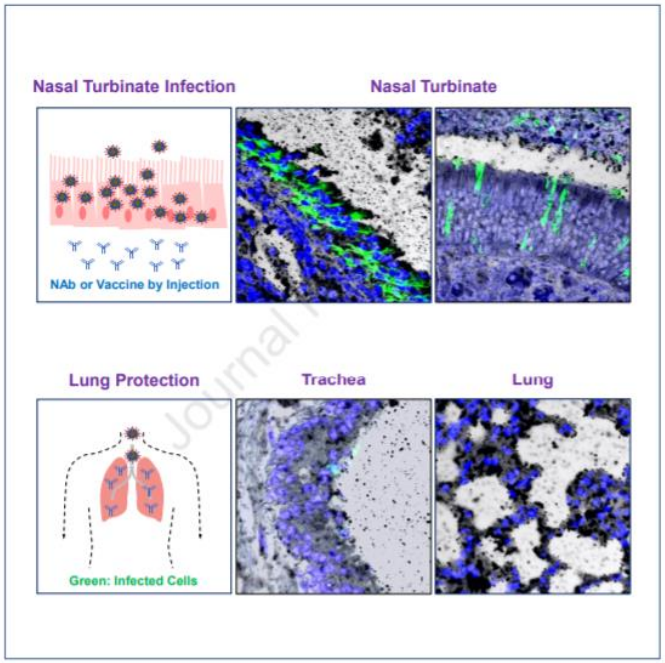
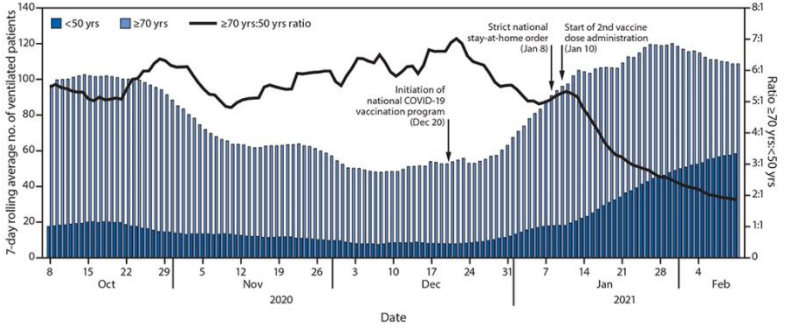
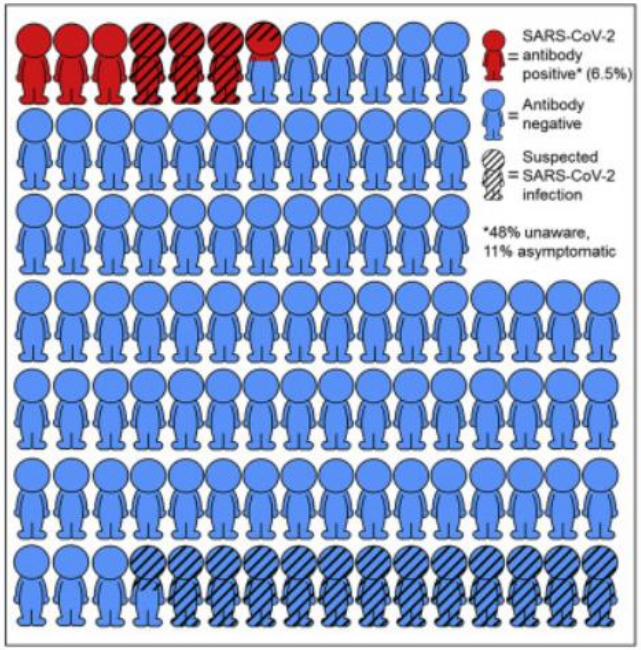
RICERCA BIBLIOGRAFICA COVID 19 SETTIMANA 01.03 – 7.03.2021 FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE DOTT.SSA ELEONORA TADDEI			
AUTORE/RIVISTA	**TITOLO**	**OUTCOME PRINCIPALE**	**ABSTRACT**
Zhou D et al Cell Host and Microbe https://www.sciencedirect.com/science/article/pii/S1931312821000986?via%3Dihub	Robust SARS-CoV-2 Infection in Nasal Turbinates after Treatment with Systemic Neutralizing Antibodies	Il criceto trattato con anticorpi neutralizzanti contro SARS-CoV-2 o sottoposto a vaccino a DNA è protetto a livello polmonare ma sviluppa una notevole infezione dei turbinati nasali : questo potrebbe sostenere l'ipotesi che la capacità di infettare, anche dopo la vaccinazione o l'infezione, è conservata.	Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is characterized by a burst in the upper respiratory portal for high transmissibility. To determine human neutralizing antibodies (HuNAbs) for entry protection, we tested three potent HuNAbs (IC50 range, 0.0007-0.35 μg/ml) against live SARS-CoV-2 infection in the golden Syrian hamster model. These HuNAbs inhibit SARS-CoV-2 infection by competing with human angiotensin converting enzyme-2 for binding to the viral receptor binding domain (RBD). Prophylactic intraperitoneal or intranasal injection of individual HuNAb or DNA vaccination significantly reduces infection in the lungs but not in the nasal turbinates of hamsters intranasally challenged with SARS-CoV-2. Although postchallenge HuNAb therapy suppresses viral loads and lung damage, robust infection is observed in nasal turbinates treated within 1-3 days. Our findings demonstrate that systemic HuNAb suppresses SARS-CoV-2 replication and injury in lungs; however, robust viral infection in

			nasal turbinate may outcompete the antibody with significant implications to subprotection, reinfection and vaccine. 
Hum C et al Drugs https://doi.org/10.1007/s40265-021-01474-5	MicroRNA Mimics or Inhibitors as Antiviral Therapeutic Approaches Against COVID-19	Ruolo dei micro-RNA (miRNA) come potenziale terapia per COVID-19.	Coronaviruses, such as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) responsible for the coronavirus disease 2019 (COVID-19) pandemic, present a significant threat to human health by inflicting a wide variety of health complications and even death. While conventional therapeutics often involve administering small molecules to fight viral infections, small non-coding RNA sequences, known as microRNAs (miRNAs/miR-), may present a novel antiviral strategy. We can take advantage of their ability to modulate host-virus interactions through mediating RNA degradation or translational inhibition. Investigations into miRNA and SARS-CoV-2 interactions can reveal novel therapeutic

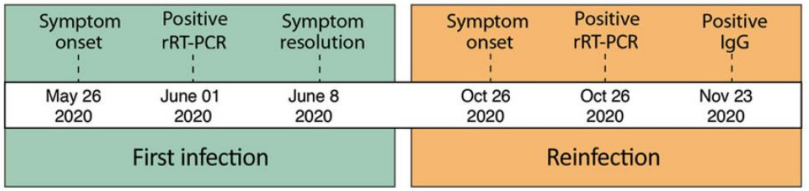
			approaches against this virus. The viral genomes of SARS-CoV-2, severe acute respiratory syndrome coronavirus (SARS-CoV), and Middle East respiratory syndrome coronavirus (MERS-CoV) were searched using the Nucleotide Basic Local Alignment Search Tool (BLASTn) for highly similar sequences, to identify potential binding sites for miRNAs hypothesized to play a role in SARS-CoV-2 infection. miRNAs that target angiotensin-converting enzyme 2 (ACE2), the receptor used by SARS-CoV-2 and SARS-CoV for host cell entry, were also predicted. Several relevant miRNAs were identified, and their potential roles in regulating SARS-CoV-2 infections were further assessed. Current treatment options for SARS-CoV-2 are limited and have not generated sufficient evidence on safety and efficacy for treating COVID-19. Therefore, by investigating the interactions between miRNAs and SARS-CoV-2, miRNA-based antiviral therapies, including miRNA mimics and inhibitors, may be developed as an alternative strategy to fight COVID-19.
Rinott E et al Morbidity and Mortality Weekly Report https://www.cdc.gov/mmwr/volumes/70/wr/mm7009e3.htm?s_cid=mm7009e3_w	Reduction in COVID-19 patients requiring mechanical ventilation following implementation of a national COVID-19 vaccination program – Israel, December 2020-February 2021	Declino del 67% del numero di persone di età superiore a 70 anni ricoverate in terapia intensiva e sottoposte a ventilazione meccanica dopo la campagna vaccinale contro SARS-CoV-2 in Israele.	Considering the vaccination rate and the expected vaccine efficacy, this study provides preliminary evidence at the population level for the reduction in risk for severe COVID-19, as manifested by need for mechanical ventilation, after vaccination with the Pfizer-BioNTech COVID-19 vaccine. These data are consistent with preliminary reports showing a reduction in COVID-19 cases and severe cases in the vaccinated population and a reduction in viral load in vaccinated persons compared with that in unvaccinated persons. Taken together, these results suggest reduced rates of severe COVID-19 following vaccination.

			FIGURE 2. Number and ratio of COVID-19 patients aged <50 and ≥70 years requiring mechanical ventilation — Israel, October 8, 2020–February 9, 2021 
Van der Hurk K et al Cell Reports Medicine https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(21)00038-0	Low awareness of past SARS-CoV-2 infection in healthy plasma donors	Sieroprevalenza di anticorpi contro SARS-CoV-2 in 3676 donatori di plasma : il 6.5% è positivo e di questi quasi la metà non pensava di aver contratto la malattia.	Awareness of infection with SARS-CoV-2 is crucial for the effectiveness of COVID-19 control measures. Here, we investigate awareness of infection and symptoms in relation to antibodies against SARS-CoV-2 in healthy plasma donors. We ask individuals donating plasma across the Netherlands between May 11th and 18th 2020 to report COVID-19 related symptoms and we test for antibodies indicative of a past infection with SARS-CoV-2. Among 3,676 with antibody and questionnaire data 239 (6.5%) are positive for SARS-CoV-2 antibodies. Of those, 48% suspect no COVID-19 despite the majority reporting symptoms. 11% of seropositive individuals report no, and 27% very mild symptoms at any time during the first peak of the epidemic. Anosmia/ageusia and fever are most strongly associated with seropositivity. Almost half of seropositive individuals do not suspect SARS-CoV-2 infection. Improved recognition of COVID-19 symptoms, in

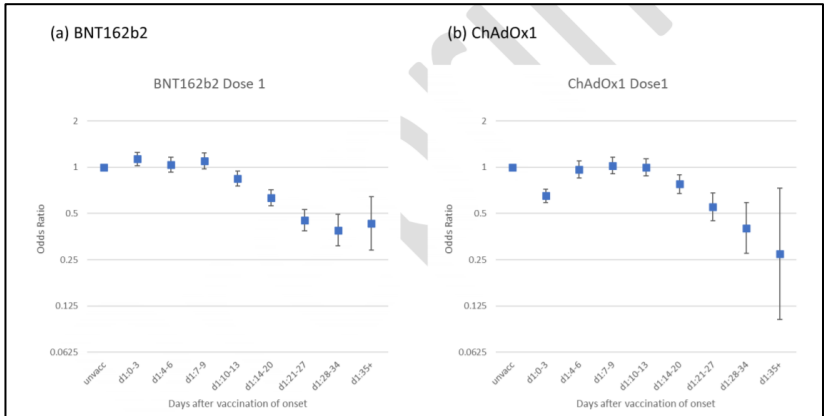
			particular anosmia/ageusia and fever, is needed to reduce widespread SARS-CoV-2 transmission. 
Nakamichi K et al Scientific Reports https://doi.org/10.1038/s41598-021-82850-9	Hospitalization and mortality associated with SARS-CoV-2 viral clades in COVID-19.	Il genoma di SARS-CoV-2 infettante 190 soggetti ricoverati e ambulatoriali afferenti a un singolo centro è stato sequenziato per stabilire se diverse varianti fossero alla base di diversi outcome clinici : non si trovano differenze fra le due varianti predominanti nel periodo marzo-aprile 2020.	The COVID-19 epidemic of 2019-20 is due to the novel coronavirus SARS-CoV-2. Following first case description in December, 2019 this virus has infected over 10 million individuals and resulted in at least 500,000 deaths world-wide. The virus is undergoing rapid mutation, with two major clades of sequence variants emerging. This study sought to determine whether SARS-CoV-2 sequence variants are associated with differing outcomes among COVID-19 patients in a single medical system. Whole genome SARS-CoV-2 RNA sequence was obtained from isolates collected from patients registered in the University of Washington Medicine health system between March 1 and April 15, 2020. Demographic and baseline clinical characteristics of patients and their outcome data including their hospitalization

