RICERCA BIBLIOGRAFICA COVID 19

SETTIMANA 21.06 – 27.06.2021

FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE

DOTT.SSA ELEONORA TADDEI

AUTORE/RIVISTA	TITOLO	OUTCOME PRINCIPALE	ABSTRACT
Food and Drug Administration https://www.fda.gov/medical-devices/safety-communications/antibody-testing-not-currently-recommended-assess-immunity-after-covid-19-vaccination-fda-safety	Antibody Testing Is Not Currently Recommended to Assess Immunity After COVID-19 Vaccination: FDA Safety Communication	Come (non) interpretare la sierologia per SARS-CoV-2 secondo l'FDA.	The U.S. Food and Drug Administration (FDA) is reminding the public and health care providers that results from currently authorized SARS-CoV-2 antibody tests should not be used to evaluate a person's level of immunity or protection from COVID-19 at any time, and especially after the person received a COVID-19 vaccination.
Karan A et al	The Risk of SARS-CoV-2 Transmission from Patients with Undiagnosed Covid-19	Più di un terzo dei pazienti che avevano avuto un compagno di stanza positivo per SARS-CoV-2 in questo	We assessed SARS-CoV-2 transmission between patients in shared rooms in an academic hospital between September 2020-April 2021. 11,290 patients were admitted to shared rooms, of whom 25 tested positive. Among 31 exposed roommates, 12 (39%) tested

<table>
<tr>
<td>CID

https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab564/6305137</td>
<td>to Roommates in a Large Academic Medical Center</td>
<td>piccolo studio ha presentato l’infezione nei 14 giorni successivi al contatto.</td>
<td>positive within 14 days. Transmission was associated with PCR cycle thresholds ≤21.

<table>
<tr><th>Covariate</th><th>Transmission+ (N=12)</th><th>Transmission- (N=19)</th><th>OR (95% CI)</th><th>p-value</th></tr>
<tr><td>Exposed Patients</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Median Age</td><td>64 (56-80)</td><td>69 (54-72)</td><td>-</td><td>0.90</td></tr>
<tr><td>Female Sex</td><td>8 (66.7%)</td><td>5 (26.3%)</td><td>5.6 [1.2-27.1]</td><td>0.03[d]</td></tr>
<tr><td>Non-White Race</td><td>6 (50.0%)</td><td>2 (10.5%)</td><td>8.5 [1.3-54.1]</td><td>0.02[d]</td></tr>
<tr><td>Exposure Duration ≥18 Hours[a]</td><td>8 (66.7%)</td><td>9 (47.4%)</td><td>2.2 [0.5-10.0]</td><td>0.30[d]</td></tr>
<tr><td>Lung Disease</td><td>2 (16.7%)</td><td>2 (10.5%)</td><td>1.7 [0.2-14.0]</td><td>0.63</td></tr>
<tr><td>Heart Failure</td><td>2 (16.7%)</td><td>3 (15.8%)</td><td>1.1 [0.2-7.5]</td><td>0.95</td></tr>
<tr><td>Cancer or Immunosuppression</td><td>3 (25.0%)</td><td>5 (26.3%)</td><td>0.9 [0.2-4.9]</td><td>0.94</td></tr>
<tr><td>Obesity</td><td>2 (16.7%)</td><td>3 (15.8%)</td><td>1.1 [0.2-7.5]</td><td>0.95</td></tr>
<tr><td>Chronic Kidney Disease</td><td>2 (16.7%)</td><td>2 (10.5%)</td><td>1.7 [0.2-14.0]</td><td>0.63</td></tr>
<tr><td>Location by Window</td><td>7 (58.3%)</td><td>8 (42.1%)</td><td>1.9 [0.4-8.3]</td><td>0.39</td></tr>
<tr><td>Index Patients[b]</td><td></td><td></td><td></td><td></td></tr>
<tr><td>PCR Cycle Threshold Value ≤21[a]</td><td>11 (91.7%)</td><td>7 (36.8%)</td><td>18.9 [2.0-179]</td><td><0.01[d]</td></tr>
<tr><td>Nebulizer Use or Other Aerosol-Generating Procedure[c]</td><td>3 (25.0%)</td><td>0 (0%)</td><td>-</td><td>-</td></tr>
<tr><td>Cough, Dyspnea, or Tachypnea</td><td>5 (41.7%)</td><td>2 (10.5%)</td><td>6.1 [0.9-39.0]</td><td>0.047[d]</td></tr>
<tr><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Delirium</td><td>1 (8.3%)</td><td>2 (10.5%)</td><td>0.8 [0.1-9.6]</td><td>0.84</td></tr>
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<td>Addeo A et al

