# RICERCA BIBLIOGRAFICA COVID 19

## SETTIMANA 22.03 – 28.03.2021

## FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE

## DOTT.SSA ELEONORA TADDEI

| AUTORE/RIVISTA | TITOLO | OUTCOME PRINCIPALE | ABSTRACT |
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| AstraZeneca<br><br>Area Stampa<br><br>https://www.astrazeneca.it/content/az-it/area-stampa/press-releases/2021/COMUNICATO_RISULTATI_STUDIO_USA.html#! | Vaccino AZD1222 per il COVID-19. Raggiunto l'endpoint primario di efficacia nell'analisi ad interim dello studio di Fase III condotto negli Stati Uniti | I comunicati stampa che precedono le pubblicazioni scientifiche non sono una novità in dopo un anno di pandemia : AstraZeneca annuncia i risultati dell'analisi ad interim del trial di fase III sul vaccino a vettore adenovirale AZD1222 (ChAdOx1 nCoV-19 ) contro SARS-CoV-2. Protocollo : https://clinicaltrials.gov/ct2/show/NCT04516746?term=NCT04516746&draw=2&rank=1 | Lo studio di fase III condotto da AstraZeneca negli Stati Uniti (US) ha dimostrato che AZD1222 ha un'efficacia statisticamente significativa del 79% nel prevenire i sintomi legati al COVID-19 e del 100% nel prevenire la malattia grave e l'ospedalizzazione.<br>Questa analisi ad interim di sicurezza ed efficacia si è basata sui dati raccolti su 32.449 partecipanti, tra i quali si sono verificati 141 casi di sintomatologia legata al COVID-19. Lo studio ha previsto una randomizzazione 2:1 tra vaccino e placebo.<br>Il profilo di efficacia di AZD1222 è risultato coerente per tutta la popolazione dello studio. In particolare, nei partecipanti di età pari o superiore ai 65 anni, l'efficacia del vaccino è risultata dell'80%. |

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| European Medicines Agency<br><br>https://www.ema.europa.eu/en/news/ema-advises-against-use-ivermectin-prevention-treatment-covid-19-outside-randomised-clinical-trials | EMA advises against use of ivermectin for the prevention or treatment of COVID-19 outside randomised clinical trials | Alla luce degli studi limitati a disposizione, l'EMA scoraggia l'uso di ivermectina per la terapia di COVID-19 al di fuori dei trial clinici. | EMA has reviewed the latest evidence on the use of ivermectin for the prevention and treatment of COVID-19 and concluded that the available data do not support its use for COVID-19 outside well-designed clinical trials.<br>In the EU, ivermectin tablets are approved for treating some parasitic worm infestations while ivermectin skin preparations are approved for treating skin conditions such as rosacea. Ivermectin is also authorised for veterinary use for a wide range of animal species for internal and external parasites.<br>Ivermectin medicines are not authorised for use in COVID-19 in the EU, and EMA has not received any application for such use. |
| Yang HS et al<br><br>JAMA<br><br>https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2777743 | Association of Age With SARS-CoV-2 Antibody Response | Studio cross sectional che valuta la differente risposta immunitaria (in termini di livelli di IgG, immunoglobuline totali, attività neutralizzante, avidità) fra pazienti di diverse fasce d'età con storia di COVID-19 : il titolo è negativamente correlato con l'età nella fascia pediatrica, mentre aumenta con l'età negli adulti (possibile ruolo di obesità e altre condizioni proinfiammatorie tipiche dell'età avanzata) ; al contrario l'avidità, ovvero la forza del legame antigene-anticorpo, è maggiore in età | Importance  Accumulating evidence suggests that children infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are more likely to manifest mild symptoms and are at a lower risk of developing severe respiratory disease compared with adults. It remains unknown how the immune response in children differs from that of adolescents and adults.<br>Objective  To investigate the association of age with the quantity and quality of SARS-CoV-2 antibody responses.<br>Design, Setting, and Participants  This cross-sectional study used 31 426 SARS-CoV-2 antibody test results from pediatric and adult patients. Data were collected from a New York City hospital from April 9 to August 31, 2020. The semiquantitative immunoglobin (Ig) G levels were compared between 85 pediatric and 3648 adult patients. Further analysis of SARS-CoV-2 antibody profiles was performed on sera from 126 patients aged 1 to 24 years.<br>Main Outcomes and Measures  SARS-CoV-2 antibody positivity rates and IgG levels were evaluated in patients from a wide range of age groups (1-102 years). SARS-CoV-2 IgG level, total antibody (TAb) level, surrogate neutralizing antibody (SNAb) activity, and antibody |

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| | | più precoce. Ancora non è chiaro perché la malattia sia generalmente più benigna nei bambini. | binding avidity were compared between children (aged 1-10 years), adolescents (aged 11-18 years), and young adults (aged 19-24 years).<br>Results Among 31 426 antibody test results (19 797 [63.0%] female patients), with 1194 pediatric patients (mean [SD] age, 11.0 [5.3] years) and 30 232 adult patients (mean [SD] age, 49.2 [17.1] years), the seroprevalence in the pediatric (197 [16.5%; 95% CI, 14.4%-18.7%]) and adult (5630 [18.6%; 95% CI, 18.2%-19.1%]) patient populations was similar. The SARS-CoV-2 IgG level showed a negative correlation with age in the pediatric population ($r = -0.45$, $P < .001$) and a moderate but positive correlation with age in adults ($r = 0.24$, $P < .001$). Patients aged 19 to 30 years exhibited the lowest IgG levels (eg, aged 25-30 years vs 1-10 years: 99 [44-180] relative fluorescence units [RFU] vs 443 [188-851] RFU). In the subset cohort aged 1 to 24 years, IgG, TAb, SNAb and avidity were negatively correlated with age (eg, IgG: $r = -0.51$; $P < .001$). Children exhibited higher median (IQR) IgG levels, TAb levels, and SNAb activity compared with adolescents (eg, IgG levels: 473 [233-656] RFU vs 191 [82-349] RFU; $P < .001$) and young adults (eg, IgG levels: 473 [233-656] RFU vs 85 [38-150] RFU; $P < .001$). Adolescents also exhibited higher median (IQR) TAb levels, IgG levels, and SNAb activity than young adults (eg, TAb levels: 961 [290-2074] RFU vs 370 [125-697]; $P = .006$). In addition, children had higher antibody binding avidity compared with young adults, but the difference was not significant.<br>Conclusions and Relevance The results of this study suggest that SARS-CoV-2 viral specific antibody response profiles are distinct in different age groups. Age-targeted strategies for disease screening and management as well as vaccine development may be warranted. |

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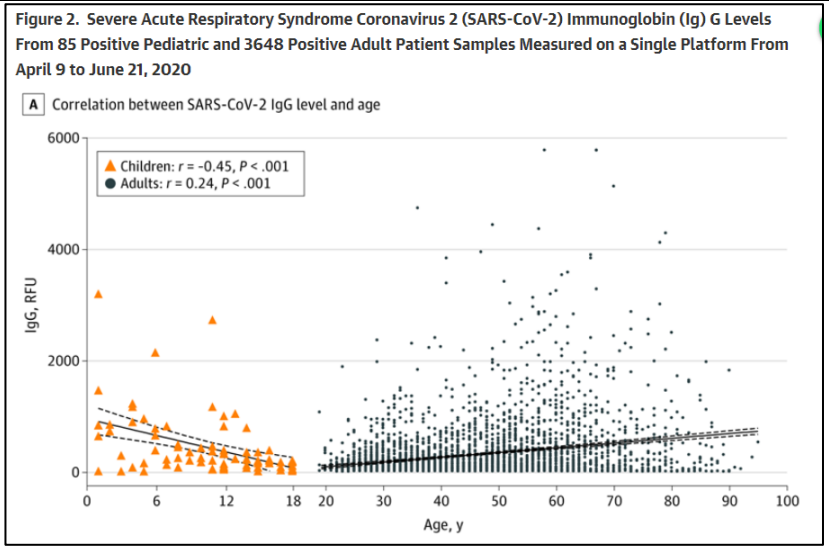
| | | | **Figure 2. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Immunoglobin (Ig) G Levels From 85 Positive Pediatric and 3648 Positive Adult Patient Samples Measured on a Single Platform From April 9 to June 21, 2020**<br>  |
| Lin AL et al<br><br>JAMA<br><br>https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2777737 | Body Weight Changes During Pandemic-Related Shelter-in-Place in a Longitudinal Cohort Study | Studio di coorte su 269 persone condotto in California nel periodo febbraio-giugno 2020, quando sono state applicate misure di « lockdown » di varia entità negli USA : si registra un aumento del peso corporeo di quasi 1 Kg/mese associato alle restrizioni agli spostamenti. | As of January 22, 2021, there were more than 98 million confirmed cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), more than 24 million of which are attributed to the US alone. Recent surges in SARS-CoV-2 and the threat of a second wave have prompted many states to reconsider reopening timelines. During the initial US surge, 45 out of 50 state governments issued shelter-in-place (SIP) orders from March 19, 2020, to April 6, 2020, to slow disease transmission. The initial SIP coincided with an observed decrease in daily step counts, likely reflective of changes in physical activity and patterns of daily living, as well as concurrent self-reported increases in snacking and overeating. We therefore sought to investigate ambulatory weight changes of a longitudinal cohort during initial SIP orders to better understand the possible downstream health implications of prolonged SIP. |

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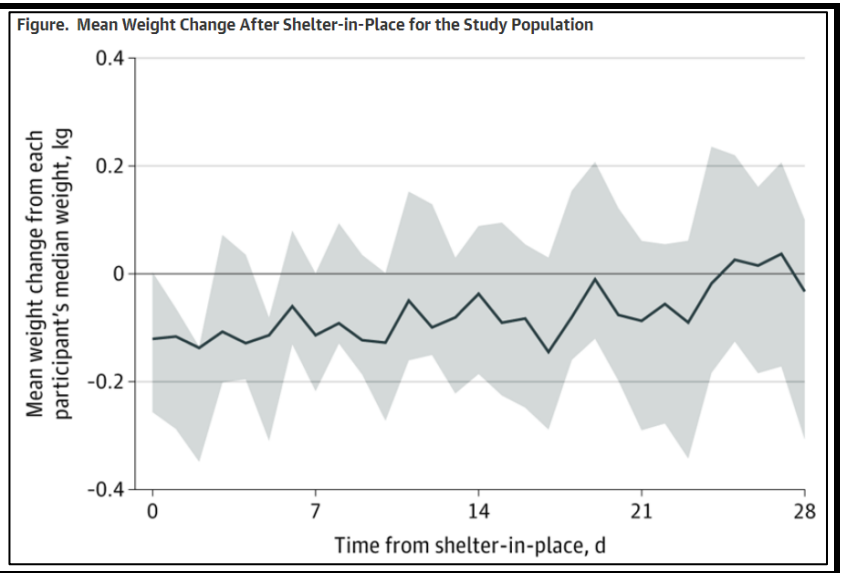
| | | |  |
| Cummins NW<br><br>Clinical Infectious Diseases<br><br>https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab220/6179767?searchresult=1 | Remdesivir: An antiviral still seeking a raison d'être | A margine di un commento su un trial clinico che valuta l'utilizzo di remdesivir nei sopravvissuti a infezione da Ebola (per cui il farmaco era stato sintetizzato), l'autore suggerisce che un antivirale ha poche possibilità di essere efficace in fase acuta di malattia – come del resto confermano gli scarsi benefici mostrati dagli studi su remdesivir e SARS-CoV-2. In pazienti ad alto rischio, per i quali divengono accettabili le difficoltà legate alla somministrazione endovena, potrebbe essere | It is likely that any viral replication that would be biologically important to inhibit therapeutically, in the context of an acute viral infection, such as EVD or COVID-19, occurs prior to: 1) the recognition of the viral infection (based on symptom or diagnostic testing), 2) initiation of treatment, and 3) accumulation of sufficient active drug in the relevant cellular and tissue compartments that would be needed to inhibit said replication. The battle is over, and the enemy has moved on before the first defensive maneuver is even begun. |

