

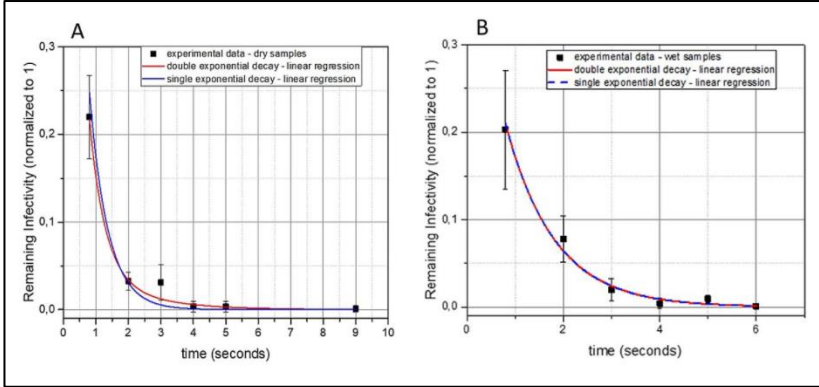
RICERCA BIBLIOGRAFICA COVID 19

SETTIMANA 4.01 -10.01.2021

FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE

DOTT.SSA ELEONORA TADDEI

| AUTORE/RIVISTA | TITOLO | OUTCOME PRINCIPALE | ABSTRACT |
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| Kirby T The Lancet https://marlin-prod.literatumonline.com/pb-assets/Lancet/pdfs/S2213260021000059.pdf | New variant of SARS-CoV-2 in UK causes surge of COVID-19 | Considerazioni sulla gestione della « variante inglese » di SARS-CoV-2 nel Regno Unito. | For most of November, 2020, England was in lockdown to force down the incidence of COVID-19 cases that had steadily increased in the late summer and autumn. Other countries in the UK (Wales, Scotland, and Northern Ireland) had also been reimposing and subsequently lifting restrictions, since each of the four nations is in charge of its own COVID-19 control plans. |
| Storm N et al Scientific Reports | Rapid and complete inactivation of SARS-CoV-2 by ultraviolet-C irradiation. | Studio che dimostra la rapida decontaminazione di superfici da SARS-CoV-2 tramite irradiazione con ultravioletti. | The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has devastated global public health systems and economies, with over 52 million people infected, millions of jobs and businesses lost, and more than 1 million deaths recorded to date. Contact with surfaces contaminated with droplets generated by infected persons through exhaling, talking, coughing and |

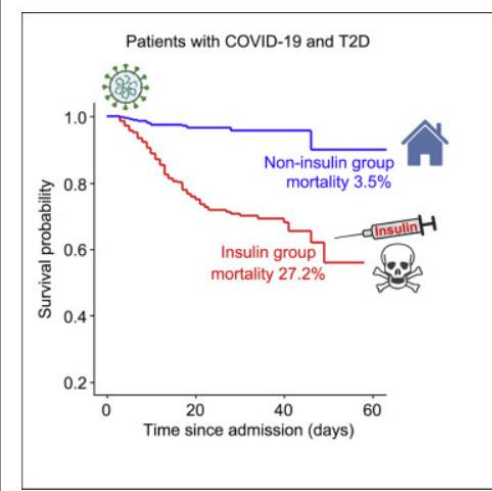
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| https://doi.org/10.1038/s41598-020-79600-8 | | | <p>sneezing is a major driver of SARS-CoV-2 transmission, with the virus being able to survive on surfaces for extended periods of time. To interrupt these chains of transmission, there is an urgent need for devices that can be deployed to inactivate the virus on both recently and existing contaminated surfaces. Here, we describe the inactivation of SARS-CoV-2 in both wet and dry format using radiation generated by a commercially available Signify ultraviolet (UV)-C light source at 254 nm. We show that for contaminated surfaces, only seconds of exposure is required for complete inactivation, allowing for easy implementation in decontamination workflows.</p>  <p>Figure A: Remaining infectivity (normalized to 1) vs time (seconds) for dry samples. The y-axis ranges from 0.0 to 0.3, and the x-axis ranges from 0 to 10. Experimental data points (black squares) show a rapid decay from approximately 0.25 at 1 second to near 0.0 by 4 seconds. Fitted curves include a double exponential decay (red line) and a single exponential decay (blue line).</p> <p>Figure B: Remaining infectivity (normalized to 1) vs time (seconds) for wet samples. The y-axis ranges from 0.0 to 0.3, and the x-axis ranges from 0 to 6. Experimental data points (black squares) show a rapid decay from approximately 0.25 at 1 second to near 0.0 by 4 seconds. Fitted curves include a double exponential decay (red line) and a single exponential decay (blue line).</p> |
| <p>Georgiu GP et al</p> <p>Irish Journal of Medical Science</p> | <p>How the language we speak determines the transmission of COVID-19.</p> | <p>La fonetica delle lingue parlate nei diversi Paesi può influenzare la trasmissione di SARS-CoV-2 ? In questo studio sembra emergere che la ricorrenza della consonante occlusiva « p » (che prevede una rapida emissione di flusso d'aria)</p> | <p>BACKGROUND: Little body of research has focused on the epidemic transmissibility and language interface. AIMS: In this paper, we aim to investigate whether (i) the feature of aspiration found in the phonological inventory of several languages and (ii) the frequency of occurrence of stop consonants are associated with the transmission of COVID-19 among humans. METHODS: The study's protocol was based on a corpus of countries infected by COVID-19 and of which the linguistic repertoire includes a widely spoken</p> |

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| https://link.springer.com/article/10.1007/s11845-020-02500-3 | | <p>sia associata al numero di riproduzione di base del virus.</p> | <p>language in individuals' everyday communication. We tested whether languages with and without aspiration differ in terms of COVID-19 reproduction number, and whether the frequency of occurrence of stop consonants in several languages correlates with the virus reproduction number. RESULTS: The results demonstrated no significant effect of aspiration on the transmission of the virus, while a positive correlation between the frequency of occurrence and transmissibility was observed only for the consonant /p/; this might suggest that languages that use /p/ more frequently might spread the virus more easily. CONCLUSIONS: The findings of this study can offer a tentative picture of how speaking specific sounds can be associated with COVID-19 transmissibility.</p> |
| <p>The Centers for Disease Control and Prevention</p> <p>https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/anaphylaxis-management.html</p> | <p>Interim considerations: preparing for the potential management of anaphylaxis after COVID-19 vaccination.</p> | <p>Indicazioni da parte dei CDC sulla individuazione e gestione dei casi di anafilassi da vaccino contro SARS-CoV-2.</p> | <p>These interim considerations provide information on preparing for the initial assessment and management of anaphylaxis following COVID-19 vaccination. Institutional practices and site-specific factors may also be considered. In all cases, appropriate medical treatment for severe allergic reactions must be immediately available in the event that an acute anaphylactic reaction occurs following administration of a COVID-19 vaccine.</p> |

| | | | <p>The following emergency equipment should be immediately available to the clinical team assessing and managing anaphylaxis.</p> <table><tr><th>Should be available at all sites</th><th>If feasible, include at sites (not required)</th></tr><tr><td>Epinephrine prefilled syringe or autoinjector*</td><td>Pulse oximeter</td></tr><tr><td>H1 antihistamine (e.g., diphenhydramine)†</td><td>Oxygen</td></tr><tr><td>Blood pressure cuff</td><td>Bronchodilator (e.g., albuterol)</td></tr><tr><td>Stethoscope</td><td>H2 antihistamine (e.g., famotidine, cimetidine)</td></tr><tr><td>Timing device to assess pulse</td><td>Intravenous fluids</td></tr><tr><td></td><td>Intubation kit</td></tr><tr><td></td><td>Adult-sized pocket mask with one-way valve (also known as cardiopulmonary resuscitation (CPR) mask)</td></tr></table> | Should be available at all sites | If feasible, include at sites (not required) | Epinephrine prefilled syringe or autoinjector* | Pulse oximeter | H1 antihistamine (e.g., diphenhydramine)† | Oxygen | Blood pressure cuff | Bronchodilator (e.g., albuterol) | Stethoscope | H2 antihistamine (e.g., famotidine, cimetidine) | Timing device to assess pulse | Intravenous fluids | | Intubation kit | | Adult-sized pocket mask with one-way valve (also known as cardiopulmonary resuscitation (CPR) mask) |
|--|---|---|---|----------------------------------|--|--|----------------|---|--------|---------------------|----------------------------------|-------------|---|-------------------------------|--------------------|--|----------------|--|---|
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| Epinephrine prefilled syringe or autoinjector* | Pulse oximeter | | | | | | | | | | | | | | | | | | |
| H1 antihistamine (e.g., diphenhydramine)† | Oxygen | | | | | | | | | | | | | | | | | | |
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| Andreano E et al MedRXiv https://doi.org/10.1101/2020.12.28.424451 | SARS-CoV-2 escape in vitro from a highly neutralizing COVID-19 convalescent plasma | Dimostrazione in vitro della capacità di SARS-CoV-2 di mutare durante esposizione in vitro al siero immune di un paziente guarito, fino a sfuggire alla neutralizzazione. Le condizioni in vivo sono certamente diverse ma tale prospettiva è rilevante per l'efficacia di terapia al plasma e vaccini. | To investigate the evolution of SARS-CoV-2 in the immune population, we co-incubated authentic virus with a highly neutralizing plasma from a COVID-19 convalescent patient. The plasma fully neutralized the virus for 7 passages, but after 45 days, the deletion of F140 in the spike N-terminal domain (NTD) N3 loop led to partial breakthrough. At day 73, an E484K substitution in the receptor-binding domain (RBD) occurred, followed at day 80 by an insertion in the NTD N5 loop containing a new glycan sequon, which generated a variant completely resistant to plasma neutralization. Computational modeling predicts that the deletion and insertion in loops N3 and N5 prevent binding of neutralizing antibodies. The recent emergence in the United Kingdom and South Africa of natural variants with similar changes suggests that SARS-CoV-2 has the potential to escape an effective immune response and that | | | | | | | | | | | | | | | | |

