RICERCA BIBLIOGRAFICA COVID 19

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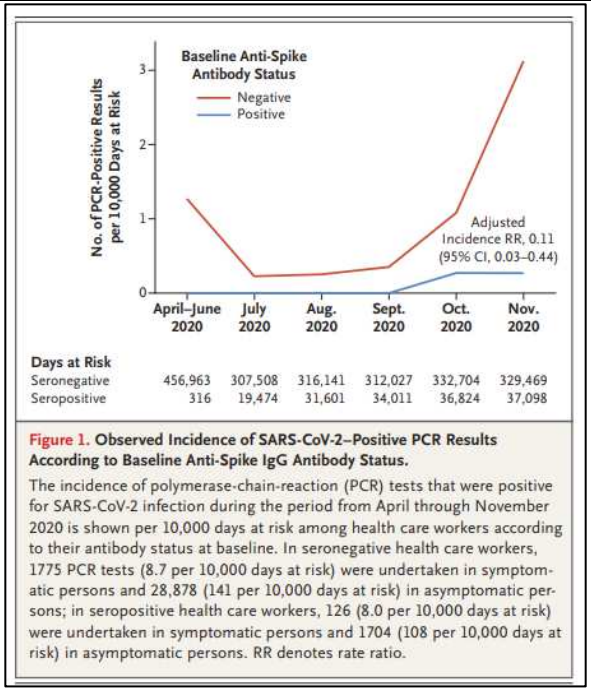
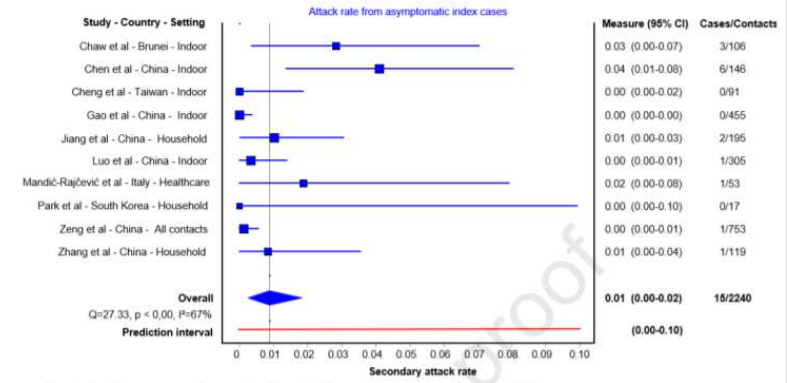
DOTT.SSA ELEONORA TADDEI

AUTORE/RIVISTA	TITOLO	OUTCOME PRINCIPALE	ABSTRACT
Lumley SF et al NEJM no reinfection after first disease in HCW.pdf	Antibody Status and Incidence of SARS-CoV-2 Infection in Health Care Workers	In uno studio condotto su 12541 Operatori sanitari a Oxford, UK, la presenza di anticorpi anti-proteina S o anti-nucleocapside di SARS-CoV-2 è associata a una riduzione sostanziale del rischio di reinfezione nei 6 mesi successivi.	BACKGROUND : The relationship between the presence of antibodies to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the risk of subsequent reinfection remains unclear. METHODS : We investigated the incidence of SARS-CoV-2 infection confirmed by polymerase chain reaction (PCR) in seropositive and seronegative health care workers attending testing of asymptomatic and symptomatic staff at Oxford University Hospitals in the United Kingdom. Baseline antibody status was determined by anti-spike (primary analysis) and anti-nucleocapsid IgG assays, and staff members were followed for up to 31 weeks. We estimated the relative incidence of PCR-positive test results and new symptomatic infection according to antibody status, adjusting for age, participant-reported gender, and changes in incidence over time. RESULTS : A total of 12,541 health care workers participated and had anti-spike IgG measured; 11,364 were followed up after

			negative antibody results and 1265 after positive results, including 88 in whom seroconversion occurred during follow-up. A total of 223 anti-spike–seronegative health care workers had a positive PCR test (1.09 per 10,000 days at risk), 100 during screening while they were asymptomatic and 123 while symptomatic, whereas 2 anti-spike–seropositive health care workers had a positive PCR test (0.13 per 10,000 days at risk), and both workers were asymptomatic when tested (adjusted incidence rate ratio, 0.11; 95% confidence interval, 0.03 to 0.44; P=0.002). There were no symptomatic infections in workers with anti-spike antibodies. Rate ratios were similar when the anti-nucleocapsid IgG assay was used alone or in combination with the anti-spike IgG assay to determine baseline status. CONCLUSIONS : The presence of anti-spike or anti-nucleocapsid IgG antibodies was associated with a substantially reduced risk of SARS-CoV-2 reinfection in the ensuing 6 months.

			 **Figure 1. Observed Incidence of SARS-CoV-2–Positive PCR Results According to Baseline Anti-Spike IgG Antibody Status.** The incidence of polymerase-chain-reaction (PCR) tests that were positive for SARS-CoV-2 infection during the period from April through November 2020 is shown per 10,000 days at risk among health care workers according to their antibody status at baseline. In seronegative health care workers, 1775 PCR tests (8.7 per 10,000 days at risk) were undertaken in symptomatic persons and 28,878 (141 per 10,000 days at risk) in asymptomatic persons; in seropositive health care workers, 126 (8.0 per 10,000 days at risk) were undertaken in symptomatic persons and 1704 (108 per 10,000 days at risk) in asymptomatic persons. RR denotes rate ratio.
Qiu X et al Clinical Microbiology and Infection https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00038-0/fulltext	Defining the role of asymptomatic and pre-symptomatic SARS-CoV-2 transmission – a living systematic review	Review sui dati relativi al contagio di SARS-CoV-2 mediato da soggetti asintomatici : sulla base della letteratura, il ruolo degli asintomatici appare ridotto e inferiore rispetto a quello dei sintomatici.	Background : Reports suggest that asymptomatic individuals (those with no symptoms at all throughout infection) with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are infectious, but the extent of transmission based on symptom status requires further study. Purpose : This living review aims to critically appraise available data about secondary attack rates from people with asymptomatic, pre-symptomatic and symptomatic SARS-CoV-2 infection. Data sources : Medline, EMBASE, China Academic Journals full-text database (CNKI), and pre-print servers were searched from 30 December 2019 to 3 July 2020 using relevant MESH terms.

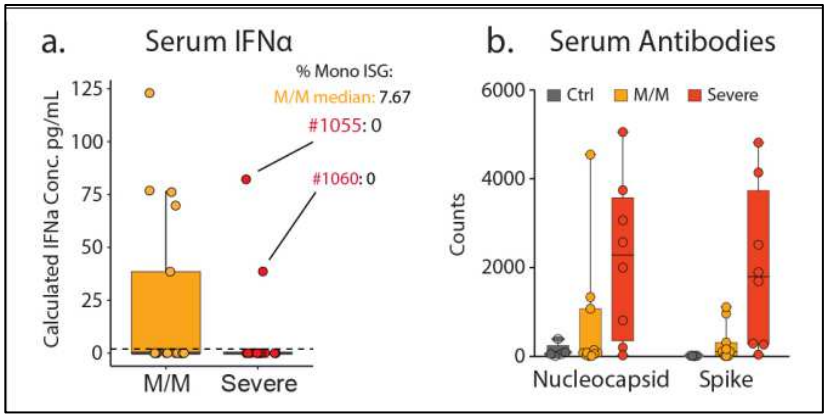
			Study selection Studies that report on contact tracing of index cases with SARS-CoV-2 infection in either English or Chinese were included. Data extraction : Two authors independently extracted data and assessed study quality and risk of bias. We calculated the secondary attack rate as the number of contacts with SARS-CoV-2, divided by the number of contacts tested. Data synthesis Of 927 studies identified, 80 were included. Summary secondary attack rate estimates were 1% (95% CI: 0%-2%) with a prediction interval of 0-10% for asymptomatic index cases in 10 studies, 7% (95% CI: 3%-11%) with a prediction interval of 1- 40% for pre-symptomatic cases in 11 studies and 6% (95% CI: 5%-8%) with a prediction interval of 5-38% for symptomatic index cases in 40 studies. The highest secondary attack rates were found in contacts who lived in the same household as the index case. Other activities associated with transmission were group activities such as sharing meals or playing board games with the index case, regardless of the disease status of the index case. Limitations : We excluded some studies because the index case or number of contacts were unclear. Conclusion : Asymptomatic patients can transmit SARS-CoV-2 to others, but our findings indicate that such individuals are responsible for fewer secondary infections than people with symptoms.

			Figure 2: Secondary attack rates from asymptomatic index cases to their contacts  For each study the secondary attack rate is reported with its 95% CI. A prediction interval at the bottom of the forest is depicted.
Tonshoff B et al JAMA Pediatrics https://jamanetwork.com/journals/jamapediatrics/fullarticle/2775656	Prevalence of SARS-CoV-2 Infection in Children and Their Parents in Southwest Germany	Studio cross-sectional su 4964 partecipanti fra cui 2482 bambini (età 1-10 anni) di cui si studia la prevalenza di infezione da SARS-CoV-2 e la concordanza genitori-figli : la prevalenza nei bambini appare bassa, inferiore a quella negli adulti testati, ma lo studio è stato eseguito in un periodo di lockdown.	Importance School and daycare closures were enforced as measures to confine the novel coronavirus disease 2019 (COVID-19) pandemic, based on the assumption that young children may play a key role in severe acute respiratory coronavirus 2 (SARS-CoV-2) spread. Given the grave consequences of contact restrictions for children, a better understanding of their contribution to the COVID-19 pandemic is of great importance. Objective To describe the rate of SARS-CoV-2 infections and the seroprevalence of SARS-CoV-2 antibodies in children aged 1 to 10 years, compared with a corresponding parent of each child, in a population-based sample. Design, Setting, and Participants This large-scale, multicenter, cross-sectional investigation (the COVID-19 BaWü study) enrolled children aged 1 to 10 years and a corresponding parent between April 22 and May 15, 2020, in southwest Germany. Exposures Potential exposure to SARS-CoV-2.

