RICERCA BIBLIOGRAFICA COVID 19

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FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE

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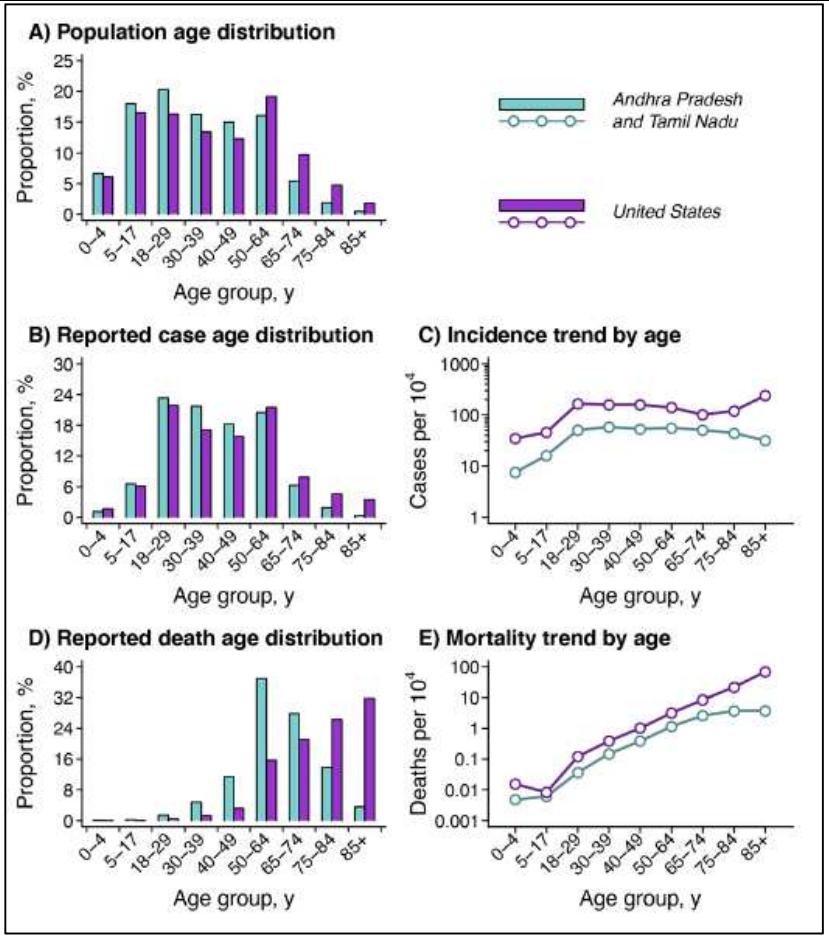
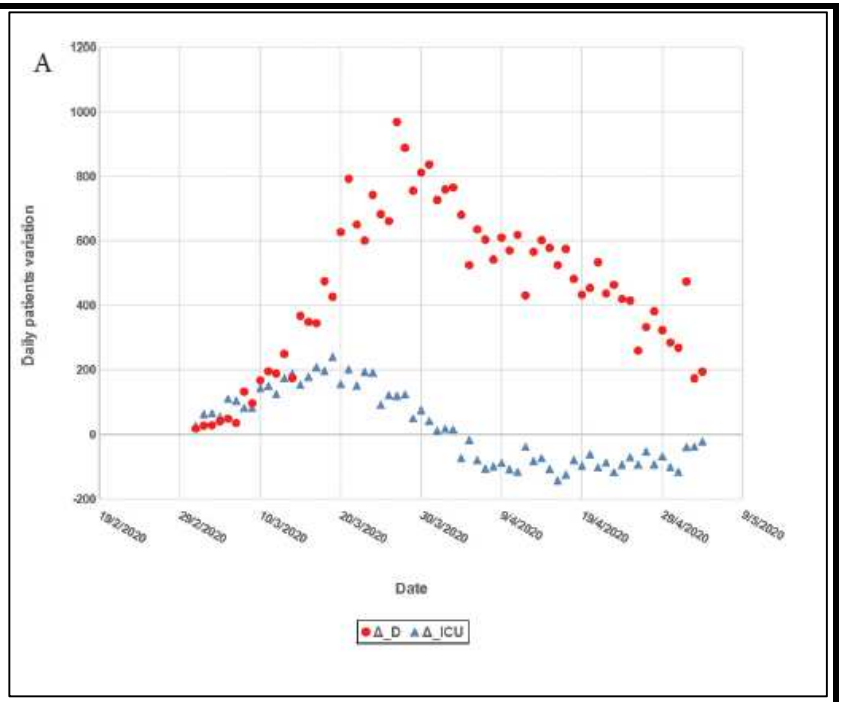
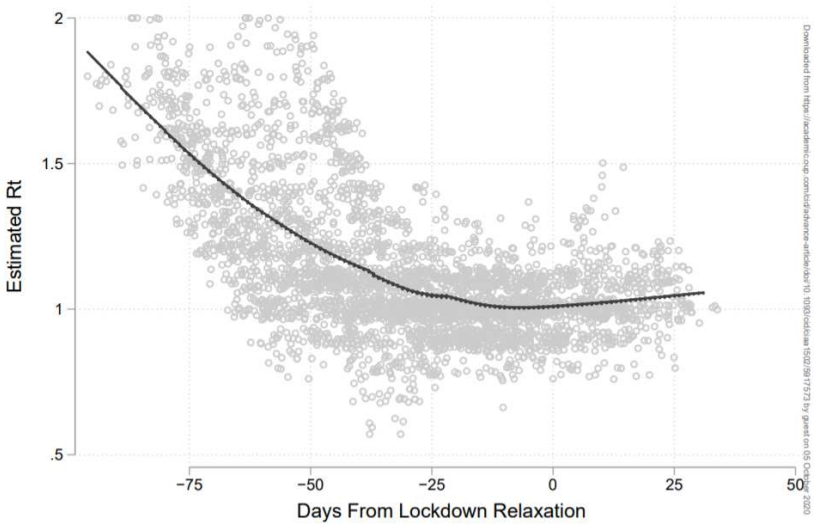
AUTORE/RIVISTA	TITOLO	OUTCOME PRINCIPALE	ABSTRACT
Laxminarayan R et al Science https://science.sciencemag.org/content/early/2020/09/29/science.abd7672	Epidemiology and transmission dynamics of COVID-19 in two Indian states	Epidemiologia dell'infezione da SARS-CoV-2 in due grandi stati indiani come paradigma della diffusione in aree a basso reddito.	Although most COVID-19 cases have occurred in low-resource countries, little is known about the epidemiology of the disease in such contexts. Data from the Indian states of Tamil Nadu and Andhra Pradesh provide a detailed view into SARS-CoV-2 transmission pathways and mortality in a high-incidence setting. Reported cases and deaths have been concentrated in younger cohorts than expected from observations in higher-income countries, even after accounting for demographic differences across settings. Among 575,071 individuals exposed to 84,965 confirmed cases, infection probabilities ranged from 4.7-10.7% for low-risk and high-risk contact types. Same-age contacts were associated with the greatest infection risk. Case-fatality ratios spanned 0.05% at ages 5-17 years to 16.6% at ages ≥85 years. Primary data are urgently needed from low-resource countries to guide control measures.

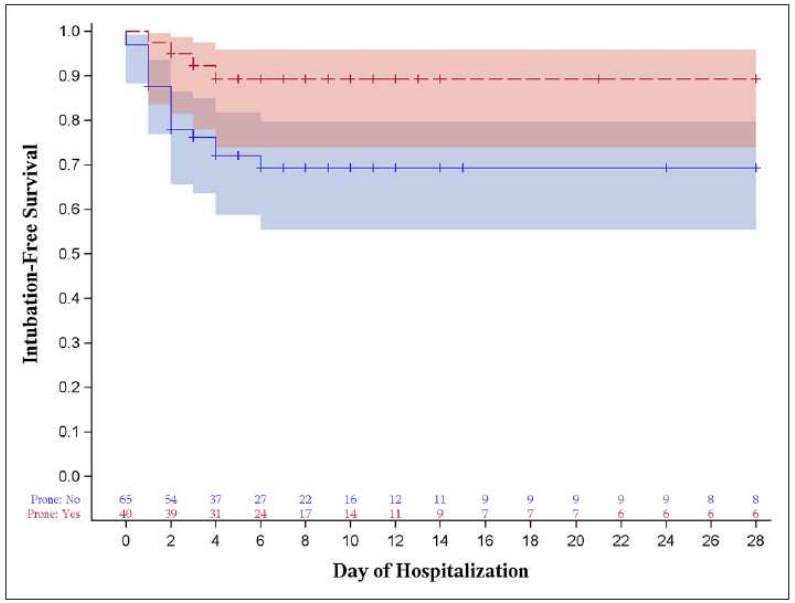
			
Ortosecco G et al Journal of Epidemiology and Global Health	First 70 Days Critical Data Trend for COVID-19 in Four Regions of Northern Italy: A Pilot Study.	Analisi dell'andamento del numero di ricoveri in rianimazione (ICU in figura) e dei decessi (D in figura) per COVID-19 in Italia - con dettaglio su quattro regioni	The new coronavirus syndrome (COVID-19) is a multi-organ pathological manifestation that, in severe forms, causes greater damage to the respiratory system, especially in the lung district with severe respiratory failure. In many cases, especially in elderly patients with high comorbidity degree, the disease can have a rapid course with a fatal outcome. Specifically, the data relating to the four Italian regions most affected by the effects of the new

https://www.atlantis-press.com/journals/jegh/125944291#volume-9		del nord - dal 24 febbraio al 4 maggio 2020.	coronavirus Severe Acute Respiratory Syndrome-CoronaVirus-2 (SARS-CoV-2), namely Lombardia, Veneto, Emilia Romagna and Piemonte, were assessed. In this work, we decided to focus the analysis only on data relating to patients admitted to the intensive care unit and to patients who died in Italy with COVID-19 in the period 24 February-4 May 2020. We used a data set where each point was an expression not of a single day, but of a longer period of time (date-points method). The article clearly identifies the phases in which the epidemic was articulated at national level and in the observed regions. Both the overall national data and the data referring to the most affected regions show an initial exponential mortality trend up to March 21st approximately. From this point the restrictive measures adopted from March 10th shows their effects and the trend first increases only linearly and then finally decreases, also thanks to the implementation of therapeutic strategies aimed at modulating respiratory distress and the clinical condition of thromboembolism, typical of critical patient COVID-19.

			
Tsai A et al Clinical Infecitous Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1502/5917573	COVID-19 transmission in the U.S. before vs. after relaxation of statewide social distancing measures.	Effetto sulla diffusione di SARS-CoV-2 dell'introduzione e dell'allentamento delle misure obbligatorie di distanziamento sociale negli USA.	BACKGROUND: Weeks after issuing social distancing orders to suppress severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission and reduce growth in cases of severe coronavirus disease 2019 (COVID-19), all U.S. states and the District of Columbia partially or fully relaxed these measures. METHODS: We identified all statewide social distancing measures that were implemented and/or relaxed in the U.S. between March 10-July 15, 2020, triangulating data from state government and third-party sources. Using segmented linear regression, we estimated the extent to which relaxation of social distancing affected epidemic control, as indicated by the time-varying, state-specific effective reproduction number (Rt). RESULTS: In the eight weeks prior to

			relaxation, mean Rt declined by 0.012 units per day (95% CI, -0.013 to -0.012), and 46/51 jurisdictions achieved Rt < 1.0 by the date of relaxation. After relaxation of social distancing, Rt reversed course and began increasing by 0.007 units per day (95% CI, 0.006-0.007), reaching a mean Rt of 1.16 eight weeks later, with only 9/51 jurisdictions maintaining Rt <1.0. Parallel models showed similar reversals in the growth of COVID-19 cases and deaths. Indicators often used to motivate relaxation at the time of relaxation (e.g. test positivity rate <5%) predicted greater post-relaxation epidemic growth. CONCLUSIONS: We detected an immediate and significant reversal in SARS-CoV-2 epidemic suppression after relaxation of social distancing measures across the U.S. Premature relaxation of social distancing measures undermined the country's ability to control the disease burden associated with COVID-19. 

