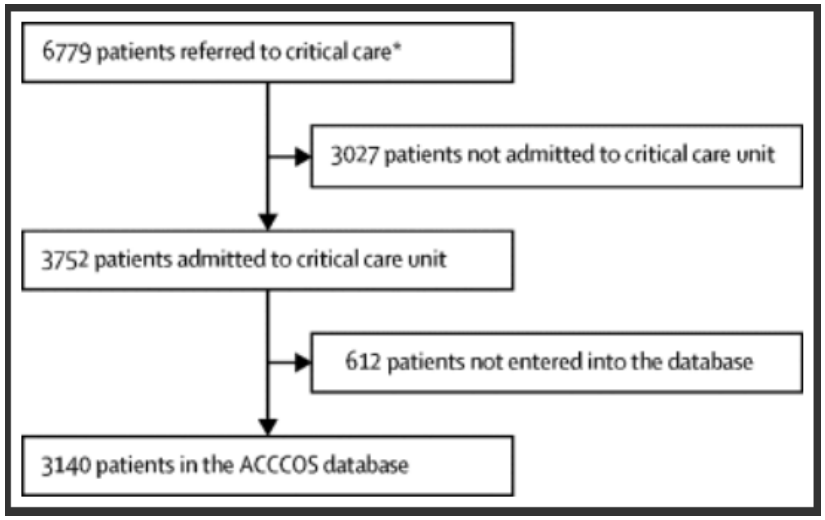
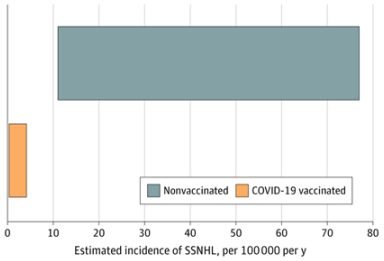
RICERCA BIBLIOGRAFICA COVID 19 SETTIMANA 24.05 – 30.05.2021 FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE DOTT.SSA ELEONORA TADDEI			
AUTORE/RIVISTA	**TITOLO**	**OUTCOME PRINCIPALE**	**ABSTRACT**
Yuan M et al Science https://science.sciencemag.org/content/early/2021/05/19/science.abh1139	Structural and functional ramifications of antigenic drift in recent SARS-CoV-2 variants	Effetto delle mutazioni tipiche delle varianti di SARS-CoV-2 sul legame con le principali famiglie di anticorpi neutralizzanti prodotte in seguito all'infezione.	Neutralizing antibodies (nAbs) elicited against the receptor-binding site (RBS) of the spike protein of wild-type SARS-CoV-2 are generally less effective against recent variants of concern. RBS residues E484, K417 and N501 are mutated in variants first described in South Africa (B.1.351) and Brazil (P.1). We analyzed their effects on ACE2 binding and K417N and E484K mutations on nAbs isolated from COVID-19 patients. Binding and neutralization of the two most frequently elicited antibody families (IGHV3-53/3-66 and IGHV1-2), which can both bind the RBS in alternate binding modes, are abrogated by K417N, E484K, or both. These effects can be structurally explained by their extensive interactions with RBS nAbs. However, nAbs to the more conserved, cross-neutralizing CR3022 and S309 sites were largely unaffected. The results have implications for next-generation vaccines and antibody therapies.

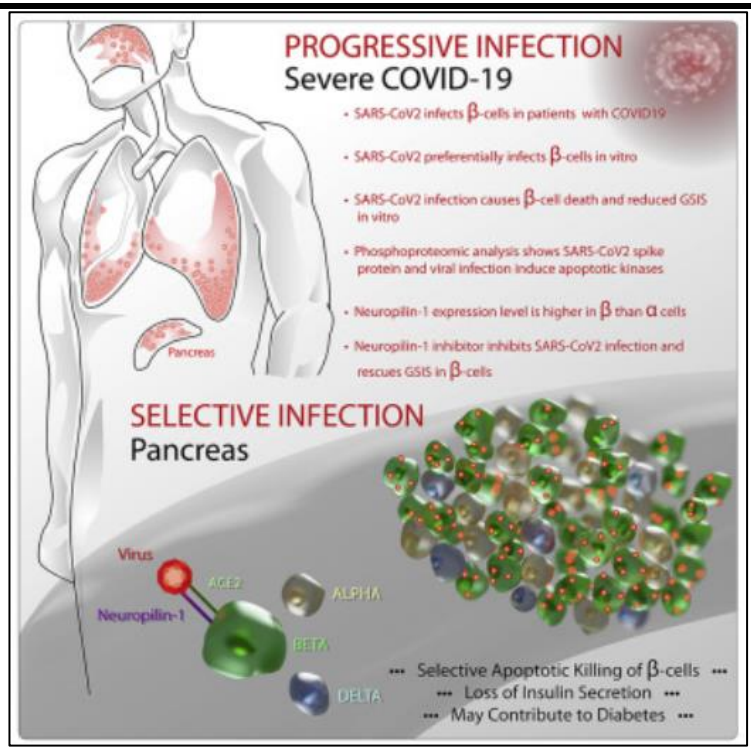
The African COVID-19 Critical Care Outcomes Study (ACCCOS) Investigators The Lancet https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00441-4/fulltext	Patient care and clinical outcomes for patients with COVID-19 infection admitted to African high-care or intensive care units (ACCCOS): a multicentre, prospective, observational cohort study	Studio di coorte multicentrico sui pazienti che hanno richiesto cure intensive per COVID-19 in 64 ospedali africani : mortalità 48%.	Background : There have been insufficient data for African patients with COVID-19 who are critically ill. The African COVID-19 Critical Care Outcomes Study (ACCCOS) aimed to determine which resources, comorbidities, and critical care interventions are associated with mortality in this patient population. Methods : The ACCCOS study was a multicentre, prospective, observational cohort study in adults (aged 18 years or older) with suspected or confirmed COVID-19 infection who were referred to intensive care or high-care units in 64 hospitals in ten African countries (ie, Egypt, Ethiopia, Ghana, Kenya, Libya, Malawi, Mozambique, Niger, Nigeria, and South Africa). The primary outcome was in-hospital mortality censored at 30 days. We studied the factors (ie, human and facility resources, patient comorbidities, and critical care interventions) that were associated with mortality in these adult patients. This study is registered on ClinicalTrials.gov, NCT04367207. Findings : From May to December, 2020, 6779 patients were referred to critical care. Of these, 3752 (55·3%) patients were admitted and 3140 (83·7%) patients from 64 hospitals in ten countries participated (mean age 55·6 years; 1890 [60·6%] of 3118 participants were male). The hospitals had a median of two intensivists (IQR 1–4) and pulse oximetry was available to all patients in 49 (86%) of 57 sites. In-hospital mortality within 30 days of admission was 48·2% (95% CI 46·4–50·0; 1483 of 3077 patients). Factors that were independently associated with mortality were increasing age per year (odds ratio 1·03; 1·02–1·04); HIV/AIDS (1·91; 1·31–2·79); diabetes (1·25; 1·01–1·56); chronic liver disease (3·48; 1·48–8·18); chronic kidney disease (1·89; 1·28–2·78); delay in admission due to a shortage of resources (2·14; 1·42–3·22); quick sequential organ failure assessment score at admission (for one

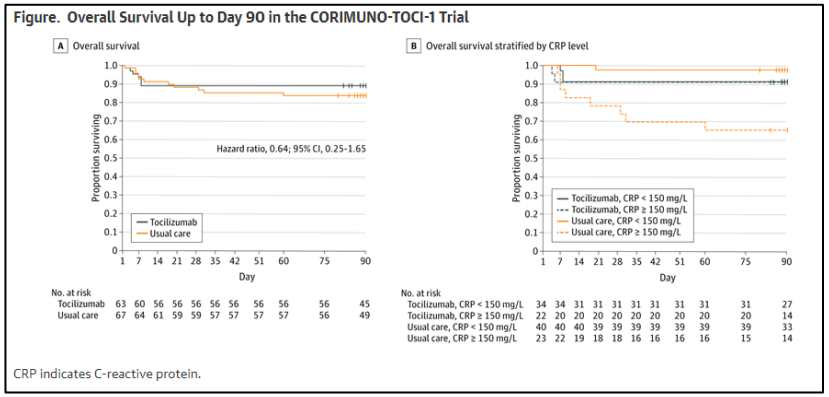
			factor [1·44; 1·01–2·04], for two factors [2·0; 1·33–2·99], and for three factors [3·66, 2·12–6·33]); respiratory support (high flow oxygenation [2·72; 1·46–5·08]; continuous positive airway pressure [3·93; 2·13–7·26]; invasive mechanical ventilation [15·27; 8·51–27·37]); cardiorespiratory arrest within 24 h of admission (4·43; 2·25–8·73); and vasopressor requirements (3·67; 2·77–4·86). Steroid therapy was associated with survival (0·55; 0·37–0·81). There was no difference in outcome associated with female sex (0·86; 0·69–1·06). Interpretation : Mortality in critically ill patients with COVID-19 is higher in African countries than reported from studies done in Asia, Europe, North America, and South America. Increased mortality was associated with insufficient critical care resources, as well as the comorbidities of HIV/AIDS, diabetes, chronic liver disease, and kidney disease, and severity of organ dysfunction at admission. 

Salyer SJ et al The Lancet https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00632-2/fulltext	The first and second waves of the COVID-19 pandemic in Africa: a cross-sectional study	Studio cross sectional dei casi di infezione da SARS-CoV-2 nel continente africano durante la prima e la seconda ondata pandemica.	Background : Although the first wave of the COVID-19 pandemic progressed more slowly in Africa than the rest of the world, by December, 2020, the second wave appeared to be much more aggressive with many more cases. To date, the pandemic situation in all 55 African Union (AU) Member States has not been comprehensively reviewed. We aimed to evaluate reported COVID-19 epidemiology data to better understand the pandemic's progression in Africa. Methods : We did a cross-sectional analysis between Feb 14 and Dec 31, 2020, using COVID-19 epidemiological, testing, and mitigation strategy data reported by AU Member States to assess trends and identify the response and mitigation efforts at the country, regional, and continent levels. We did descriptive analyses on the variables of interest including cumulative and weekly incidence rates, case fatality ratios (CFRs), tests per case ratios, growth rates, and public health and social measures in place. Findings : As of Dec 31, 2020, African countries had reported 2 763 421 COVID-19 cases and 65 602 deaths, accounting for 3·4% of the 82 312 150 cases and 3·6% of the 1 798 994 deaths reported globally. Nine of the 55 countries accounted for more than 82·6% (2 283 613) of reported cases. 18 countries reported CFRs greater than the global CFR (2·2%). 17 countries reported test per case ratios less than the recommended ten to 30 tests per case ratio range. At the peak of the first wave in Africa in July, 2020, the mean daily number of new cases was 18 273. As of Dec 31, 2020, 40 (73%) countries had experienced or were experiencing their second wave of cases with the continent reporting a mean of 23 790 daily new cases for epidemiological week 53. 48 (96%) of 50 Member States had five or more stringent public health and social measures in place by April 15, 2020, but this number had decreased to 36 (72%)

			as of Dec 31, 2020, despite an increase in cases in the preceding month. Interpretation : Our analysis showed that the African continent had a more severe second wave of the COVID-19 pandemic than the first, and highlights the importance of examining multiple epidemiological variables down to the regional and country levels over time. These country-specific and regional results informed the implementation of continent-wide initiatives and supported equitable distribution of supplies and technical assistance. Monitoring and analysis of these data over time are essential for continued situational awareness, especially as Member States attempt to balance controlling COVID-19 transmission with ensuring stable economies and livelihoods.
Formeister EJ et al JAMA https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2780288?resultClick=1	Preliminary Analysis of Association Between COVID-19 Vaccination and Sudden Hearing Loss Using US Centers for Disease Control and Prevention Vaccine Adverse Events Reporting System Data.	Nessuna associazione fra i vaccini a mRNA e la perdita dell'udito.	Between December 14, 2020, and March 2, 2021, 86 553 330 SARS-CoV-2 vaccine doses were administered in the US. Demographic and clinical characteristics of reported "most likely" cases of SSNHL are shown in the Table. Because VAERS reports are unverified, susceptible to underreporting bias, and the number of unique individuals within the vaccine cohort is not known exactly, we performed a sensitivity analysis and estimated a minimum and maximum incidence by tuning these assumptions. The results of these incidence estimates compared with the known population incidence of SSNHL are presented in the Figure and demonstrate that the incidence of SSNHL occurring after COVID-19 vaccination does not exceed that of the general population, and may be lower.

