RICERCA BIBLIOGRAFICA COVID 19

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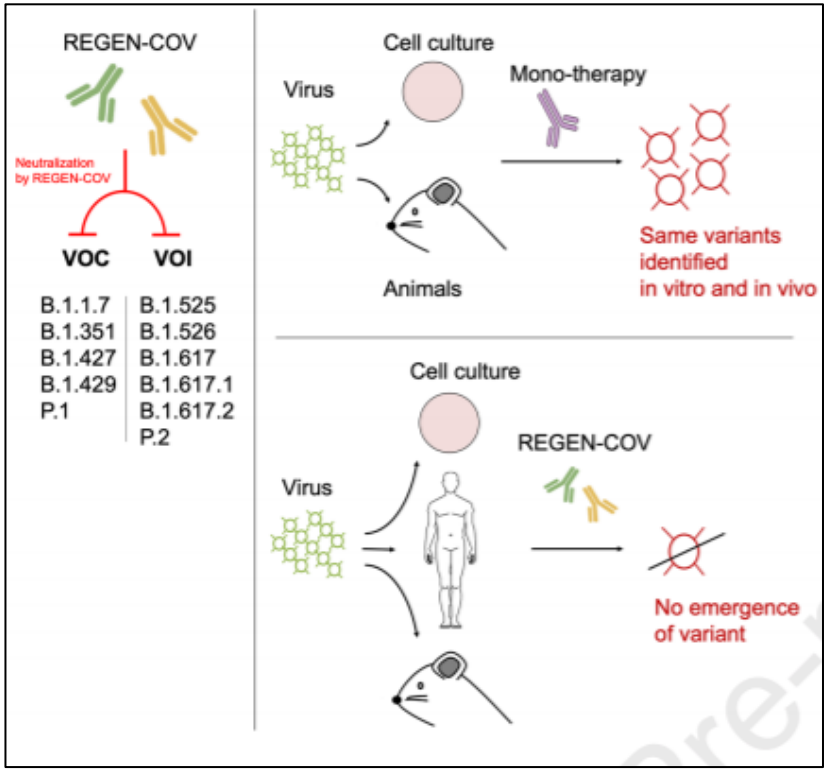
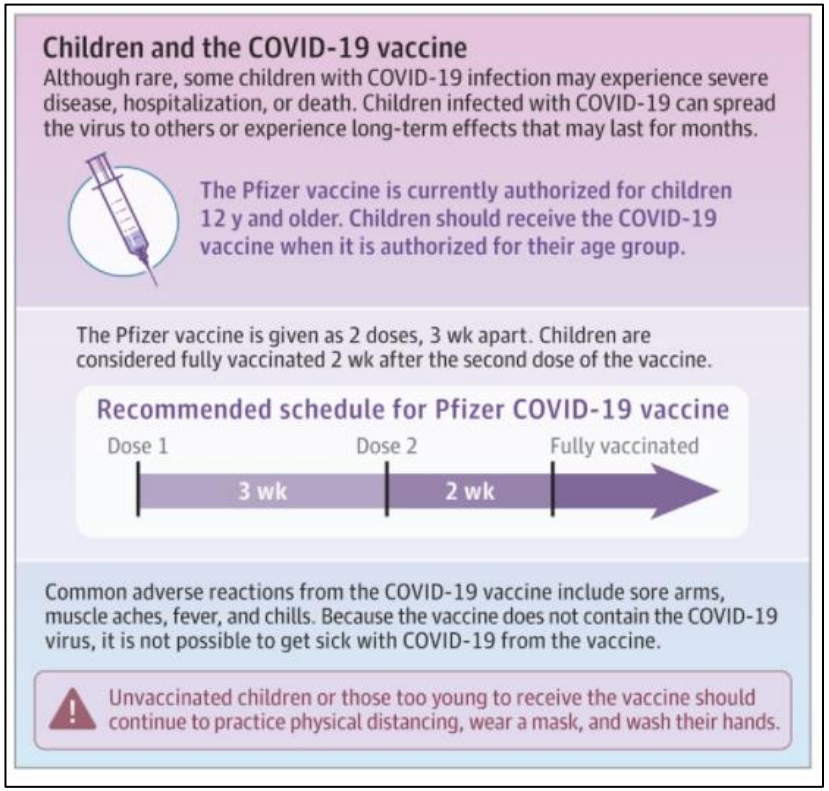
AUTORE/RIVISTA	TITOLO	OUTCOME PRINCIPALE	ABSTRACT
Copin R et al Cell https://www.cell.com/cell/fulltext/S0092-8674(21)00703-0	The monoclonal antibody combination REGEN-COV protects against SARS-CoV-2 mutational escape in preclinical and human studies	Casirivimab + imdevimab, due antiorpi monoclonali diretti contro la proteina S di SARS-CoV-2 e utilizzati nella terapia di COVID-19 sono attivi contro tutte le varianti note e se utilizzati in combinazione non favoriscono l'emergere di nuove varianti nell'umo e nell'animale da laboratorio.	Monoclonal antibodies against SARS-CoV-2 are a clinically validated therapeutic option against COVID-19. As rapidly emerging virus mutants are becoming the next major concern in the fight against the global pandemic, it is imperative that these therapeutic treatments provide coverage against circulating variants and do not contribute to development of treatment-induced emergent resistance. To this end, we investigated the sequence diversity of the spike protein and monitored emergence of virus variants in SARS-COV-2 isolates found in COVID-19 patients treated with the two-antibody combination REGEN-COV, as well as in preclinical in vitro studies using single, dual, or triple antibody combinations, and in hamster in vivo studies using REGEN-COV or single monoclonal antibody treatments. Our study demonstrates that the combination of non-competing antibodies in REGEN-COV provides protection against all current SARS-CoV-2 variants of concern/interest and also

			protects against emergence of new variants and their potential seeding into the population in a clinical setting. 
Lim ZJ et al Critical Care Medicine https://journals.lww.com/ccmjournal/Fulltext/2021/06000/A_Systematic_Re	A Systematic Review of the Incidence and Outcomes of In-Hospital Cardiac Arrests in Patients With Coronavirus Disease 2019	Revisione sistematica e metanalisi di studi riguardanti la sopravvivenza all'arresto cardiaco intraospedaliero di pazienti ricoverati o meno in terapia intensiva per COVID-19 : la sopravvivenza in terapia intensiva è maggiore e	OBJECTIVES: To investigate the incidence, characteristics, and outcomes of in-hospital cardiac arrest in patients with coronavirus disease 2019 and to describe the characteristics and outcomes for patients with in-hospital cardiac arrest within the ICU, compared with non-ICU patients with in-hospital cardiac arrest. Finally, we evaluated outcomes stratified by age. DATA SOURCES: A systematic review of PubMed, EMBASE, and preprint websites was conducted between January 1, 2020, and

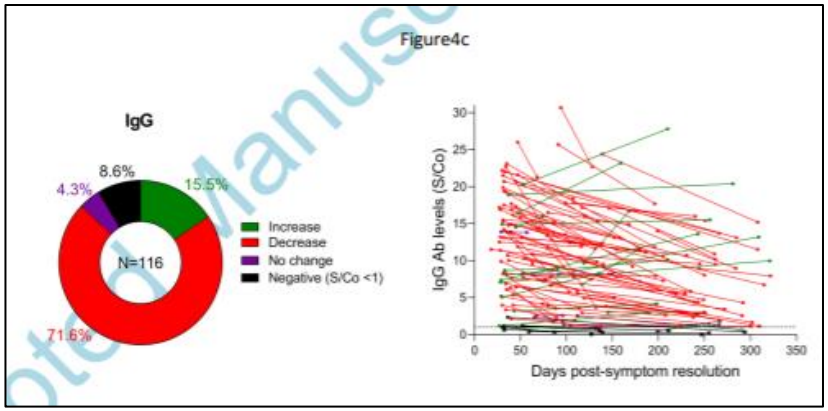
view_of_the_Incidence_and_Outcomes.3.aspx		comparabile ai dati pre-pandemia.	December 10, 2020. Prospective Register of Systematic Reviews identification: CRD42020203369. STUDY SELECTION: Studies reporting on consecutive in-hospital cardiac arrest with a resuscitation attempt among patients with coronavirus disease 2019. DATA EXTRACTION: Two authors independently performed study selection and data extraction. Study quality was assessed with the Newcastle-Ottawa Scale. Data were synthesized according to the Preferred Reporting Items for Systematic Reviews guidelines. Discrepancies were resolved by consensus or through an independent third reviewer. DATA SYNTHESIS: Eight studies reporting on 847 in-hospital cardiac arrest were included. In-hospital cardiac arrest incidence varied between 1.5% and 5.8% among hospitalized patients and 8.0–11.4% among patients in ICU. In-hospital cardiac arrest occurred more commonly in older male patients. Most initial rhythms were nonshockable (83.9%, [asystole = 36.4% and pulseless electrical activity = 47.6%]). Return of spontaneous circulation occurred in 33.3%, with a 91.7% in-hospital mortality. In-hospital cardiac arrest events in ICU had higher incidence of return of spontaneous circulation (36.6% vs 18.7%; $p < 0.001$) and relatively lower mortality (88.7% vs 98.1%; $p < 0.001$) compared with in-hospital cardiac arrest in non-ICU locations. Patients greater than or equal to 60 years old had significantly higher in-hospital mortality than those less than 60 years (93.1% vs 87.9%; $p = 0.019$). CONCLUSIONS: Approximately, one in 20 patients hospitalized with coronavirus disease 2019 received resuscitation for an in-hospital cardiac arrest. Hospital survival after in-hospital cardiac arrest within the ICU was higher than non-ICU locations and seems comparable with prepandemic survival for nonshockable rhythms.

			Although the data provide guidance surrounding prognosis after in-hospital cardiac arrest, it should be interpreted cautiously given the paucity of information surrounding treatment limitations and resource constraints during the pandemic. Further research is into actual causative mechanisms is needed.
Sprung C et al Critical Care Medicine https://journals.lww.com/ccmjournal/Fulltext/2021/06000/Reassessing_Cardiopulmonary_Resuscitation_in.11.aspx	Reassessing Cardiopulmonary Resuscitation in Hospitalized Patients With Coronavirus Disease 2019	Commento all'articolo precedente, in cui si riflette sulle indicazioni alla rianimazione cardiopolmonare (nata per pazienti con aritmie cardiache improvvise) in generale e non solo durante la pandemia di COVID-19.	The coronavirus disease 2019 (COVID-19) pandemic has caused morbidity, mortality, and an economic crisis worldwide. Necessity has required adjustments in the provision of medical care including, for the first-time in developed countries, triaging of scarce resources and considerable increased use of telemedicine as examples. Changes in procedures due to the pandemic offer an opportunity to reevaluate policies that may not be the most medically beneficial or efficient even under normal circumstances. Although cardiopulmonary resuscitation (CPR) was developed for sudden cardiac arrhythmias leading to cardiac arrest (patients too healthy to die rather than those too sick to keep living), CPR is typically performed on most dying hospitalized patients who do not have a "do-not-resuscitate" order.
Rubin R et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2780872	Could Statins Do More Than Lower Cholesterol in Patients With COVID-19?	Stato delle conoscenze in merito all'azione delle statine sul decorso di COVID-19.	Preclinical studies indicate that statins could worsen COVID-19 or at least increase the chances of infection, Italian researchers pointed out in a recent JAMA Internal Medicine article. That's because statins, along with several other classes of drugs used to treat atherosclerotic heart disease and its risk factors, upregulate angiotensin-converting enzyme 2 (ACE2) receptors, which happen to be SARS-CoV-2's gateway into cells. Yet theoretically, the authors noted, the same drugs may improve the clinical course of COVID-19 by reducing vasoconstriction, inflammation, and oxidation.