Jagan N et al Critical Care Med https://journals.lww.com/ccejournal/Fulltext/2020/10000/The_POSITIONED_Study__Prone_Positioning_in.20.aspx	The POSITIONED Study: Prone Positioning in Nonventilated Coronavirus Disease 2019 Patients—A Retrospective Analysis	Analisi retrospettiva sui dati di 105 pazienti non intubati con COVID-19: la pronazione autonoma riduce il rischio di intubazione orotracheale e di morte.	Given perceived similarities between coronavirus disease 2019 pneumonia and the acute respiratory distress syndrome, we explored whether awake self-proning improved outcomes in coronavirus disease 2019-infected patients treated in a rural medical center with limited resources during a significant local coronavirus disease 2019 outbreak. Design: Retrospective analysis of prospectively collected clinical data. Setting: Single-center rural community-based medical center in Grand Island, NE. Patients: One hundred five nonintubated, coronavirus disease-infected patients. Interventions: None. Measurements and Main Results: After patients were educated on the benefits of awake self-proning, compliance was voluntary. The primary outcome was need for intubation during the hospital stay; secondary outcomes included serial peripheral capillary oxygen saturation measured by pulse oximetry to the Fio2 ratios, in-hospital mortality, and discharge disposition. Of 105 nonintubated, coronavirus disease-infected patients, 40 tolerated awake self-proning. Patients who were able to prone were younger and had lower disease severity. The risk of intubation was lower in proned patients after adjusting for disease severity using Sequential Organ Failure Assessment scores (adjusted hazard ratio, 0.30; 95% CI, 0.09–0.96; p = 0.043) or Acute Physiology and Chronic Health Evaluation II scores (adjusted hazard ratio, 0.30; 95% CI, 0.10–0.91; p = 0.034). No prone patient died compared with 24.6% of patients who were not prone (p < 0.001; number needed to treat = 5; 95% CI, 3–8). The probability of being discharged alive and peripheral

			capillary oxygen saturation measured by pulse oximetry to the Fio2 ratios were statistically similar for both groups. Conclusions: Awake self-proning was associated with lower mortality and intubation rates in coronavirus disease 2019-infected patients. Prone positioning appears to be a safe and inexpensive strategy to improve outcomes and spare limited resources. Prospective efforts are needed to better delineate the effect of awake proning on oxygenation and to improve patients' ability to tolerate this intervention.  **Figure 1.** Time-to-intubation stratified by prone status (log-rank $p = 0.023$). *Shaded areas* represent 95% CIs.
Chaijamorn W et al Critical Care Med	Antiviral Dosing Modification for Coronavirus Disease 2019–Infected Patients	Revisione dei dati, scarsi, sull'ottimizzazione del dosaggio della terapia antivirale nei pazienti sottoposti a ECMO	Previous literature regarding coronavirus disease 2019 outlined a presence of organ dysfunction including acute respiratory distress syndrome and acute kidney injury that are linked to mortality. Several patients require extracorporeal therapy. This review aims to

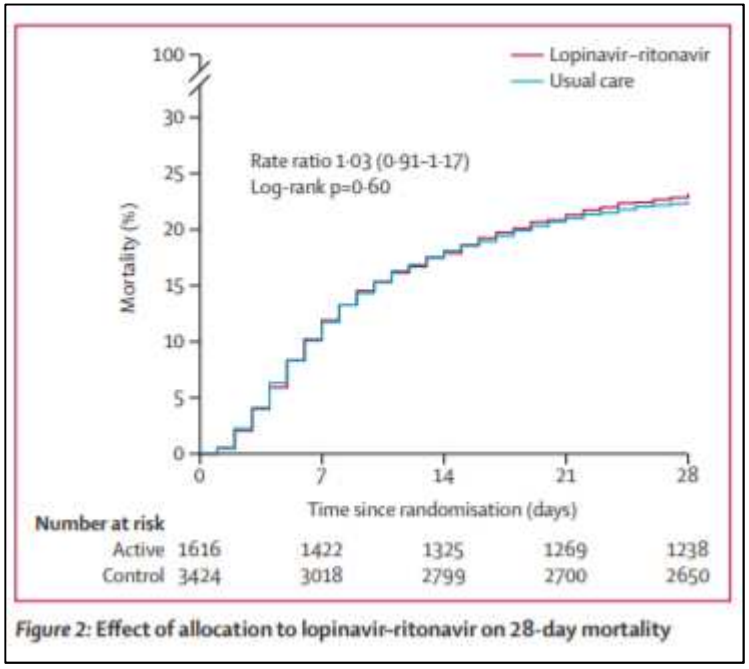
https://journals.lww.com/ccejournal/Fulltext/2020/10000/Antiviral_Dosing_Modification_for_Coronavirus.17.aspx	Receiving Extracorporeal Therapy	(ossigenazione extracorporea).	gather available published resources including physicochemical and pharmacokinetic properties and suggests antiviral drug dosing adaptation for coronavirus disease 2019–infected critically ill patients receiving extracorporeal therapy. A literature search was performed using PubMed, clinical trial registries, and bibliographic review of textbooks and review articles. Unfortunately, no standard of pharmacologic management and recommendations of drug dosing for coronavirus disease 2019 infection for critically ill patients receiving extracorporeal therapy exist due to the limited data on pharmacokinetic and clinical studies. All available extracted data were analyzed to suggest the appropriate drug dosing adjustment. Antiviral drug dosing adjustments for critically ill patients receiving extracorporeal membrane oxygenation and continuous renal replacement therapy are presented in this review. Considering pathophysiologic changes, drug properties, and extracorporeal modalities, applying our suggestions is recommended.
Carsana L et al The Lancet https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30434-5/fulltext	Pulmonary post-mortem findings in a series of COVID-19 cases from northern Italy: a two-centre descriptive study	Esito di 38 esami autoptici condotti su pazienti deceduti per COVID-19 in due centri del nord Italia in febbraio-marzo 2020: frequente presenza di danno alveolare diffuso (DAD) e di microtrombosi arteriosa.	Background: COVID-19 is characterised by respiratory symptoms, which deteriorate into respiratory failure in a substantial proportion of cases, requiring intensive care in up to a third of patients admitted to hospital. Analysis of the pathological features in the lung tissues of patients who have died with COVID-19 could help us to understand the disease pathogenesis and clinical outcomes. Methods: We systematically analysed lung tissue samples from 38 patients who died from COVID-19 in two hospitals in northern Italy between Feb 29 and March 24, 2020. The most representative areas identified at macroscopic examination were selected, and tissue blocks (median seven, range five to nine) were taken from each lung and fixed in 10% buffered formalin for at least 48 h. Tissues were assessed with use of haematoxylin and eosin staining,

			immunohistochemical staining for inflammatory infiltrate and cellular components (including staining with antibodies against CD68, CD3, CD45, CD61, TTF1, p40, and Ki-67), and electron microscopy to identify virion localisation. Findings: All cases showed features of the exudative and proliferative phases of diffuse alveolar damage, which included capillary congestion (in all cases), necrosis of pneumocytes (in all cases), hyaline membranes (in 33 cases), interstitial and intra-alveolar oedema (in 37 cases), type 2 pneumocyte hyperplasia (in all cases), squamous metaplasia with atypia (in 21 cases), and platelet–fibrin thrombi (in 33 cases). The inflammatory infiltrate, observed in all cases, was largely composed of macrophages in the alveolar lumina (in 24 cases) and lymphocytes in the interstitium (in 31 cases). Electron microscopy revealed that viral particles were predominantly located in the pneumocytes. Interpretation: The predominant pattern of lung lesions in patients with COVID-19 patients is diffuse alveolar damage, as described in patients infected with severe acute respiratory syndrome and Middle East respiratory syndrome coronaviruses. Hyaline membrane formation and pneumocyte atypical hyperplasia are frequent. Importantly, the presence of platelet–fibrin thrombi in small arterial vessels is consistent with coagulopathy, which appears to be common in patients with COVID-19 and should be one of the main targets of therapy.

Sax P NEJM – HIV and ID Observations https://blogs.jwatch.org/hiv-id-observations/	Does the White House Outbreak Invalidate the Strategy of Frequent Testing for COVID-19 Control?	Significato dei test antigenici per SARS-CoV-2 anche alla luce del recente focolaio presso la Casa Bianca negli USA.	As I've written here many times, I'm hopeful that frequent, inexpensive, rapid home testing for COVID-19 will help us climb out of this pandemic mess. Let's name it the Mina Frequent Testing Plan, after my indefatigable colleague Dr. Michael Mina who has championed it for months — most recently in a perspective published in the New England Journal of Medicine.
Anjorin AA et al Tropical Medicine and International Health https://onlinelibrary.wiley.com/doi/10.1111/tmi.13504	Comorbidities and the COVID-19 Pandemic Dynamics in Africa.	Epidemiologia di COVID-19 e delle comorbidità associate nel contesto africano.	The debate around the COVID-19 response in Africa has mostly focused on effects and implications of public health measures, in light of the socio-economic peculiarities of the continent. However, there has been limited exploration of the impact of differences in epidemiology of key comorbidities, and related healthcare factors, on the course and parameters of the pandemic. We summarize what is known about (a) the pathophysiological processes underlying the interaction of co-infections and co-morbidities in shaping prognosis of COVID-19 patients, (b) the epidemiology of key co-infections and comorbidities, and the state of related healthcare infrastructure that might shape the course of the pandemic, and (c) implications of (a) and (b) for pandemic management and post-pandemic priorities. There is a critical need to generate empirical data on clinical profiles and the predictors of morbidity and mortality from COVID-19. Improved protocols for acute febrile illness and access to diagnostic facilities, not just for SARS-CoV-2 but also other viral infections, is of urgent importance. The role of Malaria, HIV/TB and chronic malnutrition on pandemic dynamics should be further investigated. Although chronic non-communicable diseases account for a relatively lighter burden, they have a significant effect on COVID-19 prognosis, and the fragility of care-delivery systems implies that adjustments to clinical procedures and re-organization of care delivery that have been

