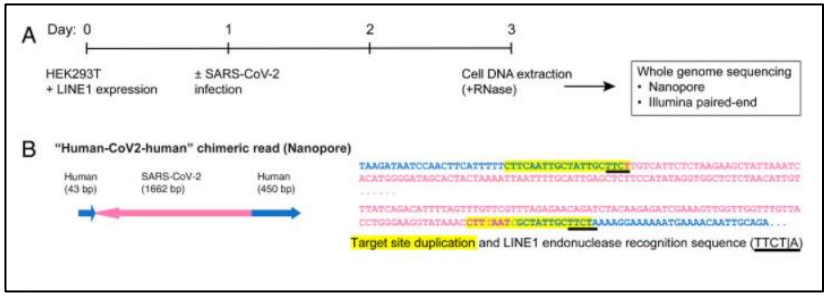
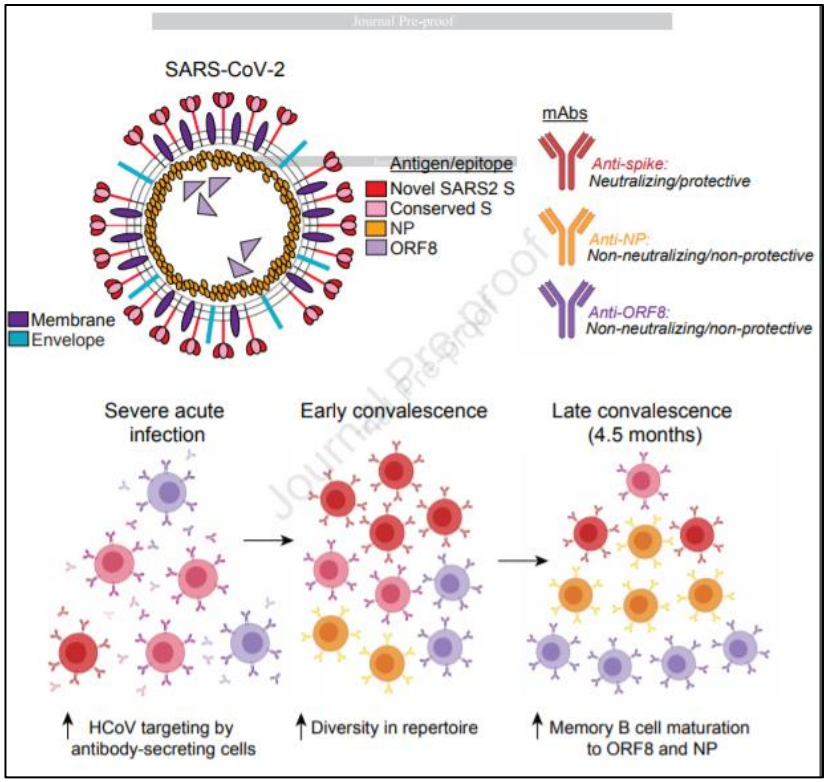
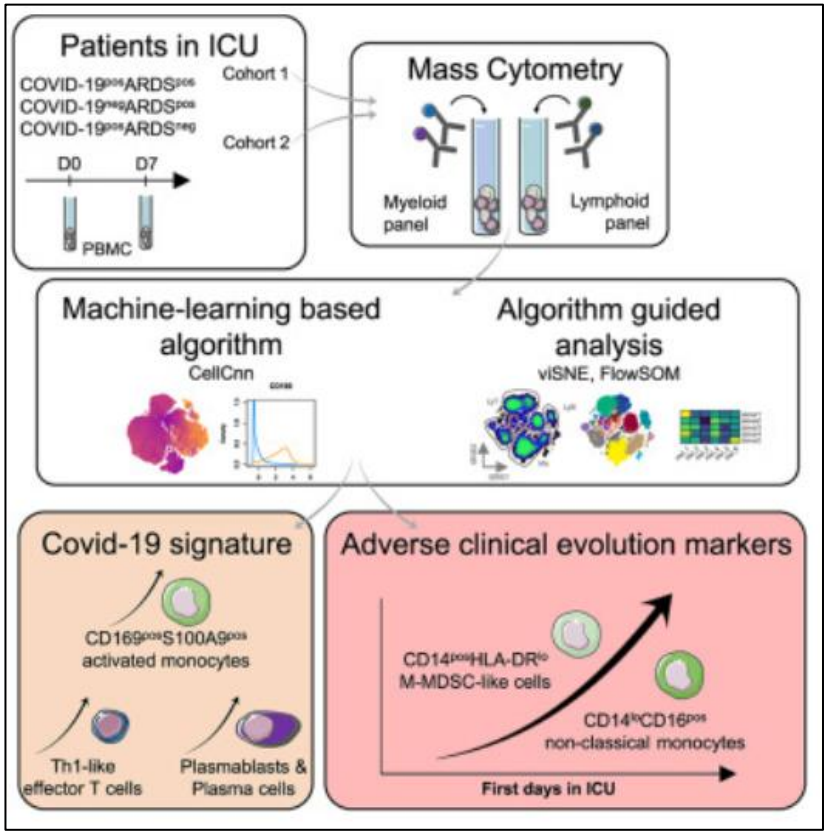
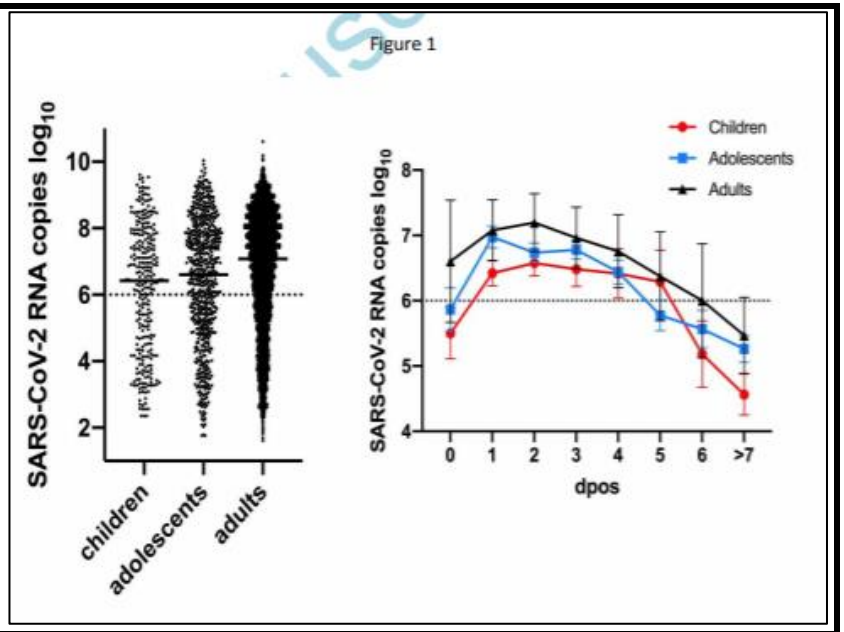
RICERCA BIBLIOGRAFICA COVID 19 SETTIMANA 10.05 – 16.05.2021 FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE DOTT.SSA ELEONORA TADDEI			
AUTORE/RIVISTA	**TITOLO**	**OUTCOME PRINCIPALE**	**ABSTRACT**
Zhang L et al PNAS https://www.pnas.org/content/118/21/e2105968118	Reverse-transcribed SARS-CoV-2 RNA can integrate into the genome of cultured human cells and can be expressed in patient-derived tissues	Alcune sequenze del genoma di SARS-CoV-2 vengono retrotrascritte con un meccanismo mediato dai retrotrasposoni cellulari; si integrano nel genoma cellulare e vengono trascritte insieme a geni della cellula, formando dei prodotti chimerici che potrebbero essere alla base della persistente positività della ricerca molecolare di SARS-CoV-2, pur in assenza di capacità di replicazione virale. Il fenomeno è stato	Prolonged detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA and recurrence of PCR-positive tests have been widely reported in patients after recovery from COVID-19, but some of these patients do not appear to shed infectious virus. We investigated the possibility that SARS-CoV-2 RNAs can be reverse-transcribed and integrated into the DNA of human cells in culture and that transcription of the integrated sequences might account for some of the positive PCR tests seen in patients. In support of this hypothesis, we found that DNA copies of SARS-CoV-2 sequences can be integrated into the genome of infected human cells. We found target site duplications flanking the viral sequences and consensus LINE1 endonuclease recognition sequences at the integration sites, consistent with a LINE1 retrotransposon-mediated, target-primed reverse transcription and retroposition mechanism. We also found, in some patient-derived tissues, evidence suggesting that a large fraction of the viral

		descritto anche per altri virus.	sequences is transcribed from integrated DNA copies of viral sequences, generating viral–host chimeric transcripts. The integration and transcription of viral sequences may thus contribute to the detection of viral RNA by PCR in patients after infection and clinical recovery. Because we have detected only subgenomic sequences derived mainly from the 3′ end of the viral genome integrated into the DNA of the host cell, infectious virus cannot be produced from the integrated subgenomic SARS-CoV-2 sequences. 
Dugan HL et al Cell https://www.cell.com/immunity/pdf/S1074-7613(21)00198-9.pdf?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS1074761321001989%3Fshowall%3Dtrue	Profiling B cell immunodominance after SARS-CoV-2 infection reveals antibody evolution to non-neutralizing viral targets	In 38 pazienti con storia di COVID-19 si osserva una « deriva » delle cellule B della memoria verso epitopi esterni alla porzione legante il recettore, che risultano non neutralizzanti ; per questo il vaccino che riporti la risposta verso gli epitopi più « utili » sarebbe utile anche nei guariti.	Dissecting the evolution of memory B cells (MBCs) against SARS-CoV-2 is critical for understanding antibody recall upon secondary exposure. Here, we utilized single-cell sequencing to profile SARS-CoV-2-reactive B cells in 38 COVID-19 patients. Using oligo-tagged antigen baits, we isolated B cells specific to the SARS-CoV-2 spike, nucleoprotein (NP), open reading frame 8 (ORF8), and endemic coronavirus (HCoV) spike proteins. SARS-CoV-2 spike-specific cells were enriched in the memory compartment of acutely infected and convalescent patients several months post symptom onset. With severe acute infection, substantial populations of endemic HCoV reactive antibody-secreting cells were identified and possessed highly mutated variable genes, signifying preexisting immunity. Finally, MBCs exhibited pronounced maturation to NP and ORF8 over time, especially in older patients. Monoclonal antibodies

