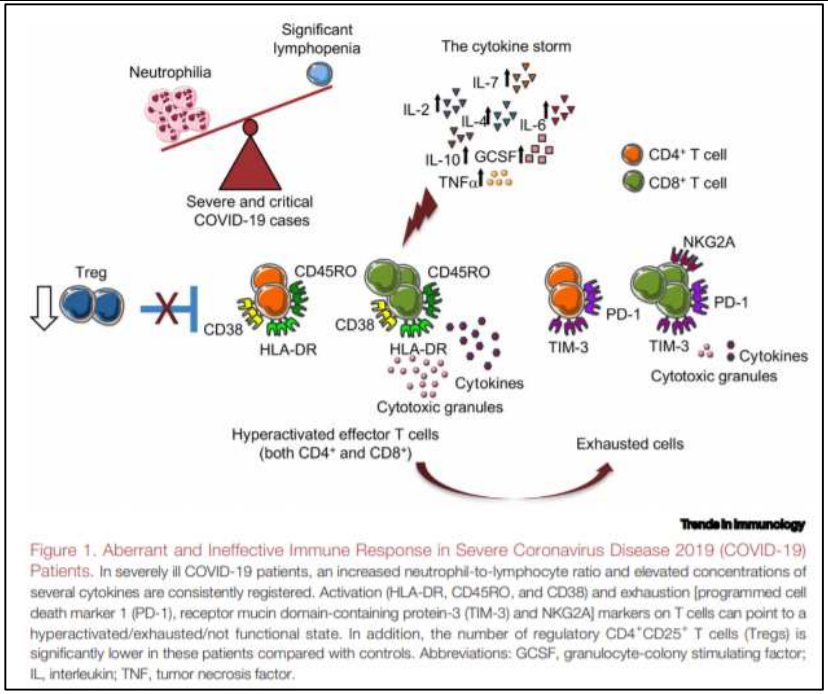
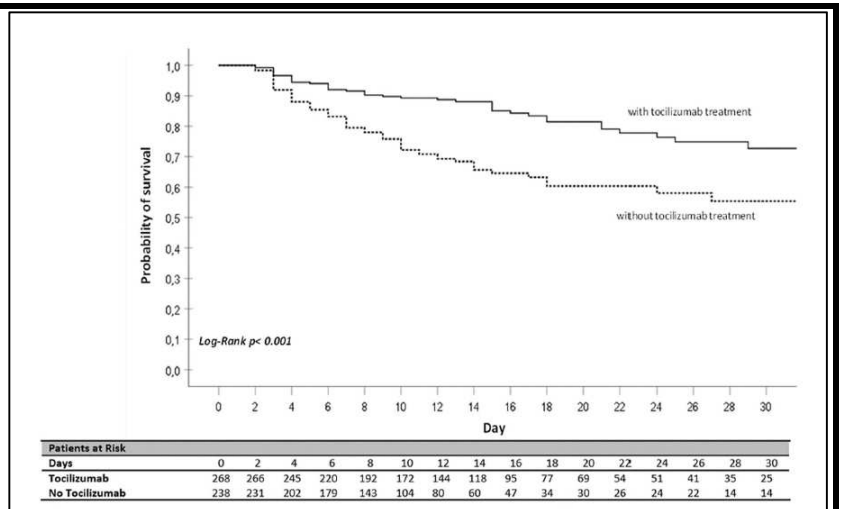
RICERCA BIBLIOGRAFICA COVID 19 SETTIMANA 07-13.11.2020 FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE DOTT.SSA ELEONORA TADDEI			
AUTORE/RIVISTA	**TITOLO**	**OUTCOME PRINCIPALE**	**ABSTRACT**
Petito E et al The Journal of Infectious Diseases https://doi.org/10.1093/infdis/jiaa756	Neutrophil more than platelet activation associates with thrombotic complications in COVID-19 patients.	Confronto dell'attivazione neutrofilica fra 36 pazienti ricoverati per COVID-19 e 31 controlli sani : associazione fra i marker di attivazione neutrofilica e la gravità di malattia e la trombosi.	BACKGROUND: SARS-CoV-2 infection is associated with hypercoagulability which predisposes to venous thromboembolism (VTE).We analyzed platelet and neutrophil activation in COVID-19 patients and their association with VTE. METHODS: Hospitalized COVID-19 patients and age- and sex-matched healthy controls were studied. Platelet and leukocyte activation, neutrophil extracellular traps (NETs), and matrix metalloproteinase-9 (MMP-9), a neutrophil-released enzyme, were measured. Four patients were re-studied after recovery. The activating effect of COVID-19 plasma on control platelets and leukocytes and the inhibiting activity of common antithrombotic agents on it were studied. RESULTS: 36 COVID-19 patients and 31 healthy controls were studied; 8/36 COVID-19 patients (22.2%) developed VTE. Platelets and neutrophils were activated in COVID-19 patients. NET, but not platelet activation, biomarkers correlated with disease severity and were associated with thrombosis. Plasmatic MMP-9 was significantly

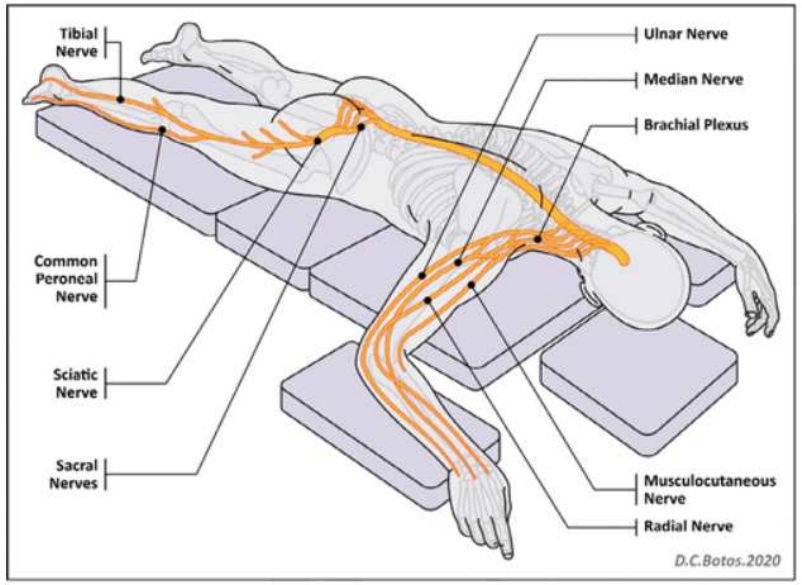
			increased in COVID-19 patients. Platelet and neutrophil activation markers, but less so NETs, normalized after recovery.In vitro, plasma from COVID-19 patients triggered platelet and neutrophil activation and NET formation, the latter blocked by therapeutic dose low-molecular weight heparin, but not by aspirin or dypiridamole. CONCLUSIONS: Platelet and neutrophil activation are key features of COVID-19 patients. NET biomarkers may help to predict clinical worsening and VTE, and may guide LMWH-treatment intensity.
De Candia P et al Trends in Immunology https://doi.org/10.1016/j.it.2020.11.002	T Cells: Warriors of SARS-CoV-2 Infection.	Ruolo dei linfociti T nella risposta immune, talvolta dannosa, nei confronti di SARS-CoV-2 in corso di infezione acuta.	Severe infection with severe acute respiratory syndrome coronavirus (SARS-CoV)-2 is characterized by massive cytokine release and T cell loss. The exaggerated host immune response, incapable of viral clearance, instead aggravates respiratory distress, as well as cardiac, and/or damage to other organs. The mortality pattern of SARS-CoV-2 infection, higher in older versus younger adults and almost absent in children, is possibly caused by the effects of age and pre-existing comorbidities on innate and adaptive immunity. Here, we speculate that the abnormal and excessive immune response to SARS-CoV-2 infection partly depends on T cell immunological memory, which is more pronounced in adults compared with children, and may significantly contribute to immunopathology and massive collateral damage in coronavirus disease 2019 (COVID-19) patients.

			 Figure 1. Aberrant and Ineffective Immune Response in Severe Coronavirus Disease 2019 (COVID-19) Patients. In severely ill COVID-19 patients, an increased neutrophil-to-lymphocyte ratio and elevated concentrations of several cytokines are consistently registered. Activation (HLA-DR, CD45RO, and CD38) and exhaustion [programmed cell death marker 1 (PD-1), receptor mucin domain-containing protein-3 (TIM-3) and NKG2A] markers on T cells can point to a hyperactivated/exhausted/not functional state. In addition, the number of regulatory CD4+CD25+ T cells (Tregs) is significantly lower in these patients compared with controls. Abbreviations: GCSF, granulocyte-colony stimulating factor; IL, interleukin; TNF, tumor necrosis factor.
Ludwig M et al International Journal of Infectious Diseases https://doi.org/10.1016/j.ijid.2020.11.204	Clinical outcomes and characteristics of patients hospitalized for Influenza or COVID-19 in Germany.	Confronto fra le caratteristiche cliniche e l'outcome di 2343 pazienti ricoverati per COVID-19 e 6762 ricoverati per influenza : la prima presenta maggiore gravità, tasso di ricovero in rianimazione e mortalità. Dire che COVID-19 è simile all'influenza non ha una base scientifica.	OBJECTIVES: Since beginning of the SARS-CoV-2 pandemic, there is a discussion about the severity of COVID-19 in comparison to infections with seasonal Influenza. The objective of this study was to compare clinical and demographic characteristics of German patients hospitalized for infection with either SARS-CoV-2 or Influenza. METHODS: This study used anonymized German healthcare claims data. Patients with a confirmed COVID-19 or Influenza diagnosis, for whom a complete hospital course was available (i.e., the patient was discharged or died in hospital) were included. The data set included detailed information on patient characteristics and hospital treatment. Patients were grouped according to whether they were transferred to intensive care unit (ICU), received mechanical ventilation (MV) or had a severe course

			of the disease (SD). Charlson-Comorbidity-Index in the eight quarters prior to hospitalization and secondary diagnoses during hospitalization were analysed. RESULTS: A total of 2343 hospitalized COVID-19 patients and 6762 hospitalized Influenza patients were included. 54% of the patients were male, with men being twice as frequent in the COVID-19 severe groups. For both diseases, patients >49 years accounted for almost three-quarters of hospital cases and hypertension, diabetes mellitus, CKD and COPD were the most common comorbidities. The proportion of cases with ICU, MV and SD was substantially higher for COVID-19 patients (ICU+: 21 vs. 13 %; MV+: 15 vs. 9%; SD+: 28 vs. 16%). Overall in-hospital mortality was more than two-fold higher in COVID-19 vs. Influenza (14 vs. 6%).). Length of ventilation and hospitalization, and the proportion of patients diagnosed with ARDS, SIRS or acute kidney injury were considerably higher in COVID-19 patients. CONCLUSIONS: COVID-19 resulted in higher in-hospital mortality and worse clinical outcomes than Influenza. This was not attributable to demographic characteristics, pre-existing comorbidities or patient triage, since the German healthcare system had not reached its limits in the pandemic. Discussions suggesting that COVID-19 and seasonal Influenza have similar severity cannot be based on clinical evidence.
Ruiz-Antoran B et al Infectious Diseases and Therapy https://doi.org/10.1007/s40121-020-00373-8	Combination of Tocilizumab and Steroids to Improve Mortality in Patients with Severe COVID-19 Infection: A Spanish, Multicenter, Cohort Study.	Studio di coorte retrospettivo multicentrico condotto in Spagna su 268 pazienti con COVID-19 trattati con tocilizumab e 238 non trattati con tocilizumab : si osserva una minore mortalità nel primo gruppo e inoltre un	BACKGROUND: We aimed to determine the impact of tocilizumab use on severe COVID-19 (coronavirus disease 19) pneumonia mortality. METHODS: We performed a multicentre retrospective cohort study in 18 tertiary hospitals in Spain from March to April 2020. Consecutive patients admitted with severe COVID-19 treated with tocilizumab were compared to patients not treated with tocilizumab, adjusting by inverse probability of the treatment weights (IPTW). Tocilizumab's effect in patients receiving steroids during the 48 h following inclusion was analysed. RESULTS: During

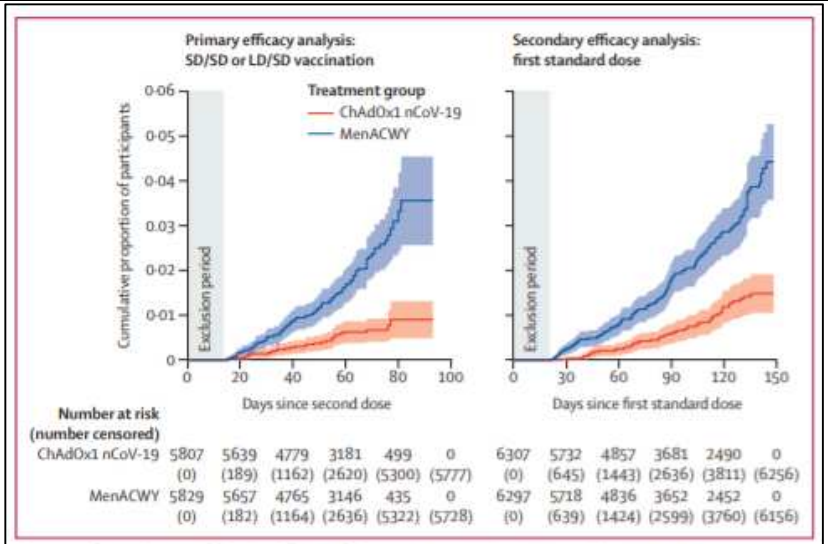
		vantaggio nell'aggiunta di tocilizumab allo steroide.	the study period, 506 patients with severe COVID-19 fulfilled the inclusion criteria. Among them, 268 were treated with tocilizumab and 238 patients were not. Median time to tocilizumab treatment from onset of symptoms was 11 days [interquartile range (IQR) 8-14]. Global mortality was 23.7%. Mortality was lower in patients treated with tocilizumab than in controls: 16.8% versus 31.5%, hazard ratio (HR) 0.514 [95% confidence interval (95% CI) 0.355-0.744], p < 0.001; weighted HR 0.741 (95% CI 0.619-0.887), p = 0.001. Tocilizumab treatment reduced mortality by 14.7% relative to no tocilizumab treatment [relative risk reduction (RRR) 46.7%]. We calculated a number necessary to treat of 7. Among patients treated with steroids, mortality was lower in those treated with tocilizumab than in those treated with steroids alone [10.9% versus 40.2%, HR 0.511 (95% CI 0.352-0.741), p = 0.036; weighted HR 0.6 (95% CI 0.449-0.804), p < 0.001] (interaction p = 0.094). CONCLUSIONS: These results show that survival of patients with severe COVID-19 is higher in those treated with tocilizumab than in those not treated and that tocilizumab's effect adds to that of steroids administered to non-intubated patients with COVID-19 during the first 48 h of presenting with respiratory failure despite oxygen therapy. Randomised controlled studies are needed to confirm these results. TRIAL REGISTRATION: European Union electronic Register of Post-Authorization Studies (EU PAS Register) identifier, EUPAS34415.