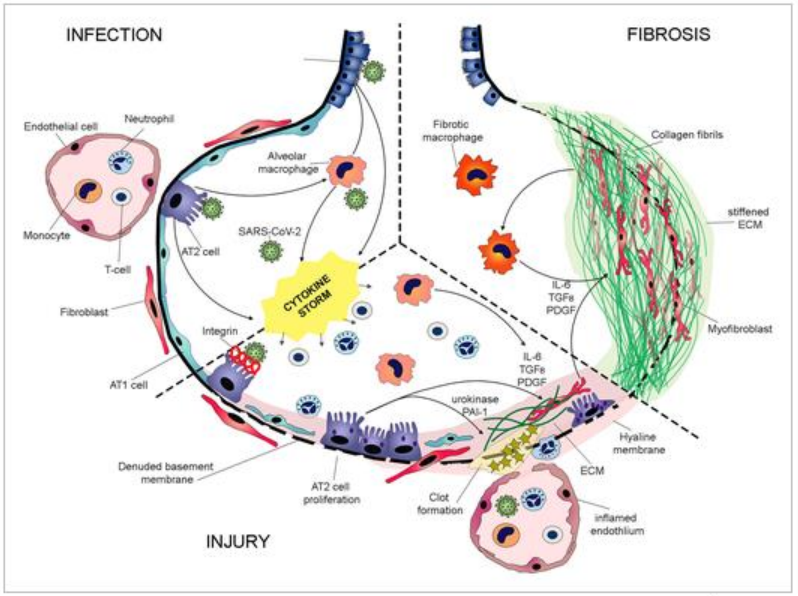
			Figure. Comparison of Estimated Incidence Range of Sudden Sensorineural Hearing Loss (SSNHL) That Occurred After COVID-19 Vaccination  Sensitivity analysis for COVID-19 vaccinated Source / Minimum incidence / Maximum incidence Cases: 40 / 147 Population size: 86 553 330[a] / 43 276 665[b] VAERS underreporting bias: 0% / 100% Incidence[c]: 0.3 / 4.1 [a]Single dose per person. [b]Two doses per person. [c]Per 100 000 per y. Based on Vaccine Adverse Events Reporting System (VAERS) reports of known SSNHL incidence, with an associated sensitivity analysis underlying determination of incidence estimates for the COVID-19 vaccine cohort.
Wu CT et al Cell Metabolism https://www.cell.com/cell-metabolism/fulltext/S1550-4131(21)00230-8	SARS-CoV-2 infects human pancreatic β-cells and elicits β-cell impairment	Le cellule beta delle isole di Langerhans esprimono scarsamente il recettore ACE2, ma possiedono altri recettori che possono consentire l'ingresso di SARS-CoV-2. Da ciò potrebbero derivare le alterazioni glicemiche spesso osservate in corso di infezione.	Emerging evidence points towards an intricate relationship between the pandemic of coronavirus disease 2019 (COVID-19) and diabetes. While pre-existing diabetes is associated with severe COVID-19, it is unclear if COVID-19 severity is a cause or consequence of diabetes. To mechanistically link COVID-19 to diabetes, we tested whether insulin-producing pancreatic β-cells can be infected by SARS-CoV-2 and cause β-cell depletion. We found that the SARS-CoV-2 receptor, ACE2 and related entry factors (TMPRSS2, NRP1, TRFC) are expressed in β-cells, with selectively high expression of NRP1. We discovered that SARS-CoV-2 infects human pancreatic β-cells in patients who succumbed to COVID-19 and selectively infects human islet β-cells in vitro. We demonstrated SARS-CoV-2 infection attenuates pancreatic insulin levels and secretion, and induces β-cell apoptosis, each rescued by NRP1 inhibition. Phosphoproteomic pathway analysis of infected islets indicates apoptotic β-cell signaling, similar to that observed in Type 1 diabetes (T1D). In summary, our study shows SARS-CoV-2 can directly induce β-cell killing.

			
Harrington P et al Leukemia https://www.nature.com/articles/s41375-021-01300-7	Single dose of BNT162b2 mRNA vaccine against SARS-CoV-2 induces high frequency of neutralising antibody and polyfunctional T-cell responses in patients with myeloproliferative neoplasms	Buona risposta alla prima dose di vaccino a mRNA contro SARS-CoV-2 in 21 pazienti con malattie mieloproliferative.	Patients with a WHO defined diagnosis of an MPN presenting to our clinic were recruited in accordance with the regional research and ethics review board, with sampling at baseline and median of 21 days (IQR 21–21) following first injection of 30 µg BNT162b2. Clinical characteristics and adverse events are summarised in Table 1, with all adverse events reported within 7 days after administration of the vaccine considered to be related to the vaccine. The vaccine was safe and generally well tolerated with 57.1% (12) patients reporting localised inflammation and 47.6% (10) of patients reporting systemic side effects including flu-like illness, fatigue and gastrointestinal symptoms, following injection.

Mariette X et al JAMA https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2780021?resultClick=1	Effectiveness of Tocilizumab in Patients Hospitalized With COVID-19 A Follow-up of the CORIMUNO-TOCI-1 Randomized Clinical Trial	Analis post hoc dei dati di un trial sull'utilizzo di tocilizumab in pazienti ospedalizzati per COVID-19, in cui si dimostra un vantaggio in sopravvivenza e necessità di ventilazione meccanica nei pazienti trattati con tocilizumab se PCR > 150 mg/dl.	We previously published a trial of tocilizumab in hospitalized patients who were receiving oxygen (rate, ≥3 L/min) but did not require high-flow or mechanical ventilation.3 The study met its primary composite end point, which was the proportion of patients who required noninvasive ventilation or intubation or who died at day 14, but found no survival difference at day 28. In this follow-up article, we extended follow-up to 90 days and examined whether survival varied with baseline CRP levels.  Figure. Overall Survival Up to Day 90 in the CORIMUNO-TOCI-1 Trial A Overall survival B Overall survival stratified by CRP level Proportion surviving Day Hazard ratio, 0.64; 95% CI, 0.25-1.65 Tocilizumab Usual care Tocilizumab, CRP < 150 mg/L Tocilizumab, CRP ≥ 150 mg/L Usual care, CRP < 150 mg/L Usual care, CRP ≥ 150 mg/L No. at risk Tocilizumab 63 60 56 56 56 56 56 56 56 56 45 Usual care 67 64 61 59 59 57 57 57 57 56 49 Tocilizumab, CRP < 150 mg/L 34 34 31 31 31 31 31 31 31 31 27 Tocilizumab, CRP ≥ 150 mg/L 22 20 20 20 20 20 20 20 20 20 14 Usual care, CRP < 150 mg/L 40 40 40 39 39 39 39 39 39 39 33 Usual care, CRP ≥ 150 mg/L 23 22 19 18 18 16 16 16 16 15 14 CRP indicates C-reactive protein.
Hodgson D et al Eurosurveillance https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.20.2100428	The potential for vaccination-induced herd immunity against the SARS-CoV-2 B.1.1.7 variant	Modello di contenimento della pandemia di COVID-19 in un contesto a bassa sieroprevalenza : in assenza di precauzioni (distanziamento, mascherine) il vaccino potrebbe prevenire nuovi casi se avesse un'efficacia superiore a 80% su tutta la popolazione, anche i bambini.	Initial reports of vaccine effectiveness against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus responsible for coronavirus disease (COVID-19), have suggested a substantial reduction of the risk of infection [1]. Nevertheless, with the emergence of more transmissible variants such as B.1.1.7 [2], how large-scale immunisation programmes against SARS-CoV-2 will perform is currently unclear. This study assesses the potential of COVID-19 vaccination to generate herd immunity and takes into account vaccine effectiveness, naturally-acquired immunity and achievable vaccination coverage (depending on the population age structure), as well as two transmissibility scenarios ((i) with pre-B.1.1.7, and (ii) with exclusively B.1.1.7 variants).

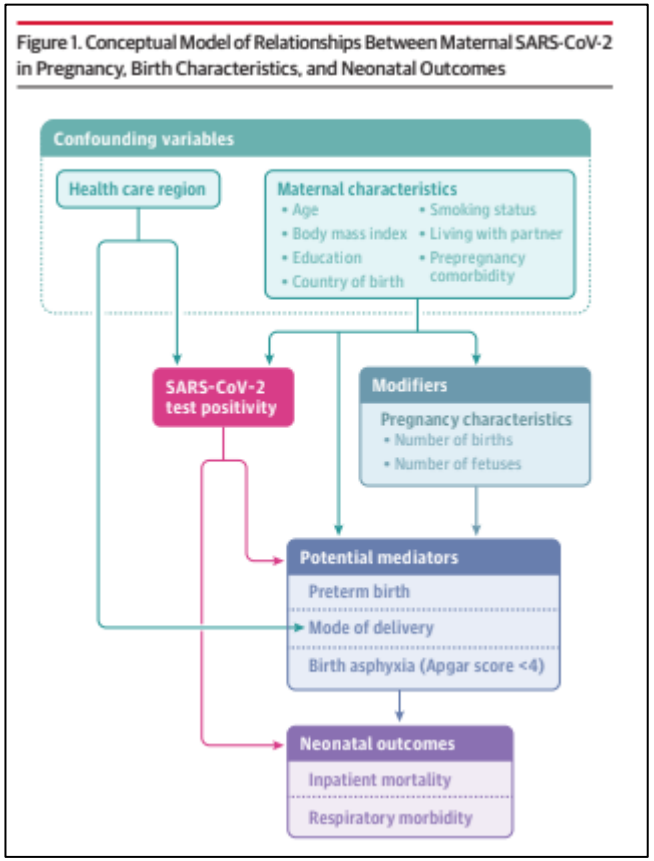
Bboum Y et al The Lancet https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00719-4/fulltext	Africa needs local solutions to face the COVID-19 pandemic	Soluzioni diversificate per gestire la pandemia di COVID-19 nel continente africano.	An important conclusion from the Article by Salyer and colleagues is the need for country-specific solutions. No one-size-fits-all approach will succeed within a continent as diverse as Africa. Countries with a high number of COVID-19 deaths desperately need vaccination to prevent further illness and deaths from severe COVID-19. Some countries might not request the vaccines because of their COVID-19 epidemiology, whereas other countries have a greater need but will be limited by the 20% allowance. By contrast, countries with low case fatality ratios could instead invest in community engagement, health system strengthening, surveillance, and case reporting to adequately handle high case counts during this wave and beyond.
Istituto Superiore di Sanità https://www.iss.it/news/-/asset_publisher/gJ3hFqMQsykM/content/id/5746202	Prevalenza e distribuzione delle varianti del virus SARS-CoV-2 di interesse per la sanità pubblica in Italia	Il rapporto integra i dati sulle varianti del virus di interesse per la sanità pubblica circolanti in Italia provenienti dall'indagine rapida di prevalenza condotta dall'Iss con quelli sulla distribuzione delle stesse varianti riportata dalle Regioni e Province Autonome (PA) e dal Laboratorio nazionale di riferimento per SARS-CoV-2 dell'Istituto Superiore Sanità.	La variante del virus SARS-CoV-2 prevalentemente circolante in Italia è la variante VOC-202012/01 (cosiddetta variante UK) - lignaggio B.1.1.7, caratterizzata da una elevata trasmissibilità. Il lignaggio P.1 (cosiddetta variante brasiliana) ha una diffusione maggiore in alcune Regioni italiane. La prevalenza di altre varianti del virus SARS-CoV-2 di interesse per la sanità pubblica è <1% nel nostro paese, ad eccezione della cosiddetta variante nigeriana (1,17%). È necessario continuare a monitorare con grande attenzione la circolazione delle varianti del virus SARS-CoV-2 ed in particolare la presenza di mutazioni riconducibili ad una maggiore trasmissibilità e/o associate ad un potenziale immune escape.
Alison J et al Immunological Reviews	COVID-19 and pulmonary fibrosis: A potential role for lung epithelial cells and fibroblasts.	Processi fisiopatologici in comune fra fibrosi polmonare e infezione da SARS-CoV-2.	The COVID-19 pandemic rapidly spread around the world following the first reports in Wuhan City, China in late 2019. The disease, caused by the novel SARS-CoV-2 virus, is primarily a respiratory condition that can affect numerous other bodily systems including the cardiovascular and gastrointestinal systems. The disease ranges

