medicines Agency https://www.ema.europa.eu/en/news/covid-19-vaccine-astrazeneca-benefits-still-outweigh-risks-despite-possible-link-rare-blood-clots	COVID-19 Vaccine AstraZeneca: benefits still outweigh the risks despite possible link to rare blood clots with low blood platelets	Parere dell'EMA sulla sicurezza del vaccino AstraZeneca contro SARS-CoV-2 e sulla possibilità molto remota che si associ a trombosi.	EMA's safety committee, PRAC, concluded its preliminary review of a signal of blood clots in people vaccinated with COVID-19 Vaccine AstraZeneca at its extraordinary meeting of 18 March 2021. The Committee confirmed that: - the benefits of the vaccine in combating the still widespread threat of COVID-19 (which itself results in clotting problems and may be fatal) continue to outweigh the risk of side effects; - the vaccine is not associated with an increase in the overall risk of blood clots (thromboembolic events) in those who receive it; - there is no evidence of a problem related to specific batches of the vaccine or to particular manufacturing sites; - however, the vaccine may be associated with very rare cases of blood clots associated with thrombocytopenia, i.e. low levels of blood platelets (elements in the blood that help it to clot) with or without bleeding, including rare cases of clots in the vessels draining blood from the brain (CVST).
Agenzia Italiana del Farmaco https://www.aifa.gov.it/web/guest/-/dopo-parere-ema-domani-riprendono-vaccinazioni-con-astrazeneca	Dopo parere EMA, domani riprendono vaccinazioni con AstraZeneca	AIFA recepisce il parere EMA in merito alla sicurezza del vaccino AstraZeneca contro SARS-CoV-2.	La raccomandazione del Comitato di Valutazione dei rischi per la Farmacovigilanza (PRAC) dell'Agenzia Europea per i Medicinali (EMA), nella riunione di oggi, 18 marzo 2021, ha confermato il favorevole rapporto beneficio/rischio del vaccino antiCovid19 AstraZeneca, escludendo una associazione tra i casi di trombosi e il vaccino COVID19. Ha inoltre escluso, sulla base dei dati disponibili, problematiche legate alla qualità e alla produzione.
Paul Erlich Institut http://www.quotidianosanita.it/allegati/allegato947417.pdf	FAQ – Temporary suspension of COVID-19 vaccine AstraZeneca	Domande e risposte sulla sospensione, ora ritirata, del vaccino AstraZeneca contro SARS-CoV-2, a cura dell'Istituto Federale di	A specific form of severe cerebral venous thrombosis associated with platelet deficiency (thrombocytopenia) and bleeding has been identified in seven cases (as of 15 March 2021) in temporal association with vaccination with COVID-19 Vaccine AstraZeneca

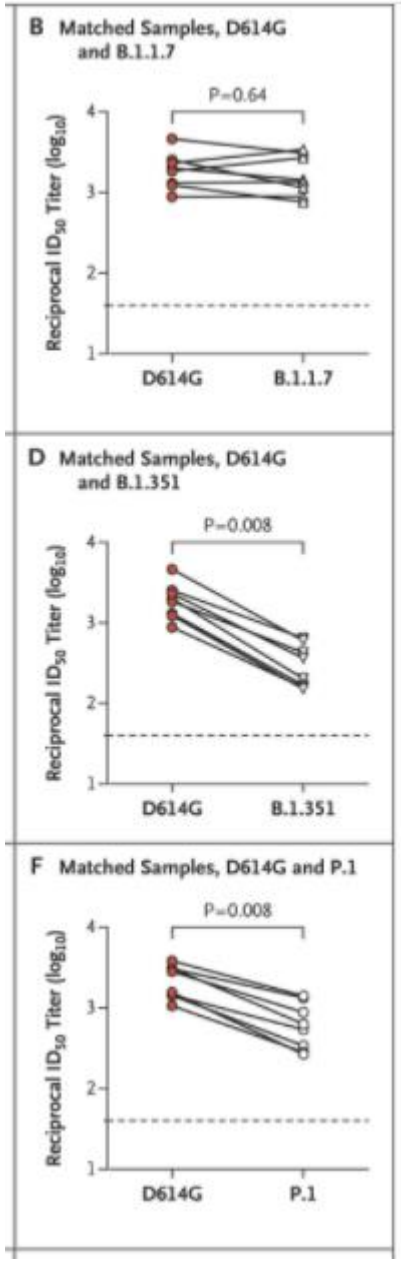
		vaccinologia tedesco che pertiene al Ministero della Salute.	
Thompson A et al BMJ https://pn.bmj.com/content/21/1/75	Cerebral venous sinus thrombosis associated with COVID-19	Trombosi dei seni venosi della dura madre in un paziente con sospetta infezione da SARS-CoV-2.	Coronavirus disease of 2019 (COVID-19) is well known to increase the risk of developing venous thromboembolism; thus, patients with COVID-19 may present to neurologists with cerebral venous sinus thrombosis. We present a patient presenting acutely with delirium, who after initial negative viral testing, was diagnosed with cerebral venous sinus thrombosis in association with COVID-19.
Hughes C et al European Journal of Case Reports in Internal Medicine https://www.ejcrim.com/index.php/EJCRIM/article/view/1691	Cerebral Venous Sinus Thrombosis as a Presentation of COVID-19	Caso di infezione da SARS-CoV-2 che si presenza con trombosi dei seni venosi cerebrali.	Coronavirus disease 19 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). We describe the case of a 59-year-old man who presented with headache, hypertension and a single episode of fever with no other symptoms. He subsequently developed unilateral weakness. Computer tomography identified a cerebral venous sinus thrombosis (CVST). A subsequent test for COVID-19 was positive. This is the first report of CVST as a presenting symptom of COVID-19 infection.
Tu TM et al Journal of Stroke and Cerebrovascular Disease https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7538072/	Cerebral Venous Thrombosis in Patients with COVID-19 Infection: a Case Series and Systematic Review	Due casi clinici di trombosi venosa cerebrale in COVID-19 e revisione della letteratura.	Background : There has been increasing reports associating the coronavirus disease 2019 (COVID-19) with thromboembolic phenomenon including ischemic strokes and venous thromboembolism. Cerebral venous thrombosis (CVT) is a rare neurovascular emergency that has been observed in some COVID-19 patients, yet much remains to be learnt of its underlying pathophysiology. Objective : We present a case series of local patients with concomitant COVID-19 infection and CVT; and aim to perform a systematic review of known cases in the current literature.