			 **Fig. 2** Probability of survival of patients with SARS-COV-2 infection according to tocilizumab exposure. Descriptive raw analysis
Fernandez CE et al Radiology https://pubs.rsna.org/doi/10.1148/radiol.2020203116	Imaging Review of Peripheral Nerve Injuries in Patients with COVID-19	Tecniche di imaging utili nella diagnosi di lesioni dei nervi periferici nei malati di COVID-19.	With surging numbers of coronavirus disease 2019 (COVID-19) patients throughout the world, neuromuscular complications and rehabilitation concerns are becoming more apparent. Peripheral nerve injury can occur in COVID-19 patients secondary to post-infectious inflammatory neuropathy, prone positioning-related stretch/compression injury, systemic neuropathy, or nerve entrapment from hematoma. Imaging of peripheral nerves in COVID-19 patients may help characterize nerve pathology, identify site and severity of nerve damage, and potentially elucidate mechanisms of injury thereby aiding the medical diagnosis and decisionmaking process. This review article aims to provide a first comprehensive summary of the current knowledge of COVID-19 and peripheral nerve imaging.

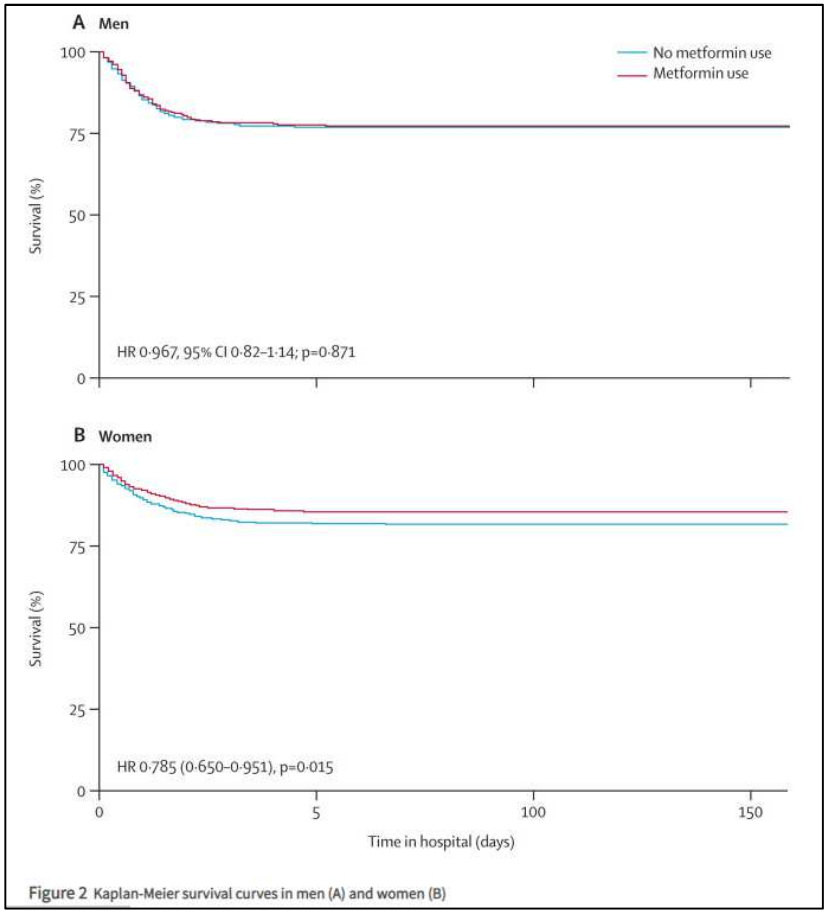
			
Friedman J et al JAMA https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2773768	Overdose-Related Cardiac Arrests Observed by Emergency Medical Services During the US COVID-19 Epidemic	Brusco aumento dei casi di arresto cardiaco per overdose di sostanze d'abuso in aprile 2020, in corrispondenza con il picco epidemico di COVID-19 negli USA.	The coronavirus disease 2019 (COVID-19) pandemic took grip of the US 2 decades into an accelerating overdose crisis that caused more than 70 000 deaths in 2019 alone.1 Front-line health care professionals and officials have sounded the alarm that the social and economic fallout from the COVID-19 pandemic may impede efforts to flatten the overdose curve. However, the state databases tracking overdose mortality often have long lags that stymie timely analysis and response. Emergency medical services (EMS) data provide a novel source of near-real-time information to track epidemiological trends during the COVID-19 pandemic. We leverage a large, national EMS database to characterize emergent trends in overdose mortality fueled by the pandemic.

Voysey M et al The Lancet https://marlin-prod.literatumonline.com/pb-assets/Lancet/pdfs/S0140673620326611.pdf	Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK	Primo trial clinico che valuta sicurezza ed efficacia di un vaccino inattivato contro SARS-CoV-2 basato su vettore adenovirale, ChAdOx1 nCoV-19 (AstraZeneca). I dati derivano da 4 trial clinici randomizzati tuttora in corso in Regno Unito, Brasile e Sudafrica che hanno coinvolto 23 848 adulti, di cui 11636 inclusi nell'analisi ad interim. Efficacia 70.4% dopo due dosi e protezione dalla malattia sintomatica 64.1% dopo almeno una dose. Elevata sicurezza.	Background : A safe and efficacious vaccine against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), if deployed with high coverage, could contribute to the control of the COVID-19 pandemic. We evaluated the safety and efficacy of the ChAdOx1 nCoV-19 vaccine in a pooled interim analysis of four trials. Methods : This analysis includes data from four ongoing blinded, randomised, controlled trials done across the UK, Brazil, and South Africa. Participants aged 18 years and older were randomly assigned (1:1) to ChAdOx1 nCoV-19 vaccine or control (meningococcal group A, C, W, and Y conjugate vaccine or saline). Participants in the ChAdOx1 nCoV-19 group received two doses containing 5×10^{10} viral particles (standard dose; SD/SD cohort); a subset in the UK trial received a half dose as their first dose (low dose) and a standard dose as their second dose (LD/SD cohort). The primary efficacy analysis included symptomatic COVID-19 in seronegative participants with a nucleic acid amplification test-positive swab more than 14 days after a second dose of vaccine. Participants were analysed according to treatment received, with data cutoff on Nov 4, 2020. Vaccine efficacy was calculated as 1−relative risk derived from a robust Poisson regression model adjusted for age. Studies are registered at ISRCTN89951424 and ClinicalTrials.gov, NCT04324606, NCT04400838, and NCT04444674. Findings : Between April 23 and Nov 4, 2020, 23 848 participants were enrolled and 11636 participants (7548 in the UK, 4088 in Brazil) were included in the interim primary efficacy analysis. In participants who received two standard doses, vaccine efficacy was 62·1% (95% CI 41·0–75·7; 27 [0·6%] of 4440 in the ChAdOx1 nCoV-19 group vs 71 [1·6%]

			of 4455 in the control group) and in participants who received a low dose followed by a standard dose, efficacy was 90·0% (67·4–97·0; three [0·2%] of 1367 vs 30 [2·2%] of 1374; pinteraction=0·010). Overall vaccine efficacy across both groups was 70·4% (95·8% CI 54·8–80·6; 30 [0·5%] of 5807 vs 101 [1·7%] of 5829). From 21 days after the first dose, there were ten cases hospitalised for COVID-19, all in the control arm; two were classified as severe COVID-19, including one death. There were 74341 person-months of safety follow-up (median 3·4 months, IQR 1·3–4·8): 175 severe adverse events occurred in 168 participants, 84 event in the ChAdOx1 nCoV-19 group and 91 in the control group. Three events were classified as possibly related to a vaccine: one in the ChAdOx1 nCoV-19 group, one in the control group, and one in a participant who remains masked to group allocation. Interpretation : ChAdOx1 nCoV-19 has an acceptable safety profile and has been found to be efficacious against symptomatic COVID-19 in this interim analysis of ongoing clinical trials.

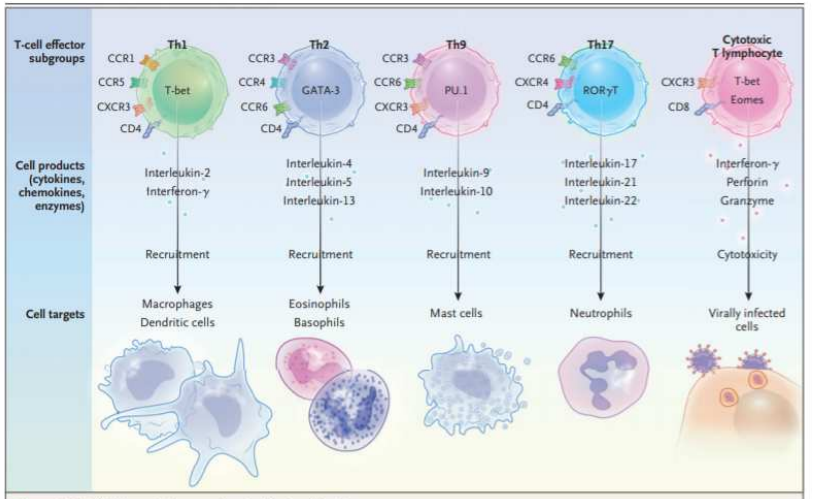
			 ***Figure:*** **Kaplan-Meier cumulative incidence of primary symptomatic, NAAT-positive COVID-19** Cumulative incidence of symptomatic COVID-19 after two doses (left) or after first standard dose in participants receiving only standard-dose vaccines (right). Grey shaded areas show the exclusion period after each dose in which cases were excluded from the analysis. Blue and red shaded areas show 95% CIs. LD/SD=low-dose prime plus standard-dose boost. MenACWY=meningococcal group A, C, W, and Y conjugate vaccine. NAAT=nucleic acid amplification test. SD/SD=two standard-dose vaccines given.
Knoll M et al The Lancet https://marlin-prod.literatumonline.com/pb-assets/Lancet/pdfs/S0140673620326234.pdf	Oxford–AstraZeneca COVID-19 vaccine efficacy	Commento allo studio precedente che evidenzia limiti e punti di forza dei trial sul vaccino Oxford-AstraZeneca.	2020 has been a difficult year for all, but has seen 58 vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) be developed and in clinical trials, with some vaccines reportedly having more than 90% efficacy against COVID-19 in clinical trials.
Bramante CT et al The Lancet	Metformin and risk of mortality in patients hospitalised with COVID-19:	Studio di coorte retrospettivo sull'effetto della metformina (almeno 90 giorni di terapia pre-	Background : Type 2 diabetes and obesity, as states of chronic inflammation, are risk factors for severe COVID-19. Metformin has cytokine-reducing and sex-specific immunomodulatory effects. Our

https://www.thelancet.com/journals/lanhl/article/PIIS2666-7568(20)30033-7/fulltext	a retrospective cohort analysis	ricovero) sulla mortalità da COVID-19 : si osserva un effetto protettivo nelle donne obese o diabetiche ricoverate. Tale effetto, di cui si ipotizza l'origine nella azione immunomodulatrice del farmaco, dovrà essere indagato in studi prospettici.	aim was to identify whether metformin reduced COVID-19-related mortality and whether sex-specific interactions exist. Methods : In this retrospective cohort analysis, we assessed de-identified claims data from UnitedHealth Group (UHG)'s Clinical Discovery Claims Database. Patient data were eligible for inclusion if they were aged 18 years or older; had type 2 diabetes or obesity (defined based on claims); at least 6 months of continuous enrolment in 2019; and admission to hospital for COVID-19 confirmed by PCR, manual chart review by UHG, or reported from the hospital to UHG. The primary outcome was in-hospital mortality from COVID-19. The independent variable of interest was home metformin use, defined as more than 90 days of claims during the year before admission to hospital. Covariates were comorbidities, medications, demographics, and state. Heterogeneity of effect was assessed by sex. For the Cox proportional hazards, censoring was done on the basis of claims made after admission to hospital up to June 7, 2020, with a best outcome approach. Propensity-matched mixed-effects logistic regression was done, stratified by metformin use. Findings : 6256 of the 15 380 individuals with pharmacy claims data from Jan 1 to June 7, 2020 were eligible for inclusion. 3302 (52·8%) of 6256 were women. Metformin use was not associated with significantly decreased mortality in the overall sample of men and women by either Cox proportional hazards stratified model (hazard ratio [HR] 0·887 [95% CI 0·782–1·008]) or propensity matching (odds ratio [OR] 0·912 [95% CI 0·777–1·071], p=0·15). Metformin was associated with decreased mortality in women by Cox proportional hazards (HR 0·785, 95% CI 0·650–0·951) and propensity matching (OR 0·759, 95% CI 0·601–0·960, p=0·021).

