

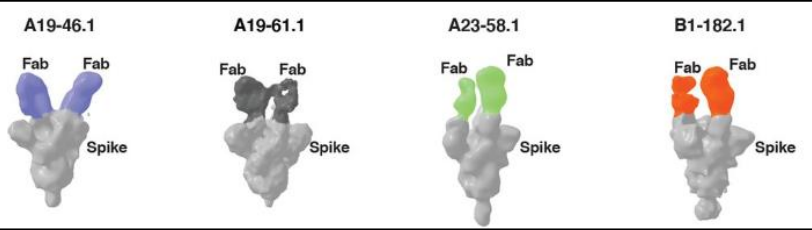
## RICERCA BIBLIOGRAFICA COVID 19

SETTIMANA 05.07 – 11.07.2021

FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE

DOTT.SSA ELEONORA TADDEI

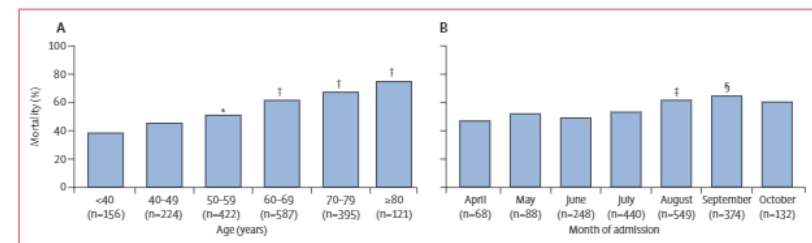
AUTORE/RIVISTA	TITOLO	OUTCOME PRINCIPALE	ABSTRACT
Bosco-Lauth AM et al  Emerging Infectious Diseases  <a href="https://wwwnc.cdc.gov/eid/article/27/8/21-0180_article">https://wwwnc.cdc.gov/eid/article/27/8/21-0180_article</a>	Peridomestic mammal susceptibility to severe acute respiratory syndrome coronavirus 2 infection	Animali selvatici suscettibili all'infezione acuta da SARS-CoV-2 : ad esempio il topo cervino, la moffetta e il woodrat dalla coda folta si infettano e diffondono il virus attraverso le secrezioni respiratorie, invece gli scoiattoli e i procioni no.	Wild animals have been implicated as the origin of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), but it is largely unknown how the virus affects most wildlife species and if wildlife could ultimately serve as a reservoir for maintaining the virus outside the human population. We show that several common peridomestic species, including deer mice, bushy-tailed woodrats, and striped skunks, are susceptible to infection and can shed the virus in respiratory secretions. In contrast, we demonstrate that cottontail rabbits, fox squirrels, Wyoming ground squirrels, black-tailed prairie dogs, house mice, and racoons are not susceptible to SARS-CoV-2 infection. Our results expand upon the existing knowledge base of susceptible species and provide evidence that human–wildlife interactions could result in continued transmission of SARS-CoV-2.

<p>Wang L et al</p> <p>Science</p> <p><a href="https://science.sciencemag.org/content/early/2021/06/30/science.abh1766/tab-article-info">https://science.sciencemag.org/content/early/2021/06/30/science.abh1766/tab-article-info</a></p>	<p>Ultrapotent antibodies against diverse and highly transmissible SARS-CoV-2 variants</p>	<p>Descrizione di 4 anticorpi monoclonali, di cui 2 « ultrapotenti », cioè neutralizzanti a concentrazioni nanomolari, diretti contro SARS-CoV-2 e attivi contro le varianti.</p>	<p>The emergence of highly transmissible SARS-CoV-2 variants of concern (VOC) that are resistant to therapeutic antibodies highlights the need for continuing discovery of broadly reactive antibodies. We identify four receptor-binding domain targeting antibodies from three early-outbreak convalescent donors with potent neutralizing activity against 23 variants including the B.1.1.7, B.1.351, P.1, B.1.429, B.1.526 and B.1.617 VOCs. Two antibodies are ultrapotent, with sub-nanomolar neutralization titers (IC<sub>50</sub> 0.3 to 11.1 ng/mL; IC<sub>80</sub> 1.5 to 34.5 ng/mL). We define the structural and functional determinants of binding for all four VOC-targeting antibodies and show that combinations of two antibodies decrease the in vitro generation of escape mutants, suggesting their potential in mitigating resistance development.</p> 
<p>Estenssoro E et al</p> <p>The Lancet</p> <p><a href="https://www.sciencedirect.com/science/article/pii/S2213260021002290?via%3DIihub">https://www.sciencedirect.com/science/article/pii/S2213260021002290?via%3DIihub</a></p>	<p>Clinical characteristics and outcomes of invasively ventilated patients with COVID-19 in Argentina (SATICOVID): a prospective, multicentre cohort study</p>	<p>Studio di coorte prospettico su 1909 pazienti sottoposti a ventilazione meccanica in ospedali diversi in Argentina per polmonite da SARS-CoV-2 : mortalità del 57%, molto elevata, attribuita in parte alla mancanza di personale e risorse anche se i fattori di rischio associati sono gli</p>	<p>Background : Although COVID-19 has greatly affected many low-income and middle-income countries, detailed information about patients admitted to the intensive care unit (ICU) is still scarce. Our aim was to examine ventilation characteristics and outcomes in invasively ventilated patients with COVID-19 in Argentina, an upper middle-income country.</p> <p>Methods : In this prospective, multicentre cohort study (SATICOVID), we enrolled patients aged 18 years or older with RT-PCR-confirmed COVID-19 who were on invasive mechanical ventilation and admitted to one of 63 ICUs in Argentina. Patient demographics and clinical, laboratory, and general management</p>

		<p>stessi che negli studi condotti in Paesi più ricchi.</p>	<p>variables were collected on day 1 (ICU admission); physiological respiratory and ventilation variables were collected on days 1, 3, and 7. The primary outcome was all-cause in-hospital mortality. All patients were followed until death in hospital or hospital discharge, whichever occurred first. Secondary outcomes were ICU mortality, identification of independent predictors of mortality, duration of invasive mechanical ventilation, and patterns of change in physiological respiratory and mechanical ventilation variables. The study is registered with ClinicalTrials.gov, NCT04611269, and is complete.</p> <p>Findings : Between March 20, 2020, and Oct 31, 2020, we enrolled 1909 invasively ventilated patients with COVID-19, with a median age of 62 years [IQR 52–70]. 1294 (67·8%) were men, hypertension and obesity were the main comorbidities, and 939 (49·2%) patients required vasopressors. Lung-protective ventilation was widely used and median duration of ventilation was 13 days (IQR 7–22). Median tidal volume was 6·1 mL/kg predicted bodyweight (IQR 6·0–7·0) on day 1, and the value increased significantly up to day 7; positive end-expiratory pressure was 10 cm H<sub>2</sub>O (8–12) on day 1, with a slight but significant decrease to day 7. Ratio of partial pressure of arterial oxygen (PaO<sub>2</sub>) to fractional inspired oxygen (FiO<sub>2</sub>) was 160 (IQR 111–218), respiratory system compliance 36 mL/cm H<sub>2</sub>O (29–44), driving pressure 12 cm H<sub>2</sub>O (10–14), and FiO<sub>2</sub> 0·60 (0·45–0·80) on day 1. Acute respiratory distress syndrome developed in 1672 (87·6%) of patients; 1176 (61·6%) received prone positioning. In-hospital mortality was 57·7% (1101/1909 patients) and ICU mortality was 57·0% (1088/1909 patients); 462 (43·8%) patients died of refractory hypoxaemia, frequently overlapping with septic shock (n=174). Cox regression identified age (hazard ratio 1·02 [95% CI 1·01–1·03]), Charlson score (1·16 [1·11–1·23]), endotracheal</p>
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intubation outside of the ICU (ie, before ICU admission; 1.37 [1.10–1.71]), vasopressor use on day 1 (1.29 [1.07–1.55]), D-dimer concentration (1.02 [1.01–1.03]), PaO<sub>2</sub>/FiO<sub>2</sub> on day 1 (0.998 [0.997–0.999]), arterial pH on day 1 (1.01 [1.00–1.01]), driving pressure on day 1 (1.05 [1.03–1.08]), acute kidney injury (1.66 [1.36–2.03]), and month of admission (1.10 [1.03–1.18]) as independent predictors of mortality.

Interpretation : In patients with COVID-19 who required invasive mechanical ventilation, lung-protective ventilation was widely used but mortality was high. Predictors of mortality in our study broadly agreed with those identified in studies of invasively ventilated patients in high-income countries. The sustained burden of COVID-19 on scarce health-care personnel might have contributed to high mortality over the course of our study in Argentina. These data might help to identify points for improvement in the management of patients in middle-income countries and elsewhere.