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| | | | vaccines and antibodies able to control emerging variants should be developed. |
| <p>Yu B et al</p> <p>Cell</p> <p>https://www.cell.com/cell-metabolism/fulltext/S1550-4131(20)30647-1?utm_medium=homepage</p> | <p>Insulin Treatment Is Associated with Increased Mortality in Patients with COVID-19 and Type 2 Diabetes</p> | <p>Studio retrospettivo su 689 pazienti diabetici ricoverati per COVID-19 : il trattamento con insulina durante il ricovero è associato a peggiore outcome.</p> | <p>COVID-19 caused by SARS-COV-2 infection can lead to multi-organ injuries and significant mortality in severe and critical patients, especially among those individuals with type 2 diabetes (T2D) as a comorbidity. While attenuated mortality was observed with aggressive glucose control, it was unclear whether therapeutic regimens including insulin treatment were beneficial for patients with COVID-19 and T2D. This retrospective study investigated 689 patients with COVID-19 and T2D from a cohort of 3,305 cases from Wuhan, China. Unexpectedly, we found that insulin treatment for patients with COVID-19 and T2D was associated with a significant increase in mortality (27.2% versus 3.5%; adjusted HR, 5.38 [2.75–10.54]). Further analysis showed that insulin treatment was associated with enhanced systemic inflammation and aggravated injuries of vital organs. Therefore, insulin treatment for patients with COVID-19 and T2D should be used with caution.</p> |

Graphical Abstract



Banerji A et al

The Journal of Allergy and Clinical Immunology: In Practice

<https://www.sciencedirect.com/science/article/pii/S2213219820314112?via%3Dihub>

mRNA Vaccines to Prevent COVID-19 Disease and Reported Allergic Reactions: Current Evidence and Approach

Revisione dell'evidenza in merito alle reazioni allergiche da vaccini a mRNA, con una disamina del contenuto dei vaccini Pfizer e Moderna e una sezione di domande-risposte per i pazienti.

The recent Food and Drug Administration (FDA) approval of two highly effective COVID-19 vaccines from Pfizer-BioNtech and Moderna has brought hope to millions of American in the midst of an ongoing global pandemic. The FDA Emergency Use Authorization guidance for both vaccines is to not administer the vaccine to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COVID-19 vaccine. The Centers for Diseases Control and Prevention (CDC) advises that all patients should be observed for 15 minutes after COVID-19 vaccination and staff must be able to identify and manage anaphylaxis. Post-FDA approval, despite very strong safety signals in both phase 3 trials, reports of possible allergic reactions have raised public concern. To provide reassurance and support during widespread vaccination across America, allergists must offer clear guidance to patients based on the best information available, but

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| | | | also in accordance with the broader recommendations of our US regulatory agencies. This review summarizes vaccine allergy epidemiology and proposes risk stratification schema: (1) for individuals with different allergy histories to safely receive their first COVID-19 vaccine and (2) for individuals who develop a reaction to their first dose of COVID-19 vaccine. |
| <p>Matezou HC et al</p> <p>The Journal of Infectious Diseases</p> <p>https://doi.org/10.1093/infdis/jiaa804</p> | <p>Association between upper respiratory tract viral load, comorbidities, disease severity and outcome of patients with SARS-CoV-2 infection</p> | <p>In un campione di 1122 pazienti la maggiore carica virale di SARS-CoV-2 nelle alte vie respiratorie (stimata con il ciclo soglia) è associata allo sviluppo di sintomi nell'analisi multivariata.</p> | <p>Background : There is limited information on the association between upper respiratory tract (URT) viral loads, host factors, and disease severity in SARS-CoV-2 infected patients.</p> <p>Methods : We studied 1,122 patients (mean age: 46 years) diagnosed by PCR. URT viral load, measured by PCR cycle threshold, was categorized as high, moderate or low.</p> <p>Results : There were 336 (29.9%) patients with comorbidities; 309 patients (27.5%) had high, 316 (28.2%) moderate, and 497 (44.3%) low viral load. In univariate analyses, compared to patients with moderate or low viral load, patients with high viral load were older, had more often comorbidities, developed symptomatic disease, were intubated and died; in addition, patients with high viral load had longer stay in intensive care unit and longer intubation compared to patients with low viral load (p-values <0.05 for all). Patients with chronic cardiovascular disease, hypertension, chronic pulmonary disease, immunosuppression, obesity and chronic neurological disease had more often high viral load (p-value<0.05 for all). Multivariate analysis found that a high viral load was associated with COVID-19. The level of viral load was not associated with any other outcome.</p> <p>Conclusions : URT viral load could be used to identify patients at higher risk for morbidity or severe outcome.</p> |

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| <p>Niwas Ret al</p> <p>Advances in Respiratory Medicine</p> <p>https://journals.viamedica.pl/advances_in_respiratory_medicine/article/view/69692</p> | <p>Clinical outcome, viral response and safety profile of chloroquine in COVID-19 patients — initial experience</p> | <p>Piccolo studio retrospettivo su 12 pazienti trattati con cloroquina e 17 controlli ricoverati per COVID-19 : i primi mostrano minore durata dei sintomi.</p> | <p>Introduction: Chloroquine and its analogues are currently being investigated for the treatment and post exposure prophylaxis of COVID-19 due to its antiviral activity and immunomodulatory activity.</p> <p>Material and methods: Confirmed symptomatic cases of COVID-19 were included in the study. Patients were supposed to receive chloroquine (CQ) 500 mg twice daily for 7 days. Due to a change in institutional protocol, initial patients received chloroquine and subsequent patients who did not receive chloroquine served as negative controls. Clinical effectiveness was determined in terms of timing of symptom resolution and conversion rate of reverse transcriptase polymerase chain reaction (RT-PCR) on day 14 and day 15 of admission.</p> <p>Results: Twelve COVID-19 patients formed the treatment arm and 17 patients were included in the control arm. The duration of symptoms among the CQ treated group (6.3 ± 2.7 days) was significantly (p-value = 0.009) lower than that of the control group (8.9 ± 2.2 days). There was no significant difference in the rate of RT-PCR negativity in both groups. 2 patients out of 12 developed diarrhea in the CQ therapy arm.</p> <p>Conclusion: The duration of symptoms among the treated group (with chloroquine) was significantly lower than that of the control group. RT-PCR conversion was not significantly different between the 2 groups.</p> |
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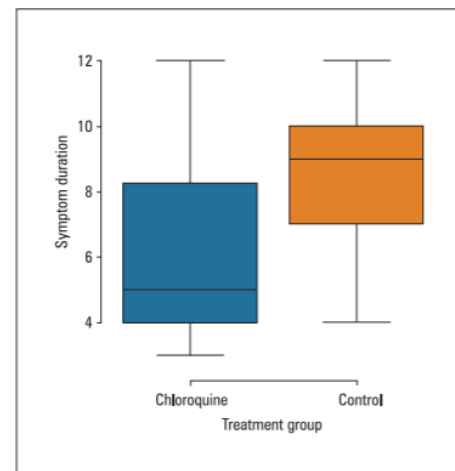


Figure 2. Box-plot showing the distribution of time-to-symptom resolution between the CQ and control arms

Couturaud F et al

JAMA

<https://jamanetwork.com/journals/jama/article-abstract/2774681>

Prevalence of Pulmonary Embolism Among Patients With COPD Hospitalized With Acutely Worsening Respiratory Symptoms

L'embolia polmonare non si verifica solo in COVID-19 : il 5.9% dei pazienti ricoverati con riacutizzazione di BPCO presentava embolia polmonare a 48 ore dal ricovero in questo studio retrospettivo su 740 pazienti (in COVID-19 le percentuali riportate in ospedalizzati non ICU sono 3-8%).

Importance The prevalence of pulmonary embolism in patients with chronic obstructive pulmonary disease (COPD) and acutely worsening respiratory symptoms remains uncertain.

Objective To determine the prevalence of pulmonary embolism in patients with COPD admitted to the hospital for acutely worsening respiratory symptoms.

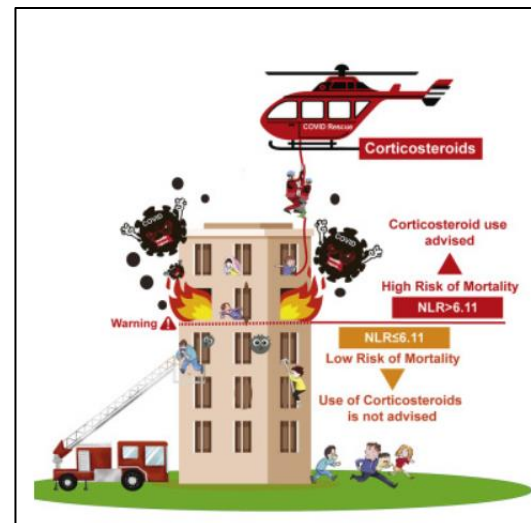
Design, Setting, and Participants Multicenter cross-sectional study with prospective follow-up conducted in 7 French hospitals. A predefined pulmonary embolism diagnostic algorithm based on Geneva score, D-dimer levels, and spiral computed tomographic pulmonary angiography plus leg compression ultrasound was applied within 48 hours of admission; all patients had 3-month follow-up. Patients were recruited from January 2014 to May 2017 and the final date of follow-up was August 22, 2017.

Exposures Acutely worsening respiratory symptoms in patients with COPD.

