RICERCA BIBLIOGRAFICA COVID 19

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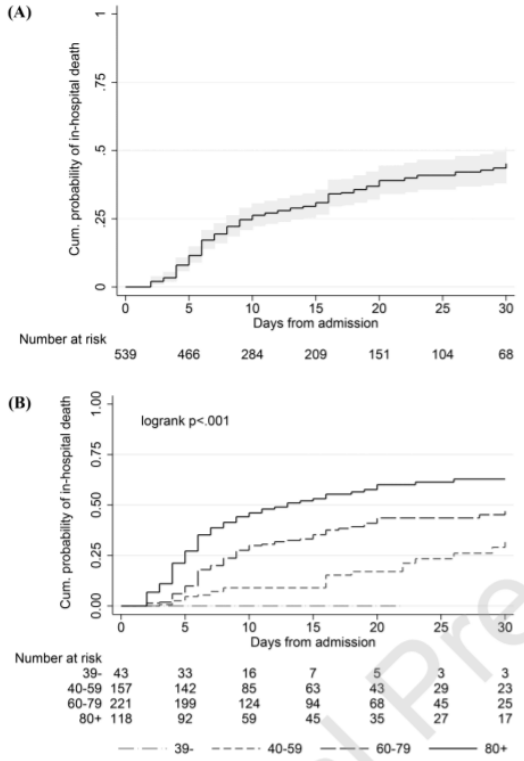
AUTORE/RIVISTA	TITOLO	OUTCOME PRINCIPALE	ABSTRACT
Li Y et al Annals of Noninvasive Electrocardiology https://onlinelibrary.wiley.com/doi/10.1111/anec.12805	Electrocardiograhic characteristics in patients with coronavirus infection: A single-center observational study.	Studio retrospettivo osservazionale sulle caratteristiche elettrocardiografiche di 135 pazienti ricoverati in un ospedale cinese per SARS-CoV-2, con ricerca di fattori associati a peggiore outcome.	BACKGROUND: A global outbreak of coronavirus disease (COVID-19), caused by severe acute respiratory coronavirus 2 (SARS-CoV-2), has emerged since December 2019, in Wuhan, China. However, electrocardiograhic (ECG) manifestations of patients with COVID-19 have not been fully described. We aim to investigate ECG characteristics in COVID-19 patients and risk factors of intensive care unit (ICU) admission. METHODS: This retrospective observational study included the patients with COVID-19 at the Wuhan Asia General hospital between February 10, and 26, 2020. Demographic, clinical, and ECG characteristics were collected, and comparisons were made between the ICU and non-ICU admission groups. Logistic regression was used to identify risk factors of ICU admission. RESULTS: Among 135 included patients (median age: 64 years [interquartile range: 48-72]), ST-T abnormalities (40%) were the most common ECG feature, followed by arrhythmias (38%). Cardiovascular disease (CVD) was presented in 48% of the patients.

			Six (4.4%) died during hospitalization, and 23 (17.0%) were admitted to the ICU. Compared with non-ICU group, the ICU group showed higher heart rate (p = .019) and P-wave duration (p = .039) and was more frequently associated with CVD (p < .001), ST-T abnormalities (p = .007), arrhythmias (p = .003), QTc interval prolongation (p = .003), and pathological Q waves (p < .001). Twenty-seven patients were re-examined ECG during admission, and 17 of them presented new findings compared with their initial ECG presentations. ST-T abnormalities (p = .040) and history of CVD (p = .0047) were associated with increased risk of ICU hospitalization. CONCLUSIONS: COVID-19 is frequently related to cardiovascular manifestations including ECG abnormalities and cardiovascular comorbidities. ST-T abnormalities and CVD at admission were associated with increased odds of ICU admission. TABLE 3 New electrographic findings in patients with COVID-19 during admission New ECG findings[a] — No. Pathological Q wave — 2 ST-T abnormality — 5 Atrial premature complex — 1 Ectopic atrial rhythm — 1 Atrial fibrillation — 3 Ventricular premature complex — 1 Limb lead low voltage — 1 Intermittent bundle branch block — 1 QTc prolongation — 1 Left ventricle hypertrophy — 3 Resolved ECG abnormalities Sinus tachycardia resolved — 1 Atrial tachycardia resolved — 1 ST-T abnormalities resolved — 1 QTc prolongation resolved — 1 [a]A total of 27 patients re-examined ECG during admission, and 10 of them presented no significant changes compared with their initial ECG results.

Sze S et al Age and Ageing https://academic.oup.com/ageing/advance-article/doi/10.1093/ageing/afaa206/5908994	The need for improved discharge criteria for hospitalised patients with COVID-19-implications for patients in long term care facilities	Disamina dei criteri di dimissione dall'ospedale dei pazienti affetti da COVID-19 in uso in vari Paesi del mondo, con attenzione ai contesti in cui non è possibile testare ripetutamente per SARS-CoV-2 ed è necessario un compromesso fra dimissione precoce e tutela della comunità di destinazione.	In the COVID-19 pandemic, patients who are older and residents of long term care facilities (LTCF) are at greatest risk of worse clinical outcomes. We reviewed discharge criteria for hospitalised COVID-19 patients from ten countries with the highest incidence of COVID-19 cases as of 26th July 2020. Five countries (Brazil, Mexico, Peru, Chile and Iran) had no discharge criteria; the remaining five (United States of America, India, Russia, South Africa and the United Kingdom) had discharge guidelines with large inter-country variability. India and Russia recommend discharge for a clinically recovered patient with two negative reverse transcription polymerase chain reaction (RT-PCR) tests 24 hours apart; the USA offers either a symptom based strategy-clinical recovery and ten days after symptom onset, or the same test-based strategy. The UK suggests that patients can be discharged when patients have clinically recovered; South Africa recommends discharge 14 days after symptom onset if clinically stable. We recommend a unified, simpler discharge criteria, based on current studies which suggest that most SARS-CoV-2 loses its infectivity by 10 days post-symptom onset. In asymptomatic cases, this can be taken as 10 days after the first positive PCR result. Additional days of isolation beyond this should be left to the discretion of individual clinician. This represents a practical compromise between unnecessarily prolonged admissions and returning highly infectious patients back to their care facilities, and is of particular importance in older patients discharged to LTCFs, residents of which may be at greatest risk of transmission and worse clinical outcomes.

Caron P et al Annales d'Endrocrinologie https://www.sciencedirect.com/science/article/pii/S0003426620312142?via%3Dihub	THYROID DISORDERS AND SARS-CoV-2 INFECTION: from pathophysiological mechanism to patient management.	Revisione sui metodi di diagnosi e trattamento delle alterazioni della funzionalità tiroidea in corso di infezione da SARS-CoV-2.	The World Health Organization (WHO) declared the COVID-19 epidemic to be a global pandemic in March 2020. COVID-19 is an infection caused by SARS-CoV-2, a coronavirus that utilizes the angiotensin-2 converting enzyme to penetrate thyroid and pituitary cells, and may result in a "cytokine storm". Based on the pathophysiological involvement of the pituitary-thyroid axis, the current review discusses the diagnosis of abnormal thyroid function test, and the management of patients presenting with thyrotoxicosis, thyroid-associated orbitopathy and hypothyroidism in the context of SARS-CoV-2 infection.
d'Arminio Monforte A et al International Journal of Infectious Diseases https://linkinghub.elsevier.com/retrieve/pii/S1201971220307530	The importance of patients' case-mix for the correct interpretation of the hospital fatality rate in COVID-19 disease.	Studio di coorte prospettico su 539 pazienti ricoverati per COVID-19 a Milano, con ricerca dei fattori associati a maggior rischio di mortalità intraospedaliera. Variazione della mortalità nei diversi momenti dell'epidemia.	OBJECTIVE: We aimed to document data on the epidemiology and factors associated with clinical course leading to death of patients hospitalised with COVID-19. METHODS: Prospective observational cohort study on patients hospitalised with COVID-19 disease in February-24(th)/May-17(th) 2020 in Milan, Italy. Uni-multivariable Cox regression analyses were performed. Death's percentage by two-weeks' intervals according to age and disease severity was analysed. RESULTS: A total of 174/539 (32.3%) patients died in hospital over 8,228 person-day follow-up; the 14-day Kaplan-Meier probability of death was 29.5% (95%CI: 25.5-34.0). Older age, burden of comorbidities, COVID-19 disease severity, inflammatory markers at admission were independent predictors of increased risk, while several drug-combinations were predictors of reduced risk of in-hospital death. The highest fatality rate, 36.5%, occurred during the 2nd-3rd week of March, when 55.4% of patients presented with severe disease, while a second peak, by the end of April, was related to the admission of older patients (55% > = 80 years) with less severe disease, 30% coming from long-term care facilities. CONCLUSIONS: The unusual fatality rate in our setting is likely to be related to age and the clinical conditions of our patients.

			These findings may be useful to better allocate resources of the national healthcare system, in case of re-intensification of COVID-19 epidemics.  **Fig 2. Kaplan-Meier estimates of cumulative probability of in-hospital death (A) and according to age strata (B).**
Servick K Science https://www.sciencemag.org/news/2020/08/how-	How will COVID-19 affect the coming flu season? Scientists struggle for clues	Prospettive sulla possibile doppia epidemia di COVID-19 e influenza nell'emisfero boreale, in base a quanto è	In March, as the Southern Hemisphere braced for winter flu season while fighting COVID-19, epidemiologist Cheryl Cohen and colleagues at South Africa's National Institute for Communicable Diseases (NICD) set up a plan to learn from the double whammy. They hoped to study interactions between seasonal respiratory viruses and SARS-CoV-2, which causes COVID-19. Does infection

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 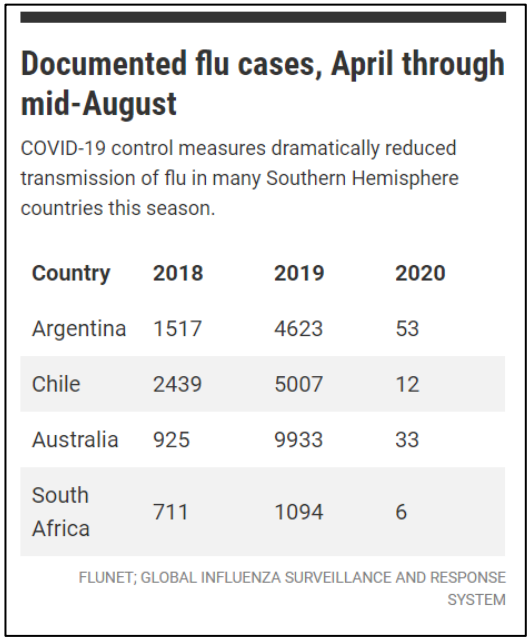
Documented flu cases, April through mid-August
COVID-19 control measures dramatically reduced transmission of flu in many Southern Hemisphere countries this season.
<table><tr><th>Country</th><th>2018</th><th>2019</th><th>2020</th></tr><tr><td>Argentina</td><td>1517</td><td>4623</td><td>53</td></tr><tr><td>Chile</td><td>2439</td><td>5007</td><td>12</td></tr><tr><td>Australia</td><td>925</td><td>9933</td><td>33</td></tr><tr><td>South Africa</td><td>711</td><td>1094</td><td>6</td></tr></table>FLUNET; GLOBAL INFLUENZA SURVEILLANCE AND RESPONSE SYSTEM</td>
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<td>Vitte J et al

