COVID- 19 REPORT (SETTIMANA DAL 17 AL 23 GENNAIO 2022)

VIROLOGIA E DIAGNOSTICA
ESTENSORE : DOTT. FRANCESCO TACCARI

ARTICOLO	ABSTRACT	CONTENUTO E COMMENTO
Berenger BM et al. Diagn Microbiol Infect Dis. Clinical evaluation of nasopharyngeal, midturbinate nasal and oropharyngeal swabs for the detection of SARS-CoV-2. https://reader.elsevier.com/reader/sd/pii/S0732889321003096?token=4F3BD0BA8DB54858	Abstract In the setting of supply chain shortages of nasopharyngeal (NP) swabs, we sought to compare the ability of nasopharyngeal, midturbinate nasal, and oropharyngeal swabs (NPS, MTS, and OPS) to detect SARS-CoV-2. Community and hospitalized participants post-COVID-19 diagnosis were swabbed and tested for SARS-CoV-2 by PCR. Thirty-six participants had all 3 swabs collected. Using detection at any site as the standard, the percent positive agreements were 90% (95% CI 74.4-96.5), 80% (70.3-94.7) and 87% (62.7-90.5) for NPS, MTS, and OPS, respectively. Subsequently, 43 participants had OPS and NPS collected. Thirty-nine were positive with a percent positive agreement of 82.1% (95% CI 67.3-91.0) for OPS and 87.2% (73.3-94.4) for NPS. Combining all 79 patients tested, 67 were positive at either site with a positive agreement was 86.5% (76.4-	Studio che confronta le performance del tampone nasofaringeo, del tampone dei turbinati nasali medi e del tampone dell'orofaringe nella rilevazione del virus SARS-CoV-2. Sono stati sottoposti a tamponi sia partecipanti ospedalizzati che non ospedalizzati, con infezione da SARS-CoV-2 accertata. Nel primo studio è stata riscontrata una percentuale di positività del 90%, 80% e 87%, rispettivamente per il tampone nasofaringeo, per quello dei turbinati nasali medi e dell'orofaringe; nel secondo studio (tampone orofaringeo vs nasofaringeo) è stata riscontrata una percentuale di positività dell 82.1% per l'orofaringeo e dell'87.2% per il nasofaringeo. Individuare il campione più appropriato, la cui raccolta sia però ben tollerata dal paziente, è un tema di cruciale importanza nella diagnosi dell'infezione da SARS-CoV-2. Tale studio sembrerebbe riscontrare nel tampone orofaringeo

9F0B84E0BD54E5C07B3143375FDEA25B59BA748E971547B84A457C7729A0A281824CC224CFDAA14A&originRegion=eu-west-1&originCreation=20220114210624	92.7) for OPS and 91.1% (81.8-95.8) for NPS. OPS are an acceptable alternative to NPS for the detection of SARS-CoV-2 infections.	una accettabile alternativa al tampone nasofaringeo, standard diagnostico di riferimento.
Araf Y et al. J Med Virol. Omicron variant of SARS-CoV-2: Genomics, transmissibility, and responses to current COVID-19 vaccines. https://onlinelibrary.wiley.com/doi/epdf/10.1002/jmv.27588	Abstract Currently, the SARS-CoV-2 has been spread worldwide as the Omicron variant. This variant is a heavily mutated virus and designated as a variant of concern by the World Health Organization (WHO). WHO cautioned that the Omicron variant of SARS-CoV-2 held a very high risk of infection, reigniting anxieties about the economy's recovery from the two-year pandemic. The extensively mutated Omicron variant is likely to spread internationally, posing a high risk of infection surges with serious repercussions in some areas. According to preliminary data, the Omicron variant of SARS-CoV-2 has a higher risk of reinfection. On the other hand, whether the current COVID-19 vaccines could effectively resistant the new strain is still under investigation. However, there is very limited information on the current situation of the Omicron variant, such as genomics, transmissibility, efficacy of vaccines, treatment, and management. This review focused on the genomics, transmission, and effectiveness of vaccines against the Omicron variant, which will be helpful for further investigation of a new variant of SARS-CoV-2.	Review sulla famigerata « Variant Of Concern » Omicron, che ne mette a fuoco la genomica, la trasmissibilità e l'efficacia dei vaccini contro di essa. In primo luogo la variante Omicron possiede un elevatissimo numero di mutazioni, 30 delle quali sono nella sequenza genomica che codifica per la proteina spike, responsabili dell'alterazione strutturale della stessa e pertanto della capacità di Omicron di sfuggire al sistema immunitario. La variante Omicron possiede inoltre un'incredibile trasmissibilità, circa 4 volte maggiore del ceppo « wild type » e 2 volte maggiore della variante Delta, caratteristica che le ha permesso una diffusione rapidissima nel mondo. Infine Omicron è stata riscontrata anche in pazienti vaccinati per SARS-CoV-2, suggerendo che la nuova variante presenta un certo grado di resistenza ai vaccini attualmente disponibili.

Barreiro P et al. J Clin Microbiol. A pilot study for the evaluation of an interferon-gamma release assay (IGRA) to measure T-cell immune responses after SARS-CoV-2 infection or vaccination in a unique cloistered cohort. https://journals.asm.org/doi/epdf/10.1128/jcm.02199-21	Abstract Background: Assessment of T-cell responses to SARS-CoV-2 antigens may be of value to determine long-lasting protection to breakthrough infections or reinfections. Interferon-gamma release assay is a validated method to test cellular immunity in mycobacterial infections and has been proposed for patients with SARS-CoV-2 infection or vaccination. Methods: Quantitative IgG to spike and qualitative IgG to nucleocapsid antigens were determined by chemiluminescence microparticle immunoassay using the Architect® platform (Abbott®), and interferon-gamma release assay against two Qiagen® proprietary mixes of SARS-CoV-2 spike protein (antigen-1 and antigen-2) were performed for a selected group of subjects. Results: A total of 121 subjects in a cloistered institution after a COVID-19 outbreak were studied. IgG-spike levels and interferon-gamma concentration were highest among subjects after two doses of vaccine, followed by patients with a longer history of past COVID-19 and no vaccination. Best cut-off for interferon-gamma assay was 25 IU/µL for all subgroups of individuals and the two sets of SARS-CoV-2 antigens studied. Conclusions: Testing T-cell response may be of clinical utility to determine immunity after exposure to SARS-CoV-2 antigens, with the interferon-gamma concentration of	Studio su 121 soggetti nei quali è stata valutata la risposta cellulare T-mediata agli antigeni di SARS-CoV-2 mediante un saggio di rilascio di interferon gamma e la risposta anticorpale IgG quantitativa nei confronti della proteina spike e qualitativa nei confronti degli antigeni del nucleocapside, mediante un test in chemiluminescenza. Sono stati riscontrati più elevati livelli di IgG-spike e più elevate concentrazioni di interferon-gamma nei soggetti vaccinati con due dosi e nei soggetti con una precedente storia di COVID-19 di più lunga durata ma non vaccinati. La risposta immunitaria al virus SARS-CoV-2 è complessa e non può essere ricondotta solamente alla risposta anticorpale : si può facilmente comprendere quindi la discutibile utilità clinica della determinazione del titolo anticorpale dopo la vaccinazione o dopo l'infezione. La determinazione della risposta cellulare T-mediata agli antigeni di SARS-CoV-2 mediante un test di rilascio di interferon gamma (metodica adeguatamente validata per le infezioni da micobatteri, ad esempio) potrebbe pertanto essere di ausilio nel determinare in maniera più esaustiva la protezione verso nuove infezioni o reinfezioni.

