RICERCA BIBLIOGRAFICA COVID 19

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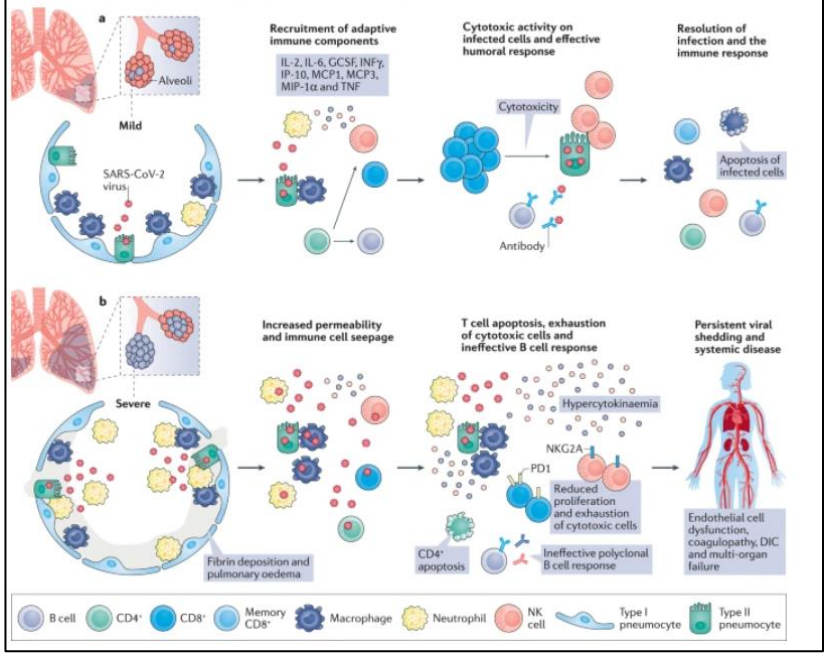
AUTORE/RIVISTA	TITOLO	OUTCOME PRINCIPALE	ABSTRACT
Perico L et al Nature https://www.nature.com/articles/s41581-020-00357-4	Immunity, endothelial injury and complement-induced coagulopathy in COVID-19	Revisione dei meccanismi patogenetici dell'infezione da SARS-CoV-2 e in particolare della disfunzione endoteliale e della microangiopatia trombotica da attivazione del complemento.	In December 2019, a novel coronavirus was isolated from the respiratory epithelium of patients with unexplained pneumonia in Wuhan, China. This pathogen, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causes a pathogenic condition that has been termed coronavirus disease 2019 (COVID-19) and has reached pandemic proportions. As of 17 September 2020, more than 30 million confirmed SARS-CoV-2 infections have been reported in 204 different countries, claiming more than 1 million lives worldwide. Accumulating evidence suggests that SARS-CoV-2 infection can lead to a variety of clinical conditions, ranging from asymptomatic to life-threatening cases. In the early stages of the disease, most patients experience mild clinical symptoms, including a high fever and dry cough. However, 20% of patients rapidly progress to severe illness characterized by atypical interstitial bilateral pneumonia, acute respiratory distress syndrome and multiorgan dysfunction. Almost 10% of these critically ill

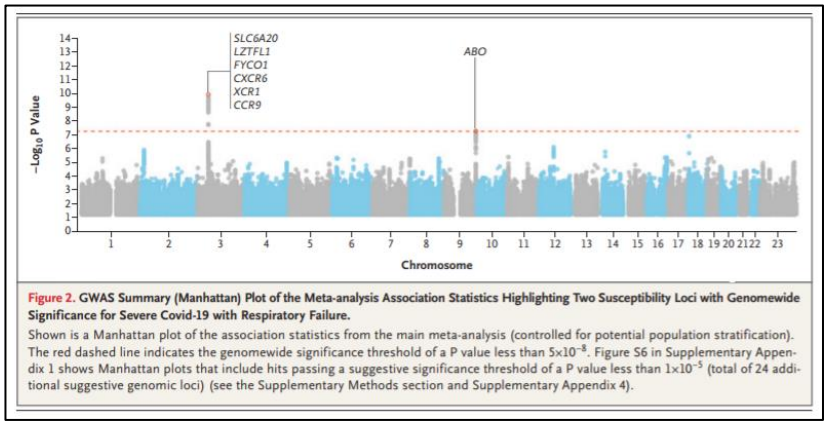
			patients subsequently die. Insights into the pathogenic mechanisms underlying SARS-CoV-2 infection and COVID-19 progression are emerging and highlight the critical role of the immunological hyper-response — characterized by widespread endothelial damage, complement-induced blood clotting and systemic microangiopathy — in disease exacerbation. These insights may aid the identification of new or existing therapeutic interventions to limit the progression of early disease and treat severe cases. **Fig. 2: Pathogenesis and outcomes of COVID-19.** 
Petrone L et al Clinical Microbiology and Infection	A whole blood test to measure SARS-CoV-2 specific response in COVID-19 patients	Test tipo IGRA (interferon-gamma release assay) su sangue intero basato sulla stimolazione con antigeni di	Objectives: To examine whether specific T-cell-responses to SARS-CoV-2 peptides can be detected in COVID-19 using a whole-blood experimental setting, which may be further explored as potential diagnostic tool.

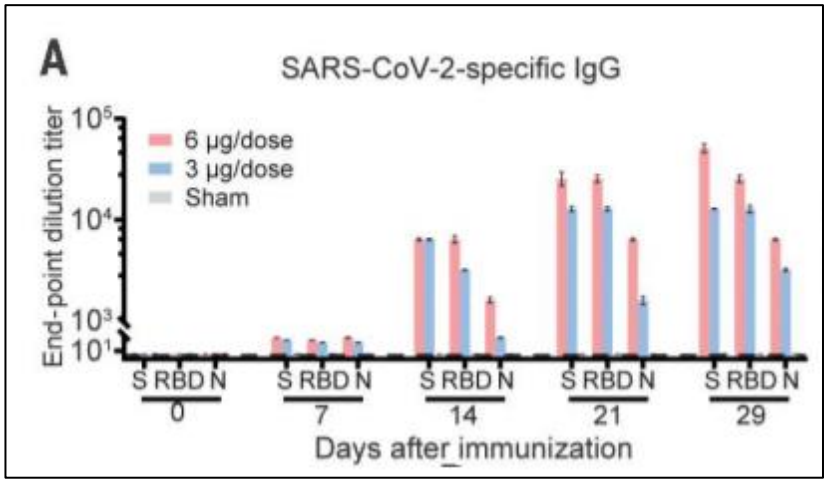
https://pubmed.ncbi.nlm.nih.gov/33045370/		SARS-CoV-2 per rilevare la risposta al virus a fine diagnostico.	Methods: We evaluated IFN-γ levels after stimulating whole-blood with spike and remainder-antigens peptides megapools (MP) derived from SARS-CoV-2 sequences; IL-1β, IL-1RA, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12p70, IL-13, IL-15, IL-17A, eotaxin, basic FGF, G-CSF, GM-CSF, IFN-γ, IP-10, MCP-1, MIP-1α, MIP-1β, PDGF, RANTES, TNF-α, VEGF were also evaluated. Results: IFN-γ-response to spike and remainder-antigens MPs was significantly increased in 35 COVID-19-patients compared to 29 "NO COVID-19"-individuals (medians spike-MP: 0.26 vs 0, p=0.0002; medians remainder-antigens-MP: 0.07 vs 0.02; p=0.02). This response was detected independently of patients' clinical parameters. IFN-γ-response to SARS-CoV-2-unrelated antigens CMV and SEB was similar in COVID-19 compared to NO-COVID-19-invididuals (median CMV: 3.46 versus 5.28, p=0.16; median SEB: 12.68 versus 15.05; p=0.1). In response to spike-MPs in COVID-19-compared to "NO COVID-19"-individuals, we found significant higher median of IL-2 (50.08 vs 0, p=0.0018), IFN-γ (90.16 vs 0, p=0.01), IL-4 (0.52 vs 0, p=0.03), IL-13 (0.84 vs 0, p=0.007) and MCP-1 (4602 vs 359.2, p=0.05). Conclusions: Immune response to SARS-CoV-2 peptides in a whole-blood assay is associated to COVID-19 and it is characterized by both Th1 and Th2 profile. This experimental approach may be useful for developing new T-cell based diagnostic tests for disease and vaccine settings.
Cantini F et al Drugs https://link.springer.com/article/10.1007/s40265-020-01421-w	Immune Therapy, or Antiviral Therapy, or Both for COVID-19: A Systematic Review	Revisione sistematica delle evidenze riguardo la terapia disponibile per l'infezione da SARS-CoV-2 nelle sue diverse fasi.	Background : Based on current evidence, recent guidelines of the National Institute of Health, USA indicated the use of remdesivir and dexamethasone for the treatment of COVID-19 patients with mild-moderate disease, not requiring high-flow oxygen. No therapeutic agent directed against the immunologic pathogenic

			mechanisms related to the cytokine release syndrome complicating the disease was indicated. Objectives : The purpose of this review was to assess the clinical impact of different therapies for COVID-19; thus, helping to identify the optimal management of the disease. To explain the rationale for the different therapeutic approaches, the characteristics of SARS-CoV-2, the pathogenesis of COVID-19, and the immune response triggered by SARS-CoV-2 infection were reported. Methods: The efficacy assessment of the different treatments was performed by a systematic review in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Available English language published articles including randomised controlled trials, open-label trials of antivirals and immune therapies extracted from Medline, Google Scholar, and MedRxiv databases were analysed. For inclusion, the primary end point of the trials had to be the efficacy as measured by the improvement of clinical features, or mortality, or the Intensive Care Unit Admission rate, or the discharge number. Case reports, paediatric studies, and studies without control group were excluded. The literature search was extended up to August 15, 2020. Results : After the removal of duplicate articles, and the exclusion of studies not meeting the eligibility criteria, 2 trials of lopinavir/ritonavir, 1 of favipiravir, 3 of remdesivir, 1 of dexamethasone, 3 of hydroxychloroquine, 2 of colchicine, 6 of tocilizumab, 1 of sarilumab, 1 of siltuximab, 2 of anakinra, 3 of baricitinib, 1 of ruxolitinib, 1 of mavrilimumab, and 1 of itolizumab were suitable for the review. Among antivirals, only remdesivir significantly reduced the time to recovery, and mortality. Data for chloroquine and hydroxychloroquine were largely inconclusive. In a