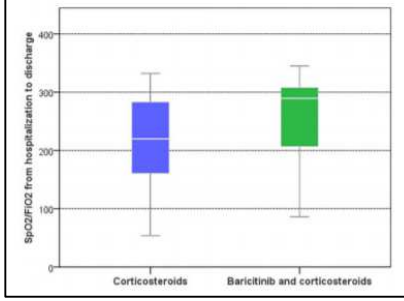
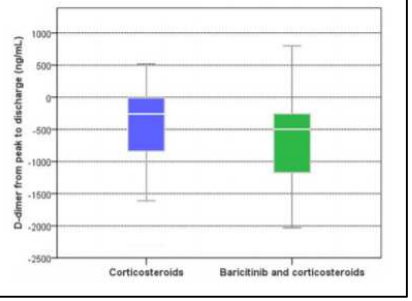
			useful in other regions are unlikely to be feasible. Africa is a large region with local variations in factors that can shape pandemic dynamics. A one-size fits all response is not optimal, but there are broad lessons relating to differences in epidemiology and healthcare delivery factors, that should be considered as part of a regional COVID-19 response framework.
Salem N et al Journal of Thrombosis and Thrombolysis https://link.springer.com/article/10.1007/s11239-020-02300-7	Thromboelastography findings in critically ill COVID-19 patients.	Studio della ipercoagulabilità tramite tromboelastografia (TEG) in 52 pazienti critici ricoverati per COVID-19.	The rate of venous and arterial thrombotic events among patients infected with severe acute respiratory syndrome coronavirus-2 (SAR-CoV-2) is high. This may be due to a hypercoagulable state induced by the severe inflammation that results from the SAR-CoV-2 infection. We aimed to determine hypercoagulable states' incidence based on thromboelastography study and its association with thrombotic events in critically ill patients with coronavirus disease 2019 (COVID-19). Fifty-two COVID-19 patients who had thromboelastography study were retrospectively included. All patients received pharmacologic thromboprophylaxis. The hypercoagulable state was observed in 16 patients (30.8%). Among them, maximum amplitude and a-angle were elevated in 75% and 25%, respectively. Reaction time and K were low in only 12.5% for both of them. Inflammatory and coagulation markers, as well as thromboprophylaxis regimens, were not associated with a hypercoagulable state. Fourteen patients (27%) experienced a total of 16 thrombotic events, including 8 (57%) deep venous thrombosis, 6 (43%) pulmonary embolism, and 2 (14.3%) arterial thrombosis. The hypercoagulable state was not significantly associated with thrombotic events. In summary, we observed a lower rate of hypercoagulable state on thromboelastography study in critically ill COVID-19 patients. Also, the hypercoagulable state was not associated with the occurrence of thrombotic events.

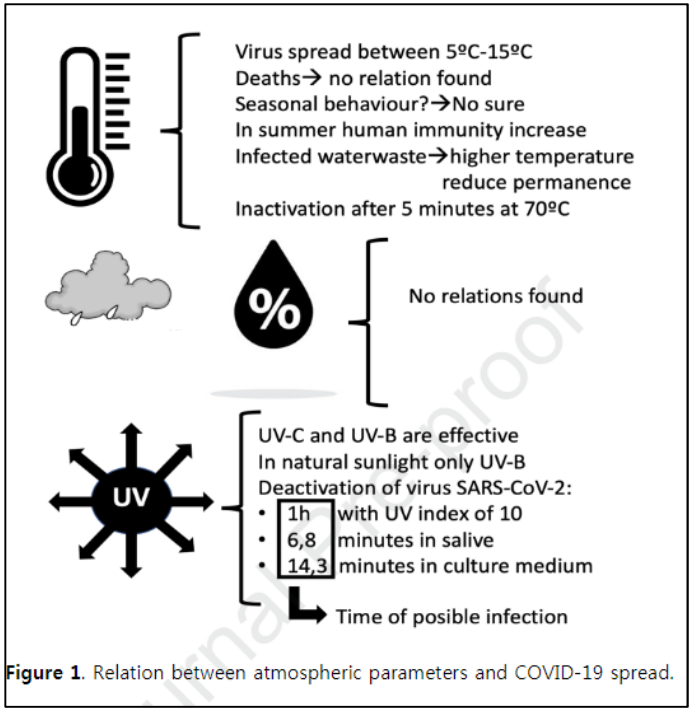
RECOVERY Collaborative Group The Lancet https://doi.org/10.1016/S0140-6736(20)32013-4	Lopinavir–ritonavir in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial.	Risultati del braccio del RECOVERY trial che confronta 1616 pazienti trattati con lopinavir/ritonavir e 3424 sottoposti a standard of care: la terapia con lopinavir/ritonavir non è supportata da alcuna evidenza di beneficio.	Background: Lopinavir–ritonavir has been proposed as a treatment for COVID-19 on the basis of in vitro activity, preclinical studies, and observational studies. Here, we report the results of a randomised trial to assess whether lopinavir–ritonavir improves outcomes in patients admitted to hospital with COVID-19. Methods: In this randomised, controlled, open-label, platform trial, a range of possible treatments was compared with usual care in patients admitted to hospital with COVID-19. The trial is underway at 176 hospitals in the UK. Eligible and consenting patients were randomly allocated to either usual standard of care alone or usual standard of care plus lopinavir–ritonavir (400 mg and 100 mg, respectively) by mouth for 10 days or until discharge (or one of the other RECOVERY treatment groups: hydroxychloroquine, dexamethasone, or azithromycin) using web-based simple (unstratified) randomisation with allocation concealment. Randomisation to usual care was twice that of any of the active treatment groups (eg, 2:1 in favour of usual care if the patient was eligible for only one active group, 2:1:1 if the patient was eligible for two active groups). The primary outcome was 28-day all-cause mortality. Analyses were done on an intention-to-treat basis in all randomly assigned participants. The trial is registered with ISRCTN, 50189673, and ClinicalTrials.gov, NCT04381936. Findings: Between March 19, 2020, and June 29, 2020, 1616 patients were randomly allocated to receive lopinavir–ritonavir and 3424 patients to receive usual care. Overall, 374 (23%) patients allocated to lopinavir–ritonavir and 767 (22%) patients allocated to usual care died within 28 days (rate ratio 1·03, 95% CI 0·91–1·17; p=0·60). Results were consistent across all prespecified subgroups of patients. We observed no significant difference in time until discharge alive from hospital (median 11 days [IQR 5 to >28] in both

			groups) or the proportion of patients discharged from hospital alive within 28 days (rate ratio 0·98, 95% CI 0·91–1·05; p=0·53). Among patients not on invasive mechanical ventilation at baseline, there was no significant difference in the proportion who met the composite endpoint of invasive mechanical ventilation or death (risk ratio 1·09, 95% CI 0·99–1·20; p=0·092). Interpretation: In patients admitted to hospital with COVID-19, lopinavir–ritonavir was not associated with reductions in 28-day mortality, duration of hospital stay, or risk of progressing to invasive mechanical ventilation or death. These findings do not support the use of lopinavir–ritonavir for treatment of patients admitted to hospital with COVID-19.  *Figure 2:* **Effect of allocation to lopinavir–ritonavir on 28-day mortality**

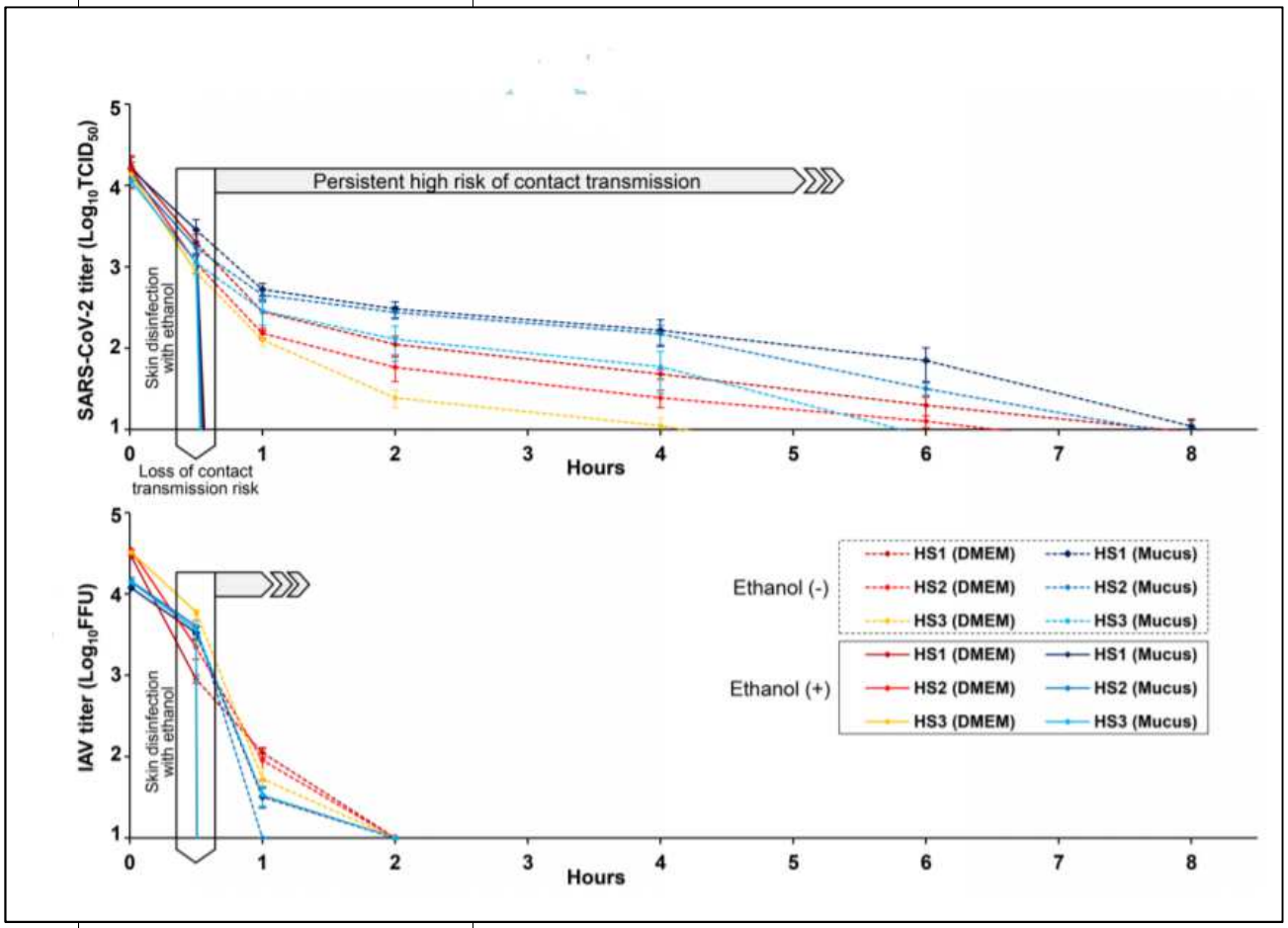
Wilt TJ et al Annals of Internal Medicine https://doi.org/10.7326/M20-5752	Remdesivir for Adults With COVID-19 : A Living Systematic Review for an American College of Physicians Practice Points.	Revisione sistematica dei dati su efficacia e sicurezza di remdesivir per pazienti con COVID-19.	Background: Few treatments exist for coronavirus disease 2019 (COVID-19). Purpose: To evaluate the effectiveness and harms of remdesivir for COVID-19. Data Sources: Several databases, tables of contents of journals, and U.S. Food and Drug Administration and company websites were searched from 1 January through 31 August 2020. Study Selection: English-language, randomized trials of remdesivir treatments for adults with suspected or confirmed COVID-19. New evidence will be incorporated using living review methods. Data Extraction: Single-reviewer abstraction and risk-of-bias assessment verified by a second reviewer; GRADE (Grading of Recommendations Assessment, Development and Evaluation) methods used for certainty-of-evidence assessments. Data Synthesis: Four randomized trials were included. In adults with severe COVID-19, remdesivir compared with placebo probably improves recovery by a large amount (absolute risk difference [ARD] range, 7% to 10%) and may result in a small reduction in mortality (ARD range, -4% to 1%) and a shorter time to recovery or clinical improvement. Remdesivir may have little to no effect on hospital length of stay. Remdesivir probably reduces serious adverse events by a moderate amount (ARD range, −6% to −8%). Compared with a 10-day remdesivir course, a 5-day course may reduce mortality, increase recovery or clinical improvement by small to moderate amounts, reduce time to recovery, and reduce serious adverse events among hospitalized patients not requiring mechanical ventilation. Recovery due to remdesivir may not vary by age, sex, symptom duration, or disease severity. Limitations: Low-certainty evidence with few published trials, including 1 preliminary report and 2 open-label trials. Trials

