RICERCA BIBLIOGRAFICA COVID 19

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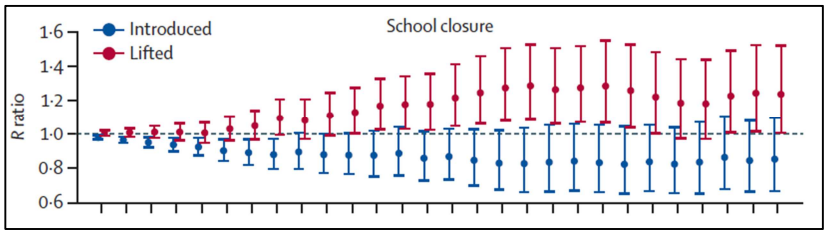
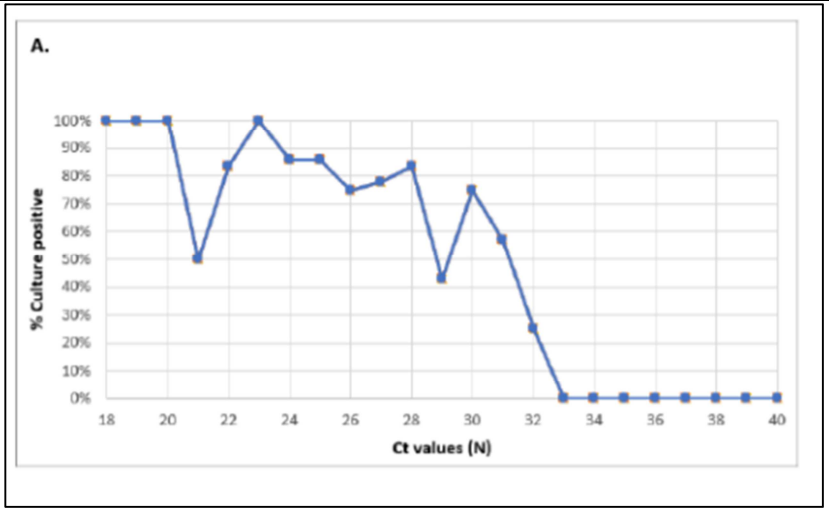
AUTORE/RIVISTA	TITOLO	OUTCOME PRINCIPALE	ABSTRACT
Li Y et al The Lancet https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30785-4/fulltext	The temporal association of introducing and lifting non-pharmaceutical interventions with the time-varying reproduction number (R) of SARS-CoV-2: a modelling study across 131 countries	Quantificazione dell'effetto dell'introduzione/sospensione di misure restrittive sulla diffusione di SARS-CoV-2 (in termini di numero di riproduzione Rt) in base ai dati di 131 Paesi.	Background Non-pharmaceutical interventions (NPIs) were implemented by many countries to reduce the transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causal agent of COVID-19. A resurgence in COVID-19 cases has been reported in some countries that lifted some of these NPIs. We aimed to understand the association of introducing and lifting NPIs with the level of transmission of SARS-CoV-2, as measured by the time-varying reproduction number (R), from a broad perspective across 131 countries. Methods In this modelling study, we linked data on daily country-level estimates of R from the London School of Hygiene & Tropical Medicine (London, UK) with data on country-specific policies on NPIs from the Oxford COVID-19 Government Response Tracker, available between Jan 1 and July 20, 2020. We defined a phase as a time period when all NPIs remained the same, and we divided the timeline of each country into individual phases based on the status

			of NPIs. We calculated the R ratio as the ratio between the daily R of each phase and the R from the last day of the previous phase (ie, before the NPI status changed) as a measure of the association between NPI status and transmission of SARS-CoV-2. We then modelled the R ratio using a log-linear regression with introduction and relaxation of each NPI as independent variables for each day of the first 28 days after the change in the corresponding NPI. In an ad-hoc analysis, we estimated the effect of reintroducing multiple NPIs with the greatest effects, and in the observed sequence, to tackle the possible resurgence of SARS-CoV-2. Findings 790 phases from 131 countries were included in the analysis. A decreasing trend over time in the R ratio was found following the introduction of school closure, workplace closure, public events ban, requirements to stay at home, and internal movement limits; the reduction in R ranged from 3% to 24% on day 28 following the introduction compared with the last day before introduction, although the reduction was significant only for public events ban (R ratio 0·76, 95% CI 0·58–1·00); for all other NPIs, the upper bound of the 95% CI was above 1. An increasing trend over time in the R ratio was found following the relaxation of school closure, bans on public events, bans on public gatherings of more than ten people, requirements to stay at home, and internal movement limits; the increase in R ranged from 11% to 25% on day 28 following the relaxation compared with the last day before relaxation, although the increase was significant only for school reopening (R ratio 1·24, 95% CI 1·00–1·52) and lifting bans on public gatherings of more than ten people (1·25, 1·03–1·51); for all other NPIs, the lower bound of the 95% CI was below 1. It took a median of 8 days (IQR 6–9) following the introduction of an NPI to observe 60% of the maximum reduction in R and even longer

			(17 days [14–20]) following relaxation to observe 60% of the maximum increase in R. In response to a possible resurgence of COVID-19, a control strategy of banning public events and public gatherings of more than ten people was estimated to reduce R, with an R ratio of 0·71 (95% CI 0·55–0·93) on day 28, decreasing to 0·62 (0·47–0·82) on day 28 if measures to close workplaces were added, 0·58 (0·41–0·81) if measures to close workplaces and internal movement restrictions were added, and 0·48 (0·32–0·71) if measures to close workplaces, internal movement restrictions, and requirements to stay at home were added. Interpretation Individual NPIs, including school closure, workplace closure, public events ban, ban on gatherings of more than ten people, requirements to stay at home, and internal movement limits, are associated with reduced transmission of SARS-CoV-2, but the effect of introducing and lifting these NPIs is delayed by 1–3 weeks, with this delay being longer when lifting NPIs. These findings provide additional evidence that can inform policy-maker decisions on the timing of introducing and lifting different NPIs, although R should be interpreted in the context of its known limitations. 
Chowdhury JF et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMclde2	Anticoagulation in Hospitalized Patients with Covid-19	Dilemma dell'anticoagulazione nei pazienti con infezione grave da SARS-CoV-2 : discussione delle opzioni disponibili.	We are in a time of unprecedented uncertainty. Clinicians may be faced with the temptation to choose intervention over caution when confronted with ill patients and limited data. We have, however, been trained to practice evidence-based medicine and must be wary of acting too quickly on new observations when the intervention may cause harm. We need more evidence to change

028217?query=featured_coronavirus			our practice.
Li M et al Science of the Total Environment https://www.sciencedirect.com/science/article/pii/S0048969720363397?via%3Dihub	Identifying novel factors associated with COVID-19 transmission and fatality using the machine learning approach.	Analisi di regressione logistica alla ricerca di fattori associati alla trasmissione e alla mortalità di COVID-19 sulla base dei dati di numerosi Paesi, spunti per comprendere meglio le dinamiche della pandemia.	The COVID-19 virus has infected more than 38 million people and resulted in more than one million deaths worldwide as of October 14, 2020. By using the logistic regression model, we identified novel critical factors associated with COVID19 cases, death, and case fatality rates in 154 countries and in the 50 U.S. states. Among numerous factors associated with COVID-19 risk, economic inequality enhanced the risk of COVID-19 transmission. The per capita hospital beds correlated negatively with COVID-19 deaths. Blood types B and AB were protective factors for COVID-19 risk, while blood type A was a risk factor. The prevalence of HIV and influenza and pneumonia was associated with reduced COVID-19 risk. Increased intake of vegetables, edible oil, protein, vitamin D, and vitamin K was associated with reduced COVID-19 risk, while increased intake of alcohol was associated with increased COVID-19 risk. Other factors included age, sex, temperature, humidity, social distancing, smoking, health investment, urbanization level, and race. High temperature is a more compelling factor mitigating COVID-19 transmission than low temperature. Our comprehensive identification of the factors affecting COVID-19 transmission and fatality may provide new insights into the COVID-19 pandemic and advise effective strategies for preventing and migrating COVID-19 spread.

Basile K et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1579/5937368	Cell-based culture of SARS-CoV-2 informs infectivity and safe de-isolation assessments during COVID-19.	Analisi dei campioni respiratori di 195 pazienti con infezione accertata da SARS-CoV-2 di variabile gravità : PCR alla diagnosi, coltura cellulare da campioni positivi con osservazione quotidiana di eventuale effetto citopatico, PCR di conferma e PCR al quarto giorno in assenza di effetto citopatico, per stabilire la associazione fra ciclo-soglia e positività colturale.	BACKGROUND: The detection of SARS-CoV-2 RNA by real-time polymerase chain reaction (PCR) in respiratory samples collected from persons recovered from COVID-19 does not necessarily indicate shedding of infective virions. By contrast, the isolation of SARS-CoV-2 using cell-based culture likely indicates infectivity, but there are limited data on the correlation between SARS-CoV-2 culture and PCR. METHODS: One hundred and ninety-five patients with varying severity of COVID-19 were tested (outpatients [n=178]), inpatients [n=12] and critically unwell patients admitted to the intensive care unit [ICU; n=5]). SARS-CoV-2 PCR positive samples were cultured in Vero C1008 cells and inspected daily for cytopathic effect (CPE). SARS-CoV-2-induced CPE was confirmed by PCR of culture supernatant. Where no CPE was observed, PCR was performed on day four to confirm absence of virus replication. Cycle threshold (Ct) of the day four PCR (Ctculture) and the PCR of the original clinical sample (Ctsample) were compared, and positive cultures were defined where Ctsample - Ctculture was >/=3. FINDINGS: Of 234 samples collected, 228 (97%) were from the upper respiratory tract. SARS-CoV-2 was only successfully isolated from samples with Ctsample </=32, including in 28/181 (15%), 19/42 (45%) and 9/11 samples (82%) collected from outpatients, inpatients, and ICU patients, respectively. The mean duration from symptom onset to culture positivity was 4.5 days (range 0-18). SARS-CoV-2 was significantly more likely to be isolated from samples collected from inpatients (p<0001) and ICU patients (p<00001) compared with outpatients respectively, and in samples with lower Ctsample. CONCLUSION: SARS-CoV-2 culture may be used as a surrogate marker for infectivity and inform de-isolation protocols.