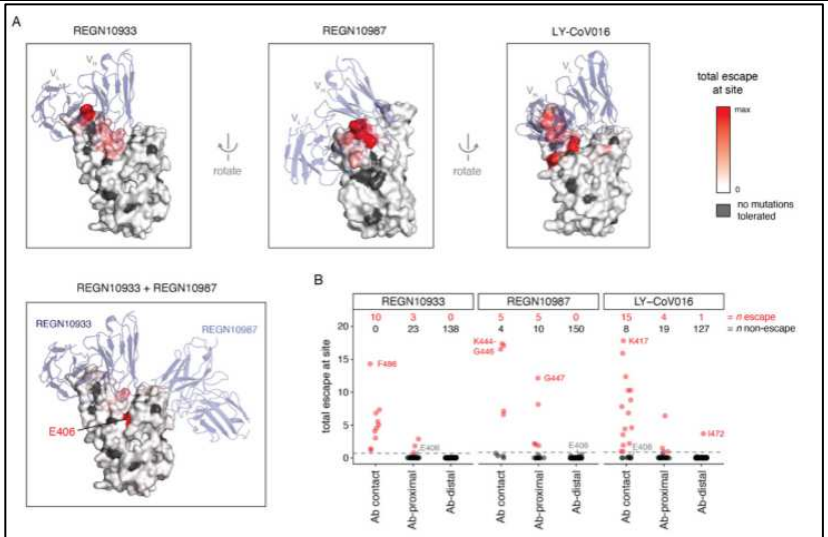
			Main Outcomes and Measures The main outcomes were infection and seroprevalence of SARS-CoV-2. Participants were tested for SARS-CoV-2 RNA from nasopharyngeal swabs by reverse transcription–polymerase chain reaction and SARS-CoV-2 specific IgG antibodies in serum by enzyme-linked immunosorbent assays and immunofluorescence tests. Discordant results were clarified by electrochemiluminescence immunoassays, a second enzyme-linked immunosorbent assay, or an in-house Luminex-based assay. Results This study included 4964 participants: 2482 children (median age, 6 [range, 1-10] years; 1265 boys [51.0%]) and 2482 parents (median age, 40 [range, 23-66] years; 615 men [24.8%]). Two participants (0.04%) tested positive for SARS-CoV-2 RNA. The estimated SARS-CoV-2 seroprevalence was low in parents (1.8% [95% CI, 1.2–2.4%]) and 3-fold lower in children (0.6% [95% CI, 0.3-1.0%]). Among 56 families with at least 1 child or parent with seropositivity, the combination of a parent with seropositivity and a corresponding child with seronegativity was 4.3 (95% CI, 1.19-15.52) times higher than the combination of a parent who was seronegative and a corresponding child with seropositivity. We observed virus-neutralizing activity for 66 of 70 IgG-positive serum samples (94.3%). Conclusions and Relevance In this cross-sectional study, the spread of SARS-CoV-2 infection during a period of lockdown in southwest Germany was particularly low in children aged 1 to 10 years. Accordingly, it is unlikely that children have boosted the pandemic. This SARS-CoV-2 prevalence study, which appears to be the largest focusing on children, is instructive for how ad hoc mass testing provides the basis for rational political decision-making in a pandemic.

			Table 4. Number of Children and Their Corresponding Parent With Seropositivity and Seronegativity Children age range, y All children / 1-5 / 6-10 Test result: Child Negative: 2426 / 34 / 1105 / 15 / 1321 / 19 Positive: 8 / 14 / 4 / 5 / 4 / 9 Mid-P McNemar test: <.001 / .02 / .003
Crane MA et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2775686	Change in Reported Adherence to Nonpharmaceutical Interventions During the COVID-19 Pandemic, April-November 2020	Sondaggio eseguito negli USA in merito alla aderenza autoriportata alle raccomandazioni per il controllo della pandemia di COVID-19 : l'aderenza si è ridotta progressivamente nel tempo, con un picco negativo in estate.	Nonpharmaceutical interventions (NPIs) have been used to mitigate the effects of the coronavirus disease 2019 (COVID-19) pandemic. Reports describe an increasing attitude of apathy or resistance toward adherence to NPIs, termed pandemic fatigue. To better describe this phenomenon in the US, we used national surveillance data to analyze reporting of adherence to protective behaviors identified as NPIs.
Heching M et al Chest https://journal.chestnet.org/article/S0012-3692(21)00100-8/fulltext	Surfactant for Treatment of ARDS in COVID-19 Patient	Ritenendo che la ARDS dell'infezione grave da SARS-CoV-2 somigli in alcuni aspetti a quella da deficit di surfattante del neonato, gli autori di questo studio hanno trattato un paziente con surfattante esogeno, con beneficio.	Patients with coronavirus disease 2019 (COVID-19) suffer from severe respiratory symptoms consistent with acute respiratory distress syndrome (ARDS). The clinical presentation of ARDS in COVID-19 is often atypical, as COVID-19 patients exhibit a disproportionate hypoxemia as compared to a relatively preserved lung mechanics. This pattern is more similar to neonatal respiratory distress syndrome (RDS) secondary to surfactant deficiency, which has been shown to benefit from exogenous surfactant. We present our experience with exogenous surfactant treatment in a COVID-19 patient suffering from COVID-19 related ARDS. The patient responded with improved oxygenation, and we believe surfactant

			was the catalyst for the successful extubation and clinical improvement of the patient.
Rappuoli R et al Proceedings of the National Academy of Sciences https://www.pnas.org/content/118/3/e2020368118	Vaccinology in the post–COVID-19 era	Prospettiva sulla vaccinologia moderna e sulle sue future applicazioni dopo l'era « COVID-19 ».	The COVID-19 pandemic is a shocking reminder of how our world would look in the absence of vaccination. Fortunately, new technologies, the pace of understanding new and existing pathogens, and the increased knowledge of the immune system allow us today to develop vaccines at an unprecedented speed. Some of the vaccine technologies that are fast-tracked by the urgency of COVID-19 may also be the answer for other health priorities, such as antimicrobial resistance, chronic infections, and cancer, that the post-COVID-19 world will urgently need to face. This perspective analyzes the way COVID-19 is transforming vaccinology and the opportunities for vaccines to have an increasingly important role in health and well-being.
Combes AJ et al Science s41586-021-03234-7_reference.pdf	Global absence and targeting of protective immune states in severe COVID-19	Una risposta anticorpale troppo "zelante" -in grado di bloccare il signalling dell'interferone alfa - caratterizza i pazienti con COVID-19 grave in questo studio.	While SARS-CoV-2 infection has pleiotropic and systemic effects in some patients, many others experience milder symptoms. We sought a holistic understanding of the severe/mild distinction in COVID-19 pathology, and its origins. We performed a whole-blood preserving single-cell analysis protocol to integrate contributions from all major cell types including neutrophils, monocytes, platelets, lymphocytes and the contents of serum. Patients with mild COVID-19 disease display a coordinated pattern of interferon-stimulated gene (ISG) expression across every cell population and these cells are systemically absent in patients with severe disease. Severe COVID-19 patients also paradoxically produce very high anti-SARS-CoV-2 antibody titers and have lower viral load as compared to mild

			disease. Examination of the serum from severe patients demonstrates that they uniquely produce antibodies that functionally block the production of the mild disease-associated ISG-expressing cells, by engaging conserved signaling circuits that dampen cellular responses to interferons. Overzealous antibody responses pit the immune system against itself in many COVID-19 patients and perhaps in other viral infections and this study defines targets for immunotherapies in severe patients to re-engage viral defense. 
White KM et al Science https://science.sciencemag.org/content/early/2021/01/22/science.abf4058.full	Plitidepsin has potent preclinical efficacy against SARS-CoV-2 by targeting the host protein eEF1A	Dimostrazione su coltura cellulare e modello murino dell'attività antivirale del farmaco antineoplastico plitidepsina, attraverso l'inibizione di una proteina eucariotica implicata nella traduzione proteica. Il farmaco, già in uso in combinazione con steroidi per il trattamento del mieloma multiplo, andrà	SARS-CoV-2 viral proteins interact with the eukaryotic translation machinery and inhibitors of translation have potent antiviral effects. Here we report that the drug plitidepsin (aplidin), which has limited clinical approval, possesses antiviral activity (IC90 = 0.88 nM) 27.5-fold more potent than remdesivir against SARS-CoV-2 in vitro, with limited toxicity in cell culture. Through the use of a drug resistant mutant, we show that the antiviral activity of plitidepsin against SARS-CoV-2 is mediated through inhibition of the known target eEF1A. We demonstrate the in vivo efficacy of plitidepsin treatment in two mouse models of SARS-CoV-2 infection with a reduction of viral replication in the lungs by two orders of magnitude using

		incontro a un trial di fase II/III nel prossimo futuro.	prophylactic treatment. Our results indicate that plitidepsin is a promising therapeutic candidate for COVID-19.
Starr TN et al Science https://science.sciencemag.org/content/early/2021/01/22/science.abf9302.full	Prospective mapping of viral mutations that escape antibodies used to treat COVID-19	Mappatura delle mutazioni a carico del frammento legante il recettore (RBD) della proteina spike di SARS-CoV-2 che consentono l'evasione dagli anticorpi monoclonali attualmente in uso.	Antibodies are a potential therapy for SARS-CoV-2, but the risk of the virus evolving to escape them remains unclear. Here we map how all mutations to SARS-CoV-2's receptor-binding domain (RBD) affect binding by the antibodies in the REGN-COV2 cocktail and the antibody LY-CoV016. These complete maps uncover a single amino-acid mutation that fully escapes the REGN-COV2 cocktail, which consists of two antibodies targeting distinct structural epitopes. The maps also identify viral mutations that are selected in a persistently infected patient treated with REGN-COV2, as well as during in vitro viral escape selections. Finally, the maps reveal that mutations escaping the individual antibodies are already present in circulating SARS-CoV-2 strains. Overall, these complete escape maps enable interpretation of the consequences of mutations observed during viral surveillance.

			 **Fig. 4. Structural context of escape mutations.** (**A**) Escape maps projected on antibody-bound RBD structures. [REGN10933 and REGN10987: PDB 6XDG (*11*); LY-CoV016: PDB 7C01 (*13*)]. Antibody heavy- and light-chain variable domains are shown as blue cartoons, and the RBD surface is colored to indicate how strongly mutations at that site mediate escape (white indicates no escape, red indicates strongest escape site for that antibody/cocktail). Sites where no mutations are functionally tolerated are colored gray. (**B**) For each antibody, sites were classified as direct antibody contacts (non-hydrogen atoms within 4 Å of antibody), antibody-proximal (4–8 Å), or antibody-distal (>8 Å). Each point indicates a site, classified as escape (red) or non-escape (black). The dashed gray line indicates the cutoff used to classify sites as escape or non-escape (see Methods for details). Red and black numbers indicate how many sites in each category are escape or non-escape sites, respectively. Interactive visualizations are at https://jbloomlab.github.io/SARS-CoV-2-RBD_MAP_clinical_Abs/ and hypothesized mechanisms of escape and additional structural details for labeled points are shown in fig. S6.
Hall V et al MedRXiv https://www.medrxiv.org/content/10.1101/2021.01.13.21249642v1	Do antibody positive healthcare workers have lower SARS-CoV-2 infection rates than antibody negative healthcare workers? Large multi-centre prospective cohort study (the SIREN study), England: June to November 2020	Studio di coorte prospettico condotto su operatori sanitari degli ospedali del Regno Unito : coloro che avevano anticorpi anti-SARS-CoV-2 positivi hanno un rischio di reinfezione inferiore dell'83% rispetto ai negativi di infettarsi nuovamente con SARS-CoV-2.	Background There is an urgent need to better understand whether individuals who have recovered from COVID-19 are protected from future SARS-CoV-2 infection. Methods A large multi-centre prospective cohort was recruited from publicly funded hospital staff in the UK. Participants attended regular SARS-CoV-2 PCR and antibody testing (every 2-4 weeks) and completed fortnightly questionnaires on symptoms and exposures. At enrolment, participants were assigned to either the positive cohort (antibody positive or prior PCR/antibody test positive) or negative cohort (antibody negative, not previously known to be

			PCR/antibody positive). Potential reinfections were clinically reviewed and classified according to case definitions (confirmed, probable, possible (subdivided by symptom-status)) depending on hierarchy of evidence. Individuals in the primary infection were excluded from this analysis if infection was confirmed by antibody only. Reinfection rates in the positive cohort were compared against new PCR positives in the negative cohort using a mixed effective multivariable logistic regression analysis. Findings Between 18 June and 09 November 2020, 44 reinfections (2 probable, 42 possible) were detected in the baseline positive cohort of 6,614 participants, collectively contributing 1,339,078 days of follow-up. This compares with 318 new PCR positive infections and 94 antibody seroconversions in the negative cohort of 14,173 participants, contributing 1,868,646 days of follow-up. The incidence density per 100,000 person days between June and November 2020 was 3.3 reinfections in the positive cohort, compared with 22.4 new PCR confirmed infections in the negative cohort. The adjusted odds ratio was 0.17 for all reinfections (95% CI 0.13-0.24) compared to PCR confirmed primary infections. The median interval between primary infection and reinfection was over 160 days. Interpretation A prior history of SARS-CoV-2 infection was associated with an 83% lower risk of infection, with median protective effect observed five months following primary infection. This is the minimum likely effect as seroconversions were not included.
Oran DP et al Annals of Internal Medicine	The Proportion of SARS-CoV-2 Infections That Are Asymptomatic: A Systematic Review.	In base a questa revisione sistematica, almeno un terzo delle infezioni da SARS-CoV-2 è asintomatica e circa un quarto di chi	Background: Asymptomatic infection seems to be a notable feature of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the pathogen that causes coronavirus disease 2019 (COVID-19), but the prevalence is uncertain.