			excluded pregnant women and adults with severe kidney or liver disease. Conclusion: In hospitalized adults with COVID-19, remdesivir probably improves recovery and reduces serious adverse events and may reduce mortality and time to clinical improvement. For adults not receiving mechanical ventilation or extracorporeal membrane oxygenation, a 5-day course of remdesivir may provide similar benefits to and fewer harms than a 10-day course.
Rodriguez-Garcia JL et al Rheumatology https://doi.org/10.1093/rheumatology/keaa587	Baricitinib improves respiratory function in patients treated with corticosteroids for SARS-CoV-2 pneumonia: an observational cohort study.	Studio di coorte osservazionale che dimostra un possibile vantaggio nell'associazione fra steroidi e l'inibiitore di Janus Kinase (JAK) baricitinib in pazienti ospedalizzati per COVID-19.	The Janus kinase (JAK) inhibitor baricitinib may block viral entry into pneumocytes and prevent cytokine storm in patients with SARS-CoV-2 pneumonia. We aimed to assess whether baricitinib improved pulmonary function in patients treated with high-dose corticosteroids for moderate to severe SARS-CoV-2 pneumonia. Methods: This observational study enrolled patients with moderate to severe SARS-CoV-2 pneumonia [arterial oxygen partial pressure (PaO2)/fraction of inspired oxygen (FiO2) <200 mmHg] who received lopinavir/ritonavir and HCQ plus either corticosteroids (CS group, n = 50) or corticosteroids and baricitinib (BCT-CS group, n = 62). The primary end point was the change in oxygen saturation as measured by pulse oximetry (SpO2)/FiO2 from hospitalization to discharge. Secondary end points included the proportion of patients requiring supplemental oxygen at discharge and 1 month later. Statistics were adjusted by the inverse propensity score weighting (IPSW). Results: A greater improvement in SpO2/FiO2 from hospitalization to discharge was observed in the BCT-CS vs CS group (mean differences adjusted for IPSW, 49; 95% CI: 22, 77; P < 0.001). A higher proportion of patients required supplemental oxygen both at discharge (62.0% vs 25.8%; reduction of the risk by 82%, OR adjusted for IPSW, 0.18; 95% CI: 0.08, 0.43; P < 0.001) and 1 month

			later (28.0% vs 12.9%, reduction of the risk by 69%, OR adjusted for IPSW, 0.31; 95% CI: 0.11, 0.86; P = 0.024) in the CS vs BCT-CS group. Conclusions: . In patients with moderate to severe SARS-CoV-2 pneumonia a combination of baricitinib with corticosteroids was associated with greater improvement in pulmonary function when compared with corticosteroids alone. FIG. 2 Boxplot of SpO_2/FiO_2 from hospitalization to discharge by treatment group  FIG. 3 Decrease in D-dimer was more pronounced with baricitinib and corticosteroids *vs* corticosteroids alone 
Shuren J et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMp2023830	Covid-19 Molecular Diagnostic Testing — Lessons Learned	Osservazioni sulle conseguenze dell'accelerazione del processo di approvazione dei test per SARS-CoV-2 da parte della FDA e sull'importanza della comprensione dei limiti dei test diagnostici ai fini di una corretta interpretazione.	On February 4, 2020, the U.S. secretary of health and human services declared that emergency use of diagnostics for SARS-CoV-2 was justified, triggering emergency authority for the Food and Drug Administration (FDA) to grant an emergency use authorization (EUA) for a device if it reasonably believes that it may be effective, rather than waiting to grant full approval when it has reasonable assurance that the device is safe and effective. This mechanism expedites access to accurate diagnostic tests during emergencies, when information gaps and false results may adversely affect patient care and public health decision making.
Fernandez-Raga M et al Environmental Research	SARS-CoV-2 Viability under Different Meteorological Conditions, Surfaces, Fluids	Revisione delle evidenze riguardo la sopravvivenza di SARS-CoV-2 sulle superfici in diverse condizioni.	Since the COVID-19 outbreak, researchers have tried to characterise the novel coronavirus SARS-CoV-2 to better understand the pathogenic mechanisms of the virus and prevent further dissemination. As a consequence, there has been a bloom in

https://www.sciencedirect.com/science/article/pii/S0013935120311907?via%3Dihub	and Transmission between Animals		scientific research papers focused on the behaviour of the virus in different environmental contexts. Nevertheless, despite these efforts and due to its novelty, available information about this coronavirus is limited, as several research studies are still ongoing. This review aims to shed light on this issue. To that end, we have examined the scientific literature to date regarding the viability of SARS-CoV-2 on surfaces and fluids or under different environmental conditions (temperature, precipitation and UV radiation). We have also addressed the role of animals in the transmission of this coronavirus.  **Figure 1**. Relation between atmospheric parameters and COVID-19 spread.

Hirose R et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1517/5917611?searchresult=1	Survival of SARS-CoV-2 and influenza virus on the human skin: Importance of hand hygiene in COVID-19	Studio della sopravvivenza di SARS-CoV-2 a confronto con Virus dell'Influenza A sulla cute umana e sua rapida inattivazione tramite igiene con gel alcolico.	Background: The stability of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on human skin remains unknown, considering the hazards of viral exposure to humans. We generated a model that allows the safe reproduction of clinical studies on the application of pathogens to human skin and elucidated the stability of SARS-CoV-2 on the human skin. Methods: We evaluated the stability of SARS-CoV-2 and influenza A virus (IAV), mixed with culture medium or upper respiratory mucus, on human skin surfaces and the dermal disinfection effectiveness of 80% (w/w) ethanol against SARS-CoV-2 and IAV. Results: SARS-CoV-2 and IAV were inactivated more rapidly on skin surfaces than on other surfaces (stainless steel/glass/plastic); the survival time was significantly longer for SARS-CoV-2 than for IAV [9.04 h (95% confidence interval: 7.96–10.2 h) vs. 1.82 h (1.65–2.00 h)]. IAV on other surfaces was inactivated faster in mucus versus medium conditions, while SARS-CoV-2 showed similar stability in the mucus and medium; the survival time was significantly longer for SARS-CoV-2 than for IAV [11.09 h (10.22–12.00 h) vs. 1.69 h (1.57–1.81 h)]. Moreover, both SARS-CoV-2 and IAV in the mucus/medium on human skin were completely inactivated within 15 s by ethanol treatment. Conclusions: The 9-h survival of SARS-CoV-2 on human skin may increase the risk of contact transmission in comparison with IAV, thus accelerating the pandemic. Proper hand hygiene is important to prevent the spread of SARS-CoV-2 infections.


SARS-CoV-2 titer (Log10TCID50)
Persistent high risk of contact transmission
Skin disinfection with ethanol
Loss of contact transmission risk
Hours
IAV titer (Log10FFU)
Skin disinfection with ethanol
Hours
Ethanol (-)
HS1 (DMEM)
HS2 (DMEM)
HS3 (DMEM)
HS1 (Mucus)
HS2 (Mucus)
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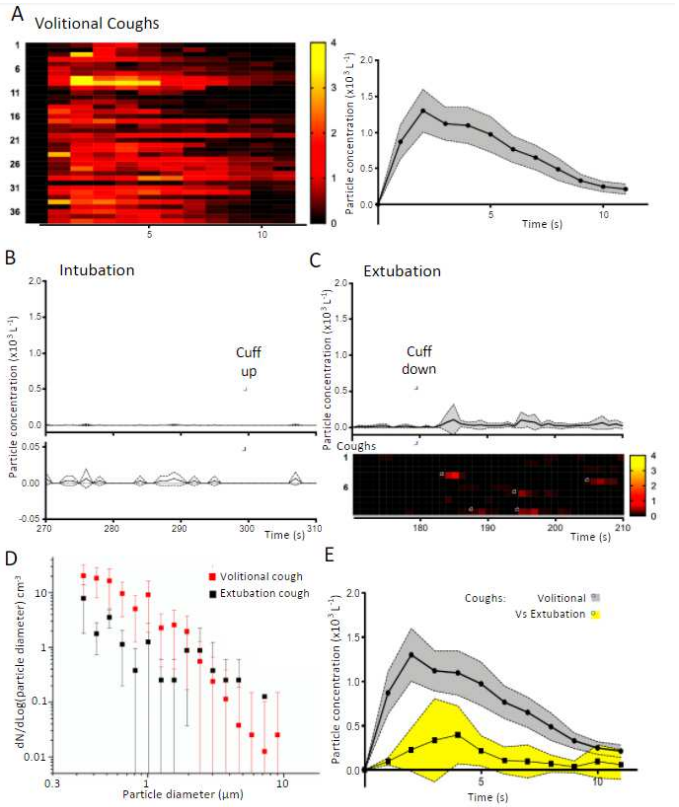
Haitao T et al Mayo Clinic Proceedings https://www.mayoclinicproceedings.org/article/S0025-6196(20)30838-7/fulltext	COVID-19 and Sex Differences: Mechanisms and Biomarkers.	Revisione delle basi molecolari delle differenze di genere nell'ambito dell'infezione da SARS-CoV-2.	Men are consistently overrepresented in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, and coronavirus disease 2019 (COVID-19) severe outcomes, including higher fatality rates. These differences are likely due to gender-specific behaviors, genetic and hormonal factors, and sex differences in biological pathways related to SARS-CoV-2 infection. Several social, behavioral, and comorbid factors are implicated in the generally worse outcomes in men compared with women. Underlying biological sex differences and their effects on COVID-19 outcomes, however, have received less attention. The present review summarizes the available literature regarding proposed molecular and cellular markers of COVID-19 infection, their associations with health outcomes, and any reported modification by sex. Biological sex differences characterized by such biomarkers exist within healthy populations and also differ with age- and sex-specific conditions, such as pregnancy and menopause. In the context of COVID-19, descriptive biomarker levels are often reported by sex, but data pertaining to the effect of patient sex on the relationship between biomarkers and COVID-19 disease severity/outcomes are scarce. Such biomarkers may offer plausible explanations for the worse COVID-19 outcomes seen in men. There is the need for larger studies with sex-specific reporting and robust analyses to elucidate how sex modifies cellular and molecular pathways associated with SARS-CoV-2. This will improve interpretation of biomarkers and clinical management of COVID-19 patients by facilitating a personalized medical approach to risk stratification, prevention, and treatment.

