RICERCA BIBLIOGRAFICA COVID 19

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FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE

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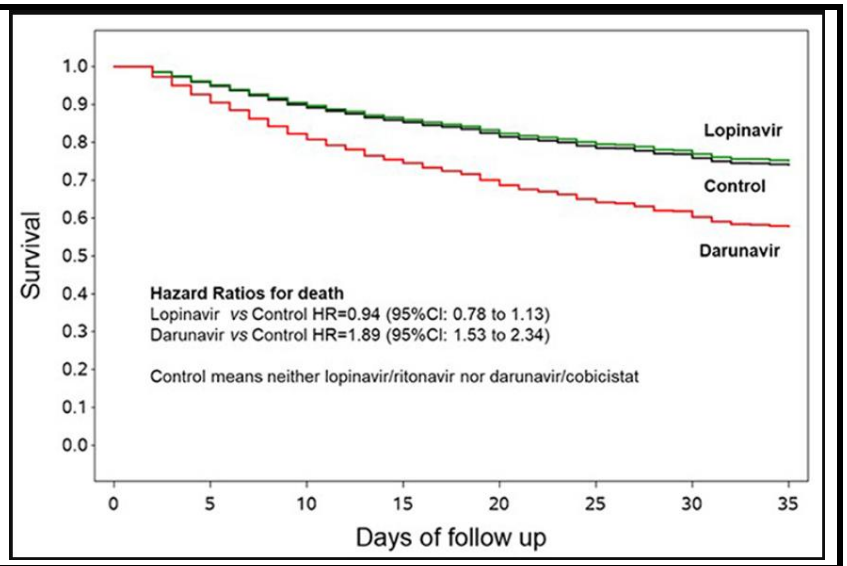
AUTORE/RIVISTA	TITOLO	OUTCOME PRINCIPALE	ABSTRACT
Tummino TA et al Science https://science.sciencemag.org/content/early/2021/06/22/science.abi4708	Drug-induced phospholipidosis confounds drug repurposing for SARS-CoV-2	L'effetto in vitro di alcuni farmaci contro SARS-CoV-2 potrebbe essere non specifco e legato al fenomeno della fosfolipidosi.	Repurposing drugs as treatments for COVID-19 has drawn much attention. Beginning with sigma receptor ligands, and expanding to other drugs from screening in the field, we became concerned that phospholipidosis was a shared mechanism underlying the antiviral activity of many repurposed drugs. For all of the 23 cationic amphiphilic drugs tested, including hydroxychloroquine, azithromycin, amiodarone, and four others already in clinical trials, phospholipidosis was monotonically correlated with antiviral efficacy. Conversely, drugs active against the same targets that did not induce phospholipidosis were not antiviral. Phospholipidosis depends on the physicochemical properties of drugs, and does not reflect specific target-based activities, rather it may be considered a toxic confound in early drug discovery. Early detection of phospholipidosis could eliminate these artifacts, enabling a focus on molecules with therapeutic potential.

Althoff KN et al CID https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab519/6294073	Antibodies to SARS-CoV-2 in All of Us Research Program Participants, January 2-March 18, 2020	Circolazione di SARS-CoV-2 negli USA prima del primo caso « ufficiale », sulla base della sierologia di una coorte di partecipanti a uno studio.	Background : With limited SARS-CoV-2 testing capacity in the US at the start of the epidemic (January – March), testing was focused on symptomatic patients with a travel history throughout February, obscuring the picture of SARS-CoV-2 seeding and community transmission. We sought to identify individuals with SARS-CoV-2 antibodies in the early weeks of the US epidemic. Methods : All of Us study participants in all 50 US states provided blood specimens during study visits from January 2 to March 18, 2020. A participant was considered seropositive if they tested positive for SARS-CoV-2 immunoglobulin G (IgG) antibodies on the Abbott Architect SARS-CoV-2 IgG ELISA and the EUROIMMUN SARS-CoV-2 ELISA in a sequential testing algorithm. Sensitivity and specificity of the Abbott and EUROIMMUNE ELISAs and the net sensitivity and specificity of the sequential testing algorithm were estimated with 95% confidence intervals. Results : The estimated sensitivity of Abbott and EUROIMMUN was 100% (107/107 [96.6%, 100%]) and 90.7% (97/107 [83.5%, 95.4%]), respectively. The estimated specificity of Abbott and EUROIMMUN was 99.5% (995/1,000 [98.8%, 99.8%]) and 99.7% (997/1,000 [99.1%, 99.9%), respectively. The net sensitivity and specificity of our sequential testing algorithm was 90.7% (97/107 [83.5%, 95.4%]) and 100.0% (1,000/1,000 [99.6%, 100%]), respectively. Of the 24,079 study participants with blood specimens from January 2 to March 18, 2020, 9 were seropositive, 7 of whom were seropositive prior to the first confirmed case in the states of Illinois, Massachusetts, Wisconsin, Pennsylvania, and Mississippi. Conclusions : Our findings indicate SARS-CoV-2 infections weeks prior to the first recognized cases in 5 US states.

Seagle EE et al CID https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab562/6305138	The landscape of candidemia during the COVID-19 pandemic	Candidemia nei pazienti con e senza COVID-19.	Background : The COVID-19 pandemic has resulted in unprecedented healthcare challenges, and COVID-19 has been linked to secondary infections. Candidemia, a fungal healthcare-associated infection, has been described in patients hospitalized with severe COVID-19. However, studies of candidemia and COVID-19 co-infection have been limited in sample size and geographic scope. We assessed differences in patients with candidemia with and without a COVID-19 diagnosis. Methods : We conducted a case-level analysis using population-based candidemia surveillance data collected through the Centers for Disease Control and Prevention's Emerging Infections Program during April–August 2020 to compare characteristics of candidemia patients with and without a positive test for COVID-19 in the 30 days before their Candida culture using chi-square or Fisher exact tests. Results : Of the 251 candidemia patients included, 64 (25.5%) were positive for SARS-CoV-2. Liver disease, solid organ malignancies, and prior surgeries were each >3 times more common in patients without COVID-19 co-infection, whereas intensive care unit-level care, mechanical ventilation, having a central venous catheter, and receipt of corticosteroids and immunosuppressants were each >1.3 times more common in patients with COVID-19. All cause in-hospital fatality was two times higher among those with COVID-19 (62.5%) than without (32.1%). Conclusions : One quarter of candidemia patients had COVID-19. These patients were less likely to have certain underlying conditions and recent surgery commonly associated with candidemia and more likely to have acute risk factors linked to COVID-19 care, including immunosuppressive medications. Given the high mortality, it is

			important for clinicians to remain vigilant and take proactive measures to prevent candidemia in patients with COVID-19.
al Jalali V et al CMI https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00342-6/fulltext	Improved immunogenicity against SARS-CoV-2 in a solid organ transplant recipient by switching vaccines	Caso di una paziente trapiantate e sottoposta a tre dosi di vaccino diverso contro SARS-CoV-2 (un ciclo con Pfizer e un richiamo con Vaxzevria).	Because of the lack of a marked antibody response, on March 30th one shot of the AZD1222 vaccine was administered. Remarkably, twenty-eight days after this vaccination another anti-spike antibody test (SARS-CoV-2 spike antibody test by Roche) detected 1963 U/ml of antibodies and a neutralizing antibody test conducted on May 20th showed an antibody titer of 1:160.
Fekkar A et al CMI https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00345-1/fulltext	COVID-19 associated pulmonary aspergillosis (CAPA): how big a problem is it?	Riflessioni sulla aspergillosi associata a COVID-19, un'entità da meglio definire.	The concept of CAPA was largely deduced from the association between influenza infection and Aspergillus superinfection, assuming similar pathophysiologic features with SARS-CoV-2, which are as yet unconfirmed. Indeed, SARS-CoV-2 pneumonia seems to be associated with less extensive airway epithelium destruction and distinct host immune response profiles compared to influenza pneumonia. In sharp contrast to the reported CAPA cases, 93% of the 41 reported COVID-19-associated mucormycosis were proven
Buonsenso D et al CID https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab559/6305136	Children and SARS-CoV-2 transmission: a step closer to better understanding and evidence-based interventions?	Discussione sul ruolo dei bambini nella trasmissione di SARS-CoV-2 e sull'impatto rispetto alla loro formazione delle misure di contenimento del contagio che comprendono la chiusura delle scuole.	The scientific community has worked incredibly hard over the past year and will continue to do so to provide evidence-based Information. With the growing number of effective vaccines and their extension to children, the aim of making schools safer is even closer. We are doing our best as clinicians and researchers. Will policy makers, with the new evidence available, do their best to guarantee the basic children's rights to health and education?

