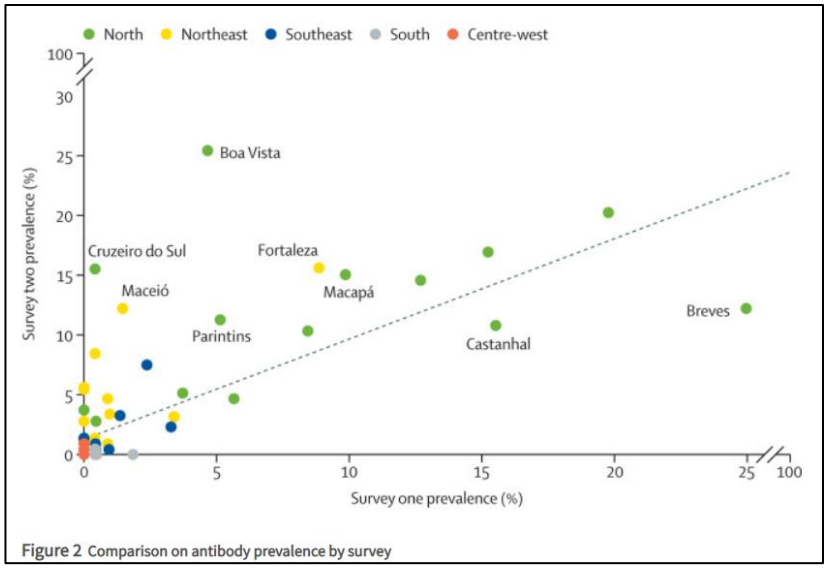
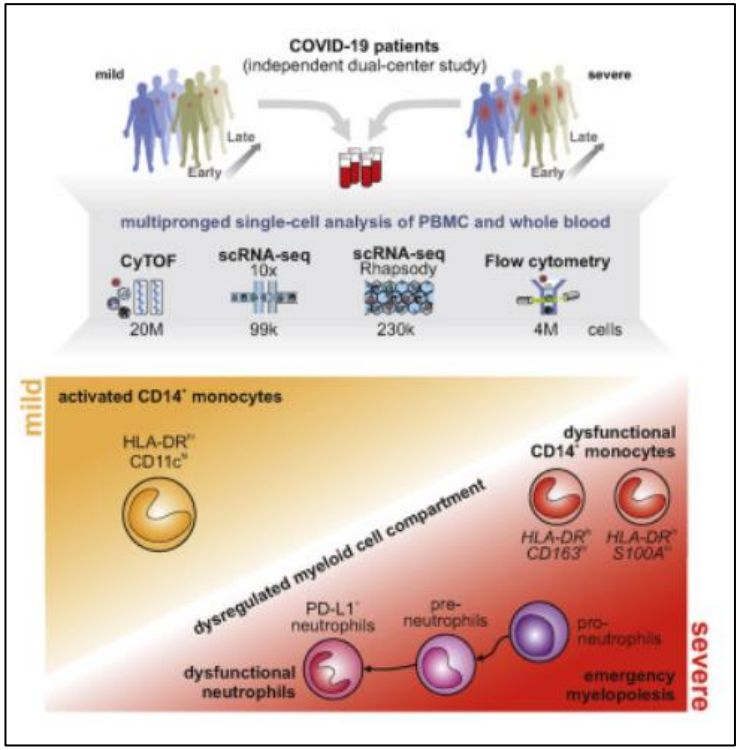
RICERCA BIBLIOGRAFICA COVID 19 SETTIMANA 28.09-04.10.2020 FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE DOTT.SSA ELEONORA TADDEI			
AUTORE/RIVISTA	**TITOLO**	**OUTCOME PRINCIPALE**	**ABSTRACT**
Hallal PC et al The Lancet https://doi.org/10.1016/S2214-109X(20)30387-9	SARS-CoV-2 antibody prevalence in Brazil: results from two successive nationwide serological household surveys	Studio cross-sectional di sieroprevalenza per SARS-CoV-2 su persone provenienti da 133 città brasiliane rappresentative di tutti gli stati del Paese. Si rileva grande eterogeneità, con maggiore prevalenza nelle persone di origine indigena e appartenenti alle classi più disagiate.	Background: Population-based data on COVID-19 are essential for guiding policies. There are few such studies, particularly from low or middle-income countries. Brazil is currently a hotspot for COVID-19 globally. We aimed to investigate severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibody prevalence by city and according to sex, age, ethnicity group, and socioeconomic status, and compare seroprevalence estimates with official statistics on deaths and cases. Methods: In this repeated cross-sectional study, we did two seroprevalence surveys in 133 sentinel cities in all Brazilian states. We randomly selected households and randomly selected one individual from all household members. We excluded children younger than 1 year. Presence of antibodies against SARS-CoV-2 was assessed using a lateral flow point-of-care test, the WONDFO SARS-CoV-2 Antibody Test (Wondfo Biotech, Guangzhou, China), using two drops of blood from finger prick samples. This lateral-flow

			assay detects IgG and IgM isotypes that are specific to the SARS-CoV-2 receptor binding domain of the spike protein. Participants also answered short questionnaires on sociodemographic information (sex, age, education, ethnicity, household size, and household assets) and compliance with physical distancing measures. Findings: We included 25 025 participants in the first survey (May 14–21) and 31 165 in the second (June 4–7). For the 83 (62%) cities with sample sizes of more than 200 participants in both surveys, the pooled seroprevalence increased from 1·9% (95% CI 1·7–2·1) to 3·1% (2·8–3·4). City-level prevalence ranged from 0% to 25·4% in both surveys. 11 (69%) of 16 cities with prevalence above 2·0% in the first survey were located in a stretch along a 2000 km of the Amazon river in the northern region. In the second survey, we found 34 cities with prevalence above 2·0%, which included the same 11 Amazon cities plus 14 from the northeast region, where prevalence was increasing rapidly. Prevalence levels were lower in the south and centre-west, and intermediate in the southeast, where the highest level was found in Rio de Janeiro (7·5% [4·2–12·2]). In the second survey, prevalence was similar in men and women, but an increased prevalence was observed in participants aged 20–59 years and those living in crowded conditions (4·4% [3·5–5·6] for those living with households with six or more people). Prevalence among Indigenous people was 6·4% (4·1–9·4) compared with 1·4% (1·2–1·7) among White people. Prevalence in the poorest socioeconomic quintile was 3·7% (3·2–4·3) compared with 1·7% (1·4–2·2) in the wealthiest quintile. Interpretation: Antibody prevalence was highly heterogeneous by country region, with rapid initial escalation in Brazil's north and northeast. Prevalence is strongly associated with Indigenous

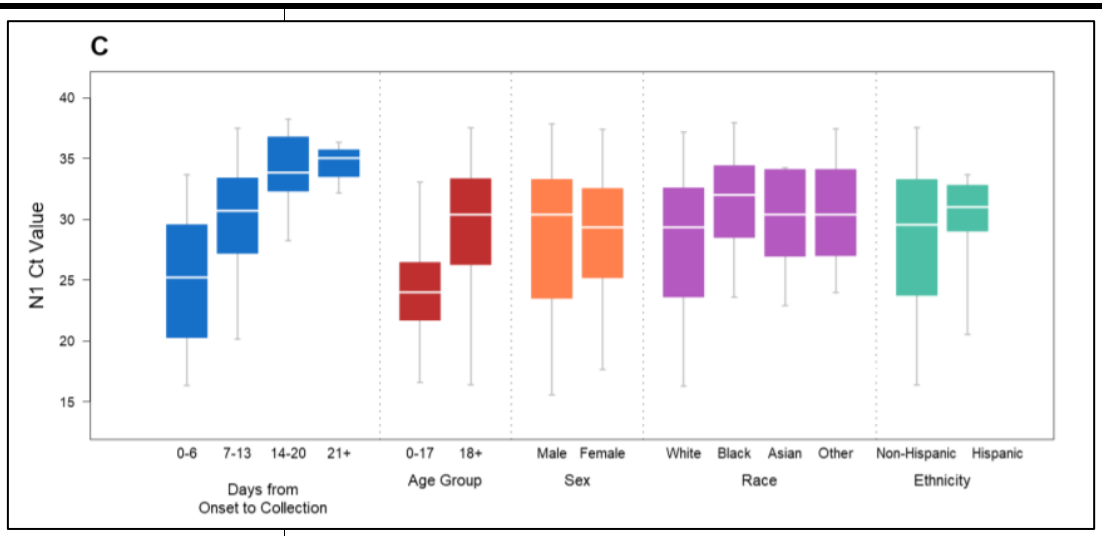
			ancestry and low socioeconomic status. These population subgroups are unlikely to be protected if the policy response to the pandemic by the national government continues to downplay scientific evidence.  Figure 2 Comparison on antibody prevalence by survey
Gupta V et al Clinical Infectious Diseases https://doi.org/10.1093/cid/ciaa1451	Asymptomatic reinfection in two healthcare workers from India with genetically distinct SARS-CoV-2.	Casi clinici di due giovani operatori sanitari (25 e 28 anni) con storia di infezione e reinfezione, sempre asintomatica, da parte di virus SARS-CoV-2 geneticamente distinti.	Dear Editor, To et al recently reported a case of SARS-CoV-2 reinfection confirmed by genome sequencing. Additional reports of genetically characterized reinfections have emerged [2, 3] raising pertinent questions on the longevity of immune response in SARS-CoV-2 infection . In all previous reports, patients had symptoms in one or both of the episodes. Here we report asymptomatic SARS-COV-2 reinfection in two healthcare workers detected during routine surveillance. The report highlights the possibility of undetected SARS-CoV-2 reinfections and the need for surveillance of SARS-CoV-2 reinfections in healthcare systems.