Cancer Cell

https://www.sciencedirect.com/science/article/pii/S1535610821003305?via%3Dihub</td>
<td>Immunogenicity of SARS-CoV-2 messenger RNA Vaccines in Patients with Cancer</td>
<td>Risposta anticorpale contro SARS-CoV-2 dopo vaccino a mRNA: neoplasie ematologiche e terapia con anti-CD20 sono fattori associati al mancato sviluppo di un titolo.</td>
<td>Patients with cancer experience higher burden of SARS-CoV-2 infection, disease severity, complications, and mortality, than the general population. SARS-CoV-2 mRNA vaccines are highly effective in the general population; however, few data are available on their efficacy in patients with cancer. Using a prospective cohort, we assessed the seroconversion rates and anti-SARS-CoV-2 spike protein antibody titers following the 1st and 2nd dose of BNT162b2 and mRNA-1273 SARS-CoV-2 vaccines in patients with cancer in U.S. and Europe from January to April 2021. Among 131 patients, most (94%) achieved seroconversion after receipt of 2 vaccine doses. Seroconversion rates and antibody titers in patients with hematological malignancy were significantly lower than those with solid tumors. None of the patients with history of anti-CD-20 antibody in the 6 months prior to vaccination developed antibody response. Antibody titers were highest for clinical surveillance or</td>
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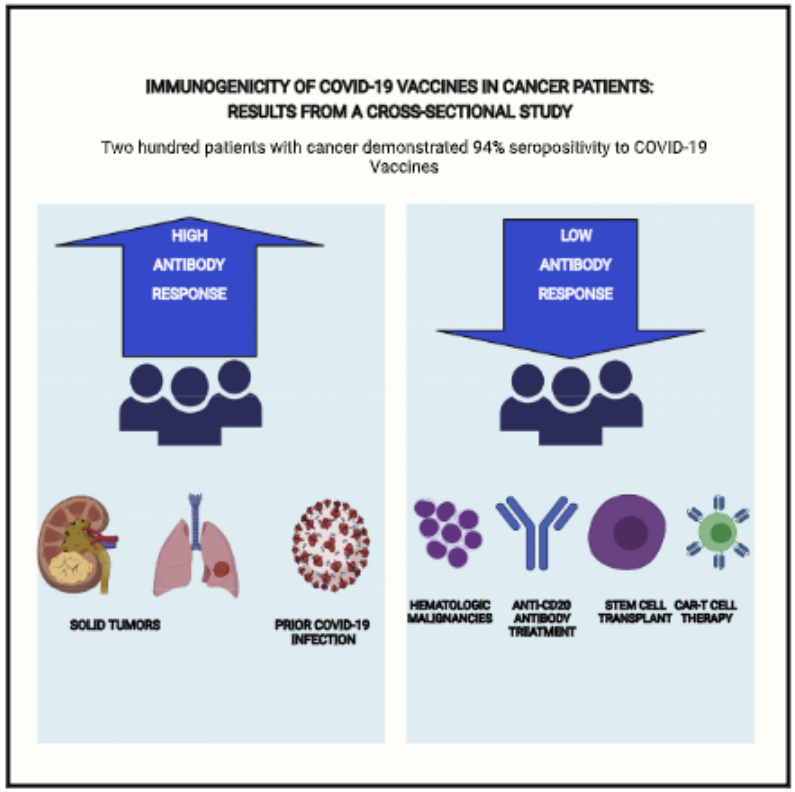
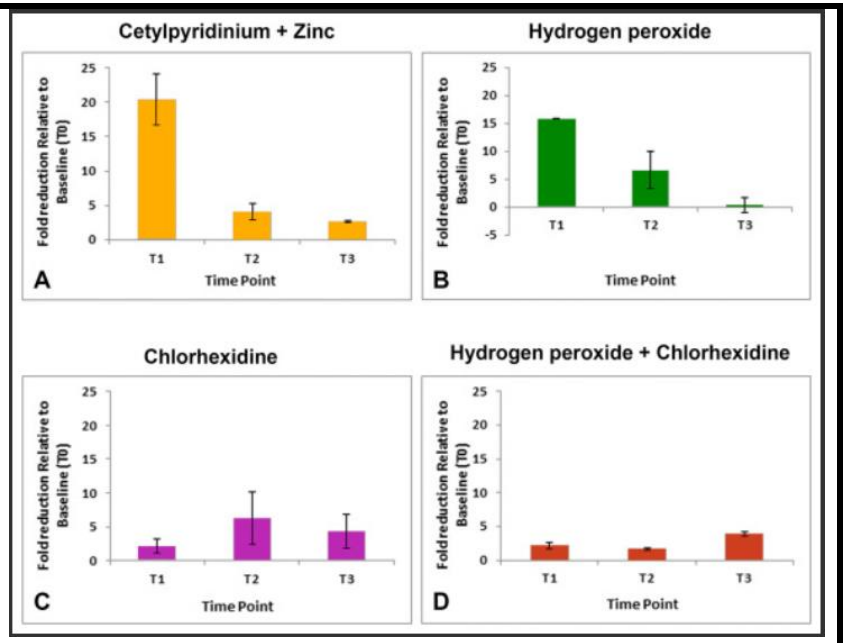
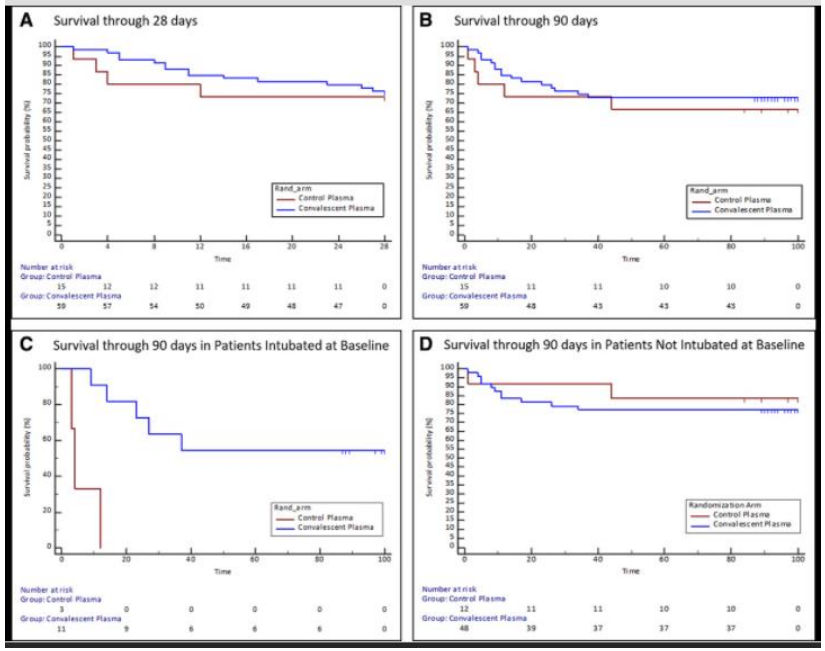
			endocrine therapy groups and lowest for cytotoxic chemotherapy or monoclonal antibody group. **Graphical abstract** 
De Paula Eduardo F et al Helyon https://www.cell.com/heliyon/fulltext/S2405-8440(21)01449-	Salivary SARS-CoV-2 load reduction with mouthwash use: a randomized pilot clinical trial	Igiene orale con collutori a base di diversi agenti antimicrobici e riduzione della carica di SARS-CoV-2.	The saliva of patients with COVID-19 has a high SARS-CoV-2 viral load. The risk of spreading the virus is high, and procedures for viral load reduction in the oral cavity are important. Little research to date has been performed on the effect of mouthwashes on the salivary SARS-CoV-2 viral load. This pilot randomized single-center clinical trial investigated whether three types of mouthwash with solutions containing either 0.075% cetylpyridinium chloride plus

3?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS2405844021014493%3Fshowall%3Dtrue			0.28% zinc lactate (CPC+Zn), 1.5% hydrogen peroxide (HP), or 0.12% chlorhexidine gluconate (CHX) reduce the SARS-CoV-2 viral load in saliva at different time points. Sixty SARS-CoV-2-positive patients were recruited and randomly partitioned into a placebo (oral rinsing with distilled water) group and other groups according to the type of mouthwash. Saliva samples were collected from the participants before rinsing (T0), immediately after rinsing (T1), 30 min after rinsing (T2), and 60 min after rinsing (T3). The salivary SARS-CoV-2 viral load was measured by qRT-PCR assays. Rinsing with HP and CPC+Zn resulted in better reductions in viral load, with 15.8±0.08- and 20.4±3.7-fold reductions at T1, respectively. Although the CPC+Zn group maintained a 2.6±0.1-fold reduction at T3, this trend was not observed for HP. HP mouthwash resulted in a significant reduction in the SARS-CoV-2 viral load up to 30 min after rinsing (6.5±3.4). The CHX mouthwash significantly reduced the viral load at T1, T2, and T3 (2.1±1.5-, 6.2±3.8-, and 4.2±2.4-fold reductions, respectively). In conclusion, mouthwash with CPC+Zinc and CHX resulted in significant reductions of the SARS-CoV-2 viral load in saliva up to 60 mins after rinsing, while HP mouthwash resulted in a significant reduction up to 30 mins after rinsing. Despite this transitory effect, these results encourage further studies and suggest that these products could be considered as risk-mitigation strategies for patients infected with SARS-CoV-2.

			
Bennett-Guerrero E et al Critical Care Med https://journals.lww.com/ccmjournal/Fulltext/2021/07000/Severe_Acute_Respiratory_Syndrome_Coronavirus_2.2.aspx	Severe Acute Respiratory Syndrome Coronavirus 2 Convalescent Plasma Versus Standard Plasma in Coronavirus Disease 2019 Infected Hospitalized Patients in New York: A Double-Blind Randomized Trial	La terapia con plasma di soggetti guariti non è associata a sopravvivenza in pazienti con infezione da SARS-CoV-2.	OBJECTIVES: Four peer-reviewed publications have reported results from randomized controlled trials of convalescent plasma for coronavirus disease 2019 infection; none were conducted in the United States nor used standard plasma as a comparator. To determine if administration of convalescent plasma to patients with coronavirus disease 2019 increases antibodies to severe acute respiratory syndrome coronavirus 2 and improves outcome. DESIGN: Double-blind randomized controlled trial. SETTING: Hospital in New York. PATIENTS: Patients with polymerase chain reaction documented coronavirus disease 2019 infection.

