The Weekly COVID-19 Literature Surveillance Summary

July 02, 2021

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COVID-19 Daily Literature Surveillance

COVID19LST

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LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or *n*-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, *n*-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or *n*-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non -randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

*** Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.**

**** As always, a systematic review is generally better than an individual study.**

How to cite the Levels of Evidence Table

OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence".
Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

** OCEBM Table of Evidence Working Group = Jeremy Howick, Iain Chalmers (James Lind Library), Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson*

EXECUTIVE SUMMARY

Epidemiology

- SARS-CoV-2 B.1.1.7 REINFECTION AFTER PREVIOUS COVID-19 IN TWO IMMUNOCOMPETENT ITALIAN PATIENTS: A double case report from the ASST Sette Laghi by microbiology researchers found, when analyzing one 56-year old patient in December 2020 with confirmed B.1.1.7. strain infection and interstitial pneumonia, the amino acid substitutions N501Y and A570D were confirmed. In another case of a 58-year old male in January 2021, with the same strain and detectable mutation, diagnosis of interstitial pneumonia necessitated treatment in the subacute medical unit. These reports provide a possible clinical profile for reinfection with the B.1.1.7 strain, and authors suggest that more cases of reinfection with B.1.1.7 are likely undetected.

- Understanding Risk for Newborns Born to SARS-CoV-2-Positive Mothers: An editorial article conducted by researchers affiliated with Columbia University Irving Medical Center in New York investigated a study performed in Sweden by Norman et al involving 88159 infants born to 87005 mothers between March 11, 2020 and January 31, 2021, in which there was a 2.6% maternal SARS-CoV-2 positivity rate. This study showed maternal SARS-CoV-2 infection in pregnancy to be associated with higher risk of newborn complications, with the risk increasing with COVID-19 disease severity. However, the incidence of positive SARS-CoV-2 PCR tests in infants was low (0.9%) with no cases progressing to pneumonia. This study provides reassuring data of low risk of neonatal infection, morbidity, and mortality, however more information is needed overall on short and long-term outcomes related to children with in utero exposure to SARS-CoV-2.

Understanding the Pathology

- Nasal ciliated cells are primary targets for SARS-CoV-2 replication in early stage of COVID-19: Investigators at the Institute for Basic Science in South Korea analyzed nasal epithelial samples from humans and nonhuman primates infected with SARS-CoV-2. By combining immunofluorescence staining and single cell RNA-sequencing, they found high levels of viral proteins in the setting of low levels of mRNA with proteins generally localized to the apical side of multiciliated cells (Figure 2, B-G) suggesting that mRNA levels poorly correlate to cellular localization. Additionally, they found that SARS-CoV-2 replication was localized to these nasal multiciliated cells when compared to oral squamous cells (Figure 4, B and C). While the findings suggest early replication in shedding epithelia of the nasal cavity, the lack of inclusion of glandular epithelial cells warrants study of these cells as potential points of replication for the virus.

Transmission & Prevention

- Effect of 2 Inactivated SARS-CoV-2 Vaccines on Symptomatic COVID-19 Infection in Adults: A Randomized Clinical Trial: An international team of researchers conducted a phase 3 randomized clinical trial on the efficacy and safety of the WIVO4 and HBO2 inactivated SARS-CoV-2 vaccines in 40,382 symptomatic COVID-19 adults. Primary efficacy end point was determined to be 72.8% ([95% CI 58.1%-84.2%]; P less than 0.001) for WIVO4 and 78.1% ([95% CI 64.8%-86.3%]; P less than 0.001) for HBO2 (Table 2, Figure 2). 100% efficacy was seen against severe COVID-19. 44.2% of participants in the WIVO4 group reported adverse reactions, 41.7% in the HBO2 group, and 46.5% in the alum-only group (Figure 3). These findings suggest the significant efficacy and safety of these two vaccines against SARS-CoV-2 infection while also demonstrating their ability to prevent further transmission.

- Persistence of Antibody and Cellular Immune Responses in COVID-19 patients over Nine Months after Infection: A cross-sectional study conducted at the Beijing Institute of Microbiology and Epidemiology assessed blood samples taken from 59 patients who recovered from COVID-19 between 257 and 343 days post-SARS-CoV-2 infection. They found at the designated time point 90% of patients possessed detectable IgG antibodies against the virus spike and nucleocapsid proteins, 60% possessed antibodies against the receptor binding domain (Figure 1), and 70% possessed specific memory B and T cell responses (Figure 2). The findings suggest that immunity against the virus largely persists at about one year after infection, though the small sample size warrants future large-scale studies.

- Quantifying the risk of SARS-CoV-2 reinfection over time: Researchers at the Health Information and Quality Authority in Ireland. performed a systematic review of of 11 cohort studies including 615,777 patients who recovered from COVID-19 to quantify risk of reinfection with SARS-Cov-2. The median follow-up was 131 days (4.4 months; range of medians: 54–210 days) and with a maximum follow-up of 10 months. They found reinfection rates to be between 0-1% (median PCR-confirmed reinfection rate: 0.27%) with no studies reporting an increase risk of infection with increasing time since recovery.

- Characteristics of COVID-19 Cases and Outbreaks at Child Care Facilities - District of Columbia, July-December 2020: In a Morbidity and Mortality Weekly Report from the CDC, researchers discuss their observational study of COVID-19 cases and outbreaks at 469 child care facilities in the District of Colombia from July-December 2020. A total of 319 cases were

identified from 112 facilities, 180 of whom were teachers or staff members. 27 facilities had 29 index cases that caused an additional 127 cases, which qualify as an outbreak. These results suggest that outbreaks at child care facilities were relatively low and implementing preventative measures can further decrease transmission.

- Indoor Air Changes and Potential Implications for SARS-CoV-2 Transmission: A review article conducted by researchers affiliated with Harvard University, University of Michigan, and HOK Architects in Chicago, Illinois provide rational for increasing the current ventilation and filtration standards for indoor spaces levels closer to hospital standards (eTable), since SARS-CoV-2 outbreaks have been largely associated with time spent indoors and low-level ventilation. Higher ventilation and filtration rates allow for rapid removal of particles from indoor air to lessen the duration of respiratory aerosols and far-field transmission (within same room by beyond 6 feet) among room occupants. Considerations for implementing these strategies include cost, minimal impact on close-contact transmission, use in spaces where masks are not worn all the time, and scale of ventilation/filtration to the amount of occupants in the rooms. Improved ventilation and filtration strategies should be a continued emphasis in buildings even after the pandemic as a holistic risk reduction strategy.

R&D: Diagnosis & Treatments

- Dynamics of anti-SARS-CoV-2 IgG antibodies post-COVID-19 in a Brazilian Amazon population: An observational cohort study conducted at the Federal University of Pará in Brazil followed 125 anti-SARS-CoV-2 antibody positive volunteers for 90 days following COVID-19 diagnosis to assess the persistence of antibodies. They found that persistence was detected after 90 days in 87 participants (69.6%) (Table 3) with symptoms lasting longer in those with persistent IgG response (greater than or equal to 21 days, compared to less than or equal to 7 days) (Table 2). The findings suggest a potentially high rate of immunity loss in this population.

- Bamlanivimab for Prevention of COVID-19: An editorial article written by a researcher affiliated with Harvard Medical School discusses a randomized, double-blind, placebo-controlled trial in 74 skilled nursing and assisted living facilities with 966 total participants to evaluate single IV 4200 mg dose of Bamlanivimab (a SARS-CoV-2 neutralizing monoclonal antibody) in COVID-19 prophylaxis. They found a significant reduction in incidence of symptomatic COVID-19 compared with placebo (8.5% vs. 15.2%, OR 0.43, 95% CI 0.28-0.68) as well as moderate to severe COVID-19 by day 57 (8.3% vs. 14.1%, OR 0.46, 95% CI 0.29-0.73). They additionally found significant decreases in viral loads in the Bamlanivimab group compared with placebo (2.44 vs. 3.64) and no COVID-19 related deaths among those in the treatment groups versus 5 deaths in the control. These findings suggest that passive immune prophylaxis with Bamlanivimab could abort outbreaks and reduce transmission in similar residential facilities.

TABLE OF CONTENTS

A RAPID SCOPING REVIEW OF COVID-19 AND VULNERABLE WORKERS: INTERSECTING OCCUPATIONAL AND PUBLIC HEALTH ISSUES

Côté D, Durant S, MacEachen E, Majowicz S, Meyer S, Huynh AT, Laberge M, Dubé J.. Am J Ind Med. 2021 May 18. doi: 10.1002/ajim.23256. Online ahead of print.
Level of Evidence: 5 - Review / Literature Review

BLUF

In a literature review of 30 studies, a multidisciplinary team of researchers associated several Canadian universities discuss COVID-19 transmission risk in essential occupations such as healthcare, retail, manufacturing, and agriculture. In these occupations, the main issues reported that increase risk of transmission were lack of PPE, inadequate health insurance, physical proximity to each other, housing conditions, and many more (Table 3). In addition, COVID-19 rates also increase with structural inequities, discrimination, and mental health issues. These findings suggest that public systems such as healthcare, legislation, workplace environment, and community network for must change for the better (Table 4).

