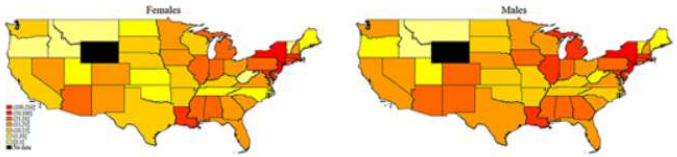
RICERCA BIBLIOGRAFICA COVID 19 SETTIMANA 7-13.09.2020 FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE DOTT.SSA ELEONORA TADDEI			
AUTORE/RIVISTA	**TITOLO**	**OUTCOME PRINCIPALE**	**ABSTRACT**
Squillace N et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1282/5901570	Therapy of SARS-Coronavirus-2 pneumonia: is there an optimal IL-6 cut-off for successful tocilizumab treatment?	Research letter in cui viene suggerito, sulla base di una casistica italiana di 32 pazienti, un cut-off di IL-6 (>135 pg/ml) associato a peggiore prognosi e minore efficacia di terapia con tocilizumab nei pazienti con COVID-19.	Jordan SC et al. showed that the use of tocilizumab in 27 patients with severe SarsCoronavirus-2 (SARS-COV-2) pneumonia was associated with reduced inflammation and risk of mechanical ventilation or death. The mean IL-6 level at baseline was 356 ± 616 pg/ml1. Few studies evaluated prognostic value of IL-6 at baseline to predict clinical benefit of tocilizumab treatment.
De Oliveira B et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-	Efficacy of Tocilizumab for treatment of severe COVID-19 Pneumonia: more evidence is needed.	Commento a un precedente lavoro retrospettivo (Jordan SC et al, Clin Infect Dis 2020; 23: ciaa812. doi: 10.1093/cid/ciaa812) sull'efficacia della terapia con tocilizumab per COVID-	In the June 23rd, 2020 edition of Clinical Infectious Diseases, Jordan et al. describe their results using tocilizumab, a humanized monoclonal antibody targeting the interleukin 6 receptor in hypoxic patients with confirmed SARS-CoV-2 pneumonia. During the current COVID19 pandemic, many different drugs, ranging from previously available antiviral drugs, cytokine inhibitors, glucocorticoids, and other inflammation modulators have been used empirically and are

article/doi/10.1093/cid/ciaa1284/5901587		19. Vengono criticate le inferenze degli autori e si sottolinea la necessità di trial clinici randomizzati per fornire adeguate evidenze a sostegno dell'utilizzo del farmaco.	simultaneously being evaluated in clinical trials. The cytokine storm that these patients are prone to in the more severe cases is well documented and is considered one of the more promising targets of treatment.
Quast T et al Journal of Public Health https://academic.oup.com/jpubhealth/advance-article/doi/10.1093/pubmed/fdaa159/5901977	Years of life lost associated with COVID-19 deaths in the United States.	Stima degli anni di vita persi (YLL) dalla popolazione USA a causa delle morti per COVID-19 : 1,2 milioni.	Background: The mortality effects of COVID-19 are a critical aspect of the disease's impact. Years of life lost (YLLs) can provide greater insight than the number of deaths by conveying the shortfall in life expectancy and thus the age profile of the decedents. Methods: We employed data regarding COVID-19 deaths in the USA by jurisdiction, gender and age group for the period 1 February 2020 through 11 July 2020. We used actuarial life expectancy tables by gender and age to estimate YLLs. Results: We estimated roughly 1.2 million YLLs due to COVID-19 deaths. The YLLs for the top six jurisdictions exceeded those for the remaining 43. On a per-capita basis, female YLLs were generally higher than male YLLs throughout the country. Conclusions: Our estimates offer new insight into the effects of COVID-19. Our findings of heterogenous rates of YLLs by geography and gender highlight variation in the magnitude of the pandemic's effects that may inform effective policy responses.

			Figure 2 contains maps of YLLs per capita by gender, where the darker shading reflects higher YLLs per capita. New York excluding New York City, and New York City are combined in the maps. The highest YLLs per capita are generally located in the northeast, with Louisiana as the one jurisdiction outside the region with the darkest shade in both maps. All of the jurisdictions on the map for males are as darkly or more darkly shaded than the corresponding jurisdictions on the females map. The jurisdictions in the northeast generally have the same shading for both genders. **Fig. 2** 
Rosat C et al Cell https://www.sciencedirect.com/science/article/pii/S0092867420311570	The Immunology of Multisystem Inflammatory Syndrome in Children with COVID-19	Studio retrospettivo condotto fra Italia e Svezia per confrontare le caratteristiche immunologiche (citochine, sottopopolazioni linfocitarie, autoanticorpi) ed ematobiochimiche di bambini sani o affetti da COVID-19 paucisintomatico, MIS-C (sindrome infiammatoria multisistemica dei bambini, rara complicanza di COVID19) e malattia di Kawasaki. Le differenze evidenziate potrebbero	SARS-CoV-2 infection is typically very mild and often asymptomatic in children. A complication is the rare Multisystem Inflammatory Syndrome in Children (MIS-C) associated with COVID-19, presenting 4-6 weeks after infection as high fever, organ dysfunction and strongly elevated markers of inflammation. The pathogenesis is unclear but has overlapping features with Kawasaki disease suggestive of vasculitis and a likely autoimmune etiology. We apply systems-level analyses of blood immune cells, cytokines and autoantibodies in healthy children, children with Kawasaki disease enrolled prior to COVID-19, children infected with SARS-CoV-2 and children presenting with MIS-C. We find that the inflammatory response in MIS-C differs from the cytokine storm of severe acute COVID-19, shares several features with Kawasaki disease, but also differs from this condition with respect to T-cell subsets, IL-17A and biomarkers associated with arterial damage. Finally, autoantibody profiling suggests multiple autoantibodies that could be involved in

guidare la terapia della MIS-C.

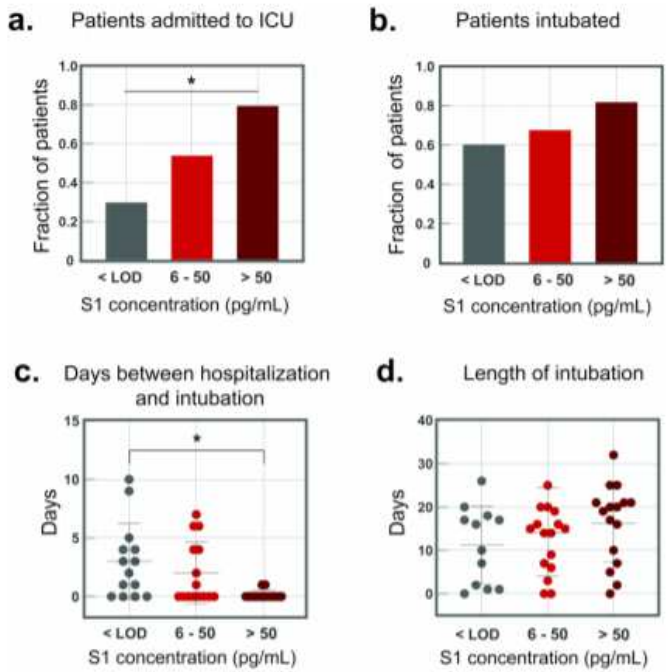
the pathogenesis of MIS-C.

	Children with COVID-19 (n = 54)		Kawasaki (n = 28)	Healthy (n = 19)	p-value
	CoV-2+ (n = 41)	MIS-C (n = 13)			
Age in months	79.8 (11.5 - 131.1)	106 (71.1 - 165.4)	24.5 (15.8 - 41.8)	29 (21 - 45.8)	p = 0.04 (CoV-2+ vs MIS-C) p < 0.001 (CoV-2+ vs HC, KD) p < 0.001 (MIS-C vs HC, KD)
Male : Female	23 : 18	8 : 3	14 : 14	5 : 7	n.s.
Platelets, 10^9/L	252 (204.8 - 298.5)	163 (126.5 - 193.5)	378 (271.5 - 485.2)	372 (294 - 408.2)	p < 0.001 (CoV-2+ vs rest) p < 0.001 (MIS-C vs HC, KD)
WBC, 10^9/L	6.4 (5.2 - 9.1)	7.9 (5.5 - 8.7)	15 (11 - 19)	9.2 (7.9 - 9.7)	p < 0.001 (CoV-2+ vs KD) p < 0.001 (MIS-C vs KD) p < 0.001 (KD vs HC)
Neutrophils, 10^9/L	2.6 (1.8 - 3.9)	6.1 (4.3 - 7.5)	10 (6.5 - 12.7)	2.5 (1.9 - 3.7)	p = 0.004 (CoV-2+ vs MIS-C) p < 0.001 (CoV-2+ vs KD) p = 0.008 (MIS-C vs HC) p = 0.009 (MIS-C vs KD) p < 0.001 (KD vs HC)
Lymphocytes, 10^9/L	2.6 (1.9 - 4)	0.7 (0.4 - 1.2)	2.4 (1.4 - 4.1)	4.7 (3.8 - 5.7)	p < 0.001 (CoV-2+ vs MIS-C) p = 0.004 (CoV-2+ vs HC) p < 0.001 (MIS-C vs HC, KD) p = 0.016 (KD vs HC)
Hb, g/dL	13 (12 - 13.9)	12.2 (10.6 - 14.8)	10.8 (10.3 - 11.2)	11.9 (11.4 - 12.3)	p = 0.014 (CoV-2+ vs HC) p < 0.001 (CoV-2+ vs KD) p = 0.001 (KD vs HC)
CRP, mg/dL	0.1 (0 - 0.5)	22.8 (18.2 - 26.5)	11.3 (8.1 - 18.8)	0	p < 0.001 (CoV-2+ vs rest) p < 0.001 (MIS-C vs HC) p < 0.001 (KD vs HC)
Ferritin, ng/mL	58 (40 - 114)	550 (360.5 - 843)	186 (142.5 - 248.5)	n.a.	p < 0.001 (CoV-2+ vs MIS-C) p = 0.003 (CoV-2+ vs KD) p < 0.001 (MIS-C vs KD)
Albumin, g/dL	4.3 (4.2 - 4.6)	29 (13.1 - 30.5)	3.7 (3.4 - 3.9)	n.a.	p = 0.001 (CoV-2+ vs MIS-C) p < 0.001 (CoV-2+ vs KD) p < 0.001 (MIS-C vs KD)
Sodium, mEq/L	139 (138 - 140)	133.5 (132.2 - 136.5)	136 (134 - 137)	n.a.	p < 0.001 (CoV-2+ vs MIS-C, KD)
Triglicerides, mg/dL	122.5 (73 - 158.5)	146 (126.2 - 171.8)	169.5 (117 - 229)	n.a.	p = 0.042 (CoV-2+ vs KD)
ALT, UI/L	18 (12 - 22)	20 (16 - 30)	38.5 (23 - 58.2)	n.a.	p < 0.01 (CoV-2+ vs KD) p = 0.041 (MIS-C vs KD)
AST, UI/L	26 (21.2 - 38.8)	26 (25.5 - 30.5)	33 (28.2 - 49.2)	n.a.	n.s