Thompson LA et al JAMA https://jamanetwork.com/journals/jamapediatrics/fullarticle/2780948	Children and COVID-19 Vaccines	Vaccinazione contro infezione da SARS-CoV-2 per i bambini : domande e risposte.	While most children have had mild or no symptoms, thousands have been hospitalized and several hundred have died. Children with underlying conditions are more likely to experience severe effects of COVID-19, but even healthy children can be severely affected. Children can spread COVID-19 to others and also can have long-term effects that last months. For these reasons, children need to be protected from COVID-19. 
Di Cadtelnuovo A et al Journal of Healthcare Engineering	Research Article Disentangling the Association of Hydroxychloroquine	Studio osservazionale retrospettivo su oltre 4000 pazienti ricoverati per COVID-19 in Italia durante la	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

https://www.researchgate.net/publication/352002163_Research_Article_Disentangling_the_Association_of_Hydroxychloroquine_Treatment_with_Mortality_in_Covid-19_Hospitalized_Patients_through_Hierarchical_Clustering	Treatment with Mortality in Covid-19 Hospitalized Patients through Hierarchical Clustering	prima « ondata » di pandemia : associazione del trattamento con idrossiclorochina con minore mortalità nel gruppo di pazienti a basso rischio (giovani e con meno comorbidità, identificati tramite un algoritmo di clustering).	study of 4,396 unselected patients hospitalized for Covid19 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, andone 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 is 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 medicationsin use and were concordant with associations with disease severity and outcome. These findings suggest aparticularly beneficial effect of HCQ within low risk Covid-19 patients and may contribute to clarifying thecurrent controversy on HCQ efficacy in Covid-19 treatment
Xiao X et al Scientific Reports	Animal sales from Wuhan wet markets immediately prior to the COVID-19 pandemic	Studio dei movimenti di animali vivi e morti passati per il mercato di Wuhan tra maggio 2017 e novembre 2019.	Here we document 47,381 individuals from 38 species, including 31 protected species sold between May 2017 and November 2019 in Wuhan's markets. We note that no pangolins (or bats) were traded, supporting reformed opinion that pangolins were not likely the spillover host at the source of the current coronavirus (COVID-19) pandemic. While we caution against the misattribution of COVID-

https://www.nature.com/articles/s41598-021-91470-2#Bib1			19's origins, the wild animals on sale in Wuhan suffered poor welfare and hygiene conditions and we detail a range of other zoonotic infections they can potentially vector. Nevertheless, in a precautionary response to COVID-19, China's Ministries temporarily banned all wildlife trade on 26th Jan 2020 until the COVID-19 pandemic concludes, and permanently banned eating and trading terrestrial wild (non-livestock) animals for food on 24th Feb 2020. These interventions, intended to protect human health, redress previous trading and enforcement inconsistencies, and will have collateral benefits for global biodiversity conservation and animal welfare.
De Giorgi V et al The Journa of Infectious Diseases https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiab295/6293992	Naturally acquired SARS-CoV-2 immunity persists for up to 11 months following infection	Su 228 donatori di plasma guariti da COVID-19 a partire da aprile 2020, 91.4% ha ancora IgG anti-SARS-CoV-2 nel follow-up, i primi fino a 11 mesi dopo la scomparsa dei sintomi.	Background : Characterizing the kinetics of the antibody response to SARS-CoV-2 is of critical importance to developing strategies that may mitigate the public health burden of COVID-19. We conducted a prospective, longitudinal analysis of COVID-19 convalescent plasma (CCP) donors at multiple time points over an 11-month period in order to determine how circulating antibody levels change over time following natural infection. Methods : From April 2020 to February 2021, we enrolled 228 donors. At each study visit, subjects either donated plasma or had study samples drawn only. Anti-SARS-CoV-2 donor testing was performed using the VITROS® Anti-SARS-CoV-2 Total and IgG assays, and an in-house fluorescence reduction neutralization assay (FRNA). Results : Anti-SARS-CoV-2 antibodies were identified in 97% of COVID-19 convalescent donors at initial presentation. In follow up analyses, of the 116 donors presenting for repeat timepoints, 91.4% of donors had detectable IgG levels up to 11 months post-symptom recovery, while 63% had detectable neutralizing titers, however, we observed that 25% of donors had neutralizing levels that dropped to an undetectable titer over time.

			Conclusion : Our data suggest that immunological memory is acquired in most individuals infected with SARS-CoV-2 and is sustained in a majority of patients for up to 11 months after recovery. 
Gostin LO et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2781010?guestAccessKey=37fc252e-9c17-478a-9a45-c6e670d52455&utm_source=silverchair&utm_medium=email&utm_campaign=article_alert-	Mandatory SARS-CoV-2 Vaccinations in K-12 Schools, Colleges/Universities, and Businesses	Discussione sull'opportunità di un obbligo vaccinale contro SARS-CoV-2 nelle scuole degli USA.	The Centers for Disease Control and Prevention (CDC) recently issued guidance that fully vaccinated individuals can safely remove masks and end social distancing in most indoor settings.1 Educational facilities and businesses are faced with whether and how to differentiate between vaccinated and unvaccinated individuals, including requiring proof of vaccination. Mandatory vaccination has historically served as a tool to reach and sustain high immunization coverage and to prevent transmission in K-12 schools, colleges/universities, and health care facilities. Vaccine mandates could extend to workers and customers in businesses to ensure safer environments. This Viewpoint examines the epidemiologic, public health, and legal considerations for mandatory SARS-CoV-2 vaccinations in each setting.

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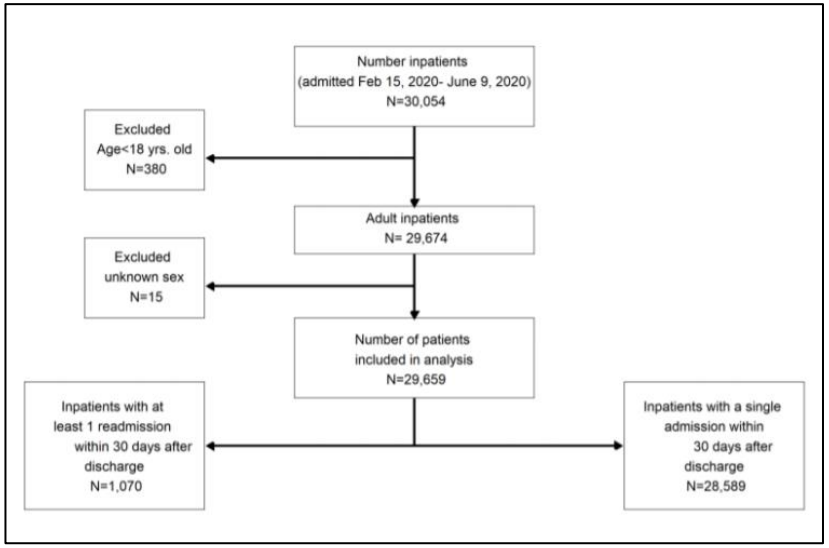
Talbot TR et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2781011?guestAccessKey=11b6e32e-7acb-4175-828b-8ffa04aeecb0&utm_source=silverchair&utm_medium=email&utm_campaign=article_alert-jama&utm_content=olf&utm_term=060721	COVID-19 Vaccination of Health Care Personnel as a Condition of Employment A Logical Addition to Institutional Safety Programs	Discussione sull'opportunità di imporre l'obbligo vaccinale contro SARS-CoV-2 al personale sanitario negli USA (dove ancora non è avvenuto).	As the SARS-CoV-2 vaccines move closer to full licensure and the data on their excellent effectiveness against both symptomatic and asymptomatic COVID-19 infection emerge, the question of whether to implement a SARS-CoV-2 vaccination policy for HCP as a condition of employment is becoming clearer. HCP should not inadvertently spread contagious infections like measles and influenza to their patients and other HCP. The time is coming to add COVID-19 to that list.
Sax P HIV and ID Observations - NEJM	We're Allowed to Say that Some COVID-19 Vaccines Are Better than Others, Right?	Pro e contro dei diversi vaccini disponibili contro SARS-CoV-2 ed expert opinio dell'Infettivologo Paul Sax.	However, if someone asked me what COVID-19 vaccine I'd recommend, based on what we know now, my answer would not be "whichever one you prefer" or "whichever one you are offered first" — especially if it were a 35-year-old woman. It would be an mRNA vaccine.

https://blogs.jwatch.org/hiv-id-observations/			
Bourguignon A et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2107051?query=featured_home	Adjunct Immune Globulin for Vaccine-Induced Thrombotic Thrombocytopenia	Trattamento di VITT (trombocitopenia trombotica immune indotta da vaccino) in tre pazienti canadesi, basato su immunoglobuline EV e anticoagulanti.	The use of high-dose intravenous immune globulin (IVIG) plus anticoagulation is recommended for the treatment of vaccine-induced immune thrombotic thrombocytopenia (VITT), a rare side effect of adenoviral vector vaccines against coronavirus disease 2019 (Covid-19). We describe the response to IVIG therapy in three of the first patients in whom VITT was identified in Canada after the receipt of the ChAdOx1 nCoV-19 vaccine. The patients were between the ages of 63 and 72 years; one was female. At the time of this report, Canada had restricted the use of the ChAdOx1 nCoV-19 vaccine to persons who were 55 years of age or older on the basis of reports that VITT had occurred primarily in younger persons. Two of the patients in our study presented with limb-artery thrombosis; the third had cerebral venous and arterial thrombosis. Variable patterns of serum-induced platelet activation were observed in response to heparin and platelet factor 4 (PF4), indicating the heterogeneity of the manifestations of VITT in serum. After the initiation of IVIG, reduced antibody-induced platelet activation in serum was seen in all three patients.
Thakkar A et al Cancer Cell	Seroconversion rates following COVID-19 vaccination amongst patients with cancer	Studio della conversione post-vaccinale anti SARS-CoV-2 in 220 pazienti affetti da neoplasie : 94%, che si riduce a 70% nei trattati con terapia immunosoppressive o trapianto di cellule staminali ematopoietiche. Il	As COVID-19 adversely affects patients with cancer, prophylactic strategies are critically needed. Using a validated antibody assay against SARS-CoV-2 spike protein, we determined a high seroconversion rate (94%) in 200 patients with cancer in New York City that had received full dosing with one of the FDA-approved COVID-19 vaccines. Comparing to solid tumors (98%), a significantly lower rate of seroconversion was observed in patients with

