RICERCA BIBLIOGRAFICA COVID 19

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FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE

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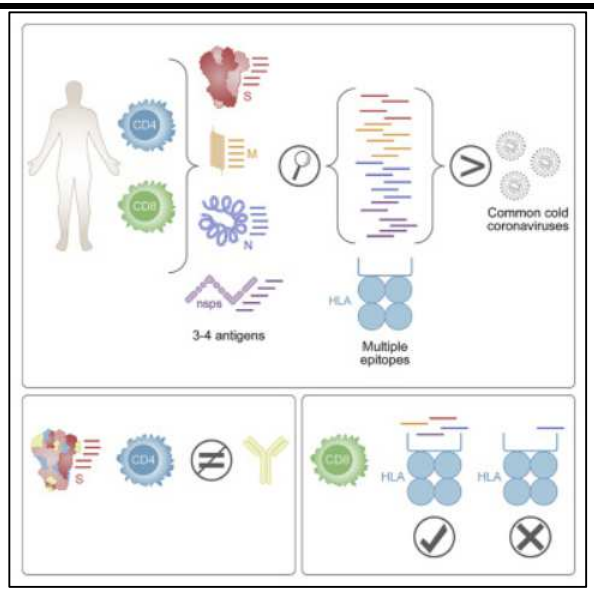
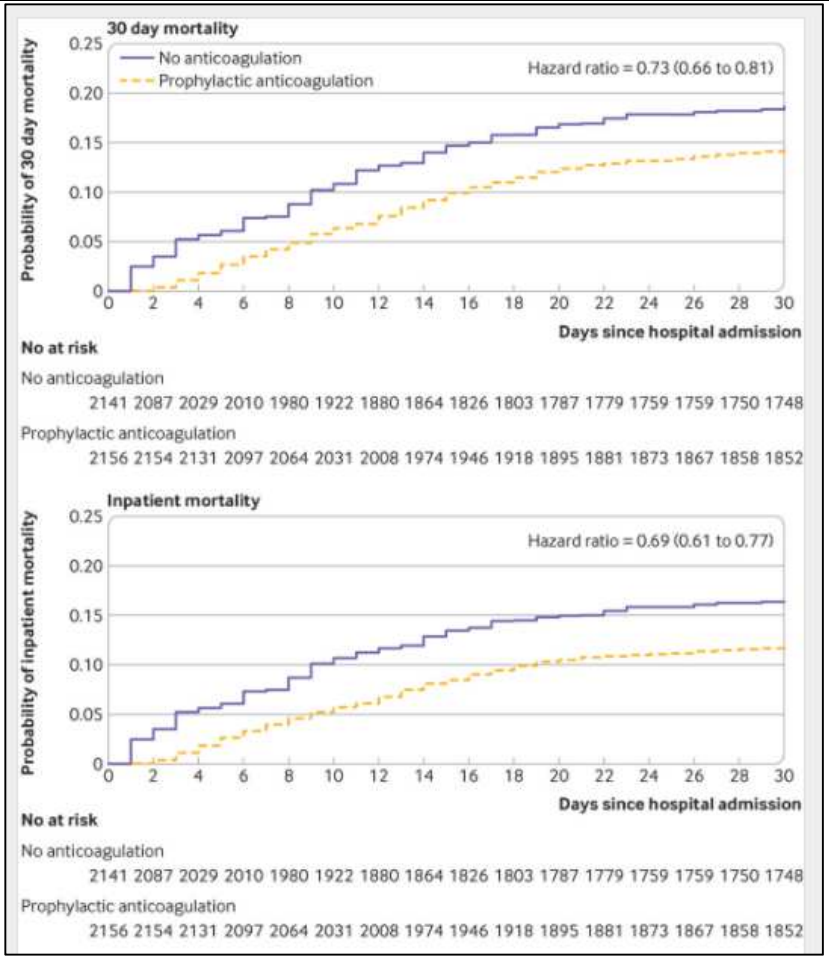
AUTORE/RIVISTA	TITOLO	OUTCOME PRINCIPALE	ABSTRACT
New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG) https://www.gov.uk/government/publications/nervtag-update-note-on-b117-severity-11-february-2021	NERVTAG: Update note on B.1.1.7 severity, 11 February 2021	Aggiornamento sui dati disponibili in merito ai tassi di ospedalizzazione e mortalità per infezione da SARS-CoV-2 variante « inglese » rispetto al wild-type: una serie di casistiche conferma l'aumento di entrambi i tassi, per quanto il rischio assoluto di morte rimanga basso.	On Thursday, 21st January, NERVTAG presented evidence to SAGE of increased disease severity in people infected with variant of concern (VOC) B.1.1.7 compared to people infected with non-VOC virus variants. In that report it was stated that 'data will accrue in coming weeks, at which time the analyses will become more definitive'. Here we report updated and additional analyses, which together strengthen the earlier finding of increased disease severity in people infected with VOC B.1.1.7 compared to other virus variants […] Based on these analyses, it is likely that infection with VOC B.1.1.7 is associated with an increased risk of hospitalisation and death compared to infection with non-VOC viruses. It should be noted that the absolute risk of death per infection remains low.

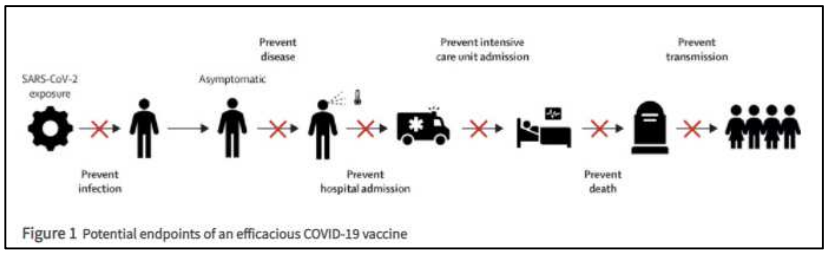
Tarke A et al Cell https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(21)00015-X?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS266637912100015X%3Fshowall%3Dtrue	Comprehensive analysis of T cell immunodominance and immunoprevalence of SARS-CoV-2 epitopes in COVID-19 cases	Gli epitopi antigenici riconosciuti dai linfociti T CD4+ e CD8+ in una coorte di 99 persone con storia di infezione da SARS-CoV-2 sono molto vari, solo in parte sovrapposti a quelli riconosciuti dagli anticorpi anti-SARS-CoV-2. Sulla base di questa osservazione, l'escape dalla risposta T-mediata non dovrebbe essere facile da realizzare per il virus.	T cells are involved in control of SARS-CoV-2 infection. To establish the patterns of immunodominance of different SARS-CoV-2 antigens and precisely measure virus-specific CD4+ and CD8+ T cells, we study epitope-specific T cell responses of 99 convalescent coronavirus disease 2019 (COVID-19) cases. The SARS-CoV-2 proteome is probed using 1,925 peptides spanning the entire genome, ensuring an unbiased coverage of human leukocyte antigen (HLA) alleles for class II responses. For HLA class I, we study an additional 5,600 predicted binding epitopes for 28 prominent HLA class I alleles, accounting for wide global coverage. We identify several hundred HLA-restricted SARS-CoV-2-derived epitopes. Distinct patterns of immunodominance are observed, which differ for CD4+ T cells, CD8+ T cells, and antibodies. The class I and class II epitopes are combined into epitope megapools to facilitate identification and quantification of SARS-CoV-2-specific CD4+ and CD8+ T cells.

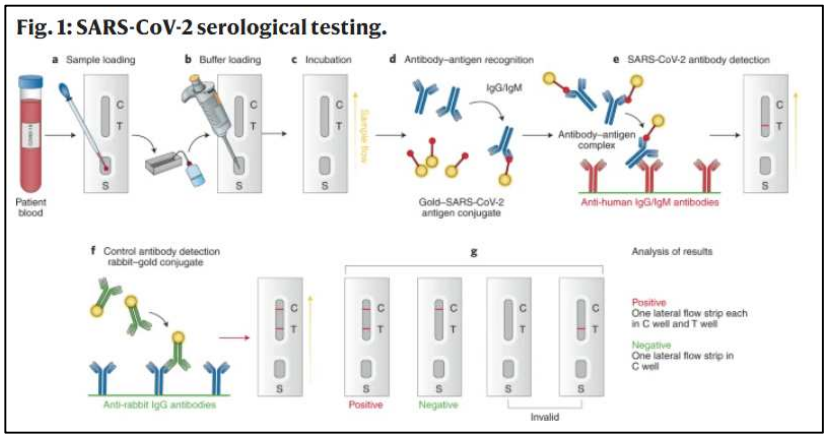
			
Rentsch CT et al The BMJ https://www.bmj.com/content/372/bmj.n311	Early initiation of prophylactic anticoagulation for prevention of coronavirus disease 2019 mortality in patients admitted to hospital in the United States: cohort study	Studio di coorte osservazionale su 4297 persone ricoverate con COVID-19 negli USA, non sottoposte precedentemente a terapia anticoagulante : l'utilizzo di anticoagulante a dosaggio profilattico entro 24 ore dal ricovero è associato a minore mortalità a 30 giorni, senza evidenza di maggior rischio di sanguinamento maggiore.	Objective : To evaluate whether early initiation of prophylactic anticoagulation compared with no anticoagulation was associated with decreased risk of death among patients admitted to hospital with coronavirus disease 2019 (covid-19) in the United States. Design : Observational cohort study. Setting Nationwide cohort of patients receiving care in the Department of Veterans Affairs, a large integrated national healthcare system. Participants : All 4297 patients admitted to hospital from 1 March to 31 July 2020 with laboratory confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and without a history of anticoagulation. Main outcome measures : The main outcome was 30 day mortality. Secondary outcomes were inpatient mortality, initiating therapeutic

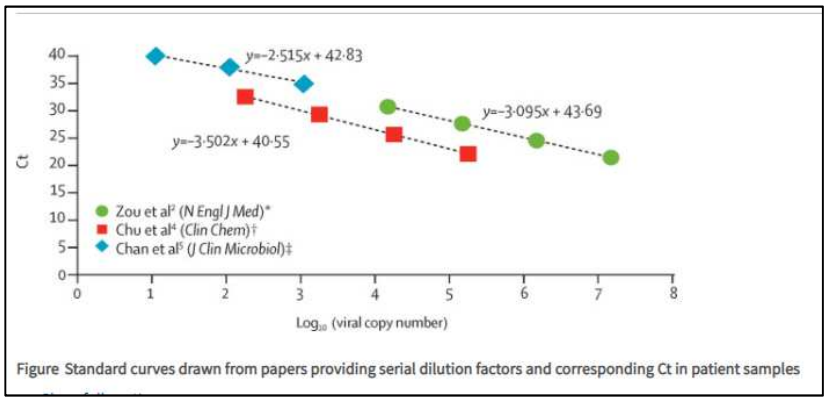
			anticoagulation (a proxy for clinical deterioration, including thromboembolic events), and bleeding that required transfusion. Results : Of 4297 patients admitted to hospital with covid-19, 3627 (84.4%) received prophylactic anticoagulation within 24 hours of admission. More than 99% (n=3600) of treated patients received subcutaneous heparin or enoxaparin. 622 deaths occurred within 30 days of hospital admission, 513 among those who received prophylactic anticoagulation. Most deaths (510/622, 82%) occurred during hospital stay. Using inverse probability of treatment weighted analyses, the cumulative incidence of mortality at 30 days was 14.3% (95% confidence interval 13.1% to 15.5%) among those who received prophylactic anticoagulation and 18.7% (15.1% to 22.9%) among those who did not. Compared with patients who did not receive prophylactic anticoagulation, those who did had a 27% decreased risk for 30 day mortality (hazard ratio 0.73, 95% confidence interval 0.66 to 0.81). Similar associations were found for inpatient mortality and initiation of therapeutic anticoagulation. Receipt of prophylactic anticoagulation was not associated with increased risk of bleeding that required transfusion (hazard ratio 0.87, 0.71 to 1.05). Quantitative bias analysis showed that results were robust to unmeasured confounding (e-value lower 95% confidence interval 1.77 for 30 day mortality). Results persisted in several sensitivity analyses. Conclusions : Early initiation of prophylactic anticoagulation compared with no anticoagulation among patients admitted to hospital with covid-19 was associated with a decreased risk of 30 day mortality and no increased risk of serious bleeding events. These findings provide strong real world evidence to support guidelines recommending the use of prophylactic anticoagulation as initial treatment for patients with covid-19 on hospital admission.

