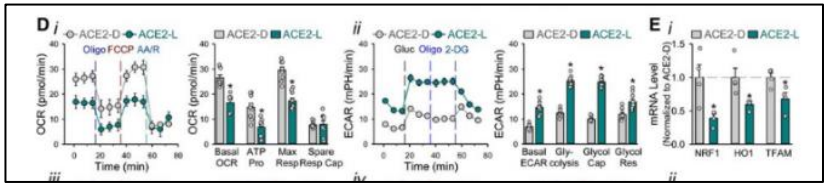
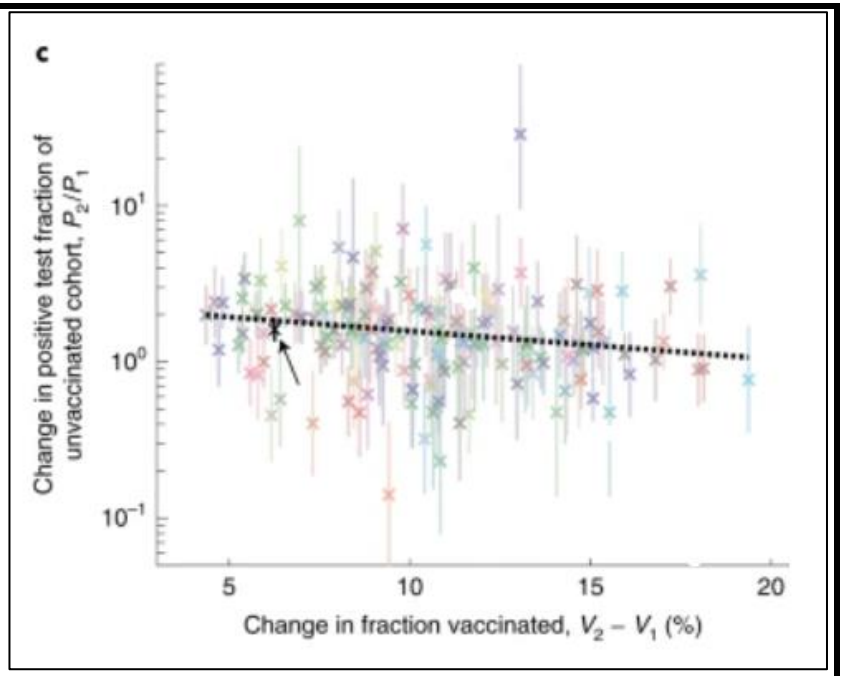
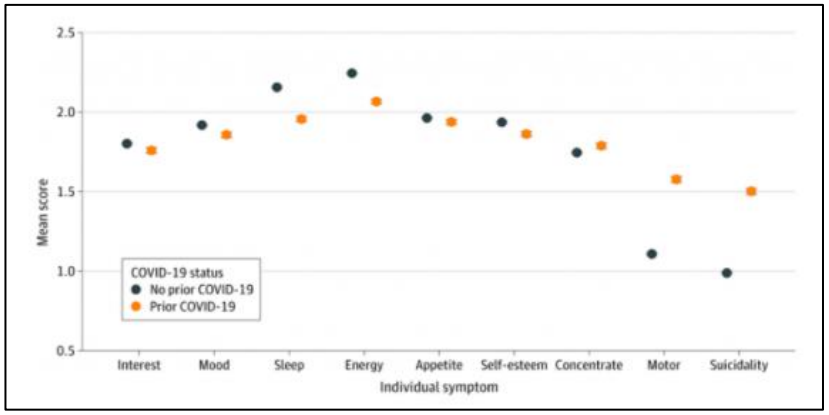
RICERCA BIBLIOGRAFICA COVID 19 SETTIMANA 14.06 – 20.06.2021 FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE DOTT.SSA ELEONORA TADDEI			
AUTORE/RIVISTA	**TITOLO**	**OUTCOME PRINCIPALE**	**ABSTRACT**
Pascarella S et al BioRXiv https://www.biorxiv.org/content/10.1101/2021.06.08.445535v1	SARS-CoV-2 B.1.617 Indian variants: are electrostatic potential changes responsible for a higher transmission rate?	La variante « indiana » di SARS-CoV-2 possiede dei sub-lineage caratterizzati da sostituzioni aminoacidiche il cui effetto è una alterazione del potenziale elettrostatico della porzione legante il recettore (RBD) della proteina S, per cui l'interazione appare favorita e la trasmissibilità del virus portatore sarebbe aumentata.	Lineage B.1.617+, also known as G/452R.V3, is a recently described SARS-CoV-2 variant under investigation (VUI) firstly identified in October 2020 in India. As of May 2021, three sublineages labelled as B.1.617.1, B.1.617.2 and B.1.617.3 have been already identified, and their potential impact on the current pandemic is being studied. This variant has 13 amino acid changes, three in its spike protein, which are currently of particular concern: E484Q, L452R and P681R. Here we report a major effect of the mutations characterizing this lineage, represented by a marked alteration of the surface electrostatic potential (EP) of the Receptor Binding Domain (RBD) of the spike protein. Enhanced RBD-EP is particularly noticeable in the B.1.617.2 sublineage, which shows multiple replacements of neutral or negatively-charged amino acids with positively-charged amino acids. We here hypothesize that this EP change can favor the interaction between the B.1.617+RBD and the negatively-charged ACE2 thus conferring a potential increase in the virus transmission.

			
Lei Y et al Circulation https://www.ahajournals.org/doi/10.1161/CIRCRESAHA.121.318902	SARS-CoV-2 Spike Protein Impairs Endothelial Function via Downregulation of ACE 2	La proteina S di SARS-CoV-2 da sola, anche se associata a uno pseudovirus non infettante, è in grado di danneggiare l'endotelio e in particolare l'attività mitocondriale, determinando stress ossidativo.	SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) infection relies on the binding of S protein (Spike glycoprotein) to ACE (angiotensin-converting enzyme) 2 in the host cells. Vascular endothelium can be infected by SARS-CoV-2,1 which triggers mitochondrial reactive oxygen species production and glycolytic shift.2 Paradoxically, ACE2 is protective in the cardiovascular system, and SARS-CoV-1 S protein promotes lung injury by decreasing the level of ACE2 in the infected lungs.3 In the current study, we show that S protein alone can damage vascular endothelial cells (ECs) by downregulating ACE2 and consequently inhibiting mitochondrial function. 

Milman O et al Nature https://www.nature.com/articles/s41591-021-01407-5	Community-level evidence for SARS-CoV-2 vaccine protection of unvaccinated individuals	Effetto della vaccinazione contro SARS-CoV-2 sugli individui non vaccinati all'interno di una popolazione.	Mass vaccination has the potential to curb the current COVID-19 pandemic by protecting individuals who have been vaccinated against the disease and possibly lowering the likelihood of transmission to individuals who have not been vaccinated. The high effectiveness of the widely administered BNT162b vaccine from Pfizer–BioNTech in preventing not only the disease but also infection with SARS-CoV-2 suggests a potential for a population-level effect, which is critical for disease eradication. However, this putative effect is difficult to observe, especially in light of highly fluctuating spatiotemporal epidemic dynamics. Here, by analyzing vaccination records and test results collected during the rapid vaccine rollout in a large population from 177 geographically defined communities, we find that the rates of vaccination in each community are associated with a substantial later decline in infections among a cohort of individuals aged under 16 years, who are unvaccinated. On average, for each 20 percentage points of individuals who are vaccinated in a given population, the positive test fraction for the unvaccinated population decreased approximately twofold. These results provide observational evidence that vaccination not only protects individuals who have been vaccinated but also provides cross-protection to unvaccinated individuals in the community.

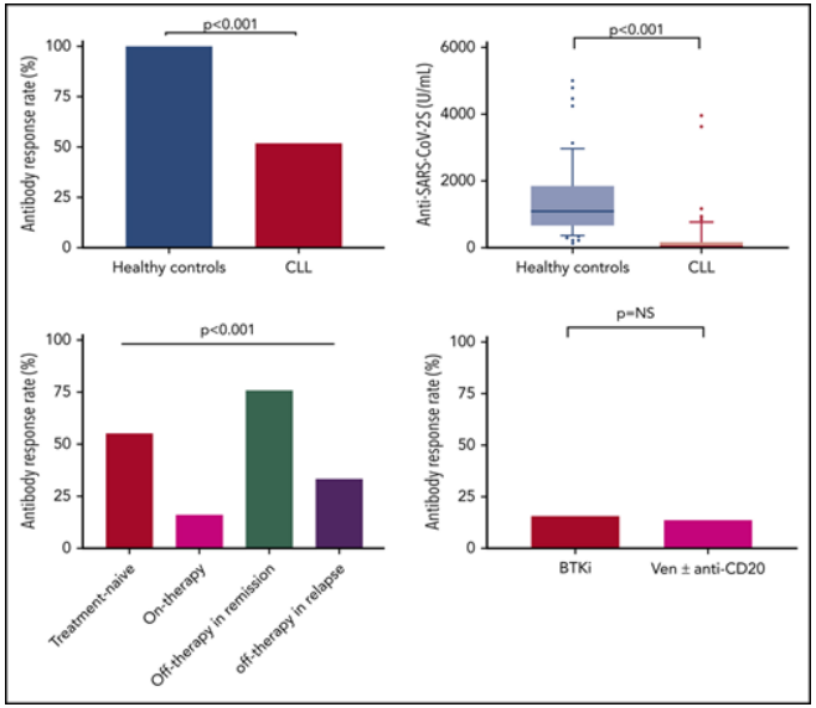
			
Aschman T et al JAMA https://jamanetwork.com/journals/jamaneurology/fullarticle/2781013?resultClick=1	Association Between SARS-CoV-2 Infection and Immune-Mediated Myopathy in Patients Who Have Died	Evidenza di miopatia infiammatoria in gran parte delle persone decedute per COVID-19 in questa casistica.	Importance Myalgia, increased levels of creatine kinase, and persistent muscle weakness have been reported in patients with COVID-19. Objective To study skeletal muscle and myocardial inflammation in patients with COVID-19 who had died. Design, Setting, and Participants This case-control autopsy series was conducted in a university hospital as a multidisciplinary postmortem investigation. Patients with COVID-19 or other critical illnesses who had died between March 2020 and February 2021 and on whom an autopsy was performed were included. Individuals for whom informed consent to autopsy was available and the postmortem interval was less than 6 days were randomly selected. Individuals who were infected with SARS-CoV-2 per polymerase

			chain reaction test results and had clinical features suggestive of COVID-19 were compared with individuals with negative SARS-CoV-2 polymerase chain reaction test results and an absence of clinical features suggestive of COVID-19. Main Outcomes and Measures Inflammation of skeletal muscle tissue was assessed by quantification of immune cell infiltrates, expression of major histocompatibility complex (MHC) class I and class II antigens on the sarcolemma, and a blinded evaluation on a visual analog scale ranging from absence of pathology to the most pronounced pathology. Inflammation of cardiac muscles was assessed by quantification of immune cell infiltrates. Results Forty-three patients with COVID-19 (median [interquartile range] age, 72 [16] years; 31 men [72%]) and 11 patients with diseases other than COVID-19 (median [interquartile range] age, 71 [5] years; 7 men [64%]) were included. Skeletal muscle samples from the patients who died with COVID-19 showed a higher overall pathology score (mean [SD], 3.4 [1.8] vs 1.5 [1.0]; 95% CI, 0-3; $P < .001$) and a higher inflammation score (mean [SD], 3.5 [2.1] vs 1.0 [0.6]; 95% CI, 0-4; $P < .001$). Relevant expression of MHC class I antigens on the sarcolemma was present in 23 of 42 specimens from patients with COVID-19 (55%) and upregulation of MHC class II antigens in 7 of 42 specimens from patients with COVID-19 (17%), but neither were found in any of the controls. Increased numbers of natural killer cells (median [interquartile range], 8 [8] vs 3 [4] cells per 10 high-power fields; 95% CI, 1-10 cells per 10 high-power fields; $P < .001$) were found. Skeletal muscles showed more inflammatory features than cardiac muscles, and inflammation was most pronounced in patients with COVID-19 with chronic courses. In some muscle specimens, SARS-CoV-2 RNA was detected by reverse transcription–polymerase chain reaction, but no evidence

