

## RICERCA BIBLIOGRAFICA COVID 19

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FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE

DOTT.SSA ELEONORA TADDEI

AUTORE/RIVISTA	TITOLO	OUTCOME PRINCIPALE	ABSTRACT
Wei EK et al  JAMA  <a href="https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2782429">https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2782429</a>	Nine Lessons Learned From the COVID-19 Pandemic for Improving Hospital Care and Health Care Delivery	Lezioni dalla pandemia di COVID-19 da integrare nella futura gestione dell'assistenza ospedaliera in circostanze « normali » ed emergenziali.	New York City (NYC) was the epicenter of the COVID-19 pandemic in the US in March 2020. A dense city of only 302 square miles, it has had 33 359 deaths and 109 192 hospitalizations due to COVID-19 as of June 15, 2021. <sup>1</sup> In guiding NYC Health + Hospitals, the largest municipal hospital system in the US, through the pandemic, we have learned a number of lessons. Although there is much to debate about the national public health response to COVID-19, <sup>2</sup> we focus on the lessons learned through COVID-19 that we believe have applicability for improving hospital care in the future. The growth of telehealth has been covered elsewhere. <sup>3,4</sup> We present 9 other lessons for improving hospital care and health care delivery.
Recalde M et al  Journal of Clinical Endocrinology and Metabolism	Body mass index and risk of COVID-19 diagnosis, hospitalisation, and death: a cohort study of 2 524 926 Catalans	Aumentato rischio di infezione e di ospedalizzazione per COVID-19 nei pazienti obesi.	Context : A comprehensive understanding of the association between body mass index (BMI) and COVID-19 is still lacking. Objective : To investigate associations between BMI and risk of COVID-19 diagnosis, hospitalisation with COVID-19, and death after

<a href="https://doi.org/10.1210/clinem/dgab546">https://doi.org/10.1210/clinem/dgab546</a>			<p>a COVID-19 diagnosis or hospitalisation (subsequent death), accounting for potential effect modification by age and sex.</p> <p>Design : Population-based cohort study.</p> <p>Setting : Primary care records covering &gt;80% of the Catalan population, linked to region-wide testing, hospital, and mortality records from March to May 2020.</p> <p>Participants : Adults (≥18 years) with at least one measurement of weight and height.</p> <p>Main outcome measures : Hazard ratios (HR) for each outcome.</p> <p>Results : We included 2 524 926 participants. After 67 days of follow-up, 57 443 individuals were diagnosed with COVID-19, 10 862 were hospitalised with COVID-19, and 2467 had a subsequent death. BMI was positively associated with being diagnosed and hospitalised with COVID-19. Compared to a BMI of 22kg/m<sup>2</sup>, the HR (95%CI) of a BMI of 31kg/m<sup>2</sup> was 1.22 (1.19-1.24) for diagnosis, and 1.88 (1.75-2.03) and 2.01 (1.86-2.18) for hospitalisation without and with a prior outpatient diagnosis, respectively. The association between BMI and subsequent death was J-shaped, with a modestly higher risk of death among individuals with BMIs ≤19kg/m<sup>2</sup> and a more pronounced increasing risk for BMIs ≥40kg/m<sup>2</sup>. The increase in risk for COVID-19 outcomes was particularly pronounced among younger patients.</p> <p>Conclusions : There is a monotonic association between BMI and COVID-19 diagnosis and hospitalisation risks, but a J-shaped one with mortality. More research is needed to unravel the mechanisms underlying these relationships.</p>
<p>Crook H et al</p> <p>BMJ</p>	<p>Long covid—mechanisms, risk factors, and management</p>	<p>Revisione sul « long COVID » e sulle sue possibilità di trattamento.</p>	<p>Since its emergence in Wuhan, China, covid-19 has spread and had a profound effect on the lives and health of people around the globe. As of 4 July 2021, more than 183 million confirmed cases of covid-19 had been recorded worldwide, and 3.97 million deaths. Recent evidence has shown that a range of persistent symptoms can remain</p>

<a href="https://www.bmj.com/content/374/bmj.n1648">https://www.bmj.com/content/374/bmj.n1648</a>			<p>long after the acute SARS-CoV-2 infection, and this condition is now coined long covid by recognized research institutes. Studies have shown that long covid can affect the whole spectrum of people with covid-19, from those with very mild acute disease to the most severe forms. Like acute covid-19, long covid can involve multiple organs and can affect many systems including, but not limited to, the respiratory, cardiovascular, neurological, gastrointestinal, and musculoskeletal systems. The symptoms of long covid include fatigue, dyspnea, cardiac abnormalities, cognitive impairment, sleep disturbances, symptoms of post-traumatic stress disorder, muscle pain, concentration problems, and headache. This review summarizes studies of the long term effects of covid-19 in hospitalized and non-hospitalized patients and describes the persistent symptoms they endure. Risk factors for acute covid-19 and long covid and possible therapeutic options are also discussed.</p>
<p>Wu S et al</p> <p>The Lancet</p> <p><a href="https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00396-0/fulltext">https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00396-0/fulltext</a></p>	<p>Safety, tolerability, and immunogenicity of an aerosolised adenovirus type-5 vector-based COVID-19 vaccine (Ad5-nCoV) in adults: preliminary report of an open-label and randomised phase 1 clinical trial</p>	<p>Efficacia e immunogenicità di un vaccino a vettore adenovirale somministrato per via aerosolica contro SARS-CoV-2.</p>	<p>Background</p> <p>SARS-CoV-2 has caused millions of deaths, and, since Aug 11, 2020, 20 intramuscular COVID-19 vaccines have been approved for use. We aimed to evaluate the safety and immunogenicity of an aerosolised adenovirus type-5 vector-based COVID-19 vaccine (Ad5-nCoV) in adults without COVID-19 from China.</p> <p>Method</p> <p>This was a randomised, single-centre, open-label, phase 1 trial done in Zhongnan Hospital (Wuhan, China), to evaluate the safety and immunogenicity of the Ad5-nCoV vaccine by aerosol inhalation in adults (≥18 years) seronegative for SARS-CoV-2. Breastfeeding or pregnant women and people with major chronic illnesses or history of allergies were excluded. Participants were enrolled and randomly assigned (1:1:1:1:1) into five groups to be vaccinated via intramuscular injection, aerosol inhalation, or both. Randomisation</p>

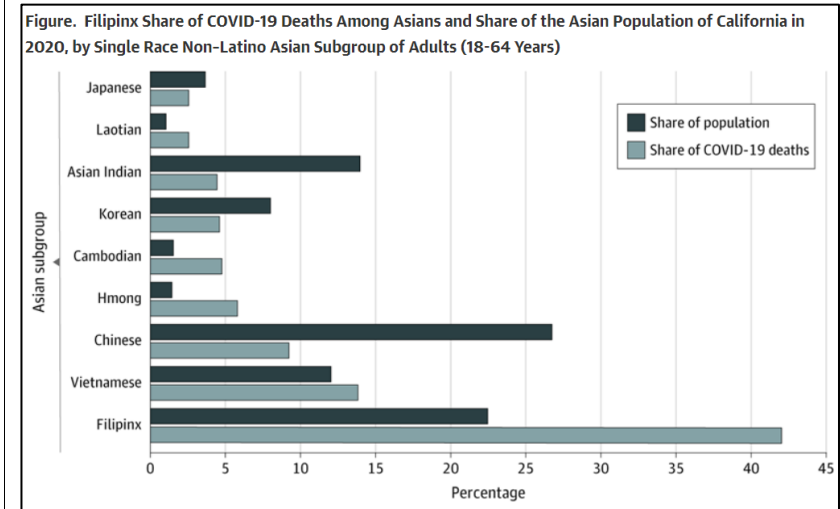
			<p>was stratified by sex and age (18–55 years or ≥56 years) using computer-generated randomisation sequences (block sizes of five). Only laboratory staff were masked to group assignment. The participants in the two aerosol groups received an initial high dose (<math>2 \times 10^{10}</math> viral particles; HDmu group) or low dose (<math>1 \times 10^{10}</math> viral particles; LDmu group) of Ad5-nCoV vaccine on day 0, followed by a booster on day 28. The mixed vaccination group received an initial intramuscular (<math>5 \times 10^{10}</math> viral particles) vaccine on day 0, followed by an aerosolised booster (<math>2 \times 10^{10}</math> viral particles) vaccine on day 28 (MIX group). The intramuscular groups received one dose (<math>5 \times 10^{10}</math> viral particles; 1Dim group) or two doses (<math>10 \times 10^{10}</math> viral particles; 2Dim group) of Ad5-nCoV on day 0. The primary safety outcome was adverse events 7 days after each vaccination, and the primary immunogenicity outcome was anti-SARS-CoV-2 spike receptor IgG antibody and SARS-CoV-2 neutralising antibody geometric mean titres at day 28 after last vaccination. This trial is registered with ClinicalTrials.gov, number NCT04552366.</p>
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Findings

Between Sept 28, 2020, and Sept 30, 2020, 230 individuals were screened for inclusion, of whom 130 (56%) participants were enrolled into the trial and randomly assigned into one of the five groups (26 participants per group). Within 7 days after vaccination, adverse events occurred in 18 (69%) in the HDmu group, 19 (73%) in the LDmu group, 19 (73%) in the MIX group, 19 (73%) in the 1Dim group, and 15 (58%) in the 2Dim group. The most common adverse events reported 7 days after the first or booster vaccine were fever (62 [48%] of 130 participants), fatigue (40 [31%] participants), and headache (46 [35%] participants). More adverse events were reported in participants who received intramuscular vaccination, including participants in the MIX group (49 [63%] of 78 participants),

