RICERCA BIBLIOGRAFICA COVID 19

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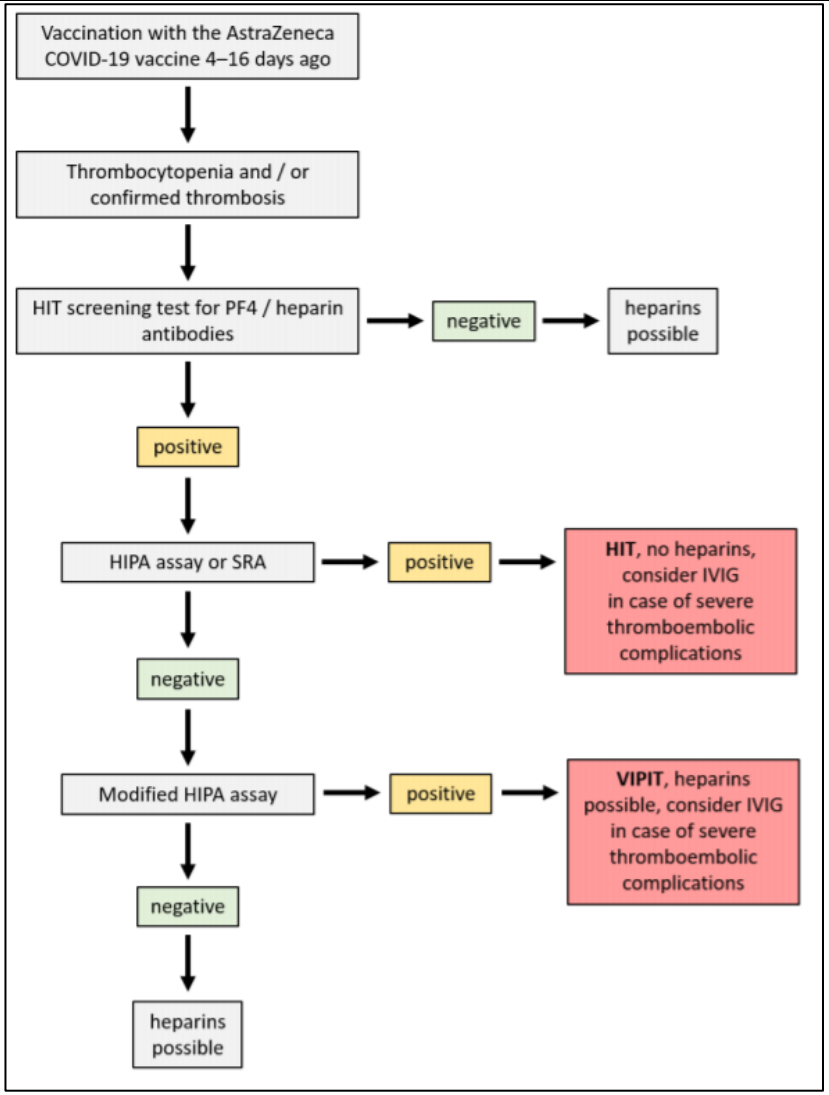
AUTORE/RIVISTA	TITOLO	OUTCOME PRINCIPALE	ABSTRACT
Greinacher A et al Preprint- not peer reviewed https://www.researchsquare.com/article/rs-362354/v1	A Prothrombotic Thrombocytopenic Disorder Resembling Heparin-Induced Thrombocytopenia Following Coronavirus-19 Vaccination	Casistica di 9 pazienti (8 donne) che hanno presentato eventi trombotici successivamente alla vaccinazione con AstraZeneca contro SARS-CoV-2 in Germania e Austria: gli autori propongono, sulla base del riscontro di un alto titolo di anticorpi anti-fattore piastrinico 4 (PF4) nei casi più gravi, un meccanismo simile a quello della trombocitopenia indotta da eparina (HIT), che spiegherebbe anche la	Background. Vaccines are important for managing the COVID-19 pandemic caused by SARS-CoV-2. However, following widespread vaccination using a recombinant adenoviral vector encoding the spike protein antigen of SARS-CoV-2 (AZD1222, AstraZeneca), reports have emerged of some vaccine recipients developing unusual thrombotic events and thrombocytopenia. We investigated whether such patients could have a prothrombotic disorder caused by platelet-activating antibodies directed against platelet factor 4 (PF4), as is known to be caused by heparin and sometimes other environmental triggers. Methods. We summarized the clinical and laboratory features of 9 patients in Germany and Austria who developed thrombosis and thrombocytopenia events following AZD1222 vaccination. Serum from four patients was used to test for anti-PF4/heparin antibodies, both by immunoassay and by platelet activation assays performed in the presence of heparin, PF4, or both.

		latenza fra vaccinazione e trombosi. L'argomento è così « scottante » che l'editor fa precedere il preprint da una nota in cui ribadisce che WHO supporta tuttora l'utilizzo del vaccino AstraZeneca.	Results. The 9 patients (8 female; median age, 36 [range, 22—49) presented with thrombosis beginning 4 to 16 days post-vaccination: 7 patients had cerebral venous thrombosis (CVT), 1 had pulmonary embolism, and 1 had splanchnic vein thrombosis and CVT; 4 patients died. None had received heparin prior to symptom onset. All four patients tested strongly positive for anti-PF4/heparin antibodies by immunoassay; all 4 patients tested strongly positive in the platelet activation assay in the presence of PF4 independently of heparin. Platelet activation was inhibited by high concentrations of heparin, Fc receptor-blocking monoclonal antibody, and intravenous immunoglobulin. Conclusions. The AZD1222 vaccine is associated with development of a prothrombotic disorder that clinically resembles heparin-induced thrombocytopenia but which shows a different serological profile. Table 2 Summary of patients presenting with prothrombotic thrombocytopenia after Coronavirus 19 vaccination in Austria (AT) and Germany (GER) February -March 2021 **Case** 1 2 3 4 5 6 7 8 9 Sex female female female female female female female female male Age, years 49 35 48 35 43 22 36 46 24 Platelet count nadir (per cubic millimeter) 13 100 31 9 23 75 29 60 11 Site of thrombosis Splanchnic vein thrombosis, aortic thrombosis, CVT PE CVT CVT CVT CVT CVT CVT CVT Onset of symptom after vaccination, days 5 10 8 4 13 7 8 14 16 Associated autoimmune disease no no no yes yes no no no no Outcome fatal recovering fatal fatal recovering recovering recovering in-hospital fatal CVT - cerebral vein thrombosis PE - pulmonary embolism

Gesellschaft für Thrombose- und Hämostaseforschung https://gth-online.org/wp-content/uploads/2021/03/GTH_Stellungnahme_AstraZeneca_engl._3_22_2021.pdf	Updated GTH statement on vaccination with the AstraZeneca COVID-19 vaccine, as of March 22, 2021	Indicazioni della Società Tedesca per la Ricerca su Trombosi ed Emostasi sull'utilizzo del vaccino AstraZeneca alla luce della possibile associazione con trombosi mediata da meccanismo simil-HIT : in caso di disturbi prolungati dopo la vaccinazione vengono proposti accertamenti finalizzati ad escludere una trombocitopenia immune pro-trombotica indotta da vaccino (VIPIT). In caso di VIPIT e trombosi clinicamente evidente, questa rispnderebbe al trattamento con immunoglobuline mentre è naturalmente controindicata l'eparina.	An important pathomechanism has been clarified within the GTH under the leadership of the Greifswald working group around Andreas Greinacher. The vaccination is likely to lead to the formation of antibodies against platelet antigens as part of the inflammatory reaction and immune stimulation. Depending on or independently of heparin, these antibodies then induce massive platelet activation via the Fc receptor in analogy to heparininduced thrombocytopenia (HIT). This mechanism (HIT mimicry) could be demonstrated in four patients with a sinus / cerebral vein thrombosis after vaccination with the AstraZeneca COVID-19 vaccine in the laboratory of Andreas Greinacher in cooperation with other GTH members. As with classical HIT, these antibodies appear 4–16 days after vaccination. This athomechanism does not rule out that the sinus / cerebral vein thromboses after vaccination with the AstraZeneca COVID-19 vaccine also have other causes.


Vaccination with the AstraZeneca COVID-19 vaccine 4–16 days ago
Thrombocytopenia and / or confirmed thrombosis
HIT screening test for PF4 / heparin antibodies
negative
heparins possible
positive
HIPA assay or SRA
positive
HIT, no heparins, consider IVIG in case of severe thromboembolic complications
negative
Modified HIPA assay
positive
VIPIT, heparins possible, consider IVIG in case of severe thromboembolic complications
negative
heparins possible

Kupferschmidt K et al Science https://www.sciencemag.org/news/2021/03/rare-clotting-disorder-may-cloud-worlds-hopes-astrazenecas-covid-19-vaccine	A rare clotting disorder may cloud the world's hopes for AstraZeneca's COVID-19 vaccine	Approfondimento dei giornalisti di Science sugli sviluppi della questione trombosi e vaccino AstraZeneca contro SARS-CoV-2.	Now, a group of researchers led by German clotting specialist Andreas Greinacher of the University of Greifswald says the highly unusual combination of symptoms—widespread blood clots and a low platelet count, sometimes with bleeding—resembles a rare side effect of the blood thinner heparin called heparin-induced thrombocytopenia (HIT).
Thompson MG et al Morbidity and Mortality Weekly Report https://www.cdc.gov/mmwr/volumes/70/wr/pdfs/mm7013e3-H.pdf	Interim Estimates of Vaccine Effectiveness of BNT162b2 and mRNA-1273 COVID-19 Vaccines in Preventing SARS-CoV-2 Infection Among Health Care Personnel, First Responders, and Other Essential and Frontline Workers — Eight U.S. Locations, December 2020–March 2021	In una coorte di 3950 tra operatori sanitari e altri lavoratori di « prima linea » sottoposti a tamponi settimanali di screening, i vaccini a mRNA contro SARS-CoV-2 (Pfizer BNT162b2 e Moderna mRNA-1273), somministrati a 2479 persone con entrambe le dosi e 477 con solo una dose, dimostrano una riduzione del rischio di infezione da SARS-CoV-2 rispetto ai non vaccinati del	What is already known about this topic? Messenger RNA (mRNA) COVID-19 vaccines have been shown to be effective in preventing symptomatic SARS-CoV-2 infection in randomized placebo-controlled Phase III trials. What is added by this report? Prospective cohorts of 3,950 health care personnel, first responders, and other essential and frontline workers completed weekly SARS-CoV-2 testing for 13 consecutive weeks. Under real-world conditions, mRNA vaccine effectiveness of full immunization (≥14 days after second dose) was 90% against SARS-CoV-2 infections regardless of symptom status; vaccine effectiveness of partial immunization (≥14 days after first dose but before second dose) was 80%. What are the implications for public health practice? Authorized mRNA COVID-19 vaccines are effective for preventing SARS-CoV-2