Frontiers in Immunology

https://www.frontiersin.org/articles/10.3389/fimmu.2020.02159/full</td>
<td>Immune Modulation as a Therapeutic Option During the SARS-CoV-2 Outbreak: The Case for Antimalarial Aminoquinolines</td>
<td>Azione antivirale e immunomodulatrice delle aminochinoline antimalariche e razionale del loro utilizzo contro SARS-CoV-2.</td>
<td>The rapid spread, severity, and lack of specific treatment for COVID-19 resulted in hasty drug repurposing. Conceptually, trials of antivirals were well-accepted, but twentieth century antimalarials sparked an impassioned global debate. Notwithstanding, antiviral and immunomodulatory effects of aminoquinolines have been investigated in vitro, in vivo and in clinical trials for more than 30 years. We review the mechanisms of action of (hydroxy)chloroquine on immune cells and networks and discuss promises and pitfalls in the fight against SARS-CoV-2, the agent of the COVID-19 outbreak.</td>
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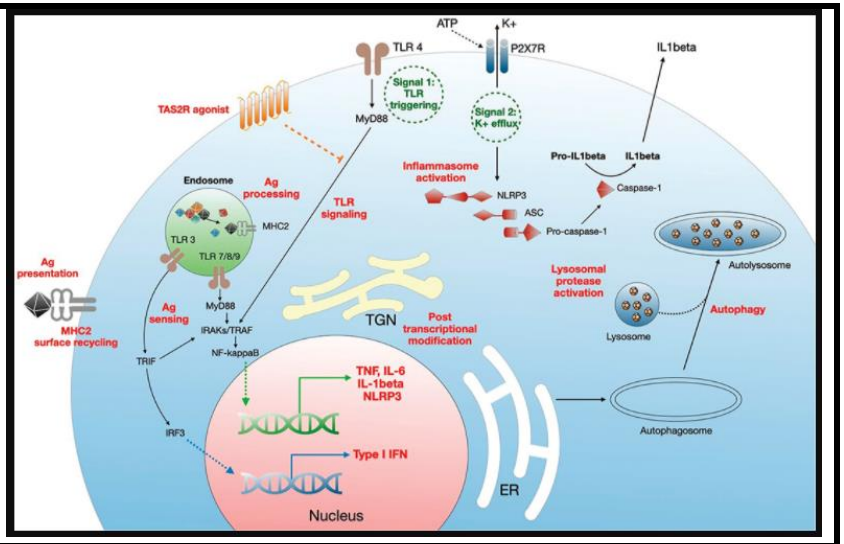
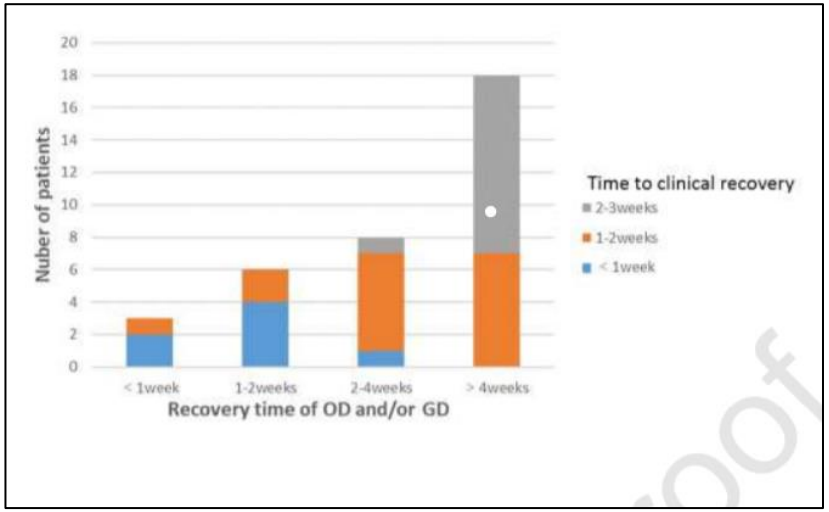
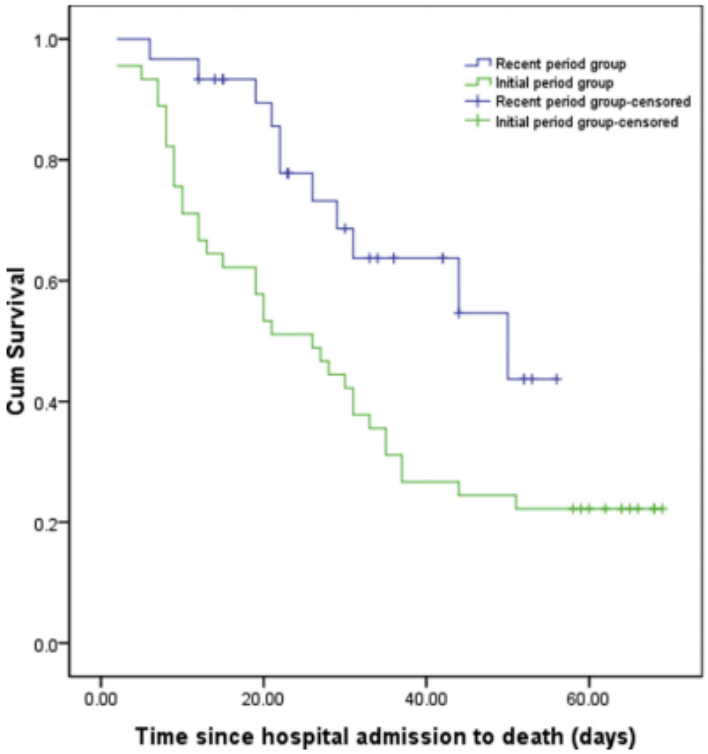
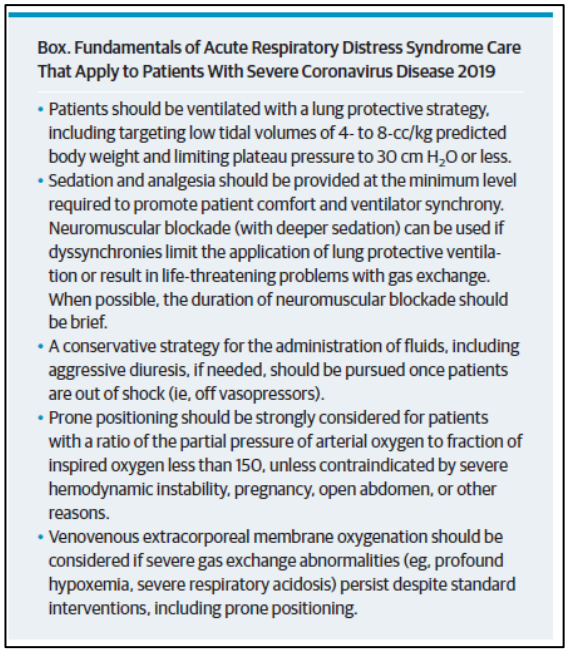
			
Li H et al International Journal of Infectious Diseases https://www.ijidonline.com/article/S1201-9712(20)30755-4/fulltext	Prevalence and recovery time of olfactory and gustatory dysfunctions of hospitalized patients with COVID19 in Wuhan, China.	Studio osservazionale retrospettivo su 196 pazienti con storia di COVID-19 in merito alla frequenza di perdita e ai tempi di recupero delle funzioni chemorecettoriali.	OBJECTIVES: To investigate olfactory and gustatory dysfunction in patients with coronavirus disease 2019 (COVID-19) in Wuhan using a telephone interview. METHODS: This retrospective telephone survey investigated 196 consecutive patients with COVID-19 discharged 3 months previously from two hospital in Wuhan, China. The characteristics of the patient's disease course and recovery time for olfactory and/or gustatory dysfunctions (OD and/or GD) were collected by telephone interview. Demographic data were collected from the patients' medical records. RESULTS: A total of 196 patients with COVID-19 completed the study. The most prevalent general symptoms consisted of fever, cough, and fatigue. 19.9% of patients reported OD and/or GD. In 87.2% of these cases, OD or GD appeared after the general symptoms. Among the patients, 51.4% had a recovery time of more than 4 weeks for OD and/or GD. Patients with COVID-19 and OD and/or GD had significantly higher rates of cardiovascular disease than patients without OD and/or GD (p = 0.002). CONCLUSION: Recovery from

			chemosensory dysfunction (OD and/or GD) was slow, with over half of the patients taking more than 4 weeks to recover. Cardiovascular disease might be related to the development of olfactory or taste disorders in patients with COVID-19. 
Wang Y et al Annals of Noninvasive Electrocardiology https://onlinelibrary.wiley.com/doi/10.1111/anec.12806	Electrocardiogram analysis of patients with different types of COVID-19.	Confronto fra le caratteristiche ECG e quelle demografiche e di alcuni esami ematici di pazienti gravi e critici con COVID-19.	BACKGROUND: Severe acute respiratory syndrome coronavirus 2 causes acute myocardial damage and arrhythmia in coronavirus disease 2019 (COVID-19) patients. Studying the changes of electrocardiogram is of great significance for the diagnosis of patients with COVID-19. METHODS: A retrospective analysis method was adopted to compare the electrocardiogram changes between COVID-19 critically severe and severe patients. Univariate and multivariate logistic regression were used to analyze the correlation of the levels of serum indexes and past medical history with ST-T changes and atrial fibrillation. And the correlation of ECG parameters with in-hospital death and ventilator use were investigated by using the same methods. RESULTS: The incidence of male, stroke, elevated cardiac troponin I (cTnI), N-terminal of the

			prohormone brain natriuretic peptide (NT-proBNP), d-dimer, high-sensitivity C-reactive protein (hs-CRP), hyperkalemia, and hypocalcemia in the critically ill patients was higher than that in severe patients. There were differences in ST-T changes, sinus tachycardia, atrial fibrillation, and atrial tachycardia between the two groups. Multivariate logistic regression analysis showed that elevated cTnI and NT-proBNP were the independent risk factors of ST-T changes. Elevated NT-proBNP and age were the independent risk factors of atrial fibrillation. Sinus tachycardia and atrial fibrillation were the independent risk factors of in-hospital death and ventilator use. CONCLUSION: ST-T changes, sinus tachycardia, and atrial fibrillation are with great significance in the diagnosis of the severity, myocardia injury, and cardiac insufficiency of COVID-19 patients. Sinus tachycardia and atrial fibrillation could be used as independent variables predicting in-hospital death and ventilator use.
Zhang Su et al Sleep Medicine https://www.sciencedirect.com/science/article/pii/S138994572030366X?via%3Dihub	Improved night shift schedule related to the mortality of critically ill patients with Corona Virus Disease 2019	Studio osservazionale retrospettivo monocentrico su 75 pazienti che confronta la mortalità dei ricoverati per COVID-19 prima e dopo l'introduzione di un nuovo schema di turnazioni mediche. Uno schema che riserva i turni diurni agli operatori « chiave » (più esperti nella gestione dell'emergenza-urgenza) sembra ridurre la mortalità.	PURPOSE: To determine the relationship between the improved night shift schedule and the mortality of critically ill patients with Corona Virus Disease 2019 (COVID-19). METHODS: According to the time of the implementation of the new night shift schedule, we divided all patients into two groups: initial period group and recent period group. The clinical electronic medical records, nursing records, laboratory findings, and radiological examinations for all patients with laboratory confirmed Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection were reviewed. Cox proportional hazard ratio (HR) models were used to determine the risk factors associated with in hospital death. RESULTS: A total of 75 patients were included in this study. Initial period group includes 45 patients and recent period group includes 30 patients. The difference in mortality between the two groups was significant,

			77.8% and 36.7%, respectively. Leukocytosis at admission and admitted to hospital before the new night shift schedule were associated with increased odds of death. CONCLUSIONS: Shift arrangement of medical staff are associated with the mortality of critically ill patients with COVID-19. The new night shift schedule might improve the continuity of treatment, thereby improving the overall quality of medical work and reducing the mortality of critically ill patients. S. Zhang et al. / Sleep Medicine 75 (2020) 354–360  Fig. 2. Survival of critically ill patients with COVID-19.

Bos LDJ et al JAMA https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2770931	Severe COVID-19 Infections—Knowledge Gained and Remaining Questions	Stato dell'arte e lacune nel trattamento dei pazienti con COVID-19 grave, a partire dalle conoscenze sulla sindrome da distress respiratorio acuto (ARDS).	Patients with acute respiratory failure due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have overwhelmed critical care capacity in some cities and countries. The mortality of patients who require critical care is high but varies widely among hospitals. Despite a rapidly increasing understanding of the pathogenesis of coronavirus disease 2019 (COVID-19), uncertainty remains about the reasons that some patients develop respiratory failure and others have no to minimal symptoms, as well as about the optimal management of patients with severe COVID-19 disease. We review the evidence for the management of patients with the acute respiratory distress syndrome (ARDS) that may apply to patients with severe COVID-19, what has been learned about treatment of these patients, and the gaps in knowledge that remain.  **Box. Fundamentals of Acute Respiratory Distress Syndrome Care That Apply to Patients With Severe Coronavirus Disease 2019** • Patients should be ventilated with a lung protective strategy, including targeting low tidal volumes of 4- to 8-cc/kg predicted body weight and limiting plateau pressure to 30 cm H_2O or less. • Sedation and analgesia should be provided at the minimum level required to promote patient comfort and ventilator synchrony. Neuromuscular blockade (with deeper sedation) can be used if dyssynchronies limit the application of lung protective ventilation or result in life-threatening problems with gas exchange. When possible, the duration of neuromuscular blockade should be brief. • A conservative strategy for the administration of fluids, including aggressive diuresis, if needed, should be pursued once patients are out of shock (ie, off vasopressors). • Prone positioning should be strongly considered for patients with a ratio of the partial pressure of arterial oxygen to fraction of inspired oxygen less than 150, unless contraindicated by severe hemodynamic instability, pregnancy, open abdomen, or other reasons. • Venovenous extracorporeal membrane oxygenation should be considered if severe gas exchange abnormalities (eg, profound hypoxemia, severe respiratory acidosis) persist despite standard interventions, including prone positioning.