			Methods : We describe two patients with concomitant COVID-19 infection and CVT from a nationwide registry in Singapore. We then conducted a literature search in PubMed and Embase using a suitable keyword search strategy from 1st December 2019 to 11th June 2020. All studies reporting CVT in COVID-19 patients were included. Results : Nine studies and 14 COVID-19 patients with CVT were studied. The median age was 43 years (IQR=36-58) and majority had no significant past medical conditions (60.0%). The time taken from onset of COVID-19 symptoms to CVT diagnosis was a median of 7 days (IQR=6-14). CVT was commonly seen in the transverse (75.0%) and sigmoid sinus (50.0%); 33.3% had involvement of the deep venous sinus system. A significant proportion of patients had raised D-dimer (75.0%) and CRP levels (50.0%). Two patients reported presence of antiphospholipid antibodies. Most patients received anticoagulation (91.7%) while overall mortality rate was 45.5%. Conclusions : The high mortality rate of CVT in COVID-19 infection warrants a high index of suspicion from physicians, and early treatment with anticoagulation should be initiated.
INSPIRATION Investigators JAMA https://jamanetwork.com/journals/jama/fullarticle/2777829	Effect of Intermediate-Dose vs Standard-Dose Prophylactic Anticoagulation on Thrombotic Events, Extracorporeal Membrane Oxygenation Treatment, or Mortality Among Patients With COVID-19 Admitted to the Intensive Care Unit The INSPIRATION Randomized Clinical Trial	La terapia anticoagulante a dose intermedia (enoxaparina 100 UI/Kg/die) non conferisce vantaggio in termini di sopravvivenza, trombosi e necessità di circolazione extracorporea (ECMO) rispetto alla profilassi standard (enoxaparina 4000 UI/die) in questo trial clinico su 562 pazienti ricoverati in terapia intensiva per COVID-19.	Importance Thrombotic events are commonly reported in critically ill patients with COVID-19. Limited data exist to guide the intensity of antithrombotic prophylaxis. Objective To evaluate the effects of intermediate-dose vs standard-dose prophylactic anticoagulation among patients with COVID-19 admitted to the intensive care unit (ICU). Design, Setting, and Participants Multicenter randomized trial with a 2 × 2 factorial design performed in 10 academic centers in Iran comparing intermediate-dose vs standard-dose prophylactic anticoagulation (first hypothesis) and statin therapy vs matching placebo (second hypothesis; not reported in this article) among adult patients admitted to the ICU with COVID-19. Patients were recruited

			between July 29, 2020, and November 19, 2020. The final follow-up date for the 30-day primary outcome was December 19, 2020. Interventions Intermediate-dose (enoxaparin, 1 mg/kg daily) (n = 276) vs standard prophylactic anticoagulation (enoxaparin, 40 mg daily) (n = 286), with modification according to body weight and creatinine clearance. The assigned treatments were planned to be continued until completion of 30-day follow-up. Main Outcomes and Measures The primary efficacy outcome was a composite of venous or arterial thrombosis, treatment with extracorporeal membrane oxygenation, or mortality within 30 days, assessed in randomized patients who met the eligibility criteria and received at least 1 dose of the assigned treatment. Prespecified safety outcomes included major bleeding according to the Bleeding Academic Research Consortium (type 3 or 5 definition), powered for noninferiority (a noninferiority margin of 1.8 based on odds ratio), and severe thrombocytopenia (platelet count <20 ×103/μL). All outcomes were blindly adjudicated. Results Among 600 randomized patients, 562 (93.7%) were included in the primary analysis (median [interquartile range] age, 62 [50-71] years; 237 [42.2%] women). The primary efficacy outcome occurred in 126 patients (45.7%) in the intermediate-dose group and 126 patients (44.1%) in the standard-dose prophylaxis group (absolute risk difference, 1.5% [95% CI, −6.6% to 9.8%]; odds ratio, 1.06 [95% CI, 0.76-1.48]; P = .70). Major bleeding occurred in 7 patients (2.5%) in the intermediate-dose group and 4 patients (1.4%) in the standard-dose prophylaxis group (risk difference, 1.1% [1-sided 97.5% CI, −∞ to 3.4%]; odds ratio, 1.83 [1-sided 97.5% CI, 0.00-5.93]), not meeting the noninferiority criteria (P for noninferiority >.99). Severe thrombocytopenia occurred only in patients assigned to the

			intermediate-dose group (6 vs 0 patients; risk difference, 2.2% [95% CI, 0.4%-3.8%]; P = .01). Conclusions and Relevance Among patients admitted to the ICU with COVID-19, intermediate-dose prophylactic anticoagulation, compared with standard-dose prophylactic anticoagulation, did not result in a significant difference in the primary outcome of a composite of adjudicated venous or arterial thrombosis, treatment with extracorporeal membrane oxygenation, or mortality within 30 days. These results do not support the routine empirical use of intermediate-dose prophylactic anticoagulation in unselected patients admitted to the ICU with COVID-19. **Figure 2. Primary Outcome in the Prespecified Primary Cohort in a Study of the Effect of Intermediate-Dose vs Standard-Dose Prophylactic Among Patients With COVID-19 Admitted to the Intensive Care Unit** 
Al-Samkari H et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2777828	Finding the Optimal Thromboprophylaxis Dose in Patients With COVID-19	Osservazioni sullo studio precedente, di cui si commentano alcuni aspetti : i pazienti non sono stati sottoposti a screening per trombosi venosa profonda (ma la trombosi occulta potrebbe essere non	Therefore, with an important contribution from the trial performed by Sadeghipour and colleagues, the preponderance of high-quality evidence at this time supports use of standard-dose thromboprophylaxis, not dose escalation, in critically ill patients with COVID-19. However, pending the publication of final results from the ATTACC, REMAP-CAP, and ACTIV-4a multiplatform trial confirming the interim report, escalated thromboprophylaxis could be appropriate in moderately ill hospitalized patients with COVID-19