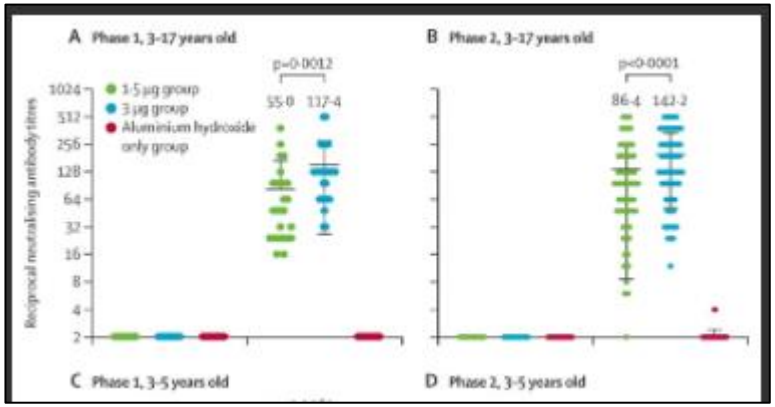
Di Castelnuovo A et al Front Med https://pubmed.ncbi.nlm.nih.gov/34179035/	Lopinavir/Ritonavir and Darunavir/Cobicistat in Hospitalized COVID-19 Patients: Findings From the Multicenter Italian CORIST Study	Studio osservazionale multicentrico italiano sulla associazione fra lopinavir/ritonavir e darunavir/ritonavir per la terapia di COVID-19 : il secondo è associato alla mortalità, il primo non è associato a variazioni della mortalità.	Background: Protease inhibitors have been considered as possible therapeutic agents for COVID-19 patients. Objectives: To describe the association between lopinavir/ritonavir (LPV/r) or darunavir/cobicistat (DRV/c) use and in-hospital mortality in COVID-19 patients. Study Design: Multicenter observational study of COVID-19 patients admitted in 33 Italian hospitals. Medications, preexisting conditions, clinical measures, and outcomes were extracted from medical records. Patients were retrospectively divided in three groups, according to use of LPV/r, DRV/c or none of them. Primary outcome in a time-to event analysis was death. We used Cox proportional-hazards models with inverse probability of treatment weighting by multinomial propensity scores. Results: Out of 3,451 patients, 33.3% LPV/r and 13.9% received DRV/c. Patients receiving LPV/r or DRV/c were more likely younger, men, had higher C-reactive protein levels while less likely had hypertension, cardiovascular, pulmonary or kidney disease. After adjustment for propensity scores, LPV/r use was not associated with mortality (HR = 0.94, 95% CI 0.78 to 1.13), whereas treatment with DRV/c was associated with a higher death risk (HR = 1.89, 1.53 to 2.34, E-value = 2.43). This increased risk was more marked in women, in elderly, in patients with higher severity of COVID-19 and in patients receiving other COVID-19 drugs. Conclusions: In a large cohort of Italian patients hospitalized for COVID-19 in a real-life setting, the use of LPV/r treatment did not change death rate, while DRV/c was associated with increased mortality. Within the limits of an observational study, these data do not support the use of LPV/r or DRV/c in COVID-19 patients.

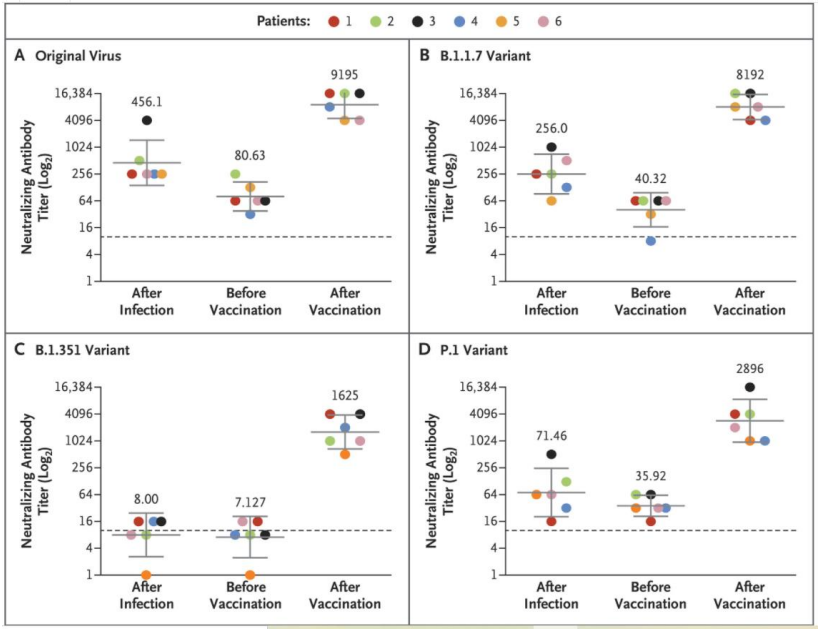
			
Borobia AM et al The Lancet https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01420-3/fulltext	Immunogenicity and reactogenicity of BNT162b2 booster in ChAdOx1-S-primed participants (CombiVacS): a multicentre, open-label, randomised, controlled, phase 2 trial	Pubblicazione definitiva dello studio spagnolo già visto in preprint sulla vaccinazione « eterologa » contro SARS-CoV-2.	Background To date, no immunological data on COVID-19 heterologous vaccination schedules in humans have been reported. We assessed the immunogenicity and reactogenicity of BNT162b2 (Comirnaty, BioNTech, Mainz, Germany) administered as second dose in participants primed with ChAdOx1-S (Vaxzevria, AstraZeneca, Oxford, UK). Methods We did a phase 2, open-label, randomised, controlled trial on adults aged 18–60 years, vaccinated with a single dose of ChAdOx1-S 8–12 weeks before screening, and no history of SARS-CoV-2 infection. Participants were randomly assigned (2:1) to receive either BNT162b2 (0·3 mL) via a single intramuscular injection (intervention group) or continue observation (control group). The primary outcome was 14-day immunogenicity, measured by immunoassays for SARS-CoV-2 trimeric spike protein and receptor binding domain (RBD). Antibody functionality was assessed using a pseudovirus

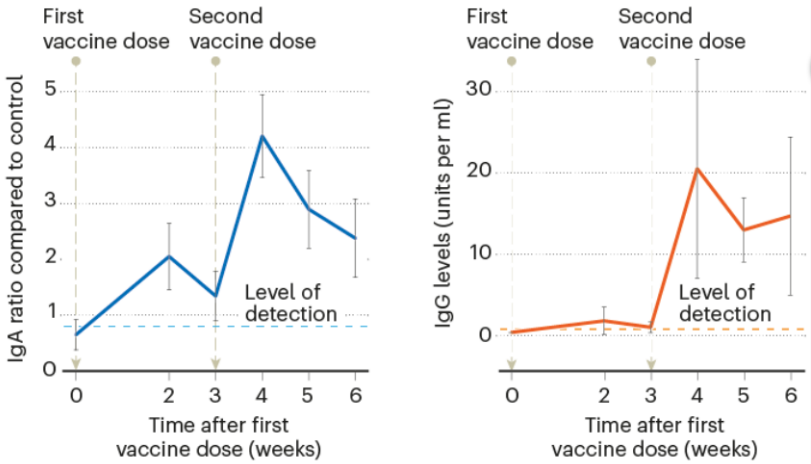
			neutralisation assay, and cellular immune response using an interferon-γ immunoassay. The safety outcome was 7-day reactogenicity, measured as solicited local and systemic adverse events. The primary analysis included all participants who received at least one dose of BNT162b2 and who had at least one efficacy evaluation after baseline. The safety analysis included all participants who received BNT162b2. This study is registered with EudraCT (2021-001978-37) and ClinicalTrials.gov (NCT04860739), and is ongoing. Findings Between April 24 and 30, 2021, 676 individuals were enrolled and randomly assigned to either the intervention group (n=450) or control group (n=226) at five university hospitals in Spain (mean age 44 years [SD 9]; 382 [57%] women and 294 [43%] men). 663 (98%) participants (n=441 intervention, n=222 control) completed the study up to day 14. In the intervention group, geometric mean titres of RBD antibodies increased from 71·46 BAU/mL (95% CI 59·84–85·33) at baseline to 7756·68 BAU/mL (7371·53–8161·96) at day 14 (p<0·0001). IgG against trimeric spike protein increased from 98·40 BAU/mL (95% CI 85·69–112·99) to 3684·87 BAU/mL (3429·87–3958·83). The interventional:control ratio was 77·69 (95% CI 59·57–101·32) for RBD protein and 36·41 (29·31–45·23) for trimeric spike protein IgG. Reactions were mild (n=1210 [68%]) or moderate (n=530 [30%]), with injection site pain (n=395 [88%]), induration (n=159 [35%]), headache (n=199 [44%]), and myalgia (n=194 [43%]) the most commonly reported adverse events. No serious adverse events were reported. Interpretation

			BNT162b2 given as a second dose in individuals prime vaccinated with ChAdOx1-S induced a robust immune response, with an acceptable and manageable reactogenicity profile. Funding
Han B et al The Lancet https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00319-4/fulltext	Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine (CoronaVac) in healthy children and adolescents: a double-blind, randomised, controlled, phase 1/2 clinical trial	Trial di fase I/II sul vaccino inattivato CoronaVac contro SARS-CoV-2 in bambini e adolescenti di età inferiore a 18 anni.	Background A vaccine against SARS-CoV-2 for children and adolescents will play an important role in curbing the COVID-19 pandemic. Here we aimed to assess the safety, tolerability, and immunogenicity of a candidate COVID-19 vaccine, CoronaVac, containing inactivated SARS-CoV-2, in children and adolescents aged 3–17 years. Methods We did a double-blind, randomised, controlled, phase 1/2 clinical trial of CoronaVac in healthy children and adolescents aged 3–17 years old at Hebei Provincial Center for Disease Control and Prevention in Zanhuang (Hebei, China). Individuals with SARS-CoV-2 exposure or infection history were excluded. Vaccine (in 0·5 mL aluminum hydroxide adjuvant) or aluminum hydroxide only (alum only, control) was given by intramuscular injection in two doses (day 0 and day 28). We did a phase 1 trial in 72 participants with an age de-escalation in three groups and dose-escalation in two blocks (1·5 µg or 3·0 µg per injection). Within each block, participants were randomly assigned (3:1) by means of block randomisation to receive CoronaVac or alum only. In phase 2, participants were randomly assigned (2:2:1) by means of block randomisation to receive either CoronaVac at 1·5 µg or 3·0 µg per dose, or alum only. All participants, investigators, and laboratory staff were masked to group allocation. The primary safety endpoint was adverse reactions within 28 days after each injection in all participants who received at least one dose. The primary immunogenicity endpoint assessed in the per-protocol population was seroconversion rate of