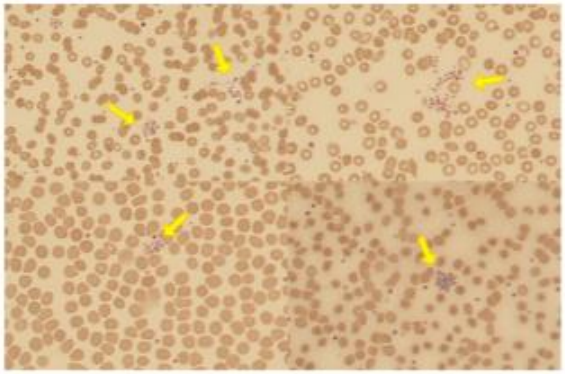
			large trial, dexamethasone 6 mg/day reduced mortality by one-third. Trials of tocilizumab and sarilumab did not definitively demonstrate efficacy. Anakinra significantly reduced the mortality in 2 trials. Three retrospective trials on a cumulative number of 145 patients, reported the efficacy of baricitinib, with significant reduction of intensive care unit admission, and deaths. These results were recently confirmed by the ACTT-2 trial. Due to paucity of studies and to the small size clinical series, the results of other immune therapies were not conclusive. Conclusions : Beyond the supportive therapy, up to now the best therapeutic approach for COVID-19 may be a three-step combination therapy, including remdesivir 100 mg/day (200 mg loading dose on first day) in the first stage of the disease, and combined dexamethasone 6 mg/day plus baricitinib 4 mg/day to target the immune dysregulation triggered by the SARS-CoV-2 infection. The promising results of anakinra should be confirmed by the ongoing RCTs.
Rodriguez JY et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1595/5929667?searchresult=1	Candida auris: a latent threat to critically ill patients with COVID-19	Descrizione di 20 casi di fungiemia in pazienti ospedalizzati per COVID-19: 19/20 candidemie, di cui 15/19 Candida non albicans e 6/19 Candida auris, endemica nel nord della Colombia.	We report 20 cases of fungemia in hospitalized patients with SARS-CoV-2 infection in 4 institutions in the northern region of Colombia from June to September 2020. We reviewed medical records and evaluated microbiological, demographic and clinical variables. Mortality was evaluated at 30 days after isolation of the yeast. Pathogen identification was performed by matrix-assisted laser desorption/ionization time-of-fight (MALDI-TOF) mass spectrometry (Bruker Daltonik, Bremen, Germany). SARS-CoV-2 infection was confirmed by RT PCR for SARSCoV-2.

Sax P HIV and ID Observations - NEJM Journal Watch https://blogs.jwatch.org/hiv-id-observations/	Does Remdesivir Actually Work?	Breve revisione critica delle evidenze a disposizione sull'efficacia di remdesivir contro l'infezione da SARS-CoV-2.	So for now, the answer to the question, "Does remdesivir actually work?" is a cautious maybe. Sometimes. For some people. Which, given the absence of anything else right now and its low toxicity, means I'd still recommend it for most hospitalized people with COVID-19 — with the hope of giving it sooner rather than later, especially for those on oxygen at high risk for disease progression. But if we can learn anything from the mental gyrations required to square these conflicting study results, it's that we definitely need more effective options.
The Severe Covid-19 GWAS Group NEJM https://www.nejm.org/doi/10.1056/NEJMoa2020283	Genomewide Association Study of Severe Covid-19 with Respiratory Failure	Studio di associazione genome-wide (GWAS) alla ricerca dei determinanti di infezione grave da SARS-CoV-2: emergono due loci, il primo contenente fra l'altro geni per recettori delle chemochine, il secondo i determinanti del sistema AB0 (rischio maggiore per il gruppo A, fattore protettivo il gruppo 0)	BACKGROUND: There is considerable variation in disease behavior among patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (Covid-19). Genomewide association analysis may allow for the identification of potential genetic factors involved in the development of Covid-19. METHODS: We conducted a genomewide association study involving 1980 patients with Covid-19 and severe disease (defined as respiratory failure) at seven hospitals in the Italian and Spanish epicenters of the SARS-CoV-2 pandemic in Europe. After quality control and the exclusion of population outliers, 835 patients and 1255 control participants from Italy and 775 patients and 950 control participants from Spain were included in the final analysis. In total, we analyzed 8,582,968 single-nucleotide polymorphisms and conducted a meta-analysis of the two case–control panels. RESULTS : We detected cross-replicating associations with rs11385942 at locus 3p21.31 and with rs657152 at locus 9q34.2, which were significant at the genomewide level ($P<5\times10-8$) in the meta-analysis of the two case–control panels (odds ratio, 1.77; 95% confidence interval [CI], 1.48 to 2.11; $P=1.15\times10-10$; and odds ratio, 1.32; 95% CI, 1.20 to 1.47; $P=4.95\times10-8$, respectively). At locus

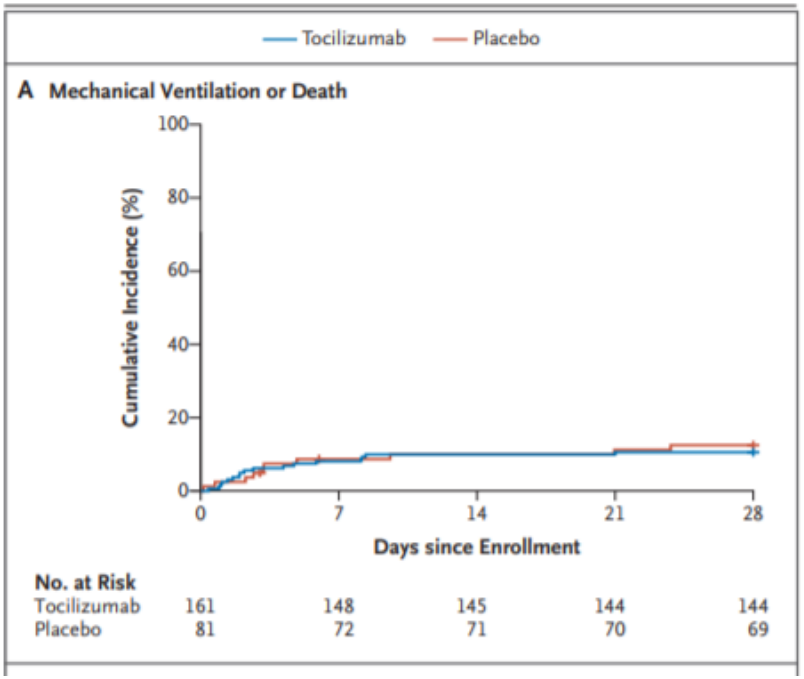
			3p21.31, the association signal spanned the genes SLC6A20, LZTFL1, CCR9, FYCO1, CXCR6 and XCR1. The association signal at locus 9q34.2 coincided with the ABO blood group locus; in this cohort, a blood-group–specific analysis showed a higher risk in blood group A than in other blood groups (odds ratio, 1.45; 95% CI, 1.20 to 1.75; P=1.48×10−4) and a protective effect in blood group O as compared with other blood groups (odds ratio, 0.65; 95% CI, 0.53 to 0.79; P=1.06×10−5). CONCLUSIONS : We identified a 3p21.31 gene cluster as a genetic susceptibility locus in patients with Covid-19 with respiratory failure and confirmed a potential involvement of the ABO blood-group system.  **Figure 2. GWAS Summary (Manhattan) Plot of the Meta-analysis Association Statistics Highlighting Two Susceptibility Loci with Genomewide Significance for Severe Covid-19 with Respiratory Failure.** Shown is a Manhattan plot of the association statistics from the main meta-analysis (controlled for potential population stratification). The red dashed line indicates the genomewide significance threshold of a P value less than 5×10^{-8}. Figure S6 in Supplementary Appendix 1 shows Manhattan plots that include hits passing a suggestive significance threshold of a P value less than 1×10^{-5} (total of 24 additional suggestive genomic loci) (see the Supplementary Methods section and Supplementary Appendix 4).
Kaser A NEJM https://www.nejm.org/doi/10.1056/NEJMe2025501	Genetic Risk of Severe Covid-19	Commento all'articolo precedente che orienta sul ruolo determinante della « sinapsi immunologica » tra linfociti T e cellule presentanti l'antigene nella patogenesi di COVID-19.	The large majority of patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have mild or no symptoms,1 whereas a small proportion of patients have respiratory compromise, acute respiratory distress syndrome, and multiorgan failure (which is often fatal). The determinants of disease severity appear to reside almost exclusively in host factors, not in viral genetic variation.

Quiang G et al Science https://science.sciencemag.org/content/369/6499/77	Development of an inactivated vaccine candidate for SARS-CoV-2	Esiti di uno studio preclinico sul candidato vaccino inattivato PiCoVacc diretto contro SARS-CoV-2, in grado di indurre anticorpi neutralizzanti nel macaco.	The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has resulted in an unprecedented public health crisis. Because of the novelty of the virus, there are currently no SARS-CoV-2–specific treatments or vaccines available. Therefore, rapid development of effective vaccines against SARS-CoV-2 are urgently needed. Here, we developed a pilot-scale production of PiCoVacc, a purified inactivated SARS-CoV-2 virus vaccine candidate, which induced SARS-CoV-2–specific neutralizing antibodies in mice, rats, and nonhuman primates. These antibodies neutralized 10 representative SARS-CoV-2 strains, suggesting a possible broader neutralizing ability against other strains. Three immunizations using two different doses, 3 or 6 micrograms per dose, provided partial or complete protection in macaques against SARS-CoV-2 challenge, respectively, without observable antibody-dependent enhancement of infection. These data support the clinical development and testing of PiCoVacc for use in humans. 