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| | | giustificato il ricorso a remdesivir nella profilassi post-esposizione. | |
| Rasmussen AL et al<br><br>Science<br><br>https://science.sciencemag.org/content/371/6535/1206 | SARS-CoV-2 transmission without symptoms | Le infezioni asintomatiche da SARS-CoV-2 sono stimate tra 17 e 30% del totale e la contagiosità degli asintomatici è molto difficile da stabilire, in quanto spesso non sono testati se non in contesti in cui si pratica lo screening universale (case di riposo, ospedali), che sono di per sé ad alto rischio di trasmissione. | Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has a potentially long incubation period and spreads opportunistically among those who are unaware they are infected. Asymptomatic COVID-19 cases are those that do not develop symptoms for the duration of infection, whereas presymptomatic cases develop symptoms later in the course of infection, but both are crucial drivers of transmission. Transmission without symptoms poses specific challenges for determining the infectious timeline and potential exposures. Early in the pandemic, most transmission was from undocumented cases, suggesting that spread was driven by people who were either asymptomatic or experiencing such mild disease that it was not recognized as COVID-19. Contagious people without observable signs of illness make infection prevention efforts vulnerable to compliance with masking, distancing, hand hygiene, symptom screening, and ultimately, people staying home when possible. The lack of widespread testing in asymptomatic individuals further complicates COVID-19 mitigation and control efforts. |

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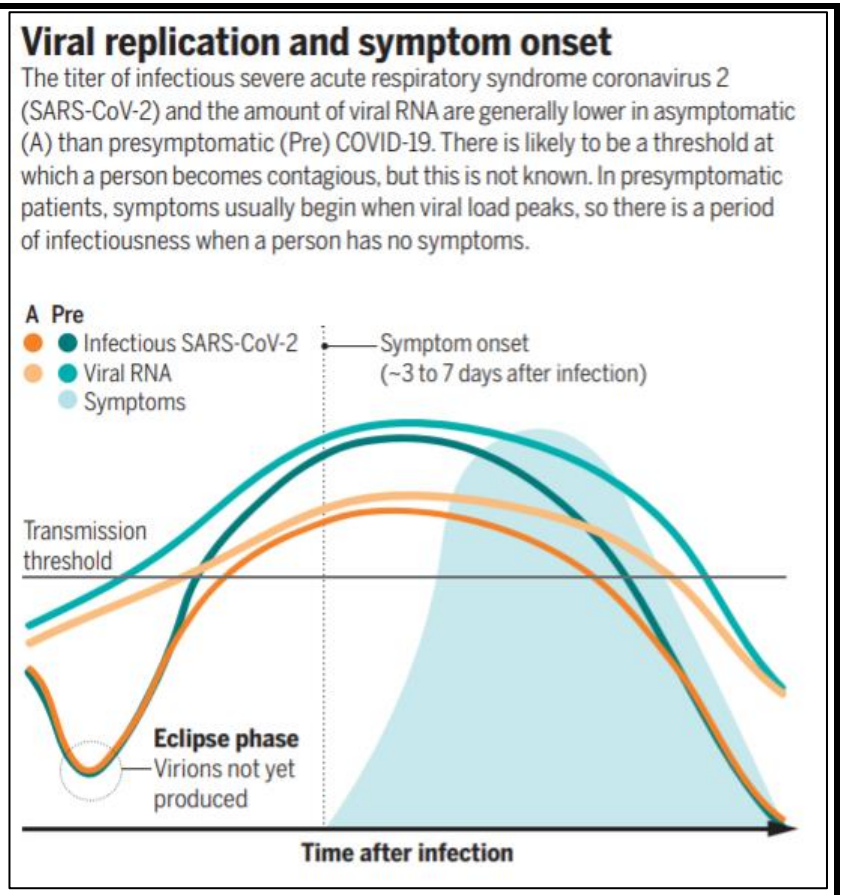
| | | |  |
| Quotidianosanità<br><br>http://www.quotidianosanita.it/cronache/articolo.php?articolo_id=93637 | Nobel. I professionisti sanitari italiani candidati a quello per “La pace”. Ecco come nasce la proposta | Candidatura al Premio Nobel per la pace del 2021 per il « corpo sanitario italiano ». La notizia non è stata divulgata dalla Fondazione Nobel, che per statuto mantiene riservate le liste dei candidati per 50 anni, ma dalla Fondazione | La proposta è stata lanciata dalla Fondazione Gorbachev [ https://gorbachevfoundation.it/associazione/ ] che, a un anno dall’inizio della pandemia, vorrebbe vedere l’alto riconoscimento conferito ai “medici, infermieri, farmacisti, psicologi, fisioterapisti, biologi, tecnici, operatori civili e militari tutti, che hanno affrontato in situazioni spesso drammatiche e proibitive l’emergenza COVID 19 con straordinaria abnegazione, molti dei quali sacrificando la |

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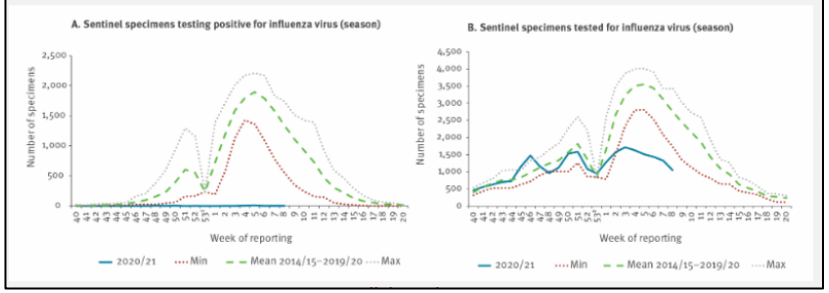
| | | proponente. Tra le altre candidature pubblicizzate, quella di Greta Thumberg. | propria vita per preservare quella degli altri e per contenere la diffusione della pandemia". |
| Adloch C et al<br><br>Eurosurveillance<br><br>https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.11.2100221 | Very little influenza in the WHO European Region during the 2020/21 season, weeks 40 2020 to 8 2021 | La stagione influenzale 2020-2021 si conferma del tutto anomala in base ai datiraccolti dal GISRS (Global Influenza Surveillance and Response System), con livelli di diffusione inferiori a quelli normalmente osservati nei mesi estivi. | We study features of influenza epidemiology in the World Health Organization (WHO) European Region from week 40 2020 to week 8 2021, a period when in usual seasons the highest influenza activity (peak of seasonal epidemic) would be expected. Results are compared to those of the previous six seasons (2014/15–2019/20).<br><br>**Figure 2.** Sentinel-surveillance-obtained numbers of (A) specimens testing positive for influenza virus and (B) specimens tested in the 2020/21 season up to week 8, compared with minimum, mean and maximum of previous seasons (weeks 40–20) in 2014/15–2019/20, WHO European Region<br><br>  <br> |
| Nalbandian A et al<br><br>Nature | Post-acute COVID-19 syndrome | Dettagliata revisione sulle caratteristiche del « long COVID », la persistenza di disturbi dopo la fase acuta di infezione da SARS-CoV-2. | Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the pathogen responsible for the coronavirus disease 2019 (COVID-19) pandemic, which has resulted in global healthcare crises and strained health resources. As the population of patients recovering from COVID-19 grows, it is paramount to establish an understanding of the healthcare issues surrounding them. COVID-19 is now recognized as a multi-organ disease with a broad spectrum of manifestations. Similarly to post-acute viral syndromes described in survivors of other virulent coronavirus epidemics, there are increasing reports of persistent and prolonged effects after acute |

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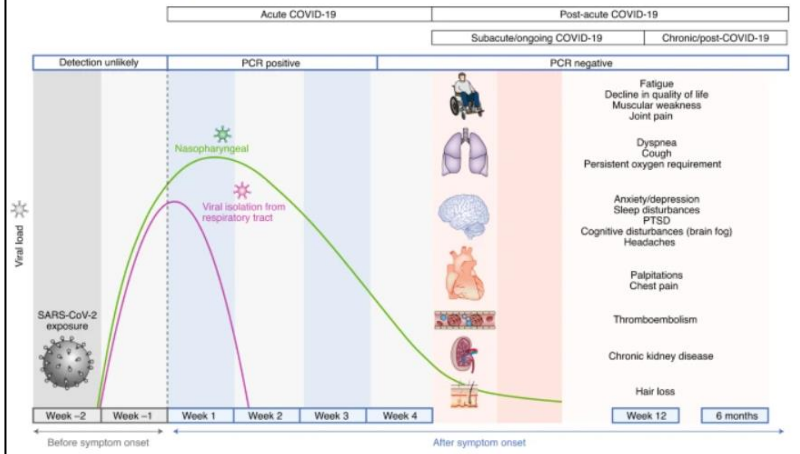
| https://www.nature.com/articles/s41591-021-01283-z | | | COVID-19. Patient advocacy groups, many members of which identify themselves as long haulers, have helped contribute to the recognition of post-acute COVID-19, a syndrome characterized by persistent symptoms and/or delayed or long-term complications beyond 4 weeks from the onset of symptoms. Here, we provide a comprehensive review of the current literature on post-acute COVID-19, its pathophysiology and its organ-specific sequelae. Finally, we discuss relevant considerations for the multidisciplinary care of COVID-19 survivors and propose a framework for the identification of those at high risk for post-acute COVID-19 and their coordinated management through dedicated COVID-19 clinics.<br><br>**Fig. 1: Timeline of post-acute COVID-19.**<br>  <br><br>Acute COVID-19 usually lasts until 4 weeks from the onset of symptoms, beyond which replication-competent SARS-CoV-2 has not been isolated. Post-acute COVID-19 is defined as persistent symptoms and/or delayed or long-term complications beyond 4 weeks from the onset of symptoms. The common symptoms observed in post-acute COVID-19 are summarized. |

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| Janiaud P et al<br><br>JAMA<br><br>https://jamanetwork.com/journals/jama/fullarticle/2777060 | Association of Convalescent Plasma Treatment With Clinical Outcomes in Patients With COVID-19<br>A Systematic Review and Meta-analysis | Metanalisi dei trial clinici randomizzati (4) sulla terapia con plasma per COVID-19 : non si dimostra un beneficio su sopravvivenza, peggioramento clinico, necessità di ventilazione meccanica, durata del ricovero. | Importance Convalescent plasma is a proposed treatment for COVID-19.<br>Objective To assess clinical outcomes with convalescent plasma treatment vs placebo or standard of care in peer-reviewed and preprint publications or press releases of randomized clinical trials (RCTs).<br>Data Sources PubMed, the Cochrane COVID-19 trial registry, and the Living Overview of Evidence platform were searched until January 29, 2021.<br>Study Selection The RCTs selected compared any type of convalescent plasma vs placebo or standard of care for patients with confirmed or suspected COVID-19 in any treatment setting.<br>Data Extraction and Synthesis Two reviewers independently extracted data on relevant clinical outcomes, trial characteristics, and patient characteristics and used the Cochrane Risk of Bias Assessment Tool. The primary analysis included peer-reviewed publications of RCTs only, whereas the secondary analysis included all publicly available RCT data (peer-reviewed publications, preprints, and press releases). Inverse variance–weighted meta-analyses were conducted to summarize the treatment effects. The certainty of the evidence was assessed using the Grading of Recommendations Assessment, Development, and Evaluation.<br>Main Outcomes and Measures All-cause mortality, length of hospital stay, clinical improvement, clinical deterioration, mechanical ventilation use, and serious adverse events.<br>Results A total of 1060 patients from 4 peer-reviewed RCTs and 10 722 patients from 6 other publicly available RCTs were included. The summary risk ratio (RR) for all-cause mortality with convalescent plasma in the 4 peer-reviewed RCTs was 0.93 (95% CI, 0.63 to 1.38), the absolute risk difference was −1.21% (95% CI, |

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| | | | −5.29% to 2.88%), and there was low certainty of the evidence due to imprecision. Across all 10 RCTs, the summary RR was 1.02 (95% CI, 0.92 to 1.12) and there was moderate certainty of the evidence due to inclusion of unpublished data. Among the peer-reviewed RCTs, the summary hazard ratio was 1.17 (95% CI, 0.07 to 20.34) for length of hospital stay, the summary RR was 0.76 (95% CI, 0.20 to 2.87) for mechanical ventilation use (the absolute risk difference for mechanical ventilation use was −2.56% [95% CI, −13.16% to 8.05%]), and there was low certainty of the evidence due to imprecision for both outcomes. Limited data on clinical improvement, clinical deterioration, and serious adverse events showed no significant differences.<br>Conclusions and Relevance Treatment with convalescent plasma compared with placebo or standard of care was not significantly associated with a decrease in all-cause mortality or with any benefit for other clinical outcomes. The certainty of the evidence was low to moderate for all-cause mortality and low for other outcomes. |
| Meyer MN et al<br><br>JAMA<br><br>https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2777776 | Trends in Health Care Worker Intentions to Receive a COVID-19 Vaccine and Reasons for Hesitancy | Esiti di un sondaggio condotto su oltre 16000 operatori sanitari negli USA in merito alla volontà di sottoporsi al vaccino ; chi è in contatto coi pazienti ha un maggiore tasso di accettazione ; la maggior parte di chi non accetta vorrebbe attendere più dati sull'impiego dei vaccini su larga scala. | Although health care workers (HCWs) can serve as ambassadors of COVID-19 vaccine acceptance, surveys have found low acceptance rates among HCWs (eg, 33.5%).1 However, those surveys were conducted before the issuance of vaccine emergency use authorizations (EUAs) by the US Food and Drug Administration (FDA). We surveyed all employees of a health care system on the eve of vaccine distribution to encourage them to receive a COVID-19 vaccine, assess their intentions to do so, and understand reasons for hesitancy. |