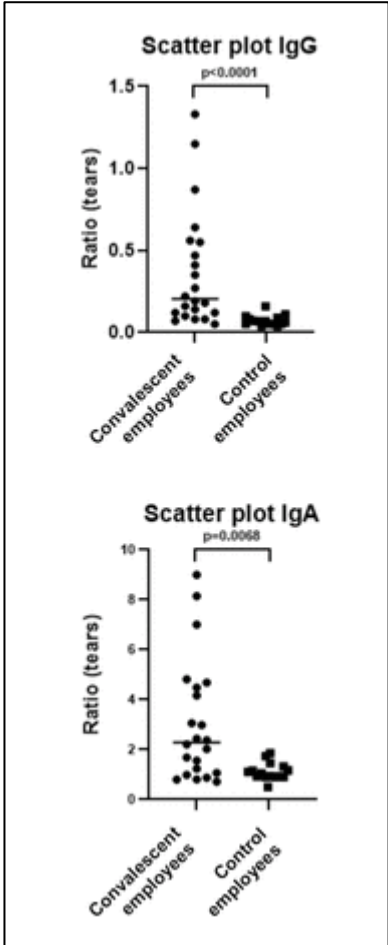
Background/aims: SARS-CoV-2 is highly contagious. More evidence concerning extrapulmonary transmission routes such as the eyes is urgently needed. Although the humoral immune response is important in the viral containment, the local response in tears has not yet been studied. The aim of our study was twofold: to assess the prevalence of both SARS-CoV-2 RNA and antibodies in tear fluid. Methods: In a first series, nasopharyngeal sampling and tear sampling by Schirmer test strips were performed in 26 acutely ill

Muyldermans A et al  
BMJ Open Ophtalmology  
<https://www.ncbi.nlm.nih.gov/research/coronaviruses/publication/34192156>

SARS-CoV-2 RNA and antibodies in tear fluid.

Presenza di RNA virale e di IgG e IgA contro SARS-CoV-2 nelle lacrime di 22 pazienti con infezione.

			<p>patients with COVID-19 to assess the presence of SARS-CoV-2 RNA by reverse transcription PCR. In a second series, IgG and IgA responses to SARS-CoV-2 spike protein in serum and tear fluid of convalescent individuals (n=22) were compared with control individuals (n=15) by ELISA. Results: SARS-CoV-2 RNA was detected in tears of 7/26 (26.9%) patients with COVID-19. None of them had ocular symptoms. Convalescent individuals displayed a significant higher ratio of IgG (<math>p&lt;0.0001</math>) and IgA (<math>p=0.0068</math>) in tears compared with control individuals. A sensitivity of 77.3% and specificity of 93.3% was observed for IgG, and 59.1% and 100% for IgA.</p> <p>Conclusions: Our results demonstrate the presence of SARS-CoV-2 RNA and a local IgG and IgA immune response in tear fluid. These data confirm the possibility of SARS-CoV-2 transmission through tear fluid and the importance of the eye as a first defence against SARS-CoV-2, indicating the potential of tears as a non-invasive surrogate for serum in monitoring the host immune response.</p>
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<p>Buckee C et al</p> <p>Nature</p> <p><a href="https://www.nature.com/articles/s41586-021-03694-x">https://www.nature.com/articles/s41586-021-03694-x</a></p>	<p>Thinking clearly about social aspects of infectious disease transmission</p>	<p>Come studiare il comportamento umano per approfondire gli aspetti sociali della trasmissione delle malattie infettive.</p>	<p>Social and cultural forces shape almost every aspect of infectious disease transmission in human populations, as well as our ability to measure, understand, and respond to epidemics. For directly transmitted infections, pathogen transmission relies on human-to-human contact, with kinship, household, and societal structures shaping contact patterns that in turn determine epidemic dynamics. Social, economic, and cultural forces also shape patterns of</p>

			<p>exposure, health-seeking behaviour, infection outcomes, the likelihood of diagnosis and reporting of cases, and the uptake of interventions. Although these social aspects of epidemiology are hard to quantify and have limited the generalizability of modelling frameworks in a policy context, new sources of data on relevant aspects of human behaviour are increasingly available. Researchers have begun to embrace data from mobile devices and other technologies as useful proxies for behavioural drivers of disease transmission, but there is much work to be done to measure and validate these approaches, particularly for policy-making. Here we discuss how integrating local knowledge in the design of model frameworks and the interpretation of new data streams offers the possibility of policy-relevant models for public health decision-making as well as the development of robust, generalizable theories about human behaviour in relation to infectious diseases.</p>
<p>Rubin R et al</p> <p>JAMA</p> <p><a href="https://jamanetwork.com/journals/jama/fullarticle/2781739">https://jamanetwork.com/journals/jama/fullarticle/2781739</a></p>	<p>Alcohol-Related Diseases Increased as Some People Drank More During the COVID-19 Pandemic</p>	<p>Aumento del consumo di alcool durante la pandemia di COVID-19. Necessario indagare il problema durante i contatti medici anche per altre ragioni, per offrire supporto alle persone.</p>	<p>Although the World Health Organization had recommended banning all alcohol sales during lockdowns, concerns arose that such a move would increase the number of people experiencing potentially life-threatening withdrawal symptoms, further taxing hospitals dealing with COVID-19.</p> <p>But, as the authors of an article early in the pandemic observed, keeping alcohol retailers open during lockdowns could have unintentionally sent the message that alcohol is essential for life, encouraging consumption. A widely circulated myth that drinking alcohol protected against COVID-19 didn't help matters.</p>
<p>SeeBle J et al</p> <p>CID</p> <p><a href="https://doi.org/10.1093/cid/ciab611">https://doi.org/10.1093/cid/ciab611</a></p>	<p>Persistent symptoms in adult patients one year after COVID-19: a prospective cohort study</p>	<p>Titolo di anticorpi ANA associato alle sequele di COVID-19 in questa coorte di 96 pazienti.</p>	<p>Background : Long COVID is defined as the persistence of symptoms beyond 3 months after SARS-CoV-2 infection. To better understand the long-term course and etiology of symptoms we analyzed a cohort of COVID-19 patients prospectively.</p>

			<p>Methods : Patients were included at 5 months after acute COVID-19 in this prospective, non-interventional follow-up study. Patients followed until 12 months after COVID-19 symptom onset (n=96, 32.3% hospitalised, 55.2% females) were included in this analysis of symptoms, quality of life (based on a SF-12 survey), laboratory parameters including antinuclear antibodies (ANA), and SARS-CoV-2 antibody levels.</p> <p>Results : At month 12, only 22.9% of patients were completely free of symptoms and the most frequent symptoms were reduced exercise capacity (56.3%), fatigue (53.1%), dyspnoea (37.5%), concentration problems (39.6%), problems finding words (32.3%), and sleeping problems (26.0%). Females showed significantly more neurocognitive symptoms than males.</p> <p>ANA titres were <math>\geq 1:160</math> in 43.6% of patients at 12 months post COVID-19 symptom onset, and neurocognitive symptom frequency was significantly higher in the group with an ANA titre <math>\geq 1:160</math> compared to <math>&lt; 1:160</math>. Compared to patients without symptoms, patients with at least one long COVID symptom at 12 months did not differ significantly with respect to their SARS-CoV-2-antibody levels, but had a significantly reduced physical and mental life quality compared to patients without symptoms.</p> <p>Conclusions : Neurocognitive long COVID symptoms can persist at least for one year after COVID-19 symptom onset, and reduce life quality significantly. Several neurocognitive symptoms were associated with ANA titre elevations. This may indicate autoimmunity as cofactor in aetiology of long COVID.</p>
Tacquard C et al  Chest	Impact of High-Dose Prophylactic Anticoagulation in Critically Ill Patients With COVID-19 Pneumonia	La profilassi anticoagulante a dose aumentata (intermedia o pari alla dose terapeutica) riduce gli eventi trombotici nei pazienti critici	<p>Background</p> <p>Because of the high risk of thrombotic complications (TCs) during SARS-CoV-2 infection, several scientific societies have proposed to</p>