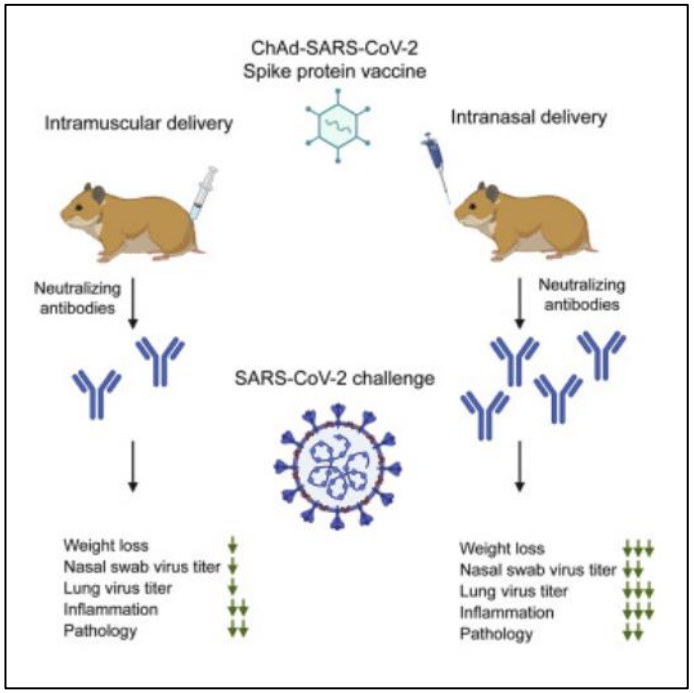
			neutralising antibody to live SARS-CoV-2 at 28 days after the second injection. This study is ongoing and is registered with ClinicalTrials.gov, NCT04551547. Findings Between Oct 31, 2020, and Dec 2, 2020, 72 participants were enrolled in phase 1, and between Dec 12, 2020, and Dec 30, 2020, 480 participants were enrolled in phase 2. 550 participants received at least one dose of vaccine or alum only (n=71 for phase 1 and n=479 for phase 2; safety population). In the combined safety profile of phase 1 and phase 2, any adverse reactions within 28 days after injection occurred in 56 (26%) of 219 participants in the 1·5 µg group, 63 (29%) of 217 in the 3·0 µg group, and 27 (24%) of 114 in the alum-only group, without significant difference (p=0·55). Most adverse reactions were mild and moderate in severity. Injection site pain was the most frequently reported event (73 [13%] of 550 participants), occurring in 36 (16%) of 219 participants in the 1·5 µg group, 35 (16%) of 217 in the 3·0 µg group, and two (2%) in the alum-only group. As of June 12, 2021, only one serious adverse event of pneumonia has been reported in the alum-only group, which was considered unrelated to vaccination. In phase 1, seroconversion of neutralising antibody after the second dose was observed in 27 of 27 participants (100·0% [95% CI 87·2–100·0]) in the 1·5 µg group and 26 of 26 participants (100·0% [86·8-100·0]) in the 3·0 µg group, with the geometric mean titres of 55·0 (95% CI 38·9–77·9) and 117·4 (87·8–157·0). In phase 2, seroconversion was seen in 180 of 186 participants (96·8% [93·1–98·8]) in the 1·5 µg group and 180 of 180 participants (100·0% [98·0–100·0]) in the 3·0 µg group, with the geometric mean titres of 86·4 (73·9–101·0) and 142·2 (124·7–162·1). There were no detectable antibody responses in the alum-only groups.

			Interpretation CoronaVac was well tolerated and safe and induced humoral responses in children and adolescents aged 3–17 years. Neutralising antibody titres induced by the 3·0 µg dose were higher than those of the 1·5 µg dose. The results support the use of 3·0 µg dose with a two-immunisation schedule for further studies in children and adolescents. 
Lustig Y et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMc2104036?query=featured_home	Neutralizing Response against Variants after SARS-CoV-2 Infection and One Dose of BNT162b2	Aumento del titolo neutralizzante contro le varianti alfa, beta e delta dopo una dose di vaccino Pfizer contro SARS-CoV-2 in 18 persone con storia di infezione naturale.	This study showed that, in our small cohort, one vaccine dose substantially increased neutralizing activity against all variants tested, with similar titers detected across patients for each variant. This highlights the importance of vaccination even in previously infected patients, given the added benefit of an increased antibody response to the variants tested. Limitations of the study include the small cohort of only women and the lack of evaluation of T-cell response. However, we think the fact that all six patients responded similarly to vaccination supports our conclusions. Further studies could investigate the effects of a second vaccine dose on neutralizing activity against variants of concern in persons who have and persons who have not been previously infected.

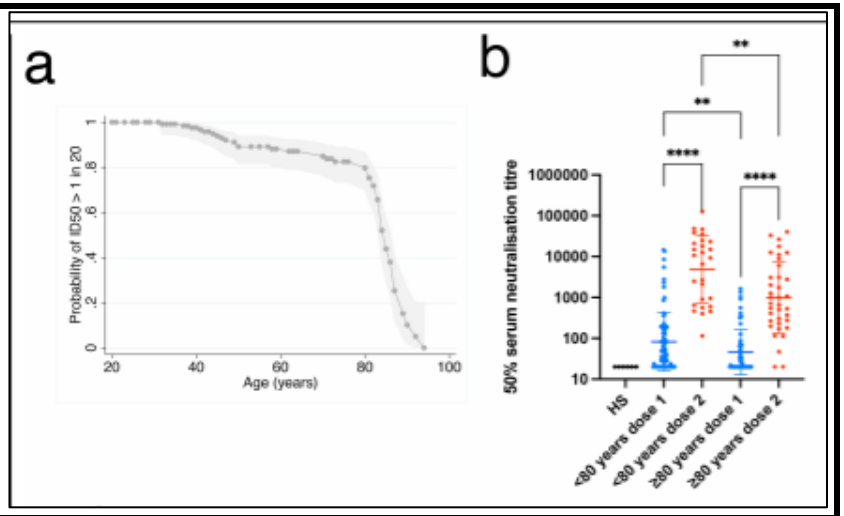
			
Hall S et al Nature https://www.nature.com/articles/d41586-021-01680-x	COVID vaccines and breastfeeding: what the data say	Riassunto delle conoscenze attuali in merito alla sicurezza della vaccinazione (almeno con vaccini a mRNA) contro SARS-CoV-2.	Unlike the yellow-fever vaccine, COVID-19 vaccines do not carry a risk of igniting an active infection. In addition, COVID-19 vaccines are extremely unlikely to cross into breast milk. The fragile messenger RNA used in the Pfizer–BioNTech and Moderna vaccines, for example, is designed to break down so quickly that it should never leave the cells where it was injected — let alone get into the bloodstream and then the breast. In fact, researchers don't expect that any of the current vaccines will be excreted into breast milk.

			BREAST-MILK BENEFITS A study of 84 lactating health-care workers found that their breast milk contains substantial levels of antibodies to the coronavirus SARS-CoV-2 for several weeks after they were vaccinated. The study looked at two antibodies, immunoglobulin A (IgA, also found in the linings of the gut and respiratory tract) and immunoglobulin G (IgG, also found in the blood). 
Di Castelnuovo A et al Journal of Helathcare Engineering https://www.hindawi.com/journals/jhe/2021/5556207/	Disentangling the Association of Hydroxychloroquine Treatment with Mortality in Covid-19 Hospitalized Patients through Hierarchical Clustering	Studio osservazionale retrospettivo su oltre 4000 pazienti ricoverati per COVID-19 in Italia, in cui si osserva che l'utilizzo di idrossiclorochina è inversamente associato alla mortalità nei soggetti più giovani con meno comorbidità.	The efficacy of hydroxychloroquine (HCQ) in treating SARS-CoV-2 infection is harshly debated, with observational and experimental studies reporting contrasting results. To clarify the role of HCQ in Covid-19 patients, we carried out a retrospective observational study of 4,396 unselected patients hospitalized for Covid-19 in Italy (February–May 2020). Patients' characteristics were collected at entry, including age, sex, obesity, smoking status, blood parameters, history of diabetes, cancer, cardiovascular and chronic pulmonary diseases, and medications in use. These were used to identify subtypes of patients with similar characteristics through hierarchical clustering based on Gower distance. Using multivariable Cox regressions, these clusters were then tested for association with mortality and modification of effect by treatment with HCQ. We identified two clusters, one of 3,913 younger patients with lower

			circulating inflammation levels and better renal function, and one of 483 generally older and more comorbid subjects, more prevalently men and smokers. The latter group was at increased death risk adjusted by HCQ (HR[CI95%] = 3.80[3.08-4.67]), while HCQ showed an independent inverse association (0.51[0.43-0.61]), as well as a significant influence of cluster∗HCQ interaction ($p < 0.001$). This was driven by a differential association of HCQ with mortality between the high (0.89[0.65-1.22]) and the low risk cluster (0.46[0.39-0.54]). These effects survived adjustments for additional medications in use and were concordant with associations with disease severity and outcome. These findings suggest a particularly beneficial effect of HCQ within low risk Covid-19 patients and may contribute to clarifying the current controversy on HCQ efficacy in Covid-19 treatment.
Bticker TL et al Cell https://www.cell.com/cell-reports/fulltext/S2211-1247(21)00798-1	A single intranasal or intramuscular immunization with chimpanzee adenovirus vectored SARS-CoV-2 vaccine protects against pneumonia in hamsters	Somministrazione intranasale di un vaccino a vetore adenovirale contro SARS-CoV-2 nel criceto, con risultati migliori dell'intramuscolo.	The development of an effective vaccine against SARS-CoV-2, the etiologic agent of COVID-19, is a global priority. Here, we compared the protective capacity of intranasal and intramuscular delivery of a chimpanzee adenovirus-vectored vaccine encoding a pre-fusion stabilized spike protein (ChAd-SARS-CoV-2-S) in Golden Syrian hamsters. While immunization with ChAd-SARS-CoV-2-S induced robust spike protein specific antibodies capable of neutralizing the virus, antibody levels in serum were higher in hamsters vaccinated by an intranasal compared to intramuscular route. Accordingly, against challenge with SARS-CoV-2, ChAd-SARS-CoV-2-S immunized hamsters were protected against less weight loss and had reduced viral infection in nasal swabs and lungs, and reduced pathology and inflammatory gene expression in the lungs, compared to ChAd-Control immunized hamsters. Intranasal immunization with ChAd-SARS-CoV-2-S provided superior protection against SARS-CoV-2 infection and inflammation in the upper respiratory tract. These

			findings support intranasal administration of the ChAd-SARS-CoV-2-S candidate vaccine to prevent SARS-CoV-2 infection, disease, and possibly transmission. 
Breton G et al bioRXiv https://www.biorxiv.org/content/10.1101/2020.12.08.416636v1.article-info	Persistent Cellular Immunity to SARS-CoV-2 Infection	Persistenza della risposta T cellulare dopo infezione da SARS-CoV-2 in 41 persone con storia di infezione.	SARS-CoV-2 is responsible for an ongoing pandemic that affected millions of individuals around the globe. To gain further understanding of the immune response in recovered individuals we measured T cell responses in paired samples obtained an average of 1.3 and 6.1 months after infection from 41 individuals. The data indicate that recovered individuals show persistent polyfunctional SARS-CoV-2 antigen specific memory that could contribute to rapid recall responses. In addition, recovered individuals show enduring immune alterations in relative numbers of CD4+ and CD8+ T cells, expression of activation/exhaustion markers, and cell division.