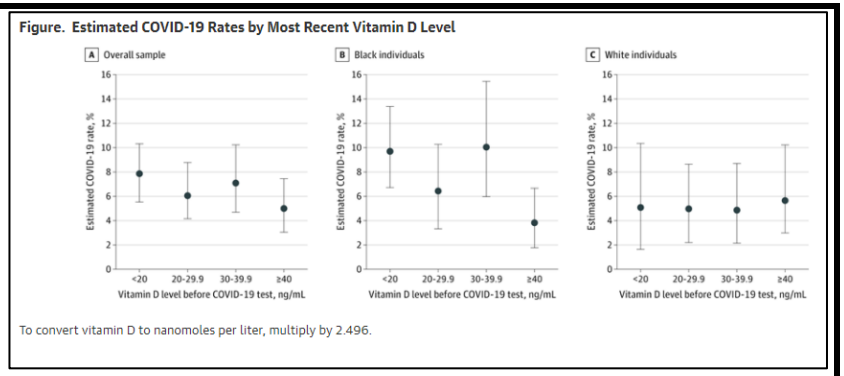
		significativa clinicamente) ; la dose standard di enoxaparina in profilassi è stata in parte adattata al peso; la popolazione studiata, dei ricoverati in terapia intensiva, potrebbe non essere quella che beneficia maggiormente della profilassi anticoagulante aumentata, in quanto già affetta da danno d'organo significativo.	while balancing known comorbidities and bleeding risks. Additional important questions pertaining to thromboprophylaxis in COVID-19 remain under active investigation, including the utility of postdischarge thromboprophylaxis and the effect of outpatient thromboprophylaxis for patients with mild COVID-19 not requiring hospital admission.
Wu K et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMc2102179	Serum Neutralizing Activity Elicited by mRNA-1273 Vaccine	La protezione conferita dal vaccino MODERNA contro SARS-CoV-2, studiata in termini di titolo neutralizzante, appare ridotta nei confronti delle varianti P.1 (« brasiliana »), B.1.427/B.1.429, B.1.1.7+E484K e B.1.351 (« sudafricana »).	Protection conferred by the mRNA-1273 vaccine against the P.1, B.1.427/B.1.429, and B.1.351 variants remains to be determined. Our findings underscore the importance of continued viral surveillance and evaluation of vaccine efficacy against new variants and may help to facilitate the establishment of correlates of protection in both nonhuman primates and humans.

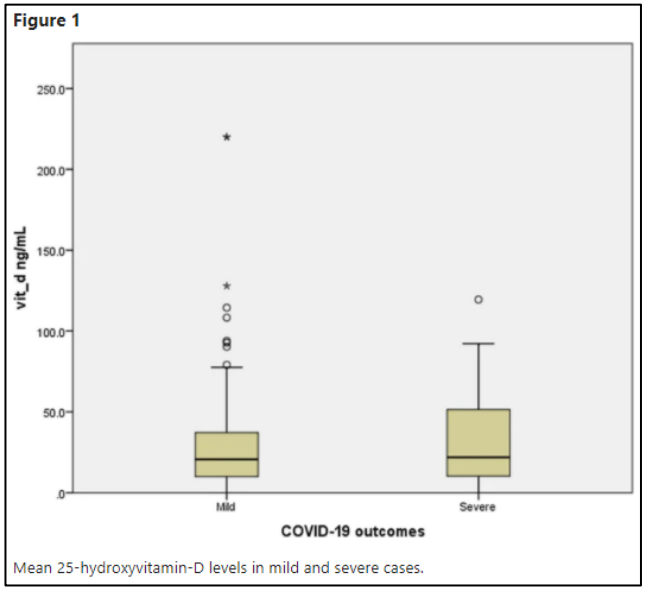

B Matched Samples, D614G and B.1.1.7
P=0.64
Reciprocal ID50 Titer (log10)
4
3
2
1
D614G
B.1.1.7
D Matched Samples, D614G and B.1.351
P=0.008
Reciprocal ID50 Titer (log10)
4
3
2
1
D614G
B.1.351
F Matched Samples, D614G and P.1
P=0.008
Reciprocal ID50 Titer (log10)
4
3
2
1
D614G
P.1

Grint DJ et al Eurosurveillance https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.11.2100256	Case fatality risk of the SARS-CoV-2 variant of concern B.1.1.7 in England, 16 November to 5 February	In base ai dati di sanità pubblica inglesi, il rischio di morte associato a infezione da variante « inglese » di SARS-CoV-2 è aumentato con hazard ratio 1.67 rispetto alle altre varianti presenti nel Paese.	The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant of concern B.1.1.7 (VOC) was first identified in Kent, United Kingdom (UK) in autumn 2020. Early analysis suggests it is more transmissible than previously circulating forms (non-VOC) [1]. It is now the dominant strain throughout the UK and is increasing in prevalence across Europe [2]. Early reports of increased mortality have not included data on individuals' comorbidities, and this information is needed to facilitate pandemic planning. Certain PCR assays for SARS-CoV-2 do not amplify one of the spike protein gene targets in this VOC. Spike gene target failure (SGTF) is therefore a proxy for VOC identification, with greater than 95% sensitivity for VOC diagnosis during the period from 16 November to 11 January [3]. Working on behalf of NHS England, we estimate the risk of death following confirmation of SARS-CoV-2 infection in England, comparing infection with VOC to non-VOC, after accounting for demographic factors and comorbidities. The code and configuration of our analysis is available online (github.com/opensafely/sgtf-cfr-research).
Meltzer DO et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2777682	Association of Vitamin D Levels, Race/Ethnicity, and Clinical Characteristics With COVID-19 Test Results	Studio di coorte su 4638 persone testate per SARS-CoV-2 e di cui si conosce il dosaggio di vitamina D durante l'anno precedente : livelli più bassi sono associati a infezione.	Importance Deficient (ie, <20 ng/mL) or insufficient (ie, 20 to <30 ng/mL) 25-hydroxyvitamin D (also known as calcifediol) levels are more common in Black individuals than White individuals and are associated with increased coronavirus disease 2019 (COVID-19) risk. Whether COVID-19 risk is associated with differences in vitamin D levels of 30 ng/mL or greater is not known. Objective To examine whether COVID-19 test results are associated with differences in vitamin D levels of 30 ng/mL or greater, including for White individuals and for Black individuals.