	25 IU/µL as the best cut-off either after infection or vaccination.	
Ramachandran A et al. J Am Coll Emerg Physicians Open Performance of Abbott ID-Now rapid nucleic amplification test for laboratory identification of COVID-19 in asymptomatic emergency department patients. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8716572/pdf/EMP2-2-e12592.pdf	Abstract Objective: We sought to evaluate the test characteristics of Abbott ID-Now as a screening tool compared to polymerase chain reaction (PCR) testing for identification of COVID in an asymptomatic emergency department population. Methods: We performed a prospective study enrolling a convenience sample of asymptomatic patients presenting to a single academic emergency department (ED) who received simultaneous testing with ID-Now and PCR per standardized ED protocols. Sensitivity, specificity, and positive and negative predictive value (PPV, NPV) of ID-Now were calculated compared to PCR. Stratified analysis by cycle threshold (Ct) values was also performed, defined as high viral load (Ct < 33) and low viral load (Ct ≥ 33). Results: A total of 3121 patients were enrolled, of whom 2895 had valid results for ID-Now and PCR. COVID prevalence was 2.6%. ID-Now had a sensitivity of 85.1% (95% CI 75.9% to 92.7%) and a specificity of 99.7% (99.5% to 99.9%). PPV and NPV were high at 87.5% (83.1% to 96.1%) and 99.6% (99.3% to 99.8%). Stratified analysis by low and high Ct values demonstrated reduction in sensitivity in patients with low viral loads: 91.7% (81.6% to 97.2%) in low Ct value patients versus 58.3% (27.7% to 84.8%) in high Ct value patients.	Studio prospettico condotto in un Pronto Soccorso su 3121 pazienti asintomatici che mira a valutare la performance di un test molecolare rapido rispetto allo standard diagnostico molecolare di riferimento. E' stata riscontrata una sensibilità del test molecolare rapido dell'85.1% e una specificità del 99.7%. E' stata inoltre prevedibilmente riscontrata una una maggior sensibilità del test nei pazienti con più alta carica virale (91.7%). In una realtà come quella del Pronto Soccorso l'idoneo e rapido inquadramento del paziente è di fondamentale importanza per il corretto allocamento dello stesso. Inoltre l'identificazione del paziente con infezione da SARS-CoV-2, asintomatico ma comunque contagioso, è cruciale. Lo strumento valutato in questo studio sembrerebbe in grado di rilevare il virus rapidamente e con buona sensibilità nella subdola categoria dei pazienti asintomatici, sebbene in presenza di una bassa carica virale tale sensibilità risulterebbe non ottimale.

	Conclusions: ID-Now had excellent performance in asymptomatic ED patients with a low rate of false positives. Cycle threshold analysis suggests a relationship between viral load and ID-Now sensitivity. Given its speed and performance in this population, ID-Now should be considered an excellent tool to support clinical decision-making in ED populations.	

COVID- 19 REPORT (SETTIMANA DAL 17 AL 23 GENNAIO 2022)

VACCINI

COMMENTO : DOTT. PIERLUIGI DEL VECCHIO E DOTT.SSA GIULIA MICHELI

ARTICOLO	ABSTRACT	CONTENUTO E COMMENTO
Walter E.B. et al. The NEJM Evaluation of the BNT162b2 Covid-19 Vaccine in Children 5 to 11 Years of Age https://www.nejm.org/doi/pdf/10.1056/NEJMoa2116298?articleTools=true	BACKGROUND Safe, effective vaccines against coronavirus disease 2019 (Covid-19) are urgently needed in children younger than 12 years of age. METHODS A phase 1, dose-finding study and an ongoing phase 2–3 randomized trial are being conducted to investigate the safety, immunogenicity, and efficacy of two doses of the BNT162b2 vaccine administered 21 days apart in children 6 months to 11 years of age. We present results for 5-to-11-year-old children. In the phase 2–3 trial, participants were randomly assigned in a 2:1 ratio to receive two doses of either the BNT162b2 vaccine at the dose level identified during the open-label phase 1 study or placebo. Immune responses 1 month after	Trial clinico randomizzato dose finding di fase 1 con una fase 2 e 3 in corso, finalizzato a valutare la sicurezza, l'efficacia e l'immunogenicità di due dosi del vaccino BNT162b2 per Sars-CoV2 in una popolazione tra i 6 mesi e gli 11 anni di vita. (n=2268 nella fase 2-3). Nella fase 2-3 del trial i partecipanti sono stati randomizzati in un rapporto di 2:1 in un gruppo ricevente due somministrazioni di BNT162b2 al dosaggio 10 ug stabilito nella fase 1 ed un gruppo ricevente placebo. Il geometric mean ratio del titolo di anticorpi neutralizzanti per Sars-CoV2, ad un mese dalla seconda dose, è risultato essere pari a 1.04 (dati confrontati con quelli di una popolazione tra i 16 ed i 25 anni vaccinata). Tale valore ha