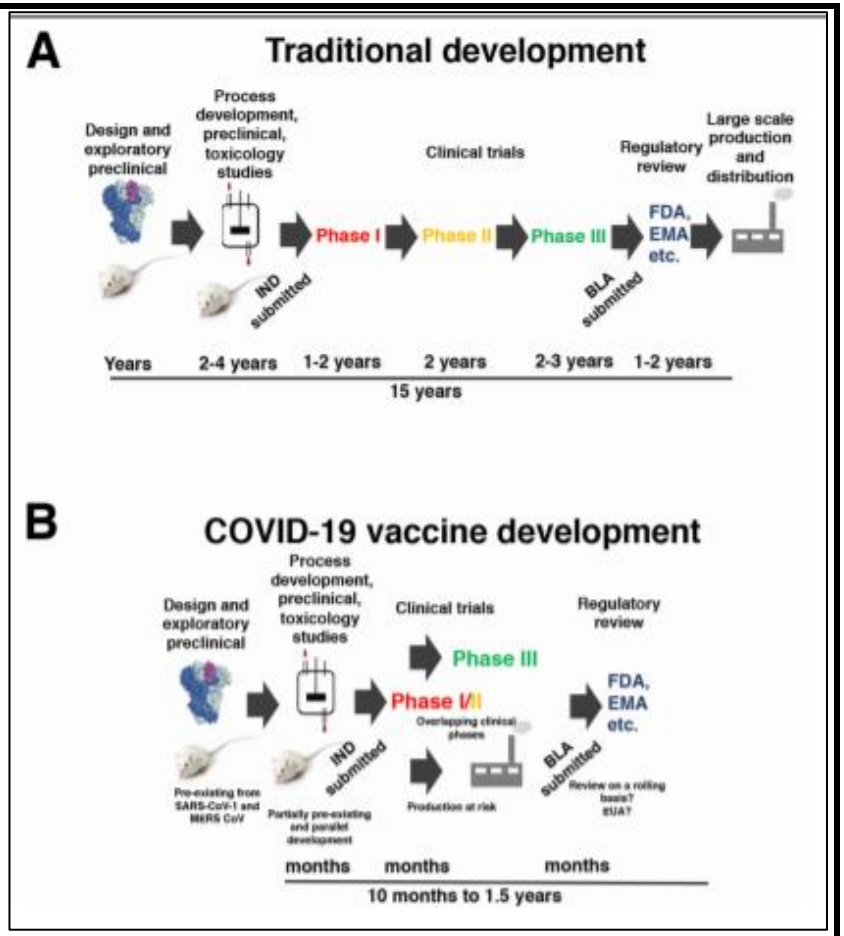
Scgultze A et al The Lancet https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30415-X/fulltext	Risk of COVID-19-related death among patients with chronic obstructive pulmonary disease or asthma prescribed inhaled corticosteroids: an observational cohort study using the OpenSAFELY platform.	Studio retrospettivo su 148557 pazienti con BPCO (broncopneumopatia cronica ostruttiva) e 818490 con asma: l'utilizzo di corticosteroidi inalatori non protegge dalla morte per COVID-19 ma sembra addirittura associato ad un aumento di mortalità (che tuttavia secondo gli Autori potrebbe essere dovuto a fattori di confondimento).	Background: Early descriptions of patients admitted to hospital during the COVID-19 pandemic showed a lower prevalence of asthma and chronic obstructive pulmonary disease (COPD) than would be expected for an acute respiratory disease like COVID-19, leading to speculation that inhaled corticosteroids (ICSs) might protect against infection with severe acute respiratory syndrome coronavirus 2 or the development of serious sequelae. We assessed the association between ICS and COVID-19-related death among people with COPD or asthma using linked electronic health records (EHRs) in England, UK. Methods: In this observational study, we analysed patient-level data for people with COPD or asthma from primary care EHRs linked with death data from the Office of National Statistics using the OpenSAFELY platform. The index date (start of follow-up) for both cohorts was March 1, 2020; follow-up lasted until May 6, 2020. For the COPD cohort, individuals were eligible if they were aged 35 years or older, had COPD, were a current or former smoker, and were prescribed an ICS or long-acting β agonist plus long-acting muscarinic antagonist (LABA–LAMA) as combination therapy within the 4 months before the index date. For the asthma cohort, individuals were eligible if they were aged 18 years or older, had been diagnosed with asthma within 3 years of the index date, and were prescribed an ICS or short-acting β agonist (SABA) only within the 4 months before the index date. We compared the outcome of COVID-19-related death between people prescribed an ICS and those prescribed alternative respiratory medications: ICSs versus LABA–LAMA for the COPD cohort, and low-dose or medium-dose and high-dose ICSs versus SABAs only in the asthma cohort. We used Cox regression models to estimate hazard ratios (HRs) and 95% CIs for the association between exposure categories and the

			outcome in each population, adjusted for age, sex, and all other prespecified covariates. We calculated e-values to quantify the effect of unmeasured confounding on our results. Findings: We identified 148 557 people with COPD and 818 490 people with asthma who were given relevant respiratory medications in the 4 months before the index date. People with COPD who were prescribed ICSs were at increased risk of COVID-19-related death compared with those prescribed LABA–LAMA combinations (adjusted HR 1·39 [95% CI 1·10–1·76]). Compared with those prescribed SABAs only, people with asthma who were prescribed high-dose ICS were at an increased risk of death (1·55 [1·10–2·18]), whereas those given a low or medium dose were not (1·14 [0·85–1·54]). Sensitivity analyses showed that the apparent harmful association we observed could be explained by relatively small health differences between people prescribed ICS and those not prescribed ICS that were not recorded in the database (e value lower 95% CI 1·43). Interpretation: Our results do not support a major role for regular ICS use in protecting against COVID-19-related death among people with asthma or COPD. Observed increased risks of COVID-19-related death can be plausibly explained by unmeasured confounding due to disease severity.
Schulte-Schrepping J et al Cell https://www.cell.com/cell/fulltext/S0092-8674(20)30992-2	Severe COVID-19 Is Marked by a Dysregulated Myeloid Cell Compartment	Studio della diversa risposa immunitaria che caratterizza l'infezione lieve e grave da SARS-CoV-2 sulla base di due coorti di pazienti. Si dimostra inoltre la presenza di alterazioni della mielopoiesi.	Coronavirus disease 2019 (COVID-19) is a mild to moderate respiratory tract infection, however, a subset of patients progress to severe disease and respiratory failure. The mechanism of protective immunity in mild forms and the pathogenesis of severe COVID-19 associated with increased neutrophil counts and dysregulated immune responses remain unclear. In a dual-center, two-cohort study, we combined single-cell RNA-sequencing and single-cell proteomics of whole-blood and peripheral-blood mononuclear cells

			to determine changes in immune cell composition and activation in mild versus severe COVID-19 (242 samples from 109 individuals) over time. HLA-DRhiCD11chi inflammatory monocytes with an interferon-stimulated gene signature were elevated in mild COVID-19. Severe COVID-19 was marked by occurrence of neutrophil precursors, as evidence of emergency myelopoiesis, dysfunctional mature neutrophils, and HLA-DRlo monocytes. Our study provides detailed insights into the systemic immune response to SARS-CoV-2 infection and reveals profound alterations in the myeloid cell compartment associated with severe COVID-19. 

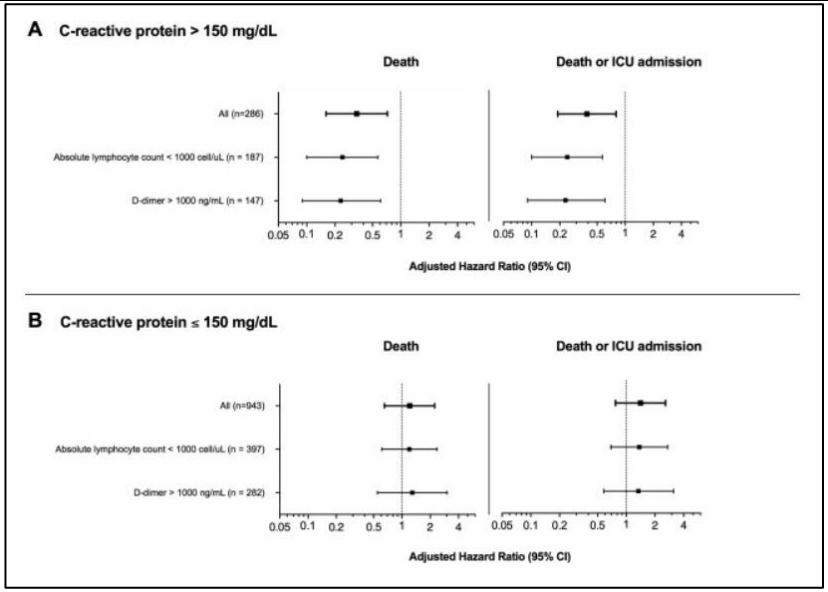
Salvatore PP et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1469/5912493?searchresult=1	Epidemiological Correlates of PCR Cycle Threshold Values in the Detection of SARS-CoV-2	Studio della correlazione fra ciclo soglia di positivizzazione della PCR per SARS-CoV-2 e caratteristiche di pazienti con COVID-19 lieve gestiti fuori dall'ospedale.	Background: Detection of SARS-CoV-2 infection has principally been performed through the use of real-time reverse-transcription PCR (rRT-PCR) testing. Results of such tests can be reported as cycle threshold (Ct) values, which may provide semi-quantitative or indirect measurements of viral load. Previous reports have examined temporal trends in Ct values over the course of a SARS-CoV-2 infection. Methods: Using testing data collected during a prospective household transmission investigation of outpatient and mild COVID-19 cases, we examined the relationship between Ct values of the viral RNA N1 target and demographic, clinical, and epidemiological characteristics collected through participant interviews and daily symptom diaries. Results: We found Ct values are lowest (corresponding to higher viral RNA concentration) soon after symptom onset and are significantly correlated with time elapsed since onset ($p<0.001$); within 7 days after symptom onset, the median Ct value was 26.5 compared with a median Ct value of 35.0 occurring 21 days after onset. Ct values were significantly lower among participants under 18 years of age ($p=0.01$) and those reporting upper respiratory symptoms at the time of sample collection ($p=0.001$) and were higher among participants reporting no symptoms ($p=0.05$). Conclusions: These results emphasize the importance of early testing for SARS-CoV-2 among individuals with symptoms of respiratory illness and allows cases to be identified and isolated when their viral shedding may be highest.

			
Kramer F Nature https://www.nature.com/articles/s41586-020-2798-3	SARS-CoV-2 vaccines in development	Aggiornamento sulle caratteristiche e le fasi di sviluppo dei più di 180 vaccini contro SARS-CoV-2 in studio nel mondo.	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in late 2019 in China and caused a coronavirus disease 2019 (COVID-19) pandemic. To mitigate the public health, economic and societal impacts of the virus, a vaccine is urgently needed. The development of SARS-CoV-2 vaccines was initiated in early January 2020 when the sequence of the virus became available and moved at record speed with one Phase I trial already starting in March 2020 and currently more than 180 vaccines in various stages of development. Phase I/II trial data is already available for several vaccine candidates and many have moved into Phase III trials. The data available so far suggests that effective and safe vaccines might become available within months rather than years.

			
Yokota I et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-	Mass screening of asymptomatic persons for SARS-CoV-2 using saliva	Esito di uno screening su 1924 persone asintomatiche cui sono stati eseguiti tampone nasofaringeo e raccolta di un campione di saliva per ricerca molecolare di SARS-CoV-2: si dimostrano elevata	Background: COVID-19 has rapidly evolved to become a global pandemic due largely to the transmission of its causative virus through asymptomatic carriers. Detection of SARS-CoV-2 in asymptomatic people is an urgent priority for the prevention and containment of disease outbreaks in communities. However, few data are available in asymptomatic persons regarding the accuracy of PCR testing. Additionally, although self-collected saliva has significant logistical advantages in mass screening, its utility as an

article/doi/10.1093/cid/ciaa1388/5911780		sensibilità e specificità per entrambe le metodiche, che mostrano alta concordanza.	alternative specimen in asymptomatic persons is yet to be determined. Methods: We conducted a mass-screening study to compare the utility of nucleic acid amplification, such as reverse transcriptase polymerase chain reaction (RT-PCR) testing, using nasopharyngeal swabs (NPS) and saliva samples from each individual in two cohorts of asymptomatic persons: the contact tracing cohort and the airport quarantine cohort. Results: In this mass-screening study including 1,924 individuals, the sensitivity of nucleic acid amplification testing with nasopharyngeal and saliva specimens were 86% (90%CI:77-93%) and 92% (90%CI:83-97%), respectively, with specificities greater than 99.9%. The true concordance probability between the nasopharyngeal and saliva tests was estimated at 0.998 (90%CI:0.996-0.999) on the estimated airport prevalence at 0.3%. In positive individuals, viral load was highly correlated between NPS and saliva. Conclusion: Both nasopharyngeal and saliva specimens had high sensitivity and specificity. Self-collected saliva is a valuable specimen to detect SARS-CoV-2 in mass screening of asymptomatic persons.
Thapa SB et al JAMA https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2771090	Clinical Outcomes of In-Hospital Cardiac Arrest in COVID-19	Caratteristiche di 54 pazienti ricoverati per COVID-19 e sottoposti a rianimazione cardiopolmonare (RCP) per arresto intraospedaliero. Nessun paziente è sopravvissuto fino ad essere dimesso.	Before the outbreak of coronavirus disease 2019 (COVID-19), 25% of patients who underwent in-hospital cardiac arrest (IHCA) survived to discharge, with the initial rhythm being nonshockable in 81% of cases.1 Despite the outbreak causing many deaths, to our knowledge, information on IHCA among this subset of patients in the US is lacking.