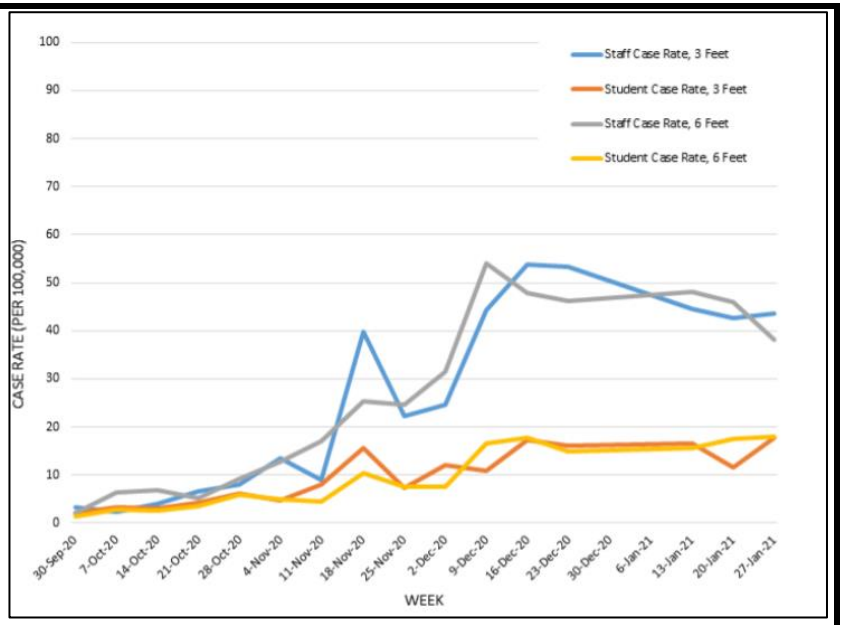
			Design, Setting, and Participants This retrospective cohort study was conducted at an academic medical center in Chicago, Illinois. Participants included individuals with data on vitamin D level within 365 days before COVID-19 testing, which was conducted from March 3 to December 30, 2020. Data were analyzed from September 11, 2020, to February 5, 2021. Exposures The last vitamin D level before COVID-19 testing was categorized as less than 20 ng/mL (ie, deficient), 20 to less than 30 ng/mL (ie, insufficient), 30 to less than 40 ng/mL, or 40 ng/mL or greater. Treatment was defined by vitamin D type and dose 14 days before COVID-19 testing and treatment changes after last vitamin D level. Main Outcomes and Measures The main outcome was a positive result for COVID-19 in polymerase chain reaction testing. Multivariable analyses tested whether previously measured vitamin D level was associated with having test results positive for COVID-19 in White individuals and in Black individuals, controlling for months and treatment changes since the vitamin D level was measured, as well as demographic characteristics and comorbidity indicators. Results A total of 4638 individuals (mean [SD] age 52.8 [19.5] years; 3205 [69%] women) had data for a vitamin D level within 1 year before COVID-19 testing, including 2288 (49%) Black individuals, 1999 (43%) White individuals, and 351 individuals (8%) who were another race/ethnicity (eg, Asian, Mideast Indian, >1 race). Stratified by vitamin D level, 1251 individuals (27%) had less than 20 ng/mL, 1267 individuals (27%) had 20 to less than 30 ng/mL, 1023 individuals (22%) had 30 to less than 40 ng/mL, and 1097 individuals (24%) had 40 ng/mL or greater. Lower vitamin D levels were more common in Black individuals (<20 ng/mL: 829 of 2288 Black individuals [36%]) than White individuals (<20 ng/mL: 315 of 1999 White individuals

			[16%]). A total of 333 individuals (7%) had test results positive for COVID-19, including 102 White individuals (5%) and 211 Black individuals (9%). Multivariate analysis controlling for time since last vitamin D level measurement was used to estimate the outcomes associated with levels 14 days before COVID-19 testing. A positive test result for COVID-19 was not significantly associated with vitamin D levels in White individuals but was associated with vitamin D levels in Black individuals (compared with ≥40 ng/mL: <20 ng/mL incidence rate ratio [IRR], 2.55 [95% CI, 1.26-5.15]; P = .009; 20 to <30 ng/mL IRR, 1.69 [95% CI, 0.75-3.84]; P = .21; 30 to <40 ng/mL IRR, 2.64 [95% CI, 1.24-5.66]; P = .01). Stratified by vitamin D level, estimated COVID-19 positivity rates in Black individuals were 9.72% (95% CI, 6.74%-13.41%) for individuals with a vitamin D level less than 20 ng/mL, 6.47% (95% CI, 3.33%-10.28%) for individuals with a vitamin D level of 20 to less than 30 ng/mL, 10.10% (95% CI, 6.00%-15.47%) for individuals with a vitamin D level of 30 to less than 40 ng/mL, and 3.82% (95% CI, 1.78%-6.68%) for individuals with a vitamin D level of 40 ng/mL or higher. Multivariate analysis in individuals with a vitamin D level of 30 ng/mL or greater found that the IRR of a positive COVID-19 test result was 0.97 (95% CI, 0.94-0.99; P = .008) per 1-ng/mL increase in vitamin D overall and 0.95 (95% CI, 0.91-0.98; P = .003) per 1-ng/mL increase in vitamin D in Black individuals. Conclusions and Relevance In this single-center retrospective cohort study, COVID-19 risk increased among Black individuals with vitamin D level less than 40 ng/mL compared with those with 40 ng/mL or greater and decreased with increasing levels among individuals with levels greater than 30 ng/mL. No significant associations were noted for White individuals. Randomized clinical trials should examine whether increasing vitamin D level to greater than 40 ng/mL affects COVID-19 risk.

