# REPORT COVID-19 (SETTIMANA 21-27 MARZO 2022)

## VIROLOGIA E DIAGNOSTICA

## ESTENSORE : DOTT. FRANCESCO TACCARI

| ARTICOLO | ABSTRACT | CONTENUTO E COMMENTO |
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| Torres M.D.T. et al.<br><br>Pre-proof (iScience)<br><br>Detection of SARS-CoV-2 with RAPID: a prospective cohort study.<br><br>https://reader.elsevier.com/reader/sd/pii/S2589004222003 25X?token=89D15D96341E8B04103A57B75117FB8A7FAB3C4FFB3103CFD0A7638306CA7EBD6E3FE22E59F19139D27490FD | Abstract<br><br>COVID-19 has killed over 5 million people worldwide. Currently available methods to detect SARS-CoV-2 are limited by their cost and need for multistep sample preparation and trained personnel. Therefore, there is an urgent need to develop fast, inexpensive, and scalable point-of-care diagnostics that can be used for mass testing. Between January and March 2021, we obtained 321 anterior nare swab samples from individuals in Philadelphia (PA, USA). For the Real-time Accurate Portable Impedimetric Detection prototype 1.0 (RAPID) test, anterior nare samples were tested via an electrochemical impedance spectroscopy (EIS) approach. The overall sensitivity, specificity, and accuracy of RAPID in this cohort study were 80.6%, 89.0% and 88.2%, respectively. We present a rapid, accurate, inexpensive (< $5.00 per unit), and scalable test for | Studio prospettico che mira a valutare le performance diagnostiche di uno strumento chiamato RAPID (Real-time Accurate Portable Impedimetric Detection prototype 1.0) che sfrutta il principio della spettroscopia di impedenza elettrochimica : RAPID è un biosensore elettrochimico che si attiva quando la proteina spike del virus SARS-CoV-2 si lega ad un elettrodo funzionalizzato con il recettore ACE2 umano. Sono stati analazzati con questo strumento 321 campioni ottenuti tamponando le fosse nasali anteriori, ottenendo una sensibilità dell'80.6%, una specificità dell'89.0% e un'accuratezza dell'88.2%. Tale metodica è estremamente economica (circa 7-10 volte meno costosa del gold standard diagnostico RT-PCR) e rapida (circa 4 minuti contro una media di 45 minuti per la RT-PCR), oltre che « point-of-care ».<br>Tale metodica che, a giudicare dai risultati di tale studio, sembra essere anche piuttosto accurata, potrebbe essere |

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| BC61463B&originRegion=eu-west-1&originCreation=20220315141700 | diagnosing COVID-19 at the point-of-care. We anticipate that further iterations of this approach will enable widespread deployment, large-scale testing, and population-level surveillance. | non solo un valido strumento da impiegare su larga scala per la rilevazione del virus SARS-CoV-2 ma potrebbe essere anche utilizzato, modificando la funzionalità degli elettrodi, per la diagnostica di altre infezioni virali, batteriche e fungine. |
| Rabalski L et al.<br><br>Clin Microbiol Infect.<br><br>Zoonotic spill-over of SARS-CoV-2: mink-adapted virus in humans.<br><br>https://www.clinicalmicrobiologyandinfection.com/action/showPdf?pii=S1198-743X%2821%2900698-4 | Abstract<br><br>Objectives: This work aimed to analyse possible zoonotic spill-over of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). We report the spill-over of mink-adapted SARS-CoV-2 from farmed mink to humans after adaptation that lasted at least 3 months.<br>Methods: Next-generation sequencing and a bioinformatic approach were applied to analyse the data.<br>Results: In an isolate obtained from an asymptomatic patient testing positive for SARS-CoV-2, we found four distinguishing mutations in the S gene that gave rise to the mink-adapted variant (G75V, M177T, Y453F, and C1247F) and others.<br>Conclusions: Zoonotic spill-over of SARS-CoV-2 can occur from mink to human. | In questo studio viene riportato un possibile spill-over del virus SARS-CoV-2 da un animale all'uomo: in particolare si tratterebbe di un ceppo virale del visone che sarebbe diventato in grado di infettare l'uomo dopo circa 3 mesi di adattamento. Per l'analisi dei dati sono state utilizzate le tecnologie del sequenziamento di ultima generazione e della bioinformatica. In un soggetto umano asintomatico è stato riscontrato un ceppo del virus che, in base all'analisi filogenetica, presenta altissima analogia con il ceppo isolato nel visone, contenente tuttavia alcune mutazione che hanno reso possibile l'adattamento in una specie differente. L'esatto ruolo delle mutazioni riscontrate nel nuovo ceppo virale non è chiaro, ma probabilmente sono funzionali ad aumentare la « fitness » virale nel nuovo ospite. Questo lavoro rappresenta una ulteriore prova a sostegno della teoria dello spill-over del virus SARS-CoV-2 da diverse specie animali all'uomo. |
| Markov PV et al.<br><br>Nat Rev Microbiol.<br><br>Antigenic evolution will lead to new SARS-CoV-2 variants with unpredictable severity. | Abstract<br><br>The comparatively milder infections with the Omicron variant and higher levels of population immunity have raised hopes for a weakening of the pandemic. We argue that the lower severity of Omicron is a coincidence and that ongoing rapid antigenic evolution is likely to produce new variants that may escape immunity and be more severe. | In questo articolo della sezione « comment » della prestigiosa rivista « Nature Reviews Microbiology » viene analizzata la relazione fra l'evoluzione antigenica del virus SARS-CoV-2 e la potenziale formazione di nuovi varianti virali in grado di generare sindromi di severità clinica imprevedibile. Secondo gli autori il concetto secondo cui l'evoluzione dei virus tenderebbe a produrre ceppi sempre meno virulenti al fine di poter aumentare la sua |