Martinez-Sanz J et al Clinical Microbiology and Infection https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30573-5/fulltext	Effects of tocilizumab on mortality in hospitalized patients with COVID-19: A multicenter cohort study.	Associazione fra terapia con tocilizumab e mortalità/ tempo al ricovero in terapia intensiva o morte in una coorte di 1229 pazienti ricoverati per COVID-19 in Spagna. Emerge un vantaggio per i pazienti con proteina C reattiva superiore a 150 mg/l trattati con tocilizumab.	OBJECTIVES: Tocilizumab has been proposed as a candidate therapy for patients with severe coronavirus disease 2019 (COVID-19), especially among those with higher systemic inflammation. Here, we investigate the association between tocilizumab use and mortality in a large cohort of hospitalized patients. METHODS: Cohort study of patients hospitalized with COVID-19 in Spain. The primary outcome was time to death and the secondary outcome time to intensive care unit admission (ICU) or death. We used inverse-probability weighting to fit marginal structural models adjusted for time-varying covariates to determine the causal relationship between tocilizumab use and the outcomes. RESULTS: A total of 1,229 patients were analyzed, with 261 patients (61 deaths) in the tocilizumab group and 969 patients (120 deaths) in the control group. In the adjusted marginal structural models, a significant interaction between tocilizumab use and high C-reactive protein (CRP) levels was detected. Tocilizumab was associated with decreased risk of death (aHR 0.34, 95% CI 0.16-0.72, p=0.005) and ICU admission or death (aHR 0.38, 95% CI 0.19-0.81, p=0.011) among patients with baseline CRP >150 mg/L, but not among those with CRP </=150 mg/L. Exploratory subgroup analyses yielded point estimates that were consistent with these findings. CONCLUSIONS: In this large observational study, tocilizumab was associated with a lower risk of death or ICU or death in patients with higher CRP levels. While the results of ongoing clinical trials of tocilizumab in patients with COVID-19 will be important to establish its safety and efficacy, our findings have implications for the design of future clinical trials.

			
Helfand BKI et al JAMA https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2771091	The Exclusion of Older Persons From Vaccine and Treatment Trials for Coronavirus Disease 2019—Missing the Target	Revisione dei criteri di inclusione di 847 trial clinici su COVID-19 (lista completa nell'Appendice allo studio): la fascia d'età 65-80 anni è ampiamente esclusa, nonostante sia la più colpita in termini di incidenza dell'infezione e mortalità.	Older adults are at greatest risk of severe disease and death due to coronavirus disease 2019 (COVID-19). Globally, persons older than 65 years comprise 9% of the population,1 yet account for 30% to 40% of cases and more than 80% of deaths.2 Unfortunately, there is a long history of exclusion of older adults from clinical trials. In response, the National Institutes of Health instituted the Inclusion Across the Lifespan policy, requiring the inclusion of older adults in clinical trials.3 Thus, we reviewed all COVID-19 treatment and vaccine trials on http://www.clinicaltrials.gov to evaluate their risk for exclusion of older adults (≥65 years).

Piechotta V et al Cochrane Library https://pubmed.ncbi.nlm.nih.gov/32648959/	Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a living systematic review	Revisione sistematica che valuta efficacia e sicurezza del trattamento con plasma di convalescenti o immunoglobuline iperimmuni per COVID-19. Le evidenze a disposizione sono scarse.	Background: Convalescent plasma and hyperimmune immunoglobulin may reduce mortality in patients with viral respiratory diseases, and are currently being investigated in trials as potential therapy for coronavirus disease 2019 (COVID-19). A thorough understanding of the current body of evidence regarding the benefits and risks is required. OBJECTIVES: To continually assess, as more evidence becomes available, whether convalescent plasma or hyperimmune immunoglobulin transfusion is effective and safe in treatment of people with COVID-19. Search methods: We searched the World Health Organization (WHO) COVID-19 Global Research Database, MEDLINE, Embase, Cochrane COVID-19 Study Register, Centers for Disease Control and Prevention COVID-19 Research Article Database and trial registries to identify completed and ongoing studies on 4 June 2020. Selection criteria: We followed standard Cochrane methodology. We included studies evaluating convalescent plasma or hyperimmune immunoglobulin for people with COVID-19, irrespective of study design, disease severity, age, gender or ethnicity. We excluded studies including populations with other coronavirus diseases (severe acute respiratory syndrome (SARS) or Middle East respiratory syndrome (MERS)) and studies evaluating standard immunoglobulin. Data collection and analysis: We followed standard Cochrane methodology. To assess bias in included studies, we used the Cochrane 'Risk of bias' tool for randomised controlled trials (RCTs), the Risk of Bias in Non-randomised Studies - of Interventions (ROBINS-I) tool for controlled non-randomised studies of interventions (NRSIs), and the assessment criteria for observational studies, provided by Cochrane Childhood Cancer for non-controlled NRSIs. MAIN RESULTS: This is the first living update of our review.

			We included 20 studies (1 RCT, 3 controlled NRSIs, 16 non-controlled NRSIs) with 5443 participants, of whom 5211 received convalescent plasma, and identified a further 98 ongoing studies evaluating convalescent plasma or hyperimmune immunoglobulin, of which 50 are randomised. We did not identify any completed studies evaluating hyperimmune immunoglobulin. Overall risk of bias of included studies was high, due to study design, type of participants, and other previous or concurrent treatments. Effectiveness of convalescent plasma for people with COVID-19 We included results from four controlled studies (1 RCT (stopped early) with 103 participants, of whom 52 received convalescent plasma; and 3 controlled NRSIs with 236 participants, of whom 55 received convalescent plasma) to assess effectiveness of convalescent plasma. Control groups received standard care at time of treatment without convalescent plasma. All-cause mortality at hospital discharge (1 controlled NRSI, 21 participants) We are very uncertain whether convalescent plasma has any effect on all-cause mortality at hospital discharge (risk ratio (RR) 0.89, 95% confidence interval (CI) 0.61 to 1.31; very low-certainty evidence). Time to death (1 RCT, 103 participants; 1 controlled NRSI, 195 participants) We are very uncertain whether convalescent plasma prolongs time to death (RCT: hazard ratio (HR) 0.74, 95% CI 0.30 to 1.82; controlled NRSI: HR 0.46, 95% CI 0.22 to 0.96; very low-certainty evidence). Improvement of clinical symptoms, assessed by need for respiratory support (1 RCT, 103 participants; 1 controlled NRSI, 195 participants) We are very uncertain whether convalescent plasma has any effect on improvement of clinical symptoms at seven days (RCT: RR 0.98, 95% CI 0.30 to 3.19), 14 days (RCT: RR 1.85, 95% CI 0.91 to 3.77; controlled NRSI: RR 1.08, 95% CI 0.91 to 1.29), and 28 days (RCT: RR 1.20, 95% CI 0.80 to 1.81; very low-certainty

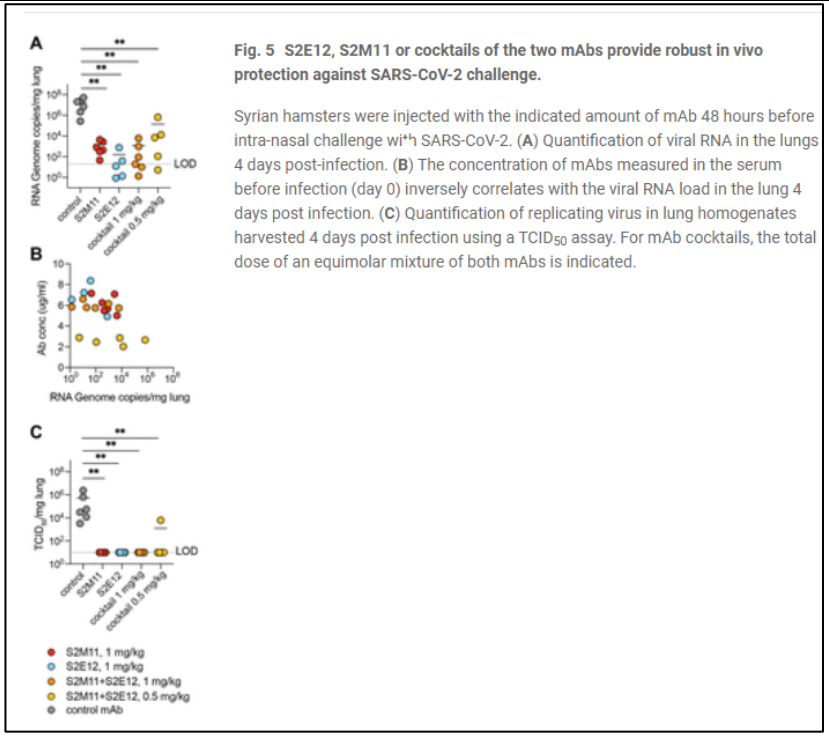
			evidence). Quality of life No studies reported this outcome. Safety of convalescent plasma for people with COVID-19 We included results from 1 RCT, 3 controlled NRSIs and 10 non-controlled NRSIs assessing safety of convalescent plasma. Reporting of adverse events and serious adverse events was variable. The controlled studies reported on adverse events and serious adverse events only in participants receiving convalescent plasma. The duration of follow-up varied. Some, but not all, studies included death as a serious adverse event. Grade 3 or 4 adverse events (13 studies, 201 participants) The studies did not report the grade of adverse events. Thirteen studies (201 participants) reported on adverse events of possible grade 3 or 4 severity. The majority of these adverse events were allergic or respiratory events. We are very uncertain whether or not convalescent plasma therapy affects the risk of moderate to severe adverse events (very low-certainty evidence). Serious adverse events (14 studies, 5201 participants) Fourteen studies (5201 participants) reported on serious adverse events. The majority of participants were from one non-controlled NRSI (5000 participants), which reported only on serious adverse events limited to the first four hours after convalescent plasma transfusion. This study included death as a serious adverse event; they reported 15 deaths, four of which they classified as potentially, probably or definitely related to transfusion. Other serious adverse events reported in all studies were predominantly allergic or respiratory in nature, including anaphylaxis, transfusion-associated dyspnoea, and transfusion-related acute lung injury (TRALI). We are very uncertain whether or not convalescent plasma affects the number of serious adverse events. Authors' conclusions: We are very uncertain whether convalescent plasma is beneficial for people admitted to hospital with COVID-19.

			For safety outcomes we also included non-controlled NRSIs. There was limited information regarding adverse events. Of the controlled studies, none reported on this outcome in the control group. There is only very low-certainty evidence for safety of convalescent plasma for COVID-19. While major efforts to conduct research on COVID-19 are being made, problems with recruiting the anticipated number of participants into these studies are conceivable. The early termination of the first RCT investigating convalescent plasma, and the multitude of studies registered in the past months illustrate this. It is therefore necessary to critically assess the design of these registered studies, and well-designed studies should be prioritised. Other considerations for these studies are the need to report outcomes for all study arms in the same way, and the importance of maintaining comparability in terms of co-interventions administered in all study arms. There are 98 ongoing studies evaluating convalescent plasma and hyperimmune immunoglobulin, of which 50 are RCTs. This is the first living update of the review, and we will continue to update this review periodically. These updates may show different results to those reported here.
Juul S et al PloS Medicine https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1003293	Interventions for treatment of COVID-19: A living systematic review with meta-analyses and trial sequential analyses (The LIVING Project)	Revisione sistematica e metanalisi sulla base di 33 trial clinici al fine di valutare l'efficacia di desametasone, remdesivir e idrossiclorochina per COVID-19.	Background: Coronavirus disease 2019 (COVID-19) is a rapidly spreading disease that has caused extensive burden to individuals, families, countries, and the world. Effective treatments of COVID-19 are urgently needed. Methods and findings: This is the first edition of a living systematic review of randomized clinical trials comparing the effects of all treatment interventions for participants in all age groups with COVID-19. We planned to conduct aggregate data meta-analyses, trial sequential analyses, network meta-analysis, and individual patient data meta-analyses. Our systematic review is based on Preferred Reporting Items for Systematic Reviews and Meta-