			<p>than those who received aerosol vaccine (13 [25%] of 52 participants) after the first vaccine vaccination. No serious adverse events were noted within 56 days after the first vaccine. At days 28 after last vaccination, geometric mean titres of SARS-CoV-2 neutralising antibody was 107 (95% CI 47–245) in the HDmu group, 105 (47–232) in the LDmu group, 396 (207–758) in the MIX group, 95 (61–147) in the 1Dim group, and 180 (113–288) in the 2Dim group. The geometric mean concentrations of receptor binding domain-binding IgG was 261 EU/mL (95% CI 121–563) in the HDmu group, 289 EU/mL (138–606) in the LDmu group, 2013 EU/mL (1180–3435) in the MIX group, 915 EU/mL (588–1423) in the 1Dim group, and 1190 EU/mL (776–1824) in the 2Dim group.</p> <p>Interpretation</p> <p>Aerosolised Ad5-nCoV is well tolerated, and two doses of aerosolised Ad5-nCoV elicited neutralising antibody responses, similar to one dose of intramuscular injection. An aerosolised booster vaccination at 28 days after first intramuscular injection induced strong IgG and neutralising antibody responses. The efficacy and cost-effectiveness of aerosol vaccination should be evaluated in future studies.</p>
<p>Iewin C et al</p> <p>JAMA</p> <p><a href="https://jamanetwork.com/journals/jama-health-forum/fullarticle/2782408">https://jamanetwork.com/journals/jama-health-forum/fullarticle/2782408</a></p>	<p>US Health Care Relies on Filipinx While Ignoring Their Health Needs</p> <p>Disguised Disparities and the COVID-19 Pandemic</p>	<p>Le persone originarie delle Filippine sono molto rappresentate fra gli operatori sanitari negli USA, ma sono anche state duramente colpite come categoria dalla pandemia.</p>	<p>In the US, Filipinx are the third largest Asian subgroup and have represented a crucial part of the country's health care workforce since the mid-20th century. Although the 2.9 million Filipinx in the US represent about 1% of the population, approximately 1 of 4 Filipinx working adults are frontline health care workers.<sup>1</sup> The COVID-19 pandemic has exacted a disproportionate toll on Filipinx communities in the US and on Filipinx health care workers, specifically. The absence of disaggregated race/ethnicity data for COVID-19 has masked how the pandemic has affected Filipinx in the US. Policy makers and researchers must recognize that these disparities are not limited to COVID-19 but are a critical example of</p>

how data aggregation under a single Asian category has hidden the health needs of the Filipinx population.



The recent COVID-19 pandemic is a treatment challenge in the acute infection stage but the recognition of chronic COVID-19 symptoms termed post-acute sequelae SARS-CoV-2 infection (PASC) may affect up to 30% of all infected individuals. The underlying mechanism and source of this distinct immunologic condition three months or more after initial infection remains elusive. Here, we investigated the presence of SARS-CoV-2 S1 protein in 46 individuals. We analyzed T-cell, B-cell, and monocytic subsets in both severe COVID-19 patients and in patients with post-acute sequelae of COVID-19 (PASC). The levels of both intermediate (CD14+, CD16+) and non-classical monocyte (CD14Lo, CD16+) were significantly elevated in PASC patients up to 15 months post-acute infection compared to healthy controls ( $P=0.002$  and  $P=0.01$ , respectively). A statistically significant number of non-classical monocytes contained SARS-CoV-2 S1 protein in both severe ( $P=0.004$ ) and PASC patients ( $P=0.02$ ) out to 15 months post-infection. Non-classical monocytes were sorted from

Patterson BK et al

MedRXiv

<https://www.biorxiv.org/content/10.1101/2021.06.25.449905v1>

Persistence of SARS CoV-2 S1 Protein in CD16+ Monocytes in Post-Acute Sequelae of COVID-19 (PASC) Up to 15 Months Post-Infection

Persistenza della proteina S di SARS-CoV-2 nei monociti di pazienti con COVID-19 grave e con sequele di COVID-19 fino a 15 mesi dalla diagnosi.

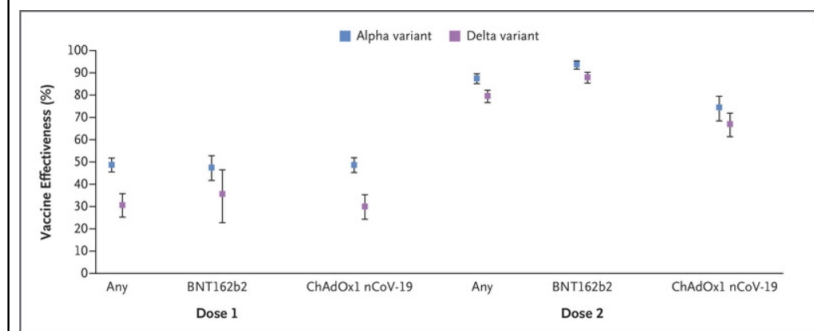
			<p>PASC patients using flow cytometric sorting and the SARS-CoV-2 S1 protein was confirmed by mass spectrometry. Cells from 4 out of 11 severe COVID-19 patients and 1 out of 26 also contained SARS-CoV-2 RNA. Non-classical monocytes are capable of causing inflammation throughout the body in response to fractalkine/CX3CL1 and RANTES/CCR5.</p>
<p>Lopez Bernal</p> <p>NEJM</p> <p><a href="https://www.nejm.org/doi/full/10.1056/NEJMoa2108891?query=featured_home">https://www.nejm.org/doi/full/10.1056/NEJMoa2108891?query=featured_home</a></p>	<p>Effectiveness of Covid-19 Vaccines against the B.1.617.2 (Delta) Variant</p>	<p>Efficacia comparabile di due dosi di vaccino Pfizer o Vaxzevria contro la variante Delta di SARS-CoV-2 rispetto alla Alfa.</p>	<p>BACKGROUND</p> <p>The B.1.617.2 (delta) variant of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (Covid-19), has contributed to a surge in cases in India and has now been detected across the globe, including a notable increase in cases in the United Kingdom. The effectiveness of the BNT162b2 and ChAdOx1 nCoV-19 vaccines against this variant has been unclear.</p> <p>METHODS</p> <p>We used a test-negative case-control design to estimate the effectiveness of vaccination against symptomatic disease caused by the delta variant or the predominant strain (B.1.1.7, or alpha variant) over the period that the delta variant began circulating. Variants were identified with the use of sequencing and on the basis of the spike (S) gene status. Data on all symptomatic sequenced cases of Covid-19 in England were used to estimate the proportion of cases with either variant according to the patients' vaccination status.</p> <p>RESULTS</p> <p>Effectiveness after one dose of vaccine (BNT162b2 or ChAdOx1 nCoV-19) was notably lower among persons with the delta variant (30.7%; 95% confidence interval [CI], 25.2 to 35.7) than among those with the alpha variant (48.7%; 95% CI, 45.5 to 51.7); the results were</p>

similar for both vaccines. With the BNT162b2 vaccine, the effectiveness of two doses was 93.7% (95% CI, 91.6 to 95.3) among persons with the alpha variant and 88.0% (95% CI, 85.3 to 90.1) among those with the delta variant. With the ChAdOx1 nCoV-19 vaccine, the effectiveness of two doses was 74.5% (95% CI, 68.4 to 79.4) among persons with the alpha variant and 67.0% (95% CI, 61.3 to 71.8) among those with the delta variant.

## CONCLUSIONS

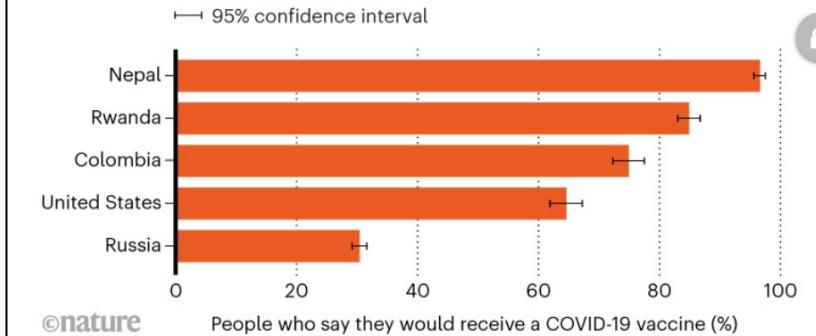
Only modest differences in vaccine effectiveness were noted with the delta variant as compared with the alpha variant after the receipt of two vaccine doses. Absolute differences in vaccine effectiveness were more marked after the receipt of the first dose. This finding would support efforts to maximize vaccine uptake with two doses among vulnerable populations.

**Figure 1.** Vaccine Effectiveness against the Alpha and Delta Variants, According to Dose and Vaccine Type.



Shown is the effectiveness of one dose and two doses of the BNT162b2 and ChAdOx1 nCoV-19 vaccines, or either vaccine ("any"), against symptomatic disease with the B.1.1.7 (alpha) or B.1.617.2 (delta) variant of the severe acute respiratory syndrome coronavirus 2. I bars indicate 95% confidence intervals.