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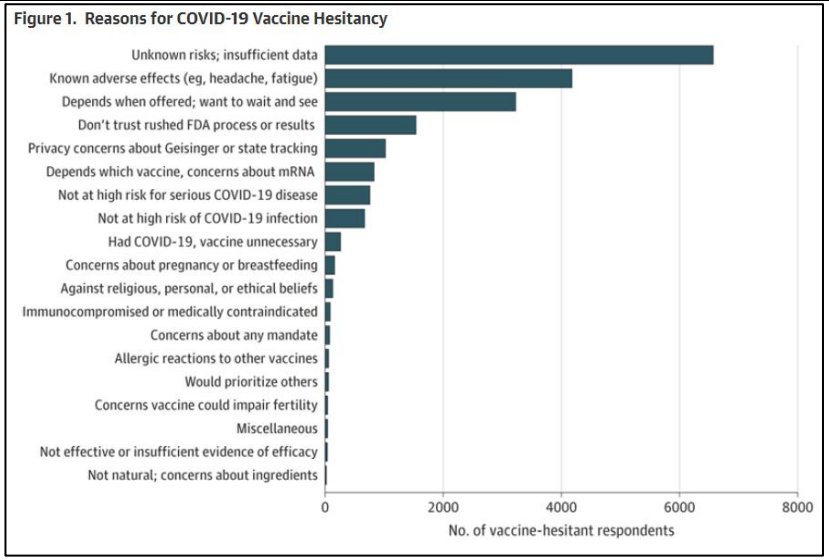
| | | |  |
| Benedict C et al<br><br>The Lancet<br><br>https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00126-0/fulltext | Could a good night's sleep improve COVID-19 vaccine efficacy? | Il sistema immunitario segue ritmi circadiani ; per questo si ipotizza che somministrare il vaccino contro SARS-CoV-2 in momenti diversi della giornata possa influenzare la risposta generata, analogamente a quanto osservato in piccoli studi su epatite A e influenza. | Thus, it is possible that administering COVID-19 vaccines in the morning might result in higher antibody titres. However, several uncertainties remain, such as how to determine the appropriate time of vaccination for night-shift workers. This group often has chronic circadian disruption and exhibits a markedly greater risk of COVID-19 diagnosis. |

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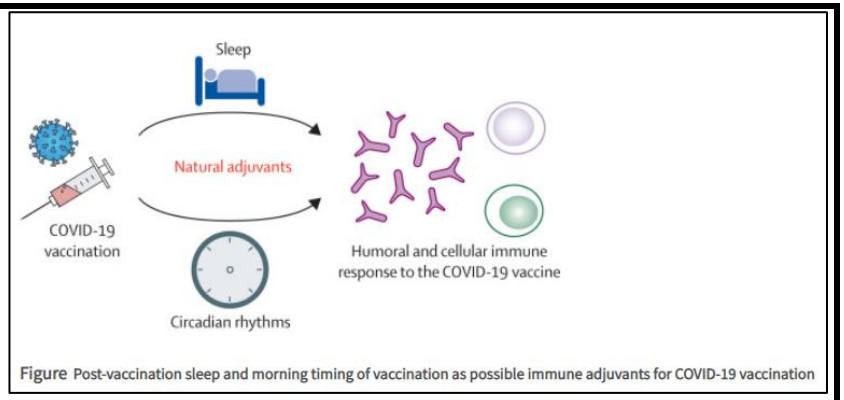
| | | |  <br>Figure Post-vaccination sleep and morning timing of vaccination as possible immune adjuvants for COVID-19 vaccination |
| Sax P<br><br>NEJM<br><br>https://www.nejm.org/covid-vaccine/faq | COVID-19 vaccines FAQs:<br><br>Are there minimum or maximum ages for patients to receive the vaccine? | Non ci sono evidenze per scoraggiare la vaccinazione nei pazienti grandi anziani, per quanto essi non siano stati inclusi nei trial clinici ; è possibile che la risposta al vaccino in questi soggetti sia subottimale. | The Pfizer/BioNTech vaccine is authorized for patients ≥16 years and the Moderna vaccine for ≥18 years. Studies in children are under way, but neither vaccine should be administered to children at this point. There is no maximum age restriction. Given the disproportionate toll that Covid-19 has taken on the elderly — essentially every study finds that older age is a risk factor for severe disease — older people should be strongly encouraged to be immunized.<br><br>One important unknown based solely on the clinical trial results is how effective the vaccines will be in the frail older population, especially those of extremely advanced age or who live in nursing homes. While this is a target population for early immunization, this particular subset of older people did not participate in the phase 3 clinical trials, because study participants had to be ambulatory and clinically stable. Since the release of the vaccines, however, we now have population-based studies showing a substantial decline in hospitalizations due to Covid-19 among people over 70, including data from nursing homes. These encouraging data suggest that |

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| | | | even though older vaccinated people have lower antibody levels than younger recipients, they still experience significant protection. |
| Keehner J et al<br><br>NEJM<br><br>https://www.nejm.org/doi/full/10.1056/NEJMc2101927 | SARS-CoV-2 Infection after Vaccination in Health Care Workers in California | 379 operatori sanitari su 36659 vaccinati con almeno una dose di vaccino a mRNA contro SARS-CoV-2 hanno presentato infezione dallo stesso virus, e di questi 7 dopo almeno due settimane dalla seconda dose. L'infezione post-vaccinale appare un evento molto raro, mentre gli autori sottolineano il problema dell'esitazione : circa il 70% degli operatori aveva aderito alla campagna vaccinale. | In the initial 31 days of the vaccination campaign, 59% of 23,234 UTSW employees received a first dose of either one of the mRNA vaccines and 30% received a second dose. Between December 15, 2020, and January 28, 2021, a total of 350 of the 23,234 employees (1.5%) who were eligible to receive the vaccine were identified as being newly infected with SARS-CoV-2. |

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| | | | **Table 1. New SARS-CoV-2 Infections among Vaccinated Health Care Workers from December 16, 2020, through February 9, 2021.**<br><br>**Days after Vaccination** / **Vaccinated Persons**<br>With New Infection (N=379) — *number*<br>Tested (N=14,604)* — *number*<br>Eligible for Testing (N=36,659)† — *number (percent)*<br><br>**Dose 1**<br>Days 1–7: 145 / 5794 / 35,673 (97.3)<br>Days 8–14: 125 / 7844 / 34,404 (93.8)<br>Days 15–21: 57 / 7958 / 32,667 (89.1)<br>Day 22 or later, before dose 2: 15 / 4286 / 32,327 (88.2)<br>**Dose 2**<br>Days 1–7: 22 / 5546 / 23,100 (63.0)<br>Days 8–14: 8 / 4909 / 16,082 (43.9)<br>Day 15 or later: 7 / 4167 / 14,990 (40.9)<br><br>* Shown are the numbers of unique health care workers who underwent testing (not the number of individual tests).<br>† Shown are the numbers and percentages of persons among 36,659 vaccinated health care workers who were eligible to undergo testing each week as of February 9, 2021. |
| Thakkar A et al<br><br>Nature | Patterns of seroconversion for SARS-CoV-2 IgG in patients with malignant disease and association with anticancer therapy | Studio retrospettivo su 261 pazienti con diagnosi di neoplasia e infezione accertata da SARS-CoV-2, di cui si studia la sieroconversione : 22 pazienti non la presentano, e la mancata | Patients with cancer have been identified in several studies to be at high risk of developing severe COVID-19; however, rates of SARS-CoV-2 IgG seroconversion and its association with cancer types and anticancer therapy remain obscure. We conducted a retrospective cohort study in patients with cancer who underwent SARS-CoV-2 IgG testing. Two hundred and sixty-one patients with a cancer diagnosis underwent SARS-CoV-2 IgG testing and demonstrated a high rate of seroconversion (92%). However, significantly lower |

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| https://www.nature.com/articles/s43018-021-00191-y | | sieroconversione appare associata a neoplasia ematologica, terapia con anti CD-20 (rituximab), terapia con CAR-T-cells, trapianto di staminali emopoietiche. A latere, lo shedding virale è significativamente più lungo in caso di neoplasie ematologiche rispetto a neoplasie solide (61 vs 33 giorni in media). | seroconversion was observed in patients with hematological malignancies (82%), patients who received anti-CD-20 antibody therapy (59%) and stem cell transplant (60%). Notably, all 17 patients who received immunotherapy, including 16 that received anti-PD-1/PD-L1 monoclonal antibodies, developed SARS-CoV-2 IgG antibodies (100% seroconversion). These data show differential rates of seroconversion in specific patient groups and bear importance for clinical monitoring and vaccination strategies that are being developed to mitigate the COVID-19 pandemic.<br><br>**Table 3 \| Associations of therapies and cancer types with SARS-CoV-2 IgG positivity**<br>**Results[a]**<br>**Type of cancer** / **SARS-CoV-2 IgG positive** / **SARS-CoV-2 IgG negative** / **OR (univariate)** / ***P* value[b] (univariate)** / **OR (multivariate)** / ***P* value (multivariate)**<br>Hematological malignancies 49 11 3.8 0.005 4.004 0.0026<br>Solid malignancies 190 11<br>Type of cancer-directed therapy<br>Anti-CD-20 therapy 10 7 0.09 0.00013<br>Stem cell transplant 6 4 0.1 0.0057<br>Endocrine therapy 70 1 8.6 0.01<br>Immunotherapy 17 0 0.38<br>[a]Univariate analysis was carried out between all treatment categories and seroconversion, only the statistically significant results are shown here. Univariate statistical test used was a two-sided Fisher's test and multivariate test was a two-sided Wald test on a logistic model. [b]*P* values are uncorrected for multiple hypothesis testing and FDR correction is provided for variables where more than two levels of analysis was performed in Supplementary Tables 9, 11 and 12. |
| Garibaldi BT et al<br><br>JAMA<br><br>https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2777863 | Comparison of Time to Clinical Improvement With vs Without Remdesivir Treatment in Hospitalized Patients With COVID-19 | Studio retrospettivo su 342 persone ricoverate per COVID-19 e trattate con remdesivir (184 anche con steroidi), a confronto con controlli appaiati per caratteristiche demografiche e cliniche. Il remdesivir è associato a più rapido miglioramento clinico. Non si riportano dati sulla durata dei sintomi | Importance : Clinical effectiveness data on remdesivir are urgently needed, especially among diverse populations and in combination with other therapies.<br>Objective : To examine whether remdesivir administered with or without corticosteroids for treatment of coronavirus disease 2019 (COVID-19) is associated with more rapid clinical improvement in a racially/ethnically diverse population.<br>Design, Setting, and Participants : This retrospective comparative effectiveness research study was conducted from March 4 to August 29, 2020, in a 5-hospital health system in the Baltimore, Maryland, and Washington, DC, area. Of 2483 individuals with confirmed severe acute respiratory syndrome coronavirus 2 |

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| | | rispetto all'inizio di remdesivir. | infection assessed by polymerase chain reaction, those who received remdesivir were matched to infected individuals who did not receive remdesivir using time-invariant covariates (age, sex, race/ethnicity, Charlson Comorbidity Index, body mass index, and do-not-resuscitate or do-not-intubate orders) and time-dependent covariates (ratio of peripheral blood oxygen saturation to fraction of inspired oxygen, blood pressure, pulse, temperature, respiratory rate, C-reactive protein level, complete white blood cell count, lymphocyte count, albumin level, alanine aminotransferase level, glomerular filtration rate, dimerized plasmin fragment D [D-dimer] level, and oxygen device). An individual in the remdesivir group with k days of treatment was matched to a control patient who stayed in the hospital at least k days (5 days maximum) beyond the matching day.<br>Exposures : Remdesivir treatment with or without corticosteroid administration.<br>Main Outcomes and Measures : The primary outcome was rate of clinical improvement (hospital discharge or decrease of 2 points on the World Health Organization severity score), and the secondary outcome, mortality at 28 days. An additional outcome was clinical improvement and time to death associated with combined remdesivir and corticosteroid treatment.<br>Results : Of 2483 consecutive admissions, 342 individuals received remdesivir, 184 of whom also received corticosteroids and 158 of whom received remdesivir alone. For these 342 patients, the median age was 60 years (interquartile range, 46-69 years), 189 (55.3%) were men, and 276 (80.7%) self-identified as non-White race/ethnicity. Remdesivir recipients had a shorter time to clinical improvement than matched controls without remdesivir treatment (median, 5.0 days [interquartile range, 4.0-8.0 days] vs 7.0 days |