https://covidreference.com/top10		titolo di IgG è superiore se si utilizza un vaccino a mRNA rispetto ai vaccini adenovirali.	hematological malignancies (85%), particularly recipients following highly immunosuppressive therapies such as anti-CD20 therapies (70%) and stem cell transplantation (73%). Patients receiving immune checkpoint inhibitor therapy (97%) or hormonal therapies (100%) demonstrated high seroconversion post-vaccination. Patients with prior COVID-19 infection demonstrated higher anti-spike IgG titers post-vaccination. Relatively lower IgG titers were observed following vaccination with the adenoviral than mRNA-based vaccines. These data demonstrate generally high immunogenicity of COVID-19 vaccination in oncology patients and identify immunosuppressed cohorts that need novel vaccination or passive immunization strategies.
Zhou H et al Cell https://www.cell.com/cell/fulltext/S0092-8674(21)00709-1	Identification of novel bat coronaviruses sheds light on the evolutionary origins of SARS-CoV-2 and related viruses	Identificazione di 4 nuovi Coronavirus simili a SARS-Cov-2 nel pipistrello *Rhinolophus pusillus.*	Despite the discovery of animal coronaviruses related to SARS-CoV-2, the evolutionary origins of this virus are elusive. We describe a meta-transcriptomic study of 411 bat samples collected from a small geographical region in Yunnan province, China, between May 2019 and November 2020. We identified 24 full-length coronavirus genomes, including four novel SARS-CoV-2 related and three SARS-CoV related viruses. Rhinolophus pusillus virus RpYN06 was the closest relative of SARS-CoV-2 in most of the genome, although it possessed a more divergent spike gene. The other three SARS-CoV-2 related coronaviruses carried a genetically distinct spike gene that could weakly bind to the hACE2 receptor in vitro. Ecological modeling predicted the co-existence of up to 23 Rhinolophus bat species, with the largest contiguous hotspots extending from South Laos and Vietnam to southern China. Our study highlights the remarkable diversity of bat coronaviruses at the local scale, including close relatives of both SARS-CoV-2 and SARS-CoV.

Zoa-Assoumou s ET AL The Lancet https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(21)00125-7/fulltext	SARS-CoV-2 emerging variants in Africa: view from Gabon	Dati sulla sorveglianza genomica di SARS-CoV-2 in Gabon nel periodo gennaio-marzo 2021: la gran parte sono « varianti » del virus, in particolare la « inglese »	Since SARS-CoV-2 appeared in late 2019 in Wuhan, China, variants have emerged around the world. The general concern is that these variants appear to cause more severe disease, spread more easily between humans, and might change the effectiveness of current treatment and vaccines. Travel-related dissemination of SARS-CoV-2 fuels the global pandemic and the spread of variants. Therefore, SARS-CoV-2 genomic surveillance would help trace the emergence and spread of variants to better understand and anticipate their impact on public health. SARS-CoV-2 genomic surveillance in Africa has been portrayed as a challenge. Nevertheless, Gabon has taken up the challenge of setting up and implementing SARS-CoV-2 genomic surveillance. Gabon's strategy in the fight against COVID-19 includes SARS-CoV-2 PCR testing of volunteers and travellers (this applies to travel into and out of Gabon, as well as interprovincial travel within Gabon); contact tracing; and treatment. Here, we report the first data of the Gabonese genomic surveillance initiative.
Bertollini R et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2781112	Associations of Vaccination and of Prior Infection With Positive PCR Test Results for SARS-CoV-2 in Airline Passengers Arriving in Qatar	Associazione fra vaccinazione contro SARS-CoV-2 o precedente infezione e positività della PCR al tampone nasofaringeo nei viaggiatori diretti verso il Qatar nel periodo febbraio-aprile 2021 : come atteso le due condizioni sono protettive.	The SARS-CoV-2 pandemic has severely affected international travel. With efficacious COVID-19 vaccines available, Qatar implemented a pilot program between February 18 and April 26, 2021, to ease travel restrictions by waiving the quarantine requirement for vaccinated residents who received their second vaccine dose at least 14 days before arrival. The program still required a polymerase chain reaction (PCR) test to be performed on each passenger upon arrival at Hamad International Airport, Qatar's international travel gate. We investigated the incidence of PCR-positive test results in arriving passengers.

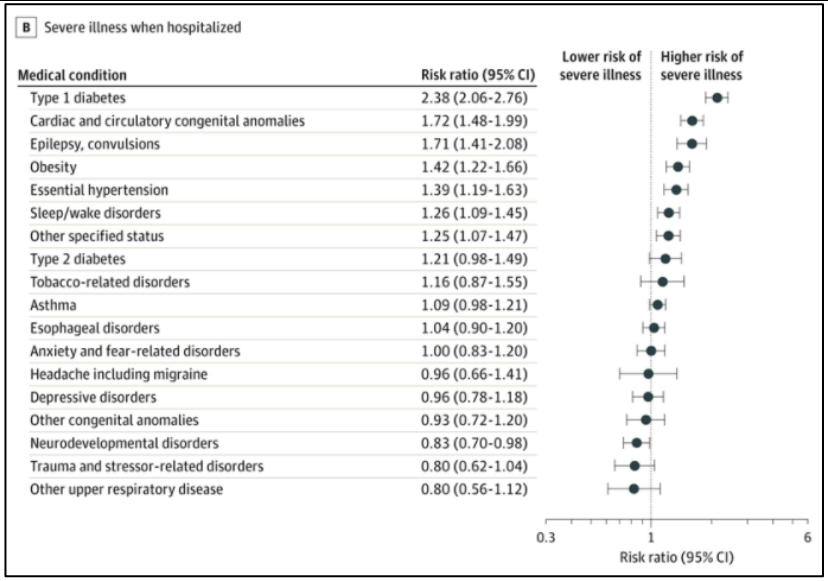
			Table. Associations of Vaccination and of Prior Infection With PCR Positivity Upon Arrival at the Airport Among Residents of Qatar Returning on International Flights PCR test results upon arrival at airport Exposure / Positive / Negative / Relative risk (95% CI) / χ^2 P value Vaccination status Vaccinated and second dose completed ≥14 d before the PCR test at the airport: 83 / 10 009 / 0.22 (0.17-0.28) / <.001 Unvaccinated and had no record of prior infection: 377 / 9715 Prior infection status Unvaccinated but record of prior infection ≥90 d before the PCR test at the airport: 78 / 7616 / 0.26 (0.21-0.34) / <.001 Unvaccinated and had no record of prior infection: 293 / 7401
Verna EC et al CID https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab464/6279074	Factors Associated with Readmission in the US Following Hospitalization with COVID-19	Fattori di rischio associati con riospedalizzazione dopo un ricovero per COVID-19 in una popolazione di quasi 30000 adulti negli USA : il 3.6% è stato nuovamente ricoverato e tali pazienti avevano maggiore probabilità di essere affetti da diabete, ipertensione, malattie cardiovascolari.	Background : Patients hospitalized for COVID-19 may experience complications following hospitalization and require readmission. This analysis estimates the rate and risk factors associated with COVID-19-related readmission and inpatient mortality. Methods : This is a retrospective cohort study utilizing deidentified chargemaster data from 297 hospitals across 40 US states on patients hospitalized with COVID-19 February 15-June 09, 2020. Demographics, comorbidities, acute conditions, and clinical characteristics of first hospitalization are summarized. Mulitvariable logistic regression was used to measure risk factor associations with 30-day readmission and in-hospital mortality. Results : Among 29,659 patients, 1,070 (3.6%) were readmitted. Readmitted patients were more likely to have diabetes, hypertension, cardiovascular disease (CVD), chronic kidney disease (CKD) vs those not readmitted (p<0.0001) and to present on first admission with acute kidney injury (15.6% vs. 9.2%), congestive heart failure (6.4% vs. 2.4%), and cardiomyopathy (2.1% vs. 0.8%) (p<0.0001). Higher odds of readmission were observed in patients age >60 vs. 1840 (odds ratio [OR]=1.92, 95% confidence interval [CI]=1.48, 2.50), and admitted in the Northeast vs. West (OR=1.43, 95% CI=1.14, 1.79) or South (OR=1.28, 95% CI=1.11, 1.49).

			Comorbidities including diabetes (OR=1.34, 95% CI=1.12, 1.60), CVD (OR=1.46, 95% CI=1.23, 1.72), CKD stage 1-5 (OR=1.51, 95% CI=1.25,1.81) and stage 5 (OR=2.27, 95% CI=1.81, 2.86) were associated with higher odds of readmission. 12.3% of readmitted patients died during second hospitalization. Conclusions : Among this large US population of patients hospitalized with COVID-19, readmission was associated with certain comorbidities and acute conditions during first hospitalization. These findings may inform strategies to mitigate risks of readmission due to COVID-19 complications. 
Corti D et al Cell	Tackling COVID-19 with neutralizing monoclonal antibodies	Revisione sugli anticorpi monoclonali disponibili per la terapia contro SARS-CoV-2.	Monoclonal antibodies (mAbs) have revolutionized the treatment of several human diseases, including cancer and autoimmunity and inflammatory conditions, and represent a new frontier for the treatment of infectious diseases. In the last 20 years, innovative methods have allowed the rapid isolation of mAbs from convalescent subjects, humanized mice, or libraries assembled in vitro and have proven that mAbs can be effective countermeasures

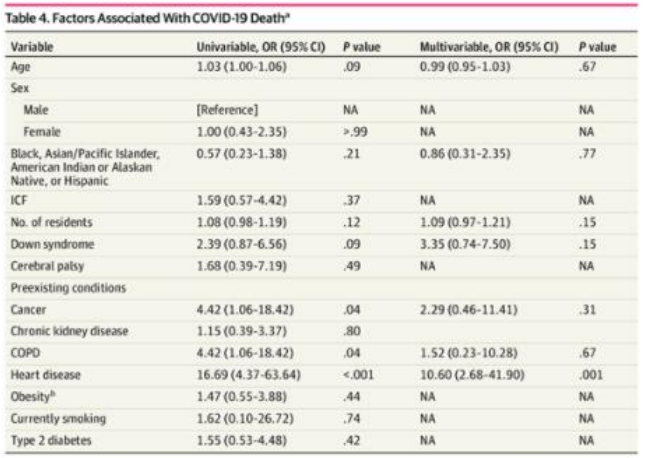
https://www.cell.com/cell/fulltext/S0092-8674(21)00602-4			against emerging pathogens. During the past year, an unprecedentedly large number of mAbs have been developed to fight coronavirus disease 2019 (COVID-19). Lessons learned from this pandemic will pave the way for the development of more mAb-based therapeutics for other infectious diseases. Here, we provide an overview of SARS-CoV-2-neutralizing mAbs, including their origin, specificity, structure, antiviral and immunological mechanisms of action, and resistance to circulating variants, as well as a snapshot of the clinical trials of approved or late-stage mAb therapeutics.
Razani N et al The Journal of Infectious Diseases https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiab298/6291889	Clarification regarding Outdoor Transmission of SARS-CoV-2 and Other Respiratory Viruses, a Systematic Review	Stima della bassa trasmissibilità di SARS-CoV-2 all'aperto (<10%).	On April 24, 2021, the Centers for Disease Control and Prevention (CDC) issued new guidance on outdoor activities. In subsequent testimony before the United States Senate, a number reported in our article, "Outdoor Transmission of SARS-CoV-2 and Other Respiratory Viruses: A Systematic Review," was cited that the proportion of SARS-CoV-2 transmission occurring in outside settings is less than 10%. We are writing to clarify how we arrived at the less than ten percent summary number. Our abstract and results sections state that "five identified studies found a low proportion of reported global SARS-CoV-2 infections occurred outdoors (<10%)." Because of the small number of heterogeneous studies we reviewed, as well as their methodological limitations, we could not provide a meta-analytically pooled estimate of the exact proportion of SARSCoV-2 transmissio. Ten percent was chosen as a conservative estimate based on the upper confidence limit of the proportion of cases attributable to outdoor settings reported in one of the studies we reviewedns that have occurred outdoors or the associated risk.