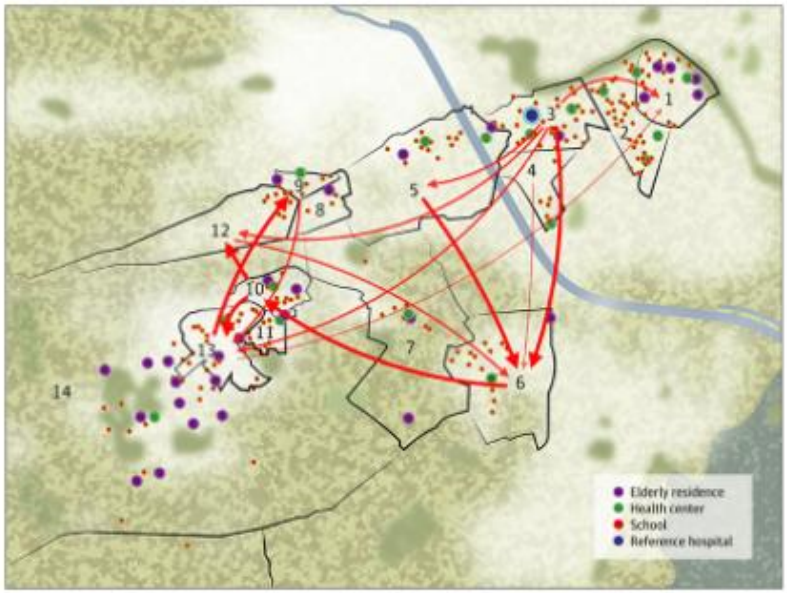
			INTERVENTIONS: Patients were randomized (4:1) to receive 2 U of convalescent plasma versus standard plasma. Antibodies to severe acute respiratory syndrome coronavirus 2 were measured in plasma units and in trial recipients. MEASUREMENTS AND MAIN RESULTS: Enrollment was terminated after emergency use authorization was granted for convalescent plasma. Seventy-four patients were randomized. At baseline, mean (sd) Acute Physiology and Chronic Health Evaluation II score (23.4 [5.6] and 22.5 [6.6]), percent of patients intubated (19% and 20%), and median (interquartile range) days from symptom onset to randomization of 9 (6–18) and 9 (6–15), were similar in the convalescent plasma versus standard plasma arms, respectively. Convalescent plasma had high neutralizing activity (median [interquartile range] titer 1:526 [1:359–1:786]) and its administration increased antibodies to severe acute respiratory syndrome coronavirus 2 by 14.4%, whereas standard plasma administration led to an 8.6% decrease (p = 0.005). No difference was observed for ventilator-free days through 28 days (primary study endpoint): median (interquartile range) of 28 (2–28) versus 28 (0–28; p = 0.86) for the convalescent plasma and standard plasma groups, respectively. A greater than or equal to 2 point improvement in the World Health Organization scale was achieved by 20% of subjects in both arms (p = 0.99). All-cause mortality through 90 days was numerically lower in the convalescent plasma versus standard plasma groups (27% vs 33%; p = 0.63) but did not achieve statistical significance. A key prespecified subgroup analysis of time to death in patients who were intubated at baseline was statistically significant; however, sample size numbers were small.

			CONCLUSIONS: Administration of convalescent plasma to hospitalized patients with coronavirus disease 2019 infection increased antibodies to severe acute respiratory syndrome coronavirus disease 2 but was not associated with improved outcome. 
Orkin AM et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2781397?guestAccessKey=e3d13505-821c-4301-b8e3-	Guidelines for Reporting Trial Protocols and Completed Trials Modified Due to the COVID-19 Pandemic and Other Extenuating Circumstances The CONSERVE 2021 Statement	Consensus su come riportare i cambi di protocollo per cause di forza maggiore – ad esempio in perido pandemico- nei trial clinici, rispettando l'etica ed evitando che ciò comprometta la validità dei risultati.	Importance Extenuating circumstances can trigger unplanned changes to randomized trials and introduce methodological, ethical, feasibility, and analytical challenges that can potentially compromise the validity of findings. Numerous randomized trials have required changes in response to the COVID-19 pandemic, but guidance for reporting such modifications is incomplete. Objective As a joint extension for the CONSORT and SPIRIT reporting guidelines, CONSERVE (CONSORT and SPIRIT Extension for RCTs Revised in Extenuating Circumstances) aims to improve

b2fdc00ac398&utm_source=silverchair&utm_medium=email&utm_campaign=article_alert-jama&utm_content=olf&utm_term=062121			reporting of trial protocols and completed trials that undergo important modifications in response to extenuating circumstances. Evidence A panel of 37 international trial investigators, patient representatives, methodologists and statisticians, ethicists, funders, regulators, and journal editors convened to develop the guideline. The panel developed CONSERVE following an accelerated, iterative process between June 2020 and February 2021 involving (1) a rapid literature review of multiple databases (OVID Medline, OVID EMBASE, and EBSCO CINAHL) and gray literature sources from 2003 to March 2021; (2) consensus-based panelist meetings using a modified Delphi process and surveys; and (3) a global survey of trial stakeholders. Findings The rapid review yielded 41 673 citations, of which 38 titles were relevant, including emerging guidance from regulatory and funding agencies for managing the effects of the COVID-19 pandemic on trials. However, no generalizable guidance for all circumstances in which trials and trial protocols might face unanticipated modifications were identified. The CONSERVE panel used these findings to develop a consensus reporting guidelines following 4 rounds of meetings and surveys. Responses were received from 198 professionals from 34 countries, of whom 90% (n = 178) indicated that they understood the concept definitions and 85.4% (n = 169) indicated that they understood and could use the implementation tool. Feedback from survey respondents was used to finalize the guideline and confirm that the guideline's core concepts were applicable and had utility for the trial community. CONSERVE incorporates an implementation tool and checklists tailored to trial reports and trial protocols for which extenuating circumstances have resulted in important modifications to the intended study procedures. The checklists include 4 sections

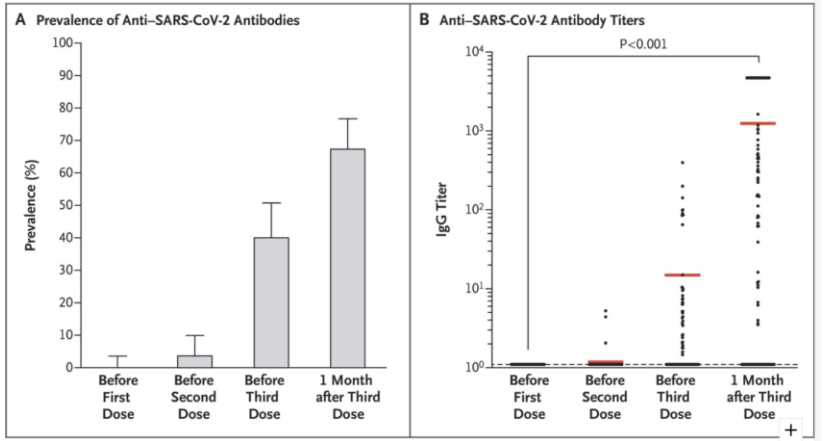
			capturing extenuating circumstances, important modifications, responsible parties, and interim data analyses. Conclusions and Relevance CONSERVE offers an extension to CONSORT and SPIRIT that could improve the transparency, quality, and completeness of reporting important modifications to trials in extenuating circumstances such as COVID-19.
Romero Garcia C et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2781191?resultClick=1	Trends in Incidence and Transmission Patterns of COVID-19 in Valencia, Spain	Studio di coorte su 2646 pazienti con COVID-19 a Valencia, in cui si osserva come avviene la trasmissione tra diverse aree della città e il ruolo degli hub ove si esegue il test.	Importance Limited information on the transmission and dynamics of SARS-CoV-2 at the city scale is available. Objective To describe the local spread of SARS-CoV-2 in Valencia, Spain. Design, Setting, and Participants This single-center epidemiological cohort study of patients with SARS-CoV-2 was performed at University General Hospital in Valencia (population in the hospital catchment area, 364 000), a tertiary hospital. The study included all consecutive patients with COVID-19 isolated at home from the start of the COVID-19 pandemic on February 19 until August 31, 2020. Exposures Cases of SARS-CoV-2 infection confirmed by the presence of IgM antibodies or a positive polymerase chain reaction test result on a nasopharyngeal swab were included. Cases in which patients with negative laboratory results met diagnostic and clinical criteria were also included. Main Outcomes and Measures The primary outcome was the characterization of dissemination patterns and connections among the 20 neighborhoods of Valencia during the outbreak. To recreate the transmission network, the inbound and outbound connections were studied for each region, and the relative risk of infection was estimated. Results In total, 2646 patients were included in the analysis. The mean (SD) age was 45.3 (22.5) years; 1203 (46%) were male and 1442 (54%) were female (data were missing for 1); and the overall