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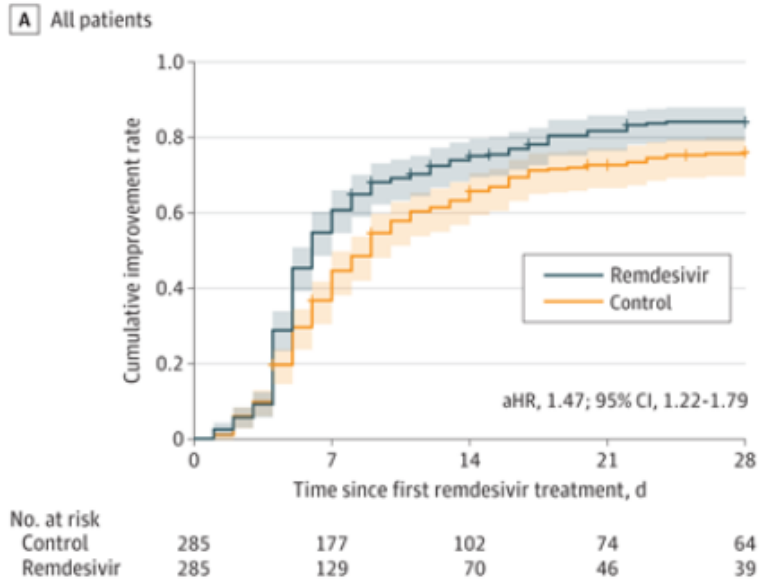
| | | | [interquartile range, 4.0-10.0 days]; adjusted hazard ratio, 1.47 [95% CI, 1.22-1.79]). Remdesivir recipients had a 28-day mortality rate of 7.7% (22 deaths) compared with 14.0% (40 deaths) among matched controls, but this difference was not statistically significant in the time-to-death analysis (adjusted hazard ratio, 0.70; 95% CI, 0.38-1.28). The addition of corticosteroids to remdesivir was not associated with a reduced hazard of death at 28 days (adjusted hazard ratio, 1.94; 95% CI, 0.67-5.57).<br>Conclusions and Relevance : In this comparative effectiveness research study of adults hospitalized with COVID-19, receipt of remdesivir was associated with faster clinical improvement in a cohort of predominantly non-White patients. Remdesivir plus corticosteroid administration did not reduce the time to death compared with remdesivir administered alone.<br>**Figure 2. Time to Clinical Improvement**<br>  <br> |

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| Olimpieri PP et al<br><br>Europe PMC<br><br>https://europepmc.org/article/PPR/PPR300812 | Mortality after remdesivir treatment of pneumonia in hospitalised patients with laboratory confirmed COVID-19: national data in the Italian real-world practice collected by the AIFA monitoring register. | Analisi del Registro AIFA sull'utilizzo di remdesivir per COVID-19, contenente oltre 16000 pazienti. La mortalità sull'intero campione a 15 giorni è 6.9%, quella a 29 giorni 11.5%. | Background. The Italian Medicines Agency (AIFA) granted reimbursement for remdesivir (Veklury®) exclusively to COVID-19 patients with pneumonia and requiring supplemental low-flow oxygen therapy and instituted a monitoring registry to control use appropriateness and to manage vials delivery. The aim of this work is to provide a picture on mortality in a large cohort of patients having these characteristics. Methods: The Remdesivir Registry (RR) collected very few and essential healthcare data necessary to manage the distribution of vials across Italian hospitals. Mortality by day 15 and 29 was estimated using the Kaplan-Meier estimator and the Cox proportional-hazards (PH) model was applied to analyse the risks connected to patient's background features relative to all-cause mortality by day 29. Findings. 16396 SARS-CoV-2 positive patients were included in the registry with a mean age of 66·3 years and a male/female ratio of 2·0/1. 2226 deaths were registered. The Kaplan–Meier estimate of national mortality by day 15 was 6·9% (95% CI: 6·5%-7·3%) while mortality by day 29 was 11·5% (95% CI: 11·0%-11·9%). Cox-adjusted estimates by day 29 shown 18·4% (IC 95% 16·9% -19·9%) mortality in the class 65 years or older. Interpretation. To the best of our knowledge, this study provided the largest figure on mortality after the remdesivir treatment of SARS-Cov2 pneumonia in the real-world context showing a dramatic effect of the age on mortality. |

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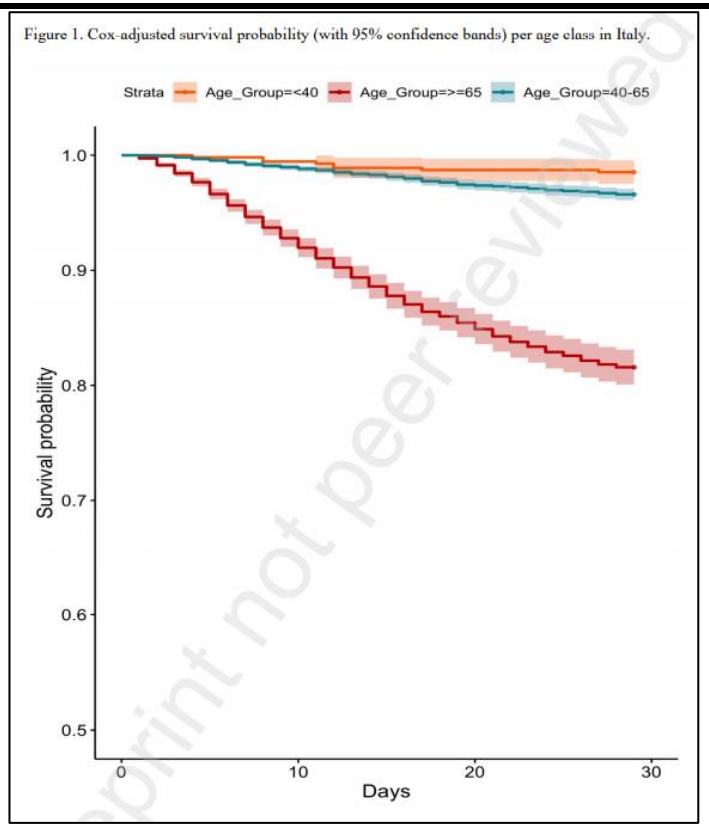
| | | |  |
| Grieco DL et al<br><br>JAMA<br><br>https://jamanetwork.com/journals/jama/fullarticle/2778088 | Effect of Helmet Noninvasive Ventilation vs High-Flow Nasal Oxygen on Days Free of Respiratory Support in Patients With COVID-19 and Moderate to Severe Hypoxemic Respiratory Failure<br>The HENIVOT Randomized Clinical Trial | Trial clinico randomizzato su 109 pazienti trattati in rianimazione per COVID-19 con pressione positiva in helmet contro cannule nasali ad alto flusso: non si dimostra una differenza fra i due trattamenti in temini di giorni senza necessità di supporto respiratorio entro | Importance High-flow nasal oxygen is recommended as initial treatment for acute hypoxemic respiratory failure and is widely applied in patients with COVID-19.<br>Objective To assess whether helmet noninvasive ventilation can increase the days free of respiratory support in patients with COVID-19 compared with high-flow nasal oxygen alone.<br>Design, Setting, and Participants Multicenter randomized clinical trial in 4 intensive care units (ICUs) in Italy between October and December 2020, end of follow-up February 11, 2021, including 109 patients with COVID-19 and moderate to severe hypoxemic |

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| | | 28 giorni. I pazienti in cannule nasali vengono più spesso intubati di quelli in helmet. | respiratory failure (ratio of partial pressure of arterial oxygen to fraction of inspired oxygen ≤200).<br>Interventions Participants were randomly assigned to receive continuous treatment with helmet noninvasive ventilation (positive end-expiratory pressure, 10-12 cm H2O; pressure support, 10-12 cm H2O) for at least 48 hours eventually followed by high-flow nasal oxygen (n = 54) or high-flow oxygen alone (60 L/min) (n = 55).<br>Main Outcomes and Measures The primary outcome was the number of days free of respiratory support within 28 days after enrollment. Secondary outcomes included the proportion of patients who required endotracheal intubation within 28 days from study enrollment, the number of days free of invasive mechanical ventilation at day 28, the number of days free of invasive mechanical ventilation at day 60, in-ICU mortality, in-hospital mortality, 28-day mortality, 60-day mortality, ICU length of stay, and hospital length of stay.<br>Results Among 110 patients who were randomized, 109 (99%) completed the trial (median age, 65 years [interquartile range {IQR}, 55-70]; 21 women [19%]). The median days free of respiratory support within 28 days after randomization were 20 (IQR, 0-25) in the helmet group and 18 (IQR, 0-22) in the high-flow nasal oxygen group, a difference that was not statistically significant (mean difference, 2 days [95% CI, −2 to 6]; P = .26). Of 9 prespecified secondary outcomes reported, 7 showed no significant difference. The rate of endotracheal intubation was significantly lower in the helmet group than in the high-flow nasal oxygen group (30% vs 51%; difference, −21% [95% CI, −38% to −3%]; P = .03). The median number of days free of invasive mechanical ventilation within 28 days was significantly higher in the helmet group than in the high-flow nasal oxygen group (28 [IQR, 13-28] vs 25 [IQR 4-28]; mean |

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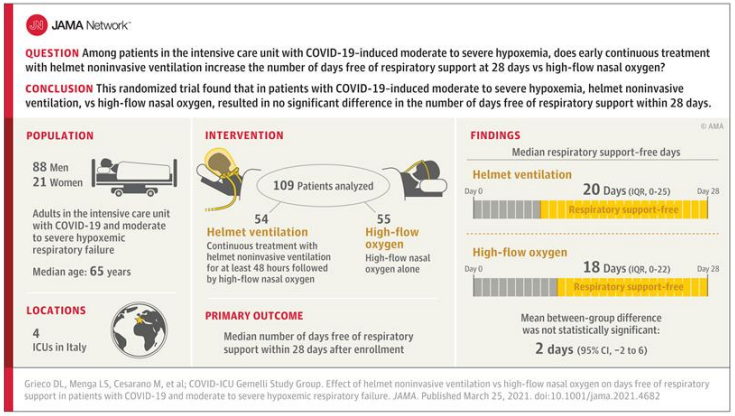
| | | | difference, 3 days [95% CI, 0-7]; P = .04). The rate of in-hospital mortality was 24% in the helmet group and 25% in the high-flow nasal oxygen group (absolute difference, −1% [95% CI, −17% to 15%]; P > .99).<br>Conclusions and Relevance Among patients with COVID-19 and moderate to severe hypoxemia, treatment with helmet noninvasive ventilation, compared with high-flow nasal oxygen, resulted in no significant difference in the number of days free of respiratory support within 28 days. Further research is warranted to determine effects on other outcomes, including the need for endotracheal intubation.<br>**Visual Abstract. Effect of Helmet Noninvasive Ventilation vs High-Flow Nasal Oxygen in COVID-19 and Moderate to Severe Hypoxemia**<br>  |
| Benenson S et al<br><br>NEJM | BNT162b2 mRNA Covid-19 Vaccine Effectiveness among Health Care Workers | Significativo calo delle nuova infezioni da SARS-CoV-2 in operatori sanitari vaccinati con vaccino Pfizer contro SARS-CoV-2 in Israele. | From the beginning of the epidemic through January 31, 2021, of the 6680 health care workers, 689 (10.3%) were infected, mostly due to exposure to Covid-19 in the community; the trends in incidence among health care workers were similar to that in the Jerusalem population (Fig. S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org). Vaccination with two doses of the Pfizer–BioNtech vaccine, given 21 days |