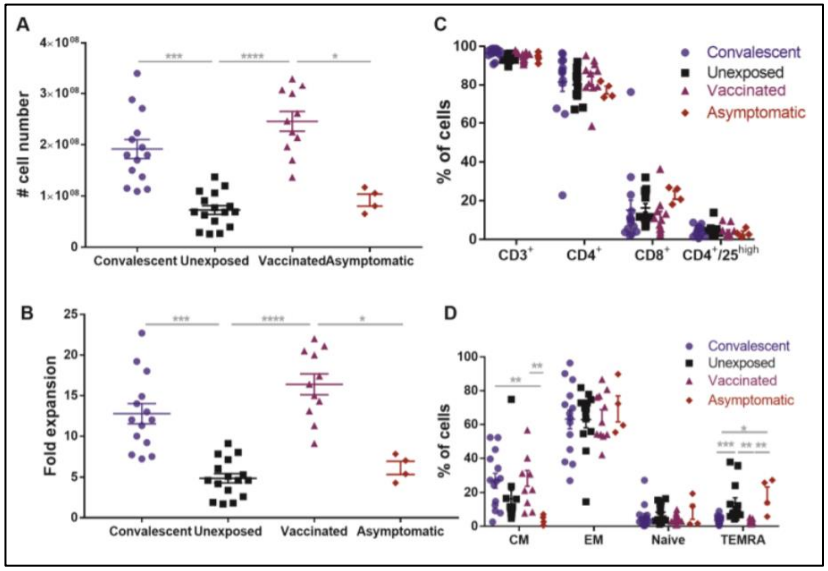
			against these targets were non-neutralizing and non-protective in vivo. These findings reveal antibody adaptation to non-neutralizing intracellular antigens during infection, emphasizing the importance of vaccination for inducing neutralizing spike-specific MBCs. 
Saunders KO et al Nature https://www.nature.com/articles/s41586-021-03594-0	Neutralizing antibody vaccine for pandemic and pre-emergent coronaviruses	Vaccinare gli animali per prevenire future zoonosi sostenute da Coronavirus potrebbe essere una futura strategia di salute globale. I vaccini a mRNA sono un a piattaforma adattabile che si presta a questo scopo.	Betacoronaviruses (betaCoVs) caused the severe acute respiratory syndrome (SARS) and Middle East Respiratory Syndrome (MERS) outbreaks, and the SARS-CoV-2 pandemic. Vaccines that elicit protective immunity against SARS-CoV-2 and betaCoVs circulating in animals have the potential to prevent future betaCoV pandemics. Here, we show that macaque immunization with a multimeric SARS-CoV-2 receptor binding domain (RBD) nanoparticle adjuvanted with

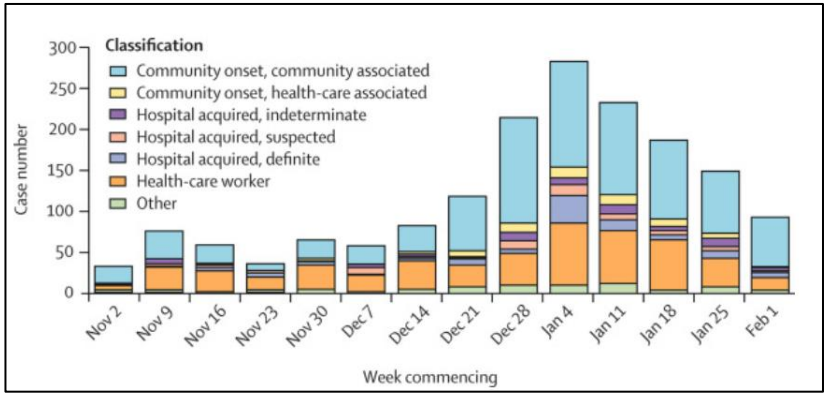
			3M-052/Alum elicited cross-neutralizing antibody (cross-nAb) responses against batCoVs, SARS-CoV-1, SARS-CoV-2, and SARS-CoV-2 variants B.1.1.7, P.1, and B.1.351. Nanoparticle vaccination resulted in a SARS-CoV-2 reciprocal geometric mean neutralization ID50 titer of 47,216, and protection against SARS-CoV-2 in macaque upper and lower respiratory tracts. Importantly, nucleoside-modified mRNA encoding a stabilized transmembrane spike or monomeric RBD also induced SARS-CoV-1 and batCoV cross-nAbs, albeit at lower titers. These results demonstrate current mRNA vaccines may provide some protection from future zoonotic betaCoV outbreaks, and provide a platform for further development of pan-betaCoV vaccines.
Roussel M et al Cell Reports Medicine https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(21)00119-1	Comparative immune profiling of acute respiratory distress syndrome patients with or without SARS-CoV2 infection	I pazienti con COVID-19 che sviluppano o meno ARDS hanno un profilo immunitario simile, che li distingue dai pazienti con ARDS dovuta ad altre cause.	Acute respiratory distress syndrome (ARDS) is the main complication of COVID-19, requiring admission to Intensive Care Unit (ICU). Despite extensive immune profiling of COVID-19 patients, to what extent COVID-19-associated ARDS differs from other causes of ARDS remains unknown. To address this question, we build 3 cohorts of patients categorize in COVID-19negARDSpos, COVID-19posARDSpos, and COVID-19posARDSneg, and compare their immune landscape analyze by high-dimensional mass cytometry on peripheral blood. A cell signature associating S100A9/calprotectin-producing CD169pos monocytes, plasmablasts, and Th1 cells is found in COVID-19posARDSpos, unlike COVID-19negARDSpos patients. Moreover, this signature is essentially share with COVID-19posARDSneg patients, suggesting that severe COVID-19 patients, whatever they experience or not ARDS, display similar immune profiles. We show an increase in CD14posHLA-DRlow and CD14lowCD16pos monocytes correlate to the occurrence of adverse events during ICU stay. We demonstrate that COVID-19-associated ARDS display a specific immune profile, and

			might benefit from personalize therapy in addition to standard ARDS management. 
Bellon M et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-	SARS-CoV-2 viral load kinetics in symptomatic children, adolescents and adults	In questa coorte di oltre 8000 individui, i bambini mostrano una carica virale di SARS-CoV-2 nel tampone nasofaringeo inferiore a quella degli adulti nella prima settimana di infezione.	SARS-CoV-2 viral load (VL) can serve as a correlate for infectious virus presence and transmission. Viral shedding kinetics over the first week of illness for symptomatic children (n=279), adolescents (n=639) and adults (n=7109) show VLs compatible with infectious virus presence, with slightly lower VL in children than adults.

article/doi/10.1093/cid/ciab396/6265276			
Misra-Hebert AD et al JAMA Health Forum https://jamanetwork.com/journals/jama-health-forum/fullarticle/2779695	COVID-19 Home Monitoring After Diagnosis and Health Care Utilization in an Integrated Health System	Gestione domiciliare di pazienti con COVID-19 negli USA, si osserva un ricorso esiguo all'ospedalizzazione nei 90 giorni successivi all'arruolamento nel programma rispetto a chi non ha accettato di partecipare.	Remote monitoring programs have been implemented for patients with suspected or confirmed COVID-191 after hospital discharge or emergency department (ED) visits. The Cleveland Clinic Health System (CCHS) established a home monitoring program (HMP) for patients with positive test results for SARS-Co-V-2. We assessed health care utilization patterns for patients enrolled in the HMP compared with similar patients who were not enrolled.
Zaslavsky AM et al JAMA https://jamanetwork.com/journals/jama-health-	Study on COVID-19 Home Monitoring—A Control Group Is Essential	Commento metdologico al lavoro precedente, in cui si osserva che il gruppo di controllo avrebbe dovuto essere costituito da pazienti cui non veniva offerto il monitoraggio a domicilio, e	Without a control group, the study by Misra-Hebert and colleagues does not provide conclusive evidence for the proposed intervention. Nonetheless, it is at least consistent with the desired treatment effect and supports reanalysis with retrospectively identified controls or a new prospectively controlled study.

forum/fullarticle/2779697		non dai pazienti che rifiutavano tale monitoraggio.	
Papayanni P et al CID https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab371/6255711	Vaccinated and convalescent donor-derived SARS-CoV-2-specific T cells as adoptive immunotherapy for high-risk COVID-19 patients	I linfociti T specifici per SARS-CoV-2 predicono l'andamento clinico dei pazienti e potrebbero essere utilizzati come terapia per i soggetti ad alto rischio.	Background : Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic poses an urgent need for the development of effective therapies for Coronavirus Disease 2019 (COVID-19). Methods : We first tested SARS-CoV-2-specific T-cell (CoV-2-ST) immunity and expansion in unexposed donors, COVID-19 infected individuals (convalescent), asymptomatic PCR-positive subjects, vaccinated individuals, non-ICU hospitalized patients and ICU patients who either recovered and were discharged (ICU recovered) or had a prolonged stay and/or died (ICU critical). CoV-2-STs were generated from all types of donors and underwent phenotypic and functional assessment. Results : We demonstrate causal relationship between the expansion of endogenous CoV-2-STs and the disease outcome; insufficient expansion of circulating CoV-2-STs, identified hospitalized patients at high-risk for an adverse outcome. CoV-2-STs with a similarly functional and non-alloreactive, albeit highly cytotoxic, profile against SARS-CoV-2 could be expanded from both convalescent and vaccinated donors generating clinical-scale, SARS-CoV-2-specific T-cell products with functional activity against both the unmutated virus and its B.1.1.7 variant. In contrast, critical COVID-19 patient-originating CoV-2-STs failed to expand, recapitulating the in vivo failure of CoV-2-specific T-cell immunity to control the infection. CoV-2-STs generated from asymptomatic PCR+ individuals presented only weak responses whereas their counterparts originating from exposed to other seasonal

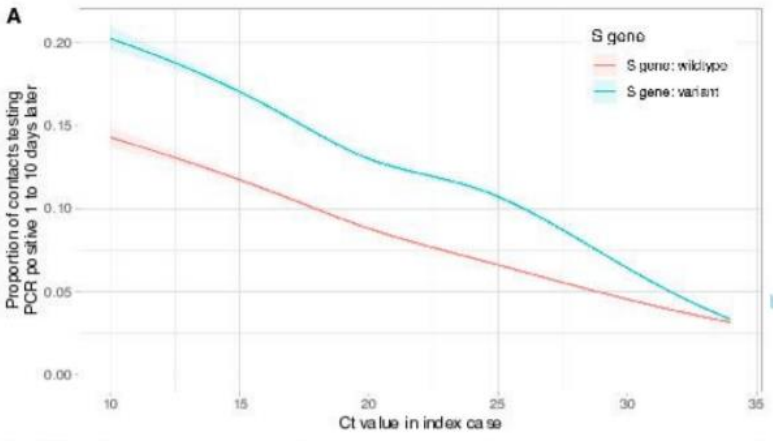
			coronaviruses subjects failed to kill the virus, thus disempowering the hypothesis of protective cross-immunity. Conclusions : Overall, we provide evidence on risk stratification of hospitalized COVID-19 patients and the feasibility of generating powerful CoV-2-ST products from both convalescent and vaccinated donors as an “off-the shelf” T-cell immunotherapy for high-risk patients. 
Hamilton WL et al The Lancet https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00251-6/fulltext?rss=yes&utm_campaign=update-	Applying prospective genomic surveillance to support investigation of hospital-onset COVID-19	Controllo dei cluster ospedalieri di SARS-CoV-2 tramite il sequenziamento dei campioni.	Here, we provide an update on our previous Article, which described the use of rapid SARS-CoV-2 genome sequencing to investigate hospital-acquired infections (HAIs) at Cambridge University Hospitals NHS Foundation Trust (CUH), Cambridge, UK. CUH experienced a substantial second wave of COVID-19 (figure). Between Nov 2, 2020, and Feb 7, 2021, 162 (14%) of 1178 patients with COVID-19 at CUH had a suspected or definite HAI (as previously defined), and 465 infected health-care workers (HCWs) were identified via the staff screening programme. Nanopore