https://www.acpjournals.org/doi/10.7326/M20-6976		riceve la diagnosi da asintomatico poi rimane tale.	Purpose: To estimate the proportion of persons infected with SARS-CoV-2 who never develop symptoms. Data Sources: Searches of Google News, Google Scholar, medRxiv, and PubMed using the keywords antibodies, asymptomatic, coronavirus, COVID-19, PCR, seroprevalence, and SARS-CoV-2. Study Selection: Observational, descriptive studies and reports of mass screening for SARS-CoV-2 that were either cross-sectional or longitudinal in design; were published through 17 November 2020; and involved SARS-CoV-2 nucleic acid or antibody testing of a target population, regardless of current symptomatic status, over a defined period. Data Extraction: The authors collaboratively extracted data on the study design, type of testing performed, number of participants, criteria for determining symptomatic status, testing results, and setting. Data Synthesis: Sixty-one eligible studies and reports were identified, of which 43 used polymerase chain reaction (PCR) testing of nasopharyngeal swabs to detect current SARS-CoV-2 infection and 18 used antibody testing to detect current or prior infection. In the 14 studies with longitudinal data that reported information on the evolution of symptomatic status, nearly three quarters of persons who tested positive but had no symptoms at the time of testing remained asymptomatic. The highest-quality evidence comes from nationwide, representative serosurveys of England (n = 365 104) and Spain (n = 61 075), which suggest that at least one third of SARS-CoV-2 infections are asymptomatic. Limitation: For PCR-based studies, data are limited to distinguish presymptomatic from asymptomatic infection. Heterogeneity precluded formal quantitative syntheses.

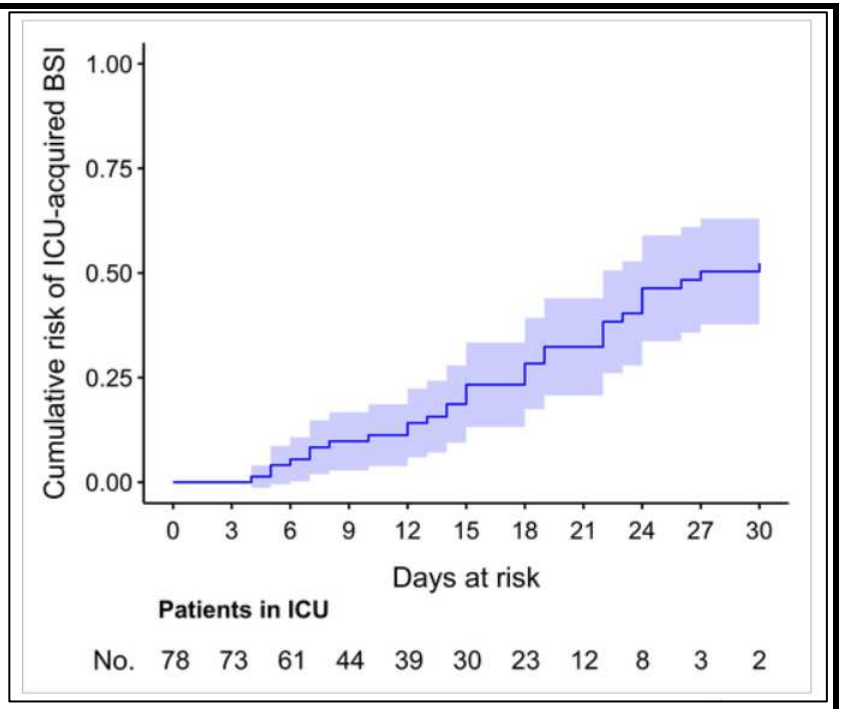
			Conclusion: Available data suggest that at least one third of SARS-CoV-2 infections are asymptomatic. Longitudinal studies suggest that nearly three quarters of persons who receive a positive PCR test result but have no symptoms at the time of testing will remain asymptomatic. Control strategies for COVID-19 should be altered, taking into account the prevalence and transmission risk of asymptomatic SARS-CoV-2 infection.
Cusumano JC et al Open Forum Infectious Diseases https://academic.oup.com/ofid/article/7/11/ofaa518/5975147	Staphylococcus aureus Bacteremia in Patients Infected With COVID-19: A Case Series	Studio osservazionale retrospettivo su 42 casi di infezione del torrente ematico da Stafilococco aureo in pazienti con COVID-19 : la sovrainfezione nosocomiale è un fattore predittivo di mortalità.	Background : Previous viral pandemics have shown that secondary bacterial infections result in higher morbidity and mortality, with Staphylococcus aureus being the primary causative pathogen. The impact of secondary S. aureus bacteremia on mortality in patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) remains unknown. Methods : This was a retrospective observational case series of patients with coronavirus disease 2019 (COVID-19) who developed secondary S. aureus bacteremia across 2 New York City hospitals. The primary end point was to describe 14-day and 30-day hospital mortality rates of patients with COVID-19 and S. aureus bacteremia. Secondary end points included predictors of 14-day and 30-day hospital mortality in patients with COVID-19 and S. aureus bacteremia. Results : A total of 42 patients hospitalized for COVID-19 with secondary S. aureus bacteremia were identified. Of these patients, 23 (54.8%) and 28 (66.7%) died at 14 days and 30 days, respectively, from their first positive blood culture. Multivariate analysis identified hospital-onset bacteremia (≥4 days from date of admission) and age as significant predictors of 14-day hospital mortality and Pitt bacteremia score as a significant predictor of 30-day hospital mortality (odds ratio [OR], 11.9; 95% CI, 2.03–114.7; P

			= .01; OR, 1.10; 95% CI, 1.03–1.20; P = .02; and OR, 1.56; 95% CI, 1.19–2.18; P = .003, respectively). Conclusions : Bacteremia with S. aureus is associated with high mortality rates in patients hospitalized with COVID-19. Further investigation is warranted to understand the impact of COVID-19 and secondary S. aureus bacteremia.
European Centers for Disease Prevention and Control Eurosurveillance https://www.ecdc.europa.eu/en/publications-data/covid-19-risk-assessment-spread-new-variants-concern-eueea-first-update	Updated rapid risk assessment from ECDC on the risk related to the spread of new SARS-CoV-2 variants of concern in the EU/EEA – first update	Aggiornamento degli ECDC sulle varianti di SARS-CoV-2 che destano « preoccupazione » : inglese, sudafricana e brasiliana. Appare molto probabile che esse giungano in Europa e potrebbe conseguirne un aumento dei casi di infezione e della pressione sul sistema sanitario.	Viruses constantly change through mutation and variations in the SARS-CoV-2 virus, due to evolution and adaptation processes, have been observed worldwide. While most emerging mutations will not have a significant impact on the spread of the virus, some mutations or combinations of mutations may provide the virus with a selective advantage, such as increased transmissibility or the ability to evade the host immune response. In this update we report new information on the spread of three virus variants (VOC 202012/01, 501Y.V2 and variant P.1). These variants are considered to be of concern because of mutations which have led to increased transmissibility and deteriorating epidemiological situations in the areas where they have recently become established. Based on the new information, the risk associated with the introduction and community spread of variants of concern has been increased to high/very high and the options for response have been adjusted to the current situation.
Johnson BA et al Nature https://www.nature.com/articles/s41586-021-03237-4	Loss of furin cleavage site attenuates SARS-CoV-2 pathogenesis	In questo studio si dimostra l'importanza di una porzione della proteina S di SARS-CoV-2 sensibile al clivaggio da parte dell'enzima furina, che se eliminata determina riduzione della replicazione virale in cellule umane.	SARS-CoV-2, a novel coronavirus (CoV)-producing worldwide pandemic1, has a furin cleavage site (PRRAR) in its spike protein that is absent in other group 2B CoVs2. To explore whether the furin cleavage site contributes to infection and pathogenesis, we generated a mutant SARS-CoV-2 deleting the furin cleavage site (ΔPRRA). SARS-CoV-2 ΔPRRA replicates had faster kinetics, improved fitness in Vero E6 cells, and reduced spike protein processing as compared to parental SARS-CoV-2. However, the

			ΔPRRA mutant had reduced replication in a human respiratory cell line and was attenuated in both hamster and K18-hACE2 transgenic mouse models of SARS-CoV-2 pathogenesis. Despite reduced disease, the ΔPRRA mutant conferred protection against rechallenge with the parental SARS-CoV-2. Importantly, COVID-19 patient sera and receptor-binding domain (RBD) monoclonal antibodies had lower neutralization values against the ΔPRRA mutant versus parental SARS-CoV-2, likely due to increased particle/PFU ratio. Together, these results demonstrate a critical role for the furin cleavage site in SARS-CoV-2 infection and highlight the importance of this site in evaluating antibody neutralization activity.
Claro IM et al Emerging Infectious Diseases https://wwwnc.cdc.gov/eid/article/27/3/21-0038_article	Local Transmission of SARS-CoV-2 Lineage B.1.1.7, Brazil, December 2020	Due casi di infezione da variante « inglese » di SARS-CoV-2 in Brasile a dicembre 2020, in due pazienti testati per sorveglianza e uno dei quali non aveva storia di viaggi all'estero; chi cerca trova!	In December 2020, research surveillance detected the B.1.1.7 lineage of severe acute respiratory syndrome coronavirus 2 in São Paulo, Brazil. Rapid genomic sequencing and phylogenetic analysis revealed 2 distinct introductions of the lineage. One patient reported no international travel. There may be more infections with this lineage in Brazil than reported.
Priesemann V et al The Lancet https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00150-1/fulltext	An action plan for pan-European defence against new SARS-CoV-2 variants	Se varianti di SARS-CoV-2 con maggiore trasmissibilità si diffonderanno in Europa, come è probabile, sarà necessario il mantenimento delle misure preventive, auspicabilmente accompagnate da adeguate misure a sostegno della popolazione.	COVID-19 cases are very high across Europe. Current measures are not reducing virus spread sufficiently, and new SARS-CoV-2 variants are emerging. The B.1.1.7 and B1.351 variants, first identified in the UK and South Africa, respectively, have spread to many European countries. Although the biological properties of these variants are yet to be characterised, epidemiological data suggest they have a higher transmissibility than the original variant. These viral properties could increase the effective reproduction number R in the population. In the case of B.1.1.7, estimates suggest R could increase from 1 to about 1.4 with no change in population behavior.