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| https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8919145/pdf/41579_2022_Article_722.pdf | | trasmissibilità non ha fondamento : la relativa bassa virulenza della più recente « variant-of-concern » Omicron sarebbe solamente una coincidenza. La virulenza sarebbe infatti del tutto indipendente dalla trasmissibilità del virus e pertanto potrebbero generarsi varianti virali non solo più trasmissibili ma contemporaneamente anche più aggressive. Un altro concetto da accantonare secondo gli autori sarebbe quello per cui la diffusione dell'immunità vaccinale o post-infezione garantirebbe in caso di reinfezione delle forme cliniche meno severe : l'evoluzione antigenica del virus potrebbe rendere infatti le nuove varianti in grado di evadere completamente la risposta immunitaria, dando luogo quindi a forme cliniche di invariata o superiore severità.<br>Le conoscenze dell'evoluzione antigenica dei virus sono ancora estremamente limitate e pertanto risulta estremamente difficile predire efficacemente quali nuove varianti potranno generarsi nel prossimo futuro e quali caratteristiche potranno avere. Dovrebbe essere attivamente promossa un'attenta e costante analisi dei meccanismi dell'evoluzione antigenica, specialmente in popolazioni bersaglio dove tale processo è massimizzato come gli immunodepressi o specie animali « permissive » in stretto contatto con l'uomo. |
| Kolodziej LM et al.<br><br>J Hosp Infect.<br><br>SARS-CoV-2 transmission risk upon return to work in RNA- | Abstract<br><br>Background: Healthcare workers (HCWs) are at risk for coronavirus disease 2019 (COVID-19) and for spreading Severe Acute Respiratory Syndrome Virus 2 (SARS-CoV-2) amongst colleagues and patients.<br>Aim: We aimed to study presence of SARS-CoV-2 RNA and possible onward transmission by HCWs upon return to work | In questo studio prospettico osservazionale viene valutata la capacità di trasmissione del virus SARS-CoV-2 di operatori sanitari che rientrano a lavoro dopo l'infezione da SARS-CoV-2. Sono stati arruolati operatori sanitari non vaccinati per SARS-CoV-2 (da maggio a settembre 2020) con un tampone nasofaringeo molecolare positivo. Al rientro a lavoro (dopo almeno 24 ore dalla risoluzione dei sintomi respiratori, in accordo con le procedure interne dell'ospedale di |

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| positive healthcare workers.<br><br>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8916832/pdf/main.pdf | after COVID-19, and association with disease severity and development of antibodies over time.<br>Methods: Unvaccinated HCWs with positive SARS-CoV-2 RT-PCR were prospectively recruited. Data on symptoms was collected via telephone questionnaires on day 2, 7, 14 and 21 after positive test. Upon return to work, repeat SARS-CoV-2 RT-PCR was performed and serum was collected. Repeat sera were collected at week 4, 8, 12 and 16 to determine antibody dynamics over time. Phylogenetic analysis was conducted to investigate possible transmission events originating from HCW with a positive repeat RT-PCR.<br>Findings: Sixty-one (84.7%) participants with mild-moderate COVID-19 had a repeat SARS-CoV-2 PCR performed upon return to work (median 13 days post symptom onset), of which 30 (49.1%) were positive with a median cycle threshold (Ct) value of 29.2 (IQR 3.0). All HCWs developed antibodies against SARS-CoV-2. No significant differences in symptomatology and presence of antibodies were found between repeat RT-PCR-positive and -negative HCWs. Eleven direct colleagues of six participants with a repeat RT-PCR Ct-value <30 tested positive after the HCW returned to work. Phylogenetic and epidemiologic analysis did not indicate onward transmission through HCW who were SARS-CoV-2 RNA positive upon return to work.<br>Conclusions: HCWs regularly return to work with sub stantial SARS-CoV-2 RNA loads. However, we found no evidence for subsequent in-hospital transmission. | riferimento) è stato ripetuto il tampone nasofaringeo molecolare per SARS-CoV-2. Per gli operatori sanitari risultati positivi al tampone nasofaringeo di controllo sono state effettuate analisi filogenetiche per valutare possibili trasmissioni sul posto di lavoro. Sessantuno (84.7%) partecipanti hanno avuto un tampone di controllo positivo (mediana 13 giorni dall'esordio dei sintomi), il 49.1% dei quali con una mediana di cicli soglia di 29.2. Undici colleghi diretti di sei partecipanti con tampone positivo al rientro con cicli soglia <30 sono risultati positivi; tuttavia le analisi epidemiologiche e filogenetiche non hanno mostrato alcuna trasmissione legata al partecipante indice.<br>Stabilire la contagiosità di un soggetto con recente infezione da SARS-CoV-2 è una questione di fondamentale importanza e numerosi studi hanno dimostrato la scarsa capacità del tampone molecolare nel decretare la fine del periodo di contagiosità. L'approccio basato sulla assenza di sintomatologia per stabilire il rientro a lavoro degli operatori sanitari proposto dagli autori dello studio dovrebbe tuttavia essere integrato con un test di laboratorio, come ad esempio il tampone antigenico che sembrerebbe più accurato del tampone molecolare nello stabilire il periodo di infettività. |

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| VACCINI<br>COMMENTO : DOTT. PIERLUIGI DEL VECCHIO E DOTT.SSA GIULIA MICHELI | | |
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| **ARTICOLO** | **ABSTRACT** | **CONTENUTO E COMMENTO** |
| Regev-Yochay G. et al.<br>The NEJM<br>Efficacy of a Fourth Dose of Covid-19 mRNA Vaccine against Omicron<br>https://www.nejm.org/doi/pdf/10.1056/NEJMc2202542 | Non disponibile | COMMENTO : Studio clinico non randomizzato open-label condotto con lo scopo di valutare l'immunogenicità e la sicurezza di una quarta dose di vaccino per Sars-CoV2 a mRNA (BNT162b2 e mRNA-1273) somministrata a 4 mesi dalla terza dose di vaccino (nell'ambito di un protocollo a tre dosi di BNT162b2). Dei 1050 operatori sanitari arruolati nel protocollo Sheba, 155 hanno ricevuto la quarta dose di vaccino Pfizer e, una settimana dopo, 120 persone hanno ricevuto invece mRNA-1273. Dopo la quarta dose in entrambi i gruppi è stato riscontrato un aumento degli anticorpi IgG contro il RBD di Sars-Cov2 e del titolo di anticorpi neutralizzanti. Tale crescita è risultata essere maggiore rispetto al valore di partenza di un fattore 9-10, maggiore anche a quella riscontrata dopo la terza dose, in assenza di particolari differenze tra i due composti utilizzati. |