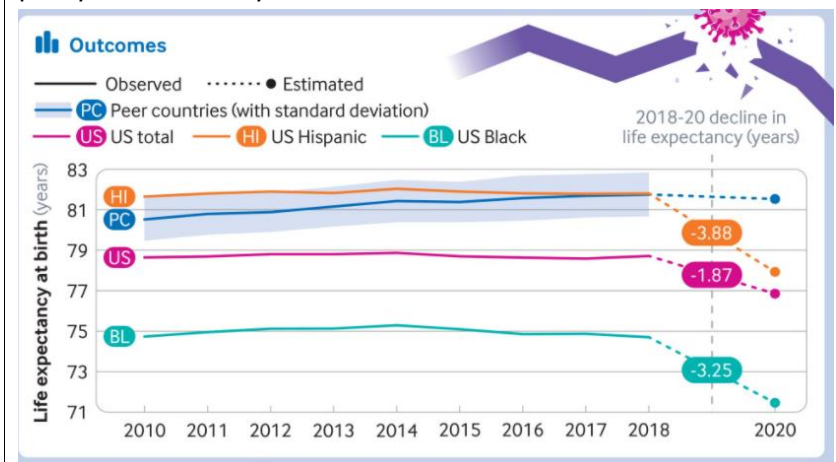


<a href="https://journal.chestnet.org/article/S0012-3692(21)00047-7/fulltext">https://journal.chestnet.org/article/S0012-3692(21)00047-7/fulltext</a>		<p>con COVID-19 in questa casistica di 538 persone ricoverate in rianimazione in Francia.</p>	<p>increase the dose of preventive anticoagulation, although arguments in favor of this strategy are inconsistent.</p> <p>Research Question</p> <p>What is the incidence of TC in critically ill patients with COVID-19 and what is the relationship between the dose of anticoagulant therapy and the incidence of TC?</p> <p>Study Design and Methods</p> <p>All consecutive patients referred to eight French ICUs for COVID-19 were included in this observational study. Clinical and laboratory data were collected from ICU admission to day 14, including anticoagulation status and thrombotic and hemorrhagic events. The effect of high-dose prophylactic anticoagulation (either at intermediate or equivalent to therapeutic dose), defined using a standardized protocol of classification, was assessed using a time-varying exposure model using inverse probability of treatment weight.</p> <p>Results</p> <p>Of 538 patients included, 104 patients experienced a total of 122 TCs with an incidence of 22.7% (95% CI, 19.2%-26.3%). Pulmonary embolism accounted for 52% of the recorded TCs. High-dose prophylactic anticoagulation was associated with a significant reduced risk of TC (hazard ratio, 0.81; 95% CI, 0.66-0.99) without increasing the risk of bleeding (HR, 1.11; 95% CI, 0.70-1.75).</p> <p>Interpretation</p> <p>High-dose prophylactic anticoagulation is associated with a reduction in thrombotic complications in critically ill patients with COVID-19 without an increased risk of hemorrhage. Randomized controlled trials comparing prophylaxis with higher doses of anticoagulants are needed to confirm these results.</p>
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<p>Woolf SH et al</p> <p>BMJ</p> <p><a href="https://www.bmj.com/content/373/bmj.n1343">https://www.bmj.com/content/373/bmj.n1343</a></p>	<p>Effect of the covid-19 pandemic in 2020 on life expectancy across populations in the USA and other high income countries: simulations of provisional mortality data</p>	<p>Riduzione dell'aspettativa di vita negli USA per l'anno 2020 rispetto al 2018, in particolare a discapito delle comunità di afroamericani e ispanici.</p>	<p>Objective To estimate changes in life expectancy in 2010-18 and during the covid-19 pandemic in 2020 across population groups in the United States and to compare outcomes with peer nations.</p> <p>Design Simulations of provisional mortality data.</p> <p>Setting US and 16 other high income countries in 2010-18 and 2020, by sex, including an analysis of US outcomes by race and ethnicity.</p> <p>Population Data for the US and for 16 other high income countries from the National Center for Health Statistics and the Human Mortality Database, respectively.</p> <p>Main outcome measures Life expectancy at birth, and at ages 25 and 65, by sex, and, in the US only, by race and ethnicity. Analysis excluded 2019 because life table data were not available for many peer countries. Life expectancy in 2020 was estimated by simulating life tables from estimated age specific mortality rates in 2020 and allowing for 10% random error. Estimates for 2020 are reported as medians with fifth and 95th centiles.</p> <p>Results Between 2010 and 2018, the gap in life expectancy between the US and the peer country average increased from 1.88 years (78.66 v 80.54 years, respectively) to 3.05 years (78.74 v 81.78 years). Between 2018 and 2020, life expectancy in the US decreased by 1.87 years (to 76.87 years), 8.5 times the average decrease in peer countries (0.22 years), widening the gap to 4.69 years. Life expectancy in the US decreased disproportionately among racial and ethnic minority groups between 2018 and 2020, declining by 3.88, 3.25, and 1.36 years in Hispanic, non-Hispanic Black, and non-Hispanic White populations, respectively. In Hispanic and non-Hispanic Black populations, reductions in life expectancy were 18 and 15 times the average in peer countries, respectively. Progress since 2010 in reducing the gap in life expectancy in the US between Black and White people was erased in 2018-20; life expectancy in</p>
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Black men reached its lowest level since 1998 (67.73 years), and the longstanding Hispanic life expectancy advantage almost disappeared.

Conclusions The US had a much larger decrease in life expectancy between 2018 and 2020 than other high income nations, with pronounced losses among the Hispanic and non-Hispanic Black populations. A longstanding and widening US health disadvantage, high death rates in 2020, and continued inequitable effects on racial and ethnic minority groups are likely the products of longstanding policy choices and systemic racism.



Sangli S et al

Annals of Internal Medicine

<https://www.acpjournals.org/doi/10.7326/L21-0244>

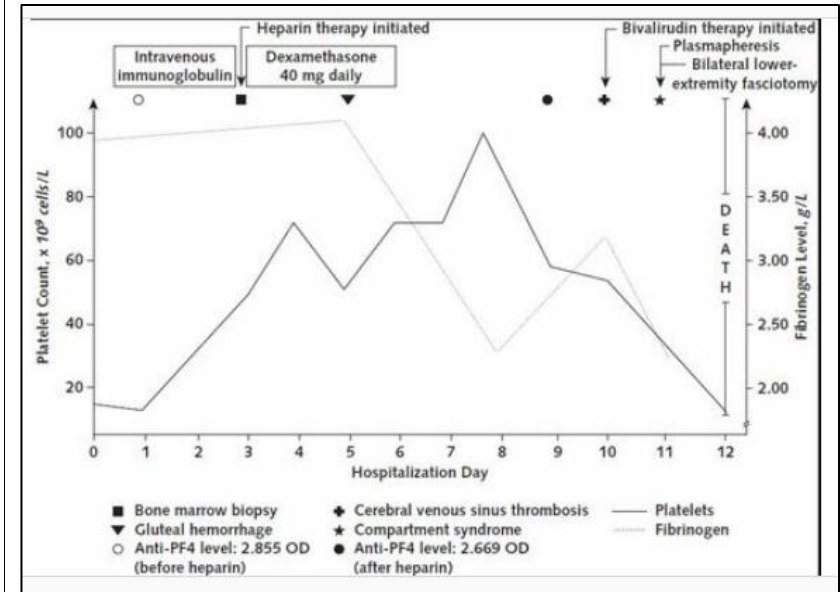
Thrombosis With Thrombocytopenia After the Messenger RNA–1273 Vaccine

Trombosi e trombocitopenia pochi giorni dopo la prima dose di vaccino Moderna a Mrna (!) in un uomo di 65 anni.

Background: Thrombosis with thrombocytopenia has been reported after vaccination against SARS-CoV-2 with 2 vaccines based on recombinant adenovirus vectors—the ChAdOx1 vaccine from AstraZeneca (1, 2) and the Ad26.COV2.S vaccine from Johnson & Johnson/Janssen (3). This syndrome is similar to heparin-induced thrombocytopenia (HIT), and it is known as vaccine-induced thrombocytopenia (VITT) or thrombocytopenia with thrombosis syndrome (TTS). To our knowledge, there are no

reports of VITT or TTS after a SARS-CoV-2 vaccine based on messenger RNA (mRNA) technology.

Objective: To describe a patient with VITT or TTS after administration of the mRNA-1273 vaccine from Moderna.



BACKGROUND : Mass vaccination campaigns to prevent coronavirus disease 2019 (Covid-19) are occurring in many countries; estimates of vaccine effectiveness are urgently needed to support decision making. A countrywide mass vaccination campaign with the use of an inactivated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine (CoronaVac) was conducted in Chile starting on February 2, 2021.

METHODS : We used a prospective national cohort, including participants 16 years of age or older who were affiliated with the public national health care system, to assess the effectiveness of the inactivated SARS-CoV-2 vaccine with regard to preventing Covid-19 and related hospitalization, admission to the intensive

Jara A et al

NEJM

[https://www.nejm.org/doi/full/10.1056/NEJMoa2107715?query=featured\\_home](https://www.nejm.org/doi/full/10.1056/NEJMoa2107715?query=featured_home)

Effectiveness of an Inactivated SARS-CoV-2 Vaccine in Chile

Efficacia nella vita reale della vaccinazione contro SARS-CoV-2 in una coorte di circa 10 milioni di persone in Cile.