			mortality was 3.7%. The incidence of SARS-CoV-2 cases was higher in neighborhoods with higher household income (β2 [for mean income per household] = 0.197; 95% CI, 0.057-0.351) and greater population density (β1 [inhabitants per km2] = 0.228; 95% CI, 0.085-0.387). Correlations with meteorological variables were not statistically significant. Neighborhood 3, where the hospital and testing facility were located, had the most outbound connections (14). A large residential complex close to the city (neighborhood 20) had the fewest connections (0 outbound and 2 inbound). Five geographically unconnected neighborhoods were of strategic importance in disrupting the transmission network. Conclusions and Relevance This study of local dissemination of SARS-COV-2 revealed nonevident transmission patterns between geographically unconnected areas. The results suggest that tailor-made containment measures could reduce transmission and that hospitals, including testing facilities, play a crucial role in disease transmission. Consequently, the local dynamics of SARS-CoV-2 spread might inform the strategic lockdown of specific neighborhoods to stop the contagion and avoid a citywide lockdown.

			Figure 4. Functional Propagation Network and Interactions Among Neighborhoods  The thickness of an arrow indicates the strength of the propagation link; thicker arrows represent stronger links, whereas thinner arrows represent weaker links.
Chan VW et al Critical Care Medicine https://journals.lww.com/ccmjournal/Fulltext/2021/07000/Transmission_of_Severe_Acute_Respiratory_Syndrome.15.aspx	Transmission of Severe Acute Respiratory Syndrome Coronavirus 1 and Severe Acute Respiratory Syndrome Coronavirus 2 During Aerosol-Generating Procedures in Critical Care: A Systematic Review and Meta-Analysis of Observational Studies	Revisione sistematica e metanalisi che valuta il rischio di trasmissione di SARS-CoV e SARS-CoV-2 tramite procedure generanti aerosol.	OBJECTIVES: To assess the risk of coronavirus transmission to healthcare workers performing aerosol-generating procedures and the potential benefits of personal protective equipment during these procedures. DATA SOURCES: MEDLINE, EMBASE, and Cochrane CENTRAL were searched using a combination of related MeSH terms and keywords. STUDY SELECTION: Cohort studies and case controls investigating common anesthetic and critical care aerosol-generating procedures and transmission of severe acute respiratory syndrome coronavirus 1, Middle East respiratory syndrome coronavirus, and severe acute

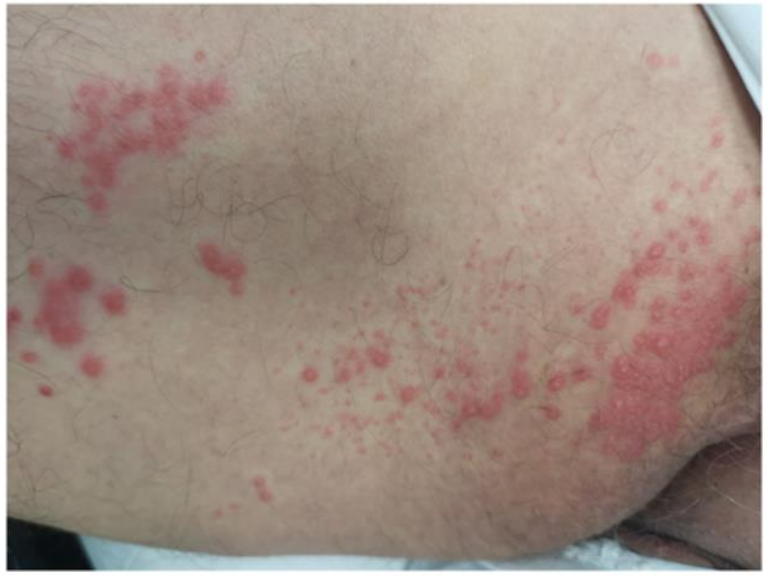
			respiratory syndrome coronavirus 2 to healthcare workers were included for quantitative analysis. DATA EXTRACTION: Qualitative and quantitative data on the transmission of severe acute respiratory syndrome coronavirus 1, severe acute respiratory syndrome coronavirus 2, and Middle East respiratory syndrome coronavirus to healthcare workers via aerosol-generating procedures in anesthesia and critical care were collected independently. The Risk Of Bias In Non-randomized Studies - of Interventions tool was used to assess the risk of bias of included studies. DATA SYNTHESIS: Seventeen studies out of 2,676 yielded records were included for meta-analyses. Endotracheal intubation (odds ratio, 6.69, 95% CI, 3.81–11.72; $p < 0.001$), noninvasive ventilation (odds ratio, 3.65; 95% CI, 1.86–7.19; $p < 0.001$), and administration of nebulized medications (odds ratio, 10.03; 95% CI, 1.98–50.69; $p = 0.005$) were found to increase the odds of healthcare workers contracting severe acute respiratory syndrome coronavirus 1 or severe acute respiratory syndrome coronavirus 2. The use of N95 masks (odds ratio, 0.11; 95% CI, 0.03–0.39; $p < 0.001$), gowns (odds ratio, 0.59; 95% CI, 0.48–0.73; $p < 0.001$), and gloves (odds ratio, 0.39; 95% CI, 0.29–0.53; $p < 0.001$) were found to be significantly protective of healthcare workers from contracting severe acute respiratory syndrome coronavirus 1 or severe acute respiratory syndrome coronavirus 2. CONCLUSIONS: Specific aerosol-generating procedures are high risk for the transmission of severe acute respiratory syndrome coronavirus 1 and severe acute respiratory syndrome coronavirus 2 from patients to healthcare workers. Personal protective equipment reduce the odds of contracting severe acute respiratory syndrome coronavirus 1 and severe acute respiratory syndrome coronavirus 2.

Burke M et al The Lancet https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00333-9/fulltext	Long COVID has exposed medicine's blind-spot	Come interpretare il cosiddetto long-COVID ? Una patologia inedita in linea con la novità del patogeno SARS-CoV-2 oppure una serie di disturbi, su scala molto ampia a causa della pandemia, che esistono anche in relazione ad altre patologie e non hanno mai trovato attenzione in medicina ?	Indeed, one of the most concerning stories emerging out of the COVID-19 pandemic is the quandary of long COVID. Long COVID, or post-acute sequelae of SARS-CoV-2 infection, is being seen in a growing number of patients reporting a constellation of symptoms after SARS-CoV-2 infection that are persistent, debilitating, and have yet to be fully explained by known or measurable mechanisms.
Holmes C The Lancet https://www.thelancet.com/journals/lanhl/article/PIIS2666-7568(21)00147-1/fulltext	Common infections and increased risk of developing dementia: compelling evidence for intervention studies	Commento a uno studio che mette in relazione le infezioni con la successiva diagnosi di demenza. Interessante in un momento di diffusione pandemica dell'infezione da SARS-CoV-2.	However, there is increasing evidence that infections might, by increasing systemic inflammation, have an indirect stimulating effect on brain inflammation, particularly in older patients or individuals with early-stage dementia. This systemic inflammatory effect might explain why diseases with aseptic inflammation—such as rheumatoid arthritis and heart disease—are independent risk factors for the development of Alzheimer's disease.
Kamar N et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMc2108861?query=featured_home	Three Doses of an mRNA Covid-19 Vaccine in Solid-Organ Transplant Recipients	Effetto di tre somministrazioni di vaccino a mRNA in una casistica di pazienti trapiantati di organo solido.	Here, we report the humoral response in a group of 101 consecutive solid-organ transplant recipients (mean [±SD] age, 58±2 years; 69% were men) who were given three doses of the messenger RNA vaccine BNT162b2 (Pfizer–BioNTech). The group included 78 kidney-transplant recipients, 12 liver-transplant recipients, 8 lung-transplant or heart-transplant recipients, and 3 pancreas-transplant recipients.