			If true, many countries that have succeeded in reducing R to 1 or less will be confronted with a novel wave of viral spread despite the current measures. Once a more contagious variant has established itself, stabilising the number of new infections will become increasingly difficult.
King KG et al American Journal of Infection Control https://www.ajicjournal.org/article/S0196-6553(21)00023-7/fulltext	An Assessment of Outpatient Clinic Room Ventilation Systems and Possible Relationship to Disease Transmission	La valutazione di 105 ambulatori medici fa osservare che la gran parte di essi non è a norma per un gran numero di funzioni per quanto riguarda l'areazione e ciò potrebbe mettere a rischio di trasmissione di infezioni, quale COVID-19, gli occupanti. Gli standard di riferimento sono quelli americani : https://www.ashrae.org/technical-resources/standards-and-guidelines/standards-addenda/ansi-ashrae-ashe-standard-170-2017-ventilation-of-health-care-facilities	Background : With healthcare shifting to the outpatient setting, this study examined whether outpatient clinics operating in business occupancy settings were conducting procedures in rooms with ventilation rates above, at, or below thresholds defined in the ANSI/ASHRAE/ASHE Standard 170 for Ventilation in Health Care Facilities and whether lower ventilation rates and building characteristics increase the risk of disease transmission. Methods : Ventilation rates were measured in 105 outpatient clinic rooms categorized by services rendered. Building characteristics were evaluated as determinants of ventilation rates, and risk of disease transmission was estimated using the Gammaitoni-Nucci model. Results : When compared to Standard 170, 10% of clinic rooms assessed did not meet the minimum requirement for general exam rooms, 39% did not meet the requirement for treatment rooms, 83% did not meet the requirement for aerosol-generating procedures, and 88% did not meet the requirement for procedure rooms or minor surgical procedures. Conclusions : Lower than standard air changes per hour were observed and could lead to an increased risk of spread of diseases when conducting advanced procedures and evaluating persons of interest for emerging infectious diseases. These findings are pertinent during the SARS-CoV-2 pandemic, as working guidelines are established for the healthcare community.

Giacobbe DR et al European Journal of Clinical Investigation https://onlinelibrary.wiley.com/doi/10.1111/eci.13319	Bloodstream infections in critically ill patients with COVID-19.	Il trattamento con antinfiammatori (tocilizumab o steroidi) è l'unico fattore che si mantiene predittore indipendente di infezione del torrente ematico in questa casistica di 78 pazienti critici con COVID-19 ricoverati in rianimazione.	BACKGROUND: Little is known about the incidence and risk of intensive care unit (ICU)-acquired bloodstream infections (BSI) in critically ill patients with coronavirus disease 2019 (COVID-19). MATERIALS AND METHODS: This retrospective, single-centre study was conducted in Northern Italy. The primary study objectives were as follows: (a) to assess the incidence rate of ICU-acquired BSI and (b) to assess the cumulative risk of developing ICU-acquired BSI. RESULTS: Overall, 78 critically ill patients with COVID-19 were included in the study. Forty-five episodes of ICU-acquired BSI were registered in 31 patients, with an incidence rate of 47 episodes (95% confidence interval [CI] 35-63) per 1000 patient-days at risk. The estimated cumulative risk of developing at least one BSI episode was of almost 25% after 15 days at risk and possibly surpassing 50% after 30 days at risk. In multivariable analysis, anti-inflammatory treatment was independently associated with the development of BSI (cause-specific hazard ratio [csHR] 1.07 with 95% CI 0.38-3.04 for tocilizumab, csHR 3.95 with 95% CI 1.20-13.03 for methylprednisolone and csHR 10.69 with 95% CI 2.71-42.17 for methylprednisolone plus tocilizumab, with no anti-inflammatory treatment as the reference group; overall P for the dummy variable = 0.003). CONCLUSIONS: The incidence rate of BSI was high, and the cumulative risk of developing BSI increased with ICU stay. Further study will clarify if the increased risk of BSI we detected in COVID-19 patients treated with anti-inflammatory drugs is outweighed by the benefits of reducing any possible pro-inflammatory dysregulation induced by SARS-CoV-2.

			
Thomson EC et al Cell https://www.cell.com/cell/fulltext/S0092-8674(21)00080-5	Circulating SARS-CoV-2 spike N439K variants maintain fitness while evading antibody-mediated immunity	La mutazione N439K nella porzione legante il recettore ACE2 della proteina spike di SARS-CoV-2 aumenta l'affinità per il recettore stesso, non determina riduzione della fitness virale e riduce l'affinità per anticorpi provenienti dal siero di pazienti guariti o monoclonali sintetizzati e approvati in uso.	SARS-CoV-2 can mutate and evade immunity, with consequences for efficacy of emerging vaccines and antibody therapeutics. Herein we demonstrate that the immunodominant SARS-CoV-2 spike (S) receptor binding motif (RBM) is a highly variable region of S, and provide epidemiological, clinical, and molecular characterization of a prevalent, sentinel RBM mutation, N439K. We demonstrate N439K S protein has enhanced binding affinity to the hACE2 receptor, and N439K viruses have similar in vitro replication fitness and cause infections with similar clinical outcomes as compared to wild-type. We show the N439K mutation confers resistance against several neutralizing monoclonal antibodies, including one authorized for emergency use by the FDA, and reduces the activity of some polyclonal sera from persons recovered from infection.

			Immune evasion mutations that maintain virulence and fitness such as N439K can emerge within SARS-CoV-2 S, highlighting the need for ongoing molecular surveillance to guide development and usage of vaccines and therapeutics.
Muik A et al bioRXiv – not peer reviewed https://www.biorxiv.org/content/10.1101/2021.01.18.426984v1	Neutralization of SARS-CoV-2 lineage B.1.1.7 pseudovirus by BNT162b2 vaccine-elicited human sera	Il siero di 16 pazienti vaccinati con BNT162b2 (Pfizer) neutralizza in egual modo SARS-CoV-2 wild-type e B.1.1.7 (variante « inglese »).	Recently, a new SARS-CoV-2 lineage called B.1.1.7 has emerged in the United Kingdom that was reported to spread more efficiently than other strains. This variant has an unusually large number of mutations with 10 amino acid changes in the spike protein, raising concerns that its recognition by neutralizing antibodies may be affected. Here, we investigated SARS-CoV-2-S pseudoviruses bearing either the Wuhan reference strain or the B.1.1.7 lineage spike protein with sera of 16 participants in a previously reported trial with the mRNA-based COVID-19 vaccine BNT162b2. The immune sera had equivalent neutralizing titers to both variants. These data, together with the combined immunity involving humoral and cellular effectors induced by this vaccine, make it unlikely that the B.1.1.7 lineage will escape BNT162b2-mediated protection.
Wu K et al bioRXiv – not peer reviewed https://www.biorxiv.org/content/10.1101/2021.01.25.427948v1	mRNA-1273 vaccine induces neutralizing antibodies against spike mutants from global SARS-CoV-2 variants	Il siero di soggetti vaccinati con mRNA-1273 (Moderna) neutralizza, con titolo neutralizzante ridotto ma comunque valido, una serie di vettori virali portatori di proteina S con diverse mutazioni, fra cui quelle tipiche delle varianti « inglese » e « sudafricana ».	Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is the causative infection of a global pandemic that has led to more than 2 million deaths worldwide. The Moderna mRNA-1273 vaccine has demonstrated ~94% efficacy in a Phase 3 study and has been approved under Emergency Use Authorization. The emergence of SARS-CoV-2 variants with mutations in the spike protein, most recently circulating isolates from the United Kingdom (B.1.1.7) and Republic of South Africa (B.1.351), has led to lower neutralization from convalescent serum by pseudovirus neutralization (PsVN) assays and resistance to certain monoclonal antibodies. Here, using two orthogonal VSV and lentivirus PsVN assays expressing spike variants of 20E (EU1), 20A.EU2, D614G-N439, mink cluster 5,

			B.1.1.7, and B.1.351 variants, we assessed the neutralizing capacity of sera from human subjects or non-human primates (NHPs) that received mRNA-1273. No significant impact on neutralization against the B.1.1.7 variant was detected in either case, however reduced neutralization was measured against the mutations present in B.1.351. Geometric mean titer (GMT) of human sera from clinical trial participants in VSV PsVN assay using D614G spike was 1/1852. VSV pseudoviruses with spike containing K417N-E484K-N501Y-D614G and full B.1.351 mutations resulted in 2.7 and 6.4-fold GMT reduction, respectively, when compared to the D614G VSV pseudovirus. Importantly, the VSV PsVN GMT of these human sera to the full B.1.351 spike variant was still 1/290, with all evaluated sera able to fully neutralize. Similarly, sera from NHPs immunized with 30 or 100µg of mRNA-1273 had VSV PsVN GMTs of ~ 1/323 or 1/404, respectively, against the full B.1.351 spike variant with a ~ 5 to 10-fold reduction compared to D614G. Individual mutations that are characteristic of the B.1.1.7 and B.1.351 variants had a similar impact on neutralization when tested in VSV or in lentivirus PsVN assays. Despite the observed decreases, the GMT of VSV PsVN titers in human vaccinee sera against the B.1.351 variant remained at ~1/300. Taken together these data demonstrate reduced but still significant neutralization against the full B.1.351 variant following mRNA-1273 vaccination.
Bellan Mattia et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2775643	Respiratory and Psychophysical Sequelae Among Patients With COVID-19 Four Months After Hospital Discharge	Studio di coorte sul follow up, in termini di funzionalità respiratoria e sequele psichiche, di 238 pazienti ricoverati per COVID-19 a Novara.	Importance Although plenty of data exist regarding clinical manifestations, course, case fatality rate, and risk factors associated with mortality in severe coronavirus disease 2019 (COVID-19), long-term respiratory and functional sequelae in survivors of COVID-19 are unknown.

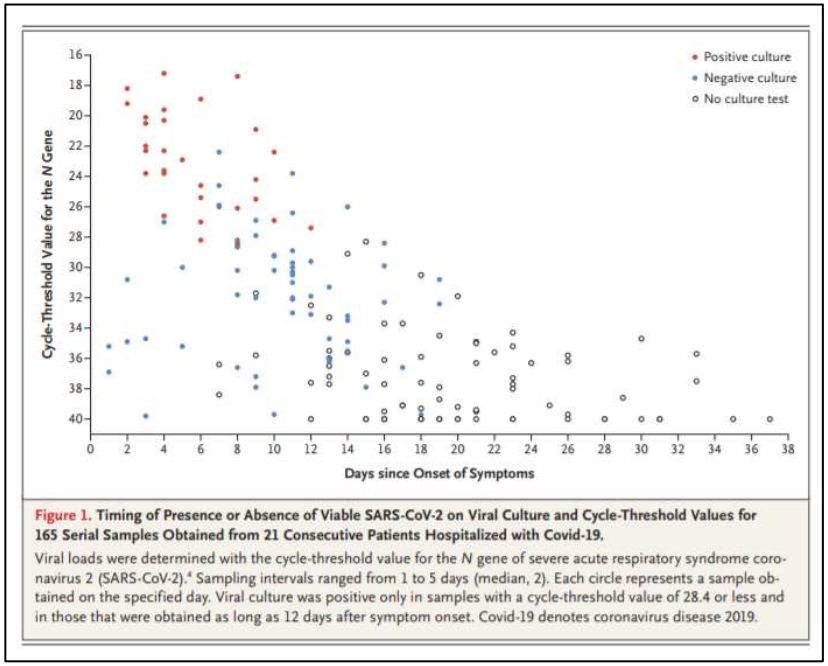
			Objective To evaluate the prevalence of lung function anomalies, exercise function impairment, and psychological sequelae among patients hospitalized for COVID-19, 4 months after discharge. Design, Setting, and Participants This prospective cohort study at an academic hospital in Northern Italy was conducted among a consecutive series of patients aged 18 years and older (or their caregivers) who had received a confirmed diagnosis of severe acute respiratory coronavirus 2 (SARS-CoV-2) infection severe enough to require hospital admission from March 1 to June 29, 2020. SARS-CoV-2 infection was confirmed via reverse transcription–polymerase chain reaction testing, bronchial swab, serological testing, or suggestive computed tomography results. Exposure Severe COVID-19 requiring hospitalization. Main Outcomes and Measures The primary outcome of the study was to describe the proportion of patients with a diffusing lung capacity for carbon monoxide (Dlco) less than 80% of expected value. Secondary outcomes included proportion of patients with severe lung function impairment (defined as Dlco <60% expected value); proportion of patients with posttraumatic stress symptoms (measured using the Impact of Event Scale–Revised total score); proportion of patients with functional impairment (assessed using the Short Physical Performance Battery [SPPB] score and 2-minute walking test); and identification of factors associated with Dlco reduction and psychological or functional sequelae. Results Among 767 patients hospitalized for severe COVID-19, 494 (64.4%) refused to participate, and 35 (4.6%) died during follow-up. A total of 238 patients (31.0%) (median [interquartile range] age, 61 [50-71] years; 142 [59.7%] men; median [interquartile range] comorbidities, 2 [1-3]) consented to participate to the study. Of these, 219 patients were able to complete both pulmonary function

tests and Dlco measurement. Dlco was reduced to less than 80% of the estimated value in 113 patients (51.6%) and less than 60% in 34 patients (15.5%). The SPPB score was suggested limited mobility (score <11) in 53 patients (22.3%). Patients with SPPB scores within reference range underwent a 2-minute walk test, which was outside reference ranges of expected performance for age and sex in 75 patients (40.5%); thus, a total of 128 patients (53.8%) had functional impairment. Posttraumatic stress symptoms were reported in a total of 41 patients (17.2%).