<table>
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<td>90% dopo 2 dosi e dell’80% dopo 1 dose.</td>
<td>infection in real-world conditions. COVID-19 vaccination is recommended for all eligible persons.
TABLE 2. Person-days, SARS-CoV-2 infections, and vaccine effectiveness among health care personnel, first responders, and other essential and frontline workers, by messenger RNA immunization status — eight U.S. locations, December 14, 2020–March 13, 2021
<table>
<tr><th></th><th></th><th colspan="2">SARS-CoV-2 infections</th><th>Unadjusted vaccine effectiveness*</th><th>Adjusted vaccine effectiveness*,†</th></tr>
<tr><th>COVID-19 immunization status</th><th>Person-days</th><th>No.</th><th>Incidence rate per 1,000 person-days</th><th>% (95% CI)</th><th>% (95% CI)</th></tr>
<tr><td>Unvaccinated</td><td>116,657</td><td>161</td><td>1.38</td><td>N/A</td><td>N/A</td></tr>
<tr><td>Partially immunized</td><td>41,856</td><td>8</td><td>0.19</td><td>82 (62–91)</td><td>80 (59–90)</td></tr>
<tr><td>≥14 days after receiving first dose only§</td><td>15,868</td><td>5</td><td>0.32</td><td></td><td></td></tr>
<tr><td>≥14 days after first dose through receipt of second dose</td><td>25,988</td><td>3</td><td>0.12</td><td></td><td></td></tr>
<tr><td>Fully immunized</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>≥14 days after second dose</td><td>78,902</td><td>3</td><td>0.04</td><td>91 (73–97)</td><td>90 (68–97)</td></tr>
</table>
Abbreviations: CI = confidence interval; N/A = not applicable.
* Vaccine effectiveness was estimated using a Cox proportional hazards model accounting for time-varying immunization status.
† Hazard ratio is adjusted for study site.
§ Participants received first dose but had not received second dose by the end of the study period.</td>
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<td>Bamidis AD et al

The Lancet

https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(21)00072-2/fulltext</td>
<td>First manifestation of adult-onset Still's disease after COVID-19</td>
<td>Caso di malattia di Still dell’adulto in paziente con storia recente di COVID-19.</td>
<td>Adult-onset Still's disease (AOSD) is a rare inflammatory disorder that usually affects young adults, with a bimodal peak at ages 15–25 years and 36–46 years. The disease is characterised by fever of more than 39°C, transient skin rash, leucocytosis, arthralgia, arthritis, or a combination of these symptoms. In addition to at least two of the aforementioned major criteria, the Yamaguchi criteria for the diagnosis of AOSD require the presence of minor criteria—ie, sore throat, lymphadenopathy, hepatomegaly or splenomegaly, abnormal liver function tests, and negative tests for antinuclear antibodies and rheumatoid factor. Infections, malignancies, and other rheumatic diseases need to be excluded. The cytokine interleukin (IL)-1 has a central role in the pathogenesis of AOSD and inhibition of IL-1β by monoclonal antibodies, and blockade of the IL-1 receptor by antagonists significantly ameliorates the disease. IL-1 drives the intense innate immune response by activating neutrophils, macrophages, and mast cells, and by leading to overexpression of several proinflammatory cytokines, including IL-6, IL-8, IL-17, IL-18, and TNF.3 Viral or bacterial infections have been proposed as potential trigger, but the exact mechanisms underlying AOSD onset remain largely unknown.4</td>
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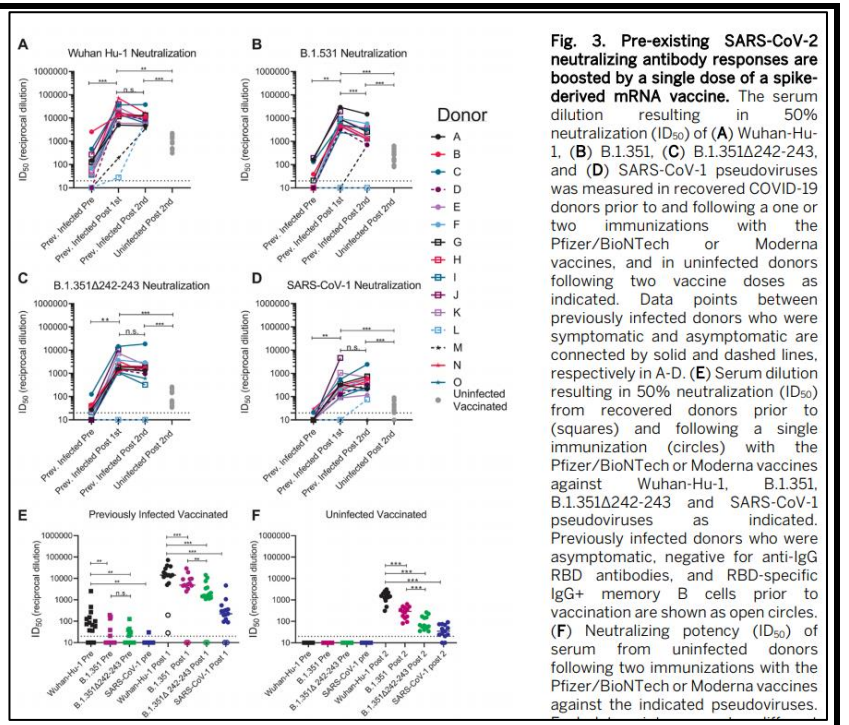
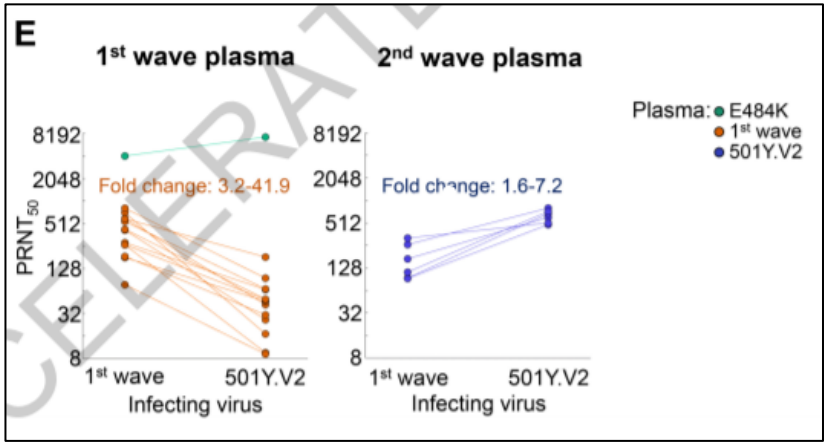
Rabagliati R et al Emerging Infectious Diseases https://wwwnc.cdc.gov/eid/article/27/5/20-4412_article	COVID-19–Associated Mold Infection in Critically Ill Patients, Chile	Sedici casi di infezione invasiva da muffe (Aspergillus, Rhizopus e Scedosporium, solo galattomannano in 8 pazienti) in corso di infezione grave da SARS-CoV-2 in immunocompetenti : da sospettare in caso di decorso complicato.	Patients with severe coronavirus disease (COVID-19) may have COVID-19–associated invasive mold infection (CAIMI) develop. We report 16 cases of CAIMI among 146 nonimmunocompromised patients with severe COVID-19 at an academic hospital in Santiago, Chile. These rates correspond to a CAIMI incidence of 11%; the mortality rate for these patients was 31.2%.
Stamatato L et al Science https://science.sciencemag.org/content/early/2021/03/24/science.abg9175	mRNA vaccination boosts cross-variant neutralizing antibodies elicited by SARS-CoV-2 infection	Il titolo anticorpale neutralizzante contro SARS-CoV-2 viene incrementato da una singola dose di vaccino a mRNA in soggetti guariti, per cui appare importante vaccinare anche i convalescenti. D'altra parte una dose ulteriore non aumenta ancora il titolo, per cui potrebbe non essere somministrata, almeno precocemente. Rimane da studiare l'andamento del titolo neutralizzante nel tempo.	Emerging SARS-CoV-2 variants have raised concerns about resistance to neutralizing antibodies elicited by previous infection or vaccination. We examined whether sera from recovered and naïve donors collected prior to, and following immunizations with existing mRNA vaccines, could neutralize the Wuhan-Hu-1 and B.1.351 variants. Pre-vaccination sera from recovered donors neutralized Wuhan-Hu-1 and sporadically neutralized B.1.351, but a single immunization boosted neutralizing titers against all variants and SARS-CoV-1 by up to 1000-fold. Neutralization was due to antibodies targeting the receptor binding domain and was not boosted by a second immunization. Immunization of naïve donors also elicited cross-neutralizing responses, but at lower titers. Our study highlights the importance of vaccinating both uninfected and previously infected persons to elicit cross-variant neutralizing antibodies.

			 **Fig. 3. Pre-existing SARS-CoV-2 neutralizing antibody responses are boosted by a single dose of a spike-derived mRNA vaccine.** The serum dilution resulting in 50% neutralization (ID_{50}) of (**A**) Wuhan-Hu-1, (**B**) B.1.351, (**C**) B.1.351Δ242-243, and (**D**) SARS-CoV-1 pseudoviruses was measured in recovered COVID-19 donors prior to and following a one or two immunizations with the Pfizer/BioNTech or Moderna vaccines, and in uninfected donors following two vaccine doses as indicated. Data points between previously infected donors who were symptomatic and asymptomatic are connected by solid and dashed lines, respectively in A-D. (**E**) Serum dilution resulting in 50% neutralization (ID_{50}) from recovered donors prior to (squares) and following a single immunization (circles) with the Pfizer/BioNTech or Moderna vaccines against Wuhan-Hu-1, B.1.351, B.1.351Δ242-243 and SARS-CoV-1 pseudoviruses as indicated. Previously infected donors who were asymptomatic, negative for anti-IgG RBD antibodies, and RBD-specific IgG+ memory B cells prior to vaccination are shown as open circles. (**F**) Neutralizing potency (ID_{50}) of serum from uninfected donors following two immunizations with the Pfizer/BioNTech or Moderna vaccines against the indicated pseudoviruses.
Cele S et al Nature https://www.nature.com/articles/s41586-021-03471-w	Escape of SARS-CoV-2 501Y.V2 from neutralization by convalescent plasma	Il plasma di soggetti guariti da COVID-19 in Sudafrica durante la seconda ondata pandemica (presenza di variante 501Y.V2, « sudafricana ») neutralizza anche il virus della prima ondata, mentre non è vero il contrario : vaccini basati sulla nuova variante dovrebbero mantenere efficacia anche sul virus non mutato.	SARS-CoV-2 variants of concern (VOC) have arisen independently at multiple locations and may reduce the efficacy of current vaccines targeting the spike glycoprotein. Here, using a live virus neutralization assay (LVNA), we compared neutralization of a non-VOC variant versus the 501Y.V2 variant using plasma collected from adults hospitalized with COVID-19 from two South African infection waves, with the second wave dominated by 501Y.V2 infections. Sequencing demonstrated that infections in first wave plasma donors were with viruses harbouring none of the 501Y.V2-defining mutations, except for one with the E484K mutation in the receptor binding domain. 501Y.V2 virus was effectively neutralized by plasma from second wave infections and first wave virus was effectively neutralized by first wave plasma. In cross-neutralization, 501Y.V2