laninf&utm_medium=email&_hsmi=126493068&_hsenc=p2ANqtz-8W7zmT-eIVeKQBB3_JITdBiiC3890qQoANcNuwbHWT9HI4fKoEzNRMERsZg6AFy-Mml7U7ZVPM1v8gRtLSsVIm_S8facGaRS9pj4KstlYyerHVQE&utm_content=126493068&utm_source=hs_email			sequencing was attempted for 513 (44%) of 1178 patients, prioritising those with hospital-onset infections, and 324 (70%) of 465 HCWs; 252 (21%) of 1178 patients and 317 (68%) of 465 HCWs had SARS-CoV-2 genomes available after quality control filtering (as previously described). Patient coverage was lower than in our previous study and for HCWs, reflecting different diagnostic testing methods and limitations on sequencing capacity. The frequency of the B.1.1.7 PANGO-lineage increased from 8% (nine of 109) in November, 2020, to 83% (257 of 311) in January, 2021. 
Lund LC et al The Lancet https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00211-5/fulltext?rss=yes&utm_campaign=update-laninf&utm_medium=email&_hsmi=126493068&_hsenc=p2ANqtz--	Post-acute effects of SARS-CoV-2 infection in individuals not requiring hospital admission: a Danish population-based cohort study	Effetti a lungo termine di COVID-19 in una coorte di persone non ricoverate per questo motivo in Danimarca, sulla base dei dati di accesso alle cure mediche: il rischio di complicanze acute appare basso, salvo per un lieve aumento del rischio di tromboembolia venosa. La dispnea è il motivo	Background : Individuals admitted to hospital for COVID-19 might have persisting symptoms (so-called long COVID) and delayed complications after discharge. However, little is known regarding the risk for those not admitted to hospital. We therefore examined prescription drug and health-care use after SARS-CoV-2 infection not requiring hospital admission. Methods : This was a population-based cohort study using the Danish prescription, patient, and health insurance registries. All individuals with a positive or negative RT-PCR test for SARS-CoV-2 in Denmark between Feb 27 and May 31, 2020, were eligible for inclusion. Outcomes of interest were delayed acute complications, chronic disease, hospital visits due to persisting symptoms, and

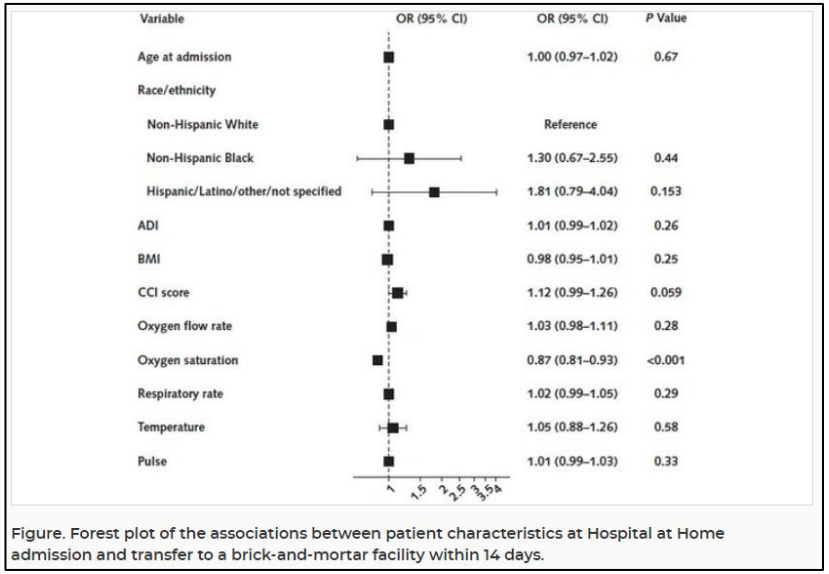
1cl0LeeZfTceiTFzdSSCjjQHfEbJjLGy9CwuCHH1eqcGlpijz8q_3hHrfujYaOStN-qPOgoKSO8x_q8BeFqXetGW63SsJYWTxtNHnJ3NQcDtlRG8&utm_content=126493068&utm_source=hs_email		principale per cui si ricercano le cure dopo la malattia da SARS-CoV-2.	prescription drug use. We used data from non-hospitalised SARS-CoV-2-positive and matched SARS-CoV-2-negative individuals from 2 weeks to 6 months after a SARS-CoV-2 test to obtain propensity score-weighted risk differences (RDs) and risk ratios (RRs) for initiation of 14 drug groups and 27 hospital diagnoses indicative of potential post-acute effects. We also calculated prior event rate ratio-adjusted rate ratios of overall health-care use. Findings : 10 498 eligible individuals tested positive for SARS-CoV-2 in Denmark from Feb 27 to May 31, 2020, of whom 8983 (85·6%) were alive and not admitted to hospital 2 weeks after their positive test. The matched SARS-CoV-2-negative reference population not admitted to hospital consisted of 80 894 individuals. Compared with SARS-CoV-2-negative individuals, SARS-CoV-2-positive individuals were not at an increased risk of initiating new drugs (RD <0·1%) except bronchodilating agents, specifically short-acting β2-agonists (117 [1·7%] of 6935 positive individuals vs 743 [1·3%] of 57 206 negative individuals; RD +0·4% [95% CI 0·1–0·7]; RR 1·32 [1·09–1·60]) and triptans (33 [0·4%] of 8292 vs 198 [0·3%] of 72 828; RD +0·1% [0·0–0·3]; RR 1·55 [1·07–2·25]). There was an increased risk of receiving hospital diagnoses of dyspnoea (103 [1·2%] of 8676 vs 499 [0·7%] of 76 728; RD +0·6% [0·4–0·8]; RR 2·00 [1·62–2·48]) and venous thromboembolism (20 [0·2%] of 8785 vs 110 [0·1%] of 78 872; RD +0·1% [0·0–0·2]; RR 1·77 [1·09–2·86]) for SARS-CoV-2-positive individuals compared with negative individuals, but no increased risk of other diagnoses. Prior event rate ratio-adjusted rate ratios of overall general practitioner visits (1·18 [95% CI 1·15–1·22]) and outpatient hospital visits (1·10 [1·05–1·16]), but not hospital admission, showed increases among SARS-CoV-2-positive individuals compared with SARS-CoV-2-negative individuals.

			Interpretation : The absolute risk of severe post-acute complications after SARS-CoV-2 infection not requiring hospital admission is low. However, increases in visits to general practitioners and outpatient hospital visits could indicate COVID-19 sequelae.
Huang L et al The Lancet https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00225-5/fulltext	Post-acute conditions of patients with COVID-19 not requiring hospital admission	Commento all'articolo precedente in cui si osserva che stimare i sintomi a lungo termine di COVID-19 solo sulla base degli accessi al sistema sanitario (cui molti individui in contesto pandemico potrebbero non ricorrere) può condurre a una sottostima.	In the study, the authors only investigated six persisting symptoms, which did not cover the whole potential clinical spectrum. In addition, the prevalence of the persistent symptoms in patients with COVID-19 was about 1%, which was lower than that in a previous study, which showed a rate of 5–15%.5 Given the inherent nature of this type of registration study, there is the possibility of greatly underestimating the actual prevalence, because there are many reasons that patients with persistent symptoms might not visit the health-care service, such as symptoms being mild, not having health insurance or access to health care, and the risk of reinfection when visiting a health-care facility during the COVID-19 pandemic. Although the number might be underestimated, SARS-CoV-2-positive individuals still more frequently developed dyspnoea than SARS-CoV-2-negative individuals, supporting the finding of greater prescription of bronchodilating agents in SARS-CoV-2-positive individuals. These findings will prompt health-care workers to focus on those patients who have recovered from COVID-19 who already have potential risk factors for dyspnoea, such as chronic pulmonary disease, heart failure, and pulmonary hypertension. Monitoring respiratory rate and oxygen saturation at home were simple and practicle ways for these patients to assess their respiratory function and health status.
DeMerle K et al JAMA	Precision Medicine for COVID-19 Phenotype Anarchy or Promise Realized?	Possibile applicare la medicina « di precisione » all'infezione da SARS-CoV-2, distinguendo precocemente	Ataxonomic revolution is occurring in medicine. Spurred by the halcyon vision of targeted "precision" therapy and enabled by access to massive electronic health data sets, high-throughput multichannel, molecular diagnostic assays, and advances in the

https://jamanetwork.com/journals/jama/fullarticle/2779924		i pazienti e cercando di prevedere il loro decorso ?	understanding of disease biology, researchers have generated a plethora of new disease subclassifications. Variably termed “phenotypes,” “endotypes,” or “subtypes,” these patient groups can share symptoms, biology, or prognosis and are proposed as the basis for precision care. The fast-paced research of SARS-CoV-2 has followed suit, with more than 60 subtypes proposed in the last year (eTable and eFigure in the Supplement). These subtypes range from simple classifications such as the H or L phenotypes of COVID-19–related acute respiratory distress syndrome to emerging groups organized from machine learning methods on large data sets. This Viewpoint examines the complexity of COVID-19 subtype classification and the implications for precision medicine.
Lee LYW et al CID https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab421/6273394	SARS-CoV-2 infectivity by viral load, S gene variants and demographic factors and the utility of lateral flow devices to prevent transmission	La carica virale del caso indice (stimata con il ciclo soglia di positivizzazione della PCR) influenza indipendentemente da altri fattori la probabilità di trasmettere l’infezione ai contatti.	Background : How SARS-CoV-2 infectivity varies with viral load is incompletely understood. Whether rapid point-of-care antigen lateral flow devices (LFDs) detect most potential transmission sources despite imperfect clinical sensitivity is unknown. Methods : We combined SARS-CoV-2 testing and contact tracing data from England between 01-September-2020 and 28-February-2021. We used multivariable logistic regression to investigate relationships between PCR-confirmed infection in contacts of community-diagnosed cases and index case viral load, S gene target failure (proxy for B.1.1.7 infection), demographics, SARS-CoV-2 incidence, social deprivation, and contact event type. We used LFD performance to simulate the proportion of cases with a PCR-positive contact expected to be detected using one of four LFDs. Results : 231,498/2,474,066(9%) contacts of 1,064,004 index cases tested PCR-positive. PCR-positive results in contacts independently increased with higher case viral loads (lower Ct values) e.g., 11.7%(95%CI 11.5-12.0%) at Ct=15 and 4.5%(4.4-4.6%) at Ct=30.