			Analysis (PRISMA) and Cochrane guidelines, and our 8-step procedure for better validation of clinical significance of meta-analysis results. We performed both fixed-effect and random-effects meta-analyses. Primary outcomes were all-cause mortality and serious adverse events. Secondary outcomes were admission to intensive care, mechanical ventilation, renal replacement therapy, quality of life, and nonserious adverse events. We used Grading of Recommendations Assessment, Development and Evaluation (GRADE) to assess the certainty of evidence. We searched relevant databases and websites for published and unpublished trials until August 7, 2020. Two reviewers independently extracted data and assessed trial methodology. We included 33 randomized clinical trials enrolling a total of 13,312 participants. All trials were at overall high risk of bias. We identified one trial randomizing 6,425 participants to dexamethasone versus standard care. This trial showed evidence of a beneficial effect of dexamethasone on all-cause mortality (rate ratio 0.83; 95% confidence interval [CI] 0.75–0.93; $p < 0.001$; low certainty) and on mechanical ventilation (risk ratio [RR] 0.77; 95% CI 0.62–0.95; $p = 0.021$; low certainty). It was possible to perform meta-analysis of 10 comparisons. Meta-analysis showed no evidence of a difference between remdesivir versus placebo on all-cause mortality (RR 0.74; 95% CI 0.40–1.37; $p = 0.34$, $I2 = 58\%$; 2 trials; very low certainty) or nonserious adverse events (RR 0.94; 95% CI 0.80–1.11; $p = 0.48$, $I2 = 29\%$; 2 trials; low certainty). Meta-analysis showed evidence of a beneficial effect of remdesivir versus placebo on serious adverse events (RR 0.77; 95% CI 0.63–0.94; $p = 0.009$, $I2 = 0\%$; 2 trials; very low certainty) mainly driven by respiratory failure in one trial. Meta-analyses and trial sequential analyses showed that we could exclude the possibility that hydroxychloroquine versus standard

			care reduced the risk of all-cause mortality (RR 1.07; 95% CI 0.97–1.19; p = 0.17; I2 = 0%; 7 trials; low certainty) and serious adverse events (RR 1.07; 95% CI 0.96–1.18; p = 0.21; I2 = 0%; 7 trials; low certainty) by 20% or more, and meta-analysis showed evidence of a harmful effect on nonserious adverse events (RR 2.40; 95% CI 2.01–2.87; p < 0.00001; I2 = 90%; 6 trials; very low certainty). Meta-analysis showed no evidence of a difference between lopinavir–ritonavir versus standard care on serious adverse events (RR 0.64; 95% CI 0.39–1.04; p = 0.07, I2 = 0%; 2 trials; very low certainty) or nonserious adverse events (RR 1.14; 95% CI 0.85–1.53; p = 0.38, I2 = 75%; 2 trials; very low certainty). Meta-analysis showed no evidence of a difference between convalescent plasma versus standard care on all-cause mortality (RR 0.60; 95% CI 0.33–1.10; p = 0.10, I2 = 0%; 2 trials; very low certainty). Five single trials showed statistically significant results but were underpowered to confirm or reject realistic intervention effects. None of the remaining trials showed evidence of a difference on our predefined outcomes. Because of the lack of relevant data, it was not possible to perform other meta-analyses, network meta-analysis, or individual patient data meta-analyses. The main limitation of this living review is the paucity of data currently available. Furthermore, the included trials were all at risks of systematic errors and random errors. Conclusions: Our results show that dexamethasone and remdesivir might be beneficial for COVID-19 patients, but the certainty of the evidence was low to very low, so more trials are needed. We can exclude the possibility of hydroxychloroquine versus standard care reducing the risk of death and serious adverse events by 20% or more. Otherwise, no evidence-based treatment for COVID-19

			currently exists. This review will continuously inform best practice in treatment and clinical research of COVID-19.
Tortorici MA et al Science https://science.sciencemag.org/content/early/2020/09/23/science.abe3354.full	Ultrapotent human antibodies protect against SARS-CoV-2 challenge via multiple mechanisms	Descrizione di due anticorpi neutralizzanti (S2E12 e S2M11) diretti contro il recettore ACE2 in grado di bloccare l'ingresso di SARS-CoV-2 nelle cellule ed efficaci su animale da esperimento.	Efficient therapeutic options are needed to control the spread of SARS-CoV-2 that has caused more than 922,000 fatalities as of September 13th, 2020. We report the isolation and characterization of two ultrapotent SARS-CoV-2 human neutralizing antibodies (S2E12 and S2M11) that protect hamsters against SARS-CoV-2 challenge. Cryo-electron microscopy structures show that S2E12 and S2M11 competitively block ACE2 attachment and that S2M11 also locks the spike in a closed conformation by recognition of a quaternary epitope spanning two adjacent receptor-binding domains. Cocktails including S2M11, S2E12 or the previously identified S309 antibody broadly neutralize a panel of circulating SARS-CoV-2 isolates and activate effector functions. Our results pave the way to implement antibody cocktails for prophylaxis or therapy, circumventing or limiting the emergence of viral escape mutants.

			 **Fig. 5 S2E12, S2M11 or cocktails of the two mAbs provide robust in vivo protection against SARS-CoV-2 challenge.** Syrian hamsters were injected with the indicated amount of mAb 48 hours before intra-nasal challenge wi[illegible]h SARS-CoV-2. (**A**) Quantification of viral RNA in the lungs 4 days post-infection. (**B**) The concentration of mAbs measured in the serum before infection (day 0) inversely correlates with the viral RNA load in the lung 4 days post infection. (**C**) Quantification of replicating virus in lung homogenates harvested 4 days post infection using a $TCID_{50}$ assay. For mAb cocktails, the total dose of an equimolar mixture of both mAbs is indicated.
Anderson EJ et al NEJM https://www.nejm.org/doi/10.1056/NEJMoa2028436	Safety and Immunogenicity of SARS-CoV-2 mRNA-1273 Vaccine in Older Adults.	Espansione di un trial clinico di fase 1 sul vaccino a RNA messaggero mRNA-1273 contro SARS-CoV-2 a includere pazienti di età medio-avanzata. Buona tollerabilità e individuazione della dose di 100 mcg da testare in trial di fase 3.	BACKGROUND: Testing of vaccine candidates to prevent infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in an older population is important, since increased incidences of illness and death from coronavirus disease 2019 (Covid-19) have been associated with an older age. METHODS: We conducted a phase 1, dose-escalation, open-label trial of a messenger RNA vaccine, mRNA-1273, which encodes the stabilized prefusion SARS-CoV-2 spike protein (S-2P) in healthy adults. The trial was expanded to include 40 older adults, who were stratified according to age (56 to 70 years or ≥71 years). All the participants were assigned sequentially to receive two doses of either 25 µg or 100 µg of vaccine administered 28 days apart.

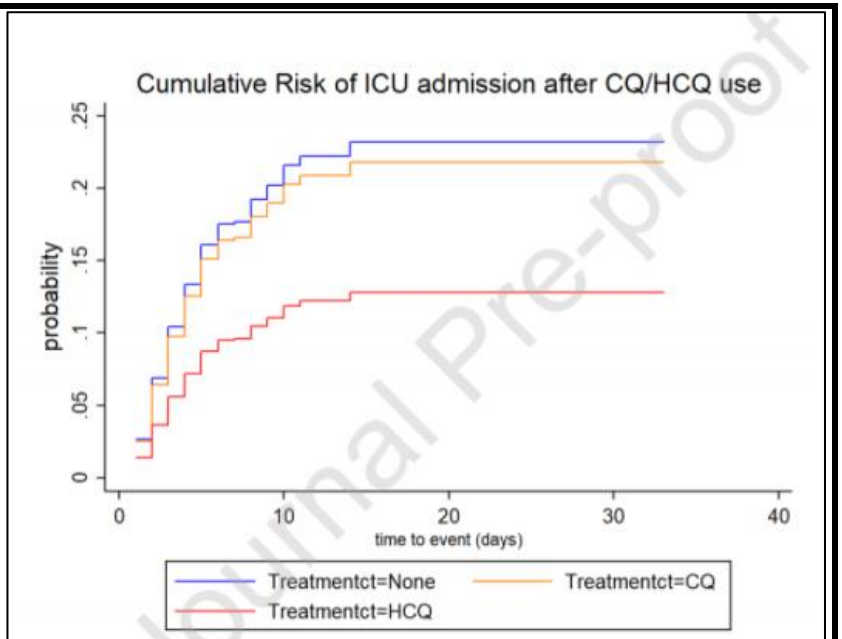
			RESULTS: Solicited adverse events were predominantly mild or moderate in severity and most frequently included fatigue, chills, headache, myalgia, and pain at the injection site. Such adverse events were dose-dependent and were more common after the second immunization. Binding-antibody responses increased rapidly after the first immunization. By day 57, among the participants who received the 25-µg dose, the anti–S-2P geometric mean titer (GMT) was 323,945 among those between the ages of 56 and 70 years and 1,128,391 among those who were 71 years of age or older; among the participants who received the 100-µg dose, the GMT in the two age subgroups was 1,183,066 and 3,638,522, respectively. After the second immunization, serum neutralizing activity was detected in all the participants by multiple methods. Binding- and neutralizing-antibody responses appeared to be similar to those previously reported among vaccine recipients between the ages of 18 and 55 years and were above the median of a panel of controls who had donated convalescent serum. The vaccine elicited a strong CD4 cytokine response involving type 1 helper T cells. CONCLUSIONS: In this small study involving older adults, adverse events associated with the mRNA-1273 vaccine were mainly mild or moderate. The 100-µg dose induced higher binding- and neutralizing-antibody titers than the 25-µg dose, which supports the use of the 100-µg dose in a phase 3 vaccine trial.
Webb BJ et al The Lancet https://www.thelancet.com/journals/lanrhe/article	Clinical criteria for COVID-19-associated hyperinflammatory syndrome: a cohort study.	Validazione di criteri per definire la sindrome da iperinfiammazione da COVID-19: fever, iperferritinemia, ratio neutrofili/linfociti, LDH o AST, D-dimero ed elevazione delle citochine (PCR,	Background: A subset of patients with COVID-19 develops a hyperinflammatory syndrome that has similarities with other hyperinflammatory disorders. However, clinical criteria specifically to define COVID-19-associated hyperinflammatory syndrome (cHIS) have not been established. We aimed to develop and validate diagnostic criteria for cHIS in a cohort of inpatients with COVID-19.

/PIIS2665-9913(20)30343-X/fulltext		interleukina-6 o trigliceridi) e loro associazione con outcome avverso in 299 pazienti ospedalizzati.	Methods: We searched for clinical research articles published between Jan 1, 1990, and Aug 20, 2020, on features and diagnostic criteria for secondary haemophagocytic lymphohistiocytosis, macrophage activation syndrome, macrophage activation-like syndrome of sepsis, cytokine release syndrome, and COVID-19. We compared published clinical data for COVID-19 with clinical features of other hyperinflammatory or cytokine storm syndromes. Based on a framework of conserved clinical characteristics, we developed a six-criterion additive scale for cHIS: fever, macrophage activation (hyperferritinaemia), haematological dysfunction (neutrophil to lymphocyte ratio), hepatic injury (lactate dehydrogenase or asparate aminotransferase), coagulopathy (D-dimer), and cytokinaemia (C-reactive protein, interleukin-6, or triglycerides). We then validated the association of the cHIS scale with in-hospital mortality and need for mechanical ventilation in consecutive patients in the Intermountain Prospective Observational COVID-19 (IPOC) registry who were admitted to hospital with PCR-confirmed COVID-19. We used a multistate model to estimate the temporal implications of cHIS. Findings: We included 299 patients admitted to hospital with COVID-19 between March 13 and May 5, 2020, in analyses. Unadjusted discrimination of the maximum daily cHIS score was 0·81 (95% CI 0·74–0·88) for in-hospital mortality and 0·92 (0·88–0·96) for mechanical ventilation; these results remained significant in multivariable analysis (odds ratio 1·6 [95% CI 1·2–2·1], p=0·0020, for mortality and 4·3 [3·0–6·0], p<0·0001, for mechanical ventilation). 161 (54%) of 299 patients met two or more cHIS criteria during their hospital admission; these patients had higher risk of mortality than patients with a score of less than 2 (24 [15%] of 138 vs one [1%] of 161) and for mechanical ventilation (73 [45%]