ABSTRACT

BACKGROUND: This article reports the results of a rapid scoping review of the literature on COVID-19 transmission risk to workers in essential sectors such as retail, health care, manufacturing, and agriculture, and more particularly the experiences of workers in precarious employment and social situations. METHODS: Following scoping review methods, we included 30 studies that varied in terms of methodology and theoretical approaches. The search included peer-reviewed articles and grey literature published between March and September 2020. RESULTS: Based on the studies reviewed, we found that COVID-19 infection and death rates increased not only with age and comorbidities, but also with discrimination and structural inequities based on racism and sexism. Racial and ethnic minority workers, including migrant workers, are concentrated in high-risk occupations and this concentration is correlated to lower socioeconomic conditions. The COVID-19 pandemic appears in the occupational health and safety spotlight as an exacerbator of already existing socioeconomic inequalities and social inequalities in health, especially in light of the intersection of issues related to racism, ethnic minority status, and sexism. CONCLUSIONS: This review provides early evidence about the limitations of institutions' responses to the pandemic, and their capacity to provide a safe and decent working environment for all workers, regardless of their employment status or the social protections they may enjoy under normal circumstances. It is also important to think about these issues in the postpandemic context, when conditions of precariousness and vulnerability persist and possibly worsen.

FIGURES

TABLE 3 Cartography of the main issues by occupational categories

Occupational categories	Authors	Main issues
Agricultural workers	Koh,[29] Tutor Marcom et al.,[10] and Alahmad et al.[21]	• Among seasonal migrant workers: Housing, communication, testing, contact tracing barriers, lack of internet connectivity, and availability of PPE • Health programmes halted to avoid staff exposure and telehealth visits were limited due to the lack of internet connectivity
Construction	Brown et al.[11]	• Previous medical condition to increase risk for COVID-19 • Inadequate health insurance coverage
Direct care staff (incl. home carers)	Ameida et al.[12] and Sterling et al.[14]	• Lack of paid sick leave • Inadequate PPE • Working long hours • Inconsistent delivery of information • Aggravation of already existing physical and mental health problems • Long-term care among migrant carers in the European Union as showcase of system deficit and precarious labour market
Factory workers	Tran et al.[15]	• Health issues before pandemic with high prevalence of respiratory system problems • Self-treatment without medication • Crowded public transportation facilities
Gig economy drivers	Apouey et al.[16]	• Instable income • Concerns for one's own health and for the future
Hotel and restaurants	Sönmez et al.[17]	• Combination of life and work stressors • Feeling of insecurity (health, financial)
Meat processing	Donahue et al.[18] and Waltenburg et al.[19]	• Lack of flexible medical leave policy • Closeness to each other • A certain number of positives asymptomatic • Disproportionate burden of illness and death among racialized minority workers
Medically trained midwives	Smith[20]	• Lack of access to PPE • Being culturally rooted in local customs, positive effect in creating trust among community members

Table 3. Cartography of the main issues by occupational categories.

TABLE 4 Cartography of the main recommendations

Level of action*	Recommendations	Studies
Individual level		
1.1 Demographic	Need to recognise specific socioeconomic status factors as being clinically relevant to people's risk of COVID-19	Khalatbari-Soltani et al.[19]
1.2 Financial	Quick action for providing better social security for those who can't afford taking sick leave	Almeida et al.[12]
Organisational level		
2.1 Workplace environment	As far as possible, provide testing facilities near industrial sites or at-risk environment to avoid travelling	Tran et al.[13]
	Need for workplace and sector-specific guidance or tailored strategies and interventions (incl. culturally responsive)	Brown et al.,[11] Sterling et al.,[14] Sönmez et al.,[17] Waltenburg et al.,[27] Smith,[20] Bui et al.,[24] Moore et al.,[25] and Poulakas and Branka[26]
	Provide better workers protection and conditions, including access to proper PPE	Brown et al.,[11] Almeida et al.,[12] Alahmad et al.,[21] Hawkins[27]
	For migrant farm workers especially, to set up strike teams to do on-farm testing and prevention	Tutor Marcom et al.[30]
	For temporary workers, to improve housing conditions and communication facilities	Alahmad et al.[21] and Koh[29]
	To address social inequality among the most vulnerable groups or among groups most at risk for unfair treatment**	Sönmez et al.,[17] Smith,[20] and Rogers et al.[31]
	Plans to ensure safe return to work, not only control methods to reduce exposures at work	Baker[23]
	Characteristics of high-risk occupations and composition of the workforce (e.g., gender, wage, PPE, policy) need to be better understood and reflected in governmental actions	Lee and Kim[32] and St-Denis[33]
2.2 Healthcare, social assistance, and insurance systems	Improved real-time data collection reporting ethnic and racial minorities hospitalisation and death	Selden and Berdahl[34]
	Develop continuous monitoring and adjustment as conditions change	Alahmad et al.[21]
	Improved access to health information	Alahmad et al.[21]
	Address the psychological health issues emerging from the health crisis	Wilson et al.[35]
	To improve health care access and insurance coverage to all	Brown et al.,[11] Almeida et al.,[12] and Alahmad et al.[21]
2.3 Community network	Involve traditional healers, health providers or village traditional health collaborators in COVID-19 health strategy	Tran et al.[13]
	Recognise the interaction between workplace environment and community	Waltenburg et al.[27]
Societal level		
3.1 Policies and legislation	Develop health strategies for the most vulnerable populations and areas***	Beana-Diez et al.[22]
	Policies to protect workers from psychological health crisis during the pandemic	Sönmez et al.[17]
	Attention needed to understand the impact of life and work conditions that may render some vulnerable groups more susceptible to COVID-19 infection	Sönmez et al.[17]

TABLE 4 (Continued)

Level of action*	Recommendations	Studies
	Provide assistance for migrant workers in the long-run	Wang et al.[36]
	Develop better interministerial coordination in the planning of services offered to newcomers	Goudet[37]
	Provide increased capacity or authority of local governments (decentralization)	Lyttelton and Zang[38]
3.2 Sociodemographic and social trends	Better integration of OHS and public health (concerted actions, databases, comorbidities)	Coggon et al.[39] and Roy
3.3 Labour market dynamics	Advocacy for a trans-sectoral and trans-national governance approach to improve migrant workers protection and support	Kuhlmann et al.[15]
3.4 Intercultural communication	To develop mitigation strategies that are culturally and linguistically responsive	Bui et al.[24]

*Classification inspired by Lederer, Loisel and Rivard's scoping review of diverse conceptualizations of work ability.[16]
**This is explicitly addressed in three studies, but it could be deducted implicitly from most of the reviewed documents.
***This might be overlapping organisational level health and social assistance dimension.

Table 4. Cartography of the main recommendations

SYMPTOMS AND FUNCTIONAL IMPAIRMENT ASSESSED 8 MONTHS AFTER MILD COVID-19 AMONG HEALTH CARE WORKERS

Havervall S, Rosell A, Phillipson M, Mangsbo SM, Nilsson P, Hober S, Thålin C.. JAMA. 2021 May 18;325(19):2015-2016. doi: 10.1001/jama.2021.5612.
Level of Evidence: 3 - Local non-random sample

BLUF

Researchers in Sweden conducted a cohort study of 2149 healthcare professionals regarding symptoms consistent with long COVID-19 after mild infection for up to 8 months. Of the participants, 323 were anti-SARS-CoV-2 IgG seropositive and 1072 were seronegative at baseline and participants with previous severe disease and those who developed seropositivity during the study were excluded. 71/323 (22%) seropositive and 254/1072 (24%) seronegative participants reported underlying chronic disease. 26% of seropositive versus 9% of seronegative participants reported at least one persistent symptom that lasted at least two months (RR, 2.9 [95% CI, 2.2-3.8]) and 15% of seropositive versus 3% of seronegative participants reported at least one symptom that lasted at least 8 months (RR, 4.4 [95% CI, 2.9-6.7]) (Table). The most common symptoms in the seropositive group were anosmia, dyspnea, and fatigue with these symptoms being reported as significantly affecting work life, home life, and social life in 8%, 12%, and 15% of seropositive individuals respectively. These results indicate that low risk individuals with mild COVID-19 experience significant long-term symptoms.