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| | | | <p>Main Outcomes and Measures The primary outcome was pulmonary embolism diagnosed within 48 hours of admission. Key secondary outcome was pulmonary embolism during a 3-month follow-up among patients deemed not to have venous thromboembolism at admission and who did not receive anticoagulant treatment. Other outcomes were venous thromboembolism (pulmonary embolism and/or deep vein thrombosis) at admission and during follow-up, and 3-month mortality, whether venous thromboembolism was clinically suspected or not.</p> <p>Results Among 740 included patients (mean age, 68.2 years [SD, 10.9 years]; 274 women [37.0%]), pulmonary embolism was confirmed within 48 hours of admission in 44 patients (5.9%; 95% CI, 4.5%-7.9%). Among the 670 patients deemed not to have venous thromboembolism at admission and who did not receive anticoagulation, pulmonary embolism occurred in 5 patients (0.7%; 95% CI, 0.3%-1.7%) during follow-up, including 3 deaths related to pulmonary embolism. The overall 3-month mortality rate was 6.8% (50 of 740; 95% CI, 5.2%-8.8%). The proportion of patients who died during follow-up was higher among those with venous thromboembolism at admission than the proportion of those without it at admission (14 [25.9%] of 54 patients vs 36 [5.2%] of 686; risk difference, 20.7%, 95% CI, 10.7%-33.8%; $P < .001$). The prevalence of venous thromboembolism was 11.7% (95% CI, 8.6%-15.9%) among patients in whom pulmonary embolism was suspected ($n = 299$) and was 4.3% (95% CI, 2.8%-6.6%) among those in whom pulmonary embolism was not suspected ($n = 441$).</p> <p>Conclusions and Relevance Among patients with chronic obstructive pulmonary disease admitted to the hospital with an acute worsening of respiratory symptoms, pulmonary embolism</p> |
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| | | | was detected in 5.9% of patients using a predefined diagnostic algorithm. Further research is needed to understand the possible role of systematic screening for pulmonary embolism in this patient population. |
| <p>European Medicines Agency</p> <p>https://www.ema.europa.eu/en/news/ema-recommends-covid-19-vaccine-moderna-authorisation-eu</p> <p>https://www.ema.europa.eu/en/medicines/human/summaries-opinion/covid-19-vaccine-moderna</p> | EMA recommends COVID-19 Vaccine Moderna for authorisation in the EU | <p>L'Agenzia europea dei farmaci raccomanda l'autorizzazione da parte della Commissione Europea del vaccino Moderna a mRNA contro SARS-CoV-2. Nel secondo link una serie di domande-risposte sul vaccino.</p> | <p>EMA has recommended granting a conditional marketing authorisation for COVID-19 Vaccine Moderna to prevent Coronavirus disease (COVID-19) in people from 18 years of age. This is the second COVID-19 vaccine that EMA has recommended for authorisation.</p> <p>EMA's human medicines committee (CHMP) has thoroughly assessed the data on the quality, safety and efficacy of the vaccine and recommended by consensus a formal conditional marketing authorisation be granted by the European Commission. This will assure EU citizens that the vaccine meets EU standards and puts in place the safeguards, controls and obligations to underpin EU-wide vaccination campaigns.</p> |
| <p>Jingjing C et al</p> <p>Cell</p> <p>https://www.cell.com/cell-metabolism/fulltext/S1550-4131(21)00002-4</p> | The neutrophil-to-lymphocyte ratio determines clinical efficacy of corticosteroid therapy in patients with COVID-19 | <p>Studio retrospettivo su oltre 12000 pazienti ospedalizzati per COVID-19 in Cina : nei casi con rapporto neutrofili/linfociti superiore a 6.11, la terapia con corticosteroidi riduce la mortalità a 60 giorni.</p> | <p>Corticosteroid therapy is now recommended as a treatment in patients with severe COVID-19. But one key question is how to objectively identify severely ill patients who may benefit from such therapy. Here, we assigned 12,862 COVID-19 cases from 21 hospitals in Hubei Province equally to a training and a validation cohort. We found that a neutrophil-to-lymphocyte ratio (NLR) > 6.11 at admission discriminated a higher risk for mortality. Importantly, however, corticosteroid treatment in such individuals was associated with a lower risk of 60-day all-cause mortality. Conversely, in individuals with an NLR ≤ 6.11 or with Type 2 Diabetes, corticosteroid treatment was not associated with reduced mortality, but rather increased risks of hyperglycemia and</p> |

infections. These results show that in the studied cohort corticosteroid treatment is associated with beneficial outcomes in a subset of COVID-19 patients who are non-diabetic and with severe symptoms as defined by NLR.



Background: SARS-CoV-2 quickly spreads in the worldwide population, imposing social restrictions to control the infection, being the massive testing another essential strategy to break the chain of transmission. Aim: To compare the performance of at-home self-collected samples - saliva and combined nasal-oropharyngeal swabs (NOP) - for SARS-CoV-2 detection in a telemedicine platform for COVID-19 surveillance. Material and methods: We analyzed 201 patients who met the criteria of suspected COVID-19. NOP sampling was combined (nostrils and oropharynx) and saliva collected using a cotton pad device. Detection of SARS-COV-2 was performed by using the Altona RealStar(R) SARS-CoV-2 RT-PCR Kit 1.0. Results: There was an overall significant agreement (kappa coefficient value of 0.58) between

Braz-Silva PH et al

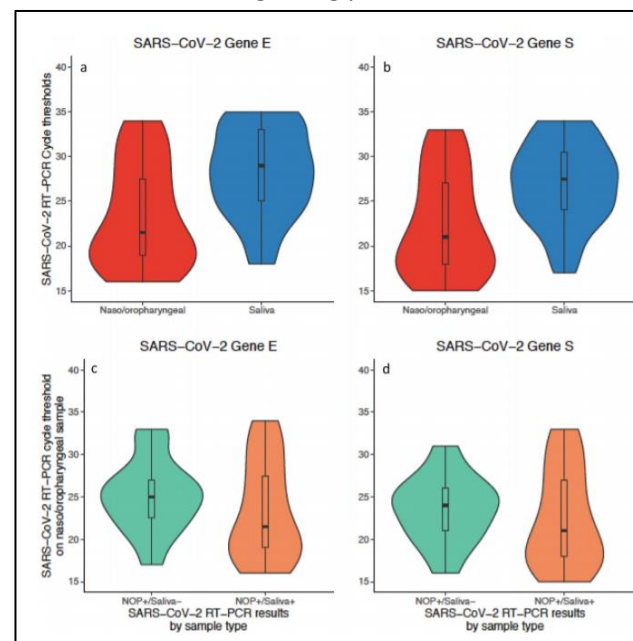
Journal of Oral
Microbiology

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7733974/>

Performance of at-home self-collected saliva and nasal-oropharyngeal swabs in the surveillance of COVID-19.

Accettabile concordanza di tampone nasofaringeo e prelievo di campione salivare eseguiti autonomamente a casa da 201 pazienti con sospetta infezione da SARS-CoV-2.

saliva and NOP. Considering results in either sample, 70 patients positive for SARS-CoV-2 were identified, with 52/70 being positive in NOP and 55/70 in saliva. This corresponds to sensitivities of 74.2% (95% CI; 63.7% to 83.1%) for NOP and 78.6% (95% CI; 67.6% to 86.6%) for saliva. Conclusion: Our data show the feasibility of using at-home self-collected samples (especially saliva), as an adequate alternative for SARS-CoV-2 detection. This new approach of testing can be useful to develop strategies for COVID-19 surveillance and for guiding public health decisions.



Elabbadi A et al
Infection

Bacterial coinfection in critically ill COVID-19 patients with severe pneumonia.

Prevalenza di sovrainfezioni batteriche in 1010 pazienti ricoverati in terapia intensiva per COVID-19. Predominanza di Stafilococco aureo.

Severe 2019 novel coronavirus infectious disease (COVID-19) with pneumonia is associated with high rates of admission to the intensive care unit (ICU). Bacterial coinfection has been reported to be rare. We aimed at describing the rate of bacterial coinfection in critically ill adult patients with severe COVID-19 pneumonia. All the patients with laboratory-confirmed severe COVID-19 pneumonia

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| https://link.springer.com/article/10.1007/s15010-020-01553-x | | | <p>admitted to the ICU of Tenon University-teaching hospital, from February 22 to May 7th, 2020 were included. Respiratory tract specimens were obtained within the first 48 h of ICU admission. During the study period, 101 patients were referred to the ICU for COVID-19 with severe pneumonia. Most patients (n = 83; 82.2%) were intubated and mechanically ventilated on ICU admission. Overall, 20 (19.8%) respiratory tract specimens obtained within the first 48 h. Staphylococcus aureus was the main pathogen identified, accounting for almost half of the early-onset bacterial etiologies. We found a high prevalence of early-onset bacterial coinfection during severe COVID-19 pneumonia, with a high proportion of S. aureus. Our data support the current WHO guidelines for the management of severe COVID-19 patients, in whom antibiotic therapy directed to respiratory pathogens is recommended.</p> |
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Table 2 Bacterial microorganism(s) identified in severe COVID-19 pneumonia

| Microorganism, <i>n</i> | Early Bacterial Coinfection [†] |
|---|--|
| Gram-positive cocci | 12 |
| <i>Staphylococcus aureus</i> | 11 |
| <i>MSSA</i> | 9 |
| <i>MRSA</i> ^a | 2 |
| <i>Streptococcus pneumoniae</i> | 1 |
| <i>Enterococcus sp.</i> | 0 |
| Gram-negative bacilli | 13 |
| <i>Enterobacteriaceae</i> | |
| <i>E. coli</i> | 2 |
| <i>Klebsiella spp.</i> | 2 |
| <i>Enterobacter, Citrobacter, Hafnia spp.</i> | 4 |
| <i>Serratia</i> | 0 |
| <i>Non-fermenting GNB</i> | |
| <i>Pseudomonas spp.</i> | 2 |
| <i>Others</i> | 0 |
| <i>Other GNB</i> | |
| <i>H. influenza</i> | 2 |
| <i>M. catarrhalis</i> | 1 |
| Other | |
| Intracellular pathogen | 0 |

^a*MRSA* methicillin-resistant *S. aureus* (MRSA), in one renal transplant recipient, and one patient without identified risk factor