Iba T et al Critical Care Medicine https://journals.lww.com/ccmjournal/Fulltext/2020/09000/Coagulopathy_of_Coronavirus_Disease_2019.15.aspx	Coagulopathy of Coronavirus Disease 2019	Review narrativa sulla coagulopatia da COVID-19. L'ampia letteratura a disposizione incoraggia l'utilizzo di profilassi antitrombotica nei pazienti ospedalizzati e la ricerca attiva di tromboembolia polmonare sulla base di indici di rischio quali elevazione di fibrinogeno e D-dimero.	Objectives: Recent studies have reported a high prevalence of thrombotic events in coronavirus disease 2019. However, the significance of thromboembolic complications has not been widely appreciated. The purpose of this review is to provide current knowledge of this serious problem. Design: Narrative review. Data Sources: Online search of published medical literature through PubMed using the term "COVID-19," "SARS," "acute respiratory distress syndrome," "coronavirus," "coagulopathy," "thrombus," and "anticoagulants." Study Selection and Data Extraction: Articles were chosen for inclusion based on their relevance to coagulopathy and thrombosis in coronavirus disease 2019, and anticoagulant therapy. Reference lists were reviewed to identify additional relevant articles. Data Synthesis: Coronavirus disease 2019 is associated with a strikingly high prevalence of coagulopathy and venous thromboembolism that may contribute to respiratory deterioration. Monitoring coagulation variables is important, as abnormal coagulation tests are related to adverse outcomes and may necessitate adjuvant antithrombotic interventions. In the initial phase of the infection, d-dimer and fibrinogen levels are increased, while activated partial prothrombin time, prothrombin time, and platelet counts are often relatively normal. Increased d-dimer levels three times the upper limit of normal may trigger screening for venous thromboembolism. In all hospitalized patients, thromboprophylaxis using low-molecular-weight heparin is currently recommended. The etiology of the procoagulant responses is complex and thought to be a result of specific interactions between host defense mechanisms and the coagulation system. Although the coagulopathy is reminiscent of disseminated

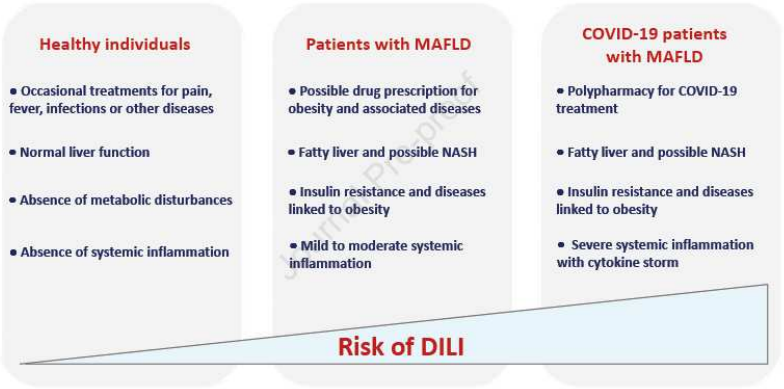
			intravascular coagulation and thrombotic microangiopathy, it has features that are markedly distinct from these entities. Conclusions: Severe acute respiratory syndrome coronavirus 2/coronavirus disease 2019 frequently induces hypercoagulability with both microangiopathy and local thrombus formation, and a systemic coagulation defect that leads to large vessel thrombosis and major thromboembolic complications, including pulmonary embolism in critically ill hospitalized patients. d-dimers and fibrinogen levels should be monitored, and all hospitalized patients should undergo thromboembolism prophylaxis with an increase in therapeutic anticoagulation in certain clinical situations.
Ogata AF et al Clinical Chemistry https://academic.oup.com/clinchem/advance-article/doi/10.1093/clinchem/hvaa213/5902449	Ultra-sensitive Serial Profiling of SARS-CoV-2 Antigens and Antibodies in Plasma to Understand Disease Progression in COVID-19 Patients with Severe Disease.	Lavoro che riporta il dosaggio di antigeni ematici di SARS-CoV-2 e dimostra una associazione significativa tra i livelli rilevati di questi e il peggioramento clinico dei pazienti (in particolare ricovero in terapia intensiva e tempo alla intubazione). Vengono inoltre confrontati i tempi di positività di antigenemie, sierologia e RT-PCR su tampone nasofaringeo.	Background : Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected over 21 million people worldwide since August 16, 2020. Compared to PCR and serology tests, SARS-CoV-2 antigen assays are underdeveloped, despite their potential to identify active infection and monitor disease progression. Methods: We used Single Molecule Array (Simoa) assays to quantitatively detect SARS-CoV-2 spike, S1 subunit, and nucleocapsid antigens in the plasma of coronavirus disease (COVID-19) patients. We studied plasma from 64 COVID-19 positive patients, 17 COVID-19 negative patients, and 34 pre-pandemic patients. Combined with Simoa anti-SARS-CoV-2 serological assays, we quantified changes in 31 SARS-CoV-2 biomarkers in 272 longitudinal plasma samples obtained for 39 COVID-19 patients. Data were analyzed by hierarchical clustering and were compared to longitudinal RT-PCR test results and clinical outcomes. Results : SARS-CoV-2 S1 and N antigens were detectable in 41 out of 64 COVID-19 positive patients. In these patients, full antigen clearance in plasma was observed a mean ± 95%CI of 5 ± 1 days after seroconversion and nasopharyngeal RT-PCR tests reported

Figure 5. Indicators of disease severity based on S1 concentrations in plasma for 64 COVID-19 positive patients. COVID-19 positive patients were separated into three groups based on S1 concentrations. The cutoff between groups 2 and 3 (50 pg/mL, 0.65 pmol/L) was chosen as five standard deviations above the LOD. The fraction of patients admitted to the ICU or who were intubated was calculated for each group independently. a.) Fraction of COVID-19 positive patients who were immediately admitted to the ICU upon presentation to the hospital. b.) Fraction of COVID-19 positive patients who were intubated during hospitalization. c.) Days between date of presentation to the hospital and intubation date for intubated COVID-19 positive patients. d.) The length of intubation for intubated COVID-19 positive patients. For all plots, significance indicated by the asterisks (*P* value <0.05).



positive results for 15 ± 5 days after viral antigen clearance. Correlation between patients with high concentrations of S1 antigen and ICU admission (77%) and time to intubation (within one day) was statistically significant.

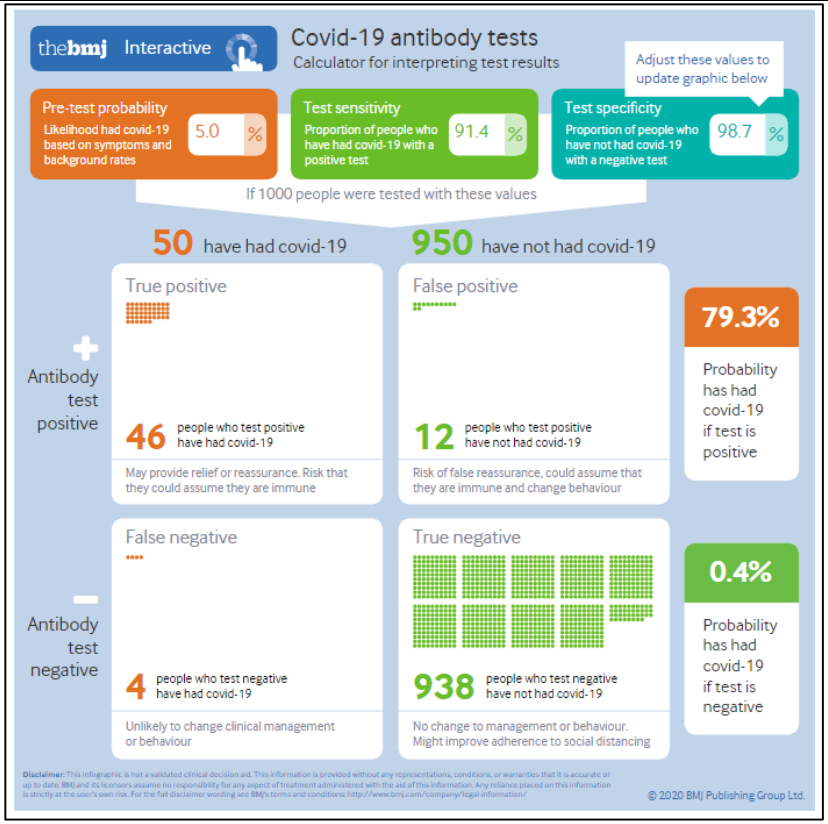
Conclusions : The reported SARS-CoV-2 Simoa antigen assay is the first to detect viral antigens in the plasma of COVID-19 positive patients to date. These data show that SARS-CoV-2 viral antigens in the blood are associated with disease progression, such as respiratory failure, in COVID-19 cases with severe disease.

Ferron PJ et al Biochimie https://www.sciencedirect.com/science/article/pii/S0300908420302030?via%3Dihub	Treatments in Covid-19 patients with pre-existing metabolic dysfunction-associated fatty liver disease: A potential threat for drug-induced liver injury?	Disamina dei meccanismi di epatotossicità presenti nei casi di infezione da SARS-CoV-2 in pazienti già affetti da steatosi epatica di origine metabolica (MAFLD). Viene illustrata nel dettaglio la tossicità epatica da farmaci (drug-induced liver injury : DILI) riconducibile ai trattamenti attualmente utilizzati in corso di COVID-19.	Obese patients who often present metabolic dysfunction-associated fatty liver disease (MAFLD) are at risk of severe presentation of coronavirus disease 2019 (COVID-19). These patients are more likely to be hospitalized and receive antiviral agents and other drugs required to treat acute respiratory distress syndrome and systemic inflammation, combat bacterial and fungal superinfections and reverse multi-organ failure. Among these pharmaceuticals, antiretrovirals such as lopinavir/ritonavir and remdesivir, antibiotics and antifungal agents can induce drug-induced liver injury (DILI), whose mechanisms are not always understood.  In the present article, we hypothesize that obese COVID-19 patients with MAFLD might be at higher risk for DILI than non-infected healthy individuals or MAFLD patients. These patients present several concomitant factors, which individually can favour DILI: polypharmacy, systemic inflammation at risk of cytokine storm, fatty liver and sometimes nonalcoholic steatohepatitis (NASH) as well as insulin resistance and other diseases linked to obesity. Hence, in obese COVID-19 patients, some drugs might cause more severe (and/or more frequent) DILI, while others might trigger the

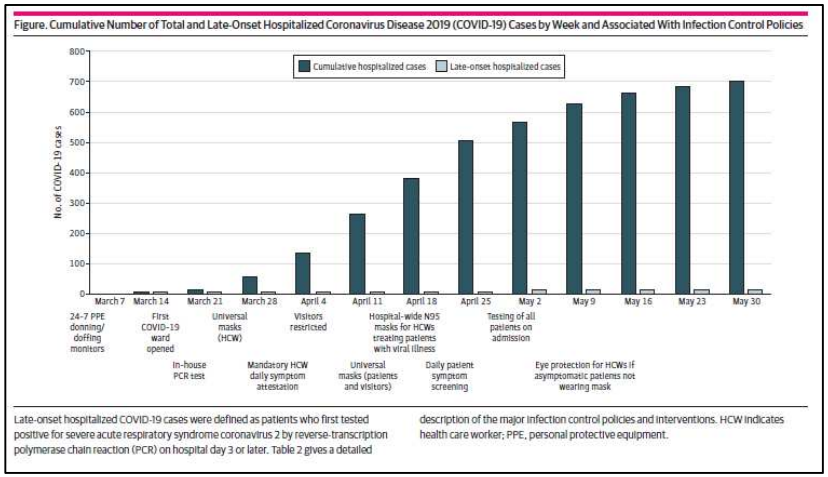
			transition of fatty liver to NASH, or worsen pre-existing steatosis, necroinflammation and fibrosis. We also present the main mechanisms whereby drugs can be more hepatotoxic in MAFLD including impaired activity of xenobiotic-metabolizing enzymes, mitochondrial dysfunction, altered lipid homeostasis and oxidative stress. Although comprehensive investigations are needed to confirm our hypothesis, we believe that the current epidemic of obesity and related metabolic diseases has extensively contributed to increase the number of cases of DILI in COVID-19 patients, which may have participated in presentation severity and death.
Martín-Rodríguez F et al Clinical Simulation in Nursing https://www.nursingsimulation.org/article/S1876-1399(20)30068-2/fulltext	Predicting Health Care Workers' Tolerance of Personal Protective Equipment: An Observational Simulation Study	Sviluppo e validazione di un modello per predire la capacità di tollerare i dispositivi di protezione individuale da parte di operatori sanitari, in base ai dati di una simulazione di 30 minuti su 96 partecipanti.	Background: More recently, due to the coronavirus disease 2019 pandemic, health care workers have to deal with clinical situations wearing personal protective equipment (PPE); however, there is a question of whether everybody will tolerate PPE equally. The main objective of this study was to develop a risk model to predict whether health care workers will tolerate wearing PPE, C category, 4B/5B/6B type, during a 30-minute simulation. Methods: A nonexperimental simulation study was conducted at the Advanced Simulation Center, Faculty of Medicine, Valladolid University (Spain) from April 3rd to 28th, 2017. Health care students and professionals were equipped with PPE and performed a 30-minute simulation. Anthropometric, physiological, and analytical variables and anxiety levels were measured before and after simulation. A scoring model was constructed. Results: Ninety-six volunteers participated in the study. Half the sample presented metabolic fatigue in the 20 minutes after finishing the simulation. The predictive model included female sex, height, muscle and bone mass, and moderate level of physical activity. The validity of the main model using all the variables presented an area under the curve of 0.86 (95% confidence interval:

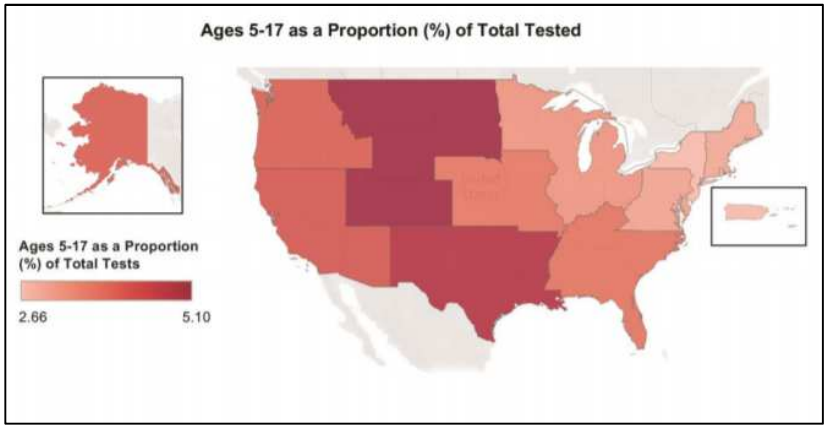
			0.786-0.935), and the validity of the model had an area under the curve of 0.725 (95% confidence interval: 0.559-0.89). Conclusions: Decision-making in biohazard incidents is a challenge for emergency team leaders. Knowledge of health care workers' physiological tolerance of PPE could improve their performance.
Jacobs JL et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1316/5902941	Detection of SARS-CoV-2 RNA in Blood of Patients with COVID-19: What Does It Mean?	Interpretazione di recenti lavori in cui i livelli di viremia dI SARS-CoV-2 (RNAemia) sembrano correlare con la gravità di malattia meglio di altri indici quali la positività del tampone nasofaringeo o la sierologia, come del resto avviene in altre infezioni virali. Gli autori ipotizzano anche un loro utilizzo per testare l'efficacia di farmaci contro SARS-CoV-2.	The SARS-CoV-2/COVID-19 pandemic has severely impacted global societies and taken hundreds of thousands of lives prematurely. A striking paradox about SARS-CoV-2 infection is the broad range of clinical manifestations – ranging from asymptomatic infection, to more severe disease requiring hospitalization, to death despite intensive care. Such a broad range of illness is characteristic of other infectious diseases including poliovirus infection for which only 1 in 100 to 1 in 1000 infections result in paralytic disease with the remainder being asymptomatic or minimally symptomatic. Initial studies of prognosis in SARS-CoV2/COVID-19 have focused on host risk factors for severe disease, which have identified older age, male sex, non-white race, and comorbidities including obesity, among others. Most studies of SARS-CoV-2 pathogenesis have focused on cellular and serologic responses, immunopathology, and qualitative or semi-quantitative measurements of SARSCoV-2 RNA in the nasopharynx. The contribution of immunopathology to COVID-19 disease severity has been established. Host response to infection is generally a well-regulated process containing complex checks and balances to avoid host injury from overactive innate or adaptive immune responses. In COVID-19, however, there can be immune dysregulation and excessive inflammatory responses that can tip the balance toward severe disease. As for most virus infections, some combination of virus- and immune-mediated damage is likely responsible for severe disease.

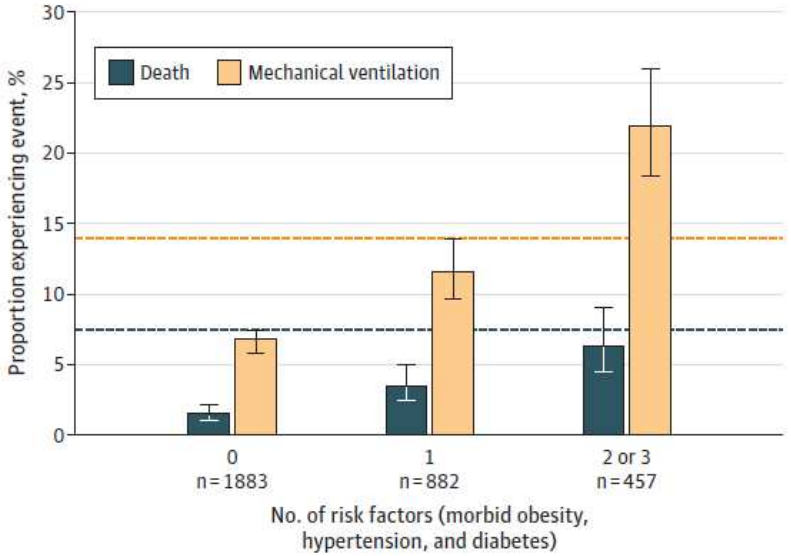
Watson J et al British Medical Journal https://www.bmj.com/content/370/bmj.m3325	Testing for SARS-CoV-2 antibodies	Articolo che fornisce alcune raccomandazioni pratiche per la prescrizione e l'nterpretazione della sierologia per SARS-CoV-2.	As the covid-19 pandemic has unfolded, interest has grown in antibody testing as a way to measure how far the infection has spread and to identify individuals who may be immune. Testing also has a clinical role, given the varying symptoms of covid-19 and false negative results of reverse transcription polymerase chain reaction (RT-PCR) tests, particularly when swabs are taken more than five days after symptom onset and sensitivity of RT-PCR tests starts to decrease. In May, the UK government announced that antibody testing should be offered to anyone having their blood taken who wants to know whether they have been infected with SARS-CoV-2, even if there is "not a specific clinical indication," yet currently there is no clear guidance for clinicians on how to interpret these results or how they fit into clinical pathways. In this article we offer an approach to antibody testing in individuals with and without symptoms suggestive of current or past SARS-CoV-2 infection.

			
Rhee C et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2770287	Incidence of Nosocomial COVID-19 in Patients Hospitalized at a Large US Academic Medical Center	Incidenza di infezioni nosocomiali da SARS-CoV-2 al Brigham and Women's Hospital (Boston). Secondo la revisione degli autori, un solo caso è stato secondario ad acquisizione intraospedaliera nelle prime 12 settimane dal primo	IMPORTANCE Some patients are avoiding essential care for fear of contracting coronavirus disease 2019 (COVID-19) in hospitals. There are few data, however, on the risk of acquiring COVID-19 in US hospitals. OBJECTIVE To assess the incidence of COVID-19 among patients hospitalized at a large US academic medical center in the 12 weeks after the first inpatient case was identified. DESIGN, SETTING, AND PARTICIPANTS This cohort study included all patients admitted to Brigham and Women's Hospital (Boston,

		positivo ricoverato per COVID19 nel centro.	Massachusetts) between March 7 and May 30, 2020. Follow-up occurred through June 17, 2020. Medical records for all patients who first tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by reverse-transcription polymerase chain reaction (RT-PCR) on hospital day 3 or later or within 14 days of discharge were reviewed. EXPOSURES A comprehensive infection control program was implemented that included dedicated COVID-19 units with airborne infection isolation rooms, personal protective equipment in accordance with US Centers for Disease Control and Prevention recommendations, personal protective equipment donning and doffing monitors, universal masking, restriction of visitors, and liberal RT-PCR testing of symptomatic and asymptomatic patients. MAIN OUTCOMES AND MEASURES Whether infection was community or hospital acquired based on timing of tests, clinical course, and exposures. RESULTS Over the 12-week period, 9149 patients (mean [SD] age, 46.1 [26.4] years; median [IQR] age, 51 years [30-67 years]; 5243 female [57.3%]) were admitted to the hospital, for whom 7394 SARS-CoV-2 RT-PCR tests were performed; 697 COVID-19 cases were confirmed, translating into 8656 days of COVID-19–related care. Twelve of the 697 hospitalized patients with COVID-19 (1.7%) first tested positive on hospital day 3 or later (median, 4 days; range, 3-15 days). Of these, only 1 case was deemed to be hospital acquired, most likely from a presymptomatic spouse who was visiting daily and diagnosed with COVID-19 before visitor Restrictions and masking were implemented. Among 8370 patients with non–COVID-19–related hospitalizations discharged through June 17, 11 (0.1%) tested positive within 14 days (median time to diagnosis, 6 days; range, 1-14 days). Only 1

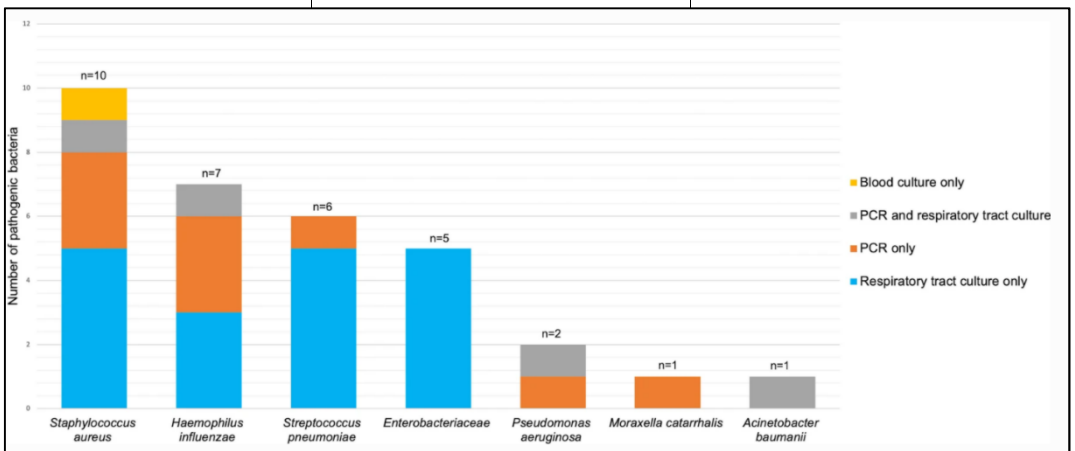
			case was deemed likely to be hospital acquired, albeit with no known exposures. CONCLUSIONS AND RELEVANCE In this cohort study of patients in a large academic medical center with rigorous infection control measures, nosocomial COVID-19 was rare during the height of the pandemic in the region. These findings may inform practices in other institutions and provide reassurance to patients concerned about contracting COVID-19 in hospitals.  Figure. Cumulative Number of Total and Late-Onset Hospitalized Coronavirus Disease 2019 (COVID-19) Cases by Week and Associated With Infection Control Policies Late-onset hospitalized COVID-19 cases were defined as patients who first tested positive for severe acute respiratory syndrome coronavirus 2 by reverse-transcription polymerase chain reaction (PCR) on hospital day 3 or later. Table 2 gives a detailed description of the major infection control policies and interventions. HCW indicates health care worker; PPE, personal protective equipment.
Guilamo-Ramos V et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1348/5902518	Reconsidering assumptions of adolescent and young adult SARS-CoV-2 transmission dynamics.	Dato il ruolo emergente di adolescenti e giovani adulti nella diffusione di SARS-CoV2, tale categoria finora poco considerata dovrebbe essere maggiormente oggetto di raccomandazioni di sanità pubblica.	Evidence regarding the important role of adolescents and young adults (AYA) in accelerating and sustaining coronavirus disease 2019 (COVID-19) outbreaks is growing. Furthermore, data suggest two known factors that contribute to high severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmissibility-presymptomatic transmission and asymptomatic case presentations-may be amplified in AYA. However, AYA have not been prioritized as a key population in the public health response to the COVID-19 pandemic. Policy decisions that limit public health attention on AYA and are driven by the assumption of insignificant