			
Mazhar F et al International Journal of Infectious Diseases https://www.ijidonline.com/article/S1201-9712(20)32186-X/fulltext	Use of hydroxychloroquine and chloroquine in COVID-19: How good is the quality of randomized controlled trials?	Analisi di 16 trial clinici sull'utilizzo di clorochina e idrossiclorochina per COVID-19 in cui si conclude che la qualità degli studi condotti finora è subottimale.	Objectives : We critically evaluated the quality of evidence and quality of harm reporting in clinical trials that evaluated the effectiveness of hydroxychloroquine (HCQ) or chloroquine (CQ) for the treatment of coronavirus disease 2019 (COVID-19). Study design and setting : Scientific databases were systematically searched to identify relevant trials of HCQ/CQ for the treatment of COVID-19 published up to 10 September 2020. The Cochrane risk-of-bias tools for randomized trials and non-randomized trials of interventions were used to assess risk of bias in the included studies. A 10-item Consolidated Standards of Reporting Trials (CONSORT) harm extension was used to assess quality of harm reporting in the included trials. Results : Sixteen trials, including fourteen randomized trials and two non-randomized trials, met the inclusion criteria. The results from the included trials were conflicting and lacked effect estimates adjusted for baseline disease severity or comorbidities in many cases, and most of the trials recruited a fairly small cohort of

			patients. None of the clinical trials met the CONSORT criteria in full for reporting harm data in clinical trials. None of the 16 trials had an overall 'low' risk of bias, while four of the trials had a 'high', 'critical', or 'serious' risk of bias. Biases observed in these trials arise from the randomization process, potential deviation from intended interventions, outcome measurements, selective reporting, confounding, participant selection, and/or classification of interventions. Conclusion : In general, the quality of currently available evidence for the effectiveness of CQ/HCQ in patients with COVID-19 is suboptimal. The importance of a properly designed and reported clinical trial cannot be overemphasized amid the COVID-19 pandemic, and its dismissal could lead to poorer clinical and policy decisions, resulting in wastage of already stretched invaluable health care resources.
Shah P et al Critical Care Medicine https://journals.lww.com/ccmjournal/Abstract/9000/Is_Cardiopulmonary_Resuscitation_Futile_in.95450.aspx	Is Cardiopulmonary Resuscitation Futile in Coronavirus Disease 2019 Patients Experiencing In-Hospital Cardiac Arrest?	Studio retrospettivo che include 63 pazienti sottoposti a rianimazione caridopolmonare per arresto cardiocircolatorio avvenuto in corso di ricovero per COVID-19 : mortalità intraospedaliera 100% indipendentemente da comorbidità, gravità di malattia e setting di ricovero.	Objectives: There is limited data regarding outcomes after in-hospital cardiac arrest among coronavirus disease 2019 patients. None of the studies have reported the outcomes of in-hospital cardiac arrest in coronavirus disease 2019 patients in the United States. We describe the characteristics and outcomes of in-hospital cardiac arrest in coronavirus disease 2019 patients in rural Southwest Georgia. Design: Retrospective cohort study. Setting: Single-center, multihospital. PATIENTS: Consecutive coronavirus disease 2019 patients who experienced in-hospital cardiac arrest with attempted resuscitation. Interventions: Attempted resuscitation with advanced cardiac life support. Measurement and Main Results: Out of 1,094 patients hospitalized for coronavirus disease 2019 during the study period, 63 patients

			suffered from in-hospital cardiac arrest with attempted resuscitation and were included in this study. The median age was 66 years, and 49.2% were males. The majority of patients were African Americans (90.5%). The most common comorbidities were hypertension (88.9%), obesity (69.8%), diabetes (60.3%), and chronic kidney disease (33.3%). Eighteen patients (28.9%) had a Charlson Comorbidity Index of 0–2. The most common presenting symptoms were shortness of breath (63.5%), fever (52.4%), and cough (46%). The median duration of symptoms prior to admission was 14 days. During hospital course, 66.7% patients developed septic shock, and 84.1% had acute respiratory distress syndrome. Prior to in-hospital cardiac arrest, 81% were on ventilator, 60.3% were on vasopressors, and 39.7% were on dialysis. The majority of in-hospital cardiac arrest (84.1%) occurred in the ICU. Time to initiation of advanced cardiac life support protocol was less than 1 minute for all in-hospital cardiac arrest in the ICU and less than 2 minutes for the remaining patients. The most common initial rhythms were pulseless electrical activity (58.7%) and asystole (33.3%). Although return of spontaneous circulation was achieved in 29% patients, it was brief in all of them. The in-hospital mortality was 100%. Conclusions: In our study, coronavirus disease 2019 patients suffering from in-hospital cardiac arrest had 100% in-hospital mortality regardless of the baseline comorbidities, presenting illness severity, and location of arrest.
Zeng HL et al The FEBS Journal https://febs.onlinelibrary.	Proteomic characteristics of bronchoalveolar lavage fluid in critical COVID-19 patients.	Analisi proteomica su lavaggio broncoalveolare di 5 pazienti con infezione da SARS-CoV-2 a confronto con 4 non infetti che evidenzia la differente espressione di 41	Up to 10-20% of patients with Coronavirus Disease 2019 (COVID-19) develop a severe pulmonary disease due to immune dysfunction and cytokine dysregulation. However, the extracellular proteomic characteristics in respiratory tract of these critical COVID-19 still remains to be investigated. In the present study, we performed a

wiley.com/doi/10.1111/febs.15609		proteine coinvolte nella risposta infiammatoria e allo stress ossidativo.	quantitative proteomic analysis of the bronchoalveolar lavage fluid (BALF) from patients with critical COVID-19 and from non-COVID-19 controls. Our study identified 358 differentially expressed BALF proteins ($p < 0.05$), among which 41 were significantly changed after using the Benjamini-Hochberg correction ($q < 0.05$). The up-regulated signaling was found to be mainly involved in inflammatory signaling and response to oxidative stress. A series of increased extracellular factors including Tenascin-C (TNC), Mucin-1 (KL-6 or MUC1), Lipocalin-2 (LCN2), periostin (POSTN), Chitinase 3-like 1 (CHI3L1 or YKL40), S100A12, as well as the antigens including lymphocyte antigen 6D /E48 antigen (LY6D), CD9 antigen, CD177 antigen, prostate stem cell antigen (PSCA) were identified. Among which, the pro-inflammatory factor TNC and KL-6, that were further validated in serum of another thirty-nine COVID-19 patients and healthy controls, showing high potentials of being biomarkers or therapeutic candidates for COVID-19. This BALF proteome associated with COVID-19 would also be a valuable resource for researches on anti-inflammatory medication and understanding the molecular mechanisms of host response.
Hoffman C et al Infection https://link.springer.com/article/10.1007/s15010-020-01538-w	Older age groups and country-specific case fatality rates of COVID-19 in Europe, USA and Canada	Nei 20 Paesi analizzati in questo studio, la proporzione di anziani fra i casi di infezione da SARS-CoV-2 differisce significativamente e si dimostra una relazione lineare fra percentuale degli infetti di età superiore a 75 anni e mortalità dell'infezione.	Purpose : To evaluate the association between the percentages of older age groups among confirmed SARS-CoV-2 infections and the country-specific case fatality rate (CFR). Methods : This ecological study analyzed data from the 20 most severely affected European countries, USA and Canada, in which national health authorities provided data on age distribution and gender among confirmed SARS-CoV-2 cases and deaths. Results : The proportion of individuals older than 70 years among confirmed SARS-CoV-2 cases differed markedly between the countries, ranging from 4.9 to 40.4%. There was a strong linear association between the proportion of individuals older than 75

years and the country-specific CFRs (R2 = 0.803 for all countries, R2 = 0.961 after exclusion of three countries with incongruent data). Each 5% point increase of this older age group among confirmed SARS-CoV-2 cases was associated with an increase in CFR of 2.5% points (95% CI 1.9–3.1).

Conclusion : Data from 20 European countries and the USA and Canada showed that the variance of crude CFR of COVID-19 is predominantly (80–96%) determined by the proportion of older individuals who are diagnosed with SARS-CoV-2. The age distribution of SARS-CoV-2 infections is still far from being homogeneous. Detailed demographic data have to be taken into account in all the analyses on COVID-19-associated mortality. We urgently call for standardized data collection by national health authorities.