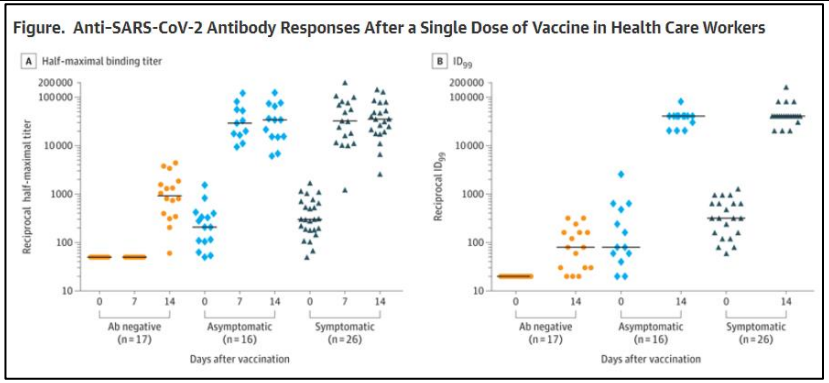
			and death were collected. Statistical and machine learning models were applied to determine if viral genetic variants were associated with specific outcomes of hospitalization or death. Full length SARS-CoV-2 sequence was obtained 190 subjects with clinical outcome data. 35 (18.4%) were hospitalized and 14 (7.4%) died from complications of infection. A total of 289 single nucleotide variants were identified. Clustering methods demonstrated two major viral clades, which could be readily distinguished by 12 polymorphisms in 5 genes. A trend toward higher rates of hospitalization of patients with Clade 2 infections was observed (p = 0.06, Fisher's exact). Machine learning models utilizing patient demographics and co-morbidities achieved area-under-the-curve (AUC) values of 0.93 for predicting hospitalization. Addition of viral clade or sequence information did not significantly improve models for outcome prediction. In summary, SARS-CoV-2 shows substantial sequence diversity in a community-based sample. Two dominant clades of virus are in circulation. Among patients sufficiently ill to warrant testing for virus, no significant difference in outcomes of hospitalization or death could be discerned between clades in this sample. Major risk factors for hospitalization and death for either major clade of virus include patient age and comorbid conditions.
Hashan MR et al EClinicalMedicine https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00051-1/fulltext	Epidemiology and clinical features of COVID-19 outbreaks in aged care facilities: A systematic review and meta-analysis	Revisione sistematica dell'impatto di COVID-19 sulle strutture per anziani : mortalità 23%, oltre un terzo dei pazienti necessita di ospedalizzazione.	Background : COVID-19 outbreaks in aged care facilities (ACFs) often have devastating consequences. However, epidemiologically these outbreaks are not well defined. We aimed to define such outbreaks in ACFs by systematically reviewing literature published during the current COVID-19 pandemic. Methods : We searched 11 bibliographic databases for literature published on COVID-19 in ACFs between December 2019 and September 2020. Original studies reporting extractable epidemiological data as part of outbreak investigations or non-

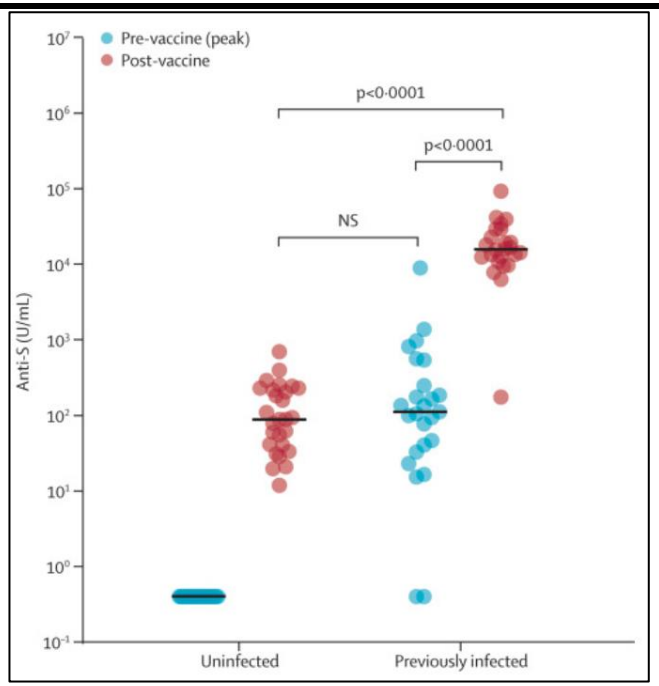
			outbreak surveillance of ACFs were included in this systematic review and meta-analysis. PROSPERO registration: CRD42020211424. Findings : We identified 5,148 publications and selected 49 studies from four continents reporting data on 214,380 residents in 8,502 ACFs with 25,567 confirmed cases of COVID-19. Aged care residents form a distinct vulnerable population with single-facility attack rates of 45% [95% CI 32–58%] and case fatality rates of 23% [95% CI 18–28%]. Of the cases, 31% [95% CI 28–34%] were asymptomatic. The rate of hospitalization amongst residents was 37% [95% CI 35–39%]. Data from 21 outbreaks identified a resident as the index case in 58% of outbreaks and a staff member in 42%. Findings from the included studies were heterogeneous and of low to moderate quality in risk of bias assessment. Interpretation : The clinical presentation of COVID-19 varies widely in ACFs residents, from asymptomatic to highly serious cases. Preventing the introduction of COVID-19 into ACFs is key, and both residents and staff are a priority group for COVID-19 vaccination. Rapid diagnosis, identification of primary and secondary cases and close contacts plus their isolation and quarantine are of paramount importance.
Nonaka CKV et al Emerging Infectious Diseases	Genomic Evidence of SARS-CoV-2 Reinfection Involving E484K Spike Mutation, Brazil	Reinfezione da SARS-CoV-2 in una donna di 45 anni in Brasile, a distanza di 5 mesi dal primo episodio e senza necessità di ospedalizzazione. I due episodi sono stati causati da due varianti del virus : B.1.1.33 e P.2 (B.1.1.28.2).	Uncertainty remains about how long the protective immune responses against severe acute respiratory syndrome coronavirus 2 persists, and suspected reinfection in recovered patients has been reported. We describe a case of reinfection from distinct virus lineages in Brazil harboring the E484K mutation, a variant associated with escape from neutralizing antibodies.

https://wwwnc.cdc.gov/eid/article/27/5/21-0191_article			
Public Health England https://www.gov.uk/government/news/new-data-show-vaccines-reduce-severe-covid-19-in-older-adults	New data show vaccines reduce severe COVID-19 in older adults	Riduzione delle infezioni sintomatiche e delle ospedalizzazioni da SARS-CoV-2 fra gli ultra-settantenni nel Regno Unito dopo un mese di campagna vaccinale.	Today Public Health England (PHE) has submitted a pre-print of a real-world study that shows that both the Pfizer and Oxford-AstraZeneca vaccines are highly effective in reducing COVID-19 infections among older people aged 70 years and over. Since January, protection against symptomatic COVID, 4 weeks after the first dose, ranged between 57 and 61% for one dose of Pfizer and between 60 and 73% for the Oxford-AstraZeneca vaccine.
Bernal JL et al Preprint, not peer-reviewed https://khub.net/documents/135939561/430986542/Early+effectiveness+of+COVID+vaccines.pdf/ffd7161c-b255-8e88-c2dc-88979fc2cc1b?t=1614617945615	Early effectiveness of COVID-19 vaccination with vBNT162b2 mRNA vaccine and ChAdOx1 adenovirus vector vaccine on symptomatic disease, hospitalisations and mortality in older adults in the UK: a test negative case control study	Lavoro in corso di revisione menzionato sul sito Public Health England (vedi sopra) i cui dati mostrano che i soggetti anziani vaccinati con Pfizer hanno una riduzione del tasso di infezione sintomatica da SARS-CoV-2, ospedalizzazione e morte, mentre per i vaccinati con una dose di AstraZeneca si hanno risultati analoghi ma non è valutabile l'effetto sulla mortalità per via del follow up insufficiente.	Objectives : To estimate the real-world effectiveness of the Pfizer/BioNTech BNT162b2 vaccine and Astrazeneca ChAdOx1 vaccine against Confirmed COVID-19, hospitalisations and deaths. To estimate effectiveness on the UK variant of concern. Design : Test negative case control design Setting : Community COVID-19 PCR testing in England Participants : All adults in England aged 70 years and older (over 7.5 million). All COVID-19 testing in the community among eligible individuals who reported symptoms between 8th December 2020 and 19 th February 2021 was included in the analysis. Interventions : One and two doses of BNT162b2 vaccine. One dose of ChAdOx1 vaccine. Main outcome measures : Symptomatic PCR confirmed SARS-CoV-2 infection, hospitalisations and deaths with COVID-19. Results : Individuals aged >=80 years vaccinated with BNT162b2 prior to 4th January, had a higher odds of testing positive in the first 9 days

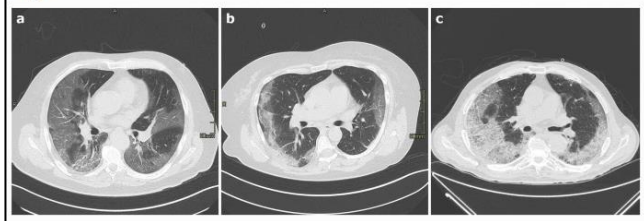
		L'ulteriore notizia positiva è l'evidente efficacia contro la variante « inglese », ormai prevalente nel Paese.	after vaccination (odds ratio up to 1.48, 95%CI 1.23-1.77), indicating that those initially targeted had a higher underlying risk of infection. Vaccine effectiveness was therefore estimated relative to the baseline post-vaccination period. Vaccine effects were noted from 10-13 days after vaccination, reaching an effectiveness of 70% (95% CI 59-78%) from 28-34 days, then plateauing. From 14 days after the second dose a vaccine effectiveness of 89% (95%CI: 85-93%) was seen. Individuals aged >=70 years vaccinated from 4 th January had a similar underlying risk of COVID-19 to unvaccinated individuals. With BNT162b2, vaccine effectiveness reached 61% (95%CI 51-69%) from 28-34 days after vaccination then plateaued. With the ChAdOx1 vaccine, vaccine effects were seen from 14-20 days after vaccination reaching an effectiveness of 60% (95%CI 41-73%) from 28-34 days and further increasing to 73% (95%CI 27-90%) from day 35 onwards. On top of the protection against symptomatic disease, cases who had been vaccinated with one dose of BNT162b2 had an additional 43% (95%CI 33-52%) lower risk of emergency hospitalisation and an additional 51% (95%CI 37-62%) lower risk of death. Cases who had been vaccinated with one dose of ChAdOx1 had an additional 37% (95% CI 3-59%) lower risk of emergency hospitalisation. There was insufficient follow-up to assess the effect of ChAdOx1 on mortality due to the later rollout of this vaccine. Combined with the effect against symptomatic disease, this indicates that a single dose of either vaccine is approximately 80% effective at preventing hospitalisation and a single dose of BNT162b2 is 85% effective at preventing death with COVID-19. Conclusion : Vaccination with either a single dose of BNT162b2 or ChAdOx1 COVID-19 vaccination was associated with a significant reduction in symptomatic SARS-CoV2 positive cases in older adults with even greater protection against severe disease. Both vaccines