https://onlinelibrary.wiley.com/doi/10.1111/imr.12977			in severity from asymptomatic through to severe acute respiratory distress requiring intensive care treatment and mechanical ventilation, which can lead to respiratory failure and death. It has rapidly become evident that COVID-19 patients can develop features of interstitial pulmonary fibrosis, which in many cases persist for as long as we have thus far been able to follow the patients. Many questions remain about how such fibrotic changes occur within the lung of COVID-19 patients, whether the changes will persist long term or are capable of resolving, and whether post-COVID-19 pulmonary fibrosis has the potential to become progressive, as in other fibrotic lung diseases. This review brings together our existing knowledge on both COVID-19 and pulmonary fibrosis, with a particular focus on lung epithelial cells and fibroblasts, in order to discuss common pathways and processes that may be implicated as we try to answer these important questions in the months and years to come.

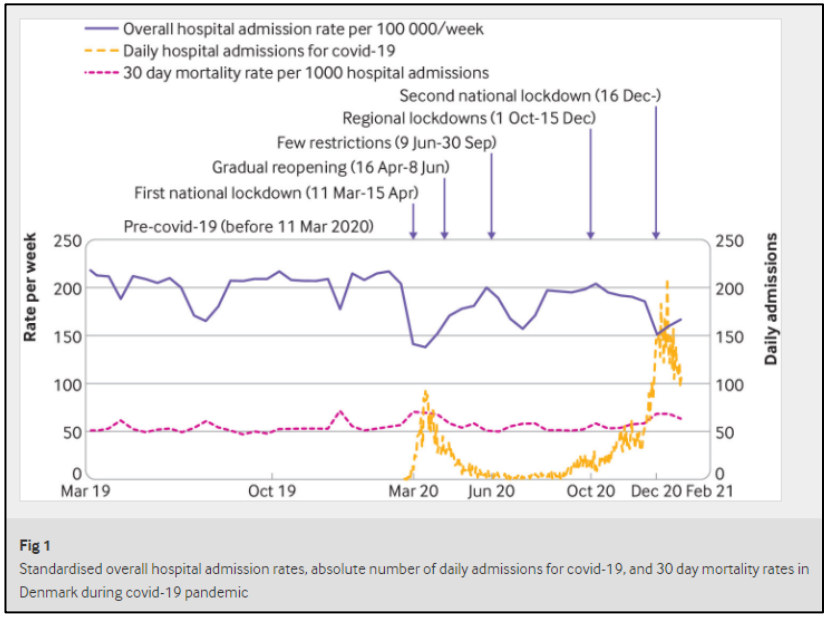
			
Wilson N et al Scientific Report https://www.nature.com/articles/s41598-021-89807-y	Estimating the impact of control measures to prevent outbreaks of COVID-19 associated with air travel into a COVID-19-free country	Modello del rischio che comportano gli ingressi dall'estero in un Paese che abbia ridotto significativamente la circolazione di SARS-CoV-2 e strategie di prevenzione.	We aimed to estimate the risk of COVID-19 outbreaks associated with air travel to a COVID-19-free country [New Zealand (NZ)]. A stochastic version of the SEIR model CovidSIM v1.1, designed specifically for COVID-19 was utilised. We first considered historical data for Australia before it eliminated COVID-19 (equivalent to an outbreak generating 74 new cases/day) and one flight per day to NZ with no interventions in place. This gave a median time to an outbreak of 0.2 years (95% range of simulation results: 3 days to 1.1 years) or a mean of 110 flights per outbreak. However, the combined use of a pre-flight PCR test of saliva, three subsequent PCR tests (on days 1, 3 and 12 in NZ), and various other interventions (mask use and contact tracing) reduced this risk to one outbreak after a median of 1.5 years (20 days to 8.1 years). A pre-flight test plus 14 days quarantine was an even more effective strategy (4.9 years; 2,594 flights). For a much lower prevalence

			(representing only two new community cases per week in the whole of Australia), the annual risk of an outbreak with no interventions was 1.2% and had a median time to an outbreak of 56 years. In contrast the risks associated with travellers from Japan and the United States was very much higher and would need quarantine or other restrictions. Collectively, these results suggest that multi-layered interventions can markedly reduce the risk of importing the pandemic virus via air travel into a COVID-19-free nation. For some low-risk source countries, there is the potential to replace 14-day quarantine with alternative interventions. However, all approaches require public and policy deliberation about acceptable risks, and continuous careful management and evaluation.
Norman M et al JAMA https://pubmed.ncbi.nlm.nih.gov/33914014/	Association of Maternal SARS-CoV-2 Infection in Pregnancy With Neonatal Outcomes	Effetto dell'infezione materna da SARS-CoV-2 in gravidanza sugli outcome neonatali in una coorte svedese.	Importance: The outcomes of newborn infants of women testing positive for SARS-CoV-2 in pregnancy is unclear. Objective: To evaluate neonatal outcomes in relation to maternal SARS-CoV-2 test positivity in pregnancy. Design, setting, and participants: Nationwide, prospective cohort study based on linkage of the Swedish Pregnancy Register, the Neonatal Quality Register, and the Register for Communicable Diseases. Ninety-two percent of all live births in Sweden between March 11, 2020, and January 31, 2021, were investigated for neonatal outcomes by March 8, 2021. Infants with malformations were excluded. Infants of women who tested positive for SARS-CoV-2 were matched, directly and using propensity scores, on maternal characteristics with up to 4 comparator infants. Exposures: Maternal test positivity for SARS-CoV-2 in pregnancy. Main outcomes and measures: In-hospital mortality; neonatal resuscitation; admission for neonatal care; respiratory, circulatory, neurologic, infectious, gastrointestinal, metabolic, and hematologic

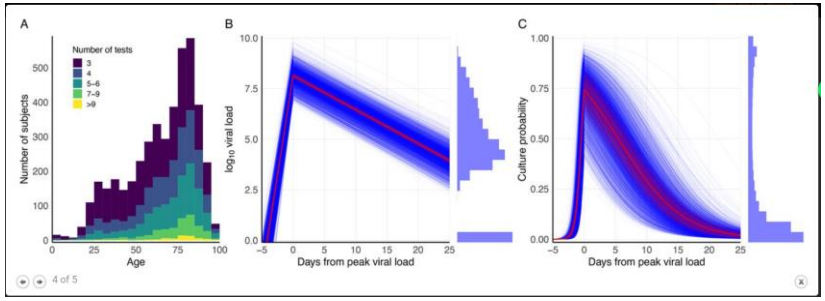
			disorders and their treatments; length of hospital stay; breastfeeding; and infant test positivity for SARS-CoV-2. Results: Of 88 159 infants (49.0% girls), 2323 (1.6%) were delivered by mothers who tested positive for SARS-CoV-2. The mean gestational age of infants of SARS-CoV-2-positive mothers was 39.2 (SD, 2.2) weeks vs 39.6 (SD, 1.8) weeks for comparator infants, and the proportions of preterm infants (gestational age <37 weeks) were 205/2323 (8.8%) among infants of SARS-CoV-2-positive mothers and 4719/85 836 (5.5%) among comparator infants. After matching on maternal characteristics, maternal SARS-CoV-2 test positivity was significantly associated with admission for neonatal care (11.7% vs 8.4%; odds ratio [OR], 1.47; 95% CI, 1.26-1.70) and with neonatal morbidities such as respiratory distress syndrome (1.2% vs 0.5%; OR, 2.40; 95% CI, 1.50-3.84), any neonatal respiratory disorder (2.8% vs 2.0%; OR, 1.42; 95% CI, 1.07-1.90), and hyperbilirubinemia (3.6% vs 2.5%; OR, 1.47; 95% CI, 1.13-1.90). Mortality (0.30% vs 0.12%; OR, 2.55; 95% CI, 0.99-6.57), breastfeeding rates at discharge (94.4% vs 95.1%; OR, 0.84; 95% CI, 0.67-1.05), and length of stay in neonatal care (median, 6 days in both groups; difference, 0 days; 95% CI, -2 to 7 days) did not differ significantly between the groups. Twenty-one infants (0.90%) of SARS-CoV-2-positive mothers tested positive for SARS-CoV-2 in the neonatal period; 12 did not have neonatal morbidity, 9 had diagnoses with unclear relation to SARS-CoV-2, and none had congenital pneumonia. Conclusions and relevance: In a nationwide cohort of infants in Sweden, maternal SARS-CoV-2 infection in pregnancy was significantly associated with small increases in some neonatal morbidities. Given the small numbers of events for many of the

			outcomes and the large number of statistical comparisons, the findings should be interpreted as exploratory. 
Bodilsen J et al BMJ https://www.bmj.com/content/373/bmj.n1135	Hospital admission and mortality rates for non-covid diseases in Denmark during covid-19 pandemic: nationwide population based cohort study	Riduzione dei ricoveri per diagnosi diverse da COVID-19 durante la prima « ondata» in Danimarca, con elevata mortalità per le stesse condizioni : impatto della pandemia sulla salute dei non infettati.	Objective To determine the incidence of hospital admissions and associated mortality rates for non-covid medical conditions during the covid-19 pandemic. Design Nationwide, population based cohort study. Setting Denmark from 13 March 2019 to 27 January 2021. Participants All Danish residents >1 year of age.