Conclusions and Relevance: These findings suggest that at 4 months after discharge, respiratory, physical, and psychological sequelae were common among patients who had been hospitalized for COVID-19.

Table 2. Logistic Regression Analysis of Risk Factors for D_{LCO} Impairment

Outcome	OR (95% CI)	*P* value
D_{LCO} <80%		
Female sex	4.33 (2.25-8.33)	<.001
Age	1.01 (0.99-1.04)	.17
Atrial fibrillation	1.48 (0.41-5.37)	.55
CKD	10.12 (2.00-51.05)	.005
ICU admission	1.32 (0.39-4.42)	.65
Modality of oxygen delivery	1.68 (1.08-2.61)	.02
COPD	2.20 (0.57-8.48)	.25
Smoking status	1.19 (0.76-1.84)	.45
D_{LCO} <60%		
Female sex	2.70 (1.11-6.55)	.03
Age	1.00 (0.97-1.04)	.70
No. of comorbidities	1.18 (0.65-2.15)	.59
CKD	4.75 (1.19-19.00)	.03
Diabetes	2.17 (0.68-6.92)	.19
ICU admission	5.76 (1.37-24.25)	.02
Modality of oxygen delivery	1.55 (0.82-2.94)	.18
COPD	5.52 (1.32-23.08)	.02
Smoking status	0.98 (0.52-1.87)	.96

Kim MC et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMc2027040?query=featured_coronavirus	Duration of Culturable SARS-CoV-2 in Hospitalized Patients with Covid-19	In 89 pazienti ricoverati per COVID-19, la negatività alla PCR del tampone nasofaringeo si ottiene dopo un periodo mediano di 34 giorni, mentre il virus non è più osservabile su coltura cellulare dopo un massimo di 12 giorni dall'esordio dei sintomi e un massimo di 3 giorni dall'apiressia.	SARS-CoV-2 was cultured in 29 of the 89 samples (33%) (Figure 1). The median time from symptom onset to viral clearance in culture was 7 days (95% confidence interval [CI], 5 to 10), and the median time from symptom onset to viral clearance on real-time RT-PCR was 34 days (lower boundary of the 95% CI, 24 days) (Fig. S1 and Table S4). The latest positive viral culture was 12 days after symptom onset (in Patient 6). Viable virus was identified until 3 days after the resolution in fever (in Patient 14). Viral culture was positive only in samples with a cycle-threshold value of 28.4 or less. The incidence of culture positivity decreased with an increasing time from symptom onset and with an increasing cycle-threshold value.  **Figure 1. Timing of Presence or Absence of Viable SARS-CoV-2 on Viral Culture and Cycle-Threshold Values for 165 Serial Samples Obtained from 21 Consecutive Patients Hospitalized with Covid-19.** Viral loads were determined with the cycle-threshold value for the *N* gene of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[4] Sampling intervals ranged from 1 to 5 days (median, 2). Each circle represents a sample obtained on the specified day. Viral culture was positive only in samples with a cycle-threshold value of 28.4 or less and in those that were obtained as long as 12 days after symptom onset. Covid-19 denotes coronavirus disease 2019.

News From the Centers for Disease Control and Prevention JAMA https://jamanetwork.com/journals/jama/fullarticle/2775458	Drug-Resistant Bacteria Outbreak Linked to COVID-19 Patient Surge	I CDC segnalano un incremento della diffusione di microrganismi multiresistenti durante la pandemia di COVID-19, come conseguenza della modifica necessaria di alcune pratiche di infection control.	Breaches in infection control practices during last spring's coronavirus disease 2019 (COVID-19) surge likely contributed to a 34-patient outbreak of carbapenem-resistant Acinetobacter baumannii (CRAB) infections at a New Jersey hospital.
Fiorenzato E et al PlosOne https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0246204	Cognitive and mental health changes and their vulnerability factors related to COVID-19 lockdown in Italy	Esiti di un sondaggio su 1215 persone alla fine di un periodo di 7-10 settimane di quarantena alla ricerca di alterazioni comportamentali e fattori di rischio per una loro maggiore gravità.	The COVID-19 pandemic and government imposed social restrictions like lockdown exposed most individuals to an unprecedented stress, increasing mental health disorders worldwide. We explored subjective cognitive functioning and mental health changes and their possible interplay related to COVID-19-lockdown. We also investigated potential risk factors to identify more vulnerable groups. Across Italy, 1215 respondents completed our Qualtrics-based online-survey during the end of a seven to 10-week imposed lockdown and home confinement (from April 29 to May 17, 2020). We found subjective cognitive functioning and mental health severely changed in association with the lockdown. Under government regulations, cognitive complaints were mostly perceived in routine tasks involving attention, temporal orientation and executive functions—with no changes in language abilities. A paradoxical effect was observed for memory, with reduced forgetfulness compared to pre-lockdown. We found higher severity and prevalence of depression, anxiety disorders, abnormal sleep, appetite changes, reduced libido and health anxiety: with mild-to-severe depression and anxiety prevalence climbing to 32 and 36 percent, respectively, under restrictions. Being female, under 45

			years, working from home or being underemployed were all identified as relevant risk factors for worsening cognition and mental health. Frequent consumers of COVID-19 mass media information or residents in highly infected communities reported higher depression and anxiety symptoms, particularly hypochondria in the latter. If similar restrictions are reimposed, governments must carefully consider these more vulnerable groups in their decisions, whilst developing effective global and long-term responses to the cognitive and mental health challenges of this type of pandemic; as well as implementing appropriate psychological interventions with specific guidelines: particularly regarding exposure to COVID-19 mass-media reports.
Karmakar M et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2775732	Association of Social and Demographic Factors With COVID-19 Incidence and Death Rates in the US	Come per molte malattie infettive, i fattori sociodemografici correlano con incidenza e mortalità di COVID-19.	Importance Descriptive data have revealed significant racial/ethnic disparities in coronavirus disease 2019 (COVID-19) cases in the US, but underlying mechanisms of disparities remain unknown. Objective To examine the association between county-level sociodemographic risk factors and US COVID-19 incidence and mortality. Design, Setting, and Participants This cross-sectional study analyzed the association between US county-level sociodemographic risk factors and COVID-19 incidence using mixed-effects negative binomial regression, and COVID-19 mortality using zero-inflated negative binomial regression. Data on COVID-19 incidence and mortality were collected from January 20 to July 29, 2020. The association of social risk factors with weekly cumulative incidence and mortality was also examined by interacting time with the index measures, using a random intercept to account for repeated measures.

			Main Outcomes and Measures Sociodemographic data from publicly available data sets, including the US Centers for Disease Control and Prevention's Social Vulnerability Index (SVI), which includes subindices of socioeconomic status, household composition and disability, racial/ethnic minority and English language proficiency status, and housing and transportation. Results As of July 29, 2020, there were a total of 4 289 283 COVID-19 cases and 147 074 COVID-19 deaths in the US. An increase of 0.1 point in SVI score was associated with a 14.3% increase in incidence rate (incidence rate ratio [IRR], 1.14; 95% CI, 1.13-1.16; P < .001) and 13.7% increase in mortality rate (IRR, 1.14; 95% CI, 1.12-1.16; P < .001), or an excess of 87 COVID-19 cases and 3 COVID-19 deaths per 100 000 population for a SVI score change from 0.5 to 0.6 in a midsize metropolitan county; subindices were also associated with both outcomes. A 0.1-point increase in the overall SVI was associated with a 0.9% increase in weekly cumulative increase in incidence rate (IRR, 1.01; 95% CI, 1.01-1.01; P < .001) and 0.5% increase in mortality rate (IRR, 1.01; 95% CI, 1.01-1.01; P < .001). Conclusions and Relevance In this cross-sectional study, a wide range of sociodemographic risk factors, including socioeconomic status, racial/ethnic minority status, household composition, and environmental factors, were significantly associated with COVID-19 incidence and mortality. To address inequities in the burden of the COVID-19 pandemic, these social vulnerabilities and their root causes must be addressed.

			Table 1. Association of Social Vulnerability Index Measures With COVID-19 Incidence and Mortality COVID-19 incidence rate[a,b] — COVID-19 mortality rate[a,c] Variable — IRR (95% CI) — *P* value — IRR (95% CI) — *P* value Overall Social Vulnerability Index[d] — 1.14 (1.13-1.16) — <.001 — 1.14 (1.12-1.16) — <.001 Socioeconomic status subindex[d] — 1.11 (1.10-1.13) — <.001 — 1.12 (1.09-1.14) — <.001 Household characteristics and disability subindex[d] — 1.02 (1.01-1.03) — .001 — 1.06 (1.04-1.08) — <.001 Racial/ethnic minority status and language subindex[d] — 1.22 (1.20-1.23) — <.001 — 1.17 (1.14-1.19) — <.001 Housing type and transportation subindex[d] — 1.10 (1.08-1.11) — <.001 — 1.08 (1.06-1.10) — <.001 Abbreviation: COVID-19, coronavirus disease 2019; IRR, incidence rate ratio. [a] Each of the independent variables was entered into a separate regression model to test the association with either COVID-19 incidence or mortality, adjusted for population density, urbanicity, and COVID-19 testing rate. Each cell represents a separate regression model. All regression models included an offset for the total number of people residing in the county. Analytic sample excluded the counties spanning New York, New York. [b] Incidence rates were estimated using mixed-effects negative binomial regression with a random intercept for state. [c] Mortality rates were estimated using mixed-effects zero-inflated negative binomial regression with a random intercept for state. Cases per 100 000 population were used to model the logit part in each model estimating excess zero count. [d] Owing to rescaling of the variables, IRR for each index shows the change in incidence or mortality for a 0.1 unit of the original index measure.
Moore JP et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2776039	SARS-CoV-2 Vaccines and the Growing Threat of Viral Variants	Le varianti di SARS-CoV-2, caratterizzate da mutazioni a carico della proteina S, potrebbero mostrare minore affinità per agli anticorpi prodotti a seguito di vaccinazione : questo sembra il caso delle varianti sudafricana e brasiliana	Variants in the S-protein that increase the amount of virus shed from an infected person or that increase its affinity for the ACE2 receptor are likely to increase virus transmission, an important problem in the context of a pandemic. Furthermore, the same or similar alterations can change the shape of the S-protein and impair or even destroy NAb binding sites. Hence, by extrapolation, vaccine efficacy might be compromised. These “escape mutations” typically arise when the virus is put under selective pressure by antibodies that limit but do not eliminate viral replication. Under these conditions, the virus might then find a way to escape this pressure and restore its ability to reproduce more efficiently. The scenario of virus evolution in the face of suboptimal immunity is one reason extending the interval between the first and second dose of a SARS-CoV-2 vaccine might be problematic.