	the second dose of BNT162b2 were immunologically bridged to those in 16-to-25-year-olds from the pivotal trial of two 30-µg doses of BNT162b2. Vaccine efficacy against Covid-19 at 7 days or more after the second dose was assessed. RESULTS During the phase 1 study, a total of 48 children 5 to 11 years of age received 10 µg, 20 µg, or 30 µg of the BNT162b2 vaccine (16 children at each dose level). On the basis of reactogenicity and immunogenicity, a dose level of 10 µg was selected for further study. In the phase 2–3 trial, a total of 2268 children were randomly assigned to receive the BNT162b2 vaccine (1517 children) or placebo (751 children). At data cutoff, the median follow-up was 2.3 months. In the 5-to-11-year-olds, as in other age groups, the BNT162b2 vaccine had a favorable safety profile. No vaccine-related serious adverse events were noted. One month after the second dose, the geometric mean ratio of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) neutralizing titers in 5-to-11-year-olds to those in 16-to-25-year-olds. was 1.04 (95% confidence interval [CI], 0.93 to 1.18), a ratio meeting the prespecified immunogenicity success criterion (lower bound of two-sided 95% CI, >0.67; geometric mean ratio point estimate, ≥0.8). Covid-19 with onset 7 days or more after the second dose was reported in three recipients of the BNT162b2 vaccine and in 16 placebo recipients (vaccine efficacy, 90.7%; 95% CI, 67.7 to 98.3). CONCLUSIONS A Covid-19 vaccination regimen consisting of two 10-µg doses of BNT162b2 administered 21 days apart	rispettato i criteri prespecificati di successo di immunogenicità. Dei riceventi le due dosi di vaccino 3 hanno sviluppato il COVID-19 almeno a 7 giorni dalla seconda dose vs. 16 nel gruppo placebo. I dati, seppur preliminari, dimostrano un buon profilo di sicurezza, immunogenicità ed efficacia nella popolazione oggetto di studio di un ciclo vaccinale con due dosi da 10 ug di BNT162b2, somministrate a distanza di 21 giorni l'una dall'altra. Bisognerà attendere ulteriori riscontri a lungo termine riguardanti la durata della risposta immunitaria ed il monitoraggio di eventuali eventi avversi, con un follow-up previsto dallo studio di almeno 4 anni.

	was found to be safe, immunogenic, and efficacious in children 5 to 11 years of age.	
Nawal Al Kaabi et al. Nature The incidence of COVID-19 infection following emergency use authorization of BBIBP-CORV inactivated vaccine in frontline workers in the United Arab Emirates https://www.nature.com/articles/s41598-021-04244-1.pdf	Based on the findings from the Phase III clinical trials of inactivated SARS COV-2 Vaccine, (BBIBPCORV) emergency use authorization (EUA) was granted for the vaccine to frontline workers in the UAE. A prospective cohort study was conducted among frontline workers to estimate the incidence rate and risk of symptomatic COVID-19 infection 14 days after the second dose of inoculation with BBIBP-CORV inactivated vaccine. Those who received two doses of the BBIBP-CORV vaccine in the period from 14th of September 2020 (first dose) to 21st of December 2020 (second dose) were followed up for COVID-19 infections. 11,322 individuals who received the two-dose BBIBP-CORV vaccine were included and were followed up post the second dose plus fourteen days. The incidence rate of symptomatic infection was 0.08 per 1000-person days (95% CI 0.07, 0.10). The estimated absolute risk of developing symptomatic infection was 0.97% (95% CI 0.77%, 1.17%). The confirmed seroconversion rate was 92.8%. There were no serious adverse events reported and no individuals suffered from severe disease. Our findings show that vaccinated individuals are likely to remain protected against symptomatic infection or becoming PCR positive for SARS COV 2 following the second dose of the vaccination.	Studio di coorte prospettico condotto tra i lavoratori degli Emirati Arabi, esposti in prima linea al rischio di contagio da Sars-CoV2 e sottoposti ad un ciclo vaccinale con due dosi di BBIBP-CORV (settembre-dicembre 2020). Si tratta di un vaccino inattivato, approvato dalla WHO nella Emergency Use Listing. 11.322 individui sono stati sottoposti alla vaccinazione con due dosi di tale composto, con un'incidenza di infezioni sintomatiche pari allo 0.08 per 1000 persone al giorno, con un rischio assoluto di sviluppare un'infezione sintomatica dello 0.97%. Il tasso di sierconversione è risultato essere del 92.8%. Non sono stati riportati eventi avversi severi dopo la somministrazione, e nessuno dei vaccinati ha sviluppato una patologia severa da Sars-CoV2. In conclusione i dati dello studio risultano promettenti, con la forte limitante di un'assenza di un gruppo di controllo di non vaccinati e considerando che in assoluto molte altre variabili possono ridurre il tasso di infezioni osservato nel periodo dello studio.

Nemet I. et al. The NEJM Third BNT162b2 Vaccination Neutralization of SARS-CoV-2 Omicron Infection https://www.nejm.org/doi/full/10.1056/NEJMc2119358?query=featured_coronavirus	To the Editor: On November 26, 2021, the World Health Organization (WHO) named the B.1.1.529 (omicron) variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first detected in South Africa, as a variant of concern.1 By November 29, 2021, three days after the announcement by the WHO, cases of infection with the omicron variant had already been detected in many other countries. Whether the BNT162b2 vaccine (Pfizer–BioNTech), which was previously shown to have 95% efficacy against coronavirus disease 2019 (Covid-19),2,3 will effectively neutralize infection with the omicron variant is unclear. We compared neutralization of omicron-infected cells in serum samples obtained from participants who had received two doses of vaccine with neutralization in samples obtained from participants who had received three doses. Microneutralization assays with wild-type virus and B.1.351 (beta), B.1.617.2 (delta), and omicron variant isolates were performed with the use of serum samples obtained from two groups of 20 health care workers. One group comprised participants who had received two doses of the BNT162b2 vaccine (mean, 165.6 days since receipt of the second dose), and the second group comprised those who had received three vaccine doses (mean, 25 days since receipt of the third dose) (Table S1 in the SupplementaryAppendix, available with the full text of this letter at NEJM.org). Significance was assessed with the use of a Wilcoxon matched-pairs signedrank test. Receipt of three vaccine doses led to better	Studio analitico in vitro, condotto in Israele, sulla neutralizzazione di cellule infettate con diverse varianti di SARS-CoV2 su campioni di siero ottenuto da operatori sanitari vaccinati con il vaccino BNT162b2, divisi in due gruppi (20 operatori ciascuno), uno comprendente coloro che hanno ricevuto 2 e l'altro 3 dosi di vaccino. I risultati mostrano una significante minore efficacia della neutralizzazione del virus wild-type e delle tre varianti di interesse (beta, delta, omicron) dai sieri ottenuti da operatori che hanno ricevuto 2 dosi del vaccino BNT162b2. Una minore efficacia di neutralizzazione contro le varianti beta ed omicron rispetto al virus wild-type e' stato osservato in entrambi i gruppi in modo simile. Limitazioni : campione piccolo, studio in vitro, maggiore distanza temporale dall'ultima dose nel gruppo con 2 dosi. Interessante notare come la vaccinazione, sia essa con due o tre dosi, sembra associarsi una ridotta efficacia della neutralizzazione in vitro per le varianti non wild-type.