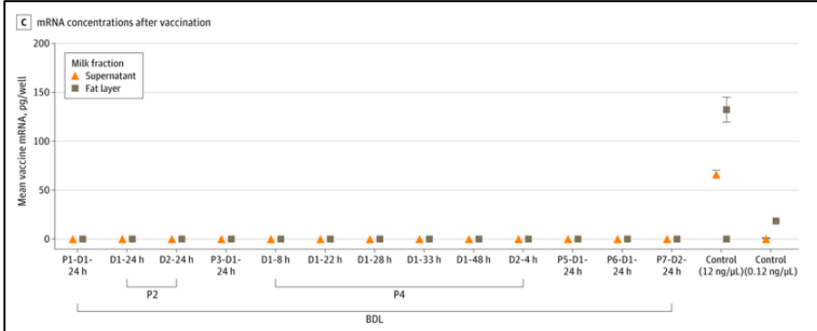
			<p>care unit (ICU), and death. We estimated hazard ratios using the extension of the Cox proportional-hazards model, accounting for time-varying vaccination status. We estimated the change in the hazard ratio associated with partial immunization (<math>\geq 14</math> days after receipt of the first dose and before receipt of the second dose) and full immunization (<math>\geq 14</math> days after receipt of the second dose). Vaccine effectiveness was estimated with adjustment for individual demographic and clinical characteristics.</p> <p>RESULTS : The study was conducted from February 2 through May 1, 2021, and the cohort included approximately 10.2 million persons. Among persons who were fully immunized, the adjusted vaccine effectiveness was 65.9% (95% confidence interval [CI], 65.2 to 66.6) for the prevention of Covid-19 and 87.5% (95% CI, 86.7 to 88.2) for the prevention of hospitalization, 90.3% (95% CI, 89.1 to 91.4) for the prevention of ICU admission, and 86.3% (95% CI, 84.5 to 87.9) for the prevention of Covid-19–related death.</p> <p>CONCLUSIONS : Our results suggest that the inactivated SARS-CoV-2 vaccine effectively prevented Covid-19, including severe disease and death, a finding that is consistent with results of phase 2 trials of the vaccine.</p>
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			<p><b>B Crude Cumulative Incidence of Covid-19</b></p> <table border="1"> <caption>Estimated data from Figure B</caption> <thead> <tr> <th>Days since February 2, 2021</th> <th>Vaccinated with one dose only (%)</th> <th>Unvaccinated (%)</th> <th>Vaccinated with two doses (%)</th> </tr> </thead> <tbody> <tr><td>0</td><td>0.0</td><td>0.0</td><td>0.0</td></tr> <tr><td>14</td><td>0.3</td><td>0.2</td><td>0.1</td></tr> <tr><td>28</td><td>0.8</td><td>0.5</td><td>0.3</td></tr> <tr><td>42</td><td>1.8</td><td>1.0</td><td>0.6</td></tr> <tr><td>56</td><td>2.8</td><td>1.5</td><td>0.9</td></tr> <tr><td>70</td><td>3.8</td><td>2.0</td><td>1.2</td></tr> <tr><td>84</td><td>4.8</td><td>2.8</td><td>1.5</td></tr> </tbody> </table>	Days since February 2, 2021	Vaccinated with one dose only (%)	Unvaccinated (%)	Vaccinated with two doses (%)	0	0.0	0.0	0.0	14	0.3	0.2	0.1	28	0.8	0.5	0.3	42	1.8	1.0	0.6	56	2.8	1.5	0.9	70	3.8	2.0	1.2	84	4.8	2.8	1.5
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<p>Brinkley-Rubinstein L et al</p> <p>NEJM</p> <p><a href="https://www.nejm.org/doi/full/10.1056/NEJMc2108479?query=featured_home">https://www.nejm.org/doi/full/10.1056/NEJMc2108479?query=featured_home</a></p>	<p>Breakthrough SARS-CoV-2 Infections in Prison after Vaccination</p>	<p>Bassa incidenza di infezioni da SARS-CoV-2 post vaccinazione in un carcere degli USA.</p>	<p>We conducted a study to analyze weekly PCR test results that were obtained in the RIDOC system from March 9 to May 6, 2021. RIDOC policy includes a 10-day isolation period for all persons who have symptoms or a positive Covid-19 test. A test-based end-of-isolation strategy was initiated on March 10. According to this protocol, if negative results were obtained on two PCR tests that had been performed 24 hours apart, isolation could end early.</p>																																
<p>Patriquin CJ et al</p> <p>NEJM</p> <p><a href="https://www.nejm.org/doi/full/10.1056/NEJMc2108479?query=featured_home">https://www.nejm.org/doi/full/10.1056/NEJMc2108479?query=featured_home</a></p>	<p>Therapeutic Plasma Exchange in Vaccine-Induced Immune Thrombotic Thrombocytopenia</p>	<p>Tre caso di VITT (trombocitopenia trombotica indotta da vaccino) refrattari alla terapia steroidea e con immunoglobuline, trattati</p>	<p>VITT is a severe complication after ChAdOx1 nCoV-19 vaccination. Up-front treatment remains anticoagulation and IVIG. Although further validation is required, we suggest that therapeutic plasma exchange may be effective for the treatment of refractory VITT.</p>																																

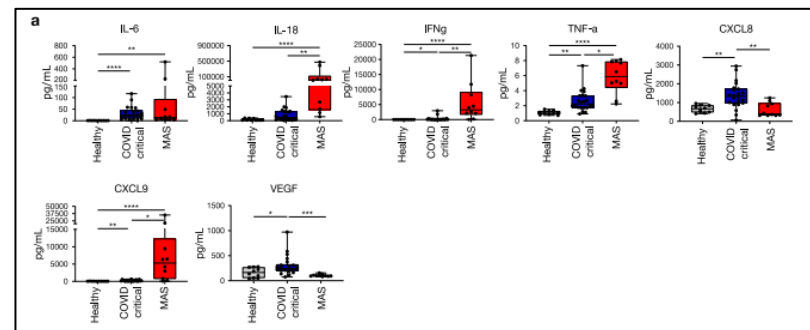
<a href="#">9465?query=featured_ho me</a>		efficacemente con plasmaferesi.	
<p>The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group</p> <p>JAMA</p> <p><a href="https://jamanetwork.com/journals/jama/fullarticle/2781880">https://jamanetwork.com/journals/jama/fullarticle/2781880</a></p>	<p>Association Between Administration of IL-6 Antagonists and Mortality Among Patients Hospitalized for COVID-19</p> <p>A Meta-analysis</p>	<p>Metanalisi di 27 trial clinici in cui si osserva che la terapia con antagonisti di interleukina 6 è associata a minore mortalità a 28 giorni in COVID-19.</p>	<p>Importance Clinical trials assessing the efficacy of IL-6 antagonists in patients hospitalized for COVID-19 have variously reported benefit, no effect, and harm.</p> <p>Objective To estimate the association between administration of IL-6 antagonists compared with usual care or placebo and 28-day all-cause mortality and other outcomes.</p> <p>Data Sources Trials were identified through systematic searches of electronic databases between October 2020 and January 2021. Searches were not restricted by trial status or language. Additional trials were identified through contact with experts.</p> <p>Study Selection Eligible trials randomly assigned patients hospitalized for COVID-19 to a group in whom IL-6 antagonists were administered and to a group in whom neither IL-6 antagonists nor any other immunomodulators except corticosteroids were administered. Among 72 potentially eligible trials, 27 (37.5%) met study selection criteria.</p> <p>Data Extraction and Synthesis In this prospective meta-analysis, risk of bias was assessed using the Cochrane Risk of Bias Assessment Tool. Inconsistency among trial results was assessed using the I<sup>2</sup> statistic. The primary analysis was an inverse variance–weighted fixed-effects meta-analysis of odds ratios (ORs) for 28-day all-cause mortality.</p> <p>Main Outcomes and Measures The primary outcome measure was all-cause mortality at 28 days after randomization. There were 9 secondary outcomes including progression to invasive mechanical ventilation or death and risk of secondary infection by 28 days.</p>

			<p>Results A total of 10 930 patients (median age, 61 years [range of medians, 52-68 years]; 3560 [33%] were women) participating in 27 trials were included. By 28 days, there were 1407 deaths among 6449 patients randomized to IL-6 antagonists and 1158 deaths among 4481 patients randomized to usual care or placebo (summary OR, 0.86 [95% CI, 0.79-0.95]; P = .003 based on a fixed-effects meta-analysis). This corresponds to an absolute mortality risk of 22% for IL-6 antagonists compared with an assumed mortality risk of 25% for usual care or placebo. The corresponding summary ORs were 0.83 (95% CI, 0.74-0.92; P &lt; .001) for tocilizumab and 1.08 (95% CI, 0.86-1.36; P = .52) for sarilumab. The summary ORs for the association with mortality compared with usual care or placebo in those receiving corticosteroids were 0.77 (95% CI, 0.68-0.87) for tocilizumab and 0.92 (95% CI, 0.61-1.38) for sarilumab. The ORs for the association with progression to invasive mechanical ventilation or death, compared with usual care or placebo, were 0.77 (95% CI, 0.70-0.85) for all IL-6 antagonists, 0.74 (95% CI, 0.66-0.82) for tocilizumab, and 1.00 (95% CI, 0.74-1.34) for sarilumab. Secondary infections by 28 days occurred in 21.9% of patients treated with IL-6 antagonists vs 17.6% of patients treated with usual care or placebo (OR accounting for trial sample sizes, 0.99; 95% CI, 0.85-1.16).</p> <p>Conclusions and Relevance In this prospective meta-analysis of clinical trials of patients hospitalized for COVID-19, administration of IL-6 antagonists, compared with usual care or placebo, was associated with lower 28-day all-cause mortality.</p>
Golan Y et al  JAMA	Evaluation of Messenger RNA From COVID-19 BTN162b2 and mRNA-1273 Vaccines in Human Milk	Nessuno dei campioni di latte materno raccolti da 4 a 48 ore dopo la somministrazione di vaccino a mRNA contro SARS-CoV-2	A total of 7 breastfeeding mothers (mean [SD] age, 37.8 [5.8] years) volunteered for this study (Table). Their children ranged in age from 1 month to 3 years. Postvaccination milk samples were collected 4 to 48 hours after administration of the BNT162b2 (n = 5) or mRNA-