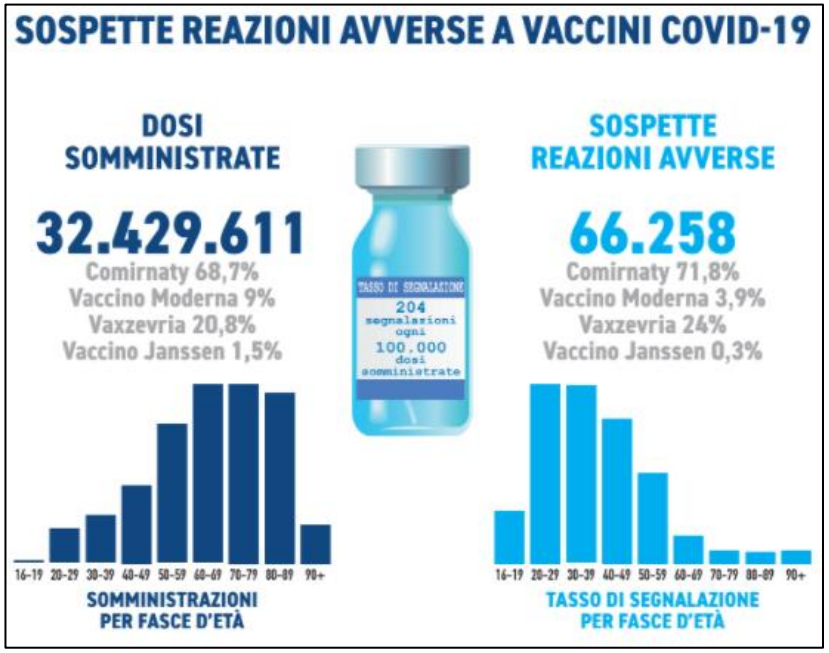
Kompaniyets L et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2780706?resultClick=1	Underlying Medical Conditions Associated With Severe COVID-19 Illness Among Children	Fattori associati a COVID-19 grave nei bambini e ragazzi di età inferiore a 18 anni in una casistica di 43,465 persone : emergono il diabete di tipo 1, l'obesità e le patologie cardiovascolari congenite.	Importance Information on underlying conditions and severe COVID-19 illness among children is limited. Objective To examine the risk of severe COVID-19 illness among children associated with underlying medical conditions and medical complexity. Design, Setting, and Participants This cross-sectional study included patients aged 18 years and younger with International Statistical Classification of Diseases, Tenth Revision, Clinical Modification code U07.1 (COVID-19) or B97.29 (other coronavirus) during an emergency department or inpatient encounter from March 2020 through January 2021. Data were collected from the Premier Healthcare Database Special COVID-19 Release, which included data from more than 800 US hospitals. Multivariable generalized linear models, controlling for patient and hospital characteristics, were used to estimate adjusted risk of severe COVID-19 illness associated with underlying medical conditions and medical complexity. Exposures Underlying medical conditions and medical complexity (ie, presence of complex or noncomplex chronic disease). Main Outcomes and Measures Hospitalization and severe illness when hospitalized (ie, combined outcome of intensive care unit admission, invasive mechanical ventilation, or death). Results Among 43 465 patients with COVID-19 aged 18 years or younger, the median (interquartile range) age was 12 (4-16) years, 22 943 (52.8%) were female patients, and 12 491 (28.7%) had underlying medical conditions. The most common diagnosed conditions were asthma (4416 [10.2%]), neurodevelopmental disorders (1690 [3.9%]), anxiety and fear-related disorders (1374 [3.2%]), depressive disorders (1209 [2.8%]), and obesity (1071 [2.5%]). The strongest risk factors for hospitalization were type 1 diabetes (adjusted risk ratio [aRR], 4.60; 95% CI, 3.91-5.42) and

			obesity (aRR, 3.07; 95% CI, 2.66-3.54), and the strongest risk factors for severe COVID-19 illness were type 1 diabetes (aRR, 2.38; 95% CI, 2.06-2.76) and cardiac and circulatory congenital anomalies (aRR, 1.72; 95% CI, 1.48-1.99). Prematurity was a risk factor for severe COVID-19 illness among children younger than 2 years (aRR, 1.83; 95% CI, 1.47-2.29). Chronic and complex chronic disease were risk factors for hospitalization, with aRRs of 2.91 (95% CI, 2.63-3.23) and 7.86 (95% CI, 6.91-8.95), respectively, as well as for severe COVID-19 illness, with aRRs of 1.95 (95% CI, 1.69-2.26) and 2.86 (95% CI, 2.47-3.32), respectively. Conclusions and Relevance This cross-sectional study found a higher risk of severe COVID-19 illness among children with medical complexity and certain underlying conditions, such as type 1 diabetes, cardiac and circulatory congenital anomalies, and obesity. Health care practitioners could consider the potential need for close observation and cautious clinical management of children with these conditions and COVID-19.

			B Severe illness when hospitalized 
Landes SD et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2780779	Risk Factors Associated With COVID-19 Outcomes Among People With Intellectual and Developmental Disabilities Receiving Residential Services	I fattori associati a peggiore outcome di COVID-19 nelle persone con disabilità sono analoghi a quelli della popolazione generale : età più avanzata e comorbidità.	Importance Although there is evidence of more severe COVID-19 outcomes, there is no information describing the risk factors for COVID-19 diagnosis and/or mortality among people with intellectual and developmental disabilities (IDD) receiving residential support services in the US. Objective To identify associations between demographic characteristics, residential characteristics, and/or preexisting health conditions and COVID-19 diagnosis and mortality for people with IDD receiving residential support services. Design, Setting, and Participants This cohort study tracked COVID-19 outcomes for 543 individuals with IDD. Participants were receiving support services from a single organization providing residential services in the 5 boroughs of New York City from March 1 to October 1, 2020. Statistical analysis was performed from December 2020 to February 2021.

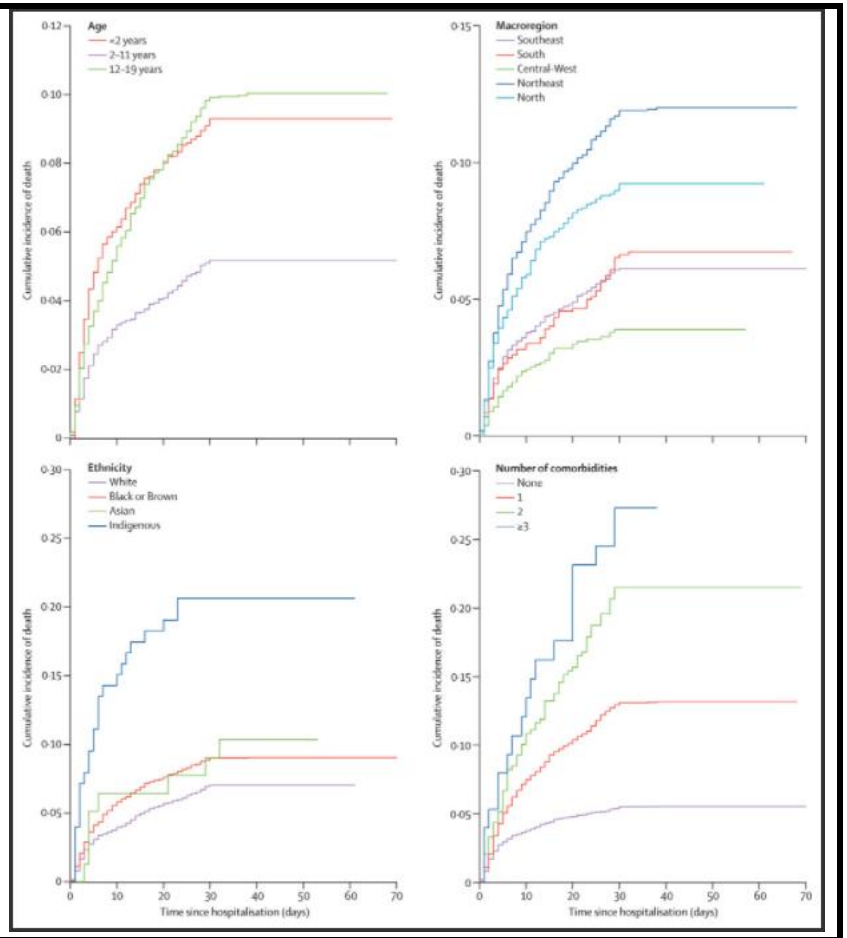
			Exposures Resident-level characteristics, including age, sex, race/ethnicity, disability status, residential characteristics, and preexisting medical conditions. Main Outcomes and Measures COVID-19 diagnosis was confirmed by laboratory test. COVID-19 mortality indicated that the individual died from COVID-19 during the course of the study. Logistic regression models were used to evaluate associations between demographic characteristics, residential characteristics, and preexisting health conditions and COVID-19 diagnosis and mortality. Results Among the 543 individuals with IDD in the study, the median (interquartile range) age was 57.0 (45-65) years; 217 (40.0%) were female, and 274 (50.5%) were Black, Asian/Pacific Islander, American Indian or Alaskan Native, or Hispanic. The case rate was 16 759 (95% CI, 13 853-20 131) per 100 000; the mortality rate was 6446 (95% CI, 4671-8832) per 100 000; and the case-fatality rate was 38.5% (95% CI, 29.1%-48.7%). Increased age (odds ratio [OR], 1.04; 95% CI, 1.02-1.06), Down syndrome (OR, 2.91; 95% CI, 1.49-5.69), an increased number of residents (OR, 1.07; 95% CI, 1.00-1.14), and chronic kidney disease (OR, 4.17; 95% CI, 1.90-9.15) were associated with COVID-19 diagnosis. Heart disease (OR, 10.60; 95% CI, 2.68-41.90) was associated with COVID-19 mortality. Conclusions and Relevance This study found that, similar to the general population, increased age and preexisting health conditions were associated with COVID-19 outcomes for people with IDD receiving residential support services in New York City. As with older adults living in nursing homes, number of residents was also associated with more severe COVID-19 outcomes. Unique to people with IDD was an increased risk of COVID-19 diagnosis for people with Down syndrome.