	neutralization of the wild-type virus and the three variants than receipt of two vaccine doses (Fig. 1). The geometric mean titers of the wildtype virus and the beta, delta, and omicron variants were 16.56, 1.27, 8.00, and 1.11, respectively, after receipt of the second vaccine dose and 891.4, 152.2, 430.5, and 107.6, respectively, after receipt of the third dose. A significantly lower neutralization efficiency of the BNT162b2 vaccine against all the tested variants of concern (beta, delta, and omicron) than against the wildtype virus was observed in samples obtained from participants who had received two doses than in those obtained from participants who had received three doses (Fig. 1B and 1D). The lower neutralization efficiency against the beta and omicron variants than against the wild-type virus was similar in samples obtained from participants who had received two doses and in those obtained from participants who had received three doses. The third dose of the BNT162b2 vaccine efficiently neutralized infection with the omicron variant (geometric mean titer, 1.11 after the second dose vs. 107.6 after the third dose) (Fig. 1A and 1C). We analyzed the neutralization efficiency of the BNT162b2 vaccine against wild-type SARSCoV-2 and the beta, delta, and omicron variants of concern. Limitations of the study include the small cohort tested and the fact that the test was only an in vitro assay. Nevertheless, we found low neutralization efficiency with two doses of the BNT162b2 vaccine against the wild-type virus and the delta variant, assessed more than	

	5 months after receipt of the second dose, and no neutralization efficiency against the omicron variant. The importance of a third vaccine dose is clear, owing to the higher neutralization efficiency (by a factor of 100) against the omicron variant after the third dose than after the second dose; however, even with three vaccine doses, neutralization against the omicron variant was lower (by a factor of 4) than that against the delta variant. The durability of the effect of the third dose of vaccine against Covid-19 is yet to be determined.	
Eyre D.W. et al. The NEJM Effect of Covid-19 Vaccination on Transmission of Alpha and Delta Variants https://www.nejm.org/doi/full/10.1056/NEJMoa2116597?query=featured_coronavirus	BACKGROUND Before the emergence of the B.1.617.2 (delta) variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), vaccination reduced transmission of SARS-CoV-2 from vaccinated persons who became infected, potentially by reducing viral loads. Although vaccination still lowers the risk of infection, similar viral loads in vaccinated and unvaccinated persons who are infected with the delta variant call into question the degree to which vaccination prevents transmission. METHODS We used contact-testing data from England to perform a retrospective observational cohort study involving adult contacts of SARS-CoV-2–infected adult index patients. We used multivariable Poisson regression to investigate associations between transmission and the vaccination status of index patients and contacts and to determine how these associations varied with the B.1.1.7 (alpha) and delta variants and time since the second vaccination. RESULTS Among 146,243 tested contacts of 108,498 index patients, 54,667 (37%) had positive SARS-CoV-2 polymerase-chain-	Studio osservazionale retrospettivo di coorte**,** svolto nel Regno Unito (1 gennaio-31 luglio 2021) nel quale sono stati studiati adulti di età maggiore di 18 anni, contatti di casi e casi indice (146243 contatti testati, 108498 indici testati) al fine di investigare associazioni tra trasmissione e stato vaccinale tra casi indice e contatti e studiare come queste cambino con le diverse varianti virali (alpha e delta) e la distanza temporale dal termine della vaccinazione. Dei 146,243 contatti testa, 52,667 (37%) sono risultati positivi al test PCR per SARS-CoV2. I vaccini BNT e ChAd si sono dimostrati associati a una minore trasmissione di SARS-CoV2 dai casi che si sono infettati nonostante la vaccinazione (adjusted rate ratio BNT162b2, 0.32; 95% confidence interval [CI], 0.21 to 0.48; and with ChAdOx1 nCoV-19, 0.48; 95% CI, 0.30 to 0.78), seppur nei casi vaccinati con BNT e in maggiormente con ChAd, questa riduzione e’ stata minore sulla trasmissione della variante

	reaction (PCR) tests. In vaccinated index patients who became infected with the alpha variant, two vaccinations with either BNT162b2 or ChAdOx1 nCoV-19 (also known as AZD1222), as compared with no vaccination, were independently associated with reduced PCR positivity in contacts (adjusted rate ratio with BNT162b2, 0.32; 95% confidence interval [CI], 0.21 to 0.48; and with ChAdOx1 nCoV-19, 0.48; 95% CI, 0.30 to 0.78). Vaccine-associated reductions in transmission of the delta variant were smaller than those with the alpha variant, and reductions in transmission of the delta variant after two BNT162b2 vaccinations were greater (adjusted rate ratio for the comparison with no vaccination, 0.50; 95% CI, 0.39 to 0.65) than after two ChAdOx1 vaccinations (adjusted rate ratio, 0.76; 95% CI, 0.70 to 0.82). Variation in cycle-threshold (Ct) values (indicative of viral load) in index patients explained 7 to 23% of vaccine-associated reductions in transmission of the two variants. The reductions in transmission of the delta variant declined over time after the second vaccination, reaching levels that were similar to those in unvaccinated persons by 12 weeks in index patients who had received ChAdOx1 nCoV-19 and attenuating substantially in those who had received BNT162b2. Protection in contacts also declined in the 3-month period after the second vaccination. CONCLUSIONS Vaccination was associated with a smaller reduction in transmission of the delta variant than of the alpha variant, and the effects of vaccination decreased over time. PCR Ct values at diagnosis of the index patient only partially explained decreased transmission.	delta che sulla variante alfa (adjusted rate ratio BNT, 0.50; 95% CI, 0.39 to 0.65; adjusted rate ratio ChAdOx1, 0.76; 95% CI, 0.70 to 0.82).). La vaccinazione e' stata associata a piu' basse cariche virali (alte Ct) nella variante alfa (non vaccinati median Ct value, 18.4; interquartile range, 15.7 to 22.5; BNT nei pazienti sintomatici, Valore mediano Ct, 27.4; interquartile range, 19.7 to 32.1 : ChAdOx, Ct mediano, 23.9; interquartile range, 18.1 to 32.5) e minor misura nella variante delta (BNT Ct mediano 18.0 (interquartile range, 15.8 to 21.8), ChAd Ct mediano 17.3 (interquartile range, 15.3 to 20.6), Non vaccinato Ct mediano 17.0 (interquartile range, 15.1 to 20.3): lo studio ha pero' mostrato che la differenza nei valori Ct alla diagnosi dei casi era attribuibile solo per il 7/23% all'effetto della vaccinazione. L'incidenza delle infezioni con la variante alfa e quelle con la delta erano minori nei contatti vaccinati con 2 dosi di BNT che in coloro vaccinati con 2 dosi di ChAd. La protezione verso la trasmissione ai contatti e' andata scemando nel periodo di 3 mesi dopo la seconda vaccinazione, in misura maggiore verso la variante delta, specialmente nei vaccinati con ChAd. I contatti erano piu' soggetti a infettarsi maggiore il tempo trascorso della seconda vaccinazione. Limitazioni : bias comportamentale (non investigati i soggetti che non avessero eseguito un test PCR), possibili altre fonti di contagio per i contatti altri che il caso, dati insufficienti su precedenti infezioni, utilizzati come proxy il periodo (10