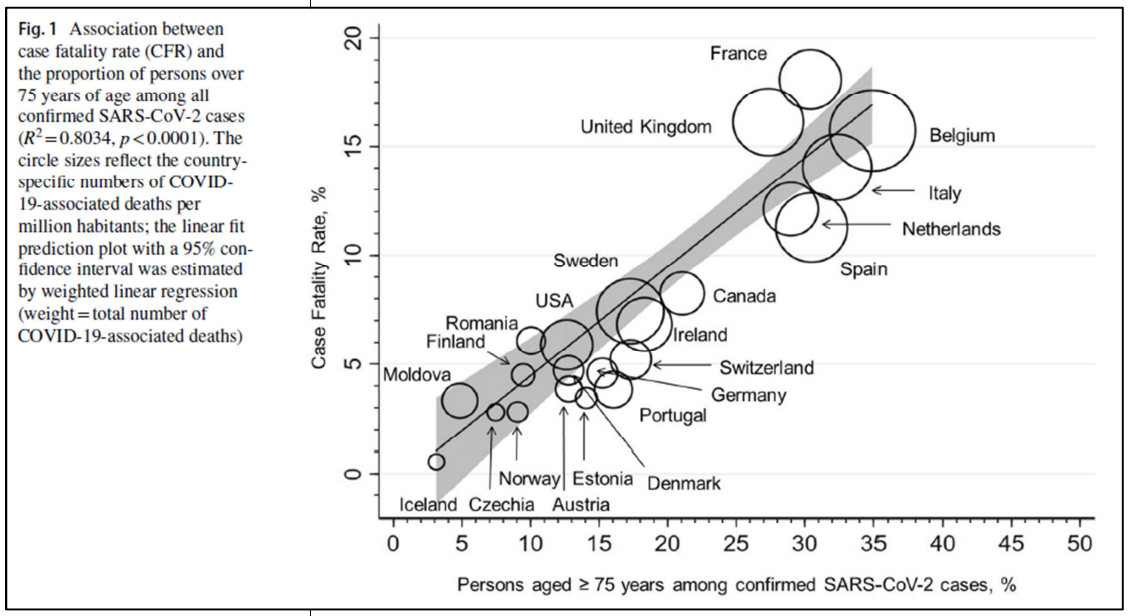
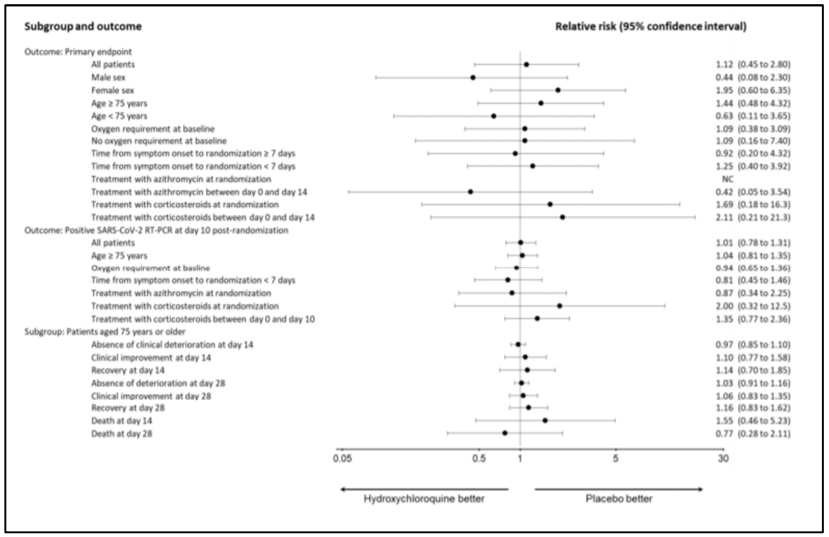
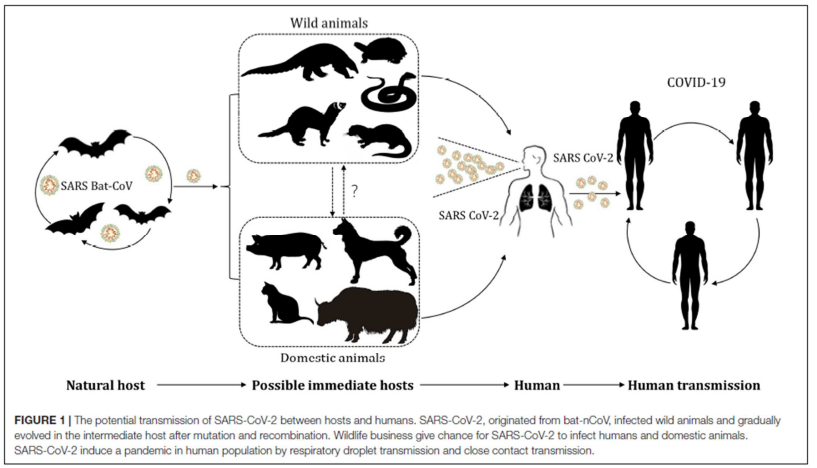


Fig. 1 Association between case fatality rate (CFR) and the proportion of persons over 75 years of age among all confirmed SARS-CoV-2 cases ($R^2 = 0.8034$, $p < 0.0001$). The circle sizes reflect the country-specific numbers of COVID-19-associated deaths per million habitants; the linear fit prediction plot with a 95% confidence interval was estimated by weighted linear regression (weight = total number of COVID-19-associated deaths)

Rafiei Y et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMp2028209?query=featured_coronavirus	The Missing Piece — SARS-CoV-2 Testing and School Reopening	Lo screening degli asintomatici per infezione da SARS-CoV-2 è la strategia necessaria, secondo gli Autori, per consentire una riapertura durevole delle scuole negli USA.	Disparities among communities in testing access and lag times exacerbate preexisting socioeconomic and racial inequities among schools. Schools that cannot quickly obtain test results are disproportionately forced to rely on extended quarantines. Given the distinctive difficulties students from low-income households face in distance learning, these disparities are particularly troubling. They also disproportionately burden children with special health needs, who may be at higher risk of Covid-19 infection and may depend on school-based services.
Dubée V et al MedRXiv https://www.medrxiv.org/content/10.1101/2020.10.19.20214940v1.full.pdf	A placebo-controlled double blind trial of hydroxychloroquine in mild-to-moderate COVID-19	Trial clinico multicentrico randomizzato, controllato con placebo, che valuta l'effetto di terapia con idrossiclorochina in pazienti con COVID-19 e fattori di rischio per gravità di malattia : nessuna differenza di outcome fra i due gruppi.	Background : The efficacy of hydroxychloroquine in coronavirus disease 2019 (COVID-19) remains controversial. Methods : We conducted a multicentre randomized double-blind placebo-controlled trial evaluating hydroxychloroquine in COVID-19 patients with at least one of the following risk factors for worsening: age ≥75 years, age between 60 and 74 years, and presence of at least one comorbidity, or need for supplemental oxygen (≤3 L/min). Eligible patients were randomized in a 1:1 ratio to receive either 800mg hydroxychloroquine on Day 0 followed by 400mg per day for 8 days or a placebo. The primary endpoint was a composite of death or tracheal intubation within 14 days following randomization. Secondary endpoints included mortality and clinical evolution at Day 14 and 28, viral shedding at Day 5 and 10. Results : The trial was stopped after 250 patients were included due to a slowdown of the pandemic in France. The intention-to-treat population comprised 123 and 124 patients in the placebo and hydroxychloroquine groups, respectively. The median age was 77 years and 151 patients required oxygen therapy. The primary endpoint occurred in nine patients in the hydroxychloroquine group and eight patients in the placebo group (relative risk 1.12; 95% confidence interval 0.45– 2.80; P=0.82). No difference was observed

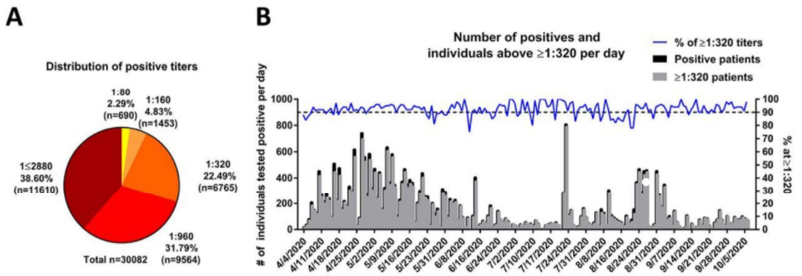
			between the two groups in any of the secondary endpoints. Conclusion : In this trial involving mainly older patients with mild-to-moderate COVID-19, patients treated with hydroxychloroquine did not experience better clinical or virological outcomes than those receiving the placebo. 
Zhao J et al Frontiers in Microbiology https://www.frontiersin.org/articles/10.3389/fmicb.2020.580137/full	The Potential Intermediate Hosts for SARS-CoV-2.	Revisione delle conoscenze sui possibili ospiti intermedi di SARS-CoV-2 che dal reservoir nel pipistrello conducono all'uomo.	The coronavirus disease 19 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become a global pandemic since the first report in Wuhan. COVID-19 is a zoonotic disease and the natural reservoir of SARS-CoV-2 seems to be bats. However, the intermediate host explaining the transmission and evolvement is still unclear. In addition to the wildlife which has access to contact with bats in the natural ecological environment and then infects humans in wildlife market, domestic animals are also able to establish themselves as the intermediate host after infected by SARS-CoV-2. Although recent studies related to SARS-CoV-2 have made a lot of progress, many