			forward transmission from AYA pose a risk to inadvertently reinvigorate local transmission dynamics. In this viewpoint, we highlight evidence regarding the increased potential of AYA to transmit SARS-CoV-2 that, to date, has received little attention, discuss adolescent and young adult specific considerations for future COVID-19 control measures, and provide applied programmatic suggestions. 
Cunningham JW et al JAMA https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2770542	Clinical Outcomes in Young US Adults Hospitalized With COVID-19	Andamento clinico e outcome di 3222 pazienti di età 18-34 anni ricoverati negli USA per COVID19. Obesità, ipertensione e sesso maschile sono indipendentemente associati a ventilazione meccanica e decesso. La presenza di multipli fattori di rischio conferisce un profilo di rischio	Coronavirus disease 2019 (COVID-19) is increasing rapidly among young adults in the US.1 Often described as a disease affecting older adults, to our knowledge, fewstudies have included younger patients to better understand their anticipated clinical trajectory. We investigated the clinical profile and outcomes of 3222 young adults (defined by theUS Census as age 18-34 years) who required hospitalization for COVID-19 in the US.

		comparabile a quello degli adulti di mezza età.	Figure. Death and Mechanical Ventilation in Young Adults With and Without Morbid Obesity, Hypertension, and Diabetes  Morbid obesity, diabetes, and hypertension were determined by *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10)* codes during coronavirus disease 2019 (COVID-19) admission. Proportions of patients experiencing death and mechanical ventilation were compared with a reference group of 8862 middle-aged (age 35-64 years) nonpregnant patients with COVID-19 with none of these conditions in the Premier database (dotted lines). Error bars refer to 95% CIs.
Atalla E et al International Journal of Clinical Practice https://pubmed.ncbi.nlm.nih.gov/32894801/	Readmissions among Patients with COVID-19.	Caratteristiche di 19 pazienti affetti da COVID19 e nuovamente ricoverati dopo la dimissione ospedaliera.	BACKGROUND: Hospital readmissions are associated with poor patient outcomes and increased health resource utilization. The need to study readmission patterns is even bigger during a pandemic because the burden is further stretching the healthcare system. METHODS: We reviewed the initial hospitalization and subsequent readmission for 19 patients with confirmed COVID-19 in the largest statewide hospital network in Rhode Island, US, from

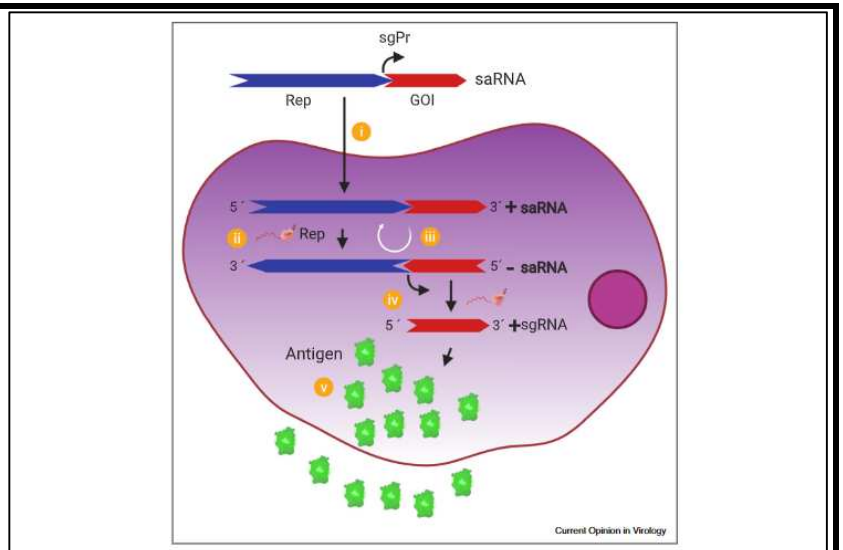
			March 1(st) through April 19(th) , 2020. We also compared the characteristics and clinical outcomes between readmitted and non-readmitted patients. RESULTS: Of the 339 hospitalized patients with COVID-19, 279 discharged alive. Among them, 19/279 were readmitted (6.8%) after a median of 5 days. There was a significantly higher rate of hypertension, diabetes, chronic pulmonary disease, liver disease, cancer, and substance abuse among the readmitted compared to non-readmitted patients. The most common reasons of readmissions happening within 12 days from discharge included respiratory distress and thrombotic episodes, while those happening at a later time included psychiatric illness exacerbations and falls. The length of stay during readmission was longer than during index admission and more demanding on healthcare resources. CONCLUSION: Among hospitalized patients with COVID-19, those readmitted had a higher burden of comorbidities than the non-readmitted. Within the first 12 days from discharge, readmission reasons were more likely to be associated with COVID-19, while those happening later were related to other reasons. Readmissions characterization may help in defining optimal timing for patient discharge and ensuring safe care transition.
Contou D et al Annals of Intensive Care https://annalsofintensivecare.springeropen.com/articles/10.1186/s13613-020-00736-x	Bacterial and viral co-infections in patients with severe SARS-CoV-2 pneumonia admitted to a French ICU.	Studio retrospettivo monocentrico su 92 pazienti ricoverati in terapia intensiva in Francia. La prevalenza di coinfezioni batteriche (diagnosi entro 48h dall'ingresso in terapia intensiva) è 28%. Gli autori propendono per la somministrazione di terapia	Background: Data on the prevalence of bacterial and viral co-infections among patients admitted to the ICU for acute respiratory failure related to SARS-CoV-2 pneumonia are lacking. We aimed to assess the rate of bacterial and viral co-infections, as well as to report the most common micro-organisms involved in patients admitted to the ICU for severe SARS-CoV-2 pneumonia. Patients and methods : In this monocenter retrospective study, we reviewed all the respiratory microbiological investigations

		antibiotica empirica, da sospendere alla negatività delle colture, per il paziente critico con COVID19.	performed within the first 48 h of ICU admission of COVID-19 patients (RT-PCR positive for SARS-CoV-2) admitted for acute respiratory failure. Results : From March 13th to April 16th 2020, a total of 92 adult patients (median age: 61 years, 1st–3rd quartiles [55–70]; males: n = 73/92, 79%; baseline SOFA: 4 [3–7] and SAPS II: 31 [21–40]; invasive mechanical ventilation: n = 83/92, 90%; ICU mortality: n = 45/92, 49%) were admitted to our 40-bed ICU for acute respiratory failure due to SARS-CoV-2 pneumonia. Among them, 26 (28%) were considered as co-infected with a pathogenic bacterium at ICU admission with no co-infection related to atypical bacteria or viruses. The distribution of the 32 bacteria isolated from culture and/or respiratory PCRs was as follows: methicillin-sensitive Staphylococcus aureus (n = 10/32, 31%), Haemophilus influenzae (n = 7/32, 22%), Streptococcus pneumoniae (n = 6/32, 19%), Enterobacteriaceae (n = 5/32, 16%), Pseudomonas aeruginosa (n = 2/32, 6%), Moraxella catarrhalis (n = 1/32, 3%) and Acinetobacter baumannii (n = 1/32, 3%). Among the 24 pathogenic bacteria isolated from culture, 2 (8%) and 5 (21%) were resistant to 3rd generation cephalosporin and to amoxicillin–clavulanate combination, respectively. Conclusions: We report on a 28% rate of bacterial co-infection at ICU admission of patients with severe SARSCoV-2 pneumonia, mostly related to Staphylococcus aureus, Haemophilus influenzae, Streptococcus pneumoniae and Enterobacteriaceae. In French patients with confirmed severe SARSCoV-2 pneumonia requiring ICU admission, our results encourage the systematic administration of an empiric antibiotic monotherapy with a 3rd generation cephalosporin, with a prompt de-escalation as soon as possible. Further larger studies are needed to assess the real prevalence and

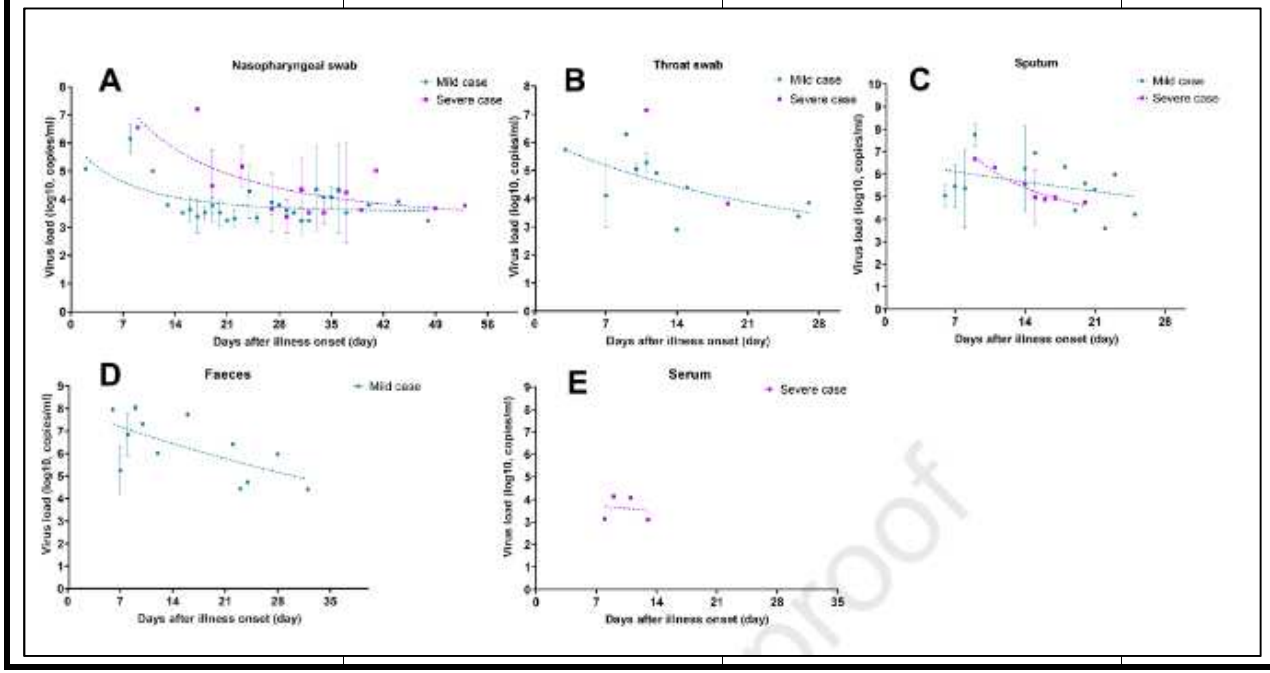


Number of each species of bacteria isolated from respiratory tract cultures (blue), multiplex PCR (red), both (grey) or blood culture (yellow) among 26 critically ill patients with severe SARS-CoV-2 pneumonia