			virus was poorly neutralized by first wave plasma, with a 15.1-fold drop relative to 501Y.V2 neutralization by second wave plasma across participants. In contrast, second wave plasma cross-neutralization of first wave virus was more effective, showing only a 2.3-fold decline relative to first wave plasma neutralization of first wave virus. While we only tested one plasma elicited by E484K alone, this potently neutralized both variants. The observed effective neutralization of first wave virus by 501Y.V2 infection elicited plasma provides preliminary evidence that vaccines based on VOC sequences could retain activity against other circulating SARS-CoV-2 lineages. 
Klein J et al medRXiv – not peer reviewed https://www.medrxiv.org/content/10.1101/2021.03.24.21253992v1	Case Study: Longitudinal immune profiling of a SARS-CoV-2 reinfection in a solid organ transplant recipient	Reinfezione da SARS-CoV-2 in un trapiantato renale sottoposto a terapia contro il rigetto acuto d'organo, di cui è stata approfonditamente studiata la risposta immunitaria.	Prior to the emergence of antigenically distinct SARS-CoV-2 variants, reinfections were reported infrequently - presumably due to the generation of durable and protective immune responses. However, case reports also suggested that rare, repeated infections may occur as soon as 48 days following initial disease onset. The underlying immunologic deficiencies enabling SARS-CoV-2 reinfections are currently unknown. Here we describe a renal transplant recipient who developed recurrent, symptomatic SARS-

			CoV-2 infection - confirmed by whole virus genome sequencing - 7 months after primary infection. To elucidate the immunological mechanisms responsible for SARS-CoV-2 reinfection, we performed longitudinal profiling of cellular and humoral responses during both primary and recurrent SARS-CoV-2 infection. We found that the patient responded to the primary infection with transient, poor-quality adaptive immune responses. The patient's immune system was further compromised by intervening treatment for acute rejection of the renal allograft prior to reinfection. Importantly, we also identified the development of neutralizing antibodies and the formation of humoral memory responses prior to SARS-CoV-2 reinfection. However, these neutralizing antibodies failed to confer protection against reinfection, suggesting that additional factors are required for efficient prevention of SARS-CoV-2 reinfection. Further, we found no evidence supporting viral evasion of primary adaptive immune responses, suggesting that susceptibility to reinfection may be determined by host factors rather than pathogen adaptation in this patient. In summary, our study suggests that a low neutralizing antibody presence alone is not sufficient to confer resistance against reinfection. Thus, patients with solid organ transplantation, or patients who are otherwise immunosuppressed, who recover from infection with SARS-CoV-2 may not develop sufficient protective immunity and are at risk of reinfection.
Tan BK et al Thorax https://thorax.bmj.com/content/early/2021/03/24/thoraxjnl-2020-215383	Arterial and venous thromboembolism in COVID-19: a study-level meta-analysis	Metanalisi sulla prevalenza di trombosi venosa profonda ed embolia polmonare nei pazienti con COVID-19 : elevata nei pazienti ricoverati in terapia intensiva, mentre è meno	Background : The prevalence of venous thromboembolic event (VTE) and arterial thromboembolic event (ATE) thromboembolic events in patients with COVID-19 remains largely unknown. Methods : In this meta-analysis, we systematically searched for observational studies describing the prevalence of VTE and ATE in COVID-19 up to 30 September 2020.

		evidente il rischio nei pazienti meno gravi.	Results : We analysed findings from 102 studies (64 503 patients). The frequency of COVID-19-related VTE was 14.7% (95% CI 12.1% to 17.6%, I2=94%; 56 studies; 16 507 patients). The overall prevalence rates of pulmonary embolism (PE) and leg deep vein thrombosis were 7.8% (95% CI 6.2% to 9.4%, I2=94%; 66 studies; 23 117 patients) and 11.2% (95% CI 8.4% to 14.3%, I2=95%; 48 studies; 13 824 patients), respectively. Few were isolated subsegmental PE. The VTE prevalence was significantly higher in intensive care unit (ICU) (23.2%, 95% CI 17.5% to 29.6%, I2=92%, vs 9.0%, 95% CI 6.9% to 11.4%, I2=95%; pinteraction<0.0001) and in series systematically screening patients compared with series testing symptomatic patients (25.2% vs 12.7%, pinteraction=0.04). The frequency rates of overall ATE, acute coronary syndrome, stroke and other ATE were 3.9% (95% CI 2.0% to to 3.0%, I2=96%; 16 studies; 7939 patients), 1.6% (95% CI 1.0% to 2.2%, I2=93%; 27 studies; 40 597 patients) and 0.9% (95% CI 0.5% to 1.5%, I2=84%; 17 studies; 20 139 patients), respectively. Metaregression and subgroup analyses failed to explain heterogeneity of overall ATE. High heterogeneity limited the value of estimates. Conclusions : Patients admitted in the ICU for severe COVID-19 had a high risk of VTE. Conversely, further studies are needed to determine the specific effects of COVID-19 on the risk of ATE or VTE in less severe forms of the disease.
Shah SA et al Thorax https://thorax.bmj.com/content/early/2021/02/04/thoraxjnl-2020-216512	Impact of COVID-19 national lockdown on asthma exacerbations: interrupted time-series analysis of English primary care data	Riduzione significativa dei ricoveri per esacerbazione di asma in Inghilterra nel periodo gennaio-agosto 2020 rispetto agli anni precedenti (2016-2019).	Background The impact of COVID-19 and ensuing national lockdown on asthma exacerbations is unclear. Methods We conducted an interrupted time-series (lockdown on 23 March 2020 as point of interruption) analysis in asthma cohort identified using a validated algorithm from a national-level primary care database, the Optimum Patient Care Database. We derived asthma exacerbation rates for every week and compared

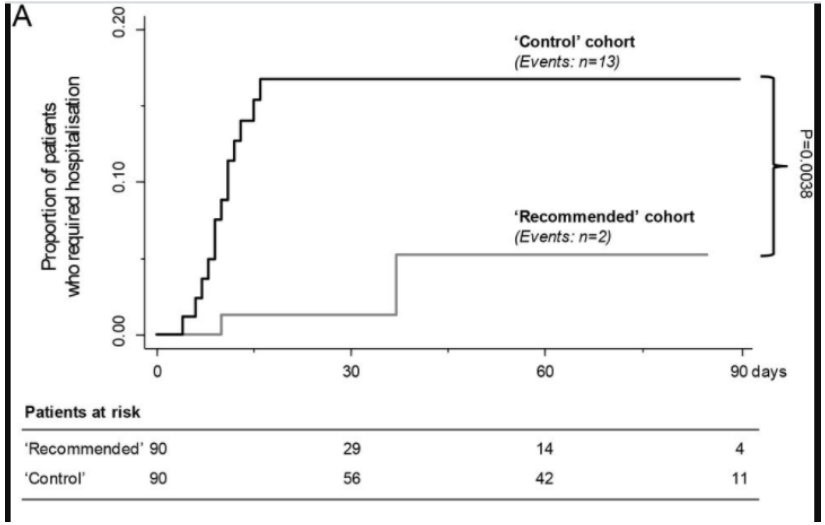
			exacerbation rates in the period: January to August 2020 with a pre-COVID-19 period and January to August 2016–2019. Exacerbations were defined as asthma-related hospital attendance/admission (including accident and emergency visit), or an acute course of oral corticosteroids with evidence of respiratory review, as recorded in primary care. We used a generalised least squares modelling approach and stratified the analyses by age, sex, English region and healthcare setting. Results From a database of 9 949 387 patients, there were 100 165 patients with asthma who experienced at least one exacerbation during 2016–2020. Of 278 996 exacerbation episodes, 49 938 (17.9%) required hospital visit. Comparing pre-lockdown to post-lockdown period, we observed a statistically significant reduction in the level (−0.196 episodes per person-year; p<0.001; almost 20 episodes for every 100 patients with asthma per year) of exacerbation rates across all patients. The reductions in level in stratified analyses were: 0.005–0.244 (healthcare setting, only those without hospital attendance/admission were significant), 0.210–0.277 (sex), 0.159–0.367 (age), 0.068–0.590 (region). Conclusions There has been a significant reduction in attendance to primary care for asthma exacerbations during the pandemic. This reduction was observed in all age groups, both sexes and across most regions in England.
Ufficio Stampa Istituto Superiore di Sanità https://www.iss.it/web/guest/primo-piano/-/asset_publisher/3f4alM	Comunicato Stampa N° 20/2021 Covid-19: in Italia la 'variante inglese' all'86,7% Il 4,0% dei casi con quella 'brasiliana'	In base al sequenziamento di campioni contenenti SARS-CoV-2 provenienti da 126 laboratori su tutto il territorio italiano, la prevalenza della variante « inglese » a metà marzo 2021 è di 86.7%, quella della	In Italia al 18 marzo scorso la prevalenza della cosiddetta 'variante inglese' del virus Sars-CoV-2 era del 86,7%, con valori oscillanti tra le singole regioni tra il 63,3% e il 100%. Per quella 'brasiliana' la prevalenza era del 4,0% (0%-32,0%), mentre le altre monitorate sono sotto lo 0,5%. La stima viene dalla nuova indagine rapida condotta dall'Iss e dal Ministero della Salute insieme ai laboratori regionali e alla Fondazione Bruno Kessler, che fa seguito a quelle

wzN1Z7/content/id/5672623		variante «brasiliana » del 4.3%.	diffuse nelle scorse settimane da cui era emersa una maggior trasmissibilità per la variante 'inglese' del 37%.
Mehta HB et al JAMA https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2777972	Risk Factors Associated With SARS-CoV-2 Infections, Hospitalization, and Mortality Among US Nursing Home Residents	Studio di coorte condotto negli USA su 482 323 persone residenti in strutture per lungodegenza, alla ricerca di fattori di rischio per infezione da SARS-CoV-2 (BMI), ospedalizzazione (BMI, etnia e stato funzionale) e morte (disabilità e decadimento cognitivo).	Importance Nursing home residents account for approximately 40% of deaths from SARS-CoV-2. Objective To identify risk factors for SARS-CoV-2 incidence, hospitalization, and mortality among nursing home residents in the US. Design, Setting, and Participants This retrospective longitudinal cohort study was conducted in long-stay residents aged 65 years or older with fee-for-service Medicare residing in 15 038 US nursing homes from April 1, 2020, to September 30, 2020. Data were analyzed from November 22, 2020, to February 10, 2021. Main Outcomes and Measures The main outcome was risk of diagnosis with SARS-CoV-2 (per International Statistical Classification of Diseases, Tenth Revision, Clinical Modification [ICD-10-CM] codes) by September 30 and hospitalization or death within 30 days after diagnosis. Three-level (resident, facility, and county) logistic regression models and competing risk models conditioned on nursing home facility were used to determine association of patient characteristics with outcomes. Results Among 482 323 long-stay residents included, the mean (SD) age was 82.7 (9.2) years, with 326 861 (67.8%) women, and 383 838 residents (79.6%) identifying as White. Among 137 119 residents (28.4%) diagnosed with SARS-CoV-2 during follow up, 29 204 residents (21.3%) were hospitalized, and 26 384 residents (19.2%) died within 30 days. Nursing homes explained 37.2% of the variation in risk of infection, while county explained 23.4%. Risk of infection increased with increasing body mass index (BMI;