			critical issues are still unaddressed. Here, we reviewed findings regarding the investigations of the intermediate host, which may inspire future investigators and provide them with plenty of information. The results demonstrate the critical role of the intermediate host in the transmission chain of SARS-CoV-2, and the efficient intervention on this basis may be useful to prevent further deterioration of COVID-19.  **FIGURE 1 |** The potential transmission of SARS-CoV-2 between hosts and humans. SARS-CoV-2, originated from bat-nCoV, infected wild animals and gradually evolved in the intermediate host after mutation and recombination. Wildlife business give chance for SARS-CoV-2 to infect humans and domestic animals. SARS-CoV-2 induce a pandemic in human population by respiratory droplet transmission and close contact transmission.
Comber L et al Reviews in Medical Virology https://onlinelibrary.wiley.com/doi/10.1002/rmv.2184	Airborne transmission of SARS-CoV-2 via aerosols.	Revisione delle evidenze riguardo la trasmissione di SARS-CoV-2 tramite aerosol : ruolo indefinito nella propagazione dell'infezione.	A key consideration in the Covid-19 pandemic is the dominant modes of transmission of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus. The objective of this review was to synthesise the evidence for the potential airborne transmission of SARS-CoV-2 via aerosols. Systematic literature searches were conducted in PubMed, Embase, Europe PMC and National Health Service UK evidence up to 27 July 2020. A protocol was published and Cochrane guidance for rapid review methodology was adhered to throughout. Twenty-eight studies were identified. Seven out of eight epidemiological studies suggest aerosol transmission may occur, with enclosed environments and poor ventilation noted as possible contextual factors. Ten of the 16 air sampling studies

			detected SARS-CoV-2 ribonucleic acid; however, only three of these studies attempted to culture the virus with one being successful in a limited number of samples. Two of four virological studies using artificially generated aerosols indicated that SARS-CoV-2 is viable in aerosols. The results of this review indicate there is inconclusive evidence regarding the viability and infectivity of SARS-CoV-2 in aerosols. Epidemiological studies suggest possible transmission, with contextual factors noted. Viral particles have been detected in air sampling studies with some evidence of clinical infectivity, and virological studies indicate these particles may represent live virus, adding further plausibility. However, there is uncertainty as to the nature and impact of aerosol transmission of SARS-CoV-2, and its relative contribution to the Covid-19 pandemic compared with other modes of transmission.
Zawawi A et al Parasite Epidemiology and Control https://linkinghub.elsevier.com/retrieve/pii/S2405673120300568	The impact of COVID-19 pandemic on malaria elimination.	La pandemia da COVID-19 pone importanti sfide per i Paesi in cui è endemica la malaria, dalle difficoltà di diagnosi differenziale al consumo di farmaci antimalarici per il trattamento di SARS-CoV-2.	SARS-CoV-2 has spread throughout the world and become the cause of the infectious coronavirus disease 2019 (COVID-19). As low- and middle-income countries shift increasingly to focus on identifying and treating COVID-19, questions are emerging about the impact this shift in focus will have on ongoing efforts to control other infectious diseases, such as malaria. This review discusses how the spread of SARS-CoV-2 in low- and middle-income countries might impact these efforts, focusing in particular on the effects of co-infection and the use of antimalarial drugs used to treat malaria as therapeutic interventions for COVID-19.
Gmehlin C et al Infection Control and Hospital Epidemiology https://www.cambridge.o	COVID-19 in Long Term Care Facilities: A Review of Epidemiology, Clinical Presentations, and Containment Interventions.	Revisione della letteratura riguardante gli aspetti epidemiologici e clinici della diffusione di SARS-CoV-2 nelle strutture di lungodengenza.	Long-term care facilities (LTCFs) and their populations have been greatly affected by the coronavirus disease 2019 (COVID-19) pandemic. In this review, we summarize the literature to describe the current epidemiology of COVID-19 in LTCFs, clinical presentations and outcomes in the LTCF population with COVID-19, containment interventions, and the role of healthcare workers in

rg/core/journals/infection-control-and-hospital-epidemiology/article/covid19-in-long-term-care-facilities-a-review-of-epidemiology-clinical-presentations-and-containment-interventions/579A45D9A871F94897DB711F852CA7BA			SARS-CoV-2 transmission in these facilities.
Fang FC et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1654/5940148	COVID-19 - Lessons Learned and Questions Remaining.	Una sintetica elencazione delle conoscenze attuali sull'infezione da SARS-CoV-2 e degli aspetti controversi dopo circa 10 mesi di pandemia.	In this article, the editors of Clinical Infectious Diseases review some of the most important lessons they have learned about the epidemiology, clinical features, diagnosis, treatment and prevention of SARS-CoV-2 infection and identify essential questions about COVID-19 that remain to be answered.
Perrone F et al Journal of Translational Medicine https://translational-medicine.biomedcentral.com/articles/10.1186/s12967-020-02573-9	Tocilizumab for patients with COVID-19 pneumonia. The single-arm TOCIVID-19 prospective trial	Trial clinico multicentrico mono-braccio per valutare l'effetto di tocilizumab EV sulla mortalità da COVID-19 in pazienti ospedalizzati: riduzione della mortalità a 30 giorni rispetto all'ipotesi nulla (mortalità prevista del 15%).	Background : Tocilizumab blocks pro-inflammatory activity of interleukin-6 (IL-6), involved in pathogenesis of pneumonia the most frequent cause of death in COVID-19 patients. Methods : A multicenter, single-arm, hypothesis-driven trial was planned, according to a phase 2 design, to study the effect of tocilizumab on lethality rates at 14 and 30 days (co-primary endpoints, a priori expected rates being 20 and 35%, respectively). A further prospective cohort of patients, consecutively enrolled after the first cohort was accomplished, was used as a secondary validation dataset. The two cohorts were evaluated jointly in an

			exploratory multivariable logistic regression model to assess prognostic variables on survival. Results : In the primary intention-to-treat (ITT) phase 2 population, 180/301 (59.8%) subjects received tocilizumab, and 67 deaths were observed overall. Lethality rates were equal to 18.4% (97.5% CI: 13.6–24.0, P = 0.52) and 22.4% (97.5% CI: 17.2–28.3, P < 0.001) at 14 and 30 days, respectively. Lethality rates were lower in the validation dataset, that included 920 patients. No signal of specific drug toxicity was reported. In the exploratory multivariable logistic regression analysis, older age and lower PaO2/FiO2 ratio negatively affected survival, while the concurrent use of steroids was associated with greater survival. A statistically significant interaction was found between tocilizumab and respiratory support, suggesting that tocilizumab might be more effective in patients not requiring mechanical respiratory support at baseline. Conclusions : Tocilizumab reduced lethality rate at 30 days compared with null hypothesis, without significant toxicity. Possibly, this effect could be limited to patients not requiring mechanical respiratory support at baseline.
Wajnberg A et al Science https://science.sciencemag.org/content/early/2020/10/27/science.abd7728	Robust neutralizing antibodies to SARS-CoV-2 infection persist for months	La maggior parte degli individui con storia di infezione lieve-moderata da SARS-CoV-2 ha una risposta anticorpale significativa contro la proteina S che dura almeno 5 mesi.	SARS-CoV-2 has caused a global pandemic with millions infected and numerous fatalities. Questions regarding the robustness, functionality, and longevity of the antibody response to the virus remain unanswered. Here we report that the vast majority of infected individuals with mild-to-moderate COVID-19 experience robust IgG antibody responses against the viral spike protein, based on a dataset of 30,082 individuals screened at Mount Sinai Health System in New York City. We also show that titers are relatively stable for at least a period approximating 5 months and that anti-spike binding titers significantly correlate with neutralization of authentic SARS-CoV-2. Our data suggests that more than 90% of

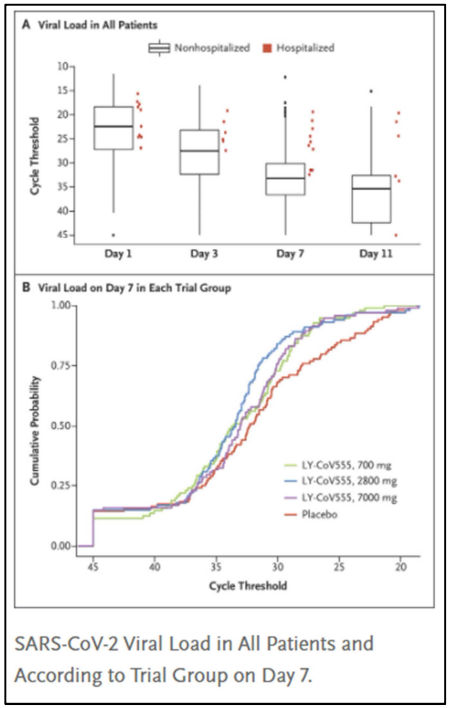
			seroconverters make detectible neutralizing antibody responses. These titers remain relatively stable for several months after infection. 
Gurumurthy C et al Nature Protocols https://www.nature.com/articles/s41596-020-00403-2	Genetically modified mouse models to help fight COVID-19.	Il topo, utile modello preclinico per lo studio di SARS-CoV-2, è naturalmente resistente all'infezione e deve essere modificato geneticamente per esprimere il recettore ACE2, con i metodi proposti in questo lavoro.	The research community is in a race to understand the molecular mechanisms of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, to repurpose currently available antiviral drugs and to develop new therapies and vaccines against coronavirus disease 2019 (COVID-19). One major challenge in achieving these goals is the paucity of suitable preclinical animal models. Mice constitute ~70% of all the laboratory animal species used in biomedical research. Unfortunately, SARS-CoV-2 infects mice only if they have been genetically modified to express human ACE2. The inherent resistance of wild-type mice to SARS-CoV-2, combined with a wealth of genetic tools that are available only for modifying mice, offers a unique opportunity to create a versatile set of genetically engineered mouse models useful for COVID-19 research. We propose three broad categories of these models and more than two dozen designs that may be useful for SARS-CoV-2 research and for fighting COVID-19.
Lundstrom K et al Viruses	Viewpoint: Origin of SARS-CoV-2.	L'origine di SARS-CoV-2 viene fatta risalire al virus del pipistrello CoV RaTG13, con il quale tuttavia	The origin of the severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) virus causing the COVID-19 pandemic has not yet been fully determined. Despite the consensus about the SARS-CoV-2 origin from bat CoV RaTG13, discrepancy to host tropism to other