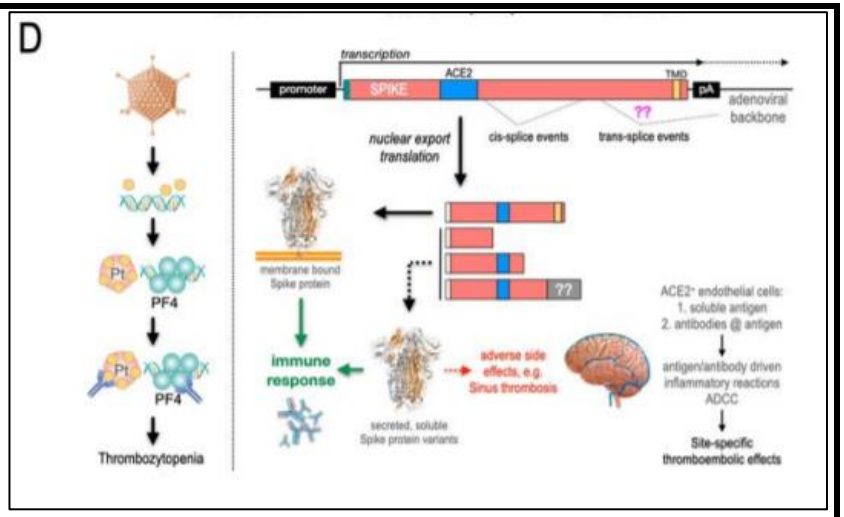
			Main outcomes measures Population based healthcare registries that encompass the entire Danish population were used to compare hospital admission and mortality rates during the covid-19 pandemic (from 11 March 2020 to 27 January 2021) with the prepandemic baseline data (from 13 March 2019 to 10 March 2020). Hospital admissions were categorised as covid-19 when patients were assigned a diagnosis code for covid-19 within five days of admission. All patients were followed until migration, death, or end of follow-up, whichever came first. Rate ratios for hospital admissions were computed using Poisson regression and were directly standardised using the Danish population on 1 January 2019 as reference. 30 day mortality rate ratios were examined by Cox regression, adjusted for age and sex, and covid-19 diagnosis was used as a competing risk. Results 5 753 179 residents were identified during 567.8 million person weeks of observation, with 1 113 705 hospital admissions among 675 447 people. Compared with the prepandemic baseline period (mean hospital admission rate 204.1 per 100 000/week), the overall hospital admission rate for non-covid-19 conditions decreased to 142.8 per 100 000/week (rate ratio 0.70, 95% confidence interval 0.66 to 0.74) after the first national lockdown, followed by a gradual return to baseline levels until the second national lockdown when it decreased to 158.3 per 100 000/week (0.78, 0.73 to 0.82). This pattern was mirrored for most major diagnosis groups except for non-covid-19 respiratory diseases, nervous system diseases, cancer, heart failure, sepsis, and non-covid-19 respiratory infections, which remained lower throughout the study period. Overall 30 day mortality rates were higher during the first national lockdown (mortality rate ratio 1.28, 95% confidence interval 1.23 to 1.32) and the second national lockdown

			(1.20, 1.16 to 1.24), and these results were similar across most major diagnosis groups. For non-covid-19 respiratory diseases, cancer, pneumonia, and sepsis, the 30 day mortality rate ratios were also higher between lockdown periods. Conclusions Hospital admissions for all major non-covid-19 disease groups decreased during national lockdowns compared with the prepandemic baseline period. Additionally, mortality rates were higher overall and for patients admitted to hospital with conditions such as respiratory diseases, cancer, pneumonia, and sepsis. Increased attention towards management of serious non-covid-19 medical conditions is warranted.  **Fig 1** Standardised overall hospital admission rates, absolute number of daily admissions for covid-19, and 30 day mortality rates in Denmark during covid-19 pandemic
Ader F et l Clinical Microbiology and Infection	An open-label randomized, controlled trial of the effect of lopinavir/ritonavir, lopinavir/ritonavir plus IFN-	Assenza di effetto sul miglioramento clinico al giorno 15 di pazienti ricoverati per COVID-19 da parte di idrossiclorochina e	Objectives We evaluated the clinical, virological and safety outcomes of lopinavir/ritonavir, lopinavir/ritonavir-interferon (IFN)-β-1a, hydroxychloroquine or remdesivir in comparison to standard of care

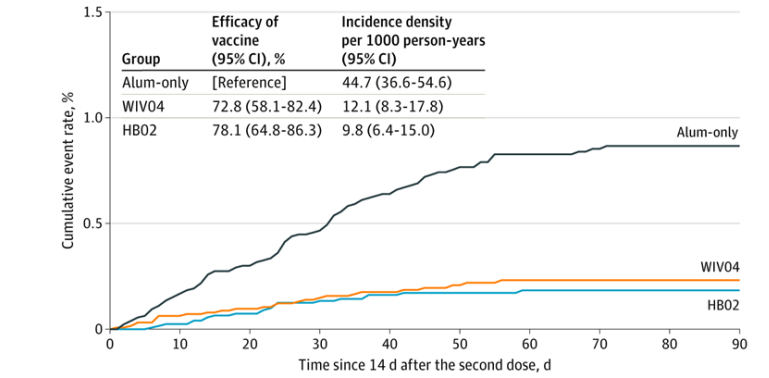
https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00259-7/fulltext	β-1a and hydroxychloroquine in hospitalized patients with COVID-19	lopinavir/ritonavir con eventuale aggiunta di interferone beta.	(control) in COVID-19 inpatients requiring oxygen and/or ventilatory support. Methods We conducted a phase 3 multi-centre open-label, randomized 1:1:1:1:1, adaptive, controlled trial (DisCoVeRy), add-on trial to Solidarity (NCT04315948, EudraCT2020-000936-23). The primary outcome was the clinical status at day 15, measured by the WHO 7-point ordinal scale. Secondary outcomes included SARS-CoV-2 quantification in respiratory specimens, pharmacokinetic and safety analyses. We report the results for the lopinavir/ritonavir-containing arms and for the hydroxychloroquine arm, which were stopped prematurely. Results The intention-to-treat population included 583 participants (lopinavir/ritonavir, n=145; lopinavir/ritonavir-IFN-β-1a, n=145; hydroxychloroquine, n=145; control, n=148), among whom 418 (71.7%) were male, the median age was 63 years (IQR, 54-71) and 211 (36.2%) had a severe disease. The day-15 clinical status was not improved with investigational treatments: lopinavir/ritonavir versus control, adjusted odds ratio (aOR) 0.83, (95% confidence interval [CI] 0.55-1.26, P=0.39); lopinavir/ritonavir-IFN-β-1a versus control, aOR 0.69 (95%CI 0.45-1.04, P=0.08); hydroxychloroquine versus control, aOR 0.93 (95%CI 0.62-1.41, P=0.75). No significant effect of investigational treatment was observed on SARS-CoV-2 clearance. Trough plasma concentrations of lopinavir and ritonavir were higher than those expected, while those of hydroxychloroquine were those expected with the dosing regimen. The occurrence of Serious Adverse Events was significantly higher in participants allocated to the lopinavir/ritonavir-containing arms. Conclusion

			In adults hospitalized for COVID-19, lopinavir/ritonavir, lopinavir/ritonavir-IFN-ß-1a and hydroxychloroquine did not improve the clinical status at day 15, nor SARS-CoV-2 clearance in respiratory tract specimens.
Jones TC et al Science https://science.sciencemag.org/content/early/2021/05/24/science.abi5273	Estimating infectiousness throughout SARS-CoV-2 infection course	Ampio studio sull'infettività dei soggetti con infezione da SARS-CoV-2 : il picco (di probabilità di isolare il virus in coltura) si avrebbe a 4.3 giorni dall'inizio dello shedding.	Two elementary parameters for quantifying viral infection and shedding are viral load and whether samples yield a replicating virus isolate in cell culture. We examined 25,381 German SARS-CoV-2 cases, including 6110 from test centres attended by pre-symptomatic, asymptomatic, and mildly-symptomatic (PAMS) subjects, 9519 who were hospitalised, and 1533 B.1.1.7 lineage infections. The youngest had mean log10 viral load 0.5 (or less) lower than older subjects and an estimated ~78% of the peak cell culture replication probability, due in part to smaller swab sizes and unlikely to be clinically relevant. Viral loads above 109 copies per swab were found in 8% of subjects, one-third of whom were PAMS, with mean age 37.6. We estimate 4.3 days from onset of shedding to peak viral load (8.1) and cell culture isolation probability (0.75). B.1.1.7 subjects had mean log10 viral load 1.05 higher than non-B.1.1.7, with estimated cell culture replication probability 2.6 times higher. 

Kowarz E et al Research Square – preprint https://assets.researchsquare.com/files/rs-558954/v1/8c30a186-e9e2-47c1-a76c-dc3bdf10c22a.pdf	"Vaccine-Induced Covid-19 Mimicry" Syndrome: Splice reactions within the SARS-CoV-2 Spike open reading frame result in Spike protein variants that may cause thromboembolic events in patients immunized with vector-based vaccines	Ipotesi del legame di una forma solubile della proteina S all'endotelio come base di eventi tromboembolici a seguito della vaccinazione con vaccini a vettore virale contro SARS-CoV-2.	During the last months many countries have started the immunization of millions of people by using vector-based vaccines. Unfortunately, severe side effects became overt during these vaccination campaigns: cerebral venous sinus thromboses (CVST), absolutely rare under normal life conditions, were found as a severe side effect that occured 4-14 days after 1st vaccinations. Besides CVST, Splanchnic Vein Thrombosis (SVT) was also observed. This type of adverse event has not been observed in the clinical studies of AstraZeneca, and therefore led immediately to a halt in vaccinations in several european countries. These events were mostly associated with thrombocytopenia, and thus, similar to the well-known Heparin-induced thrombocytopenia (HIT). Meanwhile, scientists have proposed a mechanism to explain this vaccine-induced thrombocytopenia. However, they do not provide a satisfactory explanation for the late thromboembolic events. Here, we present data that may explain these severe side effects which have been attributed to adenoviral vaccines. According to our results, transcription of wildtype and codon-optimized Spike open reading frames enables alternative splice events that lead to Cterminal truncated, soluble Spike protein variants. These soluble Spike variants may initiate severe side effects when binding to ACE2-expressing endothelial cells in blood vessels. In analogy to the thromboembolic events caused by Spike protein encoded by the SARS-CoV-2 virus, we termed the underlying disease mechanism the "Vaccine-Induced Covid-19 Mimicry" syndrome (VIC19M syndrome).