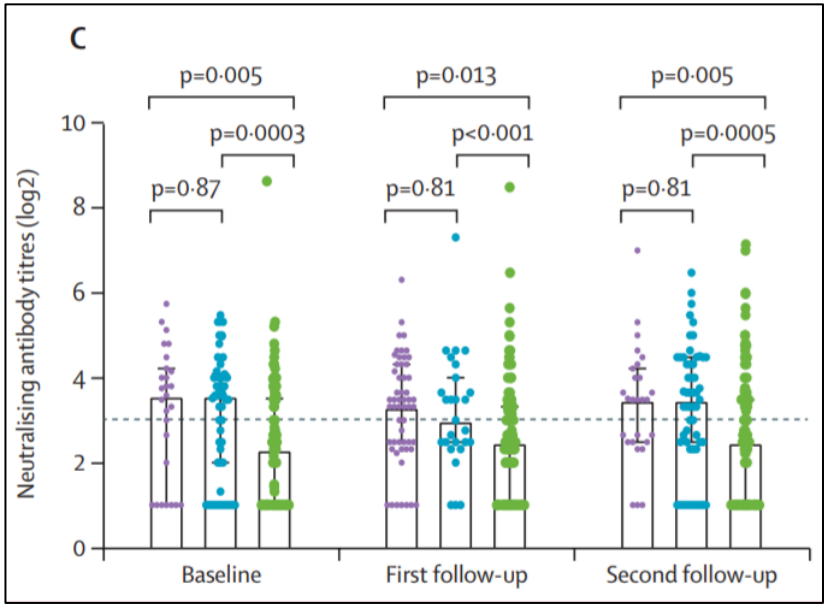
			
Jevalikar G et al Scientific Reports https://www.nature.com/articles/s41598-021-85809-y	Lack of association of baseline 25-hydroxyvitamin D levels with disease severity and mortality in Indian patients hospitalized for COVID-19	Studio osservazionale prospettico su 410 pazienti ricoverati per COVID-19, nei quali non si dimostra una associazione fra la carenza di vitamina D e l'infiammazione o gli outcome.	Vitamin D deficiency (VDD) owing to its immunomodulatory effects is believed to influence outcomes in COVID-19. We conducted a prospective, observational study of patients, hospitalized with COVID-19. Serum 25-OHD level < 20 ng/mL was considered VDD. Patients were classified as having mild and severe disease on basis of the WHO ordinal scale for clinical improvement (OSCI). Of the 410 patients recruited, patients with VDD (197,48.2%) were significantly younger and had lesser comorbidities. The levels of PTH were significantly higher in the VDD group (63.5 ± 54.4 vs. 47.5 ± 42.9 pg/mL). The proportion of severe cases (13.2% vs.14.6%), mortality (2% vs. 5.2%), oxygen requirement (34.5% vs.43.4%), ICU admission (14.7% vs.19.8%) was not significantly different between patients with or without VDD. There was no significant correlation between serum 25-OHD levels and inflammatory markers studied. Serum parathormone levels correlated with D-dimer (r 0.117, p- 0.019), ferritin (r 0.132, p-0.010), and LDH (r 0.124, p-0.018). Amongst VDD patients, 128(64.9%) were treated with oral cholecalciferol (median dose of 60,000 IU). The proportion of severe cases, oxygen, or ICU admission was not significantly different in the treated vs. untreated group. In conclusion, serum 25-OHD levels at admission did not correlate with inflammatory markers, clinical outcomes, or mortality

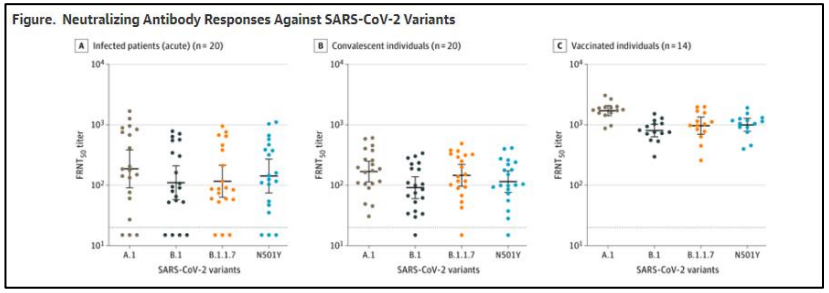
			in hospitalized COVID-19 patients. Treatment of VDD with cholecalciferol did not make any difference to the outcomes.  Mean 25-hydroxyvitamin-D levels in mild and severe cases.
Van den Berg P et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab230/6167856	Effectiveness of three versus six feet of physical distancing for controlling spread of COVID-19 among primary and secondary students and staff: A retrospective, state-wide cohort study	La prescrizione di una distanza minima interpersonale di 1 oppure 2 metri non determina differente incidenza di infezioni da SARS-CoV-2 in questo studio sulle scuole americane.	Background : National and international guidelines differ about the optimal physical distancing between students for prevention of SARS-CoV-2 transmission; studies directly comparing the impact of ≥3 versus ≥6 feet of physical distancing policies in school settings are lacking. Thus, our objective was to compare incident cases of SARS-CoV-2 in students and staff in Massachusetts public schools among districts with different physical distancing requirements. State guidance mandates masking for all school staff and for students in grades 2 and higher; the majority of districts required universal masking. Methods : Community incidence rates of SARS-CoV-2, SARS-CoV-2 cases among students in grades K-12 and staff participating in-person learning, and district infection control plans were linked. Incidence rate ratios (IRR) for students and staff members in districts with ≥3

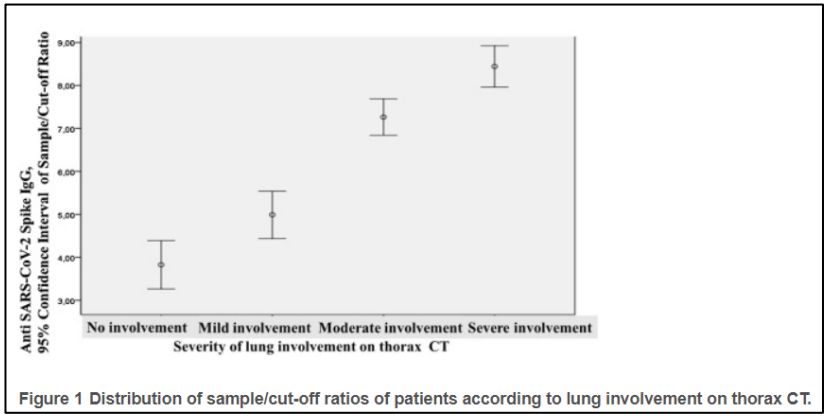
			versus ≥6 feet of physical distancing were estimated using log-binomial regression; models adjusted for community incidence are also reported. Results : Among 251 eligible school districts, 537,336 students and 99,390 staff attended in-person instruction during the 16-week study period, representing 6,400,175 student learning weeks and 1,342,574 staff learning weeks. Student case rates were similar in the 242 districts with ≥3 feet versus ≥6 feet of physical distancing between students (IRR, 0.891, 95% CI, 0.594-1.335); results were similar after adjusting for community incidence (adjusted IRR, 0.904, 95% CI, 0.616-1.325). Cases among school staff in districts with ≥3 feet versus ≥6 feet of physical distancing were also similar (IRR, 1.015, 95% CI, 0.754-1.365). Conclusions : Lower physical distancing policies can be adopted in school settings with masking mandates without negatively impacting student or staff safety.

			
He Z et al The Lancet https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00238-5/fulltext	Seroprevalence and humoral immune durability of anti-SARS-CoV-2 antibodies in Wuhan, China: a longitudinal, population-level, cross-sectional study	Studio di sieroprevalenza contro SARS-CoV-2 a Wuhan con campionamento in aprile, giugno e ottobre-dicembre 2020 : su 335 positivi seguiti per tutto il periodo di osservazione, la percentuale di persone con anticorpi neutralizzanti rimane invariata nel tempo (titolo più elevato nei sintomatici, blu in figura, rispetto agli asintomatici, verde).	Background : Wuhan was the epicentre of the COVID-19 outbreak in China. We aimed to determine the seroprevalence and kinetics of anti-SARS-CoV-2 antibodies at population level in Wuhan to inform the development of vaccination strategies. Methods : In this longitudinal cross-sectional study, we used a multistage, population-stratified, cluster random sampling method to systematically select 100 communities from the 13 districts of Wuhan. Households were systematically selected from each community and all family members were invited to community health-care centres to participate. Eligible individuals were those who had lived in Wuhan for at least 14 days since Dec 1, 2019. All eligible participants who consented to participate completed a standardised electronic questionnaire of demographic and clinical questions and self-reported any symptoms associated with COVID-19 or previous diagnosis of COVID-19. A venous blood sample was taken