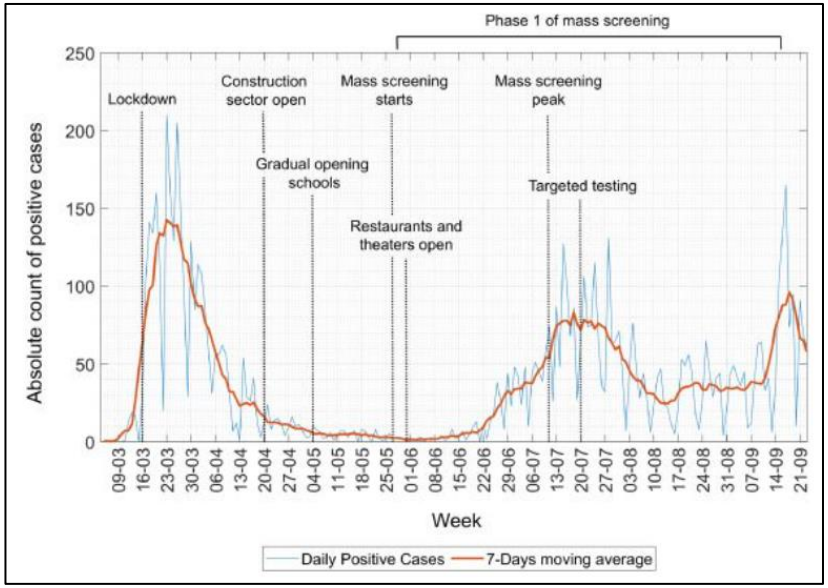
			show similar effects. Protection was maintained for the duration of follow-up (>6 weeks). A second dose of BNT162b2 provides further protection against symptomatic disease but second doses of ChAdOx1 have not yet been rolled out in England. There is a clear effect of the vaccines against the UK variant of concern.  *Figure 3: Adjusted odds ratios for confirmed case by interval after vaccination for BNT162b2 and ChAdOx1 vaccines, vaccinations administered since 4th January 2021*
Saadat S et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2777171?resultClick=1	Binding and Neutralization Antibody Titers After a Single Vaccine Dose in Health Care Workers Previously Infected With SARS-CoV-2	Di 59 operatori sanitari vaccinati contro SARS-CoV-2 con vaccini a mRNA, quelli con storia documentata di infezione pregressa da SARS-CoV-2 sviluppano un titolo anticorpale significativamente superiore dopo la prima dose di vaccino rispetto ai naive.	Current shortages in COVID-19 vaccine production and distribution have led some experts to suggest untested regimens. Persons who have had COVID-19 are thought to have protective immunity and memory responses. for at least 6 months; however, neither recall responses nor ideal vaccine dosing regimens have been studied in those previously infected with SARS-CoV-2. We assessed whether health care workers with previous COVID-19 infection could mount recall responses to a single dose of an mRNA-based COVID-19 vaccine.

			
Mainsty C et al The Lancet https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00501-8/fulltext	Antibody response to first BNT162b2 dose in previously SARS-CoV-2-infected individuals	Dopo una singola dose di vaccino Pfizer, 24 operatori sanitari con sierologia già positiva per via di un'infezione pregressa da SARS-CoV-2 sviluppano un titolo anticorpale contro S1 140 volte superiore ai naive. Non è noto quanto tale risposta sia duratura dopo una sola dose di vaccino.	We reasoned that previous infection could be analogous to immune priming. As such, a first prime vaccine dose would effectively act as boost, so a second dose might not be needed. To test this, we undertook a nested case-control analysis of 51 participants of COVIDsortium, an ongoing longitudinal observational study of health-care workers (HCWs) in London who underwent weekly PCR and quantitative serology testing from the day of the first UK lockdown on March 23, 2020, and for 16 weeks onwards. 24 of 51 HCWs had a previous laboratory-confirmed mild or asymptomatic SARS-CoV-2 infection, as confirmed by positive detection of antibodies against the SARS-CoV-2 nucleocapsid (Elecsys Anti-SARS-CoV-2 N ECLIA, Roche Diagnostics, Burgess Hill, UK) or the receptor binding domain of the SARS-CoV-2 S1 subunit of the spike protein (anti-S; Elecsys anti-SARS-CoV-2 spike ECLIA, Roche Diagnostics), whereas 27 HCWs remained seronegative. A median of 12·5 sampling timepoints per participant permitted the identification of peak antibody titres in seropositive individuals while avoiding false negatives.

			
Plante JA et al Cell Host and Microbe https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(21)00099-8?utm_medium=homepage	The Variant Gambit: COVID's Next Move	Revisione sulle varianti di SARS-CoV-2.	Over a year after its emergence, COVID-19, the disease caused by SARS-CoV-2, continues to plague the world and dominate our daily lives. Even with the development of effective vaccines, this coronavirus pandemic continues to cause a fervor with the identification of major new variants hailing from the United Kingdom, South Africa, Brazil, and California. Coupled with worries over a distinct mink strain that has caused human infections and potential for further mutations, SARS-CoV-2 variants bring concerns for increased spread and escape from both vaccine and natural infection immunity. Here, we outline factors driving SARS-CoV-2 variant evolution, explore the potential impact of specific mutations, examine the risk of further mutations, and consider the

			experimental studies needed to understand the threat these variants pose.
Lichtenauer M et al Frontiers in Cardiovascular Medicine https://doi.org/10.3389/fcvm.2021.623076	Overview of Current International Recommendations for Echocardiography Exams During the Covid-19 Pandemic and Its Local Implementation in Austria.	Indicazioni all'esecuzione di ecocardiogramma in corso di pandemia di COVID-19 : le medesime dell'epoca precedente, con DPI.	Since its first appearance in December 2019, the novel Coronavirus SARS-CoV-2 (Severe acute respiratory syndrome coronavirus 2) has spread throughout the world at rapid pace causing the coronavirus disease 2019 (Covid-19). Originating in the Chinese province Hubei, more than 91.8 million people globally have now been infected with the coronavirus and more than 1.966.000 patients have died thus far from Covid-19 (as of January 13th 2021). The virus spreads primarily by droplet infection as well as via aerosols during close physical contact. Particularly in medical examinations with close physical contact between examiner and patient, like echocardiography, the risk of contracting the virus is increased. Therefore, the use of personal protective equipment is recommended for the protection of patients and medical personnel alike. In this article, the current recommendations of international professional associations on the use of personal protective equipment and their local implementation are presented.
Carlicchi E et al Emerging Radiology https://doi.org/10.1007/s10140-021-01919-0	Chest-CT mimics of COVID-19 pneumonia-a review article	Diagnosi differenziali radiologiche di polmonite COVID-19 relata alla TAC torace.	Coronavirus disease 2019 (COVID-19) emerged in early December 2019 in China, as an acute lower respiratory tract infection and spread rapidly worldwide being declared a pandemic in March 2020. Chest-computed tomography (CT) has been utilized in different clinical settings of COVID-19 patients; however, COVID-19 imaging appearance is highly variable and nonspecific. Indeed, many pulmonary infections and non-infectious diseases can show similar CT findings and mimic COVID-19 pneumonia. In this review, we discuss clinical conditions that share a similar imaging

			appearance with COVID-19 pneumonia, in order to identify imaging and clinical characteristics useful in the differential diagnosis. **Fig. 1**  **a–c** Axial HRCT images of three different patients with COVID-19 pneumonia (**a–c**) showing bilateral, patchy ground-glass parenchymal opacities with prevalent peripheral and mid-lower lobes distribution
Wilmes P et al The Lancet https://www.sciencedirect.com/science/article/pii/S2666776221000338?via%3Dihub	SARS-CoV-2 transmission risk from asymptomatic carriers: Results from a mass screening programme in Luxembourg	Risultati di uno screening di massa eseguito in Lussemburgo per infezione da SARS-CoV-2 : vengono identificati 1099 casi, di cui due terzi sintomatici.	Background : To accompany the lifting of COVID-19 lockdown measures, Luxembourg implemented a mass screening (MS) programme. The first phase coincided with an early summer epidemic wave in 2020. Methods : rRT-PCR-based screening for SARS-CoV-2 was performed by pooling of samples. The infrastructure allowed the testing of the entire resident and cross-border worker populations. The strategy relied on social connectivity within different activity sectors. Invitation frequencies were tactically increased in sectors and regions with higher prevalence. The results were analysed alongside contact tracing data. Findings : The voluntary programme covered 49% of the resident and 22% of the cross-border worker populations. It identified 850 index cases with an additional 249 cases from contact tracing. Over-representation was observed in the services, hospitality and construction sectors alongside regional differences. Asymptomatic cases had a significant but lower secondary attack rate when compared to symptomatic individuals. Based on simulations using an agent-based SEIR model, the total number of expected cases

			would have been 42·9% (90% CI [-0·3, 96·7]) higher without MS. Mandatory participation would have resulted in a further difference of 39·7% [19·6, 59·2]. Interpretation : Strategic and tactical MS allows the suppression of epidemic dynamics. Asymptomatic carriers represent a significant risk for transmission. Containment of future outbreaks will depend on early testing in sectors and regions. Higher participation rates must be assured through targeted incentivisation and recurrent invitation. 
Van Loon W et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-	Renewed absence of SARS-CoV-2 infections in the day care context in Berlin, January 2021	In uno studio di sorveglianza su 149 bambini di 8 asili della regione di Berlino, 74 insegnanti e 472 familiari, si registrano 0 casi di infezione da SARS-CoV-2 in Settembre 2020 e Gennaio 2021,	At the January assessment, 57.9% (70/121) of children and 98.5% (65/66) of staff had visited their kindergarten at least once during the preceding two weeks (median, 8 days [range, 0-11], and 10 days [1-14], respectively). 149 children (median age, 5 years [range, 2-8]), 74 staff members (45 years [19-79]), and 472 household members (36 years [1-91]) provided a swab. Mostly cold-like symptoms

article/doi/10.1093/cid/ciab199/6155930?searchresult=1		nonostante nel secondo periodo vi fosse un aumento di casi nella stessa regione. Gli autori suggeriscono che gli asili non siano una fonte significativa di contagio.	were reported for 11.6% (17/147), 55.4% (41/74), and 24.9% (112/449) of children, staff, and household members on the day of sample collection. All tested negative for SARS-CoV-2.
Davies NG et al Science https://science.sciencemag.org/content/early/2021/03/03/science.abg3055	Estimated transmissibility and impact of SARS-CoV-2 lineage B.1.1.7 in England	Stima della trasmissibilità della variante B.1.1.7 di SARS-CoV-2 (« inglese ») e potenziali implicazioni epidemiologiche.	A novel SARS-CoV-2 variant, VOC 202012/01 (lineage B.1.1.7), emerged in southeast England in November 2020 and is rapidly spreading toward fixation. Using a variety of statistical and dynamic modelling approaches, we estimate that this variant has a 43–90% (range of 95% credible intervals 38–130%) higher reproduction number than preexisting variants. A fitted two-strain dynamic transmission model shows that VOC 202012/01 will lead to large resurgences of COVID-19 cases. Without stringent control measures, including limited closure of educational institutions and a greatly accelerated vaccine roll-out, COVID-19 hospitalisations and deaths across England in 2021 will exceed those in 2020. Concerningly, VOC 202012/01 has spread globally and exhibits a similar transmission increase (59–74%) in Denmark, Switzerland, and the United States.
Ooliver SE et al Morbidity and Mortality Weekly Report https://www.cdc.gov/mmwr/volumes/70/wr/mm7009e4.htm	The Advisory Committee on Immunization Practices' Interim Recommendation for Use of Janssen COVID-19 Vaccine	Raccomandazione all'uso del vaccino Janssen a vettore adenovirale contro SARS-CoV-2 da parte della FDA.	What is already known about this topic? On February 27, 2021, the Food and Drug Administration issued an Emergency Use Authorization (EUA) for the Janssen COVID-19 vaccine. What is added by this report? On February 28, 2021, after a transparent evidence-based review of all available data, the Advisory Committee on Immunization Practices (ACIP) issued an interim recommendation for use of the Janssen COVID-19 vaccine in persons aged ≥18 years for the prevention of COVID-19. What are the implications for public health practice? The Janssen COVID-19 vaccine has high efficacy against COVID-19–associated