Sang Hyun et al Thorax https://thorax.bmj.com/lookup/doi/10.1136/thoraxjnl-2020-215042	Upper respiratory viral load in asymptomatic individuals and mildly symptomatic patients with SARS-CoV-2 infection	Studio su 213 pazienti con infezione lieve da SARS-CoV-2 reclutati in una struttura per isolamento in Corea. Non si dimostra una differenza di carica virale (stimata tramite ciclo soglia di positivizzazione della PCR-real time) fra sintomatici e asintomatici.	Background Asymptomatic individuals with SARS-CoV-2 infection have viable viral loads and have been linked to several transmission cases. However, data on the viral loads in such individuals are lacking. We assessed the viral loads in asymptomatic individuals with SARS-CoV-2 infection in comparison with those in symptomatic patients with COVID-19. Methods Study participants were recruited from a community facility designated for the isolation of patients with mild COVID-19 in South Korea. The presence of symptoms was evaluated with a questionnaire-based survey. Viral loads in the upper respiratory tract were measured with real-time reverse transcription-PCR (RT-PCR) targeting the E, RdRp and N genes of SARS-CoV-2, with a cycle threshold (Ct) value of 40 for determining positivity. Results In 213 patients with SARS-CoV-2 infection, 41 (19%) had remained asymptomatic from potential exposure to laboratory confirmation and admission; of them, 39 (95%) underwent follow-up RT-PCR testing after a median 13 days. In 172 symptomatic patients, 144 (84%) underwent follow-up RT-PCR testing. Twenty-one (54%) asymptomatic individuals and 92 (64%) symptomatic patients tested positive for SARS-CoV-2 at follow-up. Asymptomatic individuals and symptomatic patients did not show any significant differences in the mean Ct values of the E (31.15 vs 31.43; p>0.99), RdRp (32.26 vs 32.93; p=0.92) and N (33.05 vs 33.28; p>0.99) genes. Conclusion Approximately one-fifth of the individuals without severe symptoms were asymptomatic, and their viral loads were comparable to those in symptomatic patients. A large proportion of mildly symptomatic patients with COVID-19 or asymptomatic individuals with SARS-CoV-2 showed persistent positive upper respiratory RT-PCR results at follow-up.

Buitrago-garcia Diana et al PloS Medicine http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1003346	Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: A living systematic review and meta-analysis	Revisione sistematica e metanalisi sulle caratteristiche degli asintomatici infetti da SARS-CoV-2 e sul loro ruolo nella trasmissione del virus.	Background : There is disagreement about the level of asymptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. We conducted a living systematic review and meta-analysis to address three questions: (1) Amongst people who become infected with SARS-CoV-2, what proportion does not experience symptoms at all during their infection? (2) Amongst people with SARS-CoV-2 infection who are asymptomatic when diagnosed, what proportion will develop symptoms later? (3) What proportion of SARS-CoV-2 transmission is accounted for by people who are either asymptomatic throughout infection or presymptomatic? Methods and findings : We searched PubMed, Embase, bioRxiv, and medRxiv using a database of SARS-CoV-2 literature that is updated daily, on 25 March 2020, 20 April 2020, and 10 June 2020. Studies of people with SARS-CoV-2 diagnosed by reverse transcriptase PCR (RT-PCR) that documented follow-up and symptom status at the beginning and end of follow-up or modelling studies were included. One reviewer extracted data and a second verified the extraction, with disagreement resolved by discussion or a third reviewer. Risk of bias in empirical studies was assessed with an adapted checklist for case series, and the relevance and credibility of modelling studies were assessed using a published checklist. We included a total of 94 studies. The overall estimate of the proportion of people who become infected with SARS-CoV-2 and remain asymptomatic throughout infection was 20% (95% confidence interval [CI] 17–25) with a prediction interval of 3%–67% in 79 studies that addressed this review question. There was some evidence that biases in the selection of participants influence the estimate. In seven studies of defined populations screened for SARS-CoV-2 and then followed, 31% (95% CI 26%–37%, prediction interval 24%–38%) remained

			asymptomatic. The proportion of people that is presymptomatic could not be summarised, owing to heterogeneity. The secondary attack rate was lower in contacts of people with asymptomatic infection than those with symptomatic infection (relative risk 0.35, 95% CI 0.10–1.27). Modelling studies fit to data found a higher proportion of all SARS-CoV-2 infections resulting from transmission from presymptomatic individuals than from asymptomatic individuals. Limitations of the review include that most included studies were not designed to estimate the proportion of asymptomatic SARS-CoV-2 infections and were at risk of selection biases; we did not consider the possible impact of false negative RT-PCR results, which would underestimate the proportion of asymptomatic infections; and the database does not include all sources. Conclusions : The findings of this living systematic review suggest that most people who become infected with SARS-CoV-2 will not remain asymptomatic throughout the course of the infection. The contribution of presymptomatic and asymptomatic infections to overall SARS-CoV-2 transmission means that combination prevention measures, with enhanced hand hygiene, masks, testing tracing, and isolation strategies and social distancing, will continue to be needed.
Kampf, Gunter et al The Journal of Hospital Infection https://www.journalofhospitalinfection.com/article	Potential sources, modes of transmission and effectiveness of prevention measures against SARS-CoV-2.	Rilevanza delle diverse potenziali fonti di infezione da SARS-CoV-2 ed efficacia delle misure di prevenzione.	During the current SARS-CoV-2 pandemic new studies are emerging daily providing novel information about sources, transmission risks and possible prevention measures. In this review, we aimed to comprehensively summarize the current evidence on possible sources for SARS-CoV-2, including evaluation of transmission risks and effectiveness of applied prevention measures. Next to symptomatic patients, asymptomatic or pre-symptomatic carriers are a possible source with respiratory secretions as the most likely

/S0195-6701(20)30437-0/fulltext			cause for viral transmission. Air and inanimate surfaces may be sources; however, viral RNA has been inconsistently detected. Similarly, even though SARS-CoV-2 RNA has been detected on or in personnel protective equipment, blood, urine, eyes, the gastrointestinal tract and pets, these sources are currently thought to play a negligible role for transmission. Finally, various prevention measures such as hand washing, hand disinfection, face masks, gloves, surface disinfection or physical distancing for the healthcare setting and public are analysed for their expected protective effect.
Shehabi Y et al Seminars in Respiratory and Critical Care Medicine https://www.thieme-connect.de/products/ejournals/abstract/10.1055/s-0040-1716736	Optimal Sedation and Pain Management: A Patient- and Symptom-Oriented Paradigm.	Principi di sedazione e analgesia per pazienti critici, rivisti nel contesto della pandemia da COVID-19.	In the critically ill patient, optimal pain and sedation management remains the cornerstone of achieving comfort, safety, and to facilitate complex life support interventions. Pain relief, using multimodal analgesia, is an integral component of any orchestrated approach to achieve clinically appropriate goals in critically ill patients. Sedative management, however, remains a significant challenge. Subsequent studies including most recent randomized trials have failed to provide strong evidence in favor of a sedative agent, a mode of sedation or ancillary protocols such as sedative interruption and sedative minimization. In addition, clinical practice guidelines, despite a comprehensive evaluation of relevant literature, have limitations when applied to individual patients. These limitations have been most apparent during the coronavirus disease 2019 pandemic. As such, there is a need for a mindset shift to a practical and achievable sedation strategy, driven by patients' characteristics and individual patient needs, rather than one cocktail for all patients. In this review, we present key principles to achieve patient-and symptom-oriented optimal analgesia and sedation in the critically ill patients. Sedative intensity should be proportionate to care complexity with due consideration to an individual patient's modifiers. The use of multimodal analgesics,

sedatives, and antipsychotics agents-that are easily titratable-reduces the overall quantum of sedatives and opioids, and reduces the risk of adverse events while maximizing clinical benefits. In addition, critical considerations regarding the choice of sedative agents should be given to factors such as age, medical versus operative diagnosis, and cardiovascular status. Specific populations such as trauma, neurological injury, and pregnancy should also be taken into account to maximize efficacy and reduce adverse events.

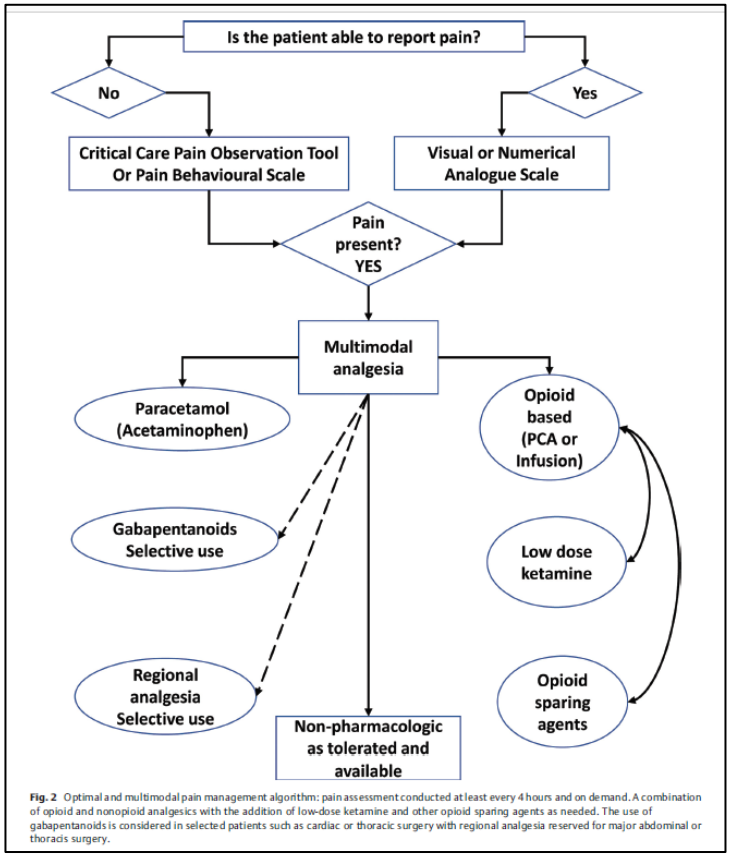
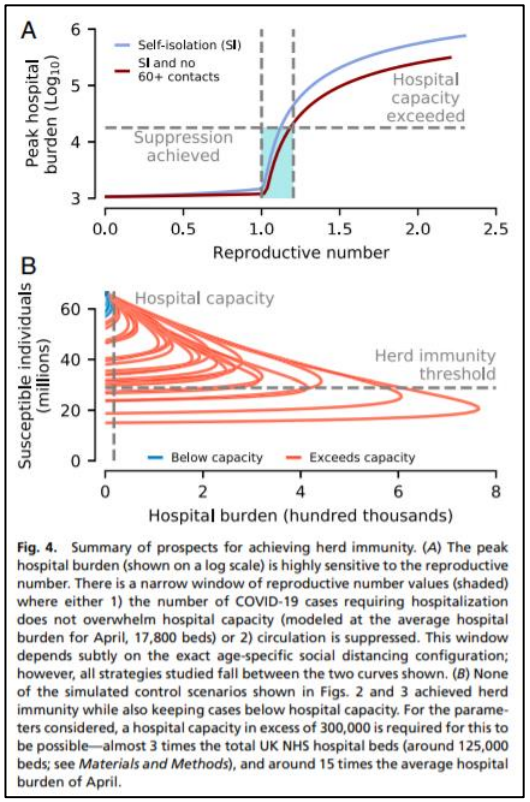


Fig. 2 Optimal and multimodal pain management algorithm: pain assessment conducted at least every 4 hours and on demand. A combination of opioid and nonopioid analgesics with the addition of low-dose ketamine and other opioid sparing agents as needed. The use of gabapentanoids is considered in selected patients such as cardiac or thoracic surgery with regional analgesia reserved for major abdominal or thoracis surgery.

Berkwits M et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2770825	The COVID-19 Pandemic and the JAMA Network	Tredici articoli di opinione a cura degli Editori di JAMA Network, relativi agli aspetti di COVID-19 di interesse nell'ambito di diverse specialità mediche.	In 13 Viewpoints in this issue, JAMA Network editors reflect on the clinical, public health, operational, and workforce issues related to COVID-19 in each of their specialties.
Weasley Long S et al medRxiv preprint https://drive.google.com/file/d/1CZzxGCgqv9VUCK1SRakWErgCpZxoevDQ/view	Molecular Architecture of Early Dissemination and Massive Second Wave of the SARS-CoV-2 Virus in a Major Metropolitan Area	Risultati del sequenziamento di 5085 genomi di SARS-CoV-2 relativi a due ondate epidemiche di COVID-19 a Houston. Non si dimostrano associazioni fra i genotipi virali e la gravità dell'infezione.	ABSTRACT We sequenced the genomes of 5,085 SARS-CoV-2 strains causing two COVID-19 disease waves in metropolitan Houston, Texas, an ethnically diverse region with seven million residents. The genomes were from viruses recovered in the earliest recognized phase of the pandemic in Houston, and an ongoing massive second wave of infections. The virus was originally introduced into Houston many times independently. Virtually all strains in the second wave have a Gly614 amino acid replacement in the spike protein, a polymorphism that has been linked to increased transmission and infectivity. Patients infected with the Gly614 variant strains had significantly higher virus loads in the nasopharynx on initial diagnosis. We found little evidence of a significant relationship between virus genotypes and altered virulence, stressing the linkage between disease severity, underlying medical conditions, and host genetics. Some regions of the spike protein - the primary target of global vaccine efforts - are replete with amino acid replacements, perhaps indicating the action of selection. We exploited the genomic data to generate defined single amino acid replacements in the receptor binding domain of spike protein that, importantly, produced decreased recognition by the neutralizing monoclonal antibody CR30022. Our study is the first analysis of the molecular architecture of SARS-CoV-2 in two infection waves in a major metropolitan region. The findings will help us to understand