			
Nawal AK et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2780562?guestAccessKey=a7a785c0-c695-4353-b4a0-73089c44ffaf&utm_source=silverchair&utm_medium=email&utm_campaign=article_alert-jama&utm_content=olf&utm_term=052621	Effect of 2 Inactivated SARS-CoV-2 Vaccines on Symptomatic COVID-19 Infection in Adults A Randomized Clinical Trial	Analisi ad interim di un trial clinico su due vaccini inattivati contro SARS-CoV-2 che mostrano elevata efficacia nel prevenire l'infezione sintomatica.	Importance Although effective vaccines against COVID-19 have been developed, additional vaccines are still needed. Objective To evaluate the efficacy and adverse events of 2 inactivated COVID-19 vaccines. Design, Setting, and Participants Prespecified interim analysis of an ongoing randomized, double-blind, phase 3 trial in the United Arab Emirates and Bahrain among adults 18 years and older without known history of COVID-19. Study enrollment began on July 16, 2020. Data sets used for the interim analysis of efficacy and adverse events were locked on December 20, 2020, and December 31, 2020, respectively. Interventions Participants were randomized to receive 1 of 2 inactivated vaccines developed from SARS-CoV-2 WIV04 (5 µg/dose; n = 13 459) and HB02 (4 µg/dose; n = 13 465) strains or an aluminum hydroxide (alum)–only control (n = 13 458); they received 2 intramuscular injections 21 days apart. Main Outcomes and Measures The primary outcome was efficacy against laboratory-confirmed symptomatic COVID-19 14 days

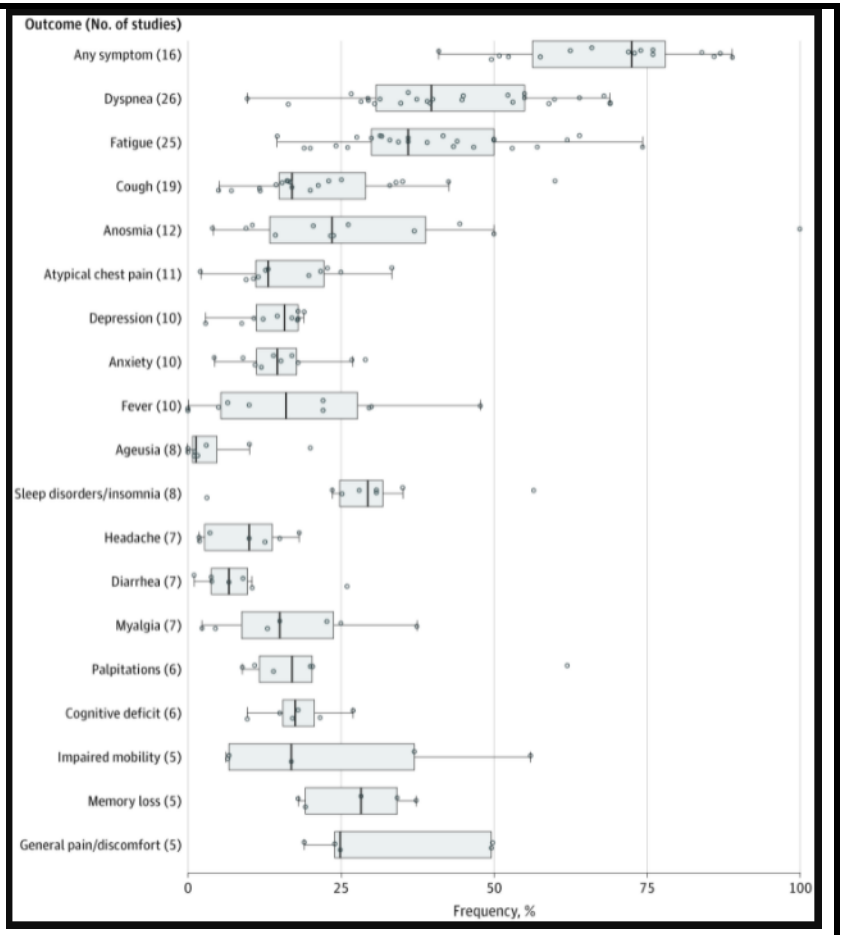
			following a second vaccine dose among participants who had no virologic evidence of SARS-CoV-2 infection at randomization. The secondary outcome was efficacy against severe COVID-19. Incidence of adverse events and reactions was collected among participants who received at least 1 dose. Results Among 40 382 participants randomized to receive at least 1 dose of the 2 vaccines or alum-only control (mean age, 36.1 years; 32 261 [84.4%] men), 38 206 (94.6%) who received 2 doses, contributed at least 1 follow-up measure after day 14 following the second dose, and had negative reverse transcriptase–polymerase chain reaction test results at enrollment were included in the primary efficacy analysis. During a median (range) follow-up duration of 77 (1-121) days, symptomatic COVID-19 was identified in 26 participants in the WIV04 group (12.1 [95% CI, 8.3-17.8] per 1000 person-years), 21 in the HB02 group (9.8 [95% CI, 6.4-15.0] per 1000 person-years), and 95 in the alum-only group (44.7 [95% CI, 36.6-54.6] per 1000 person-years), resulting in a vaccine efficacy, compared with alum-only, of 72.8% (95% CI, 58.1%-82.4%) for WIV04 and 78.1% (95% CI, 64.8%-86.3%) for HB02 ($P < .001$ for both). Two severe cases of COVID-19 occurred in the alum-only group and none occurred in the vaccine groups. Adverse reactions 7 days after each injection occurred in 41.7% to 46.5% of participants in the 3 groups; serious adverse events were rare and similar in the 3 groups (WIV04: 64 [0.5%]; HB02: 59 [0.4%]; alum-only: 78 [0.6%]). Conclusions and Relevance In this prespecified interim analysis of a randomized clinical trial, treatment of adults with either of 2 inactivated SARS-CoV-2 vaccines significantly reduced the risk of symptomatic COVID-19, and serious adverse events were rare. Data collection for final analysis is pending.

			Figure 2. Efficacy of 2 Inactivated Vaccines Against Symptomatic COVID-19 A Modified full analysis population-1  **Group** / **Efficacy of vaccine (95% CI), %** / **Incidence density per 1000 person-years (95% CI)** Alum-only / [Reference] / 44.7 (36.6-54.6) WIV04 / 72.8 (58.1-82.4) / 12.1 (8.3-17.8) HB02 / 78.1 (64.8-86.3) / 9.8 (6.4-15.0) No. of participants at risk Alum-only 12737 12206 11593 11149 10266 8319 7976 7529 1037 531 WIV04 12743 12260 11722 11256 10387 8354 8025 7594 1033 526 HB02 12726 12249 11698 11233 10366 8390 8077 7664 1031 520
The Centers for Disease Control and Prevention MMWR Morb Mortal Wkly Rep https://www.cdc.gov/mmwr/volumes/70/wr/mm7021e3.htm?s_cid=mm7021e3_w#suggestedcitation	COVID-19 Vaccine Breakthrough Infections Reported to CDC — United States, January 1–April 30, 2021	Rassegna delle infezioni da SARS-CoV-2 tra i vaccinati (oltre 100 milioni) negli USA.	A total of 10,262 SARS-CoV-2 vaccine breakthrough infections had been reported from 46 U.S. states and territories as of April 30, 2021. Among these cases, 6,446 (63%) occurred in females, and the median patient age was 58 years (interquartile range = 40–74 years). Based on preliminary data, 2,725 (27%) vaccine breakthrough infections were asymptomatic, 995 (10%) patients were known to be hospitalized, and 160 (2%) patients died. Among the 995 hospitalized patients, 289 (29%) were asymptomatic or hospitalized for a reason unrelated to COVID-19. The median age of patients who died was 82 years (interquartile range = 71–89 years); 28 (18%) decedents were asymptomatic or died from a cause unrelated to COVID-19. Sequence data were available from 555 (5%) reported cases, 356 (64%) of which were identified as SARS-CoV-2 variants of concern,§ including B.1.1.7 (199; 56%), B.1.429 (88; 25%), B.1.427 (28; 8%), P.1 (28; 8%), and B.1.351 (13; 4%).

Natori Y et al Clinical Transplantation https://doi.org/10.1111/ctr.14370	When is it Safe to perform Abdominal Transplantation in patients with prior SARS-CoV-2 infection: A Case Series.	Casistica di 14 pazienti sottoposto a trapianto di organo solido a distanza variabile da una precedente infezione da SARS-CoV-2 : 13 hanno avuto esito favorevole del trapianto.	BACKGROUND: The Coronavirus disease 2019(COVID-19) pandemic has negatively impacted worldwide organ transplantation. However, there is limited information on recipients transplanted after SARS-CoV-2 infection. A full understanding of this scenario is required, as transplantation is a lifesaving procedure and COVID-19 remains an ongoing threat. METHODS: Abdominal organ transplant recipients diagnosed with COVID-19 prior to transplantation were identified by chart review and clinical data was collected. The primary outcome was the transplant outcome including graft loss, rejection and death, and reactivation of infection posttransplant. RESULTS: We identified 14 patients who received abdominal organ transplants after symptomatic PCR confirmed SARS-CoV-2 infection; four patients had a positive PCR at the time of admission for transplantation. The median time of follow-up was 79 (22-190) days. One recipient with negative PCR before transplant tested positive 9 days after transplant. One of 14 transplanted patients developed disseminated mold infection and died 86 days after transplant. During follow-up, only one patient developed rejection; thirteen patients had favorable graft outcomes. CONCLUSIONS: We were able to perform abdominal transplantation for patients with COVID-19 before transplant, even with positive PCR at the time of transplant. Larger studies are needed to determine the time to safe transplant after SARS-CoV-2 infection.
Salzman MB et al Emerging Infectious Diseases	Multisystem inflammatory syndrome after SARS-CoV-2 infection and COVID-19 vaccination	Sindrome infiammatoria multisistemica in 6 adulti di cui 3 da poco vaccinati contro SARS-CoV-2.	We report 3 patients in California, USA, who experienced multisystem inflammatory syndrome (MIS) after immunization and severe acute respiratory syndrome coronavirus 2 infection. During the same period, 3 adults who were not vaccinated had MIS develop at a time when ≈7% of the adult patient population had received >1 vaccine.

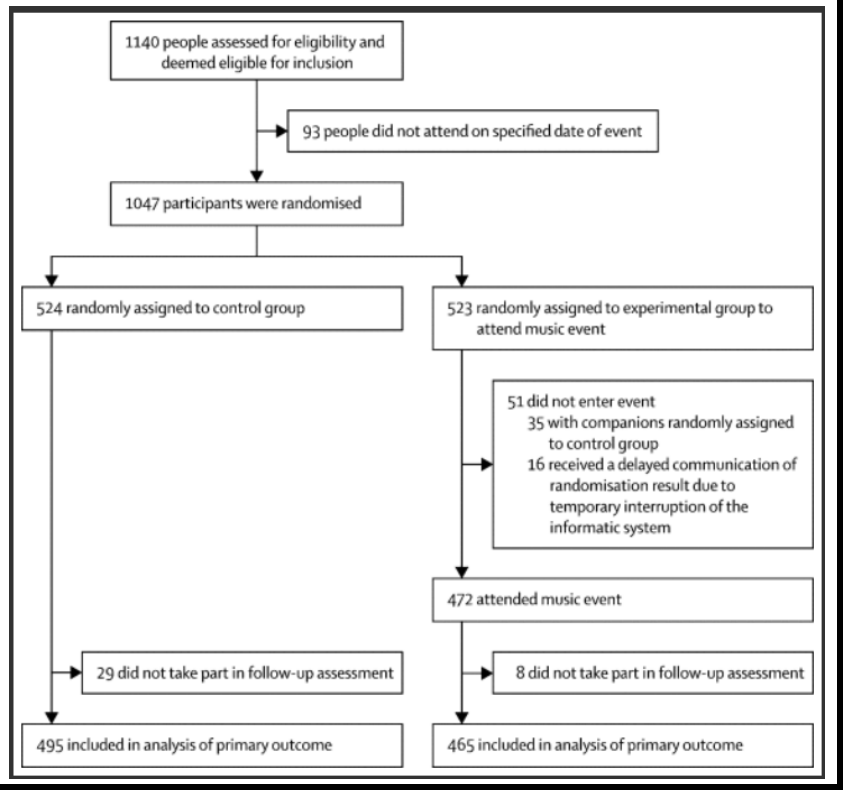
https://wwwnc.cdc.gov/eid/article/27/7/21-0594_article			
Nasserie T et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2780376	Assessment of the Frequency and Variety of Persistent Symptoms Among Patients With COVID-19 A Systematic Review	Revisione sistematica sull'argomento della persistenza dei sintomi di infezione da SARS-CoV-2 oltre 60 giorni dall'esordio di malattia o dalla diagnosi.	Importance Infection with COVID-19 has been associated with long-term symptoms, but the frequency, variety, and severity of these complications are not well understood. Many published commentaries have proposed plans for pandemic control that are primarily based on mortality rates among older individuals without considering long-term morbidity among individuals of all ages. Reliable estimates of such morbidity are important for patient care, prognosis, and development of public health policy. Objective To conduct a systematic review of studies examining the frequency and variety of persistent symptoms after COVID-19 infection. Evidence Review A search of PubMed and Web of Science was conducted to identify studies published from January 1, 2020, to March 11, 2021, that examined persistent symptoms after COVID-19 infection. Persistent symptoms were defined as those persisting for at least 60 days after diagnosis, symptom onset, or hospitalization or at least 30 days after recovery from the acute illness or hospital discharge. Search terms included COVID-19, SARS-CoV-2, coronavirus, 2019-nCoV, long-term, after recovery, long-haul, persistent, outcome, symptom, follow-up, and longitudinal. All English-language articles that presented primary data from cohort studies that reported the prevalence of persistent symptoms among individuals with SARS-CoV-2 infection and that had clearly defined and sufficient follow-up were included. Case reports, case series, and studies that described symptoms only at the time of infection