		maggio come spartiacque) e il S-gene target failure, non aggiustamenti su comorbidita' e condizioni coesistenti.

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FISIOPATOLOGIA CLINICA E TERAPIA DI COVID-19 ESTENSORI : DOTT.SSA FRANCESCA GIOVANNENZE, DOTT.SSA FRANCESCA RAFFAELLI, DOTT.SSA ELEONORA TADDEI		
ARTICOLO	**ABSTRACT**	**CONTENUTO E COMMENTO**
Pengcheng H et al Receptor binding and complex structures of human ACE2 to spike RBD from Omicron and Delta SARS-CoV-2 Cell https://www.cell.com/cell/fulltext/S0092-8674(22)00001-0	COVID-19 pandemic continues worldwide with many variants arising, especially those of variants of concern (VOCs). A recent VOC, Omicron (B.1.1.529), which obtains a large number of mutations in the receptor-binding domain (RBD) of the spike protein, has risen to intense scientific and public attention. Here we studied the binding properties between the human receptor ACE2 (hACE2) and the VOC RBDs and resolved the crystal and cryo- EM structures of the Omicron RBD-hACE2 complex, as well as the crystal structure of Delta RBD-hACE2 complex. We found that, unlike Alpha, Beta and Gamma, Omicron RBD binds to hACE2 at a similar affinity compared to that of the prototype RBD, which might be due to compensation of multiple mutations for both immune escape and transmissibility. The complex structures of Omicron-hACE2 and Delta-hACE2 reveal the	Studio della struttura cristallina dell'interazione fra la porzione legante il recettore (RBD) della proteina S (spike) della variante omicron di SARS-CoV-2 e il recettore cellulare ACE-2. Pare che le mutazioni della porzione RBD di omicron consentano una affinità simile a quella della RBD wild-type, pur conferendo un vantaggio in termini di « fuga » dal sistema immunitario. La conoscenza dettagliata dei meccanismi molecolari alla base dell'infezione da SARS-CoV-2 è alla base di una comprensione sempre più approfondita della malattia e dello sviluppo di nuove possibilità terapeutiche.

	structural basis of how RBD-specific mutations bind to hACE2.	
Jansen J et al SARS-CoV-2 infects the human kidney and drives fibrosis in kidney organoids Cell https://www.cell.com/cell-stem-cell/fulltext/S1934-5909(21)00520-8	Kidney failure is frequently observed during and after COVID-19, but it remains elusive whether this is a direct effect of the virus. Here, we report that SARS-CoV-2 directly infects kidney cells and is associated with increased tubule-interstitial kidney fibrosis in patient autopsy samples. To study direct effects of the virus on the kidney independent of systemic effects of COVID-19, we infected human induced pluripotent stem cell-derived kidney organoids with SARS-CoV-2. Single cell RNA-sequencing indicated injury and dedifferentiation of infected cells with activation of pro-fibrotic signaling pathways. Importantly, SARS-CoV-2 infection also led to increased collagen 1 protein expression in organoids. A SARS-CoV-2 protease inhibitor was able to ameliorate the infection of kidney cells by SARS-CoV-2. Our results suggest that SARS-CoV-2 can directly infect kidney cells and induce cell injury with subsequent fibrosis. These data could explain both acute kidney injury in COVID-19 patients and the development of chronic kidney disease in Long-COVID.	Dimostrazione dell'infezione diretta di cellule renali da parte di SARS-CoV-2 tramite l'utilizzo di organoidi, cioè prototipi di rene formati a partire da cellule staminali. In particolare il danno renale consiste nella fibrosi interstiziale, come dimostrato anche nelle autopsie di persone decedute dopo l'infezione da SARS-CoV-2. Considerando la rilevanza della compromissione renale nell'ambito di COVID-19, avere a disposizione modelli per studiare in vivo il fenomeno appare molto significativo.
Serviente C et al From heart to muscle: Pathophysiological	The long-term sequelae of the coronavirus disease 2019 (COVID-19) are multifaceted and, besides the lungs, impact other organs and tissues, even in cases of mild infection. Along with commonly reported symptoms such as fatigue	Disamina delle manifestazioni a lungo di termine dell'infezione da SARS-CoV-2 (cosiddetto « long COVID »), che possono essere giustificati da una disfunzione endoteliale persistente che potrebbe determinare in particolare malessere e ridotta tolleranza all'esercizio per

mechanisms underlying long-term physical sequelae from SARS-CoV-2 infection. J Appl Physiol https://doi.org/10.1152/japplphysiol.00734.2021	and dyspnea, a significant proportion of those with prior COVID-19 infection also exhibit signs of cardiac damage, muscle weakness, and ultimately, poor exercise tolerance. This review provides an overview of evidence indicating cardiac impairments and persistent endothelial dysfunction in the peripheral vasculature of those previously infected with COVID-19, irrespective of the severity of the acute phase of illness. Additionally, VO2peak appears to be lower in convalescent patients, which may stem, in part, from alterations in O2 transport such as impaired diffusional O2conductance. Together, the persistent multi-organ dysfunction induced by COVID-19 may set previously healthy individuals on a trajectory towards frailty and disease. Given the large proportion of individuals recovering from COVID-19, it is critically important to better understand the physical sequelae of COVID-19, the underlying biological mechanisms contributing to these outcomes, and the long-term effects on future disease risk. This review highlights relevant literature on the pathophysiology post-COVID-19 infection, gaps in the literature, and emphasizes the need for the development of evidence-based rehabilitation guidelines.	ridotta perfusione periferica e per peggioramento degli scambi gassosi a livello polmonare.
Ruobing W et al Human airway lineages derived from pluripotent stem cells reveal the epithelial	There is an urgent need to understand how SARS-CoV-2 infects the airway epithelium and in a subset of individuals leads to severe illness or death. Induced pluripotent stem cells (iPSCs) provide a near limitless supply of human cells that can be differentiated into cell types of interest, including airway epithelium, for disease modeling. We	Studio degli effetti dell'infezione da SARS-CoV-2 su cellule staminali pluripotenti utilizzate per creare un modello di epitelio polmonare : si osserva nel dettaglio la risposta indotta dal virus, con produzione di interferone e altri mediatori dellìinfiammazione che si oppongono all'ingresso del virus nelle cellule.