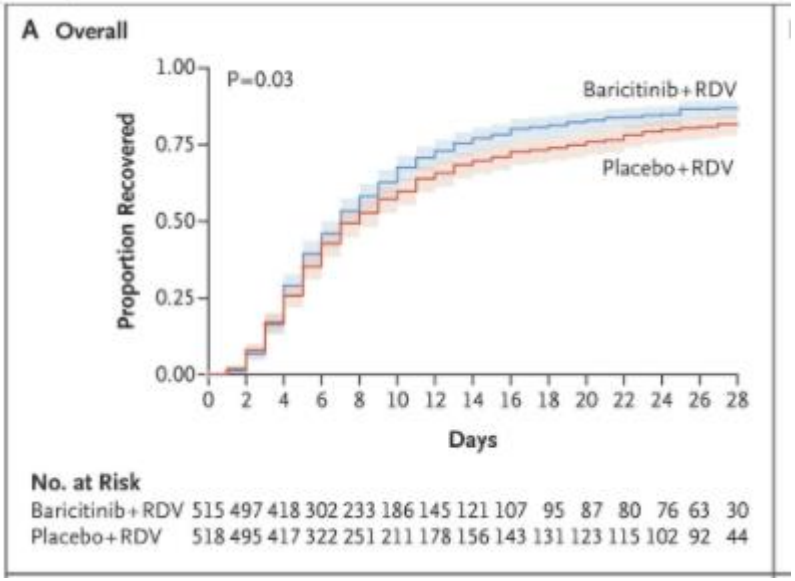
			hospitalization and death. Persons may receive any ACIP-recommended COVID-19 vaccine and are encouraged to receive the earliest vaccine available to them. Use of all EUA-authorized COVID-19 vaccines is critical in controlling the pandemic.
Schumm MA et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2777342	Filtering Facepiece Respirator (N95 Respirator) Reprocessing: A Systematic Review	Rassegna delle tecniche per riutilizzare le mascherine FFP2 in caso di carenza di dispositivi di protezione: raggi UV, perossido di idrogeno vaporizzato, calore umido e microonde sono tutti metodi efficaci, anche se gli studi specificamente condotti su SARS-CoV-2 sono pochi.	Importance The COVID-19 pandemic has resulted in a persistent shortage of personal protective equipment; therefore, a need exists for hospitals to reprocess filtering facepiece respirators (FFRs), such as N95 respirators. Objective To perform a systematic review to evaluate the evidence on effectiveness and feasibility of different processes used for decontaminating N95 respirators. Evidence Review A search of PubMed and EMBASE (through January 31, 2021) was completed for 5 types of respirator-decontaminating processes including UV irradiation, vaporized hydrogen peroxide, moist-heat incubation, microwave-generated steam, and ethylene oxide. Data were abstracted on process method, pathogen removal, mask filtration efficiency, facial fit, user safety, and processing capability. Findings Forty-two studies were included that examined 65 total types of masks. All were laboratory studies (no clinical trials), and 2 evaluated respirator performance and fit with actual clinical use of N95 respirators. Twenty-seven evaluated UV germicidal irradiation, 19 vaporized hydrogen peroxide, 9 moist-heat incubation, 10 microwave-generated steam, and 7 ethylene oxide. Forty-three types of N95 respirators were treated with UV irradiation. Doses of 1 to 2 J/cm2 effectively sterilized most pathogens on N95 respirators (>103 reduction in influenza virus [4 studies], MS2 bacteriophage [3 studies], Bacillus spores [2 studies], Escherichia virus MS2 [1 study], vesicular stomatitis virus [1 study], and Middle East respiratory syndrome virus/SARS-CoV-1 [1 study]) without

			degrading respirator components. Doses higher than 1.5 to 2 J/cm2 may be needed based on 2 studies demonstrating greater than 103 reduction in SARS-CoV-2. Vaporized hydrogen peroxide eradicated the pathogen in all 7 efficacy studies (>104 reduction in SARS-CoV-2 [3 studies] and >106 reduction of Bacillus and Geobacillus stearothermophilus spores [4 studies]). Pressurized chamber systems with higher concentrations of hydrogen peroxide caused FFR damage (6 studies), while open-room systems did not degrade respirator components. Moist heat effectively reduced SARS-CoV-2 (2 studies), influenza virus by greater than 104 (2 studies), vesicular stomatitis virus (1 study), and Escherichia coli (1 study) and preserved filtration efficiency and facial fit for 11 N95 respirators using preheated containers/chambers at 60 °C to 85 °C (5 studies); however, diminished filtration performance was seen for the Caron incubator. Microwave-generated steam (1100-W to 1800-W devices; 40 seconds to 3 minutes) effectively reduced pathogens by greater than 103 (influenza virus [2 studies], MS2 bacteriophage [3 studies], and Staphylococcus aureus [1 study]) and maintained filtration performance in 10 N95 respirators; however, damage was noted in least 1 respirator type in 4 studies. In 6 studies, ethylene oxide preserved respirator components in 16 N95 respirator types but left residual carcinogenic by-product (1 study). Conclusions and Relevance Ultraviolet germicidal irradiation, vaporized hydrogen peroxide, moist heat, and microwave-generated steam processing effectively sterilized N95 respirators and retained filtration performance. Ultraviolet irradiation and vaporized hydrogen peroxide damaged respirators the least. More research is needed on decontamination effectiveness for SARS-CoV-2 because few studies specifically examined this pathogen.

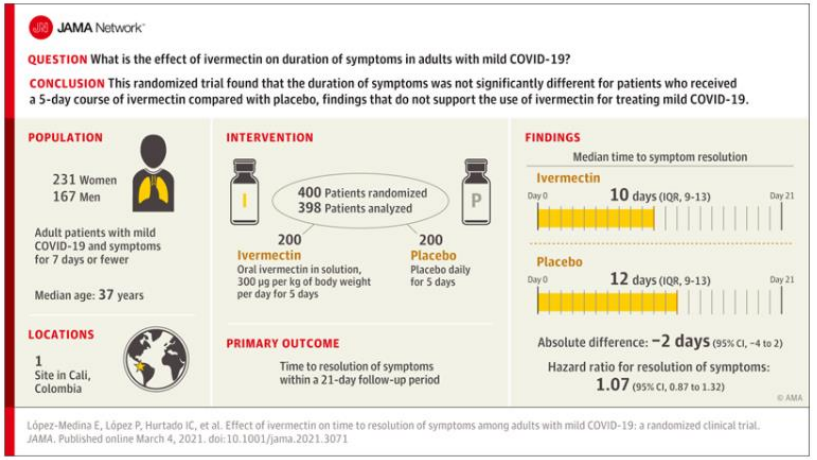
Murray CJL et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2777343	The Potential Future of the COVID-19 Pandemic Will SARS-CoV-2 Become a Recurrent Seasonal Infection?	Prospettive sul raggiungimento dell'immmunità di gregge contro SARS-CoV-2 e sulla possibilità che il virus dia luogo a picchi stagionali nel futuro : la durata dell'immunità e l'emergere di nuove varianti sono elementi cruciali.	There is growing optimism and hope that by virtue of ongoing immunization efforts, seasonality (declining infections through August), and naturally acquired immunity, by spring and early summer 2021 in the US there will be a substantial decline in the number of deaths and hospitalizations related to COVID-19. However, this optimism must be tempered by several important factors. The likelihood of achieving herd immunity against SARS-CoV-2 is low simply because not all individuals in the US are eligible to be vaccinated and a quarter of eligible individuals will likely decline to be immunized. Moreover, the vaccines do not provide full immunity against infection, and the currently available vaccines are less effective against variant B.1.351, and possibly other variants. Accordingly, the public and health systems need to plan for the possibility that COVID-19 will persist and become a recurrent seasonal disease.
Stead W JAMA https://jamanetwork.com/journals/jama/fullarticle/2776884	It's Not Your Fault	Il senso di colpa che accompagna le malattie infettive è presente anche nella pandemia di COVID-19.	COVID-19 has made this toxic combination commonplace. When we are not in the midst of a pandemic, most of us don't experience the intimacy with mortality looming over us now. Most of us, during times of peace and health, do not find ourselves in the position of wondering if we have contributed directly to the illness or death of another person. These feelings are relegated to the unlucky among us—the driver of the deadly car, the babysitter of the unwatched child who fell down stairs, the father who forgot to lock his gun safe. But COVID-19 is a lightning bolt that has come for all of us. Any of us might wake up one day and realize we shared this virus with someone else and, with it, gave sickness and death.

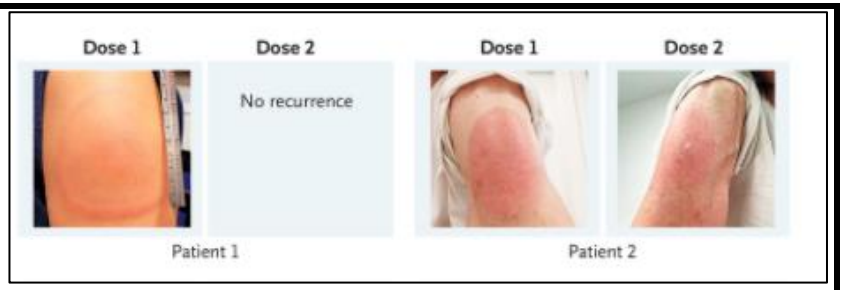
Touafchia A et al Clinical Microbiology and Infection https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00094-X/fulltext	Serious bradycardia and remdesivir for coronavirus 2019 (COVID-19): a new safety concerns	Analisi post-marketing che osserva una associazione fra bradicardia e uso di remdesivir nella terapia di COVID-19 rispetto alle altre terapie disponibili o utilizzate in precedenza. Il meccanismo alla base sarebbe un effetto diretto del farmaco sull'attività del nodo senoatriale.	Objectives : In recent clinical trials some cardiac arrhythmias were reported with use of remdesivir for COVID-19. To address this safety concern, we investigated whether use of remdesivir for COVID-19 is associated with an increased risk of bradycardia. Methods : Using VigiBase®, the World Health Organization Global Individual Case Safety Reports database, we compared the cases of bradycardia reported in COVID-19 patients exposed to remdesivir with those reported in COVID-19 patients exposed to hydroxychloroquine, lopinavir/ritonavir, tocilizumab or glucocorticoids. All reports of patients with COVID-19 registered up to the 23th of September 2020 were included. We conducted disproportionality analyses allowing the estimation of reporting odds ratios (RORs) with 95% Confident Intervals (95% CI). Results : We found 302 cardiac effects including 94 bradycardia (31%) among the 2,603 reports with remdesivir prescribed in COVID-19 patients. Most of reports were serious (75, 80%) and in 16 reports (17%) evolution was fatal. Compared with hydroxychloroquine, lopinavir/ritonavir, tocilizumab or glucocorticoids, the use of remdesivir was associated with an increased risk of reporting bradycardia (ROR 1.65; 95% CI 1.23, 2.22). Consistent results were observed in other sensitivity analyses. Conclusions : This post-marketing study in a real-world setting suggests that the use of remdesivir is significantly associated with an increased risk of reporting bradycardia and serious bradycardia when compared with the use of with hydroxychloroquine, lopinavir/ritonavir, tocilizumab or glucocorticoids. This result is in line with pharmacodynamic properties of the remdesivir.