			and/or hospitalization were excluded. A structured framework was applied to appraise study quality. Findings A total of 1974 records were identified; of those, 1247 article titles and abstracts were screened. After removal of duplicates and exclusions, 92 full-text articles were assessed for eligibility; 47 studies were deemed eligible, and 45 studies reporting 84 clinical signs or symptoms were included in the systematic review. Of 9751 total participants, 5266 (54.0%) were male; 30 of 45 studies reported mean or median ages younger than 60 years. Among 16 studies, most of which comprised participants who were previously hospitalized, the median proportion of individuals experiencing at least 1 persistent symptom was 72.5% (interquartile range [IQR], 55.0%-80.0%). Individual symptoms occurring most frequently included shortness of breath or dyspnea (26 studies; median frequency, 36.0%; IQR, 27.6%-50.0%), fatigue or exhaustion (25 studies; median frequency, 40.0%; IQR, 31.0%-57.0%), and sleep disorders or insomnia (8 studies; median 29.4%, IQR, 24.4%-33.0%). There were wide variations in the design and quality of the studies, which had implications for interpretation and often limited direct comparability and combinability. Major design differences included patient populations, definitions of time zero (ie, the beginning of the follow-up interval), follow-up lengths, and outcome definitions, including definitions of illness severity. Conclusions and Relevance This systematic review found that COVID-19 symptoms commonly persisted beyond the acute phase of infection, with implications for health-associated functioning and quality of life. Current studies of symptom persistence are highly heterogeneous, and future studies need longer follow-up, improved quality, and more standardized designs to reliably quantify risks.

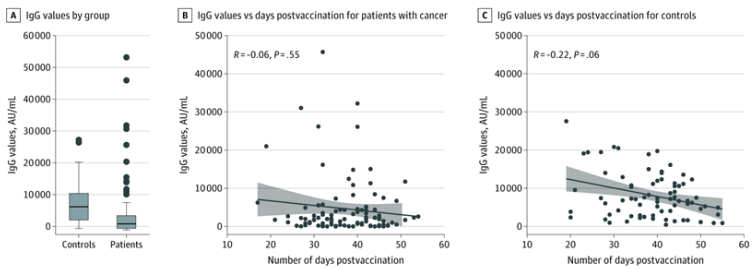
			
Epstein S et al The Lancet https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(21)00093-1/fulltext	COVID-19 vaccine prioritisation for people with disabilities	Iniquità nell'offerta vaccinale alla popolazione disabile negli USA.	For many people around the world, the COVID-19 vaccine rollout has brought unprecedented hope. For people with disabilities, vaccine prioritisation schemes are the latest aspect of the pandemic response to raise concerns. In the USA, for example, each state and territory has adopted the Centers for Disease Control and Prevention (CDC) guidelines differently. As a result, the COVID-19 vaccine rollout is uneven and has perpetuated inequities in the pandemic response.

Kuper H et al The Lancet https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(21)00077-3/fulltext	Are older people with disabilities neglected in the COVID-19 pandemic?	Le persone con disabilità e malattie croniche sono state colpite dalla pandemia in termini di isolamento, minore accesso alle cure e stress derivante dal rischio percepito.	Older people have been a central focus during the COVID-19 pandemic, as more than 90% of deaths in the UK have been among people aged 60 years or older. Messages around social distancing and high vulnerability will resonate strongly with this age group. Less often considered is that many older people have disabilities—almost half (46%) of people aged 66 years and older in the UK. Having disabilities not only increases the risk of dying from COVID-19, but potentially also increases the adverse consequences of pandemic control, yet data on these dangers are scarce.
Sparrow AK et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMp2108567?query=featured_home	Protecting Olympic Participants from Covid-19 — The Urgent Need for a Risk-Management Approach	Una pesante critica al comitato olimpico internazionale in merito all'organizzazione delle prossime Olimpiadi in periodo pandemico.	The IOC's playbooks1 are not built on scientifically rigorous risk assessment, and they fail to consider the ways in which exposure occurs, the factors that contribute to exposure, and which participants may be at highest risk. To be sure, most athletes are at low risk for serious health outcomes associated with Covid-19, but some Paralympic athletes could be in a higher-risk category. In addition, we believe the playbooks do not adequately protect the thousands of people — including trainers, volunteers, officials, and transport and hotel employees — whose work ensures the success of such a large event.
Rrevollo B et al The Lancet https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00268-1/fulltext	Same-day SARS-CoV-2 antigen test screening in an indoor mass-gathering live music event: a randomised controlled trial	Trial clinico condotto a Barcellona per valutare l'efficacia di misure di prevenzione del contagio di SARS-CoV-2 in occasione di un evento di aggregazione di massa (concerto) : persone con tampone negativo al momento dell'ingresso sono state randomizzate a tornare a casa o partecipare al	Background : The banning of mass-gathering indoor events to prevent SARS-CoV-2 spread has had an important effect on local economies. Despite growing evidence on the suitability of antigen-detecting rapid diagnostic tests (Ag-RDT) for mass screening at the event entry, this strategy has not been assessed under controlled conditions. We aimed to assess the effectiveness of a prevention strategy during a live indoor concert. Methods : We designed a randomised controlled open-label trial to assess the effectiveness of a comprehensive preventive intervention for a mass-gathering indoor event (a live concert) based on systematic same-day screening of attendees with Ag-RDTs, use of

		concerto con mascherina FFP2 in ambiente chiuso ma ben ventilato : non si è osservata differenza di nuove infezioni fra i due gruppi, per cui pare che con elevate precauzioni gli eventi al chiuso possano essere sicuri.	facial masks, and adequate air ventilation. The event took place in the Sala Apolo, Barcelona, Spain. Adults aged 18–59 years with a negative result in an Ag-RDT from a nasopharyngeal swab collected immediately before entering the event were randomised 1:1 (block randomisation stratified by age and gender) to either attend the indoor event for 5 hours or go home. Nasopharyngeal specimens used for Ag-RDT screening were analysed by real-time reverse-transcriptase PCR (RT-PCR) and cell culture (Vero E6 cells). 8 days after the event, a nasopharyngeal swab was collected and analysed by Ag-RDT, RT-PCR, and a transcription-mediated amplification test (TMA). The primary outcome was the difference in incidence of RT-PCR-confirmed SARS-CoV-2 infection at 8 days between the control and the intervention groups, assessed in all participants who were randomly assigned, attended the event, and had a valid result for the SARS-CoV-2 test done at follow-up. The trial is registered at ClinicalTrials.gov, NCT04668625. Findings : Participant enrollment took place during the morning of the day of the concert, Dec 12, 2020. Of the 1140 people who responded to the call and were deemed eligible, 1047 were randomly assigned to either enter the music event (experimental group) or continue with normal life (control group). Of the 523 randomly assigned to the experimental group, 465 were included in the analysis of the primary outcome (51 did not enter the event and eight did not take part in the follow-up assessment), and of the 524 randomly assigned to the control group, 495 were included in the final analysis (29 did not take part in the follow-up). At baseline, 15 (3%) of 495 individuals in the control group and 13 (3%) of 465 in the experimental group tested positive on TMA despite a negative Ag-RDT result. The RT-PCR test was positive in one case in each group and cell viral culture was negative in all cases. 8 days after the

			event, two (<1%) individuals in the control arm had a positive Ag-RDT and PCR result, whereas no Ag-RDT nor RT-PCR positive results were found in the intervention arm. The Bayesian estimate for the incidence between the experimental and control groups was –0·15% (95% CI –0·72 to 0·44). Interpretation : Our study provides preliminary evidence on the safety of indoor mass-gathering events during a COVID-19 outbreak under a comprehensive preventive intervention. The data could help restart cultural activities halted during COVID-19, which might have important sociocultural and economic implications. 

Massarweh A et al JAMA https://jamanetwork.com/journals/jamaoncology/fullarticle/2780584	Evaluation of Seropositivity Following BNT162b2 Messenger RNA Vaccination for SARS-CoV-2 in Patients Undergoing Treatment for Cancer	Risposta anticorpale a seguito di vaccinazione con vaccino a mRNA in una coorte di pazienti neoplastici : il titolo di IgG è inferiore rispetto ai controlli, non è noto se questo influenzi la durata e l'entità della protezione.	Importance Patients with cancer undergoing treatment are at high risk of COVID-19 following SARS-CoV-2 infection; however, their ability to produce an adequate antibody response to messenger RNA SARS-CoV-2 vaccines is unclear. Objective To evaluate rates of antispike (anti-S) antibody response to a BNT162b2 vaccine in patients with cancer who are undergoing systemic treatment vs healthy controls. Design, Setting, and Participants This prospective cohort study included 102 adult patients with solid tumors undergoing active intravenous anticancer treatment and 78 controls who received the second dose of the BNT162b2 vaccine at least 12 days before enrollment. The controls were taken from a convenience sample of the patients' family/caregivers who accompanied them to treatment. The study was conducted between February 22, 2021, and March 15, 2021 at Davidoff Cancer Center at Beilinson Hospital (Petah Tikva, Israel). Interventions Blood samples were drawn from the study participants. Serum samples were analyzed and the titers of the IgG antibodies against SARS-CoV-2 spike receptor–binding domain were determined using a commercially available immunoassay. Seropositivity was defined as 50 or greater AU/mL. Main Outcomes and Measures The primary outcome was the rate of seropositivity. Secondary outcomes included comparisons of IgG titers and identifying factors that were associated with seropositivity using univariate/multivariable analyses. Results The analysis included 180 participants, which comprised 102 patients with cancer (median [interquartile range (IQR)] age, 66 [56-72] years; 58 men [57%]) and 78 healthy controls (median [IQR] age, 62 [49-70] years; 25 men [32%]). The most common tumor type was gastrointestinal (29 [28%]). In the patient group, 92 (90%)