Bon-Sang K et al The Journal of Infectious Diseases https://academic.oup.com/jid/article/222/10/1596/5880024	Transient Lymphopenia and Interstitial Pneumonia With Endotheliitis in SARS-CoV-2–Infected Macaques	Caratteristiche dell'infezione da SARS-CoV-2 nel macaco : linfpenia e polmonite interstiziale costituiscono una sindrome COVID-19-like, utile modello per studi sulla terapia.	Using a reliable primate model is critical for developing therapeutic advances to treat humans infected with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Here, we exposed macaques to high titers of SARS-CoV-2 via combined transmission routes. We observed acute interstitial pneumonia with endotheliitis in the lungs of all infected macaques. All macaques had a significant loss of total lymphocytes during infection, which were restored over time. These data show that SARS-CoV-2 causes a coronavirus disease 2019 (COVID-19)-like disease in macaques. This new model could investigate the interaction between SARS-CoV-2 and the immune system to test therapeutic strategies.
Choucair J et al Clinical Microbiology and Infection https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30338-4/fulltext	Discrepancy in reports of COVID-19 onset of symptoms: are faulty data being collected?	L'accuratezza dei dati anamnestici riferiti dai pazienti deve essere sempre valutata criticamente ; nel corso della pandemia da COVID-19, con potenziali conseguenze nel riferire comportamenti imprudenti, la discrepanza con la realtà è probabilmente ancora maggiore.	With the medical sector overwhelmed amid the pandemic, patient interviews tend to be hastened and shortened. Healthcare providers would sometimes opt for prototyped survey charts with binary answers to screen suspicious patients in emergency rooms. However, we noticed that patients have a variable perception of their symptoms, leading to difficulty in data collection. With the virus carrying a taboo connotation in some populations, and amid the fear of quarantine, patients would deny or trivialize their symptoms. Others, seeking to be eligible for testing, would amplify their symptoms.
Azzi L Clinical Infectious Diseases https://academic.oup.com/cid/advance-	Saliva is the Key Element for SARS-CoV-2 Mass Screening	La saliva è il campione ideale per eseguire screening di massa per infezione da SARS-CoV-2 sulla popolazione asintomatica.	The current COVID-19 pandemic has shown clinicians and researchers the fundamental rôle played by asymptomatic carriers and pre-symptomatic individuals in the infectious outbreak, a feature that distinguishes SARS-CoV-2 from SARS-CoV and MERS-CoV. Recent findings have pointed out how the viral load in COVID-19 is high at the very onset of the disease and then decreases over time, underlining a probably high load also in the pre-symptomatic

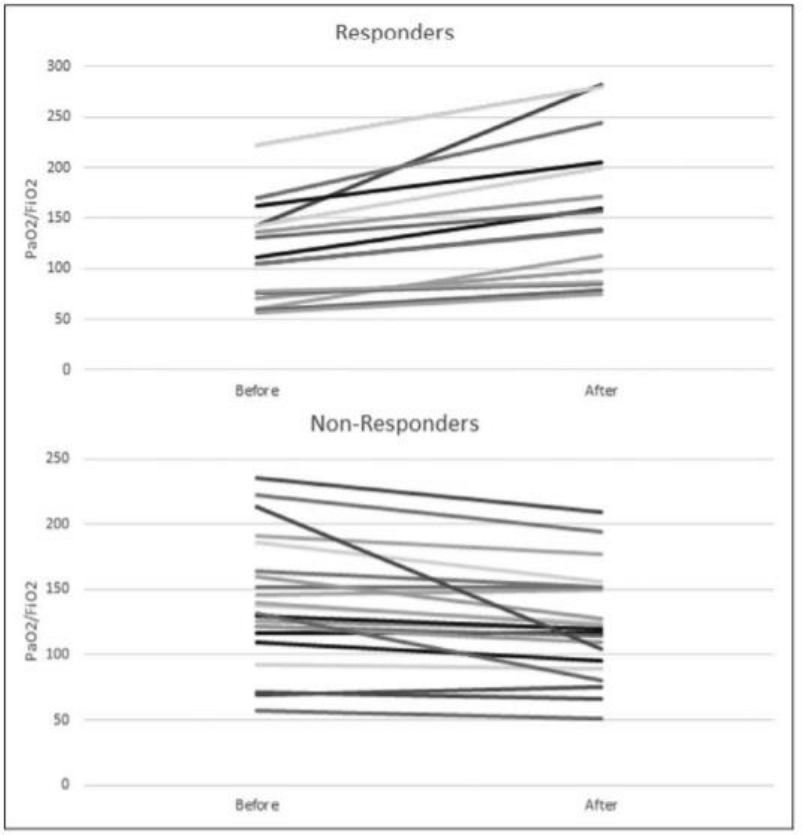
article/doi/10.1093/cid/ciaa1440/5933821			phase. Within this frame, identifying those subjects who unwittingly can spread the infection when coming into contact with their family members, or other people in social gathering spaces, is the only way to prevent new pandemic outbreaks and avert future national lockdown measures
Rampotas A et al Journal of Clinical Pathology https://www.ncbi.nlm.nih.gov/research/coronaviruses/publication/33067181	Platelet aggregates, a marker of severe COVID-19 disease.	Riscontro di aggregati piastrinici in 20 pazienti critici con infezione da SARS-CoV-2, senza piastrinopenia grave, risultato di un bilanciamento fra aumentata produzione a causa della stimolazione citochinica ed aumentata attivazione e consumo per microangiopatia trombotica.	Thrombocytopenia is common in an intensive care unit (ICU) setting due to endogenous and iatrogenic factors. Despite that, thrombocytopenia in patients with severe COVID-19 infections is surprisingly uncommon. By examining the blood film of 20 ICU patients with COVID-19, we observed the presence of platelet aggregates and macrothrombocytes indicating increased platelet activity. We compared these findings with 20 blood films of non-severe COVID-19 cases where these findings were absent. These morphology features could be consistent with severe COVID-19 infection and is further evidence of the important role that platelets play when COVID-19 manifests with thrombotic complications or respiratory failure.  **Figure 2** Peripheral films showing platelet aggregates (yellow arrows).

Stone JH et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2028836?query=featured_home	Efficacy of Tocilizumab in Patients Hospitalized with Covid-19	Trial clinico randomizzato, in doppio cieco, controllato con placebo, su 243 pazienti ospedalizzati con infezione di moderata gravità da SARS-CoV-2: la terapia con tocilizumab 8 mg/kg endovena non previene significativamente morte o necessità di intubazione.	BACKGROUND : The efficacy of interleukin-6 receptor blockade in hospitalized patients with coronavirus disease 2019 (Covid-19) who are not receiving mechanical ventilation is unclear. METHODS : We performed a randomized, double-blind, placebo-controlled trial involving patients with confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, hyperinflammatory states, and at least two of the following signs: fever (body temperature >38°C), pulmonary infiltrates, or the need for supplemental oxygen in order to maintain an oxygen saturation greater than 92%. Patients were randomly assigned in a 2:1 ratio to receive standard care plus a single dose of either tocilizumab (8 mg per kilogram of body weight) or placebo. The primary outcome was intubation or death, assessed in a time-to-event analysis. The secondary efficacy outcomes were clinical worsening and discontinuation of supplemental oxygen among patients who had been receiving it at baseline, both assessed in time-to-event analyses. RESULTS : We enrolled 243 patients; 141 (58%) were men, and 102 (42%) were women. The median age was 59.8 years (range, 21.7 to 85.4), and 45% of the patients were Hispanic or Latino. The hazard ratio for intubation or death in the tocilizumab group as compared with the placebo group was 0.83 (95% confidence interval [CI], 0.38 to 1.81; P=0.64), and the hazard ratio for disease worsening was 1.11 (95% CI, 0.59 to 2.10; P=0.73). At 14 days, 18.0% of the patients in the tocilizumab group and 14.9% of the patients in the placebo group had had worsening of disease. The median time to discontinuation of supplemental oxygen was 5.0 days (95% CI, 3.8 to 7.6) in the tocilizumab group and 4.9 days (95% CI, 3.8 to 7.8) in the placebo group (P=0.69). At 14 days, 24.6% of the patients in the tocilizumab group and 21.2% of the patients in the placebo group

			were still receiving supplemental oxygen. Patients who received tocilizumab had fewer serious infections than patients who received placebo. CONCLUSIONS : Tocilizumab was not effective for preventing intubation or death in moderately ill hospitalized patients with Covid-19. Some benefit or harm cannot be ruled out, however, because the confidence intervals for efficacy comparisons were wide. 
Mohamed OM et al European Heart Journal https://academic.oup.com/ehjqcco/advance-article/doi/10.1093/ehjqcco/qcaa079/5932442	Impact of COVID-19 on cardiac procedure activity in England and associated 30-day mortality	Significativa riduzione del numero di procedure cardiologiche (in particolare cateterismo cardiaco e impianto di device) durante la prima ondata di COVID-19	Background : Limited data exists on the impact of COVID-19 on national changes in cardiac procedure activity, including patient characteristics and clinical outcomes before and during the COVID-19 pandemic. Methods and Results : All major cardiac procedures (n = 374,899) performed between 1st January and 31st May for the years 2018,

		in Inghilterra, senza modifiche della mortalità associata.	2019 and 2020 were analysed, stratified by procedure type and time-period (pre-COVID: January-May 2018 and 2019 and January-February 2020 and COVID: March-May 2020). Multivariable logistic regression was performed to examine the odds ratio (OR) of 30-day mortality for procedures performed in the COVID period. Overall, there was a deficit of 45,501 procedures during the COVID period compared to the monthly averages (March-May) in 2018-2019. Cardiac catheterisation and device implantations were the most affected in terms of numbers (n = 19,637 and n = 10,453) whereas surgical procedures such as MVR, other valve replacement/repair, ASD/VSD repair and CABG were the most affected as a relative percentage difference (Δ) to previous years' averages. TAVR was the least affected (Δ-10.6%). No difference in 30-day mortality was observed between pre-COVID and COVID time-periods for all cardiac procedures except cardiac catheterisation (OR 1.25 95% confidence interval (CI) 1.07-1.47, p = 0.006) and cardiac device implantation (OR 1.35 95% CI 1.15-1.58, p < 0.001). Conclusion : Cardiac procedural activity has significantly declined across England during the COVID-19 pandemic, with a deficit in excess of 45000 procedures, without an increase in risk of mortality for most cardiac procedures performed during the pandemic. Major restructuring of cardiac services is necessary to deal with this deficit, which would inevitably impact long-term morbidity and mortality.
DeGrado J et al Critical Care Medicine https://journals.lww.com/ccejournal/Fulltext/2020/10000/Evaluation_of_the	Evaluation of the Efficacy and Safety of Inhaled Epoprostenol and Inhaled Nitric Oxide for Refractory	Studio retrospettivo monocentrico su 38 pazienti ricoverati in rianimazione con ARDS ed ipossia refrattaria e trattati con epoprostenolo e quindi	Objectives: The objectives of this study were to evaluate the efficacy and safety of inhaled epoprostenol and inhaled nitric oxide in patients with refractory hypoxemia secondary to coronavirus disease 2019. Design: Retrospective single-center study.