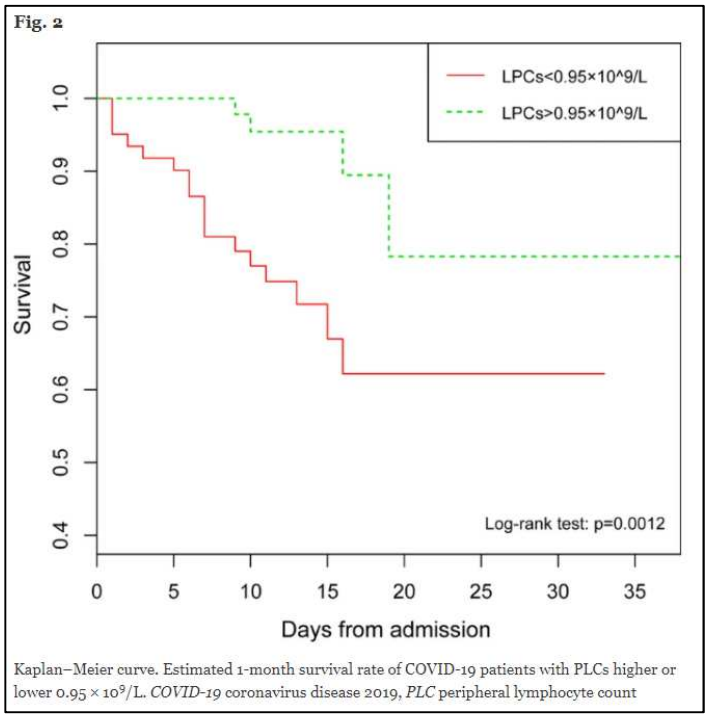
			
Li JY et al Journal of Thrombosis and Haemostasis	Clinical characteristics and risk factors for symptomatic venous thromboembolism in hospitalized COVID-19 patients: A multicenter retrospective study	Studio di coorte retrospettivo su 2779 pazienti ricoverati per COVID-19, confrontati con 23434 non affetti da COVID-19 : i primi hanno maggiore rischio di sviluppare	Background : High incidence of asymptomatic venous thromboembolism (VTE) has been observed in severe COVID-19 patients, but the characteristics of symptomatic VTE in general COVID-19 patients have not been described. Objectives : To comprehensively explore the prevalence and reliable risk prediction for VTE in COVID-19 patients.

https://onlinelibrary.wiley.com/doi/abs/10.1111/jth.15261		trombosi venosa profonda, sostenuto da fattori di rischio quali età, neoplasia, intervallo fra diagnosi di infezione e ricovero, ridotto fibrinogeno ed elevato D-dimero al ricovero.	Methods/Results : This retrospective study enrolled all COVID-19 patients with a subsequent VTE in 16 centers in China from January 1 to March 31, 2020. A total of 2779 patients were confirmed with COVID-19. In comparison with 23,434 non-COVID-19 medical inpatients, the ORs for developing symptomatic VTE in severe and non-severe hospitalized COVID-19 patients were 5.94 (95%CI 3.91 to 10.09) and 2.79 (95%CI 1.43 to 5.60), respectively. When 104 VTE cases and 208 Non-VTE cases were compared, pulmonary embolism cases had a higher rate for in-hospital death (OR 6.74, 95%CI 2.18 to 20.81). VTE developed at a median of 21 days (IQR 13.25 to 31) since onset. Independent factors for VTE were advancing age, cancer, longer interval from symptom onset to admission, lower fibrinogen and higher D-dimer on admission, and D-dimer increment (DI) ≥ 1.5 fold; of these, DI ≥ 1.5 fold had the most significant association (OR 14.18, 95%CI 6.25–32.18, P = 2.23 × 10-10). A novel model consisting of simple 3 coagulation variables (fibrinogen and D-dimer levels on admission, and DI ≥ 1.5 fold) showed good prediction for symptomatic VTE (AUC 0.865, 95%CI 0.822 to 0.907, sensitivity 0.930, specificity 0.710). Conclusions : There is an excess risk of VTE in hospitalized COVID-19 patients. The novel model can help early identification of patients who are at high risk for VTE.
Hodgson SH et al The Lancet https://www.thelancet.com/journals/laninf/article/	What defines an efficacious COVID-19 vaccine? A review of the challenges assessing the clinical efficacy of vaccines against SARS-CoV-2	Come si giudica l'efficacia di un vaccino contro l'infezione da SARS-CoV-2.	The novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has caused more than 1 million deaths in the first 6 months of the pandemic and huge economic and social upheaval internationally. An efficacious vaccine is essential to prevent further morbidity and mortality. Although some countries might deploy COVID-19 vaccines on the strength of safety and immunogenicity data alone, the goal of vaccine development is to gain direct evidence of vaccine efficacy in protecting humans

PIIS1473-3099(20)30773-8/fulltext			against SARS-CoV-2 infection and COVID-19 so that manufacture of efficacious vaccines can be selectively upscaled. A candidate vaccine against SARS-CoV-2 might act against infection, disease, or transmission, and a vaccine capable of reducing any of these elements could contribute to disease control. However, the most important efficacy endpoint, protection against severe disease and death, is difficult to assess in phase 3 clinical trials. In this Review, we explore the challenges in assessing the efficacy of candidate SARS-CoV-2 vaccines, discuss the caveats needed to interpret reported efficacy endpoints, and provide insight into answering the seemingly simple question, “Does this COVID-19 vaccine work?”  Figure 1 Potential endpoints of an efficacious COVID-19 vaccine
Maggi F et al Emerging Infectious Diseases https://wwwnc.cdc.gov/eid/article/27/4/21-0183_article	Imported SARS-COV-2 Variant P.1 Detected in Traveler Returning from Brazil to Italy	Infezione asintomatica da SARS-CoV-2 variante « brasiliana » in un uomo di 33 anni rientrato dal Brasile in Italia (via Madrid) in gennaio 2021.	We report an imported case of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant P.1 detected in an asymptomatic traveler who arrived in Italy on an indirect flight from Brazil. This case shows the risk for introduction of SARS-CoV-2 variants from indirect flights and the need for continued SARS-CoV-2 surveillance.

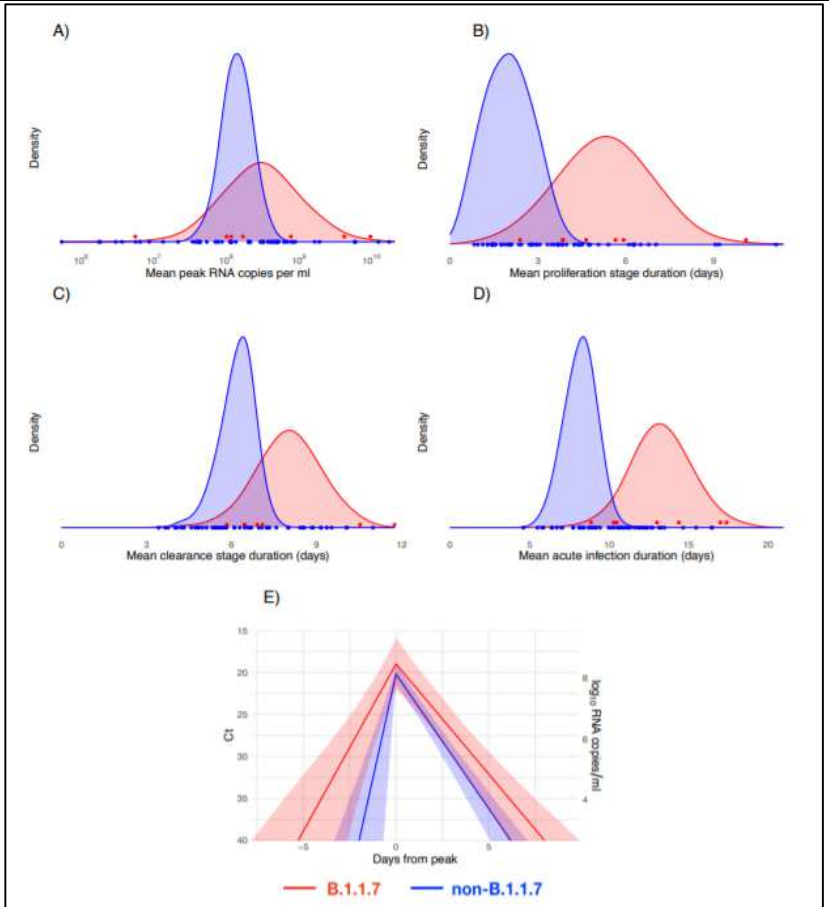
Kevadiya BD et al Nature https://www.nature.com/articles/s41563-020-00906-z	Diagnostics for SARS-CoV-2 infections	Diagnostica, di laboratorio e per immagini, dell'infezione da SARS-CoV-2.	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread to nearly every corner of the globe, causing societal instability. The resultant coronavirus disease 2019 (COVID-19) leads to fever, sore throat, cough, chest and muscle pain, dyspnoea, confusion, anosmia, ageusia and headache. These can progress to life-threatening respiratory insufficiency, also affecting the heart, kidney, liver and nervous systems. The diagnosis of SARS-CoV-2 infection is often confused with that of influenza and seasonal upper respiratory tract viral infections. Due to available treatment strategies and required containments, rapid diagnosis is mandated. This Review brings clarity to the rapidly growing body of available and in-development diagnostic tests, including nanomaterial-based tools. It serves as a resource guide for scientists, physicians, students and the public at large. **Fig. 1: SARS-CoV-2 serological testing.** 
Han MS et al	RT-PCR for SARS-CoV-2: quantitative versus qualitative	Rapide precisazioni sul significato della « carica virale » - così genericamente riportata in molti studi su COVID-19 : differenza fra	During the ongoing coronavirus disease 2019 (COVID-19) pandemic, monitoring patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) using viral kinetics or viral loads in various sample types by real-time RT-PCR has become

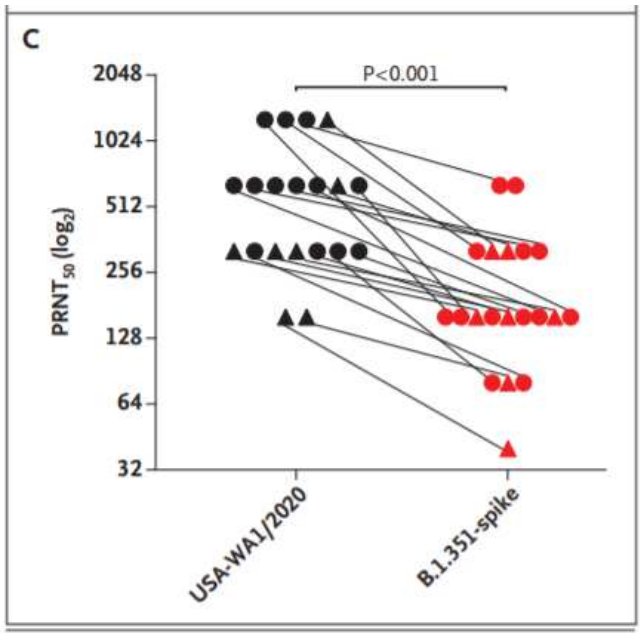
The Lancet https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30424-2/fulltext		PCR quantitativa e qualitativa, importanza della curva di calibrazione, unità di misura corrette per ogni campione.	essential. However, understanding whether the RT-PCR test results are interpreted as quantitative, qualitative, or semi-quantitative is important.  Figure Standard curves drawn from papers providing serial dilution factors and corresponding Ct in patient samples
Saibin W et al BMC Pulmonary Medicine https://bmcpulmmed.biomedcentral.com/articles/10.1186/s12890-021-01422-9	Association between peripheral lymphocyte count and the mortality risk of COVID-19 inpatients.	Una conta linfocitaria inferiore a 950/mm3 è associata a maggiore rischio di morte in questa casistica di 134 pazient ricoverati per COVID-19 a Wuhan.	BACKGROUND: To explore the relationship between peripheral lymphocyte counts (PLCs) and the mortality risk of coronavirus disease 2019 (COVID-19), as well as the potential of PLC for predicting COVID-19 hospitalized patients death. METHODS: Baseline characteristics, laboratory tests, imaging examinations, and outcomes of 134 consecutive COVID-19 hospitalized patients were collected from a tertiary hospital in Wuhan city from January 25 to February 24, 2020. Multiple regression analysis was used to analyze the relationship between the PLC at admission and mortality risk in COVID-19 patients and to establish a model for predicting death in COVID-19 hospitalized patients based on PLC. RESULTS: After adjusting for potential confounding factors, we found a non-linear relationship and threshold saturation effect between PLC and mortality risk in COVID-19 patients (infection point of PLC: 0.95 x 10(9)/L). Multiple regression analysis showed that when PLCs of COVID-19 patients were lower than 0.95 x 10(9)/L, the patients had