Livingston G et al The Lancet https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(20)30434-X/fulltext	Prevalence, management, and outcomes of SARS-CoV-2 infections in older people and those with dementia in mental health wards in London, UK: a retrospective observational study	Studio retrospettivo osservazionale che descrive le caratteristiche di 131 pazienti ricoverati in istituti di salute mentale a Londra con diagnosi di infezione da SARS-CoV-2.	Background: People living in group situations or with dementia are more vulnerable to infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Older people and those with multimorbidity have higher mortality if they become infected than the general population. However, no systematic study exists of COVID-19-related outcomes in older inpatients in psychiatric units, who comprise people from these high-risk groups. We aimed to describe the period prevalence, demographics, symptoms (and asymptomatic cases), management, and survival outcomes of COVID-19 in the older inpatient psychiatric population and people with young-onset dementia in five National Health Service Trusts in London, UK, from March 1 to April 30, 2020. Methods: In this retrospective observational study, we collected demographic data, mental health diagnoses, clinical diagnosis of COVID-19, symptoms, management, and COVID-19-related outcome data of inpatients aged 65 years or older or with dementia who were already inpatients or admitted as inpatients to five London mental health Trusts between March 1 and April 30, 2020, and information about available COVID-19-related resources (ie, testing and personal protective equipment). Patients were determined to have COVID-19 if they had a positive SARS-CoV-2 PCR test, or had relevant symptoms indicative of COVID-19, as determined by their treating physician. We calculated period prevalence of COVID-19 and analysed patients' characteristics, treatments, and outcomes. Findings: Of 344 inpatients, 131 (38%) were diagnosed with COVID-19 during the study period (period prevalence 38% [95% CI 33–43]). The mean age of patients who had COVID-19 was 75·3 years (SD 8·2); 68 (52%) were women and 47 (36%) from ethnic minority groups. 16 (12%) of 131 patients were asymptomatic and 121 (92%) had one or more disease-related comorbidity. 108 (82%) patients

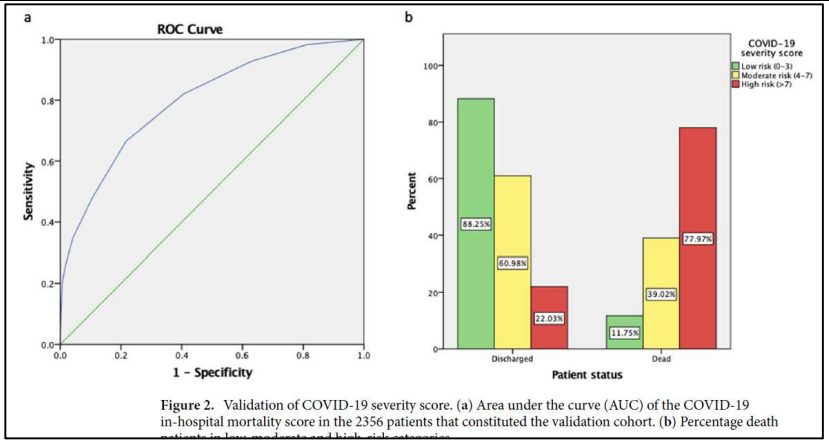
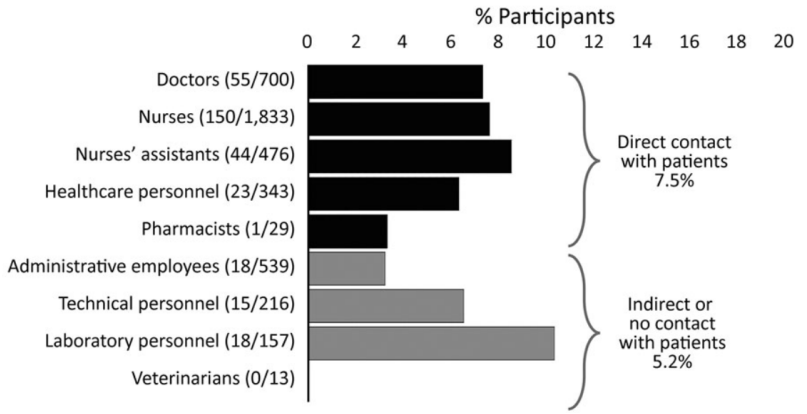
			were compulsorily detained. 74 (56%) patients had dementia, of whom 13 (18%) had young-onset dementia. On average, sites received COVID-19 testing kits 4·5 days after the first clinical COVID-19 presentation. 19 (15%) patients diagnosed with COVID-19 died during the study period, and their deaths were determined to be COVID-19 related. Interpretation: Patients in psychiatric inpatient settings who were admitted without known SARS-CoV-2 infection had a high risk of infection with SARS-CoV-2 compared with those in the community and had a higher proportion of deaths from COVID-19 than in the community. Implementation of the long-standing policy of parity of esteem for mental health and planning for future COVID-19 waves in psychiatric hospitals is urgent.
Cao B et al The Lancet https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32078-X/fulltext	Antiviral monotherapy for hospitalised patients with COVID-19 is not enough	Nel commentare i risultati recentemente pubblicati del braccio lopinavir-ritonavir del trial RECOVERY, gli autori affermano che un ruolo - probabile - degli antivirali in fase precoce di COVID-19 dovrebbe essere meglio indagato, mentre per i pazienti gravi ospedalizzati la monoterapia con antivirali è probabilmente insufficiente.	In The Lancet, the RECOVERY Collaborative Group1 report the clinical results from the RECOVERY trial—one of the largest and most productive platform trials to date among patients admitted to hospital with COVID-19—on the effectiveness of lopinavir–ritonavir treatment. Compared with the first randomised trial to investigate lopinavir–ritonavir in patients with COVID-19 by Cao and colleagues (including the authors of this Comment),2 the size of the lopinavir–ritonavir group in the RECOVERY trial was much larger and hence provides a more solid evidence base regarding possible lopinavir–ritonavir treatment effects. The trial randomly allocated 5040 patients from 176 UK hospitals (3077 men and 1963 women), and the mean age of study participants was 66·2 years (SD 15·9).1 No differences were observed between patients assigned to lopinavir–ritonavir versus usual care in the primary outcome of 28-day all-cause mortality (rate ratio 1·03, 95% CI 0·91–1·17; p=0·60) or key secondary clinical endpoints, including duration of hospital stay and the proportion of patients discharged alive from hospital. Subgroup

			analyses did not find evidence for a time-to-treatment effect or benefit in those with less severe illness. The findings of these two open-label studies support each other and conclude that lopinavir–ritonavir is not effective in improving outcomes for patients admitted to hospital with COVID-19.
NEJM Editorial Board NEJM https://www.nejm.org/doi/full/10.1056/NEJMe2029812	Dying in a Leadership Vacuum	Gli Editori di una delle più rilevanti riviste mediche del mondo rivolgono un'aspra critica ai leader politici statunitensi in merito alla gestione della pandemia di COVID-19.	Covid-19 has created a crisis throughout the world. This crisis has produced a test of leadership. With no good options to combat a novel pathogen, countries were forced to make hard choices about how to respond. Here in the United States, our leaders have failed that test. They have taken a crisis and turned it into a tragedy.
Peeples L et al Nature https://www.nature.com/articles/d41586-020-02801-8	Face masks: what the data say	La dimostrazione scientifica definitiva dell'efficacia della mascherina come misura di mitigazione della pandemia di COVID-19 è complessa ed ha forse più a che fare con lo studio del comportamento umano che non con la balistica dei droplet. Tuttavia, le evidenze disponibili fanno concludere per la sua utilità.	The science supports that face coverings are saving lives during the coronavirus pandemic, and yet the debate trundles on. How much evidence is enough?
Prather KA et al Science	Airborne transmission of SARS-CoV-2	Il punto sulla differenza fra doplet e aerosol (cut-off 100 micron) e una breve nota sulla rilevanza di	There is overwhelming evidence that inhalation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) represents a major transmission route for coronavirus disease 2019 (COVID-19). There is an urgent need to harmonize discussions about modes of virus transmission across disciplines to ensure the most effective control strategies and provide clear and consistent guidance to the

https://science.sciencemag.org/content/early/2020/10/02/science.abf0521		quest'ultimo nella trasmissione di SARS-CoV-2.	public. To do so, we must clarify the terminology to distinguish between aerosols and droplets using a size threshold of 100 µm, not the historical 5 µm (1). This size more effectively separates their aerodynamic behavior, ability to be inhaled, and efficacy of interventions.
Brown J et al Anaesthesia https://associationofanaesthetists-publications.onlinelibrary.wiley.com/doi/10.1111/anae.15292	A quantitative evaluation of aerosol generation during tracheal intubation and extubation.	In uno studio prospettico su 19 procedure di intubazione e di 14 estubazione elettiva in sala operatoria non si registra una significativa produzione di aerosol, in particolare per l'intubazione, a differenze di quanto avviene invece con la tosse. L'intubazione elettiva potrebbe non essere considerata una procedura generante aerosol.	The potential aerosolised transmission of severe acute respiratory syndrome coronavirus-2 is of global concern. Airborne precaution personal protective equipment and preventative measures are universally mandated for medical procedures deemed to be aerosol-generating. The implementation of these measures is having a huge impact on healthcare provision. There is currently a lack of quantitative evidence on the number and size of airborne particles produced during aerosol-generating procedures to inform risk assessments. To address this evidence gap, we conducted real-time, high-resolution environmental monitoring in ultraclean ventilation operating theatres during tracheal intubation and extubation sequences. Continuous sampling with an optical particle sizer allowed characterisation of aerosol generation within the zone between the patient and anaesthetist. Aerosol monitoring showed a very low background particle count (0.4 particles.l-1) allowing resolution of transient increases in airborne particles associated with airway management. A positive reference control quantitated the aerosol produced in the same setting by a volitional cough (average concentration, 732 (418) particles.l-1, n = 38). Tracheal intubation including face-mask ventilation produced very low quantities of aerosolised particles (average concentration, 1.4 (1.4) particles.l-1, n = 14, p < 0·0001 vs. cough). Tracheal extubation, particularly when the patient coughed, produced a detectable aerosol (21 (18) l-1, n = 10) which was 15-fold greater than intubation (p = 0.0004) but 35-fold less than a volitional cough (p <

			0.0001). The study does not support the designation of elective tracheal intubation as an aerosol-generating procedure. Extubation generates more detectable aerosol than intubation but falls below the current criterion for designation as a high risk aerosol-generating procedure. These novel findings from real-time aerosol detection in a routine healthcare setting provide a quantitative methodology for risk assessment that can be extended to other airway management techniques and clinical settings. They also indicate the need for reappraisal of what constitutes an aerosol-generating procedure and the associated precautions for routine anaesthetic airway management. 

Altschul D et al Scientific Reports https://www.nature.com/articles/s41598-020-73962-9	A novel severity score to predict inpatient mortality in COVID-19 patients.	Sviluppo di uno score predittivo di gravità e mortalità per COVID-19 su 2356 pazienti ospedalizzati ad Atlanta, Georgia.	COVID-19 is commonly mild and self-limiting, but in a considerable portion of patients the disease is severe and fatal. Determining which patients are at high risk of severe illness or mortality is essential for appropriate clinical decision making. We propose a novel severity score specifically for COVID-19 to help predict disease severity and mortality. 4711 patients with confirmed SARS-CoV-2 infection were included. We derived a risk model using the first half of the cohort (n = 2355 patients) by logistic regression and bootstrapping methods. The discriminative power of the risk model was assessed by calculating the area under the receiver operating characteristic curves (AUC). The severity score was validated in a second half of 2356 patients. Mortality incidence was 26.4% in the derivation cohort and 22.4% in the validation cohort. A COVID-19 severity score ranging from 0 to 10, consisting of age, oxygen saturation, mean arterial pressure, blood urea nitrogen, C-Reactive protein, and the international normalized ratio was developed. A ROC curve analysis was performed in the derivation cohort achieved an AUC of 0.824 (95% CI 0.814–0.851) and an AUC of 0.798 (95% CI 0.789–0.818) in the validation cohort. Furthermore, based on the risk categorization the probability of mortality was 11.8%, 39% and 78% for patient with low (0–3), moderate (4–6) and high (7–10) COVID-19 severity score. This developed and validated novel COVID-19 severity score will aid physicians in predicting mortality during surge periods.