<a href="https://jamanetwork.com/journals/jamapediatrics/fullarticle/2781679?resultClick=1">https://jamanetwork.com/journals/jamapediatrics/fullarticle/2781679?resultClick=1</a>		<p>conteneva mRNA in questo studio su 7 donne vaccinate durante l'allattamento.</p>	<p>1273 (n = 2) vaccines. Analysis of 13 human milk samples collected 24 hours after vaccination, including multiple time points (4 to 48 hours) from a single participant, revealed that none of the samples showed detectable levels of vaccine mRNA in any component of the milk.</p> 
<p>Vanderbeke L et al</p> <p>Nature</p> <p><a href="https://www.nature.com/articles/s41467-021-24360-w">https://www.nature.com/articles/s41467-021-24360-w</a></p>	<p>Monocyte-driven atypical cytokine storm and aberrant neutrophil activation as key mediators of COVID-19 disease severity</p>	<p>Differenze fra la tempesta citochinica nell'infezione grave da SARS-CoV-2 e nella sindrome da attivazione macrofagica.</p>	<p>Epidemiological and clinical reports indicate that SARS-CoV-2 virulence hinges upon the triggering of an aberrant host immune response, more so than on direct virus-induced cellular damage. To elucidate the immunopathology underlying COVID-19 severity, we perform cytokine and multiplex immune profiling in COVID-19 patients. We show that hypercytokinemia in COVID-19 differs from the interferon-gamma-driven cytokine storm in macrophage activation syndrome, and is more pronounced in critical versus mild-moderate COVID-19. Systems modelling of cytokine levels paired with deep-immune profiling shows that classical monocytes drive this hyper-inflammatory phenotype and that a reduction in T-lymphocytes correlates with disease severity, with CD8+ cells being disproportionately affected. Antigen presenting machinery expression is also reduced in critical disease. Furthermore, we report that neutrophils contribute to disease severity and local tissue damage by amplification of hypercytokinemia and the formation of neutrophil extracellular traps. Together our findings</p>

suggest a myeloid-driven immunopathology, in which hyperactivated neutrophils and an ineffective adaptive immune system act as mediators of COVID-19 disease severity.



To our knowledge, this is the first study to examine longer duration wearable sensor data. We found a prolonged physiological impact of COVID-19 infection, lasting approximately 2 to 3 months, on average, but with substantial intraindividual variability, which may reflect various levels of autonomic nervous system dysfunction or potentially ongoing inflammation. Transient bradycardia has been noted in a case study<sup>6</sup> approximately 9 to 15 days after symptom onset, which was also seen in our population. Our data suggest that early symptoms and larger initial RHR response to COVID-19 infection may be associated with the physiological length of recovery from this virus.

Radin JL et al

JAMA

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2781687>

Assessment of Prolonged Physiological and Behavioral Changes Associated With COVID-19 Infection

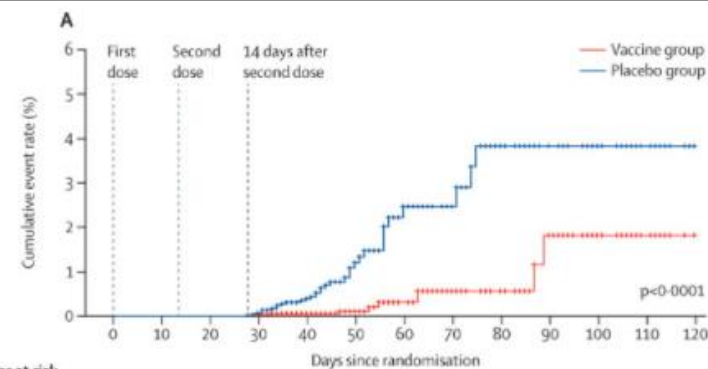
Modificazioni del ritmo cardiaco, del sonno e dell'attività motoria osservate tramite dispositivi indossabili in 875 pazienti fino a 3 mesi dopo infezione da SARS-CoV-2.

			<p><b>A</b> Change in RHR for COVID-19-positive vs COVID-19-negative individuals</p> <p><b>B</b> Change in RHR for COVID-19-positive individuals</p> <p><b>C</b> Change in sleep duration for COVID-19-positive vs COVID-19-negative individuals</p> <p><b>D</b> Change in sleep duration for COVID-19-positive individuals</p>
<p>Patel SY et al</p> <p>JAMA</p> <p><a href="https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2781811">https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2781811</a></p>	<p>Diabetes Care and Glycemic Control During the COVID-19 Pandemic in the United States</p>	<p>Riduzione delle visite in presenza e degli esami ematici, ma non dell'accesso ai farmaci, in una popolazione di diabetici nel periodo pandemico rispetto a un periodo precedente.</p>	<p>There were 1 357 029 and 1 364 522 adults with diabetes in the 2019 and 2020 cohorts, respectively, with similar baseline characteristics. In 2019, 0.3% of cohort had 1 or more telemedicine visit, compared with 29.1% of the 2020 cohort during the pandemic period.</p>

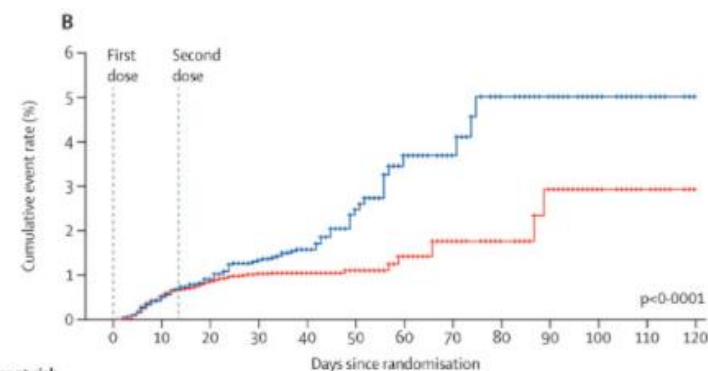
			<p><b>A</b> Proportion of patients with 1 or more outpatient visits</p> <p><b>B</b> Proportion of patients with 1 or more HbA<sub>1c</sub> tests</p> <p><b>C</b> Proportion of patients with 1 or more filled prescriptions</p> <p><b>D</b> Patient HbA<sub>1c</sub> levels</p>
<p>Goldfarb JL et al</p> <p>NEJM</p> <p><a href="https://www.nejm.org/doi/full/10.1056/NEJMp2104527?query=featured_home">https://www.nejm.org/doi/full/10.1056/NEJMp2104527?query=featured_home</a></p>	<p>Beyond the First Dose — Covid-19 Vaccine Follow-through and Continued Protective Measures</p>	<p>Percezione della necessità di una seconda dose e del livello di protezione conferito dal vaccino contro SARS-CoV-2 nella popolazione americana.</p>	<p>Despite current efforts, many Americans, including many of those who have already received a first vaccine dose, remain confused about the timing of protection and the necessity of a second dose. Moreover, a large proportion of vaccinees report being uninformed about CDC guidance regarding the need to continue to take prophylactic measures including mask wearing and avoiding crowds. Finally, our results have identified demographic groups who are most reluctant to accept these measures who would benefit from targeted outreach.</p>
<p>Tanriover MD et al</p> <p>The Lancet</p> <p><a href="https://www.thelancet.com/journals/lancet/article/">https://www.thelancet.com/journals/lancet/article/</a></p>	<p>Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac): interim results of a double-blind, randomised, placebo-</p>	<p>Trial clinico sull'efficacia di Coronavac, vaccino contro SARS-CoV-2 a virione intero inattivato : 83.5% contro l'infezione sintomatica a 2 settimane dal</p>	<p>Background : CoronaVac, an inactivated whole-virion SARS-CoV-2 vaccine, has been shown to be well tolerated with a good safety profile in individuals aged 18 years and older in phase 1/2 trials, and provided a good humoral response against SARS-CoV-2. We present the interim efficacy and safety results of a phase 3 clinical trial of CoronaVac in Turkey.</p>

<a href="#">PIIS0140-6736(21)01429-X/fulltext</a>	<p>controlled, phase 3 trial in Turkey</p>	<p>completamento della vaccinazione.</p>	<p>Methods : This was a double-blind, randomised, placebo-controlled phase 3 trial. Volunteers aged 18–59 years with no history of COVID-19 and with negative PCR and antibody test results for SARS-CoV-2 were enrolled at 24 centres in Turkey. Exclusion criteria included (but were not limited to) immunosuppressive therapy (including steroids) within the past 6 months, bleeding disorders, asplenia, and receipt of any blood products or immunoglobulins within the past 3 months. The K1 cohort consisted of health-care workers (randomised in a 1:1 ratio), and individuals other than health-care workers were also recruited into the K2 cohort (randomised in a 2:1 ratio) using an interactive web response system. The study vaccine was 3 µg inactivated SARS-CoV-2 virion adsorbed to aluminium hydroxide in a 0.5 mL aqueous suspension. Participants received either vaccine or placebo (consisting of all vaccine components except inactivated virus) intramuscularly on days 0 and 14. The primary efficacy outcome was the prevention of PCR-confirmed symptomatic COVID-19 at least 14 days after the second dose in the per protocol population. Safety analyses were done in the intention-to-treat population. This study is registered with ClinicalTrials.gov (NCT04582344) and is active but no longer recruiting.</p> <p>Findings : Among 11 303 volunteers screened between Sept 14, 2020, and Jan 5, 2021, 10 218 were randomly allocated. After exclusion of four participants from the vaccine group because of protocol deviations, the intention-to-treat group consisted of 10 214 participants (6646 [65.1%] in the vaccine group and 3568 [34.9%] in the placebo group) and the per protocol group consisted of 10 029 participants (6559 [65.4%] and 3470 [34.6%]) who received two doses of vaccine or placebo. During a median follow-up period of 43 days (IQR 36–48), nine cases of PCR-confirmed</p>
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			<p>symptomatic COVID-19 were reported in the vaccine group (31·7 cases [14·6–59·3] per 1000 person-years) and 32 cases were reported in the placebo group (192·3 cases [135·7–261·1] per 1000 person-years) 14 days or more after the second dose, yielding a vaccine efficacy of 83·5% (95% CI 65·4–92·1; <math>p&lt;0\cdot0001</math>). The frequencies of any adverse events were 1259 (18·9%) in the vaccine group and 603 (16·9%) in the placebo group (<math>p=0\cdot0108</math>) with no fatalities or grade 4 adverse events. The most common systemic adverse event was fatigue (546 [8·2%] participants in the vaccine group and 248 [7·0%] the placebo group, <math>p=0\cdot0228</math>). Injection-site pain was the most frequent local adverse event (157 [2·4%] in the vaccine group and 40 [1·1%] in the placebo group, <math>p&lt;0\cdot0001</math>).</p> <p>Interpretation : CoronaVac has high efficacy against PCR-confirmed symptomatic COVID-19 with a good safety and tolerability profile.</p>
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Number at risk (number censored)	0	10	20	30	40	50	60	70	80	90	100	110	120
Vaccine group	6646 (0)	6646 (0)	6646 (0)	5779 (1197)	4582 (3315)	1266 (724)	540 (289)	250 (43)	207 (56)	149 (93)	56 (40)	16 (15)	1 (1)
Placebo group	3568 (0)	3568 (0)	3568 (0)	3112 (623)	2488 (1667)	810 (409)	394 (156)	237 (49)	185 (46)	139 (85)	54 (37)	17 (15)	2 (2)