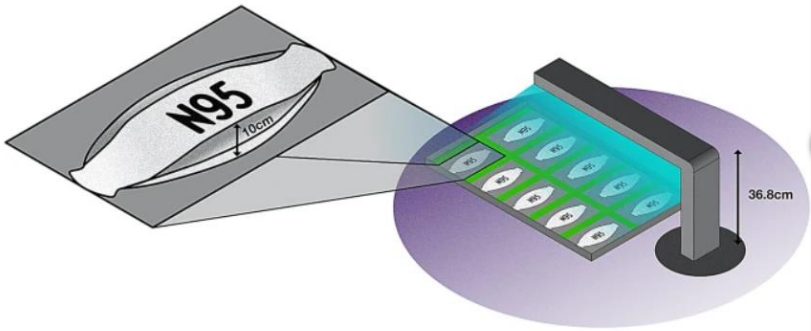
			for a direct viral infection of myofibers was found by immunohistochemistry and electron microscopy. Conclusions and Relevance In this case-control study of patients who had died with and without COVID-19, most individuals with severe COVID-19 showed signs of myositis ranging from mild to severe. Inflammation of skeletal muscles was associated with the duration of illness and was more pronounced than cardiac inflammation. Detection of viral load was low or negative in most skeletal and cardiac muscles and probably attributable to circulating viral RNA rather than genuine infection of myocytes. This suggests that SARS-CoV-2 may be associated with a postinfectious, immune-mediated myopathy.
Perlis RH et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2780928?resultClick=1	Factors Associated With Self-reported Symptoms of Depression Among Adults With and Without a Previous COVID-19 Diagnosis	Confronto dei fattori associati a depressione maggiore in persone con e senza storia di COVID-19.	Rates of major depressive symptoms are elevated after acute infection with SARS-CoV-2. A key question is whether such symptoms represent a general consequence of stress associated with acute illness or whether they reflect more specific sequelae associated with COVID-19 pathophysiology itself. To examine this possibility, in this survey study, we compared features of major depression in individuals with or without prior COVID-19 illness. 

Bollyky TJ et al The Lancet https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01323-4/fulltext	Epidemiology, not geopolitics, should guide COVID-19 vaccine donations	Riflessione sulle donazioni di vaccini contro SARS-CoV-2, acquistati dai Paesi ricchi a favore di quelli in via di sviluppo.	Vaccine donations are not the only solution to the gap that has emerged between countries with and without sufficient doses of COVID-19 vaccines. Yet, the potential number of surplus vaccine doses purchased by G7 nations is likely to be in the hundreds of millions or more. Vaccine manufacturers based in those countries have also offered to sell more than a billion doses at cost for use in low-income and middle-income countries (LMICs) in 2021, which G7 governments could buy and donate. These supplies are sufficiently large to help with near-term vaccine demands while investments are made in technology transfer to LMICs and in scaling up global manufacturing capacity for vaccines and vaccine inputs to respond to SARS-CoV-2 and future pandemic threats.
Wang Z et al Nature https://www.nature.com/articles/s41586-021-03696-9	Naturally enhanced neutralizing breadth against SARS-CoV-2 one year after infection	Stabilità della risposta anticorpale e dei linfociti B della memoria fino a 12 mesi dopo l'infezione da SARS-CoV-2 e incremento di tali componenti dopo vaccinazione (vaccino a mRNA).	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 antibodies1,2. 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 vaccines3,4. 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 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 naive individuals2,5–8. 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 concern4,9. 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.
Herishanu Y et al Blood https://ashpublications.org/blood/article/137/23/3165/475742/Efficacy-of-the-BNT162b2-mRNA-COVID-19-vaccine-in	Efficacy of the BNT162b2 mRNA COVID-19 vaccine in patients with chronic lymphocytic leukemia	La risposta anticorpale contro SARS-CoV-2 dopo vaccino Pfizer è ridotta nei pazienti con leucemia linfatica cronica, in particolare se trattati con ibrutinib, venetoclax e anticorpi anti-CD20.	Patients with chronic lymphocytic leukemia (CLL) have an increased risk for severe COVID-19 disease and mortality. The goal of this study was to determine the efficacy of COVID-19 vaccine in patients with CLL. We evaluated humoral immune responses to the BNT162b2 messenger RNA (mRNA) COVID-19 vaccine in patients with CLL and compared responses with those obtained in age-matched healthy control subjects. Patients received 2 vaccine doses, 21 days apart, and antibody titers were measured by using the Elecsys Anti-SARS-CoV-2 S assay after administration of the second dose. In a total of 167 patients with CLL, the antibody response rate was 39.5%. A comparison between 52 patients with CLL and 52 sex- and aged-matched healthy control subjects revealed a significantly reduced response rate among patients (52% vs 100%, respectively; adjusted odds ratio, 0.010; 95% confidence interval, 0.001-0.162; P < .001). The response rate was highest in patients who obtained clinical remission after treatment (79.2%), followed by 55.2% in treatment-naive patients and 16.0% in patients under treatment at the time of vaccination. In patients treated with either Bruton's tyrosine kinase inhibitors or venetoclax ± anti-CD20 antibody, response rates were considerably low (16.0% and 13.6%).

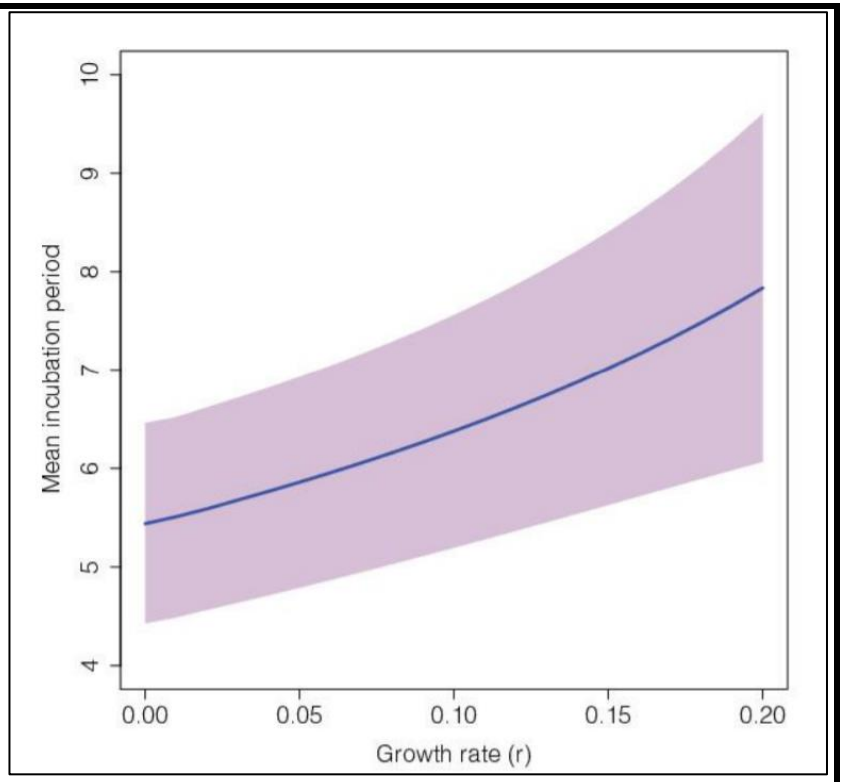
			None of the patients exposed to anti-CD20 antibodies <12 months before vaccination responded. In a multivariate analysis, the independent predictors of response were younger age, female sex, lack of currently active treatment, immunoglobulin G levels ≥550 mg/dL, and immunoglobulin M levels ≥40 mg/dL. In conclusion, antibody-mediated response to the BNT162b2 mRNA COVID-19 vaccine in patients with CLL is markedly impaired and affected by disease activity and treatment. 
Ontiveros CC et al Scientific Reports	Assessing the impact of multiple ultraviolet disinfection cycles on N95 filtering facepiece respirator integrity	Disinfezione dei filtranti N95 con radiazioni ultraviolette.	During the COVID-19 pandemic, N95 filtering facepiece respirators (FFRs) were recommended to protect healthcare workers when providing care to infected patients. Despite their single-use disposable nature, the need to disinfect and repurpose FFRs is paramount during this global emergency. The objectives of this

https://www.nature.com/articles/s41598-021-91706-1			study were to (1) determine if UV treatment has an observable impact on respirator integrity; (2) test the impact of UV treatment on N95 FFR user fit; and (3) test the impact of UV treatment on FFR integrity. Ultraviolet (UV) disinfection was assessed in maintaining N95 FFR integrity. Two models of FFRs were exposed to UV fluences ranging from 0 to 10,000 mJ cm−2 per side and subsequently tested for fit, respirator integrity, and airflow. Inspection of N95 FFRs before and after UV treatment via microscopy methods showed no observable or tactile abnormalities in the integrity of respirator material or straps. Tensile loading tests on UV-treated and untreated respirator straps also demonstrated no impact on breaking strength. Standardized fit test methods showed no compromise in user fit following UV treatment. Evaluation of particle penetration and airflow through N95 FFRs showed no impact on integrity, and average filtration efficiency did not fall below 95% for any of the respirator types or fluence levels. This work provides evidence that UV disinfection does not compromise N95 FFR integrity at UV fluences up to 10,000 mJ cm−2. UV disinfection is a viable treatment option to support healthcare professionals in their strategy against the spread of COVID-19.