[†]defined as microorganism(s) identified within the first 48 h of ICU admission. More than one bacterium was identified in 5 patients

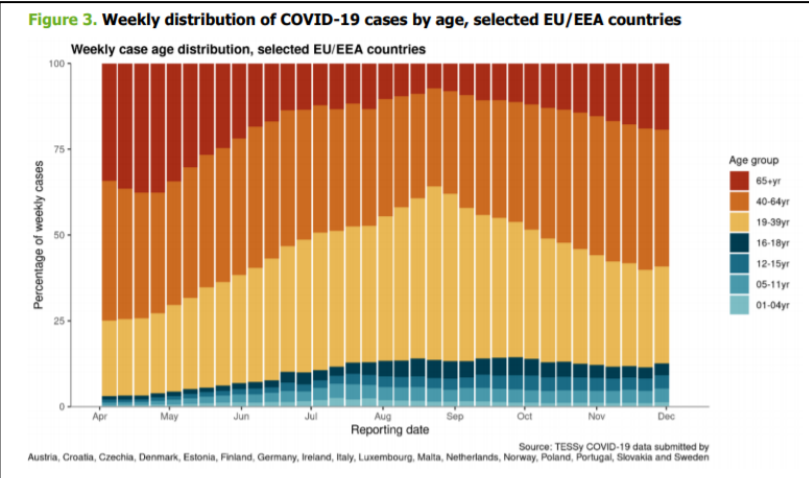
European Centre for Disease Prevention and Control

<https://www.ecdc.europa.eu/en/publications-data/children-and-school->

COVID-19 in children and the role of school settings in transmission - first update

Dati sull'impatto della chiusura delle scuole in Europa rispetto alla circolazione di SARS-CoV-2 : si tratta di una misura sicuramente dannosa per lo sviluppo dei giovani, che può dare un contributo ma

The aim of this document is to provide an update on the knowledge surrounding the role of children in the transmission of SARS-CoV-2 and the role of schools in the COVID-19 pandemic, based on the experience in the EU from August–December, 2020. This document also addresses transmission to and from staff in school settings, school-related mitigation measures including risk communication, testing, contact tracing and the efficacy of partial and full school

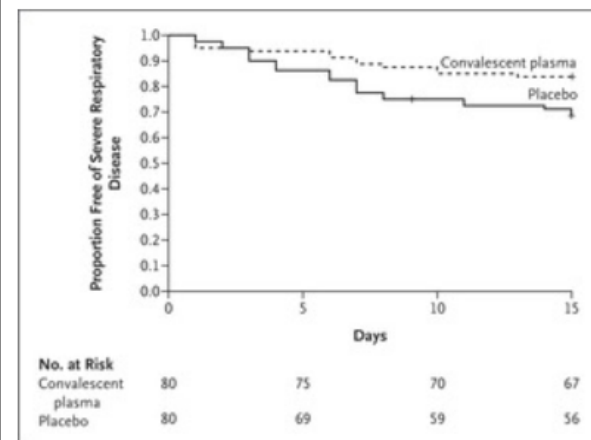
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| settings-covid-19-transmission | | <p>da sola non può arrestare il contagio.</p> | <p>closures. This document draws upon and updates evidence presented in the previous report from ECDC on this topic, which was published on August 6, 2020 [4]. This report does not consider educational settings related to young adults or adults, such as universities or vocational schools or any school with overnight stays, such as boarding schools. This report does not consider the epidemiology of COVID-19 in relation to new variants of SARS-CoV-2, for which robust evidence on the potential impact in school settings is not yet available, such as one recently observed in the United Kingdom.</p> <p>Figure 3. Weekly distribution of COVID-19 cases by age, selected EU/EEA countries</p>  <p>Source: TESSy COVID-19 data submitted by Austria, Croatia, Czechia, Denmark, Estonia, Finland, Germany, Ireland, Italy, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Slovakia and Sweden</p> |
| <p>Bhatt H et al</p> <p>Current Nutrition Report</p> <p>https://link.springer.com/article/10.1007%2Fs13668-020-00343-z</p> | <p>Should COVID-19 Mother Breastfeed her Newborn Child? A Literature Review on the Safety of Breastfeeding for Pregnant Women with COVID-19.</p> | <p>Revisione sistematica sulla opportunità di allattamento al seno da parte di madri con infezione da SARS-CoV-2 : i dati a disposizione sono scarsi ma non sufficienti per sconsigliarlo, mettendo in atto misure di protezione dai droplet.</p> | <p>PURPOSE OF REVIEW: Breastfeeding is beneficial to both the newborn and the mother. During the COVID-19 pandemic, concerns have been raised on whether the SARS-CoV-2 virus could be transmitted from COVID-19 positive mother to the newborn through breastmilk. The purpose of this review is to examine the available evidence on the risks of transmission of infection from COVID-19 mothers to their newborns through breastfeeding.</p> <p>RECENT FINDINGS: Data is very limited in this regard, with only a</p> |

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| | | | <p>few smaller case series, and case reports have been published so far. In most of the studies, breastmilk samples from COVID-19 mothers tested negative for the virus. In the case reports where the virus was detected in breastmilk and the infants were diagnosed with COVID-19, it remained unclear whether the disease was transmitted through breastmilk or direct contact or through delivery. Another hypothesis is that the viral antibodies could pass to the newborn passively through breastmilk of COVID-19 positive mothers and give immunity to the child, but data is minimal. Based on the currently available limited evidence and recognizing the benefits of breastfeeding, it may be concluded that if the health of the mother and her newborn allows, direct breastfeeding or extracted breastmilk should be encouraged by the healthcare providers after a careful discussion of the risks of vertical transmission to the mother and her family. Preventive measures should be taken by COVID-19 mothers to prevent droplet transmission of infection to the infants while breastfeeding.</p> |
| <p>Lauring AS et al</p> <p>JAMA</p> <p>https://jamanetwork.com/journals/jama/fullarticle/2775006?resultClick=1</p> | <p>Genetic Variants of SARS-CoV-2—What Do They Mean?</p> | <p>Disamina delle varianti di SARS-CoV-2, dalla « vecchia » D614G alla più recente « variante Inglese » e loro significato nell'epidemiologia dell'infezione.</p> | <p>Over the course of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, the clinical, scientific, and public health communities have had to respond to new viral genetic variants. Each one has triggered a flurry of media attention, a range of reactions from the scientific community, and calls from governments to either “stay calm” or pursue immediate countermeasures. While many scientists were initially skeptical about the significance of the D614G alteration, the emergence of the new “UK variant” —lineage B.1.1.7—has raised widespread concern. Understanding which variants are concerning, and why, requires an appreciation of virus evolution and the genomic epidemiology of SARS-CoV-2.</p> |

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| <p>Dan JM et al</p> <p>Science</p> <p>https://science.sciencemag.org/content/early/2021/01/05/science.abf4063.full</p> | <p>Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection</p> | <p>Studio su una coorte di 188 pazienti con COVID-19 (93% mai ospedalizzati) di cui viene studiata la risposta immunitaria nelle sue varie componenti (anticorpi, linfociti B e T), che appare persistente fino a 8 mesi dall'esordio.</p> | <p>Understanding immune memory to SARS-CoV-2 is critical for improving diagnostics and vaccines, and for assessing the likely future course of the COVID-19 pandemic. We analyzed multiple compartments of circulating immune memory to SARS-CoV-2 in 254 samples from 188 COVID-19 cases, including 43 samples at ≥ 6 months post-infection. IgG to the Spike protein was relatively stable over 6+ months. Spike-specific memory B cells were more abundant at 6 months than at 1 month post symptom onset. SARS-CoV-2-specific CD4+ T cells and CD8+ T cells declined with a half-life of 3-5 months. By studying antibody, memory B cell, CD4+ T cell, and CD8+ T cell memory to SARS-CoV-2 in an integrated manner, we observed that each component of SARS-CoV-2 immune memory exhibited distinct kinetics.</p> |
| <p>Tong A et al</p> <p>Critical Care Medicine</p> <p>https://journals.lww.com/ccmjournal/Abstract/9000/Core_Outcome_Measures_for_Trials_in_People_With_Coronavirus_Disease_2019_With.95396.aspx</p> | <p>Core Outcome Measures for Trials in People With Coronavirus Disease 2019</p> | <p>Una consensus di 130 partecipanti fra pazienti, operatori sanitari e popolazione generale propone una lista di outcome chiave per i trial clinici su COVID-19 : insufficienza respiratoria, insufficienza multiorgano, dispnea, guarigione e mortalità.</p> | <p>Objectives: Respiratory failure, multiple organ failure, shortness of breath, recovery, and mortality have been identified as critically important core outcomes by more than 9300 patients, health professionals, and the public from 111 countries in the global coronavirus disease 2019 core outcome set initiative. The aim of this project was to establish the core outcome measures for these domains for trials in coronavirus disease 2019.</p> <p>Design: Three online consensus workshops were convened to establish outcome measures for the four core domains of respiratory failure, multiple organ failure, shortness of breath, and recovery.</p> <p>Setting: International.</p> <p>PATIENTS: About 130 participants (patients, public, and health professionals) from 17 countries attended the three workshops.</p> <p>INTERVENTIONS: None.</p> <p>MEASUREMENTS AND MAIN RESULTS: Respiratory failure, assessed by the need for respiratory support based on the World Health</p> |