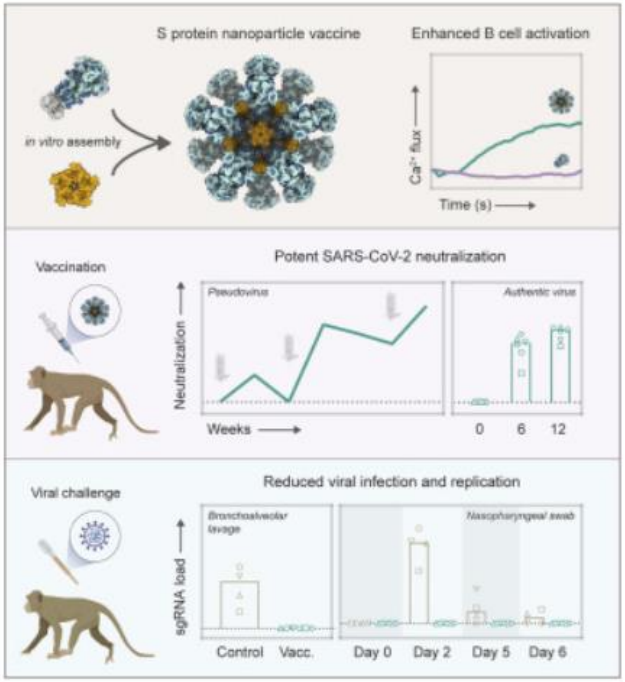
Kalil AC et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2031994	Baricitinib plus Remdesivir for Hospitalized Adults with Covid-19	Trial clinico randomizzato che confronta 515 pazienti trattati con remdesivir + baricitinibi con 518 trattati con remdesivir + placebo per COVID-19 : il baricitinib riduce il tempo di guarigione e migliora la clinica soprattutto nei pazienti trattati con alti flussi o ventilazione non invasiva.	BACKGROUND : Severe coronavirus disease 2019 (Covid-19) is associated with dysregulated inflammation. The effects of combination treatment with baricitinib, a Janus kinase inhibitor, plus remdesivir are not known. METHODS : We conducted a double-blind, randomized, placebo-controlled trial evaluating baricitinib plus remdesivir in hospitalized adults with Covid-19. All the patients received remdesivir (≤10 days) and either baricitinib (≤14 days) or placebo (control). The primary outcome was the time to recovery. The key secondary outcome was clinical status at day 15. RESULTS : A total of 1033 patients underwent randomization (with 515 assigned to combination treatment and 518 to control). Patients receiving baricitinib had a median time to recovery of 7 days (95% confidence interval [CI], 6 to 8), as compared with 8 days (95% CI, 7 to 9) with control (rate ratio for recovery, 1.16; 95% CI, 1.01 to 1.32; P=0.03), and a 30% higher odds of improvement in clinical status at day 15 (odds ratio, 1.3; 95% CI, 1.0 to 1.6). Patients receiving high-flow oxygen or noninvasive ventilation at enrollment had a time to recovery of 10 days with combination treatment and 18 days with control (rate ratio for recovery, 1.51; 95% CI, 1.10 to 2.08). The 28-day mortality was 5.1% in the combination group and 7.8% in the control group (hazard ratio for death, 0.65; 95% CI, 0.39 to 1.09). Serious adverse events were less frequent in the combination group than in the control group (16.0% vs. 21.0%; difference, −5.0 percentage points; 95% CI, −9.8 to −0.3; P=0.03), as were new infections (5.9% vs. 11.2%; difference, −5.3 percentage points; 95% CI, −8.7 to −1.9; P=0.003). CONCLUSIONS : Baricitinib plus remdesivir was superior to remdesivir alone in reducing recovery time and accelerating improvement in clinical status among patients with Covid-19,

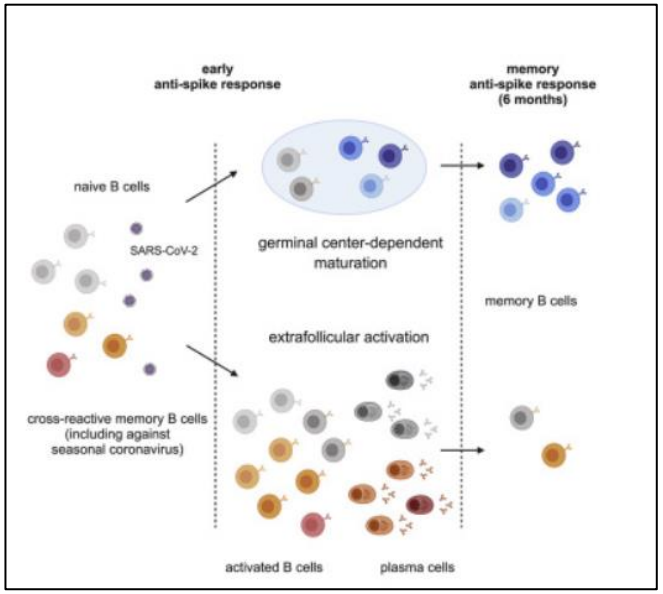
			notably among those receiving high-flow oxygen or noninvasive ventilation. The combination was associated with fewer serious adverse events. 
López-Medina E et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2777389	Effect of Ivermectin on Time to Resolution of Symptoms Among Adults With Mild COVID-19: A Randomized Clinical Trial	Trial clinico su 476 pazienti con COVID-19 lieve che confronta 5 giorni di terapia con ivermectina con placebo: il tempo di risoluzione dei sintomi non varia significativamente fra i due gruppi per cui l'utilizzo di ivermectina non appare supportato.	Importance Ivermectin is widely prescribed as a potential treatment for COVID-19 despite uncertainty about its clinical benefit. Objective To determine whether ivermectin is an efficacious treatment for mild COVID-19. Design, Setting, and Participants Double-blind, randomized trial conducted at a single site in Cali, Colombia. Potential study participants were identified by simple random sampling from the state's health department electronic database of patients with symptomatic, laboratory-confirmed COVID-19 during the study period. A total of 476 adult patients with mild disease and symptoms for 7 days or fewer (at home or hospitalized) were

			enrolled between July 15 and November 30, 2020, and followed up through December 21, 2020. Intervention Patients were randomized to receive ivermectin, 300 µg/kg of body weight per day for 5 days (n = 200) or placebo (n = 200). Main Outcomes and Measures Primary outcome was time to resolution of symptoms within a 21-day follow-up period. Solicited adverse events and serious adverse events were also collected. Results Among 400 patients who were randomized in the primary analysis population (median age, 37 years [interquartile range {IQR}, 29-48]; 231 women [58%]), 398 (99.5%) completed the trial. The median time to resolution of symptoms was 10 days (IQR, 9-13) in the ivermectin group compared with 12 days (IQR, 9-13) in the placebo group (hazard ratio for resolution of symptoms, 1.07 [95% CI, 0.87 to 1.32]; P = .53 by log-rank test). By day 21, 82% in the ivermectin group and 79% in the placebo group had resolved symptoms. The most common solicited adverse event was headache, reported by 104 patients (52%) given ivermectin and 111 (56%) who received placebo. The most common serious adverse event was multiorgan failure, occurring in 4 patients (2 in each group). Conclusion and Relevance Among adults with mild COVID-19, a 5-day course of ivermectin, compared with placebo, did not significantly improve the time to resolution of symptoms. The findings do not support the use of ivermectin for treatment of mild COVID-19, although larger trials may be needed to understand the effects of ivermectin on other clinically relevant outcomes.

			
Blumenthal KG et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMc2102131?query=featured_home	Delayed Large Local Reactions to mRNA-1273 Vaccine against SARS-CoV-2	Reazioni locali al vaccino Pfizer contro SARS-CoV-2 : 12 pazienti, con tempo mediano di insorgenza 8 giorni dopo la somministrazione, dimostrazione di aspetti ricondicibili a una reazione di ipersensibilità ritardata T-mediata alla biopsia cutanea. Tutti i pazienti sono stati sottoposti alla dose successiva, qualcuno con nuova insorgenza della lesione cutanea ma senza altri effetti avversi significativi.	Baden et al. report on a phase 3 clinical trial of the mRNA-1273 vaccine against SARS-CoV-2, and they provide information on immediate injection-site reactions, which were observed in 84.2% of the participants after the first dose. The trial also showed that delayed injection-site reactions (defined in that trial as those with an onset on or after day 8) occurred in 244 of the 30,420 participants (0.8%) after the first dose and in 68 participants (0.2%) after the second dose. These reactions included erythema, induration, and tenderness. The reactions typically resolved over the following 4 to 5 days. However, these reactions were not further characterized, and links between reactions after the first dose and those after the second dose were not provided to inform clinical care.

			
Brouwer PJM et al Cell https://www.cell.com/cell/fulltext/S0092-8674(21)00078-7	Two-component spike nanoparticle vaccine protects macaques from SARS-CoV-2 infection	Un altro vaccino a nanoparticelle sulle quali si trova la proteina S di SARS-COV-2, testato su animali da laboratorio con risposta immunitaria soddisfacente.	The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic is continuing to disrupt personal lives, global healthcare systems, and economies. Hence, there is an urgent need for a vaccine that prevents viral infection, transmission, and disease. Here, we present a two-component protein-based nanoparticle vaccine that displays multiple copies of the SARS-CoV-2 spike protein. Immunization studies show that this vaccine induces potent neutralizing antibody responses in mice, rabbits, and cynomolgus macaques. The vaccine-induced immunity protects macaques against a high-dose challenge, resulting in strongly reduced viral infection and replication in the upper and lower airways. These nanoparticles are a promising vaccine candidate to curtail the SARS-CoV-2 pandemic.

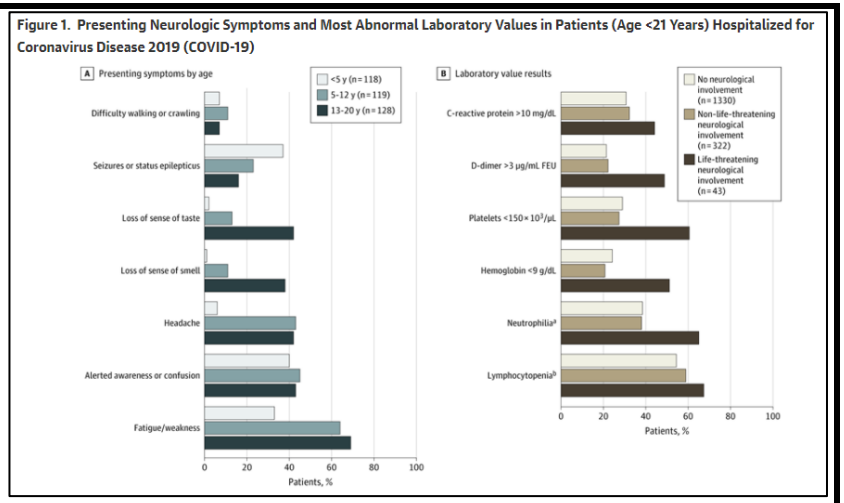
			
Sokal A et al Cell https://www.cell.com/cell/fulltext/S0092-8674(21)00093-3	Maturation and persistence of the anti-SARS-CoV-2 memory B cell response	Risposta B-cellulare all'infezione da SARS-COV-2 di varia gravità : reclutamento precoce dei linfociti B cross-reattivi con i Coronavirus stagionali e successiva maturazione di linfociti specifici per SARS-CoV-2 fino a 6 mesi dall'infezione.	Memory B cells play a fundamental role in host defenses against viruses, but to date, their role has been relatively unsettled in the context of SARS-CoV-2. We report here a longitudinal single-cell and repertoire profiling of the B cell response up to 6 months in mild and severe COVID-19 patients. Distinct SARS-CoV-2 spike-specific activated B cell clones fueled an early antibody-secreting cell burst as well as a durable synchronous germinal center response. While highly mutated memory B cells, including pre-existing cross-reactive seasonal Betacoronavirus-specific clones, were recruited early in the response, neutralizing SARS-CoV-2 RBD-specific clones accumulated with time and largely contributed to the late, remarkably stable, memory B cell pool. Highlighting germinal center maturation, these cells displayed clear accumulation of somatic

			mutations in their variable region genes over time. Overall, these findings demonstrate that an antigen-driven activation persisted and matured up to 6 months after SARS-CoV-2 infection and may provide long-term protection. 
Nishitani K et al International Orthopaedics	Self-quarantine programme and pre-operative SARS-CoV-2 PCR screening for orthopaedic elective surgery: experience from Japan	Quarantena fiduciaria di 14 giorni pre-intervento ortopedico elettivo, con esecuzione di tampone nasofaringeo per SARS-CoV-2 per rimuovere l'isolamento : su 308 pazienti, 304 si sono sottoposti al protocollo e nessuno ha avuto tampone di controllo positivo, così	PURPOSE: This study aimed to evaluate the acceptability of 14 days of self-quarantine and the positivity rate of pre-operative severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction (PCR) screening for patients undergoing elective orthopaedic surgery. METHODS: The self-quarantine programme and pre-operative SARS-CoV-2 PCR screening were initiated for patients who were scheduled for admission later than 7 May 2020 for elective orthopaedic surgery on admission. On the day of admission, the patients declared compliance with self-quarantine regulations. The admission was refused in cases of non-compliance.