<p>Kozlov M</p> <p>Nature news</p> <p><a href="https://www.nature.com/articles/d41586-021-01987-9">https://www.nature.com/articles/d41586-021-01987-9</a></p>	<p>COVID vaccines have higher approval in less-affluent countries</p>	<p>Le persone provenienti da Paesi meno ricchi sono più inclini ad accettare la vaccinazione contro SARS-CoV-2.</p>	<p>Surveys show that people in ten low- and middle-income nations are generally more eager to receive the COVID-19 jab than are people in two wealthier nations where vaccine is plentiful.</p> <div><p><b>WHERE PEOPLE ARE EAGER TO GET A COVID JAB</b></p><p>Survey data from ten low- and middle-income countries show that people there are more accepting of COVID-19 vaccines than are people in Russia and the United States.</p><table><thead><tr><th>Country</th><th>Percentage (%)</th></tr></thead><tbody><tr><td>Nepal</td><td>~95</td></tr><tr><td>Rwanda</td><td>~85</td></tr><tr><td>Colombia</td><td>~75</td></tr><tr><td>United States</td><td>~65</td></tr><tr><td>Russia</td><td>~30</td></tr></tbody></table><p>©nature</p><p>People who say they would receive a COVID-19 vaccine (%)</p><p>Source: Ref. 1</p></div>	Country	Percentage (%)	Nepal	~95	Rwanda	~85	Colombia	~75	United States	~65	Russia	~30
Country	Percentage (%)														
Nepal	~95														
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<p>Randy V</p> <p>JAMA</p> <p><a href="https://jamanetwork.com/journals/jamaoncology/fullarticle/2782038">https://jamanetwork.com/journals/jamaoncology/fullarticle/2782038</a></p>	<p>The Intersection of Societal Inequalities and Health Care Lessons Learned From the COVID-19 Pandemic</p>	<p>Disuguaglianze sociali da superare in sanità, emerse nella pandemia di COVID-19.</p>	<p>Just as it was a century ago during the 1918 influenza pandemic, the risk of dying of COVID-19 is twice as high for Black individuals compared with White individuals. During the current pandemic, Hispanic and Indigenous patients have similar mortality risk. As members of the medical profession, how do we physicians confront these disparities to progress toward equity?</p>												
<p>Kang P et al</p> <p>JAMA</p> <p><a href="https://doi.org/10.1001/jama.2021.12021">https://doi.org/10.1001/jama.2021.12021</a></p>	<p>Using Updated PubMed New Features and Functions to Enhance Literature Searches</p>	<p>Editoriale di JAMA sull'utilizzo delle funzionalità di PubMed per una ricerca efficace della letteratura.</p>	<p>PubMed is a free web-based public access resource that supports the search and retrieval of literature from the National Library of Medicine's MEDLINE database. In the past 2 years, PubMed has been updated to improve functionality and add important new features,<sup>1-3</sup> including a set of search statements to identify COVID-19 articles and a new publication filter to allow PubMed searches to retrieve early-</p>												

			release preprints. <sup>4,5</sup> This Viewpoint describes how these important new PubMed features and functions could allow clinicians to use a 3-step literature searching process to obtain real-time answers to important clinical questions.
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### Effective PubMed Searching in 3 Simple Steps

#### Step 1: Focus the Clinical Question

- Use the PICO format (patient, intervention, comparator, outcome) to concisely express the type of clinical question to be answered (eg, therapy, diagnosis, etiology, prognosis).
- Start by writing down common medical phrases that describe each PICO component of the clinical question.

#### Step 2: Use PubMed Clinical Query Filters

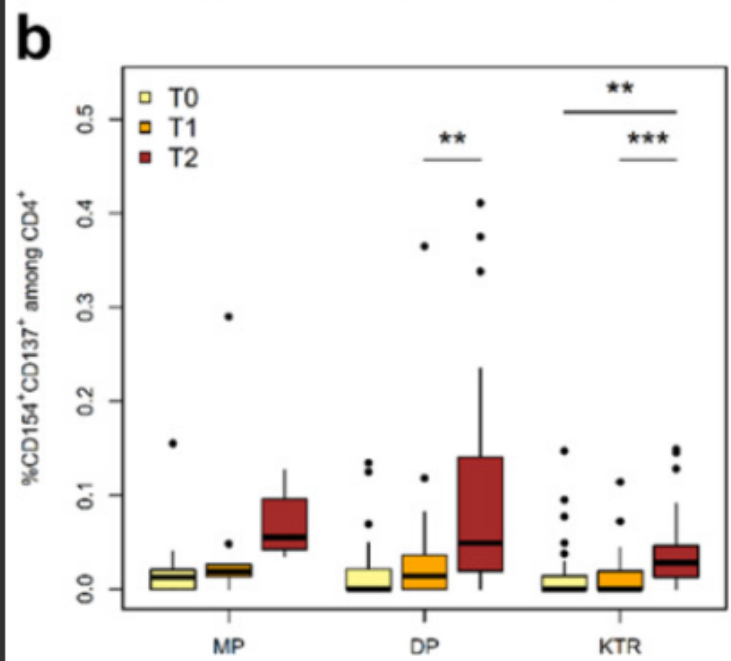
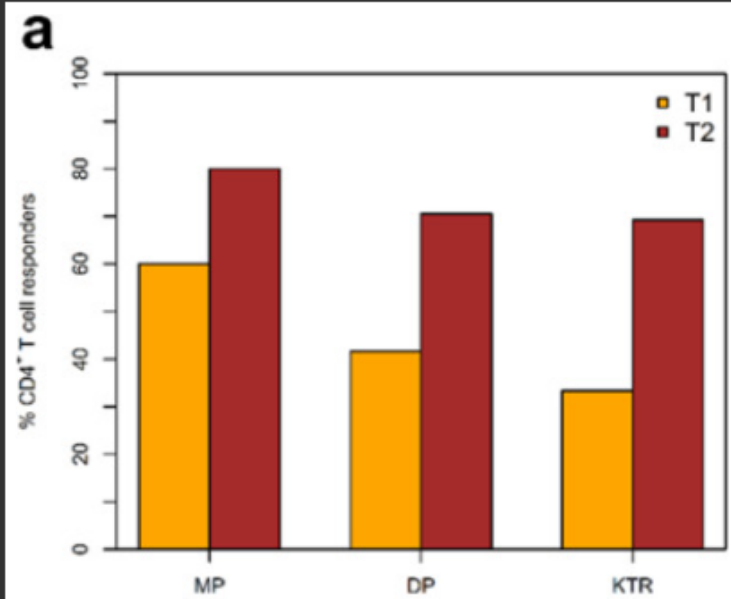
- PubMed clinical query filters are complex, multiterm search strategies implemented by using simple key terms or drop-down menus.
- Identify updated systematic reviews or meta-analyses with key search phrases and the statement (systematic review[filter] OR meta-analysis[filter]) typed into the main PubMed search page.
- Search for recent primary research studies with the clinical study categories filter most appropriate for the clinical question type (therapy, diagnosis, etiology, or prognosis) from the [clinical queries page](#) drop-down menu.
- Search for content related to COVID-19 with the COVID-19 search filter from the [clinical queries page](#) drop-down menu.
- To explicitly search for NIH-sponsored COVID-19 preprints, use key search phrases and the term *preprint[filter]* typed into any PubMed search box.

#### Step 3: Refine the Search Terms

- Every PubMed article is indexed with a controlled medical vocabulary called MeSH. PubMed automatically translates common medical phrases used in any search to appropriate MeSH terms before it conducts the search.
  - After each search, always use the "advanced" link and arrow tab (>) to determine whether PubMed has properly translated common medical phrases to appropriate MeSH terms.
  - If this translation process does not seem to have worked properly, use a different common medical phrase or use the MeSH database to find more appropriate search terms.

<p>Stumpf J et al</p> <p>The Lancet</p> <p><a href="https://www.thelancet.com/journals/lanepi/article/PIIS2666-7762(21)00155-1/fulltext">https://www.thelancet.com/journals/lanepi/article/PIIS2666-7762(21)00155-1/fulltext</a></p>	<p>Humoral and cellular immunity to SARS-CoV-2 vaccination in renal transplant versus dialysis patients: A prospective, multicenter observational study using mRNA-1273 or BNT162b2 mRNA vaccine.</p>	<p>Risposta immunitaria dopo due dosi di vaccino a mRNA in pazienti dializzati o trapiantati di rene rispetto a operatori sanitari.</p>	<p>Background : Dialysis and kidney transplant patients are vulnerable populations for COVID-19 related disease and mortality.</p> <p>Methods : We conducted a prospective study exploring the eight week time course of specific cellular (interferon-<math>\gamma</math> release assay and flow cytometry) or/and humoral immune responses (ELISA) to SARS-CoV-2 boost vaccination in more than 3100 participants including medical personnel, dialysis patients and kidney transplant recipients using mRNA vaccines BNT162b2 or mRNA-1273.</p> <p>Results : SARS-CoV-2-vaccination induced seroconversion efficacy in dialysis patients was similar to medical personnel (&gt; 95%), but markedly impaired in kidney transplant recipients (42%). T-cellular immunity largely mimicked humoral results. Major risk factors of seroconversion failure were immunosuppressive drug number and type (belatacept, MMF-MPA, calcineurin-inhibitors) as well as vaccine type (BNT162b2 mRNA). Seroconversion rates induced by mRNA-1273 compared to BNT162b2 vaccine were 97% to 88% (<math>p &lt; 0.001</math>) in dialysis and 49% to 26% in transplant patients, respectively. Specific IgG directed against the new binding domain of the spike protein (RDB) were significantly higher in dialysis patients vaccinated by mRNA-1273 (95%) compared to BNT162b2 (85%, <math>p &lt; 0.001</math>). Vaccination appeared safe and highly effective demonstrating an almost complete lack of symptomatic COVID-19 disease after boost vaccination as well as ceased disease incidences during third pandemic wave in dialysis patients.</p> <p>Conclusion : Dialysis patients exhibit a remarkably high seroconversion rate of 95% after boost vaccination, while humoral response is impaired in the majority of transplant recipients. Immunosuppressive drug number and type as well as vaccine type (BNT162b2) are major determinants of seroconversion failure in both</p>
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			dialysis and transplant patients suggesting immune monitoring and adaption of vaccination protocols.
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<p>Ikegame S et al</p> <p>Nature Communications</p> <p><a href="https://www.nature.com/articles/s41467-021-24909-9">https://www.nature.com/articles/s41467-021-24909-9</a></p>	<p>Neutralizing activity of Sputnik V vaccine sera against SARS-CoV-2 variants.</p>	<p>Siero di persone vaccinate con Sputnik presenta attività neutralizzante nei confronti delle varianti B.1.351 e della spike mutata con E484K.</p>	<p>Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected at least 180 million people since its identification as the cause of the current COVID-19 pandemic. The rapid pace of vaccine development has resulted in multiple vaccines already in use worldwide. The contemporaneous emergence of SARS-CoV-2 'variants of concern' (VOC) across diverse geographic locales underscores the need to monitor the efficacy of vaccines being administered globally. All WHO designated VOC carry spike (S) polymorphisms thought to enable escape from neutralizing antibodies. Here, we characterize the neutralizing activity of post-Sputnik V vaccination sera against the ensemble of S mutations present in alpha (B.1.1.7) and beta (B.1.351) VOC. Using de novo generated replication-competent vesicular stomatitis virus expressing various SARS-CoV-2-S in place of VSV-G (rcVSV-CoV2-S), coupled with a clonal 293T-ACE2 + TMPRSS2 + cell line optimized for highly efficient S-mediated infection, we determine that only 1 out of 12 post-vaccination serum samples shows effective neutralization (IC90) of rcVSV-CoV2-S: B.1.351 at full serum strength. The same set of sera efficiently neutralize S from B.1.1.7 and exhibit only moderately reduced activity against S carrying the E484K substitution alone. Taken together, our data suggest that control of some emergent SARS-CoV-2 variants may benefit from updated vaccines.</p>
<p>Kofman A et al</p> <p>JAMA</p> <p><a href="https://jamanetwork.com/journals/jama/fullarticle/2781945">https://jamanetwork.com/journals/jama/fullarticle/2781945</a></p>	<p>Potential COVID-19 Endgame Scenarios</p> <p>Eradication, Elimination, Cohabitation, or Conflagration?</p>	<p>Come potrebbe « finire » la storia di COVID-19.</p>	<p>[W]here on the endgame spectrum individual countries end up will dépend on both the collective choices and realities of the global community and the oft-inscrutable and perhaps unpredictable dynamics of SARS-CoV-2.</p>