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| | | In entrambi i gruppi inoltre è stata riscontrata una maggiore risposta in vivo alla variante omicron, attualmente predominante. Non sono stati riscontrati particolari eventi avversi nel corso del follow-up, se non reazioni sistemiche moderate o lievi del sito di iniezione. Nel gruppo di controllo il 25% dei partecipanti si è infettato con la variante omicron vs. il 18.3% del gruppo ricevente la quarta dose. Questi ultimi in ogni caso hanno presentato sintomi trascurabili anche se tutti in corso di infezione sono stati probabilmente infettivi, con una carica virale relativamente alta riscontrata. Le limitazioni dello studio riguardano in particolare la non randomizzazione, la differenza di una settimana nell'arruolamento dei due gruppi di intervento e il campione ridotto. |
| Wieske L. et al.<br><br>The Lancet<br><br>Humoral responses after second and third SARS-CoV-2 vaccination in patients with immune-mediated inflammatory disorders on immunosuppressants: a cohort study | Background Disease-specific studies have reported impaired humoral responses after SARS-CoV-2 vaccination in patients with immune-mediated inflammatory disorders treated with specific immunosuppressants. Disease- overarching studies, and data on recall responses and third vaccinations are scarce. Our primary objective was to investigate the effects of immunosuppressive monotherapies on the humoral immune response after SARS-CoV-2 vaccination in patients with prevalent immune-mediated inflammatory disorders.<br>Methods We did a cohort study in participants treated in outpatient clinics in seven university hospitals and one rheumatology treatment centre in the Netherlands as well as participants included in two national cohort studies on | CONTENUTO: Studio di coorte che investiga l'effetto di una terapia immunosoppressiva (monoterapia o combinata) sulla risposta immunitaria umorale al vaccino per Sars-Cov2, in pazienti con disordine infiammatorio immuno-mediato. Sono stati inclusi nello studio partecipanti di età maggiore di 18 anni, con malattie infiammatorie immuno-mediate (AR, vasculiti, LES, morbo di Crohn, SM, miastenia gravis, dermatite atopica…) vaccinati per Sars-CoV2 e non (controlli, insieme a partecipanti sani). La risposta anticorpale (IgG anti-RBD) è stata misurata dopo due dosi di vaccino, e in un sottogruppo anche dopo tre dosi (febbraio-agosto 2021). Il siero di 2339 partecipanti (1869 senza pregressa infezione e 470 con pregressa infezione) è stato analizzato. Non sono |

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| https://www.thelancet.com/action/showPdf?pii=S2665-9913%2822%2900034-0 | COVID-19-related disease severity. We included patients aged older than 18 years, diagnosed with any of the prespecified immune-mediated inflammatory disorders, who were able to understand and complete questionnaires in Dutch. Participants with immune-mediated inflammatory disorders who were not on systemic immunosuppressants and healthy participants were included as controls. Anti-receptor binding domain IgG responses and neutralisation capacity were monitored following standard vaccination regimens and a three-vaccination regimen in subgroups. Hybrid immune responsesie, vaccination after previous SARS-CoV-2 infection were studied as a proxy for recall responses.<br>Findings Between Feb 2 and Aug 1, 2021, we included 3222 participants in our cohort. Sera from 2339 participants, 1869 without and 470 participants with previous SARS-CoV-2 infection were analysed (mean age 49·9 years [SD 13·7]; 1470 [62·8%] females and 869 [37·2%] males). Humoral responses did not differ between disorders. Anti-CD20 therapy, sphingosine 1-phosphate receptor (S1P) modulators, and mycophenolate mofetil combined with corticosteroids were associated with lower relative risks for reaching seroconversion following standard vaccination (0·32 [95% CI 0·19–0·49] for anti-CD20 therapy, 0·35 [0·21–0·55] for S1P modulators, and 0·61 [0·40–0·90] for mycophenolate mofetil combined with corticosteroids). A third vaccination increased seroconversion for mycophenolate mofetil combination treatments (from | state riscontrate differenze nella risposta umorale tra le varie patologie considerate. Le terapie con anti-CD20, modulatori di S1P e micofenolato mofetile combinati con corticosteroidi sono state associate con un minor rischio relativo di raggiungere la sieroconversione rispetto alla monoterapia immunosoppressiva. La dose booster ha portato ad un incremento della sieroconversione nel gruppo in terapia di combinazione con micofenolato, ma non in maniera significativa negli altri gruppi considerati. Nei soggetti con storia di pregressa infezione da Sars-cov2 invece il vaccino ha funzionato come booster della risposta anticorpale, indipendentemente dalla terapia assunta. In conclusione, lo studio mostra un'utilità della dose booster in pazienti con malattia infiammatoria immuno-mediata in terapia con micofenolato e in ogni caso i dati suggeriscono che nonostante la riduzione del titolo anticorpale nei pazienti in terapia immmunosoppressiva, questo non si traduce nella perdita di protezione nei confronti dell'infezione, almeno non a breve distanza di tempo dalla somministrazione. |

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| | 52·6% after the second vaccination to 89·5% after the third) but not significantly for anti-CD20 therapies (from 36·8% to 45·6%) and S1P modulators (from 35·5% to 48·4%). Most other immunosuppressant groups showed moderately reduced antibody titres after standard vaccination that did not increase after a third vaccination, although seroconversion rates and neutralisation capacity were unaffected. In participants with previous SARS-CoV-2 infection, SARS-CoV-2 antibodies were boosted after vaccination, regardless of immunosuppressive treatment.<br>Interpretation Humoral responses following vaccination are impaired by specific immunosuppressants. After standard vaccination regimens, patients with immune-mediated inflammatory disorders taking most immunosuppressants show similar seroconversion to controls, although antibody titres might be moderately reduced. As neutralisation capacity and recall responses are also preserved in these patients, this is not likely to translate to loss of (short-term) protection. In patients on immunosuppressants showing poor humoral responses after standard vaccination regimens, a third vaccination resulted in additional seroconversion in patients taking mycophenolate mofetil combination treatments, whereas the effect of a third vaccination in patients on anti-CD20 therapy and S1P modulators was limited. | |