Collier DA et al Nature https://www.nature.com/articles/s41586-021-03739-1	Age-related immune response heterogeneity to SARS-CoV-2 vaccine BNT162b2	Ridotta attività neutralizzante nelle persone anziane (in particolare sopra 80 anni) vaccinate con doppia dose di vaccino Pfizer contro SARS-CoV-2 a confronto con giovani operatori sanitari : tempo di pensare a un richiamo.	Although two-dose mRNA vaccination provides excellent protection against SARS-CoV-2, data are scarce on vaccine efficacy against variants of concern (VOC) in individuals above 80 years of age1. Here we analysed immune responses following vaccination with mRNA vaccine BNT162b22 in elderly participants and younger health care workers. Serum neutralisation and binding IgG/IgA after the first vaccine dose diminished with increasing age, with a marked drop in participants over 80 years old. Sera from participants above 80 showed significantly lower neutralisation potency against B.1.1.7, B.1.351 and P.1. variants of concern as compared to wild type and were more likely to lack any neutralisation against VOC following the first dose. However, following the second dose, neutralisation against VOC was detectable regardless of age. Frequency of SARS-CoV-2 Spike specific B-memory cells was higher in elderly responders versus non-responders after first dose. Elderly participants demonstrated clear reduction in somatic hypermutation of class switched cells. SARS-CoV-2 Spike specific T-cell IFNγ and IL-2 responses decreased with increasing age, and both cytokines were secreted primarily by CD4 T cells. We conclude that the elderly are a high risk population that warrant specific measures to boost vaccine responses, particularly where variants of concern are circulating.

			
Montogomery J et al JAMA https://jamanetwork.com/journals/jamacardiology/fullarticle/2781601?resultClick=1	Myocarditis Following Immunization With mRNA COVID-19 Vaccines in Members of the US Military	Casistica di 23 giovani che hanno sviluppato miocardite entro 4 giorni dalla vaccinazione con vaccino a mRNA contro SARS-CoV-2.	Importance Myocarditis has been reported with COVID-19 but is not clearly recognized as a possible adverse event following COVID-19 vaccination. Objective To describe myocarditis presenting after COVID-19 vaccination within the Military Health System. Design, Setting, and Participants This retrospective case series studied patients within the US Military Health System who experienced myocarditis after COVID-19 vaccination between January and April 2021. Patients who sought care for chest pain following COVID-19 vaccination and were subsequently diagnosed with clinical myocarditis were included. Exposure Receipt of a messenger RNA (mRNA) COVID-19 vaccine between January 1 and April 30, 2021. Main Outcomes and Measures Clinical diagnosis of myocarditis after COVID-19 vaccination in the absence of other identified causes. Results A total of 23 male patients (22 currently serving in the military and 1 retiree; median [range] age, 25 [20-51] years)

			presented with acute onset of marked chest pain within 4 days after receipt of an mRNA COVID-19 vaccine. All military members were previously healthy with a high level of fitness. Seven received the BNT162b2-mRNA vaccine and 16 received the mRNA-1273 vaccine. A total of 20 patients had symptom onset following the second dose of an appropriately spaced 2-dose series. All patients had significantly elevated cardiac troponin levels. Among 8 patients who underwent cardiac magnetic resonance imaging within the acute phase of illness, all had findings consistent with the clinical diagnosis of myocarditis. Additional testing did not identify other etiologies for myocarditis, including acute COVID-19 and other infections, ischemic injury, or underlying autoimmune conditions. All patients received brief supportive care and were recovered or recovering at the time of this report. The military administered more than 2.8 million doses of mRNA COVID-19 vaccine in this period. While the observed number of myocarditis cases was small, the number was higher than expected among male military members after a second vaccine dose. Conclusions and Relevance In this case series, myocarditis occurred in previously healthy military patients with similar clinical presentations following receipt of an mRNA COVID-19 vaccine. Further surveillance and evaluation of this adverse event following immunization is warranted. Potential for rare vaccine-related adverse events must be considered in the context of the well-established risk of morbidity, including cardiac injury, following COVID-19 infection.

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<tr><th>Characteristic</th><th>No. (%)</th></tr>
<tr><td>Age, median (range), y</td><td>25 (20-51)</td></tr>
<tr><td>Sex</td><td></td></tr>
<tr><td>Male</td><td>23 (100)</td></tr>
<tr><td>Female</td><td>0</td></tr>
<tr><td>Military status</td><td></td></tr>
<tr><td>Currently serving</td><td>22 (96)</td></tr>
<tr><td>Retired</td><td>1 (4)</td></tr>
<tr><td>Proximate vaccine dose</td><td></td></tr>
<tr><td>Second mRNA-1273 dose</td><td>14 (61)</td></tr>
<tr><td>Second BNT162b2-mRNA dose</td><td>6 (26)</td></tr>
<tr><td>First mRNA-1273 dose</td><td>2 (9)</td></tr>
<tr><td>First BNT162b2-mRNA dose</td><td>1 (4)</td></tr>
<tr><td>Time to symptom onset, mean (range), h</td><td>50 (12-96)</td></tr>
<tr><td>Troponin level[a]</td><td></td></tr>
<tr><td>Elevated</td><td>23 (100)</td></tr>
<tr><td>Not elevated</td><td>0</td></tr>
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<td>Wang Z et al