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| https://www.nejm.org/doi/10.1056/NEJMc2101951 | | | apart,4 began on December 20, 2020. Within 8 weeks, 5297 of 6252 (84.7%) health care workers who had not been previously infected by December 20 were vaccinated. Most of the health care workers (98.9%) who had received the first dose of vaccine and were not infected by day 21 received the second dose.<br><br>Table 1. Incidence of Covid-19 among Vaccinated HCWs at HHUMC.*<br><br>Week since First Dose / Vaccinated HCWs at HHUMC: Received a First Dose of Vaccine† / Tested for SARS-CoV-2 at HHUMC‡ / Vaccinated HCWs Newly Positive for SARS-CoV-2: Positive on Testing at HHUMC / Positive on Testing at HHUMC or Community Clinics / Incidence of Covid-19 among Vaccinated HCWs: HCWs Tested at HHUMC / HCWs Tested at HHUMC or Community Clinics§<br>no. of workers / no. of workers / no./1000 workers<br>Week 1: 5297, 1152, 37, 50, 32.1, 9.4<br>Week 2: 5247, 1215, 40, 47, 32.9, 9.0<br>Week 3: 5200, 1126, 22, 29, 19.5, 5.6<br>Week 4: 5164, 685, 11, 11, 16.1, 2.1<br>Received second dose: 4864, 607, 7, 7, 11.5, 1.4<br>Did not receive second dose: 300, 78, 4, 4, 51.3, 13.3<br>Week 5: 5050, 451, 2, 3, 4.4, 0.6<br>Received second dose: 4934, 434, 2, 3, 4.6, 0.6<br>Did not receive second dose: 116, 17, 0, 0, 0, 0<br>Week 6: 4947, 309, 0, 2, 0, 0.4<br>Received second dose: 4793, 295, 0, 2, 0, 0.4<br>Did not receive second dose: 154, 14, 0, 0, 0, 0<br>Week 7: 4079, 157, 3, 5, 19.1, 1.2<br>Received second dose: 4069, 151, 3, 4, 19.9, 1.0<br>Did not receive second dose: 10, 6, 0, 1, 0, 100.0<br><br>* Health care workers (HCWs) were tested at the Hadassah Hebrew University Medical Center (HHUMC), community clinics, or both locations. Positive results on testing at community clinics were reported by the local office of the Israeli Ministry of Health to the Hadassah Infection Prevention and Control Unit.<br>† At each week since the first dose, the number of HCWs represents the number at risk (i.e., those who were not infected during the previous week).<br>‡ HCWs who were tested more than once per week were counted only once.<br>§ The denominator used to calculate incidence among the vaccinated HCWs tested at HHUMC or community clinics was the number of HCWs who received a first dose of vaccine. Systematic testing of all vaccinated HCWs was not performed; therefore, some positive cases may have been missed. |
| Frasca D et al<br><br>PLoS One<br><br>https://doi.org/10.1371/journal.pone.0245424 | Influence of obesity on serum levels of SARS-CoV-2-specific antibodies in COVID-19 patients. | Il titolo di IgG anti SARS-CoV-2 è negativamente associato con il BMI. | SARS-CoV-2 (Severe Acute Respiratory Syndrome Corona Virus-2), cause of COVID-19 (Coronavirus Disease of 2019), represents a significant risk to people living with pre-existing conditions associated with exacerbated inflammatory responses and consequent dysfunctional immunity. In this paper, we have evaluated the influence of obesity, a condition associated with chronic systemic inflammation, on the secretion of SARS-CoV-2-specific IgG antibodies in the blood of COVID-19 patients. Our hypothesis is that obesity is associated with reduced amounts of specific IgG antibodies. Results have confirmed our hypothesis and have shown that SARS-CoV-2 IgG antibodies are negatively associated with Body Mass Index (BMI) in COVID-19 obese patients, as expected based on the known influence of obesity on humoral immunity. Antibodies in COVID-19 obese patients are also |

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| | | | negatively associated with serum levels of pro-inflammatory and metabolic markers of inflammaging and pulmonary inflammation, such as SAA (serum amyloid A protein), CRP (C-reactive protein), and ferritin, but positively associated with NEFA (nonesterified fatty acids). These results altogether could help to identify an inflammatory signature with strong predictive value for immune dysfunction. Inflammatory markers identified may subsequently be targeted to improve humoral immunity in individuals with obesity and in individuals with other chronic inflammatory conditions. |
| Perez-Mies B et al<br><br>BMJ<br><br>https://thorax.bmj.com/content/early/2021/03/23/thoraxjnl-2020-216714 | Pulmonary vascular proliferation in patients with severe COVID-19: an autopsy study | Su 16 autopsie di pazienti deceduti per COVID-19, in 14 casi si osservano segni di proliferazione vascolare nei vasi polmonari. | Diffuse alveolar damage and thrombi are the most common lung histopathological lesions reported in patients with severe COVID-19. Although some studies have suggested increased pulmonary angiogenesis, the presence of vascular proliferation in COVID-19 lungs has not been well characterised. Glomeruloid-like microscopic foci and/or coalescent vascular proliferations measuring up to 2 cm were present in the lung of 14 out of 16 autopsied patients. These lesions expressed CD31, CD34 and vascular endothelial cadherin. Platelet-derived growth factor receptor-β immunohistochemistry and dual immunostaining for CD34/smooth muscle actin demonstrated the presence of pericytes. These vascular alterations may contribute to the severe and refractory hypoxaemia that is common in patients with severe COVID-19. |
| Greenhalgh t et al<br><br>BMJ | Remote management of covid-19 using home pulse oximetry and virtual ward support | Monitoraggio pulsossimetrico domiciliare per i pazienti con COVID-19. | What you need to know :<br><br>• Pulse oximeters used at home can detect hypoxia associated with acute covid-19<br>• Home oximetry requires clinical support, such as regular phone contact from a health professional in a virtual ward setting |

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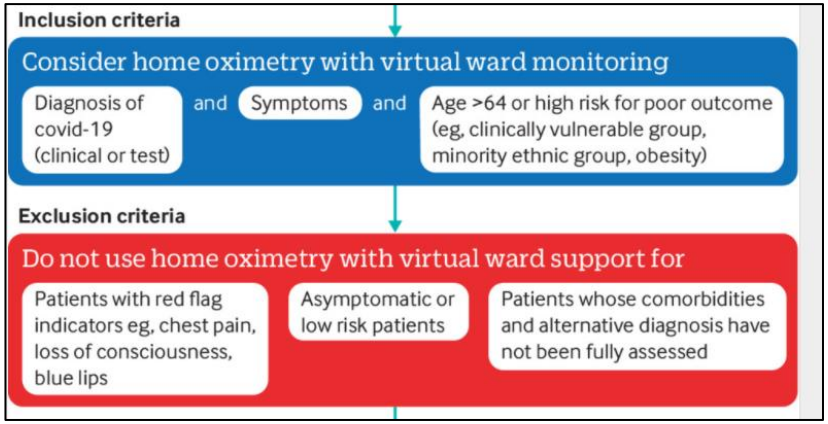
| https://www.bmj.com/content/372/bmj.n677 | | | • More research is needed to understand the safety and effectiveness of home oximetry and to optimise service models and referral pathways<br>  |
| Abdool Karim SS et al<br><br>NEJM<br><br>https://www.nejm.org/doi/10.1056/NEJMc2100362 | New SARS-CoV-2 Variants — Clinical, Public Health, and Vaccine Implications | Disamina delle varianti più significative di SARS-CoV-2. | Across the world, there are multiple variants of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (Covid-19). SARS-CoV-2 variants have been classified by the Centers for Disease Control and Prevention (CDC) as variants of interest, variants of concern, and variants of high consequence. Three new variants1 that have rapidly become dominant within their countries have aroused concerns: B.1.1.7 (also known as VOC-202012/01), 501Y.V2 (B.1.351), and P.1 (B.1.1.28.1). |

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| | | | **Table 1. Summary Results on SARS-CoV-2 Vaccine Trial Efficacy and Viral Neutralization of the B.1.1.7, P.1, and 501Y.V2 Variants, as Compared with Preexisting Variants.***<br><br>**Vaccine (Company)** \| **Preexisting Variants** \| **Neutralization by Pseudovirion or Live Viral Plaque Assay** \| **Efficacy in Settings with 501Y.V2 Variant**<br>Sample Size \| Efficacy in Preventing Clinical Covid-19 \| Efficacy in Preventing Severe Covid-19 \| B.1.1.7 Variant \| P.1 Variant \| 501Y.V2 Variant<br>no. \| % (no. of events with vaccine vs. placebo) \| % \| % \| % \| %<br>BNT162b2 (Pfizer) \| 34,922 \| 95 (8 vs. 162) \| 90 (1 vs. 9) \| Decrease by 2× \| Decrease by 6.7× \| Decrease by ≤6.5× \| NA<br>mRNA-1273 (Moderna) \| 28,207 \| 94 (11 vs. 185) \| 100 (0 vs. 30) \| Decrease by 1.8× \| Decrease by 4.5× \| Decrease by ≤8.6× \| NA<br>Sputnik V (Gamaleya) \| 19,866 \| 92 (16 vs. 62) \| 100 (0 vs. 20) \| NA \| NA \| NA \| NA<br>AZD1222 (AstraZeneca) \| 17,177 \| 67 (84 vs. 248) \| 100 (0 vs. 3) \| NA \| NA \| Decrease by ≤86× to complete immune escape \| 22‡<br>NVX-CoV2373 (Novavax) \| 15,000 \| 89 (6 vs. 56) \| 100 (0 vs. 1) \| Decrease by 1.8× \| NA \| NA \| 49‡<br>CoronaVac (Sinovac)¶<br>Brazil \| 12,396 \| 51 (NA) \| 100 (NA) \| NA \| NA \| NA \| NA<br>Turkey \| 7,371 \| 91 (3 vs. 26) \| NA \| NA \| NA \| NA \| NA<br>BBIBP-CorV (Sinopharm) \| NA \| 79 (NA) \| NA \| NA \| NA \| Decrease by 1.6× \| NA<br><br>* Data were available up to March 18, 2021. The definitions of mild, moderate, and severe coronavirus disease 2019 (Covid-19) vary across the vaccine trials. A list of references associated with these vaccines is provided in the Supplementary Appendix, available with the full text of this letter at NEJM.org. NA denotes not available, and SARS-CoV-2 severe acute respiratory syndrome coronavirus 2.<br>† Shown is the efficacy of the vaccine, as compared with placebo, against moderate-to-severe Covid-19.<br>‡ Shown is efficacy of the vaccine, as compared with placebo, against severe Covid-19 and hospitalization.<br>§ Shown is efficacy of the vaccine, as compared with placebo, against symptomatic Covid-19.<br>¶ Data are shown separately for the trial sites in Brazil and Turkey. |
| Lefrancq N et al<br><br>The Lancet<br><br>https://www.sciencedirect.com/science/article/pii/S2666776221000648?via%3Dihub | Evolution of outcomes for patients hospitalised during the first 9 months of the SARS-CoV-2 pandemic in France: A retrospective national surveillance data analysis | Nei periodi di picco epidemico di COVID-19, la probabilità di decesso e quella di entrare in rianimazione variano prevedibilmente in correlazione con l'occupazione degli ospedali. | Background : As SARS-CoV-2 continues to spread, a thorough characterisation of healthcare needs and patient outcomes, and how they have changed over time, is essential to inform planning. Methods : We developed a probabilistic framework to analyse detailed patient trajectories from 198,846 hospitalisations in France during the first nine months of the pandemic. Our model accounts for the varying age- and sex- distribution of patients, and explore changes in outcome probabilities as well as length of stay. Findings : We found that there were marked changes in the age and sex of hospitalisations over the study period. In particular, the proportion of hospitalised individuals that were >80y varied between 27% and 48% over the course of the epidemic, and was lowest during the inter-peak period. The probability of hospitalised patients entering ICU dropped from 0·25 (0·24–0·26) to 0·13 (0·12–0·14) over the four first months as case numbers fell, before rising to 0·19 (0·19–0·20) during the second wave. The probability of death followed a similar trajectory, falling from 0·25 (0·24–0·26) to 0·10 (0·09–0·11) after the first wave before increasing again during the second wave to 0·19 (0·18–0·19). Overall, we find both the |