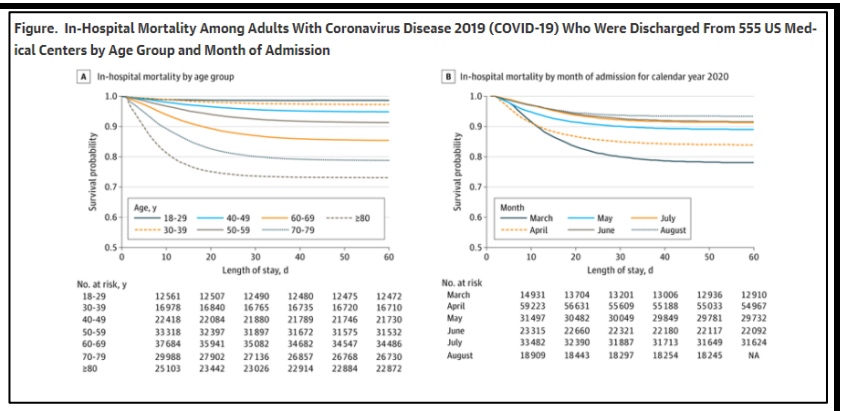
https://link.springer.com/article/10.1007%2Fs00264-021-04997-4		come nessuno dei 300 operati ha sviluppato sintomi COVID-relati dopo l'intervento. Forse è possibile solo in Giappone.	After admission, the patients underwent SARS-CoV-2 PCR screening. If PCR results were negative, isolation was terminated. If PCR results were positive, the surgery was postponed. If the patients had symptoms suspicious of coronavirus disease (COVID-19) after surgery, the PCR test was repeated. RESULTS: Overall, 308 patients (age: 63.2 +/- 18.8 years, 197 female and 111 male) were scheduled for elective orthopaedic surgery. Two patients did not agree with the requirements of self-quarantine, and two other procedures were cancelled. No non-compliance was reported; thus, the completion rate of the self-quarantine programme was 304/308 (98.7%). Finally, 304 patients underwent PCR testing, and there were no positive PCR results. After cancellations of four operations due to reasons other than COVID-19, 300 surgical procedures were performed. No patients developed COVID-19 during hospitalisation. CONCLUSIONS: Although this system is based on trusting the good behaviour of patients, accompanied by PCR screening, we believe that the results showed the efficacy of the system in safely performing orthopaedic surgery during the COVID-19 pandemic.
Pasin L et al European Journal of Internal Medicine https://doi.org/10.1016/j.ejim.2021.01.016	Anakinra for patients with COVID-19: a meta-analysis of non-randomized cohort studies	Metanalisi di 4 studi osservazionali sulla terapia con anakinra (anti IL-1) in pazienti con insufficienza respiratoria COVID-19 relata : si osserva un beneficio sulla mortalità e sulla necessità di ventilazione meccanica.	INTRODUCTION: Severe COVID-19 cases have a detrimental hyper-inflammatory host response and different cytokine-blocking biologic agents were explored to improve outcomes. Anakinra blocks the activity of both IL-1alpha and IL1beta and is approved for different autoinflammatory disorders, but it is used off-label for conditions characterized by an excess of cytokine production. Several studies on anakinra in COVID-19 patients reported positive effects. We performed a meta-analysis of all published evidence on the use of anakinra in COVID19 to investigate its effect on survival and need for mechanical ventilation. METHODS: We searched for any study performed on adult patients with acute hypoxemic failure related to 2019-nCoV infection, receiving anakinra versus any comparator.

			Primary endpoint was mortality at the longest available follow-up. Adverse effects, need for mechanical ventilation and discharge at home with no limitations were also analysed. RESULTS: Four observational studies involving 184 patients were included. Overall mortality of patients treated with anakinra was significantly lower than mortality in the control group (95% CI 0.14-0.48, p<0.0001). Moreover, patients treated with anakinra had a significantly lower risk of need for mechanical ventilation than controls (95% CI 0.250.74, p=0.002). No difference in adverse events and discharge at home with no limitations was observed. The Trial Sequential Analysis z-cumulative line reached the monitoring boundary for benefit and the required sample size. CONCLUSIONS: Administration of anakinra in COVID-19 patients was safe and might be associated with reductions in both mortality and need for mechanical ventilation. Randomized clinical trials are warranted to confirm these findings.
LaRovere KL et al JAMA https://jamanetwork.com/journals/jamaneurology/fullarticle/2777392	Neurologic Involvement in Children and Adolescents Hospitalized in the United States for COVID-19 or Multisystem Inflammatory Syndrome	Le complicanze neurologiche sono relativamente frequenti (22%) in questa casistica di 1695 pazienti di meno di 21 anni ricoverati negli USA per COVID-19. Le manifestazioni più rappresentate sono encefalopatia acuta e ictus.	Importance Coronavirus disease 2019 (COVID-19) affects the nervous system in adult patients. The spectrum of neurologic involvement in children and adolescents is unclear. Objective To understand the range and severity of neurologic involvement among children and adolescents associated with COVID-19. Setting, Design, and Participants Case series of patients (age <21 years) hospitalized between March 15, 2020, and December 15, 2020, with positive severe acute respiratory syndrome coronavirus 2 test result (reverse transcriptase-polymerase chain reaction and/or antibody) at 61 US hospitals in the Overcoming COVID-19 public health registry, including 616 (36%) meeting criteria for multisystem inflammatory syndrome in children. Patients with neurologic involvement had acute neurologic signs, symptoms, or

			diseases on presentation or during hospitalization. Life-threatening involvement was adjudicated by experts based on clinical and/or neuroradiologic features. Exposures Severe acute respiratory syndrome coronavirus 2. Main Outcomes and Measures Type and severity of neurologic involvement, laboratory and imaging data, and outcomes (death or survival with new neurologic deficits) at hospital discharge. Results Of 1695 patients (909 [54%] male; median [interquartile range] age, 9.1 [2.4-15.3] years), 365 (22%) from 52 sites had documented neurologic involvement. Patients with neurologic involvement were more likely to have underlying neurologic disorders (81 of 365 [22%]) compared with those without (113 of 1330 [8%]), but a similar number were previously healthy (195 [53%] vs 723 [54%]) and met criteria for multisystem inflammatory syndrome in children (126 [35%] vs 490 [37%]). Among those with neurologic involvement, 322 (88%) had transient symptoms and survived, and 43 (12%) developed life-threatening conditions clinically adjudicated to be associated with COVID-19, including severe encephalopathy (n = 15; 5 with splenial lesions), stroke (n = 12), central nervous system infection/demyelination (n = 8), Guillain-Barré syndrome/variants (n = 4), and acute fulminant cerebral edema (n = 4). Compared with those without life-threatening conditions (n = 322), those with life-threatening neurologic conditions had higher neutrophil-to-lymphocyte ratios (median, 12.2 vs 4.4) and higher reported frequency of D-dimer greater than 3 μg/mL fibrinogen equivalent units (21 [49%] vs 72 [22%]). Of 43 patients who developed COVID-19–related life-threatening neurologic involvement, 17 survivors (40%) had new neurologic deficits at hospital discharge, and 11 patients (26%) died.

			
Mirò O et al Chest https://journal.chestnet.org/article/S0012-3692(20)35201-6/fulltext	Frequency, Risk Factors, Clinical Characteristics, and Outcomes of Spontaneous Pneumothorax in Patients With Coronavirus Disease 2019	Studio retrospettivo caso-controllo sulle caratteristiche di 40 pazienti con COVID-19 esordito con pneumotorace spontaneo (circa 1/1000), a confronto con COVID-19 senza pneumotorace e casi di pneumotorace spontaneo senza diagnosi di COVID-19.	Background : Recent reports of patients with coronavirus disease 2019 (COVID-19) developing pneumothorax correspond mainly to case reports describing mechanically ventilated patients. The real incidence, clinical characteristics, and outcome of spontaneous pneumothorax (SP) as a form of COVID-19 presentation remain to be defined. Research Question : Do the incidence, risk factors, clinical characteristics, and outcomes of SP in patients with COVID-19 attending EDs differ compared with COVID-19 patients without SP and non-COVID-19 patients with SP? Study Design and Methods : This case-control study retrospectively reviewed all patients with COVID-19 diagnosed with SP (case group) in 61 Spanish EDs (20% of Spanish EDs) and compared them with two control groups: COVID-19 patients without SP and non-COVID-19 patients with SP. The relative frequencies of SP were estimated in COVID-19 and non-COVID-19 patients in the ED, and annual standardized incidences were estimated for both populations. Comparisons between case subjects and control subjects included

			52 clinical, analytical, and radiologic characteristics and four outcomes. Results : We identified 40 occurrences of SP in 71,904 patients with COVID-19 attending EDs (0.56‰; 95% CI, 0.40‰-0.76‰). This relative frequency was higher than that among non-COVID-19 patients (387 of 1,358,134, 0.28‰; 95% CI, 0.26‰-0.32‰; OR, 1.93; 95% CI, 1.41-2.71). The standardized incidence of SP was also higher in patients with COVID-19 (34.2 vs 8.2/100,000/year; OR, 4.19; 95% CI, 3.64-4.81). Compared with COVID-19 patients without SP, COVID-19 patients developing SP more frequently had dyspnea and chest pain, low pulse oximetry readings, tachypnea, and increased leukocyte count. Compared with non-COVID-19 patients with SP, case subjects differed in 19 clinical variables, the most prominent being a higher frequency of dysgeusia/anosmia, headache, diarrhea, fever, and lymphopenia (all with OR > 10). All the outcomes measured, including in-hospital death, were worse in case subjects than in both control groups. Interpretation : SP as a form of COVID-19 presentation at the ED is unusual (< 1‰ cases) but is more frequent than in the non-COVID-19 population and could be associated with worse outcomes than SP in non-COVID-19 patients and COVID-19 patients without SP.
Nguyen NT et al JAMA	Outcomes and Mortality Among Adults Hospitalized With COVID-19 at US Medical Centers	Analisi delle caratteristiche di 192 550 adulti ricoverati per COVID-19 negli USA : si osserva un riduzione della mortalità dall'inizio della pandemia (22% vs 6.5%) e una associazione con l'età.	Coronavirus disease 2019 (COVID-19) originally emerged from China and has since spread globally, with almost 14 million confirmed cases and more than 260 000 deaths in the US as of December 1, 2020.To date, there have been regional reports on outcomes among patients who developed serious symptoms requiring hospitalization. The objectives of our study were to examine the characteristics and outcomes among adults hospitalized with COVID-19 at US medical centers and analyze changes in mortality over the initial 6-month period of the pandemic.

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2777028			
Barsky BA et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMp2100609?query=featured_home	Vaccination plus Decarceration — Stopping Covid-19 in Jails and Prisons	Riflessione sui limiti del sistema di detenzione americano in relazione alla pandemia di COVID-19. Le soluzioni proposte sono le misure di scarcerazione e la vaccinazione, per quanto quest'ultima abbia dei limiti in un constesto epidemiologico con alto tasso di trasmissione.	Covid-19 has exposed the inadequacy of the public health infrastructure in the United States and forced us to confront associated biosocial dynamics that are driving the pandemic, including poverty, structural racism, distrust, unequal access to health care, and other social sources. But perhaps no collective preexisting condition has been more acute and preventable than that associated with the U.S. system of mass incarceration. U.S. jails and prisons house nearly 25% of the world's incarcerated population even though the United States accounts for only 4.2% of the global population.
Singh A et al Tropical Doctor	Prevention of fogging inside safety goggles for healthcare professionals during COVID-19 pandemic: A low-cost solution in resource-limited settings.	Metodi per non far appannare gli occhiali protettivi quando si indossano i DPI.	Fogging inside the safety goggles is a common problem experienced by more healthcare professionals during the COVID-19 pandemic than ever. Various anti-fogging remedies are available on the market. We have adopted a low-cost alternative that can be extremely useful in resource-limited settings.

https://journals.sagepub.com/doi/10.1177/0049475521997597			**Table 1. Methods to prevent fogging of eye goggles, with their mechanism, advantages and caveats** **Antifogging measure** / **Mechanism** / **Advantages** / **Caveats** Reversing the mask-tie around the ear / Better seal around the nasal ridge / Simple and effective method / Air may leak along the lateral margins of the mask (near the ears). Undue pressure on the skin of the ears Tightly "sealed" face mask / A correct size and properly fit mask will, by itself, prevent the exhaled air from escaping around the nasal ridge / It is easily the most important and practical measure, and should be applied in addition to any other method / Can lead to face marks, but they are temporary and cannot justify compromising with safety Application of adhesive strip on the nasal ridge -mask junction [5] / Blocks air leakage superiorly around the nasal ridge, preventing entry of air into goggles / Adhesive strips are readily available in all hospitals / Skin damage can be caused, if hypoallergenic adhesive is not used
Shen X et al Cell Host and Microbe https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(21)00102-5	SARS-CoV-2 variant B.1.1.7 is susceptible to neutralizing antibodies elicited by ancestral Spike vaccines	Il siero di soggetti guariti oppure vaccinati con i vaccini Moderna e Novavax contro SARS-CoV-2 neutralizza la variante B1.1.7 (« inglese ») di SARS-CoV-2. In sintesi, non si tratterebbe di una variante pericolosa quanto a reinfezioni o inefficacia dei vaccini.	All current vaccines for COVID-19 utilize ancestral SARS-CoV-2 Spike with the goal of generating protective neutralizing antibodies. The recent emergence and rapid spread of several SARS-CoV-2 variants carrying multiple Spike mutations raise concerns about possible immune escape. One variant, first identified in the United Kingdom (B.1.1.7, also called 501Y.V1 or 20I), contains eight Spike mutations with potential to impact antibody therapy, vaccine efficacy and risk of reinfection. Here we show that B.1.1.7 remains sensitive to neutralization, albeit at moderately reduced levels (~2-fold), by serum samples from convalescent individuals and recipients of an mRNA vaccine (mRNA-1273, (Moderna) and a protein nanoparticle vaccine (NVX-CoV2373, Novavax). A subset of monoclonal antibodies to the receptor binding domain (RBD) of Spike are less effective against the variant while others are largely unaffected. These findings indicate that variant B.1.1.7 is unlikely to be a major concern for current vaccines or for an increased risk of reinfection.