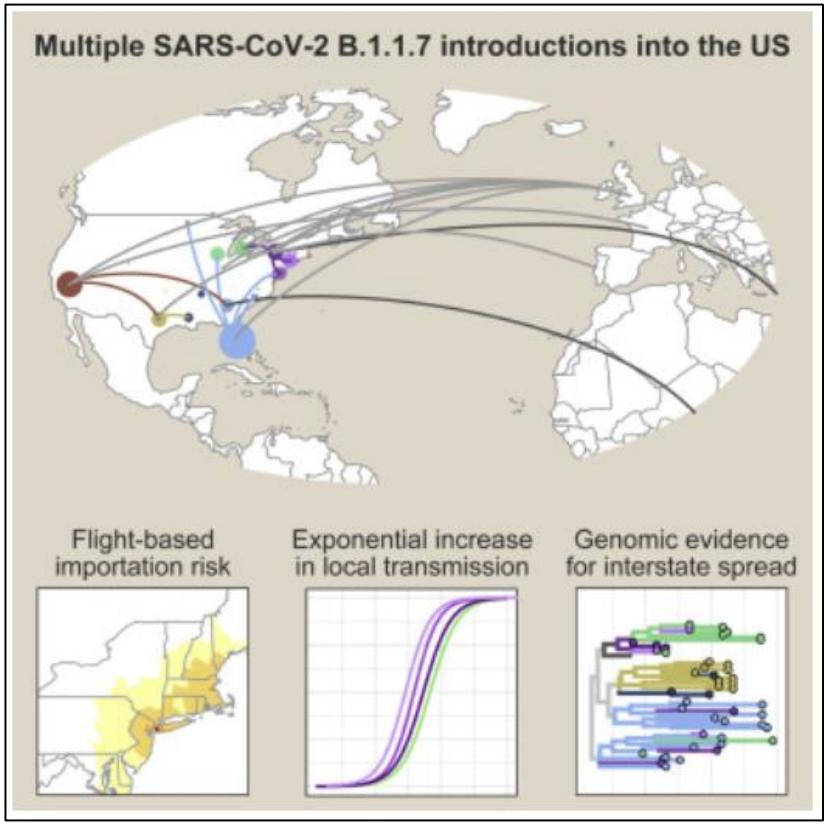
			B.1.1.7 infection increased PCR-positive results by ~50%, (e.g. 1.55-fold, 95%CI 1.49-1.61, at Ct=20). PCR-positive results were most common in household contacts (at Ct=20.1, 8.7%[95%CI 8.6-8.9%]), followed by household visitors (7.1%[6.8-7.3%]), contacts at events/activities (5.2%[4.9-5.4%]), work/education (4.6%[4.4-4.8%]), and least common after outdoor contact (2.9%[2.3-3.8%]). Contacts of children were the least likely to test positive, particularly following contact outdoors or at work/education. The most and least sensitive LFDs would detect 89.5%(89.4-89.6%) and 83.0%(82.8-83.1%) of cases with PCR-positive contacts respectively. Conclusions : SARS-CoV-2 infectivity varies by case viral load, contact event type, and age. Those with high viral loads are the most infectious. B.1.1.7 increased transmission by ~50%. The best performing LFDs detect most infectious cases. Figure 3 

Finkel Y et al Nature https://www.nature.com/articles/s41586-021-03610-3	SARS-CoV-2 uses a multipronged strategy to impede host protein synthesis	Effetti dell'infezione da SARS-CoV-2 sui meccanismi di sintesi proteica delle cellule : riduzione della traduzione e degradazione degli RNA messaggeri cellulari per « fare spazio » alla replicazione virale.	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the cause of the ongoing coronavirus disease 19 pandemic. Coronaviruses developed varied mechanisms to repress host mRNA translation to allow the translation of viral mRNAs and concomitantly block the cellular innate immune response. Although different SARS-CoV-2 proteins are implicated in host expression shutoff, a comprehensive picture of the effects of SARS-CoV-2 infection on cellular gene expression is lacking. Here, we combine RNA-sequencing, ribosome profiling and metabolic labeling of newly synthesized RNA, to comprehensively define the mechanisms that are utilized by SARS-CoV-2 to shutoff cellular protein synthesis. We show that infection leads to a global reduction in translation, but viral transcripts are not preferentially translated. Instead, we find that infection leads to accelerated degradation of cytosolic cellular mRNAs which facilitates viral takeover of the mRNA pool in infected cells. Moreover, we reveal that the translation of transcripts whose expression is induced in response to infection, including innate immune genes, is impaired. We demonstrate this impairment is likely mediated by inhibition of nuclear mRNA export, preventing newly transcribed cellular mRNAs from accessing ribosomes. Overall, our results uncover the multipronged strategy employed by SARS-CoV-2 to commandeer the translation machinery and to suppress host defenses.
Paul Sax HIV and ID Observations – NEJM https://blogs.jwatch.org/hiv-id-	Some Colleges Require COVID-19 Vaccination — Why Don't They All?	Il ruolo dei giovani adulti nella pandemia di COVID-19 e l'importanza della vaccinazione in questa fascia d'età discussi dall'infettivologo Paul Sax (Massachussets General Hospital).	Ever since the pandemic started, carefully done epidemiologic studies consistently show that older teens and young adults have the highest incidence of infection. This fact might be counterintuitive, since older people bear the disproportionate share of severe disease. As a result, the media quite regularly gets it wrong, by reporting each time when cases surge anew that "this time it's different — it's young adults."

observations/index.php/some-colleges-require-covid-19-vaccination-why-dont-they-all/2021/05/03/			
Chou SH et al Annals of Internal Medicine https://www.acpjournals.org/doi/full/10.7326/M21-0409?rfr_dat=cr_pub++0pubmed&url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org	Factors Associated With Risk for Care Escalation Among Patients With COVID-19 Receiving Home-Based Hospital Care.	Tra i pazienti gestiti a domicilio per infezione da SARS-CoV-2, il numero delle comorbidità e l'interessamento polmonare più esteso sono alla base della necessità di ricovero ospedaliero (1 paziente su 5 in questa casistica).	Background: The COVID-19 pandemic, which has resulted in more than 142 million cases globally, has challenged health care systems to rapidly transform care to address complex and dynamic resource demands. Early in the pandemic, our large integrated health system implemented the Atrium Health Hospital at Home (AH-HaH) program to deliver home-based, hospital-level care to patients with COVID-19 and increase the health system's bed capacity. Objective: To determine which AH-HaH patients were at increased risk for care escalation to traditional brick-and-mortar facilities.  Figure. Forest plot of the associations between patient characteristics at Hospital at Home admission and transfer to a brick-and-mortar facility within 14 days.

Ong DSY et al Clinical Microbiology and Infection https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00221-4/fulltext	How to interpret and use COVID-19 serology and immunology tests.	Revisione dei lavori sull'utilizzo diagnostico della sierologia per SARS-CoV-2.	BACKGROUND: Although molecular tests are considered the gold standard for coronavirus disease 2019 (COVID-19) diagnostics, serological and immunological tests may be useful in specific settings. OBJECTIVES: This review summarises the underlying principles and performance of COVID-19 serological and immunological testing. SOURCES: Selected peer-reviewed publications on COVID-19 related serology and immunology published between December 2019 and March 2021. CONTENT: Serological tests are highly specific but heterogeneous in their sensitivity for the diagnosis of COVID-19. For certain indications, including delayed disease presentations, serological tests can have added value. The presence of antibodies against SARS-CoV-2 may indicate a recent or past COVID-19 infection. Lateral flow immunoassay (LFIA) antibody tests have the advantages of being easy and fast to perform, but many have a low sensitivity in acute settings. Enzyme-linked immunosorbent assay (ELISA) and chemiluminescence immunoassays (CLIA) have higher sensitivities. Besides humoral immunity, cellular immunity is also essential for successful host defences against viruses. Enzyme-linked immunospot (ELISpot) assays can be used to measure T-cell responses against SARS-CoV-2. The presence of cross-reactive SARS-CoV-2-specific T-cells in never exposed patients suggests the possibility of cellular immunity induced by other circulating coronaviruses. T-cell responses against SARS-CoV-2 have also been detected in recovered COVID-19 patients with no detectable antibodies. IMPLICATIONS: Serological and immunological tests are primarily applied for population-based seroprevalence studies to evaluate the effectiveness of COVID-19 control measures and increase our understanding of the immunology behind COVID-19. Combining molecular diagnostics with serological tests may

			optimise the detection of COVID-19. As not all infected patients will develop antibodies against SARS-CoV-2, assessment of cellular immunity may provide complementary information on whether a patient has been previously infected with COVID-19. More studies are needed to understand the correlations of these serological and immunological parameters with protective immunity, taking into account the different circulating virus variants.
Bhatt PR et al Science https://science.sciencemag.org/content/early/2021/05/12/science.abf3546	Structural basis of ribosomal frameshifting during translation of the SARS-CoV-2 RNA genome	Fotografia di un ribosoma che traduce l'RNA messaggero di SARS-CoV-2 producendo proteine diverse a partire dallo stesso mRNA, processo noto come frameshifting, che potrebbe essere bersaglio della terapia antivirale.	Programmed ribosomal frameshifting is a key event during translation of the SARS-CoV-2 RNA genome allowing synthesis of the viral RNA-dependent RNA polymerase and downstream proteins. Here we present the cryo-electron microscopy structure of a translating mammalian ribosome primed for frameshifting on the viral RNA. The viral RNA adopts a pseudoknot structure that lodges at the entry to the ribosomal mRNA channel to generate tension in the mRNA and promote frameshifting, whereas the nascent viral polyprotein forms distinct interactions with the ribosomal tunnel. Biochemical experiments validate the structural observations and reveal mechanistic and regulatory features that influence frameshifting efficiency. Finally, we compare compounds previously shown to reduce frameshifting with respect to their ability to inhibit SARS-CoV-2 replication, establishing coronavirus frameshifting as a target for antiviral intervention.
Alpert T et al Cell https://www.cell.com/cell/fulltext/S0092-8674(21)00434-7	Early introductions and transmission of SARS-CoV-2 variant B.1.1.7 in the United States	Ricostruzione dell'introduzione della variante « inglese » di SARS-CoV-2 negli USA.	The emergence and spread of SARS-CoV-2 lineage B.1.1.7, first detected in the United Kingdom, has become a global public health concern because of its increased transmissibility. Over 2,500 COVID-19 cases associated with this variant have been detected in the United States (US) since December 2020, but the extent of establishment is relatively unknown. Using travel, genomic, and diagnostic data, we highlight that the primary ports of entry for B.1.1.7 in the US were in New York, California, and Florida.

			Furthermore, we found evidence for many independent B.1.1.7 establishments starting in early December 2020, followed by interstate spread by the end of the month. Finally, we project that B.1.1.7 will be the dominant lineage in many states by mid- to late March. Thus, genomic surveillance for B.1.1.7 and other variants urgently needs to be enhanced to better inform the public health response. 

Bertuzzi AF et al British Journal of Cancer – Nature https://www.nature.com/articles/s41416-021-01396-9	Impact of active cancer on COVID-19 survival: a matched-analysis on 557 consecutive patients at an Academic Hospital in Lombardy, Italy	In una coorte di 557 pazienti con COVID-19, di cui 46 con neoplasia attiva, la mortalità è quasi doppia in questi ultimi indipendentemente dalle altre comorbidità.	Background : The impact of active cancer in COVID-19 patients is poorly defined; however, most studies showed a poorer outcome in cancer patients compared to the general population. Methods : We analysed clinical data from 557 consecutive COVID-19 patients. Uni-multivariable analysis was performed to identify prognostic factors of COVID-19 survival; propensity score matching was used to estimate the impact of cancer. Results : Of 557 consecutive COVID-19 patients, 46 had active cancer (8%). Comorbidities included diabetes (n = 137, 25%), hypertension (n = 284, 51%), coronary artery disease (n = 114, 20%) and dyslipidaemia (n = 122, 22%). Oncologic patients were older (mean age 71 vs 65, p = 0.012), more often smokers (20% vs 8%, p = 0.009), with higher neutrophil-to-lymphocyte ratio (13.3 vs 8.2, p = 0.046). Fatality rate was 50% (CI 95%: 34.9;65.1) in cancer patients and 20.2% (CI 95%: 16.8;23.9) in the non-oncologic population. Multivariable analysis showed active cancer (HRactive: 2.26, p = 0.001), age (HRage>65years: 1.08, p < 0.001), as well as lactate dehydrogenase (HRLDH>248mU/mL: 2.42, p = 0.007), PaO2/FiO2 (HRcontinuous: 1.00, p < 0.001), procalcitonin (HRPCT>0.5ng/mL: 2.21, p < 0.001), coronary artery disease (HRyes: 1.67, p = 0.010), cigarette smoking (HRyes: 1.65, p = 0.041) to be independent statistically significant predictors of outcome. Propensity score matching showed a 1.92× risk of death in active cancer patients compared to non-oncologic patients (p = 0.013), adjusted for ICU-related bias. We observed a median OS of 14 days for cancer patients vs 35 days for other patients. Conclusion : A near-doubled death rate between cancer and non-cancer COVID-19 patients was reported. Active cancer has a negative impact on clinical outcome regardless of pre-existing clinical comorbidities.