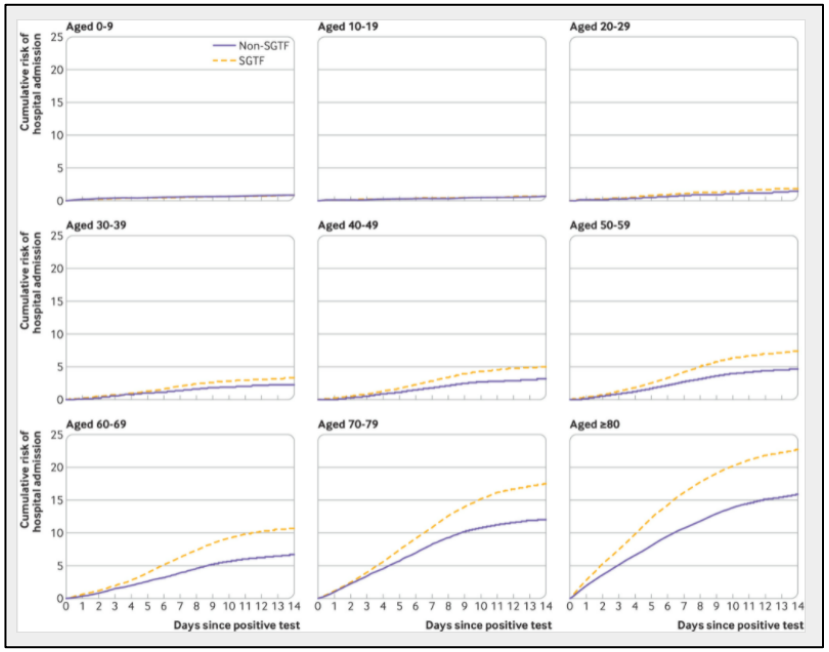
			Figure 1  Full-scale setup of N95 respirators as arranged beneath a single arm of the UV light source. The maximum respirator height was measured to be 10 cm. The top of the respirator closest to the light source receives 1142 mJ cm^{-2}, and the bottom of the respirator farthest from the light source receives 1000 mJ cm^{-2}.
Di Castelnuovo A et al Pathogens and Global Health https://www.tandfonline.com/doi/full/10.1080/20477724.2021.1936818	Hydroxychloroquine and mortality in COVID-19 patients: a systematic review and a meta-analysis of observational studies and randomized controlled trials	Revisione sistematica e metanalisi di studi di coorte e trial clinici sull'utilizzo di idrossiclorochina per COVID-19, in cui non si osserva una associazione con la mortalità.	Background: Hydroxychloroquine (HCQ) was proposed as potential treatment for COVID-19, but its association with mortality is unclear. We reviewed published literature for evidence of an association between HCQ (with or without azithromycin (AZM)) and total mortality in COVID-19 patients. Methods: Articles were retrieved until April 29th, 2021 by searching in seven databases. Data were combined using the general-variance-based method. Results: A total of 25 cohort studies (N=41,339 patients) and 11 randomized clinical trials (RCTs; N=8,709) were found. The use of HCQ was not associated with mortality in meta-analysis of RCTs (pooled risk ratio (PRR): 1.08, 95%CI: 0.97-1.20; I2=0%), but it was associated with 20% lower mortality risk (PRR=0.80, 95%CI: 0.69-0.93; I2=80%) in pooling of cohort studies. The negative association with mortality was mainly apparent by pooling cohort studies that used lower doses of HCQ (≤400 mg/day; PRR=0.69, 95%CI: 0.57-0.87). Use of HCQ+AZM (11 studies) was associated with 25% non-

			statistically significant lower mortality risk (PPR=0.75; 0.51-1.10; P=0.15). Use of HCQ was not associated with severe adverse events (PRR=1.12, 95%CI: 0.88-1.44; I2=0%). Conclusions: HCQ use was not associated with mortality in COVID-19 patients in pooling results from RCTs (high level of certainty of evidence), but it was associated with 20% mortality reduction when findings from observational studies were combined (low level of certainty of evidence). The reduction of mortality was mainly apparent in observational studies where lower doses of HCQ were used. These findings might help disentangling the debate on HCQ use in COVID-19.
Scheid JF et al Cell https://www.cell.com/cell/fulltext/S0092-8674(21)00535-3	B cell genomics behind cross-neutralization of SARS-CoV-2 variants and SARS-CoV	Studio del trascrittoma di popolazioni B cellulari che costituiscono la risposta contro SARS-CoV-2, in particolare dei target anticorpali comuni fra virus SARS-CoV e varianti di SARS-CoV-2.	Monoclonal antibodies (mAbs) are a focus in vaccine and therapeutic design to counteract severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its variants. Here, we combined B cell sorting with single-cell VDJ and RNA sequencing (RNA-seq) and mAb structures to characterize B cell responses against SARS-CoV-2. We show that the SARS-CoV-2-specific B cell repertoire consists of transcriptionally distinct B cell populations with cells producing potently neutralizing antibodies (nAbs) localized in two clusters that resemble memory and activated B cells. Cryo-electron microscopy structures of selected nAbs from these two clusters complexed with SARS-CoV-2 spike trimers show recognition of various receptor-binding domain (RBD) epitopes. One of these mAbs, BG10-19, locks the spike trimer in a closed conformation to potently neutralize SARS-CoV-2, the recently arising mutants B.1.1.7 and B.1.351, and SARS-CoV and cross-reacts with heterologous RBDs. Together, our results characterize transcriptional differences among SARS-CoV-2-specific B cells and uncover cross-neutralizing Ab targets that will inform immunogen and therapeutic design against coronaviruses.

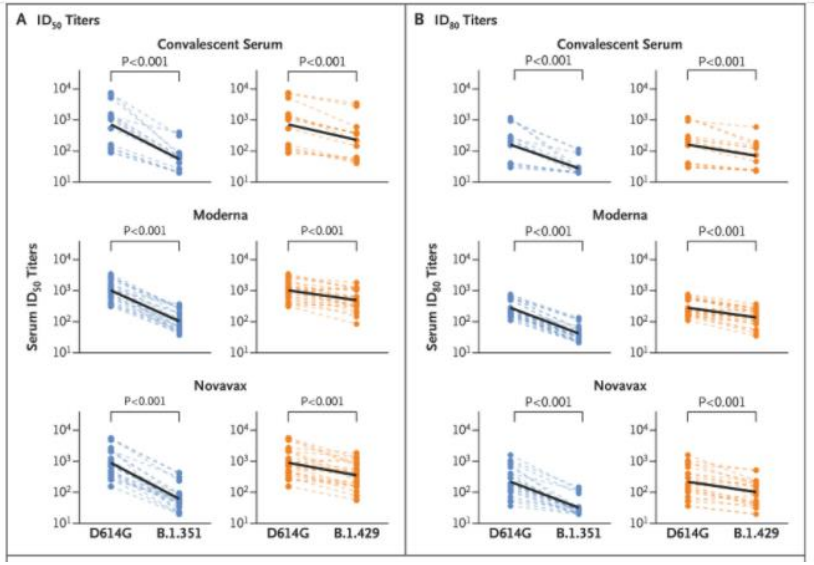
Xin H et al CID https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab501/6297425	The incubation period distribution of coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis	Revisione sistematica e metanalisi di studi che hanno stimato la durata del periodo di incubazione dell'infezione da SARS-CoV-2 : la durata media sarebbe di 6.3 giorni.	Incubation period is an important parameter to inform quarantine period and to study transmission dynamics of infectious diseases. We conducted a systematic review and meta-analysis on published estimates of the incubation period distribution of COVID-19, and showed that the pooled median of the point estimates of the mean, median and 95 th percentile for incubation period are 6.3 days (range: 1.8 to 11.9 days), 5.4 days (range: 2.0 to 17.9 days) and 13.1 days (range: 3.2 to 17.8 days) respectively. Estimates of the mean and 95 th percentile of the incubation period distribution were considerably shorter before the epidemic peak in China compared to after the peak, and variation was also noticed for different choices of methodological approach in estimation. Our findings implied that corrections may be needed before directly applying estimates of incubation period into control of or further studies on emerging infectious diseases.

			
Sheikh A et al The Lancet https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01358-1/fulltext	SARS-CoV-2 Delta VOC in Scotland: demographics, risk of hospital admission, and vaccine effectiveness	Studio osservazionale condotto in Scozia nel periodo aprile-giugno 2021, in cui si riporta la prevalenza della variante Delta (« indiana ») di SARS-CoV-2, il rischio di ospedalizzazione ad essa legato (maggiore che per la Alpha/inglese) e l'effetto della vaccinazione sulla diffusione del virus.	In summary, we show that the Delta VOC in Scotland was found mainly in younger, more affluent groups. Risk of COVID-19 hospital admission was approximately doubled in those with the Delta VOC when compared to the Alpha VOC, with risk of admission particularly increased in those with five or more relevant comorbidities. Both the Oxford–AstraZeneca and Pfizer–BioNTech COVID-19 vaccines were effective in reducing the risk of SARS-CoV-2 infection and COVID-19 hospitalisation in people with the Delta VOC, but these effects on infection appeared to be diminished when compared to those with the Alpha VOC. We had insufficient numbers of hospital admissions to compare between vaccines in

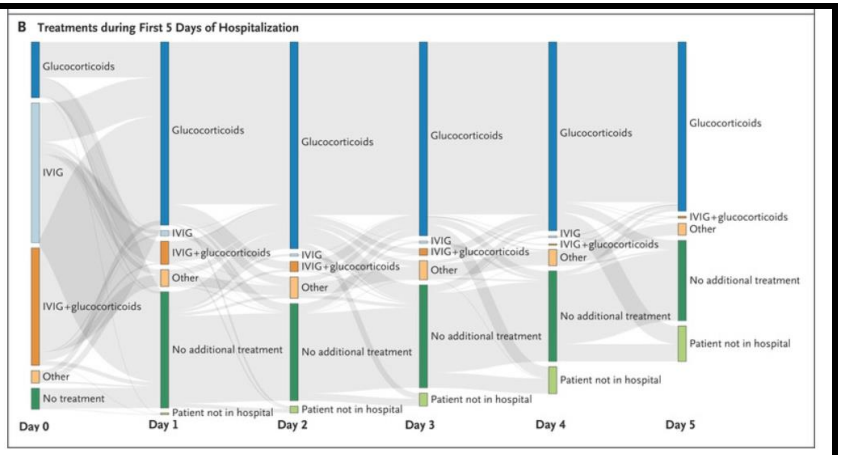
			this respect. The Oxford–AstraZeneca vaccine appeared less effective than the Pfizer–BioNTech vaccine in preventing SARS-CoV-2 infection in those with the Delta VOC. Given the observational nature of these data, estimates of vaccine effectiveness need to be interpreted with caution.
Nyberg T et al BMJ https://www.bmj.com/content/373/bmj.n1412	Risk of hospital admission for patients with SARS-CoV-2 variant B.1.1.7: cohort analysis	Rischio di ospedalizzazione per COVID-19 maggiore per chi è infettato con la variante Alpha VOC («inglese») rispetto al wild-type secondo questo studio retrospettivo svolto in Inghilterra.	Objective To evaluate the relation between diagnosis of covid-19 with SARS-CoV-2 variant B.1.1.7 (also known as variant of concern 202012/01) and the risk of hospital admission compared with diagnosis with wild-type SARS-CoV-2 variants. Design Retrospective cohort analysis. Setting Community based SARS-CoV-2 testing in England, individually linked with hospital admission data. Participants 839 278 patients with laboratory confirmed covid-19, of whom 36 233 had been admitted to hospital within 14 days, tested between 23 November 2020 and 31 January 2021 and analysed at a laboratory with an available TaqPath assay that enables assessment of S-gene target failure (SGTF), a proxy test for the B.1.1.7 variant. Patient data were stratified by age, sex, ethnicity, deprivation, region of residence, and date of positive test. Main outcome measures Hospital admission between one and 14 days after the first positive SARS-CoV-2 test. Results 27 710 (4.7%) of 592 409 patients with SGTF variants and 8523 (3.5%) of 246 869 patients without SGTF variants had been admitted to hospital within one to 14 days. The stratum adjusted hazard ratio of hospital admission was 1.52 (95% confidence interval 1.47 to 1.57) for patients with covid-19 infected with SGTF variants, compared with those infected with non-SGTF variants. The effect was modified by age (P<0.001), with hazard ratios of 0.93-1.21 in patients younger than 20 years with versus without SGTF variants, 1.29 in those aged 20-29, and 1.45-1.65 in those aged ≥30