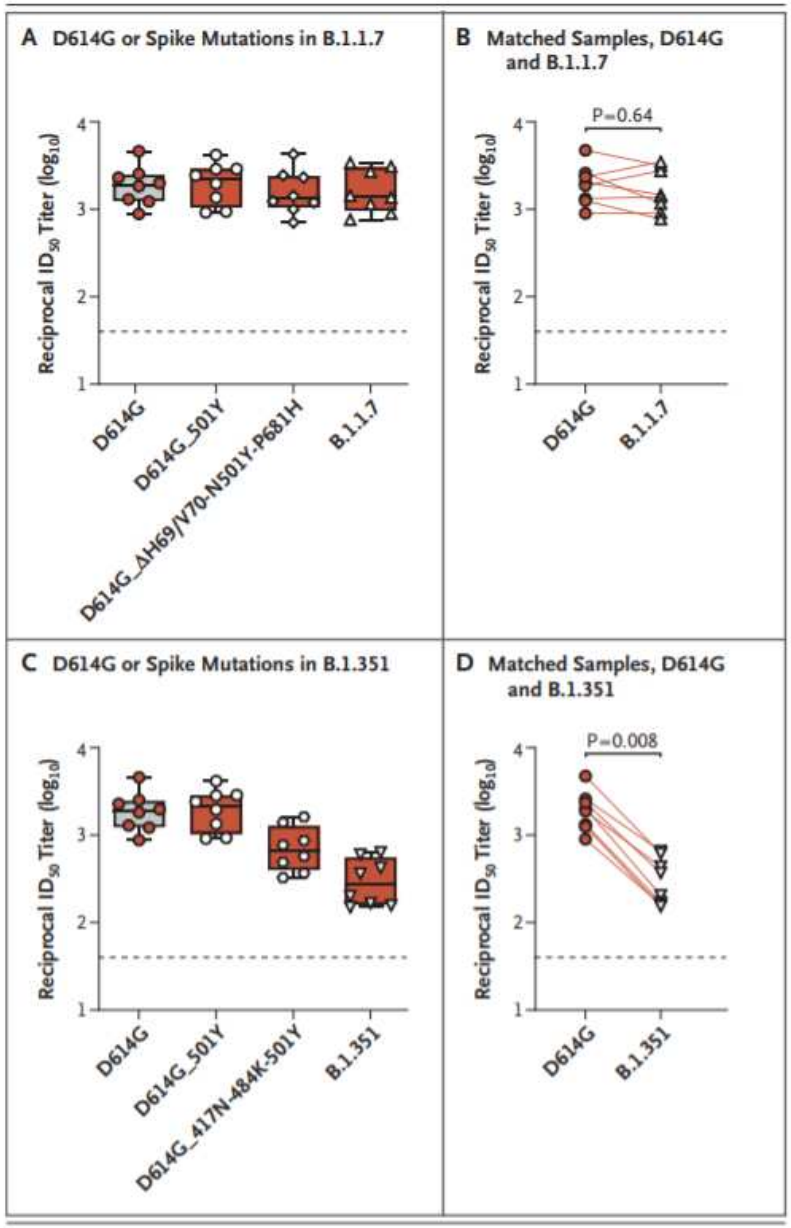
			a significantly higher mortality risk as compared to COVID-19 patient with PLCs > 0.95 x 10(9)/L (OR 7.27; 95% CI 1.10-48.25). The predictive power of PLC for death in COVID-19 patients (presented as area under the curve) was 0.78. The decision curve analysis showed that PLC had clinical utility for the prediction of death in COVID-19 inpatients. CONCLUSIONS: PLC had a non-linear relationship with mortality risk in COVID-19 inpatients. Reduced PLCs (< 0.95 x 10(9)/L) were associated with an increased mortality risk in COVID-19 inpatients. PLCs also had a potential predictive value for the death of COVID-19 inpatients. **Fig. 2**  Kaplan–Meier curve. Estimated 1-month survival rate of COVID-19 patients with PLCs higher or lower 0.95 × 10^9/L. *COVID-19* coronavirus disease 2019, *PLC* peripheral lymphocyte count

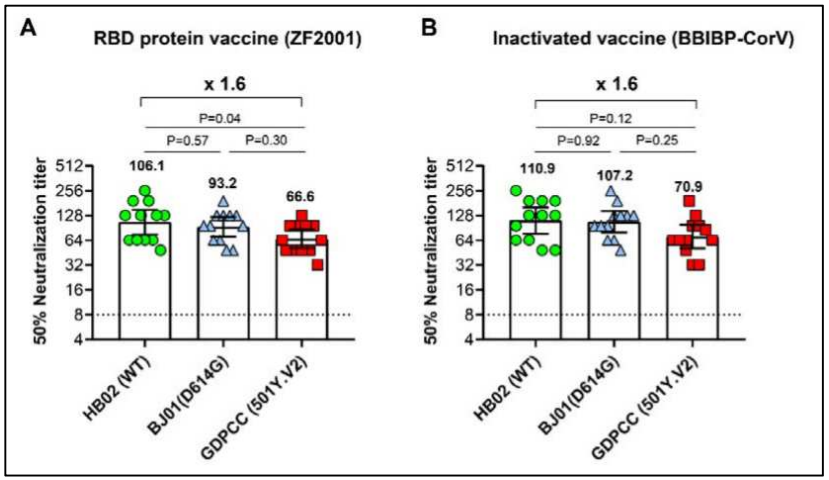
Sjoding MW et al Annals of the American Thoracic Society https://www.ncbi.nlm.nih.gov/research/coronavirus/publication/33577740	Comparing Clinical Features and Outcomes in Mechanically Ventilated Patients with COVID-19 and the Acute Respiratory Distress Syndrome.	Studio di coorte retrospettivo su 130 pazienti con COVID-19 contro 382 pazienti con ARDS per altre infezioni, tutti sottoposti a ventilazione meccanica : non si osservano differenze significative nelle caratteristiche cliniche, fisiologiche e di outcome.	RATIONALE: Patients with severe coronavirus disease 2019 (COVID-19) meet clinical criteria for the acute respiratory distress syndrome (ARDS), yet early reports suggested they differ physiologically and clinically from patients with non-COVID-19 ARDS, prompting treatment recommendations that deviate from standard evidence-based practices for ARDS. OBJECTIVES: To compare respiratory physiology, clinical outcomes, and extrapulmonary clinical features of severe COVID-19 with non-COVID ARDS. METHODS: We performed a retrospective cohort study, comparing 130 consecutive mechanically ventilated patients with severe COVID-19 with 382 consecutive mechanically ventilated patients with non-COVID-19 ARDS. Initial respiratory physiology and 28-day outcomes were compared. Extrapulmonary manifestations (inflammation, extrapulmonary organ injury, and coagulation) were compared in an exploratory analysis. RESULTS: Comparison of patients with COVID-19 and non-COVID-19 ARDS suggested small differences in respiratory compliance, ventilatory efficiency, and oxygenation. 28-day mortality was 30% in COVID-19 patients and 38% in non-COVID ARDS. In adjusted analysis, point estimates of differences in time-to-breathing-unassisted at 28 days (adjusted SHR 0.98 [95% CI 0.77-1.26]) and 28-day mortality (risk ratio = 1.01 [95% CI 0.72-1.42]) were small for COVID-19 vs. non-COVID ARDS, although the confidence intervals for these estimates include moderate differences. Patients with COVID-19 had lower neutrophil counts but did not differ in lymphocyte count or other measures of systemic inflammation. CONCLUSIONS: In this single center cohort, we found no evidence for large differences between COVID-19 and non-COVID ARDS. Many key clinical features of severe COVID-19 were similar to those of non-COVID-19 ARDS, including respiratory physiology and clinical outcomes, although our sample size

			precludes definitive conclusions. Further studies are needed to define COVID-19-specific pathophysiology before deviation from evidence-based treatment practices can be recommended.
Kissler SM et al Harvard Library – preprint https://dash.harvard.edu/handle/1/37366884	Densely sampled viral trajectories suggest longer duration of acute infection with B.1.1.7 variant relative to non-B.1.1.7 SARS-CoV-2	All'interno di un gruppo di 65 individui con infezione da SARS-COV-2 sottoposti a tamponi nasofaringei seriati, i 7 infetti da variante « inglese » mostrano una infezione di più lunga durata (tempo dalla diagnosi alla più alta concentrazione virale nel tampone e ritorno al limite inferiore di individuazione del virus).	To test whether acute infection with B.1.1.7 is associated with higher or more sustained nasopharyngeal viral concentrations, we assessed longitudinal PCR tests performed in a cohort of 65 individuals infected with SARS-CoV-2 undergoing daily surveillance testing, including seven in fected with B.1.1.7. For individuals infected with B.1.1.7, the mean duration of the proliferation phase was 5.3 days (90% credible interval [2.7, 7.8]), the mean duration of the clearance phase was 8.0 days [6.1, 9.9], and the mean overall duration of infection (proliferation plus clearance) was 13.3 days [10.1, 16.5]. These compare to a mean proliferation phase of 2.0 days [0.7, 3.3], a mean clearance phase of 6.2 days [5.1, 7.1], and a mean duration of infection of 8.2 days [6.5, 9.7] for non-B.1.1.7 virus. The peak viral concentration for B.1.1.7 was 19.0 Ct [15.8, 22.0] compared to 20.2 Ct [19.0, 21.4] for non-B.1.1.7. This converts to 8.5 log10 RNA copies/ml [7.6, 9.4] for B.1.1.7 and 8.2 log10 RNA copies/ml [7.8, 8.5] for non-B.1.1.7. These data offer evidence that SARS-CoV-2 variant B.1.1.7 may cause longer infections with similar peak viral concentration compared to non-B.1.1.7 SARS-CoV-2. This extended duration may contribute to B.1.1.7 SARS CoV-2's increased transmissibility.