			Table 4. Factors Associated With COVID-19 Death[a]  Table 4. Factors Associated With COVID-19 Death[a] Variable | Univariable, OR (95% CI) | P value | Multivariable, OR (95% CI) | P value Age | 1.03 (1.00-1.06) | .09 | 0.99 (0.95-1.03) | .67 Sex Male | [Reference] | NA | NA | NA Female | 1.00 (0.43-2.35) | >.99 | NA | NA Black, Asian/Pacific Islander, American Indian or Alaskan Native, or Hispanic | 0.57 (0.23-1.38) | .21 | 0.86 (0.31-2.35) | .77 ICF | 1.59 (0.57-4.42) | .37 | NA | NA No. of residents | 1.08 (0.98-1.19) | .12 | 1.09 (0.97-1.21) | .15 Down syndrome | 2.39 (0.87-6.56) | .09 | 3.35 (0.74-7.50) | .15 Cerebral palsy | 1.68 (0.39-7.19) | .49 | NA | NA Preexisting conditions Cancer | 4.42 (1.06-18.42) | .04 | 2.29 (0.46-11.41) | .31 Chronic kidney disease | 1.15 (0.39-3.37) | .80 COPD | 4.42 (1.06-18.42) | .04 | 1.52 (0.23-10.28) | .67 Heart disease | 16.69 (4.37-63.64) | <.001 | 10.60 (2.68-41.90) | .001 Obesity[b] | 1.47 (0.55-3.88) | .44 | NA | NA Currently smoking | 1.62 (0.10-26.72) | .74 | NA | NA Type 2 diabetes | 1.55 (0.53-4.48) | .42 | NA | NA
Agenzia Italiana del Farmaco http://www.quotidianosanita.it/allegati/allegato9563001.pdf	Rapporto sulla Sorveglianza dei vaccini COVID-19 n 5	Ultimo rapporto AIFA sull'andamento della campagna vaccinale contro SARS-CoV-2.	Nessun prodotto medicinale può essere mai considerato esente da rischi. Ognuno di noi, quando decide di servirsi di un farmaco o di sottoporsi a una vaccinazione, dovrebbe avere presente che quello che sta facendo è bilanciare i benefici con i rischi. Verificare che i benefici di un vaccino siano superiori ai rischi e ridurre questi al minimo è responsabilità delle autorità sanitarie che regolano l'immissione in commercio dei prodotti medicinali. Servirsi di un farmaco in maniera corretta, ponderata e consapevole è responsabilità di tutti. Il nostro Paese è dotato di un sistema di farmacovigilanza che, ormai da molti anni, dedica un'attenzione particolare e un apposito impianto organizzativo proprio al monitoraggio di quello che succede dopo la somministrazione di un vaccino. Si tratta di un sistema aperto, dinamico, cui tutti professionisti sanitari, pazienti, genitori, cittadini) possono inviare le proprie segnalazioni contribuendo al monitoraggio dell'uso sicuro dei vaccini e dei medicinali in genere. Inoltre, i l sistema ha piena trasparenza e offre l'accesso ai dati aggregati, interrogabili sul sito

			web dell'AIFA. È grazie a questo sistema di farmacovigilanza che è possibile realizzare questo Rapporto, che prevede un aggiornamento mensile e segue puntualmente l'andamento della campagna vaccinale contro COVID-19. Una corretta informazione è alla base di ogni scelta consapevole e questo Rapporto intende offrire a tutti un'informazione tempestiva, comprensibile e consolidata. 
Oliveira EA et al The Lancet https://www.thelancet.com/journals/lanchi/article/	Clinical characteristics and risk factors for death among hospitalised children and adolescents with COVID-19 in Brazil: an analysis of a nationwide database	Fattori associati alla mortalità dei bambini/adolescenti per COVID-19 in Brasile : età (minore mortalità nella fascia 2-11 anni, maggiore negli estremi), etnia indigena, regione di	Background COVID-19 is usually less severe and has lower case fatality in children than in adults. We aimed to characterise the clinical features of children and adolescents hospitalised with laboratory-confirmed SARS-CoV-2 infection and to evaluate the risk factors for COVID-19-related death in this population. Methods

PIIS2352-4642(21)00134-6/fulltext		provenienza più povera, comorbidità preesistenti.	We did an analysis of all patients younger than 20 years who had quantitative RT-PCR-confirmed COVID-19 and were registered in the Influenza Epidemiological Surveillance Information System (SIVEP-Gripe, a nationwide surveillance database of patients admitted to hospital with severe acute respiratory disease in Brazil), between Feb 16, 2020, and Jan 9, 2021. The primary outcome was time to recovery (discharge) or in-hospital death, evaluated by competing risks analysis using the cumulative incidence function. Findings Of the 82 055 patients younger than 20 years reported to SIVEP-Gripe during the study period, 11 613 (14·2%) had available data showing laboratory-confirmed SARS-CoV-2 infection and were included in the sample. Among these patients, 886 (7·6%) died in hospital (at a median 6 days [IQR 3–15] after hospital admission), 10 041 (86·5%) patients were discharged from the hospital, 369 (3·2%) were in hospital at the time of analysis, and 317 (2·7%) were missing information on outcome. The estimated probability of death was 4·8% during the first 10 days after hospital admission, 6·7% during the first 20 days, and 8·1% at the end of follow-up. Probability of discharge was 54·1% during the first 10 days, 78·4% during the first 20 days, and 92·0% at the end of follow-up. Our competing risks multivariate survival analysis showed that risk of death was increased in infants younger than 2 years (hazard ratio 2·36 [95% CI 1·94–2·88]) or adolescents aged 12–19 years (2·23 [1·84–2·71]) relative to children aged 2–11 years; those of Indigenous ethnicity (3·36 [2·15–5·24]) relative to those of White ethnicity; those living in the Northeast region (2·06 [1·68–2·52]) or North region (1·55 [1·22–1·98]) relative to those in the Southeast region; and those with one (2·96 [2·52–3·47]), two (4·96 [3·80–

			6·48]), or three or more (7·28 [4·56–11·6]) pre-existing medical conditions relative to those with none. Interpretation Death from COVID-19 was associated with age, Indigenous ethnicity, poor geopolitical region, and pre-existing medical conditions. Disparities in health care, poverty, and comorbidities can contribute to magnifying the burden of COVID-19 in more vulnerable and socioeconomically disadvantaged children and adolescents in Brazil.

			
Aomar-Millàn IF et al Internal and Emergency Medicine https://link.springer.com/article/10.1007/s11739-020-02600-	Anakinra after treatment with corticosteroids alone or with tocilizumab in patients with severe COVID-19 pneumonia and moderate hyperinflammation. A retrospective cohort study	Piccolo studio retrospettivo su 143 pazienti ospedalizzati con COVID-19 grave, trattati con metilprednisolone da solo o associato a tocilizumab o anakinra ; il trattamento con anakinra è	Introduction : Little evidence appears to exist for the use of anakinra, a recombinant interleukin-1 receptor antagonist, after non-response to treatment with corticosteroids alone or combined with tocilizumab in patients with severe COVID-19 pneumonia and moderate hyperinflammatory state. Patients and Methods : A retrospective observational cohort study was carried out involving 143 patients with severe COVID-19 pneumonia and moderate hyperinflammation. They received

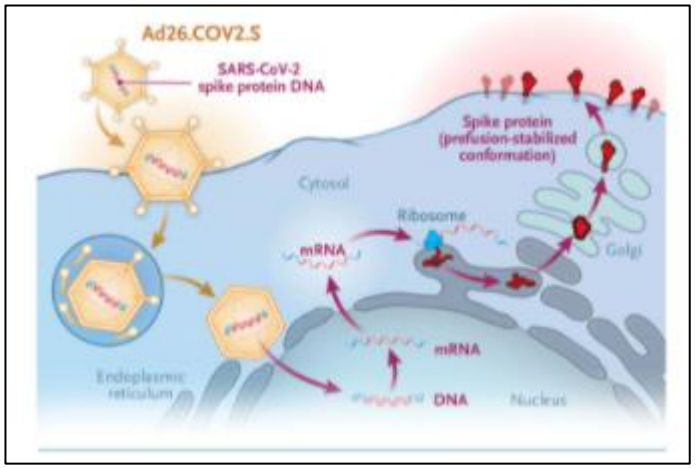
z?utm_source=toc&utm_medium=email&utm_campaign=toc_11739_16_4&utm_content=etoc_springer_20210611		associato a minore mortalità a 60 giorni.	standard therapy along with pulses of methylprednisolone (group 1) or methylprednisolone plus tocilizumab (group 2), with the possibility of receiving anakinra (group 3) according to protocol. The aim of this study was to assess the role of anakinra in the clinical course (death, admission to the intensive care ward) during the first 60 days after the first corticosteroid pulse. Clinical, laboratory, and imaging characteristics as well as infectious complications were also analyzed. Results : 74 patients (51.7%) in group 1, 59 (41.3%) patients in group 2, and 10 patients (7%) in group 3 were included. 8 patients (10.8%) in group 1 died, 6 (10.2%) in group 2, and 0 (0%) in group 3. After adjustment for age and clinical severity indices, treatment with anakinra was associated with a reduced risk of mortality (adjusted hazard ratio 0.518, 95% CI 0.265–0.910; p = 0.0437). Patients in group 3 had a lower mean CD4 count after 3 days of treatment. No patients in this group presented infectious complications. Conclusions : In patients with moderate hyperinflammatory state associated with severe COVID-19 pneumonia, treatment with anakinra after non-response to corticosteroids or corticosteroids plus tocilizumab therapy may be an option for the management of these patients and may improve their prognosis.
Hu W et al Internal and Emergency Medicine https://link.springer.com/article/10.1007/s11739-020-02515-	Disorders of sodium balance and its clinical implications in COVID-19 patients: a multicenter retrospective study	Studio retrospettivo osservazionale su 1254 pazienti con COVID-19, di cui 154 con alterazioni della sodiemia (in particolare iponatremia) che appaiono associate a un peggiore decorso.	Background : The worldwide spread of SARS-CoV-2 has infected millions of people leading to over 0.3 million mortalities. The disruption of sodium homeostasis, tends to be a common occurrence in patients with COVID-19. Methods and results : A total of 1,254 COVID-19 patients comprising 124 (9.9%) hyponatremic patients (under 135 mmol/L) and 30 (2.4%) hypernatremic patients (over 145 mmol/L) from three hospitals in Hubei, China, were enrolled in the study. The