			
Martinez DR et al Science https://science.sciencemag.org/content/early/2021/06/22/science.abi4506.full	Chimeric spike mRNA vaccines protect against Sarbecovirus challenge in mice	Vaccini basati su una proteina spike chimerica proteggono il topo dal subgenere Sarbecovirus.	The emergence of SARS-CoV in 2003 and SARS-CoV-2 in 2019 highlights the need to develop universal vaccination strategies against the broader Sarbecovirus subgenus. Using chimeric spike designs, we demonstrate protection against challenge from SARS-CoV, SARS-CoV-2, SARS-CoV-2 B.1.351, bat CoV (Bt-CoV) RsSHC014, and a heterologous Bt-CoV WIV-1 in vulnerable aged mice. Chimeric spike mRNAs induced high levels of broadly protective neutralizing antibodies against high-risk Sarbecoviruses. In contrast, SARS-CoV-2 mRNA vaccination not only showed a marked reduction in neutralizing titers against heterologous Sarbecoviruses, but SARS-CoV and WIV-1 challenge in mice resulted in breakthrough infections. Chimeric spike mRNA vaccines efficiently neutralized D614G, mink cluster five, and the UK B.1.1.7., and South African B.1.351 variants of concern. Thus, multiplexed-chimeric spikes can prevent SARS-like zoonotic coronavirus infections with pandemic potential.

Krause P et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMsr2105280?query=featured_home	SARS-CoV-2 Variants and Vaccines	Report che sintetizza le evidenze in merito al significato delle nuove varianti di SARS-CoV-2 via via emergenti e le azioni da intraprendere in contrasto.	Viral variants of concern may emerge with dangerous resistance to the immunity generated by the current vaccines to prevent coronavirus disease 2019 (Covid-19). Moreover, if some variants of concern have increased transmissibility or virulence, the importance of efficient public health measures and vaccination programs will increase. The global response must be both timely and science based.
Bohler AD et al Nature https://www.nature.com/articles/s41433-021-01610-1	Acute macular neuroretinopathy following COVID-19 vaccination	Scotoma paracentrale acuto dopo somministrazione di vaccino Vaxzevria contro SARS-CoV-2 in una giovane donna di 27 anni.	The complex immunological mechanisms of vaccines bring about an inevitable risk of immune-mediated adverse reactions. Of special interest in this time of epidemic is the safety of COVID-19 vaccines and, in particular, the emerging evidence that the ChAdOx1 nCoV-19 adenoviral vector vaccine from AstraZeneca can cause vaccine-induced immune thrombotic thrombocytopenia (VITT). We present the case of a patient who developed an acute paracentral scotoma after having received this vaccine.

			 The image displays a delicate teardrop-shaped lesion nasally to the fovea.
Eid E et al Journal of Medical Virology https://doi.org/10.1002/jmv.27036	Herpes Zoster emergence following mRNA COVID-19 Vaccine.	Riattivazione di VZV dopo vaccinazione con vaccino a mRNA contro SARS-CoV-2.	The current Sars-CoV-2 disease (COVID-19) is a multisystemic disorder of global reach that has demonstrated dire medical and socioeconomic consequences. In an effort to alleviate the morbidity and mortality associated with COVID-19 and halt viral transmission, a host of vaccines has been developed. Chief among these vaccines are the messenger RNA (mRNA vaccines that reportedly confer up to 95% protection from COVID-19 after a two-dose series.1 Common vaccine-related side effects include pain, redness, and/or swelling at the injection site, fatigue, headache, fever, and chills.1 In what follows, we describe a unique case of varicella zoster virus (VZV) reactivation emerging after vaccination with the mRNA COVID-19 vaccine.

			
Bloom JD bioRXiv - preprint https://www.biorxiv.org/content/10.1101/2021.06.18.449051v1	Recovery of deleted deep sequencing data sheds more light on the early Wuhan SARS-CoV-2 epidemic	Sequenze di SARS-COV-2 risalenti all'inizio della pandemia a Wuhan che si discostano parzialmente da quelle più studiate e considerate originarie.	The origin and early spread of SARS-CoV-2 remains shrouded in mystery. Here I identify a data set containing SARS-CoV-2 sequences from early in the Wuhan epidemic that has been deleted from the NIH's Sequence Read Archive. I recover the deleted files from the Google Cloud, and reconstruct partial sequences of 13 early epidemic viruses. Phylogenetic analysis of these sequences in the context of carefully annotated existing data suggests that the Huanan Seafood Market sequences that are the focus of the joint WHO-China report are not fully representative of the viruses in Wuhan early in the epidemic. Instead, the progenitor of known SARS-CoV-2 sequences likely contained three mutations relative to the market viruses that made it more similar to SARS-CoV-2's bat coronavirus relatives.

Ministero della Salute isrealiano Comunicato stampa https://www.gov.il/en/departments/news/21062021-02	The Ministry of Health Recommends Having Teens 12-15 Years of Age Vaccinated	Il Ministero della salute israeliano raccomanda la vaccinazione nei ragazzi di età 12-15 anni.	Following the increase in COVID-19 morbidity among children in recent days, and in light of the recent outbreaks in schools in Modi'in, Binyamina, and other places as a result of variants to the virus, an emergency meeting was held last night in the Ministry of Health between a team of experts and the Epidemic Response Team on the subject of extending vaccines to adolescents ages 12-15. During the discussion, the results of the vaccination of adolescents in Israel so far was discussed, as well as the situation in the United States, were 2.5 million adolescents have been vaccinated so far without any concerning side effects. This is following research performed in Israel which showed very rare and side effects which were not severe.
Lepak AJ et al JAMA https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2781312	Association of Changes in Seasonal Respiratory Virus Activity and Ambulatory Antibiotic Prescriptions With the COVID-19 Pandemic	Riduzione delle infezioni respiratorie virali e della prescrizione di antibiotici a domicilio « grazie » alla pandemia di SARS-CoV-2.	The COVID-19 pandemic led to numerous measures to mitigate the spread of SARS-CoV-2, including cancellations of gatherings, closure of businesses and schools, social distancing, wearing face masks, and other hygiene measures.1 These may have unintended positive associations with reducing other respiratory infections. As antibiotics are frequently inappropriately prescribed for viral respiratory diseases,2 we hypothesized that a decreased respiratory virus incidence would be associated with reduced ambulatory antibiotic orders.