<p>Nuti SV et al</p> <p>JAMA</p> <p><a href="https://jamanetwork.com/journals/jama/fullarticle/2781943">https://jamanetwork.com/journals/jama/fullarticle/2781943</a></p>	<p>Lay Epidemiology and Vaccine Acceptance</p>	<p>Diffusione di informazioni rilevanti per il singolo, coinvolgimento della politica locale e una classe medica affidabile e non giudicante potrebbero aiutare nel promuovere l'accettazione del vaccino contro SARS-CoV-2 nelle fasce di popolazione esitanti.</p>	<p>Lay epidemiology is how inferences are drawn from patterns of disease in small groups like friends and family, larger groups from social media or other sources, and even entire populations from public information or news stories.</p>
<p>Dorigatti I et al</p> <p>Nature</p> <p><a href="https://www.nature.com/articles/s41467-021-24622-7">https://www.nature.com/articles/s41467-021-24622-7</a></p>	<p>SARS-CoV-2 antibody dynamics and transmission from community-wide serological testing in the Italian municipality of Vo'</p>	<p>Esiti dello screening sierologico e molecolare della popolazione di Vo' Euganeo fra maggio e novembre 2020.</p>	<p>In February and March 2020, two mass swab testing campaigns were conducted in Vo', Italy. In May 2020, we tested 86% of the Vo' population with three immuno-assays detecting antibodies against the spike and nucleocapsid antigens, a neutralisation assay and Polymerase Chain Reaction (PCR). Subjects testing positive to PCR in February/March or a serological assay in May were tested again in November. Here we report on the results of the analysis of the May and November surveys. We estimate a seroprevalence of 3.5% (95% Credible Interval (CrI): 2.8–4.3%) in May. In November, 98.8% (95% Confidence Interval (CI): 93.7–100.0%) of sera which tested positive in May still reacted against at least one antigen; 18.6% (95% CI: 11.0–28.5%) showed an increase of antibody or neutralisation reactivity from May. Analysis of the serostatus of the members of 1,118 households indicates a 26.0% (95% CrI: 17.2–36.9%) Susceptible-Infectious Transmission Probability. Contact tracing had limited impact on epidemic suppression.</p>



			<p><b>Fig. 3: Antibody titres and dynamics at nine-month post-infection follow up.</b></p>
<p>Shotri M et al</p> <p>The Lancet</p> <p><a href="https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01642-1/fulltext">https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01642-1/fulltext</a></p>	<p>Spike-antibody waning after second dose of BNT162b2 or ChAdOx1</p>	<p>Declino del titolo anticorpale contro SARS-CoV-2 a distanza dalla seconda dose di vaccino Pfizer (due volte) o AstraZeneca (cinque volte nel periodo di osservazione).</p>	<p>To identify early indications of waning antibody levels to the spike protein (S-antibody) after complete two-dose vaccination, we did a cross-sectional analysis of fully vaccinated adults (aged <math>\geq 18</math> years) who submitted capillary blood samples for Virus Watch, a longitudinal community cohort study in England and Wales.<sup>4</sup> The study received ethical approval from the Hampstead NHS Health Research Authority Ethics Committee (20/HRA/2320). Sera were tested using Elecsys Anti-SARS-CoV-2 S and N electrochemiluminescent immunoassays (Roche Diagnostics, Basel, Switzerland); the S assay targets total antibodies to the S1 subunit of the spike protein (range 0·4–25 000 units per mL [U/mL]), whereas the N assay targets total antibodies to the full-length nucleocapsid protein, which we took as a proxy for previous SARS-CoV-2 infection (specificity 99·8% [99·3–100]).<sup>5</sup> Serological results were linked with demographic and clinical information collected at enrolment and with weekly self-reported vaccination status.</p>

<p>Thomas SJ et al</p> <p>MedRXiv</p> <p><a href="https://www.medrxiv.org/content/10.1101/2021.07.28.21261159v1.full.pdf">https://www.medrxiv.org/content/10.1101/2021.07.28.21261159v1.full.pdf</a></p>	<p>Six Month Safety and Efficacy of the BNT162b2 mRNA COVID-19 Vaccine</p>	<p>Profilo di sicurezza del vaccino Pfizer contro SARS-COV-2 a sei mesi dalla somministrazione.</p>	<p>Background: BNT162b2 is a lipid nanoparticle-formulated, nucleoside-modified RNA vaccine encoding a prefusion-stabilized, membrane-anchored SARS-CoV-2 full-length spike protein.</p> <p>BNT162b2 is highly efficacious against COVID-19 and is currently authorized for emergency use or conditional approval worldwide. At the time of authorization, data beyond 2 months postvaccination were unavailable.</p> <p>Methods: In an ongoing, placebo-controlled, observer-blinded, multinational, pivotal efficacy study, 44,165 ≥16-year-old participants and 2,264 12-15-year-old participants were randomized to receive 2 doses, 21 days apart, of 30 µg BNT162b2 or placebo. Study endpoints reported here are vaccine efficacy (VE) against laboratory-confirmed COVID-19 and safety data, both up to 6 months post-vaccination.</p> <p>Results: BNT162b2 continued to be safe and well tolerated. Few participants had adverse events leading to study withdrawal. VE against COVID-19 was 91% (95% CI 89.0–93.2) through up to 6</p>

			<p>months of follow-up, among evaluable participants and irrespective of previous SARS-CoV-2 infection. VE of 86%–100% was seen across countries and in populations with diverse characteristics of age, sex, race/ethnicity, and COVID-19 risk factors in participants without evidence of previous SARS-CoV-2 infection. VE against severe disease was 97% (95% CI 80.3– 99.9). In South Africa, where the SARS-CoV-2 variant of concern, B.1.351 (beta), was predominant, 100% (95% CI 53.5, 100.0) VE was observed.</p> <p>Conclusion: With up to 6 months of follow-up and despite a gradually declining trend in vaccine efficacy, BNT162b2 had a favorable safety profile and was highly efficacious in preventing COVID-19. (ClinicalTrials.gov number, NCT04368728).</p>
<p>Abbasi J</p> <p>JAMA</p> <p><a href="https://jamanetwork.com/journals/jama/fullarticle/2782673?guestAccessKey=9c58fb42-2958-4ac1-9807-a7269a6422b1&amp;utm_source=silverchair&amp;utm_medium=email&amp;utm_campaign=article_alert-jama&amp;utm_content=olf&amp;utm_term=072821">https://jamanetwork.com/journals/jama/fullarticle/2782673?guestAccessKey=9c58fb42-2958-4ac1-9807-a7269a6422b1&amp;utm_source=silverchair&amp;utm_medium=email&amp;utm_campaign=article_alert-jama&amp;utm_content=olf&amp;utm_term=072821</a></p>	<p>Überantibodies From Recovered COVID-19 Patients Could Spur New Therapeutics and Vaccines</p>	<p>I « migliori » anticorpi contro SARS-CoV-2 come guida per futuri monoclonali e vaccini.</p>	<p>At least a few of the patients, all of whom had mild to moderate disease, produced 4 particularly potent antibodies against the strain that infected them and a diverse range of variants that since have been detected. Two of the antibodies were “ultrapotent” at tiny concentrations across all 23 of the variants the scientists tested, including the highly transmissible B.1.1.7 (alpha), B.1.351 (beta), and B.1.617.2 (delta) versions, the researchers recently reported in Science. Combinations of some of these antibodies mitigated viral escape in laboratory experiments, a feature that could slow resistant strains from emerging in patients treated with the cocktails.</p>