bioRXiv – not peer reviewed

https://www.biorxiv.org/content/10.1101/2021.05.07.443175v1.article-info</td>
<td>Vaccination boosts naturally enhanced neutralizing breadth to SARS-CoV-2 one year after infection</td>
<td>In una coorte di 63 persone con storia di COVID-19, di cui 26 vaccinate con vaccino a mRNA, si osserva che nei vaccinati l'attività neutralizzante del siero aumenta rispetto ai non vaccinati ed è diretta anche contro le nuove varianti. La risposta rimane stabile fino a 12 mesi di follow up.</td>
<td>Over one year after its inception, the coronavirus disease-2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) remains difficult to control despite the availability of several excellent vaccines. Progress in controlling the pandemic is slowed by the emergence of variants that appear to be more transmissible and more resistant to antibodies. Here we report on a cohort of 63 COVID-19-convalescent individuals assessed at 1.3, 6.2 and 12 months after infection, 41% of whom also received mRNA vaccines. In the absence of vaccination antibody reactivity to the receptor binding domain (RBD) of SARS-CoV-2, neutralizing activity and the number of RBD-specific memory B cells remain relatively stable from 6 to 12 months. Vaccination</td>
</tr>
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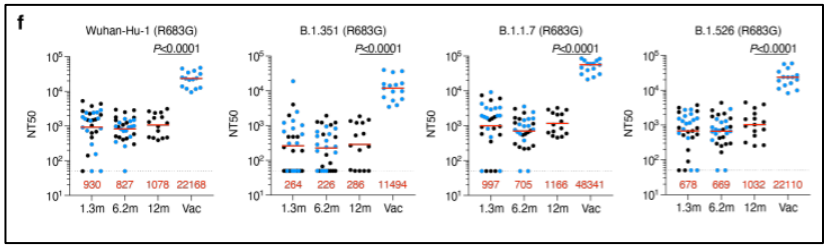
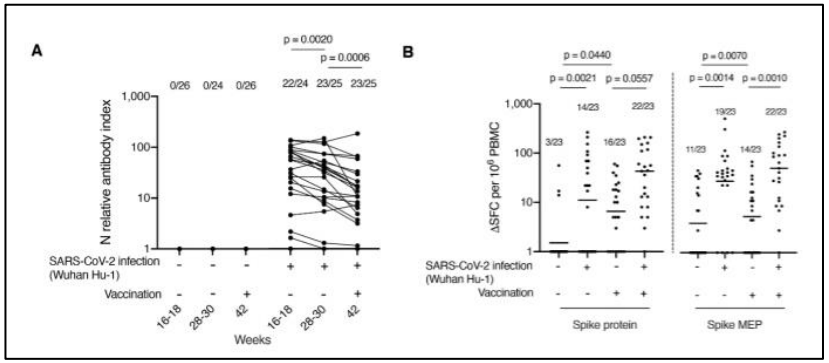
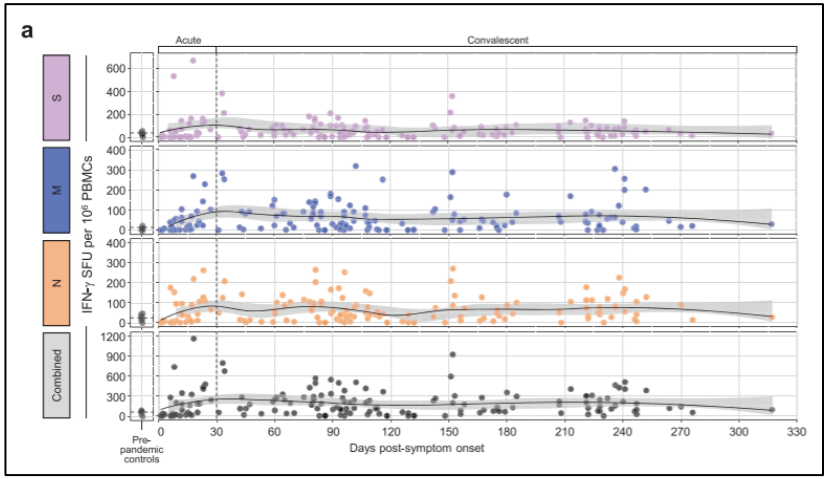
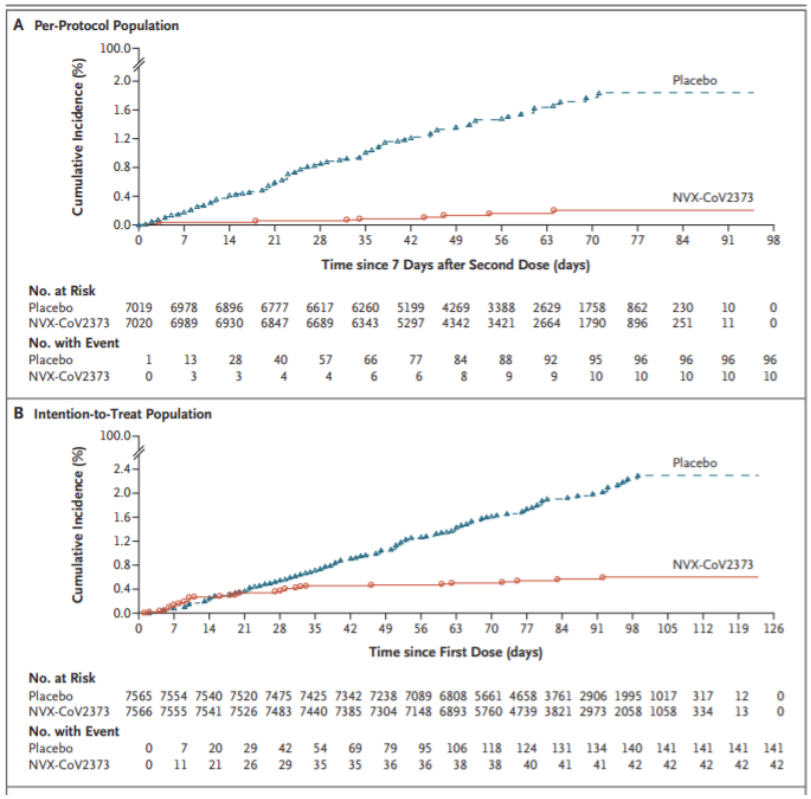
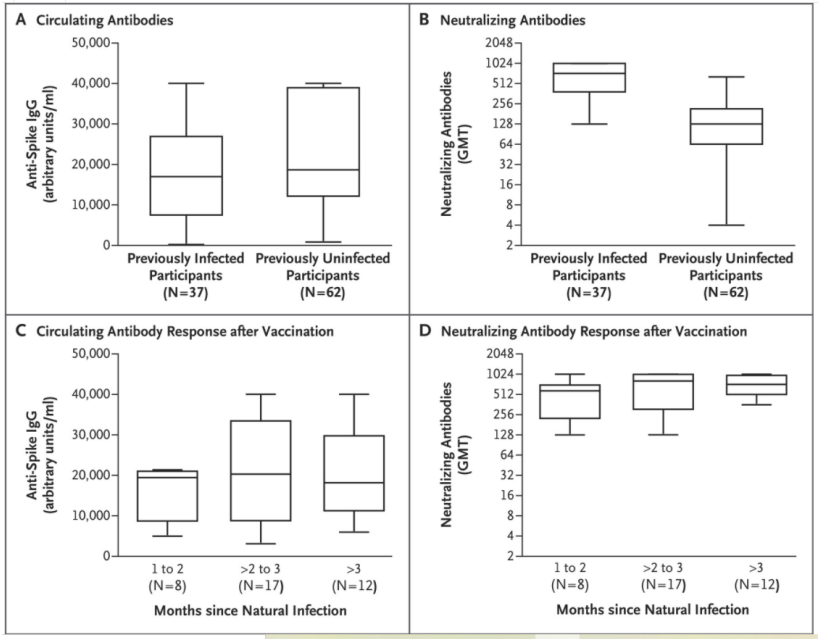
			increases all components of the humoral response, and as expected, results in serum neutralizing activities against variants of concern that are comparable to or greater than neutralizing activity against the original Wuhan Hu-1 achieved by vaccination of naïve individuals. The mechanism underlying these broad-based responses involves ongoing antibody somatic mutation, memory B cell clonal turnover, and development of monoclonal antibodies that are exceptionally resistant to SARS-CoV-2 RBD mutations, including those found in variants of concern. In addition, B cell clones expressing broad and potent antibodies are selectively retained in the repertoire over time and expand dramatically after vaccination. The data suggest that immunity in convalescent individuals will be very long lasting and that convalescent individuals who receive available mRNA vaccines will produce antibodies and memory B cells that should be protective against circulating SARS-CoV-2 variants. Should memory responses evolve in a similar manner in vaccinated individuals, additional appropriately timed boosting with available vaccines could cover most circulating variants of concern. 
Reynolds CJ et al Science	Prior SARS-CoV-2 infection rescues B and T cell responses to variants after first vaccine dose	Incremento della risposta T e B dopo una dose di vaccino a mRNA in persone con storia di COVID-19, anche contro la variante « alpha » e « beta » il che	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine rollout has coincided with the spread of variants of concern. We investigated whether single-dose vaccination, with or without prior infection, confers cross-protective immunity to variants. We analyzed T and B cell responses after first-dose vaccination with the

https://science.sciencemag.org/content/372/6549/1418		non si verifica nelle persone senza pregressa infezione dopo una sola dose.	Pfizer/BioNTech messenger RNA vaccine BNT162b2 in health care workers (HCW) followed longitudinally, with or without prior Wuhan-Hu-1 SARS-CoV-2 infection. After one dose, individuals with prior infection showed enhanced T cell immunity, antibody-secreting memory B cell response to the spike protein, and neutralizing antibodies effective against variants B.1.1.7 and B.1.351. By comparison, HCW receiving one vaccine dose without prior infection showed reduced immunity against variants. B.1.1.7 and B.1.351 spike mutations resulted in increased, abrogated, or unchanged T cell responses, depending on human leukocyte antigen (HLA) polymorphisms. Single-dose vaccination with BNT162b2 in the context of prior infection with a heterologous variant substantially enhances neutralizing antibody responses against variants. 
Jung JH et al Nature https://www.nature.com/articles/s41467-021-24377-1	SARS-CoV-2-specific T cell memory is sustained in COVID-19 convalescent patients for 10 months with successful development of stem cell-like memory T cells	Persistenza di linfociti T di memoria fino a 10 mesi dopo l'infezione da SARS-CoV-2 di tutti i livelli di gravità.	Memory T cells contribute to rapid viral clearance during re-infection, but the longevity and differentiation of SARS-CoV-2-specific memory T cells remain unclear. Here we conduct ex vivo assays to evaluate SARS-CoV-2-specific CD4+ and CD8+ T cell responses in COVID-19 convalescent patients up to 317 days post-symptom onset (DPSO), and find that memory T cell responses are maintained during the study period regardless of the severity of COVID-19. In particular, we observe sustained polyfunctionality and

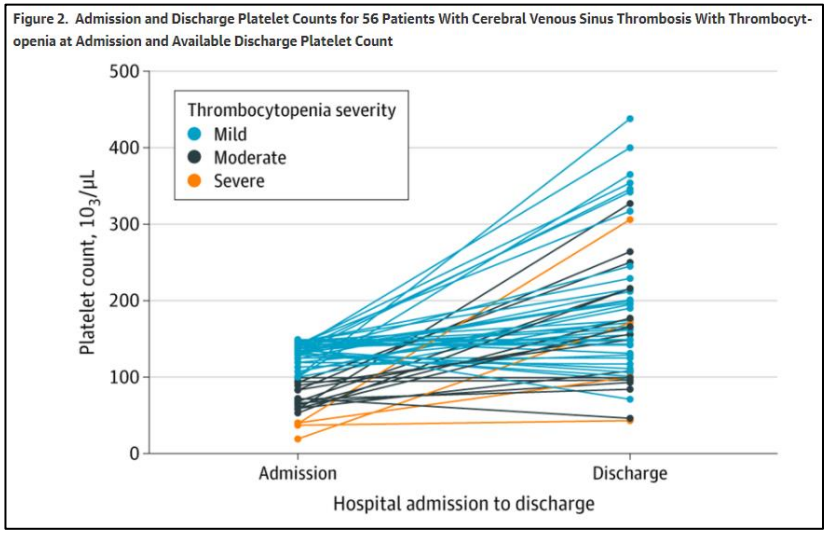
			proliferation capacity of SARS-CoV-2-specific T cells. Among SARS-CoV-2-specific CD4+ and CD8+ T cells detected by activation-induced markers, the proportion of stem cell-like memory T (TSCM) cells is increased, peaking at approximately 120 DPSO. Development of TSCM cells is confirmed by SARS-CoV-2-specific MHC-I multimer staining. Considering the self-renewal capacity and multipotency of TSCM cells, our data suggest that SARS-CoV-2-specific T cells are long-lasting after recovery from COVID-19, thus support the feasibility of effective vaccination programs as a measure for COVID-19 control. 
Heath PT et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2107659?query=featured_home	Safety and Efficacy of NVX-CoV2373 Covid-19 Vaccine	Trial clinico di fase 3 sul vaccino ricombinante a nanoparticlle contro SARS-CoV-2 Novavax basato sulla proteina spike : protezione 86.3% contro l'infezione sintomatica anche lieve da variante « alpha », 94.6% contro ceppi diversi. Nella	BACKGROUND : Early clinical data from studies of the NVX-CoV2373 vaccine (Novavax), a recombinant nanoparticle vaccine against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that contains the full-length spike glycoprotein of the prototype strain plus Matrix-M adjuvant, showed that the vaccine was safe and associated with a robust immune response in healthy adult participants. Additional data were needed regarding the efficacy, immunogenicity, and safety of this vaccine in a larger population.