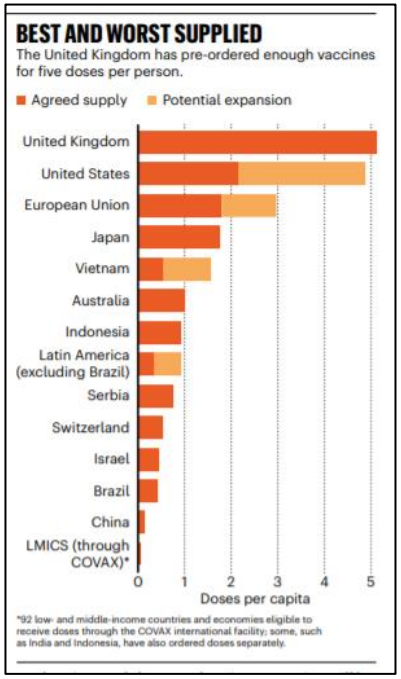
_Efficacy_and_Safety_of_Inhaled.37.aspx	Hypoxemia in Patients With Coronavirus Disease 2019	ossido nitrico per via inalatoria come broncodilatatori : un gruppo di pazienti -responders- mostra miglioramento dei parametri respiratori, anche se non emerge nessuna differenza di outcome rispetto ai non-responders.	Setting: ICUs at a large academic medical center in the United States. Patients: Thirty-eight adult critically ill patients with coronavirus disease 2019 and refractory hypoxemia treated with either inhaled epoprostenol or inhaled nitric oxide for at least 1 hour between March 1, 2020, and June 30, 2020. Interventions: Electronic chart review. Measurements and Main Results: Of 93 patients screened, 38 were included in the analysis, with mild (4, 10.5%), moderate (24, 63.2%), or severe (10, 26.3%), with acute respiratory distress syndrome. All patients were initiated on inhaled epoprostenol as the initial pulmonary vasodilator and the median time from intubation to initiation was 137 hours (68–228 h). The median change in Pao2/Fio2 was 0 (–12.8 to 31.6) immediately following administration of inhaled epoprostenol. Sixteen patients were classified as responders (increase Pao2/Fio2 > 10%) to inhaled epoprostenol, with a median increase in Pao2/Fio2 of 34.1 (24.3–53.9). The mean change in Pao2 and Spo2 was –0.55 ± 41.8 and –0.6 ± 4.7, respectively. Eleven patients transitioned to inhaled nitric oxide with a median change of 11 (3.6–24.8) in Pao2/Fio2. A logistic regression analysis did not identify any differences in outcomes or characteristics between the responders and the nonresponders. Minimal adverse events were seen in patients who received either inhaled epoprostenol or inhaled nitric oxide. Conclusions: We found that the initiation of inhaled epoprostenol and inhaled nitric oxide in patients with refractory hypoxemia secondary to coronavirus disease 2019, on average, did not produce significant increases in oxygenation metrics. However, a group of patients had significant improvement with inhaled epoprostenol and inhaled nitric oxide. Administration of inhaled epoprostenol or

			inhaled nitric oxide may be considered in patients with severe respiratory failure secondary to coronavirus disease 2019.  **Figure 2.** Pao_2/Fio_2 before and after inhaled epoprostenol in responders ($n = 16$) and nonresponders ($n = 22$).
Amato M et al Vaccines https://www.mdpi.com/2076-393X/8/3/535	Relationship between Influenza Vaccination Coverage Rate and COVID-19 Outbreak: An Italian Ecological Study	Studio dell'associazione tra vaccinazione antinfluenzale e diversi outcome dell'infezione da SARS-CoV-2 : possibile effetto protettivo rispetto a	Background: The lack of specific vaccines or drugs against coronavirus disease 2019 (COVID-19) warrants studies focusing on alternative clinical approaches to reduce the spread of this pandemic disease. In this study, we investigated whether anti-influenza vaccination plays a role in minimizing the diffusion of COVID-19 in the Italian population aged 65 and over. Methods: Four

		diffusione dell'infezione e outcome avversi.	COVID-19 outcomes were used: severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) seroprevalence, hospitalizations for COVID-19 symptoms, admissions to intensive care units for reasons related to SARS-CoV-2, and deaths attributable to COVID-19. Results: At univariate analyses, the influenza vaccination coverage rates correlated negatively with all COVID-19 outcomes (Beta ranging from −134 to −0.61; all p < 0.01). At multivariable analyses, influenza vaccination coverage rates correlated independently with SARS-CoV-2 seroprevalence (Beta (95% C.I.): −130 (−198, −62); p = 0.001), hospitalizations for COVID-19 symptoms (Beta (95% C.I.): −4.16 (−6.27, −2.05); p = 0.001), admission to intensive care units for reasons related to SARS-CoV-2 (Beta (95% C.I.): −0.58 (−1.05, −0.12); p = 0.017), and number of deaths attributable to COVID-19 (Beta (95% C.I.): −3.29 (−5.66, −0.93); p = 0.010). The R2 observed in the unadjusted analysis increased from 82% to 159% for all the considered outcomes after multivariable analyses. Conclusions: In the Italian population, the coverage rate of the influenza vaccination in people aged 65 and over is associated with a reduced spread and a less severe clinical expression of COVID-19. This finding warrants ad hoc studies to investigate the role of influenza vaccination in preventing the spread of COVID-19.
Habel JR et al Proceedings of the National Academy of Science https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7533701/	Suboptimal SARS-CoV-2-specific CD8 + T cell response associated with the prominent HLA-A*02:01 phenotype	I livelli di linfociti CD8+ nei pazienti guariti da COVID-19 sono inferiori rispetto ad altre malattie virali quali l'influenza : scopo di un vaccino ben congegnato dovrebbe essere stimolare una più elevata risposta cellulo-mediata.	An improved understanding of human T cell-mediated immunity in COVID-19 is important for optimizing therapeutic and vaccine strategies. Experience with influenza shows that infection primes CD8+ T cell memory to peptides presented by common HLA types like HLA-A2, which enhances recovery and diminishes clinical severity upon reinfection. Stimulating peripheral blood mononuclear cells from COVID-19 convalescent patients with overlapping peptides from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) led to the clonal expansion of SARS-

			CoV-2−specific CD8+ and CD4+ T cells in vitro, with CD4+ T cells being robust. We identified two HLAA*02:01-restricted SARS-CoV-2-specfic CD8+ T cell epitopes, A2/ S269–277 and A2/Orf1ab3183–3191. Using peptide−HLA tetramer enrichment, direct ex vivo assessment of A2/S269+ CD8+ and A2/ Orf1ab3183+ CD8+ populations indicated that A2/S269+ CD8+ T cells were detected at comparable frequencies (∼1.3 × 10−5) in acute and convalescent HLA-A*02:01+ patients. These frequencies were higher than those found in uninfected HLA-A*02:01+ donors (∼2.5 × 10−6), but low when compared to frequencies for influenza-specific (A2/M158) and Epstein–Barr virus (EBV)-specific (A2/BMLF1280) (∼1.38 × 10−4) populations. Phenotyping A2/S269+ CD8+ T cells from COVID-19 convalescents ex vivo showed that A2/S269+ CD8+ T cells were predominantly negative for CD38, HLA-DR, PD-1, and CD71 activation markers, although the majority of total CD8+ T cells expressed granzymes and/or perforin. Furthermore, the bias toward naïve, stem cell memory and central memory A2/S269+ CD8+ T cells rather than effector memory populations suggests that SARS-CoV-2 infection may be compromising CD8+ T cell activation. Priming with appropriate vaccines may thus be beneficial for optimizing CD8+ T cell immunity in COVID-19.
Rashed N et al Virus Disease https://link.springer.com/article/10.1007/s13337-020-00628-5	A brief outline of respiratory viral disease outbreaks: 1889–till date on the public health perspectives	Storia della pandemia influenzale fin dalle sue origini e relazioni con la attuale pandemia da SARS-CoV-2.	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is currently causing the respiratory illness termed as the coronavirus disease 2019 or the COVID-19 pandemic. Indeed, the significant increase in deaths in the current days due to influenza around the world started in 1889 is a continued public health threat because of its intermittent style of pandemic outbreaks. An array of research on the influenza viruses has been conducted especially pointing on (1) the development of the anti-viral drugs and the design of probable vaccines on trial basis, (2) the biochemical and genetic