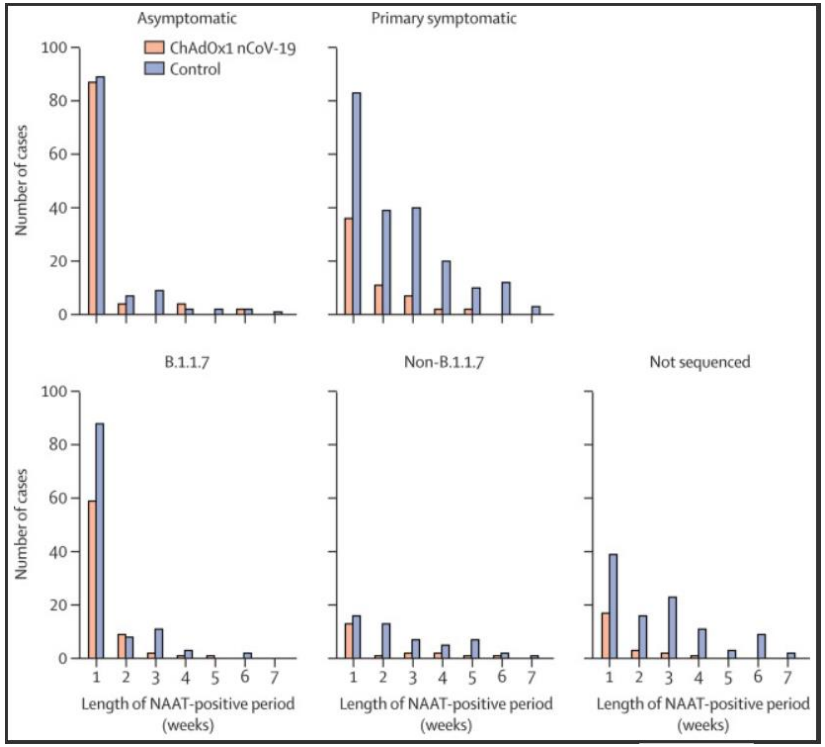
			calculated as weight in kilograms divided by height in meters squared) (eg, BMI>45 vs BMI 18.5-25: adjusted hazard ratio [aHR], 1.19; 95% CI, 1.15-1.24) but varied little by other resident characteristics. Risk of hospitalization after SARS-CoV-2 increased with increasing BMI (eg, BMI>45 vs BMI 18.5-25: aHR, 1.40; 95% CI, 1.28-1.52); male sex (aHR, 1.32; 95% CI, 1.29-1.35); Black (aHR, 1.28; 95% CI, 1.24-1.32), Hispanic (aHR, 1.20; 95% CI, 1.15-1.26), or Asian (aHR, 1.46; 95% CI, 1.36-1.57) race/ethnicity; impaired functional status (eg, severely impaired vs not impaired: aHR, 1.15; 95% CI, 1.10-1.22); and increasing comorbidities, such as renal disease (aHR, 1.21; 95% CI, 1.18-1.24) and diabetes (aHR, 1.16; 95% CI, 1.13-1.18). Risk of mortality increased with age (eg, age >90 years vs 65-70 years: aHR, 2.55; 95% CI, 2.44-2.67), impaired cognition (eg, severely impaired vs not impaired: aHR, 1.79; 95% CI, 1.71-1.86), and functional impairment (eg, severely impaired vs not impaired: aHR, 1.94; 1.83-2.05). Conclusions and Relevance These findings suggest that among long-stay nursing home residents, risk of SARS-CoV-2 infection was associated with county and facility of residence, while risk of hospitalization and death after SARS-CoV-2 infection was associated with facility and individual resident characteristics. For many resident characteristics, there were substantial differences in risk of hospitalization vs mortality. This may represent resident preferences, triaging decisions, or inadequate recognition of risk of death.
Suter F et al medRXiv – preprint, not peer reviewed	A SIMPLE, HOME-THERAPY ALGORYTHM TO PREVENT HOSPITALIZATION OF COVID-19 PATIENTS: A RETROSPECTIVE	Studio di coorte retrospettivo osservazionale dell'Istituto Mario Negri (Giuseppe Remuzzi) in cui si propone un protocollo di trattamento per i pazienti	Background Effective simple, home-treatment algorithms implemented on the basis of a pathophysiologic and pharmacologic rationale to accelerate recovery and prevent hospitalization of patients with early coronavirus disease 2019 (COVID-19) would have major implications for patients and health care providers.

https://www.medrxiv.org/content/10.1101/2021.03.25.21254296v1.full	OBSERVATIONAL MATCHED-COHORT STUDY	con infezione da SARS-CoV-2 iniziale, a domicilio : su 90 pazienti trattati fin dall'esordio dei sintomi con inibitori selettivi di COX-2 (nimesulide, celecoxib, che hanno mostrato di ridurre le citochine proinfiammatorie nel BAL in studi precedenti) e – dopo 8 giorni dall'esordio dei sintomi- anche con steroidi in più del 30% dei casi, si osserva una riduzione delle ospedalizzazioni rispetto a una coorte di controllo.	Methods This academic, matched-cohort study compared outcomes of 90 consecutive consenting patients with mild COVID-19 treated at home by their family physicians from October 2020 to January 2021 according to the proposed recommendation algorithm with those of 90 age-, sex-, and comorbidities-matched patients who received other therapeutic regimens. Primary outcome was time to resolution of major symptoms. Secondary outcomes included prevention of hospitalization. Analyses were by intention-to-treat. Findings All patients achieved complete remission. The median [IQR] time to resolution of major symptoms was 18 [14-23] days in the 'recommended' schedule cohort and 14 [7-30] days in the matched 'control' cohort (p=0·033). Minor symptoms persisted in a lower percentage of patients in the 'recommended' than in the 'control' cohort (23·3% versus 73·3%, respectively, p<0·0001) and for a shorter period (p=0·0107). Two patients in the 'recommended' cohort were hospitalized compared to 13 (14·4%) controls (Log-rank test, p=0·0038). Prevention algorithm abated the days and cumulative costs of hospitalization by >90% (from 481 to 44 days and from 296 to 28 thousand Euros, respectively. 1·2 patients had to be treated to save one hospitalization event. Interpretation Implementation of an early, home-treatment algorithm failed to accelerate recovery from major symptoms of COVID-19, but almost blunted the risk of hospitalization and related treatment costs. Evidence before this study We searched PubMed and the Cochrane Library for peer-reviewed articles published in any language up to March 19, 2021, using the search terms ("2019-nCoV" or "SARS-CoV-2" or "COVID-19") and ("early" or "outpatient" or "treatment" or "home"). Our search did not identify any randomised clinical trials or observational studies that assessed the effectiveness of

			treatment regimens targeting early mild symptoms of COVID-19 in the outpatient setting. Added value of this study In this fully academic, observational matched-cohort study, we found that early home-treatment of 90 consecutive patients with mild COVID-19 by their family physicians according to the proposed recommendation algorithm, designed on the basis of a pathophysiologic and pharmacologic rationale, significantly reduced the risk of hospitalisation compared to 90 age-, sex-, and comorbidities-matched patients who received other therapeutic regimens. Days of hospitalization and related treatment costs were reduced by more than 90%. Just 1.2 patients needed to be treated to save one hospitalization event. The 'recommended' schedule cohort required a few more days to achieve resolution of major symptoms, including fever, dyspnea, musculoskeletal pain, headache and cough compared to the 'control' cohort. Symptoms, such as anosmia and ageusia/dysgeusia, persisted less commonly and for a shorter period in the 'recommendation' than in the 'control' cohort. Implications of the available evidence The finding that the implementation of the proposed simple treatment algorithm during the initial, mild phase of COVID-19 has the potential to prevent disease progression, eventually limiting the need of hospital admission may have major implications for patients and health care providers. Indeed, preventing hospitalisations due to worsening of COVID-19 will not only save lives, but will also contribute to remarkably reduce treatment costs and to reshape health care systems that are overburdened because of the pandemic effects.

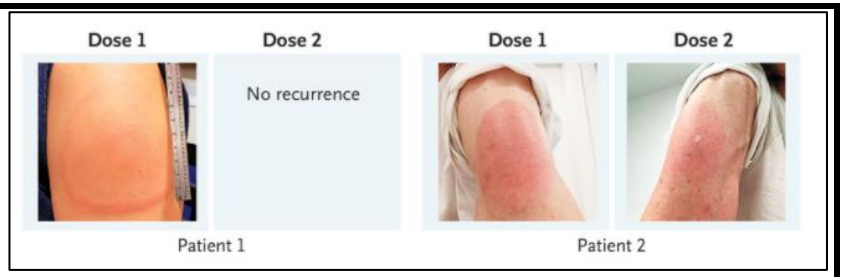
			
Niño-Taravilla C et al Emerging Infectious Diseases https://wwwnc.cdc.gov/eid/article/27/5/20-4591_article	Multisystem Inflammatory Syndrome in Children, Chile, May–August 2020	Casistica di 26 bambini (età mediana 6 anni e mezzo) con sindrome della risposta infiammatoria multisistemica (MIS-C) associata a COVID-19 (7 con tampone positivo, tutti con sierologia positiva).	We describe 26 children with multisystem inflammatory syndrome associated with coronavirus disease in the pediatric intensive care unit of Roberto del Río Hospital (Santiago, Chile). In total, 10 (38.5%) children required mechanical ventilation; 13 (50.0%) required inotropic support. In addition, 18 (69.2%) patients had echocardiographic abnormalities. No patients died.
Emary KRW et al The Lancet https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00628-0/fulltext	Efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 variant of concern 202012/01 (B.1.1.7): an exploratory analysis of a randomised controlled trial	Il vaccino AstraZeneca è efficace in termini di prevenzione dell'infezione (70.4%) da SARS-CoV-2 variante B.1.1.7 (« inglese ») anche se l'attività neutralizzante degli anticorpi prodotti è inferiore che contro i ceppi non B.1.1.7.	Background : A new variant of SARS-CoV-2, B.1.1.7, emerged as the dominant cause of COVID-19 disease in the UK from November, 2020. We report a post-hoc analysis of the efficacy of the adenoviral vector vaccine, ChAdOx1 nCoV-19 (AZD1222), against this variant. Methods : Volunteers (aged ≥18 years) who were enrolled in phase 2/3 vaccine efficacy studies in the UK, and who were randomly assigned (1:1) to receive ChAdOx1 nCoV-19 or a meningococcal conjugate control (MenACWY) vaccine, provided upper airway swabs on a weekly basis and also if they developed symptoms of