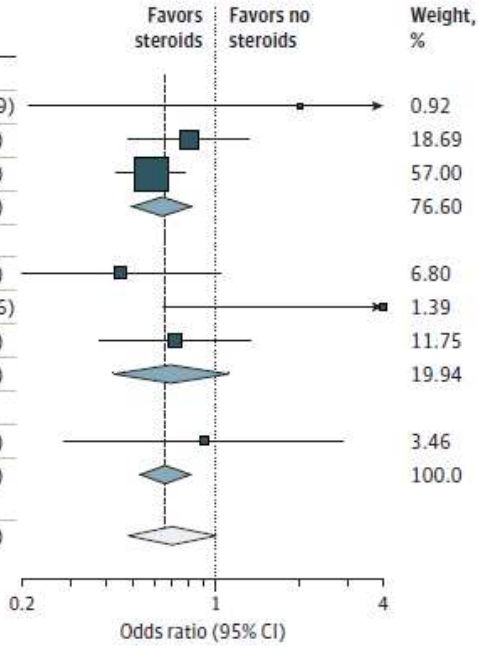
			 **Figure 2.** Validation of COVID-19 severity score. (a) Area under the curve (AUC) of the COVID-19 in-hospital mortality score in the 2356 patients that constituted the validation cohort. (b) Percentage death
Calcagno A et al Emerging Infectious Diseases https://wwwnc.cdc.gov/eid/article/27/1/20-3027_article	Risk of SARS-CoV-2 infection in healthcare workers, Turin, Italy.	Sieroprevalenza di anticorpi anti-SARS-CoV-2 fra 5444 operatori sanitari degli ospedali di Torino.	We measured severe acute respiratory syndrome coronavirus 2 spike protein subunits S1/S2 antibodies by using capillary electrophoresis and a chemiluminescence immunoassay for 5,444 active healthcare workers in Italy. Seroprevalence was 6.9% and higher among participants having contact with patients. Seroconversion was not observed in 37/213 previously infected participants. 

The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group JAMA https://jamanetwork.com/journals/jama/fullarticle/2770279	Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19	Metanalisi di 7 trial clinic randomizzati su 1703 pazienti da cui emerge che la mortalità a 28 giorni per COVID-19 è inferiore nel gruppo trattato con corticosteroidi rispetto ai trattati con standard of care o placebo.	Importance Effective therapies for patients with coronavirus disease 2019 (COVID-19) are needed, and clinical trial data have demonstrated that low-dose dexamethasone reduced mortality in hospitalized patients with COVID-19 who required respiratory support. Objective To estimate the association between administration of corticosteroids compared with usual care or placebo and 28-day all-cause mortality. Design, Setting, and Participants Prospective meta-analysis that pooled data from 7 randomized clinical trials that evaluated the efficacy of corticosteroids in 1703 critically ill patients with COVID-19. The trials were conducted in 12 countries from February 26, 2020, to June 9, 2020, and the date of final follow-up was July 6, 2020. Pooled data were aggregated from the individual trials, overall, and in predefined subgroups. Risk of bias was assessed using the Cochrane Risk of Bias Assessment Tool. Inconsistency among trial results was assessed using the I2 statistic. The primary analysis was an inverse variance–weighted fixed-effect meta-analysis of overall mortality, with the association between the intervention and mortality quantified using odds ratios (ORs). Random-effects meta-analyses also were conducted (with the Paule-Mandel estimate of heterogeneity and the Hartung-Knapp adjustment) and an inverse variance–weighted fixed-effect analysis using risk ratios. Exposures Patients had been randomized to receive systemic dexamethasone, hydrocortisone, or methylprednisolone (678 patients) or to receive usual care or placebo (1025 patients). Main Outcomes and Measures The primary outcome measure was all-cause mortality at 28 days after randomization. A secondary outcome was investigator-defined serious adverse events.

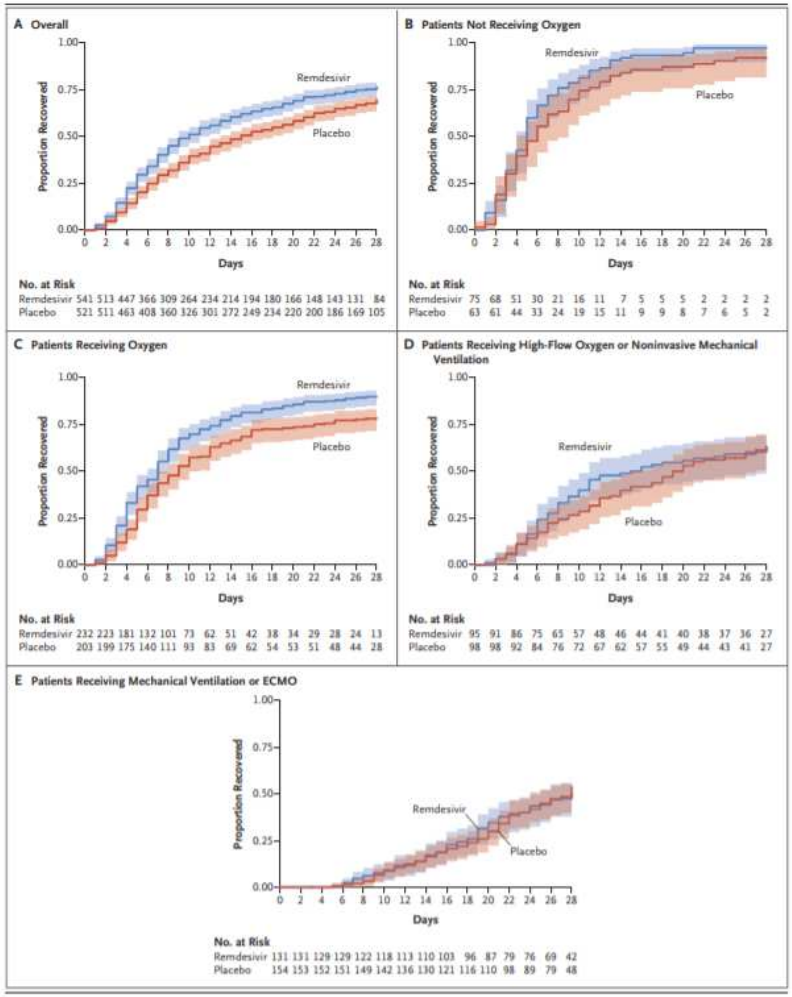
			Results A total of 1703 patients (median age, 60 years [interquartile range, 52-68 years]; 488 [29%] women) were included in the analysis. Risk of bias was assessed as “low” for 6 of the 7 mortality results and as “some concerns” in 1 trial because of the randomization method. Five trials reported mortality at 28 days, 1 trial at 21 days, and 1 trial at 30 days. There were 222 deaths among the 678 patients randomized to corticosteroids and 425 deaths among the 1025 patients randomized to usual care or placebo (summary OR, 0.66 [95% CI, 0.53-0.82]; P < .001 based on a fixed-effect meta-analysis). There was little inconsistency between the trial results (I2 = 15.6%; P = .31 for heterogeneity) and the summary OR was 0.70 (95% CI, 0.48-1.01; P = .053) based on the random-effects meta-analysis. The fixed-effect summary OR for the association with mortality was 0.64 (95% CI, 0.50-0.82; P < .001) for dexamethasone compared with usual care or placebo (3 trials, 1282 patients, and 527 deaths), the OR was 0.69 (95% CI, 0.43-1.12; P = .13) for hydrocortisone (3 trials, 374 patients, and 94 deaths), and the OR was 0.91 (95% CI, 0.29-2.87; P = .87) for methylprednisolone (1 trial, 47 patients, and 26 deaths). Among the 6 trials that reported serious adverse events, 64 events occurred among 354 patients randomized to corticosteroids and 80 events occurred among 342 patients randomized to usual care or placebo. Conclusions and Relevance In this prospective meta-analysis of clinical trials of critically ill patients with COVID-19, administration of systemic corticosteroids, compared with usual care or placebo, was associated with lower 28-day all-cause mortality.

Figure 2. Association Between Corticosteroids and 28-Day All-Cause Mortality in Each Trial, Overall, and According to Corticosteroid Drug

Drug and trial	ClinicalTrials.gov identifier	Initial dose and administration	No. of deaths/total No. of patients: Steroids	No. of deaths/total No. of patients: No steroids	Odds ratio (95% CI)	Weight, %
Dexamethasone						
DEXA-COVID 19	NCT04325061	High: 20 mg/d intravenously	2/7	2/12	2.00 (0.21-18.69)	0.92
CoDEX	NCT04327401	High: 20 mg/d intravenously	69/128	76/128	0.80 (0.49-1.31)	18.69
RECOVERY	NCT04381936	Low: 6 mg/d orally or intravenously	95/324	283/683	0.59 (0.44-0.78)	57.00
Subgroup fixed effect			166/459	361/823	0.64 (0.50-0.82)	76.60
Hydrocortisone						
CAPE COVID	NCT02517489	Low: 200 mg/d intravenously	11/75	20/73	0.46 (0.20-1.04)	6.80
COVID STEROID	NCT04348305	Low: 200 mg/d intravenously	6/15	2/14	4.00 (0.65-24.66)	1.39
REMAP-CAP	NCT02735707	Low: 50 mg every 6 h intravenously	26/105	29/92	0.71 (0.38-1.33)	11.75
Subgroup fixed effect			43/195	51/179	0.69 (0.43-1.12)	19.94
Methylprednisolone						
Steroids-SARI	NCT04244591	High: 40 mg every 12 h intravenously	13/24	13/23	0.91 (0.29-2.87)	3.46
Overall (fixed effect) $P = .31$ for heterogeneity; $I^2 = 15.6\%$			222/678	425/1025	0.66 (0.53-0.82)	100.0
Overall (random effects[a])			222/678	425/1025	0.70 (0.48-1.01)	