		popolazione studiata più di un quarto erano soggetti oltre 65 anni.	METHODS : In this phase 3, randomized, observer-blinded, placebo-controlled trial conducted at 33 sites in the United Kingdom, we assigned adults between the ages of 18 and 84 years in a 1:1 ratio to receive two intramuscular 5-µg doses of NVX-CoV2373 or placebo administered 21 days apart. The primary efficacy end point was virologically confirmed mild, moderate, or severe SARS-CoV-2 infection with an onset at least 7 days after the second injection in participants who were serologically negative at baseline. RESULTS : A total of 15,187 participants underwent randomization, and 14,039 were included in the per-protocol efficacy population. Of the participants, 27.9% were 65 years of age or older, and 44.6% had coexisting illnesses. Infections were reported in 10 participants in the vaccine group and in 96 in the placebo group, with a symptom onset of at least 7 days after the second injection, for a vaccine efficacy of 89.7% (95% confidence interval [CI], 80.2 to 94.6). No hospitalizations or deaths were reported among the 10 cases in the vaccine group. Five cases of severe infection were reported, all of which were in the placebo group. A post hoc analysis showed an efficacy of 86.3% (95% CI, 71.3 to 93.5) against the B.1.1.7 (or alpha) variant and 96.4% (95% CI, 73.8 to 99.5) against non-B.1.1.7 variants. Reactogenicity was generally mild and transient. The incidence of serious adverse events was low and similar in the two groups. CONCLUSIONS : A two-dose regimen of the NVX-CoV2373 vaccine administered to adult participants conferred 89.7% protection against SARS-CoV-2 infection and showed high efficacy against the B.1.1.7 variant.

			
Anichini G et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMc2103825?query=featured_home	SARS-CoV-2 Antibody Response in Persons with Past Natural Infection	In questo gruppo di 100 operatori sanitari di cui 39 con storia di infezione da SARS-CoV-2 si osserva che il titolo neutralizzante anti-spike dopo una sola dose di vaccino Pfizer nei guariti è superiore a quello presente dopo due dosi di vaccino nei soggetti senza storia di infezione.	The most remarkable finding of this study was the significantly lower neutralizing antibody titer after administration of a second dose of vaccine in previously uninfected patients than the titer after only a single dose of vaccine in previously infected participants. It is unclear how the neutralizing antibody titers influence the ability of the host to transmit the virus. These findings provide evidence that after the administration of a single dose of vaccine, the humoral response against SARS-CoV-2 in persons with a history of SARS-CoV-2 infection is greater than the response in previously uninfected participants who have received a second dose.

			
Van Kammen MS et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2781791	Frequency of Thrombocytopenia and Platelet Factor 4/Heparin Antibodies in Patients With Cerebral Venous Sinus Thrombosis Prior to the COVID-19 Pandemic	Studio retrospettivo su 865 pazienti con trombosi dei seni venosi cerebrali nel periodo pre-COVID19 : in quei casi erano rare la trombocitopenia e la presenza di anticorpi anti fattore piastrinico 4.	Importance Cases of cerebral venous sinus thrombosis in combination with thrombocytopenia have recently been reported within 4 to 28 days of vaccination with the ChAdOx1 nCov-19 (AstraZeneca/Oxford) and Ad.26.COV2.S (Janssen/Johnson & Johnson) COVID-19 vaccines. An immune-mediated response associated with platelet factor 4/heparin antibodies has been proposed as the underlying pathomechanism. Objective To determine the frequencies of admission thrombocytopenia, heparin-induced thrombocytopenia, and presence of platelet factor 4/heparin antibodies in patients diagnosed with cerebral venous sinus thrombosis prior to the COVID-19 pandemic. Design, Setting, and Participants This was a descriptive analysis of a retrospective sample of consecutive patients diagnosed with cerebral venous sinus thrombosis between January 1987 and March

			2018 from 7 hospitals participating in the International Cerebral Venous Sinus Thrombosis Consortium from Finland, the Netherlands, Switzerland, Sweden, Mexico, Iran, and Costa Rica. Of 952 patients, 865 with available baseline platelet count were included. In a subset of 93 patients, frozen plasma samples collected during a previous study between September 2009 and February 2016 were analyzed for the presence of platelet factor 4/heparin antibodies. Exposures Diagnosis of cerebral venous sinus thrombosis. Main Outcomes and Measures Frequencies of admission thrombocytopenia (platelet count <150 ×103/µL), heparin-induced thrombocytopenia (as diagnosed by the treating physician), and platelet factor 4/heparin IgG antibodies (optical density >0.4, in a subset of patients with previously collected plasma samples). Results Of 865 patients (median age, 40 years [interquartile range, 29-53 years], 70% women), 73 (8.4%; 95% CI, 6.8%-10.5%) had thrombocytopenia, which was mild (100-149 ×103/µL) in 52 (6.0%), moderate (50-99 ×103/µL) in 17 (2.0%), and severe (<50 ×103/µL) in 4 (0.5%). Heparin-induced thrombocytopenia with platelet factor 4/heparin antibodies was diagnosed in a single patient (0.1%; 95% CI, <0.1%-0.7%). Of the convenience sample of 93 patients with cerebral venous sinus thrombosis included in the laboratory analysis, 8 (9%) had thrombocytopenia, and none (95% CI, 0%-4%) had platelet factor 4/heparin antibodies. Conclusions and Relevance In patients with cerebral venous sinus thrombosis prior to the COVID-19 pandemic, baseline thrombocytopenia was uncommon, and heparin-induced thrombocytopenia and platelet factor 4/heparin antibodies were rare. These findings may inform investigations of the possible association between the ChAdOx1 nCoV-19 and Ad26.COV2.S

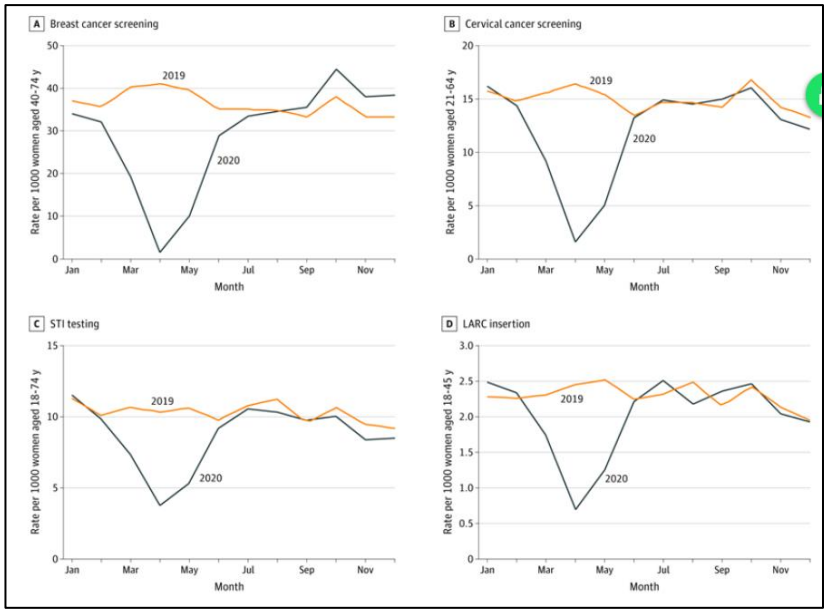
			COVID-19 vaccines and cerebral venous sinus thrombosis with thrombocytopenia.  Figure 2. Admission and Discharge Platelet Counts for 56 Patients With Cerebral Venous Sinus Thrombosis With Thrombocytopenia at Admission and Available Discharge Platelet Count
Persad G et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2781755	Ethical Considerations of Offering Benefits to COVID-19 Vaccine Recipients	Pro e contro dell'utilizzo di benefit per favorire l'adesione alla campagna vaccinale contro SARS-CoV-2.	Entry into a million-dollar lottery for getting vaccinated against COVID-19 is Ohio's offer to adults. Teens who get vaccinated receive a lottery ticket for state college tuition, room, board, and more. Other states are offering gift cards. Now many employers are offering rewards for COVID-19 vaccination. Businesses ranging from Krispy Kreme and Sam Adams beer to the Cincinnati Reds have announced discounts or prizes for vaccinated individuals. Are these benefit programs ethical? Are they useful? Are they better than

			mandates?

Objections	
Coercion	Benefits do not threaten to deprive anyone of anything they were entitled to
Exploitation	Benefits are being offered to encourage a less risky choice (vaccination), not a riskier one In any event, benefits like hazard pay are frequently offered to encourage or compensate riskier choices
Distort decision-making	Benefits improve decision-making by offsetting costs such as lost wages, childcare, and transit Lotteries do not distort decision-making any more than other approaches that harness psychological biases It is appropriate for individuals to consider how their choices affect public health and for society to encourage socially valuable choices
Corrupt vaccination's moral significance	Financial benefits do not strip medical practice or nursing of moral significance Theoretical concerns about moral significance are less important than preventing harm and improving equity
Wrong those already vaccinated	Benefits could be extended to already-vaccinated people using lotteries Treating latecomers differently from early adopters is not wrongful
Destroy public willingness to be vaccinated without pay	No empirical evidence for this Any empirical evidence needs to be weighed against value of stemming the pandemic
Make vaccination look riskier	Legitimate concern, could be addressed by appropriately calibrating benefits and targeting them to receptive groups Must be weighed against value of stemming the pandemic
Waste public funds	Legitimate concern, could be addressed by offering benefits no greater than needed to encourage vaccination