			years. The adjusted absolute risk of hospital admission within 14 days was 4.7% (95% confidence interval 4.6% to 4.7%) for patients with SGTF variants and 3.5% (3.4% to 3.5%) for those with non-SGTF variants. Conclusions The results suggest that the risk of hospital admission is higher for people infected with the B.1.1.7 variant compared with wild-type SARS-CoV-2, likely reflecting a more severe disease. The higher severity may be specific to adults older than 30 years. 
Stravalaci M et al medRXiv	Recognition and inhibition of SARS-CoV-2 by humoral innate immunity pattern recognition molecules	Interazioni fra SARS-CoV-2 e le PRM (pattern recognition molecules) che costituiscono gli effettori di una risposta innata contro il virus e la cui variabilità contribuisce alla variabile	The humoral arm of innate immunity includes diverse molecules with antibody-like functions, some of which serve as disease severity biomarkers in COVID-19. The present study was designed to conduct a systematic investigation of the interaction of humoral fluid phase pattern recognition molecules (PRM) with SARS-CoV-2. Out of 10 PRM tested, the long pentraxin PTX3 and Mannose

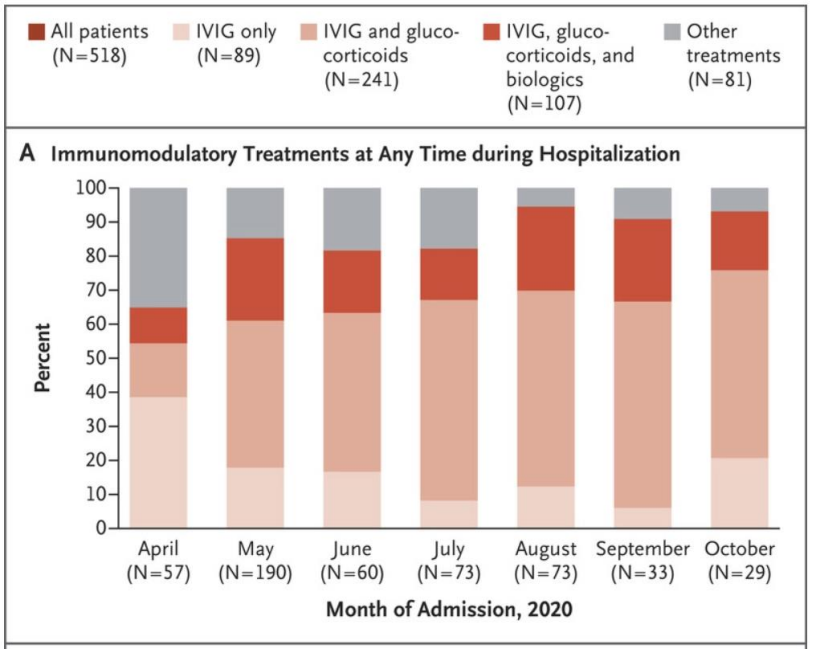
https://www.medrxiv.org/content/10.1101/2021.06.07.21258350v1		gravità di malattia fra individui.	Binding Lectin (MBL) bound the viral Nucleoprotein and Spike, respectively. MBL bound trimeric Spike, including that of variants of concern, in a glycan- dependent way and inhibited SARS-CoV-2 in three in vitro models. Moreover, upon binding to Spike, MBL activated the lectin pathway of complement activation. Genetic polymorphisms at the MBL locus were associated with disease severity. These results suggest that selected humoral fluid phase PRM can play an important role in resistance to, and pathogenesis of, COVID-19, a finding with translational implications.
Shen X et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMc2103740?query=featured_home	Neutralization of SARS-CoV-2 Variants B.1.429 and B.1.351	Attività neutralizzante del siero di convalescenti da COVID-19 o vaccinati con vaccini a mRNA contro le varianti « californiana » e « sudafricana ».	The neutralizing activity of all serum samples was tested against the B.1.429 variant and a variant of concern that first emerged in South Africa (B.1.351, also called 20H/501Y.V2). We compared this neutralizing activity to the activity the serum samples exhibited against the prototypical D614G variant. As compared with the D614G variant, we found that B.1.429 was approximately 2 to 3 times less sensitive to neutralization by convalescent serum and by serum samples obtained from vaccinated persons, whereas B.1.351 was approximately 9 to 14 times less sensitive to neutralization.

			
McArdle A et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2102968?query=featured_home	Treatment of Multisystem Inflammatory Syndrome in Children	Studio di coorte su 614 bambini con MIS-C da cui non emergono differenze di outcome in base al diverso trattamento con steroidi, immunoglobuline EV o entrambi.	BACKGROUND : Evidence is urgently needed to support treatment decisions for children with multisystem inflammatory syndrome (MIS-C) associated with severe acute respiratory syndrome coronavirus 2. METHODS : We performed an international observational cohort study of clinical and outcome data regarding suspected MIS-C that had been uploaded by physicians onto a Web-based database. We used inverse-probability weighting and generalized linear models to evaluate intravenous immune globulin (IVIG) as a reference, as compared with IVIG plus glucocorticoids and glucocorticoids alone. There were two primary outcomes: the first was a composite of inotropic support or mechanical ventilation by day 2 or later or death; the second was a reduction in disease severity on an ordinal scale by day 2. Secondary outcomes included treatment escalation and the time until a reduction in organ failure and inflammation.

			RESULTS : Data were available regarding the course of treatment for 614 children from 32 countries from June 2020 through February 2021; 490 met the World Health Organization criteria for MIS-C. Of the 614 children with suspected MIS-C, 246 received primary treatment with IVIG alone, 208 with IVIG plus glucocorticoids, and 99 with glucocorticoids alone; 22 children received other treatment combinations, including biologic agents, and 39 received no immunomodulatory therapy. Receipt of inotropic or ventilatory support or death occurred in 56 patients who received IVIG plus glucocorticoids (adjusted odds ratio for the comparison with IVIG alone, 0.77; 95% confidence interval [CI], 0.33 to 1.82) and in 17 patients who received glucocorticoids alone (adjusted odds ratio, 0.54; 95% CI, 0.22 to 1.33). The adjusted odds ratios for a reduction in disease severity were similar in the two groups, as compared with IVIG alone (0.90 for IVIG plus glucocorticoids and 0.93 for glucocorticoids alone). The time until a reduction in disease severity was similar in the three groups. CONCLUSIONS : We found no evidence that recovery from MIS-C differed after primary treatment with IVIG alone, IVIG plus glucocorticoids, or glucocorticoids alone, although significant differences may emerge as more data accrue.

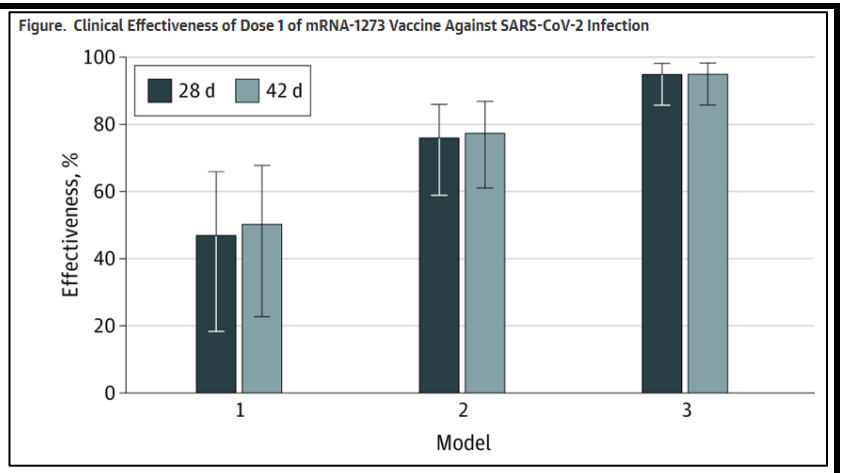
			
Son MBF et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2102605?query=featured_home	Multisystem Inflammatory Syndrome in Children — Initial Therapy and Outcomes	Revisione di un'ampia casistica di 514 bambini con sindrome infiammatoria multisistemica (MIS-C) in cui si osserva che la terapia con steroidi + immunoglobuline EV è associata a minore incidenza di danno cardiovascolare.	BACKGROUND : The assessment of real-world effectiveness of immunomodulatory medications for multisystem inflammatory syndrome in children (MIS-C) may guide therapy. METHODS : We analyzed surveillance data on inpatients younger than 21 years of age who had MIS-C and were admitted to 1 of 58 U.S. hospitals between March 15 and October 31, 2020. The effectiveness of initial immunomodulatory therapy (day 0, indicating the first day any such therapy for MIS-C was given) with intravenous immune globulin (IVIG) plus glucocorticoids, as compared with IVIG alone, was evaluated with propensity-score matching and inverse probability weighting, with adjustment for baseline MIS-C severity and demographic characteristics. The primary outcome was cardiovascular dysfunction (a composite of left ventricular dysfunction or shock resulting in the use of vasopressors) on or after day 2. Secondary outcomes included the components of the primary outcome, the receipt of adjunctive treatment (glucocorticoids in patients not already receiving glucocorticoids on day 0, a biologic, or a second dose of IVIG) on or after day 1, and persistent or recurrent fever on or after day 2.

			RESULTS : A total of 518 patients with MIS-C (median age, 8.7 years) received at least one immunomodulatory therapy; 75% had been previously healthy, and 9 died. In the propensity-score–matched analysis, initial treatment with IVIG plus glucocorticoids (103 patients) was associated with a lower risk of cardiovascular dysfunction on or after day 2 than IVIG alone (103 patients) (17% vs. 31%; risk ratio, 0.56; 95% confidence interval [CI], 0.34 to 0.94). The risks of the components of the composite outcome were also lower among those who received IVIG plus glucocorticoids: left ventricular dysfunction occurred in 8% and 17% of the patients, respectively (risk ratio, 0.46; 95% CI, 0.19 to 1.15), and shock resulting in vasopressor use in 13% and 24% (risk ratio, 0.54; 95% CI, 0.29 to 1.00). The use of adjunctive therapy was lower among patients who received IVIG plus glucocorticoids than among those who received IVIG alone (34% vs. 70%; risk ratio, 0.49; 95% CI, 0.36 to 0.65), but the risk of fever was unaffected (31% and 40%, respectively; risk ratio, 0.78; 95% CI, 0.53 to 1.13). The inverse-probability-weighted analysis confirmed the results of the propensity-score–matched analysis. CONCLUSIONS : Among children and adolescents with MIS-C, initial treatment with IVIG plus glucocorticoids was associated with a lower risk of new or persistent cardiovascular dysfunction than IVIG alone.