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| | | | <p>Organization Clinical Progression Scale, was considered pragmatic, objective, and with broad applicability to various clinical scenarios. The Sequential Organ Failure Assessment was recommended for multiple organ failure, because it was routinely used in trials and clinical care, well validated, and feasible. The Modified Medical Research Council measure for shortness of breath, with minor adaptations (recall period of 24 hr to capture daily fluctuations and inclusion of activities to ensure relevance and to capture the extreme severity of shortness of breath in people with coronavirus disease 2019), was regarded as fit for purpose for this indication. The recovery measure was developed de novo and defined as the absence of symptoms, resumption of usual daily activities, and return to the previous state of health prior to the illness, using a 5-point Likert scale, and was endorsed.</p> <p>Conclusions: The coronavirus disease 2019 core outcome set recommended core outcome measures have content validity and are considered the most feasible and acceptable among existing measures. Implementation of the core outcome measures in trials in coronavirus disease 2019 will ensure consistency and relevance of the evidence to inform decision-making and care of patients with coronavirus disease 2019.</p> |
| <p>Libster R et al</p> <p>NEJM</p> <p>https://www.nejm.org/doi/full/10.1056/NEJMoa2033700?query=featured_home</p> | <p>Early High-Titer Plasma Therapy to Prevent Severe Covid-19 in Older Adults</p> | <p>Trial clinico randomizzato in cui si dimostra una riduzione del rischio di progressione a malattia grave in pazienti anziani con COVID-19 lieve esordito da meno di 72 ore se trattati con plasma di soggetti guariti.</p> | <p>BACKGROUND Therapies to interrupt the progression of early coronavirus disease 2019 (Covid-19) remain elusive. Among them, convalescent plasma administered to hospitalized patients has been unsuccessful, perhaps because antibodies should be administered earlier in the course of illness.</p> <p>METHODS We conducted a randomized, double-blind, placebo-controlled trial of convalescent plasma with high IgG titers against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in older adult patients within 72 hours after the onset of mild Covid-19</p> |

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| | | | <p>symptoms. The primary end point was severe respiratory disease, defined as a respiratory rate of 30 breaths per minute or more, an oxygen saturation of less than 93% while the patient was breathing ambient air, or both. The trial was stopped early at 76% of its projected sample size because cases of Covid-19 in the trial region decreased considerably and steady enrollment of trial patients became virtually impossible.</p> <p>RESULTS A total of 160 patients underwent randomization. In the intention-to-treat population, severe respiratory disease developed in 13 of 80 patients (16%) who received convalescent plasma and 25 of 80 patients (31%) who received placebo (relative risk, 0.52; 95% confidence interval [CI], 0.29 to 0.94; P=0.03), with a relative risk reduction of 48%. A modified intention-to-treat analysis that excluded 6 patients who had a primary end-point event before infusion of convalescent plasma or placebo showed a larger effect size (relative risk, 0.40; 95% CI, 0.20 to 0.81). No solicited adverse events were observed.</p> <p>CONCLUSIONS</p> <p>Early administration of high-titer convalescent plasma against SARS-CoV-2 to mildly ill infected older adults reduced the progression of Covid-19.</p> |
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Time to the Development of Severe Respiratory Disease Due to Coronavirus Disease 2019, According to Trial Group in the Intention-to-Treat Analysis.

Andersen K et al

Clinical Infectious Diseases

<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1488/6067567?searchresult=1>

Association Between Chronic Use of Immunosuppressive Drugs and Clinical Outcomes From Coronavirus Disease 2019 (COVID-19) Hospitalization: A Retrospective Cohort Study in a Large US Health System

Studio di coorte retrospettivo su 2121 pazienti ricoverati negli USA con COVID-19 : il trattamento cronico con immunosoppressori non pare influenzare l'outcome dell'infezione.

Background : It is unclear whether chronic use of immunosuppressive drugs worsens or improves the severity of coronavirus disease 2019 (COVID-19), with plausible mechanisms for both.

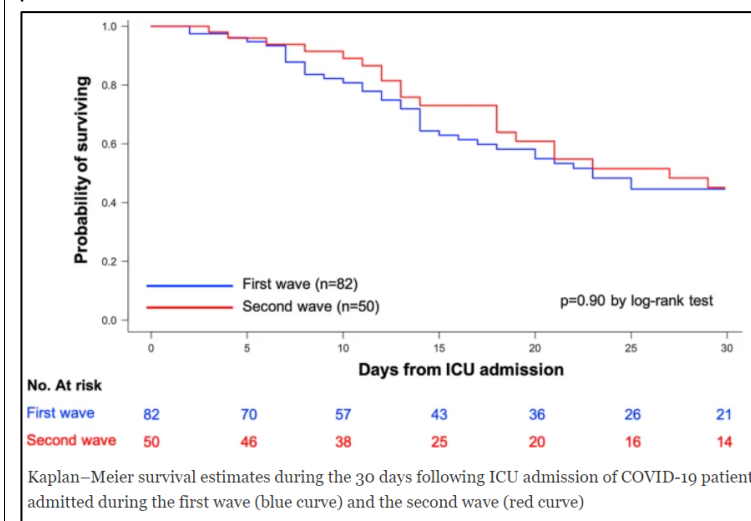
Methods : Retrospective cohort study in 2121 consecutive adults with acute inpatient hospital admission between 4 March and 29 August 2020 with confirmed or suspected COVID-19 in a large academic health system, with adjustment for confounding with propensity score-derived stabilized inverse probability of treatment weights. Chronic immunosuppression was defined as prescriptions for immunosuppressive drugs current at the time of admission. Outcomes included mechanical ventilation, in-hospital mortality, and length of stay.

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| | | | <p>Results : There were 2121 patients admitted with laboratory-confirmed (1967, 93%) or suspected (154, 7%) COVID-19 during the study period, with a median age of 55 years (interquartile range, 40–67). Of these, 108 (5%) were classified as immunosuppressed before COVID-19, primarily with prednisone (>7.5 mg/day), tacrolimus, or mycophenolate mofetil. Among the entire cohort, 311 (15%) received mechanical ventilation; the median (interquartile range) length of stay was 5.2 (2.5–10.6) days, and 1927 (91%) survived to discharge. After adjustment, there were no significant differences in the risk of mechanical ventilation (hazard ratio [HR], .79; 95% confidence interval [CI], .46–1.35), in-hospital mortality (HR, .66; 95% CI, .28–1.55), or length of stay (HR, 1.16; 95% CI, .92–1.47) among individuals with immunosuppression and counterparts.</p> <p>Conclusions : Chronic use of immunosuppressive drugs was neither associated with worse nor better clinical outcomes among adults hospitalized with COVID-19 in one US health system.</p> |
| <p>Rubin R et al</p> <p>JAMA</p> <p>https://jamanetwork.com/journals/jama/fullarticle/2775003</p> | <p>Sorting Out Whether Vitamin D Deficiency Raises COVID-19 Risk</p> | <p>Evidenze in merito al ruolo della vitamina D nella prevenzione delle infezioni e in particolare nel determinare l'esito dell'infezione da SARS-CoV-2.</p> | <p>One of the risk factors du jour for coronavirus disease 2019 (COVID-19) has been vitamin D deficiency.</p> <p>Even Anthony Fauci, MD, has said he takes a vitamin D supplement. Vitamin D “does have an impact on your susceptibility to infection,” Fauci, director of the National Institute of Allergy and Infectious Diseases, told actress Jennifer Garner in a September interview. “I would not mind recommending—and I take it myself—taking vitamin D supplements.”</p> |
| <p>Xie X et al</p> <p>BioRxiv</p> | <p>Neutralization of N501Y mutant SARS-CoV-2 by BNT162b2 vaccine-elicited sera</p> | <p>Il siero di soggetti vaccinati con BNT162b2 (Pfizer) neutralizza in ugual modo la variante N501Y di SARS-CoV-2 e il virus wild type.</p> | <p>Rapidly spreading variants of SARS-CoV-2 that have arisen in the United Kingdom and South Africa share the spike N501Y substitution, which is of particular concern because it is located in the viral receptor binding site for cell entry and increases binding to the receptor (angiotensin converting enzyme 2). We generated</p> |

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| https://www.biorxiv.org/content/10.1101/2021.01.07.425740v1 | | | isogenic N501 and Y501 SARS-CoV-2. Sera of 20 participants in a previously reported trial of the mRNA-based COVID-19 vaccine BNT162b2 had equivalent neutralizing titers to the N501 and Y501 viruses |
| <p>Meduri GU et al</p> <p>Intensive Care Medicine</p> <p>https://doi.org/10.1007/s00134-020-06289-8</p> | <p>Pharmacological principles guiding prolonged glucocorticoid treatment in ARDS</p> | <p>Metanalisi sull'utilizzo di glucocorticoidi nella ARDS.</p> | <p>Current literature addressing the pharmacological principles guiding glucocorticoid (GC) administration in ARDS is scant. This paucity of information may have led to the heterogeneity of treatment protocols and misinterpretation of available findings. GCs are agonist compounds that bind to the GC receptor (GR) producing a pharmacological response. Clinical efficacy depends on the magnitude and duration of exposure to GR. We updated the meta-analysis of randomized trials investigating GC treatment in ARDS, focusing on treatment protocols and response. We synthesized the current literature on the role of the GR in GC therapy including genomic and non-genomic effects, and integrated current clinical pharmacology knowledge of various GCs, including hydrocortisone, methylprednisolone and dexamethasone. This review addresses the role dosage, timing of initiation, mode of administration, duration, and tapering play in achieving optimal response to GC therapy in ARDS. Based on RCTs' findings, GC plasma concentration–time profiles, and pharmacodynamic studies, optimal results are most likely achievable with early intervention, an initial bolus dose to achieve close to maximal GRα saturation, followed by a continuous infusion to maintain high levels of response throughout the treatment period. In addition, patients receiving similar GC doses may experience substantial between-patient variability in plasma concentrations affecting clinical response. GC should be dose-adjusted and administered for a duration targeting clinical and laboratory improvement, followed by dose-tapering to achieve gradual recovery of the suppressed hypothalamic–pituitary–adrenal</p> |

(HPA) axis. These findings have practical clinical relevance. Future RCTs should consider these pharmacological principles in the study design and interpretation of findings.