FIGURES

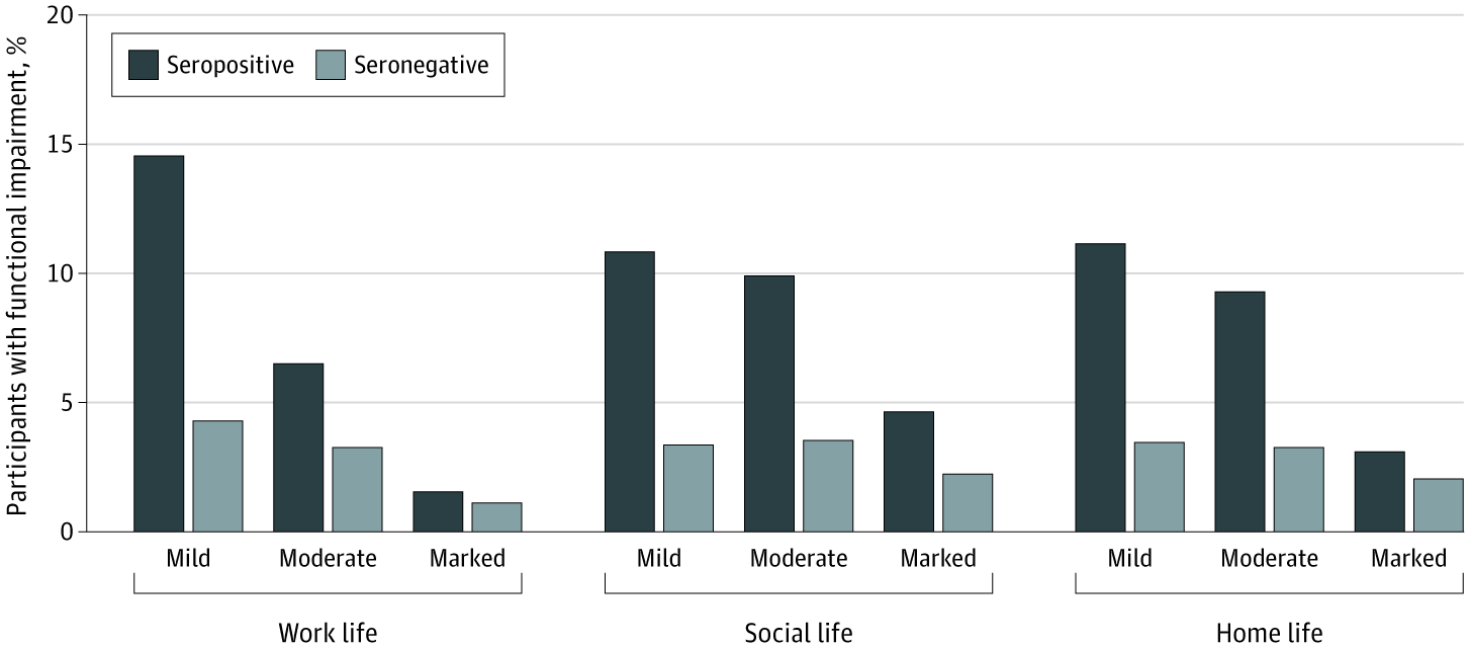


Figure. The percentage of seropositive (n = 323) and seronegative (n = 1072) participants reporting symptoms lasting at least 2 months and their related functional impairment in their work, social, and home life using the Sheehan Disability Scale (1-3, mild; 4-6, moderate; and 7-10, marked).

Table. The 10 Most Common Moderate to Severe Long-term Symptoms in Seropositive and Seronegative Participants

Duration of symptom, mo	No. (%)	
	Seropositive (n = 323)	Seronegative (n = 1072)
Any symptom		
≥2	84 (26.0)	95 (8.9)
≥4	69 (21.4)	77 (7.2)
≥8	48 (14.9)	36 (3.4)
Anosmia		
≥2	47 (14.6)	6 (0.6)
≥4	35 (10.8)	4 (0.4)
≥8	29 (9.0)	1 (0.1)
Fatigue		
≥2	27 (8.4)	57 (5.3)
≥4	22 (6.8)	47 (4.4)
≥8	13 (4.0)	16 (1.5)
Ageusia		
≥2	25 (7.7)	6 (0.6)
≥4	17 (5.3)	3 (0.3)
≥8	12 (3.7)	1 (0.1)
Dyspnea		
≥2	14 (4.3)	12 (1.1)
≥4	11 (3.4)	10 (0.9)
≥8	6 (1.9)	3 (0.3)
Sleeping disorder		
≥2	10 (3.1)	21 (2.0)
≥4	9 (2.8)	19 (1.8)
≥8	7 (2.2)	9 (0.8)
Headache		
≥2	9 (2.8)	34 (3.2)
≥4	8 (2.5)	24 (2.2)
≥8	5 (1.5)	11 (1.0)
Palpitations		
≥2	8 (2.5)	18 (1.7)
≥4	7 (1.9)	13 (1.2)
≥8	2 (0.6)	7 (0.7)
Concentration impairment		
≥2	7 (2.2)	12 (1.1)
≥4	6 (1.9)	9 (0.8)
≥8	2 (0.6)	2 (0.2)
Muscle/joint pain		
≥2	6 (1.9)	19 (1.8)
≥4	5 (1.5)	10 (0.9)
≥8	2 (0.6)	4 (0.4)
Memory impairment		
≥2	5 (1.5)	11 (1.0)
≥4	4 (1.2)	6 (0.6)
≥8	1 (0.3)	3 (0.3)

BNT162B2 MRNA VACCINATION DID NOT PREVENT AN OUTBREAK OF SARS COV-2 VARIANT 501Y.V2 IN AN ELDERLY NURSING HOME BUT REDUCED TRANSMISSION AND DISEASE SEVERITY

Bailly B, Guilpain L, Bouiller K, Chirouze C, N'Debi M, Soulier A, Demontant V, Pawlotsky JM, Rodriguez C, Fourati S.. Clin Infect Dis. 2021 May 16:ciab446. doi: 10.1093/cid/ciab446. Online ahead of print.
Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

An observational study conducted in Jura, France from March 8, 2021 to March 29, 2021, reported a SARS CoV-2 variant 501Y.V2 outbreak at a nursing home among 31 residents and 59 staff members. 50% (13/26) of vaccinated residents and 100% (5/5) annd non-vaccinated residents were infected. Non-vaccinated residents (80%, 4/5) had more severe disease when compared to vaccinated residents (15%, 2/13). Among staff members, 1 vaccinated (5.2%) and 10 non-vaccinated (25%) were infected with no severe disease development. Although based on a limited sample size, researchers concluded that the BNT162v2 mRNA vaccine (Pfizer) reduces severity and transmission of disease but not necessarily prevents outbreaks of emerging variants. They suggest that instead of relying on vaccine to prevent outbreaks in nursing homes, residential programs should conduct weekly symptom screening and viral testing post vaccination.

ABSTRACT

We report an outbreak of SARS-CoV-2 501Y.V2 in a nursing home. All non-vaccinated residents (5/5) versus half of those vaccinated with BNT162b2 (13/26) were infected. Two of 13 vaccinated versus 4 of 5 non-vaccinated residents presented severe disease. BNT162b2 did not prevent the outbreak, but reduced transmission and disease severity.

RESEARCHERS TIE SEVERE IMMUNOSUPPRESSION TO CHRONIC COVID-19 AND VIRUS VARIANTS

Abbasi J.. JAMA. 2021 May 25;325(20):2033-2035. doi: 10.1001/jama.2021.7212.
Level of Evidence: 5 - Review / Literature Review

BLUF

This article by a JAMA journalist discusses a series of case studies that illustrate sustained infection in immunocompromised individuals. She discusses how these individuals are often contagious for an extended period of time and cites research that shows that the virus evolved and adapted to treatment over a 3-month-long infection in an immunocompromised individual. She suggests that prolonged infections and suboptimal therapies can provide the evolutionary pressures for variants to emerge, which could produce a more transmissible virus and/or result in variants that are resistant to therapies or vaccines. She discusses how many researchers believe that the current SARS-CoV-2 variants of concern first arose in immunocompromised hosts and emphasizes that the healthcare community must find how best to treat COVID-19 in severely immunosuppressed patients to prevent further variants from arising.

SYMPTOMS AND CLINICAL PRESENTATION

ADULTS

SARS-COV-2 B.1.1.7 REINFECTION AFTER PREVIOUS COVID-19 IN TWO IMMUNOCOMPETENT ITALIAN PATIENTS

Novazzi F, Baj A, Genoni A, Spezia PG, Colombo A, Cassani G, Zago C, Pasciuta R, Gasperina DD, Ageno W, Severgnini P, Dentali F, Focosi D, Maggi F.. J Med Virol. 2021 May 10. doi: 10.1002/jmv.27066. Online ahead of print.
Level of Evidence: 5 - Case Report

BLUF

A double case report from the ASST Sette Laghi by microbiology researchers found, when analyzing one 56-year old patient in December 2020 with confirmed B.1.1.7. strain infection and interstitial pneumonia, the amino acid substitutions N501Y and A570D were confirmed. In another case of a 58-year old male in January 2021, with the same strain and detectable mutation, diagnosis of interstitial pneumonia necessitated treatment in the subacute medical unit. These reports provide a possible

clinical profile for reinfection with the B.1.1.7 strain, and authors suggest that more cases of reinfection with B.1.1.7 are likely undetected.