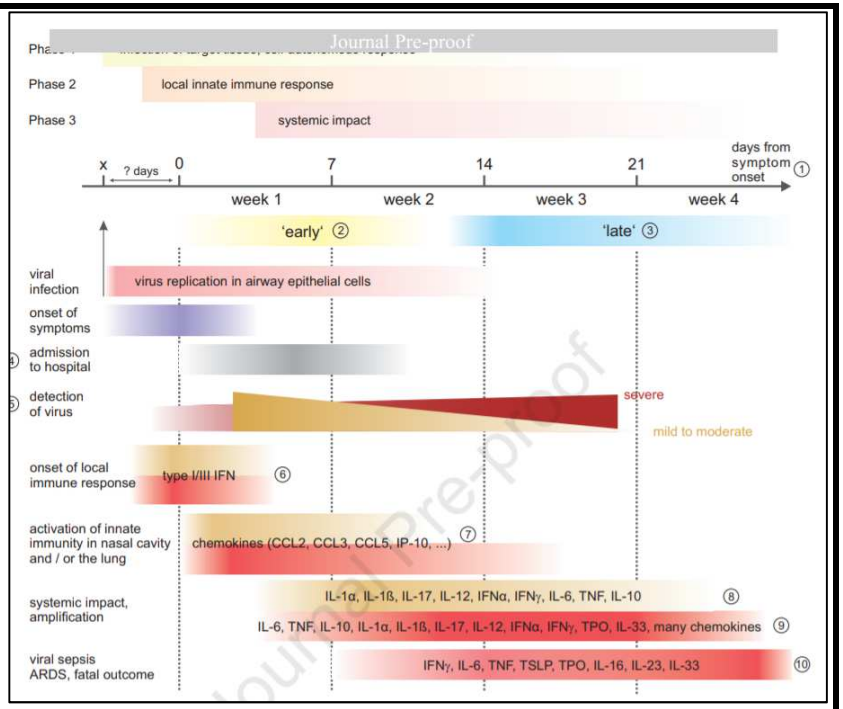
			 **Figure 1. Estimated viral trajectories for B.1.1.7 and non-B.1.1.7 SARS-CoV-2.** Posterior distributions for the mean peak viral concentration (A), mean proliferation duration (B), mean clearance duration (C), mean total duration of acute infection (D), and mean posterior viral concentration trajectory (E) for the B.1.1.7 variant (red) and non-B.1.1.7 SARS-CoV-2 (blue). In (A)–(D), distributions depict kernel density estimates obtained from 2,000 draws from the posterior distributions for each statistic. Points depict the individual-level posterior means for each statistic. In (E), solid lines depict the estimated mean viral trajectory. Shaded bands depict the 90% credible intervals for the mean viral trajectory.
Liu Y et al	Neutralizing Activity of BNT162b2-Elicited Serum — Preliminary Report	Riduzione della neutralizzazione da parte del siero di individui sottoposti a due dosi di	BNT162b2 is a nucleoside-modified RNA vaccine expressing the full-length prefusion spike glycoprotein (S) of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In a randomized, placebo-controlled clinical trial involving approximately 44,000 participants,

NEJM https://www.nejm.org/doi/full/10.1056/NEJMc2102017?query=featured_home		vaccino BNT162b2 (Pfizer) nei confronti di SARS-CoV-2 portatore delle mutazioni tipiche della variante B.1.135 (« sudafricana ») rispetto al wild-type, al portatore di D614G e al portatore di mutazioni del solo dominio N-terminale della proteina spike. Il significato in vivo di tale risultato rimane da stabilire.	immunization conferred 95% efficacy against coronavirus disease 2019 (Covid-19). 
Wu K et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMc2102179?query=featured_home	Serum Neutralizing Activity Elicited by mRNA-1273 Vaccine — Preliminary Report	Ridotta attività neutralizzante del siero di pazienti sottoposti a vaccino mRNA-1273 (Moderna) nei confronti della variante di SARS-COV-2 B.1.135 (« sudafricana ») di SARS-CoV-2, mentre è conservata l'attività nei confronti di B.1.1.7 (variante « inglese »), rispetto alla vecchia D614G. Come nello	The mRNA-1273 vaccine against SARS-CoV-2 elicited high neutralizing-antibody titers in phase 1 trial participants and has been shown to be highly efficacious in preventing symptomatic Covid-19 disease and severe disease. The recent emergence of SARS-CoV-2 variants in the United Kingdom (the B.1.1.7 lineage) and in South Africa (the B.1.351 lineage) has led to concerns about increased transmission and the potential of these variants to circumvent immunity elicited by natural infection or vaccination.

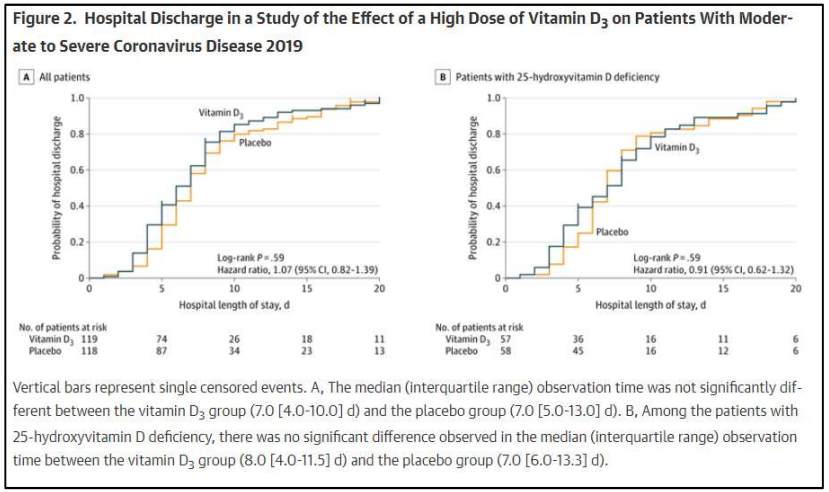
		studio precedente, non è definito il significato in vivo di tali osservazioni.	

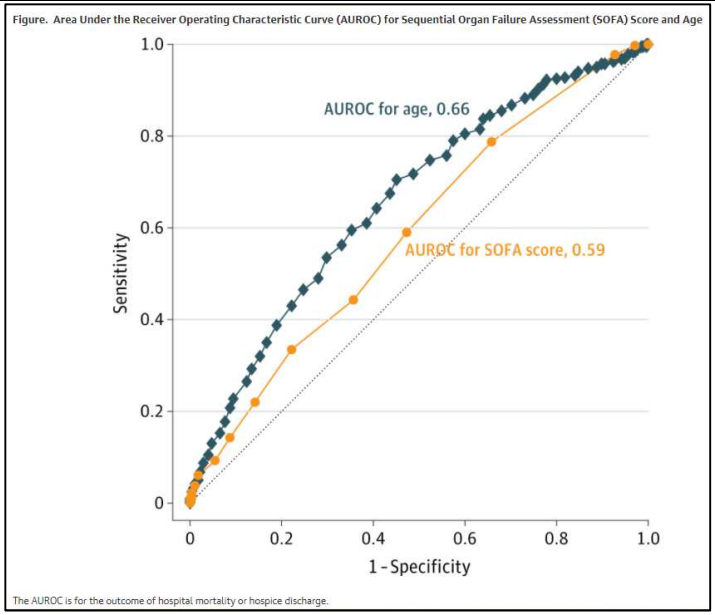
Huang B et al bioRXiv https://www.biorxiv.org/content/10.1101/2021.02.01.429069v1	Neutralization of SARS-CoV-2 VOC 501Y.V2 by human antisera elicited by both inactivated BBIBP-CorV and recombinant dimeric RBD ZF2001 vaccines	Il vaccino inattivato BBIBP-CorV e il vaccino a subunità ZF2001, entrambi di produzione cinese, inducono anticorpi in grado di neutralizzare la variante 501Y.V2 (« sudafricana ») di SARS-CoV-2 in base ai risultati di questo studio condotto su 12 sieri di persone immunizzate per ciascuno dei due vaccini.	Recently, the emerged and rapidly spreading SARS-CoV-2 variant of concern (VOC) 501Y.V2 with 10 amino acids in spike protein were found to escape host immunity induced by infection or vaccination. Global concerns have been raised for its potential to affect vaccine efficacy. Here, we evaluated the neutralization activities of two vaccines developed in China against 501Y.V2. One is licensed inactivated vaccine BBIBP-CorV and the other one is recombinant dimeric receptor-binding domain (RBD) vaccine ZF2001. Encouragingly, both vaccines largely preserved neutralizing titres, with slightly reduction, against 501Y.V2 authentic virus compare to their titres against both original SARS-CoV-2 and the currently circulating D614G virus. These data indicated that 501Y.V2 variant will not escape the immunity induced by vaccines targeting whole virus or RBD. 

Schultze JL et al Cell https://www.cell.com/cell/fulltext/S0092-8674(21)00218-X	COVID-19 and the human innate immune system	Interazione della risposta innata con SARS-CoV-2.	The introduction of SARS-CoV-2 into the human population represents a tremendous medical and economical crisis. Innate immunity - as the first line of defense of our immune system - plays a central role in combating this novel virus. Here, we provide a conceptual framework for the interaction of the human innate immune system with SARS-CoV-2 to link the clinical observations with experimental findings that have been made during the first year of the pandemic. We review evidence that variability in innate immune system components among humans is a main contributor to the heterogeneous disease courses observed for COVID-19, the disease spectrum induced by SARS-CoV-2. A better understanding of the pathophysiological mechanisms observed for cells and soluble mediators involved in innate immunity is a prerequisite for the development of diagnostic markers and therapeutic strategies targeting COVID-19. However, this will also require additional studies addressing causality of events, which is so far lacking behind.

			
Murai IH et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2776738	Effect of a Single High Dose of Vitamin D3 on Hospital Length of Stay in Patients With Moderate to Severe COVID-19 A Randomized Clinical Trial	Trial clinico su 237 pazienti ricoverati per COVID-19 in Brasile : la somministrazione di 200 000 UI di vitamina D3 non modifica la durata del ricovero, il rischio di trasferimento in terapia intensiva, di ventilazione meccanica o di decesso intraospedaliero.	Importance The efficacy of vitamin D3 supplementation in coronavirus disease 2019 (COVID-19) remains unclear. Objective To investigate the effect of a single high dose of vitamin D3 on hospital length of stay in patients with COVID-19. Design, Setting, and Participants This was a multicenter, double-blind, randomized, placebo-controlled trial conducted in 2 sites in Sao Paulo, Brazil. The study included 240 hospitalized patients with COVID-19 who were moderately to severely ill at the time of enrollment from June 2, 2020, to August 27, 2020. The final follow-up was on October 7, 2020. Interventions Patients were randomly assigned to receive a single oral dose of 200 000 IU of vitamin D3 (n = 120) or placebo (n = 120).

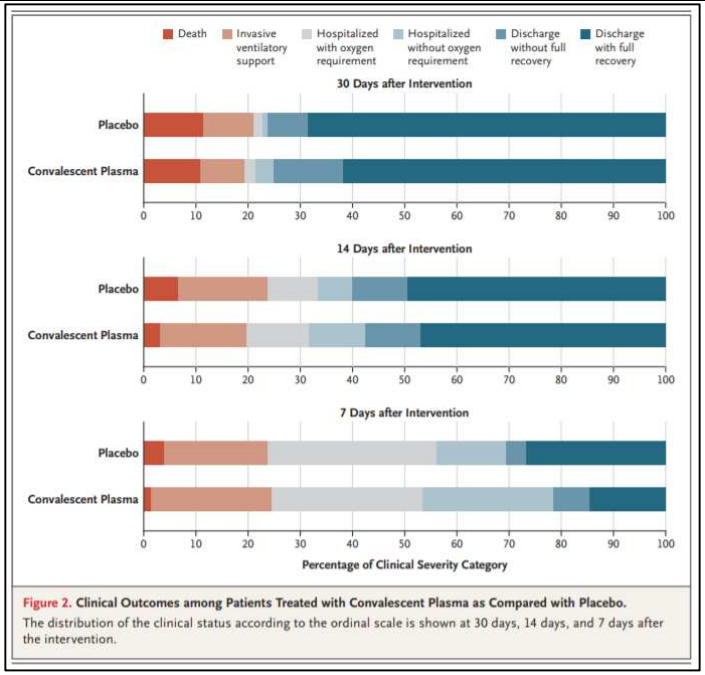
			Main Outcomes and Measures The primary outcome was length of stay, defined as the time from the date of randomization to hospital discharge. Prespecified secondary outcomes included mortality during hospitalization; the number of patients admitted to the intensive care unit; the number of patients who required mechanical ventilation and the duration of mechanical ventilation; and serum levels of 25-hydroxyvitamin D, total calcium, creatinine, and C-reactive protein. Results Of 240 randomized patients, 237 were included in the primary analysis (mean [SD] age, 56.2 [14.4] years; 104 [43.9%] women; mean [SD] baseline 25-hydroxyvitamin D level, 20.9 [9.2] ng/mL). Median (interquartile range) length of stay was not significantly different between the vitamin D3 (7.0 [4.0-10.0] days) and placebo groups (7.0 [5.0-13.0] days) (log-rank P = .59; unadjusted hazard ratio for hospital discharge, 1.07 [95% CI, 0.82-1.39]; P = .62). The difference between the vitamin D3 group and the placebo group was not significant for in-hospital mortality (7.6% vs 5.1%; difference, 2.5% [95% CI, –4.1% to 9.2%]; P = .43), admission to the intensive care unit (16.0% vs 21.2%; difference, –5.2% [95% CI, –15.1% to 4.7%]; P = .30), or need for mechanical ventilation (7.6% vs 14.4%; difference, –6.8% [95% CI, –15.1% to 1.2%]; P = .09). Mean serum levels of 25-hydroxyvitamin D significantly increased after a single dose of vitamin D3 vs placebo (44.4 ng/mL vs 19.8 ng/mL; difference, 24.1 ng/mL [95% CI, 19.5-28.7]; P < .001). There were no adverse events, but an episode of vomiting was associated with the intervention. Conclusions and Relevance Among hospitalized patients with COVID-19, a single high dose of vitamin D3, compared with placebo, did not significantly reduce hospital length of stay. The findings do