<p>Yang S et al</p> <p>The Lancet</p> <p><a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7990482/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7990482/</a></p>	<p>Safety and immunogenicity of a recombinant tandem-repeat dimeric RBD-based protein subunit vaccine (ZF2001) against COVID-19 in adults: two randomised, double-blind, placebo-controlled, phase 1 and 2 trials</p>	<p>Sicurezza e immunogenicità di un nuovo vaccino a subunità (ZF2001) contro SARS-CoV-2.</p>	<p><b>Background</b></p> <p>Although several COVID-19 vaccines have been developed so far, they will not be sufficient to meet the global demand. Development of a wider range of vaccines, with different mechanisms of action, could help control the spread of SARS-CoV-2 globally. We developed a protein subunit vaccine against COVID-19 using a dimeric form of the receptor-binding domain (RBD) of the SARS-CoV-2 spike protein as the antigen. We aimed to assess the safety and immunogenicity of this vaccine, ZF2001, and determine the appropriate dose and schedule for an efficacy study.</p> <p><b>Methods</b></p> <p>We did two randomised, double-blind, placebo-controlled, phase 1 and phase 2 trials. Phase 1 was done at two university hospitals in Chongqing and Beijing, China, and phase 2 was done at the Hunan Provincial Center for Disease Control and Prevention in Xiangtan, China. Healthy adults aged 18–59 years, without a history of SARS-CoV or SARS-CoV-2 infection, an RT-PCR-positive test result for SARS-CoV-2, a history of contact with confirmed or suspected COVID-19 cases, and severe allergies to any component of the vaccine were eligible for enrolment. In phase 1, participants were randomly assigned (2:2:1) to receive three doses of the vaccine (25 µg or 50 µg) or placebo intramuscularly, 30 days apart. In phase 2, participants were randomly assigned (1:1:1:1:1:1) to receive the vaccine (25 µg or 50 µg) or placebo intramuscularly, 30 days apart, in either a two-dose schedule or a three-dose schedule. Investigators, participants, and the laboratory team were masked to group allocation. For phase 1, the primary outcome was safety, measured by the occurrence of adverse events and serious adverse events. For phase 2, the primary outcome was safety and immunogenicity (the seroconversion rate</p>
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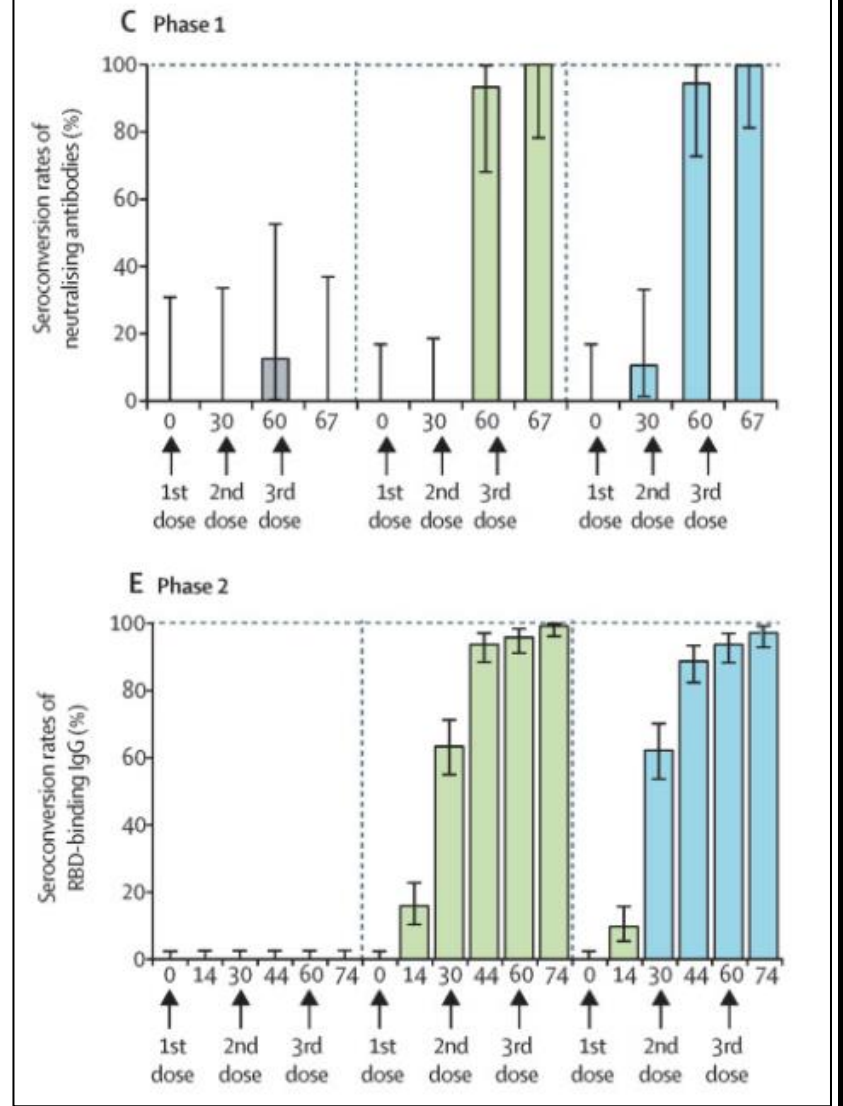
and the magnitude, in geometric mean titres [GMTs], of SARS-CoV-2-neutralising antibodies). Analyses were done on an intention-to-treat and per-protocol basis. These trials are registered with ClinicalTrials.gov (NCT04445194 and NCT04466085) and participant follow-up is ongoing.

Findings

Between June 22 and July 3, 2020, 50 participants were enrolled into the phase 1 trial and randomly assigned to receive three doses of placebo (n=10), the 25 µg vaccine (n=20), or the 50 µg vaccine (n=20). The mean age of participants was 32·6 (SD 9·4) years. Between July 12 and July 17, 2020, 900 participants were enrolled into the phase 2 trial and randomly assigned to receive two doses of placebo (n=150), 25 µg vaccine (n=150), or 50 µg vaccine (n=150), or three doses of placebo (n=150), 25 µg vaccine (n=150), or 50 µg vaccine (n=150). The mean age of participants was 43·5 (SD 9·2) years. In both phase 1 and phase 2, adverse events reported within 30 days after vaccination were mild or moderate (grade 1 or 2) in most cases (phase 1: six [60%] of ten participants in the placebo group, 14 [70%] of 20 in the 25 µg group, and 18 [90%] of 20 in the 50 µg group; phase 2: 37 [25%] of 150 in the two-dose placebo group, 43 [29%] of 150 in the two-dose 25 µg group, 50 [33%] of 150 in the two-dose 50 µg group, 47 [31%] of 150 in the three-dose placebo group, 72 [48%] of 150 in the three-dose 25 µg group, and 65 [43%] of 150 in the three-dose 50 µg group). In phase 1, two (10%) grade 3 or worse adverse events were reported in the 50 µg group. In phase 2, grade 3 or worse adverse events were reported by 18 participants (four [3%] in the two-dose 25 µg vaccine group, two [1%] in the two-dose 50 µg vaccine group, two [1%] in the three-dose placebo group, four [3%] in the three-dose 25 µg vaccine group, and six [4%] in the three-dose

50 µg vaccine group), and 11 were considered vaccine related (two [1%] in the two-dose 25 µg vaccine group, one [1%] in the two-dose 50 µg vaccine group, one [1%] in the three-dose placebo group, two [1%] in the three-dose 25 µg vaccine group, and five [3%] in the three-dose 50 µg vaccine group); seven participants reported serious adverse events (one [1%] in the two-dose 25 µg vaccine group, one [1%] in the two-dose 50 µg vaccine group, two [1%] in the three-dose placebo group, one [1%] in the three-dose 25 µg vaccine group, and two [1%] in the three-dose 50 µg vaccine group), but none was considered vaccine related. In phase 2, on the two-dose schedule, seroconversion rates of neutralising antibodies 14 days after the second dose were 76% (114 of 150 participants) in the 25 µg group and 72% (108 of 150) in the 50 µg group; on the three-dose schedule, seroconversion rates of neutralising antibodies 14 days after the third dose were 97% (143 of 148 participants) in the 25 µg group and 93% (138 of 148) in the 50 µg group. In the two-dose groups in phase 2, the SARS-CoV-2-neutralising GMTs 14 days after the second dose were 17·7 (95% CI 13·6–23·1) in the 25 µg group and 14·1 (10·8–18·3) in the 50 µg group. In the three-dose groups in phase 2, the SARS-CoV-2-neutralising GMTs 14 days after the third dose were 102·5 (95% CI 81·8–128·5) in the 25 µg group and 69·1 (53·0–90·0) in the 50 µg group.

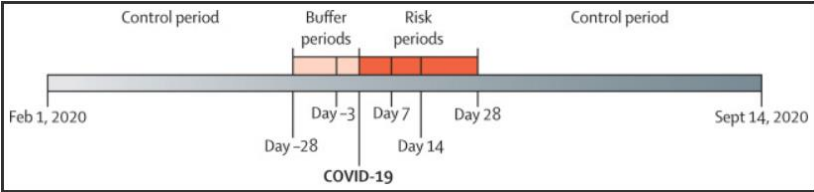
Interpretation  
The protein subunit vaccine ZF2001 appears to be well tolerated and immunogenic. The safety and immunogenicity data from the phase 1 and 2 trials support the use of the 25 µg dose in a three-dose schedule in an ongoing phase 3 trial for large-scale evaluation of ZF2001's safety and efficacy.