			
Guimaraes PO et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2101643?query=featured_home	Tofacitinib in Patients Hospitalized with Covid-19 Pneumonia	Trial clinico SU 289 pazienti ricoverati per polmonite da SARS-CoV-2 : la terapia con tofacitinib (anti JAK) è associata a minore insufficienza respiratoria e mortalità a 28 giorni rispetto al placebo, in aggiunta alla terapia standard.	BACKGROUND : The efficacy and safety of tofacitinib, a Janus kinase inhibitor, in patients who are hospitalized with coronavirus disease 2019 (Covid-19) pneumonia are unclear. METHODS : We randomly assigned, in a 1:1 ratio, hospitalized adults with Covid-19 pneumonia to receive either tofacitinib at a dose of 10 mg or placebo twice daily for up to 14 days or until hospital discharge. The primary outcome was the occurrence of death or respiratory failure through day 28 as assessed with the use of an eight-level ordinal scale (with scores ranging from 1 to 8 and higher scores indicating a worse condition). All-cause mortality and safety were also assessed. RESULTS : A total of 289 patients underwent randomization at 15 sites in Brazil. Overall, 89.3% of the patients received glucocorticoids during hospitalization. The cumulative incidence of

			death or respiratory failure through day 28 was 18.1% in the tofacitinib group and 29.0% in the placebo group (risk ratio, 0.63; 95% confidence interval [CI], 0.41 to 0.97; P=0.04). Death from any cause through day 28 occurred in 2.8% of the patients in the tofacitinib group and in 5.5% of those in the placebo group (hazard ratio, 0.49; 95% CI, 0.15 to 1.63). The proportional odds of having a worse score on the eight-level ordinal scale with tofacitinib, as compared with placebo, was 0.60 (95% CI, 0.36 to 1.00) at day 14 and 0.54 (95% CI, 0.27 to 1.06) at day 28. Serious adverse events occurred in 20 patients (14.1%) in the tofacitinib group and in 17 (12.0%) in the placebo group. CONCLUSIONS : Among patients hospitalized with Covid-19 pneumonia, tofacitinib led to a lower risk of death or respiratory failure through day 28 than placebo.
Shimabukuro TT et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2104983?query=featured_home	Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons	Revisione delle evidenze sull'utilizzo di vaccini a mRNA contro SARS-CoV-2 in gravidanza	BACKGROUND : Many pregnant persons in the United States are receiving messenger RNA (mRNA) coronavirus disease 2019 (Covid-19) vaccines, but data are limited on their safety in pregnancy. METHODS : From December 14, 2020, to February 28, 2021, we used data from the "v-safe after vaccination health checker" surveillance system, the v-safe pregnancy registry, and the Vaccine Adverse Event Reporting System (VAERS) to characterize the initial safety of mRNA Covid-19 vaccines in pregnant persons. RESULTS : A total of 35,691 v-safe participants 16 to 54 years of age identified as pregnant. Injection-site pain was reported more frequently among pregnant persons than among nonpregnant women, whereas headache, myalgia, chills, and fever were reported less frequently. Among 3958 participants enrolled in the v-safe pregnancy registry, 827 had a completed pregnancy, of which 115 (13.9%) resulted in a pregnancy loss and 712 (86.1%) resulted in a live birth (mostly among participants with vaccination in the third

			trimester). Adverse neonatal outcomes included preterm birth (in 9.4%) and small size for gestational age (in 3.2%); no neonatal deaths were reported. Although not directly comparable, calculated proportions of adverse pregnancy and neonatal outcomes in persons vaccinated against Covid-19 who had a completed pregnancy were similar to incidences reported in studies involving pregnant women that were conducted before the Covid-19 pandemic. Among 221 pregnancy-related adverse events reported to the VAERS, the most frequently reported event was spontaneous abortion (46 cases). CONCLUSIONS : Preliminary findings did not show obvious safety signals among pregnant persons who received mRNA Covid-19 vaccines. However, more longitudinal follow-up, including follow-up of large numbers of women vaccinated earlier in pregnancy, is necessary to inform maternal, pregnancy, and infant outcomes.
Gupta K et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2781173?resultClick=1	Incidence of SARS-CoV-2 Infection in Health Care Workers After a Single Dose of mRNA-1273 Vaccine	Il vaccino MODERNA contro SARS-CoV-2 riduce l'incidenza di infezioni da SARS-CoV-2 in questa coorte di operatori sanitari a partire da 8 giorni dopo la prima dose.	This study demonstrated an association between receipt of mRNA-1273 vaccine and a reduction in SARS-CoV-2 infection in HCWs beginning 8 days after dose 1. These real-world findings reflect vaccination solely with mRNA-1273 and are consistent with aggregated data for BNT162b2 and mRNA-1273 in HCWs.4-6 The first-dose risk reduction of 95% after day 14 highlights the potential for vaccination with mRNA-1273 to rapidly mitigate surges of vaccine-sensitive SARS-CoV-2 infection in HCWs.

			
Broman LM et al The Lancet https://www.thelancet.com/action/showPdf?pii=S2213-2600%2821%2900262-9	Extracorporeal membrane oxygenation for COVID-19 during first and second waves	Andamento di pazienti trattati con ECMO per COVID-19 durante la pandemia.	We analysed the continuous provision of ECMO for patients with COVID-19 during the first and second waves from the EuroECMO survey. Our results indicate that the clinical picture has changed during the second wave (between Sept 15, 2020, and March 8, 2021). Fatality and successful weaning curves approach each other, indicating an increase in mortality compared with weaning and survival (figure 1). An analysis of the deceased to weaned ratio during 2020 shows a significantly increasing trend over time (figure 2). During the spring and early summer of 2020, this ratio was less than 1—ie, the number of weaned (survivors from ECMO) was higher than the number of deceased. Currently, this ratio is more than 1, indicating worse outcome (p<0·006; median–median linear regression).

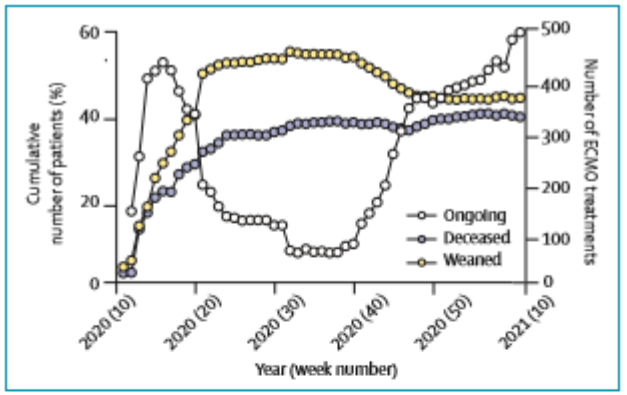


Figure 1: **Cumulative outcome of ECMO for COVID-19**
ECMO support from March 12, 2020, to March 8, 2021. First wave, defined from disease onset to Sept 14, 2020. Second wave defined from Sept 15, 2020, to March 8, 2021. ECMO=extracorporeal membrane oxygenation.

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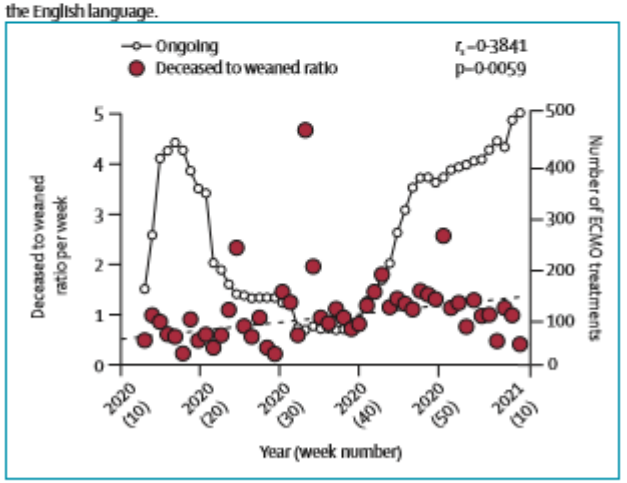
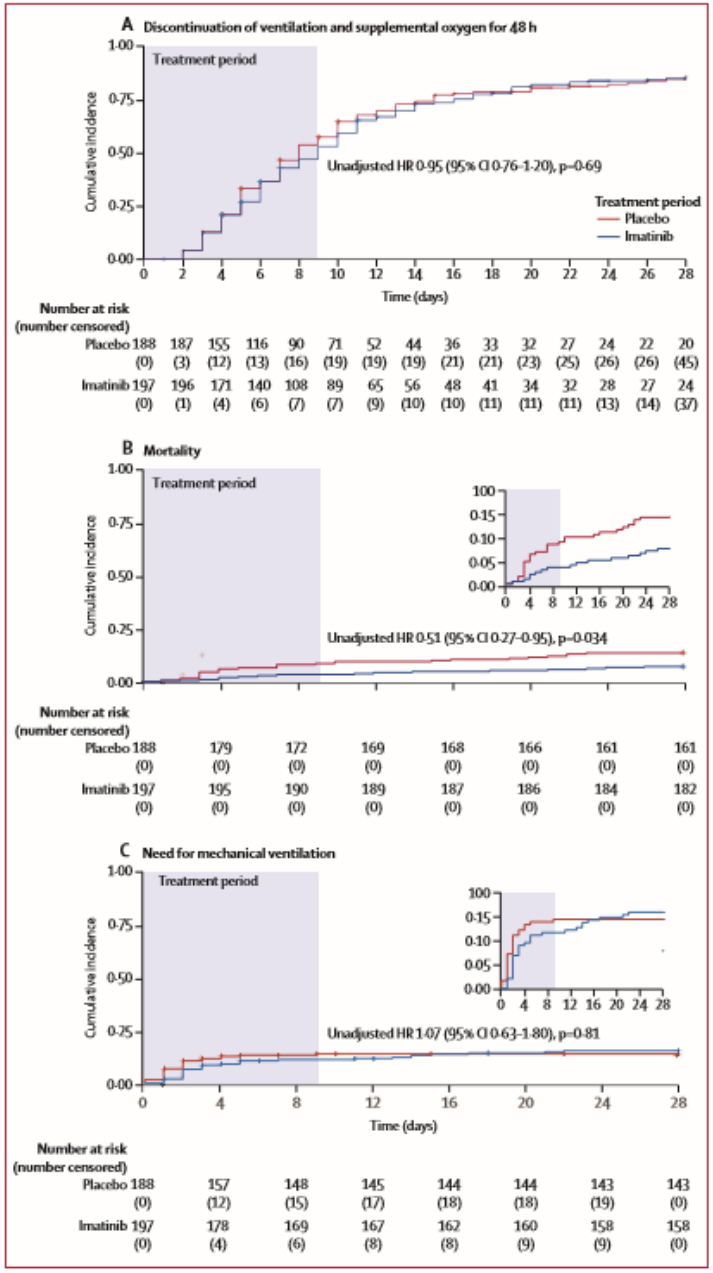


Figure 2: **Relationship between survivors and patients deceased from COVID-19 supported with ECMO**
Median–median linear regression (dashed line). First wave defined from disease onset to Sept 14, 2020. Second wave defined from Sept 15, 2020, to March 8, 2021. ECMO=extracorporeal membrane oxygenation.