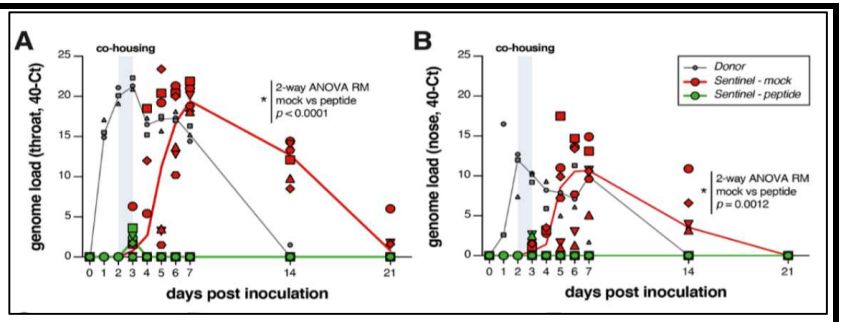
			not support the use of a high dose of vitamin D3 for treatment of moderate to severe COVID-19.  **Figure 2. Hospital Discharge in a Study of the Effect of a High Dose of Vitamin D_3 on Patients With Moderate to Severe Coronavirus Disease 2019** Vertical bars represent single censored events. A, The median (interquartile range) observation time was not significantly different between the vitamin D_3 group (7.0 [4.0-10.0] d) and the placebo group (7.0 [5.0-13.0] d). B, Among the patients with 25-hydroxyvitamin D deficiency, there was no significant difference observed in the median (interquartile range) observation time between the vitamin D_3 group (8.0 [4.0-11.5] d) and the placebo group (7.0 [6.0-13.3] d).
Raschke RA et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2776737	Discriminant Accuracy of the SOFA Score for Determining the Probable Mortality of Patients With COVID-19 Pneumonia Requiring Mechanical Ventilation	Studio retrospettivo su 674 pazienti ricoverati in terapia intensiva e sottoposti a ventilazione meccanica per COVID-19 : il punteggio SOFA non è accurato per predire la mortalità in questa popolazione.	The coronavirus disease 2019 (COVID-19) pandemic has raised concern regarding the capacity to provide care for a surge of critically ill patients that might require excluding patients with a low probability of short-term survival from receiving mechanical ventilation. A survey identified 26 unique COVID-19 triage policies, of which 20 used some form of the Sequential Organ Failure Assessment (SOFA) score. However, studies performed in 2016 and 2017 have shown only moderate discriminant accuracy of the SOFA score for predicting survival in intensive care unit (ICU) patients with sepsis and an area under the receiver operating characteristic curve (AUROC) of 0.74 to 0.75.3,4 We hypothesized that the SOFA score might be less accurate in patients requiring mechanical ventilation for COVID-19 pneumonia because such patients generally have severe single-organ dysfunction and less variation in SOFA scores.

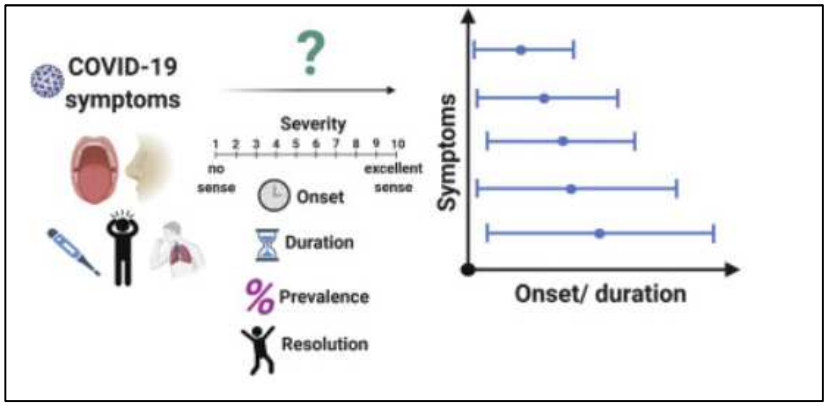
			
Libster R et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2033700?query=featured_home	Early High-Titer Plasma Therapy to Prevent Severe Covid-19 in Older Adults	Trial clinico su 160 pazienti con COVID-19 lieve, randomizzati entro 72 ore dall'esordio a ricevere plasma di soggetti guariti o placebo : si osserva una riduzione della progressione a malattia grave.	BACKGROUND : Therapies to interrupt the progression of early coronavirus disease 2019 (Covid-19) remain elusive. Among them, convalescent plasma administered to hospitalized patients has been unsuccessful, perhaps because antibodies should be administered earlier in the course of illness. METHODS : We conducted a randomized, double-blind, placebo-controlled trial of convalescent plasma with high IgG titers against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in older adult patients within 72 hours after the onset of mild Covid-19 symptoms. The primary end point was severe respiratory disease, defined as a respiratory rate of 30 breaths per minute or more, an oxygen saturation of less than 93% while the patient was breathing ambient air, or both. The trial was stopped early at 76% of its projected sample size because cases of Covid-19 in the trial region

			decreased considerably and steady enrollment of trial patients became virtually impossible. RESULTS : A total of 160 patients underwent randomization. In the intention-to-treat population, severe respiratory disease developed in 13 of 80 patients (16%) who received convalescent plasma and 25 of 80 patients (31%) who received placebo (relative risk, 0.52; 95% confidence interval [CI], 0.29 to 0.94; P=0.03), with a relative risk reduction of 48%. A modified intention-to-treat analysis that excluded 6 patients who had a primary end-point event before infusion of convalescent plasma or placebo showed a larger effect size (relative risk, 0.40; 95% CI, 0.20 to 0.81). No solicited adverse events were observed. CONCLUSIONS : Early administration of high-titer convalescent plasma against SARS-CoV-2 to mildly ill infected older adults reduced the progression of Covid-19.
Simonovich VA et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2031304?query=featured_home	A Randomized Trial of Convalescent Plasma in Covid-19 Severe Pneumonia	Trial clinico randomizzato su pazienti ospedalizzati per COVID-19, di cui 228 assegnati a terapia con plasma contro 105 assegnati a placebo, con tempo mediano dall'esordio all'arruolamento 8 giorni : non si osservano differenze di outcome a 30 giorni.	BACKGROUND : Convalescent plasma is frequently administered to patients with Covid-19 and has been reported, largely on the basis of observational data, to improve clinical outcomes. Minimal data are available from adequately powered randomized, controlled trials. METHODS : We randomly assigned hospitalized adult patients with severe Covid-19 pneumonia in a 2:1 ratio to receive convalescent plasma or placebo. The primary outcome was the patient's clinical status 30 days after the intervention, as measured on a six-point ordinal scale ranging from total recovery to death. RESULTS : A total of 228 patients were assigned to receive convalescent plasma and 105 to receive placebo. The median time from the onset of symptoms to enrollment in the trial was 8 days (interquartile range, 5 to 10), and hypoxemia was the most frequent

			severity criterion for enrollment. The infused convalescent plasma had a median titer of 1:3200 of total SARS-CoV-2 antibodies (interquartile range, 1:800 to 1:3200). No patients were lost to follow-up. At day 30 day, no significant difference was noted between the convalescent plasma group and the placebo group in the distribution of clinical outcomes according to the ordinal scale (odds ratio, 0.83; 95% confidence interval [CI], 0.52 to 1.35; P=0.46). Overall mortality was 10.96% in the convalescent plasma group and 11.43% in the placebo group, for a risk difference of −0.46 percentage points (95% CI, −7.8 to 6.8). Total SARS-CoV-2 antibody titers tended to be higher in the convalescent plasma group at day 2 after the intervention. Adverse events and serious adverse events were similar in the two groups. CONCLUSIONS : No significant differences were observed in clinical status or overall mortality between patients treated with convalescent plasma and those who received placebo.

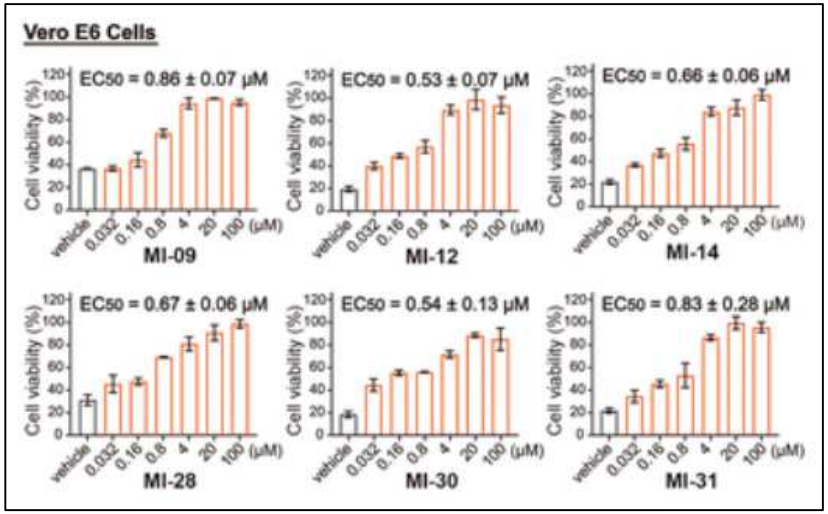
			 **Figure 2. Clinical Outcomes among Patients Treated with Convalescent Plasma as Compared with Placebo.** The distribution of the clinical status according to the ordinal scale is shown at 30 days, 14 days, and 7 days after the intervention.
De Vries RD et al Science https://science.sciencemag.org/content/early/2021/02/16/science.abf4896	Intranasal fusion inhibitory lipopeptide prevents direct-contact SARS-CoV-2 transmission in ferrets	Messa a punto di un lipopeptide in grado di inibire la fusione della proteina spike di SARS-CoV-2 con la membrana delle cellule bersaglio ; se somministrato per via intranasale a furetti messi a contatto con esemplari infetti, impedisce la trasmissione dell'infezione.	Containment of the COVID-19 pandemic requires reducing viral transmission. SARS-CoV-2 infection is initiated by membrane fusion between the viral and host cell membranes, mediated by the viral spike protein. We have designed lipopeptide fusion inhibitors that block this critical first step of infection, and based on in vitro efficacy and in vivo biodistribution selected a dimeric form for evaluation in an animal model. Daily intranasal administration to ferrets completely prevented SARS-CoV-2 direct-contact transmission during 24-hour co-housing with infected animals, under stringent conditions that resulted in infection of 100% of untreated animals. These lipopeptides are highly stable and thus may readily translate into safe and effective intranasal prophylaxis to reduce transmission of SARS-CoV-2.