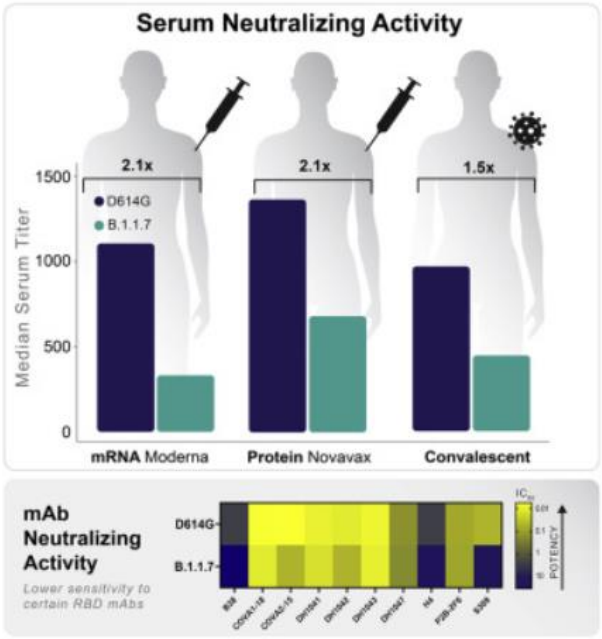
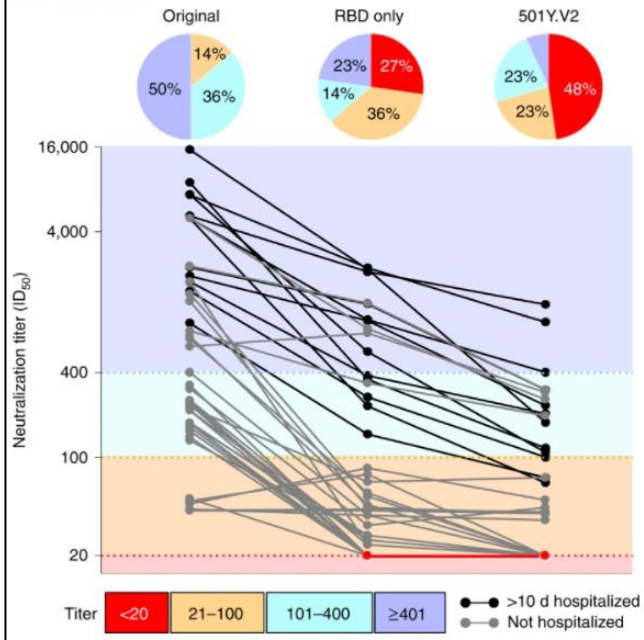
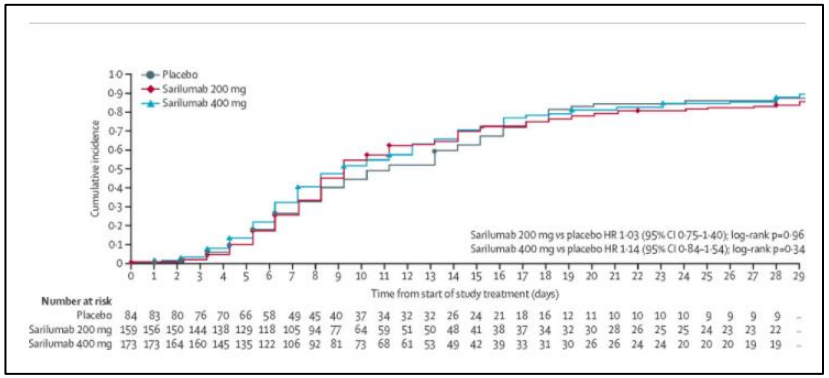
			
Wibmer CK et al Nature https://www.nature.com/articles/s41591-021-01285-x	SARS-CoV-2 501Y.V2 escapes neutralization by South African COVID-19 donor plasma	La variante B.1.351 (“sudafricana”) di SARS-CoV-2 portatrice delle mutazioni K417 ed E484 non viene legata dai più comuni anticorpi monoclonali e sfugge alla neutralizzazione, anche se non al legame, con il plasma dei soggetti guariti in Sudafrica.	SARS-CoV-2 501Y.V2 (B.1.351), a novel lineage of coronavirus causing COVID-19, contains substitutions in two immunodominant domains of the spike protein. Here, we show that pseudovirus expressing 501Y.V2 spike protein completely escapes three classes of therapeutically relevant antibodies. This pseudovirus also exhibits substantial to complete escape from neutralization, but not binding, by convalescent plasma. These data highlight the prospect of reinfection with antigenically distinct variants and foreshadows reduced efficacy of spike-based vaccines.

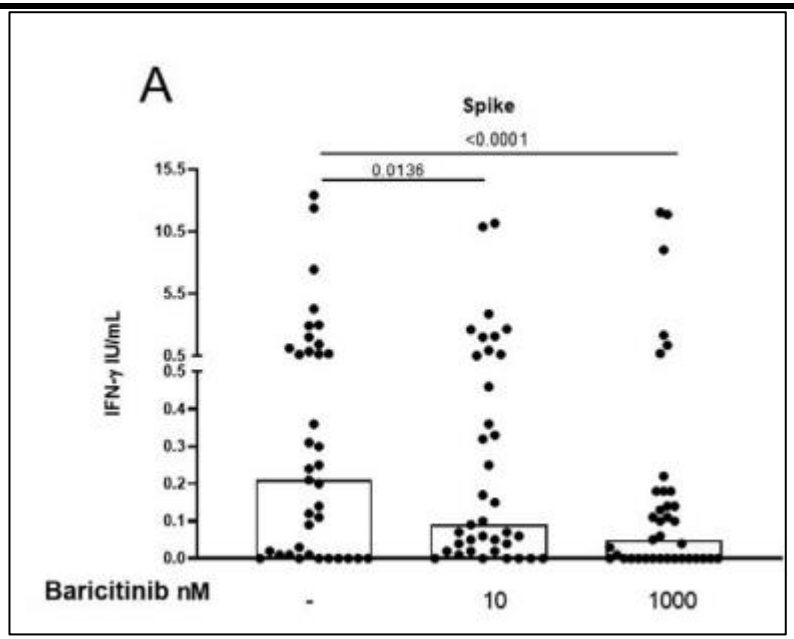
			Fig. 2: SARS-CoV-2 501Y.V2 increased resistance to neutralization by convalescent plasma/serum.  Plasma/serum collected from individuals infected with SARS-CoV-2 was assessed for neutralization to the original lineage (Wuhan-1 D614G, left), an RBD chimeric mutant containing K417N, E484K and N501Y substitutions only (middle) or the 501Y.V2 lineage pseudovirus. Twelve of the samples were collected from donors hospitalized for >10 d with COVID-19 (black). The graph is colored according to the magnitude of neutralization titer, with ID_{50} greater or lesser than 1:400 colored dark or light blue, respectively and titer <100 colored orange. The limit of detection (knockout) was an ID_{50} < 20 (red). Pie charts above each set of data points summarize the proportion of samples in each titer group.
De Souza WM et al The Lancet – preprint https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3793486	Levels of SARS-CoV-2 Lineage P.1 Neutralization by Antibodies Elicited after Natural Infection and Vaccination	La variante P.1 (« brasiliana ») di SARS-CoV-2 isolata da due pazienti sfugge alla neutralizzazione da parte di siero convalescente e di soggetti vaccinati con CoronaVac.	Background: A new SARS-CoV-2 lineage, named P.1 (20J/501Y.V3), has recently been detected in Brazil. Mutations accrued by the P.1 lineage include amino acid changes in the receptor-binding domain of the spike protein that also are reported in variants of concern in the United Kingdom (B.1.1.7) and South Africa (B.1.325). Methods: We isolated two P.1-containing specimens from nasopharyngeal and bronchoalveolar lavage samples of patients of

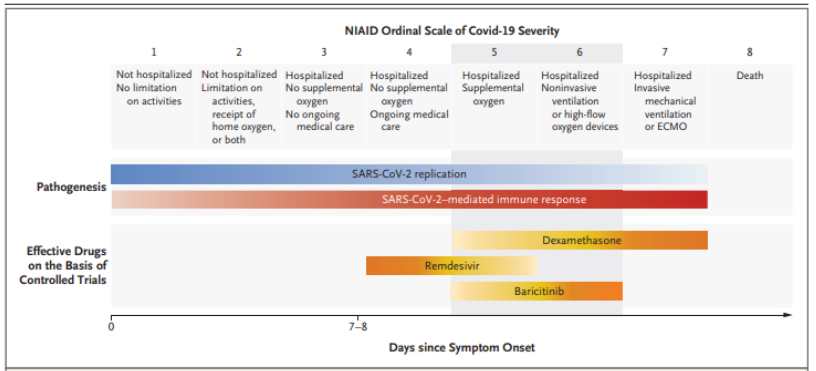
			Manaus, Brazil. We measured neutralization of the P.1 virus after incubation with the plasma of 19 COVID-19 convalescent blood donors and recipients of the chemically-inactivated CoronaVac vaccine and compared these results to neutralization of a SARS-CoV-2 B-lineage previously circulating in Brazil. Findings: The immune plasma of COVID-19 convalescent blood donors had 6-fold less neutralizing capacity against the P.1 than against the B-lineage. Moreover, five months after booster immunization with CoronaVac, plasma from vaccinated individuals failed to efficiently neutralize P.1 lineage isolates. Interpretation: These data indicate that the P.1 lineage may escape from neutralizing antibodies generated in response to polyclonal stimulation against previously circulating variants of SARS-CoV-2.
Lescure F et al The Lancet https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00099-0/fulltext	Sarilumab in patients admitted to hospital with severe or critical COVID-19: a randomised, double-blind, placebo-controlled, phase 3 trial	Trial clinico di fase 3 su 416 pazienti con COVID-19 ricoverati con necessità di ossigenoterapia trattati con sarilumab 400 mg EV, 200 mg EV o placebo : non si dimostrano differenze di miglioramento clinico al giorno 29 e di mortalità.	Background : Elevated proinflammatory cytokines are associated with greater COVID-19 severity. We aimed to assess safety and efficacy of sarilumab, an interleukin-6 receptor inhibitor, in patients with severe (requiring supplemental oxygen by nasal cannula or face mask) or critical (requiring greater supplemental oxygen, mechanical ventilation, or extracorporeal support) COVID-19. Methods : We did a 60-day, randomised, double-blind, placebo-controlled, multinational phase 3 trial at 45 hospitals in Argentina, Brazil, Canada, Chile, France, Germany, Israel, Italy, Japan, Russia, and Spain. We included adults (≥18 years) admitted to hospital with laboratory-confirmed SARS-CoV-2 infection and pneumonia, who required oxygen supplementation or intensive care. Patients were randomly assigned (2:2:1 with permuted blocks of five) to receive intravenous sarilumab 400 mg, sarilumab 200 mg, or placebo. Patients, care providers, outcome assessors, and investigators remained masked to assigned intervention throughout the course of the study. The primary endpoint was time to clinical