<p>Bhuyan P et al</p> <p>The Lancet</p> <p><a href="https://doi.org/10.1016/S0140-6736(21)01693-7">https://doi.org/10.1016/S0140-6736(21)01693-7</a></p>	<p>Very rare thrombosis with thrombocytopenia after second AZD1222 dose: a global safety database analysis.</p>	<p>La VITT dopo la seconda dose di vaccino AstraZeneca è estremamente rara.</p>	<p>Since COVID-19 vaccine roll-out, very rare cases of thrombosis with thrombocytopenia syndrome (TTS), which has been referred to as vaccine-induced immune thrombotic thrombocytopenia, have been reported. Here we describe case details of TTS identified in the AstraZeneca global safety database, which captures all spontaneously reported adverse events from real-world use of its medicines and vaccines worldwide.</p>
<p>Katsoularis I et al</p> <p>The Lancet</p> <p><a href="https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00896-5/fulltext">https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00896-5/fulltext</a></p>	<p>Risk of acute myocardial infarction and ischaemic stroke following COVID-19 in Sweden: a self-controlled case series and matched cohort study</p>	<p>COVID-19 come fattore di rischio per infarto e ictus in un'ampia casistica svedese.</p>	<p><b>Background</b>  COVID-19 is a complex disease targeting many organs. Previous studies highlight COVID-19 as a probable risk factor for acute cardiovascular complications. We aimed to quantify the risk of acute myocardial infarction and ischaemic stroke associated with COVID-19 by analysing all COVID-19 cases in Sweden.</p> <p><b>Methods</b>  This self-controlled case series (SCCS) and matched cohort study was done in Sweden. The personal identification numbers of all patients with COVID-19 in Sweden from Feb 1 to Sept 14, 2020, were identified and cross-linked with national inpatient, outpatient, cancer, and cause of death registers. The controls were matched on age, sex, and county of residence in Sweden. International Classification of Diseases codes for acute myocardial infarction or ischaemic stroke were identified in causes of hospital admission for all patients with COVID-19 in the SCCS and all patients with COVID-19 and the matched control individuals in the matched cohort study. The SCCS method was used to calculate the incidence rate ratio (IRR) for first acute myocardial infarction or ischaemic stroke following COVID-19 compared with a control period. The matched cohort study was used to determine the increased risk that COVID-19 confers compared with the background population of increased acute</p>



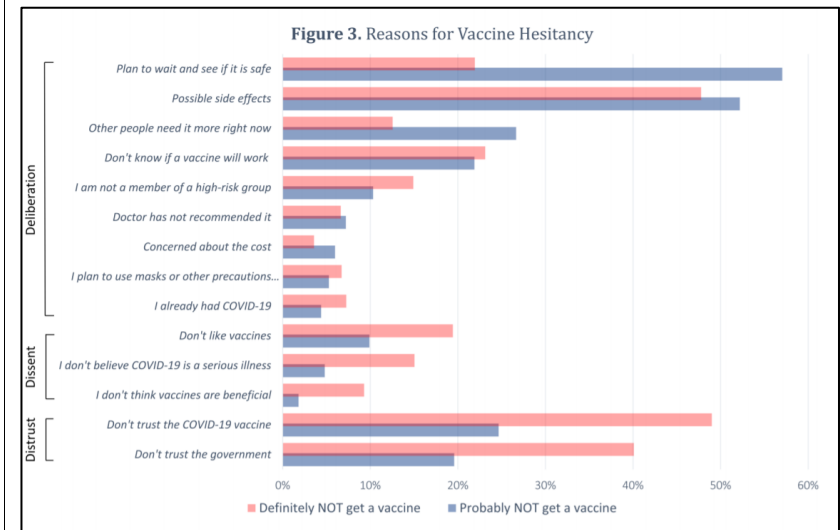
			<p>myocardial infarction or ischaemic stroke in the first 2 weeks following COVID-19.</p> <p>Findings</p> <p>86 742 patients with COVID-19 were included in the SCCS study, and 348 481 matched control individuals were also included in the matched cohort study. When day of exposure was excluded from the risk period in the SCCS, the IRR for acute myocardial infarction was 2·89 (95% CI 1·51–5·55) for the first week, 2·53 (1·29–4·94) for the second week, and 1·60 (0·84–3·04) in weeks 3 and 4 following COVID-19. When day of exposure was included in the risk period, IRR was 8·44 (5·45–13·08) for the first week, 2·56 (1·31–5·01) for the second week, and 1·62 (0·85–3·09) for weeks 3 and 4 following COVID-19. The corresponding IRRs for ischaemic stroke when day of exposure was excluded from the risk period were 2·97 (1·71–5·15) in the first week, 2·80 (1·60–4·88) in the second week, and 2·10 (1·33–3·32) in weeks 3 and 4 following COVID-19; when day of exposure was included in the risk period, the IRRs were 6·18 (4·06–9·42) for the first week, 2·85 (1·64–4·97) for the second week, and 2·14 (1·36–3·38) for weeks 3 and 4 following COVID-19. In the matched cohort analysis excluding day 0, the odds ratio (OR) for acute myocardial infarction was 3·41 (1·58–7·36) and for stroke was 3·63 (1·69–7·80) in the 2 weeks following COVID-19. When day 0 was included in the matched cohort study, the OR for acute myocardial infarction was 6·61 (3·56–12·20) and for ischaemic stroke was 6·74 (3·71–12·20) in the 2 weeks following COVID-19.</p> <p>Interpretation</p> <p>Our findings suggest that COVID-19 is a risk factor for acute myocardial infarction and ischaemic stroke. This indicates that acute myocardial infarction and ischaemic stroke represent a part of the</p>
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			<p>clinical picture of COVID-19, and highlights the need for vaccination against COVID-19.</p>  <p>The diagram illustrates the clinical picture of COVID-19 over time. It features a horizontal timeline starting from February 1, 2020, and ending on September 14, 2020. The timeline is divided into four main sections: 'Control period' (from Feb 1 to Day -28), 'Buffer periods' (from Day -28 to Day 7), 'Risk periods' (from Day 7 to Day 28), and another 'Control period' (from Day 28 to Sept 14, 2020). The 'Buffer periods' and 'Risk periods' are highlighted with orange and red shading, respectively. Specific dates marked on the timeline include Feb 1, 2020, Day -28, Day -3, Day 7, Day 14, Day 28, and Sept 14, 2020. The label 'COVID-19' is centered below the timeline.</p>
<p>Alwan NA</p> <p>Science</p> <p><a href="https://doi.org/10.1126/science.abg7113">https://doi.org/10.1126/science.abg7113</a></p>	<p>The road to addressing Long Covid</p>	<p>Come affrontare in modo aperto e ragionevole il « long COVID ».</p>	<p>Long Covid is likely the first illness in history that has been defined by patients through social media platforms such as Twitter and Facebook. People with Long Covid formed a movement that demanded recognition of what was happening to them. During the first wave of the pandemic in 2020, online testimonials of prolonged symptoms following severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection were the only source of reassurance to others with a similar experience, including this author (2). In the absence of any guidance or recognition about the possibility of a persistent illness, peer support is all that people with Long Covid had. Many previously healthy and active people described persistent symptoms of the acute illness that fluctuated, with new symptoms appearing weeks later. In many countries, most nonhospitalized people did not have lab confirmation of SARS-CoV-2 infection owing to lack of access to community testing, so their symptoms remained without a diagnosis.</p>

			<p><b>Meeting the need of Long Covid</b></p> <p>The public health response to the COVID-19 pandemic needs to adequately address the direct long-term effects of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in the context of the ongoing pandemic. An adequate response should incorporate the 4 Rs: Reporting, Recognition (including Rehabilitation), and Research.</p> <div> <div>  <p><b>Reporting</b></p> <ul style="list-style-type: none"> <li>• Universal and frequently updated case definitions</li> <li>• Disease registries</li> <li>• Follow-up after infection to assess recovery</li> <li>• Pandemic and postpandemic morbidity surveillance systems</li> <li>• Direct link to prevention policy decisions</li> <li>• Informing health and social care planning</li> </ul> </div> <div>  <p><b>Recognition</b></p> <ul style="list-style-type: none"> <li>• Listening, believing, and avoiding stereotypes.</li> <li>• Thorough clinical assessment and investigations</li> <li>• Inclusive diagnostic criteria</li> <li>• Personalized treatment and rehabilitation</li> <li>• Equitable care pathways</li> <li>• Multidisciplinary care</li> <li>• Employment rights and occupational health</li> </ul> </div> <div>  <p><b>Research</b></p> <ul style="list-style-type: none"> <li>• Risk factors</li> <li>• Prognosis and progression</li> <li>• Predictors of recovery</li> <li>• Pathophysiology</li> <li>• Therapeutics</li> <li>• Role of vaccination</li> <li>• Reinfection</li> <li>• Inequalities and stigma</li> <li>• Economic and services burden</li> <li>• Long Covid in children</li> </ul> </div> </div>
<p>Hoan K et al</p> <p>CID</p> <p><a href="https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab633/6323151">https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab633/6323151</a></p>	<p>Deliberation, Dissent, and Distrust: Understanding distinct drivers of COVID-19 vaccine hesitancy in the United States</p>	<p>Predittori di esitazione nel sottoporsi alla vaccinazione contro SARS-CoV-2 negli USA.</p>	<p><b>Background</b></p> <p>Despite the availability of safe and efficacious COVID-19 vaccines, a significant proportion of the American public remains unvaccinated and does not appear immediately interested in receiving the vaccine.</p> <p><b>Methods</b></p> <p>In this study, we analyzed data from the U.S. Census Bureau's Household Pulse Survey, a biweekly cross-sectional survey of U.S. households. We estimated the prevalence of vaccine hesitancy across states and nationally and assessed the predictors of vaccine hesitancy and vaccine rejection. Additionally, we examined the underlying reasons for vaccine hesitancy, grouped into thematic categories.</p>

## Results

A total of 459,235 participants were surveyed from January 6 to March 29, 2021. While vaccine uptake increased from 7.7 to 47 percent, vaccine hesitancy rates remained relatively fixed: overall, 10.2 percent reported that they would probably not get a vaccine, and 8.2 percent would definitely not get a vaccine. Income, education, and state political leaning strongly predicted vaccine hesitancy. However, while both female sex and Black race were factors predicting hesitancy, among those who were hesitant, these same characteristics predicted vaccine reluctance rather than rejection. Those who expressed reluctance invoked mostly “deliberative” reasons while those who rejected the vaccine were also likely to invoke reasons of “dissent” and “distrust”.