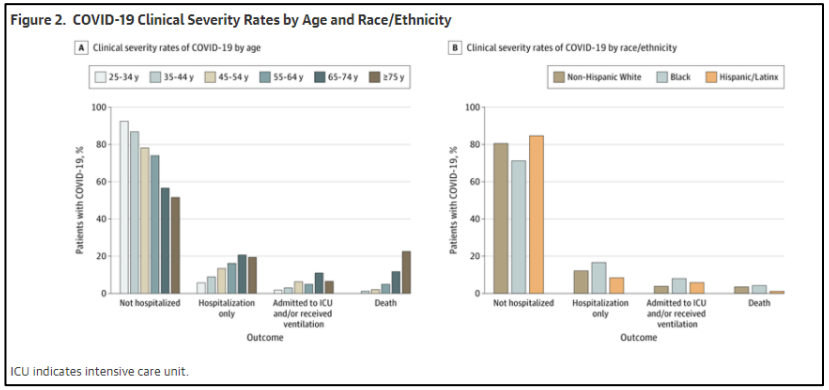
			for immunological testing on April 14–15, 2020. Blood samples were tested for the presence of pan-immunoglobulins, IgM, IgA, and IgG antibodies against SARS-CoV-2 nucleocapsid protein and neutralising antibodies were assessed. We did two successive follow-ups between June 11 and June 13, and between Oct 9 and Dec 5, 2020, at which blood samples were taken. Findings : Of 4600 households randomly selected, 3599 families (78·2%) with 9702 individuals attended the baseline visit. 9542 individuals from 3556 families had sufficient samples for analyses. 532 (5·6%) of 9542 participants were positive for pan-immunoglobulins against SARS-CoV-2, with a baseline adjusted seroprevalence of 6·92% (95% CI 6·41–7·43) in the population. 437 (82·1%) of 532 participants who were positive for pan-immunoglobulins were asymptomatic. 69 (13·0%) of 532 individuals were positive for IgM antibodies, 84 (15·8%) were positive for IgA antibodies, 532 (100%) were positive for IgG antibodies, and 212 (39·8%) were positive for neutralising antibodies at baseline. The proportion of individuals who were positive for pan-immunoglobulins who had neutralising antibodies in April remained stable for the two follow-up visits (162 [44·6%] of 363 in June, 2020, and 187 [41·2%] of 454 in October–December, 2020). On the basis of data from 335 individuals who attended all three follow-up visits and who were positive for pan-immunoglobulins, neutralising antibody levels did not significantly decrease over the study period (median 1/5·6 [IQR 1/2·0 to 1/14·0] at baseline vs 1/5·6 [1/4·0 to 1/11·2] at first follow-up [p=1·0] and 1/6·3 [1/2·0 to 1/12·6] at second follow-up [p=0·29]). However, neutralising antibody titres were lower in asymptomatic individuals than in confirmed cases and symptomatic individuals. Although titres of IgG decreased over time, the proportion of individuals who had IgG antibodies did not decrease

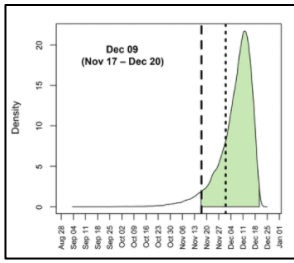
			substantially (from 30 [100%] of 30 at baseline to 26 [89·7%] of 29 at second follow-up among confirmed cases, 65 [100%] of 65 at baseline to 58 [92·1%] of 63 at second follow-up among symptomatic individuals, and 437 [100%] of 437 at baseline to 329 [90·9%] of 362 at second follow-up among asymptomatic individuals). Interpretation : 6·92% of a cross-sectional sample of the population of Wuhan developed antibodies against SARS-CoV-2, with 39·8% of this population seroconverting to have neutralising antibodies. Our durability data on humoral responses indicate that mass vaccination is needed to effect herd protection to prevent the resurgence of the epidemic. 
Strugnell R et al The Lancet	Sustained neutralising antibodies in the Wuhan population suggest durable	Commento all'articolo precedente in cui si sottolinea l'opportunità della vaccinazione contro SARS-CoV-2.	SARS-CoV-2 infections were first reported in Wuhan, China, in 2019,1 and quickly became a global pandemic, as declared on March 11, 2020.2 SARS-CoV-2 is highly infectious3 and COVID-19 is variable in

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00434-7/fulltext	protection against SARS-CoV-2		its presentation, with many infected individuals, as detected by viral nucleic acid screening, being asymptomatic.
Edara V V et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2777898	Neutralizing Antibodies Against SARS-CoV-2 Variants After Infection and Vaccination	Attività neutralizzante del siero di 20 individui in fase acuta di infezione da SARS-CoV-2, 20 guariti e 14 vaccinati con vaccino MODERNA a mRNA contro 4 ceppi virali (« wildtype », portatore di sostituzione D614G, B.1.1.7 e portatore di N501Y) : non si osservano differenze significative tra i ceppi.	Serum neutralizing antibodies rapidly appear after SARS-CoV-2 infection1 and vaccination2 and are maintained for several months.3,4 The emergence of SARS-CoV-2 variants has raised concerns about the breadth of neutralizing-antibody responses. We compared the neutralizing-antibody response to 4 variants in infected and vaccinated individuals to determine how mutations within the spike protein are associated with virus neutralization.  Figure. Neutralizing Antibody Responses Against SARS-CoV-2 Variants A Infected patients (acute) (n = 20) B Convalescent individuals (n = 20) C Vaccinated individuals (n = 14) FRNT50 titer A.1 B.1 B.1.1.7 N501Y SARS-CoV-2 variants
Basaran S et al International Journal of Infectious Diseases https://www.ijidonline.com/article/S1201-9712(21)00249-6/fulltext	The effect of tocilizumab, anakinra, and prednisolone on antibody response to SARS-CoV-2 in patients with COVID-19: A prospective cohort study with multivariate analysis of factors affecting the antibody response.	Studio prospettico su 518 pazienti con infezione da SARS-CoV-2 trattati con tocilizumab (anti IL-6), anakinra (anti IL-1) o prednisolone : tali terapie non sono associate a variazioni del titolo di IgG, che è invece linearmente associato alla gravità dell'interessamento polmonare.	Objectives : Disease severity, previous medications, immunosuppresive agents could affect the antibody response against SARS-CoV-2. We aimed to analyze variables affecting the humoral response to SARS-CoV-2. Methods : In this prospective cohort study, we included adult patients who recovered from COVID-19 and were admitted to COVID-19 follow-up unit. We defined 8 patient groups in accordance with the results of thorax CT, SARS-CoV-2 PCR test, and tocilizumab or anakinra use during active disease. Anti-S IgG antibodies were determined by ELISA in serum samples. Anti-S positive and negative cases were compared.