Number at risk (number censored)	0	10	20	30	40	50	60	70	80	90	100	110	120
Vaccine group	6646 (34)	6583 (209)	6348 (684)	5653 (1022)	4629 (3311)	1317 (753)	562 (305)	256 (44)	212 (45)	165 (105)	60 (41)	19 (18)	1 (1)
Placebo group	3568 (17)	3536 (104)	3415 (351)	3051 (524)	2519 (1669)	838 (419)	412 (168)	243 (51)	189 (38)	151 (96)	55 (38)	17 (15)	2 (2)

	Vaccine group (n=6646)	Placebo group (n=3568)
Between first and second dose	48	27
From second dose to 14 days after second dose	17	17
More than 14 days after second dose	9	32
Total (any time after randomisation)	74	76

<p>Gaythorpe KA et al</p> <p>Scientific Reports</p> <p><a href="https://www.nature.com/articles/s41598-021-92500-9">https://www.nature.com/articles/s41598-021-92500-9</a></p>	<p>Children's role in the COVID-19 pandemic: a systematic review of early surveillance data on susceptibility, severity, and transmissibility</p>	<p>Il ruolo dei bambini nella pandemia di COVID-19 non è chiaro.</p>	<p>SARS-CoV-2 infections have been reported in all age groups including infants, children, and adolescents. However, the role of children in the COVID-19 pandemic is still uncertain. This systematic review of early studies synthesises evidence on the susceptibility of children to SARS-CoV-2 infection, the severity and clinical outcomes in children with SARS-CoV-2 infection, and the transmissibility of SARS-CoV-2 by children in the initial phases of the COVID-19 pandemic. A systematic literature review was conducted in PubMed. Reviewers extracted data from relevant, peer-reviewed studies published up to July 4th 2020 during the first wave of the SARS-CoV-2 outbreak using a standardised form and assessed quality using the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies. For studies included in the meta-analysis, we used a random effects model to calculate pooled estimates of the proportion of children considered asymptomatic or in a severe or critical state. We identified 2775 potential studies of which 128 studies met our inclusion criteria; data were extracted from 99, which were then quality assessed. Finally, 29 studies were considered for the meta-analysis that included information of symptoms and/or severity, these were further assessed based on patient recruitment. Our pooled estimate of the proportion of test positive children who were asymptomatic was 21.1% (95% CI: 14.0–28.1%), based on 13 included studies, and the proportion of children with severe or critical symptoms was 3.8% (95% CI: 1.5–6.0%), based on 14 included studies. We did not identify any studies designed to assess transmissibility in children and found that susceptibility to infection in children was highly variable across studies. Children's susceptibility to infection and onward transmissibility relative to adults is still unclear and varied widely between studies. However, it is evident that most children</p>
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			<p>experience clinically mild disease or remain asymptotically infected. More comprehensive contact-tracing studies combined with serosurveys are needed to quantify children's transmissibility relative to adults. With children back in schools, testing regimes and study protocols that will allow us to better understand the role of children in this pandemic are critical.</p>
<p>Vouga M et al</p> <p>Scientific Reports</p> <p><a href="https://www.nature.com/articles/s41598-021-92357-y">https://www.nature.com/articles/s41598-021-92357-y</a></p>	<p>Maternal outcomes and risk factors for COVID-19 severity among pregnant women</p>	<p>Sono fattori di rischio associati a un decorso grave di COVID-19 in gravidanza le comorbidità polmonari, l'ipertensione e il diabete secondo questo studio caso-scontrollo su 926 gravide infette.</p>	<p>Pregnant women may be at higher risk of severe complications associated with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which may lead to obstetrical complications. We performed a case control study comparing pregnant women with severe coronavirus disease 19 (cases) to pregnant women with a milder form (controls) enrolled in the COVI-Preg international registry cohort between March 24 and July 26, 2020. Risk factors for severity, obstetrical and immediate neonatal outcomes were assessed. A total of 926 pregnant women with a positive test for SARS-CoV-2 were included, among which 92 (9.9%) presented with severe COVID-19 disease. Risk factors for severe maternal outcomes were pulmonary comorbidities [aOR 4.3, 95% CI 1.9–9.5], hypertensive disorders [aOR 2.7, 95% CI 1.0–7.0] and diabetes [aOR 2.2, 95% CI 1.1–4.5]. Pregnant women with severe maternal outcomes were at higher risk of caesarean section [70.7% (n = 53/75)], preterm delivery [62.7% (n = 32/51)] and newborns requiring admission to the neonatal intensive care unit [41.3% (n = 31/75)]. In this study, several risk factors for developing severe complications of SARS-CoV-2 infection among pregnant women were identified including pulmonary comorbidities, hypertensive disorders and diabetes. Obstetrical and neonatal outcomes appear to be influenced by the severity of maternal disease.</p>

<p>Kofman A et al</p> <p>JAMA</p> <p><a href="https://jamanetwork.com/journals/jama/fullarticle/2781945?guestAccessKey=823567ee-3c02-483f-9169-ed64989be74e&amp;utm_source=silverchair&amp;utm_medium=email&amp;utm_campaign=article_alert-jama&amp;utm_content=olf&amp;utm_term=070821">https://jamanetwork.com/journals/jama/fullarticle/2781945?guestAccessKey=823567ee-3c02-483f-9169-ed64989be74e&amp;utm_source=silverchair&amp;utm_medium=email&amp;utm_campaign=article_alert-jama&amp;utm_content=olf&amp;utm_term=070821</a></p>	<p>Potential COVID-19 Endgame Scenarios</p> <p>Eradication, Elimination, Cohabitation, or Conflagration?</p>	<p>Quale futuro per la pandemia di COVID-19.</p>	<p>Only a year ago, much of the world was united in lockdown in the midst of the first outbreak of COVID-19. Today, the global experience is widely divergent. Israel, New Zealand, Vietnam, and Brunei may well be approaching elimination. The United Kingdom, the United States, and China, for their part, appear to exist in a state of cohabitation. In contrast, India, other parts of Southeast Asia, and much of South America appear to be weighed down by a conflagration-like state.</p>
<p>Gurdasani D et al</p> <p>The Lancet</p> <p><a href="https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01589-0/fulltext">https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01589-0/fulltext</a></p>	<p>Mass infection is not an option: we must do more to protect our young</p>	<p>Eliminare le misure di contenimento di SARS-CoV-2 significa consentire l'infezione di milioni di persone non vaccinate, per lo più giovani : una decisione rischiosa secondo l'autore di questo articolo.</p>	<p>As the third wave of the pandemic takes hold across England, the UK Government plans to further re-open the nation. Implicit in this decision is the acceptance that infections will surge, but that this does not matter because vaccines have “broken the link between infection and mortality”.<sup>1</sup> On July 19, 2021—branded as Freedom Day—almost all restrictions are set to end. We believe this decision is dangerous and premature.</p>
<p>Yang H et al</p> <p>JAMA</p> <p><a href="https://jamanetwork.com/journals/jama-health-">https://jamanetwork.com/journals/jama-health-</a></p>	<p>Factors Associated With Chinese Adults' Vaccine Acceptance</p>	<p>Risultati di un sondaggio su oltre 12000 adulti in Cina in merito alla vaccinazione contro SARS-CoV-2 : maggiore conoscenza è associata a maggiore volontà di ricevere il vaccino.</p>	<p>A large-scale, nationally representative, random sample of 14 378 Chinese adults were invited to participate in this internet-based survey. The survey was conducted following the guidelines by the American Association for Public Opinion Research (AAPOR). Participants consented before responding to the questionnaire, responded anonymously, and could terminate their participation at any point.</p>

[forum/fullarticle/2781918](https://jamanetwork.com/forums/fullarticle/2781918)

**Table 1. Descriptive Statistics (n=12 651)**

Characteristic	No. (% in category or mean of variable) <sup>a</sup>	Mean of willingness to be vaccinated <sup>b</sup>	Willing to be vaccinated, % <sup>c</sup>
Age, mean (SD), y	12 649 (mean [SD], 36.6 [14.6])	NA	NA
Gender			
Women	6145 (48.6)	4.2	84.4
Men	6504 (51.4)	4.3	87.2
Monthly household income, mean (SD), ¥10 000	11 876 (mean [SD], 1.7 [1.6])	NA	NA
Education			
With college degree	9484 (75.0)	4.3	86.8
Without college degree	3162 (25.0)	4.2	83.0
Marital status			
Married	7715 (61.0)	4.3	85.9
Not married	4936 (39.0)	4.3	85.8
Location			
Rural	1382 (10.9)	4.3	85.8
Urban	11 269 (89.1)	4.3	85.9
Province			
Hubei	631 (5.0)	4.3	89.2
Other	12 020 (95.0)	4.3	85.7

Eshun-Wilson I et al

JAMA

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2781723>

Public Preferences for Social Distancing Policy Measures to Mitigate the Spread of COVID-19 in Missouri

La maggior parte dei partecipanti a questo sondaggio per oltre 2000 persone negli USA accetta di buon grado le restrizioni che impediscono i grandi eventi, mentre ad esempio si desidera conservare la possibilità di frequentare locali all'aperto.