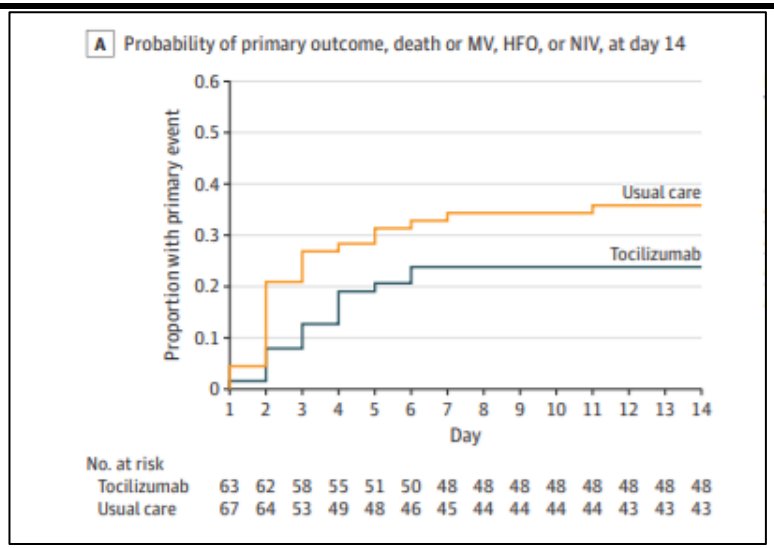
			aspects underlying the viral pathogenicity, (3) the viral epidemiology, and on (4) the protective immunity against the influenza viruses. Current review briefly discussed the epidemic/ pandemic history of influenza and correlated with the current epidemiology, the possible preventive measures that may be taken by the public health professionals as well as to increase the protective awareness among the general people. The viral reassortments during the initiation of pandemics have also been focused based on the previous literatures.
Crooke SN et al Nature https://www.nature.com/articles/s41598-020-70864-8	Immunoinformatic identification of B cell and T cell epitopes in the SARS-CoV-2 proteome	Analisi del proteoma di SARS-CoV-2 alla ricerca di epitopi di linfociti T e B, potenziali target di un vaccino peptidico.	A novel coronavirus (SARS-CoV-2) emerged from China in late 2019 and rapidly spread across the globe, infecting millions of people and generating societal disruption on a level not seen since the 1918 influenza pandemic. A safe and effective vaccine is desperately needed to prevent the continued spread of SARS-CoV-2; yet, rational vaccine design efforts are currently hampered by the lack of knowledge regarding viral epitopes targeted during an immune response, and the need for more in-depth knowledge on betacoronavirus immunology. To that end, we developed a computational workflow using a series of open-source algorithms and webtools to analyze the proteome of SARS-CoV-2 and identify putative T cell and B cell epitopes. Utilizing a set of stringent selection criteria to filter peptide epitopes, we identified 41 T cell epitopes (5 HLA class I, 36 HLA class II) and 6 B cell epitopes that could serve as promising targets for peptide-based vaccine development against this emerging global pathogen. To our knowledge, this is the first study to comprehensively analyze all 10 (structural, non-structural and accessory) proteins from SARS-CoV-2 using predictive algorithms to identify potential targets for vaccine development.

			Download PDF
Callaway E Nature https://www.nature.com/articles/d41586-020-02450-x	The unequal scramble for coronavirus vaccines — by the numbers	Lotta – impari – fra le nazioni del mondo per l'approvvigionamento di vaccini anti – SARS-CoV-2 una volta disponibili.	Wealthy countries have struck deals to buy more than two billion doses of coronavirus vaccine in a scramble that could leave limited supplies in the coming year. Meanwhile, an international effort to acquire vaccines for low- and middle-income countries is struggling to gain traction. Most experts say that late 2020 or early 2021 is the soonest vaccines could be approved and rolled out; they must first undergo large-scale phase III clinical trials to assess their effectiveness and safety. (Russia has approved a vaccine for limited use, but it hasn't completed phase III trials.) 

Zanettini C et al medRXiv https://www.medrxiv.org/content/10.1101/2020.06.24.20129817v1	Influenza Vaccination and COVID19 Mortality in the USA	Associazione fra vaccinazione antinfluenzale nella popolazione di età superiore a 65 anni e e mortalità per COVID-19 : potenziale effetto protettivo.	COVID-19 mortality rate is higher in the elderly and in those with preexisting chronic medical conditions. The elderly also suffer from increased morbidity and mortality from seasonal influenza infection, and thus annual influenza vaccination is recommended for them. In this study, we explore a possible area-level association between influenza vaccination coverage in people aged 65 years and older and the number of deaths from COVID-19. To this end, we used COVID-19 data until June 10, 2020 together with population health data for the United States at the county level. We fit quasi-Poisson regression models using influenza vaccination coverage in the elderly population as the independent variable and the number of deaths from COVID-19 as the outcome variable. We adjusted for a wide array of potential confounding variables using both county-level generalized propensity scores for influenza vaccination rates, as well as direct adjustment. Our results suggest that influenza vaccination coverage in the elderly population is negatively associated with mortality from COVID-19. This finding is robust to using different analysis periods, different thresholds for inclusion of counties, and a variety of methodologies for confounding adjustment. In conclusion, our results suggest a potential protective effect of the influenza vaccine on COVID-19 mortality in the elderly population. The significant public health implications of this possibility point to an urgent need for studying the relationship between influenza vaccination and COVID-19 mortality at the individual level, to investigate both the epidemiology and any underlying biological mechanism.
Olivier H et al JAMA	Effect of Tocilizumab vs Usual Care in Adults Hospitalized	Trial clinico randomizzato su 163 pazienti con polmonite da SARS-CoV-2 e necessità di ossigenoterapia, trattati con tocilizumab EV o	IMPORTANCE Severe pneumonia with hyperinflammation and elevated interleukin-6 is a common presentation of coronavirus disease 2019 (COVID-19).

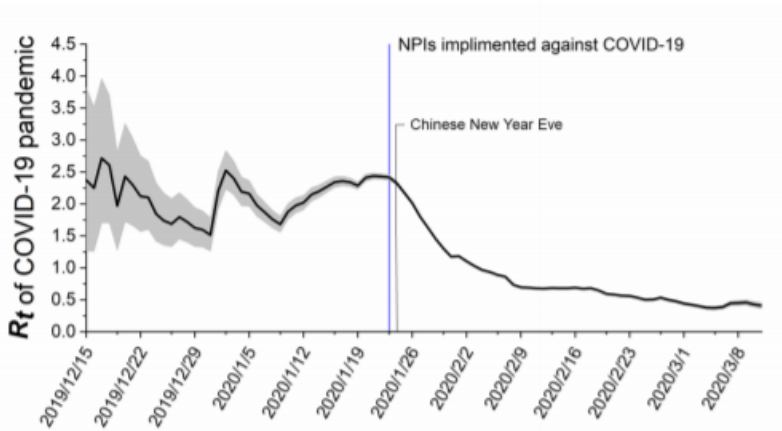
file:///C:/Users/pc/Downloads/Effect%20of%20Tocilizumab%20vs%20Usual%20Care%20in%20Adults%20Hospitalized.pdf	With COVID-19 and Moderate or Severe Pneumonia	standard of care : possibile riduzione del rischio di ventilazione non invasiva, ventilazione meccanica e morte a 14 giorni.	OBJECTIVE To determine whether tocilizumab (TCZ) improves outcomes of patients hospitalized with moderate-to-severe COVID-19 pneumonia. DESIGN, SETTING, AND PARTICPANTS This cohort-embedded, investigator-initiated, multicenter, open-label, bayesian randomized clinical trial investigating patients with COVID-19 and moderate or severe pneumonia requiring at least 3 L/min of oxygen but without ventilation or admission to the intensive care unit was conducted between March 31, 2020, to April 18, 2020, with follow-up through 28 days. Patients were recruited from 9 university hospitals in France. Analyses were performed on an intention-to-treat basis with no correction for multiplicity for secondary outcomes. INTERVENTIONS Patients were randomly assigned to receive TCZ, 8 mg/kg, intravenously plus usual care on day 1 and on day 3 if clinically indicated (TCZ group) or to receive usual care alone (UC group). Usual care included antibiotic agents, antiviral agents, corticosteroids, vasopressor support, and anticoagulants. MAIN OUTCOMES AND MEASURES Primary outcomes were scores higher than 5 on the World Health Organization 10-point Clinical Progression Scale (WHO-CPS) on day 4 and survival without need of ventilation (including noninvasive ventilation) at day 14. Secondary outcomes were clinical status assessed with the WHO-CPS scores at day 7 and day 14, overall survival, time to discharge, time to oxygen supply independency, biological factors such as C-reactive protein level, and adverse events. RESULTS Of 131 patients, 64 patients were randomly assigned to the TCZ group and 67 to UC group; 1 patient in the TCZ group withdrew consent and was not included in the analysis. Of

			the 130 patients, 42 were women (32%), and median (interquartile range) age was 64 (57.1-74.3) years. In the TCZ group, 12 patients had a WHO-CPS score greater than 5 at day 4 vs 19 in the UC group (median posterior absolute risk difference [ARD] −9.0%; 90% credible interval [CrI], −21.0 to 3.1), with a posterior probability of negative ARD of 89.0% not achieving the 95% predefined efficacy threshold. At day 14, 12% (95% CI −28% to 4%) fewer patients needed noninvasive ventilation (NIV) or mechanical ventilation (MV) or died in the TCZ group than in the UC group (24% vs 36%, median posterior hazard ratio [HR] 0.58; 90% CrI, 0.33-1.00), with a posterior probability of HR less than 1 of 95.0%, achieving the predefined efficacy threshold. The HR for MV or death was 0.58 (90% CrI, 0.30 to 1.09). At day 28, 7 patients had died in the TCZ group and 8 in the UC group (adjusted HR, 0.92; 95% CI 0.33-2.53). Serious adverse events occurred in 20 (32%) patients in the TCZ group and 29 (43%) in the UC group (P = .21). CONCLUSIONS AND RELEVANCE In this randomized clinical trial of patients with COVID-19 and pneumonia requiring oxygen support but not admitted to the intensive care unit, TCZ did not reduce WHO-CPS scores lower than 5 at day 4 but might have reduced the risk of NIV, MV, or death by day 14. No difference on day 28 mortality was found. Further studies are necessary for confirming these preliminary results.

			
Axfors C et al MedRXiv https://www.medrxiv.org/content/10.1101/2020.09.16.20194571v2	Mortality outcomes with hydroxychloroquine and chloroquine in COVID-19: an international collaborative meta-analysis of randomized trials	Metanalisi su 63 trial clinici riguardanti la terapia con idrossiclorochina e clorochina per COVID-19 : aumentata mortalità con idrossiclorochina, nessun beneficio con clorochina.	Substantial COVID-19 research investment has been allocated to randomized clinical trials (RCTs) on hydroxychloroquine/chloroquine, which currently face recruitment challenges or early discontinuation. We aimed to estimate the effects of hydroxychloroquine and chloroquine on survival in COVID-19 from all currently available RCT evidence, published and unpublished. We conducted a rapid meta-analysis of ongoing, completed, or discontinued RCTs on hydroxychloroquine or chloroquine treatment for any COVID-19 patients (protocol: https://osf.io/QESV4/). We systematically identified unpublished RCTs (ClinicalTrials.gov, WHO International Clinical Trials Registry Platform, Cochrane COVID-registry up to June 11, 2020), and published RCTs (PubMed, medRxiv and bioRxiv up to October 16, 2020). All-cause mortality was extracted (publications/preprints) or requested from investigators and combined in random-effects meta-analyses, calculating odds ratios (ORs) with 95% confidence intervals (CIs), separately for hydroxychloroquine and chloroquine.