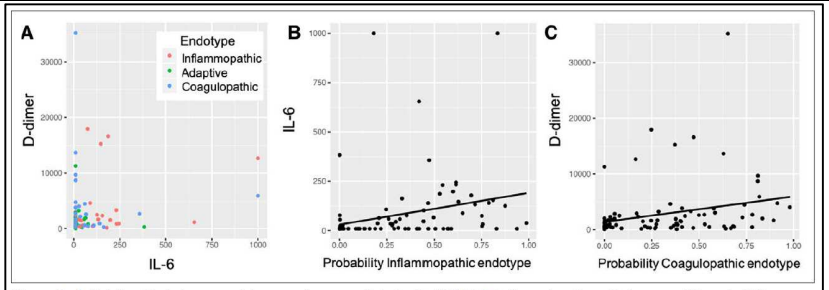
			There was no significant reduction in mortality among men (HR 0·957, 95% CI 0·82–1·14; p=0·689 by Cox proportional hazards). Interpretation : Metformin was significantly associated with reduced mortality in women with obesity or type 2 diabetes who were admitted to hospital for COVID-19. Prospective studies are needed to understand mechanism and causality. If findings are reproducible, metformin could be widely distributed for prevention of COVID-19 mortality, because it is safe and inexpensive.  Figure 2 Kaplan-Meier survival curves in men (A) and women (B)

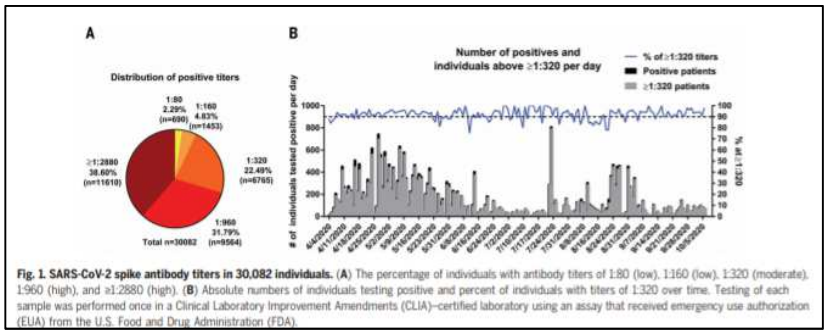
Butt JH et al BMJ Open https://bmjopen.bmj.com/content/10/12/e044421	Association between statin use and outcomes in patients with coronavirus disease 2019 (COVID-19): a nationwide cohort study	Esito di uno studio di coorte osservazionale sull'associazione fra terapia con statine (di cui è stato proposto un effetto alternativamente benefico e dannoso in studi precedenti) e mortalità da COVID-19 in Danimarca : nessuna differenza fra esposti e non esposti.	Objective To investigate the association between recent statin exposure and risk of severe COVID-19 infection and all-cause mortality in patients with COVID-19 in Denmark. Design and setting Observational cohort study using data from Danish nationwide registries. Participants Patients diagnosed with COVID-19 from 22 February 2020 to 17 May 2020 were followed from date of diagnosis until outcome of interest, death or 17 May 2020. Interventions Use of statins, defined as a redeemed drug prescription in the 6 months prior to COVID-19 diagnosis. Primary and secondary outcome measures All-cause mortality, severe COVID-19 infection and the composite. Results The study population comprised 4842 patients with COVID-19 (median age 54 years (25th–75th percentile, 40–72), 47.1% men), of whom 843 (17.4%) redeemed a prescription of statins. Patients with statin exposure were more often men and had a greater prevalence of comorbidities. The median follow-up was 44 days. After adjustment for age, sex, ethnicity, socioeconomic status and comorbidities, statin exposure was not associated with a significantly different risk of mortality (HR 0.96 (95% CI 0.78 to 1.18); 30-day standardised absolute risk (SAR), 9.8% (8.7% to 11.0%) vs 9.5% (8.2% to 10.8%); SAR difference, −0.4% (−1.9% to 1.2%)), severe COVID-19 infection (HR 1.16 (95% CI 0.95 to 1.41); 30-day SAR, 13.0% (11.8% to 14.2%) vs 14.9% (12.8% to 17.1%); SAR difference, 1.9% (−0.7% to 4.5%)), and the composite outcome of all-cause mortality or severe COVID-19 infection (HR 1.05 (95% CI 0.89 to 1.23); 30-day SAR, 17.6% (16.4% to 18.8%) vs 18.2% (16.4% to 20.1%); SAR difference, 0.6% (−1.6% to 2.9%)). The results were consistent across subgroups of age, sex and presumed indication for statin therapy. Among patients with statin exposure, there was no

			difference between statin drug or treatment intensity with respect to outcomes. Conclusions Recent statin exposure in patients with COVID-19 infection was not associated with an increased or decreased risk of all-cause mortality or severe infection.
Fajgenbaum DC et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMra2026131?query=featured_home	Cytokine Storm	La tempesta citochinica, o sindrome da rilascio di citochine, è un fenomeno descritto in relazione a numerose condizioni non solo infettive e non è facilmente distinguibile da una risposta infiammatoria appropriata. Revisione delle caratteristiche cliniche e delle opzioni terapeutiche per contrastarla, con una sezione dedicata a COVID-19.	The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has reminded us of the critical role of an effective host immune response and the devastating effect of immune dysregulation. This year marks 10 years since the first description of a cytokine storm that developed after chimeric antigen receptor (CAR) T-cell therapy1 and 27 years since the term was first used in the literature to describe the engraftment syndrome of acute graft-versus-host disease after allogeneic hematopoietic stem-cell transplantation.2 The term “cytokine release syndrome” was coined to describe a similar syndrome after infusion of muromonab-CD3 (OKT3).3 Cytokine storm and cytokine release syndrome are life-threatening systemic inflammatory syndromes involving elevated levels of circulating cytokines and immune-cell hyperactivation that can be triggered by various therapies, pathogens, cancers, autoimmune conditions, and monogenic disorders.

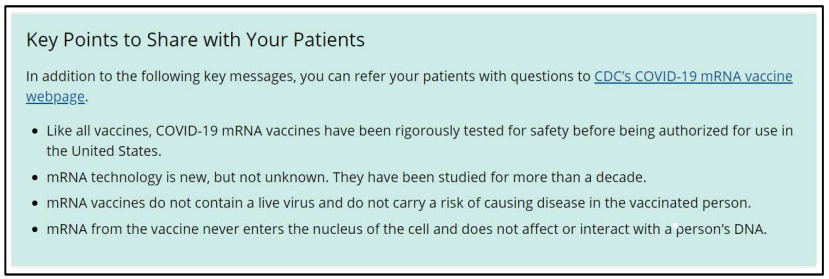
			 **Figure 3. T-Cell Effector Subgroups Involved in Cytokine Storm.** The master transcription factors (T-bet, GATA-3, PU.1, RORγT, and eomesodermin [eomes]), effector molecules, and cell targets are shown for the following T-cell subgroups: types 1, 2, 9, and 17 helper T (Th1, Th2, Th9, and Th17, respectively) cells and cytotoxic T lymphocytes.
Sweeney TE et al Critical Care Medicine https://journals.lww.com/ccmjournal/Abstract/9000/Validation_of_Inflammopathic,_Adaptive,_and.95419.aspx	Validation of Inflammopathic, Adaptive, and Coagulopathic Sepsis Endotypes in Coronavirus Disease 2019	Studio di coorte osservazionale su 97 pazienti ricoverati per COVID-19 ai quali viene applicato uno schema classificativo della sepsi di origine batterica – validato dagli stessi autori - per assegnarli a tre categorie : « inflammopatica » (gravi, risposta infiammatoria prevalente), « adattativa » (meno gravi, risposta immunitaria adattativa prevalente) e « coagulopatica » (gravi,	Objectives: Complex critical syndromes like sepsis and coronavirus disease 2019 may be composed of underling “endotypes,” which may respond differently to treatment. The aim of this study was to test whether a previously defined bacterial sepsis endotypes classifier recapitulates the same clinical and immunological endotypes in coronavirus disease 2019. Design: Prospective single-center observational cohort study. Setting: Patients were enrolled in Athens, Greece, and blood was shipped to Inflammatix (Burlingame, CA) for analysis. Patients: Adult patients within 24 hours of hospital admission with coronavirus disease 2019 confirmed by polymerase chain reaction and chest radiography.

		coagulazione sregolata). Le tre categorie si applicano anche alla sepsi di origine virale, che sembra caratterizzare l'infezione da SARS-CoV-2.	Interventions: None. Measurements and Main results: We studied 97 patients with coronavirus disease 2019, of which 50 went on to severe respiratory failure (SRF) and 16 died. We applied a previously defined 33-messenger RNA classifier to assign endotype (Inflammopathic, Adaptive, or Coagulopathic) to each patient. We tested endotype status against other clinical parameters including laboratory values, severity scores, and outcomes. Patients were assigned as Inflammopathic (29%), Adaptive (44%), or Coagulopathic (27%), similar to our prior study in bacterial sepsis. Adaptive patients had lower rates of SRF and no deaths. Coagulopathic and Inflammopathic endotypes had 42% and 18% mortality rates, respectively. The Coagulopathic group showed highest D-dimers, and the Inflammopathic group showed highest C-reactive protein and interleukin-6 levels. Conclusions: Our predefined 33-messenger RNA endotypes classifier recapitulated immune phenotypes in viral sepsis (coronavirus disease 2019) despite its prior training and validation only in bacterial sepsis. Further work should focus on continued validation of the endotypes and their interaction with immunomodulatory therapy.

			 **Figure 2. A**, Relationship between endotypes, D-dimers, and interleukin (IL)-6. **B**, IL-6 as a function of Inflammopathic probabilities. The linear regression shows R-squared = 0.08, $p < 0.01$. **C**, D-dimer as a function of Coagulopathic endotype probabilities. The linear regression shows R-squared = 0.07; $p < 0.01$.
Verweij PE et al The Lancet https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30591-0/fulltext	Fungal infections should be part of the core outcome set for COVID-19	Gli outcome dell'infezione da SARS-CoV-2 stabiliti dal WHO per uniformare la letteratura dovrebbero includere, secondo gli autori di questo articolo, anche le sovrainfezione fungine : in particolare, l'aspergillosi polmonare associata a COVID-19 (CAPA) è un evento di frequenza rilevante nei ricoverati in terapia intensiva.	In response to the needs of the rapidly evolving COVID-19 outbreak, the Clinical Characterisation and Management Working Group of the WHO Research and Development Blueprint programme, the International Forum for Acute Care Trialists, and the International Severe Acute Respiratory and Emerging Infections Consortium published a minimum set of common outcome measures for studies of COVID-19. A core outcome set is crucial in the setting of an evolving research response to the COVID-19 pandemic and will greatly facilitate pooling of data across cohort studies and clinical trials.1 The proposed minimal outcome set involves a broad range of parameters, including organ dysfunction, biochemical parameters, radiological findings, secondary infections, duration of intervention, quality of life, pregnancy outcomes, and resource use.1 It is surprising that only bacterial and viral secondary infections are considered in the proposed set, without mention of fungal coinfections. There are indications that the frequency of bacterial coinfections in patients with COVID-19 might be low, whereas up to 30% of patients admitted to the intensive care unit (ICU) were reported to develop invasive pulmonary aspergillosis.

Wanberg A et al Science https://science.sciencemag.org/content/370/6521/1227	Robust neutralizing antibodies to SARS-CoV-2 infection persist for months	Studio della sierologia contro SARS-CoV-2 di 30.082 persone con infezione lieve-moderata : la maggioranza degli individui sviluppa IgG e le mantiene per un periodo di circa 5 mesi.	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused a global pandemic with millions infected and more than 1 million fatalities. Questions regarding the robustness, functionality, and longevity of the antibody response to the virus remain unanswered. Here, on the basis of a dataset of 30,082 individuals screened at Mount Sinai Health System in New York City, we report that the vast majority of infected individuals with mild-to-moderate COVID-19 experience robust immunoglobulin G antibody responses against the viral spike protein. We also show that titers are relatively stable for at least a period of about 5 months and that anti-spike binding titers significantly correlate with neutralization of authentic SARS-CoV-2. Our data suggest that more than 90% of seroconverters make detectable neutralizing antibody responses. These titers remain relatively stable for several months after infection.  **Fig. 1. SARS-CoV-2 spike antibody titers in 30,082 individuals.** (**A**) The percentage of individuals with antibody titers of 1:80 (low), 1:160 (low), 1:320 (moderate), 1:960 (high), and ≥1:2880 (high). (**B**) Absolute numbers of individuals testing positive and percent of individuals with titers of 1:320 over time. Testing of each sample was performed once in a Clinical Laboratory Improvement Amendments (CLIA)–certified laboratory using an assay that received emergency use authorization (EUA) from the U.S. Food and Drug Administration (FDA).
Katsouras C et al European Journal of Neurology	Greater decline of acute stroke admissions compared with acute coronary syndromes during COVID-19 outbreak in Greece: Cerebro/Cardiovascular	Calo degli accessi ospedalieri per ictus e, in minor misura, per sindrome coronarica acuta durante la pandemia da COVID-19 in	BACKGROUND: A remarkable decline in admissions for acute stroke and acute coronary syndrome (ACS) has been reported in countries severely hit by the COVID-19 pandemic. However, limited data are available from countries with less COVID-19 burden focusing on concurrent stroke and ACS hospitalisation rates from the same population. METHODS: The study was conducted in three

https://doi.org/10.1111/ene.14666	implications amidst a second wave surge.	Grecia rispetto all'anno precedente.	geographically and demographically representative COVID-19 referral university hospitals in Greece. We recorded the rate of stroke and ACS hospital admissions during a 6-week period of the COVID-19 outbreak in 2020 and compared them with the rates of the corresponding period in 2019. RESULTS: We found a greater relative reduction of stroke admissions (51% [35 vs 71]; incidence rate ratio [IRR]: 0.49, p=0.001) compared with ACS admissions (27% [123 vs 168]; IRR: 0.73, p=0.009) during the COVID-19 outbreak (p=0.097). Fewer older (>65 years) patients (Stroke: 34.3 vs 45.1%, OR: 0.64, p=0.291; ACS: 39.8 vs 54.2%, OR: 0.56, p=0.016) were admitted during the COVID-19 compared with the control period. CONCLUSIONS: Hospitalisation rates both for stroke and ACS were reduced during the COVID-19 outbreak in a country with strict social distancing measures, low COVID-19 incidence and low population mortality. Lack of triggers for stroke and ACS during social distancing/quarantining may explain these observations. However, medical care avoidance attitudes among cerbro/cardiovascular patients should be dissipated amidst the rising second COVID-19 wave.
Amendola A et al Emerging Infectious Diseases https://wwwnc.cdc.gov/eid/article/27/2/20-4632_article	Evidence of SARS-CoV-2 RNA in an Oropharyngeal Swab Specimen, Milan, Italy, Early December 2019	Presenza di RNA di SARS-CoV-2 nel tampone nasofaringeo di un bambino testato per sospetto morbillo (negativo) a Milano in dicembre 2019, prima che la diffusione di COVID-19 fosse nota in Italia.	We identified severe acute respiratory syndrome coronavirus 2 RNA in an oropharyngeal swab specimen collected from a child with suspected measles in early December 2019, ≈3 months before the first identified coronavirus disease case in Italy. This finding expands our knowledge on timing and mapping of novel coronavirus transmission pathways.