https://www.mdpi.com/1999-4915/12/11/1203		sussistono differenze che potrebbero essersi prodotte tanto nell'animale che dopo il passaggio nell'uomo.	human Coronaviruses exist. SARS-CoV-2 also possesses some differences in its S protein receptor-binding domain, glycan-binding N-terminal domain and the surface of the sialic acid-binding domain. Despite similarities based on cryo-EM and biochemical studies, the SARS-CoV-2 shows higher stability and binding affinity to the ACE2 receptor. The SARS-CoV-2 does not appear to present a mutational "hot spot" as only the D614G mutation has been identified from clinical isolates. As laboratory manipulation is highly unlikely for the origin of SARS-CoV-2, the current possibilities comprise either natural selection in animal host before zoonotic transfer or natural selection in humans following zoonotic transfer. In the former case, despite SARS-CoV-2 and bat RaTG13 showing 96% identity some pangolin Coronaviruses exhibit very high similarity to particularly the receptor-binding domain of SARS-CoV-2. In the latter case, it can be hypothesized that the SARS-CoV-2 genome has adapted during human-to-human transmission and based on available data, the isolated SARS-CoV-2 genomes derive from a common origin. Before the origin of SARS-CoV-2 can be confirmed additional research is required.
Lerner AM et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2772459	Preventing the Spread of SARS-CoV-2 With Masks and Other "Low-tech" Interventions	In attesa di un vaccino efficace, disamina delle misure preventive utili contro la diffusione di SARS-Cov-2.	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the cause of coronavirus disease 2019 (COVID-19), has caused a global pandemic of historic proportions in the 10 months since cases were first reported in Wuhan, China, in December 2019, with worldwide morbidity, mortality, and disruptions to society. Ultimately, a safe and effective vaccine will be essential to control the pandemic and allow resumption of the many activities of normal life. While results of phase 3 trials for multiple candidate vaccines are on the near horizon, "low-tech" tools to prevent the spread of SARS-CoV-2 are essential, and it must be emphasized that these interventions will still be needed after a vaccine is initially

			available. Even if one or more vaccines have high efficacy and uptake in the population, it will take at least several months for enough people to be vaccinated to confer herd immunity on a population basis.
Luo X et al Scandinavian Journal of Iimmunology https://onlinelibrary.wiley.com/doi/10.1111/sji.12989	T-cell immunobiology and cytokine storm of COVID-19.	I livelli di linfociti T e di citochine in corso di infezione da SARS-CoV-2 sono associati alla gravità di malattia.	2019 coronavirus disease (COVID-19) presents as a newly recognized pneumonia and could rapidly progress into acute respiratory distress syndrome which has brought about a global pandemic. Until now, no curative therapy has been strongly recommended for COVID-19 except for personalized supportive care. T cells and virus-specific T cells are essential to protect against virus infection, including COVID-19. Delayed immune reconstitution (IR) and cytokine storm (CS) remain serious obstacles for the cure of COVID-19. Most COVID-19 patients, especially among elderly patients, had marked lymphopenia and increased neutrophils, but T cell counts in severe COVID-19 patients surviving the disease gradually restored later. Elevated pro-inflammatory cytokines, particularly IL-6, IL-10, IL-2, and IL-17, and exhausted T cells are found in peripheral blood and the lungs. It suggests that Thymosin alpha1 and adoptive COVID-19-specific T cells could improve IR while convalescent plasma, IL-6 blockade, mesenchymal stem cells, and corticosteroids could suppress CS. More clinical studies in this field worldwide are urgently warranted to pave the way for therapy of COVID-19 in the future.
Juan Y et al Nature Communications https://www.nature.com/articles/s41467-020-19238-2	Disease burden and clinical severity of the first pandemic wave of COVID-19 in Wuhan, China.	Stima dell'effetto della « prima ondata » di infezione da SARS-CoV-2 A Wuhan, al fine di fornire una guida per il futuro.	The novel coronavirus disease 2019 (COVID-19) was first reported in Wuhan, China, where the initial wave of intense community transmissions was cut short by interventions. Using multiple data sources, here we estimate the disease burden and clinical severity by age of COVID-19 in Wuhan from December 1, 2019 to March 31, 2020. Our estimates account for the sensitivity of the laboratory assays, prospective community screenings, and healthcare seeking

			behaviors. Rates of symptomatic cases, medical consultations, hospitalizations and deaths were estimated at 796 (95% CI: 703-977), 489 (472-509), 370 (358-384), and 36.2 (35.0-37.3) per 100,000 persons, respectively. The COVID-19 outbreak in Wuhan had a higher burden than the 2009 influenza pandemic or seasonal influenza in terms of hospitalization and mortality rates, and clinical severity was similar to that of the 1918 influenza pandemic. Our comparison puts the COVID-19 pandemic into context and could be helpful to guide intervention strategies and preparedness for the potential resurgence of COVID-19.
Chivukula RR et al Journal of Intensive Care Medicine https://journals.sagepub.com/doi/10.1177/0885066620969132	Evidence-Based Management of the Critically Ill Adult With SARS-CoV-2 Infection.	I pazienti con infezione grave da SARS-CoV-2 hanno molte caratteristiche in comune con la classica ARDS : disamina delle principali evidenze al riguardo.	Human infection by the novel viral pathogen SARS-CoV-2 results in a clinical syndrome termed Coronavirus Disease 2019 (COVID-19). Although the majority of COVID-19 cases are self-limiting, a substantial minority of patients develop disease severe enough to require intensive care. Features of critical illness associated with COVID-19 include hypoxemic respiratory failure, acute respiratory distress syndrome (ARDS), shock, and multiple organ dysfunction syndrome (MODS). In most (but not all) respects critically ill patients with COVID-19 resemble critically ill patients with ARDS due to other causes and are optimally managed with standard, evidence-based critical care protocols. However, there is naturally an intense interest in developing specific therapies for severe COVID-19. Here we synthesize the rapidly expanding literature around the pathophysiology, clinical presentation, and management of COVID-19 with a focus on those points most relevant for intensivists tasked with caring for these patients. We specifically highlight evidence-based approaches that we believe should guide the identification, triage, respiratory support, and general ICU care of critically ill patients infected with SARS-CoV-2. In addition, in light of the pressing need and growing enthusiasm for targeted COVID-19

			therapies, we review the biological basis, plausibility, and clinical evidence underlying these novel treatment approaches.
Chen P et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2029849?query-featured_coronavirus=	SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19	Trial clinico di fase 2 su pazienti con recente diagnosi di infezione da SARS-CoV-2 trattati con anticorpo neutralizzante LY-CoV555 contro placebo : per i trattati con la dose maggiore, riduzione della carica virale su tampone nasofaringeo, risultato di incerto significato clinico.	BACKGROUND : Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease 2019 (Covid-19), which is most frequently mild yet can be severe and life-threatening. Virus-neutralizing monoclonal antibodies are predicted to reduce viral load, ameliorate symptoms, and prevent hospitalization. METHODS In this ongoing phase 2 trial involving outpatients with recently diagnosed mild or moderate Covid-19, we randomly assigned 452 patients to receive a single intravenous infusion of neutralizing antibody LY-CoV555 in one of three doses (700 mg, 2800 mg, or 7000 mg) or placebo and evaluated the quantitative virologic end points and clinical outcomes. The primary outcome was the change from baseline in the viral load at day 11. The results of a preplanned interim analysis as of September 5, 2020, are reported here. RESULTS : At the time of the interim analysis, the observed mean decrease from baseline in the log viral load for the entire population was −3.81, for an elimination of more than 99.97% of viral RNA. For patients who received the 2800-mg dose of LY-CoV555, the difference from placebo in the decrease from baseline was −0.53 (95% confidence interval [CI], −0.98 to −0.08; P=0.02), for a viral load that was lower by a factor of 3.4. Smaller differences from placebo in the change from baseline were observed among the patients who received the 700-mg dose (−0.20; 95% CI, −0.66 to 0.25; P=0.38) or the 7000-mg dose (0.09; 95% CI, −0.37 to 0.55; P=0.70). On days 2 to 6, the patients who received LY-CoV555 had a slightly lower severity of symptoms than those who received

			placebo. The percentage of patients who had a Covid-19–related hospitalization or visit to an emergency department was 1.6% in the LY-CoV555 group and 6.3% in the placebo group. CONCLUSIONS : In this interim analysis of a phase 2 trial, one of three doses of neutralizing antibody LY-CoV555 appeared to accelerate the natural decline in viral load over time, whereas the other doses had not by day 11.  SARS-CoV-2 Viral Load in All Patients and According to Trial Group on Day 7.
Chan NC et al JAMA https://jamanetwork.com/journals/jama/fullarticle/	Peripheral Oxygen Saturation in Older Persons Wearing Nonmedical Face Masks in Community Settings	La mascherina chirurgica non provoca desaturazione in questa piccola coorte di 25 pazienti anziani.	Based on the evidence that nonmedical face masks prevent the spread of severe acute respiratory syndrome coronavirus many governments are mandating the wearing of masks in the community. However, fueled partly by claims on social media that masks can cause hypoxia and are therefore dangerous, concerns have emerged about the safety of wearing face masks. We

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<td>examined whether wearing nonmedical face masks was associated with a change in oxygen saturation.