Aman J et al The Lancet https://www.thelancet.com/action/showPdf?pii=S2213-2600%2821%2900237-X	Imatinib in patients with severe COVID-19: a randomised, double-blind, placebo-controlled, clinical trial	Trial clinico sulla terapia con imatinib/placebo in aggiunta alla terapia standard in cui non si dimostra un beneficio del farmaco nel ridurre il tempo allo svezzamento dalla ventilazione.	Background The major complication of COVID-19 is hypoxaemic respiratory failure from capillary leak and alveolar oedema. Experimental and early clinical data suggest that the tyrosine-kinase inhibitor imatinib reverses pulmonary capillary leak. Methods This randomised, double-blind, placebo-controlled, clinical trial was done at 13 academic and non-academic teaching hospitals in the Netherlands. Hospitalised patients (aged ≥18 years) with COVID-19, as confirmed by an RT-PCR test for SARS-CoV-2, requiring supplemental oxygen to maintain a peripheral oxygen saturation of greater than 94% were eligible. Patients were excluded if they had severe pre-existing pulmonary disease, had pre-existing heart failure, had undergone active treatment of a haematological or non-haematological malignancy in the previous 12 months, had cytopenia, or were receiving concomitant treatment with medication known to strongly interact with imatinib. Patients were randomly assigned (1:1) to receive either oral imatinib, given as a loading dose of 800 mg on day 0 followed by 400 mg daily on days 1–9, or placebo. Randomisation was done with a computer-based clinical data management platform with variable block sizes (containing two, four, or six patients), stratified by study site. The primary outcome was time to discontinuation of mechanical ventilation and supplemental oxygen for more than 48 consecutive hours, while being alive during a 28-day period. Secondary outcomes included safety, mortality at 28 days, and the need for invasive mechanical ventilation. All efficacy and safety analyses were done in all randomised patients who had received at least one dose of study medication (modified intention-to-treat population). This study is registered with the EU Clinical Trials Register (EudraCT 2020–001236–10).

			Findings Between March 31, 2020, and Jan 4, 2021, 805 patients were screened, of whom 400 were eligible and randomly assigned to the imatinib group (n=204) or the placebo group (n=196). A total of 385 (96%) patients (median age 64 years [IQR 56–73]) received at least one dose of study medication and were included in the modified intention-to-treat population. Time to discontinuation of ventilation and supplemental oxygen for more than 48 h was not significantly different between the two groups (unadjusted hazard ratio [HR] 0·95 [95% CI 0·76–1·20]). At day 28, 15 (8%) of 197 patients had died in the imatinib group compared with 27 (14%) of 188 patients in the placebo group (unadjusted HR 0·51 [0·27–0·95]). After adjusting for baseline imbalances between the two groups (sex, obesity, diabetes, and cardiovascular disease) the HR for mortality was 0·52 (95% CI 0·26–1·05). The HR for mechanical ventilation in the imatinib group compared with the placebo group was 1·07 (0·63–1·80; p=0·81). The median duration of invasive mechanical ventilation was 7 days (IQR 3–13) in the imatinib group compared with 12 days (6–20) in the placebo group (p=0·0080). 91 (46%) of 197 patients in the imatinib group and 82 (44%) of 188 patients in the placebo group had at least one grade 3 or higher adverse event. The safety evaluation revealed no imatinib-associated adverse events. Interpretation The study failed to meet its primary outcome, as imatinib did not reduce the time to discontinuation of ventilation and supplemental oxygen for more than 48 consecutive hours in patients with COVID-19 requiring supplemental oxygen. The observed effects on survival (although attenuated after adjustment for baseline imbalances) and duration of mechanical ventilation suggest that imatinib might confer clinical benefit in hospitalised

			patients with COVID-19, but further studies are required to validate these findings.


A Discontinuation of ventilation and supplemental oxygen for 48 h
Treatment period
Cumulative incidence
1·00
0·75
0·50
0·25
0·00
Unadjusted HR 0·95 (95% CI 0·76–1·20), p=0·69
Treatment period
Placebo
Imatinib
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28
Time (days)
Number at risk
(number censored)
Placebo 188 187 155 116 90 71 52 44 36 33 32 27 24 22 20
(0) (3) (12) (13) (16) (19) (19) (19) (21) (21) (23) (25) (26) (26) (45)
Imatinib 197 196 171 140 108 89 65 56 48 41 34 32 28 27 24
(0) (1) (4) (6) (7) (7) (9) (10) (10) (11) (11) (11) (13) (14) (37)
B Mortality
Treatment period
Cumulative incidence
1·00
0·75
0·50
0·25
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0 4 8 12 16 20 24 28
Unadjusted HR 0·51 (95% CI 0·27–0·95), p=0·034
Number at risk
(number censored)
Placebo 188 179 172 169 168 166 161 161
(0) (0) (0) (0) (0) (0) (0) (0)
Imatinib 197 195 190 189 187 186 184 182
(0) (0) (0) (0) (0) (0) (0) (0)
C Need for mechanical ventilation
Treatment period
Cumulative incidence
1·00
0·75
0·50
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0·00
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0·05
0 4 8 12 16 20 24 28
Unadjusted HR 1·07 (95% CI 0·63–1·80), p=0·81
0 4 8 12 16 20 24 28
Time (days)
Number at risk
(number censored)
Placebo 188 157 148 145 144 144 143 143
(0) (12) (15) (17) (18) (18) (19) (0)
Imatinib 197 178 169 167 162 160 158 158
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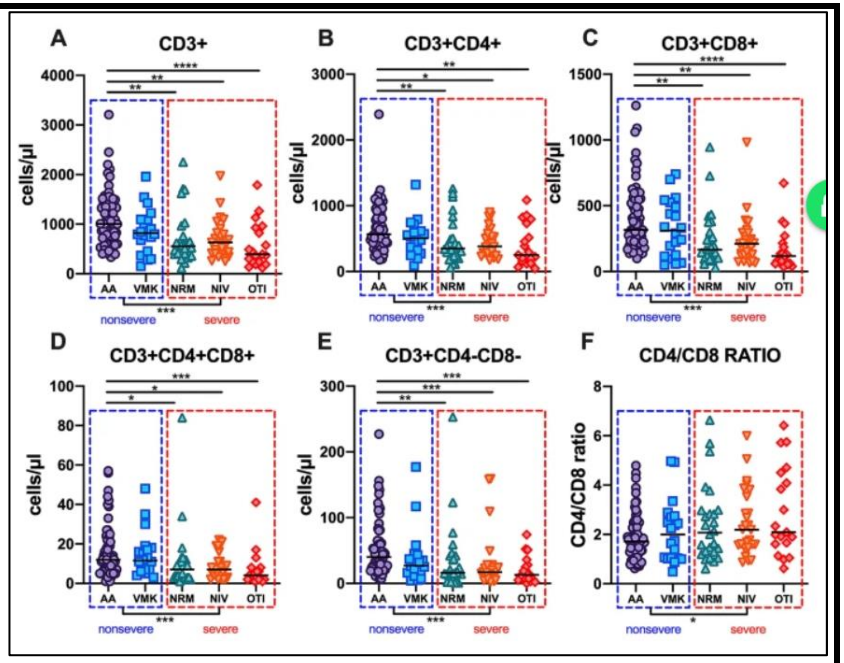
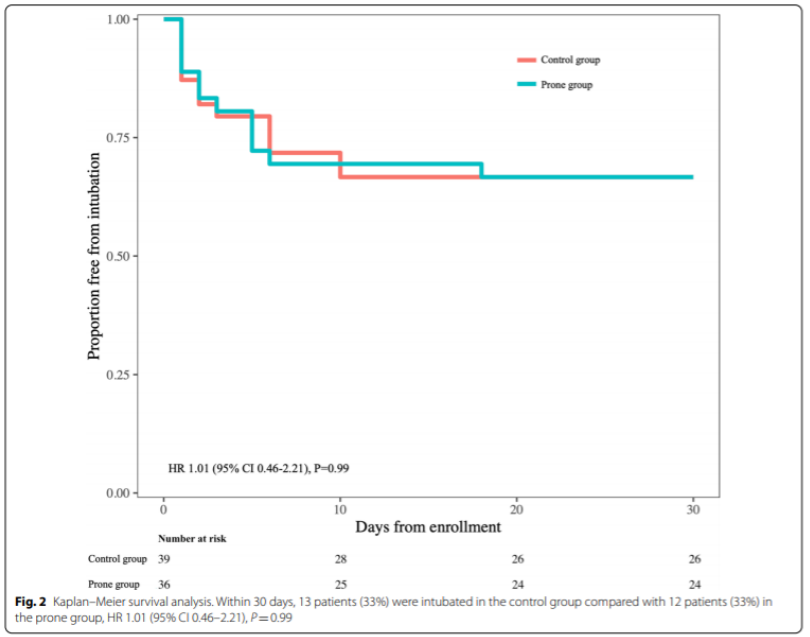
Demonbreun AR et al The Journal of Infectious Diseases https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiab314/6297423	COVID-19 mRNA vaccination generates greater IgG levels in women compared to men	Differenti livelli anticorpali contro SARS-CoV-2 fra uomini e donne in questa corte vaccinata con vaccini a mRNA.	Question : Is antibody response to COVID-19 mRNA vaccination similar in women and men? Findings : In a community cohort without prior COVID-19 infection, the first vaccine dose produced higher IgG levels and percent inhibition of spike-ACE2 receptor binding, a surrogate measure of virus neutralization, in women compared to men (7.0µg/ml; 51.6% vs 3.3µg/ml; 36.4%). After two doses, IgG levels remained significantly higher for women (30.4µg/ml) compared to men (20.6µg/ml), while percent inhibition was similar (98.4% vs 97.7%). Meaning: Sex-specific antibody response to mRNA vaccination informs future efforts to understand vaccine protection and side effects.
Agenzia Italiana del Farmaco https://www.aifa.gov.it/-/modifica-registro-anticorpi-monoclonali-covid-19-1	Modifica Registro - anticorpi monoclonali COVID-19	Modificate le indicazioni di utilizzo di anticorpi monoclonali contro COVID-19 : trattamento della malattia lieve-moderata negli adulti che non necessitano di ospedalizzazione di età superiore a 65 anni, indipendentemente dalla presenza di altri fattori di rischio.	Si informano gli utenti dei Registri Farmaci sottoposti a Monitoraggio che, a seguito della pubblicazione delle Determine AIFA nella GU n.142 del 16.06.2021, a partire dal 17.06.2021 è possibile utilizzare i medicinali bamlanivimab e etesevimab-(Eli-Lilly), casirivimab e imdevimab-(Regeneron®/Roche), in regime di rimborsabilità SSN, per la seguente indicazione terapeutica: Trattamento della malattia da coronavirus 2019 (COVID-19) lieve o moderata, negli adulti e adolescenti di età pari o superiore a 12 anni non ospedalizzati per COVID-19, che non necessitano di ossigenoterapia supplementare per COVID-19 e che sono ad alto rischio di progressione a COVID-19 severa. Il Registro è stato modificato, rispetto alla iniziale versione, modificando l'elenco dei "fattori di rischio", anche in relazione al fattore rappresentato dall'età del paziente, e consentirà il trattamento di ogni paziente con 65 anni o più, indipendentemente dalla presenza di altri fattori di rischio.