As many countries in Europe, France faced a second wave COVID-19 pandemic since September, 2020. During the first wave, intensivists faced an unprecedented massive admission of patients with COVID-19 pneumonia requiring invasive mechanical ventilation, sometimes leading to ICUs saturation. They discovered the stereotypical course of this previously unknown disease with its own specificities including the need for deep sedation and neuromuscular blockade, the increased risk of thrombotic and hemorrhagic events, and the prolonged duration of mechanical ventilation with high rate of delirium. Importantly, several randomized controlled trials conducted during this first wave highlighted the beneficial effects of early administration of glucocorticoids for critically ill COVID-19 patients.



Contou D et al

Critical Care

<https://ccforum.biomedcentral.com/articles/10.1186/s13054-020-03449-6>

Comparison between first and second wave among critically ill COVID-19 patients admitted to a French ICU: no prognostic improvement during the second wave?

Nessuna differenza di mortalità fra i malati della prima e seconda ondata di COVID-19 in una rianimazione francese.

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| <p>Cohen JB et al</p> <p>The Lancet</p> <p>https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30558-0/fulltext</p> | <p>Continuation versus discontinuation of renin–angiotensin system inhibitors in patients admitted to hospital with COVID-19: a prospective, randomised, open-label trial</p> | <p>Trial clinico multicentrico condotto in diversi Paesi del mondo che non dimostra alcuna differenza nel decorso di COVID-19 nei pazienti ospedalizzati che hanno continuato o interrotto un trattamento con inibitori del sistema renina-angiotensina-aldosterone.</p> | <p>Background : Biological considerations suggest that renin–angiotensin system inhibitors might influence the severity of COVID-19. We aimed to evaluate whether continuing versus discontinuing renin–angiotensin system inhibitors (angiotensin-converting enzyme inhibitors or angiotensin receptor blockers) affects outcomes in patients admitted to hospital with COVID-19.</p> <p>Methods : The REPLACE COVID trial was a prospective, randomised, open-label trial done at 20 large referral hospitals in seven countries worldwide. Eligible participants were aged 18 years and older who were admitted to hospital with COVID-19 and were receiving a renin–angiotensin system inhibitor before admission. Individuals with contraindications to continuation or discontinuation of renin–angiotensin system inhibitor therapy were excluded. Participants were randomly assigned (1:1) to continuation or discontinuation of their renin–angiotensin system inhibitor using permuted block randomisation, with allocation concealed using a secure web-based randomisation system. The primary outcome was a global rank score in which participants were ranked across four hierarchical tiers incorporating time to death, duration of mechanical ventilation, time on renal replacement or vasopressor therapy, and multiorgan dysfunction during the hospitalisation. Primary analyses were done in the intention-to-treat population. The REPLACE COVID trial is registered with ClinicalTrials.gov, NCT04338009.</p> <p>Findings : Between March 31 and Aug 20, 2020, 152 participants were enrolled and randomly assigned to either continue or discontinue renin–angiotensin system inhibitor therapy (continuation group n=75; discontinuation group n=77). Mean age of participants was 62 years (SD 12), 68 (45%) were female, mean body-mass index was 33 kg/m² (SD 8), and 79 (52%) had diabetes. Compared with discontinuation of renin–angiotensin system</p> |
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| | | | <p>inhibitors, continuation had no effect on the global rank score (median rank 73 [IQR 40–110] for continuation vs 81 [38–117] for discontinuation; β-coefficient 8 [95% CI –13 to 29]). There were 16 (21%) of 75 participants in the continuation arm versus 14 (18%) of 77 in the discontinuation arm who required intensive care unit admission or invasive mechanical ventilation, and 11 (15%) of 75 participants in the continuation group versus ten (13%) of 77 in the discontinuation group died. 29 (39%) participants in the continuation group and 28 (36%) participants in the discontinuation group had at least one adverse event (χ^2 test of adverse events between treatment groups $p=0.77$). There was no difference in blood pressure, serum potassium, or creatinine during follow-up across the two groups.</p> <p>Interpretation : Consistent with international society recommendations, renin–angiotensin system inhibitors can be safely continued in patients admitted to hospital with COVID-19.</p> |
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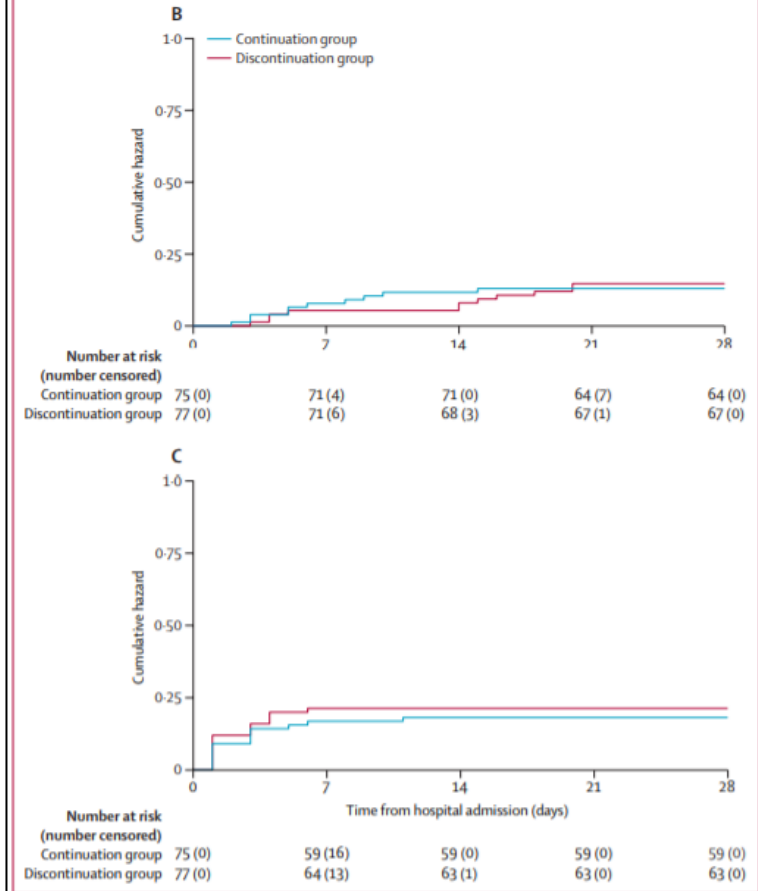
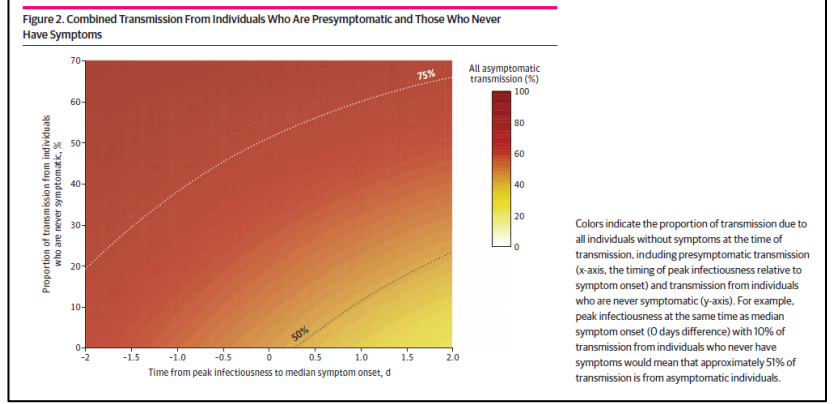


Figure 2: Outcomes for the primary endpoint, all-cause death, and intensive care unit admission or invasive mechanical ventilation

(A) The distribution of the primary endpoint (hierarchical rank score) in the continuation and discontinuation groups. The x-axis (and shaded area) shows the frequency density of rank distributions in each treatment group, the white dots show the median global rank score, the solid boxes show the IQR, and the vertical lines show the upper-adjacent and lower-adjacent values. (B) The cumulative hazard for all-cause death. (C) The cumulative hazard for intensive care unit admission or invasive mechanical ventilation.

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| <p>Johansson MA et al</p> <p>JAMA</p> <p>https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2774707</p> | <p>SARS-CoV-2 Transmission From People Without COVID-19 Symptoms.</p> | <p>Modello di diffusione di SARS-CoV-2 basato sui dati pubblicati, che stima nel 59% la quota di contagi attribuibile a persone asintomatiche. Per questo motivo le misure preventive universali quali l'utilizzo delle mascherine, il distanziamento e l'igiene delle mani saranno a lungo necessarie.</p> | <p>Importance: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the etiology of coronavirus disease 2019 (COVID-19), is readily transmitted person to person. Optimal control of COVID-19 depends on directing resources and health messaging to mitigation efforts that are most likely to prevent transmission, but the relative importance of such measures has been disputed. Objective: To assess the proportion of SARS-CoV-2 transmissions in the community that likely occur from persons without symptoms. Design, Setting, and Participants: This decision analytical model assessed the relative amount of transmission from presymptomatic, never symptomatic, and symptomatic individuals across a range of scenarios in which the proportion of transmission from people who never develop symptoms (ie, remain asymptomatic) and the infectious period were varied according to published best estimates. For all estimates, data from a meta-analysis was used to set the incubation period at a median of 5 days. The infectious period duration was maintained at 10 days, and peak infectiousness was varied between 3 and 7 days (-2 and +2 days relative to the median incubation period). The overall proportion of SARS-CoV-2 was varied between 0% and 70% to assess a wide range of possible proportions. Main Outcomes and Measures: Level of transmission of SARS-CoV-2 from presymptomatic, never symptomatic, and symptomatic individuals. Results: The baseline assumptions for the model were that peak infectiousness occurred at the median of symptom onset and that 30% of individuals with infection never develop symptoms and are 75% as infectious as those who do develop symptoms. Combined, these baseline assumptions imply that persons with infection who never develop symptoms may account for approximately 24% of all transmission. In this base case, 59% of all transmission came from asymptomatic transmission,</p> |
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comprising 35% from presymptomatic individuals and 24% from individuals who never develop symptoms. Under a broad range of values for each of these assumptions, at least 50% of new SARS-CoV-2 infections was estimated to have originated from exposure to individuals with infection but without symptoms. Conclusions and Relevance: In this decision analytical model of multiple scenarios of proportions of asymptomatic individuals with COVID-19 and infectious periods, transmission from asymptomatic individuals was estimated to account for more than half of all transmissions. In addition to identification and isolation of persons with symptomatic COVID-19, effective control of spread will require reducing the risk of transmission from people with infection who do not have symptoms. These findings suggest that measures such as wearing masks, hand hygiene, social distancing, and strategic testing of people who are not ill will be foundational to slowing the spread of COVID-19 until safe and effective vaccines are available and widely used.