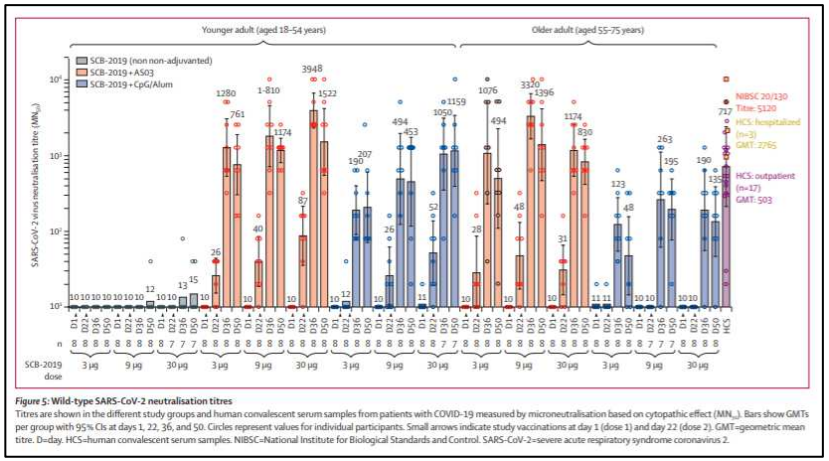
Veiga CV et al BMJ https://www.bmj.com/content/372/bmj.n84	Effect of tocilizumab on clinical outcomes at 15 days in patients with severe or critical coronavirus disease 2019: randomised controlled trial	Piccolo trial clinico multicentrico condotto in Brasile che confronta lo standard of care con e senza aggiunta di una dose di tocilizumab 8 mg/Kg EV : interruzione precoce per un inaspettato eccesso di mortalità nel gruppo tocilizumab a 15 giorni.	Objective To determine whether tocilizumab improves clinical outcomes for patients with severe or critical coronavirus disease 2019 (covid-19). Design Randomised, open label trial. Setting Nine hospitals in Brazil, 8 May to 17 July 2020. Participants Adults with confirmed covid-19 who were receiving supplemental oxygen or mechanical ventilation and had abnormal levels of at least two serum biomarkers (C reactive protein, D dimer, lactate dehydrogenase, or ferritin). The data monitoring committee recommended stopping the trial early, after 129 patients had been enrolled, because of an increased number of deaths at 15 days in the tocilizumab group. Interventions Tocilizumab (single intravenous infusion of 8 mg/kg) plus standard care (n=65) versus standard care alone (n=64). Main outcome measure The primary outcome, clinical status measured at 15 days using a seven level ordinal scale, was analysed as a composite of death or mechanical ventilation because the assumption of odds proportionality was not met. Results A total of 129 patients were enrolled (mean age 57 (SD 14) years; 68% men) and all completed follow-up. All patients in the tocilizumab group and two in the standard care group received tocilizumab. 18 of 65 (28%) patients in the tocilizumab group and 13 of 64 (20%) in the standard care group were receiving mechanical ventilation or died at day 15 (odds ratio 1.54, 95% confidence interval 0.66 to 3.66; P=0.32). Death at 15 days occurred in 11 (17%) patients in the tocilizumab group compared with 2 (3%) in the standard care group (odds ratio 6.42, 95% confidence interval 1.59

			to 43.2). Adverse events were reported in 29 of 67 (43%) patients who received tocilizumab and 21 of 62 (34%) who did not receive tocilizumab. Conclusions In patients with severe or critical covid-19, tocilizumab plus standard care was not superior to standard care alone in improving clinical outcomes at 15 days, and it might increase mortality.
McCreary EK et al BMJ https://www.bmj.com/content/372/bmj.n244	Covid-19 controversies: the tocilizumab chapter	Confronto fra i trial clinici pubblicati finora sulla terapia con tocilizumab per COVID-19 : i dati non sono sufficienti per dismettere questo farmaco, la selezione della popolazione da trattare potrebbe essere la chiave per utilizzarlo in modo proficuo.	Tocilizumab, a humanized monoclonal antibody that inhibits interleukin 6 mediated signaling by blocking interleukin 6 from binding to receptors, was an early front runner in the race to find treatments for severely ill patients. However, conflicting results from several randomized clinical trials, along with corticosteroids becoming standard care for patients admitted to hospital who required oxygen, tempered enthusiasm for its use. Now, in a linked paper, Veiga and colleagues (doi:10.1136/bmj.n84) report a randomized trial from Brazil that compared tocilizumab with standard care in 129 patients with covid-19.10 Surprisingly, the trial was stopped early because tocilizumab was associated with increased deaths at day 15 (17% v 3%, odds ratio 6.42, 95% confidence interval 1.59 to 43.2). So, should tocilizumab be abandoned? The answer is not straightforward.
Williamson L The Lancet https://www.thelancet.com/journals/lanres/article/	Living with bronchiectasis during the COVID-19 pandemic	Storia di una paziente bronchiectasica ai tempi della pandemia di COVID-19 (la mascherina in pubblico va comunque indossata).	Bronchiectasis is a chronic lung disease characterised by inflammation of the airways, mucociliary dysfunction, mucus plugging, and progressive structural damage. Patients experience a persistent cough, sputum production, and recurrent infections, accompanied by the radiological findings of dilated and thickened bronchi. Each infection causes damage to the airways, and over time this damage can lead to reduced oxygen reaching vital organs.

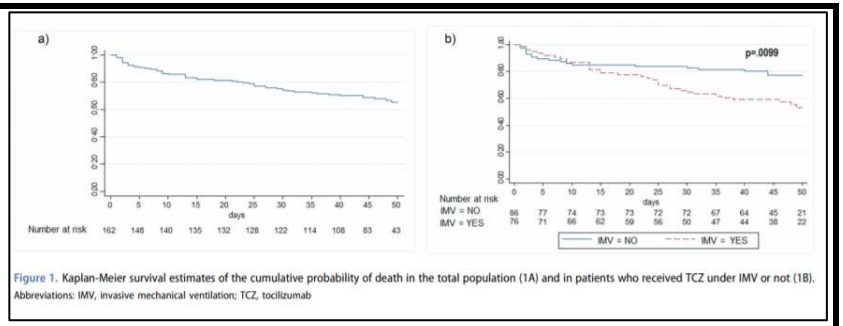
PIIS2213-2600(21)00074-6/fulltext			According to the British Lung Foundation, in excess of 300 000 people could be living with bronchiectasis in the UK. There's no cure for bronchiectasis, but patients can typically live a normal life with treatment, which aims to prevent further lung damage and infection.
Rubin EJ et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMe2101618?query=featured_home	Audio Interview: A Covid-19 Conversation with Anthony Fauci	Una conversazione su COVID-19 con Anthony Fauci.	The continuing spread of SARS-CoV-2 remains a Public Health Emergency of International Concern. What physicians need to know about transmission, diagnosis, and treatment of Covid-19 is the subject of ongoing updates from infectious disease experts at the Journal. In this audio interview conducted on January 27, 2021, the editors are joined by Dr. Anthony Fauci, U.S. Chief Medical Advisor, to discuss Covid-19 testing, therapeutics, and vaccines.
Li C et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab083/6124512?searchresult=1	Absence of vaccine-enhanced disease with unexpected positive protection against SARS-CoV-2 by inactivated vaccine given within three days of virus challenge in Syrian hamster model	In questo studio è stato valutato l'andamento dell'infezione da SARS-CoV-2 nel criceto sottoposto contestualmente a vaccino contro SARS-CoV-2 con virione inattivato: la somministrazione del vaccino immediatamente prima, dopo o contemporaneamente all'infezione non provoca effetti paradossi ma sembra migliorare il decorso dell'infezione stessa.	Background : Mass vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is ongoing amidst widespread transmission during the Coronavirus Disease 2019 (COVID-19) pandemic. Disease phenotypes of SARS-CoV-2 exposure occurring around the time of vaccine administration have not been described. Methods : Two-dose (14 days apart) vaccination regimen with a formalin-inactivated whole virion SARS-CoV-2 in golden Syrian hamster model was established. To investigate the disease phenotypes of a one-dose regimen given 3 days prior (D-3), 1 (D1) or 2 (D2) days after, or on the day (D0) of virus challenge, we monitored the serial clinical severity, tissue histopathology, virus burden, and antibody response of the vaccinated hamsters. Results : The one-dose vaccinated hamsters had significantly lower clinical disease severity score, body weight loss, lung histology score, nucleocapsid protein expression in lung, infectious virus titres

			in the lung and nasal turbinate, inflammatory changes in intestines and a higher serum neutralizing antibody or IgG titre against the spike receptor-binding domain or nucleocapsid protein when compared to unvaccinated controls. These improvements were particularly noticeable in D-3, but also in D0, D1 and even D2 vaccinated hamsters to varying degrees. No increased eosinophilic infiltration was found in the nasal turbinate, lung, and intestine after virus challenge. Significantly higher serum titre of fluorescent foci microneutralization inhibition antibody was detected in D1 and D2 vaccinated hamsters at day 4 post-challenge compared to controls despite undetectable neutralizing antibody titre. Conclusions : Vaccination just before or soon after exposure to SARS-CoV-2 does not worsen disease phenotypes and may even ameliorate infection.
Richmond P et al The Lancet https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00241-5/fulltext	Safety and immunogenicity of S-Trimer (SCB-2019), a protein subunit vaccine candidate for COVID-19 in healthy adults: a phase 1, randomised, double-blind, placebo-controlled trial	Trial clinico di fase I condotto in Australia su un vaccino a subunità contro SARS-CoV-2 adiuvato con due differenti molecole (AS03 e CPG/Alum) : si osserva buona immunogenicità di entrambi i candidati, per i quali proseguirà la sperimentazione.	Background : As part of the accelerated development of vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), we report a dose-finding and adjuvant justification study of SCB-2019, a protein subunit vaccine candidate containing a stabilised trimeric form of the spike (S)-protein (S-Trimer) combined with two different adjuvants. Methods : Our study is a phase 1, randomised, double-blind placebo-controlled trial at a specialised clinical trials centre in Australia. We enrolled healthy adult volunteers in two age groups: younger adults (aged 18–54 years) and older adults (aged 55–75 years). Participants were randomly allocated either vaccine or placebo using a list prepared by the study funder. Participants were to receive two doses of SCB-2019 (either 3 µg, 9 µg, or 30 µg) or a placebo (0·9% NaCl) 21 days apart. SCB-2019 either had no adjuvant