			
Klein H et al Clinical Microbiology and Infection https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00083-5/fulltext	Onset, duration and unresolved symptoms, including smell and taste changes, in mild COVID-19 infections. A cohort study in Israeli patients	Follow up telefonico di 103 pazienti adulti con COVID-19 lieve in Israele in merito ai sintomi di esordio e persistenti.	Objectives : This study aims to characterize longitudinal symptoms of mild COVID-19 patients for a period of six months, and potentially aid in disease management. Methods : Phone interviews were conducted with 103 mild COVID-19 patients in Israel, over a six-month period (April 2020 to October 2020). Patients were recruited via social media and word to mouth and were interviewed up to 4 times, depending on their unresolved symptoms reports. Inclusion criteria required participants to be Israeli residents aged ≥18 years, with positive COVID-19 RT-PCR results and non-severe symptoms. Symptoms' onset, duration, severity, and resolution were analyzed. Results : 44% (45/103), 41% (42/103), 39% (40/103) or 38% (39/103) of the patients experienced headache, fever, muscle ache, or dry cough as the first symptom respectively. Smell and taste changes were experienced 3.9 ± 5.4 and 4.6 ± 5.7 days (mean ± SD) after disease onset, respectively. Among prevalent symptoms, fever had the shortest duration (5.8 ± 8.6 days), and taste and smell changes were the longest-lasting symptoms (17.2 ± 17.6 and 18.9 ± 19.7 days, durations censored at 60 days). Longer recovery of the sense of smell correlated with the extent of smell change. At the six-month follow-up, 46% (47/103) of the patients had at least one unresolved symptom, most commonly fatigue (22%, 23/103), smell

			and taste changes (15%, 15/103 and 8%, 8/103 respectively), and breathing difficulties (8%, 8/103). Conclusions : Long-lasting effects of mild COVID-19 manifested in almost half of the participants reporting at least one unresolved symptom after six months. 
Lee JT et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab148/6142945?searchresult=1	Clinical and Laboratory Findings in Patients with Potential SARS-CoV-2 Reinfection, May–July 2020	Disamina di 73 pazienti con sospetta reinfezione da SARS-CoV-2, di cui 19 caratterizzate da riesacerbazione dei sintomi con tampone molecolare positivo, dal quale però non si ottiene virus che cresce in coltura (9 campioni disponibili) né un ciclo soglia della PCR sufficientemente basso (16 campioni disponibili). Si rimanda alle linee guida CDC per la gestione delle sospette reinfezioni :	Background : We investigated patients with potential SARS-CoV-2 reinfection in the United States during May–July 2020. Methods : We conducted case finding for patients with potential SARS-CoV-2 reinfection through the Emerging Infections Network. Cases reported were screened for laboratory and clinical findings of potential reinfection followed by requests for medical records and laboratory specimens. Available medical records were abstracted to characterize patient demographics, comorbidities, clinical course, and laboratory test results. Submitted specimens underwent further testing, including RT-PCR, viral culture, whole genome sequencing, subgenomic RNA PCR, and testing for anti-SARS-CoV-2 total antibody. Results : Among 73 potential reinfection patients with available records, 30 patients had recurrent COVID-19 symptoms explained by alternative diagnoses with concurrent SARS-CoV-2 positive RT-

		https://www.cdc.gov/coronavirus/2019-ncov/php/invest-criteria.html	PCR, 24 patients remained asymptomatic after recovery but had recurrent or persistent RT-PCR, and 19 patients had recurrent COVID-19 symptoms with concurrent SARS-CoV-2 positive RT-PCR but no alternative diagnoses. These 19 patients had symptom recurrence a median of 57 days after initial symptom onset (interquartile range: 47 – 76). Six of these patients had paired specimens available for further testing, but none had laboratory findings confirming reinfections. Testing of an additional three patients with recurrent symptoms and alternative diagnoses also did not confirm reinfection. Conclusions : We did not confirm SARS-CoV-2 reinfection within 90 days of the initial infection based on the clinical and laboratory characteristics of cases in this investigation. Our findings support current CDC guidance around quarantine and testing for patients who have recovered from COVID-19.
Alhazzani W et al Critical Care Medicine https://pubmed.ncbi.nlm.nih.gov/33555780/	Surviving Sepsis Campaign Guidelines on the Management of Adults With Coronavirus Disease 2019 (COVID-19) in the ICU: First Update	Linee guida Surviving Sepsis Campaign sulla gestione del malato critico con COVID-19 ; da notare una debole raccomandazione a non utilizzare dosi terapeutiche di anticoagulanti in prevenzione delle trombosi, se non nell'ambito di trial clinici.	BACKGROUND: The coronavirus disease 2019 pandemic continues to affect millions worldwide. Given the rapidly growing evidence base, we implemented a living guideline model to provide guidance on the management of patients with severe or critical coronavirus disease 2019 in the ICU. METHODS: The Surviving Sepsis Campaign Coronavirus Disease 2019 panel has expanded to include 43 experts from 14 countries; all panel members completed an electronic conflict-of-interest disclosure form. In this update, the panel addressed nine questions relevant to managing severe or critical coronavirus disease 2019 in the ICU. We used the World Health Organization's definition of severe and critical coronavirus disease 2019. The systematic reviews team searched the literature for relevant evidence, aiming to identify systematic reviews and clinical trials. When appropriate, we performed a random-effects meta-analysis to summarize treatment

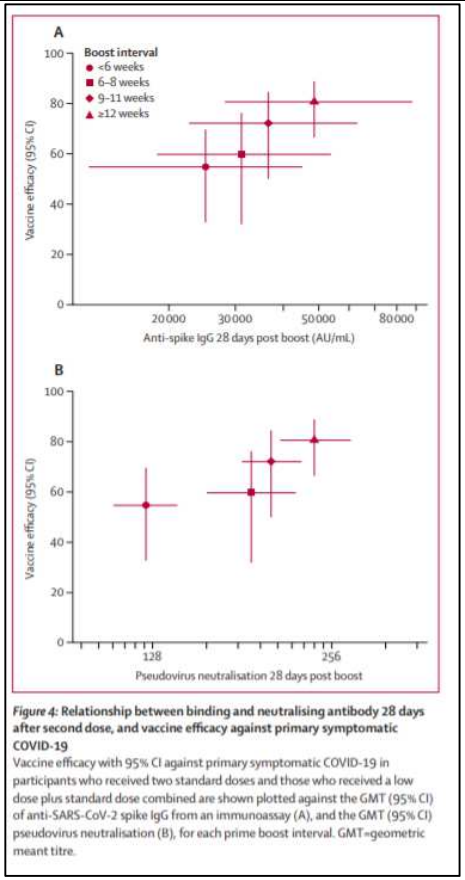
			effects. We assessed the quality of the evidence using the Grading of Recommendations, Assessment, Development, and Evaluation approach, then used the evidence-to-decision framework to generate recommendations based on the balance between benefit and harm, resource and cost implications, equity, and feasibility. RESULTS: The Surviving Sepsis Campaign Coronavirus Diease 2019 panel issued nine statements (three new and six updated) related to ICU patients with severe or critical coronavirus disease 2019. For severe or critical coronavirus disease 2019, the panel strongly recommends using systemic corticosteroids and venous thromboprophylaxis but strongly recommends against using hydroxychloroquine. In addition, the panel suggests using dexamethasone (compared with other corticosteroids) and suggests against using convalescent plasma and therapeutic anticoagulation outside clinical trials. The Surviving Sepsis Campaign Coronavirus Diease 2019 panel suggests using remdesivir in nonventilated patients with severe coronavirus disease 2019 and suggests against starting remdesivir in patients with critical coronavirus disease 2019 outside clinical trials. Because of insufficient evidence, the panel did not issue a recommendation on the use of awake prone positioning. CONCLUSION: The Surviving Sepsis Campaign Coronavirus Diease 2019 panel issued several recommendations to guide healthcare professionals caring for adults with critical or severe coronavirus disease 2019 in the ICU. Based on a living guideline model the recommendations will be updated as new evidence becomes available.

Jingxin Q et al Science https://science.sciencemag.org/content/early/2021/02/17/science.abf1611	SARS-CoV-2 Mpro inhibitors with antiviral activity in a transgenic mouse model	Sintesi di due antivirali diretti contro la proteasi Mpro di SARS-CoV-2 ed efficaci su coltura cellulare e modello murino.	The COVID-19 pandemic caused by the SARS-CoV-2 virus continually poses serious threats to global public health. The main protease (Mpro) of SARS-CoV-2 plays a central role in viral replication. We designed and synthesized 32 new bicycloproline-containing Mpro inhibitors derived from either Boceprevir or Telaprevir, both of which are approved antivirals. All compounds inhibited SARS-CoV-2 Mpro activity in vitro with IC50 values ranging from 7.6 to 748.5 nM. The co-crystal structure of Mpro in complex with MI-23, one of the most potent compounds, revealed its interaction mode. Two compounds (MI-09 and MI-30) showed excellent antiviral activity in cell-based assays. In a SARS-CoV-2 infection transgenic mouse model, oral or intraperitoneal treatment with MI-09 or MI-30 significantly reduced lung viral loads and lung lesions. Both also displayed good pharmacokinetic properties and safety in rats. 
Voysey M et al The Lancet	Single-dose administration and the influence of the timing of the booster dose on immunogenicity and	Analisi dei dati di 4 trial clinici per un totale di 17178 partecipanti sull'efficacia del vaccino	Background : The ChAdOx1 nCoV-19 (AZD1222) vaccine has been approved for emergency use by the UK regulatory authority, Medicines and Healthcare products Regulatory Agency, with a regimen of two standard doses given with an interval of 4–12

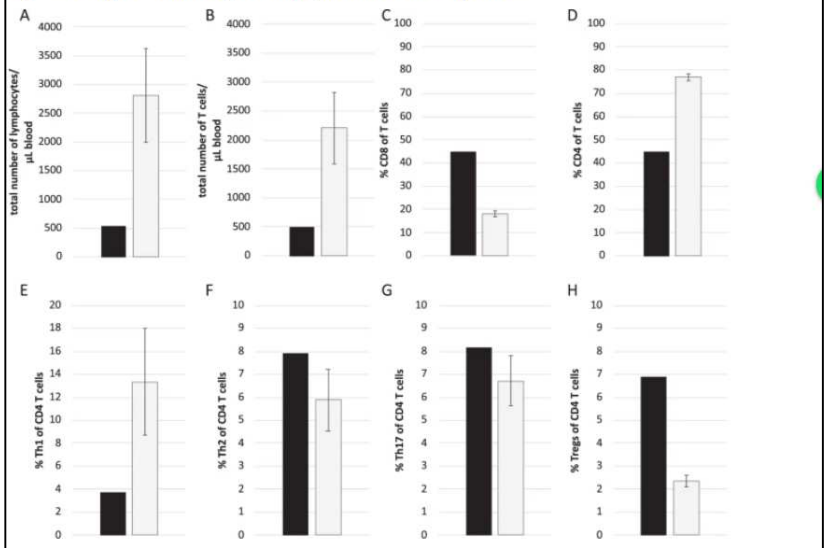
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00432-3/fulltext	efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials	AstraZeneca contro SARS-CoV-2, che confermano l'efficacia dell 66.7% contro l'infezione sintomatica, come nell'analisi ad interim precedentemente pubblicata; l'efficacia dopo una singola dose è invece del 76% (apparentemente maggiore che dopo due dosi, ma la differenza non è statisticamente significativa). Nei soggetti sottoposti a due dosi, la protezione dall'infezione sintomatica è maggiore in quelli con distanza maggiore fra le due, fino a 12 settimane, coerentemente con quanto osservato per altri vaccini. Questo dato può sostenere la politica di dilazionare la seconda somministrazione, ma poiché il follow up dei vaccinati arriva fino al giorno 90 non si possono esprimere giudizi sulla durata dell'immunità e sulle conseguenze a lungo termine del somministrare una dose sola.	weeks. The planned roll-out in the UK will involve vaccinating people in high-risk categories with their first dose immediately, and delivering the second dose 12 weeks later. Here, we provide both a further prespecified pooled analysis of trials of ChAdOx1 nCoV-19 and exploratory analyses of the impact on immunogenicity and efficacy of extending the interval between priming and booster doses. In addition, we show the immunogenicity and protection afforded by the first dose, before a booster dose has been offered. Methods : We present data from three single-blind randomised controlled trials—one phase 1/2 study in the UK (COV001), one phase 2/3 study in the UK (COV002), and a phase 3 study in Brazil (COV003)—and one double-blind phase 1/2 study in South Africa (COV005). As previously described, individuals 18 years and older were randomly assigned 1:1 to receive two standard doses of ChAdOx1 nCoV-19 (5 × 1010 viral particles) or a control vaccine or saline placebo. In the UK trial, a subset of participants received a lower dose (2·2 × 1010 viral particles) of the ChAdOx1 nCoV-19 for the first dose. The primary outcome was virologically confirmed symptomatic COVID-19 disease, defined as a nucleic acid amplification test (NAAT)-positive swab combined with at least one qualifying symptom (fever ≥37·8°C, cough, shortness of breath, or anosmia or ageusia) more than 14 days after the second dose. Secondary efficacy analyses included cases occuring at least 22 days after the first dose. Antibody responses measured by immunoassay and by pseudovirus neutralisation were exploratory outcomes. All cases of COVID-19 with a NAAT-positive swab were adjudicated for inclusion in the analysis by a masked independent endpoint review committee. The primary analysis included all participants who were SARS-CoV-2 N protein seronegative at baseline, had had at least 14 days of follow-up after the second dose, and had no evidence of