			the origin, composition, and trajectory of future infection waves, and the potential effect of the host immune response and therapeutic maneuvers on SARS CoV-2 evolution. IMPORTANCE There is concern about second and subsequent waves Of COVID-19 caused by the SARS-CoV-2 coronavirus occurring in communities globally that had an initial disease wave. Metropolitan Houston, Texas, with a population of 7 million, is experiencing a massive second disease wave that began in late May 2020. To understand SARS CoV-2 molecular population genomic architecture, evolution, and relationship between virus genotypes and patient features, we sequenced the genomes of 5,085 SARS-CoV-2 strains from these two waves. Our study provides the first molecular characterization of SARS-CoV-2 strains causing two distinct COVID-19 disease waves.
Brett TS et al PNAS https://doi.org/10.1073/pnas.2008087117	Transmission dynamics reveal the impracticality of COVID-19 herd immunity strategies.	La prospettiva di favorire l'immunità di gregge contro SARS-CoV-2 è impraticabile secondo i risultati di questa simulazione, in particolare per il rischio di sovraccarico insostenibile del sistema sanitario.	The rapid growth rate of COVID-19 continues to threaten to overwhelm healthcare systems in multiple countries. In response, severely affected countries have had to impose a range of public health strategies achieved via nonpharmaceutical interventions. Broadly, these strategies have fallen into two categories: 1) "mitigation," which aims to achieve herd immunity by allowing the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus to spread through the population while mitigating disease burden, and 2) "suppression," aiming to drastically reduce SARS-CoV-2 transmission rates and halt endogenous transmission in the target population. Using an age-structured transmission model, parameterized to simulate SARS-CoV-2 transmission in the United Kingdom, we assessed the long-term prospects of success using both of these approaches. We simulated a range of different nonpharmaceutical intervention scenarios incorporating social distancing applied to differing age groups. Our modeling confirmed

			that suppression of SARS-CoV-2 transmission is possible with plausible levels of social distancing over a period of months, consistent with observed trends. Notably, our modeling did not support achieving herd immunity as a practical objective, requiring an unlikely balancing of multiple poorly defined forces. Specifically, we found that 1) social distancing must initially reduce the transmission rate to within a narrow range, 2) to compensate for susceptible depletion, the extent of social distancing must be adaptive over time in a precise yet unfeasible way, and 3) social distancing must be maintained for an extended period to ensure the healthcare system is not overwhelmed.  **Fig. 4.** Summary of prospects for achieving herd immunity. (*A*) The peak hospital burden (shown on a log scale) is highly sensitive to the reproductive number. There is a narrow window of reproductive number values (shaded) where either 1) the number of COVID-19 cases requiring hospitalization does not overwhelm hospital capacity (modeled at the average hospital burden for April, 17,800 beds) or 2) circulation is suppressed. This window depends subtly on the exact age-specific social distancing configuration; however, all strategies studied fall between the two curves shown. (*B*) None of the simulated control scenarios shown in Figs. 2 and 3 achieved herd immunity while also keeping cases below hospital capacity. For the parameters considered, a hospital capacity in excess of 300,000 is required for this to be possible—almost 3 times the total UK NHS hospital beds (around 125,000 beds; see *Materials and Methods*), and around 15 times the average hospital burden of April.

Pereyra D et al The Lancet https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(20)30286-6/fulltext	Routine haematological parameters in COVID-19 prognosis.	Analisi retrospettiva su 210 pazienti ricoverati per COVID-19 in Austria. Non è possibile predire l'outcome avverso sulla base di una serie di esami ematologici (piastrine, frazione neutrofili/linfociti e nemmeno D-dimero).	In The Lancet Haematology, Danying Liao and colleagues reported a cohort of 380 patients with COVID-19 who were admitted to hospital in Wuhan, China, between Jan 23, and Feb 23, 2020. The authors evaluated haematological characteristics and risk factors for classification of disease severity and outcome prediction for patients with COVID-19.1 In line with previous studies, coagulation parameters were deranged in patients with severe or fatal COVID-19, with D-dimer concentrations being significantly elevated, prompting their use as a biomarker for patient outcome. The features of COVID-19-associated coagulopathy are unique and incompletely understood. The reported data underline the relevance of coagulopathies as a major threat in patients with COVID-19. Although we agree with the clinical relevance, we want to point out that the ability of haematological indicators to predict disease severity and patient outcome seems to vary between cohorts.
Doi Y et al Antimicrobial Agents and Chemotherapy https://doi.org/10.1128/AAC.01897-20	A prospective, randomized, open-label trial of early versus late favipiravir in hospitalized patients with COVID-19.	Studio della clearance virale su 69 pazienti con infezione asintomatica o lieve da SARS-CoV-2, randomizzati a terapia con favipiravir con diversa tempistica di inizio.	Favipiravir is an oral broad-spectrum inhibitor of viral RNA-dependent RNA polymerase that is approved for treatment of influenza in Japan. We conducted a prospective, randomized, open-label, multicenter trial of favipiravir for the treatment of COVID-19 at 25 hospitals across Japan. Eligible patients were adolescents and adults admitted with COVID-19 who were asymptomatic or mildly ill and had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. Patients were randomly assigned at a 1:1 ratio to early or late favipiravir therapy (the same regimen starting on day 6 instead of day 1). The primary endpoint was viral clearance by day 6. The secondary endpoint was change in viral load by day 6. Exploratory endpoints included time to defervescence and resolution of symptoms. Eighty-nine patients were enrolled, of whom 69 were virologically evaluable. Viral clearance occurred

within 6 days in 66.7% and 56.1% of the early and late treatment groups (adjusted hazard ratio [aHR], 1.42; 95% confidence interval [95% CI], 0.76–2.62). Of 30 patients who had a fever (≥37.5°C) on day 1, time to defervescence was 2.1 days and 3.2 days in the early and late treatment groups (aHR, 1.88; 95%CI, 0.81–4.35). During therapy, 84.1% developed transient hyperuricemia. Favipiravir did not significantly improve viral clearance as measured by RT-PCR by day 6 but was associated with numerical reduction in time to defervescence. Neither disease progression nor death occurred to any of the patients in either treatment group during the 28-day participation.

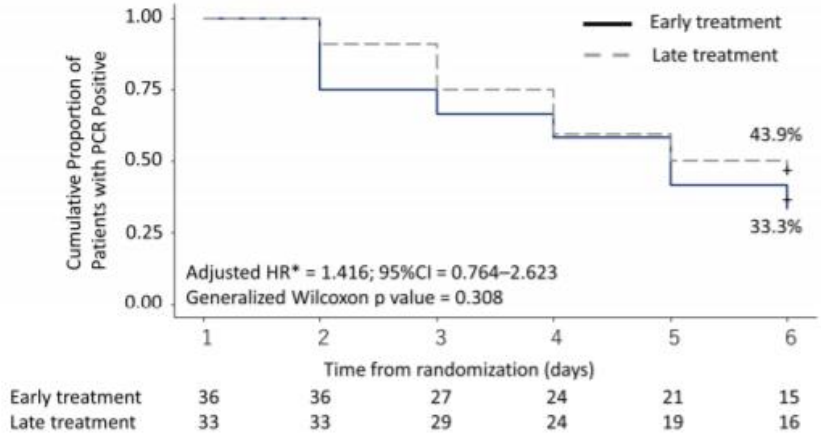
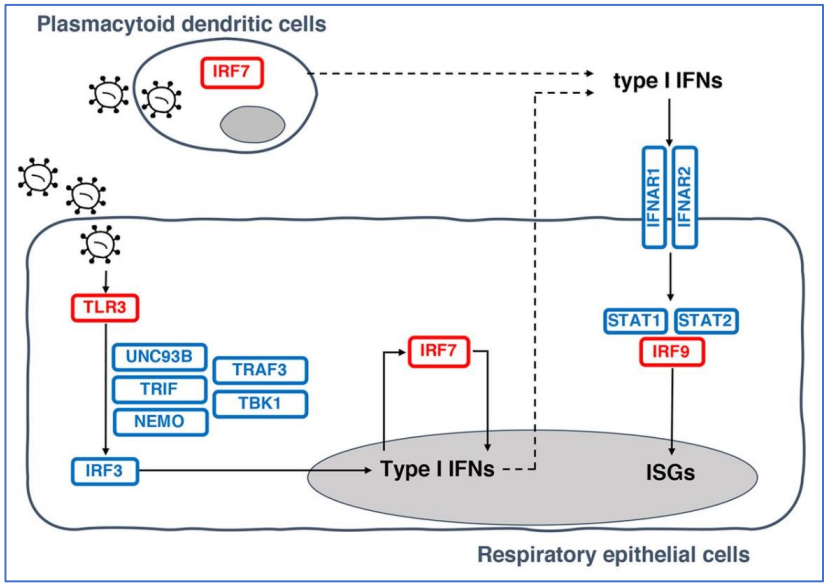
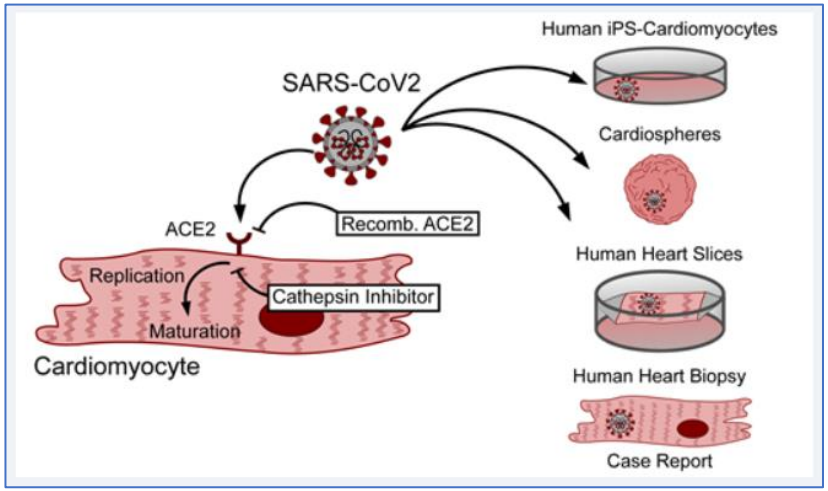
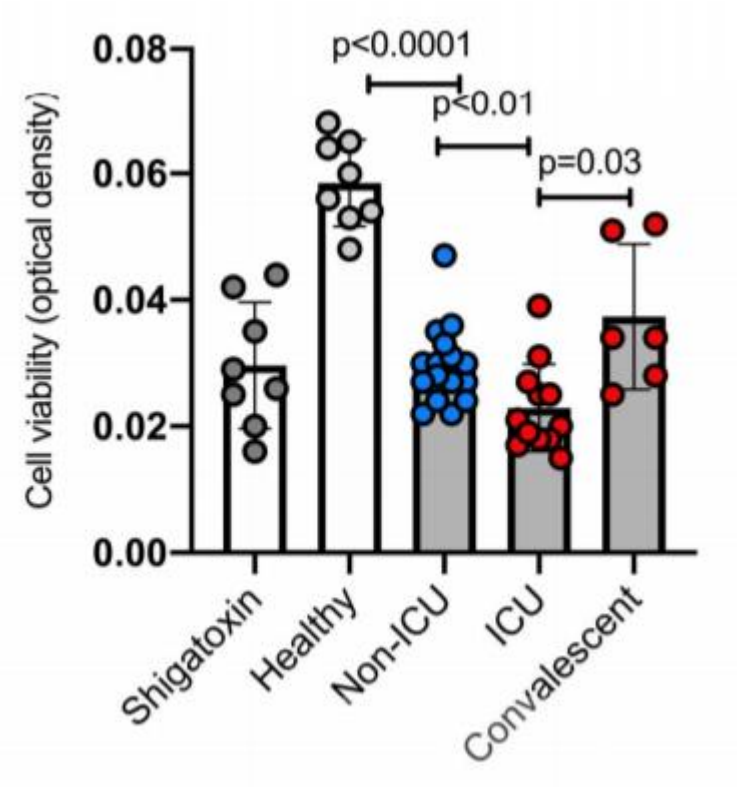


Figure 2. Viral clearance by day 6 among the infected intention-to-treat population. HR is adjusted for age and days between collection of the SARS-CoV-2-positive specimen and enrollment.

Zhang Q et al Science https://science.sciencemag.org/content/early/2020/09/23/science.abd4570.full	Inborn errors of type I IFN immunity in patients with life-threatening COVID-19	Studio basato sul sequenziamento del genoma di 659 pazienti ospedalizzati per polmonite grave COVID-19 relata, alla ricerca di mutazioni associate alla gravità di malattia (a partire da mutazioni note correlate al rischio di influenza grave). I pazienti gravi hanno errori congeniti della via di sintesi di Interferon-I.	Clinical outcome upon infection with SARS-CoV-2 ranges from silent infection to lethal COVID-19. We have found an enrichment in rare variants predicted to be loss-of-function (LOF) at the 13 human loci known to govern TLR3- and IRF7-dependent type I interferon (IFN) immunity to influenza virus, in 659 patients with life-threatening COVID-19 pneumonia, relative to 534 subjects with asymptomatic or benign infection. By testing these and other rare variants at these 13 loci, we experimentally define LOF variants in 23 patients (3.5%), aged 17 to 77 years, underlying autosomal recessive or dominant deficiencies. We show that human fibroblasts with mutations affecting this pathway are vulnerable to SARS-CoV-2. Inborn errors of TLR3- and IRF7-dependent type I IFN immunity can underlie life-threatening COVID-19 pneumonia in patients with no prior severe infection. 