			were seropositive for SARS-CoV 2 antispike IgG antibodies after the second vaccine dose, whereas in the control group, all were seropositive. The median IgG titer in the patients with cancer was significantly lower than that in the controls (1931 [IQR, 509-4386] AU/mL vs 7160 [IQR, 3129-11 241] AU/mL; P < .001). In a multivariable analysis, the only variable that was significantly associated with lower IgG titers was treatment with chemotherapy plus immunotherapy (β, −3.5; 95% CI, −5.6 to −1.5). Conclusions and Relevance In this cohort study of patients with cancer who were receiving active systemic therapy, 90% of patients exhibited adequate antibody response to the BNT162b2 vaccine, although their antibody titers were significantly lower than those of healthy controls. Further research into the clinical relevance of lower titers and their durability is required. Nonetheless, the data support vaccinating patients with cancer as a high priority, even during therapy. **Figure. IgG Values**  B and C, Greyed areas represent 95% CIs.
Sun L et al JAMA	Immune Responses to SARS-CoV-2 Among Patients With Cancer What Can Seropositivity Tell Us?	Influenza delle neoplasie sulla risposta immunitaria contro SARS-CoV-2.	Patients with cancer are at risk for immune dysregulation related to underlying malignant disease as well as receipt of immunomodulatory cancer therapy. A notable concern is that patients with cancer may not mount a robust protective immune response to SARS-CoV-2 infection or vaccination. This risk seems

https://jamanetwork.com/journals/jamaoncology/fullarticle/2780585			most pronounced in patients with hematologic cancers: in a study of 167 patients with chronic lymphocytic leukemia in Israel who had received both doses of the BNT162b2 messenger RNA (mRNA) vaccine (Pfizer-BioNTech) for COVID-19, only 39.5% had a positive antibody response, and this proportion was even lower (16%) among patients on active treatment. Patients with solid malignant neoplasms may have a more preserved immune response—of 261 patients with cancer in New York City who had tested positive for SARS-CoV-2, the rate of seroconversion was 94.5% for those with solid tumors compared with 81.7% with hematologic cancers.
Yazaki S et al JAMA https://jamanetwork.com/journals/jamaoncology/fullarticle/2780583	Difference in SARS-CoV-2 Antibody Status Between Patients With Cancer and Health Care Workers During the COVID-19 Pandemic in Japan	I pazienti con neoplasie (di ogni tipo) non hanno una sieroprevalenza di SARS-CoV-2 superiore a quella degli operatori sanitari in questo studio cross-sectional condotto in Giappone ; tuttavia i livelli anticorpali sono significativamente inferiori nei pazienti neoplastici, a suggerire una influenza della malattia di base e dei trattamenti sulla risposta immunitaria.	Importance Patients with cancer and health care workers (HCWs) are at high risk of SARS-CoV-2 infection. Assessing the antibody status of patients with cancer and HCWs can help understand the spread of COVID-19 in cancer care. Objective To evaluate serum SARS-CoV-2 antibody status in patients with cancer and HCWs during the COVID-19 pandemic in Japan. Design, Setting, and Participants Participants were enrolled for this prospective cross-sectional study between August 3 and October 30, 2020, from 2 comprehensive cancer centers in the epidemic area around Tokyo, Japan. Patients with cancer aged 16 years or older and employees were enrolled. Participants with suspected COVID-19 infection at the time of enrollment were excluded. Exposures Cancer of any type and cancer treatment, including chemotherapy, surgery, immune checkpoint inhibitors, radiotherapy, and targeted molecular therapy. Main Outcomes and Measures Seroprevalence and antibody levels in patients with cancer and HCWs. Seropositivity was defined as positivity to nucleocapsid IgG (N-IgG) and/or spike IgG (S-IgG). Serum levels of SARS-CoV-2 IgM and IgG antibodies against the

			nucleocapsid and spike proteins were measured by chemiluminescent enzyme immunoassay. Results A total of 500 patients with cancer (median age, 62.5 years [range, 21-88 years]; 265 men [55.4%]) and 1190 HCWs (median age, 40 years [range, 20-70 years]; 382 men [25.4%]) were enrolled. In patients with cancer, 489 (97.8%) had solid tumors, and 355 (71.0%) had received anticancer treatment within 1 month. Among HCWs, 385 (32.3%) were nurses or assistant nurses, 266 (22.4%) were administrative officers, 197 (16.6%) were researchers, 179 (15.0%) were physicians, 113 (9.5%) were technicians, and 50 (4.2%) were pharmacists. The seroprevalence was 1.0% (95% CI, 0.33%-2.32%) in patients and 0.67% (95% CI, 0.29%-1.32%) in HCWs (P = .48). However, the N-IgG and S-IgG antibody levels were significantly lower in patients than in HCWs (N-IgG: β, −0.38; 95% CI, −0.55 to −0.21; P < .001; and S-IgG: β, −0.39; 95% CI, −0.54 to −0.23; P < .001). Additionally, among patients, N-IgG levels were significantly lower in those who received chemotherapy than in those who did not (median N-IgG levels, 0.1 [interquartile range (IQR), 0-0.3] vs 0.1 [IQR, 0-0.4], P = .04). In contrast, N-IgG and S-IgG levels were significantly higher in patients who received immune checkpoint inhibitors than in those who did not (median N-IgG levels: 0.2 [IQR, 0.1-0.5] vs 0.1 [IQR, 0-0.3], P = .02; S-IgG levels: 0.15 [IQR, 0-0.3] vs 0.1[IQR, 0-0.2], P = .02). Conclusions and Relevance In this cross-sectional study of Japanese patients with cancer and HCWs, the seroprevalence of SARS-CoV-2 antibodies did not differ between the 2 groups; however, findings suggest that comorbid cancer and treatment with systemic therapy, including chemotherapy and immune checkpoint inhibitors, may influence the immune response to SARS-CoV-2.

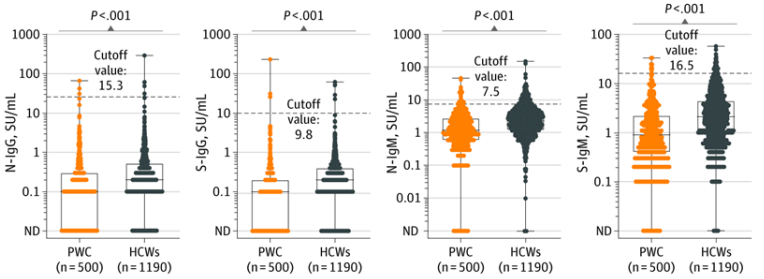
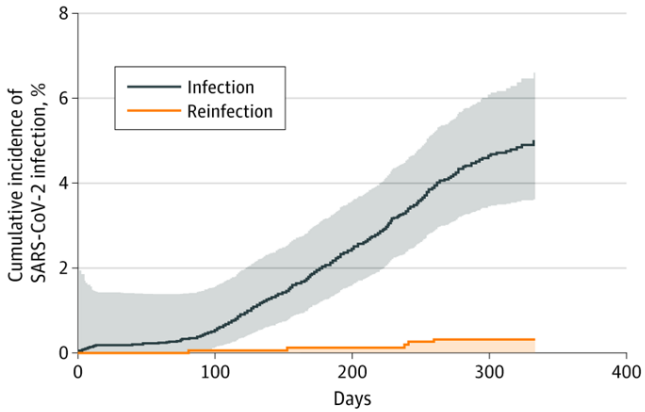
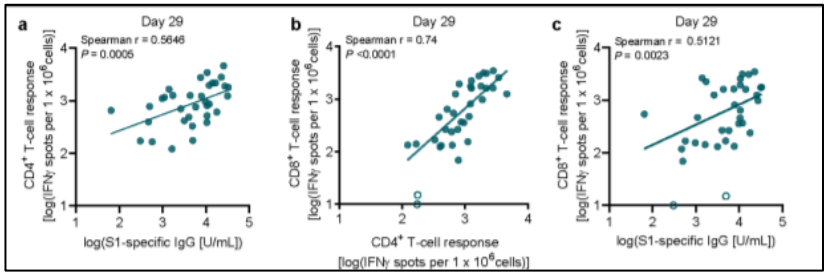
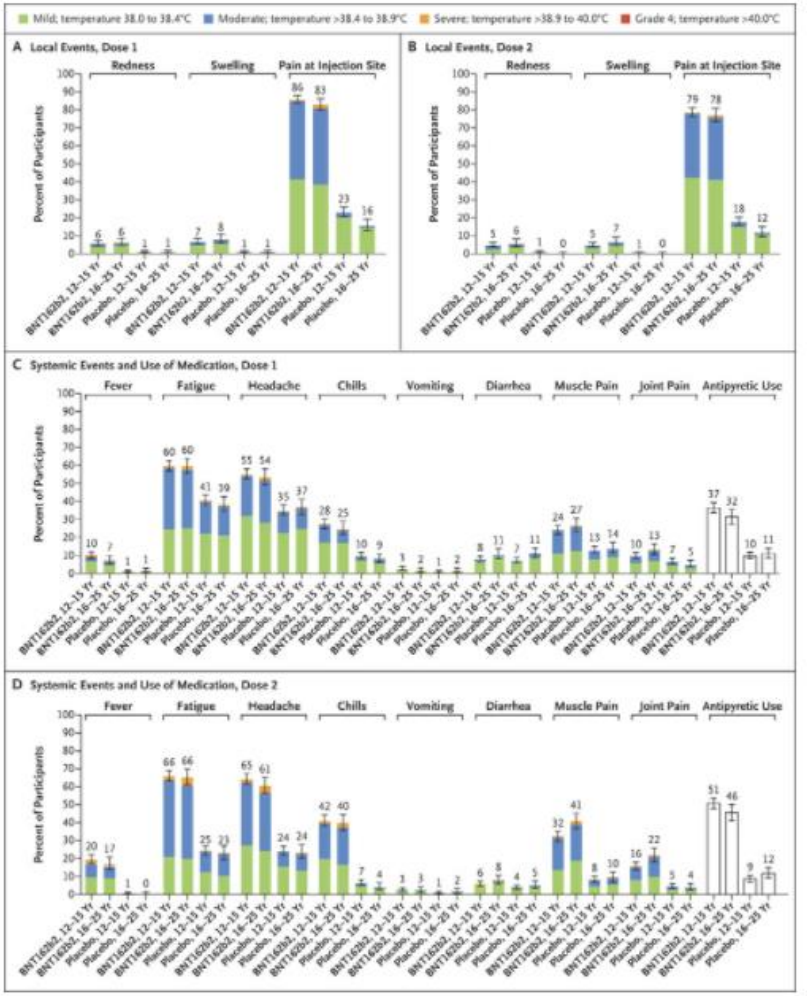
			Figure 2. SARS-CoV-2 Antibody Levels in Patients With Cancer (PWC) and Health Care Workers (HCWs) **Source** / **N-IgG (SU/mL) Median (IQR)** / **S-IgG (SU/mL) Median (IQR)** / **N-IgM (SU/mL) Median (IQR)** / **S-IgM (SU/mL) Median (IQR)** PWC: 0.1 (0-0.3) / 0.1 (0-0.2) / 1.24 (0.62-2.73) / 0.9 (0.4-2.2) HCWs: 0.2 (0.1-0.5) / 0.2 (0.1-0.4) / 2.38 (1.23-4.40) / 2.1 (1.0-4.4)  Nucleocapsid IgG (N-IgG), spike IgG (S-IgG), nucleocapsid IgM (N-IgM), and spike IgM (S-IgM) antibody levels were compared between PW and HCWs in the intention-to-treat population. The dots depict antibody levels. The boxes represents the first quartile, median, and third quartile; whiskers represent minimum and maximum values. ND indicates not detected.
Vitale J et al JAMA https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2780557	Assessment of SARS-CoV-2 Reinfection 1 Year After Primary Infection in a Population in Lombardy, Italy	Le reinfezioni da SARS-CoV-2 sono un evento molto raro in questa casistica del nord Italia.	We investigated the incidence of SARS-CoV-2 primary infection and reinfection among individuals who, during the first wave of the pandemic in Italy (February to July 2020), underwent diagnostic reverse-transcriptase–polymerase chain reaction (PCR). Symptomatic and asymptomatic patients of any age, who were recruited in several screening and contact-tracing programs, were included.