Becker NV et al JAMA https://jamanetwork.com/journals/jama-health-forum/fullarticle/2781692	Utilization of Women's Preventive Health Services During the COVID-19 Pandemic	Studio su oltre 680000 donne iscritte a programmi di prevenzione negli USA, che mostra come le attività di prevenzione (screening per neoplasie, malattie a trasmissione sessuale, contraccezione non di emergenza) siano state sfruttate in modo significativamente minore durante la pandemia rispetto all'anno precedente.	Importance The association of the COVID-19 pandemic with women's preventive health care use is unknown. Objective To describe utilization of women's preventive health services. Design, Setting, and Participants Cross-sectional study of women aged 18 to 74 years enrolled in a commercial health maintenance organization in Michigan. Exposures COVID-19 pandemic (2019-2020). Main Outcomes and Measures Adjusted odds ratios (AORs) of receiving breast cancer screening, cervical cancer screening, sexually transmitted infection (STI) screening, long-acting reversible contraception (LARC) insertions, and pharmacy-obtained contraception, adjusted for month, age, county, zip code characteristics (per-capita income, non-White percentage of population, non–English-proficient percentage of population), and plan designation (primary plan holder vs dependent). Results The study population included 685 373 women aged 18 to 74 years, enrolled for 13 000 715 person-months, of whom 10 061 275 person-months (77.4%) were among women aged 25 to 64 years and 8 020 215 (61.7%) were the primary plan holder, with mean zip code per capita income of $33 708, 20.2% mean zip code non-White population, and 3.4% mean zip code non–English-speaking population. For services requiring an in-person visit (breast cancer screening, cervical cancer screening, STI testing, and LARC insertions), utilization declined by 60% to 90% during the spring of 2020, with a nadir in April 2020, after which utilization for all services recovered to close to 2019 levels by July 2020. Claims for pharmacy-obtained hormonal contraceptives in 2020 were consistently 15% to 30% lower than 2019. The AORs of a woman receiving a given preventive service in 2020 compared with 2019

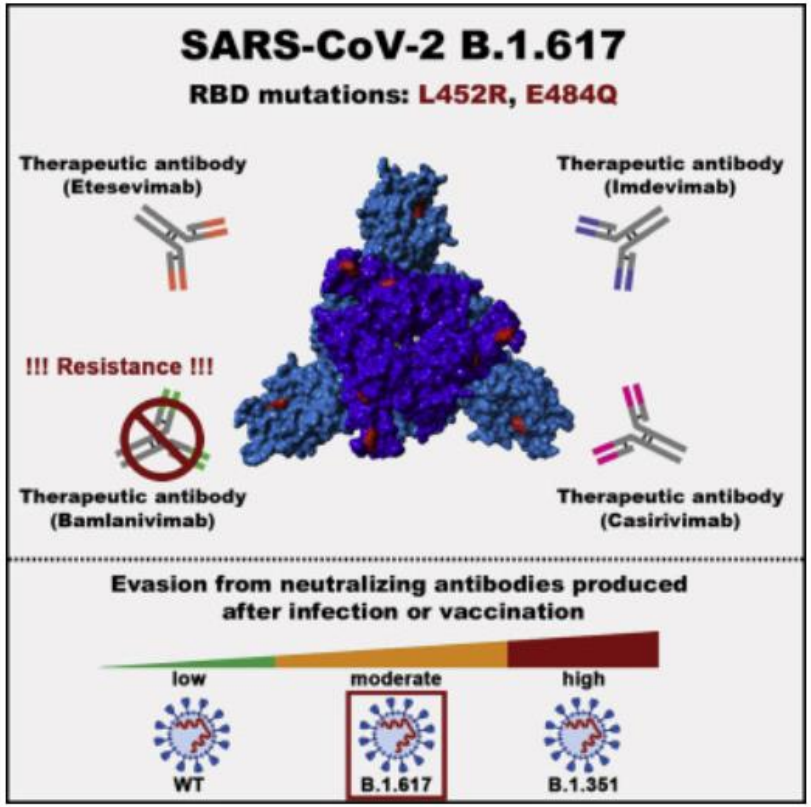
were significantly lower for breast cancer screening (AOR, 0.80; 95% CI, 0.79-0.80), cervical cancer screening (AOR, 0.80; 95% CI, 0.80-0.81), STI screening (AOR, 0.83; 95% CI, 0.82-0.84), LARC insertion (AOR, 0.87; 95% CI, 0.84-0.90), and pharmacy-obtained contraception (AOR, 0.73; 95% CI, 0.72-0.74) (all P < .001).
Conclusions and Relevance In this cross-sectional study of women enrolled in a large US commercial health maintenance organization plan, the COVID-19 pandemic was associated with large but transient declines in rates of breast cancer screening, cervical cancer screening, STI screening, and LARC insertions, and moderate persistent declines in pharmacy-obtained hormonal contraceptives. The overall odds of a woman receiving a given preventive service in 2020 was 20% to 30% lower than 2019. Further research into disparities in access to care and the health outcomes of decreased use of these key health services is warranted.



Thompson LA et al JAMA https://jamanetwork.com/journals/jamapediatrics/fullarticle/2781110	Return to Play After COVID-19 Infection in Children	Come riprendere l'attività sportiva dopo COVID-19 nei bambini e quali sintomi sorvegliare per sospettare precocemente una MIS-C.	As the pandemic continues, children may experience long-term effects from COVID-19 infections. Because children may become "long haulers" or develop multisystem inflammatory syndrome in children (MIS-C), close monitoring after a COVID-19 diagnosis is important. In addition, children who are athletes require a separate return-to-play evaluation before they return to competitive sports or physical activities.
Lee SA et al Scientifica Reports https://www.nature.com/articles/s41598-021-92323-8	Increased risk of acute kidney injury in coronavirus disease patients with renin–angiotensin–aldosterone-system blockade use: a systematic review and meta-analysis	L'utilizzo di inibitori dell'asse renina angiotensina aldosterone è associato all'insufficienza rénale acuta in pazienti ricoverati per COVID-19 secondo questa metanalisi.	Acute kidney injury (AKI) is a severe complication of coronavirus disease (COVID-19) that negatively affects its outcome. Concern had been raised about the potential effect of renin–angiotensin–aldosterone system (RAAS) blockades on renal outcomes in COVID-19 patients. However, the association between RAAS blockade use and incident AKI in COVID-19 patients has not been fully understood. We investigated the association between RAAS blockade exposure and COVID-19-related AKI in hospitalized patients through meta-analysis. Electronic databases were searched up to 24th December 2020. Summary estimates of pooled odds ratio (OR) of COVID-19-related AKI depending on RAAS blockade exposure were obtained through random-effects model. The random-effect meta-analysis on fourteen studies (17,876 patients) showed that RAAS blockade use was significantly associated with increased risk of incident AKI in hospitalized COVID-19 patients (OR 1.68; 95% confidence interval 1.19–2.36). Additional analysis showed that the association of RAAS blockade use on COVID-19-related AKI remains significant even after stratification by drug class and AKI severity. RAAS blockade use is significantly associated with the incident AKI in hospitalized COVID-19 patients. Therefore, careful monitoring of renal complications is recommended for

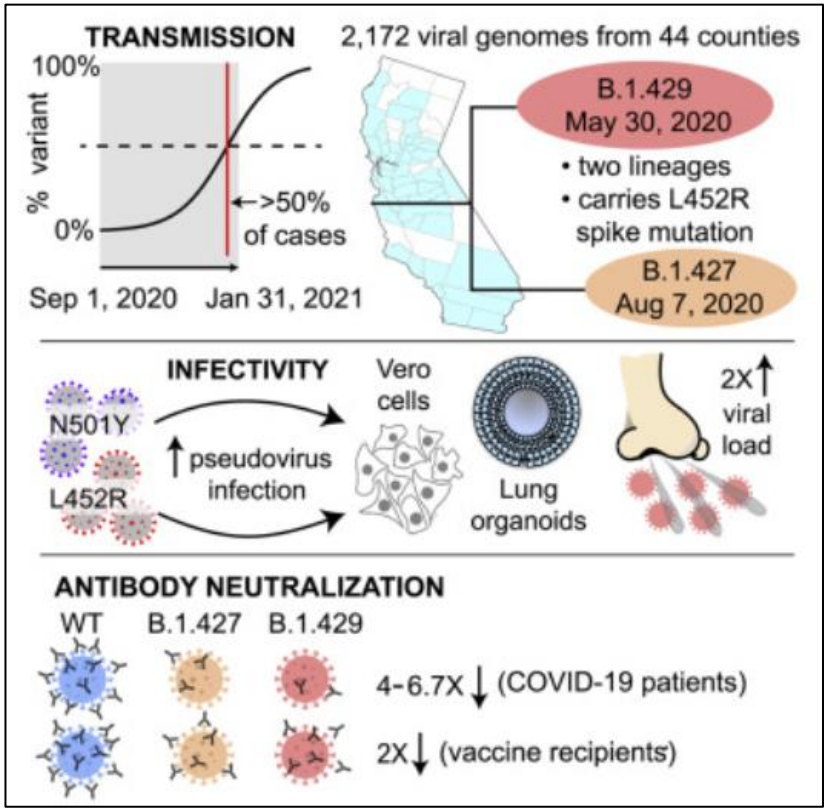
			COVID-19 patients with recent RAAS blockade use due to the potential risk of AKI.
Knabl L et al Nature Communications medicine https://www.nature.com/articles/s43856-021-00007-1	High SARS-CoV-2 seroprevalence in children and adults in the Austrian ski resort of Ischgl	Andamento dei contagi nella località sciistica di Ischgl in Austria, epicentro della prima ondata.	Background In early March 2020, a SARS-CoV-2 outbreak in the ski resort Ischgl in Austria initiated the spread of SARS-CoV-2 throughout Austria and Northern Europe. Methods Between April 21st and 27th 2020, a cross-sectional epidemiologic study targeting the full population of Ischgl (n = 1867), of which 79% could be included (n = 1473, incl. 214 children), was performed. For each individual, the study involved a SARS-CoV-2 PCR, antibody testing and structured questionnaires. A mathematical model was used to help understand the influence of the determined seroprevalence on virus transmission. Results The seroprevalence was 42.4% (95% confidence interval (CI) 39.8–44.7). Individuals under 18 showed a significantly lower seroprevalence of 27.1% (95% CI 21.3-33.6) than adults (45%; 95% CI 42.2–47.7; OR of 0.455, 95% CI 0.356–0.682, $p < 0.001$). Of the seropositive individuals, 83.7% had not been diagnosed to have had SARS-CoV-2 infection previously. The clinical course was generally mild. Over the previous two months, two COVID-19-related deaths had been recorded, corresponding to an infection fatality rate of 0.25% (95% CI 0.03–0.91). Only 8 (0.5 %) individuals were newly diagnosed to be infected with SARS-CoV-2 during this study.