9?utm_source=toc&utm_medium=email&utm_campaign=toc_11739_16_4&utm_content=etoc_springer_20210611			relationships between sodium balance disorders in COVID-19 patients, its clinical features, implications, and the underlying causes were presented. Hyponatremia patients were observed to be elderly, had more comorbidities, with severe pneumonic chest radiographic findings. They were also more likely to have a fever, nausea, higher leukocyte and neutrophils count, and a high sensitivity C-reactive protein (HS-CRP). Compared to normonatremia patients, renal insufficiency was common in both hyponatremia and hypernatremia patients. In addition, hyponatremia patients required extensive treatment with oxygen, antibiotics, and corticosteroids. The only significant differences between the hypernatremia and normonatremia patients were laboratory findings and clinical complications, and patients with hypernatremia were more likely to use traditional Chinese medicine for treatment compared to normonatremia patients. This study indicates that severity of the disease, the length of stay in the hospital of surviving patients, and mortality were higher among COVID-19 patients with sodium balance disorders. Conclusion : Sodium balance disorder, particularly hyponatremia, is a common condition among hospitalized patients with COVID-19 in Hubei, China, and it is associated with a higher risk of severe illness and increased in-hospital mortality.
Hughes R et al Multiple Sclerosis and Related Disorders https://www.msard-journal.com/article/S221	COVID-19 in ocrelizumab-treated people with multiple sclerosis.	In una ampia coorte di pazienti con sclerosi multipla in trattamento con ocrelizumab (anti-CD20), l'andamento di COVID-19 non si discosta da quello della popolazione generale.	BACKGROUND: There are limited data on the impact of coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on people with multiple sclerosis (MS). OBJECTIVE: To better understand SARS-CoV-2 infection in ocrelizumab-treated people with MS. METHODS: Internal Roche/Genentech data sources: Cases of COVID-19 from ongoing Roche/Genentech clinical trials and from post-marketing use of ocrelizumab until July 31, 2020 were identified and assessed

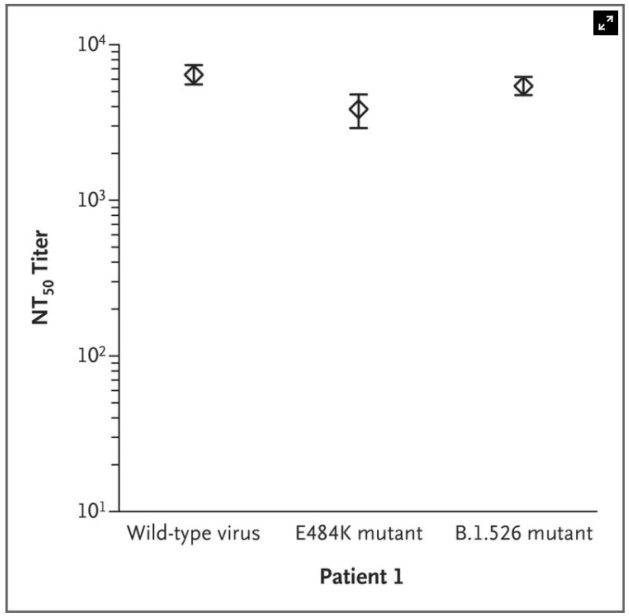
1-0348(20)30799-9/fulltext			using descriptive statistics. External real-world data (RWD) source: An MS COVID-19 cohort and an ocrelizumab-treated MS COVID-19 cohort were identified and assessed from the OPTUM de-identified COVID-19 electronic health record (EHR) database. RESULTS: Roche/Genentech clinical trial data: There were 51 (1.3%) suspected or confirmed cases of COVID-19 identified from 4,000 patients ongoing in 10 Roche/Genentech clinical trials. Of these, 26 (51%) were confirmed COVID-19 and 25 (49%) were suspected COVID-19. Sixteen (31.4%) patients were hospitalized. COVID-19 severity was mild to moderate in most patients (35, 68.6%). Ten (19.6%) patients had severe disease and there were three (5.9%) fatal cases. Most patients (43, 84.3%) recovered or were recovering. There was no association apparent between duration of exposure to ocrelizumab and COVID-19. Among COVID-19 patients with previous serum immunoglobulin status (27/51, 52.9%), all (27/27, 100%) had IgG levels within the normal range. Roche/Genentech post-marketing safety database data: There were 307 post-marketing cases of COVID-19 in the Roche/Genentech global safety database. Of these, 263 (85.7%) were confirmed and 44 (14.3%) were suspected COVID-19. 100 (32.6%) patients were hospitalized. COVID-19 was asymptomatic, mild or moderate in 143 (46.6%) patients, severe in 52 (16.9%) patients, and critical in 15 (4.9%) patients. There were 17 (5.5%) fatal cases. Information on severity was not reported in 80 (26.1%) cases. Most patients (211, 68.7%) recovered or were recovering at the time of the report. External RWD data source: As of July 13, 2020, the OPTUM() database included EHRs for almost 1.2 million patients with suspected COVID-19, 130,500 of whom met the criteria for confirmed/clinically diagnosed COVID-19. A total of 357 patients with MS with confirmed COVID-19 were identified. Forty-eight (13.4%) were treated with ocrelizumab, of whom 12

			(25.0%) were hospitalized and one died (2.1%). Similar rates of hospitalization, invasive ventilation, and death were observed in the ocrelizumab-treated and non-ocrelizumab-treated MS cohorts. Across the Roche/Genentech and RWD sources assessed, age, male sex, and the presence of comorbidities such as hypertension were associated with a more severe disease course of COVID-19. There was a higher number of comorbidities present in hospitalized versus non-hospitalized patients. CONCLUSIONS: This assessment provides evidence that COVID-19 in ocrelizumab-treated people with MS is predominantly mild to moderate in severity with most patients not requiring hospitalization; in line with data reported from the general population and MS datasets. Risk factors known to be associated with severe COVID-19 outcomes in the general population also appear to influence COVID-19 severity in ocrelizumab-treated people with MS. Case fatality rates for ocrelizumab-treated people with MS were within published ranges for the general population and other MS cohorts.
Camell CD et al Science https://science.sciencemag.org/content/early/2021/06/07/science.abe4832	Senolytics reduce coronavirus-related mortality in old mice	Le cellule senescenti esposte a SARS-CoV-2 reagiscono favorendo l'ingresso del virus e contrastando la produzione di sostanze antivirali nel topo, il che potrebbe spiegare l'andamento peggiore dell'infezione negli organismi « anziani ».	The COVID-19 pandemic has revealed the pronounced vulnerability of the elderly and chronically-ill to SARS-CoV-2-induced morbidity and mortality. Cellular senescence contributes to inflammation, multiple chronic diseases, and age-related dysfunction, but effects on responses to viral infection are unclear. Here, we demonstrate that senescent cells (SnC) become hyper-inflammatory in response to pathogen-associated molecular patterns (PAMPs), including SARS-CoV-2 Spike protein-1, increasing expression of viral entry proteins and reducing anti-viral gene expression in non-SnCs through a paracrine mechanism. Old mice acutely infected with pathogens that included a SARS-CoV-2-related mouse β-coronavirus experienced increased senescence and inflammation with nearly

			100% mortality. Targeting SnCs using senolytic drugs before or after pathogen exposure significantly reduced mortality, cellular senescence, and inflammatory markers and increased anti-viral antibodies. Thus, reducing the SnC burden in diseased or aged individuals should enhance resilience and reduce mortality following viral infection, including SARS-CoV-2.
Sadoff J et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2101544?query=featured_home	Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine against Covid-19	Trial clinico di fase III su efficacia di una singola dose di vaccino Janssen contro SARS-CoV-2 nel prevenire la malattia sintomatica a distanza di almeno 14 o almeno 28 giorni dalla somministrazione : rispettivamente 66.9% e 66.1% per la malattia moderata-grave nei due intervalli, 76.7% e 85.4% per la malattia grave-critica.	BACKGROUND : The Ad26.COV2.S vaccine is a recombinant, replication-incompetent human adenovirus type 26 vector encoding full-length severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein in a prefusion-stabilized conformation. METHODS : In an international, randomized, double-blind, placebo-controlled, phase 3 trial, we randomly assigned adult participants in a 1:1 ratio to receive a single dose of Ad26.COV2.S (5×1010 viral particles) or placebo. The primary end points were vaccine efficacy against moderate to severe–critical coronavirus disease 2019 (Covid-19) with an onset at least 14 days and at least 28 days after administration among participants in the per-protocol population who had tested negative for SARS-CoV-2. Safety was also assessed. RESULTS : The per-protocol population included 19,630 SARS-CoV-2–negative participants who received Ad26.COV2.S and 19,691 who received placebo. Ad26.COV2.S protected against moderate to severe–critical Covid-19 with onset at least 14 days after administration (116 cases in the vaccine group vs. 348 in the placebo group; efficacy, 66.9%; adjusted 95% confidence interval [CI], 59.0 to 73.4) and at least 28 days after administration (66 vs. 193 cases; efficacy, 66.1%; adjusted 95% CI, 55.0 to 74.8). Vaccine efficacy was higher against severe–critical Covid-19 (76.7% [adjusted 95% CI, 54.6 to 89.1] for onset at ≥14 days and 85.4%

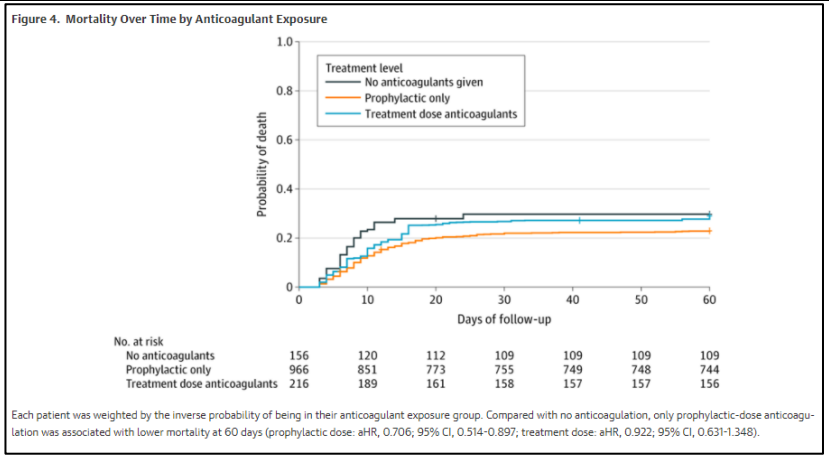
			[adjusted 95% CI, 54.2 to 96.9] for onset at ≥28 days). Despite 86 of 91 cases (94.5%) in South Africa with sequenced virus having the 20H/501Y.V2 variant, vaccine efficacy was 52.0% and 64.0% against moderate to severe–critical Covid-19 with onset at least 14 days and at least 28 days after administration, respectively, and efficacy against severe–critical Covid-19 was 73.1% and 81.7%, respectively. Reactogenicity was higher with Ad26.COV2.S than with placebo but was generally mild to moderate and transient. The incidence of serious adverse events was balanced between the two groups. Three deaths occurred in the vaccine group (none were Covid-19–related), and 16 in the placebo group (5 were Covid-19–related). CONCLUSIONS : A single dose of Ad26.COV2.S protected against symptomatic Covid-19 and asymptomatic SARS-CoV-2 infection and was effective against severe–critical disease, including Hospitalization and death. Safety appeared to be similar to that in other phase 3 trials of Covid-19 vaccines. 