			COVID-19 disease (a cough, a fever of 37·8°C or higher, shortness of breath, anosmia, or ageusia). Swabs were tested by nucleic acid amplification test (NAAT) for SARS-CoV-2 and positive samples were sequenced through the COVID-19 Genomics UK consortium. Neutralising antibody responses were measured using a live-virus microneutralisation assay against the B.1.1.7 lineage and a canonical non-B.1.1.7 lineage (Victoria). The efficacy analysis included symptomatic COVID-19 in seronegative participants with a NAAT positive swab more than 14 days after a second dose of vaccine. Participants were analysed according to vaccine received. Vaccine efficacy was calculated as 1 − relative risk (ChAdOx1 nCoV-19 vs MenACWY groups) derived from a robust Poisson regression model. This study is continuing and is registered with ClinicalTrials.gov, NCT04400838, and ISRCTN, 15281137. Findings : Participants in efficacy cohorts were recruited between May 31 and Nov 13, 2020, and received booster doses between Aug 3 and Dec 30, 2020. Of 8534 participants in the primary efficacy cohort, 6636 (78%) were aged 18–55 years and 5065 (59%) were female. Between Oct 1, 2020, and Jan 14, 2021, 520 participants developed SARS-CoV-2 infection. 1466 NAAT positive nose and throat swabs were collected from these participants during the trial. Of these, 401 swabs from 311 participants were successfully sequenced. Laboratory virus neutralisation activity by vaccine-induced antibodies was lower against the B.1.1.7 variant than against the Victoria lineage (geometric mean ratio 8·9, 95% CI 7·2–11·0). Clinical vaccine efficacy against symptomatic NAAT positive infection was 70·4% (95% CI 43·6–84·5) for B.1.1.7 and 81·5% (67·9–89·4) for non-B.1.1.7 lineages. Interpretation : ChAdOx1 nCoV-19 showed reduced neutralisation activity against the B.1.1.7 variant compared with a non-B.1.1.7

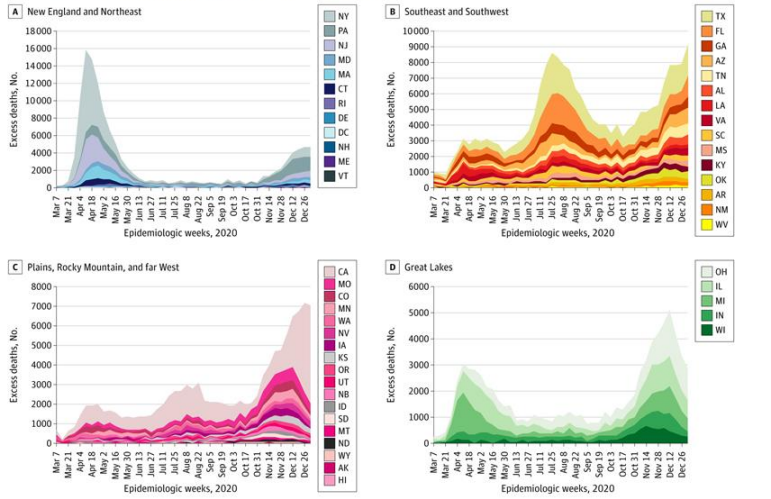
			variant in vitro, but the vaccine showed efficacy against the B.1.1.7 variant of SARS-CoV-2. 
Jarhult JD et al Scientific Reports https://www.nature.com/articles/s41598-021-86500-y	The impact of viremia on organ failure, biomarkers and mortality in a Swedish cohort of critically ill COVID-19 patients.	Una RNA-emia di SARS-CoV-2 superiore a 1000 copie/ml non predice la mortalità per COVID-19 in una coorte svedese.	The spread of virus via the blood stream has been suggested to contribute to extra-pulmonary organ failure in Coronavirus disease 2019 (COVID-19). We assessed SARS-CoV-2 RNAemia (RNAemia) and the association between RNAemia and inflammation, organ failure and mortality in critically ill COVID-19 patients. We included all patients with PCR verified COVID-19 and consent admitted to ICU. SARS-CoV-2 RNA copies above 1000/ml measured by PCR in plasma was defined as RNAemia and used as surrogate for viremia. In this cohort of 92 patients 59 (64%) were invasively ventilated. RNAemia was found in 31 patients (34%). Hypertension and

			corticosteroid treatment was more common in patients with RNAemia. Extra-pulmonary organ failure biomarkers and the extent of organ failure were similar in patients with and without RNAemia, but the former group had more renal replacement therapy and higher mortality (26 vs 16%; 35 vs 16%, respectively, p = 0.04). RNAemia was not an independent predictor of death at 30 days after adjustment for age. SARS-CoV2 RNA copies in plasma is a common finding in ICU patients with COVID-19. Although viremia was not associated with extra pulmonary organ failure it was more common in patients who did not survive to 30 days after ICU admission.
Leal T et al Journal of Gastroenterology and Hepatology https://journals.lww.com/eurojgh/pages/default.aspx	Gastrointestinal manifestations of COVID-19: results from a European centre.	Prevalenza elevata di sintomi gastrointestinali associati a COVID-19 in questa coorte di pazienti in Portogallo.	BACKGROUND: Infection due to severe acute respiratory syndrome coronavirus 2 is typically associated with a respiratory syndrome, but gastrointestinal symptoms have been described in early reports from China. However, data from European centres are scarce. OBJECTIVES: We aimed to characterise the gastrointestinal manifestations of patients with coronavirus disease 2019 (COVID-19) and their disease course. METHODS: Patients admitted at our centre between March and April 2020 with diagnosis of COVID-19 were included. Asymptomatic patients or those without symptom information were excluded. Clinical features, laboratory data and disease severity (mechanical ventilation, intensive care admission or death) were analysed. RESULTS: Two-hundred one patients were included (median age 71 years; 56.2% male). Digestive symptoms were reported by 60 (29.9%) patients during the disease course, being part of the disease presentation in 34 (16.9%). The most frequent were diarrhoea in 36 patients (17.9%). Patients with gastrointestinal symptoms were younger (P = 0.032), had higher haemoglobin levels (P = 0.002) and lower C-reactive protein (P = 0.045) and potassium levels (P = 0.004). Patients with digestive

			symptoms had less severe disease (28.3 vs. 44.0%; P = 0.038). Regarding liver damage, aspartate aminotransferase (AST) was elevated in 65.2% of patients and alanine aminotransferase (ALT) in 62.7%, but these patients did not present a more severe disease (elevated AST P = 0.062; elevated ALT P = 0.276). CONCLUSION: A significant portion of COVID-19 patients have digestive symptoms, mostly at presentation. This should be taken into account in order to keep a high level of suspicion to reach an early diagnosis and setup infection control measures to control the transmission rate. This subgroup of patients appears to have a less severe disease course.
Blumenthal KG et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMc2102131?query=featured_home	Delayed Large Local Reactions to mRNA-1273 Vaccine against SARS-C	Reazioni di ipersensibilità ritardata al vaccino MODERNA contro SARS-CoV-2, da tenere presenti per evitare accertamenti superflui. Degli stessi autori abbiamo già letto un articolo sulle reazioni allergiche su JAMA https://jamanetwork.com/journals/jama/fullarticle/2777417): decisamente una casistica ben utilizzata.	We have also observed delayed large local reactions to the mRNA-1273 vaccine, with a median onset on day 8 (range, 4 to 11) after the first dose. These reactions had a variable appearance (Figure 1). Here, we report on a series of 12 patients with these reactions, all of which appeared near the injection site after complete resolution of the initial local and systemic symptoms associated with vaccination. Five of the reactions were grade 3 plaques (≥10 cm in diameter) (Table 1). Some patients had concurrent systemic adverse effects, and among these patients, 2 had additional skin findings. Most patients received treatment for their symptoms (e.g., with ice and antihistamines). Some patients received glucocorticoids (topical, oral, or both), and 1 patient received antibiotic therapy for presumptive cellulitis. The symptoms resolved a median of 6 days after onset (range, 2 to 11).

			
Hall MA et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMp2104289?query=featured_home	"Vaccine Passport" Certification — Policy and Ethical Considerations	Controversie legate al rilascio di passaporti vaccinali per SARS-CoV-2.	Using Covid-19 vaccine passports to tailor restrictions, however, has drawn staunch opposition based on several weighty concerns.1 First, while vaccine supply remains limited, privileging people who are fortunate enough to have gained early access is morally questionable. Second, even after supply constraints ease, rates of vaccination among racial minorities and low-income populations seem likely to remain disproportionately low; relatedly, if history is a guide, programs that confer social privilege on the basis of "fitness" can lead to invidious discrimination. Third, the extent of protection conferred by vaccination, particularly against new variants, is not yet well understood, nor is the potential for viral transmission by people who have been vaccinated. Fourth, privileging the vaccinated will penalize people with religious or philosophical objections to vaccination. Finally, we lack a consensus approach to accurately certifying vaccination.
Peng J et al Clinical Infectious Diseases https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ci	Estimation of secondary household attack rates for emergent spike L452R SARS-CoV-2 variants detected by genomic surveillance at a community-based testing site in San Francisco	Lieve incremento del tasso di attacco delle varianti di SARS-CoV-2 "California" e "West Coast" (B.1.427 e B.1.429) diffuse nell'area di San Francisco a Gennaio 2021 rispetto a quanto avveniva in novembre 2020.	Background : Sequencing of the SARS-CoV-2 viral genome from patient samples is an important epidemiological tool for monitoring and responding to the pandemic, including the emergence of new mutations in specific communities. Methods : SARS-CoV 2 genomic sequences were generated from positive samples collected, along with epidemiological metadata, at a walk-up, rapid testing site in the Mission District of San Francisco, California during November 22-December 1, 2020 and January 10-

ab283/6206738?searchresult=1			29, 2021. Secondary household attack rates and mean sample viral load were estimated and compared across observed variants. Results : A total of 12,124 tests were performed yielding 1,099 positives. From these, 928 high quality genomes were generated. Certain viral lineages bearing spike mutations, defined in part by L452R, S13I, and W152C, comprised 54.4% of the total sequences from January, compared to 15.7% in November. Household contacts exposed to the “California” or “West Coast” variants (B.1.427 and B.1.429) were at higher risk of infection compared to household contacts exposed to lineages lacking these variants (0.36 vs 0.29, RR=1.28; 95% CI:1.00-1.64). The reproductive number was estimated to be modestly higher than other lineages spreading in California during the second half of 2020. Viral loads were similar among persons infected with West Coast versus non-West Coast strains, as was the proportion of individuals with symptoms (60.9% vs 64.3%). Conclusions : The increase in prevalence, relative household attack rates, and reproductive number are consistent with a modest transmissibility increase of the West Coast variants.
Woolf SH et al JAMA https://jamanetwork.com/journals/jama/fullarticle/2778361	Excess Deaths From COVID-19 and Other Causes in the US, March 1, 2020, to January 2, 2021	Incremento di decessi (oltre 500.000 persone) negli USA fra Marzo 2020 e Gennaio 2021, dovuto in parte a COVID-19 e in parte ad altre patologie, come probabile conseguenza di peggiore assistenza medica durante la pandemia.	A study analyzing US mortality in March-July 2020 reported a 20% increase in excess deaths, only partly explained by COVID-19. Surges in excess deaths varied in timing and duration across states and were accompanied by increased mortality from non–COVID-19 causes.1 This study updates the analysis for the remainder of 2020.