			Prespecified subgroup analyses included patient setting, diagnostic confirmation, control type, and publication status. Sixty-three trials were potentially eligible. We included 14 unpublished trials (1308 patients) and 14 publications/preprints (9011 patients). Results for hydroxychloroquine are dominated by RECOVERY and WHO SOLIDARITY, two highly pragmatic trials, which employed relatively high doses and included 4716 and 1853 patients, respectively (67% of the total sample size). The combined OR on all-cause mortality for hydroxychloroquine was 1.11 (95% CI: 1.02, 1.20; I2=0%; 26 trials; 10,012 patients) and for chloroquine 1.77 (95%CI: 0.15, 21.13, I2=0%; 4 trials; 307 patients). We identified no subgroup effects. We found that treatment with hydroxychloroquine was associated with increased mortality in COVID-19 patients, and there was no benefit of chloroquine. Findings have unclear generalizability to outpatients, children, pregnant women, and people with comorbidities.
Burki TK The Lancet https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30508-7/fulltext	Double threat of COVID-19 and influenza	Il sovrapporsi della pandemia influenzale con quella da SARS-CoV-2 presenta una sfida per i sistemi sanitari dell'emisfero boreale.	At the time of publication, it looks like the second wave of COVID-19 is well underway in Europe. The weekly tally of new cases has been steadily rising for more than 2 months, but the past few weeks have seen accelerated transmission. Cases have also been trending upwards in the USA. Oct 14, 2020, saw the nation register the highest number of new cases of COVID-19 since Aug 7. In general, countries are much better prepared than they were when severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) first exploded onto the scene. But October also marks the beginning of the flu season in the northern hemisphere. If both viruses surge simultaneously, even the best resourced health-care systems would be hard pressed to cope.

Lei H et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1584/5932276	Different transmission dynamics of COVID-19 and influenza suggest the relative efficiency of isolation/quarantine and social distancing against COVID-19 in China.	Le misure di distanziamento sociale, pur riducendo significativamente la diffusione dell'infezione, potrebbero non essere sufficienti ad arginare la pandemia da COVID-19 in Cina.	BACKGROUND: Non-pharmaceutical interventions (NPIs) against Coronavirus Disease 2019 (COVID-19) are vital to reducing the transmission risks. However, the relative efficiency of social distancing against COVID-19 remains controversial, since social distancing and isolation/quarantine were implemented almost at the same time in China. METHODS: In this study, surveillance data of COVID-19 and seasonal influenza in the year 2018-2020 were used to quantify the relative efficiency of NPIs against COVID-19 in China, since isolation/quarantine was not used for the influenza epidemics. Given that the relative age-dependent susceptibility to influenza and COVID-19 may vary, an age-structured Susceptible-Infected-Recovered model was built to explore the efficiency of social distancing against COVID-19 under different population susceptibility scenarios. RESULTS: The mean effective reproductive number, Rt, of COVID-19 before NPIs was 2.12 (95% confidential interval (CI): 2.02-2.21). By March 11, 2020, the overall reduction in Rt of COVID-19 was 66.1% (95% CI: 60.1%-71.2%). In the epidemiological year 2019/20, influenza transmissibility reduced by 34.6% (95% CI: 31.3%-38.2%) compared with that in the epidemiological year 2018/19. Under the observed contact patterns changes in China, social distancing had similar efficiency against COVID-19 in three different scenarios. By assuming same efficiency of social distancing against seasonal influenza and COVID-19 transmission, isolation/quarantine and social distancing could lead to a 48.1% (95% CI: 35.4%-58.1%) and 34.6% (95% CI: 31.3%-38.2%) reduction of the transmissibility of COVID-19. CONCLUSIONS: Though isolation/quarantine is more effective than social distancing, given that typical basic reproductive number of COVID-19 is 2-3, isolation/quarantine alone could not contain the COVID-19 pandemic effectively in China.

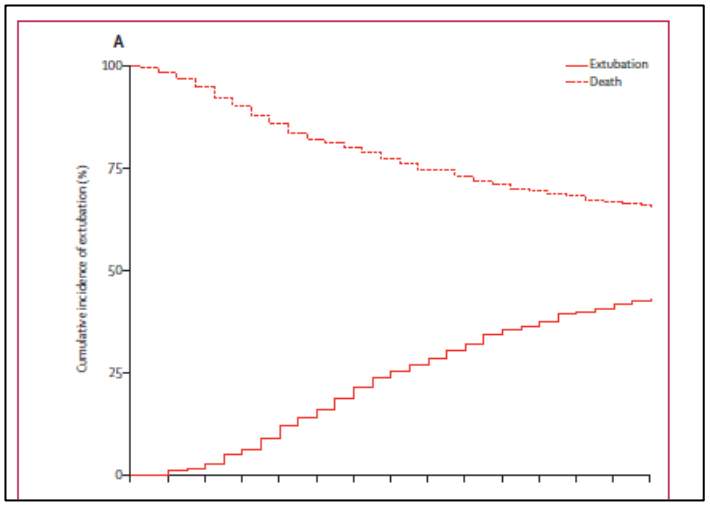
			Figure 4B 
Guzzetta G et al Emerging Infectious Diseases	Impact of a Nationwide Lockdown on SARS-CoV-2 Transmissibility, Italy.	Effetto a 14 giorni del lockdown imposto in Italia in Marzo 2020 sul numero di riproduzione (R0, Rt) dell'infezione da SARS-CoV-2.	On March 11, 2020, Italy imposed a national lockdown to curtail the spread of severe acute respiratory syndrome coronavirus 2. We estimate that, 14 days after lockdown, the net reproduction number had dropped below 1 and remained stable at >>0.76 (95% CI 0.67-0.85) in all regions for >3 of the following weeks.
Ucciferri C et al World Journal of Clinical Cases https://doi.org/10.12998/wjcc.v8.i19.4280	Role of monoclonal antibody drugs in the treatment of COVID-19.	Stato dell'arte sull'uso dei farmaci immunomodulatori, fra cui gli anticorpi monoclonali, nell'infezione da SARS-CoV-2.	Currently clinicians all around the world are experiencing a pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The clinical presentation of this pathology includes fever, dry cough, fatigue and acute respiratory distress syndrome that can lead to death infected patients. Current studies on coronavirus disease 2019 (COVID-19) continue to highlight the urgent need for an effective therapy. Numerous therapeutic strategies have been used until now but, to date, there is no specific effective treatment for SARS-CoV-2 infection. Elevated inflammatory cytokines have been reported in patients with COVID-19. Evidence suggests that elevated cytokine levels, reflecting a

			hyperinflammatory response secondary to SARS-CoV-2 infection, are responsible for multi-organ damage in patients with COVID-19. For these reason, numerous randomized clinical trials are currently underway to explore the effectiveness of biopharmaceutical drugs, such as, interleukin-1 blockers, interleukin-6 inhibitors, Janus kinase inhibitors, in COVID-19. The aim of the present paper is to briefly summarize the pathogenetic rationale and the state of the art of therapeutic strategy blocking hyperinflammation.
Wathelet M et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2772154	Factors Associated With Mental Health Disorders Among University Students in France Confined During the COVID-19 Pandemic	Esiti di un sondaggio su 69 054 studenti universitari francesi in merito alle loro condizioni di salute mentale durante il lockdown in aprile-maggio 2020 : necessità di misure di prevenzione dei disturbi mentali in vista di una nuova ondata pandemica.	IMPORTANCE The coronavirus disease 2019 (COVID-19) pandemic and quarantine measures have raised concerns regarding their psychological effects on populations. Among the general population, university students appear to be particularly susceptible to experiencing mental health problems. OBJECTIVES To measure the prevalence of self-reported mental health symptoms, to identify associated factors, and to assess care seeking among university students who experienced the COVID-19 quarantine in France. DESIGN, SETTING, AND PARTICIPANTS This survey study collected data from April 17 to May 4, 2020, from 69 054 students living in France during the COVID-19 quarantine. All French universities were asked to send an email to their students asking them to complete an online questionnaire. The targeted population was approximately 1 600 000 students. EXPOSURE Living in France during the COVID-19 quarantine. MAIN OUTCOMES AND MEASURES The rates of self-reported suicidal thoughts, severe distress, stress, anxiety, and depression were assessed using the 22-item Impact of Events Scale–Revised, the 10-item Perceived Stress Scale, the 20-item State-Trait Anxiety Inventory (State subscale), and the 13-item Beck Depression Inventory, respectively. Covariates were sociodemographic

			characteristics, precariousness indicators (ie, loss of income or poor quality housing), health-related data, information on the social environment, and media consumption. Data pertaining to care seeking were also collected. Multivariable logistic regression analyses were performed to identify risk factors. RESULTS A total of 69 054 students completed the survey (response rate, 4.3%). The median (interquartile range) age was 20 (18-22) years. The sample was mainly composed of women (50 251 [72.8%]) and first-year students (32 424 [47.0%]). The prevalence of suicidal thoughts, severe distress, high level of perceived stress, severe depression, and high level of anxiety were 11.4%(7891 students), 22.4%(15 463 students), 24.7%(17 093 students), 16.1%(11 133 students), and 27.5% (18 970 students), respectively, with 29 564 students (42.8%) reporting at least 1 outcome, among whom 3675 (12.4%) reported seeing a health professional. Among risk factors identified, reporting at least 1 mental health outcome was associated with female gender (odds ratio [OR], 2.10; 95%CI, 2.02-2.19; P < .001) or nonbinary gender (OR, 3.57; 95%CI, 2.99-4.27; P < .001), precariousness (loss of income: OR, 1.28; 95%CI, 1.22-1.33; P < .001; low-quality housing: OR, 2.30; 95%CI, 2.06-2.57; P < .001), history of psychiatric follow-up (OR, 3.28; 95%CI, 3.09-3.48; P < .001), symptoms compatible with COVID-19 (OR, 1.55; 95%CI, 1.49-1.61; P < .001), social isolation (weak sense of integration: OR, 3.63; 95%CI, 3.35-3.92; P < .001; low quality of social relations: OR, 2.62; 95%CI, 2.49-2.75; P < .001), and low quality of the information received (OR, 1.56; 95%CI, 1.49-1.64; P < .001) CONCLUSIONS AND RELEVANCE The results of this survey study suggest a high prevalence of mental health issues among students who experienced quarantine, underlining the need to reinforce