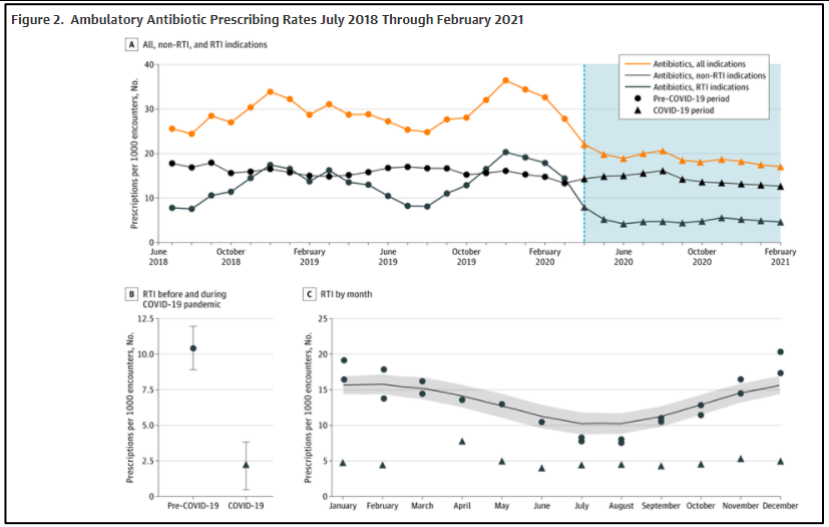
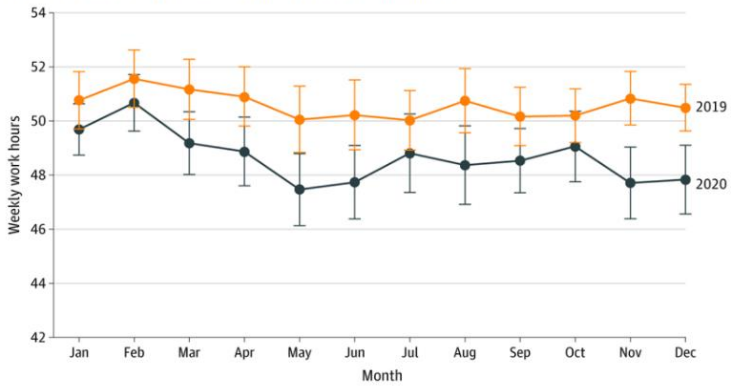
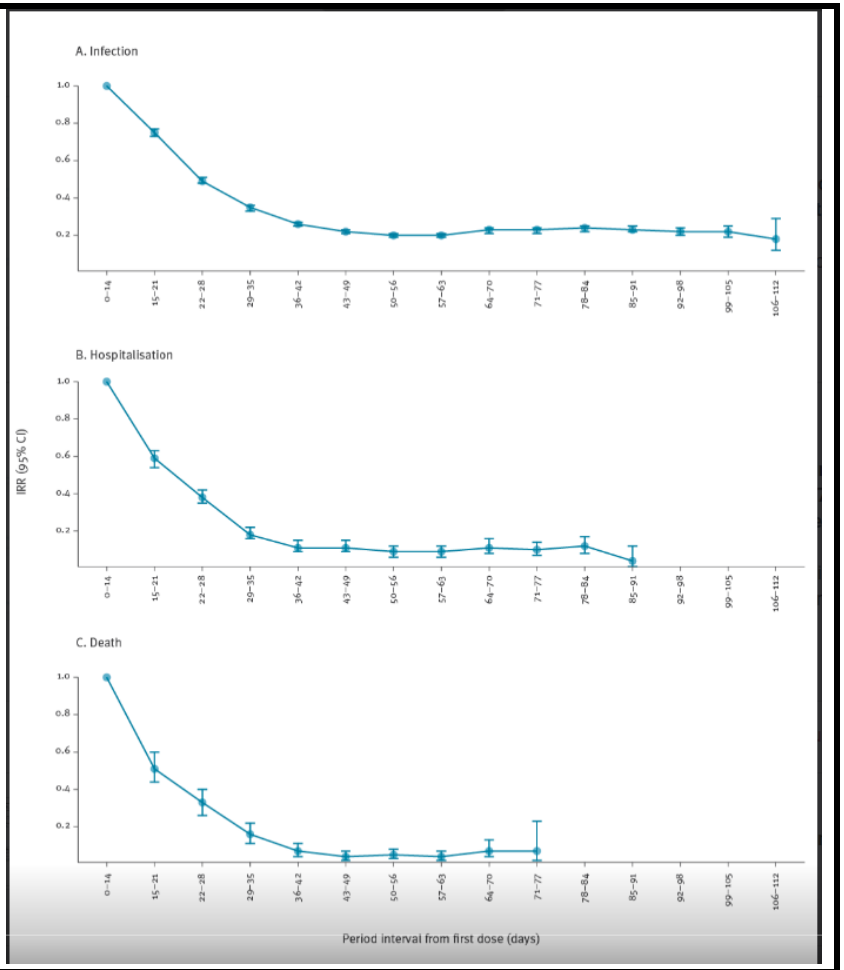
			
Robinson LB et al JAMA https://jamanetwork.com/journals/jamadermatology/fullarticle/2781364	Incidence of Cutaneous Reactions After Messenger RNA COVID-19 Vaccines	Reazioni cutanee dopo vaccino a mRNA contro SARS-CoV-2 in una ampia popolazione di oltre 40000 operatori sanitari : 1.9% dopo la prima dose, di cui oltre 80% non ricorrenti alla seconda dose.	Mucocutaneous reactions, such as pruritus, urticaria, and angioedema, may occur after COVID-19 messenger RNA (mRNA) vaccination. To our knowledge, the incidence of these reactions and recurrence with subsequent vaccination has not been described. Cutaneous reactions may contribute to unnecessary avoidance of future vaccination doses.
Hu X et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2781284	Changes in Physician Work Hours and Patterns During the COVID-19 Pandemic	Riduzione delle ore lavorative e degli impieghi a tempo pieno per una casistica di circa 2500 medici negli USA dall'inizio della pandemia di COVID-19.	The COVID-19 pandemic has been associated with loss of revenue, reduced work hours, and reduced earnings for physicians in the United States. Furthermore, pandemic restrictions and related regulatory changes allowing physicians greater flexibilities potentially altered physicians' work activities and environments. We analyzed a longitudinal data set to examine changes in US physician work hours and activities before and after the COVID-19 pandemic emerged.

			Figure. Physicians' Mean Weekly Work Hours, January 2019 to December 2020 
Mateo-Urdiales A et al Eurosurveillance https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.25.2100507	Risk of SARS-CoV-2 infection and subsequent hospital admission and death at different time intervals since first dose of COVID-19 vaccine administration, Italy, 27 December 2020 to mid-April 2021	Riduzione dell'incidenza di infezioni, ospedalizzazioni e decessi in Italia nel periodo dicembre-aprile 2021 a seguito dell0introduzione dei vaccini contro SARS-CoV-2.	To assess the real-world impact of vaccines on COVID-19 related outcomes, we analysed data from over 7 million recipients of at least one COVID-19 vaccine dose in Italy. Taking 0–14 days post-first dose as reference, the SARS-CoV-2 infection risk subsequently decreased, reaching a reduction by 78% (incidence rate ratios (IRR): 0.22; 95% CI: 0.21–0.24) 43–49 days post-first dose. Similarly, hospitalisation and death risks decreased, with 89% (IRR: 0.11; 95% CI: 0.09–0.15) and 93% (IRR: 0.07; 95% CI: 0.04–0.11) reductions 36–42 days post-first dose. Our results support ongoing vaccination campaigns.

			
Mazzola A et al CID https://academic.oup.com/cid/advance-	Poor Antibody Response after Two Doses of SARS-CoV-2 vaccine in Transplant Recipients	Ridotta risposta anticorpale dopo la seconda dose di vaccino Pfizer contro SARS-CoV-2 in 133 trapiantati d'organo.	A low anti-spike antibody response of 28.6% was observed 28 days after BNT162b2 vaccine second dose among 133 solid organ transplant-recipients without previous COVID-19. No serious adverse events were recorded. Four severe COVID-19 cases were reported between or after the two doses. Our data suggests to change the vaccine strategy.

article/doi/10.1093/cid/ciab580/6309017			
Sehmer A et al JAMA https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2781367?resultClick=1	Association of COVID-19 Vaccination and Facial Nerve Palsy A Case-Control Study	Non associazione fra paralisi di Bell e vaccinazione con Pfizer contro SARS-CoV-2.	Importance Peripheral facial nerve (Bell) palsy has been reported and widely suggested as a possible adverse effect of the BNT162b2 (Pfizer-BioNTech) COVID-19 vaccine. Israel is currently the leading country in vaccination rates per capita, exclusively using the BNT162b2 vaccine, and all residents of Israel are obligatory members of a national digital health registry system. These factors enable early analysis of adverse events. Objective To examine whether the BNT162b2 vaccine is associated with an increased risk of acute-onset peripheral facial nerve palsy. Design, Setting, and Participants This case-control study was performed from January 1 to February 28, 2021, at the emergency department of a tertiary referral center in central Israel. Patients admitted for facial nerve palsy were matched by age, sex, and date of admission with control patients admitted for other reasons. Exposures Recent vaccination with the BNT162b2 vaccine. Main Outcomes and Measures Adjusted odds ratio for recent exposure to the BNT162b2 vaccine among patients with acute-onset peripheral facial nerve palsy. The proportion of patients with Bell palsy exposed to the BNT162b2 vaccine was compared between groups, and raw and adjusted odds ratios for exposure to the vaccine were calculated. A secondary comparison with the overall number of patients with facial nerve palsy in preceding years was performed. Results Thirty-seven patients were admitted for facial nerve palsy during the study period, 22 (59.5%) of whom were male, and their mean (SD) age was 50.9 (20.2) years. Among recently vaccinated