			Figure. Excess Deaths by Regions, March 1, 2020, to January 2, 2021  State data plotted from 8 regions, as defined by the US Bureau of Economic Analysis. Surge patterns were independently examined for each of the 8 regions (Supplement); epidemic patterns were similar and could be merged as shown, except a bimodal pattern in the Great Lakes region was distinctive and plotted separately. Negative excess deaths were plotted as zero. State-level data are available on request.
Jolliffe DA et al The Lancet https://www.thelancet.com/journals/landia/article/PIIS2213-8587(21)00051-6/fulltext	Vitamin D supplementation to prevent acute respiratory infections: a systematic review and meta-analysis of aggregate data from randomised controlled trials	Metanalisi su trial clinici randomizzati che rileva come l'assunzione quotidiana di una dose di 400-1000 UI di vitamina D sia associata a minore prevalenza di infezioni respiratorie acute rispetto a chi non la assumeva; non è indagato l'effetto specifico su COVID-19.	Background : A 2017 meta-analysis of data from 25 randomised controlled trials (RCTs) of vitamin D supplementation for the prevention of acute respiratory infections (ARIs) revealed a protective effect of this intervention. We aimed to examine the link between vitamin D supplementation and prevention of ARIs in an updated meta-analysis. Methods : For this systematic review and meta-analysis, we searched MEDLINE, Embase, the Cochrane Central Register of Controlled Trials, Web of Science, and the ClinicalTrials.gov registry for studies listed from database inception to May 1, 2020. Double-blind RCTs of vitamin D3, vitamin D2, or 25-hydroxyvitamin D (25[OH]D) supplementation for any duration, with a placebo or low-dose vitamin D control, were eligible if they had been approved by a research ethics committee, and if ARI incidence was collected prospectively and prespecified as an efficacy outcome. Studies

			reporting results of long-term follow-up of primary RCTs were excluded. Aggregated study-level data, stratified by baseline 25(OH)D concentration and age, were obtained from study authors. Using the proportion of participants in each trial who had one or more ARIs, we did a random-effects meta-analysis to obtain pooled odds ratios (ORs) and 95% CIs to estimate the effect of vitamin D supplementation on the risk of having one or more ARIs (primary outcome) compared with placebo. Subgroup analyses were done to estimate whether the effects of vitamin D supplementation on the risk of ARI varied according to baseline 25(OH)D concentration (<25 nmol/L vs 25·0–49·9 nmol/L vs 50·0–74·9 nmol/L vs >75·0 nmol/L), vitamin D dose (daily equivalent of <400 international units [IU] vs 400–1000 IU vs 1001–2000 IU vs >2000 IU), dosing frequency (daily vs weekly vs once per month to once every 3 months), trial duration (≤12 months vs >12 months), age at enrolment (<1·00 years vs 1·00–15·99 years vs 16·00–64·99 years vs ≥65·00 years), and presence versus absence of airway disease (ie, asthma only, COPD only, or unrestricted). Risk of bias was assessed with the Cochrane Collaboration Risk of Bias Tool. The study was registered with PROSPERO, CRD42020190633. Findings : We identified 1528 articles, of which 46 RCTs (75 541 participants) were eligible. Data for the primary outcome were obtained for 48 488 (98·1%) of 49 419 participants (aged 0–95 years) in 43 studies. A significantly lower proportion of participants in the vitamin D supplementation group had one or more ARIs (14 332 [61·3%] of 23 364 participants) than in the placebo group (14 217 [62·3%] of 22 802 participants), with an OR of 0·92 (95% CI 0·86–0·99; 37 studies; I2=35·6%, pheterogeneity=0·018). No significant effect of vitamin D supplementation on the risk of having one or more ARIs was observed for any of the subgroups defined by

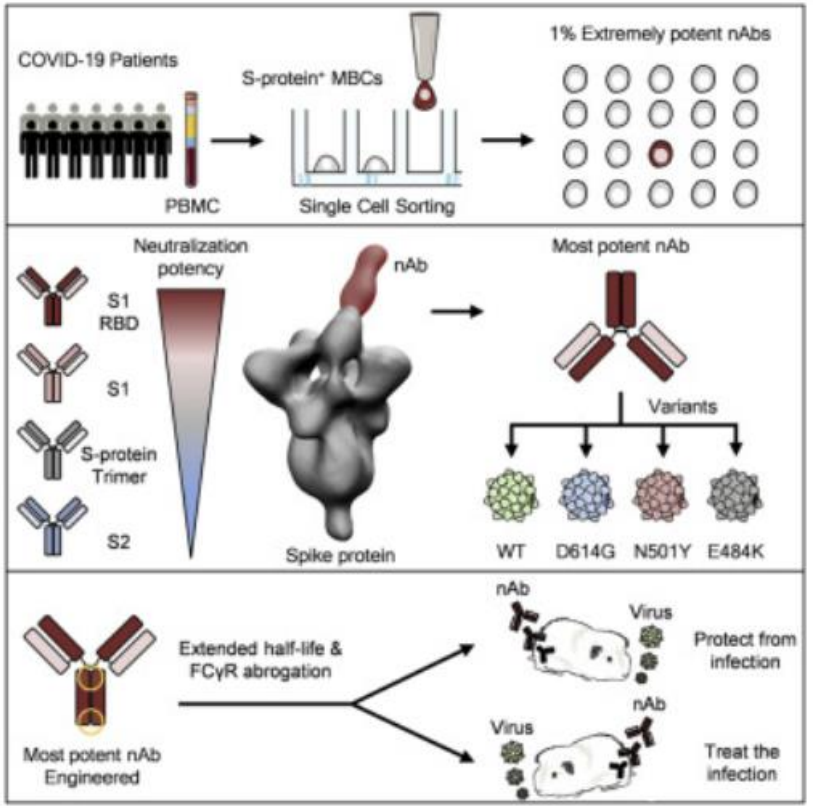
			baseline 25(OH)D concentration. However, protective effects of supplementation were observed in trials in which vitamin D was given in a daily dosing regimen (OR 0·78 [95% CI 0·65–0·94]; 19 studies; I2=53·5%, pheterogeneity=0·003), at daily dose equivalents of 400–1000 IU (0·70 [0·55–0·89]; ten studies; I2=31·2%, pheterogeneity=0·16), for a duration of 12 months or less (0·82 [0·72–0·93]; 29 studies; I2=38·1%, pheterogeneity=0·021), and to participants aged 1·00–15·99 years at enrolment (0·71 [0·57–0·90]; 15 studies; I2=46·0%, pheterogeneity=0·027). No significant interaction between allocation to the vitamin D supplementation group versus the placebo group and dose, dose frequency, study duration, or age was observed. In addition, no significant difference in the proportion of participants who had at least one serious adverse event in the vitamin supplementation group compared with the placebo group was observed (0·97 [0·86–1·07]; 36 studies; I2=0·0%, pheterogeneity=0·99). Risk of bias within individual studies was assessed as being low for all but three trials. Interpretation : Despite evidence of significant heterogeneity across trials, vitamin D supplementation was safe and overall reduced the risk of ARI compared with placebo, although the risk reduction was small. Protection was associated with administration of daily doses of 400–1000 IU for up to 12 months, and age at enrolment of 1·00–15·99 years. The relevance of these findings to COVID-19 is not known and requires further investigation.
Aveyard P et al The Lancet https://www.thelancet.com/journals/lanres/article/	Association between pre-existing respiratory disease and its treatment, and severe COVID-19: a population cohort study	Studio su una coorte di oltre 8 milioni di pazienti adulti dai registri di Medicina del territorio inglese, di cui lo 0.2% ricoverati per COVID-19 fra gennaio e aprile 2020 : le persone con	Background : Previous studies suggested that the prevalence of chronic respiratory disease in patients hospitalised with COVID-19 was lower than its prevalence in the general population. The aim of this study was to assess whether chronic lung disease or use of inhaled corticosteroids (ICS) affects the risk of contracting severe COVID-19.

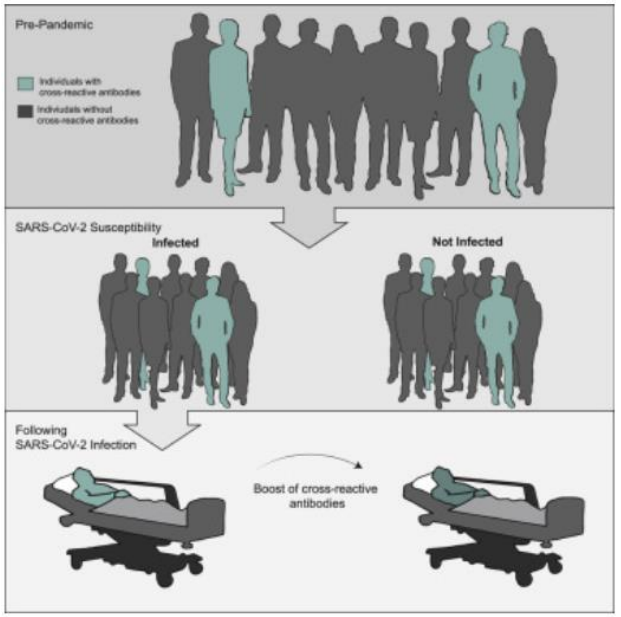
PIIS2213-2600(21)00095-3/fulltext		malattie respiratorie pregresse hanno un maggiore rischio di ospedalizzazione, ma il ricovero in Rianimazione è poco frequente ; pazienti con BPCO e interstiziopatie hanno un rischio lievemente aumentato di COVID-19 grave,.	Methods : In this population cohort study, records from 1205 general practices in England that contribute to the QResearch database were linked to Public Health England's database of SARS-CoV-2 testing and English hospital admissions, intensive care unit (ICU) admissions, and deaths for COVID-19. All patients aged 20 years and older who were registered with one of the 1205 general practices on Jan 24, 2020, were included in this study. With Cox regression, we examined the risks of COVID-19-related hospitalisation, admission to ICU, and death in relation to respiratory disease and use of ICS, adjusting for demographic and socioeconomic status and comorbidities associated with severe COVID-19. Findings : Between Jan 24 and April 30, 2020, 8 256 161 people were included in the cohort and observed, of whom 14 479 (0·2%) were admitted to hospital with COVID-19, 1542 (<0·1%) were admitted to ICU, and 5956 (0·1%) died. People with some respiratory diseases were at an increased risk of hospitalisation (chronic obstructive pulmonary disease [COPD] hazard ratio [HR] 1·54 [95% CI 1·45–1·63], asthma 1·18 [1·13–1·24], severe asthma 1·29 [1·22–1·37; people on three or more current asthma medications], bronchiectasis 1·34 [1·20–1·50], sarcoidosis 1·36 [1·10–1·68], extrinsic allergic alveolitis 1·35 [0·82–2·21], idiopathic pulmonary fibrosis 1·59 [1·30–1·95], other interstitial lung disease 1·66 [1·30–2·12], and lung cancer 2·24 [1·89–2·65]) and death (COPD 1·54 [1·42–1·67], asthma 0·99 [0·91–1·07], severe asthma 1·08 [0·98–1·19], bronchiectasis 1·12 [0·94–1·33], sarcoidosis 1·41 [0·99–1·99), extrinsic allergic alveolitis 1·56 [0·78–3·13], idiopathic pulmonary fibrosis 1·47 [1·12–1·92], other interstitial lung disease 2·05 [1·49–2·81], and lung cancer 1·77 [1·37–2·29]) due to COVID-19 compared with those without these diseases. Admission to ICU was