			prevention, surveillance, and access to care.
Elbaum L et al Current Problems in Cardiology https://www.sciencedirect.com/science/article/pii/S0146280620301924?via%3Dihub	Managing Patients With ST-Elevation Myocardial Infarction at the Epicenter of the COVID-19 Pandemic.	Casistica di 20 pazienti con STEMI trattati in un ospedale di New York in marzo-aprile 2020, di cui 12 positivi per infezione da SARS-CoV-2 : l'approccio invasivo è associato a migliore outcome indipendentemente dall'infezione, il che incoraggia una valutazione caso per caso e non standardizzata in base alla positività per SARS-CoV-2.	During the coronavirus disease 2019 (COVID-19) pandemic, strained acute care resources, the potential for rapid clinical decompensation, and concerns about staff safety has prompted a conservative management approach for acute coronary syndrome patients. We present our experience of COVID-19 patients at Elmhurst Hospital Center presenting with ST-Elevation Myocardial Infarction and compared outcomes of invasive vs conservative treatment strategies.
Aschwanden C Nature https://www.nature.com/articles/d41586-020-02948-4	The false promise of herd immunity for COVID-19	Critica all'idea che una diffusione incontrollata dell'infezione da SARS-CoV-2 possa risolvere il problema della pandemia e chiarimenti sul concetto di « immunità di gregge ».	Why proposals to largely let the virus run its course — embraced by Donald Trump's administration and others — could bring "untold death and suffering".
Aranda P et al Recent Patents on Nanotechnology	Nanotechnology research and patents on coronavirus and COVID-19: a review.	Applicazione della ricerca sulle nanotecnologie all'infezione da SARS-CoV-2.	Nanotechnology can alleviate the current challenges posed by the COVID-19 pandemic. Viral particles of coronaviruses including SARS-CoV-2 as well as other enveloped viruses like the Influenza virus could be considered as an approximation to functional core-shell nanoparticles and therefore, their study enters the realm of nanotechnology. Current research investigation and recent patents

https://www.eurekaselect.com/187084/article			dealing with aspects of immunogenic and non-immunogenic prophylaxis, detection and diagnosis as well as therapeutics and treatments are introduced and discussed in the present review.
Botta M et al The Lancet https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30459-8/fulltext	Ventilation management and clinical outcomes in invasively ventilated patients with COVID-19 (PRoVENT-COVID): a national, multicentre, observational cohort study	Studio retrospettivo multicentrico condotto nei Paesi Bassi su 553 pazienti sottoposti a ventilazione meccanica per COVID-19 : parametri di ventilazione e outcome.	Background : Little is known about the practice of ventilation management in patients with COVID-19. We aimed to describe the practice of ventilation management and to establish outcomes in invasively ventilated patients with COVID-19 in a single country during the first month of the outbreak. Methods : PRoVENT-COVID is a national, multicentre, retrospective observational study done at 18 intensive care units (ICUs) in the Netherlands. Consecutive patients aged at least 18 years were eligible for participation if they had received invasive ventilation for COVID-19 at a participating ICU during the first month of the national outbreak in the Netherlands. The primary outcome was a combination of ventilator variables and parameters over the first 4 calendar days of ventilation: tidal volume, positive end-expiratory pressure (PEEP), respiratory system compliance, and driving pressure. Secondary outcomes included the use of adjunctive treatments for refractory hypoxaemia and ICU complications. Patient-centred outcomes were ventilator-free days at day 28, duration of ventilation, duration of ICU and hospital stay, and mortality. PRoVENT-COVID is registered at ClinicalTrials.gov (NCT04346342). Findings : Between March 1 and April 1, 2020, 553 patients were included in the study. Median tidal volume was 6·3 mL/kg predicted bodyweight (IQR 5·7–7·1), PEEP was 14·0 cm H2O (IQR 11·0–15·0), and driving pressure was 14·0 cm H2O (11·2–16·0). Median respiratory system compliance was 31·9 mL/cm H2O (26·0–39·9). Of the adjunctive treatments for refractory hypoxaemia, prone

			positioning was most often used in the first 4 days of ventilation (283 [53%] of 530 patients). The median number of ventilator-free days at day 28 was 0 (IQR 0–15); 186 (35%) of 530 patients had died by day 28. Predictors of 28-day mortality were gender, age, tidal volume, respiratory system compliance, arterial pH, and heart rate on the first day of invasive ventilation. Interpretation : In patients with COVID-19 who were invasively ventilated during the first month of the outbreak in the Netherlands, lung-protective ventilation with low tidal volume and low driving pressure was broadly applied and prone positioning was often used. The applied PEEP varied widely, despite an invariably low respiratory system compliance. The findings of this national study provide a basis for new hypotheses and sample size calculations for future trials of invasive ventilation for COVID-19. These data could also help in the interpretation of findings from other studies of ventilation practice and outcomes in invasively ventilated patients with COVID-19. 

Von Kohorn I et al Journal of the Pediatric Infectious Diseases Society https://academic.oup.com/jpids/advance-article/doi/10.1093/jpids/piaa127/5934825	In Utero SARS-CoV-2 Infection	Caso di trasmissione materno-fetale in utero di SARS-CoV-2, con dimostrazione della presenza del virus su tampone nasofaringeo del neonato e sangue cordonale.	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is transmitted primarily via respiratory secretions. Evidence for in utero transmission is growing but not definitive. Reports to date describe detection of SARS-CoV-2 specific IgM in neonatal serum, nucleic acids in neonatal serum and stool, nucleic acids in neonatal nasopharyngeal (NP) secretions, and nucleic acids on placental surfaces and tissues.To our knowledge, no one has reported SARS-CoV-2 RNA in cord blood associated with neonatal infection. We present a case of neonatal infection with viral RNA in cord blood that supports in utero transmission of SARS-CoV-2 and provides insight into hematogenous spread from mother to fetus. This study was exempted by the Institutional Review Board at Holy Cross Hospital.
Gervasi SF et al BMJ - British Journal of Sports Medicine https://bjsm.bmj.com/content/early/2020/10/04/bjsports-2020-102789	Is extensive cardiopulmonary screening useful in athletes with previous asymptomatic or mild SARS-CoV-2 infection?	Studio di coorte su una squadra di giocatori di calcio professionisti, alcuni dei quali con storia di infezione lieve da SARS-CoV-2, al fine di identificare le indagini appropriate per la ripresa dell'attività agonistica dopo infezione da SARS-CoV-2 : secondo i risultati ottenuti, uno screening cardiologico e respiratorio estensivo non è necessario.	Objective During the COVID-19 pandemic, it is essential to understand if and how to screen SARS-CoV-2-positive athletes to safely resume training and competitions. The aim of this study is to understand which investigations are useful in a screening protocol aimed at protecting health but also avoiding inappropriate examinations. Methods We conducted a cohort study of a professional soccer team that is based on an extensive screening protocol for resuming training during the COVID-19 pandemic. It included personal history, antigen swabs, blood tests, spirometry, resting/stress-test ECG with oxygen saturation monitoring, echocardiogram, Holter and chest CT. We also compared the findings with prior data from the same subjects before infection and with data from SARS-CoV-2-negative players. Results None of the players had positive swab and/or anti-SARS-CoV-2 IgM class antibodies. Out of 30 players, 18 (60%) had IgG class antibodies. None had suffered severe SARS-CoV-2-related

			disease, 12 (66.7%) had complained of mild COVID-19-related symptoms and 6 (33.3%) were asymptomatic. None of the players we examined revealed significant cardiovascular abnormalities after clinical recovery. A mild reduction in spirometry parameters versus pre-COVID-19 values was observed in all athletes, but it was statistically significant ($p<0.05$) only in SARS-CoV-2-positive athletes. One SARS-CoV-2-positive player showed increased troponin I level, but extensive investigation did not show signs of myocardial damage. Conclusion In this small cohort of athletes with previous asymptomatic/mild SARS-CoV-2 infection, a comprehensive screening protocol including blood tests, spirometry, resting ECG, stress-test ECG with oxygen saturation monitoring and echocardiogram did not identify relevant anomalies. While larger studies are needed, extensive cardiorespiratory and haematological screening in athletes with asymptomatic/mild SARS-CoV-2 infection appears unnecessary.

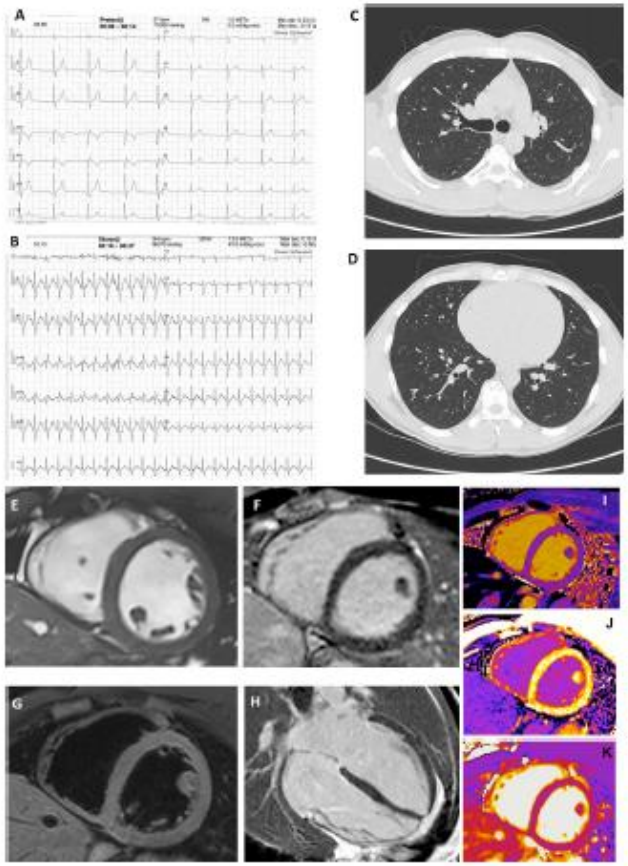
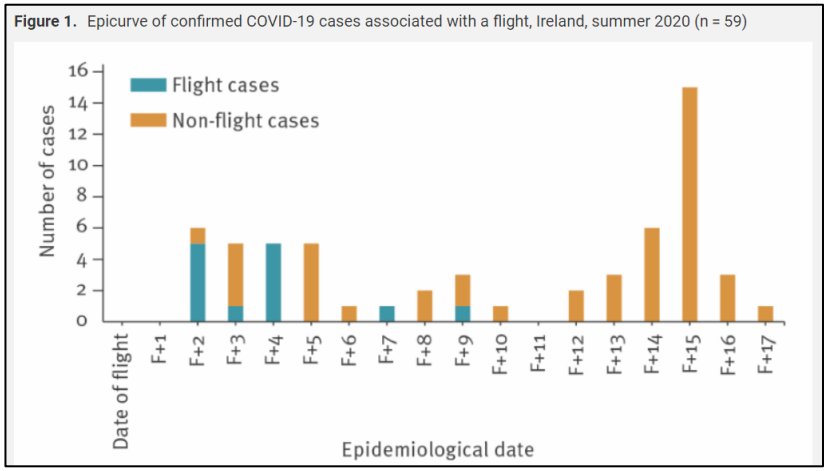