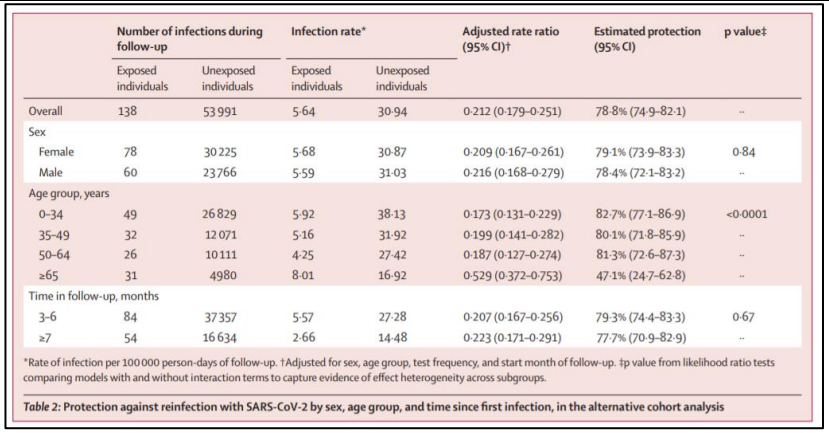
			Results : A total of 518 patients were included in the study. SARS-CoV-2 IgG antibodies were positive in 82.8% of patients. SARS-CoV-2 PCR positivity, extent of lung involvement on CT, and time to antibody testing were independently associated with antibody positivity. Tocilizumab, anakinra or prednisolone use was not a factor affecting the antibody response. The rate of antibody response and sample/CO values among antibody positive patients showed a linear relationship with the extent of lung involvement on CT. Conclusions : The use of tocilizumab, anakinra, and prednisolone for COVID-19 did not affect the antibody response against SARS-CoV-2. The main driver of antibody response among patients with COVID-19 was the extent of pulmonary involvement on CT.  Figure 1 Distribution of sample/cut-off ratios of patients according to lung involvement on thorax CT.
Salter A et al JAMA https://jamanetwork.com/journals/jamaneurology/fullarticle/2777735	Outcomes and Risk Factors Associated With SARS-CoV-2 Infection in a North American Registry of Patients With Multiple Sclerosis	Esito di uno studio cross sectional su persone con sclerosi multipla affette da COVID-19 : la recente terapia con corticosteroidi è un fattore associato a mortalità.	Importance Emergence of SARS-CoV-2 causing COVID-19 prompted the need to gather information on clinical outcomes and risk factors associated with morbidity and mortality in patients with multiple sclerosis (MS) and concomitant SARS-CoV-2 infections. Objective To examine outcomes and risk factors associated with COVID-19 clinical severity in a large, diverse cohort of North American patients with MS.

			Design, Setting, and Participants This analysis used deidentified, cross-sectional data on patients with MS and SARS-CoV-2 infection reported by health care professionals in North American academic and community practices between April 1, 2020, and December 12, 2020, in the COVID-19 Infections in MS Registry. Health care professionals were asked to report patients after a minimum of 7 days from initial symptom onset and after sufficient time had passed to observe the COVID-19 disease course through resolution of acute illness or death. Data collection began April 1, 2020, and is ongoing. Exposures Laboratory-positive SARS-CoV-2 infection or highly suspected COVID-19. Main Outcomes and Measures Clinical outcome with 4 levels of increasing severity: not hospitalized, hospitalization only, admission to the intensive care unit and/or required ventilator support, and death. Results Of 1626 patients, most had laboratory-positive SARS-CoV-2 infection (1345 [82.7%]), were female (1202 [74.0%]), and had relapsing-remitting MS (1255 [80.4%]). A total of 996 patients (61.5%) were non-Hispanic White, 337 (20.8%) were Black, and 190 (11.7%) were Hispanic/Latinx. The mean (SD) age was 47.7 (13.2) years, and 797 (49.5%) had 1 or more comorbidity. The overall mortality rate was 3.3% (95% CI, 2.5%-4.3%). Ambulatory disability and older age were each independently associated with increased odds of all clinical severity levels compared with those not hospitalized after adjusting for other risk factors (nonambulatory: hospitalization only, odds ratio [OR], 2.8 [95% CI, 1.6-4.8]; intensive care unit/required ventilator support, OR, 3.5 [95% CI, 1.6-7.8]; death, OR, 25.4 [95% CI, 9.3-69.1]; age [every 10 years]: hospitalization only, OR, 1.3 [95% CI, 1.1-1.6]; intensive care

			unit/required ventilator support, OR, 1.3 [95% CI, 0.99-1.7]; death, OR, 1.8 [95% CI, 1.2-2.6]). Conclusions and Relevance In this registry-based cross-sectional study, increased disability was independently associated with worse clinical severity including death from COVID-19. Other risk factors for worse outcomes included older age, Black race, cardiovascular comorbidities, and recent treatment with corticosteroids. Knowledge of these risk factors may improve the treatment of patients with MS and COVID-19 by helping clinicians identify patients requiring more intense monitoring or COVID-19 treatment. 
Pekar J et al Science https://science.sciencemag.org/content/early/2021/03/17/science.abf8003	Timing the SARS-CoV-2 index case in Hubei province	Modello predittivo dell'esordio della pandemia di COVID-19 in Cina, che si collocherebbe a metà ottobre 2019.	Understanding when SARS-CoV-2 emerged is critical to evaluating our current approach to monitoring novel zoonotic pathogens and understanding the failure of early containment and mitigation efforts for COVID-19. We employed a coalescent framework to combine retrospective molecular clock inference with forward epidemiological simulations to determine how long SARS-CoV-2 could have circulated prior to the time of the most recent common ancestor. Our results define the period between mid-October and mid-November 2019 as the plausible interval when the first case of SARS-CoV-2 emerged in Hubei province. By characterizing the likely dynamics of the virus before it was discovered, we show that over