Stowe J t al JAMA https://jamanetwork.com/journals/jama/fullarticle/2774088	Stillbirths During the COVID-19 Pandemic in England, April-June 2020	Incidenza di aborti spontanei oltre la 24 settimana nel periodo aprile-giugno 2020 in Inghilterra : nessuna differenza rispetto all'anno precedente.	Pregnant women have an increased risk of infectious diseases, including respiratory infections such as influenza, and are included on the coronavirus disease 2019 (COVID-19) UK clinically vulnerable list. Little is known about the risk of COVID-19 to unborn children, with data limited to a case series of 3 stillbirth deliveries in pregnant women with confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and a single London hospital reporting a higher rate of stillbirth deliveries during the pandemic period compared with a prepandemic period. To provide more robust data, we used national and regional hospitalization data in England to assess the risk of stillbirths during the COVID-19 pandemic.
The Centers fo Disease Control and Prevention https://www.cdc.gov/vaccines/covid-19/hcp/mrna-vaccine-basics.html	Understanding and Explaining mRNA COVID-19 Vaccines	Materiale informativo dei CDC per comprendere e spiegare ai pazienti il funzionamento dei vaccini a RNA messaggero.	Within the next month, messenger RNA vaccines—also called mRNA vaccines—are likely to be some of the first COVID-19 vaccines authorized for use in the United States. This page provides vaccine information for healthcare professionals and vaccine providers and tips for explaining mRNA vaccines to patients and answering questions about how mRNA vaccines work, their safety profile, and common misconceptions.  Key Points to Share with Your Patients In addition to the following key messages, you can refer your patients with questions to CDC's COVID-19 mRNA vaccine webpage. • Like all vaccines, COVID-19 mRNA vaccines have been rigorously tested for safety before being authorized for use in the United States. • mRNA technology is new, but not unknown. They have been studied for more than a decade. • mRNA vaccines do not contain a live virus and do not carry a risk of causing disease in the vaccinated person. • mRNA from the vaccine never enters the nucleus of the cell and does not affect or interact with a person's DNA.

Pardi N et al Nature https://www.nature.com/articles/nrd.2017.243	mRNA vaccines — a new era in vaccinology	Revisione risalente al 2018 che illustra le caratteristiche dei vaccini a RNA messaggero.	mRNA vaccines represent a promising alternative to conventional vaccine approaches because of their high potency, capacity for rapid development and potential for low-cost manufacture and safe administration. However, their application has until recently been restricted by the instability and inefficient in vivo delivery of mRNA. Recent technological advances have now largely overcome these issues, and multiple mRNA vaccine platforms against infectious diseases and several types of cancer have demonstrated encouraging results in both animal models and humans. This Review provides a detailed overview of mRNA vaccines and considers future directions and challenges in advancing this promising vaccine platform to widespread therapeutic use.

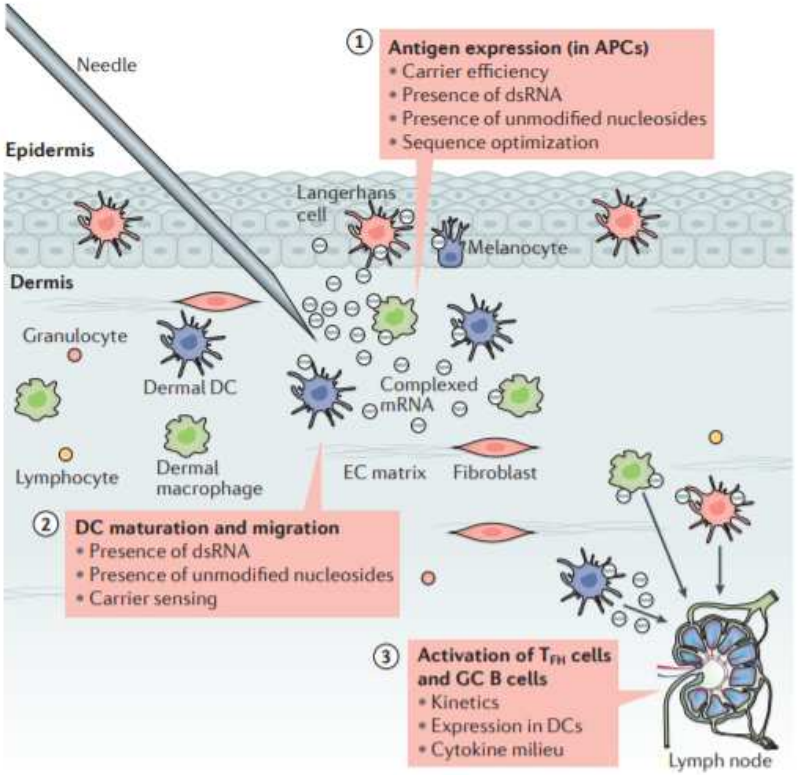
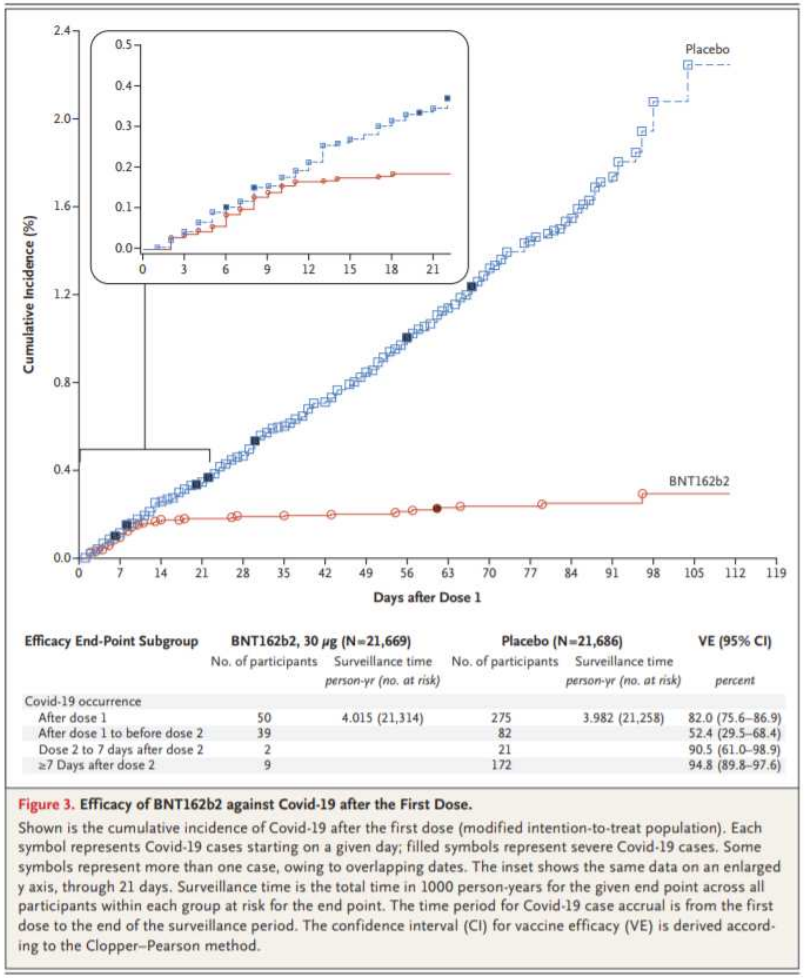
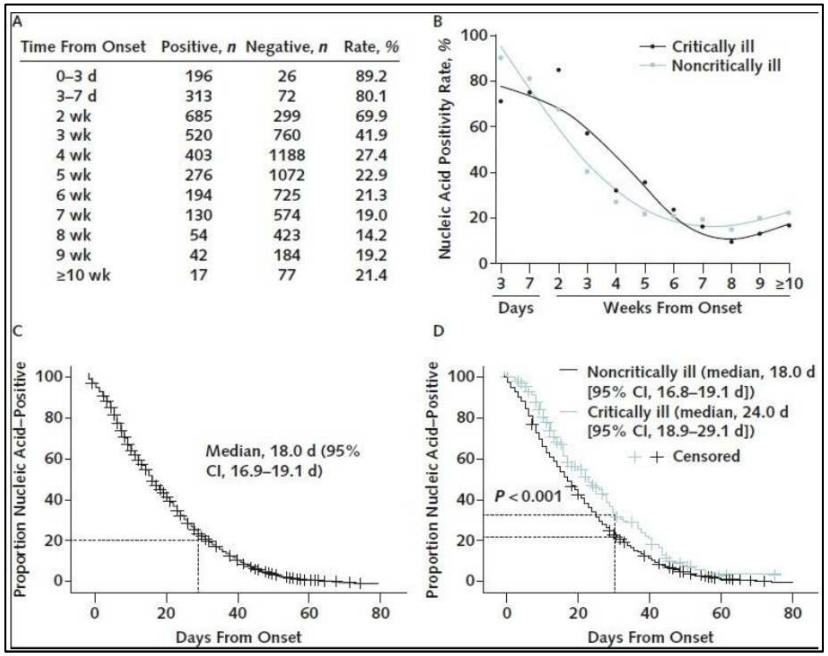


Figure 3 | **Considerations for effectiveness of a directly injected mRNA vaccine.** For an injected mRNA vaccine, major considerations for effectiveness include the following: the level of antigen expression in professional antigen-presenting cells (APCs), which is influenced by the efficiency of the carrier, by the presence of pathogen-associated molecular patterns (PAMPs) in the form of double-stranded RNA (dsRNA) or unmodified nucleosides and by the level of optimization of the RNA sequence (codon usage, G:C content, 5′ and 3′ untranslated regions (UTRs) and so on); dendritic cell (DC) maturation and migration to secondary lymphoid tissue, which is increased by PAMPs; and the ability of the vaccine to activate robust T follicular helper (T_{FH}) cell and germinal centre (GC) B cell responses — an area that remains poorly understood. An intradermal injection is shown as an example. EC, extracellular.

Polack FP et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2034577?query=featured_home	Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine	Risultati ad interim di un trial tuttora in corso su efficacia e sicurezza del vaccino a RNA messaggero BNT162b2 (Pfizer e BioNTech) contro SARS-CoV-2: dopo due dosi e a due mesi dall'inizio dello studio, si osserva efficacia 95% nel prevenire l'infezione e bassa incidenza di effetti avversi gravi.	BACKGROUND : Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and the resulting coronavirus disease 2019 (Covid-19) have afflicted tens of millions of people in a worldwide pandemic. Safe and effective vaccines are needed urgently. METHODS : In an ongoing multinational, placebo-controlled, observer-blinded, pivotal efficacy trial, we randomly assigned persons 16 years of age or older in a 1:1 ratio to receive two doses, 21 days apart, of either placebo or the BNT162b2 vaccine candidate (30 µg per dose). BNT162b2 is a lipid nanoparticle–formulated, nucleoside-modified RNA vaccine that encodes a prefusion stabilized, membrane-anchored SARS-CoV-2 full-length spike protein. The primary end points were efficacy of the vaccine against laboratory-confirmed Covid-19 and safety. RESULTS : A total of 43,548 participants underwent randomization, of whom 43,448 received injections: 21,720 with BNT162b2 and 21,728 with placebo. There were 8 cases of Covid-19 with onset at least 7 days after the second dose among participants assigned to receive BNT162b2 and 162 cases among those assigned to placebo; BNT162b2 was 95% effective in preventing Covid-19 (95% credible interval, 90.3 to 97.6). Similar vaccine efficacy (generally 90 to 100%) was observed across subgroups defined by age, sex, race, ethnicity, baseline body-mass index, and the presence of coexisting conditions. Among 10 cases of severe Covid-19 with onset after the first dose, 9 occurred in placebo recipients and 1 in a BNT162b2 recipient. The safety profile of BNT162b2 was characterized by short-term, mild-to-moderate pain at the injection site, fatigue, and headache. The incidence of serious adverse events was low and was similar in the vaccine and placebo groups. CONCLUSIONS : A two-dose regimen of BNT162b2 conferred 95% protection against Covid-19 in persons 16 years of age or older.