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<td>patients (21 [56.7%]), the mean (SD) time from vaccination to occurrence of palsy was 9.3 (4.2 [range, 3-14]) days from the first dose and 14.0 (12.6 [range, 1-23]) days from the second dose. Among 74 matched controls (2:1 ratio) with identical age, sex, and admittance date, a similar proportion were vaccinated recently (44 [59.5%]). The adjusted odds ratio for exposure was 0.84 (95% CI, 0.37-1.90; P = .67). Furthermore, analysis of the number of admissions for facial nerve palsy during the same period in preceding years (2015-2020) revealed a relatively stable trend (mean [SD], 26.8 [5.8]; median, 27.5 [range, 17-35]).
Conclusions and Relevance In this case-control analysis, no association was found between recent vaccination with the BNT162b2 vaccine and risk of facial nerve palsy.

Table 2. Distribution of Vaccinated and Nonvaccinated Patients Among Cases With New-Onset Peripheral Facial Nerve Palsy and Matched Controls
<table><tr><th>Patient group</th><th>No. of cases</th><th>No. of controls</th><th>Total No.</th></tr><tr><td>Vaccinated</td><td>21</td><td>44</td><td>65</td></tr><tr><td>Nonvaccinated</td><td>16</td><td>30</td><td>46</td></tr><tr><td>Total</td><td>37</td><td>74</td><td>111</td></tr></table></td>
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<td>Tamaki A et al

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https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2781368?resultClick=1</td>
<td>Incidence of Bell Palsy in Patients With COVID-19</td>
<td>Associazione fra paralisi di Bell e COVID-19, maggiore rispetto a quella fra paralisi e vaccino.</td>
<td>The present analysis found a higher incidence of BP in patients with COVID-19 (0.08%). This translates to approximately 82 per 100 000 patients with COVID-19. The rate of recurrent BP in patients with previous BP at the time of COVID-19 diagnosis was 8.6%. This analysis found a statistically significant higher risk of BP in patients with COVID-19 compared with those who were vaccinated against the disease. The data suggest that rates of BP are higher in patients with COVID-19, and this incidence exceeds the reported incidence of BP in those who have received a COVID-19 vaccine.</td>
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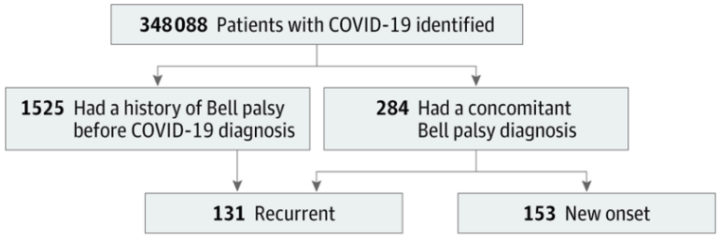
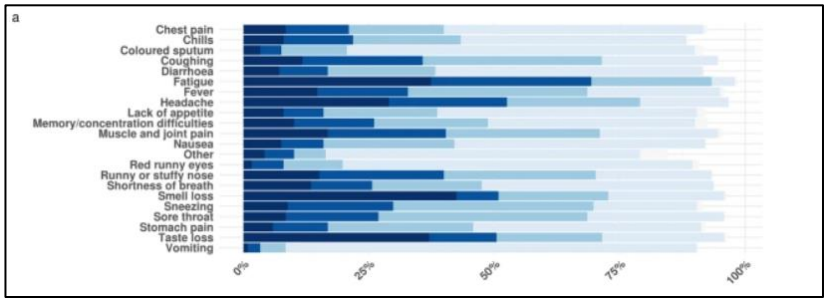
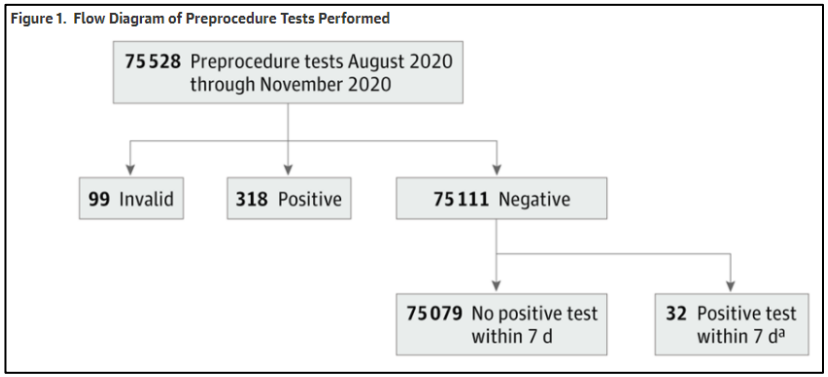
			Figure. Participant Flow Chart 
Gobeil SMC et al Science https://science.sciencemag.org/content/early/2021/06/23/science.abi6226	Effect of natural mutations of SARS-CoV-2 on spike structure, conformation, and antigenicity	Vantaggi strutturali delle varianti di SARS-CoV-2 in termini di affinità recettoriale e trasmissibilità.	SARS-CoV-2 variants with multiple spike mutations enable increased transmission and antibody resistance. Here, we combine cryo-EM, binding and computational analyses to study variant spikes, including one that was involved in transmission between minks and humans, and others that originated and spread in human populations. All variants showed increased ACE2 receptor binding and increased propensity for RBD up states. While adaptation to mink resulted in spike destabilization, the B.1.1.7 (UK) spike balanced stabilizing and destabilizing mutations. A local destabilizing effect of the RBD E484K mutation was implicated in resistance of the B.1.1.28/P.1 (Brazil) and B.1.351 (South Africa) variants to neutralizing antibodies. Our studies revealed allosteric effects of mutations and mechanistic differences that drive either inter-species transmission or escape from antibody neutralization.
Cai Y et al Science https://science.sciencemag.org/content/early/2021/06/23/science.abi9745	Structural basis for enhanced infectivity and immune evasion of SARS-CoV-2 variants	Struttura delle proteine S delle varianti alfa e beta di SARS-CoV-2 e delle mutazioni più favorevoli in termini di vantaggio selettivo per il virus.	Several fast-spreading variants of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have become the dominant circulating strains in the COVID-19 pandemic. We report here cryo-EM structures of the full-length spike (S) trimers of the B.1.1.7 and B.1.351 variants, as well as their biochemical and antigenic properties. Amino acid substitutions in the B.1.1.7 protein increase the accessibility of its receptor binding domain and also the binding affinity for receptor angiotensin-converting enzyme 2 (ACE2). The enhanced receptor engagement may account for the increased