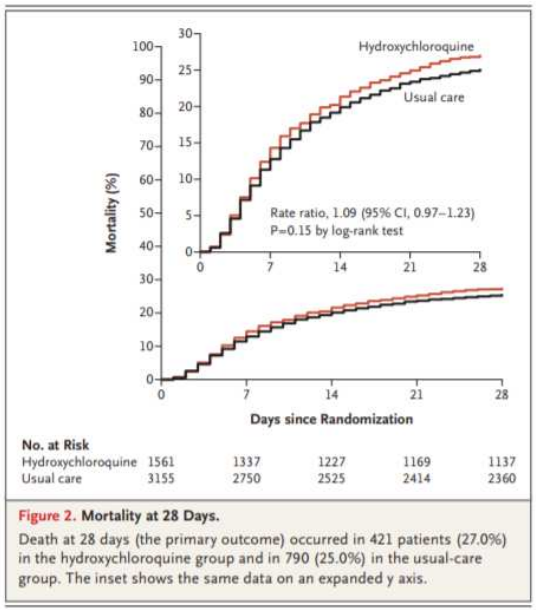


Beigel JH et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2007764?query=featured_coronavirus	Remdesivir for the Treatment of Covid-19 — Final Report	Trial clinico randomizzato controllato con placebo su 1062 pazienti trattati per 10 giorni con remdesivir o placebo per polmonite da SARS-CoV-2 di gravità variabile. Si dimostra riduzione significativa del tempo di guarigione nel gruppo remdesivir.	BACKGROUND: Although several therapeutic agents have been evaluated for the treatment of coronavirus disease 2019 (Covid-19), no antiviral agents have yet been shown to be efficacious. METHODS: We conducted a double-blind, randomized, placebo-controlled trial of intravenous remdesivir in adults who were hospitalized with Covid-19 and had evidence of lower respiratory tract infection. Patients were randomly assigned to receive either remdesivir (200 mg loading dose on day 1, followed by 100 mg daily for up to 9 additional days) or placebo for up to 10 days. The primary outcome was the time to recovery, defined by either discharge from the hospital or hospitalization for infection-control purposes only. RESULTS: A total of 1062 patients underwent randomization (with 541 assigned to remdesivir and 521 to placebo). Those who received remdesivir had a median recovery time of 10 days (95% confidence interval [CI], 9 to 11), as compared with 15 days (95% CI, 13 to 18) among those who received placebo (rate ratio for recovery, 1.29; 95% CI, 1.12 to 1.49; P<0.001, by a log-rank test). In an analysis that used a proportional-odds model with an eight-category ordinal scale, the patients who received remdesivir were found to be more likely than those who received placebo to have clinical improvement at day 15 (odds ratio, 1.5; 95% CI, 1.2 to 1.9, after adjustment for actual disease severity). The Kaplan–Meier estimates of mortality were 6.7% with remdesivir and 11.9% with placebo by day 15 and 11.4% with remdesivir and 15.2% with placebo by day 29 (hazard ratio, 0.73; 95% CI, 0.52 to 1.03). Serious adverse events were reported in 131 of the 532 patients who received remdesivir (24.6%) and in 163 of the 516 patients who received placebo (31.6%).

			CONCLUSIONS: Our data show that remdesivir was superior to placebo in shortening the time to recovery in adults who were hospitalized with Covid-19 and had evidence of lower respiratory tract infection. (Funded by the National Institute of Allergy and Infectious Diseases and others; ACTT-1 ClinicalTrials.gov number, NCT04280705. opens in new tab.) 

Hu B et al Nature Reviews Microbiology https://www.nature.com/articles/s41579-020-00459-7	Characteristics of SARS-CoV-2 and COVID-19.	Il punto sulle conoscenze dopo 10 mesi dalla diffusione di SARS-CoV-2: microbiologia, epidemiologia, clinica, terapia e prospettive future.	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a highly transmissible and pathogenic coronavirus that emerged in late 2019 and has caused a pandemic of acute respiratory disease, named 'coronavirus disease 2019' (COVID-19), which threatens human health and public safety. In this Review, we describe the basic virology of SARS-CoV-2, including genomic characteristics and receptor use, highlighting its key difference from previously known coronaviruses. We summarize current knowledge of clinical, epidemiological and pathological features of COVID-19, as well as recent progress in animal models and antiviral treatment approaches for SARS-CoV-2 infection. We also discuss the potential wildlife hosts and zoonotic origin of this emerging virus in detail. **Fig. 1: Timeline of the key events of the COVID-19 outbreak.** 
Jamaludin S et al Annals of Medicine and Surgery https://www.sciencedirect.com/science/article/pii/	COVID-19 exit strategy: Transitioning towards a new normal.	Proposte per una nuova normalità in corso di pandemia da COVID-19.	The COVID-19 outbreak from the SARS-CoV-2 virus has shocking us with its fast transmission and deadly complication. Due to that, the movement restriction has been enforced to contain this pandemic. Recently, there is an increasing pressure to restart and resurrect social and economic sectors, and to allow people to get back to work. This must be well planned before the movement restriction is lifted. Because of that, this paper aims to review and make

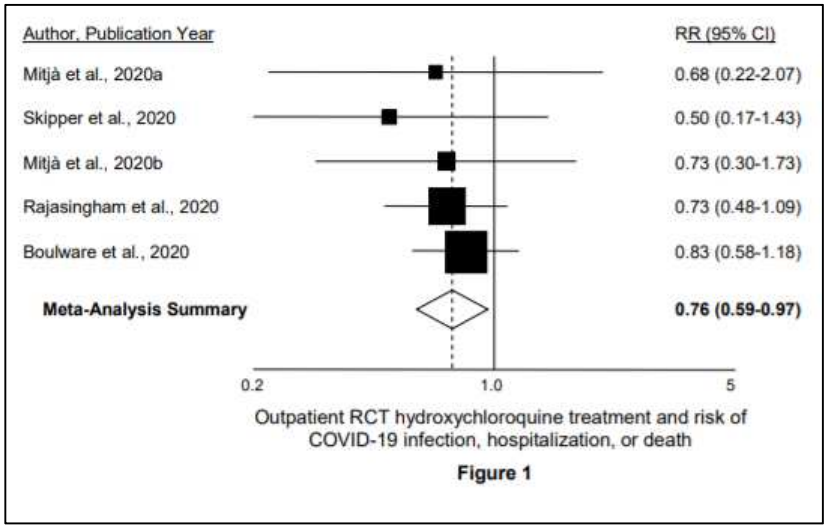
S2049080120303514?via%3Dihub			recommendations on the new normal for our daily activities and works. Firstly, the social and economic sectors must be opening in phases by emphasizing safety and health than an economic recovery. In the meantime, the WHO recommendations on social distancing and personal hygiene must be adapted and become a new normal. Because of that, the government and local authorities should develop a soft landing approach based on the WHO recommendations. Next, the community must be engaged and empowered to do their parts in preventing the spread of COVID-19. From the new normal recommendations, the people can continue their daily routines, and at the same time can reduce COVID-19 transmission. However, medical possibilities are not considered while compiling these new normals and procedures. The population must adapt and embrace the new normal to control, reduce and prevent the spreading of COVID-19, as it could be with us for a long time.
RECOVERY Collaborative Group NEJM https://www.nejm.org/doi/10.1056/NEJMoa2022926	Effect of Hydroxychloroquine in Hospitalized Patients with Covid-19	Risultati del braccio di RECOVERY su idrossiclorochina: non differenza di mortalità a 28 giorni fra gli ospedalizzati per COVID-19 trattati con idrossiclorochina rispetto a standard of care.	BACKGROUND: Hydroxychloroquine and chloroquine have been proposed as treatments for coronavirus disease 2019 (Covid-19) on the basis of in vitro activity and data from uncontrolled studies and small, randomized trials. METHODS: In this randomized, controlled, open-label platform trial comparing a range of possible treatments with usual care in patients hospitalized with Covid-19, we randomly assigned 1561 patients to receive hydroxychloroquine and 3155 to receive usual care. The primary outcome was 28-day mortality. RESULTS: The enrollment of patients in the hydroxychloroquine group was closed on June 5, 2020, after an interim analysis determined that there was a lack of efficacy. Death within 28 days occurred in 421 patients (27.0%) in the hydroxychloroquine group and in 790 (25.0%) in the usual-care group (rate ratio, 1.09; 95%

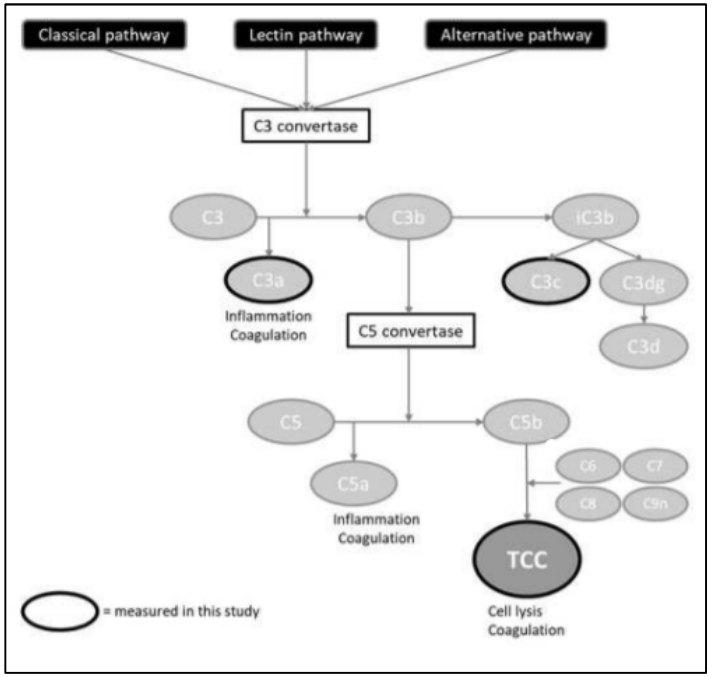
			confidence interval [CI], 0.97 to 1.23; P=0.15). Consistent results were seen in all prespecified subgroups of patients. The results suggest that patients in the hydroxychloroquine group were less likely to be discharged from the hospital alive within 28 days than those in the usual-care group (59.6% vs. 62.9%; rate ratio, 0.90; 95% CI, 0.83 to 0.98). Among the patients who were not undergoing mechanical ventilation at baseline, those in the hydroxychloroquine group had a higher frequency of invasive mechanical ventilation or death (30.7% vs. 26.9%; risk ratio, 1.14; 95% CI, 1.03 to 1.27). There was a small numerical excess of cardiac deaths (0.4 percentage points) but no difference in the incidence of new major cardiac arrhythmia among the patients who received hydroxychloroquine. CONCLUSIONS: Among patients hospitalized with Covid-19, those who received hydroxychloroquine did not have a lower incidence of death at 28 days than those who received usual care.  **Figure 2. Mortality at 28 Days.** Death at 28 days (the primary outcome) occurred in 421 patients (27.0%) in the hydroxychloroquine group and in 790 (25.0%) in the usual-care group. The inset shows the same data on an expanded y axis.