ABSTRACT

To date only one case of SARS-COV-2 B.1.1.7 reinfection has been reported (1). We report here two more such reinfection cases in Lombardy residents that, nevertheless the ECDC statement of a period from 45 to 90 days to confirm a reinfection (2), experimented a second infection from a B.1.1.7 variant of SARS CoV-2 only one month after the first one. In both cases interstitial pneumonia requiring intubation or oxygen support was present at the time of first infection, whereas the second one was characterized by very mild development. This article is protected by copyright. All rights reserved.

PREGNANT PERSONS

UNDERSTANDING RISK FOR NEWBORNS BORN TO SARS-COV-2-POSITIVE MOTHERS

Dumitriu D, Gyamfi-Bannerman C.. JAMA. 2021 May 25;325(20):2051-2052. doi: 10.1001/jama.2021.6210.

Level of Evidence: 5 - Expert Opinion

BLUF

An editorial article conducted by researchers affiliated with Columbia University Irving Medical Center in New York investigated a study performed in Sweden by Norman et al involving 88159 infants born to 87005 mothers between March 11, 2020 and January 31, 2021, in which there was a 2.6% maternal SARS-CoV-2 positivity rate. This study showed maternal SARS-CoV-2 infection in pregnancy to be associated with higher risk of newborn complications, with the risk increasing with COVID-19 disease severity. However, the incidence of positive SARS-CoV-2 PCR tests in infants was low (0.9%) with no cases progressing to pneumonia. This study provides reassuring data of low risk of neonatal infection, morbidity, and mortality, however more information is needed overall on short and long-term outcomes related to children with in utero exposure to SARS-CoV-2.

UNDERSTANDING THE PATHOLOGY

DIAGNOSE SARS-COV-2 ASSOCIATED GUILLAIN-BARRE SYNDROME UPON APPROPRIATE CRITERIA AND AFTER EXCLUSION OF DIFFERENTIALS

Finsterer J.. J Med Virol. 2021 Jun 3. doi: 10.1002/jmv.27129. Online ahead of print.
Level of Evidence: 5 - Expert Opinion

BLUF

A research physician from Austria critically reviewed a case study diagnosing Guillian-Barre syndrome (GBS) after COVID infection and discussed diagnostic limitations including failure to rule out critical ill neuropathy/myopathy (CINP/CIMP), lack of discussion of potentially neurotoxic anti-COVID medications, and lack of inflammatory marker elevations in CSF studies. He suggests that clinicians rule out other causes of neuropathies in COVID patients and avoid anchoring on the diagnosis of GBS.

NASAL CILIATED CELLS ARE PRIMARY TARGETS FOR SARS-COV-2 REPLICATION IN EARLY STAGE OF COVID-19

Ahn JH, Kim J, Hong SP, Choi SY, Yang MJ, Ju YS, Kim YT, Kim HM, Rahman MDT, Chung MK, Hong SD, Bae H, Lee CS, Koh GY.. J Clin Invest. 2021 May 18:148517. doi: 10.1172/JCI148517. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

Investigators at the Institute for Basic Science in South Korea analyzed nasal epithelial samples from humans and nonhuman primates infected with SARS-CoV-2. By combining immunofluorescence staining and single cell RNA-sequencing, they found high levels of viral proteins in the setting of low levels of mRNA with proteins generally localized to the apical side of multiciliated cells (Figure 2, B-G) suggesting that mRNA levels poorly correlate to cellular localization. Additionally, they found that SARS-CoV-2 replication was localized to these nasal multiciliated cells when compared to oral squamous cells (Figure 4, B and C). While the findings suggest early replication in shedding epithelia of the nasal cavity, the lack of inclusion of glandular epithelial cells warrants study of these cells as potential points of replication for the virus.

ABSTRACT

The upper respiratory tract is compromised in the early period of COVID-19, but SARS-CoV-2 tropism at the cellular level is not fully defined. Unlike recent single cell RNA-sequencing analyses indicating uniformly low mRNA expression of SARS-CoV-2 entry-related host molecules in all nasal epithelial cells, we show that the protein levels are relatively high and their localizations are restricted to the apical side of multiciliated epithelial cells. In addition, we provide evidence in COVID-19 patients that SARS-CoV-2 is massively detected and replicated within the multiciliated cells. We observed these findings during the early stage of COVID-19, when infected ciliated cells are rapidly replaced by differentiating precursor cells. Moreover, our analyses reveal that SARS-CoV-2 cellular tropism is restricted to the nasal ciliated versus oral squamous epithelium. These results imply that targeting ciliated cells of the nasal epithelium during the early stage of COVID-19 could be an ideal strategy to prevent SARS-CoV-2 propagation.

FIGURES

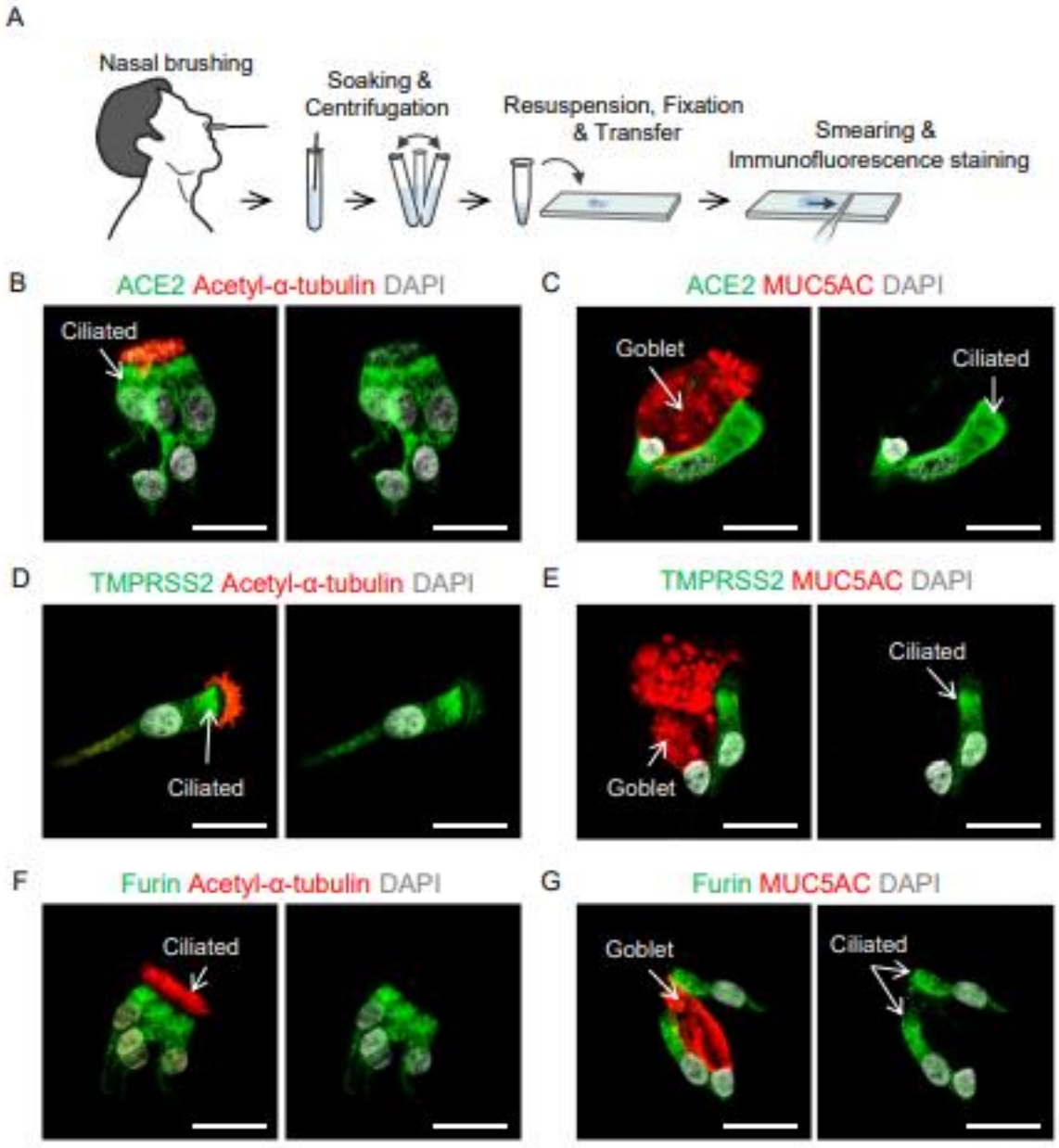


Figure 2. Human nasal cytology reveals SARS-CoV-2 entry molecules are located at the apical side of multiciliated cells

(A) Schematic diagram of a series of procedures for human nasal cytology by nasal brushing and preparation of nasal cell smear onto slide.