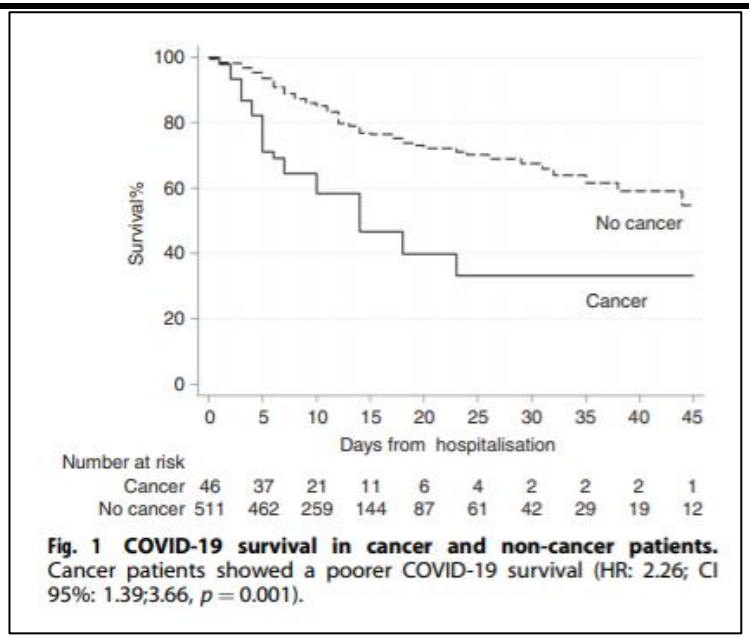
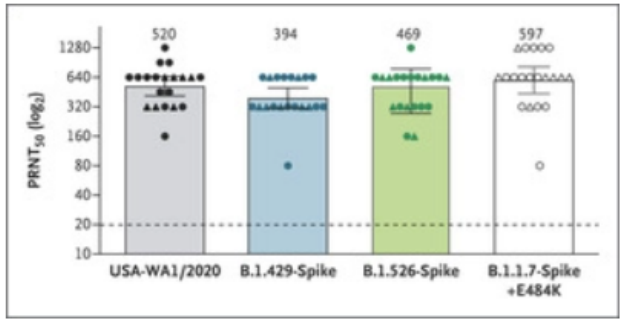
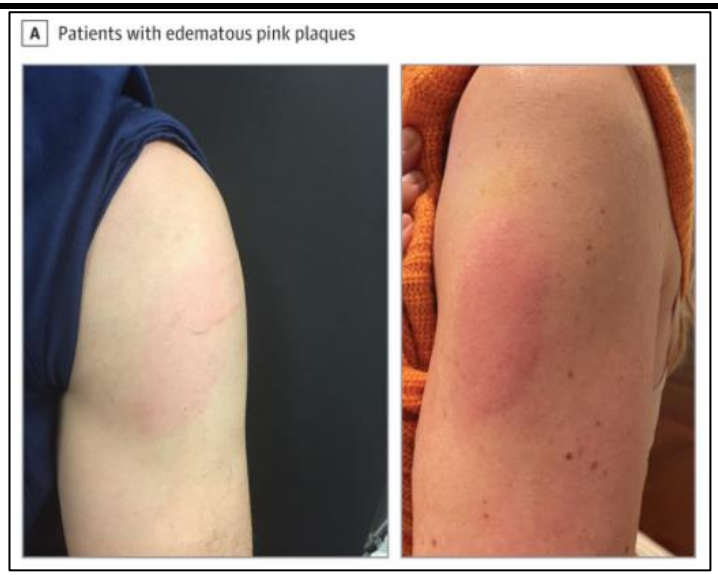
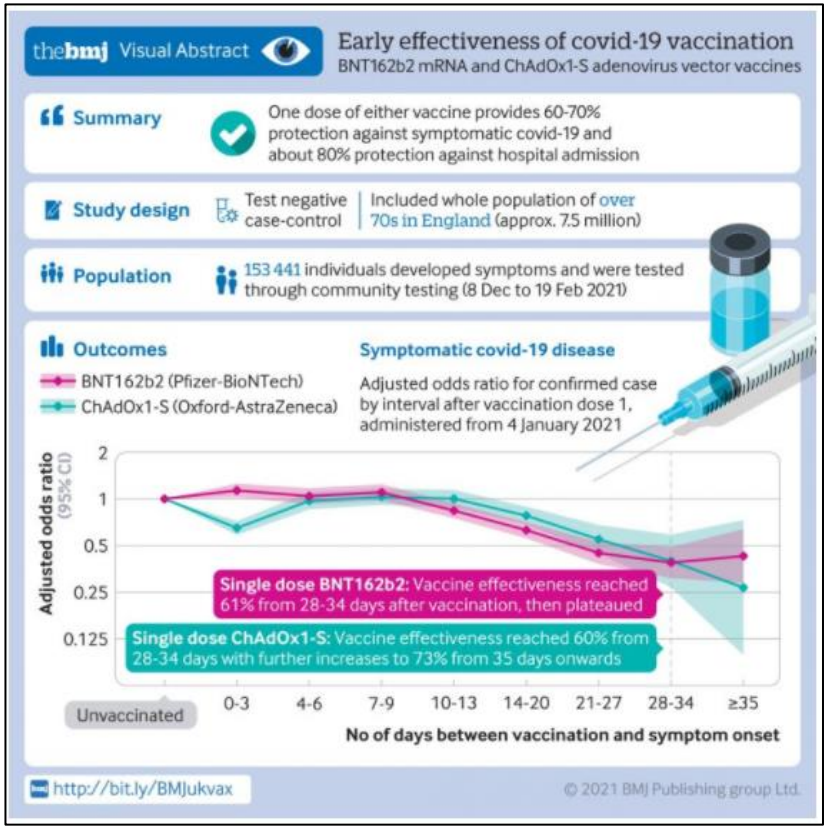
			 **Fig. 1 COVID-19 survival in cancer and non-cancer patients.** Cancer patients showed a poorer COVID-19 survival (HR: 2.26; CI 95%: 1.39;3.66, $p = 0.001$).
Liu Y et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMc2106083?query=featured_home	BNT162b2-Elicited Neutralization against New SARS-CoV-2 Spike Variants	Il siero di persone vaccinate con vaccino Pfizer contro SARS-CoV-2 neutralizza in vitro le varianti B.1.429-spike, B.1.526-spike, and B.1.1.7-spike+E484K.	All the serum samples neutralized USA-WA1/2020 and the variant viruses at titers of 1:80 or higher. The geometric mean neutralizing titers against USA-WA1/2020, B.1.429-spike, B.1.526-spike, and B.1.1.7-spike+E484K viruses were 520, 394, 469, and 597, respectively (Figure 1 and Table S1). Thus, as compared with neutralization of USA-WA1/2020, neutralization of B.1.1.7-spike+E484K and B.1.526-spike viruses was approximately equivalent, and neutralization of B.1.429-spike was slightly lower, possibly reflecting the influence of the L452R mutation, which appears to be under positive selective pressure.3 Our results suggest that, as compared with the previously reported neutralization of B.1.1.7-spike, the additional E484K mutation, which is also found in the B.1.351 and B.1.526 lineages, caused little compromise to neutralization.

			Figure 1.  Serum Neutralization of New Variant Strains of SARS-CoV-2 after Two Doses of BNT162b2 Vaccine.
Johnston MS et al JAMA https://jamanetwork.com/journals/jamadermatology/fullarticle/2779643?resultClick=1	Delayed Localized Hypersensitivity Reactions to the Moderna COVID-19 Vaccine A Case Series	Descrizione di una casistica di reazioni di ipersensibilità ritardata al vaccino MODERNA contro SARS-CoV-2, che non costituiscono una controindicazione a somministrare il richiamo.	Importance In response to the coronavirus disease 2019 (COVID-19) pandemic, 2 mRNA vaccines (Pfizer-BioNTech and Moderna) received emergency use authorization from the US Food and Drug Administration in December 2020. Some patients in the US have developed delayed localized cutaneous vaccine reactions that have been dubbed “COVID arm.” Objective To describe the course of localized cutaneous injection-site reactions to the Moderna COVID-19 vaccine, subsequent reactions to the second vaccine dose, and to characterize the findings of histopathologic examination of the reaction. Design, Setting, and Participants This retrospective case series study was performed at Yale New Haven Hospital, a tertiary medical center in New Haven, Connecticut, with 16 patients referred with localized cutaneous injection-site reactions from January 20 through February 12, 2021.

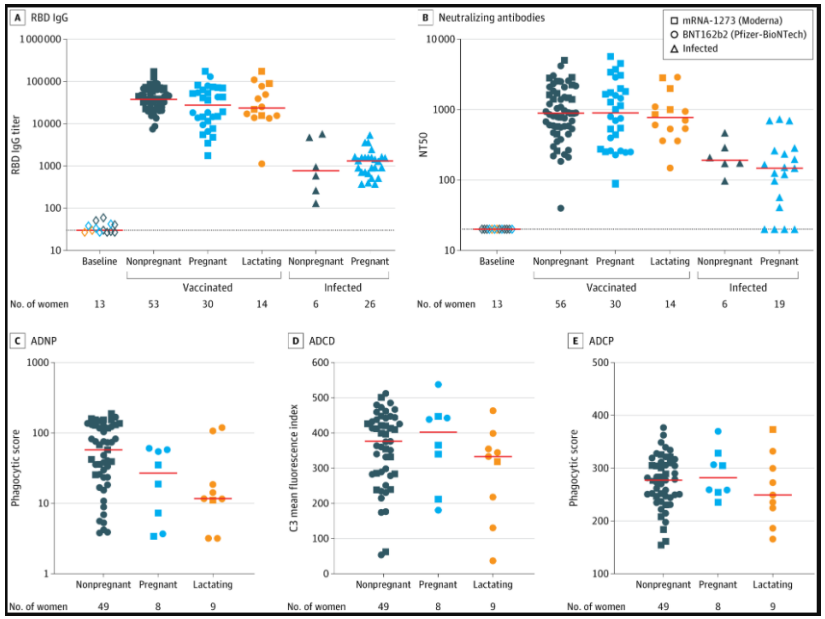
			Main Outcomes and Measures We collected each patient's demographic information, a brief relevant medical history, clinical course, and treatment (if any); and considered the findings of a histopathologic examination of 1 skin biopsy specimen. Results Of 16 patients (median [range] age, 38 [25-89] years; 13 [81%] women), 14 patients self-identified as White and 2 as Asian. The delayed localized cutaneous reactions developed in a median (range) of 7 (2-12) days after receiving the Moderna COVID-19 vaccine. These reactions occurred at or near the injection site and were described as pruritic, painful, and edematous pink plaques. None of the participants had received the Pfizer-BioNTech vaccine. Results of a skin biopsy specimen demonstrated a mild predominantly perivascular mixed infiltrate with lymphocytes and eosinophils, consistent with a dermal hypersensitivity reaction. Of participants who had a reaction to first vaccine dose (15 of 16 patients), most (11 patients) developed a similar localized injection-site reaction to the second vaccine dose; most (10 patients) also developed the second reaction sooner as compared with the first-dose reaction. Conclusions and Relevance Clinical and histopathologic findings of this case series study indicate that the localized injection-site reactions to the Moderna COVID-19 vaccine are a delayed hypersensitivity reaction. These reactions may occur sooner after the second dose, but they are self-limited and not associated with serious vaccine adverse effects. In contrast to immediate hypersensitivity reactions (eg, anaphylaxis, urticaria), these delayed reactions (dubbed "COVID arm") are not a contraindication to subsequent vaccination.