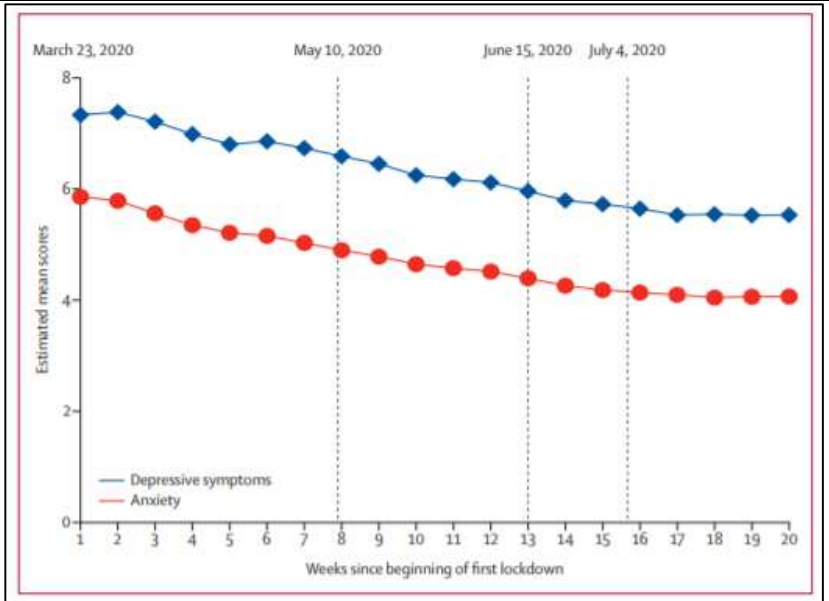
			Safety over a median of 2 months was similar to that of other viral vaccines.  **Efficacy End-Point Subgroup** — **BNT162b2, 30 μg (N=21,669)**: No. of participants; Surveillance time *person-yr (no. at risk)* — **Placebo (N=21,686)**: No. of participants; Surveillance time *person-yr (no. at risk)* — **VE (95% CI)** *percent* Covid-19 occurrence After dose 1: 50; 4.015 (21,314); 275; 3.982 (21,258); 82.0 (75.6–86.9) After dose 1 to before dose 2: 39; 82; 52.4 (29.5–68.4) Dose 2 to 7 days after dose 2: 2; 21; 90.5 (61.0–98.9) ≥7 Days after dose 2: 9; 172; 94.8 (89.8–97.6) **Figure 3. Efficacy of BNT162b2 against Covid-19 after the First Dose.** Shown is the cumulative incidence of Covid-19 after the first dose (modified intention-to-treat population). Each symbol represents Covid-19 cases starting on a given day; filled symbols represent severe Covid-19 cases. Some symbols represent more than one case, owing to overlapping dates. The inset shows the same data on an enlarged y axis, through 21 days. Surveillance time is the total time in 1000 person-years for the given end point across all participants within each group at risk for the end point. The time period for Covid-19 case accrual is from the first dose to the end of the surveillance period. The confidence interval (CI) for vaccine efficacy (VE) is derived according to the Clopper–Pearson method.
Lombardi F et al Clinical Microbiology and Infection	No evidence of SARS-CoV-2 circulation in HIV-infected patients between December	Sieroprevalenza (positività di IgG tramite due differenti saggi commerciali ELISA) di SARS-CoV-2 su 451 persone	In this monocentric cross-sectional study we evaluated the IgG seroprevalence of SARS-CoV-2 infection in HIV-infected outpatients who frequented our university hospital “Fondazione Policlinico

https://pubmed.ncbi.nlm.nih.gov/33278571/	2019 and February 2020 in Rome, Italy	HIV-positive afferenti al Policlinico Gemelli di Roma : 0% in marzo 2020.	Universitario A. Gemelli IRCCS", in Rome between December 1st 49 , 2019 and February 29th 50 , 2020.
Yu F et al Annals of Internal Medicine https://www.acpjournals.org/doi/10.7326/M20-3337	Dynamics and Correlation Among Viral Positivity, Seroconversion, and Disease Severity in COVID-19	Studio retrospettivo su 2142 pazienti con storia di COVID-19 a Wuhan, Cina : picco di positività del tampone molecolare a 3 giorni dall'esordio dei sintomi, picco di sieroconversione a 5 settimane, maggiore durata dello shedding virale nei pazienti con infezione critica.	Background: The understanding of viral positivity and seroconversion during the course of coronavirus disease 2019 (COVID-19) is limited. Objective: To describe patterns of viral polymerase chain reaction (PCR) positivity and evaluate their correlations with seroconversion and disease severity. Design: Retrospective cohort study. Setting: 3 designated specialty care centers for COVID-19 in Wuhan, China. Participants: 3192 adult patients with COVID-19. Measurements: Demographic, clinical, and laboratory data. Results: Among 12 780 reverse transcriptase PCR tests for severe acute respiratory syndrome coronavirus 2 that were done, 24.0% had positive results. In 2142 patients with laboratory-confirmed COVID-19, the viral positivity rate peaked within the first 3 days. The median duration of viral positivity was 24.0 days (95% CI, 18.9 to 29.1 days) in critically ill patients and 18.0 days (CI, 16.8 to 19.1 days) in noncritically ill patients. Being critically ill was an independent risk factor for longer viral positivity (hazard ratio, 0.700 [CI, 0.595 to 0.824]; P < 0.001). In patients with laboratory-confirmed COVID-19, the IgM-positive rate was 19.3% in the first week, peaked in the fifth week (81.5%), and then decreased steadily to around 55% within 9 to 10 weeks. The IgG-positive rate was 44.6% in the first week, reached 93.3% in the fourth week, and then remained high. Similar antibody responses were seen in clinically diagnosed cases. Serum inflammatory markers remained higher in

			critically ill patients. Among noncritically ill patients, a higher proportion of those with persistent viral positivity had low IgM titers (<100 AU/mL) during the entire course compared with those with short viral positivity. Limitation: Retrospective study and irregular viral and serology testing. Conclusion: The rate of viral PCR positivity peaked within the initial few days. Seroconversion rates peaked within 4 to 5 weeks. Dynamic laboratory index changes corresponded well to clinical signs, the recovery process, and disease severity. Low IgM titers (<100 AU/mL) are an independent risk factor for persistent viral positivity.  A Time From Onset / Positive, *n* / Negative, *n* / Rate, % 0–3 d / 196 / 26 / 89.2 3–7 d / 313 / 72 / 80.1 2 wk / 685 / 299 / 69.9 3 wk / 520 / 760 / 41.9 4 wk / 403 / 1188 / 27.4 5 wk / 276 / 1072 / 22.9 6 wk / 194 / 725 / 21.3 7 wk / 130 / 574 / 19.0 8 wk / 54 / 423 / 14.2 9 wk / 42 / 184 / 19.2 ≥10 wk / 17 / 77 / 21.4

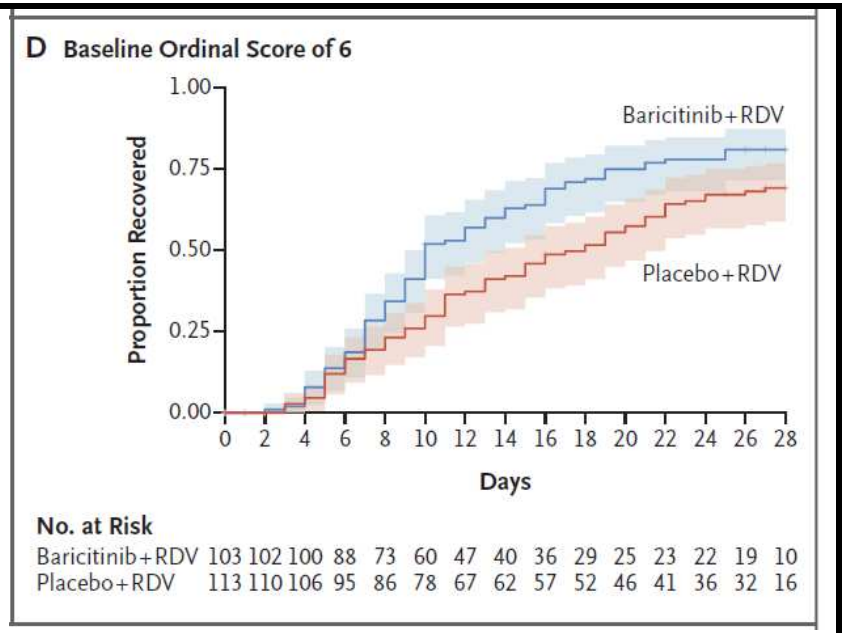
FDA Briefing Document https://www.fda.gov/media/144245/download	Vaccines and Related Biological Products Advisory Committee Meeting December 10, 2020	Documento che contiene i dettagli della sperimentazione del vaccino a mRNA BNT162b2 (Pfizer e BioNTech) contro SARS-CoV-2, attualmente al vaglio della FDA americana.	On November 20, 2020, Pfizer and BioNTech (the Sponsor) submitted an Emergency Use Authorization (EUA) request to FDA for an investigational COVID-19 vaccine (BNT162b2) intended to prevent COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The vaccine is based on the SARS-CoV-2 spike glycoprotein (S) antigen encoded by RNA and formulated in lipid nanoparticles (LNPs). The proposed use under an EUA is "for active immunization for the prevention of COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older." The proposed dosing regimen is 2 doses, 30 µg each, administered 21 days apart.
Fancourt D et al The Lancet https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(20)30482-X/fulltext	Trajectories of anxiety and depressive symptoms during enforced isolation due to COVID-19 in England: a longitudinal observational study	Studio osservazionale su 36520 adulti in Inghilterra che riporta l'andamento dei sintomi di ansia e depressione, tramite scale di valutazione, durante le 20 settimane successive all'inizio del « lockdown » : ad elevati livelli iniziali è seguita una riduzione per entrambe le patologie, come per adattamento alle nuove circostanze. In evidenza anche i fattori associati a maggiori sintomi di ansia e depressione.	Background : There is major concern about the impact of the global COVID-19 outbreak on mental health. Several studies suggest that mental health deteriorated in many countries before and during enforced isolation (ie, lockdown), but it remains unknown how mental health has changed week by week over the course of the COVID-19 pandemic. This study aimed to explore the trajectories of anxiety and depression over the 20 weeks after lockdown was announced in England, and compare the growth trajectories by individual characteristics. Methods : In this prospective longitudinal observational study, we analysed data from the UCL COVID-19 Social Study, a panel study weighted to population proportions, which collects information on anxiety (using the Generalised Anxiety Disorder assessment) and depressive symptoms (using the Patient Health Questionnaire) weekly in the UK since March 21, 2020. We included data from adults living in England who had at least three repeated measures between March 23 and Aug 9, 2020. Analyses were done using latent growth models, which were fitted to account for sociodemographic and health covariates.

			Findings : Between March 23, and Aug 9, data from over 70 000 adults were collected in the UCL COVID-19 Social Study. When including participants living in England with three follow-up measures and no missing values, our analytic sample consisted of 36 520 participants. The average depression score was 6·6 (SD=6·0, range 0–27) and the average anxiety score 5·7 (SD=5·6, range 0–21) in week 1. Anxiety and depression levels both declined across the first 20 weeks following the introduction of lockdown in England (b=–1·93, SE=0·26, p<0·0001 for anxiety; b=–2·52, SE=0·28, p<0·0001 for depressive symptoms). The fastest decreases were seen across the strict lockdown period (between weeks 2 and 5), with symptoms plateauing as further lockdown easing measures were introduced (between weeks 16 and 20). Being a woman or younger, having lower educational attainment, lower income, or pre-existing mental health conditions, and living alone or with children were all risk factors for higher levels of anxiety and depression at the start of lockdown. Many of these inequalities in experiences were reduced as lockdown continued, but differences were still evident 20 weeks after the start of lockdown. Interpretation : These data suggest that the highest levels of depression and anxiety occurred in the early stages of lockdown but declined fairly rapidly, possibly because individuals adapted to circumstances. Our findings emphasise the importance of supporting individuals in the lead-up to future lockdowns to try to reduce distress, and highlight that groups already at risk for poor mental health before the pandemic have remained at risk throughout lockdown and its aftermath.

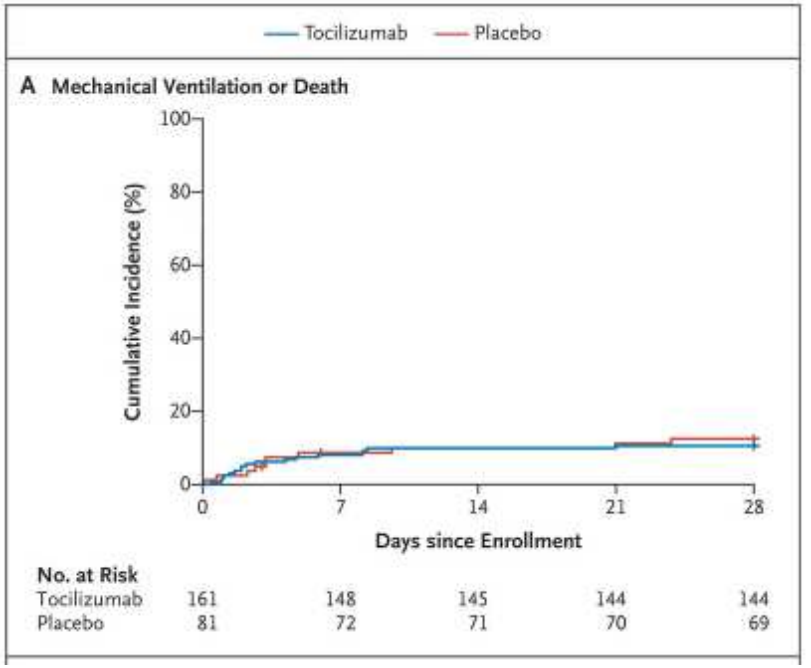
			 ***Figure 1:*** **Predicted growth trajectories of estimated mean anxiety and depressive symptom scores** Scores on anxiety were measured using the Generalised Anxiety Disorder assessment (range of scores: 0–21) and scores on depressive symptoms were measured using the Patient Health Questionnaire (range of scores: 0–27). On March 23, the first lockdown commenced in England. On May 10, it was announced that strict lowdown was being eased. On June 15, non-essential retail was reopened. On July 4, further public amenities were reopened.
Baylis F et al The Lancet https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30918-X/fulltext	A public health ethic should inform policies on COVID-19 immunity passports	La proposta di introdurre un « passaporto immunitario » per SARS-CoV-2 sulla base del quale consentire maggiore libertà di movimento agli immuni è stata avanzata su molti fronti. Secondo gli Autori di questa lettera, si tratta di una soluzione potenzialmente dannosa per la comunità.	In their Personal View, Rebecca Brown and colleagues1 argue for the implementation of so-called COVID-19 immunity passports to allow individuals presumed immune to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to move through society under reduced social distancing and other restrictions. Brown and colleagues contend that constraining these individuals' freedom of movement is a serious breach of personal liberty. We vehemently reject the political philosophy of liberal individualism that undergirds this argument and thus the conclusion in support of immunity passports.