(B-G) Representative images showing abundant ACE2, TMPRSS2 and furin in apical side of acetylated--tubulin+ multiciliated cells, but very low or absent in MUC5AC+ goblet cells in the smeared nasal cells. Scale bars, 25 µm. Similar findings were observed in n = 3 healthy volunteers from two independent experiments.

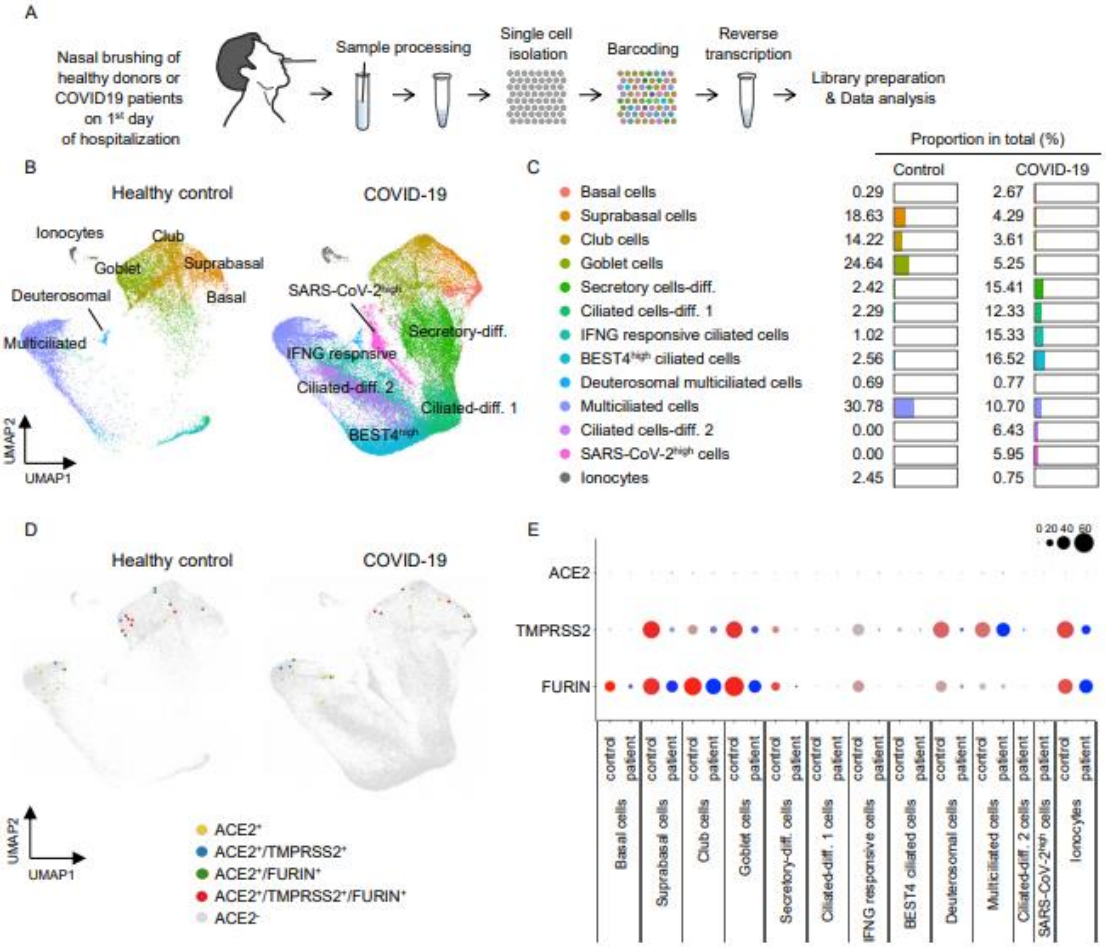


Figure 4. Comparison of cellular composition and SARS-CoV-2 entry molecular gene expression in nasal epithelial cells between healthy donors and COVID-19 patients
(A) Schematic diagram depicting a series of procedures for scRNA-seq of nasal epithelial cells from COVID-19 patients.
(B) UMAP plot comparing unsupervised clustering of nasal epithelial cell subsets between healthy controls and COVID-19 patients.
(C) List and proportion plots comparing proportion of each epithelial cell subset in total clustered epithelial cells between healthy controls and COVID-19 patients.
(D) Unsupervised clustering projected on 2D UMAP plot comparing distributions of ACE2+, ACE2+/TMPRSS2+, ACE2+/Furin+, ACE2+/TMRPSS2+/Furin+ cells across total pooled nasal epithelial cells between healthy controls and COVID-19 patients.
(E) Dot plot heatmap comparing expressions of SARS-CoV-2 entry molecule genes per each cell cluster between healthy controls and COVID-19 patients.

EFFECT OF 2 INACTIVATED SARS-COV-2 VACCINES ON SYMPTOMATIC COVID-19 INFECTION IN ADULTS: A RANDOMIZED CLINICAL TRIAL

Al Kaabi N, Zhang Y, Xia S, Yang Y, Al Qahtani MM, Abdulrazzaq N, Al Nusair M, Hassany M, Jawad JS, Abdalla J, Hussein SE, Al Mazrouei SK, Al Karam M, Li X, Yang X, Wang W, Lai B, Chen W, Huang S, Wang Q, Yang T, Liu Y, Ma R, Hussain ZM, Khan T, Saifuddin Fasihuddin M, You W, Xie Z, Zhao Y, Jiang Z, Zhao G, Zhang Y, Mahmoud S, ElTantawy I, Xiao P, Koshy A, Zaher WA, Wang H, Duan K, Pan A, Yang X.. JAMA. 2021 May 26. doi: 10.1001/jama.2021.8565. Online ahead of print.
Level of Evidence: 2 - Randomized trial or observational study with dramatic effect

BLUF

An international team of researchers conducted a phase 3 randomized clinical trial on the efficacy and safety of the WIVO4 and HBO2 inactivated SARS-CoV-2 vaccines in 40,382 symptomatic COVID-19 adults. Primary efficacy end point was determined to be 72.8% ([95% CI 58.1%-84.2%]; P less than 0.001) for WIVO4 and 78.1% ([95% CI 64.8%-86.3%]; P less than 0.001) for HBO2 (Table 2, Figure 2). 100% efficacy was seen against severe COVID-19. 44.2% of participants in the WIVO4 group reported adverse reactions, 41.7% in the HBO2 group, and 46.5% in the alum-only group (Figure 3). These findings suggest the significant efficacy and safety of these two vaccines against SARS-CoV-2 infection while also demonstrating their ability to prevent further transmission.

SUMMARY

- 30,470 people received the WIVO4 vaccine, 13,470 received the HBO2 vaccine, and 13,471 served as controls receiving aluminum hydroxide only.
- The most common adverse effects included pain at injection site and headache.

ABSTRACT

Importance: Although effective vaccines against COVID-19 have been developed, additional vaccines are still needed. Objective: To evaluate the efficacy and adverse events of 2 inactivated COVID-19 vaccines. Design, Setting, and Participants: Prespecified interim analysis of an ongoing randomized, double-blind, phase 3 trial in the United Arab Emirates and Bahrain among adults 18 years and older without known history of COVID-19. Study enrollment began on July 16, 2020. Data sets used for the interim analysis of efficacy and adverse events were locked on December 20, 2020, and December 31, 2020, respectively. Interventions: Participants were randomized to receive 1 of 2 inactivated vaccines developed from SARS-CoV-2 WIV04 (5 microg/dose; n = 13 459) and HB02 (4 microg/dose; n = 13 465) strains or an aluminum hydroxide (alum)-only control (n = 13 458); they received 2 intramuscular injections 21 days apart. Main Outcomes and Measures: The primary outcome was efficacy against laboratory-confirmed symptomatic COVID-19 14 days following a second vaccine dose among participants who had no virologic evidence of SARS-CoV-2 infection at randomization. The secondary outcome was efficacy against severe COVID-19. Incidence of adverse events and reactions was collected among participants who received at least 1 dose. Results: Among 40 382 participants randomized to receive at least 1 dose of the 2 vaccines or alum-only control (mean age, 36.1 years; 32 261 [84.4%] men), 38 206 (94.6%) who received 2 doses, contributed at least 1 follow-up measure after day 14 following the second dose, and had negative reverse transcriptase-polymerase chain reaction test results at enrollment were included in the primary efficacy analysis. During a median (range) follow-up duration of 77 (1-121) days, symptomatic COVID-19 was identified in 26 participants in the WIV04 group (12.1 [95% CI, 8.3-17.8] per 1000 person-years), 21 in the HB02 group (9.8 [95% CI, 6.4-15.0] per 1000 person-years), and 95 in the alum-only group (44.7 [95% CI, 36.6-54.6] per 1000 person-years), resulting in a vaccine efficacy, compared with alum-only, of 72.8% (95% CI, 58.1%-82.4%) for WIV04 and 78.1% (95% CI, 64.8%-86.3%) for HB02 (P < .001 for both). Two severe cases of COVID-19 occurred in the alum-only group and none occurred in the vaccine groups. Adverse reactions 7 days after each injection occurred in 41.7% to 46.5% of participants in the 3 groups; serious adverse events were rare and similar in the 3 groups (WIV04: 64 [0.5%]; HB02: 59 [0.4%]; alum-only: 78 [0.6%]). Conclusions and Relevance: In this prespecified interim analysis of a randomized clinical trial, treatment of adults with either of 2 inactivated SARS-CoV-2 vaccines significantly reduced the risk of symptomatic COVID-19, and serious adverse events were rare. Data collection for final analysis is pending. Trial Registration: ClinicalTrials.gov Identifier: NCT04510207; Chinese Clinical Trial Registry: ChiCTR2000034780.