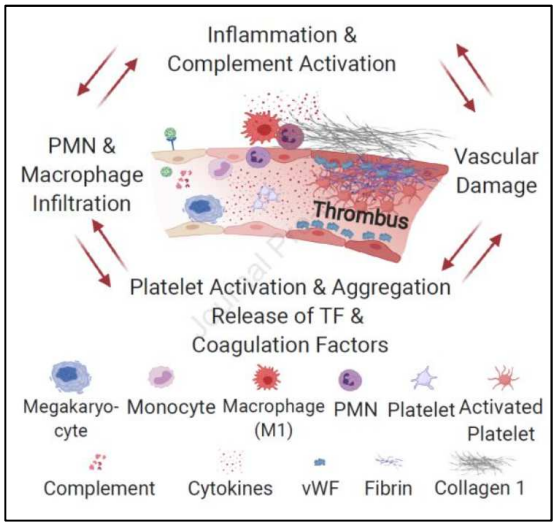
Wang Y et al European Journal of Pharmacology https://www.sciencedirect.com/science/article/pii/S0014299920307263?via%3Dihub	Tissue distributions of antiviral drugs affect their capabilities of reducing viral loads in COVID-19 treatment.	Ipotesi sull'impatto della distribuzione tissutale dei farmaci anti-SARS-CoV-2 sulla riduzione della carica virale.	Repurposing of approved antiviral drugs against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a promising strategy to treat Coronavirus disease 2019 (COVID-19) patients. Previously we reported our hypothesis that the antiviral drugs with high lung distributions might benefit COVID-19 patients by reducing viral loads. So far, chloroquine, lopinavir, hydroxychloroquine, azithromycin, favipiravir, ribavirin, darunavir, remdesivir, and umifenovir have been tested in COVID-19 clinical trials. Here we validated our hypothesis by comparing the pharmacokinetics profiles of these drugs and their capabilities of reducing viral load in clinical trials. According to bulk RNA and single cell RNA sequencing analysis, we found that high expression of both angiotensin converting enzyme 2 (ACE2) and transmembrane Serine Protease 2 (TMPRSS2) makes the lung and intestine vulnerable to SARS-CoV-2. Hydroxychloroquine, chloroquine, and favipiravir, which were highly distributed to the lung, were reported to reduce viral loads in respiratory tract of COVID-19 patients. Conversely, drugs with poor lung distributions, including lopinavir/ritonavir, umifenovir and remdesivir, were insufficient to inhibit viral replication. Lopinavir/ritonavir might inhibit SARS-CoV-2 in the GI tract according to their distribution profiles. We concluded here that the antiviral drugs should be distributed straight to the lung tissue for reducing viral loads in respiratory tract of COVID-19 patients. Additionally, to better evaluate antiviral effects of drugs that target the intestine, the stool samples should also be collected for viral RNA test in the future.
Stevenson DR et al Clinical Infectious Diseases	Improving Antimicrobial Stewardship in Critically-Ill Patients with COVID-19	Proposte di stewardship antimicrobica in base ai dati di 77 pazienti ricoverati in	We reviewed all microbiology results for 77 COVID-19 patients admitted to Intensive Care (ICU) at a London UK hospital between 01/03/2020 and 30/04/2020 from admission to discharge (obtaining local approvals). Our aim was to develop an approach supporting

https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1559/5920705?searchresult=1		terapia intensiva per COVID-19.	antimicrobial stewardship, as all patients were commenced on antibiotics upon ICU admission, 75% changed to a second antibiotic, 55% to a third (only 9% and 14% prompted by culture results respectively).
Baum A et al Science https://science.sciencemag.org/content/early/2020/10/08/science.abe2402	REGN-COV2 antibodies prevent and treat SARS-CoV-2 infection in rhesus macaques and hamsters	Effetti sull'animale da esperimento di una miscela di due anticorpi diretti contro la proteina S di SARS-CoV-2 utilizzati in profilassi o terapia.	An urgent global quest for effective therapies to prevent and treat COVID-19 disease is ongoing. We previously described REGN-COV2, a cocktail of two potent neutralizing antibodies (REGN10987+REGN10933) targeting non-overlapping epitopes on the SARS-CoV-2 spike protein. In this report, we evaluate the in vivo efficacy of this antibody cocktail in both rhesus macaques, which may model mild disease, and golden hamsters, which may model more severe disease. We demonstrate that REGN-COV-2 can greatly reduce virus load in lower and upper airways and decrease virus induced pathological sequalae when administered prophylactically or therapeutically in rhesus macaques. Similarly, administration in hamsters limits weight loss and decreases lung titers and evidence of pneumonia in the lungs. Our results provide evidence of the therapeutic potential of this antibody cocktail.
Del Rio C et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2771581	Long-term Health Consequences of COVID-19	Riflessioni su una "sindrome post-acuzie" da SARS-CoV-2.	With more than 30 million documented infections and 1 million deaths worldwide, the coronavirus disease 2019 (COVID-19) pandemic continues unabated. The clinical spectrum of severe acute respiratory syndrome coronavirus (SARS-CoV) 2 infection ranges from asymptomatic infection to life-threatening and fatal disease. Current estimates are that approximately 20 million people globally have "recovered"; however, clinicians are observing and reading reports of patients with persistent severe symptoms and even substantial end-organ dysfunction after SARS-CoV-2 infection. Because COVID-19 is a new disease, much about the clinical course

			remains uncertain—in particular, the possible long-term health consequences, if any.
Ladapo JA et al medRXiv https://www.medrxiv.org/content/10.1101/2020.09.30.20204693v1	Randomized Controlled Trials of Early Ambulatory Hydroxychloroquine in the Prevention of COVID-19 Infection, Hospitalization, and Death: Meta-Analysis	Revisione sistematica e metanalisi che suggerisce che la terapia con idrossiclorochina riduca l'incidenza dell'outcome composito comprendente nuove infezioni, ospedalizzazione e decesso per COVID-19.	Objective--To determine if hydroxychloroquine (HCQ) reduces the incidence of new illness, hospitalization or death among outpatients at risk for or infected with SARS-CoV-2 (COVID-19). Design--Systematic review and meta-analysis of randomized clinical trials. Data sources--Search of MEDLINE, EMBASE, PubMed, medRxiv, PROSPERO, and the Cochrane Central Register of Controlled Trials. Also review of reference lists from recent meta-analyses. Study selection--Randomized clinical trials in which participants were treated with HCQ or placebo/standard-of-care for pre-exposure prophylaxis, post-exposure prophylaxis, or outpatient therapy for COVID-19. Methods--Two investigators independently extracted data on trial design and outcomes. Medication side effects and adverse reactions were also assessed. The primary outcome was COVID-19 hospitalization or death. When unavailable, new COVID-19 infection was used. We calculated random effects meta-analysis according to the method of DerSimonian and Laird. Heterogeneity between the studies was evaluated by calculation of Cochran Q and I2 parameters. An Egger funnel plot was drawn to investigate publication bias. We also calculated the fixed effects meta-analysis summary of the five studies. All calculations were done in Excel, and results were considered to be statistically significant at a two-sided threshold of P=.05. Results--Five randomized controlled clinical trials enrolling 5,577 patients were included. HCQ was associated with a 24% reduction in COVID-19 infection, hospitalization or death, P=.025 (RR, 0.76 [95% CI, 0.59 to 0.97]). No serious adverse cardiac events were reported. The most common side effects were gastrointestinal. Conclusion--Hydroxychloroquine use in outpatients reduces the incidence of the composite outcome of COVID-19

			infection, hospitalization, and death. Serious adverse events were not reported and cardiac arrhythmia was rare. Systematic review registration--This review was not registered.  **Figure 1**
de Nooijer AH et al The Journal of Infectious Diseases https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiaa646/5920660	Complement activation in the disease course of COVID-19 and its effects on clinical outcomes	Studio prospettico che dimostra differenza significativa dei livelli circolanti di alcuni fattori del complemento fra pazienti con COVID-19 e controlli sani e inoltre associazione di tali livelli con la gravità di malattia.	Background: Excessive activation of immune responses in coronavirus disease 2019 (COVID-19) is considered to be related to disease severity, complications and mortality. The complement system is an important component of innate immunity and can stimulate inflammation, but its role in COVID-19 is unknown. Methods: A prospective, longitudinal, single center study was performed in hospitalized COVID-19 patients. Plasma concentrations of complement factors C3a, C3c, and terminal complement complex (TCC) were assessed at baseline and during hospital admission. In parallel, routine laboratory and clinical parameters were collected from medical files and analyzed. Results: Complement factors C3a, C3c and TCC were significantly increased in plasma of COVID-19 patients compared to healthy controls ($p<0.05$). These complement factors were especially

			elevated in ICU patients during the entire disease course ($p<0.005$ for C3a and TCC). More intense complement activation was observed in patients that deceased and in patients with thromboembolic events. Conclusions: COVID-19 patients demonstrate activation of the complement system, which is related to disease severity. This pathway may be involved in the dysregulated pro-inflammatory response associated with increased mortality and thromboembolic complications. Components of the complement system might have potential as prognostic markers for disease severity and as therapeutic targets in COVID-19. 

Aid M et al Cell https://www.cell.com/cell/pdf/S0092-8674(20)31311-8.pdf?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0092867420313118%3Fshowall%3Dtrue	Vascular Disease and Thrombosis in SARS-CoV-2 Infected Rhesus Macaques	Studio della fisiopatologia dell'infezione da SARS-CoV-2 tramite esame istologico del polmone di macachi rhesus e pazienti umani, oltre ad analisi del trascrittoma su lavaggio broncoalveolare e sangue periferico.	The COVID-19 pandemic has led to extensive morbidity and mortality throughout the world. Clinical features that drive SARS-CoV-2 pathogenesis in humans include inflammation and thrombosis, but the mechanistic details underlying these processes remain to be determined. In this study, we demonstrate endothelial disruption and vascular thrombosis in histopathologic sections of lungs from both humans and rhesus macaques infected with SARS-CoV-2. To define key molecular pathways associated with SARS-CoV-2 pathogenesis in macaques, we performed transcriptomic analyses of bronchoalveolar lavage (BAL) and peripheral blood and proteomic analyses of serum. We observed macrophage infiltrates in lung and upregulation of macrophage, complement, platelet activation, thrombosis, and proinflammatory markers, including C-reactive protein, MX1, IL-6, IL-1, IL-8, TNFα, and NF-κB. These results suggest a model in which critical interactions between inflammatory and thrombosis pathways lead to SARS-CoV-2 induced vascular disease. Our findings suggest potential therapeutic targets for COVID-19. 

Rogers R et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1548/5920703	Convalescent plasma for patients with severe COVID-19: a matched cohort study.	Confronto fra una coorte di 64 pazienti trattati con plasma iperimmune e 177 pazienti trattati con standard of care per COVID-19: non differenza di mortalità tra i due gruppi, tendenza verso un maggiore tasso di dimissione ospedaliera nella fascia d'età superiore a 65 anni.	Background: The efficacy of convalescent plasma (CP) for the treatment of COVID-19 remains unclear. Methods: In a matched cohort analysis of hospitalized patients with severe COVID-19, the impact of CP treatment on in-hospital mortality was evaluated using univariate and multivariate Cox proportionalhazards models, and the impact of CP treatment on time to hospital discharge was assessed using a stratified log-rank analysis. Results: 64 patients who received CP a median of 7 days after symptom onset were compared to a matched control group of 177 patients. The incidence of in-hospital mortality was 12.5% and 15.8% in the CP and control groups, respectively (p = 0.52). There was no significant difference in the risk of inhospital mortality between the two groups (adjusted hazard ratio [aHR] 0.93, 95% confidence interval [CI] 0.39 – 2.20). The overall rate of hospital discharge was not significantly different between the two groups (rate ratio [RR] 1.28, 95% CI 0.91 – 1.81), although there was a significantly increased rate of hospital discharge among patients 65-years-old or greater who received CP (RR 1.86, 95% CI 1.03 – 3.36). There was a greater than expected frequency of transfusion reactions in the CP group (2.8% reaction rate observed per unit transfused). Conclusions: We did not demonstrate a significant difference in risk of mortality or rate of hospital discharge between the CP and control groups. There was a signal for improved outcomes among the elderly, and further adequately powered randomized studies should target this subgroup when assessing the efficacy of CP treatment.