Blasi C Infection Control & Hospital Epidemiology https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/iodine-mouthwashes-as-deterrents-against-severe-acute-respiratory-syndrome-coronavirus-2-sarscov2/E4E0EC39491A7284F40B01F0E77F2EA4	IODINE MOUTHWASHES AS DETERRENTS AGAINST SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 (SARS-CoV-2)	Disinfettanti orali a base di iodio come misura preventiva dell'infezione da SARS-CoV-2.	It is known that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) enters the body via the eyes, nose and mouth and infects the upper respiratory tract causing the initial clinical symptoms. After the exposure, a period of incubation mainly at the level of the oropharynx, lasts from 5 to 6 days allowing the replication of organisms to reach the number of particles that can spread to the rest of the body, giving rise to symptomatic disease, organ damage, and death. As this incubation phase and progress of disease is dependent on the rate of replication and viral levels, a possible means to curb the proliferation of the virus after its entry into the upper respiratory tract is rinsing and gargling with iodine mouthwashes. A number of in vitro studies support this possibility.
Kalil AC et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2031994	Baricitinib plus Remdesivir for Hospitalized Adults with Covid-19	Trial clinico randomizzato, in doppio cieco, controllato con placebo, che valuta il trattamento con remdesivir e baricitinib contro remdesivir e placebo in pazienti affetti da COVID-19 : il maggior vantaggio in termini di tempo di guarigione e tempo al miglioramento clinico si dimostra nel gruppo dei pazienti più gravi dal punto di vista respiratorio.	BACKGROUND : Severe coronavirus disease 2019 (Covid-19) is associated with dysregulated inflammation. The effects of combination treatment with baricitinib, a Janus kinase inhibitor, plus remdesivir are not known. METHODS : We conducted a double-blind, randomized, placebo-controlled trial evaluating baricitinib plus remdesivir in hospitalized adults with Covid-19. All the patients received remdesivir (≤10 days) and either baricitinib (≤14 days) or placebo (control). The primary outcome was the time to recovery. The key secondary outcome was clinical status at day 15. RESULTS : A total of 1033 patients underwent randomization (with 515 assigned to combination treatment and 518 to control). Patients receiving baricitinib had a median time to recovery of 7 days (95% confidence interval [CI], 6 to 8), as compared with

			8 days (95% CI, 7 to 9) with control (rate ratio for recovery, 1.16; 95% CI, 1.01 to 1.32; P = 0.03), and a 30% higher odds of Improvement in clinical status at day 15 (odds ratio, 1.3; 95% CI, 1.0 to 1.6). Patients receiving high-flow oxygen or noninvasive ventilation at enrollment had a time to recovery of 10 days with combination treatment and 18 days with control (rate ratio for recovery, 1.51; 95% CI, 1.10 to 2.08). The 28-day mortality was 5.1% in the combination group and 7.8% in the control group (hazard ratio for death, 0.65; 95% CI, 0.39 to 1.09). Serious adverse events were less frequent in the combination group than in the control group (16.0% vs. 21.0%; difference, −5.0 percentage points; 95% CI, −9.8 to −0.3; P = 0.03), as were new infections (5.9% vs. 11.2%; difference, −5.3 percentage points; 95% CI, −8.7 to −1.9; P = 0.003). CONCLUSIONS : Baricitinib plus remdesivir was superior to remdesivir alone in reducing recovery time and accelerating improvement in clinical status among patients with Covid-19, notably among those receiving high-flow oxygen or noninvasive ventilation. The combination was associated with fewer serious adverse events. (Funded by the National Institute of Allergy and Infectious Diseases; ClinicalTrials.gov number, NCT04401579.)

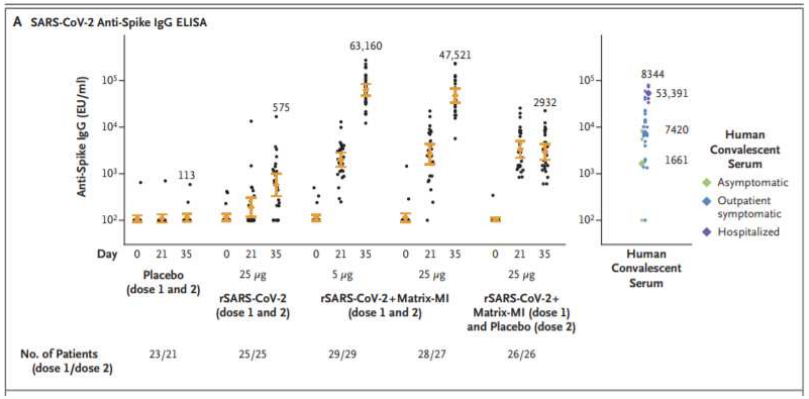
			
Stone JH et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2028836?query=featured_home	Efficacy of Tocilizumab in Patients Hospitalized with Covid-19	Trial clinico randomizzato, in doppio cieco, controllato con placebo che valuta l'efficacia della terapia con tocilizumab 8 mg/Kg EV : non si riesce a dimostrare un beneficio quanto a ricorso alla ventilazione non invasiva, mortalità, peggioramento clinico e tempo alla sospensione dell'ossigenoterapia.	BACKGROUND : The efficacy of interleukin-6 receptor blockade in hospitalized patients with coronavirus disease 2019 (Covid-19) who are not receiving mechanical ventilation is unclear. METHODS : We performed a randomized, double-blind, placebo-controlled trial involving patients with confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, hyperinflammatory states, and at least two of the following signs: fever (body temperature >38°C), pulmonary infiltrates, or the need for supplemental oxygen in order to maintain an oxygen saturation greater than 92%. Patients were randomly assigned in a 2:1 ratio to receive standard care plus a single dose of either tocilizumab (8 mg per kilogram of body weight) or placebo. The primary outcome was intubation or death, assessed in a time-to-event analysis. The secondary efficacy outcomes were clinical worsening and discontinuation of supplemental oxygen among patients who had

			been receiving it at baseline, both assessed in time-to-event analyses. RESULTS : We enrolled 243 patients; 141 (58%) were men, and 102 (42%) were women. The median age was 59.8 years (range, 21.7 to 85.4), and 45% of the patients were Hispanic or Latino. The hazard ratio for intubation or death in the tocilizumab group as compared with the placebo group was 0.83 (95% confidence interval [CI], 0.38 to 1.81; P=0.64), and the hazard ratio for disease worsening was 1.11 (95% CI, 0.59 to 2.10; P=0.73). At 14 days, 18.0% of the patients in the tocilizumab group and 14.9% of the patients in the placebo group had had worsening of disease. The median time to discontinuation of supplemental oxygen was 5.0 days (95% CI, 3.8 to 7.6) in the tocilizumab group and 4.9 days (95% CI, 3.8 to 7.8) in the placebo group (P=0.69). At 14 days, 24.6% of the patients in the tocilizumab group and 21.2% of the patients in the placebo group were still receiving supplemental oxygen. Patients who received tocilizumab had fewer serious infections than patients who received placebo. CONCLUSIONS : Tocilizumab was not effective for preventing intubation or death in moderately ill hospitalized patients with Covid-19. Some benefit or harm cannot be ruled out, however, because the confidence intervals for efficacy comparisons were wide.

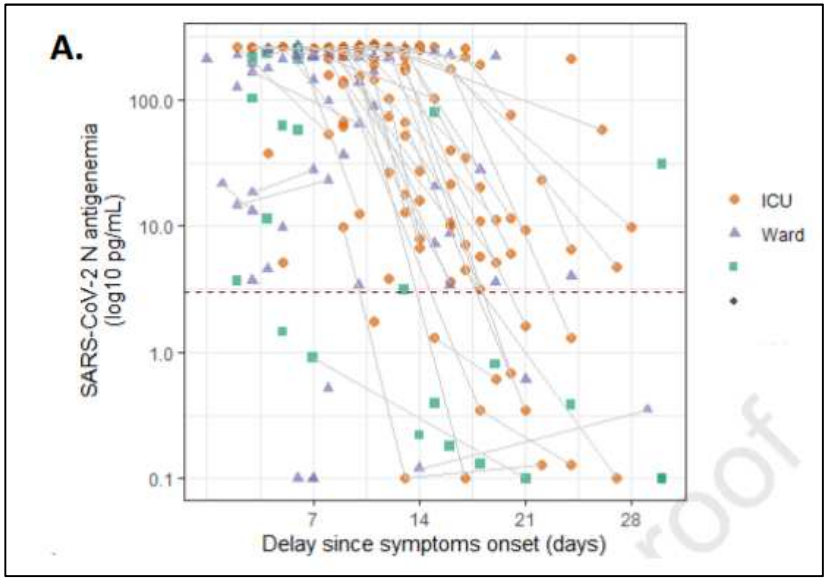
			
Cattelan AM et al BMC Infectious Diseases https://doi.org/10.1186/s12879-020-05647-7	Clinical characteristics and laboratory biomarkers changes in COVID-19 patients requiring or not intensive or sub-intensive care: a comparative study.	Fattori associati al trasferimento in terapia intensiva/subintensiva in 303 pazienti ricoverati per COVID-19.	BACKGROUND: Identifying risk factors for severe novel-coronavirus disease (COVID-19) is useful to ascertain which patients may benefit from advanced supportive care. The study offers a description of COVID-19 patients, admitted to a general ward for a non-critical clinical picture, with the aim to analyse the differences between those transferred to the intensive (ICU) and/or sub-intensive care (SICU) units and those who were not. METHODS: This observational retrospective study includes all COVID-19 patients admitted to the Infectious Diseases Unit. Clinical, laboratory, radiological and treatment data were collected. The primary outcome was a composite of need of transfer to the ICU and/or SICU during the hospitalization. Patients who did not require to be transferred are defined as Group 1; patients who were transferred to the ICU and/or SICU are defined as Group 2. Demographic, clinical

			characteristics and laboratory findings at the 1st, 3rd and last measurements were compared between the two groups. RESULTS: 303 were included. The median age was 62 years. 69 patients (22.8%) met the primary outcome and were defined as Group 2. The overall fatality rate was 6.8%. Group 2 patients were predominantly male (76.8% vs. 55.1%, p < 0.01), had a higher fatality rate (14.5% vs. 3.8%, p < 0,01), had more hypertension (72.4% vs. 44%, p < 0,01) and diabetes (31.9% vs. 21%, p = 0.04) and were more likely to present dry cough (49.3% vs. 25.2%, p < 0.01). Overall, chest X-ray at admission showed findings suggestive of pneumonia in 63.2%, and Group 2 were more likely to develop pathological findings during the hospitalization (72.7% vs. 17.2%, p = 0.01). At admission, Group 2 presented significantly higher neutrophil count, aspartate-transaminase and C-Reactive-Protein. At the 3rd measurement, Group 2 presented persistently higher neutrophil count, hepatic inflammation markers and C-Reactive-Protein. Group 1 presented a shorter duration from admission to negativization of follow-up swabs (20 vs. 35 days, p < 0.01). CONCLUSIONS: The presence of comorbidities and the persistent observation of abnormal laboratory findings should be regarded as predisposing factors for clinical worsening.
Kkeech C et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2026920?query=featured_home	Phase 1–2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine	Trial di fase 1-2 su sicurezza e immunogenicità di un vaccino ricombinante contro SARS-CoV-2 : a 35 giorni dalla vaccinazione, risposta anticorpale superiore ai controlli con storia di malattia naturale e nessun effetto avverso grave.	BACKGROUND : NVX-CoV2373 is a recombinant severe acute respiratory syndrome coronavirus 2 (rSARS-CoV-2) nanoparticle vaccine composed of trimeric full-length SARS-CoV-2 spike glycoproteins and Matrix-M1 adjuvant. METHODS : We initiated a randomized, placebo-controlled, phase 1–2 trial to evaluate the safety and immunogenicity of the rSARS-CoV-2 vaccine (in 5-µg and 25-µg doses, with or without Matrix-M1 adjuvant, and with observers unaware of trial-group assignments) in 131 healthy adults. In phase 1, vaccination comprised two

			intramuscular injections, 21 days apart. The primary outcomes were reactogenicity; laboratory values (serum chemistry and hematology), according to Food and Drug Administration toxicity scoring, to assess safety; and IgG anti–spike protein response (in enzyme-linked immunosorbent assay [ELISA] units). Secondary outcomes included unsolicited adverse events, wild-type virus neutralization (microneutralization assay), and T-cell responses (cytokine staining). IgG and microneutralization assay results were compared with 32 (IgG) and 29 (neutralization) convalescent serum samples from patients with Covid-19, most of whom were symptomatic. We performed a primary analysis at day 35. RESULTS : After randomization, 83 participants were assigned to receive the vaccine with adjuvant and 25 without adjuvant, and 23 participants were assigned to receive placebo. No serious adverse events were noted. Reactogenicity was absent or mild in the majority of participants, more common with adjuvant, and of short duration (mean, ≤2 days). One participant had mild fever that lasted 1 day. Unsolicited adverse events were mild in most participants; there were no severe adverse events. The addition of adjuvant resulted in enhanced immune responses, was antigen dose–sparing, and induced a T helper 1 (Th1) response. The two-dose 5-µg adjuvanted regimen induced geometric mean anti-spike IgG (63,160 ELISA units) and neutralization (3906) responses that exceeded geometric mean responses in convalescent serum from mostly symptomatic Covid-19 patients (8344 and 983, respectively). CONCLUSIONS : At 35 days, NVX-CoV2373 appeared to be safe, and it elicited immune responses that exceeded levels in Covid-19 convalescent serum. The Matrix-M1 adjuvant induced CD4+ T-cell responses that were biased toward a Th1 phenotype.