			(S-Trimer protein alone) or was adjuvanted with AS03 or CpG/Alum. The assigned treatment was administered in opaque syringes to maintain masking of assignments. Reactogenicity was assessed for 7 days after each vaccination. Humoral responses were measured as SCB-2019 binding IgG antibodies and ACE2-competitive blocking IgG antibodies by ELISA and as neutralising antibodies by wild-type SARS-CoV-2 microneutralisation assay. Cellular responses to pooled S-protein peptides were measured by flow-cytometric intracellular cytokine staining. This trial is registered with ClinicalTrials.gov, NCT04405908; this is an interim analysis and the study is continuing. Findings : Between June 19 and Sept 23, 2020, 151 volunteers were enrolled; three people withdrew, two for personal reasons and one with an unrelated serious adverse event (pituitary adenoma). 148 participants had at least 4 weeks of follow-up after dose two and were included in this analysis (database lock, Oct 23, 2020). Vaccination was well tolerated, with two grade 3 solicited adverse events (pain in 9 µg AS03-adjuvanted and 9 µg CpG/Alum-adjuvanted groups). Most local adverse events were mild injection-site pain, and local events were more frequent with SCB-2019 formulations containing AS03 adjuvant (44–69%) than with those containing CpG/Alum adjuvant (6–44%) or no adjuvant (3–13%). Systemic adverse events were more frequent in younger adults (38%) than in older adults (17%) after the first dose but increased to similar levels in both age groups after the second dose (30% in older and 34% in younger adults). SCB-2019 with no adjuvant elicited minimal immune responses (three seroconversions by day 50), but SCB-2019 with fixed doses of either AS03 or CpG/Alum adjuvants induced high titres and seroconversion rates of binding and neutralising antibodies in both younger and older adults (anti-SCB-

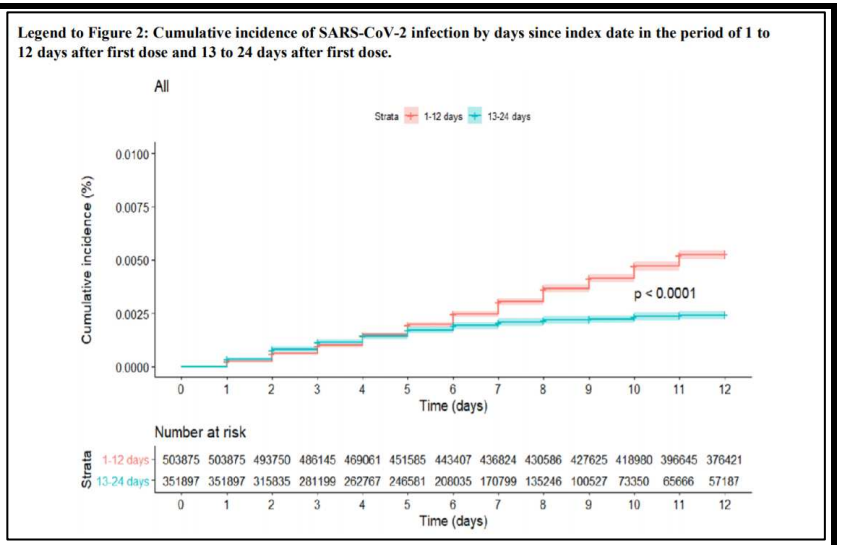
			2019 IgG antibody geometric mean titres at day 36 were 1567–4452 with AS03 and 174–2440 with CpG/Alum). Titres in all AS03 dose groups and the CpG/Alum 30 µg group were higher than were those recorded in a panel of convalescent serum samples from patients with COVID-19. Both adjuvanted SCB-2019 formulations elicited T-helper-1-biased CD4+ T-cell responses. Interpretation : The SCB-2019 vaccine, comprising S-Trimer protein formulated with either AS03 or CpG/Alum adjuvants, elicited robust humoral and cellular immune responses against SARS-CoV-2, with high viral neutralising activity. Both adjuvanted vaccine formulations were well tolerated and are suitable for further clinical development. Funding : Clover Biopharmaceuticals and the Coalition for Epidemic Preparedness Innovations.  *Figure 5:* **Wild-type SARS-CoV-2 neutralisation titres** Titres are shown in the different study groups and human convalescent serum samples from patients with COVID-19 measured by microneutralisation based on cytopathic effect (MN_{50}). Bars show GMTs per group with 95% CIs at days 1, 22, 36, and 50. Circles represent values for individual participants. Small arrows indicate study vaccinations at day 1 (dose 1) and day 22 (dose 2). GMT=geometric mean titre. D=day. HCS=human convalescent serum samples. NIBSC=National Institute for Biological Standards and Control. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

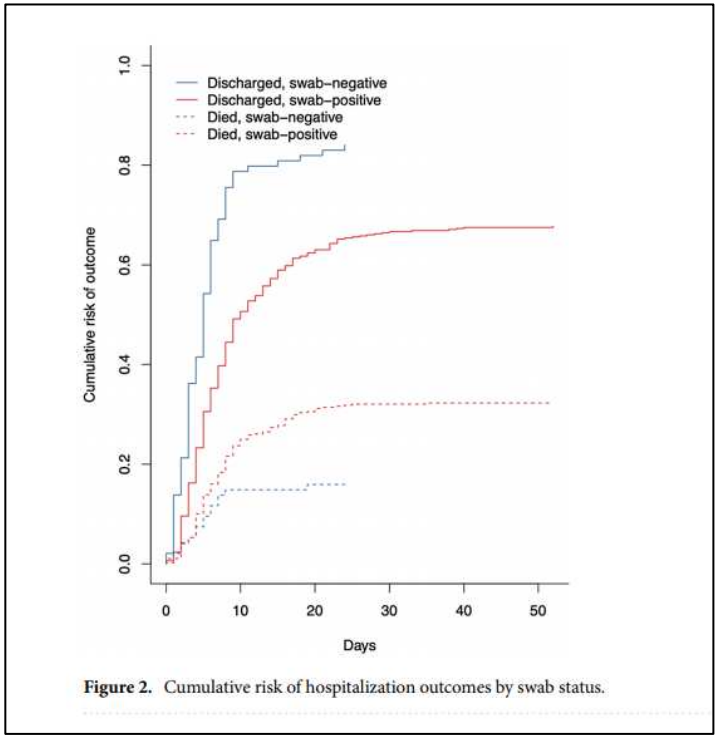
Chamorro-de-Vega E et al Expert review of Clinical Pharmacology https://www.tandfonline.com/doi/full/10.1080/17512433.2021.1875819	Clinical course of severe patients with COVID-19 treated with tocilizumab: report from a cohort study in Spain	Studio di coorte retrospettivo sulle caratteristiche di 162 pazienti ricoverati per COVID-19 in Spagna e trattati con tocilizumab : elevata mortalità, maggiore nel gruppo sottoposto a ventilazione meccanica, ed elevata incidenza di infezioni batteriche.	Background: We report the long-term outcomes, changes in laboratory parameters, the incidence of secondary nosocomial infections and treatment cost of a Spanish cohort of patients with severe COVID-19 that received tocilizumab (TCZ). Methods: Retrospective cohort of PCR confirmed adult patients who received TCZ from March 1 to 24, 2020 in a tertiary hospital was analyzed. Patients were followed up until 10 May 2020. Results: We included 162 patients (median age 64 years; 70.4% male). At time of TCZ administration, 48.1% of patients were on invasive mechanical ventilation (IMV). Over a median follow-up of 53 days, 46.9% of patients were discharge in good conditions and 19.8% were still hospitalized. The overall mortality was 33.3%, being higher in patients on IMV than those who did not (46.2% vs 26.7%, $P < 0.001$). A significant improvement in the lymphocyte count, C-reactive protein, lactate dehydrogenase, and D-dimer was observed. Overall, 43.2% patients presented nosocomial infections, causing death in 8%. Infections were more prevalent in ICU units (63.0% vs 17.1%, $P < 0.001$). The total cost of TCZ was €371,784. Conclusions: Among the patients who used TCZ, one third died, regardless the improvement in some inflammatory biomarkers. The incidence of secondary nosocomial infections was high.

			 Figure 1. Kaplan-Meier survival estimates of the cumulative probability of death in the total population (1A) and in patients who received TCZ under IMV or not (1B). Abbreviations: IMV, invasive mechanical ventilation; TCZ, tocilizumab
Richier Q et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab081/6124471?searchresult=1	Tocilizumab in COVID-19: Give it time!	Commento a una review e metanalisi sulla terapia con tocilizumab pubblicata su CID alcuni mesi fa (https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1445/5910379) che concludeva per una riduzione della mortalità e un NNT (number needed to treat) di 11 nei pazienti con COVID-19. Secondo gli autori, il farmaco merita di essere ancora studiato.	TCZ is not a magic bullet but in our case, where antiviral drugs seems to have little or no effect, it is important to let time to TCZ, which is, as Huang et al. recalls, well tolerated.
Plotkin SA et al CID https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab068/6121304	Accelerate COVID-19 Vaccine Rollout by Delaying the Second Dose of mRNA Vaccines	Discussione sull'opportunità di rimandare la seconda dose dei vaccini contro SARS-CoV-2 negli USA (come avviene già in UK e Israele) al fine di somministrare la prima dose a un maggiore numero di	We urge consideration of interim use of single doses in the United States in order to extend vaccination to as many people as possible. Based on immunologic principles, sensitization with single doses would still allow boosting with a second dose several months later, when supplies improve.

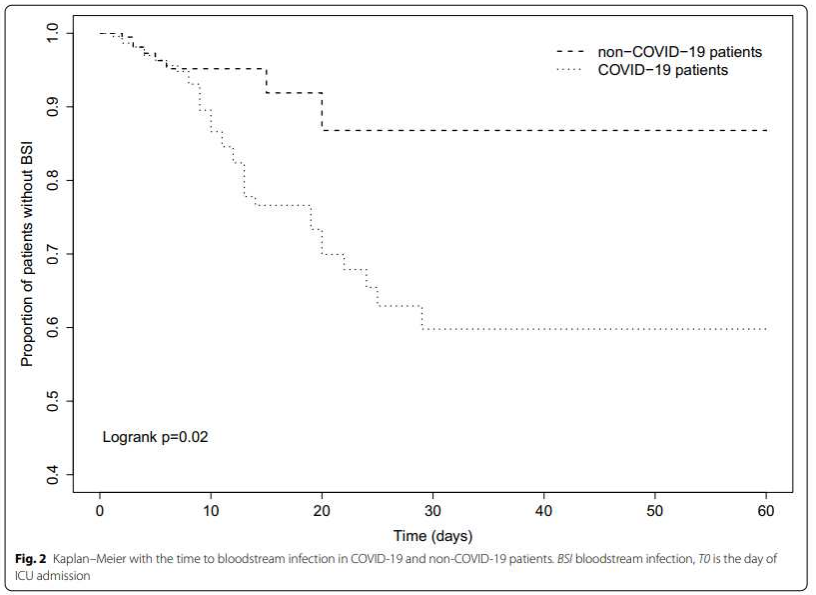
		persone. Gli autori di questa Letter sono favorevoli, ritenendo che più persone sarebbero protette per un numero sufficiente di mesi e che il booster sarebbe efficace anche a distanza. Qui la risposta contraria, secondo cui il rischio di selezionare varianti resistenti a vaccino è troppo elevato: https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab070/6121510	
Chodick G et al MedRXiv – not peer reviewed https://www.medrxiv.org/content/10.1101/2021.01.27.21250612v1	The effectiveness of the first dose of BNT162 b 2 vaccine in reducing SARS-CoV-2 infection 13-24 days after immunization: real-world evidence	Studio di coorte retrospettivo su 351.897 persone sottoposte alla prima dose di vaccino BNT162b2 (Pfizer) contro SARS-CoV-2 in Israele : nei giorni da 13 a 24 dopo la prima dose, si ha una riduzione del 51.4% del rischio relativo di infezione rispetto ai giorni 1-12, confermando il dato del trial di fase III. Si tratta in ogni caso di un follow up brevissimo (gli ultimi vaccini in questo studio sono stati	Background BNT162b2 vaccines showed high efficacy against COVID-19 in a randomized controlled phase-III trial. A vaccine effectiveness evaluation in real life settings is urgently needed, especially given the global disease surge. Hence, we assessed the short-term effectiveness of the first dose of BNT162b2-vaccine against SARS-CoV-2 infection. Given the BNT162b2 Phase-III results, we hypothesized that the cumulative incidence of SARS-CoV-2 infection among vaccinees will decline after 12 days following immunization compared to the incidence during the preceding days. Methods We conducted a retrospective cohort study using data from 2.6 million-member state-mandated health provider in Israel. Study population consisted of all members aged 16 or above years who were vaccinated with BNT162b2-vaccine between December/19/2020 and January/15/2021. We collected information regarding medical history and positive SARS-CoV-2 polymerase