## Conclusion

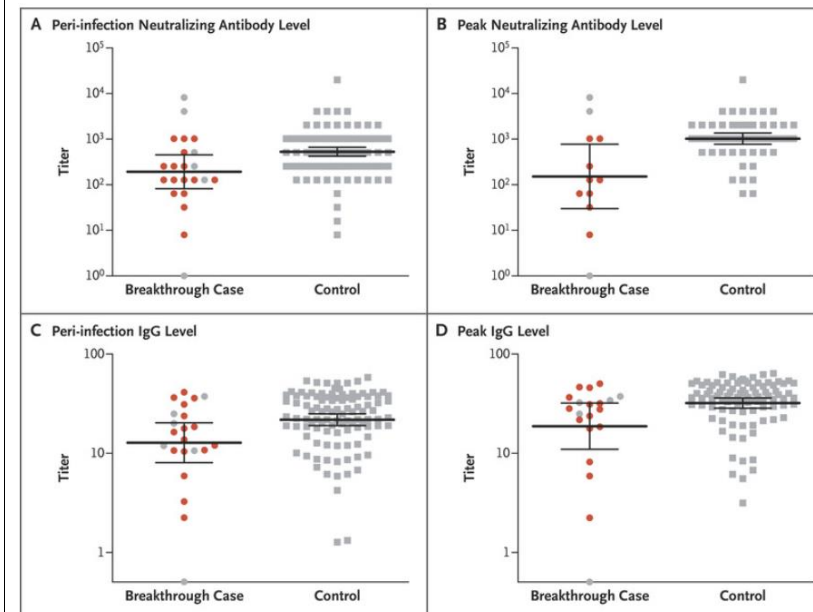
Vaccine hesitancy comprises a sizable proportion of the population and is large enough to threaten achieving herd immunity. Distinct

			subgroups of hesitancy have distinctive socio-demographic associations as well as cognitive and affective predilections. Segmented public health solutions are needed to target interventions and optimize vaccine uptake.
Cohen CA et al  JAMA  <a href="https://doi.org/10.1038/s41467-021-24938-4">https://doi.org/10.1038/s41467-021-24938-4</a>	SARS-CoV-2 specific T cell responses are lower in children and increase with age and time after infection.	Risposta T cellulare meno spiccata nei bambini rispetto agli adulti.	SARS-CoV-2 infection of children leads to a mild illness and the immunological differences with adults are unclear. Here, we report SARS-CoV-2 specific T cell responses in infected adults and children and find that the acute and memory CD4+ T cell responses to structural SARS-CoV-2 proteins increase with age, whereas CD8+ T cell responses increase with time post-infection. Infected children have lower CD4+ and CD8+ T cell responses to SARS-CoV-2 structural and ORF1ab proteins when compared with infected adults, comparable T cell polyfunctionality and reduced CD4+ T cell effector memory. Compared with adults, children have lower levels of antibodies to $\beta$ -coronaviruses, indicating differing baseline immunity. Total T follicular helper responses are increased, whilst monocyte numbers are reduced, indicating rapid adaptive coordination of the T and B cell responses and differing levels of inflammation. Therefore, reduced prior $\beta$ -coronavirus immunity and reduced T cell activation in children might drive milder COVID-19 pathogenesis.
Krantz MS et al  JAMA  <a href="https://doi.org/10.1001/jamainternmed.2021.3779">https://doi.org/10.1001/jamainternmed.2021.3779</a>	Safety Evaluation of the Second Dose of Messenger RNA COVID-19 Vaccines in Patients With Immediate Reactions to the First Dose.	Tolleranza della seconda dose di vaccino Pfizer dopo reazione allergica alla prima.	There were 189 patients who participated in this study (mean [SD] age, 43 (14) years; 163 women [86%]) (Table). Of the mRNA COVID-19 vaccine first-dose reactions evaluated, 130 (69%) were to Moderna and 59 (31%) to Pfizer-BioNTech. The most frequently reported first-dose reactions were flushing or erythema (53 [28%]), dizziness or lightheadedness (49 [26%]), tingling (46 [24%]), throat tightness (41 [22%]), hives (39 [21%]), and wheezing or shortness of breath (39 [21%]). Thirty-two (17%) met anaphylaxis criteria.

			<p>A total of 159 patients (84%) received a second dose. Antihistamine premedication before the second dose was given in 47 patients (30%). All 159 patients, including 19 individuals with first-dose anaphylaxis, tolerated the second dose. Thirty-two (20%) reported immediate and potentially allergic symptoms that were associated with the second dose that were self-limited, mild, and/or resolved with antihistamines alone.</p>
<p>Brown CM et al</p> <p>MMWR</p> <p><a href="http://dx.doi.org/10.15585/mmwr.mm7031e2">http://dx.doi.org/10.15585/mmwr.mm7031e2</a></p>	<p>Outbreak of SARS-CoV-2 Infections, Including COVID-19 Vaccine Breakthrough Infections, Associated with Large Public Gatherings — Barnstable County, Massachusetts, July 2021</p>	<p>Cluster di infezioni riconducibili a grandi raduni negli USA, verosimilmente sostenute dalla trasmissibilità della variante Delta di SARS-CoV-2.</p>	<p>What is already known about this topic?</p> <p>Variants of SARS-CoV-2 continue to emerge. The B.1.617.2 (Delta) variant is highly transmissible.</p> <p>What is added by this report?</p> <p>In July 2021, following multiple large public events in a Barnstable County, Massachusetts, town, 469 COVID-19 cases were identified among Massachusetts residents who had traveled to the town during July 3–17; 346 (74%) occurred in fully vaccinated persons. Testing identified the Delta variant in 90% of specimens from 133 patients. Cycle threshold values were similar among specimens from patients who were fully vaccinated and those who were not.</p> <p>What are the implications for public health practice?</p> <p>Jurisdictions might consider expanded prevention strategies, including universal masking in indoor public settings, particularly for large public gatherings that include travelers from many areas with differing levels of SARS-CoV-2 transmission.</p>
<p>Bergwerk M et al</p> <p>NEJM</p> <p><a href="https://www.nejm.org/doi/full/10.1056/NEJMoa21">https://www.nejm.org/doi/full/10.1056/NEJMoa21</a></p>	<p>Covid-19 Breakthrough Infections in Vaccinated Health Care Workers</p>	<p>Trentanove infezioni da SARS-CoV-2 in operatori sanitari vaccinati con Pfizer in Israele.</p>	<p>Background : Despite the high efficacy of the BNT162b2 messenger RNA vaccine against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), rare breakthrough infections have been reported, including infections among health care workers. Data are needed to characterize these infections and define correlates of breakthrough and infectivity.</p>

<a href="#">09072?query=featured_home</a>			<p>Methods : At the largest medical center in Israel, we identified breakthrough infections by performing extensive evaluations of health care workers who were symptomatic (including mild symptoms) or had known infection exposure. These evaluations included epidemiologic investigations, repeat reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assays, antigen-detecting rapid diagnostic testing (Ag-RDT), serologic assays, and genomic sequencing. Correlates of breakthrough infection were assessed in a case–control analysis. We matched patients with breakthrough infection who had antibody titers obtained within a week before SARS-CoV-2 detection (peri-infection period) with four to five uninfected controls and used generalized estimating equations to predict the geometric mean titers among cases and controls and the ratio between the titers in the two groups. We also assessed the correlation between neutralizing antibody titers and N gene cycle threshold (Ct) values with respect to infectivity.</p> <p>Results : Among 1497 fully vaccinated health care workers for whom RT-PCR data were available, 39 SARS-CoV-2 breakthrough infections were documented. Neutralizing antibody titers in case patients during the peri-infection period were lower than those in matched uninfected controls (case-to-control ratio, 0.361; 95% confidence interval, 0.165 to 0.787). Higher peri-infection neutralizing antibody titers were associated with lower infectivity (higher Ct values). Most breakthrough cases were mild or asymptomatic, although 19% had persistent symptoms (&gt;6 weeks). The B.1.1.7 (alpha) variant was found in 85% of samples tested. A total of 74% of case patients had a high viral load (Ct value, &lt;30) at some point during their infection; however, of these patients, only 17 (59%) had a positive result on concurrent Ag-RDT. No secondary infections were documented.</p>
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Conclusions : Among fully vaccinated health care workers, the occurrence of breakthrough infections with SARS-CoV-2 was correlated with neutralizing antibody titers during the peri-infection period. Most breakthrough infections were mild or asymptomatic, although persistent symptoms did occur.



#### BACKGROUND

The efficacy and safety of tofacitinib, a Janus kinase inhibitor, in patients who are hospitalized with coronavirus disease 2019 (Covid-19) pneumonia are unclear.

#### METHODS

We randomly assigned, in a 1:1 ratio, hospitalized adults with Covid-19 pneumonia to receive either tofacitinib at a dose of 10 mg or placebo twice daily for up to 14 days or until hospital discharge. The primary outcome was the occurrence of death or respiratory failure through day 28 as assessed with the use of an eight-level ordinal scale