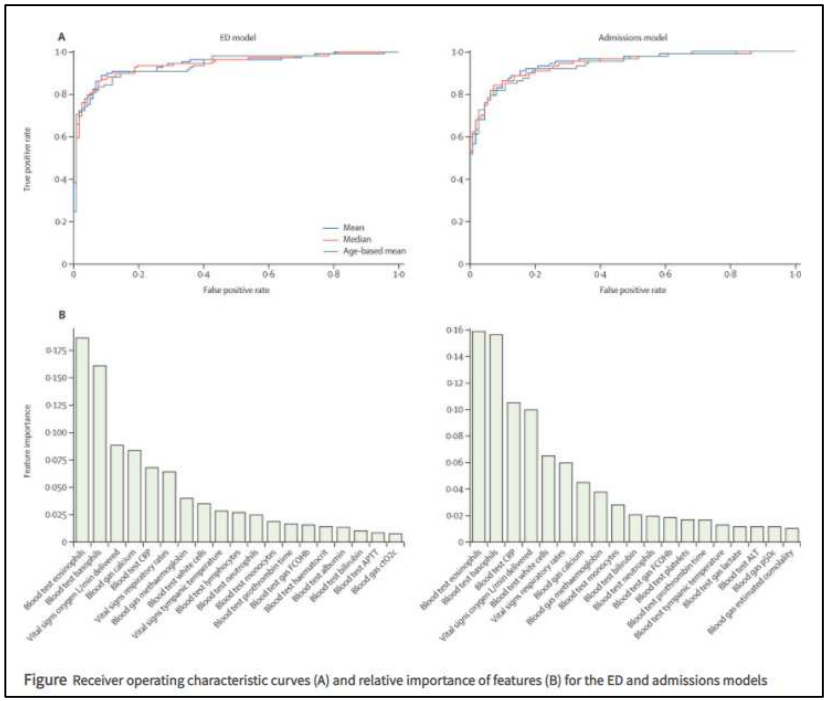
			
Meyerowitz E et al The Lancet https://doi.org/10.1016/S1473-3099(20)30837-9	Towards an accurate and systematic characterisation of persistently asymptomatic infection with SARS-CoV-2.	Suggerimenti per individuare correttamente e i soggetti persistentemente asintomatici con infezione da SARS-CoV-2, il cui ruolo appare rilevante nella trasmissione dell'infezione.	People with persistently asymptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection experience no symptoms throughout the course of infection, and pre-symptomatic individuals become infectious days before they report symptoms. Transmission of SARS-CoV-2 from individuals without symptoms contributes to pandemic spread, but the extent of transmission from persistently asymptomatic individuals remains unknown. We describe three methodological issues that hinder attempts to estimate this proportion. First, incomplete symptom assessment probably overestimates the asymptomatic fraction. Second, studies with inadequate follow-up misclassify pre-symptomatic individuals. Third, serological studies might identify people with previously unrecognised infection, but reliance on poorly defined antibody responses and retrospective symptom assessment might result in misclassification. We provide recommendations regarding definitions, detection, documentation, and follow-up to improve the identification and evaluation of people with persistently asymptomatic SARS-CoV-2 infection and their contacts. Accurate characterisation of the persistently asymptomatic fraction of

			infected individuals might shed light on COVID-19 pathogenesis and transmission dynamics, and inform public health responses.
Hingrat Q et al Clinical Microbiology and Infection https://doi.org/10.1016/j.cmi.2020.11.025	Detection of SARS-CoV-2 N-antigen in blood during acute COVID-19 provides a sensitive new marker and new testing alternatives.	Valutazione dell'efficacia di un test ELISA per antigene N di SARS-CoV-2 su siero o plasma da utilizzare per la diagnosi di infezione : specificità 98.4%, sensibilità 79.3%, che sale al 93% se si preleva il campione entro 14 giorni dall'esordio dei sintomi.	OBJECTIVES: Molecular assays on nasopharyngeal swabs remain the cornerstone of COVID-19 diagnostic. The high technicalities of nasopharyngeal sampling and molecular assays, as well as scarce resources of reagents, limit our testing capabilities. Several strategies failed, to date, to fully alleviate this testing process (e.g. saliva sampling or antigen testing on nasopharyngeal samples). We assessed the clinical performances of SARS-CoV-2 nucleocapsid antigen (N-antigen) ELISA detection in serum or plasma using the COVID-19 Quantigene(R) (AAZ, France) assay. METHODS: Performances were determined on 63 sera from 63 non-COVID patients and 227 serum samples (165 patients) from the French COVID and CoV-CONTACT cohorts with RT-PCR confirmed SARS-CoV-2 infection, including 142 serum (114 patients) obtained within 14 days after symptoms' onset. RESULTS: Specificity was 98.4% (95% confidence interval [CI], 95.3 to 100). Sensitivity was 79.3% overall (180/227, 95% CI, 74.0 to 84.6) and 93.0% (132/142, 95% CI, 88.7 to 97.2) within 14 days after symptoms onset. 91 included patients had a sera and nasopharyngeal swabs collected in the same 24 hours. Among those with high nasopharyngeal viral loads, i.e. Ct value below 30 and 33, only 1/50 and 4/67 tested negative for N-antigenemia, respectively. Among those with a negative nasopharyngeal RT-PCR, 8/12 presented positive N-antigenemia; the lower respiratory tract was explored for 6 of these 8 patients, showing positive RT-PCR in 5 cases. CONCLUSION: This is the first evaluation of a commercially available serum N-antigen detection assay. It presents a robust specificity and sensitivity within the first

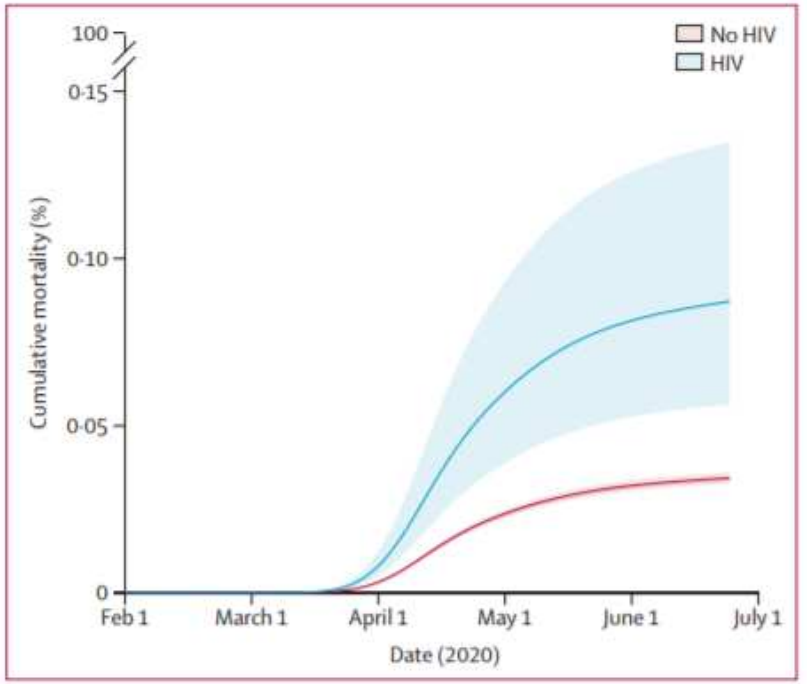
			14 days after symptoms onset. This approach provides a valuable new option for COVID-19 diagnosis, only requiring a blood draw and easily scalable in all clinical laboratories. 
Larosa E et al Euro Surveillance https://doi.org/10.2807/1560-7917.ES.2020.25.49.2001911	Secondary transmission of COVID-19 in preschool and school settings in northern Italy after their reopening in September 2020: a population-based study.	Incidenza di trasmissione di SARS-CoV-2 in 36 scuole (1248 individui e 1200 contatti, 38 casi secondari) della pronvincia di Reggio Emilia nel periodo 1 settembre-15 ottobre 2020 : tasso di attacco 3.2%, maggiore nella fascia d'età > 10 anni.	We report epidemiological investigations of transmission of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in 41 classes of 36 schools in Reggio Emilia province, northern Italy, from their reopening on 1 September to 15 October 2020. The overall secondary case attack rate was 3.2%, reaching 6.6% in middle and high schools. More timely isolation and testing of classmates could be effective in reducing virus transmission in this setting.

Soltan AAS et al The Lancet https://www.thelancet.com/journals/landig/article/PIIS2589-7500(20)30274-0/fulltext	Rapid triage for COVID-19 using routine clinical data for patients attending hospital: development and prospective validation of an artificial intelligence screening test	Studio di machine-learning in cui si insegna a un algoritmo a escludere i casi di COVID-19 fra gli accessi in pronto soccorso e fra i pazienti ricoverati, sulla base di dati clinici, emogasanalitici e degli esami ematici, raggiungendo un valore predittivo negativo di 99% e 98.5%.	Background : The early clinical course of COVID-19 can be difficult to distinguish from other illnesses driving presentation to hospital. However, viral-specific PCR testing has limited sensitivity and results can take up to 72 h for operational reasons. We aimed to develop and validate two early-detection models for COVID-19, screening for the disease among patients attending the emergency department and the subset being admitted to hospital, using routinely collected health-care data (laboratory tests, blood gas measurements, and vital signs). These data are typically available within the first hour of presentation to hospitals in high-income and middle-income countries, within the existing laboratory infrastructure. Methods : We trained linear and non-linear machine learning classifiers to distinguish patients with COVID-19 from pre-pandemic controls, using electronic health record data for patients presenting to the emergency department and admitted across a group of four teaching hospitals in Oxfordshire, UK (Oxford University Hospitals). Data extracted included presentation blood tests, blood gas testing, vital signs, and results of PCR testing for respiratory viruses. Adult patients (>18 years) presenting to hospital before Dec 1, 2019 (before the first COVID-19 outbreak), were included in the COVID-19-negative cohort; those presenting to hospital between Dec 1, 2019, and April 19, 2020, with PCR-confirmed severe acute respiratory syndrome coronavirus 2 infection were included in the COVID-19-positive cohort. Patients who were subsequently admitted to hospital were included in their respective COVID-19-negative or COVID-19-positive admissions cohorts. Models were calibrated to sensitivities of 70%, 80%, and 90% during training, and performance was initially assessed on a held-out test set generated by an 80:20 split stratified by patients with COVID-19 and balanced

			equally with pre-pandemic controls. To simulate real-world performance at different stages of an epidemic, we generated test sets with varying prevalences of COVID-19 and assessed predictive values for our models. We prospectively validated our 80% sensitivity models for all patients presenting or admitted to the Oxford University Hospitals between April 20 and May 6, 2020, comparing model predictions with PCR test results. Findings : We assessed 155 689 adult patients presenting to hospital between Dec 1, 2017, and April 19, 2020. 114 957 patients were included in the COVID-negative cohort and 437 in the COVID-positive cohort, for a full study population of 115 394 patients, with 72 310 admitted to hospital. With a sensitive configuration of 80%, our emergency department (ED) model achieved 77·4% sensitivity and 95·7% specificity (area under the receiver operating characteristic curve [AUROC] 0·939) for COVID-19 among all patients attending hospital, and the admissions model achieved 77·4% sensitivity and 94·8% specificity (AUROC 0·940) for the subset of patients admitted to hospital. Both models achieved high negative predictive values (NPV; >98·5%) across a range of prevalences (≤5%). We prospectively validated our models for all patients presenting and admitted to Oxford University Hospitals in a 2-week test period. The ED model (3326 patients) achieved 92·3% accuracy (NPV 97·6%, AUROC 0·881), and the admissions model (1715 patients) achieved 92·5% accuracy (97·7%, 0·871) in comparison with PCR results. Sensitivity analyses to account for uncertainty in negative PCR results improved apparent accuracy (ED model 95·1%, admissions model 94·1%) and NPV (ED model 99·0%, admissions model 98·5%). Interpretation : Our models performed effectively as a screening test for COVID-19, excluding the illness with high-confidence by use

			of clinical data routinely available within 1 h of presentation to hospital. Our approach is rapidly scalable, fitting within the existing laboratory testing infrastructure and standard of care of hospitals in high-income and middle-income countries.  Figure Receiver operating characteristic curves (A) and relative importance of features (B) for the ED and admissions models
Bhaskaran K et al The Lancet https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(20)30305-2/fulltext	HIV infection and COVID-19 death: a population-based cohort analysis of UK primary care data and linked national death registrations within the OpenSAFELY platform	Ampio studio di coorte retrospettivo volto a indagare l'associazione fra mortalità per COVID-19 e infezione da HIV : si dimostra un aumentato rischio (HR 2.59 dopo correzione per altri fattori di rischio), in particolare nelle persone di colore.	Background : Whether HIV infection is associated with risk of death due to COVID-19 is unclear. We aimed to investigate this association in a large-scale population-based study in England. Methods : We did a retrospective cohort study. Working on behalf of NHS England, we used the OpenSAFELY platform to analyse routinely collected electronic primary care data linked to national death registrations. We included all adults (aged ≥18 years) alive and in follow-up on Feb 1, 2020, and with at least 1 year of continuous registration with a general practitioner before this date.

			People with a primary care record for HIV infection were compared with people without HIV. The outcome was COVID-19 death, defined as the presence of International Classification of Diseases 10 codes U07.1 or U07.2 anywhere on the death certificate. Cox regression models were used to estimate the association between HIV infection and COVID-19 death; they were initially adjusted for age and sex, then we added adjustment for index of multiple deprivation and ethnicity, and then for a broad range of comorbidities. Interaction terms were added to assess effect modification by age, sex, ethnicity, comorbidities, and calendar time. Results : 17 282 905 adults were included, of whom 27 480 (0·16%) had HIV recorded. People living with HIV were more likely to be male, of Black ethnicity, and from a more deprived geographical area than the general population. 14 882 COVID-19 deaths occurred during the study period, with 25 among people with HIV. People living with HIV had higher risk of COVID-19 death than those without HIV after adjusting for age and sex: hazard ratio (HR) 2·90 (95% CI 1·96–4·30; p<0·0001). The association was attenuated, but risk remained high, after adjustment for deprivation, ethnicity, smoking and obesity: adjusted HR 2·59 (95% CI 1·74–3·84; p<0·0001). There was some evidence that the association was larger among people of Black ethnicity: HR 4·31 (95% CI 2·42–7·65) versus 1·84 (1·03–3·26) in non-Black individuals (p-interaction=0·044). Interpretation : People with HIV in the UK seem to be at increased risk of COVID-19 mortality. Targeted policies should be considered to address this raised risk as the pandemic response evolves.