			previous SARS-CoV-2 infection from NAAT swabs. Safety was assessed in all participants who received at least one dose. The four trials are registered at ISRCTN89951424 (COV003) and ClinicalTrials.gov, NCT04324606 (COV001), NCT04400838 (COV002), and NCT04444674 (COV005). Findings : Between April 23 and Dec 6, 2020, 24 422 participants were recruited and vaccinated across the four studies, of whom 17 178 were included in the primary analysis (8597 receiving ChAdOx1 nCoV-19 and 8581 receiving control vaccine). The data cutoff for these analyses was Dec 7, 2020. 332 NAAT-positive infections met the primary endpoint of symptomatic infection more than 14 days after the second dose. Overall vaccine efficacy more than 14 days after the second dose was 66·7% (95% CI 57·4–74·0), with 84 (1·0%) cases in the 8597 participants in the ChAdOx1 nCoV-19 group and 248 (2·9%) in the 8581 participants in the control group. There were no hospital admissions for COVID-19 in the ChAdOx1 nCoV-19 group after the initial 21-day exclusion period, and 15 in the control group. 108 (0·9%) of 12 282 participants in the ChAdOx1 nCoV-19 group and 127 (1·1%) of 11 962 participants in the control group had serious adverse events. There were seven deaths considered unrelated to vaccination (two in the ChAdOx1 nCov-19 group and five in the control group), including one COVID-19-related death in one participant in the control group. Exploratory analyses showed that vaccine efficacy after a single standard dose of vaccine from day 22 to day 90 after vaccination was 76·0% (59·3–85·9). Our modelling analysis indicated that protection did not wane during this initial 3-month period. Similarly, antibody levels were maintained during this period with minimal waning by day 90 (geometric mean ratio [GMR] 0·66 [95% CI 0·59–0·74]). In the participants who received two standard doses, after the second

			dose, efficacy was higher in those with a longer prime-boost interval (vaccine efficacy 81·3% [95% CI 60·3–91·2] at ≥12 weeks) than in those with a short interval (vaccine efficacy 55·1% [33·0–69·9] at <6 weeks). These observations are supported by immunogenicity data that showed binding antibody responses more than two-fold higher after an interval of 12 or more weeks compared with an interval of less than 6 weeks in those who were aged 18–55 years (GMR 2·32 [2·01–2·68]). Interpretation : The results of this primary analysis of two doses of ChAdOx1 nCoV-19 were consistent with those seen in the interim analysis of the trials and confirm that the vaccine is efficacious, with results varying by dose interval in exploratory analyses. A 3-month dose interval might have advantages over a programme with a short dose interval for roll-out of a pandemic vaccine to protect the largest number of individuals in the population as early as possible when supplies are scarce, while also improving protection after receiving a second dose.

			 ***Figure 4:*** **Relationship between binding and neutralising antibody 28 days after second dose, and vaccine efficacy against primary symptomatic COVID-19** Vaccine efficacy with 95% CI against primary symptomatic COVID-19 in participants who received two standard doses and those who received a low dose plus standard dose combined are shown plotted against the GMT (95% CI) of anti-SARS-CoV-2 spike IgG from an immunoassay (A), and the GMT (95% CI) pseudovirus neutralisation (B), for each prime boost interval. GMT=geometric meant titre.
Kadire SR et al Delayed Second Dose versus Standard Regimen for Covid-19 Vaccination https://www.nejm.org/doi/full/10.1056/NEJMclde2	Delayed Second Dose versus Standard Regimen for Covid-19 Vaccination	Scenario proposto dal New England in cui, con l'aiuto di due consulenti esperti di orientamento opposto, si deve decidere se ritardare la seconda dose di vaccino contro SARS-CoV-2 per destinare invece la prima dose a un maggior numero	You chair the Governor's task force on rollout of the Covid-19 vaccine. Given concerns about the limited availability of the two-dose mRNA vaccine, you have been asked to weigh in on the debate regarding the most effective use of the currently available doses. Should people who have already received a first dose of vaccine have their second dose delayed by a number of months until there is a greater supply, so that more people can receive a first dose? Or should those who have gotten the first dose receive the second dose according to the standard schedule, 3 to 4 weeks after the first

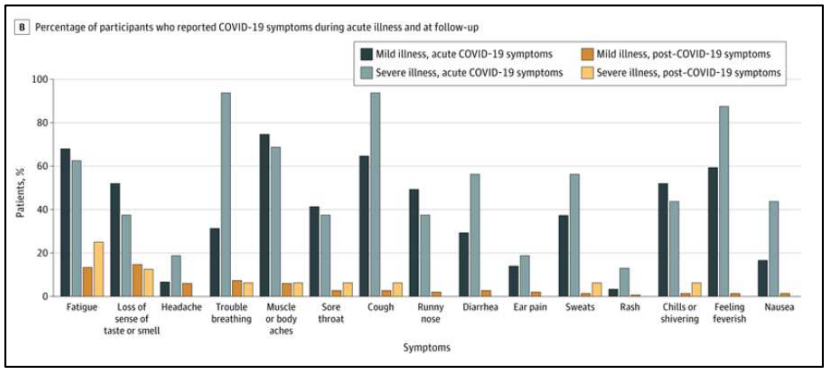
101987?query=featured_home		di persone. Un argomento importante che viene menzionato è quello della credibilità di fronte all'opinione pubblica: si riconosce che cambiare strategia vaccinale potrebbe essere deleterio ai fini dell'accettazione del vaccino.	dose, as recommended by the Food and Drug Administration (FDA)? You must consider the benefits and risks of the two approaches, on both individual and population levels, and decide what to recommend to the task force.
Reuken PA et al Leukemia https://www.nature.com/articles/s41375-021-01175-8	Severe clinical relapse in an immunocompromised host with persistent SARS-CoV-2 infection	Esacerbazione di COVID-19, dovuta a persistenza di SARS-CoV-2 per 4 mesi in una paziente di 56 anni con linfoma follicolare trattata con rituximab (anti-CD20). Si dimostra una grave linfopenia e in particolare l'assenza di linfociti B, alla base della mancata produzione di anticorpi.	Whether people who have recovered from COVID-19 can be re-infected by SARS-CoV-2 is a matter of debate. Antibodies against SARS-CoV-2 can be detected in up to 98.6% of patients after infection, but only in 67% of patients with CLL. In this context, anti-CD20 therapy is of special interest, as the memory B-cells are crucial for the development of immunity against SARS-CoV-2. A recent study from China has revealed that the failure to mount a robust humoral response against SARS-CoV-2 is associated with re-detection of SARS-CoV-2 in 7.3% of patients. In addition, patients with hematological malignancies are also more vulnerable to a severe course.

			Fig. 2: Analysis of leukocyte subpopulations of the patient.  **A**–**D** Absolute numbers of CD3 + T cells and percentages of CD3 + CD8 + cytotoxic T cells and CD3 + CD4 + T helper (Th) cells in the blood of the patient (black bars) and six controls (gray bars). **E**–**H** Frequencies of Th1 ($CXCR3^+CCR6^-CCR4^-CXCR5^-$), Th2 ($CXCR3^-CCR6^-CCR4^+CXCR5^-$), Th17 ($CXCR3^-CCR6^+CCR4^+CXCR5^-$), and Treg ($CD25^+CD127^-CCR4^+HLA\text{-}DR^-$) cells among $CD3^+CD4^+$ T cells in the patient (black bars) and controls (gray bars).
Amit S et al The Lancet https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00448-7/fulltext	Early rate reductions of SARS-CoV-2 infection and COVID-19 in BNT162b2 vaccine recipients	Dopo la vaccinazione di operatori sanitari con il vaccino Pfizer anti-SARS-CoV-2 in Israele si osserva una riduzione 30% del tasso di infezioni sintomatiche entro 14 giorni dalla prima dose e del 75% nel periodo 14-28 giorni dopo la prima dose. Questo incoraggia secondo gli autori l'eventuale scelta di dilazionare la seconda dose	In December, 2020, the Israeli Government approved the BNT162b2 COVID-19 vaccine and initiated a national immunisation campaign prioritising health-care workers (HCWs), as in other countries. This campaign coincided with a third wave of COVID-19, peaking at 10 116 daily new cases by mid-January, 2021. The Sheba Medical Centre, Israel's largest hospital with 9647 HCWs, began staff vaccination on Dec 19, 2020. All HCWs, excluding those with previous SARS-CoV-2 infection, were eligible for vaccination. Clinical trial data of BNT162b2 vaccine estimated an early vaccine efficacy in preventing COVID-19 of 52·4% before dose two, and 90.5% on days 2–7 after dose two. A recent analysis of BNT162b2 vaccine data estimated vaccine efficacy of 89–91% during days 15–28 after the

		di vaccino ove necessario, per quanto i dati sugli effetti a lungo termine di questa politica non siano disponibili.	first dose. We examined early reductions in SARS-CoV-2 infection and COVID-19 rates in vaccinated HCWs.
Olliaro P The Lancet https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00075-X/fulltext	What does 95% COVID-19 vaccine efficacy really mean?	Un vaccino « efficace al 95% » non protegge il 95% dei vaccinati, ma riduce del 95% il numero di nuove infezioni nella popolazione vaccinata rispetto a quella non vaccinata.	Simple mathematics helps. If we vaccinated a population of 100 000 and protected 95% of them, that would leave 5000 individuals diseased over 3 months, which is almost the current overall COVID-19 case rate in the UK. Rather, a 95% vaccine efficacy means that instead of 1000 COVID-19 cases in a population of 100 000 without vaccine (from the placebo arm of the abovementioned trials, approximately 1% would be ill with COVID-19 and 99% would not) we would expect 50 cases (99·95% of the population is disease-free, at least for 3 months).
Mallapaty S Nature https://www.nature.com/articles/d41586-021-00450-z	Can COVID vaccines stop transmission? Scientists race to find answers	La prevenzione dell'infezione (e non solo della malattia sintomatica) da SARS-CoV-2 non è stata studiata sistematicamente in tutti i trial clinici sui vaccini eseguiti negli scorsi mesi. In particolare abbiamo a disposizione solo dati dai trial di Moderna e AstraZeneca che indicano una riduzione fra metà e due terzi delle infezioni asintomatiche.	As countries roll out vaccines that prevent COVID-19, studies are under way to determine whether shots can also stop people from getting infected and passing on the SARS-CoV-2 virus. Vaccines that prevent transmission could help to bring the pandemic under control if they are given to enough people.