Iannetta M et al Scientific Reports https://www.nature.com/articles/s41598-021-90983-0	Baseline T-lymphocyte subset absolute counts can predict both outcome and severity in SARS-CoV-2 infected patients: a single center study	Conta dei linfociti T associata all'outcome in questa casistica di 160 pazienti ricoverati per COVID-19.	The aim of this study was to evaluate the role of baseline lymphocyte subset counts in predicting the outcome and severity of COVID-19 patients. Hospitalized patients confirmed to be infected with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) were included and classified according to in-hospital mortality (survivors/nonsurvivors) and the maximal oxygen support/ventilation supply required (nonsevere/severe). Demographics, clinical and laboratory data, and peripheral blood lymphocyte subsets were retrospectively analyzed. Overall, 160 patients were retrospectively included in the study. T-lymphocyte subset (total CD3+, CD3+ CD4+, CD3+ CD8+, CD3+ CD4+ CD8+ double positive [DP] and CD3+ CD4− CD8− double negative [DN]) absolute counts were decreased in nonsurvivors and in patients with severe disease compared to survivors and nonsevere patients ($p < 0.001$). Multivariable logistic regression analysis showed that absolute counts of CD3+ T-lymphocytes < 524 cells/µl, CD3+ CD4+ < 369 cells/µl, and the number of T-lymphocyte subsets below the cutoff (T-lymphocyte subset index [TLSI]) were independent predictors of in-hospital mortality. Baseline T-lymphocyte subset counts and TLSI were also predictive of disease severity (CD3+ < 733 cells/µl; CD3+ CD4+ < 426 cells/µl; CD3+ CD8+ < 262 cells/µl; CD3+ DP < 4.5 cells/µl; CD3+ DN < 18.5 cells/µl). The evaluation of peripheral T-lymphocyte absolute counts in the early stages of COVID-19 might represent a useful tool for identifying patients at increased risk of unfavorable outcomes.

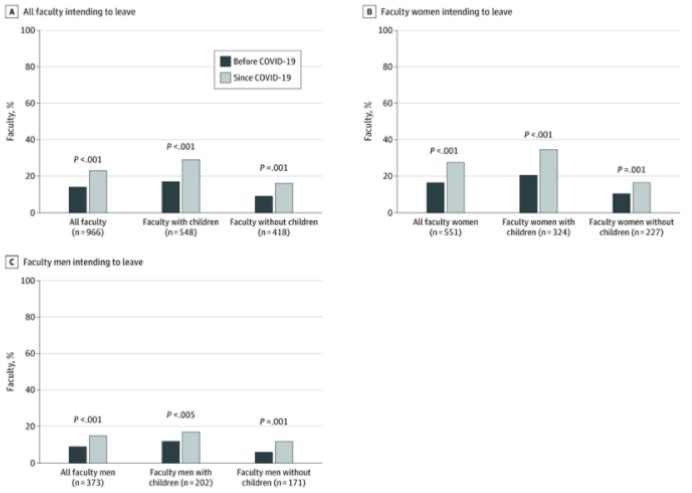
			
Campbell F et al Eurosurveillance https://doi.org/10.2807/1560-7917.ES.2021.26.24.2100509	Increased transmissibility and global spread of SARS-CoV-2 variants of concern as at June 2021.	Numeri di riproduzione di base delle varianti conosciute di SARS-CoV-2 che fanno pensare a un vantaggio futuro della « indiana »/delta sulle altre.	We present a global analysis of the spread of recently emerged SARS-CoV-2 variants and estimate changes in effective reproduction numbers at country-specific level using sequence data from GISAID. Nearly all investigated countries demonstrated rapid replacement of previously circulating lineages by the World Health Organization-designated variants of concern, with estimated transmissibility increases of 29% (95% CI: 24–33), 25% (95% CI: 20–30), 38% (95% CI: 29–48) and 97% (95% CI: 76–117), respectively, for B.1.1.7, B.1.351, P.1 and B.1.617.2.
Garcia-Ruiz I et al CMI	Congenital infection of SARS-CoV-2 in live-born neonates: a population-based descriptive study	Studio osservazonale su 45 casi di infezione congenita da SARS-CoV-2 (44 madri, una gravidanza gemellare) con studio degli annessi embrionari.	Objective : This study aimed to evaluate the evidence of mother-to-child transmission of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Methods : This is a descriptive, multicenter, observational study in nine tertiary care hospitals throughout Spain. The study population

https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00336-0/fulltext			was women with COVID-19 during pregnancy. Mother-to-child transmission was defined as positive real-time reverse-transcriptase-polymerase-chain-reaction (RT-PCR) of SARS-CoV-2 in amniotic fluid, cord blood, placenta or neonatal nasopharyngeal swabs taken immediately after birth. Results : We included 43 singleton pregnant women and one twin pregnancy, thus we obtained 45 samples of placenta, amniotic fluid and umbilical cord blood. The median gestational age at diagnosis was 34.7 weeks (range 14 to 41.3). The median interval between positive RT-PCR and delivery was 21.5 days (range 0 to 141 days). Fourteen women (31.8%, 95%CI 18.6-47.6%) were positive at the time of delivery. There was one singleton pregnancy with SARS-CoV-2 RT-PCR positive in the placenta, amniotic fluid and umbilical cord blood (2.2%, 95%CI 0.1-11.8%). Nasopharyngeal aspiration was performed on 38 neonates at birth, all of which were negative (0%, 95%CI 0-9.3%). In 11 neonates the nasopharyngeal aspiration was repeated at 24-48 hours, and one returned positive (9.1%, 95%CI 0.2-41.3%). Conclusions : The presence of the SARS-CoV-2 in placenta, amniotic fluid and cord blood shows that mother-to-child transmission is possible but uncommon.
Rosen J et al Critical Care https://ccforum.biomedcentral.com/articles/10.1186/s13054-021-03602-9	Awake prone positioning in patients with hypoxemic respiratory failure due to COVID-19: the PROFLO multicenter randomized clinical trial	Nessun vantaggio nella pronazione da svegli nei pazienti con insufficienza respiratoria per COVID-19 rispetto alla necessità di ventilazione meccanica in questo trial su 75 pazienti.	Background : The effect of awake prone positioning on intubation rates is not established. The aim of this trial was to investigate if a protocol for awake prone positioning reduces the rate of endotracheal intubation compared with standard care among patients with moderate to severe hypoxemic respiratory failure due to COVID-19. Methods : We conducted a multicenter randomized clinical trial. Adult patients with confirmed COVID-19, high-flow nasal oxygen or noninvasive ventilation for respiratory support and a PaO2/FiO2

			ratio ≤ 20 kPa were randomly assigned to a protocol targeting 16 h prone positioning per day or standard care. The primary endpoint was intubation within 30 days. Secondary endpoints included duration of awake prone positioning, 30-day mortality, ventilator-free days, hospital and intensive care unit length of stay, use of noninvasive ventilation, organ support and adverse events. The trial was terminated early due to futility. Results : Of 141 patients assessed for eligibility, 75 were randomized of whom 39 were allocated to the control group and 36 to the prone group. Within 30 days after enrollment, 13 patients (33%) were intubated in the control group versus 12 patients (33%) in the prone group (HR 1.01 (95% CI 0.46–2.21), P = 0.99). Median prone duration was 3.4 h [IQR 1.8–8.4] in the control group compared with 9.0 h per day [IQR 4.4–10.6] in the prone group (P = 0.014). Nine patients (23%) in the control group had pressure sores compared with two patients (6%) in the prone group (difference − 18% (95% CI − 2 to − 33%); P = 0.032). There were no other differences in secondary outcomes between groups. Conclusions : The implemented protocol for awake prone positioning increased duration of prone positioning, but did not reduce the rate of intubation in patients with hypoxemic respiratory failure due to COVID-19 compared to standard care.

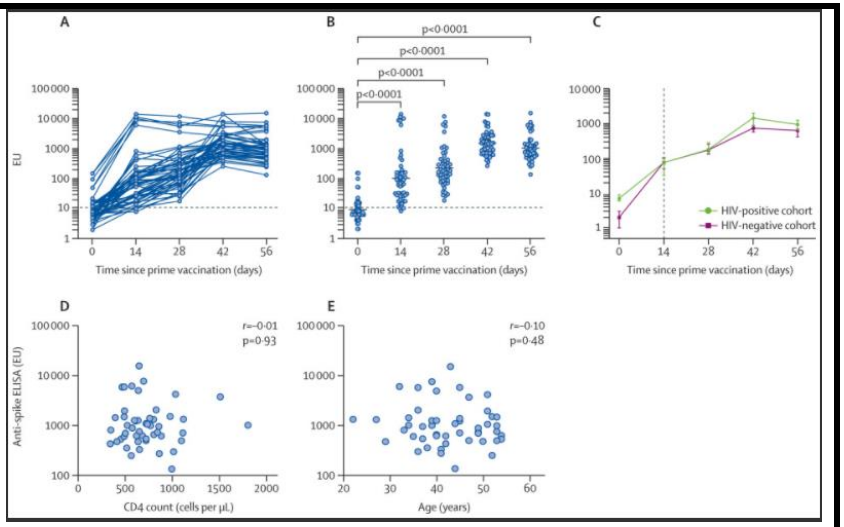
			 **Fig. 2** Kaplan–Meier survival analysis. Within 30 days, 13 patients (33%) were intubated in the control group compared with 12 patients (33%) in the prone group, HR 1.01 (95% CI 0.46–2.21), $P = 0.99$
Walter K et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2781358	Lung Transplants for COVID-19—The Option of Last Resort	Commento sull'impiego di trapianto di polmone nel trattamento della polmonite di gravità estrema da COVID-19.	After many weeks on a ventilator in the intensive care unit (ICU) at Chicago's Northwestern Memorial Hospital, 28-year-old Mayra Ramirez was critically ill with COVID-19. A paralegal who had enjoyed running 5K races, her lungs were now ravaged. She developed severe acute respiratory distress syndrome (ARDS) and required extracorporeal membrane oxygenation (ECMO)—a respite for her lungs that provided oxygen by continuously pumping her blood through an artificial lung machine. She had sepsis and her kidneys and liver were beginning to fail.
Matulevicious SA et al JAMA	Academic Medicine Faculty Perceptions of Work-Life Balance Before and Since the COVID-19 Pandemic	Effetto della pandemia di COVID-19 sulla percezione dello stress legato al lavoro e sui progetti futuri di 1186 accademici in ambito medico : le donne	Importance How the COVID-19 pandemic has affected academic medicine faculty's work-life balance is unknown. Objective To assess the association of perceived work-life conflict with academic medicine faculty intention to leave, reducing