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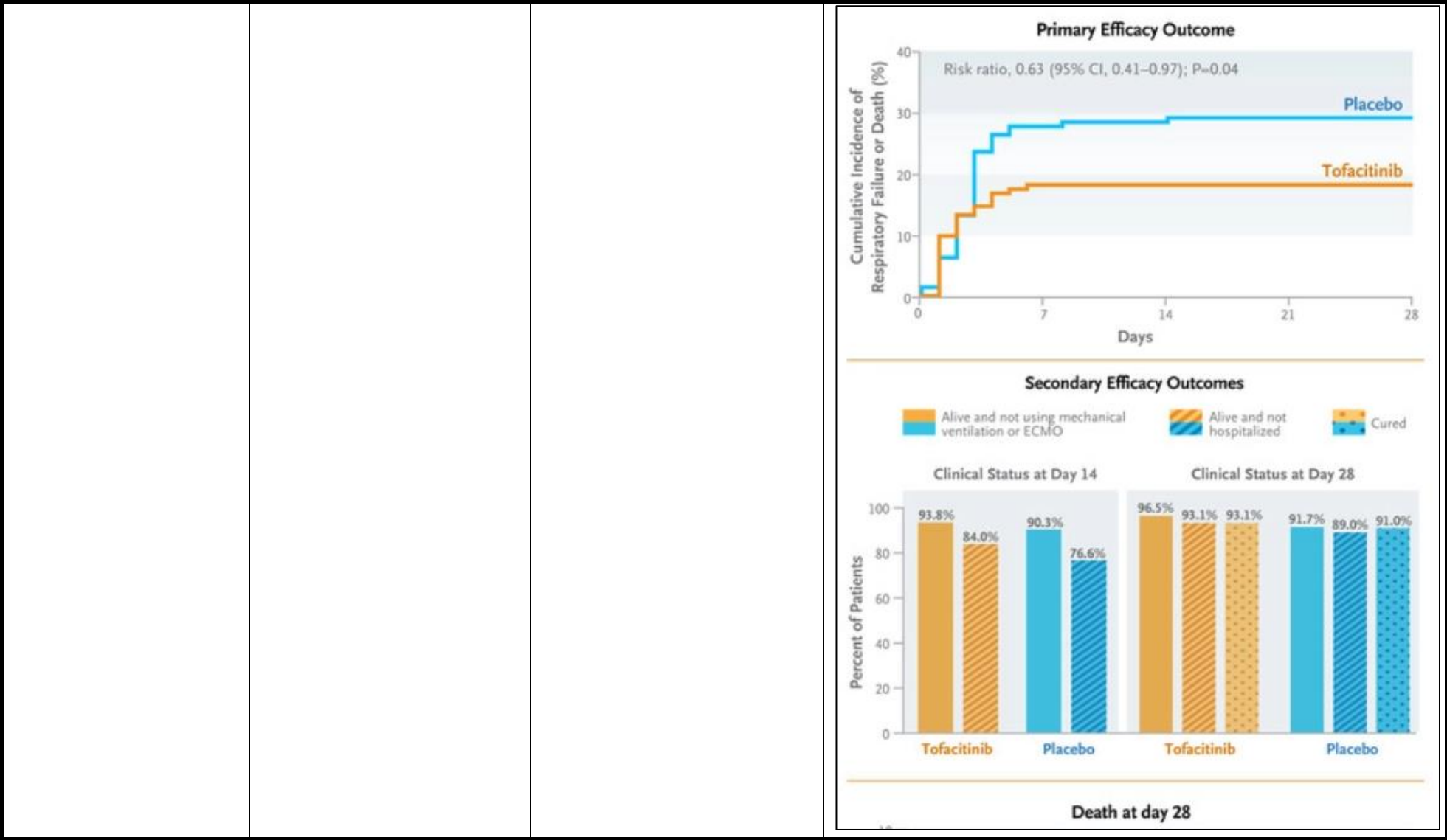
[https://www.nejm.org/doi/full/10.1056/NEJMoa2101643?query=featured\\_home](https://www.nejm.org/doi/full/10.1056/NEJMoa2101643?query=featured_home)

Tofacitinib in Patients Hospitalized with Covid-19 Pneumonia

L'inibitore di JAK tofacitinib è associato a minore rischio di insufficienza respiratoria e morte a 28 giorni nei pazienti ospedalizzati per COVID-19.



			<p>(with scores ranging from 1 to 8 and higher scores indicating a worse condition). All-cause mortality and safety were also assessed.</p> <p><b>RESULTS</b></p> <p>A total of 289 patients underwent randomization at 15 sites in Brazil. Overall, 89.3% of the patients received glucocorticoids during hospitalization. The cumulative incidence of death or respiratory failure through day 28 was 18.1% in the tofacitinib group and 29.0% in the placebo group (risk ratio, 0.63; 95% confidence interval [CI], 0.41 to 0.97; P=0.04). Death from any cause through day 28 occurred in 2.8% of the patients in the tofacitinib group and in 5.5% of those in the placebo group (hazard ratio, 0.49; 95% CI, 0.15 to 1.63). The proportional odds of having a worse score on the eight-level ordinal scale with tofacitinib, as compared with placebo, was 0.60 (95% CI, 0.36 to 1.00) at day 14 and 0.54 (95% CI, 0.27 to 1.06) at day 28. Serious adverse events occurred in 20 patients (14.1%) in the tofacitinib group and in 17 (12.0%) in the placebo group.</p> <p><b>CONCLUSIONS</b></p> <p>Among patients hospitalized with Covid-19 pneumonia, tofacitinib led to a lower risk of death or respiratory failure through day 28 than placebo.</p>
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<p>Soraas A et al</p> <p>JAMA</p> <p><a href="https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2782531">https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2782531</a></p>	<p>Self-reported Memory Problems 8 Months After COVID-19 Infection</p>	<p>Incidenza di problemi di memoria autoriportati in una coorte di oltre 13000 adulti, di cui quelli con COVID-19 studiati fino a 8 mesi di distanza dalla diagnosi.</p>	<p>COVID-19 is an airway disease that also affects the nervous system.<sup>1</sup> Therefore, neurological and neurocognitive symptoms may be a part of the postacute sequelae of SARS-CoV-2 infection (PASC) syndrome. PASC may be found to affect a high proportion of people who had mild cases of COVID-19, and there is an urgent need for a detailed description of PASC in nonhospitalized patients.<sup>2,3</sup> This cohort study examines self-reported memory problems 8 months after COVID-19 infection.</p> <p>Figure. Proportion of Participants Reporting Memory Problems 8 Months After Baseline</p> <table><caption>Data for Figure: Proportion of Participants Reporting Memory Problems 8 Months After Baseline</caption><thead><tr><th>SARS-CoV-2 status at baseline</th><th>Proportion of Participants Reporting Memory Problems (%)</th></tr></thead><tbody><tr><td>Positive</td><td>~11.2</td></tr><tr><td>Negative</td><td>~4.3</td></tr><tr><td>Untested</td><td>~2.4</td></tr></tbody></table>	SARS-CoV-2 status at baseline	Proportion of Participants Reporting Memory Problems (%)	Positive	~11.2	Negative	~4.3	Untested	~2.4
SARS-CoV-2 status at baseline	Proportion of Participants Reporting Memory Problems (%)										
Positive	~11.2										
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<p>Ceban F et al</p> <p>JAMA</p> <p><a href="https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2782453">https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2782453</a></p>	<p>Association Between Mood Disorders and Risk of COVID-19 Infection, Hospitalization, and Death</p> <p>A Systematic Review and Meta-analysis</p>	<p>Revisione sistematica alla ricerca di una associazione fra disturbi dell’umore preesistenti e outcome avverso di COVID-19 : le persone con disturbi dell’umore possono essere considerate una categoria a</p>	<p>Importance Preexisting noncommunicable diseases (eg, diabetes) increase the risk of COVID-19 infection, hospitalization, and death. Mood disorders are associated with impaired immune function and social determinants that increase the risk of COVID-19. Determining whether preexisting mood disorders represent a risk of COVID-19 would inform public health priorities.</p>								

		<p>rischio di ospedalizzazione e morte.</p>	<p><b>Objective</b> To assess whether preexisting mood disorders are associated with a higher risk of COVID-19 susceptibility, hospitalization, severe complications, and death.</p> <p><b>Data Sources</b> Systematic searches were conducted for studies reporting data on COVID-19 outcomes in populations with and without mood disorders on PubMed/MEDLINE, The Cochrane Library, PsycInfo, Embase, Web of Science, Google/Google Scholar, LitCovid, and select reference lists. The search timeline was from database inception to February 1, 2021.</p> <p><b>Study Selection</b> Primary research articles that reported quantitative COVID-19 outcome data in persons with mood disorders vs persons without mood disorders of any age, sex, and nationality were selected. Of 1950 articles identified through this search strategy, 21 studies were included in the analysis.</p> <p><b>Data Extraction and Synthesis</b> The modified Newcastle-Ottawa Scale was used to assess methodological quality and risk of bias of component studies. Reported adjusted odds ratios (ORs) were pooled with unadjusted ORs calculated from summary data to generate 4 random-effects summary ORs, each corresponding to a primary outcome.</p> <p><b>Main Outcomes and Measures</b> The 4 a priori primary outcomes were COVID-19 susceptibility, COVID-19 hospitalization, COVID-19 severe events, and COVID-19 death. The hypothesis was formulated before study search. Outcome measures between individuals with and without mood disorders were compared.</p> <p><b>Results</b> This review included 21 studies that involved more than 91 million individuals. Significantly higher odds of COVID-19 hospitalization (OR, 1.31; 95% CI, 1.12-1.53; P = .001; n = 26 554 397) and death (OR, 1.51; 95% CI, 1.34-1.69; P &lt; .001; n = 25 808 660) were found in persons with preexisting mood disorders compared</p>
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			<p>with those without mood disorders. There was no association between mood disorders and COVID-19 susceptibility (OR, 1.27; 95% CI, 0.73-2.19; n = 65 514 469) or severe events (OR, 0.94; 95% CI, 0.87-1.03; n = 83 240). Visual inspection of the composite funnel plot for asymmetry indicated the presence of publication bias; however, the Egger regression intercept test result was not statistically significant.</p> <p>Conclusions and Relevance The results of this systematic review and meta-analysis examining the association between preexisting mood disorders and COVID-19 outcomes suggest that individuals with preexisting mood disorders are at higher risk of COVID-19 hospitalization and death and should be categorized as an at-risk group on the basis of a preexisting condition.</p>
<p>Oh ES et al</p> <p>JAMA</p> <p><a href="https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2782534">https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2782534</a></p>	<p>Post-acute Sequelae of SARS-CoV-2 Infection and Subjective Memory Problems</p>	<p>Piché la sensazione soggettiva di lacune mnesiche è associata a deficit cognitivo nel futuro, i problemi di memoria riportati nell'ambito delle sequele di COVID-19 meritano approfondimento.</p>	<p>As of June 7, 2021, there are more than 168 000 000 survivors of COVID-19 worldwide. Approximately 72% of survivors report at least 1 symptom persisting 30 days or more beyond the acute illness, and symptoms frequently persist even among patients who were relatively young and never hospitalized.<sup>1</sup> Commonly reported symptoms include fatigue, shortness of breath, anxiety, depression, insomnia, and cognitive impairment.<sup>1</sup> Given the emerging public health crisis represented by this burden of survivorship, there is an urgent need for understanding postacute sequelae of SARS-CoV-2 (PASC).</p>