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| Masset, Christophe et al.<br><br>Kidney International, Volume 101, Issue 4, 825 - 826<br><br>A fourth SARS-CoV-2 mRNA vaccine in strictly seronegative kidney transplant recipients<br><br>https://www.kidney-international.org/article/S0085-2538(22)00093-X/fulltext | Non disponibile | COMMENTO : lettera all'editore di due centri universitari francesi sull'esperienza sulla quarta dose booster di vaccino a mRNA in pazienti sottoposti a trapianto renali e seronegativi ad un mese dalla terza dose. Di 49 non responder, il 42,8% ha seroconvertito, ma solo 4 di loro hanno ottenuto una risposta considerabile come neutralizzante. Non si sono dimostrate differenze statisticamente significative, ma il gruppo con risposta umorale dopo la quarta dose era caratterizzato da minor uso di steroidi (47% vs 64%), minor linfopenia (63% vs 75%), maggior impiego di BNT162b (86% vs 68%) e un maggior intervallo tra una dose e l'altra (93 vs 82 giorni). Una storia di rigetto acuto provato da biopsia sembra piu' frequente nel gruppo sieronegativo, la cui significativita' clinica e' piuttosto difficile da stimare (episodi che risalgono a piu' di 5 anni prima).<br><br>La risposta si e' mostrata pertanto globalmente piuttosto debole. |

# REPORT COVID-19 (SETTIMANA 21-27 MARZO 2022)

## 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 |
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| Duvignaud A et al<br><br>CMI<br><br>Inhaled ciclesonide for outpatient treatment of COVID-19 in adults at risk of adverse outcomes: a randomised controlled trial (COVERAGE)<br><br>https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(22)00108-2/fulltext | Objectives: To assess the efficacy of inhaled ciclesonide in reducing the risk of adverse outcomes in COVID-19 outpatients at risk of developing severe illness.<br><br>Methods: COVERAGE is an open-label, randomised controlled trial. Outpatients with documented COVID-19, risk factors for aggravation, symptoms <7 days and absence of criteria for hospitalisation are randomly allocated to either a control arm or one of several experimental arms, including inhaled ciclesonide. The primary efficacy endpoint is COVID-19 worsening (hospitalisation, oxygen therapy at home, or death) by Day 14. Other endpoints are adverse events, maximal follow-up score on the WHO OSCI, sustained alleviation of symptoms, cure, and RT-PCR and blood parameter evolution at Day 7. The trial's Safety Monitoring Board reviewed the first interim analysis of the ciclesonide arm and recommended halting it for futility. The | Trial clinico randomizzato open-label su 217 pazienti con COVID-19 non ospedalizzati, trattati con ciclesonide (steroide) per via inalatoria con endpoint primario il peggioramento clinico entro il giorno 14 dalla diagnosi. Si conclude per una insufficiente evidenza di beneficio degli steroidi inalatori in COVID-19. |

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| | results of this analysis are reported here.<br><br>Results: The analysis involved 217 participants (control 107, ciclesonide 110), including 111 women and 106 men. Their median age was 63 years [Interquartile range (IQR) 59-68]. 157/217 (72.4%) had at least one comorbidity. The median time since first symptom was 4 days [IQR 3-5]. During the 28-day follow-up, 2 participants died (control 2/107 [1.9%], ciclesonide 0), 4 received oxygen therapy at home and were not hospitalized (control 2/107 [1.9%], ciclesonide 2/110 [1.8%]) and 24 were hospitalised (control 10/107 [9.3%], ciclesonide 14/110 [12.7%]). In intent-to-treat analysis of observed data, 26 participants reached the composite primary endpoint by Day14, including 12/106 (11. 3%, 95% CI 6.0 to 18.9%) in the control arm and 14/106 (13.2%; 95% CI 7.4 to 21.2%) in the ciclesonide arm. Secondary outcomes were similar for both arms.<br><br>Conclusions: Our findings are consistent with the European Medicines Agency's COVID-19 taskforce statement that there is currently insufficient evidence that inhaled corticosteroids are beneficial for people with COVID-19. | |
| Li C et al<br><br>CID<br><br>Severe acute respiratory syndrome | Background:<br>The role of SARS-CoV-2 in the pathogenesis of testicular damage is uncertain.<br><br>Methods: We investigated the virological, pathological, and | Studio di fisiopatologia in cui si valuta l'effetto di SARS-CoV-2 sul testicolo del criceto, in considerazione della rilevanza di questa eventuale localizzazione dell'infezione umana : si osserva un danno testicolare con flogosi, emorragia, necrosi, degenerazione dei tubuli seminiferi e alterata spermatogenesi dopo infezione dell'animale per via endonasale. In cronico si osservano nell'animale vari gradi di |

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| coronavirus 2 (SARS-CoV-2) infections by intranasal or testicular inoculation induces testicular damage preventable by vaccination in golden Syrian hamsters<br><br>https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac142/6530400 | immunological changes in testes of hamsters challenged by SARS-CoV-2 wild-type and its variants by intranasal or direct testicular inoculation using influenza virus A(H1N1)pdm09 as control.<br><br>Results: Besides self-limiting respiratory tract infection, intranasal SARS-CoV-2 challenge caused acute decrease in sperm count, and serum testosterone and inhibin B at 4 to 7 days post-infection (dpi), and subsequently reduced testicular size and weight, and serum sex hormone level at 42 to 120 dpi. Acute histopathological damage with varying degree of testicular inflammation, haemorrhage, and necrosis, degeneration of seminiferous tubules and disruption of orderly spermatogenesis were seen with increasing virus inoculum. Degeneration and necrosis of Sertoli and Leydig cells were found. Though viral loads and SARS-CoV-2 nucleocapid (N) protein expression were markedly lower in testicular than lung tissues, direct intra-testicular injection showed N expressing interstitial cells and epididymal epithelial cells. Control intranasal or intra-testicular challenge by A(H1N1)pdm09 showed no testicular infection or damage. From 7 to 120 dpi, degeneration and apoptosis of seminiferous tubules, immune complex deposition and depletion of spermatogenic cell and spermatozoa persisted. Intranasal challenge with Omicron and Delta variants could also induce similar testicular changes. These testicular damages can be prevented by | atrofia testicolare, il che suggerisce l'importanza di un follow up in ambito riproduttivo dei pazienti con storia di COVID-19, per intercettare possibili conseguenze della malattia sulla fertilità. |