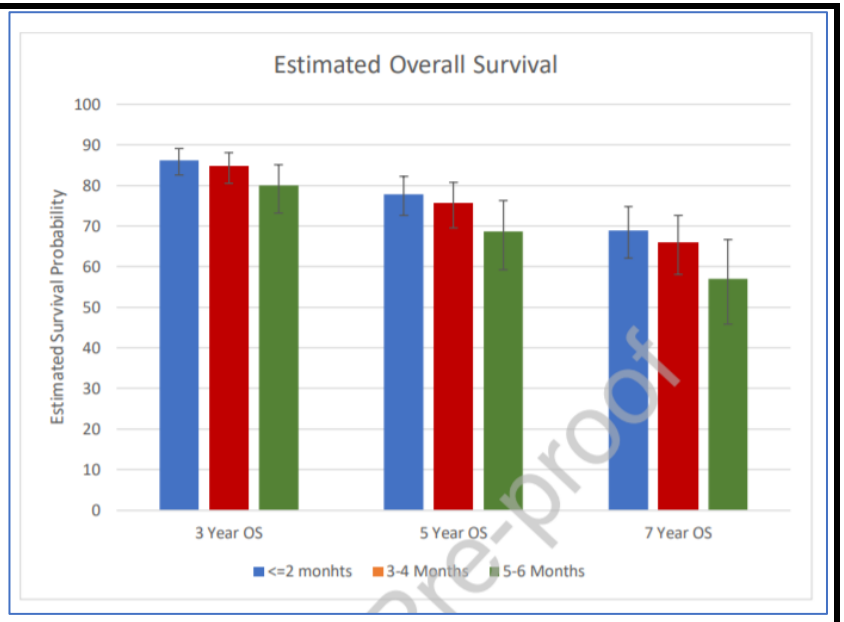
Bojkova D et al Cardiovascular Research https://academic.oup.com/cardiovascres/advance-article/doi/10.1093/cvr/cvaa267/5910550	SARS-CoV-2 infects and induces cytotoxic effects in human cardiomyocytes.	Dimostrazione dell'infezione di cardiomiociti da parte di SARS-CoV-2 su coltura cellulare, su un modello di organo tridimensionale, su sezioni di tessuto cardiaco e nei cardiomiociti provenienti da un paziente infetto.	AIMS: Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has emerged as a global pandemic. SARS-CoV-2 infection can lead to elevated markers of cardiac injury associated with higher risk of mortality. It is unclear whether cardiac injury is caused by direct infection of cardiomyocytes or is mainly secondary to lung injury and inflammation. Here, we investigate whether cardiomyocytes are permissive for SARS-CoV-2 infection. METHODS AND RESULTS: Two strains of SARS-CoV-2 infected human induced pluripotent stem cell-derived cardiomyocytes (iPS-CMs) as demonstrated by detection of intracellular double-stranded viral RNA and viral spike glycoprotein expression. Increasing concentrations of viral RNA are detected in supernatants of infected cardiomyocytes, which induced infections in Caco-2 cell lines, documenting productive infections. SARS-COV-2 infection and induced cytotoxic and proapoptotic effects associated with it abolished cardiomyocyte beating. RNA sequencing confirmed a transcriptional response to viral infection as demonstrated by the up-regulation of genes associated with pathways related to viral response and interferon signalling, apoptosis, and reactive oxygen stress. SARS-CoV-2 infection and cardiotoxicity was confirmed in a 3D cardiosphere tissue model. Importantly, viral spike protein and viral particles were detected in living human heart slices after infection with SARS-CoV-2. Coronavirus particles were further observed in cardiomyocytes of a patient with COVID-19. Infection of iPS-CMs was dependent on cathepsins and angiotensin-converting enzyme 2 (ACE2), and was blocked by remdesivir. CONCLUSIONS: This study demonstrates that SARS-CoV-2 infects cardiomyocytes in vitro in an ACE2- and cathepsin-dependent manner. SARS-CoV-2 infection of cardiomyocytes is inhibited by the antiviral drug remdesivir.

			TRANSLATIONAL PERSPECTIVE: Although this study cannot address whether cardiac injury and dysfunction in COVID-19 patients is caused by direct infection of cardiomyocytes, the demonstration of direct cardiotoxicity in cardiomyocytes, organ mimics, human heart slices and human hearts warrants the further monitoring of cardiotoxic effects in COVID-19 patients. 
Rauch A et al Circulation https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.120.050907	Endotheliopathy is induced by plasma from critically-ill patients and associated with organ failure in severe COVID-19	La risposta infiammatoria sregolata che caratterizza l'infezione da SARS-CoV-2 può indurre direttamente un danno endoteliale, come dimostrato esponendo *in vitro* cellule endoteliali polmonari al plasma di soggetti con COVID-19.	Lung histological analyses revealed the presence of vascular inflammation and severe endothelial injury as a direct consequence of intracellular SARS-CoV-2 infection and ensuing host inflammatory response in COVID-191. Endothelial cells promote coagulation following injury, leading to widespread formation of microthrombi, provoking microcirculatory failure or large-vessel thrombosis. Growing evidence suggests that microvascular thrombosis is a major pathophysiological event in COVID-19 pathogenesis.

			Damaged endothelial cells could be closely implicated in the pro-thrombotic state commonly reported in severe intensive care unit (ICU)-patients. How SARS-CoV-2 exerts its cytopathic effects is still a matter of debate and ultrastructural evidence of direct viral replication in endothelial cells remains to be demonstrated. Although direct viral tissue damage is a plausible mechanism of injury, endothelial damage and thrombo-inflammation associated with dysregulated immune responses, inducing microvascular thrombosis, represents an attractive alternative hypothesis. 

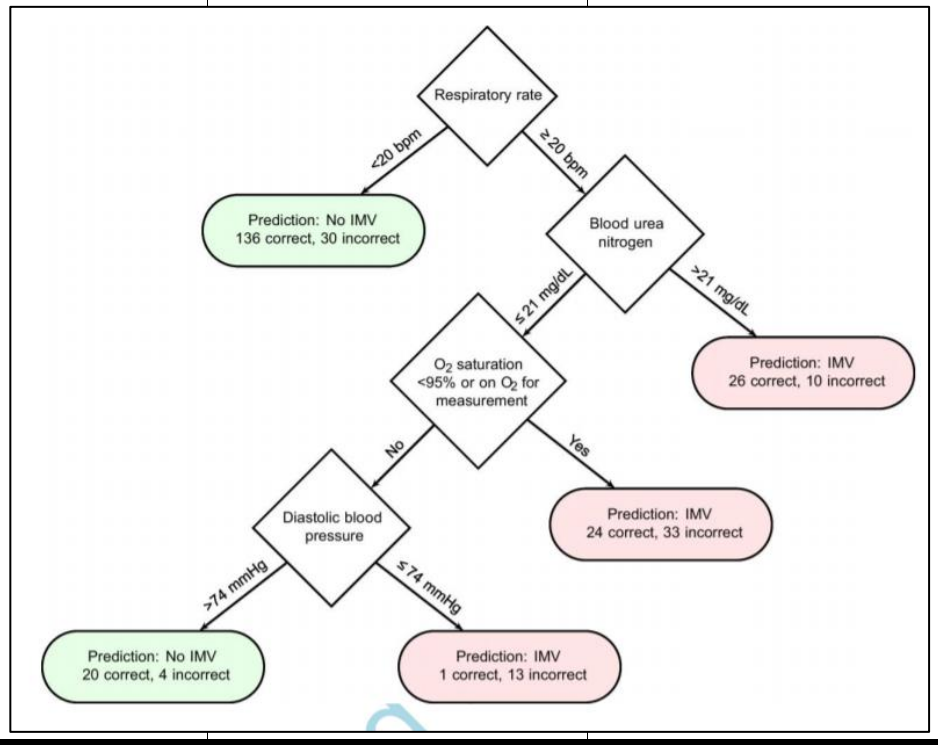
Pereson MJ et al Journal of Medical Virology https://onlinelibrary.wiley.com/doi/10.1002/jmv.26545	Phylogenetic analysis of SARS-CoV-2 in the first months since its emergence.	Analisi dei genomi di SARS-CoV-2 da ospite umano disponibili sul database GISAID al fine di ricostruirne l'evoluzione dall'inizio della pandemia. La regione codificante per la proteina S di superficie è tra le più altamente variabili.	During the first months of SARS-CoV-2 evolution in a new host, contrasting hypotheses have been proposed about the way the virus has evolved and diversified worldwide. The aim of this study was to perform a comprehensive evolutionary analysis to describe the human outbreak and the evolutionary rate of different genomic regions of SARS-CoV-2. The molecular evolution in nine genomic regions of SARS-CoV-2 was analyzed using three different approaches: phylogenetic signal assessment, emergence of amino acid substitutions, and Bayesian evolutionary rate estimation in eight successive fortnights since the virus emergence. All observed phylogenetic signals were very low and tree topologies were in agreement with those signals. However, after four months of evolution, it was possible to identify regions revealing an incipient viral lineage formation despite the low phylogenetic signal, since fortnight 3. Finally, the SARS-CoV-2 evolutionary rate for regions nsp3 and S, the ones presenting greater variability, was estimated as 1.37 x 10(-3) and 2.19 x 10(-3) substitution/site/year, respectively. In conclusion, results from this work about the variable diversity of crucial viral regions and determination of the evolutionary rate are consequently decisive to understand essential features of viral emergence. In turn, findings may allow the first time characterization of the evolutionary rate of S protein, crucial for vaccine development.
Ginsburg KB et al Urology https://www.goldjournal.net/article/S0090-4295(20)31150-X/fulltext	Association of Surgical Delay and Overall Survival in Patients with T2 Renal Masses: Implications for Critical Clinical Decision-Making during the COVID-19 Pandemic.	Fra gli effetti indiretti di COVID-19, il ritardo nell'esecuzione di interventi chirurgici ha conseguenze potenzialmente gravi, in particolare per i pazienti oncologici. Studio retrospettivo che tenta di	OBJECTIVE: To test for an association between surgical delay and overall survival (OS) for patients with T2 renal masses. Many health care systems are balancing resources to manage the current COVID-19 pandemic resulting in surgical delay in patients with large renal masses. METHODS: Using Cox proportional hazard models, we analyzed data from the National Cancer Database for patients undergoing extirpative surgery for clinical T2N0M0 renal masses

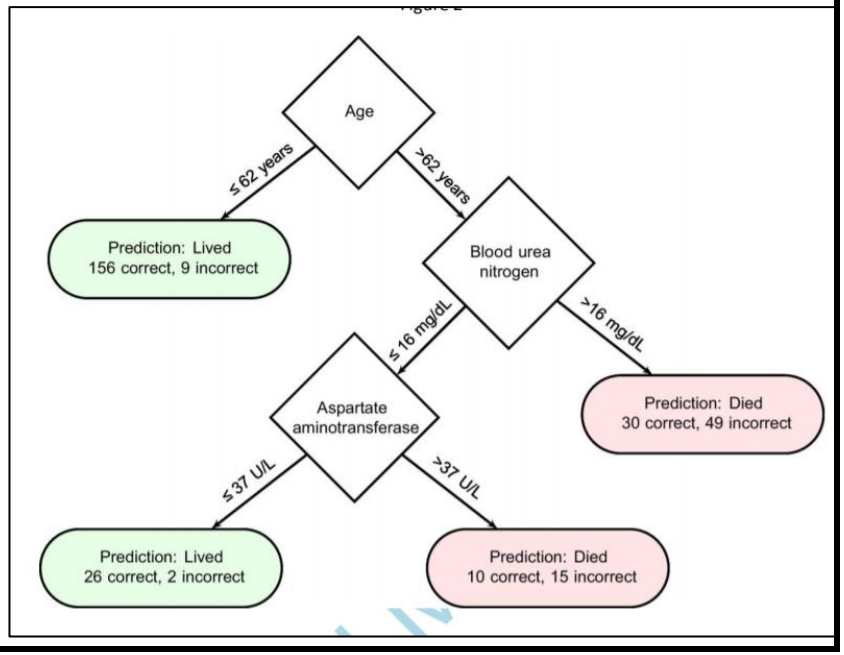
		stabilire un limite massimo di ritardo, non dannoso in termini di sopravvivenza,per pazienti con neoplasia renale in stadio T2 candidati a nefrectomia.	between 2004 and 2015. Study outcomes were to assess for an association between surgical delay with overall survival and pathologic stage. RESULTS: We identified 11,848 patients who underwent extirpative surgery for clinical T2 renal masses. Compared with patients undergoing surgery within 2 months of diagnosis, we found worse OS for patients with a surgical delay of 3-4 months (HR 1.12, 95% CI 1.00-1.25) or 5-6 months (HR 1.51, 95% CI 1.19-1.91). Considering only healthy patients with CCI=0, worse OS was associated with surgical delay of 5-6 months (HR 1.68, 95% CI 1.21-2.34, p=0.002) but not 3-4 months (HR 1.08, 95% CI 0.93-1.26, p=0.309). Pathologic stage (pT or pN) was not associated with surgical delay. CONCLUSIONS: Prolonged surgical delay (5-6 months) for patients with T2 renal tumors appears to have a negative impact on OS while shorter surgical delay (3-4 months) was not associated with worse OS in healthy patients. The data presented in this study may help patients and providers to weigh the risk of surgical delay vs. the risk of iatrogenic SARS-CoV-2 exposure during resurgent waves COVID-19 pandemic.