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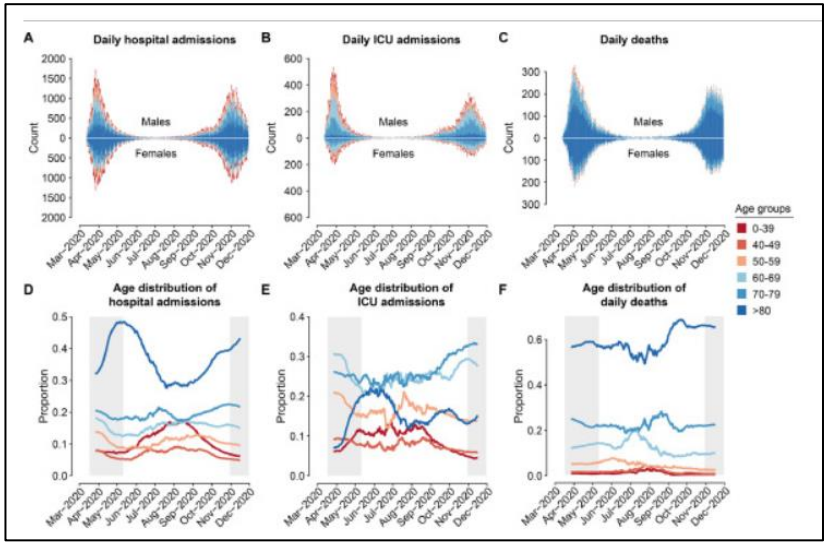
| | | | probability of death and the probability of entering ICU were significantly correlated with COVID-19 ICU occupancy.<br>Interpretation : There are large scale trends in patients outcomes by age, sex and over time. These need to be considered in ongoing healthcare planning efforts.<br>  |
| Salyer SJ et al<br><br>The Lancet<br><br>https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00632-2/fulltext | The first and second waves of the COVID-19 pandemic in Africa: a cross-sectional study | Confronto fra la prima e la seconda (peggiore) « ondata » di COVID-19 in Africa. | Background : Although the first wave of the COVID-19 pandemic progressed more slowly in Africa than the rest of the world, by December, 2020, the second wave appeared to be much more aggressive with many more cases. To date, the pandemic situation in all 55 African Union (AU) Member States has not been comprehensively reviewed. We aimed to evaluate reported COVID-19 epidemiology data to better understand the pandemic's progression in Africa.<br>Methods : We did a cross-sectional analysis between Feb 14 and Dec 31, 2020, using COVID-19 epidemiological, testing, and mitigation strategy data reported by AU Member States to assess trends and identify the response and mitigation efforts at the |

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| | | | country, regional, and continent levels. We did descriptive analyses on the variables of interest including cumulative and weekly incidence rates, case fatality ratios (CFRs), tests per case ratios, growth rates, and public health and social measures in place.<br>Findings : As of Dec 31, 2020, African countries had reported 2 763 421 COVID-19 cases and 65 602 deaths, accounting for 3·4% of the 82 312 150 cases and 3·6% of the 1 798 994 deaths reported globally. Nine of the 55 countries accounted for more than 82·6% (2 283 613) of reported cases. 18 countries reported CFRs greater than the global CFR (2·2%). 17 countries reported test per case ratios less than the recommended ten to 30 tests per case ratio range. At the peak of the first wave in Africa in July, 2020, the mean daily number of new cases was 18 273. As of Dec 31, 2020, 40 (73%) countries had experienced or were experiencing their second wave of cases with the continent reporting a mean of 23 790 daily new cases for epidemiological week 53. 48 (96%) of 50 Member States had five or more stringent public health and social measures in place by April 15, 2020, but this number had decreased to 36 (72%) as of Dec 31, 2020, despite an increase in cases in the preceding month.<br>Interpretation : Our analysis showed that the African continent had a more severe second wave of the COVID-19 pandemic than the first, and highlights the importance of examining multiple epidemiological variables down to the regional and country levels over time. These country-specific and regional results informed the implementation of continent-wide initiatives and supported equitable distribution of supplies and technical assistance. Monitoring and analysis of these data over time are essential for continued situational awareness, especially as Member States |

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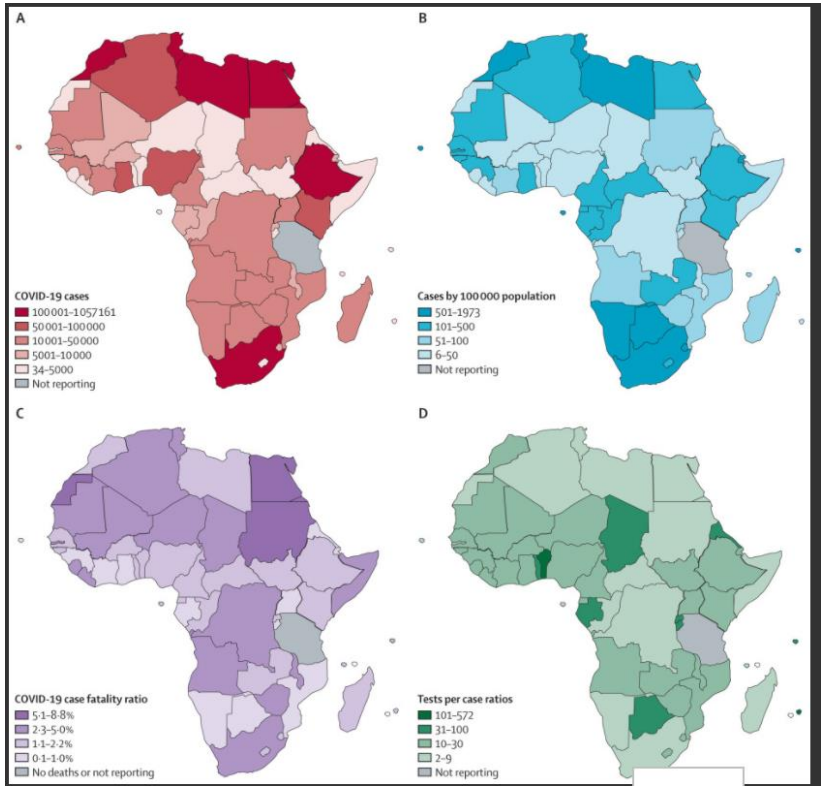
| | | | attempt to balance controlling COVID-19 transmission with ensuring stable economies and livelihoods.<br>  |
| U.S. Department of Health and Human Services<br><br>Public Health Emergency<br><br>https://www.phe.gov/emergency/events/COVID19 | Update on COVID-19 variants and impact on bamlanivimab distribution | L'anticorpo monoclonale contro SARS-CoV-2 bamlanivimab non è più distribuito da solo negli USA, a causa dei dati di resistenza da parte delle varianti. Si ritiene che il farmaco conservi efficacia, e quindi possa ancora essere | Given the sustained increase in SARS-CoV-2 viral variants in the United States that are resistant to bamlanivimab administered alone, and the availability of other authorized monoclonal antibody therapies that are expected to retain activity to these variants, the U.S. Government, in coordination with Eli Lilly and Company, will stop the distribution of bamlanivimab alone starting today, March 24, 2021. |

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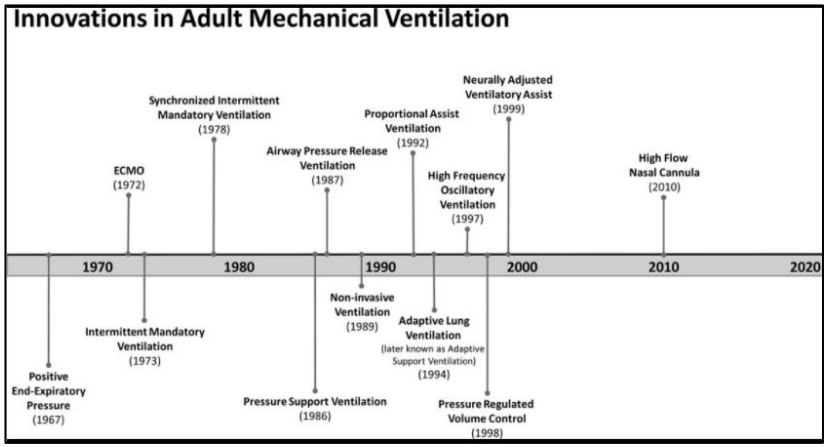
| /investigation-MCM/Bamlanivimab/Pages/default.aspx | | somministrato, insieme ad altri monoclonali. | |
| MacIntyre N et al<br><br>Critical Care Medicine<br><br>https://journals.lww.com/ccmjournal/Fulltext/2021/04000/Fifty_Years_of_Mechanical_Ventilation_1970s_to.2.aspx?context=FeaturedArticles&collectionId=3 | Fifty Years of Mechanical Ventilation—1970s to 2020 | Una storia della ventilazione meccanica e degli studi fondamentali in questo ambito. | Many of these positive-pressure ventilation (PPV) features have emerged over the last 50 years and are the result of technical advances and the translation of extensive basic and applied clinical research into clinical practice—much of which has been published in Critical Care Medicine over its 50 years of existence. This review looks back on these last 5 decades and has grouped the discussions into the decade in which a development first had real impact. It is an attempt to chronicle the important innovations, discoveries, and randomized trials that have transformed the simple concept of “in goes the good air, out goes the bad air” into the sophisticated life support system in common use today.<br>  |

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| Yang S et al<br><br>The Lancet<br><br>https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00127-4/fulltext | Safety and immunogenicity of a recombinant tandem-repeat dimeric RBD-based protein subunit vaccine (ZF2001) against COVID-19 in adults: two randomised, double-blind, placebo-controlled, phase 1 and 2 trials | Esiti di due trial di fase I e II su sicurezza e immunogenicità del vaccino ZF2001 contro SARS-CoV-2. Si tratta di un vaccino a subunità proteiche, già in corso di valutazione in uno studio di fase III. | Background : Although several COVID-19 vaccines have been developed so far, they will not be sufficient to meet the global demand. Development of a wider range of vaccines, with different mechanisms of action, could help control the spread of SARS-CoV-2 globally. We developed a protein subunit vaccine against COVID-19 using a dimeric form of the receptor-binding domain (RBD) of the SARS-CoV-2 spike protein as the antigen. We aimed to assess the safety and immunogenicity of this vaccine, ZF2001, and determine the appropriate dose and schedule for an efficacy study.<br>Methods : We did two randomised, double-blind, placebo-controlled, phase 1 and phase 2 trials. Phase 1 was done at two university hospitals in Chongqing and Beijing, China, and phase 2 was done at the Hunan Provincial Center for Disease Control and Prevention in Xiangtan, China. Healthy adults aged 18–59 years, without a history of SARS-CoV or SARS-CoV-2 infection, an RT-PCR-positive test result for SARS-CoV-2, a history of contact with confirmed or suspected COVID-19 cases, and severe allergies to any component of the vaccine were eligible for enrolment. In phase 1, participants were randomly assigned (2:2:1) to receive three doses of the vaccine (25 μg or 50 μg) or placebo intramuscularly, 30 days apart. In phase 2, participants were randomly assigned (1:1:1:1:1:1) to receive the vaccine (25 μg or 50 μg) or placebo intramuscularly, 30 days apart, in either a two-dose schedule or a three-dose schedule. Investigators, participants, and the laboratory team were masked to group allocation. For phase 1, the primary outcome was safety, measured by the occurrence of adverse events and serious adverse events. For phase 2, the primary outcome was safety and immunogenicity (the seroconversion rate and the magnitude, in geometric mean titres [GMTs], of SARS-CoV-2-neutralising antibodies). Analyses were done on an intention-to-treat and per- |

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| | | | protocol basis. These trials are registered with ClinicalTrials.gov (NCT04445194 and NCT04466085) and participant follow-up is ongoing.<br>Findings : Between June 22 and July 3, 2020, 50 participants were enrolled into the phase 1 trial and randomly assigned to receive three doses of placebo (n=10), the 25 μg vaccine (n=20), or the 50 μg vaccine (n=20). The mean age of participants was 32·6 (SD 9·4) years. Between July 12 and July 17, 2020, 900 participants were enrolled into the phase 2 trial and randomly assigned to receive two doses of placebo (n=150), 25 μg vaccine (n=150), or 50 μg vaccine (n=150), or three doses of placebo (n=150), 25 μg vaccine (n=150), or 50 μg vaccine (n=150). The mean age of participants was 43·5 (SD 9·2) years. In both phase 1 and phase 2, adverse events reported within 30 days after vaccination were mild or moderate (grade 1 or 2) in most cases (phase 1: six [60%] of ten participants in the placebo group, 14 [70%] of 20 in the 25 μg group, and 18 [90%] of 20 in the 50 μg group; phase 2: 37 [25%] of 150 in the two-dose placebo group, 43 [29%] of 150 in the two-dose 25 μg group, 50 [33%] of 150 in the two-dose 50 μg group, 47 [31%] of 150 in the three-dose placebo group, 72 [48%] of 150 in the three-dose 25 μg group, and 65 [43%] of 150 in the three-dose 50 μg group). In phase 1, two (10%) grade 3 or worse adverse events were reported in the 50 μg group. In phase 2, grade 3 or worse adverse events were reported by 18 participants (four [3%] in the two-dose 25 μg vaccine group, two [1%] in the two-dose 50 μg vaccine group, two [1%] in the three-dose placebo group, four [3%] in the three-dose 25 μg vaccine group, and six [4%] in the three-dose 50 μg vaccine group), and 11 were considered vaccine related (two [1%] in the two-dose 25 μg vaccine group, one [1%] in the two-dose 50 μg vaccine group, one [1%] in the three-dose placebo group, two [1%] in the three-dose 25 μg vaccine group, and |