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| <p>Xiu N et al</p> <p>Cell</p> <p>https://www.cell.com/cell/fulltext/S0092-8674(21)00004-0</p> | <p>Multi-organ Proteomic Landscape of COVID-19 Autopsies</p> | <p>Analisi proteomica di 144 campioni autoptici su 7 organi prelevati da 19 persone decedute per COVID-19, rispetto a controlli deceduti per altre cause, al fine di indagare le alterazioni alla base della gravità della malattia.</p> | <p>The molecular pathology of multi-organ injuries in COVID-19 patients remains unclear, preventing effective therapeutics development. Here, we report a proteomic analysis of 144 autopsy samples from seven organs in 19 COVID-19 patients. We quantified 11,394 proteins in these samples, in which 5336 were perturbed in the COVID-19 patients compared to controls. Our data showed that cathepsin L1, rather than ACE2, was significantly upregulated in the lung from the COVID-19 patients. Systemic hyperinflammation and dysregulation of glucose and fatty acid metabolism were detected in multiple organs. We also observed dysregulation of key factors involved in hypoxia, angiogenesis, blood coagulation and fibrosis in multiple organs from the COVID-19 patients. Evidence for testicular injuries include reduced Leydig cells, suppressed cholesterol biosynthesis and sperm mobility. In summary, this study depicts a multi-organ proteomic landscape of COVID-19 autopsies that furthers our understanding of the biological basis of COVID-19 pathology.</p> |
| <p>Salama C et al</p> <p>NEJM</p> <p>https://www.nejm.org/doi/full/10.1056/NEJMoa2030340?query=featured_home</p> | <p>Tocilizumab in Patients Hospitalized with Covid-19 Pneumonia</p> | <p>Trial clinico randomizzato su 389 pazienti ospedalizzati con polmonite COVID-19 relata (con attenzione alla rappresentazione delle minoranze etniche) non ventilati meccanicamente, trattati con standard of care e tocilizumab EV/placebo : nei trattati con tocilizumab vi è minor rischio di ricorso a ventilazione meccanica, ma non si dimostra un</p> | <p>BACKGROUND : Coronavirus disease 2019 (Covid-19) pneumonia is often associated with hyperinflammation. Despite the disproportionate incidence of Covid-19 among underserved and racial and ethnic minority populations, the safety and efficacy of the anti–interleukin-6 receptor antibody tocilizumab in patients from these populations who are hospitalized with Covid-19 pneumonia are unclear.</p> <p>METHODS : We randomly assigned (in a 2:1 ratio) patients hospitalized with Covid-19 pneumonia who were not receiving mechanical ventilation to receive standard care plus one or two doses of either tocilizumab (8 mg per kilogram of body weight intravenously) or placebo. Site selection was focused on the</p> |

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| | | <p>vantaggio di sopravvivenza a 28 giorni.</p> | <p>inclusion of sites enrolling high-risk and minority populations. The primary outcome was mechanical ventilation or death by day 28.</p> <p>RESULTS : A total of 389 patients underwent randomization, and the modified intention-to-treat population included 249 patients in the tocilizumab group and 128 patients in the placebo group; 56.0% were Hispanic or Latino, 14.9% were Black, 12.7% were American Indian or Alaska Native, 12.7% were non-Hispanic White, and 3.7% were of other or unknown race or ethnic group. The cumulative percentage of patients who had received mechanical ventilation or who had died by day 28 was 12.0% (95% confidence interval [CI], 8.5 to 16.9) in the tocilizumab group and 19.3% (95% CI, 13.3 to 27.4) in the placebo group (hazard ratio for mechanical ventilation or death, 0.56; 95% CI, 0.33 to 0.97; P=0.04 by the log-rank test). Clinical failure as assessed in a time-to-event analysis favored tocilizumab over placebo (hazard ratio, 0.55; 95% CI, 0.33 to 0.93). Death from any cause by day 28 occurred in 10.4% of the patients in the tocilizumab group and 8.6% of those in the placebo group (weighted difference, 2.0 percentage points; 95% CI, -5.2 to 7.8). In the safety population, serious adverse events occurred in 38 of 250 patients (15.2%) in the tocilizumab group and 25 of 127 patients (19.7%) in the placebo group.</p> <p>CONCLUSIONS : In hospitalized patients with Covid-19 pneumonia who were not receiving mechanical ventilation, tocilizumab reduced the likelihood of progression to the composite outcome of mechanical ventilation or death, but it did not improve survival. No new safety signals were identified.</p> |
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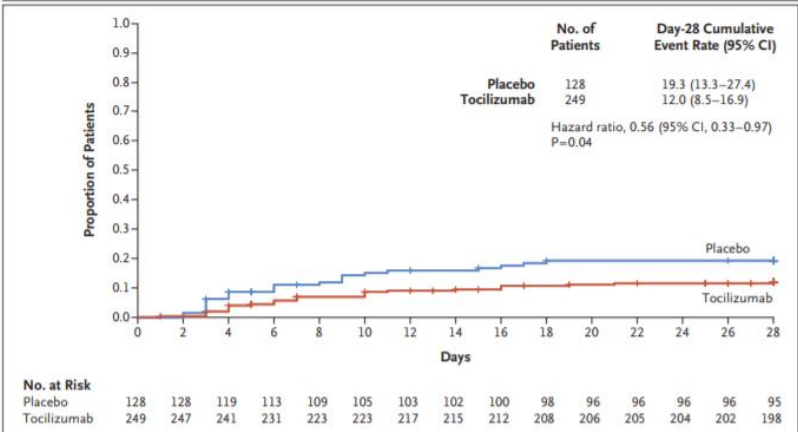
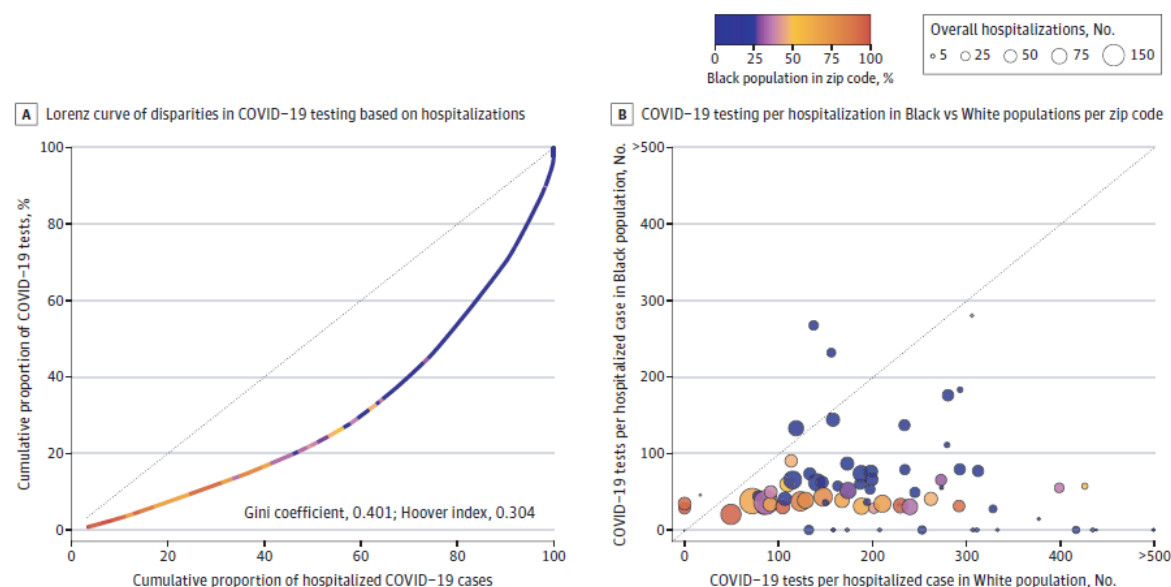
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| | | |  <p>Figure 2. Time to Mechanical Ventilation or Death by Day 28 in the Modified Intention-to-Treat Population.</p> <p>The cumulative proportion of patients was estimated with the Kaplan–Meier method and compared in the two groups with the use of the stratified log-rank test. The stratified Cox proportional-hazards model was used to estimate the hazard ratio and 95% confidence interval. Data on patients who did not receive mechanical ventilation or who died on or before day 28 were censored at day 28 or the date of the last available follow-up, whichever occurred first.</p> |
| <p>Mody A et al</p> <p>JAMA</p> <p>https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2774715</p> | <p>Using Lorenz Curves to Measure Racial Inequities in COVID-19 Testing</p> | <p>Studio della distribuzione dei test per SARS-CoV-2 in diverse province degli USA, in cui si dimostra che essi non sono stati effettuati in numero proporzionale alla gravità di interessamento di una determinata comunità.</p> | <p>Racial disparities have been widely documented during the coronavirus disease 2019 (COVID-19) pandemic, but there has been limited focus on equitable allocation of the pandemic’s most critical but limited resource: COVID-19 testing. Equitable testing is paramount to a successful COVID-19 response and is essential for early case detection, self-isolation, and overall prevention of onward transmission. We adapted a well-established tool for measuring inequity from economics—the Lorenz curve—to put forth a metric for quantifying COVID-19 related inequities.</p> |

Figure. Disparities in Coronavirus Disease 2019 (COVID-19) Testing Relative to Hospitalizations in 7 Counties in the St Louis Region, March 14, 2020, to August 10, 2020



Davidson BL et al

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Pharyngeal Antisepsis to
Reduce COVID-19
Pneumonia

L'antisepsi dell'orofaringe prima del riposo notturno, periodo in cui avviene l'aspirazione di materiale verso le basse vie aeree, potrebbe ridurre il rischio di infezione da SARS-CoV-2 abbattendo la carica virale, in analogia a quanto dimostrato ad esempio con il gonococco.