responses to SARS-CoV-2 infection. Am J Physiol Lung Cell Mol Physiol https://doi.org/10.1152/ajplung.00397.2021	present a human iPSC-derived airway epithelial platform, composed of the major airway epithelial cell types, that is permissive to SARS-CoV-2 infection. Subsets of iPSC-airway cells express the SARS-CoV-2 entry factors ACE2 and TMPRSS2. Multiciliated cells are the primary initial target of SARS-CoV-2 infection. Upon infection with SARS-CoV-2, iPSC-airway cells generate robust interferon and inflammatory responses and treatment with remdesivir or camostat methylate causes a decrease in viral propagation and entry, respectively. In conclusion, iPSC-derived airway cells provide a physiologically relevant in vitro model system to interrogate the pathogenesis of, and develop treatment strategies for, COVID-19 pneumonia.	
Lippi G et al What We Know (and Do not Know) Regarding the Pathogenesis of Pulmonary Thrombosis in COVID-19. Semin Thromb Hemost https://doi.org/10.1055/s-0041-1742091	The clinical course of coronavirus disease 2019 (COVID-19) is often complicated by the onset of venous thrombosis and thromboembolism (VTE), encompassing also pulmonary thrombosis. Recent statistics attests that the cumulative frequency of VTE can be as high as 30% in COVID-19 hospitalized patients, increasing to nearly 40 to 70% (depending on systematic screening) in those with severe illness, mechanical ventilation, or intensive care unit admission. The risk of venous thrombosis seems mostly limited to the active phase of disease, and is directly associated with some genetic (i.e., inherited prothrombotic predisposition) and demographical factors (male sex, overweight/obesity), disease severity (risk increasing progressively from hospitalization to development of severe	Revisione dei meccanismi di tromboembolia polmonare caratteristici di COVID-19 : embolia polmonare vera e propria a partenza da una trombosi venosa profonda, trombosi per contiguità con un focolaio di polmonite, trombosi diffusa che coinvolge anche il polmone nell'ambito di uno stato di infiammazione generalizzato.

	illness, being the highest in patients needing mechanical ventilation and/or intensive care), presence and extent of pulmonary disease, coexistence of multiple risk factors (immobilization, mechanical ventilation, co- or superinfections), along with increased values of inflammatory and thrombotic biomarkers. At least three different phenotypes of pulmonary thrombosis may develop in COVID-19 patients, one caused by typical embolization from peripheral venous thrombosis (e.g., deep vein thrombosis), a second type triggered by local inflammation of nearby pulmonary tissue, and a third one mostly attributable to the prothrombotic state consequent to the pronounced systemic inflammatory response (i.e., the so-called cytokine storm) that is frequently observed in COVID-19. Although the pathogenesis of these three conditions has different features, their discrimination is essential for diagnostic and therapeutic purposes. The prognosis of COVID-19 patients who develop pulmonary thrombosis is also considerably worse than those who do not, thus probably needing frequent monitoring and more aggressive therapeutic management.	
Meyer H et al Computed tomography-defined body composition as prognostic markers for	BACKGROUND: Low skeletal muscle mass (LSMM) and visceral fat areas can be assessed by cross-sectional images. These parameters are associated with several clinically relevant factors in various disorders with predictive and prognostic implications. Our aim was to establish the effect of computed tomography (CT)-defined LSMM and fat areas	Osservazione di una associazione fra ridotta massa muscolare/elevata massa adiposa viscerale, stimate tramite tomografia computerizzata, e outcome dell'infezione da SARS-CoV-2 : la possibilità di prédire quali pazienti avranno un outcome peggiore è molto utile per una allocazione razionale delle risorse.

unfavourable outcomes and in-hospital mortality in coronavirus disease 2019. J Cachexia Sarcopenia Muscle https://doi.org/10.1002/jcsm.12868	on unfavourable outcomes and in-hospital mortality in coronavirus disease 2019 (COVID-19) patients based on a large patient sample. METHODS: MEDLINE library, Cochrane, and Scopus databases were screened for the associations between CT-defined LSMM as well as fat areas and in-hospital mortality in COVID-19 patients up to September 2021. In total, six studies were suitable for the analysis and included into the present analysis. RESULTS: The included studies comprised 1059 patients, 591 men (55.8%) and 468 women (44.2%), with a mean age of 60.1 years ranging from 48 to 66 years. The pooled prevalence of LSMM was 33.6%. The pooled odds ratio for the effect of LSMM on in-hospital mortality in univariate analysis was 5.84 [95% confidence interval (CI) 1.07-31.83]. It was 2.73 (95% CI 0.54-13.70) in multivariate analysis. The pooled odds ratio of high visceral fat area on unfavourable outcome in univariate analysis was 2.65 (95% CI 1.57-4.47). CONCLUSIONS: Computed tomography-defined LSMM and high visceral fat area have a relevant association with in-hospital mortality in COVID-19 patients and should be included as relevant prognostic biomarkers into clinical routine.	
Jayk Bernal A et al Molnupiravir for Oral Treatment of Covid-19 in Nonhospitalized Patients	BACKGROUND New treatments are needed to reduce the risk of progression of coronavirus disease 2019 (Covid-19). Molnupiravir is an oral, small-molecule antiviral prodrug that is active against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).	Trial clinico di fase 3 su 1433 pazienti con infezione da SARS-CoV-2, non ospedalizzati ma sintomatici, trattati con l'antivirale molnupiravir contro placebo per 5 giorni, iniziando il trattamento entro 5 giorni dall'esordio dei sintomi : si osserva una riduzione del rischio di ospedalizzazione. Esclusi i vaccinati e le persone con storia di infezione pregressa da SARS-CoV-2. Pur tenendo conto del

NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2116044?query=featured_coronavirus	METHODS We conducted a phase 3, double-blind, randomized, placebo-controlled trial to evaluate the efficacy and safety of treatment with molnupiravir started within 5 days after the onset of signs or symptoms in nonhospitalized, unvaccinated adults with mild-to-moderate, laboratory-confirmed Covid-19 and at least one risk factor for severe Covid-19 illness. Participants in the trial were randomly assigned to receive 800 mg of molnupiravir or placebo twice daily for 5 days. The primary efficacy end point was the incidence hospitalization or death at day 29; the incidence of adverse events was the primary safety end point. A planned interim analysis was performed when 50% of 1550 participants (target enrollment) had been followed through day 29. RESULTS A total of 1433 participants underwent randomization; 716 were assigned to receive molnupiravir and 717 to receive placebo. With the exception of an imbalance in sex, baseline characteristics were similar in the two groups. The superiority of molnupiravir was demonstrated at the interim analysis; the risk of hospitalization for any cause or death through day 29 was lower with molnupiravir (28 of 385 participants [7.3%]) than with placebo (53 of 377 [14.1%]) (difference, −6.8 percentage points; 95% confidence interval, −11.3 to −2.4; P=0.001). In the analysis of all participants who had undergone randomization, the percentage of participants who were hospitalized or died	fatto che si tratti di uno studio condotto sui non vaccinati, ridurre l'ospedalizzazione significa ridurre la pressione sui sistemi sanitari, il che rende i trattamenti domiciliari come molnupiravir molto promettenti.

	through day 29 was lower in the molnupiravir group than in the placebo group (6.8% [48 of 709] vs. 9.7% [68 of 699]; difference, −3.0 percentage points; 95% confidence interval, −5.9 to −0.1). Results of subgroup analyses were largely consistent with these overall results; in some subgroups, such as patients with evidence of previous SARS-CoV-2 infection, those with low baseline viral load, and those with diabetes, the point estimate for the difference favored placebo. One death was reported in the molnupiravir group and 9 were reported in the placebo group through day 29. Adverse events were reported in 216 of 710 participants (30.4%) in the molnupiravir group and 231 of 701 (33.0%) in the placebo group. CONCLUSIONS Early treatment with molnupiravir reduced the risk of hospitalization or death in at-risk, unvaccinated adults with Covid-19.	
Gottlieb RL et al Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients NEJM	BACKGROUND Remdesivir improves clinical outcomes in patients hospitalized with moderate-to-severe coronavirus disease 2019 (Covid-19). Whether the use of remdesivir in symptomatic, nonhospitalized patients with Covid-19 who are at high risk for disease progression prevents hospitalization is uncertain. METHODS We conducted a randomized, double-blind, placebo-controlled trial involving nonhospitalized patients with	Trial clinico su 562 pazienti con infezione da SARS-CoV-2, sintomatici e non ospedalizzati ma con almeno un fattore di rischio di progressione a malattia grave, randomizzati a ricevere o placebo o l'antivirale Remdesivir per 3 giorni, entro 7 giorni dall'esordio dei sintomi : riduzione dell'87% del rischio di ospedalizzazione nel gruppo trattato con 3 dosi di farmaco. Esclusi i pazienti vaccinati o con storia di precedente infezione da SARS-CoV-2, per cui la popolazione studiata riflette solo parzialmente le caratteristiche dei pazienti di oggi.

https://www.nejm.org/doi/full/10.1056/NEJMoa2116846?query=featured_coronavirus	Covid-19 who had symptom onset within the previous 7 days and who had at least one risk factor for disease progression (age ≥60 years, obesity, or certain coexisting medical conditions). Patients were randomly assigned to receive intravenous remdesivir (200 mg on day 1 and 100 mg on days 2 and 3) or placebo. The primary efficacy end point was a composite of Covid-19–related hospitalization or death from any cause by day 28. The primary safety end point was any adverse event. A secondary end point was a composite of a Covid-19–related medically attended visit or death from any cause by day 28. RESULTS A total of 562 patients who underwent randomization and received at least one dose of remdesivir or placebo were included in the analyses: 279 patients in the remdesivir group and 283 in the placebo group. The mean age was 50 years, 47.9% of the patients were women, and 41.8% were Hispanic or Latinx. The most common coexisting conditions were diabetes mellitus (61.6%), obesity (55.2%), and hypertension (47.7%). Covid-19–related hospitalization or death from any cause occurred in 2 patients (0.7%) in the remdesivir group and in 15 (5.3%) in the placebo group (hazard ratio, 0.13; 95% confidence interval [CI], 0.03 to 0.59; P=0.008). A total of 4 of 246 patients (1.6%) in the remdesivir group and 21 of 252 (8.3%) in the placebo group had a Covid-19–related medically attended visit by day 28 (hazard ratio, 0.19; 95% CI, 0.07 to 0.56). No patients had	

	died by day 28. Adverse events occurred in 42.3% of the patients in the remdesivir group and in 46.3% of those in the placebo group. CONCLUSIONS Among nonhospitalized patients who were at high risk for Covid-19 progression, a 3-day course of remdesivir had an acceptable safety profile and resulted in an 87% lower risk of hospitalization or death than placebo.	

COVID- 19 REPORT (SETTIMANA DAL 17 AL 23 GENNAIO 2022)

SANITA' PUBBLICA, EPIDEMIOLOGIA, EPIDEMIOLOGIA BIOMOLECOLARE ESTENSORI : DOTT. SSA PAOLA DEL GIACOMO- DOTT. FRANCESCO V. SEGALA		
ARTICOLO	ABSTRACT	CONTENUTO
Dr. Francis Collins NIH.gov Latest on Omicron Variant and COVID-19 Vaccine Protection. https://directorsblog.nih.gov/2021/12/14/the-latest-on-the-	Not available	Risultati preliminari sembrano documentare un calo significativo degli anticorpi neutralizzanti contro questa variante nelle persone che hanno ricevuto un ciclo di due dosi di vaccino mRNA. Tuttavia, i risultati iniziali degli studi condotti sia in laboratorio che nel mondo reale mostrano che le persone che ricevono una dose booster, possono essere meglio protette. Sebbene questi dati siano preliminari, suggeriscono che la dose di richiamo aiuterà a proteggere le persone già vaccinate da possibili infezioni gravi da Omicron durante i mesi invernali.