			
Vital de Oliveira L et al Revista da Associação Médica Brasileira https://www.scielo.br/scielo.php?script=sci_arttext&pid=S0104-42302020001400130&tlng=en	Current evidence of SARS-CoV-2 vertical transmission: an integrative review.	Revisione delle conoscenze attuali riguardo la trasmissione verticale di SARS-CoV-2, che appare possibile ma rara. Non vi sono evidenze sufficienti per ritenere che il parto naturale aumenti il rischio di trasmissione.	OBJECTIVE: To review the current scientific evidence of vertical transmission related to coronavirus disease 2019 (COVID-19). METHODS: An integrative review was performed by two independent researchers, based on the literature available in the MEDLINE (via PubMed) and LILACS databases, using the descriptors "pregnancy" AND "COVID-19" AND "vertical transmission". This search included case reports or case series published up until 17th June 2020 in English or Portuguese. After reading the articles available in their entirety, those related specifically to the potential risks of vertical transmission of COVID-19 during pregnancy were selected. We initially found a total of 57 articles; 26 were carefully screened and 15 were finally selected. RESULTS: Pregnancy can make women more susceptible to infections, especially by viral pathogens, given the various physiological and immunological changes that occur to maintain maternal-fetal balance. It is

			speculated that the fetus may be a possible target for COVID-19. Few studies (3 out of 15) in our analysis have found positive results for SARS-CoV-2 in fetal membranes, placenta, and in newborns right after birth. Additionally, no difference was noticed when comparing different modes of delivery, and seems reasonable to assume that pregnant women with stable clinical conditions can be encouraged for vaginal delivery. CONCLUSION: Further studies with a great number of cases are warranted to elucidate whether the virus may be vertically transmitted to the fetus and if any maternal conditions can influence that. Our findings seem to demonstrate that vertical transmission is possible but quite unusual.
Jackson B et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1459/5911241	Predictors at admission of mechanical ventilation and death in an observational cohort of adults hospitalized with COVID-19.	Studio di coorte osservazionale retrospettivo su 297 adulti ricoverati per COVID-19 alla ricerca dei fattori presenti all'ingresso in ospedale e associati a ventilazione meccanica e decesso. La pneumopatia cronica non è associata alla mortalità.	BACKGROUND: Coronavirus disease (COVID-19) can cause severe illness and death. Predictors of poor outcome collected on hospital admission may inform clinical and public health decisions. METHODS: We conducted a retrospective observational cohort investigation of 297 adults admitted to eight academic and community hospitals in Georgia, United States, during March 2020. Using standardized medical record abstraction, we collected data on predictors including admission demographics, underlying medical conditions, outpatient antihypertensive medications, recorded symptoms, vital signs, radiographic findings, and laboratory values. We used random forest models to calculate adjusted odds ratios (aORs) and 95% confidence intervals (CI) for predictors of invasive mechanical ventilation (IMV) and death. RESULTS: Compared with age <45 years, ages 65-74 years and >/=75 years were predictors of IMV (aOR 3.12, CI 1.47-6.60; aOR 2.79, CI 1.23-6.33) and the strongest predictors for death (aOR 12.92, CI 3.26-51.25; aOR 18.06, CI 4.43-73.63). Comorbidities associated with death (aORs from 2.4 to 3.8, p <0.05) included end-stage renal disease, coronary artery disease, and neurologic disorders, but not

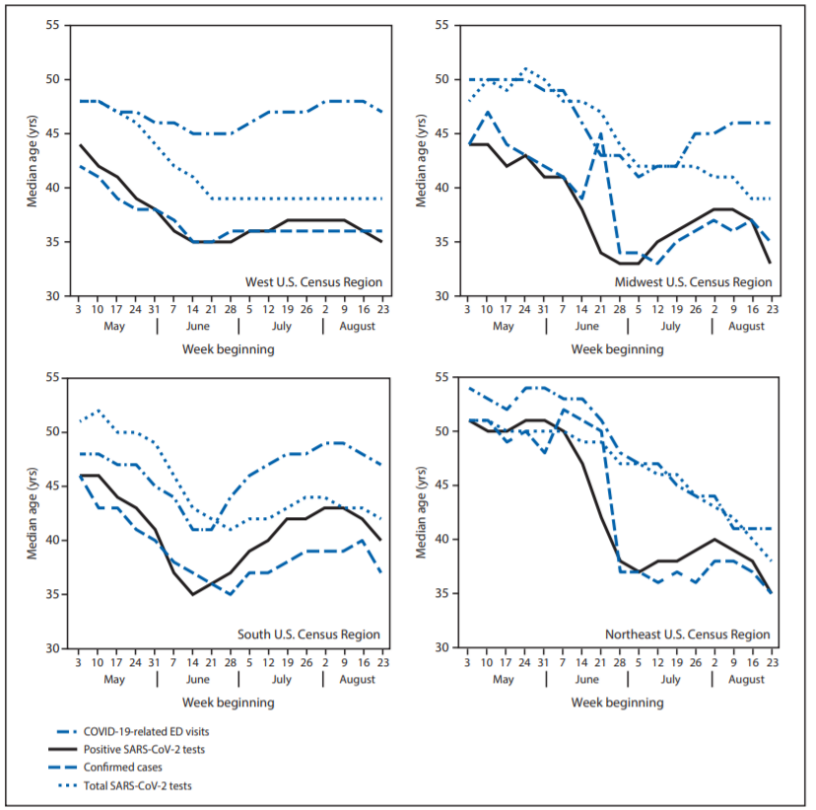
pulmonary disease, immunocompromise, or hypertension. Pre-hospital use vs. non-use of angiotensin receptor blockers (aOR 2.02, CI 1.03-3.96) and dihydropyridine calcium channel blockers (aOR 1.91, CI 1.03-3.55) were associated with death. CONCLUSIONS: After adjustment for patient and clinical characteristics, older age was the strongest predictor of death, exceeding comorbidities, abnormal vital signs, and laboratory test abnormalities. That coronary artery disease, but not chronic lung disease, was associated with death among hospitalized patients warrants further investigation, as do associations between certain antihypertensive medications and death.

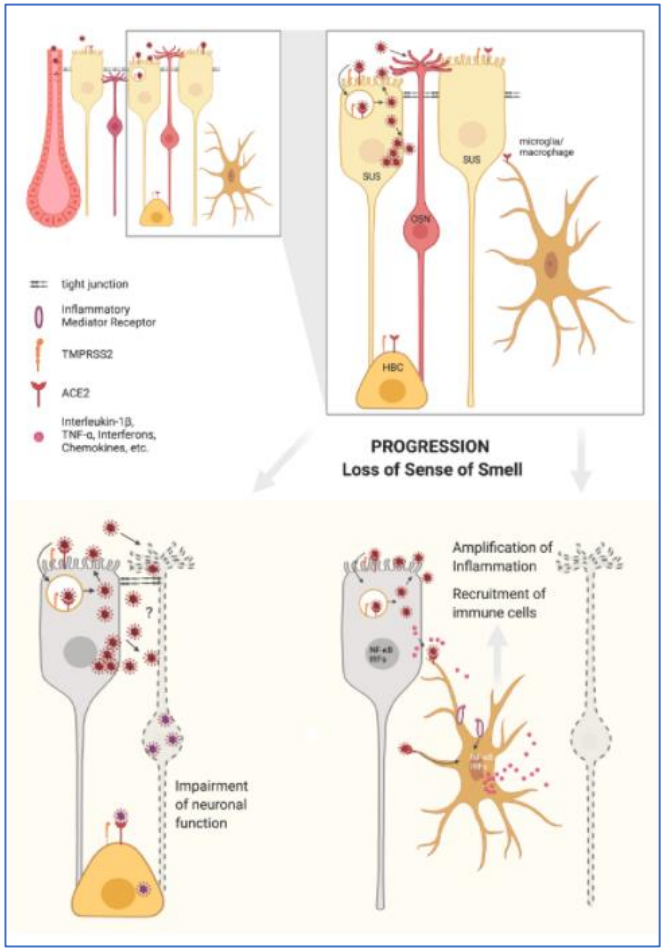




Bartoletti M et al Clinical Microbiology and Infection https://linkinghub.elsevier.com/retrieve/pii/S1198743X20305632	Efficacy of corticosteroid treatment for hospitalized patients with severe COVID-19: a multicenter study.	Studio osservazionale multicentrico su 513 pazienti con infezione grave da SARS-CoV-2. Il trattamento con steroidi è associato a riduzione della mortalità solo nel sottogruppo dei pazienti critici (paO2/FiO2 < 200 mmHg all'ingresso).	OBJECTIVES: To assess the efficacy of corticosteroids in patients with coronavirus disease 2019 (COVID-19) METHODS: Multicenter observational study from February 22 through June 30, 2020. We included consecutive adult patients with severe COVID-19 defined as respiratory rate >/=30 breath per minute, oxygen saturation </=93% on ambient air or arterial partial pressure of oxygen to fraction of inspired oxygen </=300 mmHg. We excluded patients treated with other immunomodulant drugs, receiving low dose of corticosteroids and those receiving corticosteroids after 72h from admission. The primary endpoint was 30-day mortality form hospital admission. The main exposure variable was corticosteroid therapy at dosage of >/=0.5 mg/kg of prednisone equivalents. It was introduced as binomial covariate in a logistic regression model for primary endpoint and inverse probability of treatment weighting using the propensity score. RESULTS: Of 1717 patients with COVID-19 evaluated, 513 patients were included in the study; of these 170 (33%) were treated with corticosteroids. During the hospitalization 166 (34%) patients reached the primary outcome [60/170 (35%) in the corticosteroid group and 106/343 (31%) in the non-corticosteroid group]. At multivariable analysis corticosteroid treatment was not associated with lower 30-day mortality rate [aOR 0.59 (0.20-1.74), p=0.33]. After inverse probability of treatment weighting, corticosteroids were not associated to lower 30-day mortality [average treatment effect 0.05 (95% -0.02 to 0.09), p=0.12]. However, subgroup analysis revealed that in patients with PO2/FiO2 < 200 mmHg at admission [135 patients, 52 (38%) treated with corticosteroids] corticosteroid treatment was associated to a lower risk of 30-day mortality [23/52 (44%) vs 45/83 (54%), aOR 0.20 (95%CI 0.04 to 0.90), p=0.036]. CONCLUSION: Our study shows

			that the effect of corticosteroid treatment on mortality might be limited to critically ill COVID-19 patients.
Boehmer TK et al Morbidity and Mortality Weekly Report https://www.cdc.gov/mmwr/volumes/69/wr/mm6939e1.htm?s_cid=mm6939e1_w	Changing Age Distribution of the COVID-19 Pandemic — United States, May–August 2020.	Osservazione della diffusione di SARS-CoV-2 nella fascia d'età 20-29 anni in Giugno-Agosto nel sud degli USA, seguita entro 15 giorni da una nuova ondata nella fascia d'età superiore a 60 anni, a dimostrare una probabile trasmissione dai più giovani ai più anziani in comunità.	What is already known about this topic? Early in the pandemic, COVID-19 incidence was highest among older adults. What is added by this report? During June–August 2020, COVID-19 incidence was highest in persons aged 20–29 years, who accounted for >20% of all confirmed cases. Younger adults likely contribute to community transmission of COVID-19. Across the southern United States in June 2020, increases in percentage of positive SARS-CoV-2 test results among adults aged 20–39 years preceded increases among those aged ≥60 years by 4–15 days. What are the implications for public health practice? Strict adherence to community mitigation strategies and personal preventive behaviors by younger adults is needed to help reduce infection and subsequent transmission to persons at higher risk for severe illness.