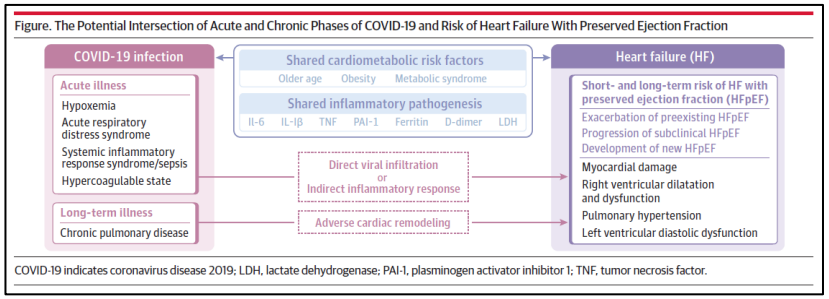
			vs three [2%]). In the multistate model, using daily cHIS score as a time-dependent variable, the cHIS hazard ratio for worsening from low to moderate oxygen requirement was 1·4 (95% CI 1·2–1·6), from moderate oxygen to high-flow oxygen 2·2 (1·1–4·4), and to mechanical ventilation 4·0 (1·9–8·2). Interpretation: We proposed and validated criteria for hyperinflammation in COVID-19. This hyperinflammatory state, cHIS, is commonly associated with progression to mechanical ventilation and death. External validation is needed. The cHIS scale might be helpful in defining target populations for trials and immunomodulatory therapies.
Mondelli M et al The Lancet https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30678-2/fulltext	Low risk of SARS-CoV-2 transmission by fomites in real-life conditions.	Corrispondenza che fa riferimento a due studi degli stessi autori in cui si dimostra che il rischio di infezione da SARS-CoV-2 tramite superfici contaminate in ospedale è trascurabile, in presenza di procedure standard di disinfezione.	We read with interest the Comment by Emanuel Goldman highlighting experiments done under controlled laboratory conditions that suggest persistence of severe acute respiratory syndrome coronavirus (SARS-CoV-2) on inanimate surfaces for days, with potential implications for viral transmission. Yet, at the same time, Goldman laments the absence of real-life studies investigating the infectious potential of SARS-CoV-2 on contaminated inanimate material and patient fomites, particularly in high-risk hospital wards. A study done in a hospital environment showed that most surfaces were contaminated, including air-conditioning vents, bed rails, bedside lockers, and rarely, toilets. Of note, environmental surface contamination declined after week of illness, and intriguingly, no surface contamination was detected in intensive care unit (ICU) rooms. A limitation of the study by Chia and colleagues is that no attempt was made to culture SARS-CoV-2 from the environmental swabs, which would have helped to understand the significance of SARS-CoV-2 RNA positive samples in terms of infectious potential.

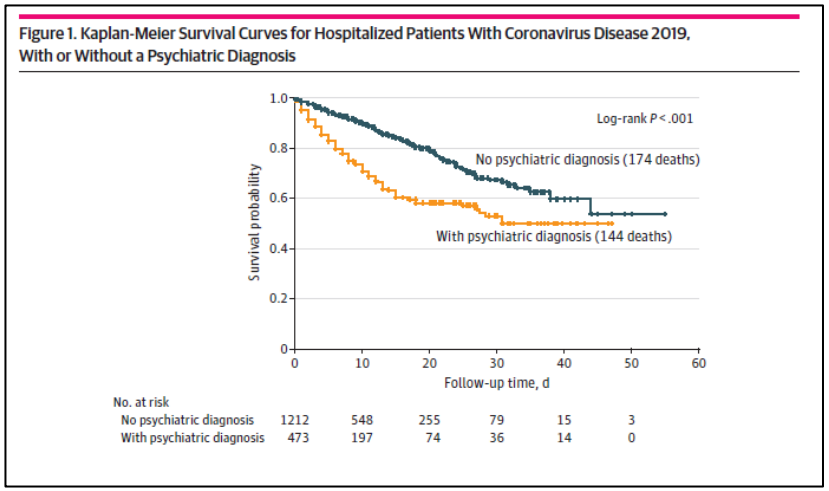
Ayerbe L et al Internal ed Emergency Medicine https://www.researchgate.net/publication/342658876_The_association_of_treatment_with_hydroxychloroquine_and_hospital_mortality_in_Covid-19_patients	The association of treatment with hydroxychloroquine and hospital mortality in COVID-19 patients	Studio retrospettivo su 2075 pazienti ricoverati per COVID-19 che dimostra un minor rischio di mortalità nei pazienti trattati con idrossiclorochina rispetto ai non trattati.	This study investigates the association between the treatment with hydroxychloroquine and mortality in patients admitted with COVID-19. Routinely recorded, clinical data, up to the 24th of April 2020, from the 2075 patients with COVID-19, admitted in 17 hospitals in Spain between the 1st of March and the 20th of April 2020 were used. The following variables were extracted for this study: age, gender, temperature, and saturation of oxygen on admission, treatment with hydroxychloroquine, azithromycin, heparin, steroids, tocilizumab, a combination of lopinavir with ritonavir, and oseltamivir, together with data on mortality. Multivariable logistic regression models were used to investigate the associations. At the time of collecting the data, 301 patients had died, 1449 had been discharged home from the hospitals, 240 were still admitted, and 85 had been transferred to hospitals not included in the study. Median follow-up time was 8 (IQR 5–12) days. Hydroxychloroquine had been used in 1857 patients. Hydroxychloroquine was associated with lower mortality when the model was adjusted for age and gender, with OR (95% CI): 0.44 (0.29–0.67). This association remained significant when saturation of oxygen<90% and temperature>37 °C were added to de model with OR 0.45 (0.30–0.68) p<0.001, and also when all the other drugs, and time of admission, were included as covariates. The association between hydroxychloroquine and lower mortality observed in this study can be acknowledged by clinicians in hospitals and in the community. Randomized-controlled trials to assess the causal efects of hydroxychloroquine in diferent therapeutic regimes are required.

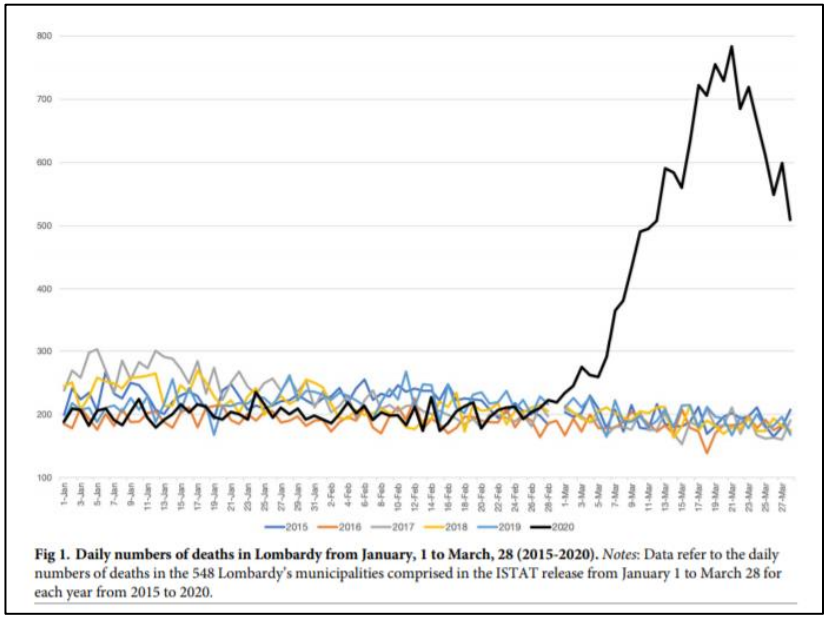
Lammers AJJ et al International Journal of Infectious Diseases https://www.sciencedirect.com/science/article/pii/S1201971220321755	Early Hydroxychloroquine but not Chloroquine use reduces ICU admission in COVID-19 patients	Studio di coorte condotto nei Paesi Bassi su 1064 pazienti trattati con clorochina, idrossiclorochina o nessun farmaco per COVID-19. Si dimostra minor rischio di ricovero in terapia intensiva per i trattati con idrossiclorochina.	Background: The global push for the use of hydroxychloroquine (HCQ) and chloroquine (CQ) against COVID-19 resulted in an ongoing discussion about the effectivity and toxicity of these drugs. Recent studies report no effect of (H)CQ on 28 day-mortality. We investigated the effect of HCQ and CQ in hospitalized patients on the non-ICU COVID-ward. Methods: A nationwide, observational cohort study was performed in The Netherlands. Hospitals were given the opportunity to decide independently on the use of three different COVID-19 treatment strategies: HCQ or CQ, or no treatment. We compared the outcome between these groups. The primary outcomes were 1) death on the COVID-19 ward, and 2) transfer to the Intensive Care Unit (ICU). Results: The analysis contained 1064 patients from 14 hospitals: 566 patients received treatment with either HCQ (n = 189) or CQ (n = 377), and 498 patients received no treatment. In a multivariate propensity matched weighted competing regression analysis, there was no significant effect of (H)CQ on mortality on the COVID-ward. HCQ however was associated with a significant decreased risk of transfer to the ICU (Hazard ratio (HR) = 0.47, 95%CI = 0.27–0.82, p = 0.008), when compared to controls. This effect was not found in the CQ group (HR = 0.80; 95%CI = 0.55–1.15, p = 0.207), and remained significant after competing risk analysis. Conclusion: The results of this observational study demonstrate a lack of effect of (H)CQ on non-ICU mortality. However, we show that the use of HCQ - but not CQ - is associated with 53% decreased risk of transfer of COVID-19 patients from the regular ward to the ICU. Recent prospective studies have reported on 28 days all-cause mortality only, therefore additional prospective data on the early effect of HCQ in preventing transfer to the ICU is still needed.

			 Figure 2B. Cumulative risk of transfer to ICU.
Abella BS et al JAMA https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2771265	Efficacy and Safety of Hydroxychloroquine vs Placebo for Pre-exposure SARS-CoV-2 Prophylaxis Among Health Care Workers: A Randomized Clinical Trial	Trial clinic randomizzato, controllato con placebo, in doppio cieco, che non riesce a dimostrare alcuna efficacia della profilassi con idrossiclorochina nel prevenire l'infezione da SARS-CoV-2 negli operatori sanitari esposti a pazienti con COVID-19.	IMPORTANCE Health care workers (HCWs) caring for patients with coronavirus disease 2019 (COVID-19) are at risk of exposure to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Currently, to our knowledge, there is no effective pharmacologic prophylaxis for individuals at risk. OBJECTIVE To evaluate the efficacy of hydroxychloroquine to prevent transmission of SARS-CoV-2 in hospital-based HCWs with exposure to patients with COVID-19 using a pre-exposure prophylaxis strategy. DESIGN, SETTING, AND PARTICIPANTS This randomized, double-blind, placebo-controlled clinical trial (the Prevention and Treatment of COVID-19 With Hydroxychloroquine Study) was

			conducted at 2 tertiary urban hospitals, with enrollment from April 9, 2020, to July 14, 2020; follow-up ended August 4, 2020. The trial randomized 132 full-time, hospital-based HCWs (physicians, nurses, certified nursing assistants, emergency technicians, and respiratory therapists), of whom 125 were initially asymptomatic and had negative results for SARS-CoV-2 by nasopharyngeal swab. The trial was terminated early for futility before reaching a planned enrollment of 200 participants. INTERVENTIONS Hydroxychloroquine, 600mg, daily, or size-matched placebo taken orally for 8 weeks. MAIN OUTCOMES AND MEASURES The primary outcomewas the incidence of SARS-CoV-2 infection as determined by a nasopharyngeal swab during the 8 weeks of treatment. Secondary outcomes included adverse effects, treatment discontinuation, presence of SARS-CoV-2 antibodies, frequency of QTc prolongation, and clinical outcomes for SARS-CoV-2–positive participants. RESULTS Of the 132 randomized participants (median age, 33 years [range, 20-66 years]; 91 women [69%]), 125 (94.7%) were evaluable for the primary outcome. There was no significant difference in infection rates in participants randomized to receive hydroxychloroquine compared with placebo (4 of 64 [6.3%] vs 4 of 61 [6.6%]; P > .99). Mild adverse events were more common in participants taking hydroxychloroquine compared with placebo (45%vs 26%; P = .04); rates of treatment discontinuation were similar in both arms (19% vs 16%; P = .81). The median change in QTc (baseline to 4-week evaluation) did not differ between arms (hydroxychloroquine: 4 milliseconds; 95%CI, −9 to 17; vs placebo: 3 milliseconds; 95%CI, −5 to 11; P = .98). Of the 8 participants with positive results for SARS-CoV-2 (6.4%), 6 developed viral symptoms; none required hospitalization, and all clinically recovered.