omicron-variant-and-vaccine-protection/		Vale anche la pena notare che la variante Omicron per lo più non ha mutazioni in porzioni del suo genoma che sono target di altri componenti dell'immunità indotta dal vaccino, comprese le cellule T. Queste cellule fanno parte della seconda linea di difesa del nostro organismo e sono generalmente più difficili da evitare per i virus. Sebbene le cellule T non possano prevenire l'infezione, aiutano a proteggere dalla malattia più grave.
Abdullah F., et al. Int J Infect Dis Decreased severity of disease during the first global omicron variant covid-19 outbreak in a large hospital in Tshwane, South Africa. https://www.ijidonline.com/action/showPdf?pii=S1201-9712%2821%2901256-X	Introduction: The coronavirus disease 2019 (COVID-19) first reported in Wuhan China in December 2019 is a global pandemic that is threatening the health and wellbeing of people worldwide. To date there have been more than 274 million reported cases and 5.3 million deaths. The Omicron variant first documented in the City of Tshwane, Gauteng Province, South Africa on 9 November 2021 led to exponential increases in cases and a sharp rise in hospital admissions. The clinical profile of patients admitted at a large hospital in Tshwane is compared with previous waves. Methods: The methods should describe what study design you employed for the study and what your sample size was, as it is this is mainly results. 466 hospital COVID-19 admissions since 14 November 2021 were compared to 3976 prior admissions since 4 May 2020. Ninety-eight patient records at peak bed occupancy during the outbreak were reviewed for primary indication for admission, clinical severity,	Dai dati emersi in questo studio condotto in una città del Sud Africa la polmonite COVID-19 causata dalla variante Omicron sarebbe presente solo in circa un terzo dei pazienti ricoverati e in oltre il 70% di questi pazienti sarebbe di grado lieve-moderato. La mortalità confrontata con l'ondata precedente (prevalentemente causata dalla variante Delta) sarebbe del 4.5% vs. 21.3%.

	oxygen supplementation level, vaccination and prior COVID-19 infection. Provincial and city-wide daily cases and reported deaths hospitalizations and excess deaths data were sourced from the NICD, the National Department of Health and the South African Medical Research Council. Results: Deaths and ICU admissions were 4.5% vs 21.3% ($p<0.00001$), and 1% vs 4.3% ($p<0.00001$); length of stay was 4.0 days vs 8.8 days; and mean age was 39 years vs 49 years for the Omicron and previous waves respectively. Admissions peaked and declined rapidly with peak bed occupancy at 51% of highest previous peak. Sixty two (63%) patients in COVID-19 wards had incidental COVID-19 following a positive SARS-CoV-2 PCR test . Only one third (36) had COVID-19 pneumonia, of which 72% had mild to moderate disease. The remaining 38% required high care or ICU admission. Fewer than half (45%) of patients in COVID-19 wards compared to 99.5% in the first wave required oxygen supplementation. City and provincial rates show decoupling of cases, hospitalisations and deaths compared to previous waves, corroborating the clinical findings of milder omicron disease in the hospital.	

	Conclusion: There was decreased severity of disease in the Omicron driven fourth wave in the City of Tshwane, its first global epicentre.	
European Centre for Disease Prevention and Control Guidance on quarantine of close contacts to COVID-19 cases and isolation of COVID-19 cases, in the current epidemiological situation, 7 January 2022. https://www.ecdc.europa.eu/en/covid-19/prevention-and-control/quarantine-and-isolation	Not available	Queste sono le nuove indicazioni dell'ECDC riguardo la gestione dei contatti stretti di casi di COVID-19. Tali indicazioni tengono conto della possibile presenza di contesti con pressione sul sistema sanitario più elevata o addirittura « estrema«. In risposta a esigenze legate ad una maggiore pressione sui sistemi sanitari la quarantena per i soggetti vaccinati è stata molto ridimensionata sia in termini di durata che di misure.
Eyre, D. W., et al. NEJM Effect of Covid-19 Vaccination on Transmission of Alpha and Delta Variants.	BACKGROUND Before the emergence of the B.1.617.2 (delta) variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), vaccination reduced transmission of SARS-CoV-2 from vaccinated persons who became infected, potentially by reducing viral loads. Although vaccination still lowers the risk of infection, similar viral loads in vaccinated and unvaccinated persons who are infected with the delta variant call into question the degree to which vaccination prevents transmission. METHODS We	Studio osservazionale su contatti di casi accertati di COVID che valuta gli effetti dei vaccini Pfizer ed AstraZeneca sulla trasmissione della variante alpha e Delta di SARS-CoV-2. I contatti stretti di casi di COVID-19 che avevano ricevuto il vaccino BNT162b2 avevano un rischio inferiore di risultare positivi durante le 14 settimane dopo la seconda vaccinazione rispetto a coloro che avevano ricevuto ChAdOx1 nCoV-19, anche se l'effetto protettivo di BNT162b2 svaniva più rapidamente.

https://www.nejm.org/doi/pdf/10.1056/NEJMoa2116597?articleTools=true	used contact-testing data from England to perform a retrospective observational cohort study involving adult contacts of SARS-CoV-2–infected adult index patients. We used multivariable Poisson regression to investigate associations between transmission and the vaccination status of index patients and contacts and to determine how these associations varied with the B.1.1.7 (alpha) and delta variants and time since the second vaccination. RESULTS Among 146,243 tested contacts of 108,498 index patients, 54,667 (37%) had positive SARS-CoV-2 polymerase-chain-reaction (PCR) tests. In index patients who became infected with the alpha variant, two vaccinations with either BNT162b2 or ChAdOx1 nCoV-19 (also known as AZD1222), as compared with no vaccination, were independently associated with reduced PCR positivity in contacts (adjusted rate ratio with BNT162b2, 0.32; 95% confidence interval [CI], 0.21 to 0.48; and with ChAdOx1 nCoV-19, 0.48; 95% CI, 0.30 to 0.78). Vaccine-associated reductions in transmission of the delta variant were smaller than those with the alpha variant, and reductions in transmission of the delta variant after two BNT162b2 vaccinations were greater (adjusted rate ratio for the comparison with no vaccination, 0.50; 95% CI, 0.39 to 0.65) than after two ChAdOx1 nCoV-19 vaccinations (adjusted rate ratio,	

	0.76; 95% CI, 0.70 to 0.82). Variation in cycle-threshold (Ct) values (indicative of viral load) in index patients explained 7 to 23% of vaccine-associated reductions in transmission of the two variants. The reductions in transmission of the delta variant declined over time after the second vaccination, reaching levels that were similar to those in unvaccinated persons by 12 weeks in index patients who had received ChAdOx1 nCoV-19 and attenuating substantially in those who had received BNT162b2. Protection in contacts also declined in the 3-month period after the second vaccination. CONCLUSIONS Vaccination was associated with a smaller reduction in transmission of the delta variant than of the alpha variant, and the effects of vaccination decreased over time. PCR Ct values at diagnosis of the index patient only partially explained decreased transmission.	