**Importance** Policies to promote social distancing can minimize COVID-19 transmission but come with substantial social and economic costs. Quantifying relative preferences among the public for such practices can inform locally relevant policy prioritization and optimize uptake.

**Objective** To evaluate relative utilities (ie, preferences) for COVID-19 pandemic social distancing strategies against the hypothetical risk of acquiring COVID-19 and anticipated income loss.

**Design, Setting, and Participants** This survey study recruited individuals living in the Missouri area from May to June 2020 via randomly distributed unincentivized social media advertisements and local recruitment platforms for members of minority racial and ethnic groups. Participants answered 6 questions that asked them to choose between 2 hypothetical counties where business

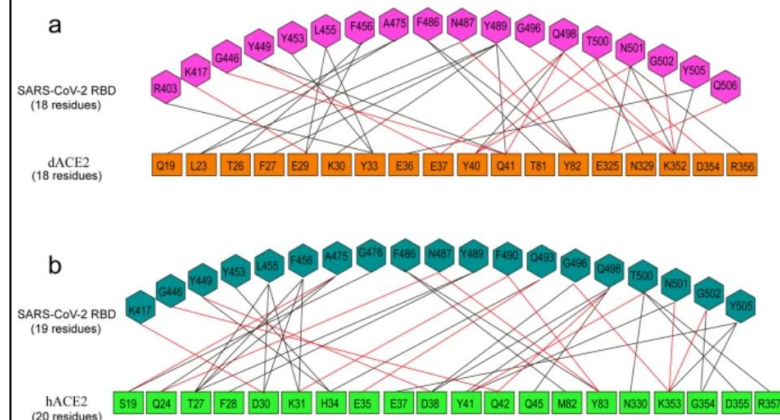
			<p>closures, social distancing policy duration, COVID-19 infection risk, and income loss varied.</p> <p><b>Main Outcomes and Measures</b> Reweighted population-level relative preferences (utilities) for social distancing policies, subgroups, and latent classes.</p> <p><b>Results</b> The survey had a 3% response rate (3045 of 90 320). Of the 2428 respondents who completed the survey, 1669 (75%) were 35 years and older, 1536 (69%) were women, and 1973 (89%) were White. After reweighting to match Missouri population demographic characteristics, the strongest preference was for the prohibition of large gatherings (mean preference, -1.43; 95% CI, -1.67 to -1.18), with relative indifference to the closure of social and lifestyle venues (mean preference, 0.05; 95% CI, -0.08 to 0.17). There were weak preferences to keep outdoor venues (mean preference, 0.50; 95% CI, 0.39 to 0.61) and schools (mean preference, 0.18; 95% CI, 0.05 to 0.30) open. Latent class analysis revealed 4 distinct preference phenotypes in the population: risk averse (48.9%), conflicted (22.5%), prosocial (14.9%), and back to normal (13.7%), with men twice as likely as women to belong to the back to normal group than the risk averse group (relative risk ratio, 2.19; 95% CI, 1.54 to 3.12).</p> <p><b>Conclusions And relevance</b> In this survey study using a discrete choice experiment, public health policies that prohibited large gatherings, as well as those that closed social and lifestyle venues, appeared to be acceptable to the public. During policy implementation, these activities should be prioritized for first-phase closures. These findings suggest that policy messages that address preference heterogeneity (eg, focusing on specific preference subgroups or targeting men) could improve adherence to social distancing measures for COVID-19 and future pandemics.</p>
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			<p><b>Figure 1. Mean Preferences for Social Distancing Measures in the Population</b></p> <table border="1"><caption>Data for Figure 1: Mean Preferences for Social Distancing Measures</caption><thead><tr><th>Measure</th><th>Mean Preference (95% CI)</th></tr></thead><tbody><tr><td>Duration: 2 vs 1 months</td><td>-0.2</td></tr><tr><td>Duration: 3 vs 1 months</td><td>-0.1</td></tr><tr><td>Large gatherings permitted</td><td>-1.3</td></tr><tr><td>Social venues open</td><td>0.1</td></tr><tr><td>Outdoor venues open</td><td>0.4</td></tr><tr><td>Schools open</td><td>0.2</td></tr><tr><td>Risk of infection: 15% vs 5%</td><td>-1.0</td></tr><tr><td>Risk of infection: 30% vs 5%</td><td>-2.8</td></tr><tr><td>Income loss: 15% vs 5%</td><td>-0.7</td></tr><tr><td>Income loss: 25% vs 5%</td><td>-1.5</td></tr></tbody></table>	Measure	Mean Preference (95% CI)	Duration: 2 vs 1 months	-0.2	Duration: 3 vs 1 months	-0.1	Large gatherings permitted	-1.3	Social venues open	0.1	Outdoor venues open	0.4	Schools open	0.2	Risk of infection: 15% vs 5%	-1.0	Risk of infection: 30% vs 5%	-2.8	Income loss: 15% vs 5%	-0.7	Income loss: 25% vs 5%	-1.5
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Income loss: 15% vs 5%	-0.7																								
Income loss: 25% vs 5%	-1.5																								
<p>Cadegiani FA et al</p> <p>MedRXiv -not peer reviewed</p> <p><a href="https://www.medrxiv.org/content/10.1101/2021.06.22.21259318v1">https://www.medrxiv.org/content/10.1101/2021.06.22.21259318v1</a></p>	<p><b>Efficacy of Proxalutamide in Hospitalized COVID-19 Patients: A Randomized, Double-Blind, Placebo-Controlled, Parallel-Design Clinical Trial</b></p>	<p>L'antagonista non steroideo del recettore degli androgeni proxalutamide interferisce nel meccanismo di infezione cellulare di SARS-CoV-2. In questo trial su 645 pazienti si osserva che la terapia con questo farmaco in pazienti non ventilati riduce la mortalità e aumenta il tasso di guarigione a 14 giorni.</p>	<p><b>Background</b> Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infectivity is mediated by the androgen-promoted protease, transmembrane protease, serine 2 (TMPRSS2). Previously, we have shown that treatment with proxalutamide, a non-steroidal androgen receptor antagonist, accelerates viral clearance and clinical remission in outpatients with coronavirus disease 2019 (COVID-19) compared to placebo. The effects in hospitalized COVID-19 patients were unknown.</p> <p><b>Methods</b> Men and women hospitalized but not requiring mechanical ventilation were randomized (1:1 ratio) to receive 300 mg of proxalutamide per day or placebo for 14 days. The study was conducted at eight sites in the state of Amazonas, Brazil. The primary outcome measure was the clinical status (8-point ordinal scale) at 14-days post-randomization. The primary efficacy endpoint was the 14-day recovery ratio (alive hospital discharge [scores 1, 2]).</p> <p><b>Findings</b> A total of 645 patients were randomized (317 received proxalutamide, 328 placebo) and underwent intention-to-treat analysis. The 14-day median ordinal scale score in the proxalutamide group was 1 (interquartile range [IQR]=1–2) versus 7 (IQR=2–8) for placebo, <math>P&lt;0.001</math>. The 14-day recovery rate was 81.4% for proxalutamide and 35.7% for placebo (recovery ratio,</p>																						