Table 2. Oxygen Saturation Before, While, and After Wearing Nonmedical Face Masks

<table>
<tr><th></th><th>Spo_2 mean (SD), %</th></tr>
<tr><td>No. of participants</td><td>25</td></tr>
<tr><td>Before mask wearing, Spo_2 reading</td><td></td></tr>
<tr><td>1</td><td>96.1 (1.3)</td></tr>
<tr><td>2</td><td>95.8 (2.1)</td></tr>
<tr><td>3</td><td>96.3 (1.6)</td></tr>
<tr><td>Pooled mean Spo_2, % (95% CI)[a]</td><td>96.1 (95.5-96.7)</td></tr>
<tr><td>While mask wearing, Spo_2 reading</td><td></td></tr>
<tr><td>1</td><td>96.4 (1.2)</td></tr>
<tr><td>2</td><td>96.5 (1.3)</td></tr>
<tr><td>3</td><td>96.7 (1.1)</td></tr>
<tr><td>Pooled mean Spo_2, % (95% CI)[a]</td><td>96.5 (96.1-97.0)</td></tr>
<tr><td>After mask wearing, Spo_2 reading</td><td></td></tr>
<tr><td>1</td><td>96.4 (1.3)</td></tr>
<tr><td>2</td><td>96.4 (1.4)</td></tr>
<tr><td>3</td><td>96.2 (1.4)</td></tr>
<tr><td>Pooled mean Spo_2, % (95% CI)[a]</td><td>96.3 (95.8-96.8)</td></tr>
</table>
Abbreviation: Spo_2, oxygen saturation measured using a portable oximeter.
[a] 95% CIs are 2-sided.</td>
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<td>Mueller AA et al

Cell

https://www.cell.com/cell-reports-</td>
<td>Inflammatory biomarker trends predict respiratory decline in COVID-19 patients</td>
<td>Studio di coorte retrospettivo in cui si dimostra una associazione fra il trend crescente del valore di proteina C reattiva durante le prime 48 ore di</td>
<td>In this single-center retrospective cohort analysis of hospitalized COVID-19 patients, we investigate whether inflammatory biomarker levels predict respiratory decline in patients who initially present with stable disease. Examination of C-reactive protein (CRP) trends reveals that a rapid rise in CRP levels precedes respiratory deterioration and intubation, while CRP levels plateau in patients</td>
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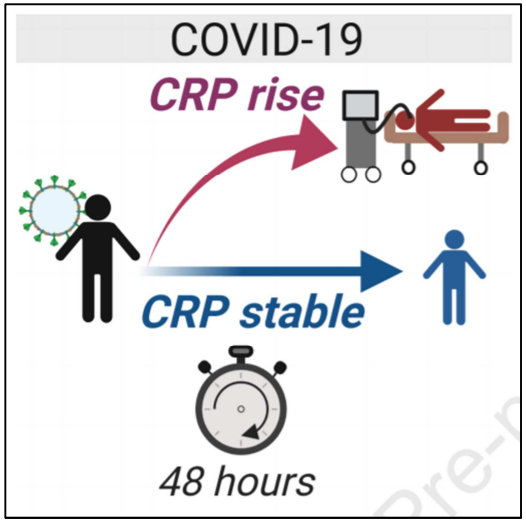
medicine/pdf/S2666-3791(20)30188-9.pdf?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS2666379120301889%3Fshowall%3Dtrue		ospedalizzazione e il peggioramento clinico nei pazienti ricoverati per COVID-19.	that remain stable. Increasing CRP during the first 48 hours of hospitalization is a better predictor (with higher sensitivity) of respiratory decline than initial CRP levels or ROX indices (a physiological score). CRP, the pro-inflammatory cytokine IL-6 and physiological measures of hypoxemic respiratory failure are correlated, which suggests a mechanistic link. Our work shows that rising CRP predicts subsequent respiratory deterioration in COVID-19 and may suggest mechanistic insights and a potential role for targeted immunomodulation in a subset of patients early during hospitalization. 
Petersen I et al Clinical Epidemiology https://doi.org/10.2147/CLEP.S276825	Three Quarters of People with SARS-CoV-2 Infection are Asymptomatic: Analysis of English Household Survey Data.	Stima di sensibilità, specificità, valore predittivo positivo e negativo dei sintomi (febbre, tosse e perdita di gusto/olfatto) rispetto all'infezione da SARS-CoV-2 : tre quarti dei positivi sono asintomatici.	Background: To reduce transmission of SARS-CoV-2, it is important to identify those who are infectious. However, little is known about what proportion of infectious people are asymptomatic and potential "silent" transmitters. We evaluated the value of COVID-19 symptoms as a marker for SARS-CoV-2 infection from a representative English survey. Methods: We used data from the Office for National Statistics Coronavirus (COVID-19) Infection Survey pilot study. We estimated sensitivity, specificity, the

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<td>proportion of asymptomatic cases (1 - sensitivity), positive predictive value (PPV) and negative predictive value (NPV) of COVID-19 symptoms as a marker of infection using results of the SARS-CoV-2 test as the "gold standard". Results: In total, there were 36,061 individuals with a SARS-CoV-2 test between 26 April and 27 June 2020. Of these, 625 (1.7%) reported symptoms on the day of the test. There were 115 (0.32%) with a positive SARS-CoV-2 test result. Of the 115, there were 27 (23.5%) who were symptomatic and 88 (76.5%) who were asymptomatic on the day of the test. Focusing on those with specific symptoms (cough, and/or fever, and/or loss of taste/smell), there were 158 (0.43%) with such symptoms on the day of the test. Of the 115 with a positive SARS-CoV-2, there were 16 (13.9%) reporting symptoms. In contrast, 99 (86.1%) did not report specific symptoms on the day of the test. The PPV for all symptoms was 4.3% and for the specific symptoms 10.1%. The specificity and NPV of symptoms were above 98%. Conclusion: COVID-19 symptoms are poor markers of SARS-CoV-2. Thus, 76.5% of this random sample who tested positive reported no symptoms, and 86.1% reported none of those specific to COVID-19. A more widespread testing programme is necessary to capture "silent" transmission and potentially prevent and reduce future outbreaks.
<table>
<tr><th></th><th colspan="2">Estimates (95% Confidence Intervals)</th></tr>
<tr><th></th><th>All Symptoms</th><th>Specific Symptoms</th></tr>
<tr><td>Sensitivity</td><td>23.5% (16.1% to 32.3%)</td><td>13.9% (8.2% to 21.6%)</td></tr>
<tr><td>Asymptomatic on the day of the test (1-sensitivity)</td><td>76.5% (67.7% to 83.9%)</td><td>86.1% (78.4% to 91.8%)</td></tr>
<tr><td>Specificity</td><td>98.3% (98.2% to 98.5%)</td><td>99.6% (99.5% to 99.7%)</td></tr>
<tr><td>Positive Predictive Values (PPV)</td><td>4.3% (2.9% to 6.2%).</td><td>10.1% (5.9% to 15.9%)</td></tr>
<tr><td>Negative Predictive Values (NPV)</td><td>99.8% (99.7% to 99.8%)</td><td>99.7% (99.7% to 99.8%)</td></tr>
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<td>Fajnzylber J et al