			the predictors of co-infection together with its prognostic impact on critically ill patients with severe SARS-CoV-2 pneumonia.
Ballesteros-Briones MC et al Current Opinion in Virology https://www.sciencedirect.com/science/article/pii/S1879625720300705?via%3Dihub	A new generation of vaccines based on alphavirus self-amplifying RNA.	Caratteristiche e vantaggi dei vaccini basati su RNA auto-amplificante (saRNA), derivati dal genoma di flavivirus e alfavirus, con potenziali applicazioni contro SARS-CoV-2.	DNA or mRNA vaccines have potential advantages over conventional vaccines since they are easier to manufacture and have higher safety profiles. In particular, self-amplifying RNA (saRNA) derived from alphavirus expression vectors has shown to be very efficient to induce humoral and cellular responses against many antigens in preclinical models, being superior to non-replicating mRNA and DNA. This is mainly due to the fact that saRNA can provide very high expression levels and simultaneously induces strong innate responses, potentiating immunity. saRNA can be administered as viral particles or DNA, but direct delivery as RNA represents a safer and more simple approach. Although saRNA can be delivered as naked RNA, in vivo transfection can be enhanced by electroporation or by complexing it with cationic lipids or polymers. Alphavirus saRNA could have broad application to vaccinate against human pathogens, including emerging ones like SARS-CoV-2, for which clinical trials have been recently initiated.

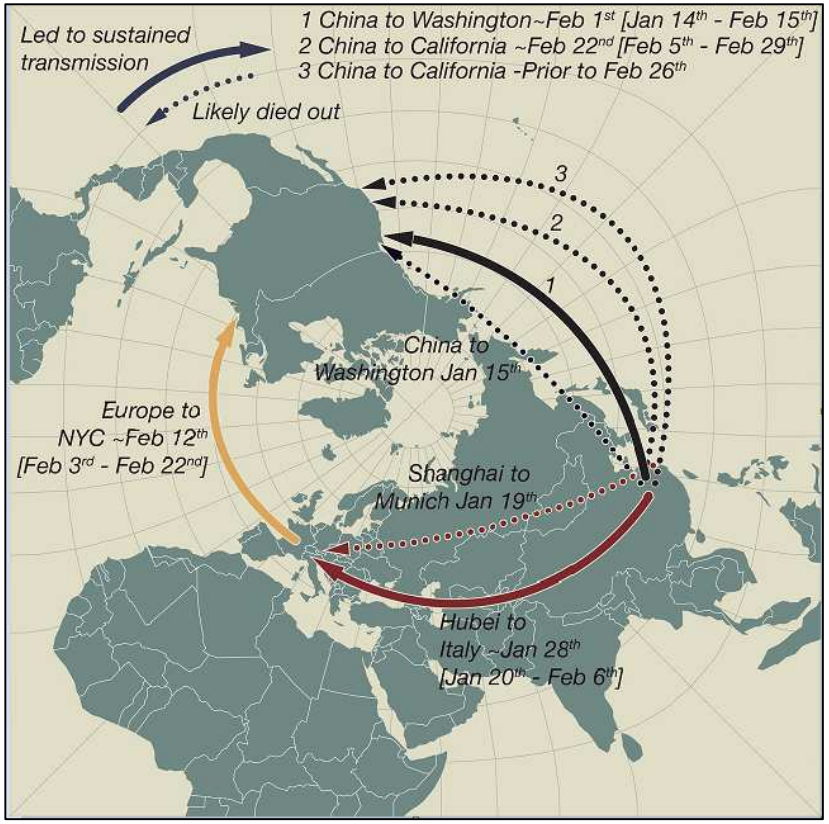
			 saRNA vectors based on alphavirus. The saRNA vector is a positive strand RNA containing the genes coding for the viral replicase (Rep) and the gene of interest (GOI) downstream of a subgenomic promoter (sgPr). Upon entry of saRNA into cells (i) Rep can be translated, being able to use saRNA as template to make a complementary negative saRNA (-saRNA) strand (ii). Rep can also use this negative RNA as template to make more saRNA (+saRNA), allowing its self-amplification (iii). In addition, Rep can recognize the sgPr in the negative strand from which a subgenomic mRNA (+sgRNA) of positive polarity is synthesized (iv). sgRNA can be translated to produce the desired antigen at very high levels, which will be secreted if having an appropriate signal peptide (v). Both +saRNA and +sgRNA contain a cap at the 5end and are polyadenilated (not shown).
Sun J et al Clinical Microbiology and Infection https://www.sciencedirect.com/science/article/pii/S1198743X20305279?via%3Dihub	The kinetics of viral load and antibodies to SARS-CoV-2.	Studio della cinetica della carica virale di SARS-CoV-2 su vari liquidi biologici, dei livelli anticorpali e dell' attività di anticorpi neutralizzanti in 35 pazienti con storia di COVID-19 con diversi livelli di gravità ricoverati nel Guangdong, China.	OBJECTIVES: To understand persistence of the virus in body fluids and immune response of infected host to severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), an agent of coronavirus disease 2019 (COVID-19). METHODS: We determined the kinetics of viral load in several body fluids through real time reverse transcription polymerase chain reaction (rRT-PCR), serum antibodies of IgA, IgG and IgM by enzyme linked immunosorbent assay (ELISA), and neutralizing antibodies by microneutralization assay in 35 COVID-19 cases from two hospitals in Guangdong, China. RESULTS: We found higher viral loads and prolonged shedding of virus RNA in severe cases of COVID-19 in nasopharyngeal (1.3x10(6) vs 6.4x10(4), p<0.05; 7 approximately 8w) and throat (6.9x10(6) vs 2.9x10(5), p<0.05; 4 approximately 5w), while comparable in

			sputum samples (5.5x10(6) vs 0.9x10(6), p<0.05; 4 approximately 5w). Viraemia was rarely detected (2.8%, n=1/35). We detected early seroconversion of IgA and IgG at 1(st) week after illness onset (day 5, 5.7%, n=2/35). Neutralizing antibodies were produced in the second week, and observed in all 35 included cases after 3(rd) week illness onset. The levels of neutralizing antibodies correlated with IgG (rs=0.85, p<0.05; kappa=0.85) and IgA (rs=0.64, p<0.05; kappa=0.61) in severe, but not mild cases (IgG, rs=0.42, kappa=0.33; IgA, rs=0.32, kappa=0.22). No correlation with IgM in either severe (rs=0.17, kappa=0.06) or mild cases (rs=0.27, kappa=0.15) was found. CONCLUSIONS: We revealed a prolonged shedding of virus RNA in upper respiratory tract, and evaluated the consistency production of IgG, IgA, IgM and neutralizing antibodies in COVID-19 cases.



Kim Y et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1345/5902973	Sustained responses of neutralizing antibodies against MERS-CoV in recovered patients and their therapeutic applicability.	Studio della persistenza di anticorpi anti-MERS su siero di 70 pazienti guariti la cui infezione risale all'epidemia del 2015 in Corea del Sud e i cui campioni sono stati prelevati nei 3 anni successivi. Il titolo, l'attvità neutralizzante e le celllule B di memoria persistono a distanza. Alla prova biologica su topo infettato da MERS-CoV, il siero dei pazienti con titolo anticorpale elevato determina riduzione della carica virale e riduce la mortalità, il che suggerisce la necessità di selezionare adeguatamente i donatori di plasma per uso terapeutico.	BACKGROUND: Zoonotic coronaviruses have emerged as a global threat by causing fatal respiratory infections. Given the lack of specific antiviral therapies, application of human convalescent plasma retaining neutralizing activity could be a viable therapeutic option that can bridge this gap. METHODS: We traced antibody responses and memory B cells in peripheral blood collected from 70 recovered MERS-CoV patients for three years after the 2015 outbreak in South Korea. We also used a mouse infection model to examine whether the neutralizing activity of collected sera could provide therapeutic benefit in vivo upon lethal MERS-CoV challenge. RESULTS: Anti-spike-specific IgG responses, including neutralizing activity and antibody-secreting memory B cells, persisted for up to 3 years, especially in MERS patients that suffered from severe pneumonia. Mean antibody titers gradually decreased annually by less than two fold. Levels of antibody responses were significantly correlated with fever duration, viral shedding periods, and maximum viral loads observed during infection periods. In a transgenic mice model challenged with lethal doses of MERS-CoV, a significant reduction in viral loads and enhanced survival was observed when therapeutically treated with human plasma retaining high neutralizing titer (> 1/5,000). However, this failed to reduce pulmonary pathogenesis, as revealed by pathological changes in lungs and initial weight loss. CONCLUSIONS: High titers of neutralizing activity are required for suppressive effect on the viral replication but may not be sufficient to reduce inflammatory lesions upon fatal infection. Therefore, immune sera with high neutralizing activity must be carefully selected for plasma therapy of zoonotic coronavirus infection.

Ng YPM et al American Journal of Perinatology https://www.thieme-connect.de/products/ejournals/abstract/10.1055/s-0040-1716506	Breastfeeding in COVID-19: A Pragmatic Approach.	Disamina delle possibilità di allattamento durante il periodo dell'epidemia da SARS-CoV-2, in considerazone delle preferenze dei genitori e delle possibilità del sistema assistenziale.	The novel coronavirus disease 2019 (COVID-19) pandemic has resulted in changes to perinatal and neonatal care, concentrating on minimizing risks of transmission to the newborn and health care staff while ensuring medical care is not compromised for both mother and infant. Current recommendations on infant care and feeding when mother has COVID-19 ranges from mother–infant separation and avoidance of human milk feeding, to initiation of early skin-to-skin contact and direct breastfeeding. Health care providers fearing risks of severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) maternal–infant transmission may veer toward restricted breastfeeding practices. We reviewed guidelines and published literature and propose three options for infant feeding depending on various scenarios. Option A involves direct breastfeeding with the infant being cared for by the mother or caregiver. In option B, the infant is cared for by another caregiver and receives mother's expressed milk. In the third option, the infant is not breastfed directly and does not receive mother's expressed milk. We recommend joint decision making by parents and the health care team. This decision is also flexible as situation changes. We also provide a framework for counseling mothers on these options using a visual aid and a corresponding structured training program for health care providers. Future research questions are also proposed. We conclude that evidence and knowledge about COVID-19 and breastfeeding are still evolving. Our options can provide a quick and flexible reference guide that can be adapted to local needs.
Worobey et al Science	The emergence of SARS-CoV-2 in Europe and North America	Lavoro che traccia origine e diffusione mondiale di SARS-CoV-2 a partire da un'accurata analisi filogenetica e dei flussi di	Accurate understanding of the global spread of emerging viruses is critically important for public health responses and for anticipating and preventing future outbreaks. Here, we elucidate when, where and how the earliest sustained SARS-CoV-2 transmission networks

https://science.sciencemag.org/content/early/2020/09/11/science.abc8169		popolazioni. Per quanto riguarda l'Italia, viene rigettata l'ipotesi di un'origine del focolaio italiano dalla Germania.	became established in Europe and North America. Our results suggest that rapid early interventions successfully prevented early introductions of the virus into Germany and the US from taking hold. Other, later introductions of the virus from China to both Italy and to Washington State founded the earliest sustained European and North America transmission networks. Our analyses demonstrate the effectiveness of public health measures in preventing onward transmission and show that intensive testing and contact tracing could have prevented SARS-CoV-2 from becoming established. 