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| | | | five [3%] in the three-dose 50 μg vaccine group); seven participants reported serious adverse events (one [1%] in the two-dose 25 μg vaccine group, one [1%] in the two-dose 50 μg vaccine group, two [1%] in the three-dose placebo group, one [1%] in the three-dose 25 μg vaccine group, and two [1%] in the three-dose 50 μg vaccine group), but none was considered vaccine related. In phase 2, on the two-dose schedule, seroconversion rates of neutralising antibodies 14 days after the second dose were 76% (114 of 150 participants) in the 25 μg group and 72% (108 of 150) in the 50 μg group; on the three-dose schedule, seroconversion rates of neutralising antibodies 14 days after the third dose were 97% (143 of 148 participants) in the 25 μg group and 93% (138 of 148) in the 50 μg group. In the two-dose groups in phase 2, the SARS-CoV-2-neutralising GMTs 14 days after the second dose were 17·7 (95% CI 13·6–23·1) in the 25 μg group and 14·1 (10·8–18·3) in the 50 μg group. In the three-dose groups in phase 2, the SARS-CoV-2-neutralising GMTs 14 days after the third dose were 102·5 (95% CI 81·8–128·5) in the 25 μg group and 69·1 (53·0–90·0) in the 50 μg group.<br>Interpretation : The protein subunit vaccine ZF2001 appears to be well tolerated and immunogenic. The safety and immunogenicity data from the phase 1 and 2 trials support the use of the 25 μg dose in a three-dose schedule in an ongoing phase 3 trial for large-scale evaluation of ZF2001's safety and efficacy. |

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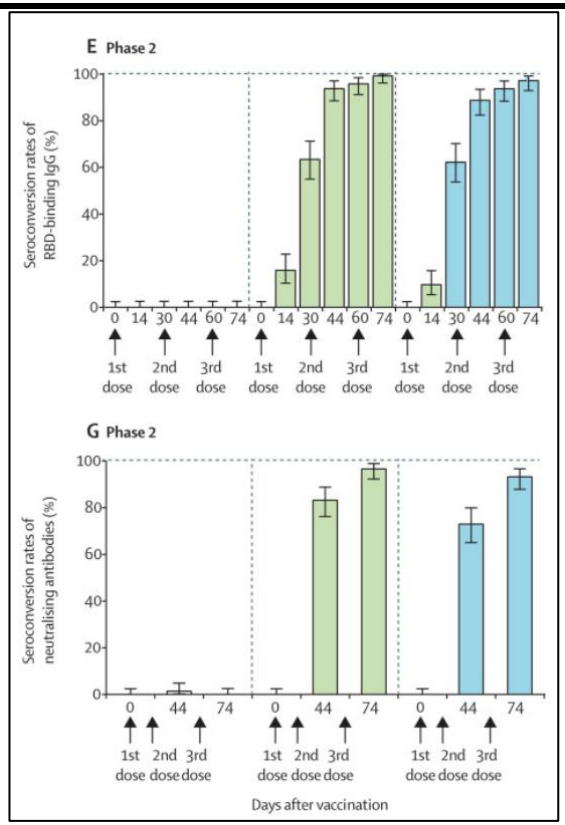
| | | |  |
| Lin X et al<br><br>Cell Reports Medicine<br><br>https://www.cell.com/cell-reports- | A comprehensive analysis and resource to use CRISPR-Cas13 for broad-spectrum targeting of RNA viruses | I CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)- Cas sono sistemi di modifica degli acidi nucleici originanti da una forma di immunità dei procarioti. Hanno la potenzialità di essere diretti contro l'RNA virale, ad esempio quello di SARS-CoV-2, e costituire una | The COVID-19 pandemic caused by SARS-CoV-2 and variants has led to significant mortality. We recently reported that an RNA-targeting CRISPR-Cas13 system, termed prophylactic antiviral CRISPR in human (PAC-MAN), offered an antiviral strategy against SARS-CoV-2 and influenza A virus. Here, we expand in silico analysis to use PAC-MAN to target a broad spectrum of human- or livestock-infectious RNA viruses with high specificity, coverage, and predicted efficiency. Our analysis reveals that a minimal set of 14 crRNAs is able to target >90% of human-infectious viruses across 10 RNA virus families. We predict that a set of 5 experimentally validated crRNAs can target |

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| medicine/fulltext/S2666-3791(21)00061-6 | | futura arma contro le infezioni. | new SARS-CoV-2 variant sequences with zero mismatches. We also build an online resource (crispr-pacman.stanford.edu) to support community use of CRISPR-Cas13 for broad-spectrum RNA virus targeting. Our work provides a new bioinformatic resource for using CRISPR-Cas13 to target diverse RNA viruses in order to facilitate development of CRISPR-based antivirals. |
| Ohashi H et al<br><br>iScience<br><br>https://www.cell.com/iscience/fulltext/S2589-0042(21)00335-7 | Potential anti-COVID-19 agents, Cepharanthine and Nelfinavir, and their usage for combination treatment | Nell'ambito del cosiddetto « repurposing » di farmaci già esistenti contro SARS-CoV-2, questo studio analizza le potenzialità di cefarantina (antinfiammatorio che blocca l'ingresso di SARS-CoV-2 nelle cellule in vitro) e dell'antiretrovirale nelfinavir (inibitore della proteasi virale). Viene proposta una azione sinergica, da valutare con studi clinici. | Antiviral treatments targeting the coronavirus disease 2019 are urgently required. We screened a panel of already-approved drugs in a cell culture model of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and identified two new agents having higher antiviral potentials than the drug candidates such as Remdesivir and Chroloquine in VeroE6/TMPRSS2 cells: the anti-inflammatory drug Cepharanthine and HIV protease inhibitor Nelfinavir. Cepharanthine inhibited SARS-CoV-2 entry through the blocking of viral binding to target cells, whilst Nelfinavir suppressed viral replication partly by protease inhibition. Consistent with their different modes of action, synergistic effect of this combined treatment to limit SARS-CoV-2 proliferation was highlighted. Mathematical modeling in vitro antiviral activity coupled with the calculated total drug concentrations in the lung predicts that Nelfinavir will shorten the period until viral clearance by 4.9-days and the combining Cepharanthine/Nelfinavir enhanced their predicted efficacy. These results warrant further evaluation of the potential anti-SARS-CoV-2 activity of Cepharanthine and Nelfinavir. |

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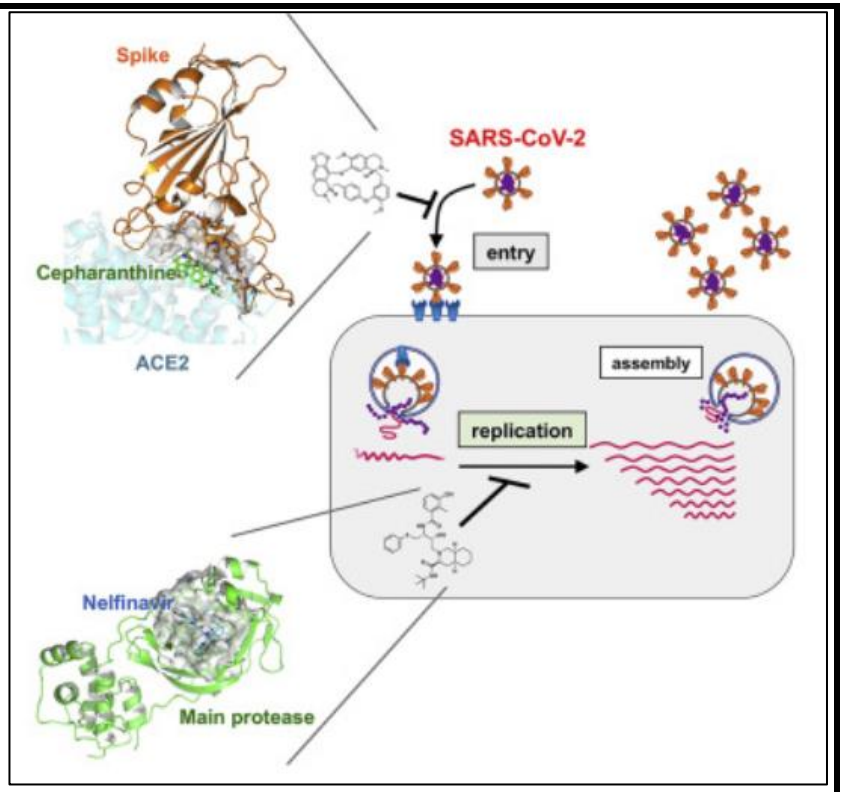
| | | |  |
| Wu P et al<br><br>Clinical Infectious Diseases<br><br>https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab271/6193430?searchresult=1 | Assessing asymptomatic, pre-symptomatic and symptomatic transmission risk of SARS-CoV-2 | Studio su casi e contatti di infezione da SARS-CoV-2 in Cina : il tasso d'attacco dei sintomatici è 4.1% contro 1.1% degli asintomatici, e le infezioni secondarie a casi asintomatici sono a propria volta asintomatiche nel 50% dei casi. | Background : The relative contributions of asymptomatic, pre-symptomatic and symptomatic transmission of SARS-CoV-2 have not been clearly measured although control measures may differ in response to the risk of spread posed by different types of cases. Methods : We collected detailed information on transmission events and symptom status based on laboratory-confirmed patient data and contact tracing data from four provinces and one municipality in China. We estimated the variation in risk of transmission over time, and the severity of secondary infections, by symptomatic status of the infector. |

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| | | | Results : There were 393 symptomatic index cases with 3136 close contacts and 185 asymptomatic index cases with 1078 close contacts included into the study. The secondary attack rate among close contacts of symptomatic and asymptomatic index cases were 4.1% (128/3136) and 1.1% (12/1078), respectively, corresponding to a higher transmission risk from symptomatic cases than from asymptomatic cases (OR: 3.79, 95% CI: 2.06, 6.95). Approximately 25% (32/128) and 50% (6/12) of the infected close contacts were asymptomatic from symptomatic and asymptomatic index cases, respectively, while more than one third (38%) of the infections in the close contacts of symptomatic cases were attributable to exposure to the index cases before symptom onset. Infected contacts of asymptomatic index cases were more likely to be asymptomatic and less likely to be severe.<br>Conclusions : Asymptomatic and pre-symptomatic transmission play an important role in spreading infection, although asymptomatic cases pose a lower risk of transmission than symptomatic cases. Early case detection and effective test-and-trace measures are important to reduce transmission. |
| Boldrini M et al<br><br>JAMA<br><br>https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2778090 | How COVID-19 Affects the Brain | Meccanismi fisiopatologici proposti per spiegare l'interessamento del sistema nervoso centrale in COVID-19. | Some patients present with anosmia, cognitive and attention deficits (ie, brain fog), new-onset anxiety, depression, psychosis, seizures, and even suicidal behavior. These present before, during, and after respiratory symptoms and are unrelated to respiratory insufficiency,1 suggesting independent brain damage. Follow-ups conducted in Germany and the United Kingdom found post–COVID-19 NPs in 20% to 70% of patients, even in young adults, and lasting months after respiratory symptoms resolved, suggesting brain involvement persists. |