			transmissibility. The B.1.351 variant has evolved to reshape antigenic surfaces of the major neutralizing sites on the S protein, making it resistant to some potent neutralizing antibodies. These findings provide structural details on how SARS-CoV-2 has evolved to enhance viral fitness and immune evasion.
McEwen AE et al CID https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab581/6309019	Variants of concern are overrepresented among post-vaccination breakthrough infections of SARS-CoV-2 in Washington State	Le infezioni da SARS-CoV-2 dopo soggetti vaccinati sono tutte dovute a varianti in questo piccolo gruppo di 20 pazienti consecutivi in un centro.	Across 20 vaccine breakthrough cases detected at our institution, all 20 (100%) infections were due to variants of concern (VOC) and had a median Ct of 20.2 (IQR=17.1-23.3). When compared to 5174 contemporaneous samples sequenced in our laboratory, VOC were significantly enriched among breakthrough infections ($p < .05$).
Rrenaud M et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2781319?resultClick=1	Clinical Outcomes for Patients With Anosmia 1 Year After COVID-19 Diagnosis	Il 96% dei pazienti di questa piccola casistica recupera l'olfatto a 12 mesi dall'insorgenza di anosmia per COVID-19.	More than 1 year into the pandemic, we describe the long-term prognosis for a cohort of patients with COVID-19–related anosmia, most of whom (96.1%) objectively recovered by 12 months. Our findings suggest that an additional 10% gain in recovery can be expected at 12 months, compared with studies with 6 months of follow-up that found only 85.9% of patients with recovery.4 This supports findings from fundamental animal research, involving both imaging studies and postmortem pathology, suggesting that COVID-19–related anosmia is likely due to peripheral inflammation.
Bliddal S et al Scientific Reports https://www.nature.com/articles/s41598-021-92045-x	Acute and persistent symptoms in non-hospitalized PCR-confirmed COVID-19 patients	Su 445 persone con infezione da SARS-CoV-2 e non ospedalizzate, un terzo ha sintomi persistenti per più di 4 settimane dalla diagnosi, in particolare astenia e difficoltà di concentrazione.	Reports of persistent symptoms after hospitalization with COVID-19 have raised concern of a "long COVID" syndrome. This study aimed at determining the prevalence of and risk factors for acute and persistent symptoms in non-hospitalized patients with polymerase chain reaction (PCR) confirmed COVID-19. We conducted a cohort study of non-hospitalized participants identified via the Danish Civil Registration System with a SARS-CoV-2-positive PCR-test and available biobank samples. Participants received a digital

			questionnaire on demographics and COVID-19-related symptoms. Persistent symptoms: symptoms > 4 weeks (in sensitivity analyses > 12 weeks). We included 445 participants, of whom 34% were asymptomatic. Most common acute symptoms were fatigue, headache, and sneezing, while fatigue and reduced smell and taste were most severe. Persistent symptoms, most commonly fatigue and memory and concentration difficulties, were reported by 36% of 198 symptomatic participants with follow-up > 4 weeks. Risk factors for persistent symptoms included female sex (women 44% vs. men 24%, odds ratio 2.7, 95% CI 1.4–5.1, p = 0.003) and BMI (odds ratio 1.1, 95% CI 1.0–1.2, p = 0.001). In conclusion, among non-hospitalized PCR-confirmed COVID-19 patients one third were asymptomatic while one third of symptomatic participants had persistent symptoms illustrating the heterogeneity of disease presentation. These findings should be considered in health care planning and policy making related to COVID-19. 
Lythgoe MP et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2781352	Comparison of COVID-19 Vaccine Approvals at the US Food and Drug Administration, European Medicines Agency, and Health Canada	Ricostruzione dell'approvazione dei diversi vaccini disponibili contro SARS-CoV-2 in USA ed Europa.	On the 1-year anniversary of the World Health Organization (WHO) declaring COVID-19 a global pandemic, the development and rollout of safe and effective vaccines has fueled optimism for greater pandemic control. During the COVID-19 pandemic, medicine regulators have faced significant pressure from both the public and governments to expedite vaccine approval, while grappling with the challenges of novel vaccine clinical development and ensuring

			public trust and confidence in COVID-19 vaccines.1 Recognizing the gravity of this public health emergency, medicine regulators have introduced or activated accelerated mechanisms for restricted approval or permitted use of unapproved medical products in predefined circumstances (eg, Emergency Use Authorizations [EUA]).2 We investigated COVID-19 vaccine approvals at 3 medicine regulatory agencies, the US Food and Drug Administration (FDA), European Medicines Agency (EMA), and Health Canada (HC), characterized and contrasted regulatory review times, and analyzed the clinical evidence supporting authorization. **Table 1. COVID-19 Vaccine Approval by Regulatory Agency** Table 1. COVID-19 Vaccine Approval by Regulatory Agency US Food and Drug Administration / European Medicines Agency / Health Canada COVID-19 Vaccine; Submission date; Authorization date[a]; Time for review, (d); Submission date; Authorization date[b]; Time for review, (d); Submission date; Authorization date[c]; Time for review, (d) Pfizer-BioNTech (BNT162b2); 11/20/2020; 12/11/2020; 21; 11/30/2020; 12/21/2020; 21; 10/09/2020; 12/09/2020; 61 Moderna (mRNA-1273); 11/30/2020; 12/18/2020; 18; 11/30/2020; 01/06/2021; 37; 10/12/2020; 12/23/2020; 72 Janssen (Ad26.COV2.S); 02/04/2021; 02/27/2021; 23; 02/16/2021; 03/11/2021; 23; 11/30/2020; 03/05/2021; 95 Oxford or AstraZeneca (ChAdOx1); NA; NA; NA[d]; 01/11/2021; 01/29/2021; 18; 10/01/2020; 02/26/2021; 148 Median review time, (range), d; 21 (18-23); 22 (18-37); 84 (61-148) Abbreviation: NA, not applicable. [a] Vaccine approved under Emergency Use Authorization. [b] Vaccine approved under Conditional Marketing Authorization. [c] Vaccine authorized with specific terms and conditions. [d] Vaccine not approved.
Roberts SC et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2781353	Utility of Mass SARS-CoV-2 Testing of Asymptomatic Patients Before Ambulatory and Inpatient Preplanned Procedures Requiring Moderate Sedation or General Anesthesia	Esito di oltre 75000 mila test per SARS-CoV-2 in pazienti asintomatici destinati a procedure ambulatoriali e utilità dello screening.	Systematic management of procedures during the COVID-19 crisis is a priority to (1) detect and care appropriately for patients with COVID-19, (2) prevent outbreaks, and (3) safely maintain routine health care activities. SARS-CoV-2 presents unique challenges, as an estimated 50% of infections occur through asymptomatic transmission, and clinical screening may miss contagious patients.1,2 These factors complicate settings where aerosol-generating procedures (AGPs) are performed, potentially exposing health care personnel (HCP) to SARS-CoV-2 transmission. Furthermore, patients with COVID-19 have increased risks of postprocedural complications, and current guidelines suggest that testing asymptomatic patients prior to preplanned procedures may

			help to mitigate these risks.3 We describe our mass preprocedure SARS-CoV-2 nucleic acid amplification testing (NAAT) during a period of high community transmission. 
Rosner CM et al Circulation https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.121.055891	Myocarditis Temporally Associated with COVID-19 Vaccination	Casistica di 7 pazienti maschi di età inferiore a 40 anni con sviluppo di miocardite entro 7 giorni da vaccinazione contro SARS-CoV-2 (6 a mRNA, 1 J&J).	We present a case series of 7 patients hospitalized for acute myocarditis-like illness following COVID-19 vaccination, from 2 US medical centers in Falls Church, VA and Dallas, TX. All were males < 40 years of age and of White or Hispanic race/ethnicity (Table). Only 1 patient reported prior history of COVID-19 infection. Six patients received mRNA (Moderna or Pfizer/BioNTech) and received the adenovirus (Johnson & Johnson) vaccine. All patients presented 3-7 days post vaccination with acute onset chest pain and biochemical evidence of myocardial injury, by cardiac troponin I.
Smith MJ et al The Lancet https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01244-7/fulltext	What constitutes success in the roll-out of COVID-19 vaccines?	Come misurare il successo delle campagne vaccinali contro SARS-CoV-2.	The path of least resistance is the familiar enemy of equity. In addition to speed, countries should be evaluated on metrics that correspond to the actual public health objectives that vaccination programmes should seek to achieve: the extent to which populations at greatest risk (eg, of death, hospitalisation, exposure, or transmission) are being vaccinated; and the extent to which disparities exist among populations eligible to be vaccinated. Measuring success in terms of these additional metrics might

			compel countries to ensure vaccines are not only deployed rapidly, but also effectively and equitably.