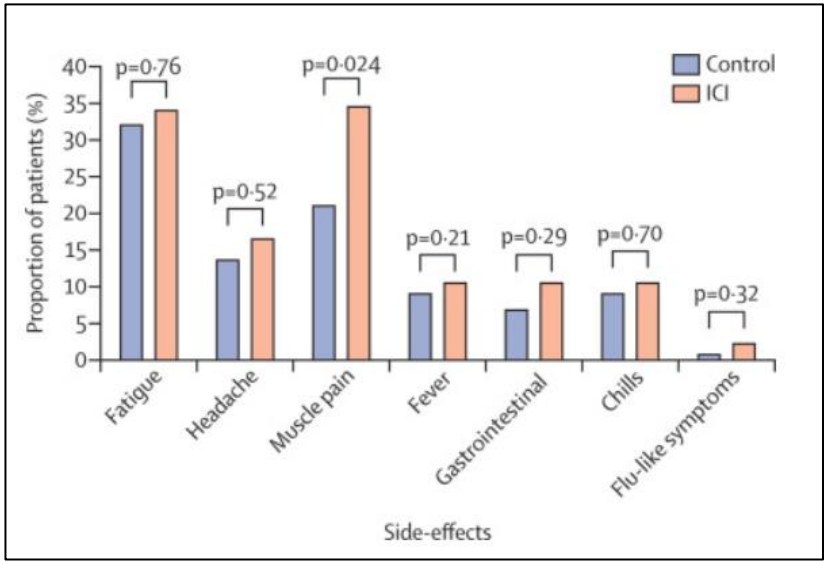
			rare, but the HR for people with asthma was 1·08 (0·93–1·25) and severe asthma was 1·30 (1·08–1·58). In a post-hoc analysis, relative risks of severe COVID-19 in people with respiratory disease were similar before and after shielding was introduced on March 23, 2020. In another post-hoc analysis, people with two or more prescriptions for ICS in the 150 days before study start were at a slightly higher risk of severe COVID-19 compared with all other individuals (ie, no or one ICS prescription): HR 1·13 (1·03–1·23) for hospitalisation, 1·63 (1·18–2·24) for ICU admission, and 1·15 (1·01–1·31) for death. Interpretation : The risk of severe COVID-19 in people with asthma is relatively small. People with COPD and interstitial lung disease appear to have a modestly increased risk of severe disease, but their risk of death from COVID-19 at the height of the epidemic was mostly far lower than the ordinary risk of death from any cause. Use of inhaled steroids might be associated with a modestly increased risk of severe COVID-19.
Chmielewska B et al The Lancet https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(21)00079-6/fulltext	Effects of the COVID-19 pandemic on maternal and perinatal outcomes: a systematic review and meta-analysis	Revisione sistematica e metanalisi che mostra l'impatto negativo in termini di mortalità materna e infantile della pandemia di COVID-19.	Background : The COVID-19 pandemic has had a profound impact on health-care systems and potentially on pregnancy outcomes, but no systematic synthesis of evidence of this effect has been undertaken. We aimed to assess the collective evidence on the effects on maternal, fetal, and neonatal outcomes of the pandemic. Methods : We did a systematic review and meta-analysis of studies on the effects of the pandemic on maternal, fetal, and neonatal outcomes. We searched MEDLINE and Embase in accordance with PRISMA guidelines, from Jan 1, 2020, to Jan 8, 2021, for case-control studies, cohort studies, and brief reports comparing maternal and perinatal mortality, maternal morbidity, pregnancy complications, and intrapartum and neonatal outcomes before and during the pandemic. We also planned to record any additional

			maternal and offspring outcomes identified. Studies of solely SARS-CoV-2-infected pregnant individuals, as well as case reports, studies without comparison groups, narrative or systematic literature reviews, preprints, and studies reporting on overlapping populations were excluded. Quantitative meta-analysis was done for an outcome when more than one study presented relevant data. Random-effects estimate of the pooled odds ratio (OR) of each outcome were generated with use of the Mantel-Haenszel method. This review was registered with PROSPERO (CRD42020211753). Findings : The search identified 3592 citations, of which 40 studies were included. We identified significant increases in stillbirth (pooled OR 1·28 [95% CI 1·07–1·54]; I2=63%; 12 studies, 168 295 pregnancies during and 198 993 before the pandemic) and maternal death (1·37 [1·22–1·53; I2=0%, two studies [both from low-income and middle-income countries], 1 237 018 and 2 224 859 pregnancies) during versus before the pandemic. Preterm births before 37 weeks' gestation were not significantly changed overall (0·94 [0·87–1·02]; I2=75%; 15 studies, 170 640 and 656 423 pregnancies) but were decreased in high-income countries (0·91 [0·84–0·99]; I2=63%; 12 studies, 159 987 and 635 118 pregnancies), where spontaneous preterm birth was also decreased (0·81 [0·67–0·97]; two studies, 4204 and 6818 pregnancies). Mean Edinburgh Postnatal Depression Scale scores were higher, indicating poorer mental health, during versus before the pandemic (pooled mean difference 0·42 [95% CI 0·02–0·81; three studies, 2330 and 6517 pregnancies). Surgically managed ectopic pregnancies were increased during the pandemic (OR 5·81 [2·16–15·6]; I2=26%; three studies, 37 and 272 pregnancies). No overall significant effects were identified for other outcomes included in the quantitative analysis: maternal gestational diabetes; hypertensive disorders of pregnancy;

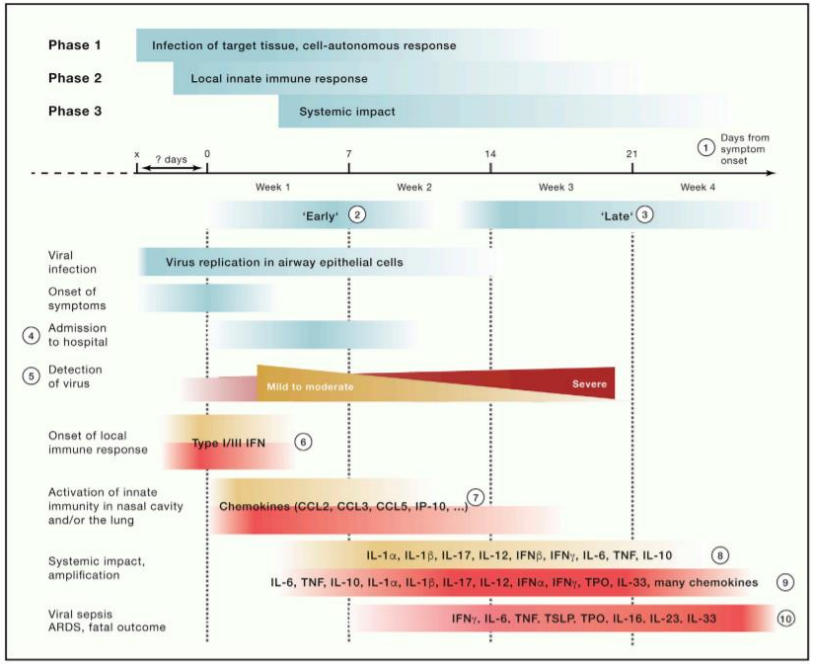
			preterm birth before 34 weeks', 32 weeks', or 28 weeks' gestation; iatrogenic preterm birth; labour induction; modes of delivery (spontaneous vaginal delivery, caesarean section, or instrumental delivery); post-partum haemorrhage; neonatal death; low birthweight (<2500 g); neonatal intensive care unit admission; or Apgar score less than 7 at 5 min. Interpretation : Global maternal and fetal outcomes have worsened during the COVID-19 pandemic, with an increase in maternal deaths, stillbirth, ruptured ectopic pregnancies, and maternal depression. Some outcomes show considerable disparity between high-resource and low-resource settings. There is an urgent need to prioritise safe, accessible, and equitable maternity care within the strategic response to this pandemic and in future health crises.
Andreano E et al Cell https://www.cell.com/cell/fulltext/S0092-8674(21)00224-5	Extremely potent human monoclonal antibodies from COVID-19 convalescent patients	Procedura di selezione di anticorpi monoclonali da 14 pazienti convalescenti da infezione da SARS-CoV-2.	Human monoclonal antibodies are safe, preventive, and therapeutic tools that can be rapidly developed to help restore the massive health and economic disruption caused by the coronavirus disease 2019 (COVID-19) pandemic. By single-cell sorting 4,277 SARS-CoV-2 spike protein-specific memory B cells from 14 COVID-19 survivors, 453 neutralizing antibodies were identified. The most potent neutralizing antibodies recognized the spike protein receptor-binding domain, followed in potency by antibodies that recognize the S1 domain, the spike protein trimer, and the S2 subunit. Only 1.4% of them neutralized the authentic virus with a potency of 1–10 ng/mL. The most potent monoclonal antibody, engineered to reduce the risk of antibody-dependent enhancement and prolong half-life, neutralized the authentic wild-type virus and emerging variants containing D614G, E484K, and N501Y substitutions. Prophylactic and therapeutic efficacy in the hamster model was observed at 0.25 and 4 mg/kg respectively in absence of Fc functions.