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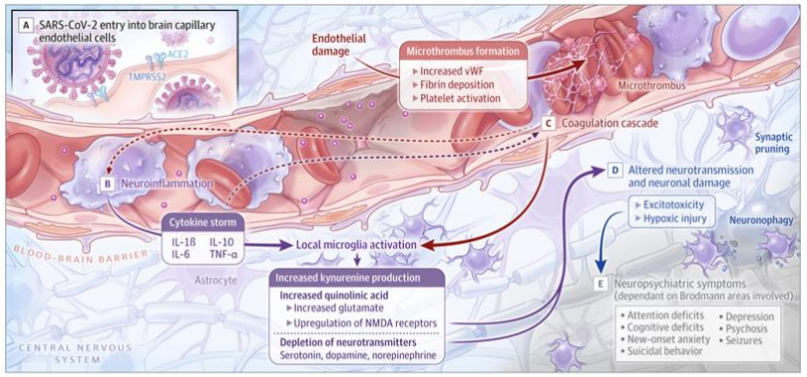
| | | | **Figure. Brain Vascular Injury, Neurotransmitter System Dysfunction, Thrombotic Events, Neuronal Damage, and Neuropsychiatric Symptoms**<br>  <br><br>A, SARS-CoV-2 invades endothelial cells via transmembrane angiotensin-converting enzyme 2 (ACE2) receptor, enabled by transmembrane protease, serine 2 (TMPRSS2). B, Cytokine elevation and microglia activation result in increased kynurenine, quinolinic acid, and glutamate, and neurotransmitter depletion. C, Coagulation cascade and elevation of von Willebrand factor (vWF) lead to thrombotic events. D, Altered neurotransmission, excitotoxicity by increased glutamate, and hypoxic injury contribute to neuronal dysfunction and loss. E, Neuropsychiatric symptoms differ depending on the Brodmann area involved. IL indicates interleukin; NMDA, *N*-methyl-D-aspartate; TNF, tumor necrosis factor. |
| Meppiel E et al<br><br>Clinical Microbiology and Infection<br><br>https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30698-4/fulltext | Neurologic manifestations associated with COVID-19: a multicentre registry | Studio retrospettivo su 222 casi di COVID-19 con manifestazioni neurologiche in Francia. | Objectives : To provide an overview of the spectrum, characteristics and outcomes of neurologic manifestations associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.<br>Methods : We conducted a single-centre retrospective study during the French coronavirus disease 2019 (COVID-19) epidemic in March–April 2020. All COVID-19 patients with de novo neurologic manifestations were eligible.<br>Results : We included 222 COVID-19 patients with neurologic manifestations from 46 centres in France. Median (interquartile range, IQR) age was 65 (53–72) years and 136 patients (61.3%) were male. COVID-19 was severe or critical in 102 patients (45.2%). The most common neurologic diseases were COVID-19–associated encephalopathy (67/222, 30.2%), acute ischaemic cerebrovascular syndrome (57/222, 25.7%), encephalitis (21/222, 9.5%) and Guillain-Barré syndrome (15/222, 6.8%). Neurologic manifestations |

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| | | | appeared after the first COVID-19 symptoms with a median (IQR) delay of 6 (3–8) days in COVID-19–associated encephalopathy, 7 (5–10) days in encephalitis, 12 (7–18) days in acute ischaemic cerebrovascular syndrome and 18 (15–28) days in Guillain-Barré syndrome. Brain imaging was performed in 192 patients (86.5%), including 157 magnetic resonance imaging (70.7%). Among patients with acute ischaemic cerebrovascular syndrome, 13 (22.8%) of 57 had multiterritory ischaemic strokes, with large vessel thrombosis in 16 (28.1%) of 57. Brain magnetic resonance imaging of encephalitis patients showed heterogeneous acute nonvascular lesions in 14 (66.7%) of 21. Cerebrospinal fluid of 97 patients (43.7%) was analysed, with pleocytosis found in 18 patients (18.6%) and a positive SARS-CoV-2 PCR result in two patients with encephalitis. The median (IQR) follow-up was 24 (17–34) days with a high short-term mortality rate (28/222, 12.6%).<br>Conclusions : Clinical spectrum and outcomes of neurologic manifestations associated with SARS-CoV-2 infection were broad and heterogeneous, suggesting different underlying pathogenic processes. |
| European Centre for Disease Prevention and Control<br><br>https://www.ecdc.europa.eu/en/publications-data/methods-detection-and-identification-sars-cov-2-variants | Methods for the detection and identification of SARS-CoV-2 variants | Indicazioni sui metodi per identificare le infezioni da varianti di SARS-CoV-2 : il gold standard è il sequenziamento, cui si possono affiancare metodi basati sulla PCR. | This technical guidance provides guidance to laboratories, microbiology experts and relevant stakeholders in making decisions on establishing or scaling up capability and capacity to detect and identify circulating SARS-CoV-2 variants, and in making decisions on which technologies to use and for which objective. |

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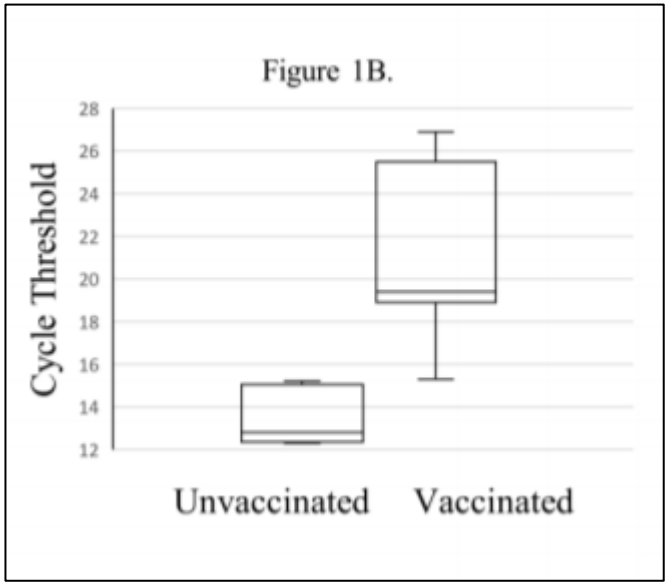
| McEllistrem MC et al<br><br>Clinical Infectious Diseases<br><br>https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab263/6188727 | Single dose of a mRNA SARS-CoV-2 vaccine is associated with lower nasopharyngeal viral load among nursing home residents with asymptomatic COVID-19 | Dopo una sola dose di vaccino Pfizer ricevuta entro 3 settimane prima, gli anziani di una casa di riposo sottoposti a tamponi di screening mostrano, se positivi, una significativa riduzione della carica di SARS-CoV-2 (stimata con ciclo-soglia della PCR) rispetto ai non vaccinati. | In nursing home residents with asymptomatic COVID-19 diagnosed through twice-weekly surveillance testing, single dose BNT162b2 vaccination (Pfizer-BioNTech) was associated with -2.4 mean log10 lower nasopharyngeal viral load than detected in absence of vaccination (p=0.004). Since viral load is linked to transmission, single dose mRNA SARS-CoV-2 vaccination may help control outbreaks.<br>  <br> |
| Avouac J et al<br><br>The Lancet<br><br>https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(21)00059-X/fulltext | COVID-19 outcomes in patients with inflammatory rheumatic and musculoskeletal diseases treated with rituximab: a cohort study | Studio di coorte su 1090 persone con malattie reumatologiche che hanno avuto infezione da SARS-CoV-2 : nel gruppo in terapia con rituximab (anti-CD20) si osserva malattia più grave e maggiore durata di ospedalizzazione, mentre | Background : Various observations have suggested that the course of COVID-19 might be less favourable in patients with inflammatory rheumatic and musculoskeletal diseases receiving rituximab compared with those not receiving rituximab. We aimed to investigate whether treatment with rituximab is associated with severe COVID-19 outcomes in patients with inflammatory rheumatic and musculoskeletal diseases.<br>Methods : In this cohort study, we analysed data from the French RMD COVID-19 cohort, which included patients aged 18 years or |

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| | | non si riesce a dimostrare una maggiore mortalità. I pazienti più gravi avevano ricevuto rituximab fino a un momento significativamente più vicino all'infezione rispetto ai meno gravi. | older with inflammatory rheumatic and musculoskeletal diseases and highly suspected or confirmed COVID-19. The primary endpoint was the severity of COVID-19 in patients treated with rituximab (rituximab group) compared with patients who did not receive rituximab (no rituximab group). Severe disease was defined as that requiring admission to an intensive care unit or leading to death. Secondary objectives were to analyse deaths and duration of hospital stay. The inverse probability of treatment weighting propensity score method was used to adjust for potential confounding factors (age, sex, arterial hypertension, diabetes, smoking status, body-mass index, interstitial lung disease, cardiovascular diseases, cancer, corticosteroid use, chronic renal failure, and the underlying disease [rheumatoid arthritis vs others]). Odds ratios and hazard ratios and their 95% CIs were calculated as effect size, by dividing the two population mean differences by their SD. This study is registered with ClinicalTrials.gov, NCT04353609. Findings : Between April 15, 2020, and Nov 20, 2020, data were collected for 1090 patients (mean age 55·2 years [SD 16·4]); 734 (67%) were female and 356 (33%) were male. Of the 1090 patients, 137 (13%) developed severe COVID-19 and 89 (8%) died. After adjusting for potential confounding factors, severe disease was observed more frequently (effect size 3·26, 95% CI 1·66–6·40, p=0·0006) and the duration of hospital stay was markedly longer (0·62, 0·46–0·85, p=0·0024) in the 63 patients in the rituximab group than in the 1027 patients in the no rituximab group. 13 (21%) of 63 patients in the rituximab group died compared with 76 (7%) of 1027 patients in the no rituximab group, but the adjusted risk of death was not significantly increased in the rituximab group (effect size 1·32, 95% CI 0·55–3·19, p=0·53). |

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| | | | Interpretation : Rituximab therapy is associated with more severe COVID-19. Rituximab will have to be prescribed with particular caution in patients with inflammatory rheumatic and musculoskeletal diseases. |
| Patel Z et al<br><br>Journa of Ultrasound in Medicine<br><br>https://onlinelibrary.wiley.com/doi/10.1002/jum.15706 | Diaphragm and Phrenic Nerve Ultrasound in COVID-19 Patients and Beyond: Imaging Technique, Findings, and Clinical Applications. | Review sullo studio ecografico del diaframma in COVID-19. | The diaphragm, the principle muscle of inspiration, is an under-recognized contributor to respiratory disease. Dysfunction of the diaphragm can occur secondary to lung disease, prolonged ventilation, phrenic nerve injury, neuromuscular disease, and central nervous system pathology. In light of the global pandemic of coronavirus disease 2019 (COVID-19), there has been growing interest in the utility of ultrasound for evaluation of respiratory symptoms including lung and diaphragm sonography. Diaphragm ultrasound can be utilized to diagnose diaphragm dysfunction, assess severity of dysfunction, and monitor disease progression. This article reviews diaphragm and phrenic nerve ultrasound and describes clinical applications in the context of COVID-19. |
| Fayol A et al<br><br>ESC Heart Failure<br><br>https://onlinelibrary.wiley.com/doi/10.1002/ehf2.13315 | Cardiac performance in patients hospitalized with COVID-19: a 6 month follow-up study. | Persistenza di disfuzione diastolica a sei mesi in pazienti con danno miocardico (rialzo delle troponine) in corso di infezione da SARS-CoV-2. | AIMS: Myocardial injury is frequently observed in patients hospitalized with coronavirus disease 2019 (COVID-19) pneumonia. Different cardiac abnormalities have been reported during the acute COVID-19 phase, ranging from infra-clinic elevations of myocardial necrosis biomarkers to acute cardiac dysfunction and myocarditis. There is limited information on late cardiac sequelae in patients who have recovered from acute COVID-19 illness. We aimed to document the presence and quantify the extent of myocardial functional alterations in patients hospitalized 6 months earlier for COVID-19 infection. METHODS AND RESULTS: We conducted a prospective echocardiographic evaluation of 48 patients (mean age 58 +/- 13 years, 69% male) hospitalized 6 +/- 1 month earlier for a laboratory-confirmed and symptomatic COVID-19. Thirty-two (66.6%) had pre-existing cardiovascular risks factors |

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| | | | (systemic hypertension, diabetes, or dyslipidaemia), and three patients (6.2%) had a known prior myocardial infarction. Sixteen patients (33.3%) experienced myocardial injury during the index COVID-19 hospitalization as identified by a rise in cardiac troponin levels. Six months later, 60.4% of patients still reported clinical symptoms including exercise dyspnoea for 56%. Echocardiographic measurements under resting conditions were not different between patients with versus without myocardial injury during the acute COVID-19 phase. In contrast, low-level exercise (25W for 3 min) induced a significant increase in the average E/e' ratio (10.1 +/- 4.3 vs. 7.3 +/- 11.5, P = 0.01) and the systolic pulmonary artery pressure (33.4 +/- 7.8 vs. 25.6 +/- 5.3 mmHg, P = 0.02) in patients with myocardial injury during the acute COVID-19 phase. Sensitivity analyses showed that these alterations of left ventricular diastolic markers were observed regardless of whether of cardiovascular risk factors or established cardiac diseases indicating SARS-CoV-2 infection as a primary cause. CONCLUSIONS: Six months after the acute COVID-19 phase, significant cardiac diastolic abnormalities are observed in patients who experienced myocardial injury but not in patients without cardiac involvement. |