			
Abramowicz M et al The Medical Letter on Drugs and Therapeutics - JAMA https://jamanetwork.com/journals/jama/fullarticle/2774326	An EUA for Bamlanivimab—A Monoclonal Antibody for COVID-19	Caratteristiche dei pazienti per cui è stata rilasciata dalla FDA una autorizzazione emergenziale all'uso dell'anticorpo monoclonale Bamlanivimab, bloccante della proteina S di SARS-CoV-2 : infezione lieve-moderata, esclusi i pazienti ricoverati e trattati con ossigenoterapia.	The investigational neutralizing IgG1 monoclonal antibody bamlanivimab (LY-CoV555; Lilly) has been granted an FDA Emergency Use Authorization (EUA) for treatment of recently diagnosed mild to moderate COVID-19 in patients who are ≥12 years old, weigh at least 40 kg, and are at high risk for progressing to severe disease and/or hospitalization (see Box).1

Sonnweber T et al European Respiratory Journal https://doi.org/10.1183/13993003.03481-2020	Cardiopulmonary recovery after COVID-19 - an observational prospective multi-center trial.	Studio osservazionale multicentrico che valuta il danno cardiopolmonare a 60 e 100 giorni dalla diagnosi di COVID-19 in 145 pazienti : il 63% ha ancora alterazioni alla TAC torace, ma senza segni radiologici di fibrosi ; il 21% presenza una riduzione della capacità di diffusione ; la persistenza di sintomi è molto frequente.	BACKGROUND: After the 2002/2003 SARS outbreak, 30% of survivors exhibited persisting structural pulmonary abnormalities. The long-term pulmonary sequelae of coronavirus disease 2019 (COVID-19) are yet unknown, and comprehensive clinical follow-up data are lacking. METHODS: In this prospective, multicentre, observational study, we systematically evaluated the cardiopulmonary damage in subjects recovering from COVID-19 at 60 and 100 days after confirmed diagnosis. We conducted a detailed questionnaire, clinical examination, laboratory testing, lung function analysis, echocardiography, and thoracic low-dose computed tomography (CT). RESULTS: Data from 145 COVID-19 patients were evaluated, and 41% of all subjects exhibited persistent symptoms 100 days after COVID-19 onset, with dyspnea being most frequent (36%). Accordingly, patients still displayed an impaired lung function, with a reduced diffusing capacity in 21% of the cohort being the most prominent finding. Cardiac impairment, including a reduced left ventricular function or signs of pulmonary hypertension, was only present in a minority of subjects. CT scans unveiled persisting lung pathologies in 63% of patients, mainly consisting of bilateral ground-glass opacities and/or reticulation in the lower lung lobes, without radiological signs of pulmonary fibrosis. Sequential follow-up evaluations at 60 and 100 days after COVID-19 onset demonstrated a vast improvement of both, symptoms and CT abnormalities over time. CONCLUSION: A relevant percentage of post-COVID-19 patients presented with persisting symptoms and lung function impairment along with pulmonary abnormalities more than 100 days after the diagnosis of COVID-19. However, our results indicate a significant improvement in symptoms and cardiopulmonary status over time.

Moehring RW et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1705/6030989?searchresult=1	Compiling Observational Research During a Pandemic: A Necessary Bridge	Valore degli studi osservazionali durante la pandemia da COVID-19 e commento alla metanalisi di Malgie et al sulla terapia con tocilizumab (settembre 2020, https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1445/5910379)	Coronavirus disease 2019 (COVID-19) has altered the scientific landscape, upending a great many things we had wrongly assumed were immutable. Gone are the days, if indeed they ever existed, when studies came out at a deliberate pace, with a pause for reflection and synthesis. Press releases and nonreviewed preprints offer the sneak peeks that were once the purview of abstracts at scientific meetings. And the pace is torrential—all occurring at a time when practicing clinicians are stretched thin managing high clinical volumes and the associated burnout. As of early June 2020, there were an astonishing 674 active interventional COVID-19 trials, of which 21 were randomized, controlled trials (RCTs) with tocilizumab [1]. In fact, this editorial became a striking example of this phenomenon. We submitted it on 14 October 2020. In the week that followed, 3 tocilizumab RCTs were published, along with another large observational cohort [2–5]. In the face of such rapid churn, it is tempting to question whether there is value in compiling retrospective, observational cohorts at all. Maybe we should just sit back and bide our time until the RCTs arrive.
Brainard J et al Eurosurveillance https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.49.2000725	Community use of face masks and similar barriers to prevent respiratory illness such as COVID-19: a rapid scoping review	Revisione sistematica sull'efficacia dell'utilizzo di mascherina da parte della popolazione nel prevenire le infezioni respiratorie : meno 6-15% in base alla letteratura disponibile.	Background : Evidence for face-mask wearing in the community to protect against respiratory disease is unclear. Aim : To assess effectiveness of wearing face masks in the community to prevent respiratory disease, and recommend improvements to this evidence base. Methods : We systematically searched Scopus, Embase and MEDLINE for studies evaluating respiratory disease incidence after face-mask wearing (or not). Narrative synthesis and random-effects meta-analysis of attack rates for primary and secondary prevention were performed, subgrouped by design, setting, face barrier type, and who wore the mask. Preferred outcome was influenza-like illness. Grading of Recommendations, Assessment, Development

			and Evaluations (GRADE) quality assessment was undertaken and evidence base deficits described. Results : 33 studies (12 randomised control trials (RCTs)) were included. Mask wearing reduced primary infection by 6% (odds ratio (OR): 0.94; 95% CI: 0.75–1.19 for RCTs) to 61% (OR: 0.85; 95% CI: 0.32–2.27; OR: 0.39; 95% CI: 0.18–0.84 and OR: 0.61; 95% CI: 0.45–0.85 for cohort, case–control and cross-sectional studies respectively). RCTs suggested lowest secondary attack rates when both well and ill household members wore masks (OR: 0.81; 95% CI: 0.48–1.37). While RCTs might underestimate effects due to poor compliance and controls wearing masks, observational studies likely overestimate effects, as mask wearing might be associated with other risk-averse behaviours. GRADE was low or very low quality. Conclusion : Wearing face masks may reduce primary respiratory infection risk, probably by 6–15%. It is important to balance evidence from RCTs and observational studies when their conclusions widely differ and both are at risk of significant bias. COVID-19-specific studies are required.
Del Borrello G et al Journal of Thrombosis and Haemostasis https://onlinelibrary.wiley.com/doi/10.1111/jth.15216	SARS-CoV-2 Associated Coagulopathy And Thromboembolism Prophylaxis In Children: A Single Centre Observational Study.	Studio prospettico osservazionale su 35 pazienti pediatrici ospedalizzati con COVID-19, in cui si riporta scarsa alterazione delle prove di emocoagulazione e degli indici di flogosi, salvo nei casi di sindrome infiammatoria multisistemica (MIS-C).	BACKGROUND: Multiple investigators have described an increased incidence of thromboembolic events in SARS-CoV-2 infected individuals. Data concerning haemostatic complications in children hospitalised for COVID-19/MIS-C are scant. OBJECTIVES: To share our experience in managing SARS-CoV-2 associated pro-coagulant state in hospitalised children. METHODS: D-dimer values were recorded at diagnosis in children hospitalised for SARS-CoV-2 related manifestations. In moderately to critically ill patients and MIS-C cases, coagulation and inflammatory markers were checked at multiple time-points and median results were compared. Pro-thrombotic risk factors were appraised for each child and

			thromboprophylaxis was started in selected cases. RESULTS: 35 patients were prospectively enrolled. D-dimer values did not discriminate COVID-19 of differing severity, whereas were markedly different between the COVID-19 and the MIS-C cohorts. In both cohorts, D-dimer and C Reactive Protein levels increased upon clinical worsening but were not accompanied by decreased fibrinogen or platelet values, with all parameters returning to normal upon disease resolution. 6 patients had multiple thrombotic risk factors and were started on pharmacological thromboprophylaxis. No deaths, thrombotic or bleeding complications occurred. CONCLUSIONS: COVID-19 pediatric patients show mildly altered coagulation and inflammatory parameters; on the other hand, MIS-C cases show laboratory signs of an inflammatory driven pro-coagulant status. Universal anticoagulant prophylaxis in hospitalised children with SARS-CoV-2 related manifestations is not warranted, but may be offered to patients with other pro-thrombotic risk factors in the context of a multi-modal therapeutic approach.

			<table><tr><th>Clinical category</th><th>Age</th><th>Gender (F/M)</th><th>Comorbidities (Y/N)</th><th>D-Dimer# (ng/mL)</th><th>CRP* (mg/L)</th></tr><tr><td>Mild COVID-19 (14)</td><td>9 m (10 d - 17 y)</td><td>4/10</td><td>2/16</td><td>800 (200-1800*)</td><td>4 (0-20)</td></tr><tr><td>Moderate COVID-19 (10)</td><td>3,5 y (2 m - 5,5 y)</td><td>2/8</td><td>3/7</td><td>900 (200-1700)</td><td>5 (0-76)</td></tr><tr><td>Severe-critical COVID-19 (6)</td><td>7,5 y (9 m - 19 y)</td><td>3/3</td><td>6/0</td><td>800 (100-2750**)</td><td>25 (3-42)</td></tr><tr><td>MIS-C (6)</td><td>6,8 y (4,5 - 12,5 y)</td><td>3/3</td><td>0/6</td><td>1900 (1300-4400)</td><td>215 (120-300)</td></tr></table>
Li K et al Virology Journal https://doi.org/10.1186/s12985-020-01461-4	Comparative analysis of clinical features of SARS-CoV-2 and adenovirus infection among children	Studio caso-controllo che confronta le caratteristiche cliniche e laboratoristiche di bambini con infezione da SARS-CoV-2 e da Adenovirus umano : 72 coppie di bambini a confronto mostrano che l'infezione da adenovirus è maggiormente sintomatica e determina maggior alterazioni ematobiochimiche.	BACKGROUND: The new emerging coronavirus disease 2019 (COVID-19) overall shares similar symptoms with other common respiratory viral infections. We aimed in this study to compare COVID-19 and human adenovirus (HAdV) infections in pediatric patients regarding the frequencies of major clinical symptoms and the potential disparities in laboratory and imaging parameters. METHODS: Following a case-control-like design, we built 72 age-matched pediatric COVID-19 and HAdV patient pairs. Their early symptoms and laboratory and imaging characteristics were then retrieved and compared. RESULTS: Fever and cough were the most common symptoms for both infections but were seen more often in HAdV than in COVID-19 patients (92% vs. 66% and 60% vs. 18%, respectively). Compared with COVID-19 patients, children with HAdV infection had statistically significantly higher values of neutrophil count, neutrophil percentage, activated partial thromboplastin time, prothrombin time, lactate dehydrogenase, C-reactive protein, procalcitonin but lower values of lymphocyte

			percentage, total bilirubin, potassium and sodium. Thoracic computed tomography also revealed more anomalies in HAdV patients than in COVID-19 patients (95% vs. 67%). CONCLUSIONS: COVID-19 is an overall less symptomatic and less severe infection at admission compared to HAdV respiratory infection in pediatric population.
Caballero A et al Clinical and Translational Immunology https://doi.org/10.1002/cti2.1218	Treatment of COVID-19 patients with the anti-CD6 antibody itolizumab.	Trial open label condotto a Cuba su 70 pazienti ricoverati per COVID-19 di variabile gravità e trattati con itolizumab, anticorpo monoclonale inibitore del recettore CD6 dei linfociti T, in aggiunta a terapia standard : apparente effetto positivo su prevenzione del peggioramento della funzionalità polmonare, tempo alla ventilazione meccanica, durata della ventilazione, mortalità a 14 giorni. Si registrano 3 casi di eventi avversi gravi (anafilassi).	Objectives: COVID-19 can lead to a hyperinflammatory state. CD6 is a glycoprotein expressed on mature T lymphocytes which is a crucial regulator of the T-cell activation. Itolizumab is a humanised antibody targeting CD6. Nonclinical and clinical data in autoimmune diseases indicate that it lowers multiple cytokines primarily involving the Th1/Th17 pathway. The primary objective of this study was to assess the impact of itolizumab in arresting the lung function deterioration of COVID-19 patients. Secondary objectives included safety, duration of ventilation, 14-day mortality and evaluation of interleukin 6 concentration. Methods: Patients with confirmed SARS-CoV-2 received itolizumab in combination with other therapies included in the national protocol for COVID-19. Results: Seventy critical, severe or moderate patients were treated with itolizumab in 10 Cuban hospitals. Median age was 68, and 94% had comorbidities. After 72 h, most patients improved the PO2/FiO2 ratio and reduced FiO2 requirements. Ventilation time was 8 days for critical and 1 day for severe cases. Ten patients had related adverse events while 3 subjects developed related serious events. In 30 patients, interleukin 6 decreased in individuals with high level and did not change in those with lower concentration. Fourteen-day lethality rate was 4% and 18% for moderate and severe patients, respectively. The proportion of moderate or severe patients with ventilation or death at day 14 was 9.8%. Time to treatment, neurological manifestations and biomarkers such as NLR were

			significantly associated with higher lethality. Conclusions: The opportune administration of itolizumab might interrupt the hyperinflammatory cascade and prevent COVID-19 morbidity and mortality.
Luo Y et al PeerJ Life and Environment https://peerj.com/articles/10459/	Characteristics and outcomes of hemodialysis patients with COVID-19: a retrospective single center study.	Confronto retrospettivo fra 16 pazienti emodializzati e 62 non emodializzati ricoverati per COVID-19 : si conferma il maggior rischio di outcome avverso per i primi, tipicamente affetti da maggior carico di comorbidità.	Background: The coronavirus 19 (COVID-19) pandemic has heightened the threat to the health and lives of patients with comorbid diseases. Infection by COVID-19 is especially detrimental to patients on hemodialysis. In this study, we evaluated the clinical characteristics, laboratory findings, treatments and prognoses of hemodialysis patients with COVID-19. Methods: A total of 16 hemodialysis patients with COVID-19 were recruited from Wuhan Fourth Hospital from 5 February to 20 March 2020 for a retrospective, single-center study. A total of 62 non-dialysis patients with COVID-19 were the control group. We collected data on the clinical characteristics, laboratory findings, treatments, and clinical outcomes of patients affected by the virus. Results: Hemodialysis patients with COVID-19 had a lower incidence of fever (P = 0.001) and relatively higher incidence of pre-admission comorbidities and shortness of breath than non-dialysis patients with COVID-19 (75% vs. 61%, P = 0.467 50% vs. 33.87%, P = 0.248). Hemodialysis patients had lower levels of hemoglobin (P < 0.001), white blood cell counts (P = 0.015), neutrophils (P = 0.016), AST (P = 0.037), ALT (P < 0.001) and procalcitonin (P < 0.001), and higher levels of D-dimer (P < 0.001) and thrombin time (P < 0.001). Hemodialysis patients had a higher incidence of pulmonary effusion, cord-like high-density shadows, pleural thickening, and atelectasis (P < 0.05). Hemodialysis patients also had relatively higher rates of mortality and prolonged hospital stays compared with the control group. Conclusions: Hemodialysis patients typically present with multiple comorbidities and are considered to be a high-risk group for COVID-

			19 infections. Hemodialysis patients with COVID-19 may have prolonged hospital stays and unfavorable prognoses and should be closely monitored.