Table 2. Incident COVID-19 Cases and Vaccine Efficacy 14 Days After 2 Doses of Immunization[a]

Outcome	WIV04 vaccine group	HB02 vaccine group	Alum-only group
Primary analysis: incident symptomatic cases			
No. of participants	12 743	12 726	12 737
No. of incident cases	26	21	95
Person-years	2140.2	2143.3	2125.6
Incidence density per 1000 person-years (95% CI)	12.1 (8.3-17.8)	9.8 (6.4-15.0)	44.7 (36.6-54.6)
Vaccine efficacy (95% CI), %	72.8 (58.1-82.4)	78.1 (64.8-86.3)	[Reference]
Secondary analysis: incident severe cases			
No. of participants	12 743	12 726	12 737
No. of incident cases	0	0	2
Person-years	2140.2	2143.3	2125.6
Incidence density per 1000 person-years (95% CI)	0 (NA)	0 (NA)	9 (1.0-34.0)
Vaccine efficacy (95% CI), %	100 (NA)	100 (NA)	[Reference]
Post hoc analysis: incident symptomatic and asymptomatic cases[b]			
No. of participants	12 727	12 713	12 722
No. of incident cases	42	31	116
Person-years	2135.5	2139.6	2121.0
Incidence density per 1000 person-years (95% CI)	19.7 (14.5-26.6)	14.5 (10.2-20.6)	54.7 (45.6-65.6)
Vaccine efficacy (95% CI), %	64.0 (48.8-74.7)	73.5 (60.6-82.2)	[Reference]

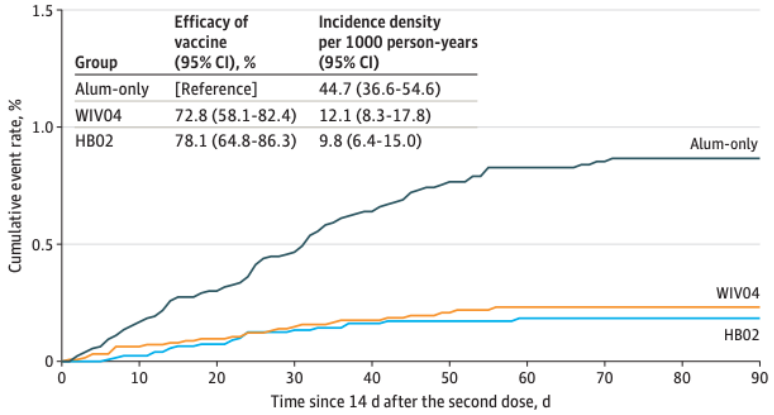
Abbreviations: alum, aluminum hydroxide; NA, not applicable.

[a] The analyses were conducted in the modified full analysis population-1, which included those who received 2 doses, contributed at least 1 efficacy follow-up visit, and had negative polymerase chain reaction test results at enrollment. A Poisson regression model with log-link function was used, with the number of incident cases as the dependent variable, treatment group as the independent variable, and person-years as the offset. Incidence density with its 95% CI was estimated using the least-square method. If the number of cases in any of the groups was less than 5, the exact method was used to estimate the incidence rate, vaccine efficacy, and 95% CI using StatXact software.

[b] Forty-four participants were excluded from the analysis because they had asymptomatic COVID-19 between the first dose and 14 days after the second dose.

Figure 2. Efficacy of 2 Inactivated Vaccines Against Symptomatic COVID-19

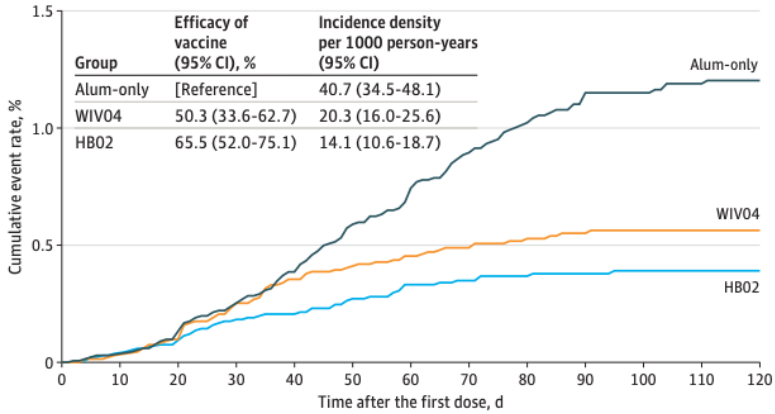
A Modified full analysis population-1



No. of participants at risk

Alum-only	12737	12206	11593	11149	10266	8319	7976	7529	1037	531
WIV04	12743	12260	11722	11256	10387	8354	8025	7594	1033	526
HB02	12726	12249	11698	11233	10366	8390	8077	7664	1031	520

B Full analysis population-1

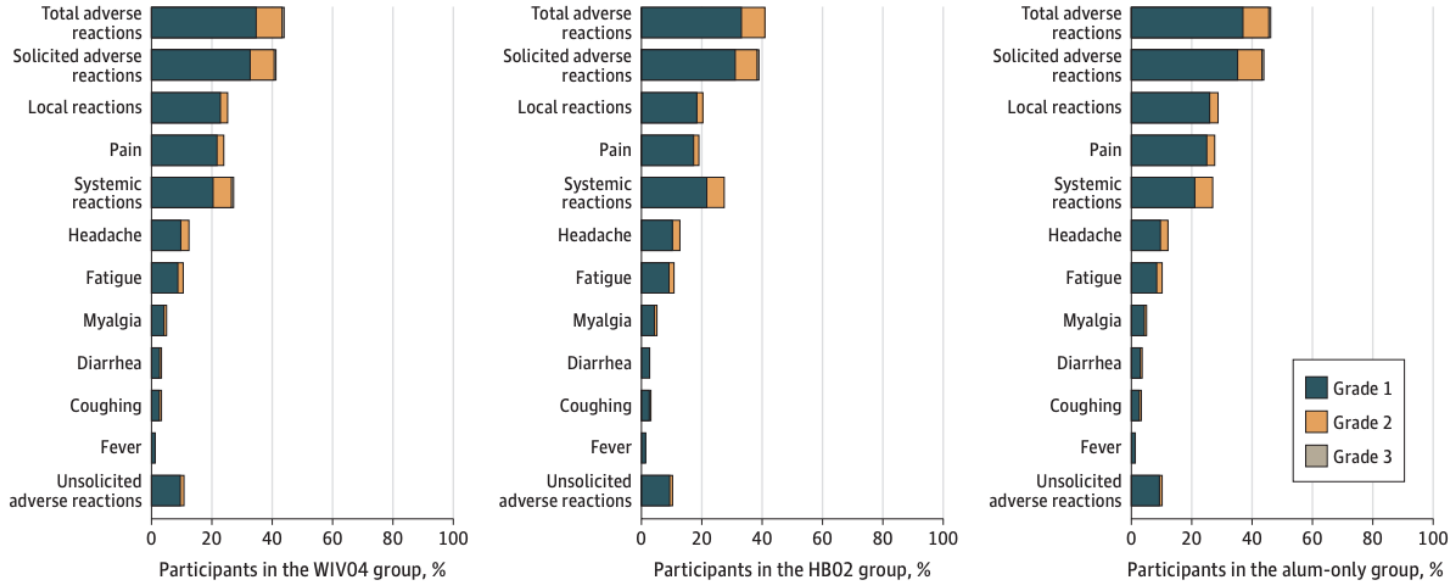


No. of participants at risk

Alum-only	13425	13273	12981	12749	12594	11857	11501	10900	9672	8041	7728	7430	665
WIV04	13428	13294	12979	12771	12622	11984	11614	11012	9780	8074	7772	7502	665
HB02	13436	13300	12993	12781	12624	11953	11618	11008	9783	8134	7844	7573	653

A, Cumulative event rates of confirmed symptomatic COVID-19 cases 14 days following a second vaccine dose among participants who received 2 doses, contributed at least 1 efficacy follow-up visit, and had negative polymerase chain reaction test results at enrollment (modified full analysis population-1). Median (interquartile range) observation times for all groups was 77 (47-78) days. B, Cumulative event rates of confirmed symptomatic COVID-19 cases after the first dose among participants who received at least 1 dose, contributed at least 1 efficacy follow-up visit, and had negative polymerase chain reaction test results at enrollment (full analysis population-1). Median (interquartile range) observation times for all the groups were 112 (82-113) days. Alum indicates aluminum hydroxide.