			
Lopez Bernal J et al BMJ https://www.bmj.com/content/373/bmj.n1088	Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study	Studio su oltre 156000 persone di età superiore a 70 anni in Inghilterra, in cui si valuta la prevalenza di infezioni sintomatiche da SARS-CoV-2, ospedalizzazione e morte con COVID-19 confrontando i non vaccinati con i vaccinati (Pfizer o AstraZeneca) : efficacia del 61% del vaccino BNT162b2, nei giorni 28-34 dalla vaccinazione completa, invece 73% con il ChAdOx1-	Objective To estimate the real world effectiveness of the Pfizer-BioNTech BNT162b2 and Oxford-AstraZeneca ChAdOx1-S vaccines against confirmed covid-19 symptoms (including the UK variant of concern B.1.1.7), admissions to hospital, and deaths. Design Test negative case-control study. Setting Community testing for covid-19 in England. Participants 156 930 adults aged 70 years and older who reported symptoms of covid-19 between 8 December 2020 and 19 February 2021 and were successfully linked to vaccination data in the National Immunisation Management System. Interventions Vaccination with BNT162b2 or ChAdOx1-S. Main outcome measures Primary outcomes were polymerase chain reaction confirmed symptomatic SARS-CoV-2 infections, admissions to hospital for covid-19, and deaths with covid-19. Results Participants aged 80 years and older vaccinated with BNT162b2 before 4 January 2021 had a higher odds of testing

		S a partire dal giorno 35. Con Pfizer, riduzione del 43% del rischio di ospedalizzazione urgente (37% per Astrazeneca) e del 51% del rischio di morte (non valutabile per Astrazeneca per follow up troppo breve).	positive for covid-19 in the first nine days after vaccination (odds ratio up to 1.48, 95% confidence interval 1.23 to 1.77), indicating that those initially targeted had a higher underlying risk of infection. Vaccine effectiveness was therefore compared with the baseline post-vaccination period. Vaccine effects were noted 10 to 13 days after vaccination, reaching a vaccine effectiveness of 70% (95% confidence interval 59% to 78%), then plateauing. From 14 days after the second dose a vaccination effectiveness of 89% (85% to 93%) was found compared with the increased baseline risk. Participants aged 70 years and older vaccinated from 4 January (when ChAdOx1-S delivery commenced) had a similar underlying risk of covid-19 to unvaccinated individuals. With BNT162b2, vaccine effectiveness reached 61% (51% to 69%) from 28 to 34 days after vaccination, then plateaued. With ChAdOx1-S, effects were seen from 14 to 20 days after vaccination, reaching an effectiveness of 60% (41% to 73%) from 28 to 34 days, increasing to 73% (27% to 90%) from day 35 onwards. On top of the protection against symptomatic disease, a further 43% (33% to 52%) reduced risk of emergency hospital admission and 51% (37% to 62%) reduced risk of death was observed in those who had received one dose of BNT162b2. Participants who had received one dose of ChAdOx1-S had a further 37% (3% to 59%) reduced risk of emergency hospital admission. Follow-up was insufficient to assess the effect of ChAdOx1-S on mortality. Combined with the effect against symptomatic disease, a single dose of either vaccine was about 80% effective at preventing admission to hospital with covid-19 and a single dose of BNT162b2 was 85% effective at preventing death with covid-19. Conclusion Vaccination with either one dose of BNT162b2 or ChAdOx1-S was associated with a significant reduction in

			symptomatic covid-19 in older adults, and with further protection against severe disease. Both vaccines showed similar effects. Protection was maintained for the duration of follow-up (>6 weeks). A second dose of BNT162b2 was associated with further protection against symptomatic disease. A clear effect of the vaccines against the B.1.1.7 variant was found. 
Collier AY et al JAMA	Immunogenicity of COVID-19 mRNA Vaccines in Pregnant and Lactating Women	I vaccini a mRNA contro SARS-CoV-2 sono immunogeni in questa piccola coorte di 30 donne	Importance Pregnant women are at increased risk of morbidity and mortality from COVID-19 but have been excluded from the phase 3 COVID-19 vaccine trials. Data on vaccine safety and immunogenicity in these populations are therefore limited.

https://jamanetwork.com/journals/jama/fullarticle/2780202		in gravidanza e 16 in allattamento ; inoltre gli anticorpi prodotti si trovano nel sangue cordonale e nel latte materno.	Objective To evaluate the immunogenicity of COVID-19 messenger RNA (mRNA) vaccines in pregnant and lactating women, including against emerging SARS-CoV-2 variants of concern. Design, Setting, and Participants An exploratory, descriptive, prospective cohort study enrolled 103 women who received a COVID-19 vaccine from December 2020 through March 2021 and 28 women who had confirmed SARS-CoV-2 infection from April 2020 through March 2021 (the last follow-up date was March 26, 2021). This study enrolled 30 pregnant, 16 lactating, and 57 neither pregnant nor lactating women who received either the mRNA-1273 (Moderna) or BNT162b2 (Pfizer-BioNTech) COVID-19 vaccines and 22 pregnant and 6 nonpregnant unvaccinated women with SARS-CoV-2 infection. Main Outcomes and Measures SARS-CoV-2 receptor binding domain binding, neutralizing, and functional nonneutralizing antibody responses from pregnant, lactating, and nonpregnant women were assessed following vaccination. Spike-specific T-cell responses were evaluated using IFN-γ enzyme-linked immunospot and multiparameter intracellular cytokine–staining assays. Humoral and cellular immune responses were determined against the original SARS-CoV-2 USA-WA1/2020 strain as well as against the B.1.1.7 and B.1.351 variants. Results This study enrolled 103 women aged 18 to 45 years (66% non-Hispanic White) who received a COVID-19 mRNA vaccine. After the second vaccine dose, fever was reported in 4 pregnant women (14%; SD, 6%), 7 lactating women (44%; SD, 12%), and 27 nonpregnant women (52%; SD, 7%). Binding, neutralizing, and functional nonneutralizing antibody responses as well as CD4 and CD8 T-cell responses were present in pregnant, lactating, and nonpregnant women following vaccination. Binding and neutralizing

			antibodies were also observed in infant cord blood and breast milk. Binding and neutralizing antibody titers against the SARS-CoV-2 B.1.1.7 and B.1.351 variants of concern were reduced, but T-cell responses were preserved against viral variants. Conclusion and Relevance In this exploratory analysis of a convenience sample, receipt of a COVID-19 mRNA vaccine was immunogenic in pregnant women, and vaccine-elicited antibodies were transported to infant cord blood and breast milk. Pregnant and nonpregnant women who were vaccinated developed cross-reactive antibody responses and T-cell responses against SARS-CoV-2 variants of concern. 
Simpson AN et al JAMA	Perinatal Outcomes During the COVID-19 Pandemic in Ontario, Canada	Le nascite pretermine e di neonati morti non sono aumentate durante la prima « ondata » di pandemia di	We performed a population-based cohort study in Ontario, Canada, using linked databases at ICES (formerly Institute for Clinical Evaluative Sciences). Data use without consent is authorized under section 45 of Ontario's Personal Health Information Protection Act;

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<td>https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2779783</td>
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<td>COVID-19 secondo questo studio condotto in Ontario.</td>
<td>thus, review by a research ethics board was not required. We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting in epidemiology guideline.
Table. Multivariable Generalized Estimating Equation Logistic Regression Analyses to Determine the Odds of Adverse Perinatal Outcomes During the Pandemic Period Compared With the Historical Period
Table. Multivariable Generalized Estimating Equation Logistic Regression Analyses to Determine the Odds of Adverse Perinatal Outcomes During the Pandemic Period Compared With the Historical Period
<table><tr><th rowspan="2">Outcome</th><th colspan="2">Births, No. (%)</th><th colspan="2">OR (95% CI)</th></tr><tr><th>Pandemic group (n = 67 747)</th><th>Historical group (n = 348 633)</th><th>Unadjusted</th><th>Adjusted[a]</th></tr><tr><td>Preterm birth (<37 wk GA)</td><td>5103 (7.5)</td><td>26 216 (7.5)</td><td>1.00 (0.95-1.04)</td><td>0.99 (0.97-1.03)</td></tr><tr><td>Stillbirth</td><td>347 (0.5)</td><td>1799 (0.5)</td><td>0.99 (0.89-1.11)</td><td>0.99 (0.89-1.11)</td></tr><tr><td>Extreme preterm birth (<28 wk GA)</td><td>406 (0.6)</td><td>2254 (0.6)</td><td>0.90 (0.78-1.04)</td><td>0.91 (0.80-1.03)</td></tr><tr><td>Very preterm birth (<32 wk GA)</td><td>807 (1.2)</td><td>4531 (1.3)</td><td>0.89 (0.80-0.99)[b]</td><td>0.91 (0.85-0.98)[b]</td></tr><tr><td>Severe small for GA</td><td>3826 (5.6)</td><td>19 225 (5.5)</td><td>1.02 (0.98-1.07)</td><td>1.02 (0.98-1.08)</td></tr><tr><td>Neonatal intensive care unit admission</td><td>8526 (12.6)</td><td>43 049 (12.3)</td><td>1.01 (0.93-1.10)</td><td>1.01 (0.94-1.08)</td></tr><tr><td>Neonatal death</td><td></td><td></td><td></td><td></td></tr><tr><td>Early</td><td>83 (0.1)</td><td>539 (0.2)</td><td>0.75 (0.50-1.14)</td><td>0.77 (0.51-1.15)</td></tr><tr><td>Late</td><td>30 (0.0)</td><td>165 (0.0)</td><td>0.91 (0.52-1.60)</td><td>0.96 (0.61-1.51)</td></tr></table>Abbreviations: GA, gestational age; OR, odds ratio.
[a] Adjusted analysis included the following variables: maternal age at index birth (continuous), parity (number of births ≥20 weeks' GA, continuous), singleton vs multiple birth (binary), Aggregated Diagnosis Groups score (continuous), income quintile (categorical, with 1 as the lowest and 5 as the highest), rural residence (binary, urban vs rural), preexisting hypertension (binary), preexisting diabetes (binary), pregnancy conceived with assisted reproductive technology (binary), short interbirth interval (<18 months, binary), and history of preterm birth (binary).
[b] Denotes significance. Observations with missing variables were excluded from the model.</td>
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<td>Chin ET et al