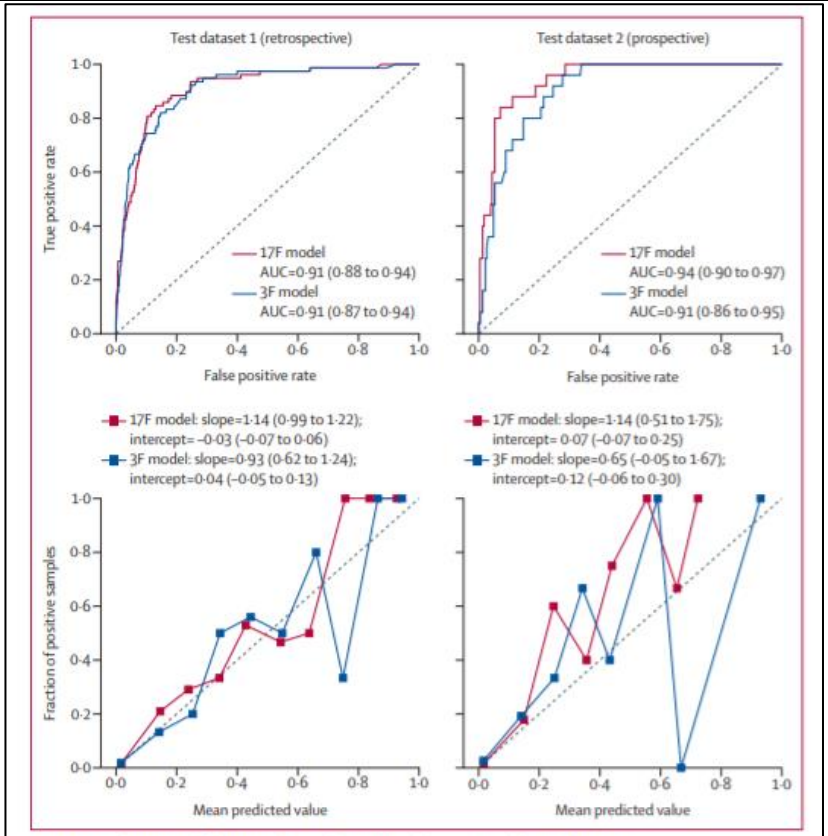
			FIGURE 2. Weekly median age of persons with COVID-19–like illness-related emergency department (ED) visits,* positive SARS-CoV-2 reverse transcription–polymerase chain reaction (RT-PCR) test results,† and confirmed COVID-19 cases,§ and of persons for whom all SARS-CoV-2 RT-PR tests were conducted,¶ by U.S. Census region** — United States, May 3–August 29, 2020 
Glezer I et al Journal of Neurochemistry https://onlinelibrary.wiley.com/doi/10.1111/jnc.15197	Viral infection and smell loss: The case of COVID-19.	Analisi dell'anosmia come sintomo delle infezioni virali e disamina dei possibili meccanismi fisiopatologici di questo fenomeno nell'ambito dell'infezione da SARS-CoV-2.	Olfactory disorders have been increasingly reported in individuals infected with SARS-CoV-2, the virus causing the coronavirus disease 2019 (COVID-19). Losing the sense of smell has a strong impact on the quality of life, since it may lead to malnutrition, weight loss, food poisoning, depression, and exposure to dangerous chemicals. Individuals who suffer from anosmia (inability to smell) also cannot sense the flavor of food, which is a combination of taste and smell. Interestingly, infected individuals have reported sudden loss of

			smell with no congested nose, as is frequently observed in common colds or other upper respiratory tract infections. These observations suggest that SARS-CoV-2 infection leads to olfactory loss through a distinct mechanism, which is still unclear. This article provides an overview of olfactory loss and the recent findings relating to COVID-19. Possible mechanisms of SARS-CoV-2 induced olfactory loss are also discussed. 

Cozzi A et al European Journal of Radiology https://www.ejradiology.com/article/S0720-048X(20)30461-7/fulltext	Chest x-ray in the COVID-19 pandemic: Radiologists' real-world reader performance.	Studio retrospettivo osservazionale condotto a Milano sulla performance, in termini di sensibilità, specificità e accuratezza, di Radiologi con diversi livelli di esperienza nell'interpretazione di RX torace per la diagnosi di infezione da SARS-CoV-2.	PURPOSE: To report real-world diagnostic performance of chest x-ray (CXR) readings during the COVID-19 pandemic. METHODS: In this retrospective observational study we enrolled all patients presenting to the emergency department of a Milan-based university hospital from February 24th to April 8th 2020 who underwent nasopharyngeal swab for reverse transcriptase-polymerase chain reaction (RT-PCR) and anteroposterior bedside CXR within 12h. A composite reference standard combining RT-PCR results with phone-call-based anamnesis was obtained. Radiologists were grouped by CXR reading experience (Group-1, >10 years; Group-2, <10 years), diagnostic performance indexes were calculated for each radiologist and for the two groups. RESULTS: Group-1 read 435 CXRs (77.0 % disease prevalence): sensitivity was 89.0 %, specificity 66.0 %, accuracy 83.7 %. Group-2 read 100 CXRs (73.0 % prevalence): sensitivity was 89.0 %, specificity 40.7 %, accuracy 76.0 %. During the first half of the outbreak (195 CXRs, 66.7 % disease prevalence), overall sensitivity was 80.8 %, specificity 67.7 %, accuracy 76.4 %, Group-1 sensitivity being similar to Group-2 (80.6 % versus 81.5 %, respectively) but higher specificity (74.0 % versus 46.7 %) and accuracy (78.4 % versus 69.0 %). During the second half (340 CXRs, 81.8 % prevalence), overall sensitivity increased to 92.8 %, specificity dropped to 53.2 %, accuracy increased to 85.6 %, this pattern mirrored in both groups, with decreased specificity (Group-1, 58.0 %; Group-2, 33.3 %) but increased sensitivity (92.7 % and 93.5 %) and accuracy (86.5 % and 81.0 %, respectively). CONCLUSIONS: Real-world CXR diagnostic performance during the COVID-19 pandemic showed overall high sensitivity with higher specificity for more experienced radiologists. The increase in accuracy over time strengthens CXR role as a first line examination in suspected COVID-19 patients.

Rahman MM et al Veterinary Medicine and Science https://onlinelibrary.wiley.com/doi/10.1002/vms3.360	Coronaviruses in wild birds - A potential and suitable vector for global distribution.	Revisione dei dati sulla diffusione di SARS-CoV-2 tra i volatili selvatici e loro ruolo nella trasmissione dei Coronavirus e in particolare di SARS-CoV-2.	The recurrent appearance of novel coronaviruses (CoVs) and the mortality and morbidity caused by their outbreaks aroused a widespread response among the global science community. Wild birds' high biodiversity, perching and migratory activity, ability to travel long distances and possession of a special adaptive immune system may make them alarming sources of zoonotic CoV-spreading vectors. This review gathers the available evidence on the global spread of CoVs in wild birds to date. The major wild birds associated with different types of CoVs are Anseriformes, Charadriiformes, Columbiformes, Pelecaniformes, Galliformes, Passeriformes, Psittaciformes, Accipitriformes, Ciconiiformes, Gruiformes and so on. However, the main type of CoVs found in wild birds is gammacoronavirus, followed by deltacoronavirus. Consequently, it is imperative to enable thorough research and continuous monitoring to fill the study gap in terms of understanding their role as zoonotic vectors and the frequent appearance of novel CoVs.
Yadaw AS et al The Lancet https://www.thelancet.com/journals/landig/article/PIIS2589-7500(20)30217-X/fulltext	Clinical features of COVID-19 mortality: development and validation of a clinical prediction model	Generazione, con tecniche di machine learning, di un modello predittivo della mortalità per COVID-19 a partire dai dati di una coorte di pazienti di New York. Il modello finale risulta accurato e si basa su tre caratteristiche: età, saturazione minima di ossigeno e tipo di trattamento (ricovero o gestione extraospedaliera).	Background: The COVID-19 pandemic has affected millions of individuals and caused hundreds of thousands of deaths worldwide. Predicting mortality among patients with COVID-19 who present with a spectrum of complications is very difficult, hindering the prognostication and management of the disease. We aimed to develop an accurate prediction model of COVID-19 mortality using unbiased computational methods, and identify the clinical features most predictive of this outcome. Methods: In this prediction model development and validation study, we applied machine learning techniques to clinical data from a large cohort of patients with COVID-19 treated at the Mount Sinai Health System in New York City, NY, USA, to predict mortality. We analysed patient-level data captured in the Mount Sinai Data Warehouse database for individuals with a confirmed diagnosis of

			COVID-19 who had a health system encounter between March 9 and April 6, 2020. For initial analyses, we used patient data from March 9 to April 5, and randomly assigned (80:20) the patients to the development dataset or test dataset 1 (retrospective). Patient data for those with encounters on April 6, 2020, were used in test dataset 2 (prospective). We designed prediction models based on clinical features and patient characteristics during health system encounters to predict mortality using the development dataset. We assessed the resultant models in terms of the area under the receiver operating characteristic curve (AUC) score in the test datasets. Findings: Using the development dataset (n=3841) and a systematic machine learning framework, we developed a COVID-19 mortality prediction model that showed high accuracy (AUC=0·91) when applied to test datasets of retrospective (n=961) and prospective (n=249) patients. This model was based on three clinical features: patient's age, minimum oxygen saturation over the course of their medical encounter, and type of patient encounter (inpatient vs outpatient and telehealth visits). Interpretation: An accurate and parsimonious COVID-19 mortality prediction model based on three features might have utility in clinical settings to guide the management and prognostication of patients affected by this disease. External validation of this prediction model in other populations is needed.

			 ***Figure 3*: Performance of the mortality prediction models on two validation datasets** Evaluation results for test datasets 1 (A) and 2 (B) are shown here in terms of the ROC curves obtained, as well as their AUC scores, with 95% CIs in parentheses. Calibration curves of the 3F and 17F models on test datasets 1 (C) and 2 (D), with the slopes and intercepts of all the curves, along with their 95% CIs in parentheses. AUC=area under the ROC curve. ROC=receiver operating characteristic.
Russel MV et al JAMA	Susceptibility to SARS-CoV-2 Infection Among Children and Adolescents Compared With Adults A Systematic Review and Meta-analysis	Revisione sistematica e metanalisi sul ruolo di bambini e adolescenti nella trasmissione di SARS-CoV-2 a confronto con gli adulti. Molti studi pubblicati non sono utilizzabili nella	IMPORTANCE The degree to which children and adolescents are infected by and transmit severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) is unclear. The role of children and adolescents in transmission of SARS-CoV-2 is dependent on susceptibility, symptoms, viral load, social contact patterns, and behavior. OBJECTIVE To systematically review the susceptibility to

https://jamanetwork.com/journals/jamapediatrics/fullarticle/2771181		metanalisi, tuttavia emerge una minore suscettibilità all'infezione nei bambini di età inferiore ai 10-14 anni, che dunque potrebbero avere un ruolo ridotto nella trasmissione del virus.	and transmission of SARS-CoV-2 among children and adolescents compared with adults. DATA SOURCES PubMed and medRxiv were searched from database inception to July 28, 2020, and a total of 13 926 studies were identified, with additional studies identified through hand searching of cited references and professional contacts. STUDY SELECTION Studies that provided data on the prevalence of SARS-CoV-2 in children and adolescents (younger than 20 years) compared with adults (20 years and older) derived from contact tracing or population screening were included. Single-household studies were excluded. DATA EXTRACTION AND SYNTHESIS PRISMA guidelines for abstracting datawere followed, which was performed independently by 2 reviewers. Quality was assessed using a critical appraisal checklist for prevalence studies. Random-effects meta-analysis was undertaken. MAIN OUTCOMES AND MEASURES Secondary infection rate (contact-tracing studies) or prevalence or seroprevalence (population screening studies) among children and adolescents compared with adults. RESULTS A total of 32 studies comprising 41 640 children and adolescents and 268 945 adults met inclusion criteria, including 18 contact-tracing studies and 14 population screening studies. The pooled odds ratio of being an infected contact in children compared with adults was 0.56 (95%CI, 0.37-0.85), with substantial heterogeneity (I2 = 94.6%). Three school-based contact-tracing studies found minimal transmission from child or teacher index cases. Findings from population screening studies were heterogenous and were not suitable for meta-analysis. Most studies were consistent with lower seroprevalence in children compared with adults, although seroprevalence in adolescents appeared similar to adults. CONCLUSIONS AND RELEVANCE In this meta-