Figure 3. Common Adverse Reactions and Grades Within 7 Days After 2 Doses in the Safety Analysis Set



The safety analysis population included all participants who received at least 1 dose. Only adverse reactions that occurred in at least 2% of participants are included; see eTable 5 in Supplement 2 for details of all adverse reactions (including common and less common adverse reactions). Participants with more than 1 adverse reaction in a specific reaction category were only counted once; for example, if they had the same symptom (eg, injection-site pain) after each dose or if they had more than 1 symptom in the reaction class (total, systemic, and local), they were only counted once in that adverse reaction class. Participants with both lower- and higher-grade adverse events were counted once in the higher-grade total adverse events. Grading scales for systemic and local adverse events are detailed in the protocol in Supplement 1. Alum indicates aluminum hydroxide.

PERSISTENCE OF ANTIBODY AND CELLULAR IMMUNE RESPONSES IN COVID-19 PATIENTS OVER NINE MONTHS AFTER INFECTION

Yao L, Wang GL, Shen Y, Wang ZY, Zhan BD, Duan LJ, Lu B, Shi C, Gao YM, Peng HH, Wang GQ, Wang DM, Jiang MD, Cao GP, Ma MJ.. J Infect Dis. 2021 May 12:jiab255. doi: 10.1093/infdis/jiab255. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A cross-sectional study conducted at the Beijing Institute of Microbiology and Epidemiology assessed blood samples taken from 59 patients who recovered from COVID-19 between 257 and 343 days post-SARS-CoV-2 infection. They found at the designated time point 90% of patients possessed detectable IgG antibodies against the virus spike and nucleocapsid proteins, 60% possessed antibodies against the receptor binding domain (Figure 1), and 70% possessed specific memory B and T cell responses (Figure 2). The findings suggest that immunity against the virus largely persists at about one year after infection, though the small sample size warrants future large-scale studies.

ABSTRACT

BACKGROUND: The duration of humoral and T and cell response after the infection of SARS-CoV-2 remains unclear.
METHODS: We performed a cross-sectional study to assess the virus-specific antibody and memory T and B cell responses in COVID-19 patients up to 343 days after infection. Neutralizing antibodies and antibodies against the receptor-binding domain, spike, and nucleoprotein of SARS-CoV-2 were measured. Virus-specific memory T and B cell responses were analyzed.
RESULTS: We enrolled 59 COVID-19 patients, including 38 moderate, 16 mild, and five asymptomatic patients; 31 (52.5%) were men, and 28 (47.5%) were women. The median age was 41 (interquartile range [IQR]: 30-55). The median day from symptom onset to enrollment was 317 days (range 257 to 343 days). We found that approximately 90% of patients still have detectable IgG antibodies against spike and nucleocapsid proteins and neutralizing antibodies against pseudovirus, whereas ~60% of patients had detectable IgG antibodies against receptor binding domain and surrogate virus-neutralizing antibodies. SARS-CoV-2-specific IgG + memory B cell and IFN-gamma secreting T cell responses were detectable in over 70% of patients.
CONCLUSIONS: SARS-CoV-2-specific immune memory response persists in most patients nearly one year after infection, which provides a promising sign for prevention from reinfection and vaccination strategy.

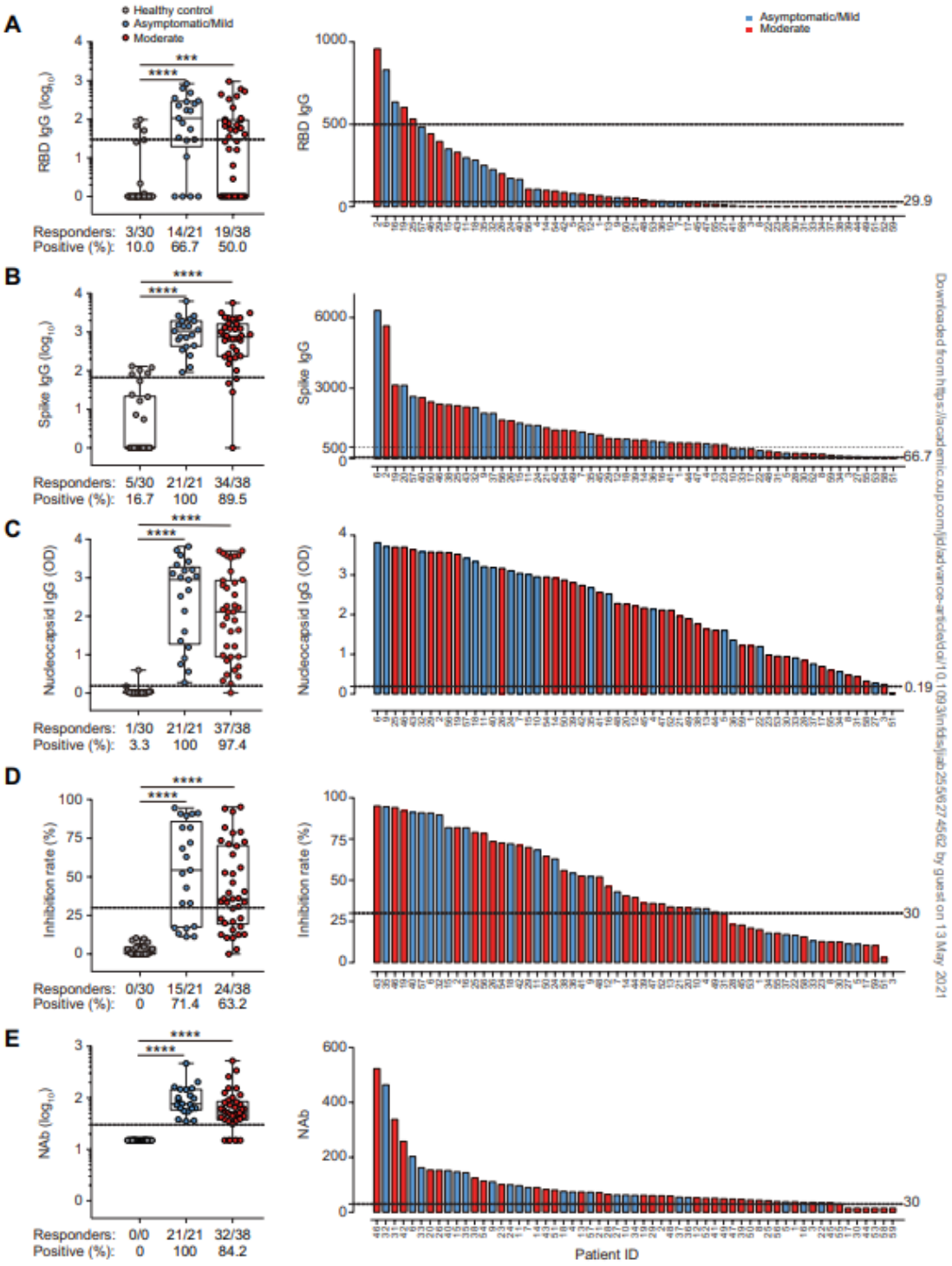


Figure 1. SARS-CoV-2-specific antibody response in recovered patients 9-11 months after infection. (A-E) Left, IgG antibodies against the receptor-binding domain (RBD), spike, and nucleocapsid of SARS-CoV-2 and neutralizing antibodies (NAb) of RBD-ACE2 binding inhibition and pseudovirus in serum samples collected from patients and healthy controls. Right, ranked anti-RBD, anti-spike, and anti- nucleocapsid IgG titers as well as RBD-ACE2 binding inhibition rate and pseudovirus NAb titer of each COVID-19 patients. Each dot represents a titer, OD value, or inhibition rate for each serum sample. The black dashed line indicates the threshold for positivity (anti-RBD IgG=29.9, anti-S IgG=66.7, anti-N IgG=0.19, inhibition rate=30%, and NAb=30). Boxplots indicate median and interquartile range (IQR); and the whiskers represent 1.5 times the IQR. Kruskal-Wallis test and Dunn's multiple comparison test using false discovery rate was used for the comparisons. ***p < 0.001, and ****p < 0.0001.