			CONCLUSIONS AND RELEVANCE In this randomized clinical trial, although limited by early termination, there was no clinical benefit of hydroxychloroquine administered daily for 8 weeks as pre-exposure prophylaxis in hospital-based HCWs exposed to patients with COVID-19.
Freaney PM et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2771385	COVID-19 and Heart FailureWith Preserved Ejection Fraction	COVID-19 può essere associato a scompenso cardiaco con frazione di eiezione preservata (HFpEF) tramite diversi meccanismi: infiltrazione diretta del miocardio, infiammazione, fibrosi cardiaca. Può inoltre esacerbare o smascherare uno scompenso pregresso.	Patients with preexisting cardiovascular disease (CVD) whodevelop coronavirus disease 2019 (COVID-19) have worse outcomes than patients without CVD.1 Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can directly or indirectly lead tomyocardial injury. Although fulminant viral myocarditis due to COVID-19 appears to be uncommon, recent data, althoughlimited, suggest that directmyocardial injurymay occur in some individuals.  Figure. The Potential Intersection of Acute and Chronic Phases of COVID-19 and Risk of Heart Failure With Preserved Ejection Fraction COVID-19 infection Acute illness Hypoxemia Acute respiratory distress syndrome Systemic inflammatory response syndrome/sepsis Hypercoagulable state Long-term illness Chronic pulmonary disease Shared cardiometabolic risk factors Older age Obesity Metabolic syndrome Shared inflammatory pathogenesis IL-6 IL-1β TNF PAI-1 Ferritin D-dimer LDH Direct viral infiltration or Indirect inflammatory response Adverse cardiac remodeling Heart failure (HF) Short- and long-term risk of HF with preserved ejection fraction (HFpEF) Exacerbation of preexisting HFpEF Progression of subclinical HFpEF Development of new HFpEF Myocardial damage Right ventricular dilatation and dysfunction Pulmonary hypertension Left ventricular diastolic dysfunction COVID-19 indicates coronavirus disease 2019; LDH, lactate dehydrogenase; PAI-1, plasminogen activator inhibitor 1; TNF, tumor necrosis factor.
Li L et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2771037	Association of a Prior Psychiatric Diagnosis With Mortality Among Hospitalized Patients With Coronavirus Disease 2019 (COVID-19) Infection	Studio di coorte condotto negli USA su 1685 pazienti ricoverati per COVID-19 in cui si dimostra l'associazione di una diagnosi psichiatrica pregressa con la mortalità.	Psychiatric disorders are associated with shortened life expectancy (ie, shortened by as much as 10 years). There is a concern that psychiatric comorbidity might increase Coronavirus Disease 2019 (COVID-19)–related mortality, as suggested by prior preliminary studies of cardiac and infectious disease outcomes. A large population study in Demark suggested that an a priori diagnosis of depression was associated with a higher 30-day mortality for those hospitalized for an infection. Here, we evaluate the association between having any prior psychiatric diagnosis and COVID-19–

			related mortality of hospitalized patients with COVID-19. 
Burki T The Lancet https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7508526/	The online anti-vaccine movement in the age of COVID-19	Su Facebook, le pagine anti-vacciniste hanno 31 milioni di follower e il numero è in crescita su tutti i social media. Questa tendenza potrebbe avere conseguenze al di là dell'epidemia di COVID-19 e impone di riflettere su eventuali misure per scoraggiare la disinformazione.	A new report by the Centre for Countering Digital Hate (CCDH) has lambasted social media companies for allowing the anti-vaccine movement to remain on their platforms. The report's authors noted that social media accounts held by so-called anti-vaxxers have increased their following by at least 7·8 million people since 2019. "The decision to continue hosting known misinformation content and actors left online anti-vaxxers ready to pounce on the opportunity presented by coronavirus", stated the report. The CCDH warned that the growing anti-vaccine movement could undermine the roll-out of any future vaccine against COVID-19.

Buonanno P et al PloS One https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0239569	Estimating the severity of COVID-19: Evidence from the Italian epicenter	Stima del numero di morti in eccesso attribuibili a COVID-19 e del numero di contagiati in Lombardia e a Bergamo in marzo 2020: i dati ufficiali sottostimano il fenomeno.	We provide results on the level of COVID-19 excess mortality in the Italian region of Lombardy and in the province of Bergamo using official and original data sources. Since February 2020 Lombardy and in particular the province of Bergamo have been severely hit by the novel COVID-19 infectious disease. Combining official statistics, retrospective data and original data (i.e., obituaries and death notices) we provide a tentative estimate of the number of deaths either directly or indirectly, associated with COVID-19 as well as the total number of persons infected. Our findings suggest that the reported number of deaths attributable to COVID-19 identified by public authorities accounts only for one half of the observed excess mortality between March 2020 and previous years.  **Fig 1. Daily numbers of deaths in Lombardy from January, 1 to March, 28 (2015-2020).** *Notes*: Data refer to the daily numbers of deaths in the 548 Lombardy's municipalities comprised in the ISTAT release from January 1 to March 28 for each year from 2015 to 2020.

Cioffi A et al Ethics, Medicine and Public Health https://www.sciencedirect.com/science/article/pii/S2352552520301390?via%3Dihub	The decline of COVID-19-related deaths and the risk of underestimating the pandemic	La riduzione di mortalità da COVID-19 che si registra attualmente nel mondo ha numerose possibili spiegazioni, che non autorizzano a ridurre l'attenzione nei confronti della prevenzione del contagio.	COVID-19 pandemic has put a strain on the stability of National Health Systems and society itself. The decline in COVID-19-related mortality is positive. However, we do not know the reason for this decline associated with a rise in infection in many countries of the world. For these reasons, this is not the time to lower our guard and excessively reduce preventive strategies against COVID-19.
Daviet F et al Circulation https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.120.049015	Heparin Induced Thrombocytopenia in Severe COVID-19 Patients	Rassegna retrospettiva delle caratteristiche di pazienti ricoverati in terapia intensiva per COVID-19 andati incontro a episodio di trombocitopenia indotta da eparina (HIT).	As the COVID-19 pandemic has spread throughout the world, important efforts have been made to describe its physiopathology and complications. In critically ill COVID-19 patients, a systemic inflammatory response associated with endothelial activation is observed. Indeed, a high rate of thrombotic complications has been described, including deep vein thrombosis. While the mechanisms of thrombosis are still unclear, anticoagulation with high doses of heparin has been proposed for these patients.
Blake Sullivan C et al JAMA https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2771362	Cerebrospinal Fluid Leak After Nasal Swab Testing for Coronavirus Disease 2019	Perdita di liquor come temibile complicanza dell'esecuzione di un tampone nasofaringeo; tuttavia, la paziente aveva un difetto preesistente della base cranica.	In March 2020, coronavirus disease 2019 (COVID-19) emerged as a global pandemic. Testing for presence of active severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is 1 pillar of the global response. In particular, nasopharyngeal, anterior nasal, and midturbinate swabs are 3 of the 5 methods for initial diagnostic specimen collection recommended by the US Centers for Disease Control and Prevention (CDC). However, complications associated with nasal swab testing are not well characterized. We describe the first case of a cerebrospinal fluid (CSF) leak after nasal testing for COVID-19, to our knowledge.
Tyan K et al	Considerations for the Selection and Use of	Guida alla selezione dei prodotti più adeguati alla	Proper disinfection using adequate disinfecting agents will be necessary for infection control strategies against coronavirus

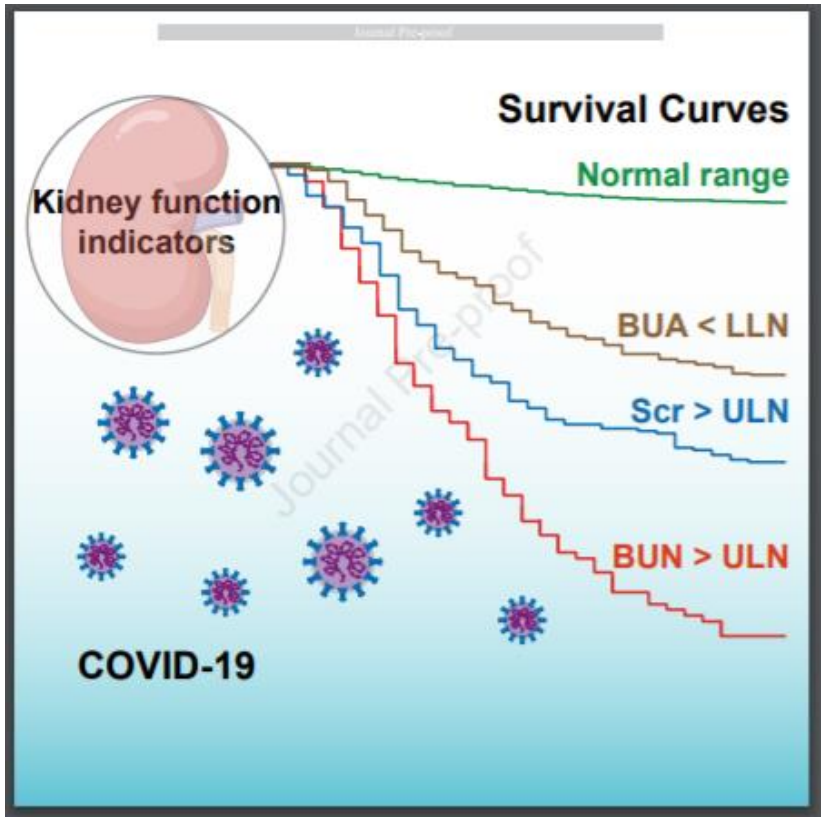
Open Forum Infectious Diseases https://academic.oup.com/ofid/article/7/9/ofaa396/5899802	Disinfectants Against SARS-CoV-2 in a Health Care Setting.	disinfezione contro SARS-CoV-2 in ambiente sanitario.	disease 2019 (COVID-19). However, limited guidance exists on effective surface disinfectants or best practices for their use against severe acute respiratory coronavirus 2. We outlined a process of fully characterizing over 350 products on the Environmental Protection Agency List N, including pH, method of delivery, indication for equipment sterilization, and purchase availability. We then developed a streamlined set of guidelines to help rapidly evaluate and select suitable disinfectants from List N, including practicality, efficacy, safety, and cost/availability. This resource guides the evaluation of ideal disinfectants amidst practical considerations posed by the COVID-19 pandemic.