JAMA</td>
<td>SARS-CoV-2 viral load is associated with increased disease severity and mortality</td>
<td>La carica di SARS-CoV-2, in particolare la viremia, è associata alla gravità di malattia in questo studio su</td>
<td>The relationship between SARS-CoV-2 viral load and risk of disease progression remains largely undefined in coronavirus disease 2019 (COVID-19). Here, we quantify SARS-CoV-2 viral load from participants with a diverse range of COVID-19 disease severity,</td>
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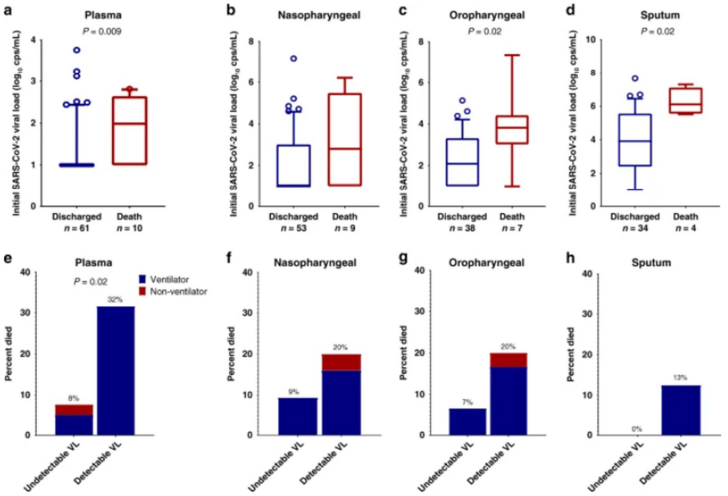
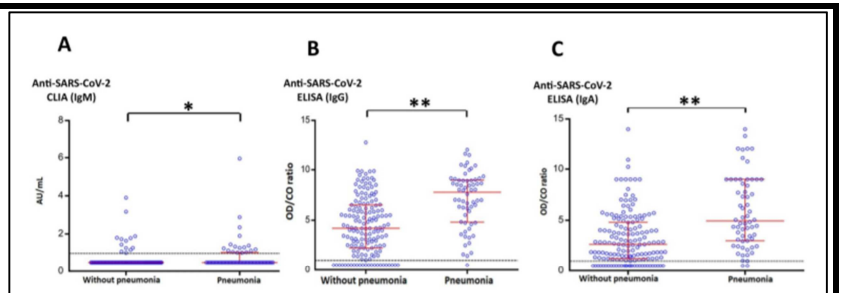
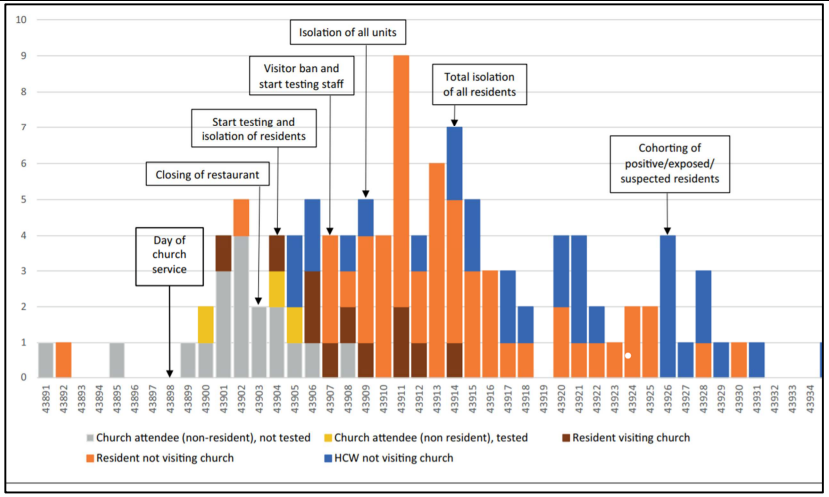
https://www.nature.com/articles/s41467-020-19057-5		235 pazienti fra ospedalizzati per COVID-19, gestiti a domicilio e asintomatici.	including those requiring hospitalization, outpatients with mild disease, and individuals with resolved infection. We detected SARS-CoV-2 plasma RNA in 27% of hospitalized participants, and 13% of outpatients diagnosed with COVID-19. Amongst the participants hospitalized with COVID-19, we report that a higher prevalence of detectable SARS-CoV-2 plasma viral load is associated with worse respiratory disease severity, lower absolute lymphocyte counts, and increased markers of inflammation, including C-reactive protein and IL-6. SARS-CoV-2 viral loads, especially plasma viremia, are associated with increased risk of mortality. Our data show that SARS-CoV-2 viral loads may aid in the risk stratification of patients with COVID-19, and therefore its role in disease pathogenesis should be further explored. **Fig. 3: SARS-CoV-2 viral load and risk of death.**  **a–d** Participants who died had higher initial viral loads compared to those who survived to discharge. The center line depicts the median value, the whiskers depict the 10–90 percentile. *P* values are from a two-tailed Wilcoxon rank sum test. **e–h** Percent of participants who eventually died categorized by detectable viral load and disease severity at the time of initial sampling. VL viral load, cps copies. *P* values are from a two-tailed Fishers exact test.

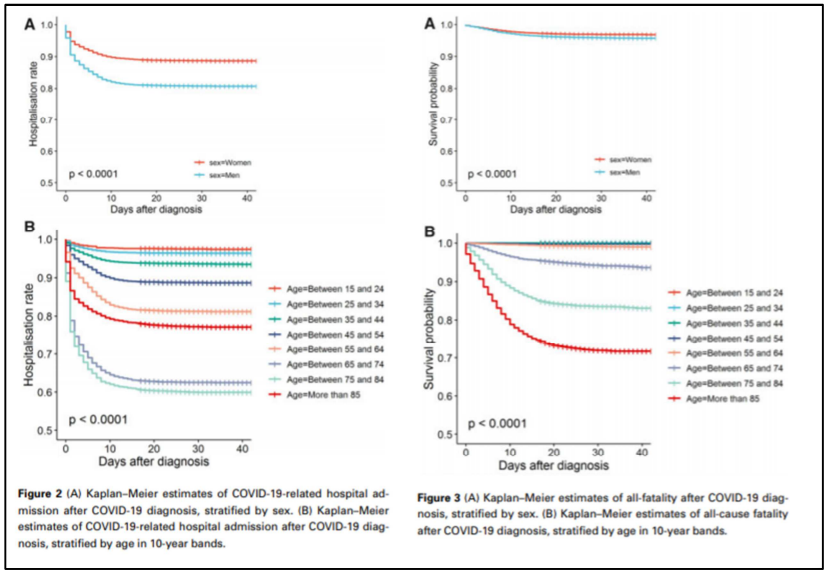
Chirathaworn C et al PLoS One https://doi.org/10.1371/journal.pone.0236905	SARS-CoV-2 RNA shedding in recovered COVID-19 cases and the presence of antibodies against SARS-CoV-2 in recovered COVID-19 cases and close contacts, Thailand, April-June 2020.	Studio sulla storia naturale di infezione da SARS-CoV-2 : di 217 pazienti guariti da COVID-19 in Thailandia il 6.6% rimane positivo per SARS-CoV-2 al tampone nasofaringeo fino a un massimo di 105 giorni e 88.5% ha IgG anti-SARS-CoV-2 nelle 4-12 settimane dall'esordio.	Coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Although Thailand has been fairly effective at controlling the spread of COVID-19, continued disease surveillance and information on antibody response in recovered patients and their close contacts remain necessary in the absence of approved vaccines and antivirals. Here, we examined 217 recovered COVID-19 patients to assess their viral RNA shedding and residual antibodies against SARS-CoV-2. We also evaluated antibodies in blood samples from 308 close contacts of recovered COVID-19 patients. We found that viral RNA remained detectable in 6.6% of recovered COVID-19 cases and up to 105 days. IgM, IgG, and IgA antibodies against SARS-CoV-2 were detected in 13.8%, 88.5%, and 83.4% of the recovered cases 4-12 weeks after disease onset, respectively. Higher levels of antibodies detected were associated with severe illness patients experienced while hospitalized. Fifteen of the 308 contacts (4.9%) of COVID-19 cases tested positive for IgG antibodies, suggesting probable exposure. Viral clearance and the pattern of antibody responses in infected individuals are both crucial for effectively combating SARS-CoV-2. Our study provides additional information on the natural history of this newly emerging disease related to both natural host defenses and antibody duration.

			 **Fig 2. The association between the antibodies against SARS-CoV-2 and symptoms of recovered COVID-19 cases.** The levels of IgM (A), IgG (B), and IgA (C) antibodies against SARS-CoV-2 in recovered COVID-19 cases with and without pneumonia are represented as dots. Bars represent median values (middle line) and 1× the upper and lower interquartile range (IQR) (upper and lower lines). The levels of IgM, IgG, and IgA antibodies against SARS-CoV-2 were significantly higher in patients with pneumonia than in those without pneumonia. * $p = 0.0002$, ** $p < 0.00001$.
Burrel S et al International Journal of Infectious Diseases https://doi.org/10.1016/j.ijid.2020.10.040	Co-infection of SARS-CoV-2 with other respiratory viruses and performance of lower respiratory tract samples for the diagnosis of COVID-19.	Caratteristiche di 21 pazienti (7% del campione esaminato) con coinfezione da SARS-CoV-2 e altri virus respiratori.	OBJECTIVES: We performed a study during the early outbreak period of coronavirus disease 2019 (COVID-19) and the seasonal epidemics of other respiratory viral infections in order to describe the extent of co-infections of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with other respiratory viruses. A second objective consisted in the comparison of the diagnostic performances of URT and LRT samples for SARS-CoV-2 infection and to compare diagnostic performances of upper and lower respiratory tract (URT and LRT) samples for SARS-CoV-2 infection. METHODS: From January 25(th) through March 29(th), 2020, all URT and LRT samples collected from patients with suspected COVID-19 received in the virology laboratory of Pitie-Salpetriere University Hospital (Paris, France) were tested simultaneously for SARS-CoV-2 and other respiratory viruses. RESULTS: A total of 1423 consecutive patients were tested: 677 (47.6%) males, 746 (52.4%) females, median age of 50 [1-103] years. Twenty-one (1.5%) patients were positive for both SARS-CoV-2 and other respiratory viruses. The detection rate of SARS-CoV-2 was significantly higher in LRT than in URT (53.6% versus 13.4%; P < 0.0001). The analysis of paired samples from 117 (8.2%) patients showed that SARS-CoV-2 load was lower in URT than in LRT samples in 65% of cases. CONCLUSION:

			The detection of other respiratory viruses in patients during epidemic period cannot rule out SARS-CoV-2 co-infection. Furthermore, LRT samples increases the accuracy of diagnosis of COVID-19.
Voeten HACM et al Clinical Infectious Diseases https://doi.org/10.1093/cid/ciaa1664	Unravelling the modes of transmission of SARS-CoV-2 during a nursing home outbreak: looking beyond the church super-spread event.	Studio di un presunto fenomeno di super-spreading di SARS-CoV-2 in occasione di una cerimonia religiosa presso una casa di riposo nei Paesi Bassi : una analisi più accurata dei casi mostra che si è trattato in realtà di 8 cluster di infezione diversi (ceppi distinti di SARS-CoV-2) probabilmente dovuti a introduzioni dall'esterno , da parte di visitatori.	BACKGROUND: An outbreak of COVID-19 in a nursing home in the Netherlands, following an on-site church service held on March 8 th, 2020, triggered an investigation to unravel sources and chain(s) of transmission. METHODS: Epidemiological data were collected from registries and through a questionnaire among church attendees. Symptomatic residents and healthcare workers (HCWs) were tested for SARS-CoV-2 by RT-PCR and subjected to whole genome sequencing (WGS). Sequences from a selection of people from the same area were included as community reference. RESULTS: After the church service, 30 of 39 attendees (77%) developed symptoms; 14 were tested and were positive for COVID-19 (11 residents and 3 non-residents). In the following five weeks, 62 of 300 residents (21%) and 30 of 640 HCWs (5%) tested positive for COVID-19; 21 of 62 residents (34%) died. The outbreak was controlled through a cascade of measures. WGS of samples from residents and HCWs identified a diversity of sequence types, grouped into eight clusters. Seven resident church attendees all were infected with distinct viruses, four of which belonged to two larger clusters in the nursing home. CONCLUSIONS: Although initial investigation suggested the church service as source of the outbreak, detailed analysis showed a more complex picture, most consistent with widespread regional circulation of the virus in the weeks before the outbreak, and multiple introductions into the nursing home before the visitor ban. The findings underscore the importance of careful outbreak investigations to understand SARS-CoV-2 transmission to develop evidence-based mitigation measures.

			
Plante JA et al Nature https://www.biorxiv.org/content/10.1101/2020.09.01.278689v1	Spike mutation D614G alters SARS-CoV-2 fitness	Una mutazione della proteina S di SARS-CoV-2 emersa nel corso della pandemia conferirebbe maggiore tendenza a sviluppare una elevata carica virale nelle alte vie aeree (favorendo così la trasmissione) ma non nei polmoni. Inoltre, il ceppo mutato sarebbe ugualmente riconosciuto dalla risposta indotta dai vaccini attualmente in studio.	A spike protein mutation D614G became dominant in SARS-CoV-2 during the COVID-19 pandemic. However, the impact on viral spread and vaccine efficacy remains to be defined. Here, we engineer the D614G mutation in the USA-WA1/2020 strain and characterize its effect. D614G enhances replication on human lung epithelial cells and primary human airway tissues through an improved infectivity of virions. Hamsters infected with the G614 variant produced higher infectious titers in the nasal washes and trachea, but not lungs, confirming clinical evidence that the D614G mutation enhances viral loads in the upper respiratory tract of COVID-19 patients and may increases transmission. Sera from D614-infected hamsters exhibit modestly higher neutralization titers against G614 virus than against D614 virus, indicating that (i) the mutation may not reduce the ability of vaccines in clinical trials to protect against COVID-19 and (ii) therapeutic antibodies should be tested against the circulating G614 virus. Together with clinical findings, our work underscores the importance of this mutation in viral spread, vaccine efficacy, and antibody therapy.

Prieto-Alhambra D et al International Journal of Epidemiology https://academic.oup.com/ije/advance-article/doi/10.1093/ije/dyaa190/5942697	Filling the gaps in the characterization of the clinical management of COVID-19: 30-day hospital admission and fatality rates in a cohort of 118 150 cases diagnosed in outpatient settings in Spain	Studio di coorte condotto in Catalogna su 118150 pazienti con diagnosi di infezione da SARS-CoV-2 dei quali vengono descritte le caratteristiche fin dal momento della diagnosi e inoltre, per 95467 casi, l'outcome dell'infezione : ospedalizzati 15%, morti a 30 giorni 4%.	Background : Currently, there is a missing link in the natural history of COVID-19, from first (usually milder) symptoms to hospitalization and/or death. To fill in this gap, we characterized COVID-19 patients at the time at which they were diagnosed in outpatient settings and estimated 30-day hospital admission and fatality rates. Methods : This was a population-based cohort study. Data were obtained from Information System for Research in Primary Care (SIDIAP)—a primary-care records database covering >6 million people (>80% of the population of Catalonia), linked to COVID-19 reverse transcriptase polymerase chain reaction (RT-PCR) tests and hospital emergency, inpatient and mortality registers. We included all patients in the database who were ≥15 years old and diagnosed with COVID-19 in outpatient settings between 15 March and 24 April 2020 (10 April for outcome studies). Baseline characteristics included socio-demographics, co-morbidity and previous drug use at the time of diagnosis, and polymerase chain reaction (PCR) testing and results. Study outcomes included 30-day hospitalization for COVID-19 and all-cause fatality. Results : We identified 118 150 and 95 467 COVID-19 patients for characterization and outcome studies, respectively. Most were women (58.7%) and young-to-middle-aged (e.g. 21.1% were 45–54 years old). Of the 44 575 who were tested with PCR, 32 723 (73.4%) tested positive. In the month after diagnosis, 14.8% (14.6–15.0) were hospitalized, with a greater proportion of men and older people, peaking at age 75–84 years. Thirty-day fatality was 3.5% (95% confidence interval: 3.4% to 3.6%), higher in men, increasing with age and highest in those residing in nursing homes [24.5% (23.4% to 25.6%)].

			Conclusion : COVID-19 infections were widespread in the community, including all age–sex strata. However, severe forms of the disease clustered in older men and nursing-home residents. Although initially managed in outpatient settings, 15% of cases required hospitalization and 4% died within a month of first symptoms. These data are instrumental for designing deconfinement strategies and will inform healthcare planning and hospital-bed allocation in current and future COVID-19 outbreaks.  **Figure 2** (A) Kaplan–Meier estimates of COVID-19-related hospital admission after COVID-19 diagnosis, stratified by sex. (B) Kaplan–Meier estimates of COVID-19-related hospital admission after COVID-19 diagnosis, stratified by age in 10-year bands. **Figure 3** (A) Kaplan–Meier estimates of all-fatality after COVID-19 diagnosis, stratified by sex. (B) Kaplan–Meier estimates of all-cause fatality after COVID-19 diagnosis, stratified by age in 10-year bands.
Achar A et al Cells https://doi.org/10.3390/cells9112360	COVID-19-Associated Neurological Disorders: The Potential Route of CNS Invasion and Blood-Brain Relevance.	Disturbi neurologici associati all'infezione da SARS-CoV-2 e revisione dei meccanismi di dianno neurologico, dalla invasione del sistema nervoso centrale alla flogosi e al danno di barriera emato-encefalica.	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel human coronavirus that has sparked a global pandemic of the coronavirus disease of 2019 (COVID-19). The virus invades human cells through the angiotensin-converting enzyme 2 (ACE2) receptor-driven pathway, primarily targeting the human respiratory tract. However, emerging reports of neurological manifestations demonstrate the neuroinvasive potential of SARS-CoV-2. This review highlights the possible routes by which SARS-CoV-2 may

			invade the central nervous system (CNS) and provides insight into recent case reports of COVID-19-associated neurological disorders, namely ischaemic stroke, encephalitis, encephalopathy, epilepsy, neurodegenerative diseases, and inflammatory-mediated neurological disorders. We hypothesize that SARS-CoV-2 neuroinvasion, neuroinflammation, and blood-brain barrier (BBB) dysfunction may be implicated in the development of the observed disorders; however, further research is critical to understand the detailed mechanisms and pathway of infectivity behind CNS pathogenesis.
Bugalia S et al Mathematical Biosciences and Engineering http://www.aimspress.com/article/10.3934/mbe.2020318	Mathematical modeling of COVID-19 transmission: the roles of intervention strategies and lockdown.	Un altro modello matematico che tenta di predire l'andamento dell'epidemia da COVID-19 sulla base dei dati dell'India e che suggerisce l'utilità di aumentare la capacità di testare e isolare gli infetti rispetto a un « lockdown » generalizzato.	An outbreak of rapidly spreading coronavirus established human to human transmission and now became a pandemic across the world. The new confirmed cases of infected individuals of COVID-19 are increasing day by day. Therefore, the prediction of infected individuals has become of utmost important for health care arrangements and to control the spread of COVID-19. In this study, we propose a compartmental epidemic model with intervention strategies such as lockdown, quarantine, and hospitalization. We compute the basic reproduction number (R0), which plays a vital role in mathematical epidemiology. Based on R0, it is revealed that the system has two equilibrium, namely disease-free and endemic. We also demonstrate the non-negativity and boundedness of the solutions, local and global stability of equilibria, transcritical bifurcation to analyze its epidemiological relevance. Furthermore, to validate our system, we fit the cumulative and new daily cases in India. We estimate the model parameters and predict the near future scenario of the disease. The global sensitivity analysis has also been performed to observe the impact of different parameters on R0. We also investigate the dynamics of disease in respect of different situations of lockdown, e.g., complete lockdown, partial

			lockdown, and no lockdown. Our analysis concludes that if there is partial or no lockdown case, then endemic level would be high. Along with this, the high transmission rate ensures higher level of endemicity. From the short time prediction, we predict that India may face a crucial phase (approx 6000000 infected individuals within 140 days) in near future due to COVID-19. Finally, numerical results show that COVID-19 may be controllable by reducing the contacts and increasing the efficacy of lockdown.