			Figure. Cumulative Incidence of SARS-Cov-2 Infection  No. days at risk RT-PCR positive 10988 137085 325798 496586 RT-PCR negative 31742 491579 2040576 3499503 RT-PCR indicates reverse-transcriptase–polymerase chain reaction.
Sahin U et al Nature https://www.nature.com/articles/s41586-021-03653-6	BNT162b2 vaccine induces neutralizing antibodies and poly-specific T cells in humans	Il vaccino Pfizer contro SARS-CoV-2 stimola una rusposta umorale e cellulare contro il virus.	BNT162b2, a lipid nanoparticle (LNP) formulated nucleoside-modified messenger RNA (mRNA) that encodes the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) spike glycoprotein (S) stabilized in the prefusion conformation, has demonstrated 95% efficacy in preventing coronavirus disease-19 (COVID-19)1. Here we extend our previous phase 1/2 trial report2 and present BNT162b2 prime/boost induced immune response data from a second phase 1/2 trial in healthy adults (18-55 years of age). BNT162b2 elicited strong antibody responses, with SARS-CoV-2 serum 50% neutralizing geometric mean titers up to 3.3-fold above those observed in COVID-19 human convalescent samples (HCS) one week post-boost. BNT162b2-elicited sera neutralized 22 pseudoviruses bearing SARS-CoV-2 S variants. Most participants had a strong IFNγ- or IL-2-positive CD8+ and CD4+ T helper type 1 (TH1) T cell response, detectable throughout the full observation period of nine weeks following the boost. pMHC multimer technology

			identified several BNT162b2-induced epitopes that were presented by frequent MHC alleles and conserved in mutant strains. One week post-boost, epitope-specific CD8+ T cells of the early differentiated effector-memory phenotype comprised 0.02-2.92% of total circulating CD8+ T cells and were detectable (0.01-0.28%) eight weeks later. In summary, BNT162b2 elicits an adaptive humoral and poly-specific cellular immune response against epitopes conserved in a broad range of variants at well tolerated doses. 
Frenck RW et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2107456?query=featured_home	Safety, Immunogenicity, and Efficacy of the BNT162b2 Covid-19 Vaccine in Adolescents	Efficacia e sicurezza del vaccino Pfizer contro SARS-CoV-2 nella fascia d'età 12-15 anni.	BACKGROUND : Until very recently, vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had not been authorized for emergency use in persons younger than 16 years of age. Safe, effective vaccines are needed to protect this population, facilitate in-person learning and socialization, and contribute to herd immunity. METHODS : In this ongoing multinational, placebo-controlled, observer-blinded trial, we randomly assigned participants in a 1:1 ratio to receive two injections, 21 days apart, of 30 µg of BNT162b2 or placebo. Noninferiority of the immune response to BNT162b2 in 12-to-15-year-old participants as compared with that in 16-to-25-year-old participants was an immunogenicity objective. Safety (reactogenicity and adverse events) and efficacy against confirmed coronavirus disease 2019 (Covid-19; onset, ≥7 days after dose 2) in the 12-to-15-year-old cohort were assessed.

			RESULTS : Overall, 2260 adolescents 12 to 15 years of age received injections; 1131 received BNT162b2, and 1129 received placebo. As has been found in other age groups, BNT162b2 had a favorable safety and side-effect profile, with mainly transient mild-to-moderate reactogenicity (predominantly injection-site pain [in 79 to 86% of participants], fatigue [in 60 to 66%], and headache [in 55 to 65%]); there were no vaccine-related serious adverse events and few overall severe adverse events. The geometric mean ratio of SARS-CoV-2 50% neutralizing titers after dose 2 in 12-to-15-year-old participants relative to 16-to-25-year-old participants was 1.76 (95% confidence interval [CI], 1.47 to 2.10), which met the noninferiority criterion of a lower boundary of the two-sided 95% confidence interval greater than 0.67 and indicated a greater response in the 12-to-15-year-old cohort. Among participants without evidence of previous SARS-CoV-2 infection, no Covid-19 cases with an onset of 7 or more days after dose 2 were noted among BNT162b2 recipients, and 16 cases occurred among placebo recipients. The observed vaccine efficacy was 100% (95% CI, 75.3 to 100). CONCLUSIONS : The BNT162b2 vaccine in 12-to-15-year-old recipients had a favorable safety profile, produced a greater immune response than in young adults, and was highly effective against Covid-19.

			Figure 2. Local Reactions and Systemic Events Reported within 7 Days after Administration of BNT162b2 or Placebo. 
Staibano P et al JAMA	Association of Tracheostomy With Outcomes in Patients With COVID-19 and SARS-CoV-2 Transmission Among Health Care Professionals	Secondo questa revisione sistematica e metanalisi, la tracheostomia nei pazienti con COVID-19 è una procedura sicura per il	Importance Approximately 5% to 15% of patients with COVID-19 require invasive mechanical ventilation (IMV) and, at times, tracheostomy. Details regarding the safety and use of tracheostomy in treating COVID-19 continue to evolve.

https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2780431?resultClick=1	A Systematic Review and Meta-analysis	personale sanitario ; inoltre sembra ridurre la dirata di degenza in rianimazione.	Objective To evaluate the association of tracheostomy with COVID-19 patient outcomes and the risk of SARS-CoV-2 transmission among health care professionals (HCPs). Data Sources EMBASE (Ovid), Medline (Ovid), and Web of Science from January 1, 2020, to March 4, 2021. Study Selection English-language studies investigating patients with COVID-19 who were receiving IMV and undergoing tracheostomy. Observational and randomized clinical trials were eligible (no randomized clinical trials were found in the search). All screening was performed by 2 reviewers (P.S. and M.L.). Overall, 156 studies underwent full-text review. Data Extraction and Synthesis We performed data extraction in accordance with Meta-analysis of Observational Studies in Epidemiology guidelines. We used a random-effects model, and ROBINS-I was used for the risk-of-bias analysis. Main Outcomes and Measures SARS-CoV-2 transmission between HCPs and levels of personal protective equipment, in addition to complications, time to decannulation, ventilation weaning, and intensive care unit (ICU) discharge in patients with COVID-19 who underwent tracheostomy. Results Of the 156 studies that underwent full-text review, only 69 were included in the qualitative synthesis, and 14 of these 69 studies (20.3%) were included in the meta-analysis. A total of 4669 patients were included in the 69 studies, and the mean (range) patient age across studies was 60.7 (49.1-68.8) years (43 studies [62.3%] with 1856 patients). We found that in all studies, 1854 patients (73.8%) were men and 658 (26.2%) were women. We found that 28 studies (40.6%) investigated either surgical tracheostomy or percutaneous dilatational tracheostomy. Overall, 3 of 58 studies (5.17%) identified a small subset of HCPs who

developed COVID-19 that was associated with tracheostomy. Studies did not consistently report the number of HCPs involved in tracheostomy. Among the patients, early tracheostomy was associated with faster ICU discharge (mean difference, 6.17 days; 95% CI, −11.30 to −1.30), but no change in IMV weaning (mean difference, −2.99 days; 95% CI, −8.32 to 2.33) or decannulation (mean difference, −3.12 days; 95% CI, −7.35 to 1.12). There was no association between mortality or perioperative complications and type of tracheostomy. A risk-of-bias evaluation that used ROBINS-I demonstrated notable bias in the confounder and patient selection domains because of a lack of randomization and cohort matching. There was notable heterogeneity in study reporting.

Conclusions and Relevance : The findings of this systematic review and meta-analysis indicate that enhanced personal protective equipment is associated with low rates of SARS-CoV-2 transmission during tracheostomy. Early tracheostomy in patients with COVID-19 may reduce ICU stay, but this finding is limited by the observational nature of the included studies.

Table. Risk-of-Bias Assessment in 14 Studies Using ROBINS-I

Table. Risk-of-Bias Assessment in 14 Studies Using ROBINS-I

	ROBINS-I domains							
Study	Confounders	Participant selection	Interventions	Deviation from intended intervention	Missing data	Outcome measurement	Reported result	Overall
Avilés-Jurado et al,[14] 2020	Moderate	Low	Low	Low	Low	Moderate	Moderate	Low
QEHB CAT,[24] 2020	Moderate	Moderate	Low	Low	Low	Moderate	Moderate	Moderate
Botti et al,[21] 2021	Serious	Moderate	Serious	Unclear	Unclear	Moderate	Serious	Serious
Glibbery et al,[33] 2020	Serious	Moderate	Moderate	Low	Moderate	Serious	Moderate	Moderate
Krishnamoorthy et al,[35] 2020	Moderate	Serious	Serious	Unclear	Serious	Moderate	Serious	Serious
Long et al,[38] 2020	Serious	Serious	Low	Low	Moderate	Moderate	Serious	Moderate
Rosano et al,[58] 2020	Moderate	Moderate	Low	Unclear	Low	Low	Moderate	Moderate
Rovira et al,[59] 2021	Moderate	Moderate	Low	Unclear	Low	Low	Moderate	Low
Sancho et al,[60] 2020	Moderate	Serious	Low	Unclear	Low	Low	Low	Low
Takhar et al,[66] 2020	Serious	Serious	Low	Unclear	Low	Low	Low	Low
Takhar et al,[67] 2020	Serious	Serious	Moderate	Low	Moderate	Serious	Serious	Serious
Yeung et al,[73] 2020	Serious	Serious	Moderate	Unclear	Moderate	Serious	Serious	Serious
Zhang et al,[74] 2020	Critical	Critical	Serious	Unclear	Serious	Serious	Serious	Serious
Zuazua-Gonzalez et al,[78] 2020	Serious	Serious	Moderate	Unclear	Low	Low	Moderate	Moderate

Abbreviation: QEHB CAT, Queen Elizabeth Hospital Birmingham COVID-19 airway team.

Schulz C et al Emerging Infectious Diseases https://wwwnc.cdc.gov/eid/article/27/7/20-4670_article	Prolonged SARS-CoV-2 RNA Shedding from Therapy Cat after Cluster Outbreak in Retirement Home	In una casa di riposo in Germania c'era un gatto cui è stata diagnosticata l'infezione asintomatica da SARS-CoV-2 con prolungato shedding virale; in quella casa di riposo si è verificato un cluster di infezioni negli ospiti, ma in base al sequenziamento la conclusione è che siano stati gli uomini a trasmettere l'infezione al gatto.	We report a therapy cat in a nursing home in Germany infected with severe acute respiratory syndrome coronavirus 2 during a cluster outbreak in the home residents. Although we confirmed prolonged presence of virus RNA in the asymptomatic cat, genome sequencing showed no further role of the cat in human infections on site.