Manabe Y et al Open Forum Infectious Diseases https://doi.org/10.1093/ofid/ofaa648	Self-Collected Oral Fluid Saliva Is Insensitive Compared With Nasal-Oropharyngeal Swabs in the Detection of Severe Acute Respiratory Syndrome Coronavirus 2 in Outpatients.	Confrontando 171 campioni appaiati di tampone nasofaringeo e salivare di pazienti non ospedalizzati con infezione da SARS-CoV-2, la saliva non è sufficientemente sensibile.	Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic control will require widespread access to accurate diagnostics. Salivary sampling circumvents swab supply chain bottlenecks, is amenable to self-collection, and is less likely to create an aerosol during collection compared with the nasopharyngeal swab. Methods: We compared real-time reverse-transcription polymerase chain reaction Abbott m2000 results from matched salivary oral fluid (gingival crevicular fluid collected in an Oracol device) and nasal-oropharyngeal (OP) self-collected specimens in viral transport media from a nonhospitalized, ambulatory cohort of coronavirus disease 2019 (COVID-19) patients at multiple time points. Results: There were 171 matched specimen pairs. Compared with nasal-OP swabs, 41.6% of the oral fluid samples were positive. Adding spit to the oral fluid percent collection device increased the percent positive agreement from 37.2% (16 of 43) to 44.6% (29 of 65). The positive percent agreement was highest in the first 5 days after symptoms and decreased thereafter. All of the infectious nasal-OP samples (culture positive on VeroE6 TMPRSS2 cells) had a matched SARS-CoV-2 positive oral fluid sample. Conclusions: In this study of nonhospitalized SARS-CoV-2-infected persons, we demonstrate lower diagnostic sensitivity of self-collected oral fluid compared with nasal-OP specimens, a difference that was especially prominent more than 5 days from symptom onset. These data do not justify the routine use of oral fluid collection for diagnosis of SARS-CoV-2 despite the greater ease of collection. It also underscores the importance of considering the method of saliva specimen collection and the time from symptom onset especially in outpatient populations.

Benard A et al Nature https://doi.org/10.1038/s41467-021-21310-4	Interleukin-3 is a predictive marker for severity and outcome during SARS-CoV-2 infections.	Studio multicentrico su pazienti ospedalizzati con COVID-19 : i bassi livelli di interleukina 3 sono associati alla gravità, alla carica virale nel tampone nasofaringeo e alla mortalità dei pazienti.	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a worldwide health threat. In a prospective multicentric study, we identify IL-3 as an independent prognostic marker for the outcome during SARS-CoV-2 infections. Specifically, low plasma IL-3 levels is associated with increased severity, viral load, and mortality during SARS-CoV-2 infections. Patients with severe COVID-19 exhibit also reduced circulating plasmacytoid dendritic cells (pDCs) and low plasma IFNalpha and IFNlambda levels when compared to non-severe COVID-19 patients. In a mouse model of pulmonary HSV-1 infection, treatment with recombinant IL-3 reduces viral load and mortality. Mechanistically, IL-3 increases innate antiviral immunity by promoting the recruitment of circulating pDCs into the airways by stimulating CXCL12 secretion from pulmonary CD123(+) epithelial cells, both, in mice and in COVID-19 negative patients exhibiting pulmonary diseases. This study identifies IL-3 as a predictive disease marker for SARS-CoV-2 infections and as a potential therapeutic target for pulmunory viral infections.
Laracy J et al Open Forum Infectious Diseases https://doi.org/10.1093/ofid/ofab029	HIV-1 Infection Does Not Change Disease Course or Inflammatory Pattern of SARS-CoV-2-Infected Patients Presenting at a Large Urban Medical Center in New York City.	Studio di coorte retrospettivo su 68 pazienti con HIV e COVID-19 a confronto ciascuno con 4 controlli non-HIV : gli HIV sono più facilmente ricoverati, ma la mortalità a 30 giorni e la necessità di ventilazione meccanica non differiscono fra i ricoverati dei due gruppi.	Background: The clinical impact of coronavirus disease 2019 (COVID-19) among people with HIV (PWH) remains unclear. In this retrospective cohort study of COVID-19, we compared clinical outcomes and laboratory parameters among PWH and controls. Methods: Sixty-eight PWH diagnosed with COVID-19 were matched 1:4 to patients without known HIV diagnosis, drawn from a study population of all patients who were diagnosed with COVID-19 at an academic urban hospital. The primary outcome was death/discharge to hospice within 30 days of hospital presentation. Results: PWH were more likely to be admitted from the emergency department than patients without HIV (91% vs 71%; P = .001). We observed no statistically significant difference between admitted PWH and patients without HIV in terms of 30-day mortality rate

			(19% vs 13%, respectively) or mechanical ventilation rate (18% vs 20%, respectively). PWH had higher erythrocyte sedimentation rates than controls on admission but did not differ in other inflammatory marker levels or nasopharyngeal/oropharyngeal severe acute respiratory syndrome coronavirus 2 viral load estimated by reverse transcriptase polymerase chain reaction cycle thresholds. Conclusions: HIV infection status was associated with a higher admission rate; however, among hospitalized patients, PWH did not differ from HIV-uninfected controls by rate of mechanical ventilation or death/discharge to hospice.
Logue JK et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2776560	Sequelae in Adults at 6 Months After COVID-19 Infection	Follow up di 177 con infezione documentata da SARS-CoV-2 (solo 16 ricoverati) fino a 9 mesi dalla diagnosi : circa un terzo riporta sintomi persistenti.	Many individuals experience persistent symptoms and a decline in health-related quality of life (HRQoL) after coronavirus disease 2019 (COVID-19) illness. Existing studies have focused on hospitalized individuals 30 to 90 days after illness onset and have reported symptoms up to 110 days after illness. Longer-term sequelae in outpatients have not been well characterized. 
Robertson JFR et al The Lancet	Delayed second dose of the BNT162b2 vaccine: innovation or misguided conjecture?	Differire la seconda somministrazione di vaccino BNT162b2 (Pfizer) non è una scelta supportata da evidenze scientifiche, a	We strongly support vaccination against COVID-19 with the Pfizer-BioNTech COVID-19 mRNA vaccine BNT162b2 when adhering to the 3-week dosing schedule that was found highly effective in the phase 3 randomised clinical trial—regarded as the gold standard. However we do not support the second dose being delayed to 12 weeks, as

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00455-4/fulltext		differenza che per il vaccino AstraZeneca, fanno notare gli autori di questo commento.	implemented by UK Chief Medical Officers. The latter followed recommendations by the Joint Committee on Vaccination and Immunisation (JCVI), based on unplanned, retrospective analysis and unwarranted assumptions. The UK is currently the only country to have adopted a maximal 12 weeks delay. How science-led is the UK strategy? Is it innovative and world-leading, or scientifically fallacious, resulting in an unproven dosing schedule introduced without fully informed patient consent? What are the potential risks, for individuals and the population?
Jeffery-Smith A et al Eurosurveillance https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.5.2100092	Antibodies to SARS-CoV-2 protect against re-infection during outbreaks in care homes, September and October 2020 separator	Due case di riposo i cui occupanti e lavoratori erano stati colpiti dalla prima ondata di COVID-19 sono state monitorate nel tempo : a distanza di 4 mesi, con la seconda ondata, si osserva un solo caso di reinfezione (sempre asintomatica e in assenza di anticorpi neutralizzanti dopo il primo episodio) fra i sieropositivi.	In autumn 2020, two care homes in London, United Kingdom (UK) with high rates of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) seropositivity following outbreaks in the first wave of the coronavirus disease (COVID-19) pandemic experienced a second COVID-19 outbreak. Outbreak investigations and SARS-CoV-2 serology were repeated to assess the role of antibodies in protecting against SARS-CoV-2 re-infection.
Czeisler ME et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2776559	Follow-up Survey of US Adult Reports of Mental Health, Substance Use, and Suicidal Ideation During the COVID-19 Pandemic, September 2020	Esito di un sondaggio condotto su oltre 5000 adulti negli USA a settembre 2020, a confronto con i risultati di aprile 2020: la prevalenza di disturbi come ansia e depressione rimane stabile, a suggerire secondo	Adverse mental health symptoms among US adults were more prevalent during the early phase (April-June 2020) of the coronavirus disease 2019 (COVID-19) pandemic compared with prepandemic estimates (eg, 3-fold increased prevalences of anxiety and depression symptoms, 2-fold increased prevalence of suicidal ideation). In June 2020, 2238 (40.9%) of 5470 US adults reported adverse mental or behavioral health symptoms. During this time, the prevalence of symptoms was lower in adults aged 65 years or

		gli autori che si tratti di fenomeni non solamente legati alla risposta alla pandemia.	older (141 of 933 [15.1%]) than in young adults aged 18 to 24 years (547 of 731 [74.9%]; P < .001). Given suggestions that acute increases in the prevalence of adverse mental health symptoms may represent a transient response to mass trauma, we sought to determine whether these patterns persisted in September 2020 and to examine disproportionately affected demographic groups.
Shah P et al Critical Care Medicine https://journals.lww.com/ccmjournal/Fulltext/2021/02000/Is_Cardiopulmonary_Resuscitation_Futile_in.4.aspx	Is Cardiopulmonary Resuscitation Futile in Coronavirus Disease 2019 Patients Experiencing In-Hospital Cardiac Arrest?	Un altro studio sulla mortalità intraospedaliera dopo arresto cardiaco in pazienti con COVID-19 : 100% in una casistica di 63 persone, indipendentemente dalle condizioni di base.	Objectives: There is limited data regarding outcomes after in-hospital cardiac arrest among coronavirus disease 2019 patients. None of the studies have reported the outcomes of in-hospital cardiac arrest in coronavirus disease 2019 patients in the United States. We describe the characteristics and outcomes of in-hospital cardiac arrest in coronavirus disease 2019 patients in rural Southwest Georgia. Design: Retrospective cohort study. Setting: Single-center, multihospital. PATIENTS: Consecutive coronavirus disease 2019 patients who experienced in-hospital cardiac arrest with attempted resuscitation. Interventions: Attempted resuscitation with advanced cardiac life support. Measurement and Main Results: Out of 1,094 patients hospitalized for coronavirus disease 2019 during the study period, 63 patients suffered from in-hospital cardiac arrest with attempted resuscitation and were included in this study. The median age was 66 years, and 49.2% were males. The majority of patients were African Americans (90.5%). The most common comorbidities were hypertension (88.9%), obesity (69.8%), diabetes (60.3%), and chronic kidney disease (33.3%). Eighteen patients (28.9%) had a Charlson Comorbidity Index of 0–2. The most common presenting symptoms were shortness of breath (63.5%), fever (52.4%), and cough (46%). The median duration of symptoms prior to admission

			was 14 days. During hospital course, 66.7% patients developed septic shock, and 84.1% had acute respiratory distress syndrome. Prior to in-hospital cardiac arrest, 81% were on ventilator, 60.3% were on vasopressors, and 39.7% were on dialysis. The majority of in-hospital cardiac arrest (84.1%) occurred in the ICU. Time to initiation of advanced cardiac life support protocol was less than 1 minute for all in-hospital cardiac arrest in the ICU and less than 2 minutes for the remaining patients. The most common initial rhythms were pulseless electrical activity (58.7%) and asystole (33.3%). Although return of spontaneous circulation was achieved in 29% patients, it was brief in all of them. The in-hospital mortality was 100%. Conclusions: In our study, coronavirus disease 2019 patients suffering from in-hospital cardiac arrest had 100% in-hospital mortality regardless of the baseline comorbidities, presenting illness severity, and location of arrest.
Pfizer.com/ News https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-submit-covid-19-vaccine-stability-data	Pfizer and BioNTech Submit COVID-19 Vaccine Stability Data at Standard Freezer Temperature to the U.S. FDA	Il vaccino Pfizer contro SARS-CoV-2 può essere conservato a una temperatura fra -25 e -15°C come indicato in questo comunicato stampa dell'azienda. I dati sono al vaglio della FDA per un eventuale aggiornamento delle indicazioni sul prodotto.	NEW YORK and MAINZ, GERMANY, February 19, 2021 — Pfizer Inc. (NYSE: PFE) and BioNTech SE (Nasdaq: BNTX) today announced the submission of new data to the U.S. Food and Drug Administration (FDA) demonstrating the stability of their COVID-19 vaccine when stored at -25°C to -15°C (-13°F to 5°F), temperatures more commonly found in pharmaceutical freezers and refrigerators. The data have been submitted to the FDA to support a proposed update to the U.S. Emergency Use Authorization (EUA) Prescribing Information, which would allow for vaccine vials to be stored at these temperatures for a total of two weeks as an alternative or complement to storage in an ultra-low temperature freezer.