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| | vaccination.<br><br>Conclusions: SARS-CoV-2 can cause acute testicular damage with subsequent chronic asymmetric testicular atrophy and associated hormonal changes despite a self-limiting pneumonia in hamsters. Awareness of possible hypogonadism and subfertility is important in managing convalescent COVID-19 males. | |
| Gatti et al<br><br>CMI<br><br>Clinical outcome in solid organ transplant recipients affected by COVID-19 compared to general population: a systematic review and meta-analysis<br><br>https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(22)00116-1/fulltext | Background : A significant increased risk of complications and mortality in immunocompromised patients affected by COVID-19 has been described. However, the impact of COVID-19 in solid organ transplant (SOT) recipients is an issue still on debate, due to conflicting evidence emerged from different observational studies.<br><br>Objective : We performed a systematic review with meta-analysis to assess the clinical outcome in SOT recipients with COVID-19 compared to general population.<br><br>Data source : PubMed-MEDLINE and Scopus were independently searched until 13 October 2021.<br><br>Study eligibility criteria : Prospective or retrospective observational studies comparing clinical outcome in SOT recipients versus general populations affected by COVID-19. Primary endpoint was 30-day mortality. | Revisione sistematica e metanalisi degli outcome di pazienti con COVID-19 sottoposti a trapianto di organo solido, a confronto con la popolazione generale di trapiantati senza infezione : nessun eccesso di mortalità fra gli infetti, ma aumentato rischio di ricovero in Rianimazione e di insufficienza renale acuta. |

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| | Participants : Patients with confirmed COVID-19.<br><br>Intervention : Solid organ transplant recipients.<br><br>Assessment of risk of bias : Quality of included studies was independently assessed according to ROBINS-I tool for observational studies.<br><br>Methods of data synthesis : Meta-analysis was performed by pooling odds ratio (OR) retrieved from studies providing adjustment for confounders using a random-effect model with inverse variance method. Multiple subgroup and sensitivity analyses were conducted to investigate source of heterogeneity.<br><br>Results : 3,501 articles were screened, and thirty-one observational studies (N=590,375; 5,759 SOT recipients vs. 584,616 general population) were included in the meta-analyses. No difference in 30-day mortality rate was found in primary analysis including studies providing adjustment for confounders (N=17; 3,752 SOT recipients vs. 159,745 general population; OR 1.13, 95%CI 0.94-1.35; I2=33.9%). No evidence of publication bias was reported. Higher risk of ICU admission (OR 1.56, 95%CI 1.03-2.63) and occurrence of acute kidney injury (OR 2.50 95%CI 1.81-3.45) was found in SOT recipients.<br><br>Conclusions : No increased risk in mortality was found in SOT | |

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| | recipients affected by COVID-19 compared to general population when adjusted for demographic and clinical features and COVID-19 severity. | |
| Zazhytska M et al<br><br>Cell<br><br>Non-cell-autonomous disruption of nuclear architecture as a potential cause of COVID-19-induced anosmia<br><br>https://www.cell.com/cell/fulltext/S0092-8674(22)00135-0 | SARS-CoV-2 infects less than 1% of cells in the human body, yet it can cause severe damage in a variety of organs. Thus, deciphering the non-cell-autonomous effects of SARS-CoV-2 infection is imperative for understanding the cellular and molecular disruption it elicits. Neurological and cognitive defects are among the least understood symptoms of COVID-19 patients, with olfactory dysfunction being their most common sensory deficit. Here, we show that both in humans and hamsters, SARS-CoV-2 infection causes widespread downregulation of olfactory receptors (ORs) and of their signaling components. This non-cell-autonomous effect is preceded by a dramatic reorganization of the neuronal nuclear architecture, which results in dissipation of genomic compartments harboring OR genes. Our data provide a potential mechanism by which SARS-CoV-2 infection alters the cellular morphology and the transcriptome of cells it cannot infect, offering insight to its systemic effects in olfaction and beyond. | Il deficit olfattivo legato a COVID-19 è un fenomeno tanto ampiamente riconosciuto quanto incompreso nei suoi meccanismi fisiopatologici : in questo studio si osserva che sia nell'uomo che nel criceto l'infezione da SARS-CoV-2 provoca una down-regolazione dei recettori olfattivi, con riorganizzazione dell'architettura del nucleo cellulare del neurone e la perdita della compartimentazione dei geni che codificano per i recettori stessi. In sintesi, il fenomeno dell'iposmia avrebbe origine da un danno che origina fin dalla trascrizione genica. |
| Corey L et al<br><br>JAMA<br><br>Expanding Efforts and Support to Respond to | Considerable inferential data indicate that immunocompromised persons with persistent COVID-19 infection may be involved in the generation of SARS-CoV-2 variants of concern globally.1-3 The largest immunocompromised population worldwide is people living with HIV. Although tremendous gains have been made in | Interessante discussione sulla importanza del supporto a una risposta alla pandemia di HIV/AIDS, in particolare in termini di inclusione di tutte le persone in un percorso di cura, anche durante la pandemia di COVID-19. |

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| the HIV and COVID-19 Intersecting Pandemics<br><br>https://jamanetwork.com/journals/jama/fullarticle/2790239 | providing access to lifesaving antiretroviral therapy, only approximately 50% of the estimated 37.7 million people living with HIV globally are optimally treated.4 The emergence of the SARS-CoV-2 Omicron variant is a stark illustration of the intersecting COVID-19 and HIV pandemics, highlighting the interrelationships and detrimental effects each of these infectious diseases has on the other.5 HIV infection is a risk factor for increased mortality from COVID-19, even more so when HIV is not controlled by antiretroviral therapy,6 and emerging data suggest that immunosuppression may be facilitating the development of SARS-CoV-2 variants of concern. | |
| Puskarich MA et al<br><br>JAMA<br><br>Efficacy of Losartan in Hospitalized Patients With COVID-19–Induced Lung Injury A Randomized Clinical Trial<br><br>https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790162 | Importance SARS-CoV-2 viral entry may disrupt angiotensin II (AII) homeostasis, contributing to COVID-19 induced lung injury. AII type 1 receptor blockade mitigates lung injury in preclinical models, although data in humans with COVID-19 remain mixed.<br><br>Objective To test the efficacy of losartan to reduce lung injury in hospitalized patients with COVID-19.<br><br>Design, Setting, and Participants This blinded, placebo-controlled randomized clinical trial was conducted in 13 hospitals in the United States from April 2020 to February 2021. Hospitalized patients with COVID-19 and a respiratory sequential organ failure assessment score of at least 1 and not already using a renin-angiotensin-aldosterone system (RAAS) inhibitor were eligible for participation. Data were | Trial clinico randomizzato controllato con placebo eseguito in 13 centri degli USA nel periodo aprile 2020 – febbraio 2021 su 205 pazienti ospedalizzati con polmonite da SARS-CoV-2 e trattati con il sartano losartan o con placebo in aggiunta alla terapia standard per COVID-19 : non si osserva un miglioramento degli scambi gassosi (paO2/FiO2) a 7 giorni nei trattati con losartan, che dunque non appare utile nel trattamento di COVID-19. |