Kilaru AS et al Academic Emergency Medicine https://onlinelibrary.wiley.com/doi/10.1111/acem.14117	Return Hospital Admissions Among 1419 Covid-19 Patients Discharged from Five US Emergency Departments	Incidenza e caratteristiche dei pazienti che tornano in ospedale e vengono ricoverati dopo essere stati dimessi dal pronto soccorso con diagnosi di COVID-19. Fascia d'età 40-59 anni, febbre o ipossia alla presentazione (spO2 <95%) e radiografia del torace alterata sono fattori di rischio per il ricovero « di ritorno ».	Although many ED patients with known or suspected Covid-19 require hospital admission, the majority are discharged home. Concern for surges in hospital occupancy compel emergency providers to preserve inpatient resources and discern which patients benefit most from admission. Even in the absence of surge conditions, patients may prefer to recover at home if safe to do so. However, some patients with Covid-19 experience delayed decompensation. Patients may develop serious illness several days after initial symptoms and require respiratory support. Additional complications, including venous thromboembolism, myocarditis, and acute kidney injury, may also require advanced therapies. It is not known how often and which patients with Covid-19 return to the hospital following initial evaluation in the ED. To date, prediction models have focused on the risk of critical illness among hospitalized patients. In this study, we describe the incidence of return hospital admission within 72 hours for patients with Covid-19 who were discharged from the ED upon initial presentation. We also evaluate patient characteristics associated with return hospital admission.
Shah GL et al The Journal of Clinical Investigation https://www.jci.org/articles/view/141777	Favorable outcomes of COVID-19 in recipients of hematopoietic cell transplantation	Esito dell'infezione da SARS-CoV-2 e ricerca di variabili associate alla gravità di malattia in 77 pazienti con storia di trapianto di cellule staminali ematopoietiche o terapia con CAR (chimeric antigen receptor) T cells. Inoltre, studio delle sottopopolazioni linfocitarie in corso di infezione.	BACKGROUND. Understanding outcomes and immunologic characteristics of cellular therapy recipients with SARS-CoV-2 is critical to performing these potentially life-saving therapies in the COVID-19 era. In this study of recipients of allogeneic (Allo) and autologous (Auto) hematopoietic cell transplant and CD19-directed chimeric antigen receptor T cell therapy (CAR-T) at Memorial Sloan Kettering Cancer Center, we aimed to identify clinical variables associated with COVID-19 severity and assess lymphocyte populations. METHODS. We retrospectively investigated patients diagnosed between March 15th and May 7th, 2020. In a subset of patients,

Figure 3: Outcomes and Disease Severity. A. Highest Supplemental Oxygen Given by Disease Status. B. COVID Disease Severity by Hematologic Malignancy Status. 77 patients (Allo n=35, Auto n =37, CAR T n=5). Severity of COVID-19 was defined as mild (no hospitalization required), moderate (hospitalization required), or severe (intensive care unit (ICU) required or goals of care changed to comfort care rather than escalation to the ICU).

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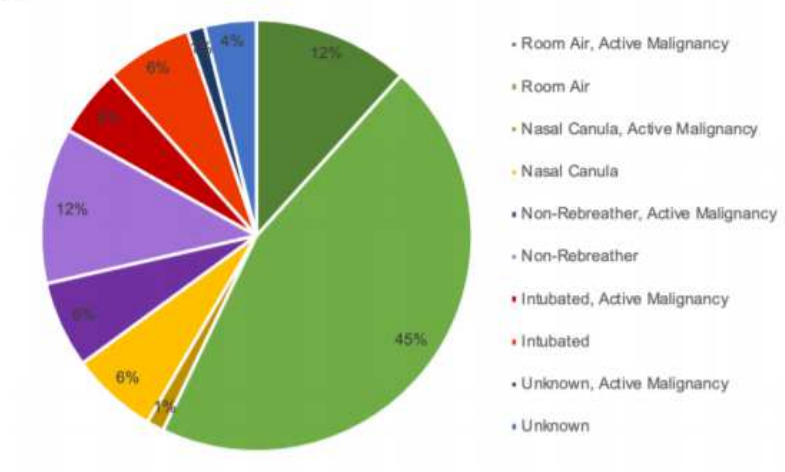

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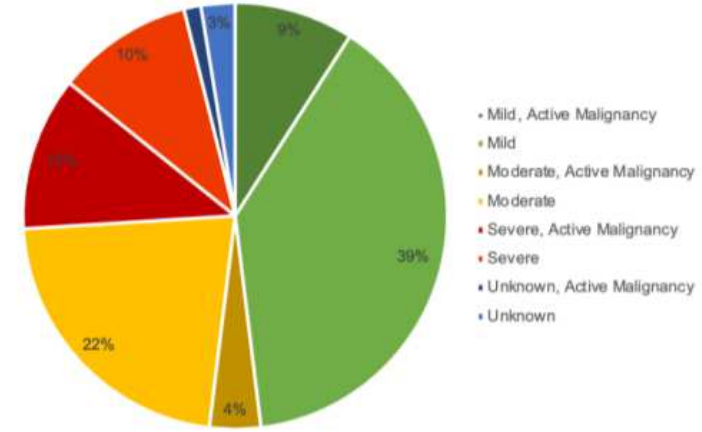


lymphocyte immunophenotyping, quantitative real-time PCR from nasopharyngeal swabs, and SARS-CoV-2 antibody status were available.

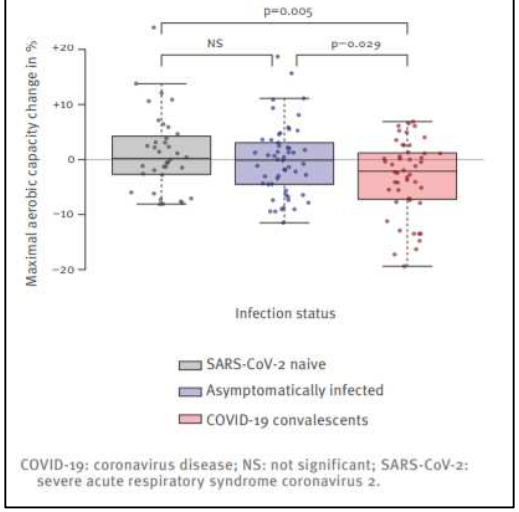
RESULTS. We identified 77 SARS-CoV-2 + cellular therapy recipients (Allo = 35, Auto = 37, CAR-T = 5; median time from cellular therapy 782 days (IQR 354,1611). Overall survival at 30 days was 78%. Clinical variables significantly associated with the composite endpoint of non-rebreather or higher oxygen requirement and death (n events = 25/77) included number of co-morbidities (HR 5.41, P = 0.004), infiltrates (HR 3.08, P = 0.032), and neutropenia (HR 1.15, P = 0.04). Worsening graft-versus-host-disease was not identified among Allo subjects. Immune profiling revealed reductions and rapid recovery in lymphocyte populations across lymphocyte subsets. Antibody responses were seen in a subset of patients.

CONCLUSION. In this series of Allo, Auto, and CAR-T recipients, we report overall favorable clinical outcomes for COVID-19 patients without active malignancy and provide preliminary insights into the lymphocyte populations that are key for the anti-viral response and immune reconstitution.

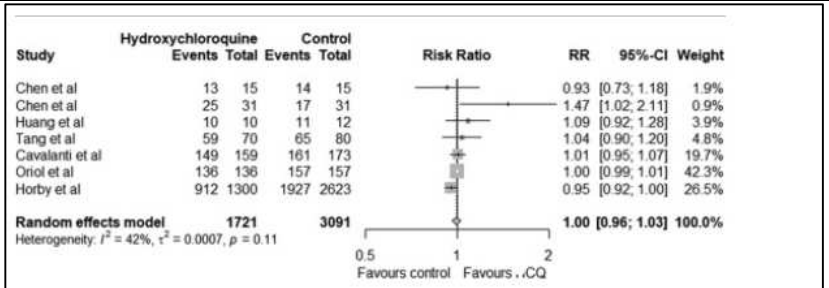
The Lancet Infectious Diseases Editorial Board The Lancet https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30706-4/fulltext	Curing COVID-19	Breve commento ai risultati ottenuti finora negli studi che valutano diverse terapie per COVID-19 : ad esclusione dei corticosteroidi, l'utilizzo di nessun altro farmaco è sostenuto da solide evidenze. Per gli Autori, la riduzione di mortalità osservata negli ultimi mesi di epidemia a livello mondiale è probabilmente dovuta alla diagnosi di un maggiore denominatore di casi piuttosto che all'effetto delle terapie utilizzate.	As the COVID-19 pandemic moves into its 10th month, greater patient survival suggests that treatment of severe disease has improved. How much of this improvement is due to better supportive care and how much to pharmaceuticals is a matter of debate. Given the huge effort that the biomedical community has put into finding drugs to treat COVID-19, with thousands of trials completed and ongoing, it's worth taking stock of the evidence for what has worked and what has not.
Lund LC et al PloS Medicine https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1003308	Adverse outcomes and mortality in users of non-steroidal anti-inflammatory drugs who tested positive for SARS-CoV-2: A Danish nationwide cohort study.	Ampio studio di coorte condotto in Danimarca per indagare l'associazione della terapia con antinfiammatori non steroidei (FANS) con mortalità a 30 giorni per infezione da SARS-CoV-2 e altri outcome sfavorevoli : nessuna associazione dimostrata.	BACKGROUND: Concerns over the safety of non-steroidal anti-inflammatory drug (NSAID) use during severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection have been raised. We studied whether use of NSAIDs was associated with adverse outcomes and mortality during SARS-CoV-2 infection. METHODS AND FINDINGS: We conducted a population-based cohort study using Danish administrative and health registries. We included individuals who tested positive for SARS-CoV-2 during the period 27 February 2020 to 29 April 2020. NSAID users (defined as individuals having filled a prescription for NSAIDs up to 30 days before the SARS-CoV-2 test) were matched to up to 4 non-users on calendar week of the test date and propensity scores based on age, sex, relevant comorbidities, and use of selected prescription drugs. The main outcome was 30-day mortality, and NSAID users were

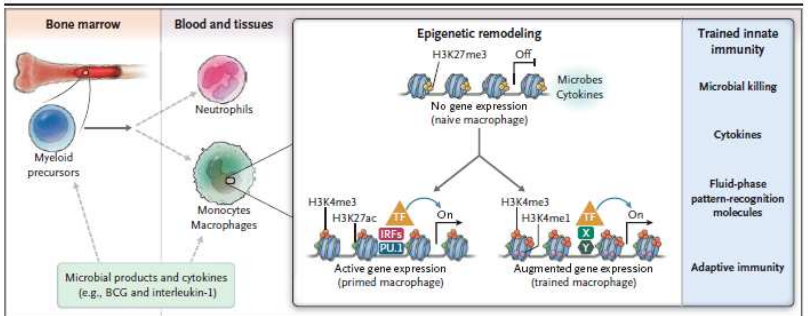
			compared to non-users using risk ratios (RRs) and risk differences (RDs). Secondary outcomes included hospitalization, intensive care unit (ICU) admission, mechanical ventilation, and acute renal replacement therapy. A total of 9,236 SARS-CoV-2 PCR-positive individuals were eligible for inclusion. The median age in the study cohort was 50 years, and 58% were female. Of these, 248 (2.7%) had filled a prescription for NSAIDs, and 535 (5.8%) died within 30 days. In the matched analyses, treatment with NSAIDs was not associated with 30-day mortality (RR 1.02, 95% CI 0.57 to 1.82, p = 0.95; RD 0.1%, 95% CI -3.5% to 3.7%, p = 0.95), risk of hospitalization (RR 1.16, 95% CI 0.87 to 1.53, p = 0.31; RD 3.3%, 95% CI -3.4% to 10%, p = 0.33), ICU admission (RR 1.04, 95% CI 0.54 to 2.02, p = 0.90; RD 0.2%, 95% CI -3.0% to 3.4%, p = 0.90), mechanical ventilation (RR 1.14, 95% CI 0.56 to 2.30, p = 0.72; RD 0.5%, 95% CI -2.5% to 3.6%, p = 0.73), or renal replacement therapy (RR 0.86, 95% CI 0.24 to 3.09, p = 0.81; RD -0.2%, 95% CI -2.0% to 1.6%, p = 0.81). The main limitations of the study are possible exposure misclassification, as not all individuals who fill an NSAID prescription use the drug continuously, and possible residual confounding by indication, as NSAIDs may generally be prescribed to healthier individuals due to their side effects, but on the other hand may also be prescribed for early symptoms of severe COVID-19. CONCLUSIONS: Use of NSAIDs was not associated with 30-day mortality, hospitalization, ICU admission, mechanical ventilation, or renal replacement therapy in Danish individuals who tested positive for SARS-CoV-2. TRIAL REGISTRATION: The European Union electronic Register of Post-Authorisation Studies EUPAS34734.