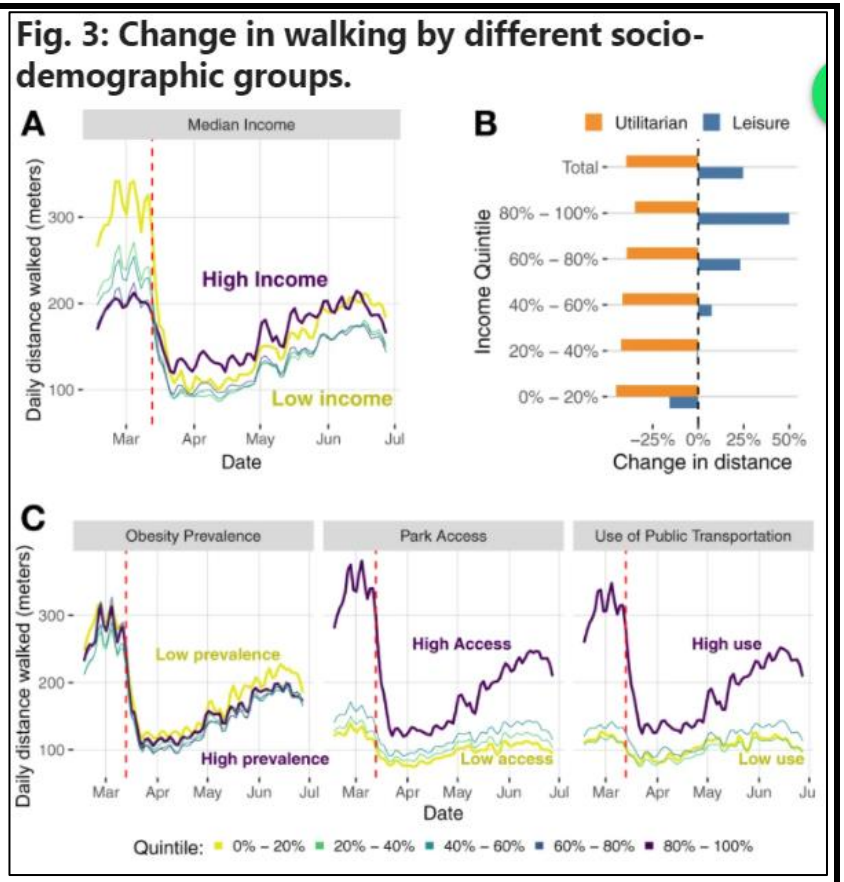
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2780956		progettano in numero maggiore, rispetto a prima della pandemia, di abbandonare l'attività accademica per incompatibilità con la vita personale.	employment to part time, or declining leadership opportunities before and since the COVID-19 pandemic. Design, Settings, and Participants An anonymous online survey of medical, graduate, and health professions school faculty was conducted at a single large, urban academic medical center between September 1 and September 25, 2020. Main Outcomes and Measures Self-assessed intention to leave, reducing employment to part time, or turning down leadership opportunities because of work-life conflict before and since the COVID-19 pandemic. Results Of the 1186 of 3088 (38%) of faculty members who answered the survey, 649 (55%) were women and 682 (58%) were White individuals. Respondents were representative of the overall faculty demographic characteristics except for an overrepresentation of female faculty respondents and underrepresentation of Asian faculty respondents compared with all faculty (female faculty: 649 [55%] vs 1368 [44%]; Asian faculty: 259 [22%] vs 963 [31%]). After the start of the COVID-19 pandemic, faculty were more likely to consider leaving or reducing employment to part time compared with before the pandemic (leaving: 225 [23%] vs 133 [14%]; P < .001; reduce hours: 281 [29%] vs 206 [22%]; P < .001). Women were more likely than men to reduce employment to part time before the COVID-19 pandemic (153 [28%] vs 44 [12%]; P < .001) and to consider both leaving or reducing employment to part time since the COVID-19 pandemic (leaving: 154 [28%] vs 56 [15%]; P < .001; reduce employment: 215 [40%] vs 49 [13%]; P < .001). Faculty with children were more likely to consider leaving and reducing employment since the COVID-19 pandemic compared with before the pandemic (leaving: 159 [29%] vs 93 [17%]; P < .001; reduce employment: 213 [40%] vs 130 [24%];

			P < .001). Women with children compared with women without children were also more likely to consider leaving since the COVID-19 pandemic than before (113 [35%] vs 39 [17%]; P < .001). Working parent faculty and women were more likely to decline leadership opportunities both before (faculty with children vs without children: 297 [32%] vs 84 [9%]; P < .001; women vs men: 206 [29%] vs 47 [13%]; P < .001) and since the COVID-19 pandemic (faculty with children vs faculty without children: 316 [34%] vs 93 [10 %]; P < .001; women vs men: 148 [28%] vs 51 [14%]; P < .001). Conclusions and Relevance In this survey study, the perceived stressors associated with work-life integration were higher in women than men, were highest in women with children, and have been exacerbated by the COVID-19 pandemic. The association of both gender and parenting with increased perceived work-life stress may disproportionately decrease the long-term retention and promotion of junior and midcareer women faculty. **Figure 1. Intent to Leave the University of Texas Southwestern Before and Since COVID-19** 

Frater J et al The Lancet https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(21)00103-X/fulltext	Safety and immunogenicity of the ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 in HIV infection: a single-arm substudy of a phase 2/3 clinical trial	Sotto-studio clinico di fase 2/3 che ha arruolato 54 adulti con infezione da HIV in terapia, con viremia non rilevabile e conta dei CD4+ superiore a 350 ; i pazienti sono stati sottoposti a vaccino Vaxzevria/Astrazeneca contro SARS-CoV, con risultati di sicurezza e immunogenicità positivi.	Background : Data on vaccine immunogenicity against SARS-CoV-2 are needed for the 40 million people globally living with HIV who might have less functional immunity and more associated comorbidities than the general population. We aimed to explore safety and immunogenicity of the ChAdOx1 nCoV-19 (AZD1222) vaccine in people with HIV. Methods : In this single-arm open-label vaccination substudy within the protocol of the larger phase 2/3 trial COV002, adults aged 18–55 years with HIV were enrolled at two HIV clinics in London, UK. Eligible participants were required to be on antiretroviral therapy (ART), with undetectable plasma HIV viral loads (<50 copies per mL), and CD4 counts of more than 350 cells per µL. A prime-boost regimen of ChAdOx1 nCoV-19, with two doses was given 4–6 weeks apart. The primary outcomes for this substudy were safety and reactogenicity of the vaccine, as determined by serious adverse events and solicited local and systemic reactions. Humoral responses were measured by anti-spike IgG ELISA and antibody-mediated live virus neutralisation. Cell-mediated immune responses were measured by ex-vivo IFN-γ enzyme-linked immunospot assay (ELISpot) and T-cell proliferation. All outcomes were compared with an HIV-uninfected group from the main COV002 study within the same age group and dosing strategy and are reported until day 56 after prime vaccination. Outcomes were analysed in all participants who received both doses and with available samples. The COV002 study is registered with ClinicalTrials.gov, NCT04400838, and is ongoing. Findings : Between Nov 5 and Nov 24, 2020, 54 participants with HIV (all male, median age 42·5 years [IQR 37·2–49·8]) were enrolled and received two doses of ChAdOx1 nCoV-19. Median CD4 count at enrolment was 694·0 cells per µL (IQR 573·5–859·5). No serious

			adverse events occurred. Local and systemic reactions occurring during the first 7 days after prime vaccination included pain at the injection site (26 [49%] of 53 participants with available data), fatigue (25 [47%]), headache (25 [47%]), malaise (18 [34%]), chills (12 [23%]), muscle ache (19 [36%]), joint pain (five [9%]), and nausea (four [8%]), the frequencies of which were similar to the HIV-negative participants. Anti-spike IgG responses by ELISA peaked at day 42 (median 1440 ELISA units [EUs; IQR 704–2728]; n=50) and were sustained until day 56 (median 941 EUs [531–1445]; n=49). We found no correlation between the magnitude of the anti-spike IgG response at day 56 and CD4 cell count (p=0·93) or age (p=0·48). ELISpot and T-cell proliferative responses peaked at day 14 and 28 after prime dose and were sustained to day 56. Compared with participants without HIV, we found no difference in magnitude or persistence of SARS-CoV-2 spike-specific humoral or cellular responses (p>0·05 for all analyses). Interpretation : In this study of people with HIV, ChAdOx1 nCoV-19 was safe and immunogenic, supporting vaccination for those well controlled on ART.

			
Hunter RF et al Nature https://www.nature.com/articles/s41467-021-23937-9	Effect of COVID-19 response policies on walking behavior in US cities	Le « camminate » durante il lock down – non dovendo recarsi fisicamente a lavoro – sarebbero state appannaggio di persone appartenenti a classi ad alto reddito in questo studio condotto su 10 aree metropolitane degli USA ; chi camminava poco e utilizzava i mezzi pubblici per lavorare già prima della pandemia, nelle classi a più basso reddito, non ha potuto cambiare abitudini.	The COVID-19 pandemic is causing mass disruption to our daily lives. We integrate mobility data from mobile devices and area-level data to study the walking patterns of 1.62 million anonymous users in 10 metropolitan areas in the United States. The data covers the period from mid-February 2020 (pre-lockdown) to late June 2020 (easing of lockdown restrictions). We detect when users were walking, distance walked and time of the walk, and classify each walk as recreational or utilitarian. Our results reveal dramatic declines in walking, particularly utilitarian walking, while recreational walking has recovered and even surpassed pre-pandemic levels. Our findings also demonstrate important social patterns, widening existing inequalities in walking behavior. COVID-19 response measures have a larger impact on walking behavior for those from low-income areas and high use of public transportation. Provision of equal opportunities to support walking is key to opening up our society and economy.

			
Jawad NK et al The Lancet https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00925-9/fulltext	Refugee access to COVID-19 vaccines in Lebanon	Discussione sull'accessibilità alle cure e in particolare ai vaccini per COVID-19 in un Paese che ospita un énorme numero di rifugiati come il Libano.	In Lebanon, refugees make up approximately 30% of the population. Refugees live in high-density camps with scarce access to clean water, sanitation, and hygiene services, which leaves these individuals highly vulnerable during an infectious disease outbreak. According to the non-profit organisation Anera, public health interventions have been scarce across refugee camps since the beginning of the COVID-19 pandemic. Consequently, COVID-19 deaths were elevated among Syrian and Palestinian refugees in

			Lebanon, with a fatality rate that is four times and three times the national average, respectively.