			analysis, there is preliminary evidence that children and adolescents have lower susceptibility to SARS-CoV-2, with an odds ratio of 0.56 for being an infected contact compared with adults. There is weak evidence that children and adolescents play a lesser role than adults in transmission of SARS-CoV-2 at a population level. This study provides no information on the infectivity of children.
Fisher J et al Annals of Surgery https://journals.lww.com/annalsofsurgery/Abstract/9000/Increase_in_Pediatric_Perforated_Appendicitis_in.94185.aspx	Increase in Pediatric Perforated Appendicitis in the New York City Metropolitan Region at the Epicenter of the COVID-19 Outbreak.	Osservazione di un aumento della prevalenza di appendicite complicata da perforazione nei bambini che hanno acceduto all'ospedale nel periodo di picco di COVID-19 a New York rispetto ai 5 anni precedenti.	OBJECTIVE: The aim of the study was to determine whether perforated appendicitis rates in children were influenced by the Coronavirus disease 2019 (COVID-19) surge. BACKGROUND: Disruption of care pathways during a public health crisis may prevent children from obtaining prompt assessment for surgical conditions. Progression of appendicitis to perforation is influenced by timeliness of presentation. In the context of state-mandated controls and public wariness of hospitals, we investigated the impact of the COVID-19 outbreak on perforated appendicitis in children. STUDY DESIGN: We conducted an analysis of all children presenting to 3 hospital sites with acute appendicitis between March 1 and May 7, 2020, corresponding with the peak COVID-19 outbreak in the New York City region. Control variables were collected from the same institutions for the preceding 5 years. The primary outcome measure was appendiceal perforation. RESULTS: Fifty-five children presented with acute appendicitis over 10 weeks. Compared to a 5-year control cohort of 1291 patients, we observed a higher perforation rate (45% vs 27%, odds ratio 2.23, 95% confidence interval 1.29-3.85, P = 0.005) and longer mean duration of symptoms in children with perforations (71 +/- 39 vs 47 +/- 27 h, P = 0.001) during the COVID-19 period. There were no differences in perforation rates (55% vs 59%, P = 0.99) or median length of stay (1.0 vs 3.0 days, P = 0.58) among children screening positive or negative for SARS-CoV-2. CONCLUSIONS: Children in the epicenter

			of the COVID-19 outbreak demonstrated higher rates of perforated appendicitis compared to historical controls. Preoperative detection of SARS-CoV-2 was not associated with inferior outcomes. Although children likely avoid much of the morbidity directly linked to COVID-19, disruption to local healthcare delivery systems may negatively impact other aspects of pediatric surgical disease.
Ho EP et al Age and Ageing https://academic.oup.com/ageing/advance-article/doi/10.1093/ageing/afaa205/5908995	COVID 19: Prioritise Autonomy, Beneficence and Conversations Before Score-based Triage	Con lo sperato appiattimento della curva dei contagi da SARS-CoV-2, il triage di ammissione delle persone anziane in terapia intensiva dovrebbe prevedere una valutazione caso per caso che non escluda a priori i pazienti in età avanzata.	At the start of the COVID-19 pandemic, mounting demand overwhelmed critical care surge capacities, triggering implementation of triage protocols to determine ventilator allocation. Relying on triage scores to ration care, while relieving clinicians from making morally distressing decisions under high situational pressure, distracts clinicians from what is essentially deeply humanistic issues entrenched in this protracted public health crisis. Such an approach will become increasingly untenable as countries flatten their epidemic curves. Decisions regarding ICU admission are particularly challenging in older people, who are most likely to require critical care, but for whom benefits are most uncertain. Before applying score-based triage, physicians must first discern if older people will benefit from critical care (beneficence) and second, if he wants critical care (autonomy). When deliberating beneficence, physicians should steer away from solely using age-stratified survival probabilities from epidemiological data. Instead, decisions must be based on individualised risk-stratification that encompasses evidence-based predictors of adverse outcomes specific to older adults. Survival will also need to be weighed against burden of treatment, as well as longer-term functional deficits and quality-of-life. By identifying the robust older people who may benefit from critical care, clinicians should proceed to elicit his values and preferences that would determine the treatment most aligned with his best interest. During these dialogues, physicians

			must truthfully convey the emergent clinical reality, discern the older person's therapeutic goals and discuss the feasibility of achieving them. Given that COVID-19 is here to stay, these conversations aimed at achieving goal-cordant care must become a new clinical norm.
Canetta C et al Autonomic Neuroscience https://www.autonomicneuroscience.com/article/S1566-0702(20)30168-5/fulltext	Syncope at SARS-CoV-2 onset.	Caratteristiche di 35 pazienti con storia di sincope all'esordio di infezione da SARS-CoV-2. Data l'assenza di anomalie neurologiche o cardiologiche rilevabili, gli autori postulano una predisposizione individuale all'inadeguatezza della tachicardia compensatoria per questi pazienti.	We describe clinical and laboratory findings in 35 patients tested positive for SARS-CoV-2 by reverse transcriptase-polymerase chain reaction on nasopharyngeal swab experiencing one or multiple syncope at disease onset. Clinical neurologic and cardiologic examination, and electrocardiographic findings were normal. Chest computed tomography showed findings consistent with interstitial pneumonia. Arterial blood gas analysis showed low pO2, pCO2, and ratio of arterial oxygen partial pressure to fractional inspired oxygen (PaO2/FiO2) indicating hypocapnic hypoxemia. Patients who presented with syncope showed significantly lower heart rate as compared to 68 SARS-CoV-2 positive that did not. Such poorer than expected compensatory heart rate increase may have led to syncope based on individual susceptibility. We speculate that SARS-CoV-2 could have caused angiotensin-converting enzyme-2 (ACE2) receptor internalization in the nucleus of the solitary tract and other midbrain nuclei, impairing baroreflex and chemoreceptor response, and inhibiting the compensatory tachycardia during acute hypocapnic hypoxemia.
Pavoni V et al Thrombosis research https://www.thrombosisresearch.com/article/S004	Venous thromboembolism and bleeding in critically ill COVID-19 patients treated with higher than standard low molecular weight	Analisi retrospettiva dei dati di 42 pazienti ricoverati in terapia intensiva per COVID-19 e trattati con enoxaparina a dosaggio variabile più cardioaspirina secondo un protocollo interno, sulla base del D-	BACKGROUND: Critically ill COVID-19 patients have a clear pattern of inflammation and hypercoagulable state. The main aim of the study was to evaluate the outcome of severe COVID-19 patients basing on prothrombotic risk factors (i.e. D-dimer). We also evaluated the impact of different doses of low molecular weight heparin (LMWH) on the incidence of bleedings. METHODS: The data of forty-two patients admitted to the Intensive Care Unit (ICU) were

9-3848(20)30517-X/fulltext	heparin doses and aspirin: A call to action.	dimero all'ingresso. I pazienti più gravi hanno alta incidenza di tromboembolia e maggiore outcome avverso nonostante la terapia. Non si verificano sanguinamenti maggiori nei trattati con eparina a dose terapeutica.	retrospectively analyzed. On ICU admission, patients with D-dimer<3000ng/mL (Group 1) received enoxaparin 4000 UI (6000 UI, if body mass index >35) subcutaneously b.i.d. and patients with D-dimer>/=3000ng/mL (Group 2) received enoxaparin 100UI/kg every 12h. Aspirin was administered to all patients once a day. RESULTS: Both groups presented a high incidence of perivascular thrombosis (40.9% in Group 1 and 30% in Group 2). Patients of Group 2 suffered a higher incidence of venous thromboembolism (VTE) than Group 1 (65% vs 13.6%, p=0.001). One patient (4.5%) of Group 1 and three patients (15%) of Group 2 suffered from minor bleeding; no patient had major bleeding. Group 2 had a longer ICU and hospital stay than Group 1 (11.5+/-5.6 vs 9.0+/-4.8 and 30+/-4.9 vs 21+/-2.3, p<0.05, respectively) as well as increased ICU mortality (25% vs 9.1%). CONCLUSIONS: More severe critically ill COVID-19 patients have a high incidence of VTE and worse outcome, despite the use of heparin at the therapeutic dose. However, the use of heparin did not increase the incidence of bleeding complications.

Table 3
Outcome measures of studied population stratified on D-dimer value [Group 1 (D-dimer < 3000 ng/mL), Group 2 (D-dimer ≥ 3000 ng/mL)].

	Total patients n = 42	Group 1 n = 22 (52.3%)	Group 2 n = 20 (47.6%)	p value
Length of ICU stay (days)	11.8 ± 5.1	9.0 ± 4.8	11.5 ± 5.6	0.040*
Length of hospital stay (days)	30 ± 4.9	21 ± 2.3	30 ± 4.9	0.002*
ICU mortality, n (%)	7 (16.7)	2 (9.1)	5 (25)	0.167
Hospital mortality, n (%)	9 (21.4)	4 (18.1)	5 (25)	0.590
Minor bleedings, n (%)	4 (9.5)	1 (4.5)	3 (15)	0.249
Airway bleedings, n (%)	2 (4.7)	0	2 (10)	
Macroscopic hematuria, n (%)	2 (4.7)	1 (4.5)	1 (5)	
Major bleedings, n (%)	0	0	0	–
VTE, n (%)	16 (38)	3 (13.6)	13 (65`	0.001*
PE, n (%)	3 (7.1)	1 (4.5)	2 (10)	
Proximal DVT, n (%)	13 (30.9)	2 (9.1)	11 (55)	
Perivascular thrombosis, n (%)	15 (35.7)	9 (40.9)	6 (30)	0.461
Internal jugular vein, n (%)	10 (23.8)	6 (27.3)	4 (20)	
Subclavian vein, n (%)	1 (2.4)	1 (4.5)	0	
Femoral vein, n (%)	4 (9.5)	2 (9.1)	2 (10)	

ICU: Intensive Care Unit; VTE: venous thromboembolism; PE: pulmonary embolism; DVT: deep vein thrombosis.
Data are expressed by mean ± SD or number (percentage).
* $p < 0.05$.

Setti L et al BMJ Open https://bmjopen.bmj.com/content/10/9/e039338	Potential role of particulate matter in the spreading of COVID-19 in Northern Italy: first observational study based on initial epidemic diffusion.	Studio che mostra un'associazione fra eccesso di particelle PM10 e infezioni da SARS-CoV-2, proponendo questo fattore come un determinante del contagio.	OBJECTIVES: A number of studies have shown that the airborne transmission route could spread some viruses over a distance of 2 meters from an infected person. An epidemic model based only on respiratory droplets and close contact could not fully explain the regional differences in the spread of COVID-19 in Italy. On March 16th 2020, we presented a position paper proposing a research hypothesis concerning the association between higher mortality rates due to COVID-19 observed in Northern Italy and average concentrations of PM10 exceeding a daily limit of 50 microg/m(3). METHODS: To monitor the spreading of COVID-19 in Italy from February 24th to March 13th (the date of the Italian lockdown), official daily data for PM10 levels were collected from all Italian provinces between February 9th and February 29th, taking into account the maximum lag period (14 days) between the infection and diagnosis. In addition to the number of exceedances of the daily limit value of PM10, we also considered population data and daily travelling information for each province. RESULTS: Exceedance of the daily limit value of PM10 appears to be a significant predictor of infection in univariate analyses ($p<0.001$). Less polluted provinces had a median of 0.03 infections over 1000 residents, while the most polluted provinces showed a median of 0.26 cases. Thirty-nine out of 41 Northern Italian provinces resulted in the category with the highest PM10 levels, while 62 out of 66 Southern provinces presented low PM10 concentrations ($p<0.001$). In Milan, the average growth rate before the lockdown was significantly higher than in Rome (0.34 vs 0.27 per day, with a doubling time of 2.0 days vs 2.6, respectively), thus suggesting a basic reproductive number R0>6.0, comparable with the highest values estimated for China. CONCLUSION: A significant association has been found between the

geographical distribution of daily PM10 exceedances and the initial spreading of COVID-19 in the 110 Italian provinces.

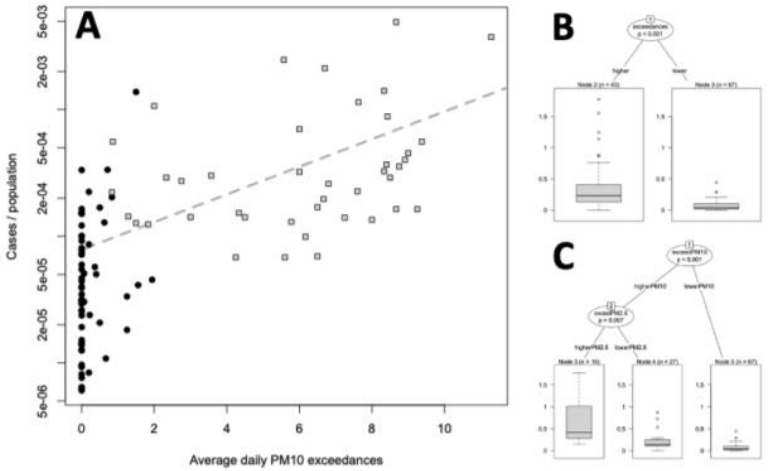


Figure 3 Relationship between the daily limit value of exceedances of PM_{10} and COVID-19 case ratios over the population in Italian provinces. (A) Scatter plot on a semilogarithmic scale relating the proportion of COVID-19 cases of the population of northern (grey squares) and southern (black bullets) Italian provinces vs the average daily limit value of exceedances of PM_{10}. The dashed binomial (logistic) regression is characterised by an increasing slope of 0.25 ($p<0.001$). (B) Box plots showing that—with a 1.29 cut-off value of exceedance of PM_{10}—the proportion of COVID-19 cases is greater ($p<0.001$) in the most polluted provinces (39 out of 41 located in Northern Italy) than the less polluted provinces, mainly located in Southern Italy (62 out of 66). (C) Box plots showing that even considering $PM_{2.5}$ exceedance rates (despite 39% missing data due to the absence of monitoring stations for $PM_{2.5}$) the proportion of COVID-19 in Po Valley might be stratified consistently ($p<0.001$) with PM_{10} data presented in figure 1B–E.