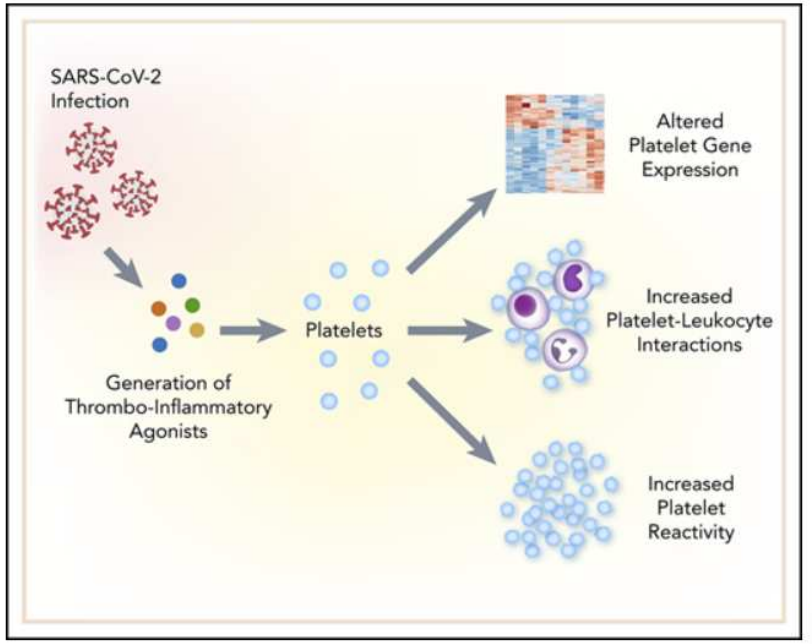
Brinder R et al The Journal of Infectious Diseases https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiaa575/5903399	Environmental and Aerosolized SARS-CoV-2 Among Hospitalized COVID-19 Patients.	Bassa prevalenza della positività per SARS-CoV-2 di fomiti e aerosol provenienti dalle stanze di ospedale di 20 pazienti con COVID-19, il che suggerisce basso rischio di trasmissione tramite oggetti inanimati.	During April and May 2020, we studied 20 hospitalized COVID-19 patients, their hospital rooms (fomites and aerosols), and their close contacts for molecular and culture evidence of SARS-CoV-2 virus. Among the more than 400 samples, we found molecular evidence of virus in most sample types, especially the nasopharygeal (NP), saliva, and fecal samples, but the prevalence of molecular positivity among fomites and aerosols was low. The agreement between NP swab and saliva positivity was high (89.5%, Kappa 0.79). Two NP swabs collected from patients on one and seven days post-symptom onset had evidence of infectious virus (2 passages over 14 days in Vero E6 cells). In summary, the low molecular prevalence and lack of viable SARS-CoV-2 virus in fomites and air samples implied low nosocomial risk SARS-CoV-2 transmission through inanimate objects or aerosols.
Temmam S et al One Health https://www.sciencedirect.com/science/article/pii/S2352771420302652?via%3Dihub	Absence of SARS-CoV-2 infection in cats and dogs in close contact with a cluster of COVID-19 patients in a veterinary campus.	Assenza di anticorpi anti-SARS-CoV-2 in 12 cani e 9 gatti vissuti a stretto contatto con persone positive per SARS-CoV-2.	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which originated in Wuhan, China, in 2019, is responsible for the COVID-19 pandemic. It is now accepted that the wild fauna, probably bats, constitute the initial reservoir of the virus, but little is known about the role pets can play in the spread of the disease in human communities, knowing the ability of SARS-CoV-2 to infect some domestic animals. In this cross-sectional study, we tested the antibody response in a cluster of 21 domestic pets (9 cats and 12 dogs) living in close contact with their owners (belonging to a veterinary community of 20 students) in which two students tested positive for COVID-19 and several others (n=11/18) consecutively showed clinical signs (fever, cough, anosmia, etc.) compatible with COVID-19 infection. Although a few pets presented many clinical signs indicative for a coronavirus infection, no antibodies against SARS-CoV-2 were detectable in their blood one month after the index case was reported, using an immunoprecipitation assay.

			These original data can serve a better evaluation of the host range of SARS-CoV-2 in natural environment exposure conditions.
Crameri GAG et al Eurosurveillance https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.36.2001542	Reduced maximal aerobic capacity after COVID-19 in young adult recruits, Switzerland, May 2020.	Studio su 199 giovani uomini e donne Svizzeri: si dimostra una riduzione della performance fisica a distanza dalla guarigione in chi ha avuto COVID-19 sintomatico, rispetto agli asintomatici e ai controlli mai infettati.	In March 2020, we observed an outbreak of COVID-19 among a relatively homogenous group of 199 young (median age 21 years; 87% men) Swiss recruits. By comparing physical endurance before and in median 45 days after the outbreak, we found a significant decrease in predicted maximal aerobic capacity in COVID-19 convalescent but not in asymptomatically infected and SARS-CoV-2 naive recruits. This finding might be indicative of lung injury after apparently mild COVID-19 in young adults. **FIGURE** Difference in predicted maximal aerobic capacity before and after COVID-19 outbreak by infection status among recruits, Switzerland, May 2020  COVID-19: coronavirus disease; NS: not significant; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

Pathak SK et al Daiabetes and Metabolic Syndrome https://www.sciencedirect.com/science/article/pii/S1871402120303362?via%3Dihub	No benefit of hydroxychloroquine in COVID-19: Results of Systematic Review and Meta-Analysis of Randomized Controlled Trials".	Metanalisi di trial clinici randomizzati che conclude per una assenza di beneficio nell'utilizzo di clorochina nei pazienti affetti da COVID-19 lieve-moderato.	Background and aims : Coronavirus pandemic is currently a global public health emergency with no definitive treatment guidelines. We conducted a systematic review and meta-analysis of the literature evaluating the efficacy of hydroxychloroquine and its related formulations in COVID-19 patients. Methods : A systematic search of PubMed, Scopus, MedRxiv data and Cochrane Central Register of Clinical Trials for published articles that reported the outcomes of COVID-19 patients treated with hydroxychloroquine or its compounds was done. We identified 1071 published studies and 7 studies were included in the analysis. Results : The study population consisted of a total of 4984 patients, of which 1721 (34.5%) received hydroxychloroquine or its congeners (HCQ group) while 3091 (62.01%) received standard of care or had included antiviral medication (control group). The pooled estimate of successful treatment in the hydroxychloroquine group and the control group was 77.45% and 77.87% respectively, which indicated similar clinical outcomes in patients treated with hydroxychloroquine compared to the control group. The odds ratio of a favourable outcome with hydroxychloroquine was 1.11 (95 CI 0.72 to 1.69) (p = 0.20). The pooled risk difference of favourable outcome with hydroxychloroquine versus control group was 0.00 (95 CI -0.03 to 0.03) which was statistically not significant (p = 0.10). Conclusions: The present evidence shows no benefit of hydroxychloroquine in patients affected by mild to moderate COVID-19 disease. However, now several trials on HCQ are ongoing and hopefully more data will be available soon. Hence, the management of COVID-19 is set to change for better in the future.

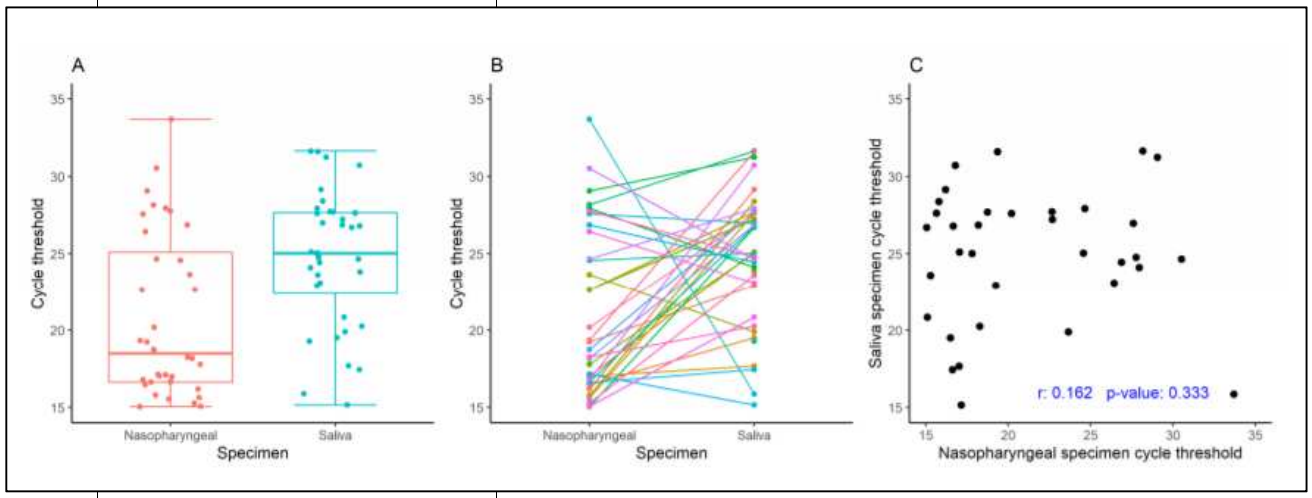
			 Download : Download high-res image (211KB) Download : Download full-size image Fig. 2. Forest plot illustrating the relative risk (RR) for favourable outcome between Treatment group (hydroxychloroquine) and control group in COVID-19 patients.
Mantovani A et al. NEJM https://www.nejm.org/doi/full/10.1056/NEJMcibr2011679	Trained Innate Immunity, Epigenetics, and Covid-19	La cosiddetta « trained innate immunity », considerata alla base degli effetti ad ampio spettro a seguito della vaccinazione con Bacillo di Calmette-Guérin (BCG), deriva dal fatto che cellule della linea mieloide o loro precursori subiscano una duratura modificazione epigenetica a seguito del contatto con un microrganismo. Essa potrebbe avere un ruolo nella risposta a SARS-CoV-2.	Innate immunity is mediated by different cell types and cell-associated or fluid-phase patternrecognition molecules and plays a key role in tissue repair and resistance against pathogens. Exposure to selected vaccines, such as bacille Calmette–Guérin (BCG) or microbial components, can increase the baseline tone of innate immunity and trigger pathogen-agnostic antimicrobial resistance (known as trained innate immunity). Such training is directly relevant to resistance against infectious diseases, including Covid-19. A recent study by de Laval et al. pinpoints a driver of durable innate immune memory conferred by myeloid cells (monocytes, macrophages, and neutrophils).