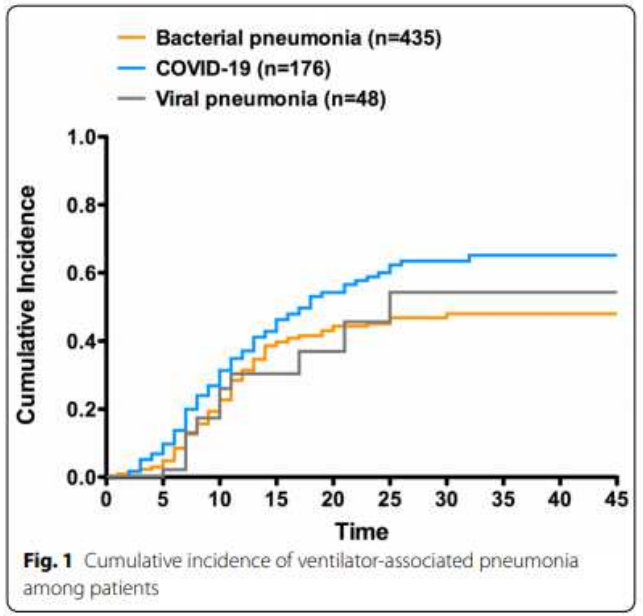
		somministrati meno di due settimane fa), per cui non si possono trarre conclusioni sulla protezione a più lungo termine. In questo studio la definizione di caso si basa sul tampone positivo e non sulla necessaria presenza di sintomi, a differenza del trial di fase III.	chain reaction test from days after first dose to January/17/2021. Daily and cumulative infection rates in days 13-24 were compared to days 1-12 after first dose using Kaplan-Meier survival analysis and generalized linear models. Findings Data of 503,875 individuals (mean age 59.7 years SD=14.7, 47.8% males) were analyzed, of whom 351,897 had 13-24 days of follow-up. The cumulative incidence of SARS-CoV-2 infection was 0.57% (n=2484) during days 1-12 and 0.27% (n=614) in days 13-24. A 51.4% relative risk reduction (RRR) was calculated in weighted-average daily incidence of SARS-CoV-2 infection from 43.41-per-100,000(SE=12.07) in days 1-12 to 21.08-per-100,000(SE=6.16) in days 13-24 following immunization. The decrement in incidence was evident from day 18 after first dose. Similar RRRs were calculated in individuals aged 60 or above (44.5%), younger individuals (50.2%), females (50.0%) and males (52.1%). Findings were similar in sub-populations and patients with various comorbidities. Conclusions We demonstrated an effectiveness of 51% of BNT162b2 vaccine against SARS-CoV-2 infection 13-24 days after immunization with the first dose. Immunization with the second dose should be continued to attain the anticipated protection.

			Legend to Figure 2: Cumulative incidence of SARS-CoV-2 infection by days since index date in the period of 1 to 12 days after first dose and 13 to 24 days after first dose. 
Middleton P et al Scientific Reports https://do<i.org/10.1038/s41598-021-81930-0	Characteristics and outcomes of clinically diagnosed RT-PCR swab negative COVID-19: a retrospective cohort study.	Studio retrospettivo su 94 pazienti che hanno ricevuto diagnosi clinica di COVID-19 a tampone negativo : a confronto con un gruppo di controllo a tampone positivo, i « negativi » hanno un decorso più lieve, tuttavia si tratta di un gruppo di pazienti che presenta difficoltà di diagnosi e gestione.	Patients with strong clinical features of COVID-19 with negative real time polymerase chain reaction (RT-PCR) SARS-CoV-2 testing are not currently included in official statistics. The scale, characteristics and clinical relevance of this group are not well described. We performed a retrospective cohort study in two large London hospitals to characterize the demographic, clinical, and hospitalization outcome characteristics of swab-negative clinical COVID-19 patients. We found 1 in 5 patients with a negative swab and clinical suspicion of COVID-19 received a clinical diagnosis of COVID-19 within clinical documentation, discharge summary or death certificate. We compared this group to a similar swab positive cohort and found similar demographic composition, symptomology and laboratory findings. Swab-negative clinical COVID-19 patients had better outcomes, with shorter length of hospital stay, reduced need for > 60% supplementary oxygen and reduced mortality. Patients with strong clinical features of COVID-19 that are swab-negative are a common clinical challenge. Health systems must

			recognize and plan for the management of swab-negative patients in their COVID-19 clinical management, infection control policies and epidemiological assessments.  **Figure 2.** Cumulative risk of hospitalization outcomes by swab status.
Buetti N et al Intensive Care https://doi.org/10.1007/s00134-021-06346-w	COVID-19 increased the risk of ICU-acquired bloodstream infections: a case-cohort study from the multicentric OUTCOMEREA network.	Studio di coorte prospettico condotto in Francia su 235 pazienti con COVID-19 ricoverati in rianimazione, a confronto con 235 controlli non affetti da COVID-19 : COVID-19 è un fattore di maggior rischio di infezioni	PURPOSE: The primary objective of this study was to investigate the risk of ICU bloodstream infection (BSI) in critically ill COVID-19 patients compared to non-COVID-19 patients. Subsequently, we performed secondary analyses in order to explain the observed results. METHODS: We conducted a matched case-cohort study, based on prospectively collected data from a large ICU cohort in France. Critically ill COVID-19 patients were matched with similar non-COVID-19 patients. ICU-BSI was defined by an infection onset

		del torrente ematico dopo 7 giorni di degenza in rianimazione, mentre all'interno della coorte COVID appaiono fattori di rischio le terapie con tocilizumab o anakinra, ma non con corticosteroidi.	occurring > 48 h after ICU admission. We estimated the effect of COVID-19 on the probability to develop an ICU-BSI using proportional subdistribution hazards models. RESULTS: We identified 321 COVID-19 patients and 1029 eligible controls in 6 ICUs. Finally, 235 COVID-19 patients were matched with 235 non-COVID-19 patients. We observed 43 ICU-BSIs, 35 (14.9%) in the COVID-19 group and 8 (3.4%) in the non-COVID-19 group (p </= 0.0001), respectively. ICU-BSIs of COVID-19 patients were more frequently of unknown source (47.4%). COVID-19 patients had an increased probability to develop ICU-BSI, especially after 7 days of ICU admission. Using proportional subdistribution hazards models, COVID-19 increased the daily risk to develop ICU-BSI (sHR 4.50, 95% CI 1.82-11.16, p = 0.0012). Among COVID-19 patients (n = 235), a significantly increased risk for ICU-BSI was detected in patients who received tocilizumab or anakinra (sHR 3.20, 95% CI 1.31-7.81, p = 0.011) but not corticosteroids. CONCLUSIONS: Using prospectively collected multicentric data, we showed that the ICU-BSI risk was higher for COVID-19 than non-COVID-19 critically ill patients after seven days of ICU stay. Clinicians should be particularly careful on late ICU-BSIs in COVID-19 patients. Tocilizumab or anakinra may increase the ICU-BSI risk.

			 **Fig. 2** Kaplan–Meier with the time to bloodstream infection in COVID-19 and non-COVID-19 patients. *BSI* bloodstream infection, *T0* is the day of ICU admission
Llitjos JF et al Annals of Intensive Care https://doi.org/10.1186/s13613-021-00812-w	Increased susceptibility to intensive care unit-acquired pneumonia in severe COVID-19 patients: a multicentre retrospective cohort study.	Studio di coorte multicentrico che confronta 176 pazienti ricoverati in rianimazione per COVID-19 con due coorti storiche di pazienti critici in merito allo sviluppo di polmonite nosocomiale : COVID-19 è un fattore di rischio indipendente per polmonite nosocomiale.	BACKGROUND: The aim of this study is to determine whether severe COVID-19 patients harbour a higher risk of ICU-acquired pneumonia. METHODS: This retrospective multicentre cohort study comprised all consecutive patients admitted to seven ICUs for severe COVID-19 pneumonia during the first COVID-19 surge in France. Inclusion criteria were laboratory-confirmed SARS-CoV-2 infection and requirement for invasive mechanical ventilation for 48 h or more. Control groups were two historical cohorts of mechanically ventilated patients admitted to the ICU for bacterial or non-SARS-CoV-2 viral pneumonia. The outcome of interest was the development of ICU-acquired pneumonia. The determinants of ICU-acquired pneumonia were investigated in a multivariate competing risk analysis. RESULT: One hundred and seventy-six patients with severe SARS-CoV-2 pneumonia admitted to the ICU between March 1st and 30th June of 2020 were included into the study. Historical

			control groups comprised 435 patients with bacterial pneumonia and 48 ones with viral pneumonia. ICU-acquired pneumonia occurred in 52% of COVID-19 patients, whereas in 26% and 23% of patients with bacterial or viral pneumonia, respectively ($p < 0.001$). Times from initiation of mechanical ventilation to ICU-acquired pneumonia were similar across the three groups. In multivariate analysis, the risk of ICU-acquired pneumonia remained independently associated with underlying COVID-19 (SHR = 2.18; 95 CI 1.2-3.98, p = 0.011). CONCLUSION: COVID-19 appears an independent risk factor of ICU-acquired pneumonia in mechanically ventilated patients with pneumonia. Whether this is driven by immunomodulatory properties by the SARS-CoV-2 or this is related to particular processes of care remains to be investigated.  **Fig. 1** Cumulative incidence of ventilator-associated pneumonia among patients

Agenzia Italiana del Farmaco https://www.aifa.gov.it/documents/20142/1289678/Comunicato_AIFA_626.pdf/265e16d3-921e-cc38-fdc1-d854c1f18ef8	AIFA: autorizzato vaccino AstraZeneca	Comunicato stampa AIFA sull'autorizzazione all'uso del vaccino AstraZeneca contro SARS-CoV-2, preferenzialmente nella fascia d'età 18-55 anni.	Nel tentativo di contestualizzare le migliori condizioni di utilizzo di questo vaccino rispetto agli altri vaccini disponibili (BioNTech/Pfizer e Moderna) e sottolineando che una valutazione conclusiva potrà avvenire solo al termine degli studi clinici in corso, la CTS ha suggerito: 1. Un utilizzo preferenziale dei vaccini a RNA messaggero nei soggetti più anziani e/o più fragili. Per la definizione di specifiche categorie di rischio si rimanda a quanto previsto dal piano strategico per la vaccinazione anti SARS-CoV2/COVID-19 del Ministero della Salute. 2. Un utilizzo preferenziale del vaccino AstraZeneca, in attesa di acquisire ulteriori dati, in soggetti tra i 18 e i 55 anni, per i quali sono disponibili evidenze maggiormente solide.