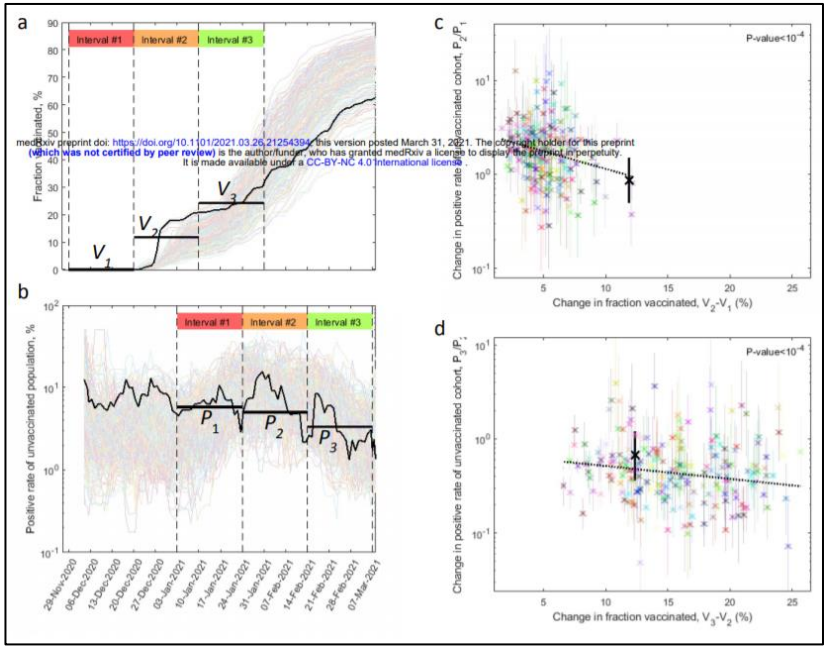
			
Anderson EM et al Cell https://www.cell.com/cell/fulltext/S0092-8674(21)00160-4	Seasonal human coronavirus antibodies are boosted upon SARS-CoV-2 infection but not associated with protection	Circa il 20% di una coorte di persone con infezione da SARS-CoV-2 possedeva anticorpi contro i Coronavirus endemici, ma questi non conferivano protezione contro infezione o ospedalizzazione per COVID-19.	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has rapidly spread within the human population. Although SARS-CoV-2 is a novel coronavirus, most humans had been previously exposed to other antigenically distinct common seasonal human coronaviruses (hCoVs) before the coronavirus disease 2019 (COVID-19) pandemic. Here, we quantified levels of SARS-CoV-2-reactive antibodies and hCoV-reactive antibodies in serum samples collected from 431 humans before the COVID-19 pandemic. We then quantified pre-pandemic antibody levels in serum from a separate cohort of 251 individuals who became PCR-confirmed infected with

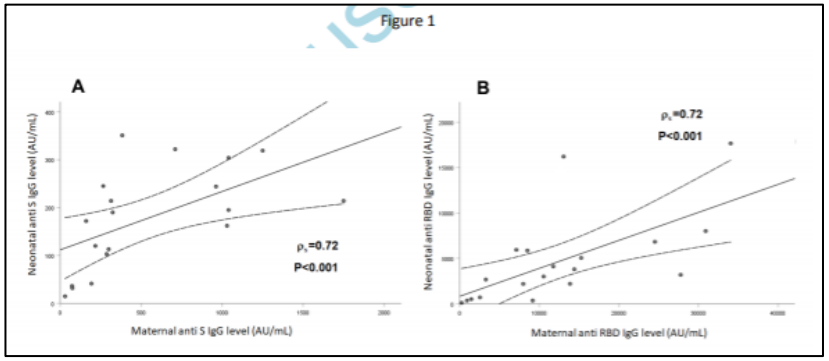
			SARS-CoV-2. Finally, we longitudinally measured hCoV and SARS-CoV-2 antibodies in the serum of hospitalized COVID-19 patients. Our studies indicate that most individuals possessed hCoV-reactive antibodies before the COVID-19 pandemic. We determined that ~20% of these individuals possessed non-neutralizing antibodies that cross-reacted with SARS-CoV-2 spike and nucleocapsid proteins. These antibodies were not associated with protection against SARS-CoV-2 infections or hospitalizations, but they were boosted upon SARS-CoV-2 infection. 
Waissengrin B et al The Lancet https://www.thelancet.com/journals/lanonc/article	Short-term safety of the BNT162b2 mRNA COVID-19 vaccine in patients with cancer treated with immune checkpoint inhibitors	Sicurezza e tollerabilità del vaccino Pfizer contro SARS-CoV-2 in 137 pazienti neoplastici trattati con farmaci inibitori dei	Between Jan 11 and Feb 25, 2021, 170 patients who were being treated with immune checkpoint inhibitors were offered the vaccine and surveyed. 33 (19%) refused the vaccination, mostly due to fear of side-effects. 137 (81%) patients received the first vaccination dose, of whom 134 (98%) received the second dose. Three patients died after the first dose, one due to COVID-19, and

/PIIS1470-2045(21)00155-8/fulltext		checkpoint cellulari in Israele.	two due to disease progression. Characteristics of the remaining 134 patients are presented in the appendix p 1. The most common side-effects after the first dose were local, with 28 (21%) of 134 patients reporting pain at the site of injection. Systemic side-effects included fatigue (five [4%]), headache (three [2%]), muscle pain (three [2%]), and chills (one [1%]). 
Hughes S Medscape https://www.medscape.com/viewarticle/948560	AstraZeneca COVID Vaccine: Clotting Disorder Mechanism Revealed?	Riassunto degli approfondimenti condotti sui casi di trombosi venosa successivi a vaccinazione con vaccino AstraZeneca contro SARS-CoV-2 (circa 1-2 per milione), di cui si sospetta un meccanismo simile alla trombocitopenia indotta da eparina (HIT) sulla base dei risultati già	The European Medicines Agency (EMA) continues to reassure the public about the safety of the AstraZeneca COVID-19 vaccine, although several countries have imposed new restrictions on the product, owing to its link to a rare clotting disorder. Use of the vaccine has been suspended for individuals younger than 55 or 60 years in several European countries and in Canada after reports of a prothrombotic disorder and thrombocytopenia, mainly in younger individuals. Now, more information on the prothrombotic disorder has become available. The vaccine appears to be linked to a condition that

		riportati del gruppo di Greinacher in Germania.	clinically resembles heparin-induced thrombocytopenia (HIT) and that occurs mainly in younger women.
Giovannetti M et al Science https://science.sciencemag.org/content/early/2021/03/17/science.abf8003/tab-e-letters	Response to Timing the SARS-CoV-2 index case in Hubei province by Pekar J et al	La datazione dell'inizio della circolazione di SARS-CoV-2 in Cina, stimata da Pekar in un articolo già presentato in questa bibliografia, era stata studiata con risultati analoghi in un precedente lavoro italiano risalente a febbraio 2020, notevole perché basato su dati molto meno numerosi per l'analisi filogenetica (https://pubmed.ncbi.nlm.nih.gov/32048560/).	[…] coalescent framework based on a combination of retrospective phylodynamic inference and prospective epidemiological simulations, helped by the unprecedented number of cases and more than 800K SARS-2-CoV genomes generated, allowed to determine the cryptic circulation of SARS-CoV-2 with its probable introduction between mid-October and mid-November 2019. In this line, worthy of mention is the early observation made by Benvenuto et al who, by employing a molecular clock model, could date back to the fourth week of November 2019 (95%HPD: September 28, 2019; December 21, 2019) the origin of this novel pathogen. This dating, which is consistent with the estimation made by Pekar et al remains quite noticeable in consideration of the very limited set of data, particularly regarding the paucity of SARS-CoV-2 complete genomes available at the beginning of the epidemic, that of course may justify its particular wide 95% HPD.
Schultze JL et al Cell https://www.cell.com/cell/fulltext/S0092-8674(21)00218-X	COVID-19 and the human innate immune system	Ruolo dell'immunità innata nell'infezione umana da SARS-CoV-2.	The introduction of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) into the human population represents a tremendous medical and economic crisis. Innate immunity—as the first line of defense of our immune system—plays a central role in combating this novel virus. Here, we provide a conceptual framework for the interaction of the human innate immune system with SARS-CoV-2 to link the clinical observations with experimental findings that have been made during the first year of the pandemic. We review evidence that variability in innate immune system components among humans is a main contributor to the heterogeneous disease courses observed for coronavirus disease 2019 (COVID-19), the

			disease spectrum induced by SARS-CoV-2. A better understanding of the pathophysiological mechanisms observed for cells and soluble mediators involved in innate immunity is a prerequisite for the development of diagnostic markers and therapeutic strategies targeting COVID-19. However, this will also require additional studies addressing causality of events, which so far are lagging behind. 
Milman O et al medRXiv – not peer reviewed	SARS-CoV-2 infection risk among unvaccinated is negatively associated with community-level vaccination rates	Vaccinando gli adulti si riduce consensualmente il numero di nuovi positivi nei ragazzi di età inferiore a 16 anni, come si osserva in questo studio in corso di	Mass vaccination has the potential to curb the current COVID-19 pandemic by protecting vaccinees from the disease and possibly lowering the chance of transmission to unvaccinated individuals. The high effectiveness of the widely-administered BNT162b vaccine in preventing not only the disease but also infection suggests a potential for a population-level effect, critical for disease eradication. However, this putative effect is difficult to observe,

https://www.medrxiv.org/content/10.1101/2021.03.26.21254394v2		pubblicazione condotto in Israele.	especially in light of highly fluctuating spatio-temporal epidemic dynamics. Here, analyzing vaccination records and test results collected during a rapid vaccine rollout for a large population from 223 geographically defined communities, we find that the rates of vaccination in each community are highly correlated with a later decline in infections among a cohort of under 16 years old which are unvaccinated. These results provide observational evidence that vaccination not only protects individual vaccinees but also provides cross-protection to unvaccinated individuals in the community. 
Rottenstreich A et al Clinical Infectious Diseases	Efficient maternofetal transplacental transfer of anti- SARS-CoV-2 spike antibodies after antenatal	Gli anticorpi anti SARS-CoV-2 sono trasmessi per via transplacentare in 20 gravide vaccinate con il vaccino Pfizer.	Maternal and cord blood sera were collected from 20 parturients who received the BNT162b2 vaccine. All women and infants were positive for anti S- and anti-RBD-specific IgG. Cord blood antibody concentrations were correlated to maternal levels and to time since

https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab266/6209876?searchresult=1	SARS-CoV-2 BNT162b2 mRNA vaccination		vaccination. Antenatal SARS-CoV-2 vaccination may provide maternal and neonatal protection. 
Pfizer Biontech https://www.pfizer.com/science/coronavirus/vaccine/additional-population-studies	STUDIES IN ADDITIONAL POPULATIONS Children Under 12	Aggiornamenti sul trial Pfizer sull'utilizzo del vaccino a mRNA contro SARS-CoV-2 nei bambini di età compresa fra 6 mesi e 11 anni, i cui risultati sono attesi nella seconda metà del 2021.	In March 2021, Pfizer and BioNTech dosed the first healthy children in a global Phase 1/2/3 continuous study to further evaluate the safety, tolerability, and immunogenicity of the Pfizer-BioNTech COVID-19 vaccine in children 11 years to 6 month old.