Alter G et al Nature https://www.nature.com/articles/s41586-021-03681-2	Immunogenicity of Ad26.COV2.S vaccine against SARS-CoV-2 variants in humans	Risposta neutralizzante nei confronti di alcune varianti di SARS-CoV-2 dopo vaccinazione con Ad26.COV2.S (Janssen): minore titolo anticorpale nei confronti della « sudafricana » e « brasiliana » (NB : sappiamo che questi nomi, così come le sigle, sono in disuso secondo la WHO!) ma immunità T cellulare conservata.	The Ad26.COV2.S vaccine has demonstrated clinical efficacy against symptomatic COVID-19, including against the B.1.351 variant that is partially resistant to neutralizing antibodies. However, the immunogenicity of this vaccine in humans against SARS-CoV-2 variants of concern remains unclear. Here we report humoral and cellular immune responses from 20 Ad26.COV2.S vaccinated individuals from the COV1001 phase 1/2 clinical trial2 against the original SARS-CoV-2 strain WA1/2020 as well as against the B.1.1.7, CAL.20C, P.1., and B.1.351 variants of concern. Ad26.COV2.S induced median pseudovirus neutralizing antibody titers that were 5.0- and 3.3-fold lower against the B.1.351 and P.1 variants, respectively, as compared with WA1/2020 on day 71 following vaccination. Median binding antibody titers were 2.9- and 2.7-fold lower against the B.1.351 and P.1 variants, respectively, as compared with WA1/2020. Antibody-dependent cellular phagocytosis, complement deposition, and NK cell activation responses were largely preserved against the B.1.351 variant. CD8 and CD4 T cell responses, including central and effector memory responses, were comparable among the WA1/2020, B.1.1.7, B.1.351, P.1, and CAL.20C variants. These data show that neutralizing antibody responses induced by Ad26.COV2.S were reduced against the B.1.351 and P.1 variants, but functional non-neutralizing antibody responses and T cell responses were largely preserved against SARS-CoV-2 variants. These findings have implications for vaccine protection against SARS-CoV-2 variants of concern.
Hacisuleyman E et al NEJM	Vaccine Breakthrough Infections with SARS-CoV-2 Variants	Descrizione di due casi di infezione da SARS-CoV-2 a distanza di 2 settimane dalla seconda dose di un vaccino a mRNA, con dimostrazione	Emerging variants of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are of clinical concern. In a cohort of 417 persons who had received the second dose of BNT162b2 (Pfizer–BioNTech) or mRNA-1273 (Moderna) vaccine at least 2 weeks previously, we

https://www.nejm.org/doi/full/10.1056/NEJMoa2105000?query=featured_home		di infezione da varianti e delle mutazioni presenti : le varianti costituiscono un potenziale rischio almeno per alcune persone vaccinate.	identified 2 women with vaccine breakthrough infection. Despite evidence of vaccine efficacy in both women, symptoms of coronavirus disease 2019 developed, and they tested positive for SARS-CoV-2 by polymerase-chain-reaction testing. Viral sequencing revealed variants of likely clinical importance, including E484K in 1 woman and three mutations (T95I, del142–144, and D614G) in both. These observations indicate a potential risk of illness after successful vaccination and subsequent infection with variant virus, and they provide support for continued efforts to prevent and diagnose infection and to characterize variants in vaccinated persons. **Figure 4.** Neutralization Assays for Antibodies to the Wuhan-Hu-1 Isolate, the E484K Variant, and the B.1.526 Variant. 

Vaughn VM et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2780927	Trends in Venous Thromboembolism Anticoagulation in Patients Hospitalized With COVID-19	Sempre più pazienti ricoverati per COVID-19 hanno ricevuto anticoagulanti, a dose profilattica o terapeutica, secondo questo studio di coorte che analizza il periodo marzo-giugno 2020. Solo l'anticoagulante a dose profilattica è associato a ridotta mortalità a 60 giorni.	Importance Venous thromboembolism (VTE) is a common complication of COVID-19. It is not well understood how hospitals have managed VTE prevention and the effect of prevention strategies on mortality. Objective To characterize frequency, variation across hospitals, and change over time in VTE prophylaxis and treatment-dose anticoagulation in patients hospitalized for COVID-19, as well as the association of anticoagulation strategies with in-hospital and 60-day mortality. Design, Setting, and Participants This cohort study of adults hospitalized with COVID-19 used a pseudorandom sample from 30 US hospitals in the state of Michigan participating in a collaborative quality initiative. Data analyzed were from patients hospitalized between March 7, 2020, and June 17, 2020. Data were analyzed through March 2021. Exposures Nonadherence to VTE prophylaxis (defined as missing ≥2 days of VTE prophylaxis) and receipt of treatment-dose or prophylactic-dose anticoagulants vs no anticoagulation during hospitalization. Main Outcomes and Measures The effect of nonadherence and anticoagulation strategies on in-hospital and 60-day mortality was assessed using multinomial logit models with inverse probability of treatment weighting. Results Of a total 1351 patients with COVID-19 included (median [IQR] age, 64 [52-75] years; 47.7% women, 48.9% Black patients), only 18 (1.3%) had a confirmed VTE, and 219 (16.2%) received treatment-dose anticoagulation. Use of treatment-dose anticoagulation without imaging ranged from 0% to 29% across hospitals and increased over time (adjusted odds ratio [aOR], 1.46; 95% CI, 1.31-1.61 per week). Of 1127 patients who ever received

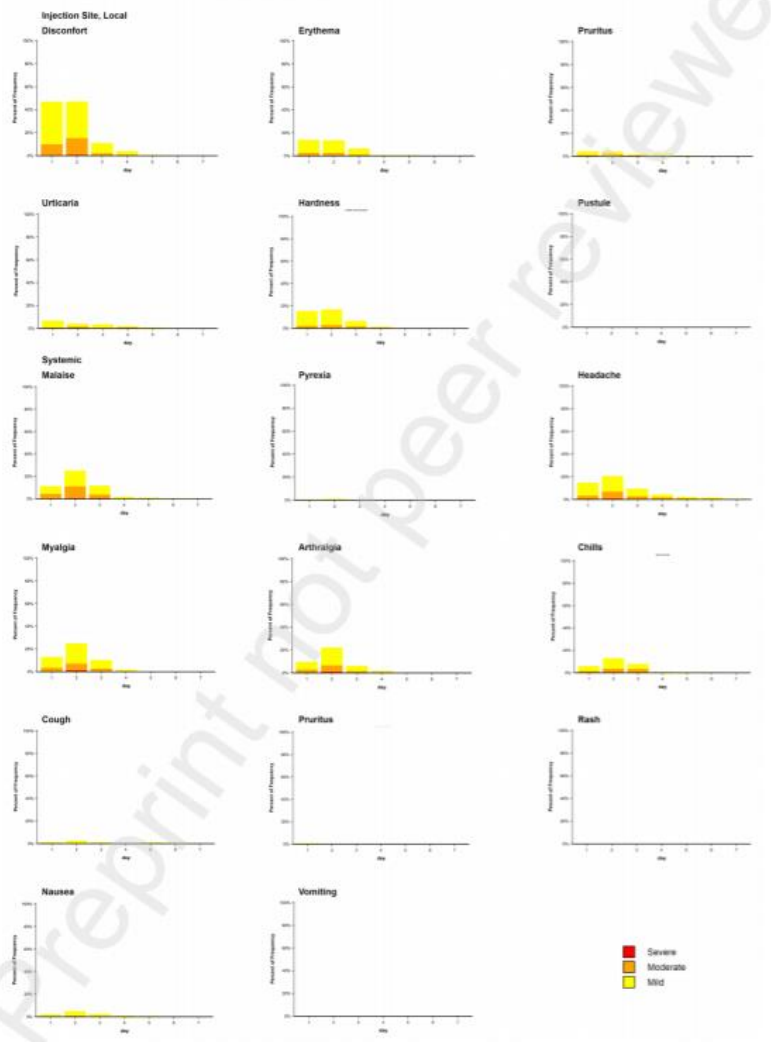
			anticoagulation, 392 (34.8%) missed 2 or more days of prophylaxis. Missed prophylaxis varied from 11% to 61% across hospitals and decreased markedly over time (aOR, 0.89; 95% CI, 0.82-0.97 per week). VTE nonadherence was associated with higher 60-day (adjusted hazard ratio [aHR], 1.31; 95% CI, 1.03-1.67) but not in-hospital mortality (aHR, 0.97; 95% CI, 0.91-1.03). Receiving any dose of anticoagulation (vs no anticoagulation) was associated with lower in-hospital mortality (only prophylactic dose: aHR, 0.36; 95% CI, 0.26-0.52; any treatment dose: aHR, 0.38; 95% CI, 0.25-0.58). However, only the prophylactic dose of anticoagulation remained associated with lower mortality at 60 days (prophylactic dose: aHR, 0.71; 95% CI, 0.51-0.90; treatment dose: aHR, 0.92; 95% CI, 0.63-1.35). Conclusions and Relevance This large, multicenter cohort of patients hospitalized with COVID-19, found evidence of rapid dissemination and implementation of anticoagulation strategies, including use of treatment-dose anticoagulation. As only prophylactic-dose anticoagulation was associated with lower 60-day mortality, prophylactic dosing strategies may be optimal for patients hospitalized with COVID-19.

			
Ministero della Salute https://www.trovanorme.salute.gov.it/norme/renderNormsanPdf?anno=2021&codLeg=81053&parte=1%20&serie=null	Circolare 11 giugno 2021 - Aggiornamento parere CTS vaccini.	Il Ministero della Salute recepisce il parere del CTS che, data l'evoluzione favorevole dello scenario epidemiologico e dunque l'evoluzione del rapporto rischio/beneficio connesso alla vaccinazione con Vaxzevria (AstraZeneca) contro SARS-CoV-2 nelle persone di età inferiore a 60 anni, raccomanda l'uso di tale vaccino solo al di sopra dei 60 anni di età. Per i più giovani che hanno già ricevuto la prima dose, viene raccomandata una seconda dose con vaccino a mRNA.	Facendo seguito alle note circolari prot. n° 14358-07/04/2021-DGPRE, prot. n° 16722-21/04/2021-DGPRE e prot. n°19748-05/05/2021-DGPRE, si inoltra il parere del Comitato tecnico scientifico di cui all'Ordinanza del Capo del Dipartimento della Protezione Civile n. 751 del 2021, acquisito con prot. n° 26245-11/06/2021-DGPRE (ALLEGATO 1), relativo ai vaccini Vaxzevria e Janssen. Alla luce di tali indicazioni il vaccino Vaxzevria viene somministrato solo a persone di età uguale o superiore ai 60 anni (ciclo completo). Per persone che hanno ricevuto la prima dose di tale vaccino e sono al di sotto dei 60 anni di età, il ciclo deve essere completato con una seconda dose di vaccino a mRNA (Comirnaty o Moderna), da somministrare ad una distanza di 8-12 settimane dalla prima dose.