			<p>2.28; 95% CI 1.95–2.66 [P&lt;0.001]). The 28-day all-cause mortality rate was 11.0% for proxalutamide versus 49.4% for placebo (hazard ratio, 0.16; 95% CI 0.11–0.24). The median post-randomization time to recovery was 5 days (IQR=3– 8) for proxalutamide versus 10 days (IQR=6–15) for placebo.</p> <p>Interpretation Hospitalized COVID-19 patients not requiring mechanical ventilation receiving proxalutamide had a 128% higher recovery rate than those treated with placebo. All-cause mortality was reduced by 77.7% over 28 days.</p>
<p>Quinn SC et al</p> <p>NEJM</p> <p><a href="https://www.nejm.org/doi/full/10.1056/NEJMp2103104?query=featured_home">https://www.nejm.org/doi/full/10.1056/NEJMp2103104?query=featured_home</a></p>	<p>Addressing Vaccine Hesitancy in BIPOC Communities — Toward Trustworthiness, Partnership, and Reciprocity</p>	<p>Le comunità di afroamericani, indigeni e le minoranze negli USA hanno avuto conseguenze più pesanti dalla pandemia di COVID-19 e sono anche gravate da scetticismo nei confronti dei vaccini. Questo deriverebbe da sfiducia nelle istituzioni, un problema da affrontare.</p>	<p>It is essential to remember that hesitancy doesn't mean refusal, and in fact, skepticism can be protective for BIPOC communities. However, we believe it's time to shift the focus from a sole emphasis on changing hearts and minds among members of BIPOC communities to ensuring that institutions are trustworthy, transparent, and engaged with communities during the vaccine rollout. Making our institutions — particularly health care, public health, and government — more trustworthy will require listening to community voices, preparing public health and health care organizations to respectfully engage with BIPOC communities, and becoming more client-centered, including viewing hesitancy and barriers to vaccine uptake through the eyes of members of the BIPOC community.</p>
<p>Zhang Z et al</p> <p>Nature</p> <p><a href="https://www.nature.com/articles/s41467-021-24326-y">https://www.nature.com/articles/s41467-021-24326-y</a></p>	<p>The molecular basis for SARS-CoV-2 binding to dog ACE2</p>	<p>Struttura cristallina del legame fra ACE2 e porzione legante il recettore della proteina S di SARS-CoV-2 nel cane : le interazioni sono un po' meno numerose che nell'uomo ma l'infezione è possibile.</p>	<p>SARS-CoV-2 can infect many domestic animals, including dogs. Herein, we show that dog angiotensin-converting enzyme 2 (dACE2) can bind to the SARS-CoV-2 spike (S) protein receptor binding domain (RBD), and that both pseudotyped and authentic SARS-CoV-2 can infect dACE2-expressing cells. We solved the crystal structure of RBD in complex with dACE2 and found that the total number of contact residues, contact atoms, hydrogen bonds and salt bridges at the binding interface in this complex are slightly fewer than those in</p>

the complex of the RBD and human ACE2 (hACE2). This result is consistent with the fact that the binding affinity of RBD to dACE2 is lower than that of hACE2. We further show that a few important mutations in the RBD binding interface play a pivotal role in the binding affinity of RBD to both dACE2 and hACE2. Our work reveals a molecular basis for cross-species transmission and potential animal spread of SARS-CoV-2, and provides new clues to block the potential transmission chains of this virus.

**Fig. 2: Interaction interface in the RBD/dACE2 complex and the RBD/hACE2 complex.**



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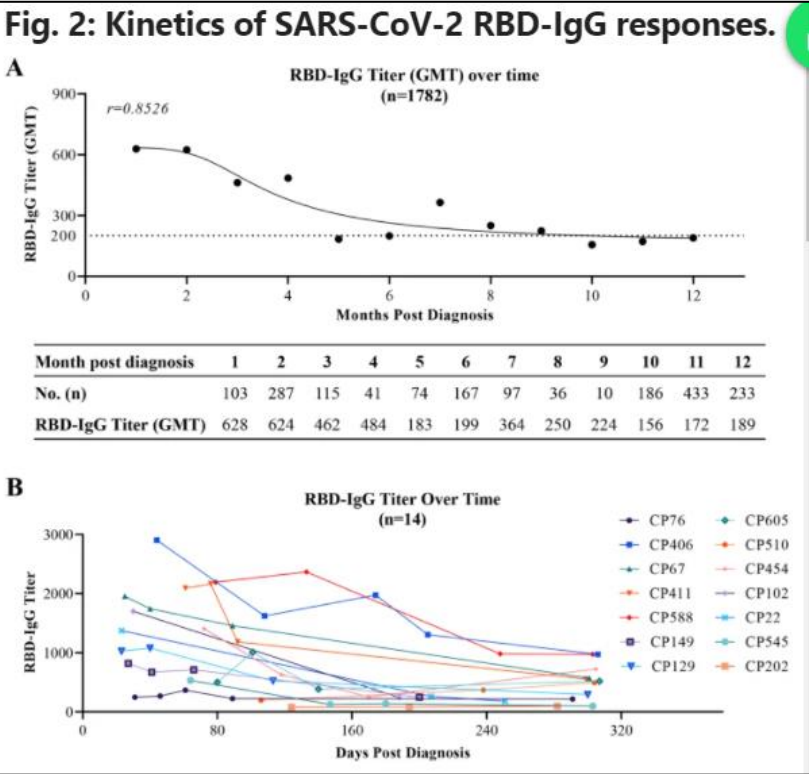
<https://www.nature.com/articles/s41467-021-24230-5>

Twelve-month specific IgG response to SARS-CoV-2 receptor-binding domain among COVID-19 convalescent plasma donors in Wuhan

Studio della presenza di IgG anti RBD di SARS-CoV-2 fino a 12 mesi dopo l'infezione in una coorte di oltre 1700 pazienti di Wuhan : riduzione progressiva del titolo con stabilizzazione al 64% circa di quello iniziale dopo 9 mesi.

To investigate the duration of humoral immune response in convalescent coronavirus disease 2019 (COVID-19) patients, we conduct a 12-month longitudinal study through collecting a total of 1,782 plasma samples from 869 convalescent plasma donors in Wuhan, China and test specific antibody responses. The results show that positive rate of IgG antibody against receptor-binding domain of spike protein (RBD-IgG) to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the COVID-19 convalescent plasma donors exceeded 70% for 12 months post diagnosis. The

level of RBD-IgG decreases with time, with the titer stabilizing at 64.3% of the initial level by the 9th month. Moreover, male plasma donors produce more RBD-IgG than female, and age of the patients positively correlates with the RBD-IgG titer. A strong positive correlation between RBD-IgG and neutralizing antibody titers is also identified. These results facilitate our understanding of SARS-CoV-2-induced immune memory to promote vaccine and therapy development.





<p>Gargano J et al</p> <p>MMWR</p> <p><a href="https://www.cdc.gov/mmwr/volumes/70/wr/mm7027e2.htm?s_cid=mm7027e2_w">https://www.cdc.gov/mmwr/volumes/70/wr/mm7027e2.htm?s_cid=mm7027e2_w</a></p>	<p>Use of mRNA COVID-19 vaccine after reports of myocarditis among vaccine recipients</p>	<p>Rischio-beneficio dell'utilizzo di vaccini a mRNA a fronte dei casi di miocardite riportati nella popolazione molto giovane.</p>	<p>What is already known about this topic?</p> <p>An elevated risk for myocarditis among mRNA COVID-19 vaccinees has been observed, particularly in males aged 12–29 years.</p> <p>What is added by this report?</p> <p>On June 23, 2021, the Advisory Committee on Immunization Practices concluded that the benefits of COVID-19 vaccination to individual persons and at the population level clearly outweighed the risks of myocarditis after vaccination.</p> <p>What are the implications for public health practice?</p> <p>Continued use of mRNA COVID-19 vaccines in all recommended age groups will prevent morbidity and mortality from COVID-19 that far exceed the number of cases of myocarditis expected. Information regarding the risk for myocarditis with mRNA COVID-19 vaccines should be disseminated to providers to share with vaccine recipients.</p>
<p>Wiegmann PM et al</p> <p>JAMA</p> <p><a href="https://jamanetwork.com/journals/jama-health-forum/fullarticle/2781916">https://jamanetwork.com/journals/jama-health-forum/fullarticle/2781916</a></p>	<p>Balancing Quality and Speed in the Market Approval of Diagnostic Tests</p>	<p>Esperienza di USA, Corea e Regno Unito nell'approvazione rapida di test diagnostici per SARS-CoV-2.</p>	<p>The novelty of the SARS-CoV-2 virus accounted for the early delay of mass testing and necessitated the development of new detection methods. These methods included molecular, antigen, and antibody tests, all of which have specific strengths and weaknesses. These developments and the subsequent commercialization of diagnostic tests required coordination from a wide array of stakeholders in the testing ecosystem—scientists, test manufacturers, clinical laboratories, and others. This coordination is challenging; consequently, COVID-19 tests available on the market vary substantially in their sensitivity and specificity.</p>
<p>Bilinski J et al</p> <p>BMJ</p>	<p>Rapid resolution of COVID-19 after faecal microbiota transplantation</p>	<p>Due casi di trapianto fecale per trattare la colite da Clostridium difficile in pazienti con coinfezione da SARS-CoV-2, con potenziali</p>	<p>Recent publications demonstrate that SARS-CoV-2 may undergo prolonged shedding in stool, and that gut microbiome perturbations associate with COVID-19 severity. Faecal microbiota transplant (FMT) restores a damaged gut microbiome and may impact on</p>

<a href="https://gut.bmj.com/content/gutjnl/early/2021/06/25/gutjnl-2021-325010.full.pdf">https://gut.bmj.com/content/gutjnl/early/2021/06/25/gutjnl-2021-325010.full.pdf</a>		<p>interessanti implicazioni immunologiche.</p>	<p>immune responses, including in the respiratory system ('gut–lung axis'); such microbiome-immune signalling may result in lung-epithelial resistance to SARS-CoV-2. We describe two interesting cases of patients treated with FMT primarily to treat <i>Clostridioides difficile</i> infection (CDI), but which coincidentally were performed just before initial symptoms of coexisting COVID-19.</p>
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