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| | analyzed from April 19 to August 24, 2021.<br><br>Interventions Losartan 50 mg orally twice daily vs equivalent placebo for 10 days or until hospital discharge.<br><br>Main Outcomes and Measures The primary outcome was the imputed arterial partial pressure of oxygen to fraction of inspired oxygen (Pao2:Fio2) ratio at 7 days. Secondary outcomes included ordinal COVID-19 severity; days without supplemental o2, ventilation, or vasopressors; and mortality. Losartan pharmacokinetics and RAAS components (AII, angiotensin-[1-7] and angiotensin-converting enzymes 1 and 2)] were measured in a subgroup of participants.<br><br>Results A total of 205 participants (mean [SD] age, 55.2 [15.7] years; 123 [60.0%] men) were randomized, with 101 participants assigned to losartan and 104 participants assigned to placebo. Compared with placebo, losartan did not significantly affect Pao2:Fio2 ratio at 7 days (difference, −24.8 [95%, −55.6 to 6.1]; P = .12). Compared with placebo, losartan did not improve any secondary clinical outcomes and led to fewer vasopressor-free days than placebo (median [IQR], 9.4 [9.1-9.8] vasopressor-free days vs 8.7 [8.2-9.3] vasopressor-free days).<br><br>Conclusions and Relevance This randomized clinical trial found that initiation of orally administered losartan to hospitalized patients with COVID-19 and acute lung injury | |

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| | did not improve Pao2:Fio2 ratio at 7 days. These data may have implications for ongoing clinical trials. | |
| Allotey J et al<br><br>The BMJ<br><br>SARS-CoV-2 positivity in offspring and timing of mother-to-child transmission: living systematic review and meta-analysis<br><br>https://www.bmj.com/content/376/bmj-2021-067696 | Objectives To assess the rates of SARS-CoV-2 positivity in babies born to mothers with SARS-CoV-2 infection, the timing of mother-to-child transmission and perinatal outcomes, and factors associated with SARS-CoV-2 status in offspring.<br><br>Design Living systematic review and meta-analysis.<br><br>Data sources Major databases between 1 December 2019 and 3 August 2021.<br><br>Study selection Cohort studies of pregnant and recently pregnant women (including after abortion or miscarriage) who sought hospital care for any reason and had a diagnosis of SARS-CoV-2 infection, and also provided data on offspring SARS-CoV-2 status and risk factors for positivity. Case series and case reports were also included to assess the timing and likelihood of mother-to-child transmission in SARS-CoV-2 positive babies.<br><br>Data extraction Two reviewers independently extracted data and assessed study quality. A random effects model was used to synthesise data for rates, with associations reported using odds ratios and 95% confidence intervals. Narrative | Ampia revisione sistematica di quasi 500 lavori sulla trasmissione verticale di SARS-CoV-2 dalla madre al feto, oppure al neonato durante il parto o in epoca perinatale; il fenomeno è descritto in tutti e tre i casi, ma appare estremamente raro e associato alla gravità dell'infezione materna. |

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| | syntheses were performed when meta-analysis was inappropriate. The World Health Organization classification was used to categorise the timing of mother-to-child transmission (in utero, intrapartum, early postnatal).<br><br>Results 472 studies (206 cohort studies, 266 case series and case reports; 28952 mothers, 18237 babies) were included. Overall, 1.8% (95% confidence interval 1.2% to 2.5%; 140 studies) of the 14271 babies born to mothers with SARS-CoV-2 infection tested positive for the virus with reverse transcriptase polymerase chain reaction (RT-PCR). Of the 592 SARS-CoV-2 positive babies with data on the timing of exposure and type and timing of tests, 14 had confirmed mother-to-child transmission: seven in utero (448 assessed), two intrapartum (18 assessed), and five during the early postnatal period (70 assessed). Of the 800 SARS-CoV-2 positive babies with outcome data, 20 were stillbirths, 23 were neonatal deaths, and eight were early pregnancy losses; 749 babies were alive at the end of follow-up. Severe maternal covid-19 (odds ratio 2.4, 95% confidence interval 1.3 to 4.4), maternal death (14.1, 4.1 to 48.0), maternal admission to an intensive care unit (3.5, 1.7 to 6.9), and maternal postnatal infection (5.0, 1.2 to 20.1) were associated with SARS-CoV-2 positivity in offspring. Positivity rates using RT-PCR varied between regions, ranging from 0.1% (95% confidence interval 0.0% to 0.3%) in studies from North America to 5.7% (3.2% to 8.7%) in studies from Latin America and the Caribbean. | |

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| | Conclusion SARS-CoV-2 positivity rates were found to be low in babies born to mothers with SARS-CoV-2 infection. Evidence suggests confirmed vertical transmission of SARS-CoV-2, although this is likely to be rare. Severity of maternal covid-19 appears to be associated with SARS-CoV-2 positivity in offspring.<br><br>Systematic review registration PROSPERO CRD42020178076.<br><br>Readers' note This article is a living systematic review that will be updated to reflect emerging evidence. Updates may occur for up to two years from the date of original publication. | |