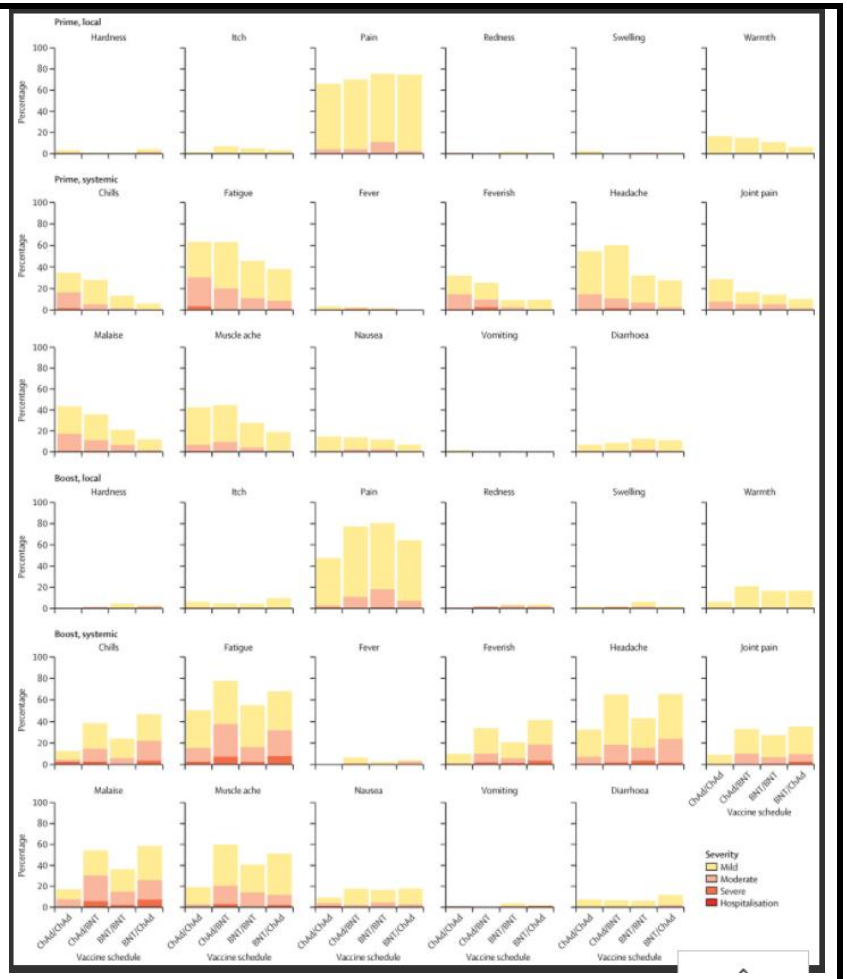
Borobia AM et al Preprint – not peer reviewed https://www.actasanitaria.com/wp-content/uploads/2021/06/SSRN-id3854768.pdf	Reactogenicity and immunogenicity of BNT162b2 in subjects having received a first dose of 2 ChAdOx1S: initial results of a randomised, adaptive, phase 2 trial (CombiVacS)	In una coorte di 663 adulti di età inferiore a 60 anni (media 44 anni) che avevano ricevuto la prima dose di vaccino Vaxzevria/Astrazeneca contro SARS-CoV-2, 2/3 hanno ricevuto a distanza di almeno 8 settimane un richiamo con vaccino Pfizer a mRNA, con una risposta significativa in termini di titolo di IgG neutralizzanti e risposta T-cellulare (studiata tramite un saggio basato su IFN-gamma). Gli effetti avversi sono stati lievi.	Background : There are no immunological data on SARS-CoV-2 heterologous vaccinations schedules in humans. We assessed the immunogenicity and reactogenicity of BNT162b2 (Comirnaty, BioNTech) administered as second dose in participants primed with ChAdOx1-S (Vaxzevria, Astra Zeneca). Methods : We did a phase 2, open-label, adaptive, randomised, controlled clinical trial on adults under 60 years old, vaccinated with a single dose of ChAdOx1-S between 8 and 12 weeks before screening, and no history of SARS-CoV-2 infection (EudraCT No. 2021-001978-37 and NCT04860739).Participants were randomly assigned (2:1) to receive BNT162b2 (0.3 mL, single intramuscular injection) or observation. The primary outcomes were 7-day reactogenicity and 14-day anti-spike IgG response, measured by immunoassays covering SARS-CoV-2 trimeric spike protein and receptor binding domain (RBD). Antibodies functionality and cellular immune response were assessed using a pseudovirus neutralization assay and IFN-gamma immunoassay, respectively. Findings : Between April 24 and April 30, 2021, 676 individuals were randomized (n=450 intervention group, n=226 control group) at 5 sites in Spain, and 663 (441 and 222, respectively) completed the study up to day 14 (mean age 44 [SD 9], 56·5% female). In the intervention group, geometric mean titres (GMT) of IgG-RBD increased from 71·46 BAU/mL (95% CI 59·84-85·33) at baseline to 56·68 (7371·53; 8161·96) at day 14 ($p < 0·0001$). IgG against trimeric spike-protein increased from 98·4 [85.69–112.99] to 3684·87 [3429·87–3958·83]). 100% participants exhibited neutralizing antibodies 14 days after BNT162b2 administration, in comparison to 34.1% at enrolment. A 4-fold increase in cellular immune response was also observed. Reactions were predominantly mild (68·3%) or

			moderate (29·9%), and consisted more frequently on injection site pain (88·2%), induration (35·5%), headache (44·4%) and myalgia (43·3%). 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.

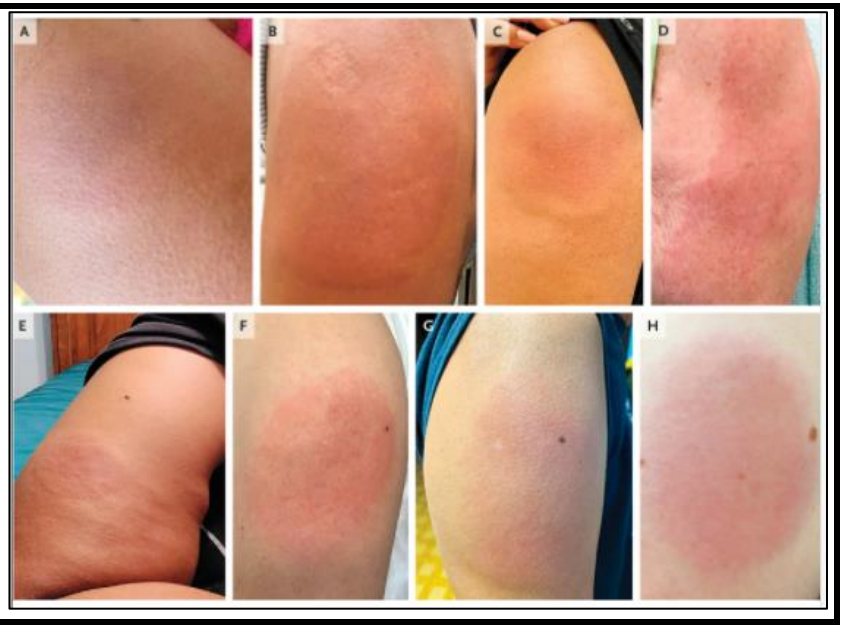
Figure 5. Solicited local and systemic adverse reactions in first 7 days after vaccination as recorded in participant symptom electronic diaries



Ministero de Ciencia e Informacion https://www.isciii.es/Noticias/Noticias/Paginas/Noticias/Presentaci%c3%b3n-resultados-preliminares-CombivacS.aspx	El uso combinado de las vacunas de AstraZeneca y Pfizer contra el SARS-CoV-2 ofrece una potente respuesta inmunitaria	Comunicato stampa del Ministero della Scienza spagnolo e dell'Istituto Caros III in merito ai risultati dello studio CombivacS [testo in Spagnolo].	Los primeros resultados señalan que esta pauta de vacunación heteróloga es altamente inmunogénica y no presenta problemas de reactogenicidad postvacunación diferentes a los ya comunicados en el uso homólogo (en solitario) de esas mismas vacunas; es decir, la respuesta del sistema inmunitario se potencia mucho tras la segunda dosis de la vacuna Comirnaty, mientras que los efectos adversos observados entran dentro de lo esperado, son de carácter leve o moderado y se restringen mayoritariamente a los primeros 2-3 días después de recibir la vacuna. En ningún caso se ha comunicado un ingreso hospitalario secundario al uso de esta pauta de vacunación dentro de este ensayo clínico.
Shaw RH et al The Lancet https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01115-6/fulltext	Heterologous prime-boost COVID-19 vaccination: initial reactogenicity data	Dati iniziali di sicurezza dal trial Com-COV in corso nel Regno Unito, in cui 830 adulti di età superiore a 50 anni ricevono una prima dose con vaccino Vaxzevria/Astrazeneca contro SARS-CoV-2 e quindi vengono randomizzati a ricevere la seconda dose con vaccino a Pfizer mRNA : gli effetti avversi per chi riceve la vaccinazione « eterologa » appaiono più frequenti, anche se di breve durata e al momento non si sono registrate ospedalizzazioni per questo motivo.	Com-COV (ISRCTN 69254139) is a UK multi-centre, participant-masked, randomised heterologous prime-boost COVID-19 vaccination study comparing all four prime-boost permutations of the ChAd and BNT vaccines both at 28-day and 84-day prime-boost intervals. Participants are 50 years and older with no or mild-to-moderate, well controlled comorbidity and were recruited across eight sites. The protocol is available online.

			
Callaway E et al Nature https://www.nature.com/articles/d41586-021-01359-3	Mix-and-match COVID vaccines trigger potent immune response	Commento ai due lavori precedenti in merito all'utilizzo di una strategia di vaccinazione « eterologa » contro SARS-CoV-2. Rimane aperta la questione delle	Preliminary results from a trial of more than 600 people are the first to show the benefits of combining different vaccines.

		eventuali dosi successive alla seconda.	
Samarakoon U et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMc2108620?query=featured_home	Delayed Large Local Reactions to mRNA Covid-19 Vaccines in Blacks, Indigenous Persons, and People of Color	Rassegna iconografica di reazioni avverse locali ritardate dopo vaccini a mRNA contro SARS-CoV-2 in persone di etnia non caucasica.	From February 10, 2021, through April 23, 2021, a total of 1422 reports of postvaccination reactions were submitted to a Covid-19 vaccine allergy case registry (https://allergyresearch.massgeneral.org. opens in new tab). Of these reactions, 510 (36%) were delayed large local reactions that were reported by patients (64%) and clinicians (36%). The mean (±SD) age of the patients with delayed large local reactions was 50±15 years (range, 21 to 91), and the majority were women (472 [93%]). Delayed large local reactions were reported after the receipt of the mRNA-1273 vaccine in 459 patients (90%), after the receipt of the BNT162b2 vaccine in 35 (7%), and after the receipt of other or unknown Covid-19 vaccines in 16 (3%).

			 A B C D E F G H