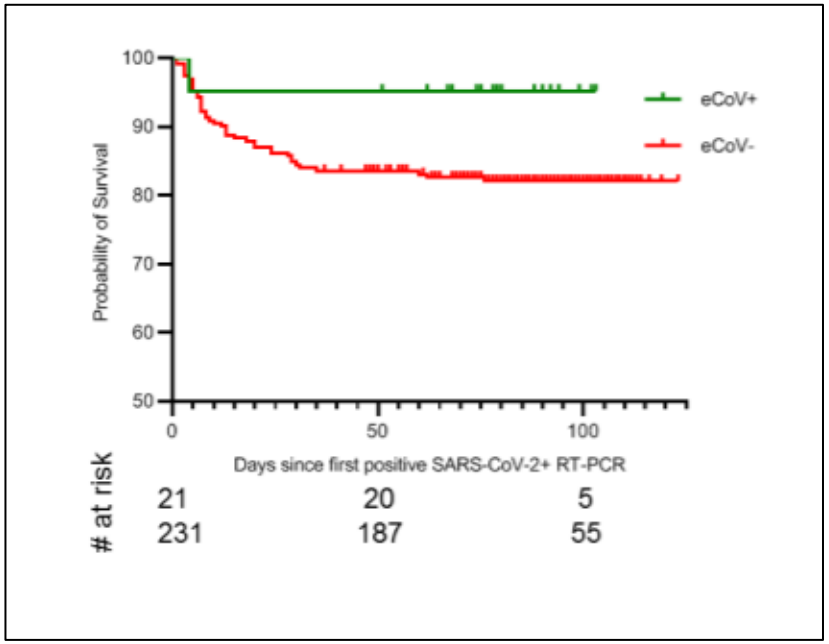
Table 1. Considerations for the Selection of a Disinfectant Against SARS-CoV-2

Consideration	Key Questions
Efficacy against SARS-CoV-2	• Does this product have an emerging viral pathogen claim? • What is the wet-contact time required to kill SARS-CoV-2?
Safety profile	• What is the pH of the product? • Does the product have potential for toxicity or irritation?
Practicality (ease of use, surface compatibility)	• What is the method of delivery (premoistened wipe, spray, concentrate requiring dilution, etc.)? • Can this product be delivered through multiple modalities to allow for flexibility (spray bottle with dry wipe packs vs saturating wipe rolls in a bucket, etc.)? • What surface types/equipment is the disinfectant compatible with?
Availability and cost	• Is this product currently commercially available, and will it remain available for repurchase? • Is this product economical for the health care institution?

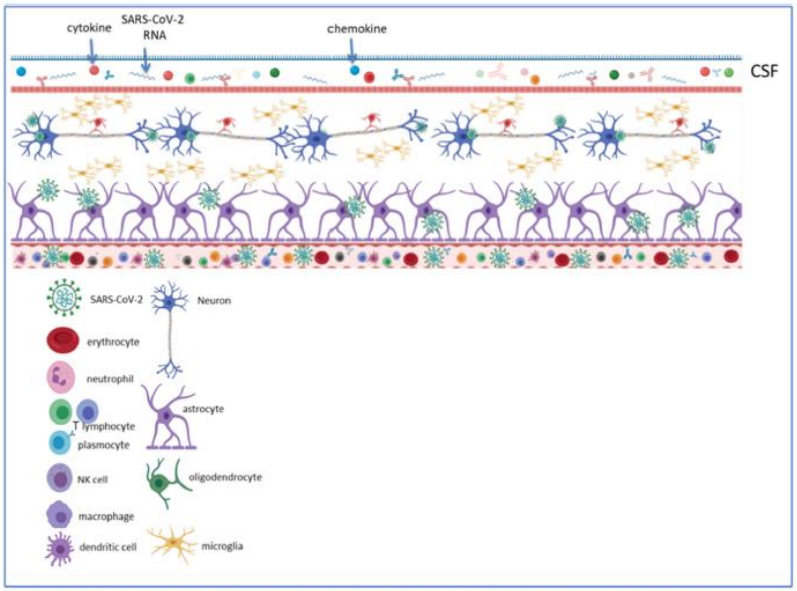
Abbreviation: SARS-CoV-2, severe acute respiratory coronavirus 2.

Goldman JD et al medRxiv https://doi.org/10.1101/2020.09.22.20192443	Reinfection with SARS-CoV-2 and Failure of Humoral Immunity: a case report.	Descrizione della durata dello shedding virale di 176 pazienti testati per SARS-CoV-2. Nel caso di un paziente sessantenne con storia di polmonite in marzo 2020, si dimostra una reinfezione sintomatica in luglio dovuta a un virus filogeneticamente distinto e una ridotta risposta anticorpale.	Recovery from COVID-19 is associated with production of anti-SARS-CoV-2 antibodies, but it is uncertain whether these confer immunity. We describe viral RNA shedding duration in hospitalized patients and identify patients with recurrent shedding. We sequenced viruses from two distinct episodes of symptomatic COVID-19 separated by 144 days in a single patient, to conclusively describe reinfection with a new strain harboring the spike variant D614G. With antibody and B cell analytics, we show correlates of adaptive immunity, including a differential response to D614G. Finally, we discuss implications for vaccine programs and begin to define benchmarks for protection against reinfection from SARS-CoV-2.
Liu YM et aò Med https://www.cell.com/med/pdf/S2666-6340(20)30017-9.pdf?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS266663402030017 9%3Fshowall%3Dtrue	Kidney function indicators predict adverse outcomes of COVID-19	Studio retrospettivo su 12413 pazienti ricoverati per COVID-19: creatinina e azoto ureico elevati e acido urico ridotto all'ingresso sono associati alla mortalità per ogni causa.	Background. The coronavirus disease 2019 (COVID-19) is an emerged respiratory infectious disease with kidney injury as a part of the clinical complications. However, the dynamic change of kidney function and its association with COVID-19 prognosis are largely unknown. Methods. In this multicenter retrospective cohort study, we analyzed clinical characteristics, medical history, laboratory tests, and treatment data of 12,413 COVID-19 patients. The patient cohort was stratified according to the severity of the outcome into three groups: non-severe, severe, and death. Findings. The prevalence of elevated blood urea nitrogen (BUN), elevated serum creatinine (Scr), and decreased blood uric acid (BUA) at admission was 6.29%, 5.22%, 11.66%, respectively. The trajectories showed elevation of BUN level and Scr level, as well as a reduction of BUA level during 28 days after admission in death cases. Increased all-cause mortality risk was associated with elevated baseline levels of BUN and Scr, and decreased level of BUA.

			Conclusion. The dynamic changes of the three kidney function markers were associated with different severity and poor prognosis of COVID-19 patients. BUN showed close association and high potential for predicting adverse outcomes in COVID-19 patients for severity stratification and triage. 
Sagar M et al Journal of Clinical Investigation	Recent endemic coronavirus infection is associated with less severe COVID-19.	Differenza di gravità e outcome di COVID-19 fra 875 pazienti con storia recente di infezione da parte dei Coronavirus	Four different endemic coronaviruses (eCoVs) are etiologic agents for the seasonal "common cold," and these eCoVs share extensive sequence homology with human severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Here, we show that individuals with as

https://dm5migu4zj3pb.cloudfront.net/manuscripts/143000/143380/cache/143380.1-20200930130923-covered-253bed37ca4c1ab43d105aefdf7b5536.pdf		endemici (eCoV) e 15053 pazienti non recentemente infettati, a suggerire una cross-reattività che potrebbe conferire un vantaggio immunitario.	compared to without a relatively recent documented eCoV were tested at greater frequency for respiratory infections but had similar rate of SARS-CoV-2 acquisition. Importantly, the patients with a previously detected eCoV had less severe coronavirus disease-2019 (COVID-19) illness. Our observations suggest that pre-existing immune responses against endemic human coronaviruses can mitigate disease manifestations from SARS-CoV-2 infection. 
Pitscheider L et al European Journal of Neurology	Muscle involvement in SARS-CoV-2 infection.	Analisi retrospettiva delle caratteristiche di 351 pazienti ricoverati per infezione da SARS-CoV-2 e 258 per influenza, al fine di confrontare i marker e la	BACKGROUND: Since the outbreak of the SARS-CoV-2 pandemic several reports indicated neurological involvement in COVID-19 disease. Muscle involvement has also been reported as evidenced by creatine kinase (CK) elevations and reports of myalgia. METHODS: CK, markers of inflammation, pre-existing diseases and statin use were extracted from records of Austrian hospitalized COVID-19 patients. Disease severity was classified as severe in case

https://onlinelibrary.wiley.com/doi/10.1111/ene.14564		gravità del danno muscolare.	of intensive care unit (ICU) admission or mortality. COVID-19 patients were additionally compared to a historical group of hospitalized influenza patients. RESULTS: 351 patients with SARS-CoV-2 and 258 with influenza were included in the final analysis. CK was elevated in 27% of COVID-19 and in 28% of influenza patients. CK was higher in severe COVID-19 as were markers of inflammation. CK correlated significantly with inflammation markers, which had an independent impact on CK when adjusted for demographic variables and disease severity. Compared to influenza patients, COVID-19 patients were older, more frequent male, had more comorbidities and more frequently a severe disease course. Nevertheless, influenza patients had higher baseline CK than COVID-19, and 35.7% of ICU admitted patients had CK levels > 1000 U/l compared to only 4.7% of ICU-admitted COVID-19 patients. CONCLUSIONS: HyperCKemia occurs in a similar frequency in COVID-19 and influenza infection. CK levels were lower in COVID-19 than in influenza in mild and severe disease. CK levels strongly correlate with disease severity and markers of inflammation. To date it remains unclear whether hyperCKemia is due to a virus-triggered inflammatory response or direct muscle toxicity.
Lima M et al Current Treatment Options in Neurology https://link.springer.com/article/10.1007%2Fs11940-020-00647-z	Unraveling the Possible Routes of SARS-COV-2 Invasion into the Central Nervous System	Vie di invasione neuronale ed ematogena del sistema nervoso centrale da parte di SARS-CoV-2.	Purpose of Review: To describe the possible neuroinvasion pathways of Severe Acute Respiratory Syndrome-related Coronavirus-2 (SARS-CoV-2), the virus responsible for the Coronavirus disease-19 (Covid-19) pandemic. Recent Findings: We present data regarding the family of Coronaviruses (CoVs) and the central nervous system (CNS), and describe parallels between SARS-CoV-2 and other members of the family, which have been investigated in more depth and combine these findings with the recent advancements regarding SARS-CoV-2. Summary: SARS-CoV-2 like other CoVs is neuroinvasive, neurotropic and neurovirulent.

			Two main pathways of CNS penetration seem to be the strongest candidates, the hematogenous and the neuronal. Tauhe olfactory route in particular appears to play a significant role in neuroinvasion of coronaviruses and SARS-CoV-2, as well. However, existing data suggest that other routes, involving the nasal epithelium in general, lymphatic tissue and the CSF may also play roles in SARS-CoV-2 invasion into the CNS.  **Fig. 3. The CNS microenvironment following SARS-CoV-2 infection.** Spread of SARS-CoV-2 from lungs to the CNS can most likely be achieved through the haematogenous route. In addition, it can enter the CNS through the olfactory bulb, and once the infectious agent persists due to the inability of the immune system to control/suppress viral replication, the virus may reach the whole brain and the CSF, and participate in demyelination. In the hematogenous route, SARS-CoV-2 may gain access by infecting endothelial cells of the blood-brain-barrier, epithelial cells of the blood-cerebrospinal fluid barrier in the choroid plexus, or it may indeed use inflammatory cells as "Trojan horse" to obtain access into the CNS. Experimental data suggest that primary glial cultures can secrete a series of inflammatory cytokines participating in the perpetuation of viral infection and further inflicting CNS tissue damage. The role of astrocytes in the machinery of SARS-CoV-2 mediated CNS pathology is yet undetermined and remains to be defined.
Pericas J et al Infectioin	Hospital at home for the management of COVID-19: preliminary experience with 63 patients.	Caratteristiche ed esito di 63 pazienti con COVID-19 dimessi precocemente o interamente gestiti fuori dall'ospedale grazie ad una	Alternatives to conventional hospitalization are needed to increase health systems resilience in the face of COVID-19 pandemic. Herein, we describe the characteristics and outcomes of 63 patients admitted to a single HaH during the peak of COVID-19 in Barcelona. Our results suggest that HaH seems to be a safe and efficacious