Figure 1 Instrumental findings in a player with increased troponin I level. In the only SARS-CoV-2-positive player (asymptomatic) with increased troponin I level, resting (A) and stress-test (B) ECG were normal. Chest CT at the level of the plane passing through the upper right lobar bronchus (C) and of the plane passing through lung bases (D) was absolutely normal. (E–M) Cardiac magnetic resonance images acquired using a 1.5 T Siemens Aera (Siemens Healthcare, Erlangen, Germany). (E) Short-axis cine balanced steady-state free precession showed normal left ventricle end-diastolic volume, wall thickness and motion. (F) Short-axis T2 image showed no oedema. (G, H) Short-axis and four-chamber views showed no alteration of late gadolinium enhancement. (I, J) Short-axis T1 native and T1 postcontrast maps showed normal values of T1 and extracellular volume. (K) T2 map showed no oedema.

Mallapaty S Nature https://www.nature.com/articles/d41586-020-02972-4	Why COVID outbreaks look set to worsen this winter	La possibilie stagionalità di SARS-CoV-2 non è accertata, tuttavia il cambiamento delle condizioni climatiche (basse temperature e minore umidità) e delle abitudini umane nei mesi invernali probabilmente favoriranno la sua diffusione.	Infections caused by many respiratory viruses, including influenza and some coronaviruses, swell in winter and drop in summer. Researchers say it's too early in the COVID-19 pandemic to say whether SARS-CoV-2 will become a seasonal virus. But growing evidence suggests that a small seasonal effect will probably contribute to bigger outbreaks in winter, on the basis of what is known about how the virus spreads and how people behave in colder months.
Murphy N et al EuroSurveillance https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.42.2001624	A large national outbreak of COVID-19 linked to air travel, Ireland, summer 2020.	Descrizione di 59 casi di infezione da SARS-CoV-2 riconducibili direttamente o indirettamente a un volo intercontinentale della durata di 7 ore atterrato in Irlanda l'estate scorsa.	An outbreak of 59 cases of coronavirus disease (COVID-19) originated with 13 cases linked by a 7h, 17% occupancy flight into Ireland, summer 2020. The flight-associated attack rate was 9.8-17.8%. Spread to 46 non-flight cases occurred country-wide. Asymptomatic/pre-symptomatic transmission in-flight from a point source is implicated by 99% homology across the virus genome in five cases travelling from three different continents. Restriction of movement on arrival and robust contact tracing can limit propagation post-flight. **Figure 1.** Epicurve of confirmed COVID-19 cases associated with a flight, Ireland, summer 2020 (n = 59) 

Pringle JC et al Morbidity and Mortality Weekly Report https://www.cdc.gov/mmwr/volumes/69/wr/mm6943e1.htm?s_cid=mm6943e1_w	COVID-19 in a Correctional Facility Employee Following Multiple Brief Exposures to Persons with COVID-19 — Vermont, July–August 2020.	Caso di infezione di una guardia carceraria negli USA la cui fonte ipotetica sarebbero i contatti ripetuti ma molto brevi con 6 detenuti - in seguito risultati positivi asintomatici – nel corso di una giornata. Tali contatti non soddisfano rigorosamente la definizione di « contatto stretto » (revisionati i filmati di ogni incontro), per cui inizialmente il soggetto non era stato posto in isolamento.	On August 11, 2020, a confirmed case of coronavirus disease 2019 (COVID-19) in a male correctional facility employee (correctional officer) aged 20 years was reported to the Vermont Department of Health (VDH). On July 28, the correctional officer had multiple brief encounters with six incarcerated or detained persons (IDPs)* while their SARS-CoV-2 test results were pending.
Agarwal A et al BMJ https://www.bmj.com/content/371/bmj.m3939	Convalescent plasma in the management of moderate covid-19 in adults in India: open label phase II multicentre randomised controlled trial (PLACID Trial)	Trial multicentrico di fase II condotto in India su 464 adulti ricoverati per COVID-19 di gravità moderata, trattati con plasma di soggetti guariti più standard of care oppure con le sole cure standard (che includono antivirali, steroidi, anti-IL6): non si dimostra alcun beneficio del plasma sulla progressione di malattia o sulla mortalità per ogni causa.	Objective To investigate the effectiveness of using convalescent plasma to treat moderate coronavirus disease 2019 (covid-19) in adults in India. Design Open label, parallel arm, phase II, multicentre, randomised controlled trial. Setting 39 public and private hospitals across India. Participants 464 adults (≥18 years) admitted to hospital (screened 22 April to 14 July 2020) with confirmed moderate covid-19 (partial pressure of oxygen in arterial blood/fraction of inspired oxygen (PaO2/FiO2) ratio between 200 mm Hg and 300 mm Hg or a respiratory rate of more than 24/min with oxygen saturation 93% or less on room air): 235 were assigned to convalescent plasma with best standard of care (intervention arm) and 229 to best standard of care only (control arm).

			Interventions Participants in the intervention arm received two doses of 200 mL convalescent plasma, transfused 24 hours apart. The presence and levels of neutralising antibodies were not measured a priori; stored samples were assayed at the end of the study. Main outcome measure Composite of progression to severe disease (PaO_2/FiO_2 <100 mm Hg) or all cause mortality at 28 days post-enrolment. Results Progression to severe disease or all cause mortality at 28 days after enrolment occurred in 44 (19%) participants in the intervention arm and 41 (18%) in the control arm (risk difference 0.008 (95% confidence interval −0.062 to 0.078); risk ratio 1.04, 95% confidence interval 0.71 to 1.54). Conclusion Convalescent plasma was not associated with a reduction in progression to severe covid-19 or all cause mortality. This trial has high generalisability and approximates convalescent plasma use in real life settings with limited laboratory capacity. A priori measurement of neutralising antibody titres in donors and participants might further clarify the role of convalescent plasma in the management of covid-19.

			Table 4 | Comparison of secondary outcomes between convalescent plasma therapy (intervention arm) and best standard of care (control arm) in per protocol analysis (n=451). Values are numbers (percentages) unless stated otherwise **Secondary outcomes** / **Intervention arm** / **Control arm** / **Unadjusted risk ratio (95% CI)** Resolution of symptoms on day 7: Shortness of breath (n=362) / 140/183 (76) / 119/181 (66) / 1.16 (1.02 to 1.32) Fever (n=138) / 66/67 (98) / 65/71 (92) / 1.08 (0.99 to 1.16) Cough (n=274) / 102/127 (80) / 111/147 (76) / 1.06 (0.94 to 1.2) Fatigue (n=306) / 114/156 (73) / 92/153 (60) / 1.21 (1.02 to 1.42) Negative conversion of SARS-CoV-2 RNA: Day 3 (n=367) / 79/184 (43) / 67/183 (37) / 1.2 (0.9 to 1.5) Day 7 (n=342) / 117/173 (68) / 93/169 (55) / 1.2 (1.04 to 1.5) Median (interquartile range) total hospital stay (days); No with event / 14 (10-19); n=227 / 13 (10-18); n=224 / 0.2* Median (interquartile range) total days of respiratory support; No with event / 9 (6-13); n=227 / 10 (6-13); n=224 / 0.7* Median (interquartile range) days of respiratory support post-enrolment; No with event / 6 (3-9); n=227 / 6 (4-10); n=224 / 0.5* Type of mechanical ventilation during hospital stay: Invasive / 19/227 (8) / 19/224 (8) / 0.99 (0.54 to 1.81) Non-invasive / 31/227 (14) / 37/224 (16) / 0.8 (0.5 to 1.3) Vasopressor support after enrolment / 10/225 (4) / 8/221 (4) / 1.2 (0.5 to 3.05) SARS-CoV-2=severe acute respiratory syndrome coronavirus 2; RNA=ribonucleic acid. *Continuous variables—Mann-Whitney U test applied and P values reported. All changes are measured from day of enrolment.
Baig AM et al The Journal of Medical Virology https://onlinelibrary.wiley.com/doi/10.1002/jmv.26624	Chronic COVID Syndrome: Need for an appropriate medical terminology for Long-COVID and COVID Long-Haulers.	La persistenza di disturbi dopo l'infezione acuta da SARS-CoV-2 merita una definizione rigorosa, ad esempio « Sindrome Cronica da COVID », piuttosto che nomi informali attualmente utilizzati in letteratura come « long-COVID ».	With the ongoing pandemic of coronavirus diseases (COVID-19) caused by SARS-CoV-2, there has been a surge in research and publications related to its pathogenesis and the clinical presentation of the affected patients. Many aspects of this novel virus have raised confusion including the naming of the virus and the disease it causes, the staging of its clinical presentation to highlight a few such occurrences. An emerging aspect of the clinical presentation related to COVID-19 is the long-term effects, which in the absence of any consensus has been termed as long-covid and long-haulers in recent publications. As the COVID-19 is a zoonotic infection and comes under a medically related disease, the term chronic covid syndrome (CCS) would be a more traditional way of symbolizing the so-called long-covid and long-haulers in COVID-19. Though the renaming of this chronic state of now well-recognized chronicity seen in COVID-19 would not affect its prognosis, this is much needed to recognize this entity with a more appropriate nomenclature as published work is making its way into databases like Google Scholar and PubMed.