NEJM

https://www.nejm.org/doi/full/10.1056/NEJMc2105282?query=featured_home</td>
<td>Covid-19 Vaccine Acceptance in California State Prisons</td>
<td>Accettazione (scarsa nei giovani afroamericani, anche se reversibile con il counselling) della vaccinazione contro SARS-CoV-2 fra i detenuti negli USA.</td>
<td>Most of the residents who were offered vaccines in the first 10 weeks of this program accepted, and the percentages of older and more medically vulnerable residents who accepted are similar to those reported in long-term care facilities. However, acceptance was markedly lower among residents at low risk for severe illness from Covid-19 and among non-Hispanic minorities, especially Black residents. Fewer than half of young, Black residents accepted at least one dose, a finding that may reflect mistrust in correctional authorities and clinicians or a lack of access to reliable information on vaccine safety and efficacy. However, an encouraging finding was that a substantial proportion of residents who had initially declined a first dose later accepted a reoffer — an important indication that hesitancy is not necessarily fixed.</td>
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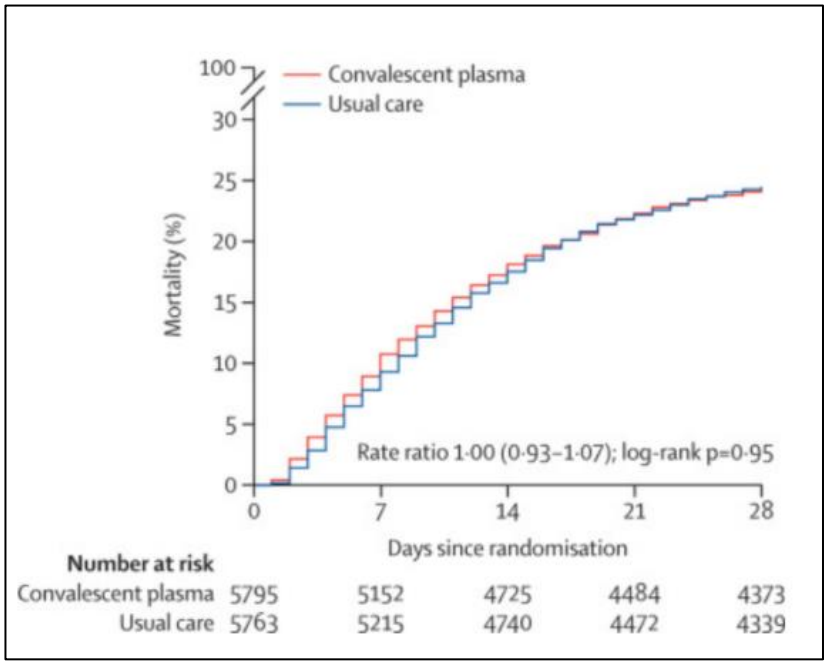
The Centers for Disease Control and Prevention https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated-guidance.html	Guidance for Fully Vaccinated People	Negli USA, le persone vaccinate con un ciclo completo contro SARS-CoV-2 possono smettere di applicare le norme di distanziamento sociale e di indossare la mascherina e non devono essere testate dopo contato con un caso di infezione, salvo contesti particolari. Un forte incentivo alla vaccinazione da parte dei CDC.	Update that fully vaccinated people no longer need to wear a mask or physically distance in any setting, except where required by federal, state, local, tribal, or territorial laws, rules, and regulations, including local business and workplace guidance Update that fully vaccinated people can refrain from testing following a known exposure unless they are residents or employees of a correctional or detention facility or a homeless shelter
Romero-Brufau S et al BMJ https://www.bmj.com/content/373/bmj.n1087	Public health impact of delaying second dose of BNT162b2 or mRNA-1273 covid-19 vaccine: simulation agent based modeling study	Simulazione dell'effetto di ritardare la seconda dose di vaccini contro SARS-CoV-2, vaccinado più persone con la prima dose : nei soggetti di età inferiore a 65 anni la mortalità per il virus sarebbe ridotta.	Objective To estimate population health outcomes with delayed second dose versus standard schedule of SARS-CoV-2 mRNA vaccination. Design Simulation agent based modeling study. Setting Simulated population based on real world US county. Participants The simulation included 100 000 agents, with a representative distribution of demographics and occupations. Networks of contacts were established to simulate potentially infectious interactions though occupation, household, and random interactions. Interventions Simulation of standard covid-19 vaccination versus delayed second dose vaccination prioritizing the first dose. The simulation runs were replicated 10 times. Sensitivity analyses included first dose vaccine efficacy of 50%, 60%, 70%, 80%, and 90% after day 12 post-vaccination; vaccination rate of 0.1%, 0.3%, and 1% of population per day; assuming the vaccine prevents only symptoms but not asymptomatic spread (that is, non-sterilizing vaccine); and an alternative vaccination strategy that implements

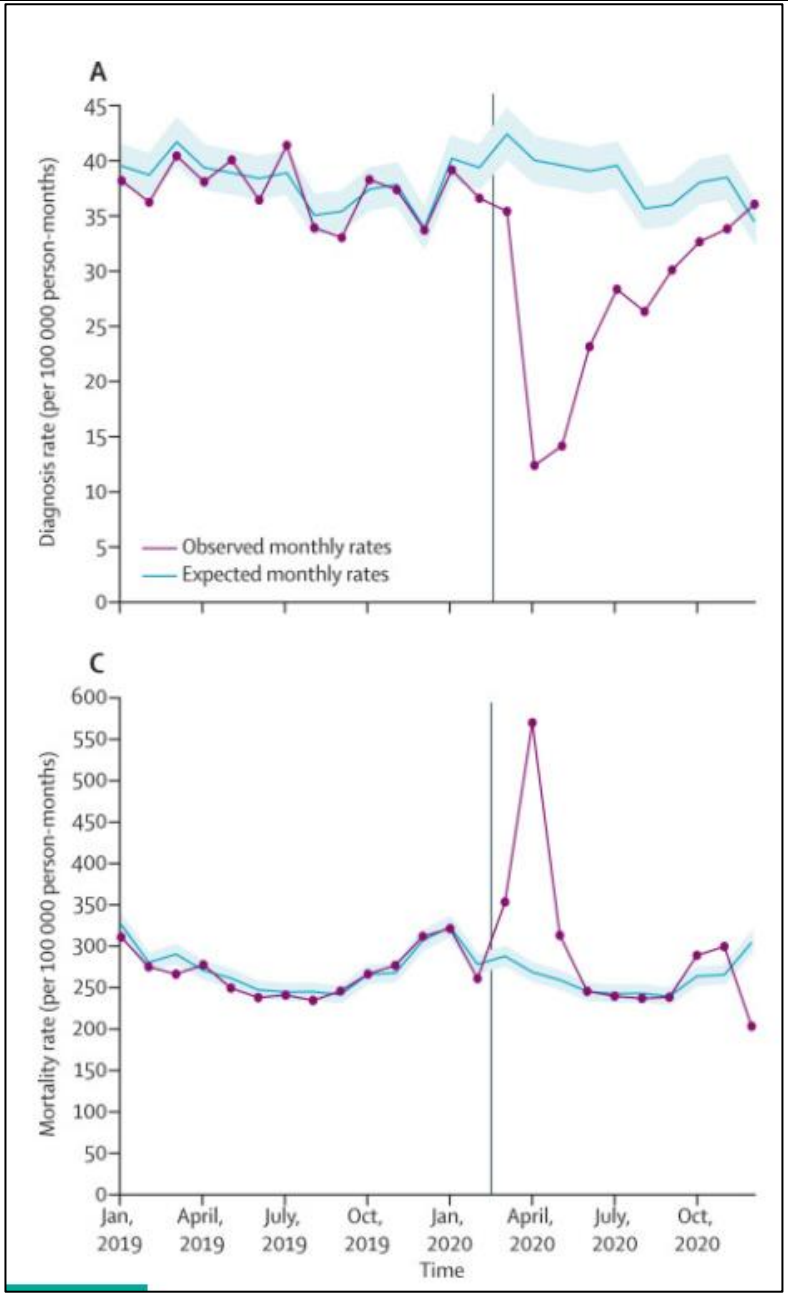
			delayed second dose for people under 65 years of age, but not until all those above this age have been vaccinated. Main outcome measures Cumulative covid-19 mortality, cumulative SARS-CoV-2 infections, and cumulative hospital admissions due to covid-19 over 180 days. Results Over all simulation replications, the median cumulative mortality per 100 000 for standard dosing versus delayed second dose was 226 v 179, 233 v 207, and 235 v 236 for 90%, 80%, and 70% first dose efficacy, respectively. The delayed second dose strategy was optimal for vaccine efficacies at or above 80% and vaccination rates at or below 0.3% of the population per day, under both sterilizing and non-sterilizing vaccine assumptions, resulting in absolute cumulative mortality reductions between 26 and 47 per 100 000. The delayed second dose strategy for people under 65 performed consistently well under all vaccination rates tested. Conclusions A delayed second dose vaccination strategy, at least for people aged under 65, could result in reduced cumulative mortality under certain conditions.
Decaro N et al Emerging Infectious Diseases https://pubmed.ncbi.nlm.nih.gov/33979566/	Possible Human-to-Dog Transmission of SARS-CoV-2, Italy, 2020	Stesso virus SARS-CoV-2 in un cane e nei membri della famiglia cui appartiene, a indicare una possibile trasmissione.	We detected severe acute respiratory syndrome coronavirus 2 in an otherwise healthy poodle living with 4 family members who had coronavirus disease. We observed antibodies in serum samples taken from the dog, indicating seroconversion. Full-length genome sequencing showed that the canine and human viruses were identical, suggesting human-to-animal transmission.
Colitti B et L Emerging Infectious Diseases	Cross-sectional serosurvey of companion animals housed with SARS-CoV-2–infected owners, Italy	Il 20% dei gatti e il 3% dei cani che vivevano con persone con infezione da SARS-CoV-2 in questa casistica hanno a propria	We conducted a serologic survey among dogs and cats in Italy to detect antibodies against severe acute respiratory syndrome virus 2 (SARS-CoV-2). We found that SARS-CoV-2 seroprevalence was higher among cats (16.2%) than dogs (2.3%). In addition,

https://wwwnc.cdc.gov/eid/article/27/7/20-3314_article		volta sierologia positiva. Non si può stabilire la direzione della trasmissione tra uomo e animale.	seroprevalence was higher among animals living in close contact with SARS-CoV-2–positive owners.
RECOVERY Collaborative Group https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00897-7/fulltext	Convalescent plasma in patients admitted to hospital with COVID-19 (RECOVERY): a randomised controlled, open-label, platform trial.	Il plasma di soggetti guariti non migliora l'outcome di COVID-19, nemmeno se ad alto titolo, nemmeno in base alla durata dei sintomi o l'entità di ossigenoterapia necessaria.	Background : Many patients with COVID-19 have been treated with plasma containing anti-SARS-CoV-2 antibodies. We aimed to evaluate the safety and efficacy of convalescent plasma therapy in patients admitted to hospital with COVID-19. Methods : This randomised, controlled, open-label, platform trial (Randomised Evaluation of COVID-19 Therapy [RECOVERY]) is assessing several possible treatments in patients hospitalised with COVID-19 in the UK. The trial is underway at 177 NHS hospitals from across the UK. Eligible and consenting patients were randomly assigned (1:1) to receive either usual care alone (usual care group) or usual care plus high-titre convalescent plasma (convalescent plasma group). The primary outcome was 28-day mortality, analysed on an intention-to-treat basis. The trial is registered with ISRCTN, 50189673, and ClinicalTrials.gov, NCT04381936. Findings : Between May 28, 2020, and Jan 15, 2021, 11558 (71%) of 16287 patients enrolled in RECOVERY were eligible to receive convalescent plasma and were assigned to either the convalescent plasma group or the usual care group. There was no significant difference in 28-day mortality between the two groups: 1399 (24%) of 5795 patients in the convalescent plasma group and 1408 (24%) of 5763 patients in the usual care group died within 28 days (rate ratio 1·00, 95% CI 0·93–1·07; p=0·95). The 28-day mortality rate ratio was similar in all prespecified subgroups of patients, including in those patients without detectable SARS-CoV-2 antibodies at randomisation. Allocation to convalescent plasma had no significant effect on the proportion of patients discharged from hospital within