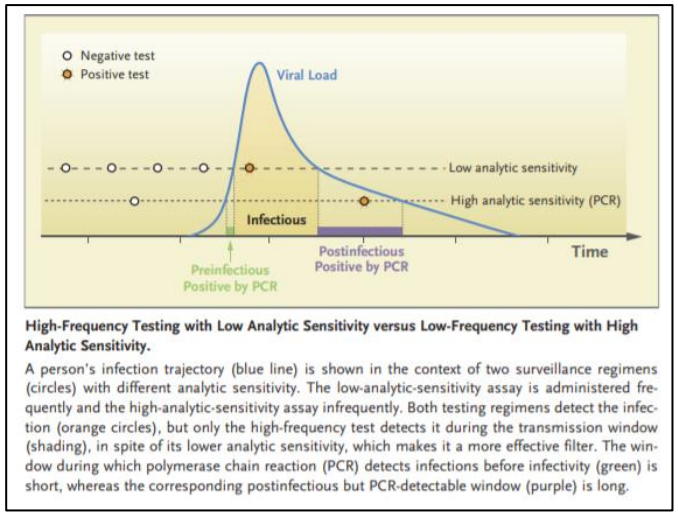
https://link.springer.com/article/10.1007/s15010-020-01527-z		unità di cure domiciliari: 3 ri-ospedalizzazioni, nessun decesso, una prospettiva per mitigare la carenza di posti letto alla ripresa dell'epidemia.	alternative to conventional hospitalization for accurately selected patients with COVID-19.
Di Castelnuovo A et al Vascular Pharmacology https://pubmed.ncbi.nlm.nih.gov/32992048/	RAAS inhibitors are not associated with mortality in COVID-19 patients: findings from an observational multicenter study in Italy and a meta-analysis of 19 studies	Da uno studio retrospettivo osservazionale multicentrico italiano su 4069 pazienti non emerge una associazione fra uso di ACE-inibitori e/o sartani e mortalità per COVID-19. Ciò è confermato anche da una metanalisi degli studi disponibili.	Objective: The hypothesis that been set forward that use of Renin Angiotensin Aldosterone System (RAAS) inhibitors is associated with COVID-19 severity. We set-up a multicenter Italian collaboration (CORIST Project, ClinicalTrials.gov ID: NCT04318418) to retrospectively investigate the relationship between RAAS inhibitors and COVID-19 in-hospital mortality. We also carried out an updated meta-analysis on the relevant studies. Methods: We analyzed 4,069 unselected patients with laboratory-confirmed SARS-CoV-2 infection and hospitalized in 34 clinical centers in Italy from February 19, 2020 to May 23, 2020. The primary end-point in a time-to event analysis was in-hospital death, comparing patients who received angiotensin-converting-enzyme inhibitors (ACE-I) or angiotensin-receptor blockers (ARB) with patients who did not. Articles for the meta-analysis were retrieved until July 13th, 2020 by searching in web-based libraries, and data were combined using the general variance-based method. Results: Out of 4,069 COVID-19 patients, 13.5% and 13.3% received ACE-I or ARB, respectively. Use of neither ACE-I nor ARB was associated with mortality (multivariable hazard ratio (HR) adjusted also for COVID-19 treatments: 0.96, 95% confidence interval 0.77-1.20 and HR=0.89, 0.67-1.19 for ACE-I and ARB, respectively). Findings were similar restricting the analysis to hypertensive (N=2,057) patients (HR=1.00, 0.78-1.26 and HR=0.88, 0.65-1.20) or when ACE-I or ARB were considered as a single group. Results from

			the meta-analysis (19 studies, 29,057 COVID-19 adult patients, 9,700 with hypertension) confirmed the absence of association. Conclusions: In this observational study and meta-analysis of the literature, ACE-I or ARB use was not associated with severity or in-hospital mortality in COVID-19 patients.
Oliva A et al Journal of Patient Sefety https://pubmed.ncbi.nlm.nih.gov/32941344/	Liability of Health Care Professionals and Institutions During COVID-19 Pandemic in Italy: Symposium Proceedings and Position Statement	Esiti di un simposio in tema di responsabilità degli operatori sanitari e degli istituti di cura all'epoca di COVID-19.	Background: On May 12, 2020, a symposium titled "Liability of healthcare professionals and institutions during COVID-19 pandemic" was held in Italy with the participation of national experts in malpractice law, hospital management, legal medicine, and clinical risk management. The symposium's rationale was the highly likely inflation of criminal and civil proceedings concerning alleged errors committed by health care professionals and decision makers during the COVID-19 pandemic. Its aim was to identify and discuss the main issues of legal and medicolegal interest and thus to find solid solutions in the spirit of preparedness planning. Methods: There were 5 main points of discussion: (A) how to judge errors committed during the pandemic because of the application of protocols and therapies based on no or weak evidence of efficacy, (B) whether hospital managers can be considered liable for infected health care professionals who were not given adequate personal protective equipment, (C) whether health care professionals and institutions can be considered liable for cases of infected inpatients who claim that the infection was transmitted in a hospital setting, (D) whether health care institutions and hospital managers can be considered liable for the hotspots in long-term care facilities/care homes, and (E) whether health care institutions and hospital managers can be considered liable for the worsening of chronic diseases. Results and conclusion: Limitation of the liability to the cases of gross negligence (with an explicit definition of this term), a no-fault

			system with statal indemnities for infected cases, and a rigorous methodology for the expert witnesses were proposed as key interventions for successfully facing future proceedings.
Di Castelnuovo A et al Nutrition, Metabolism and Cardiovascular Diseases https://pubmed.ncbi.nlm.nih.gov/32912793/	Common cardiovascular risk factors and in-hospital mortality in 3,894 patients with COVID-19: survival analysis and machine learning-based findings from the multicentre Italian CORIST Study	Studio retrospettivo osservazionale multicentrico condotto su 3894 pazienti ricoverati per COVID-19 alla ricerca, tramite tecniche di machine learning, di fattori associati alla mortalità.	Background and aims: There is poor knowledge on characteristics, comorbidities and laboratory measures associated with risk for adverse outcomes and in-hospital mortality in European Countries. We aimed at identifying baseline characteristics predisposing COVID-19 patients to in-hospital death. Methods and results: Retrospective observational study on 3894 patients with SARS-CoV-2 infection hospitalized from February 19th to May 23rd, 2020 and recruited in 30 clinical centres distributed throughout Italy. Machine learning (random forest)-based and Cox survival analysis. 61.7% of participants were men (median age 67 years), followed up for a median of 13 days. In-hospital mortality exhibited a geographical gradient, Northern Italian regions featuring more than twofold higher death rates as compared to Central/Southern areas (15.6% vs 6.4%, respectively). Machine learning analysis revealed that the most important features in death classification were impaired renal function, elevated C reactive protein and advanced age. These findings were confirmed by multivariable Cox survival analysis (hazard ratio (HR): 8.2; 95% confidence interval (CI) 4.6-14.7 for age ≥85 vs 18-44 y); HR = 4.7; 2.9-7.7 for estimated glomerular filtration rate levels <15 vs ≥ 90 mL/min/1.73 m2; HR = 2.3; 1.5-3.6 for C-reactive protein levels ≥10 vs ≤ 3 mg/L). No relation was found with obesity, tobacco use, cardiovascular disease and related-comorbidities. The associations between these variables and mortality were substantially homogenous across all sub-groups analyses.

			Conclusions: Impaired renal function, elevated C-reactive protein and advanced age were major predictors of in-hospital death in a large cohort of unselected patients with COVID-19, admitted to 30 different clinical centres all over Italy.
Nelde A et al Nature Immunology https://www.nature.com/articles/s41590-020-00808-x	SARS-CoV-2-derived peptides define heterologous and COVID-19-induced T cell recognition	Identificazione di epitopi di SARS-CoV-2 identificati dai linfociti T.	T cell immunity is central for the control of viral infections. To characterize T cell immunity, but also for the development of vaccines, identification of exact viral T cell epitopes is fundamental. Here we identify and characterize multiple dominant and subdominant SARS-CoV-2 HLA class I and HLA-DR peptides as potential T cell epitopes in COVID-19 convalescent and unexposed individuals. SARS-CoV-2-specific peptides enabled detection of post-infectious T cell immunity, even in seronegative convalescent individuals. Cross-reactive SARS-CoV-2 peptides revealed pre-existing T cell responses in 81% of unexposed individuals and validated similarity with common cold coronaviruses, providing a functional basis for heterologous immunity in SARS-CoV-2 infection. Diversity of SARS-CoV-2 T cell responses was associated with mild symptoms of COVID-19, providing evidence that immunity requires recognition of multiple epitopes. Together, the proposed SARS-CoV-2 T cell epitopes enable identification of heterologous and post-infectious T cell immunity and facilitate development of diagnostic, preventive and therapeutic measures for COVID-19.

Denina M et al The Pediatric Infectious Disease Journal https://journals.lww.com/pidj/Abstract/9000/Sequelae_of_COVID_19_in_Hospitalized_Children__A.96024.aspx	Sequelae of COVID-19 in Hospitalized Children: A 4-Months Follow-Up.	Caratteristiche di una coorte di 25 bambini con storia di COVID-19 in cui si dimostrano scarse sequele a distanza.	Little is known about the sequelae of SARS-CoV-2 infection in children. In a COVID-19 dedicated clinic, we followed-up for 4 months 25 children previously hospitalized for COVID-19, performing clinical, laboratory, and lung ultrasound evaluation. Mid-term sequelae were rarely observed in our COVID-19 children's cohort.
Karatayev VA et al Proceedings of the National Academy of Science https://www.pnas.org/content/117/39/24575	Local lockdowns outperform global lockdown on the far side of the COVID-19 epidemic curve	In base a un modello sviluppato per l'Ontario, Canada, ogni realtà locale (provincia) dovrebbe poter stabilire criteri propri per l'inizio di un periodo di lockdown.	During the COVID-19 pandemic, decision makers are grappling with how to reopen (and possibly reclose) their jurisdictions as the number of cases ebbs and flows. Establishing a criterion for each county/municipality to open and close based on their case count has appeal, given the wide disparity in COVID-19 rates in urban versus rural settings. Our simulation model is based on the geography, epidemiology, and travel patterns of Ontario, Canada. It shows that the county-by-county approach causes fewer days of closure and impacts fewer people than a strategy that opens or closes the entire province together. This is true even if individuals begin traveling to reopened counties with higher frequency. The county-by-county strategy is most effective when the criteria are coordinated.
Pollard MS et al JAMA	Changes in Adult Alcohol Use and Consequences During the COVID-19 Pandemic in the US	Questionario condotto su 6000 adulti per valutare la modifica del consumo di alcool prima e dopo la pandemia da COVID-19.	As stay-at-home orders began in some US states as a mitigation strategy for coronavirus disease 2019 (COVID-19) transmission, Nielsen reported a 54% increase in national sales of alcohol for the week ending March 21, 2020, compared with 1 year before; online sales increased 262% from 2019. Three weeks later, the World Health Organization warned that alcohol use during the pandemic

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2770975			may potentially exacerbate health concerns and risk-taking behaviors.This study examines individual-level changes in alcohol use and consequences associated with alcohol use in US adults, as well as demographic disparities, from before to during the COVID-19 pandemic.
Mina M et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMp2025631	Rethinking Covid-19 Test Sensitivity — A Strategy for Containment	Riflessione sulle caratteristiche ideali di un test per lo screening di SARS-CoV-2 nella popolazione.	It's time to change how we think about the sensitivity of testing for Covid-19. The Food and Drug Administration (FDA) and the scientific community are currently almost exclusively focused on test sensitivity, a measure of how well an individual assay can detect viral protein or RNA molecules. Critically, this measure neglects the context of how the test is being used. Yet when it comes to the broad screening the United States so desperately needs, context is fundamental. The key question is not how well molecules can be detected in a single sample but how effectively infections can be detected in a population by the repeated use of a given test as part of an overall testing strategy — the sensitivity of the testing regimen.  **High-Frequency Testing with Low Analytic Sensitivity versus Low-Frequency Testing with High Analytic Sensitivity.** A person's infection trajectory (blue line) is shown in the context of two surveillance regimens (circles) with different analytic sensitivity. The low-analytic-sensitivity assay is administered frequently and the high-analytic-sensitivity assay infrequently. Both testing regimens detect the infection (orange circles), but only the high-frequency test detects it during the transmission window (shading), in spite of its lower analytic sensitivity, which makes it a more effective filter. The window during which polymerase chain reaction (PCR) detects infections before infectivity (green) is short, whereas the corresponding postinfectious but PCR-detectable window (purple) is long.