Antiseptic mouthwash use to control coronavirus disease 2019 (COVID-19) has been proposed, disputed, and dismissed without understanding the proposal and without serious consideration of merits and counterarguments. Adding a proven, safe, and evidence-based clinically reasonable measure to existing approaches of universal masking and social distancing, while awaiting a safe and effective vaccine, seems a constructive approach worth implementing and observing for efficacy. We describe how adding pharyngeal antisepsis, "washing the throat," before sleeping, when healthy adults of all ages aspirate material from above the larynx, can help protect individuals against COVID-19 pneumonia and,

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| | | | hence, help protect society. We also address critiques presented against widespread adoption of pharyngeal antisepsis. |
| Wood S et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMms2033790?query=featured_home | Beyond Politics — Promoting Covid-19 Vaccination in the United States | Idee di comunicazione per promuovere in modo efficace la vaccinazione contro SARS-CoV-2 fra i pazienti. | The United States has invested more than \$10 billion in Operation Warp Speed to fast-track SARS-CoV-2 vaccines from conception to market in 1 year. The result is 11 candidates reaching the final stage of Food and Drug Administration testing — a phenomenal improvement over past development timelines. Indeed, two SARS-CoV-2 vaccines are already available to Americans. Given this level of investment, skill, and good fortune in developing a vaccine, it will be tragic if we fail to curtail the virus because Americans refuse to be vaccinated. |
| Callaway E et al Nature https://www.nature.com/articles/d41586-021-00031-0 | Could new COVID variants undermine vaccines? Labs scramble to find out | Aggiornamento sugli studi in corso per comprendere se le varianti più recentemente emerse di SARS-CoV-2 possano vanificare lo sforzo vaccinale. | As concern grows over faster-spreading variants of coronavirus, labs worldwide are racing to unpick the biology of these viruses. Scientists want to understand why SARS-CoV-2 variants identified in the United Kingdom and South Africa seem to be spreading so quickly, and whether they might diminish the potency of vaccines or overcome natural immunity and lead to spate of reinfections. |
| CDC COVID-19 Response Team; Food and Drug Administration Morbidity and Mortality Weekly Report https://www.cdc.gov/mmwr/volumes/70/wr/mm7 | Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine — United States, December 14–23, 2020 | Report di 21 casi di anafilassi a seguito della somministrazione di quasi 2 milioni di dosi del vaccino Pfizer contro SARS-CoV-2 negli USA. | What is already known about this topic? Anaphylaxis is a severe, life-threatening allergic reaction that occurs rarely after vaccination. What is added by this report? During December 14–23, 2020, monitoring by the Vaccine Adverse Event Reporting System detected 21 cases of anaphylaxis after administration of a reported 1,893,360 first doses of the Pfizer-BioNTech COVID-19 vaccine (11.1 cases per million doses); 71% of these occurred within 15 minutes of vaccination. |

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| 002e1.htm?s_cid=mm7002e1_w | | | <p>What are the implications for public health practice?</p> <p>Locations administering COVID-19 vaccines should adhere to CDC guidance for use of COVID-19 vaccines, including screening recipients for contraindications and precautions, having the necessary supplies available to manage anaphylaxis, implementing the recommended postvaccination observation periods, and immediately treating suspected cases of anaphylaxis with intramuscular injection of epinephrine.</p> |
| <p>Quinti I et al</p> <p>Expert Review of Clinical Immunology</p> <p>https://www.tandfonline.com/doi/full/10.1080/1744666X.2021.1873767</p> | <p>Clinical management of patients with primary immunodeficiencies during the COVID-19 pandemic.</p> | <p>Revisione delle letterature sull'impatto di COVID-19 sulle persone con immunodeficienze congenite : numericamente scarso, forse per la tendenza ad aderire scrupolosamente alle misure di prevenzione.</p> | <p>Introduction: Patients affected by Inborn Errors of Immunity (IEI) represent a potential group-at-risk in the current COVID-19 pandemic. Studies on large and small cohorts of IEI reported a huge variability clinical manifestations associated to SARS-Cov-2, ranging from asymptomatic, mild, moderate/severe to death. A great impulse to improve remote assistance programs and to switch to home-based treatment to reduce mobility and face to face contacts has been implemented.</p> <p>Areas covered: The authors completed a comprehensive review of the literature by searching the PubMed database for studies on large and small cohorts and case reports of IEI patients with COVID-19, with the aim to provide useful information for their clinical management during the COVID-19 pandemic.</p> <p>Expert opinion: Surprisingly, a low number of IEI patients affected by SARS-Cov-2 were reported with a risk to die for COVID-19 overlapping that of the general population. The low number might be explained by the choice of most physicians to inform early in the pandemic about safety measures, to switch most of the IEI patients to home therapy and to remote assistance. The guidelines issued by the scientific societies and periodically updated, represent the best tool for the clinical management of IEI patients.</p> |

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| <p>Krone M et al</p> <p>Euro Surveill</p> <p>https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.1.2001365</p> | <p>Control of a COVID-19 outbreak in a nursing home by general screening and cohort isolation in Germany, March to May 2020.</p> | <p>Efficacia di test universale e isolamento nel controllare un cluster di infezione da SARS-CoV-2 in una casa di riposo in Germania : adeguate risorse per garantire tale approccio appaiono irrinunciabili.</p> | <p>Elderly care facilities have become a major focus of coronavirus disease (COVID-19) control. Here, we describe an outbreak of COVID-19 in a nursing home in Germany from 8 March to 4 May 2020 (58 days), and the effect of an intervention of general screening and cohort isolation. COVID-19 cases among residents and staff were recorded on a daily basis from the first positive SARS-CoV-2 test from a resident on 8 March 2020, until 4 May 2020 when the last staff member was classified COVID-19 negative. Eighty of 160 residents (50%) and 37 of 135 staff members (27%) tested positive for SARS-CoV-2. Twenty-seven of the 80 residents were asymptomatic but tested positive during the first general screening. Cohort isolation of SARS-CoV-2 positive residents by reorganising the facility proved to be a major effort. After the intervention, four further asymptomatic residents tested positive in follow-up screenings within a period of 6 days, and were possibly infected prior to the intervention. Thereafter, no further infections were recorded among residents. The described outbreak was controlled by implementing general screening and rigorous cohort isolation, providing a blueprint for similar facilities.</p> |
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| | | | <p>Number of newly diagnosed COVID-19 cases among nursing home residents and staff by test result date, Wuerzburg, Germany, 8 March–4 May 2020 (n = 160 residents, n = 135 staff)</p> <p>COVID-19: coronavirus disease; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.</p> |
| <p>Demartini B et al</p> <p>Frontiers in Psychiatry</p> <p>https://www.frontiersin.org/articles/10.3389/fpsy.2020.561345/full</p> | <p>Early Psychiatric Impact of COVID-19 Pandemic on the General Population and Healthcare Workers in Italy: A Preliminary Study.</p> | <p>Esito di un sondaggio su 432 persone in merito all'impatto psicologico dei primi mesi di pandemia di COVID-19 in Lombardia : i più colpiti da sintomi di ansia, depressione e burnout sono giovani, donne e operatori sanitari, rispetto ai quali sono auspicabili misure di sostegno.</p> | <p>Introduction: Since February 2020, the outbreak of COVID-19 spread to several countries worldwide, including Italy. In this study, we aimed to assess the psychopathological impact of the pandemic across the general population of Lombardy, the most affected Italian region, and to compare the prevalence of psychiatric symptoms between the general public and healthcare workers.</p> <p>Methods: Four hundred and thirty-two participants completed an online survey including: the Depression, Anxiety and Stress Scale–21 items (DASS-21), the Impact of Event Scale—Revised (IES-R) and the Pittsburgh Sleep Quality Index (PQSI). Healthcare workers were also asked to complete the Maslach Burnout Inventory (MBI).</p> <p>Results: At the DASS-21, 33.3% of the responders presented pathological levels of stress, 25.5% of anxiety, and 35.9% of depression. At the IES-R, 13.9% appeared at risk of developing Post-Traumatic Stress Disorder (PTSD). At the PQSI, 57.6% presented sleep disturbances. Female gender and younger age predicted</p> |

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| | | | <p>higher scores of distress. Healthcare workers presented higher levels of psychiatric symptoms than the general public. Moreover, working in contact with COVID-19 patients predicted higher scores at the IES-R subscale Intrusion.</p> <p>Conclusion: Our results showed that about a third of our sample presented symptoms of stress, anxiety, and depression during the first month of the COVID-19 pandemic outbreak in Lombardy; more than half of the responders presented sleep disturbances, and 13% appeared at risk of PTSD. Italian authorities should develop specific strategies to guarantee psychological support to the population of Lombardy, with particular attention to women, young people, and healthcare workers exposed to COVID-19 patients.</p> |
| <p>Iacobucci G et al</p> <p>BMJ</p> <p>https://www.bmj.com/content/372/bmj.n18</p> | <p>Covid-19 vaccination: What's the evidence for extending the dosing interval?</p> | <p>Domande e risposte sulla decisione del Regno Unito di prolungare l'intervallo fra le due dosi di vaccino anti-SARS-CoV-2 (Pfizer e Astra-Zeneca), motivata dalla volontà di somministrare almeno una dose a più persone possibile.</p> | <p>On 30 December the four UK chief medical officers announced that the second doses of the covid vaccines should be given towards the end of 12 weeks rather than in the previously recommended 3-4 weeks. Gareth Iacobucci and Elisabeth Mahase look at the questions this has raised</p> |