# REPORT COVID-19 (SETTIMANA 21-27 MARZO 2022)

| SANITA' PUBBLICA, EPIDEMIOLOGIA, EPIDEMIOLOGIA BIOMOLECOLARE<br>ESTENSORI : DOTT. SSA PAOLA DEL GIACOMO- DOTT. FRANCESCO V. SEGALA | | |
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| **ARTICOLO** | **ABSTRACT** | **CONTENUTO E COMMENTO** |
| COVID-19 Excess Mortality Collaborators*<br><br>The Lancet<br><br>Estimating excess mortality due to the COVID-19 pandemic: a systematic analysis of COVID-19-related mortality, 2020–21<br><br>https://www.thelancet.com/journals/lancet/article/PIIS0140- | **Background.** Mortality statistics are fundamental to public health decision making. Mortality varies by time and location, and its measurement is affected by well known biases that have been exacerbated during the COVID-19 pandemic. This paper aims to estimate excess mortality from the COVID-19 pandemic in 191 countries and territories, and 252 subnational units for selected countries, from Jan 1, 2020, to Dec 31, 2021.<br><br>**Methods.** All-cause mortality reports were collected for 74 countries and territories and 266 subnational locations (including 31 locations in low-income and middle-income countries) that had reported either weekly or monthly deaths from all causes during the pandemic in 2020 and 2021, and for up to 11 year previously. In addition, we obtained excess mortality data for 12 states in India. Excess | L'eccesso di mortalità – definito come la differenza netta tra il numero di morti (per tutte le cause) registrato e/o stimato durante la pandemia, e il numero di morti "attese" sulla base dei trend di mortalità registrati negli anni precedenti – è un indicatore cruciale per stimare l'impatto della pandemia in termini di sanità pubblica. Tale valore si scosta dalla mortalità registrata perché, da un lato, non è influenzato dalla sottostima diagnostica (differenza tra numero di casi diagnosticati e reale numero di infezioni) e, dall'altro, tiene in considerazione anche dell'eccesso di mortalità determinato dallo stravolgimento dei sistemi sanitari secondario alla pandemia, e quindi del numero dei morti in eccesso per patologie diverse dalla COVID-19 che non sono state prese correttamente in carico nel periodo di pandemia.<br><br>I dati per questa analisi sono stati raccolti dai registri nazionali di 74, da gennaio 2008 fino a dicembre 2021, normalizzando le anomalie di mortalità dovute, ad esempio, |

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| 6736(21)02796-3/fulltext | mortality over time was calculated as observed mortality, after excluding data from periods affected by late registration and anomalies such as heat waves, minus expected mortality. Six models were used to estimate expected mortality; final estimates of expected mortality were based on an ensemble of these models. Ensemble weights were based on root mean squared errors derived from an out-of-sample predictive validity test. As mortality records are incomplete worldwide, we built a statistical model that predicted the excess mortality rate for locations and periods where all-cause mortality data were not available. We used least absolute shrinkage and selection operator (LASSO) regression as a variable selection mechanism and selected 15 covariates, including both covariates pertaining to the COVID-19 pandemic, such as seroprevalence, and to background population health metrics, such as the Healthcare Access and Quality Index, with direction of effects on excess mortality concordant with a meta-analysis by the US Centers for Disease Control and Prevention. With the selected best model, we ran a prediction process using 100 draws for each covariate and 100 draws of estimated coefficients and residuals, estimated from the regressions run at the draw level using draw-level input data on both excess mortality and covariates. Mean values and 95% uncertainty intervals were then generated at national, regional, and global levels. Out-of-sample predictive validity testing was done on the basis of our final | ad ondate di calore. La mortalità attesa è stata quindi calcolata estrapolata dall'utilizzo di 6 modelli matematici differenti, applicando il modello predittivo anche a nazioni che non forniscono dati di mortalità.<br>Sulla base di tale analisi, sebbene le morti COVID-relate riportate ufficialmente nel periodo di tempo intercorrente tra il 1 gennaio 2020 e il 31 dicembre 2021 sono state 5,94 milioni, gli autori stimano che l'eccesso di mortalità rispetto all'atteso sia stato, in tutto il mondo, di 18 milioni di morti. L'eccesso di mortalità per 100.000 unità di popolazione è risultato eterogeno, a seconda delle aree geografiche, raggiungendo i valori più alti in Asia Meridionale, Nord Africa, Medio Oriente e Est Europa. Le nazioni che hanno assistito all'eccesso di mortalità per 100.000 individui più elevato sono inoltre state, nell'ordine: Russia, Messico, Brasile e USA.<br><br>Questo studio mette in evidenzia il reale impatto della pandemia sulla mortalità mondiale, stimandolo circa 3 volte superiore ai report ufficiali. |

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| | model specification.<br><br>**Findings.** Although reported COVID-19 deaths between Jan 1, 2020, and Dec 31, 2021, totalled 5·94 million worldwide, we estimate that 18·2 million (95% uncertainty interval 17·1–19·6) people died worldwide because of the COVID-19 pandemic (as measured by excess mortality) over that period. The global all-age rate of excess mortality due to the COVID-19 pandemic was 120·3 deaths (113·1–129·3) per 100000 of the population, and excess mortality rate exceeded 300 deaths per 100000 of the population in 21 countries. The number of excess deaths due to COVID-19 was largest in the regions of south Asia, north Africa and the Middle East, and eastern Europe. At the country level, the highest numbers of cumulative excess deaths due to COVID-19 were estimated in India (4·07 million [3·71–4·36]), the USA (1·13 million [1·08–1·18]), Russia (1·07 million [1·06–1·08]), Mexico (798000 [741000–867000]), Brazil (792000 [730000–847000]), Indonesia (736000 [594000–955000]), and Pakistan (664000 [498000–847000]). Among these countries, the excess mortality rate was highest in Russia (374·6 deaths [369·7–378·4] per 100000) and Mexico (325·1 [301·6–353·3] per 100000), and was similar in Brazil (186·9 [172·2–199·8] per 100000) and the USA (179·3 [170·7–187·5] per 100000).<br><br>**Interpretation.** The full impact of the pandemic has been much greater than what is indicated by reported deaths due to COVID-19 alone. Strengthening death registration systems | |

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| | around the world, long understood to be crucial to global public health strategy, is necessary for improved monitoring of this pandemic and future pandemics. In addition, further research is warranted to help distinguish the proportion of excess mortality that was directly caused by SARS-CoV-2 infection and the changes in causes of death as an indirect consequence of the pandemic. | |
| Pertwee E at al.<br><br>An epidemic of uncertainty: rumors, conspiracy theories and vaccine hesitancy<br><br>Nature Medicine<br><br>https://www.nature.com/articles/s41591-022-01728-z | The COVID-19 'infodemic' continues to undermine trust in vaccination efforts aiming to bring an end to the pandemic. However, the challenge of vaccine hesitancy is not only a problem of the information ecosystem and it often has little to do with the vaccines themselves. In this Perspective, we argue that the epidemiological and social crises brought about by COVID-19 have magnified widely held social anxieties and trust issues that, in the unique circumstances of this global pandemic, have exacerbated skepticism toward vaccines. We argue that trust is key to overcoming vaccine hesitancy, especially in a context of widespread social uncertainty brought about by the pandemic, where public sentiment can be volatile. Finally, we draw out some implications of our argument for strategies to build vaccine confidence. | Una delle più grandi sfide di sanità pubblica dall'inizio della pandemia è stato arginare la cosiddetta « infodemia », ovvero l'epidemia di disinformazione relativa alla COVID-19 e, soprattutto, alla relativa campagna vaccinale. In questo perspective article, gli autori suppongono che il fenomeno dell'esitazione vaccinale non affondi le sue radici nella bassa qualità del sistema informativo sui vaccini in sé, quanto nella perdita di fiducia nei confronti dell'autorità sanitaria, in un sentimento di esclusione dalla vita politica e, infine, in un inasprimento dell'ansia sociale riguardante la velocità dello sviluppo tecnologico.<br>In sostanza, gli autori sottolineano come, per combattere efficacemente l'esitazione vaccinale, le campagne di salute pubblica debbano, più che espandere e rafforzare il sistema informatio, lavorare sul riconsolidamento di un sentimento di fiducia nei confronti delle istituzioni. |