			improvement of two or more points (seven point scale ranging from 1 [death] to 7 [discharged from hospital]) in the modified intention-to-treat population. The key secondary endpoint was proportion of patients alive at day 29. Safety outcomes included adverse events and laboratory assessments. Findings : Between March 28 and July 3, 2020, of 431 patients who were screened, 420 patients were randomly assigned and 416 received placebo (n=84 [20%]), sarilumab 200 mg (n=159 [38%]), or sarilumab 400 mg (n=173 [42%]). At day 29, no significant differences were seen in median time to an improvement of two or more points between placebo (12·0 days [95% CI 9·0 to 15·0]) and sarilumab 200 mg (10·0 days [9·0 to 12·0]; hazard ratio [HR] 1·03 [95% CI 0·75 to 1·40]; log-rank p=0·96) or sarilumab 400 mg (10·0 days [9·0 to 13·0]; HR 1·14 [95% CI 0·84 to 1·54]; log-rank p=0·34), or in proportions of patients alive (77 [92%] of 84 patients in the placebo group; 143 [90%] of 159 patients in the sarilumab 200 mg group; difference −1·7 [−9·3 to 5·8]; p=0·63 vs placebo; and 159 [92%] of 173 patients in the sarilumab 400 mg group; difference 0·2 [−6·9 to 7·4]; p=0·85 vs placebo). At day 29, there were numerical, non-significant survival differences between sarilumab 400 mg (88%) and placebo (79%; difference +8·9% [95% CI −7·7 to 25·5]; p=0·25) for patients who had critical disease. No unexpected safety signals were seen. The rates of treatment-emergent adverse events were 65% (55 of 84) in the placebo group, 65% (103 of 159) in the sarilumab 200 mg group, and 70% (121 of 173) in the sarilumab 400 mg group, and of those leading to death 11% (nine of 84) were in the placebo group, 11% (17 of 159) were in the sarilumab 200 mg group, and 10% (18 of 173) were in the sarilumab 400 mg group. Interpretation : This trial did not show efficacy of sarilumab in patients admitted to hospital with COVID-19 and receiving

			supplemental oxygen. Adequately powered trials of targeted immunomodulatory therapies assessing survival as a primary endpoint are suggested in patients with critical COVID-19. 
Kramer DB et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMp2102146?query=featured_home	Choices in a Crisis — Individual Preferences among SARS-CoV-2 Vaccines	Se la disponibilità di vaccini contro SARS-CoV-2 aumenterà come auspicato, sarà necessario riflettere sulla possibilità per i pazienti di scegliere il vaccino cui sottoporsi.	The extraordinarily swift development of effective vaccines against SARS-CoV-2 offers new optimism about combating the Covid-19 pandemic. So far, vaccine demand far exceeds supply, and people generally cannot choose which vaccine they receive. In the United States, this lack of choice has generated little debate given the similar mechanism of action, number of required doses, safety profile, and efficacy of the two vaccines approved in December 2020, both based on mRNA technology. However, the Food and Drug Administration (FDA) has now granted emergency use authorization (EUA) for a third vaccine and may consider additional vaccines for EUA. As real-world experience with vaccination accumulates, meaningful differences in effectiveness against new SARS-CoV-2 variants and adverse reaction rates may emerge, along with new information about relative effectiveness in preventing transmission. Thus, the question of whether individual vaccinees should be able to choose which vaccine they receive will become increasingly salient.

Petrone L et al Journal of Infection https://pubmed.ncbi.nlm.nih.gov/33639176/	In-vitro evaluation of the immunomodulatory effects of Baricitinib: Implication for COVID-19 therapy	Osservazione in vitro dell'effetto immunomodulatore di baricitinib (inibitore di JAK) che dermina una ridotta produzione di Interferone-gamma e altri fattori solubili dell'immunità.	Objective: Baricitinib seems a promising therapy for COVID-19. To fully-investigate its effects, we in-vitro evaluated the impact of baricitinib on the SARS-CoV-2-specific-response using the whole-blood platform. Methods: We evaluated baricitinib effect on the IFN-γ -release and on a panel of soluble factors by multiplex-technology after stimulating whole-blood from 39 COVID-19 patients with SARS-CoV-2 antigens. Staphylococcal Enterotoxin B (SEB) antigen was used as a positive control. Results: In-vitro exogenous addition of baricitinib significantly decreased IFN-γ response to spike- (median: 0.21, IQR: 0.01–1; spike+baricitinib 1000 nM median: 0.05, IQR: 0–0.18; $p < 0.0001$) and to the remainder-antigens (median: 0.08 IQR: 0–0.55; remainder-antigens+baricitinib 1000 nM median: 0.03, IQR: 0–0.14; $p = 0.0013$). Moreover, baricitinib significantly decreased SEB-induced response (median: 12.52, IQR: 9.7–15.2; SEB+baricitinib 1000 nM median: 8, IQR: 1.44–12.16; $p < 0.0001$). Baricitinib did modulate other soluble factors besides IFN-γ , significantly decreasing the spike-specific-response mediated by IL-17, IL-1β, IL-6, TNF-α, IL-4, IL-13, IL-1ra, IL-10, GM-CSF, FGF, IP-10, MCP-1, MIP-1β ($p \leq 0.0156$). The baricitinib-decreased SARS-CoV-2-specific-response was observed mainly in mild/moderate COVID-19 and in those with lymphocyte count ≥1 × 103/μl. Conclusions: Exogenous addition of baricitinib decreases the in-vitro SARS-CoV-2-specific response in COVID-19 patients using a whole-blood platform. These results are the first to show the effects of this therapy on the immune-specific viral response.

			
Goletti D et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMe2034982	Baricitinib Therapy in Covid-19 Pneumonia — An Unmet Need Fulfilled	Commento al lavoro di Kalil et al (riportato più in alto) che mostra l'effetto di baricitinib in aggiunta a desametasone nei pazienti con COVID-19 e insufficienza respiratoria.	By confirming the results of the previous open-label studies showing the beneficial effects of baricitinib for Covid-19 treatment, ACTT-2 provides the highest grade of evidence on the efficacy of the drug, which acts through the inhibition of JAK1 and JAK2 and consequently blocks the immune cascade and reduces viral replication.10 The reported highest efficacy of baricitinib in patients with ordinal scores of 5 and 6 allows expansion of the therapeutic armamentarium against Covid-19 pneumonia, mainly in patients receiving oxygen support without invasive mechanical ventilation.

			 Figure 1. Evidence-based Efficacy of Covid-19 Therapies, According to Disease Severity.
Martinez MW et al JAMA https://jamanetwork.com/journals/jamacardiology/fullarticle/2777308	Prevalence of Inflammatory Heart Disease Among Professional Athletes With Prior COVID-19 Infection Who Received Systematic Return-to-Play Cardiac Screening	Su 789 atleti professionisti con storia di COVID-19 lieve o asintomatico sottoposti a una valutazione cardiologica approfondita prima della ripresa dell'attività agonistica, 5 (0.6%) avevano segni di patologia infiammatoria cardiaca alla risonanza che hanno controindicato l'attività agonistica. Per gli altri, dopo la ripresa dell'attività non si sono osservati eventi avversi cardiaci.	Importance The major North American professional sports leagues were among the first to return to full-scale sport activity during the coronavirus disease 2019 (COVID-19) pandemic. Given the unknown incidence of adverse cardiac sequelae after COVID-19 infection in athletes, these leagues implemented a conservative return-to-play (RTP) cardiac testing program aligned with American College of Cardiology recommendations for all athletes testing positive for COVID-19. Objective To assess the prevalence of detectable inflammatory heart disease in professional athletes with prior COVID-19 infection, using current RTP screening recommendations. Design, Setting, and Participants This cross-sectional study reviewed RTP cardiac testing performed between May and October 2020 on professional athletes who had tested positive for COVID-19. The professional sports leagues (Major League Soccer, Major League Baseball, National Hockey League, National Football League, and the men's and women's National Basketball Association) implemented mandatory cardiac screening requirements for all players who had tested positive for COVID-19 prior to resumption of team-organized sports activities.

			Exposures Troponin testing, electrocardiography (ECG), and resting echocardiography were performed after a positive COVID-19 test result. Interleague, deidentified cardiac data were pooled for collective analysis. Those with abnormal screening test results were referred for additional testing, including cardiac magnetic resonance imaging and/or stress echocardiography. Main Outcomes and Measures The prevalence of abnormal RTP test results potentially representing COVID-19–associated cardiac injury, and results and outcomes of additional testing generated by the initial screening process. Results The study included 789 professional athletes (mean [SD] age, 25 [3] years; 777 men [98.5%]). A total of 460 athletes (58.3%) had prior symptomatic COVID-19 illness, and 329 (41.7%) were asymptomatic or paucisymptomatic (minimally symptomatic). Testing was performed a mean (SD) of 19 (17) days (range, 3-156 days) after a positive test result. Abnormal screening results were identified in 30 athletes (3.8%; troponin, 6 athletes [0.8%]; ECG, 10 athletes [1.3%]; echocardiography, 20 athletes [2.5%]), necessitating additional testing; 5 athletes (0.6%) ultimately had cardiac magnetic resonance imaging findings suggesting inflammatory heart disease (myocarditis, 3; pericarditis, 2) that resulted in restriction from play. No adverse cardiac events occurred in athletes who underwent cardiac screening and resumed professional sport participation. Conclusions and Relevance This study provides large-scale data assessing the prevalence of relevant COVID-19–associated cardiac pathology with implementation of current RTP screening recommendations. While long-term follow-up is ongoing, few cases of inflammatory heart disease have been detected, and a safe return to professional sports activity has thus far been achieved.

Moore JP JAMA https://jamanetwork.com/journals/jama/fullarticle/2777390	Approaches for Optimal Use of Different COVID-19 Vaccines. Issues of Viral Variants and Vaccine Efficacy	Spunti per l'ottimizzazione dell'uso dei vaccini contro SARS-CoV-2, dalla combinazione alla singola dose per i guariti.	The efforts of the Biden administration to accelerate rollout of COVID-19 vaccines are enabling more adults in the US to be vaccinated each week. As of February 28, 2021, an estimated more than 48 million people have received at least 1 vaccine dose. Provided enough people are vaccinated, the US might be able to transition back toward prepandemic life at some point this year. However, one scenario that could adversely affect the vaccine program is the further evolution and spread of viral variants that are resistant to vaccine-induced neutralizing antibodies. It is prudent to discuss possible strategies to minimize the potential effects of this problem, and other scenarios for maximizing the benefit of available and future vaccine supplies.
Gerussi V et al Vaccines https://doi.org/10.3390/vaccines9020172	Vaccine Hesitancy among Italian Patients Recovered from COVID-19 Infection towards Influenza and Sars-Cov-2 Vaccination.	Quasi la metà di 599 persone intervistate con storia di COVID-19 è restia a ricevere in futuro il vaccino per influenza e per SARS-CoV-2 e ciò vale anche per chi è stato ospedalizzato.	We aimed to assess the attitude towards influenza and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccinations among coronavirus disease 2019 (COVID-19) recovered patients. We performed a cross-sectional study consisting of a standardized telephone interview carried out between September and November 2020 targeting a cohort of adult in- and out-patients that had recovered from COVID-19 after the first wave (March-May 2020) at Udine Hospital (Italy). Overall, 599 people participated (320 female, median age 53 years) and most had experienced an acute COVID-19 with mild illness (409, 68.3%). The majority were hesitant or undecided towards influenza (327, 54.6%) and SARS-CoV-2 (353, 59.2%) vaccines. Older age, public work exposure, and previous 2019 flu shots were the main factors associated with a positive attitude toward both vaccinations ($p < 0.05$). Being hospitalized during the acute COVID-19 phase was associated with the willingness to get a flu shot (94/272, 34.5%) but not SARS-CoV-2

			vaccine (70/244, 28.7%). Vaccine hesitancy is diffuse and multifactorial also among COVID-19 recovered.