			two-thirds of SARS-CoV-2-like zoonotic events would be self-limited, dying out without igniting a pandemic. Our findings highlight the shortcomings of zoonosis surveillance approaches for detecting highly contagious pathogens with moderate mortality rates.  **Fig. 1 Posterior distribution for the time of the most recent common ancestor (tMRCA) of 583 sampled SARS-CoV-2 genomes circulating in China between December 2019 and April 2020.** Inference was performed using a strict molecular clock and a Bayesian Skyline coalescent prior. Shaded area denotes 95% HPD. Long-dashed line is 17 November 2019, and short-dashed line is 01 December 2019.
Hansen CH et al The Lancet https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00575-4/fulltext	Assessment of protection against reinfection with SARS-CoV-2 among 4 million PCR-tested individuals in Denmark in 2020: a population-level observational study	Studio osservazionale condotto in Danimarca sulla popolazione con infezione da SARS-CoV-2 durante la prima e la seconda « ondata » epidemica. Chi è stato positivo ha una protezione del 78-80.5% contro la reinfezione, che si riduce però a 47% nelle persone di età superiore a 65 anni. Queste dovrebbero avere la priorità per la vaccinazione, anche se sono già state infette.	Background : The degree to which infection with SARS-CoV-2 confers protection towards subsequent reinfection is not well described. In 2020, as part of Denmark's extensive, free-of-charge PCR-testing strategy, approximately 4 million individuals (69% of the population) underwent 10·6 million tests. Using these national PCR-test data from 2020, we estimated protection towards repeat infection with SARS-CoV-2. Methods : In this population-level observational study, we collected individual-level data on patients who had been tested in Denmark in 2020 from the Danish Microbiology Database and analysed infection rates during the second surge of the COVID-19 epidemic, from Sept 1 to Dec 31, 2020, by comparison of infection rates between individuals with positive and negative PCR tests during the first surge (March to May, 2020). For the main analysis, we excluded people who tested positive for the first time between the two surges and those who died before the second surge. We did an alternative cohort analysis, in which we compared infection rates throughout the year between those with and without a previous confirmed infection at least 3 months earlier, irrespective of date. We also investigated whether differences were found by age group, sex, and

			time since infection in the alternative cohort analysis. We calculated rate ratios (RRs) adjusted for potential confounders and estimated protection against repeat infection as 1 – RR. Findings : During the first surge (ie, before June, 2020), 533 381 people were tested, of whom 11 727 (2·20%) were PCR positive, and 525 339 were eligible for follow-up in the second surge, of whom 11 068 (2·11%) had tested positive during the first surge. Among eligible PCR-positive individuals from the first surge of the epidemic, 72 (0·65% [95% CI 0·51–0·82]) tested positive again during the second surge compared with 16 819 (3·27% [3·22–3·32]) of 514 271 who tested negative during the first surge (adjusted RR 0·195 [95% CI 0·155–0·246]). Protection against repeat infection was 80·5% (95% CI 75·4–84·5). The alternative cohort analysis gave similar estimates (adjusted RR 0·212 [0·179–0·251], estimated protection 78·8% [74·9–82·1]). In the alternative cohort analysis, among those aged 65 years and older, observed protection against repeat infection was 47·1% (95% CI 24·7–62·8). We found no difference in estimated protection against repeat infection by sex (male 78·4% [72·1–83·2] vs female 79·1% [73·9–83·3]) or evidence of waning protection over time (3–6 months of follow-up 79·3% [74·4–83·3] vs ≥7 months of follow-up 77·7% [70·9–82·9]). Interpretation : Our findings could inform decisions on which groups should be vaccinated and advocate for vaccination of previously infected individuals because natural protection, especially among older people, cannot be relied on.

	Number of infections during follow-up		Infection rate*		Adjusted rate ratio (95% CI)†	Estimated protection (95% CI)	p value‡
	Exposed individuals	Unexposed individuals	Exposed individuals	Unexposed individuals			
Overall	138	53 991	5·64	30·94	0·212 (0·179–0·251)	78·8% (74·9–82·1)	..
Sex							
Female	78	30 225	5·68	30·87	0·209 (0·167–0·261)	79·1% (73·9–83·3)	0·84
Male	60	23 766	5·59	31·03	0·216 (0·168–0·279)	78·4% (72·1–83·2)	..
Age group, years							
0–34	49	26 829	5·92	38·13	0·173 (0·131–0·229)	82·7% (77·1–86·9)	<0·0001
35–49	32	12 071	5·16	31·92	0·199 (0·141–0·282)	80·1% (71·8–85·9)	..
50–64	26	10 111	4·25	27·42	0·187 (0·127–0·274)	81·3% (72·6–87·3)	..
≥65	31	4980	8·01	16·92	0·529 (0·372–0·753)	47·1% (24·7–62·8)	..
Time in follow-up, months							
3–6	84	37 357	5·57	27·28	0·207 (0·167–0·256)	79·3% (74·4–83·3)	0·67
≥7	54	16 634	2·66	14·48	0·223 (0·171–0·291)	77·7% (70·9–82·9)	..

*Rate of infection per 100 000 person-days of follow-up. †Adjusted for sex, age group, test frequency, and start month of follow-up. ‡p value from likelihood ratio tests comparing models with and without interaction terms to capture evidence of effect heterogeneity across subgroups.

Table 2: **Protection against reinfection with SARS-CoV-2 by sex, age group, and time since first infection, in the alternative cohort analysis**

Dye C et al Science https://science.sciencemag.org/content/371/6535/1184	COVID-19 vaccination passports	Discussione sull'introduzione di un passaporto vaccinale per COVID-19 (analogo a quello per la febbre gialla e altre infezioni) e sui problemi legati alla creazione di disparità che potrebbero derivarne.	As countries grow eager to reignite their economies and people increasingly yearn for mobility and normalcy in life, pressure is mounting for some form of COVID-19 health status certificate that would support these desires. There has already been an explosion of COVID-19 passport initiatives for domestic use and international travel. But scientific, legal, and ethical concerns abound with such documentation. Given the high stakes, what is the path forward?
Rubin R JAMA https://jamanetwork.com/journals/jama/fullarticle/2777785	COVID-19 Vaccines vs Variants—Determining How Much Immunity Is Enough	La domanda chiave sui vaccini contro SARS-CoV-2, cui potremo rispondere accumulando esperienza dal mondo reale, è : quante persone vaccinate si infettano e hanno bisogno di ospedalizzazione ? I dati di sierologia sono poco informativi.	As COVID-19 cases resulting from infection with SARS-CoV-2 variants accumulate in the US and around the world, one question looms large: How well do the COVID-19 vaccines developed so far protect against these novel coronavirus spinoffs? Regardless of the platform on which the vaccine is based, Fauci said, "you still have a fixed immunogen and a virus that's changing. Sooner or later, you're going to get a mutant that evades that."

Aschwanden C Nature https://www.nature.com/articles/d41586-021-00728-2	Five reasons why COVID herd immunity is probably impossible	Le ragioni del titolo sono : incertezza della non trasmissibilità da parte dei vaccinati contro SARS-CoV-2; iniquità nella distribuzione del vaccino ; possibile effetto delle varianti sull'efficacia del vaccino ; incerta durata dell'immunità ; comportamenti più promiscui nei vaccinati che alzerebbero la soglia di « immunità di gregge ». La riduzione drastica dei casi di malattia grave sarebbe un presupposto di per sé molto significativo in vista del ritorno alla normalità.	Even with vaccination efforts in full force, the theoretical threshold for vanquishing COVID-19 looks to be out of reach.