			Conclusions Ischgl was hit early and hard by SARS-CoV-2 leading to a high local seroprevalence of 42.4%, which was lower in individuals below the age of 18 than in adults. Mathematical modeling suggests that a drastic decline of newly infected individuals in Ischgl by the end of April occurred due to the dual impact from the non-pharmacological interventions and a high immunization of the Ischgl population.
Hoffmann M et al Cell https://www.cell.com/cell-reports/fulltext/S2211-1247(21)00828-7	SARS-CoV-2 variant B.1.617 is resistant to Bamlanivimab and evades antibodies induced by infection and vaccination	Resistenza della variante « indicana » all'anticorpo monoclonale bamlanivimab.	The emergence of SARS-CoV-2 variants threatens efforts to contain the COVID-19 pandemic. The number of COVID-19 cases and deaths in India has risen steeply and a SARS-CoV-2 variant, B.1.617, is believed to be responsible for many of these cases. The spike protein of B.1.617 harbors two mutations in the receptor binding domain, which interacts with the ACE2 receptor and constitutes the main target of neutralizing antibodies. Therefore, we analyze whether B.1.617 is more adept in entering cells and/or evades antibody responses. B.1.617 enters two out of eight cell lines tested with roughly 50% increased efficiency and is equally inhibited by two entry inhibitors. In contrast, B.1.617 is resistant against Bamlanivimab, an antibody used for COVID-19 treatment. B.1.617 evades antibodies induced by infection or vaccination, although less so than the B.1.351 variant. Collectively, our study reveals that antibody evasion of B.1.617 may contribute to the rapid spread of this variant.

			
Pieh C et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2781462	Assessment of Mental Health of High School Students During Social Distancing and Remote Schooling During the COVID-19 Pandemic in Austria	Dopo un anno di didattica a distanza, più della metà dei 3052 ragazzi (14-20 anni) studiati in questo lavoro ha sintomi depressivi, quasi la metà manifesta ansia e quasi un quarto insonnia ; l'ideazione suicidaria interessa il 36.9%.	To get the COVID-19 pandemic under control, many countries have imposed lockdown measures or remote schooling. This study assessed mental health in high school students aged 14 to 20 years after 1 semester of attending school remotely and almost a year of social distancing in Austria.

Ropper AH et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMra2106545?query=featured_home	Cerebral Venous Thrombosis	Una review su come riconoscere e trattare la trombosi venosa centrale, con riferimento anche ai vaccini a mRNA contro SARS-CoV-2.	Cerebral venous thrombosis is characterized by infarction with focal neurologic deficits and increased intracranial pressure. As a very rare complication of some vaccines against Covid-19, the disorder is accompanied by disseminated intravascular coagulation and hemorrhage.
Thompson MG et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2107058?query=featured_home	Prevention and Attenuation of Covid-19 with the BNT162b2 and mRNA-1273 Vaccines	Studio di coorte propettico su 3975 operatori sanitari vaccinati con vaccini a mRNA, in cui si osserva una efficacia del 91% contro l'infezione per chi ha eseguito un ciclo completo di due dosi da almeno 2 settimane.	BACKGROUND : Information is limited regarding the effectiveness of the two-dose messenger RNA (mRNA) vaccines BNT162b2 (Pfizer–BioNTech) and mRNA-1273 (Moderna) in preventing infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and in attenuating coronavirus disease 2019 (Covid-19) when administered in real-world conditions. METHODS : We conducted a prospective cohort study involving 3975 health care personnel, first responders, and other essential and frontline workers. From December 14, 2020, to April 10, 2021, the participants completed weekly SARS-CoV-2 testing by providing mid-turbinate nasal swabs for qualitative and quantitative reverse-transcriptase–polymerase-chain-reaction (RT-PCR) analysis. The formula for calculating vaccine effectiveness was 100%×(1−hazard ratio for SARS-CoV-2 infection in vaccinated vs. unvaccinated participants), with adjustments for the propensity to be vaccinated, study site, occupation, and local viral circulation. RESULTS : SARS-CoV-2 was detected in 204 participants (5%), of whom 5 were fully vaccinated (≥14 days after dose 2), 11 partially vaccinated (≥14 days after dose 1 and <14 days after dose 2), and 156 unvaccinated; the 32 participants with indeterminate vaccination status (<14 days after dose 1) were excluded. Adjusted vaccine effectiveness was 91% (95% confidence interval [CI], 76 to

			97) with full vaccination and 81% (95% CI, 64 to 90) with partial vaccination. Among participants with SARS-CoV-2 infection, the mean viral RNA load was 40% lower (95% CI, 16 to 57) in partially or fully vaccinated participants than in unvaccinated participants. In addition, the risk of febrile symptoms was 58% lower (relative risk, 0.42; 95% CI, 0.18 to 0.98) and the duration of illness was shorter, with 2.3 fewer days spent sick in bed (95% CI, 0.8 to 3.7). CONCLUSIONS : Authorized mRNA vaccines were highly effective among working-age adults in preventing SARS-CoV-2 infection when administered in real-world conditions, and the vaccines attenuated the viral RNA load, risk of febrile symptoms, and duration of illness among those who had breakthrough infection despite vaccination.
Deng X et al Cell https://www.cell.com/cell/fulltext/S0092-8674(21)00505-5	Transmission, infectivity, and neutralization of a spike L452R SARS-CoV-2 variant	Caratterizzazione della variante di SARS-CoV-2 B.1.427/B.1.429 diffusa in California, caratterizzata da maggiore contagiosità rispetto alle precedenti e più note varianti in vivo.	We identified an emerging severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant by viral whole-genome sequencing of 2,172 nasal/nasopharyngeal swab samples from 44 counties in California, a state in the western United States. Named B.1.427/B.1.429 to denote its two lineages, the variant emerged in May 2020 and increased from 0% to >50% of sequenced cases from September 2020 to January 2021, showing 18.6%–24% increased transmissibility relative to wild-type circulating strains. The variant carries three mutations in the spike protein, including an L452R substitution. We found 2-fold increased B.1.427/B.1.429 viral shedding in vivo and increased L452R pseudovirus infection of cell cultures and lung organoids, albeit decreased relative to pseudoviruses carrying the N501Y mutation common to variants B.1.1.7, B.1.351, and P.1. Antibody neutralization assays revealed 4.0- to 6.7-fold and 2.0-fold decreases in neutralizing titers from convalescent patients and vaccine recipients, respectively. The increased prevalence of a more transmissible variant in California

			exhibiting decreased antibody neutralization warrants further investigation. 
Bennett-Guerrero E et al Critical Care Medicine https://journals.lww.com/ccmjournal/Fulltext/2021/07000/Severe_Acute_Respiratory_Syndrome_Coronavirus_2.2.aspx	Severe Acute Respiratory Syndrome Coronavirus 2 Convalescent Plasma Versus Standard Plasma in Coronavirus Disease 2019 Infected Hospitalized Patients in New York: A Double-Blind Randomized Trial	Il trattamento con plasma di soggetti guariti rispetto a plasma generico non modifica l'outcome in questo piccolo trial su 74 pazienti ricoverati per COVID-19, di cui circa un quinto intubati.	OBJECTIVES: Four peer-reviewed publications have reported results from randomized controlled trials of convalescent plasma for coronavirus disease 2019 infection; none were conducted in the United States nor used standard plasma as a comparator. To determine if administration of convalescent plasma to patients with coronavirus disease 2019 increases antibodies to severe acute respiratory syndrome coronavirus 2 and improves outcome. DESIGN: Double-blind randomized controlled trial. SETTING: Hospital in New York.

			PATIENTS: Patients with polymerase chain reaction documented coronavirus disease 2019 infection. INTERVENTIONS: Patients were randomized (4:1) to receive 2 U of convalescent plasma versus standard plasma. Antibodies to severe acute respiratory syndrome coronavirus 2 were measured in plasma units and in trial recipients. MEASUREMENTS AND MAIN RESULTS: Enrollment was terminated after emergency use authorization was granted for convalescent plasma. Seventy-four patients were randomized. At baseline, mean (sd) Acute Physiology and Chronic Health Evaluation II score (23.4 [5.6] and 22.5 [6.6]), percent of patients intubated (19% and 20%), and median (interquartile range) days from symptom onset to randomization of 9 (6–18) and 9 (6–15), were similar in the convalescent plasma versus standard plasma arms, respectively. Convalescent plasma had high neutralizing activity (median [interquartile range] titer 1:526 [1:359–1:786]) and its administration increased antibodies to severe acute respiratory syndrome coronavirus 2 by 14.4%, whereas standard plasma administration led to an 8.6% decrease (p = 0.005). No difference was observed for ventilator-free days through 28 days (primary study endpoint): median (interquartile range) of 28 (2–28) versus 28 (0–28; p = 0.86) for the convalescent plasma and standard plasma groups, respectively. A greater than or equal to 2 point improvement in the World Health Organization scale was achieved by 20% of subjects in both arms (p = 0.99). All-cause mortality through 90 days was numerically lower in the convalescent plasma versus standard plasma groups (27% vs 33%; p = 0.63) but did not achieve statistical significance. A key prespecified subgroup analysis of time to death in patients who were intubated at baseline was statistically significant; however, sample size numbers were small.

			CONCLUSIONS: Administration of convalescent plasma to hospitalized patients with coronavirus disease 2019 infection increased antibodies to severe acute respiratory syndrome coronavirus disease 2 but was not associated with improved outcome.