			 **Figure 1. Cellular and Molecular Mechanisms Underlying Trained Innate Immunity.** Exposure to microbial signals, particularly from bacille Calmette–Guérin (BCG), and to cytokines trains myelomonocytic cells with enhanced effector function against microbial agents. Training can occur at the level of bone marrow hematopoietic stem cells or of mature macrophages. Training-mediated augmentation of myelomonocytic-cell function depends on reshaping of the epigenetic landscape driven at the level of stem cells by the pioneering transcription factor (TF) CCAAT/enhancer-binding protein β (C/EBPβ),[2] transcription of long noncoding RNA, and metabolic rewiring. Trained myeloid cells show enhanced killing capacity and increased production of cytokines, chemokines, and fluid-phase pattern-recognition molecules. Moreover, they are better suited to triggering adaptive immune responses. Training is likely to underlie the off-target pathogen-agnostic function of BCG and possibly other vaccines. Interferon regulatory factors (IRFs) and PU.1 are TFs. X and Y indicate TFs that are involved in the regulation of specific genes in trained macrophages.
Manne BK et al Blood https://ashpublications.org/blood/article/136/11/1317/461106/Platelet-gene-expression-and-function-in-patients	Platelet gene expression and function in patients with COVID-19	L'nfezione da SARS-CoV-2 determina una alterazione dell'espressione genica nelle piastrine circolanti dei pazienti affetti, per quanto queste siano sprovviste del recettore ACE2. Ciò altera la attivazione e aggregazione piastrinica e potrebbe contribuire alla diatesi trombofilica tipica di COVID-19.	There is an urgent need to understand the pathogenesis of coronavirus disease 2019 (COVID-19). In particular, thrombotic complications in patients with COVID-19 are common and contribute to organ failure and mortality. Patients with severe COVID-19 present with hemostatic abnormalities that mimic disseminated intravascular coagulopathy associated with sepsis, with the major difference being increased risk of thrombosis rather than bleeding. However, whether severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection alters platelet function to contribute to the pathophysiology of COVID-19 remains unknown. In this study, we report altered platelet gene expression and functional responses in patients infected with SARS-CoV-2. RNA sequencing demonstrated distinct changes in the gene-expression profile of circulating platelets of COVID-19 patients. Pathway analysis revealed differential gene-expression changes in pathways associated with protein ubiquitination, antigen presentation, and mitochondrial dysfunction. The receptor for SARS-CoV-2 binding, angiotensin-converting enzyme 2 (ACE2), was not detected by

			messenger RNA (mRNA) or protein in platelets. Surprisingly, mRNA from the SARS-CoV-2 N1 gene was detected in platelets from 2 of 25 COVID-19 patients, suggesting that platelets may take-up SARS-COV-2 mRNA independent of ACE2. Resting platelets from COVID-19 patients had increased P-selectin expression basally and upon activation. Circulating platelet-neutrophil, -monocyte, and -T-cell aggregates were all significantly elevated in COVID-19 patients compared with healthy donors. Furthermore, platelets from COVID-19 patients aggregated faster and showed increased spreading on both fibrinogen and collagen. The increase in platelet activation and aggregation could partially be attributed to increased MAPK pathway activation and thromboxane generation. These findings demonstrate that SARS-CoV-2 infection is associated with platelet hyperreactivity, which may contribute to COVID-19 pathophysiology. 

Lee JC et al American Journal of Rhinology and Allergy https://journals.sagepub.com/doi/10.1177/1945892420957853	A systematic review of the neuropathologic findings of post-viral olfactory dysfunction: implications and novel insights for the COVID-19 pandemic	Revisione della letteratura sui meccanismi di alterazione dell'olfatto post-infezione virale : un fenomeno complesso di origine multifattoriale.	BACKGROUND: Post-viral olfactory dysfunction is a common cause of both short- and long-term smell alteration. The coronavirus pandemic further highlights the importance of post-viral olfactory dysfunction. Currently, a comprehensive review of the neural mechanism underpinning post-viral olfactory dysfunction is lacking. OBJECTIVES: To synthesize the existing primary literature related to olfactory dysfunction secondary to viral infection, detail the underlying pathophysiological mechanisms, highlight relevance for the current COVID-19 pandemic, and identify high impact areas of future research. METHODS: PubMed and Embase were searched to identify studies reporting primary scientific data on post-viral olfactory dysfunction. Results were supplemented by manual searches. Studies were categorized into animal and human studies for final analysis and summary. RESULTS: A total of 38 animal studies and 7 human studies met inclusion criteria and were analyzed. There was significant variability in study design, experimental model, and outcome measured. Viral effects on the olfactory system varies significantly based on viral substrain but generally include damage or alteration in components of the olfactory epithelium and/or the olfactory bulb. CONCLUSIONS: The mechanism of post-viral olfactory dysfunction is highly complex, virus-dependent, and involves a combination of insults at multiple levels of the olfactory pathway. This will have important implications for future diagnostic and therapeutic developments for patients infected with COVID-19.

Procop GW et al Journal of Clinical Microbiology https://jcm.asm.org/content/early/2020/09/03/JCM.01946-20	A direct comparison of enhanced saliva to nasopharyngeal swab for the detection of SARS-CoV-2 in symptomatic patients	Concordanza di esito della PCR real-time (RT) per SARS-CoV-2 fra tampone nasofaringeo e saliva in 224 persone testate. I due campioni sono comparabili per rilevamento qualitativo di SARS-CoV-2, anche se il ciclo soglia della PCR è più elevato per i campioni di saliva, che hanno carica virale mediamente più bassa.	Background: The ongoing COVID-19 pandemic has resulted in shortages in nasopharyngeal swabs (NPS) and viral transport media, necessitating the search for alternate diagnostic specimens, such as saliva. We directly compared matched saliva and NPS specimens from symptomatic patients suspected of having COVID-19.Methods: An enhanced saliva specimen (ie strong sniff, elicited cough, and collection of saliva/secretions) was collected without transport media prior to NPS from 224 patients with symptoms deemed consistent with COVID-19. Both specimens were tested with the CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel (4 February 2020 version), with the NPS result used as the reference standard.Results: Of the 216 patients included in the final analysis, there was a 100% Positive Percent Agreement (38/38 positive specimens) and 99.4% Negative Percent Agreement (177/178 negative specimens). The one discrepant specimen had the presence of SARS-CoV-2 confirmed in the saliva specimen using an alternate FDA EUA assay. The overall mean difference in crossing threshold (Ct) values for the positive NPS and saliva specimens was -3.61 (95% C.I. -5.78 to -1.44, p = 0.002).Conclusion: An enhanced saliva specimen performed as well as NPS for the qualitative detection of SARS-CoV-2 in symptomatic patients, albeit the overall mean viral load in saliva was lower.

			
Graffigna G et al PloS One https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0238613	Measuring Italian citizens' engagement in the first wave of the COVID-19 pandemic containment measures : a cross-sectional study	Risultati di un questionario online condotto su 1000 cittadini italiani al fine di individuare i fattori associati a coinvolgimento e adesione alle misure di contenimento di SARS-CoV-2 : il cittadino poco coinvolto è tendenzialmente preoccupato per il proprio stato di salute ma non fiducioso di poterlo determinare con le proprie scelte.	BACKGROUND: In January 2020, the coronavirus disease 2019 (COVID-19) started to spread in Italy. The Italian government adopted urgent measures to slow its spread. Enforcing compliance with such measures is crucial in order to enhance their effectiveness. Engaging citizens in the COVID-19 preventive process is urgent today both in Italy and around the world. However, to the best of our knowledge, no previous studies have investigated the role of health engagement in predicting citizens' compliance with health emergency containment measures. METHOD: An online survey was administered between February 28 and March 4, 2020 on a representative sample of 1000 Italians. The questionnaire included a measure of health engagement (Patient Health Engagement Scale), a 5-item Likert scale ranging from 1 to 7, resulting in 4 positions that describe the psychological readiness to be active in one's own health management, and a series of ad hoc items intended to measure citizens' perceived susceptibility and severity of the disease, orientation towards health management,

			trust in institutional bodies, health habits and food consumption. To investigate the relationship between health engagement and these variables, ANOVA analysis, logistic regression and contingency tables with Pearson's chi-squared analysis have been carried out. RESULTS: Less engaged people show higher levels of perceived susceptibility to the virus and severity of the disease; they are less trustful of scientific and healthcare authorities, they feel less self-effective in managing their own health - both in normal conditions and under stress - and are less prone to cooperate with healthcare professionals. Low levels of health engagement also are associated with a change in the usual purchase behavior. CONCLUSIONS: The Patient Health Engagement model (PHE) provides a useful framework for understanding how people will respond to health threats such as pandemics. Therefore, intervention studies should focus on raising their levels of engagement to increase the effectiveness of educational initiatives intended to promote preventive behaviors.
Carrillo-Vega MF et al PloS One https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0238905	Early estimation of the risk factors for hospitalization and mortality by COVID-19 in Mexico	Ricerca dei fattori associati a ospedalizzazione e mortalità da COVID-19 su 10544 pazienti con infezione moderato-grave. Si conferma in entrambi i casi il ruolo di sesso maschile, età avanzata, ipertensione, obesità e diabete, oltre a maggiore mortalità per pazienti ospedalizzati, con polmonite e sottoposti a ventilazione meccanica.	BACKGROUND: Due to a high prevalence of chronic non-degenerative diseases, it is suspected that COVID 19 poses a high risk of fatal complications for the Mexican population. The present study aims to estimate the risk factors for hospitalization and death in the Mexican population infected by SARS-CoV-2. METHODS AND FINDINGS: We used the publicly available data released by the Epidemiological Surveillance System for Viral Respiratory Diseases of the Mexican Ministry of Health (Secretaria de Salud, SSA). All records of positive SARS-CoV-2 cases were included. Two multiple logistic regression models were fitted to estimate the association between hospitalization and mortality, with other covariables. Data on 10,544 individuals (57.68% men), with mean age 46.47+/-15.62, were analyzed. Men were about 1.54 times more likely to be

			hospitalized than women (p<0.001, 95% C.I. 1.37-1.74); individuals aged 50-74 and >/=74 were more likely to be hospitalized than people aged 25-49 (OR 2.05, p<0.001, 95% C.I. 1.81-2.32, and OR 3.84, p<0.001, 95% C.I. 2.90-5.15, respectively). People with hypertension, obesity, and diabetes were more likely to be hospitalized than people without these comorbidities (p<0.01). Men had more risk of death in comparison to women (OR = 1.53, p<0.001, 95% C.I. 1.30-1.81) and individuals aged 50-74 and >/=75 were more likely to die than people aged 25-49 (OR 1.96, p<0.001, 95% C.I. 1.63-2.34, and OR 3.74, p<0.001, 95% C.I. 2.80-4.98, respectively). Hypertension, obesity, and diabetes presented in combination conveyed a higher risk of dying in comparison to not having these diseases (OR = 2.10; p<0.001, 95% C.I. 1.50-2.93). Hospitalization, intubation and pneumonia entail a higher risk of dying (OR 5.02, p<0.001, 95% C.I. 3.88-6.50; OR 4.27, p<0.001, 95% C.I. 3.26-5.59, and OR = 2.57; p<0.001, 95% C.I. 2.11-3.13, respectively). Our study's main limitation is the lack of information on mild (asymptomatic) or moderate cases of COVID-19. CONCLUSIONS: The present study points out that in Mexico, where an important proportion of the population has two or more chronic conditions simultaneously, a high mortality rate is a serious risk for those infected by SARS-CoV-2.