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| Van der Linden S et al.<br><br>Misinformation: susceptibility, spread, and interventions to immunize the public<br><br>Nature Medicine<br><br>https://www.nature.com/articles/s41591-022-01713-6 | The spread of misinformation poses a considerable threat to public health and the successful management of a global pandemic. For example, studies find that exposure to misinformation can undermine vaccination uptake and compliance with public-health guidelines. As research on the science of misinformation is rapidly emerging, this conceptual Review summarizes what we know along three key dimensions of the infodemic: susceptibility, spread, and immunization. Extant research is evaluated on the questions of why (some) people are (more) susceptible to misinformation, how misinformation spreads in online social networks, and which interventions can help to boost psychological immunity to misinformation. Implications for managing the infodemic are discussed. | Review narrativa esplorante le tre dimensioni dell'epidemia di disinformazione COVID-relata, o « infodemia » : suscettibilità, diffusione e immunità.<br>Per quanto riguarda la vulnerabilità alla disinformazione, l'autore sottolinea l'importanza dei fenomeni della « verità illusoria », ovvero la verità che viene ritenuta tale in quanto insistentemente ripetuta e di « motivated reasoning » ovvero il processo cognitivo per cui un individuo inizia il suo ragionamento su un particolare tema con l'obiettivo di raggiungere una conclusione precisa. Quest'ultimo processo cognitivo, ad esempio, viene spesso utilizzato per giustificare un'informazione falsa che porta un contributo positivo ad una particolare causa politica.<br>La review analizza poi la diffusione della disinformazione attraverso i social media e, analogamente a quanto avverrebbe per un'epidemia virale, analizza la sua dinamica attraverso una stima del R0, descrivendolo come la dinamica di diffusione di un'informazione falsa in seguito alla sus esposizione sui social media, in quanto, sottolinea l'autore, le informazioni false si trasmettono 6 volte più velocemente delle informazioni vere.<br>Infine, la review si concentra sulle possibili strategie per contenere la diffusione dell'infodemia : dal più tradizionale « fact checking », consistente dell'analizzare gli elementi di incongruità di un'informazione falsa assieme ad un individuo già esposto alla stessa, fino alla più recente « terapia profilattica » che, analogamente a quanto avverrebbe per un vaccino, postula che individui non ancora esposti alla disinformazione, se sottoposti a delle fake news più deboli accoppiate da forti confutazioni, possono essere in grado di consolidare dei meccanismi logici e cognitivi in grado di proteggerli da una futura informazione falsa. |

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| Bartsch S et al.<br><br>Lancet Publich Health<br><br>Maintaining face mask use before and after achieving different COVID-19 vaccination coverage levels: a modelling study<br><br>https://www.sciencedirect.com/science/article/pii/S2468266722000408 | **Background.** Face mask wearing has been an important part of the response to the COVID-19 pandemic. As vaccination coverage progresses in countries, relaxation of such practices is increasing. Subsequent COVID-19 surges have raised the questions of whether face masks should be encouraged or required and for how long. Here, we aim to assess the value of maintaining face masks use indoors according to different COVID-19 vaccination coverage levels in the USA.<br><br>**Methods.** In this computational simulation-model study, we developed and used a Monte Carlo simulation model representing the US population and SARS-CoV-2 spread. Simulation experiments compared what would happen if face masks were used versus not used until given final vaccination coverages were achieved. Different scenarios varied the target vaccination coverage (70–90%), the date these coverages were achieved (Jan 1, 2022, to July 1, 2022), and the date the population discontinued wearing face masks.<br><br>**Findings.** Simulation experiments revealed that maintaining face mask use (at the coverage seen in the USA from March, 2020, to July, 2020) until target vaccination coverages were achieved was cost-effective and in many cases cost saving from both the societal and third-party payer perspectives across nearly all scenarios explored. Face mask use was estimated to be cost-effective and usually cost saving when | Studio di modello matematico confrontante due scenari : cosa sarebbe successo se, in parallelo alla diffusione della campagna vaccinale, a) le mascherine non fossero state o b) fossero state usate.<br>Tale simulazione mette in evidenza come l'utilizzo delle mascherine fino al raggiungimento di una copertura vaccinale del 70-90% sia conveniente, dal punto di vista economico, in tutti gli scenari esplorati. In particolare, perché il beneficio sia più pronunciato se l'utilizzo delle mascherine viene rinforzato nei mesi invernali e prolungato fino a 2-10 settimane dal raggiungimento della soglia vaccinale. Ovviamente, la comparsa di varianti che riducono l'efficacia dei vaccini non fa che consolidare l'efficace e la convenienza economica delle mascherine. |

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| | the cost of face masks per person per day was ≤US$1·25. In all scenarios, it was estimated to be cost-effective to maintain face mask use for about 2–10 weeks beyond the date that target vaccination coverage (70–90%) was achieved, with this added duration being longer when the target coverage was achieved during winter versus summer. Factors that might increase the transmissibility of the virus (eg, emergence of the delta [B.1.617.2] and omicron [B.1.1.529] variants), or decrease vaccine effectiveness (eg, waning immunity or escape variants), or increase social interactions among certain segments of the population, only increased the cost savings or cost-effectiveness provided by maintaining face mask use.<br><br>Interpretation<br>Our study provides strong support for maintaining face mask use until and a short time after achieving various final vaccination coverage levels, given that maintaining face mask use can be not just cost-effective, but even cost saving. The emergence of the omicron variant and the prospect of future variants that might be more transmissible and reduce vaccine effectiveness only increases the value of face masks. | |