			28 days (3832 [66%] patients in the convalescent plasma group vs 3822 [66%] patients in the usual care group; rate ratio 0·99, 95% CI 0·94–1·03; p=0·57). Among those not on invasive mechanical ventilation at randomisation, there was no significant difference in the proportion of patients meeting the composite endpoint of progression to invasive mechanical ventilation or death (1568 [29%] of 5493 patients in the convalescent plasma group vs 1568 [29%] of 5448 patients in the usual care group; rate ratio 0·99, 95% CI 0·93–1·05; p=0·79). Interpretation : In patients hospitalised with COVID-19, high-titre convalescent plasma did not improve survival or other prespecified clinical outcomes. 

Moreno GK et al CID https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab343/6274297	SARS-CoV-2 transmission in intercollegiate athletics not fully mitigated with daily antigen testing	Nessun sistema è infallibile per prevenire il contagio di un virus, ad esempio i test antigenici ripetuti non hanno impedito alcune trasmissioni in un gruppo di atleti universitari.	Background : High-frequency, rapid-turnaround SARS-CoV-2 testing continues to be proposed as a way of efficiently identifying and mitigating transmission in congregate settings. However, two SARS-CoV-2 outbreaks occurred among intercollegiate university athletic programs during the fall 2020 semester despite mandatory directly observed daily antigen testing. Methods : During the fall 2020 semester, athletes and staff in both programs were tested daily using Quidel's Sofia SARS Antigen Fluorescent Immunoassay (FIA), with positive antigen results requiring confirmatory testing with real-time reverse transcription polymerase chain reaction (RT-PCR). We used genomic sequencing to investigate transmission dynamics in these two outbreaks. Results : In Outbreak 1, 32 confirmed cases occurred within a university athletics program after the index patient attended a meeting while infectious despite a negative antigen test on the day of the meeting. Among isolates sequenced from Outbreak 1, 24 (92%) of 26 were closely related, suggesting sustained transmission following an initial introduction event. In Outbreak 2, 12 confirmed cases occurred among athletes from two university programs that faced each other in an athletic competition despite receiving negative antigen test results on the day of the competition. Sequences from both teams were closely related and distinct from viruses circulating in Team 1's community, suggesting transmission during intercollegiate competition in Team 2's community. Conclusions : These findings suggest that antigen testing alone, even when mandated and directly observed, may not be sufficient as an intervention to prevent SARS-CoV-2 outbreaks in congregate settings, and highlight the importance of supplementing serial antigen testing with appropriate mitigation strategies to prevent SARS-CoV-2 outbreak in congregate settings.

Carr J et al The Lancet https://www.thelancet.com/journals/landia/article/PIIS2213-8587(21)00116-9/fulltext	Impact of COVID-19 on diagnoses, monitoring, and mortality in people with type 2 diabetes in the UK	Meno nuove diagnosi di diabète mellito di tipo 2 rispetto all'atteso nel Regno Unito in aprile 2020, all'apice della prima ondata di pandemia.	In April 2020, the rate reduction (RR) of new diagnoses of type 2 diabetes in primary care practices in England was 0·70 (95% CI 0·68–0·71) when compared with 10-year (January, 2010 to February, 2020) historical trends (figure A), with similar reductions in other UK nations (0·68 [0·70–0·66]). Older individuals (ie, those aged 65 years and older), men, and people from deprived areas had the greatest reductions in diagnosis rates (data not shown). The reduced diagnosis rates in April were mirrored by the reduced rates of new metformin prescriptions in general practices in England when compared with 10-year historical trends (0·53 [0·51–0·55].


A
Diagnosis rate (per 100 000 person-months)
45
40
35
30
25
20
15
10
5
0
Observed monthly rates
Expected monthly rates
C
Mortality rate (per 100 000 person-months)
600
550
500
450
400
350
300
250
200
150
100
50
0
Jan, 2019
April, 2019
July, 2019
Oct, 2019
Jan, 2020
April, 2020
July, 2020
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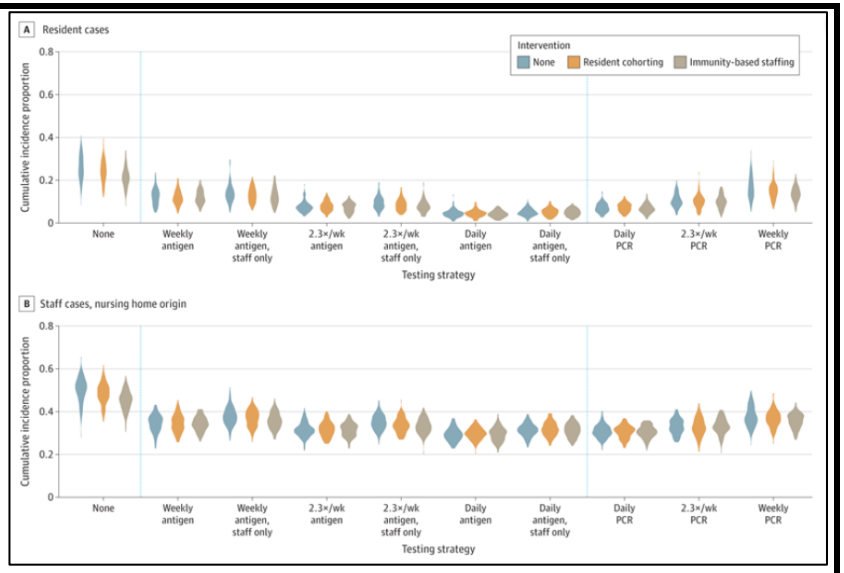
Time

Holmdahl I et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2779870	Estimation of Transmission of COVID-19 in Simulated Nursing Homes With Frequent Testing and Immunity-Based Staffing	Simulazione dell'andamento delle infezioni da SARS-CoV-2 in una casa di riposo con 100 ospiti e 100 membri dello staff : appaiare ospiti guariti e staff « suscettibile » (contando sui DPI) e viceversa ospiti suscettibili e staff immune appare la migliore strategia di prevenzione. Naturalmente la disponibilità di un test quotidiano, anche solo dello staff, ridurrebbe in modo significativo la diffusione, anche se ad un costo elevato.	Importance Nursing homes and other long-term care facilities have been disproportionately impacted by the COVID-19 pandemic. Strategies are urgently needed to reduce transmission in these high-risk populations. Objective To evaluate COVID-19 transmission in nursing homes associated with contact-targeted interventions and testing. Design, Setting, and Participants This decision analytical modeling study developed an agent-based susceptible–exposed–infectious (asymptomatic/symptomatic)–recovered model between July and September 2020 to examine SARS-CoV-2 transmission in nursing homes. Residents and staff of a simulated nursing home with 100 residents and 100 staff split among 3 shifts were modeled individually; residents were split into 2 cohorts based on COVID-19 diagnosis. Data were analyzed from September to October 2020. Exposures In the resident cohorting intervention, residents who had recovered from COVID-19 were moved back from the COVID-19 (ie, infected with SARS-CoV-2) cohort to the non–COVID-19 (ie, susceptible and uninfected with SARS-CoV-2) cohort. In the immunity-based staffing intervention, staff who had recovered from COVID-19 were assumed to have protective immunity and were assigned to work in the non–COVID-19 cohort, while susceptible staff worked in the COVID-19 cohort and were assumed to have high levels of protection from personal protective equipment. These interventions aimed to reduce the fraction of people's contacts that were presumed susceptible (and therefore potentially infected) and replaced them with recovered (immune) contacts. A secondary aim of was to evaluate cumulative incidence of SARS-CoV-2 infections associated with 2 types of screening tests (ie, rapid antigen testing and polymerase chain reaction [PCR] testing) conducted with varying frequency.

			Main Outcomes and Measures Estimated cumulative incidence proportion of SARS-CoV-2 infection after 3 months. Results Among the simulated cohort of 100 residents and 100 staff members, frequency and type of testing were associated with smaller outbreaks than the cohorting and staffing interventions. The testing strategy associated with the greatest estimated reduction in infections was daily antigen testing, which reduced the mean cumulative incidence proportion by 49% in absence of contact-targeted interventions. Under all screening testing strategies, the resident cohorting intervention and the immunity-based staffing intervention were associated with reducing the final estimated size of the outbreak among residents, with the immunity-based staffing intervention reducing it more (eg, by 19% in the absence of testing) than the resident cohorting intervention (eg, by 8% in the absence of testing). The estimated reduction in transmission associated with these interventions among staff varied by testing strategy and community prevalence. Conclusions and Relevance These findings suggest that increasing the frequency of screening testing of all residents and staff, or even staff alone, in nursing homes may reduce outbreaks in this high-risk setting. Immunity-based staffing may further reduce spread at little or no additional cost and becomes particularly important when daily testing is not feasible.

			
Drossinos Y et al Health Science Reports https://onlinelibrary.wiley.com/doi/10.1002/hsr2.275	Droplets and aerosols: An artificial dichotomy in respiratory virus transmission.	Revisione della distinzione fra trasmissione via « droplet » e « aerosol », che secondo gli autori andrebbe superata per riferirsi solo a trasmissione « aerea » in contrapposizione alla trasmissione da contatto.	In the medical literature, three mutually non-exclusive modes of pathogen transmission associated with respiratory droplets are usually identified: contact, droplet, and airborne (or aerosol) transmission. The demarcation between droplet and airborne transmission is often based on a cut-off droplet diameter, most commonly 5 mum. We argue here that the infectivity of a droplet, and consequently the transmissivity of the virus, as a function of droplet size is a continuum, depending on numerous factors (gravitational settling rate, transport, and dispersion in a turbulent air jet, viral load and viral shedding, virus inactivation) that cannot be adequately characterized by a single droplet diameter. We propose instead that droplet and aerosol transmission should be replaced by a unique airborne transmission mode, to be distinguished from contact transmission.