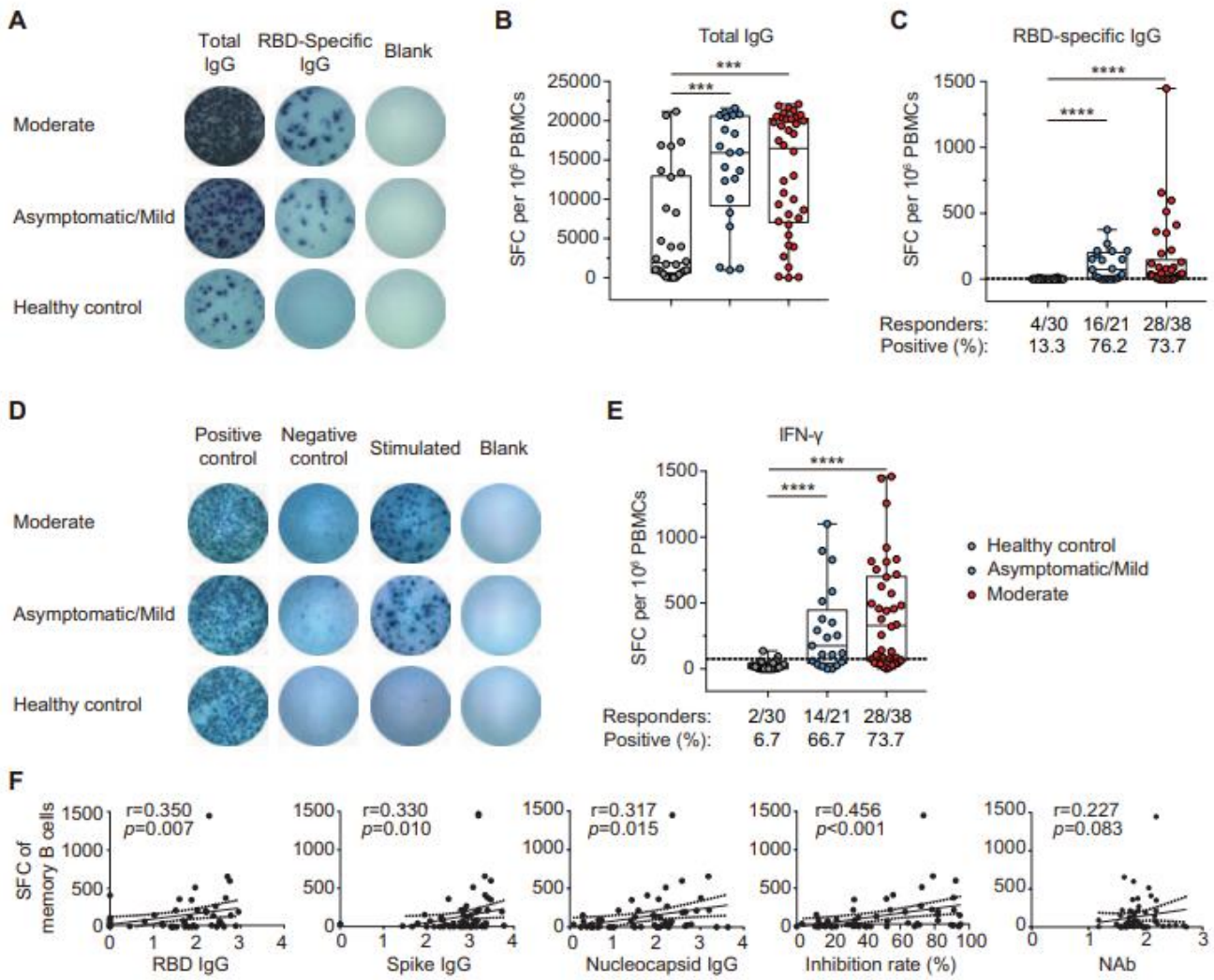


Figure 2. B and T cells responses to SARS-CoV-2 in COVID-19 convalescent patients. (A) A representative ELISpot of total IgG+ and SARS-CoV RBD-specific IgG+ memory B cells from each type of subjects. (B) Total IgG+ memory B cell counting in patients and healthy controls. (C) RBDspecific IgG+ memory B cell counting in patients and healthy controls. (D) A representative ELISpot of IFN-γ producing T cells against a defined peptide pool of S/N/M and ORF3a/7a from each type of subjects, with blank as negative control and anti-CD3 as positive controls. (E) Summary data of patients studied according to S/N/M and ORF3a/7a in patients and healthy controls. (F) Correlations between spot-forming cells (SFC) of memory B cells and antibody responses. The dotted line indicates the cut-off for positive responses (RBD-specific IgG secreting memory B cells=3, and IFN-γsecreting T cells=75). Boxplots indicate median and interquartile range (IQR); and the whiskers

represent 1.5 times the IQR. Data in the graph (B, C, and E) represented as SFC per 1x106 PBMC, and each point on the dot plot represents an individual subject. Kruskal-Wallis test and Dunn's multiple comparison test using false discovery rate was used for the comparisons in panel B, C, and E. ***p < 0.001, ****p < 0.0001. Spearman correlations were used in panel F. S, spike; N, nucleoprotein; M, membrane protein; ORF, open reading frame.

ASYMPTOMATIC AND SYMPTOMATIC SARS-COV-2 INFECTIONS AFTER BNT162B2 VACCINATION IN A ROUTINELY SCREENED WORKFORCE

Tang L, Hijano DR, Gaur AH, Geiger TL, Neufeld EJ, Hoffman JM, Hayden RT.. JAMA. 2021 May 6. doi: 10.1001/jama.2021.6564. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A retrospective cohort study conducted at St. Jude Children's Research Hospital analyzing 5217 workers from December 17, 2020 to March 20, 2021 by a bio-statistician found that the incidence rate ratio—the ratio of diagnosed cases per person-days of follow-up in vaccinated compared with unvaccinated groups—steadily decreased in participants receiving both one and two doses of the BNT162b2 (Pfizer-BioNTech) vaccine (Table 1). They also reported lower cumulative incidence of asymptomatic screening positive test results and symptoms (Figure 1), but the study design and unequal follow-up schedules warrant future studies.

*One author reported serving as a consultant to Pfizer and another reported serving on advisory boards for Roche Molecular, Quidel Corporation, and Inflammatix outside the submitted work.

FIGURES

Table. Estimated Incidence Rate Ratio Against Any SARS-CoV-2 Infection and Asymptomatic or Symptomatic/Contact SARS-CoV-2 Infection[a]

Vaccination status	Follow-up time, person-days (No. at risk)	Any positive test result		Asymptomatic screening positive test result		Screening positive test result based on the presence of symptoms or known COVID-19 exposure	
		No.	IRR (95% CI)[b]	No.	IRR (95% CI)	No.	IRR (95% CI)
Unvaccinated total follow-up[c]	149 718 (2165)	185		79		106	
Vaccinated total follow-up	198 480 (3052)	51	0.21 (0.15-0.28)	29	0.28 (0.18-0.42)	22	0.16 (0.10-0.25)
Vaccinated periods							
0-11 d after dose 1	32 807 (3052)	24	0.59 (0.39-0.91)	10	0.58 (0.30-1.12)	14	0.60 (0.35-1.05)
≥12 d after dose 1 and before dose 2	32 481 (2942)	17	0.42 (0.26-0.70)	10	0.58 (0.30-1.13)	7	0.30 (0.14-0.65)
0-6 d after dose 2	16 492 (2776)	4	0.20 (0.07-0.53)	3	0.35 (0.11-1.09)	1	0.09 (0.01-0.61)
≥7 d after dose 2	116 700 (2724)	6	0.04 (0.02-0.09)	6	0.10 (0.04-0.22)	0	0[d]

Abbreviation: IRR, incidence rate ratio.

[a] Follow-up periods for unvaccinated employees began on December 17, 2020, or on their first asymptomatic screening date, whichever was later. Individuals who received vaccines other than BNT162b2 were censored on vaccination. Follow-up periods for vaccinated workers began when they received their first dose. Workers who remained SARS-CoV-2 negative during follow-up were censored on March 20, 2021, or on the employment termination date, whichever was earlier. No person contributed to both groups. Individuals with prior COVID-19 exposure were excluded.

[b] Incidence rate ratio is the ratio of confirmed COVID-19 cases per person-days of follow-up in vaccinated compared with unvaccinated groups.

[c] The unvaccinated group was treated as the reference group for all calculations.

[d] 95% CI does not apply.

Table 1. Estimated Incidence Rate Ratio Against Any SARS-CoV-2 Infection and Asymptomatic or Symptomatic/Contact SARS-CoV-2 Infectiona

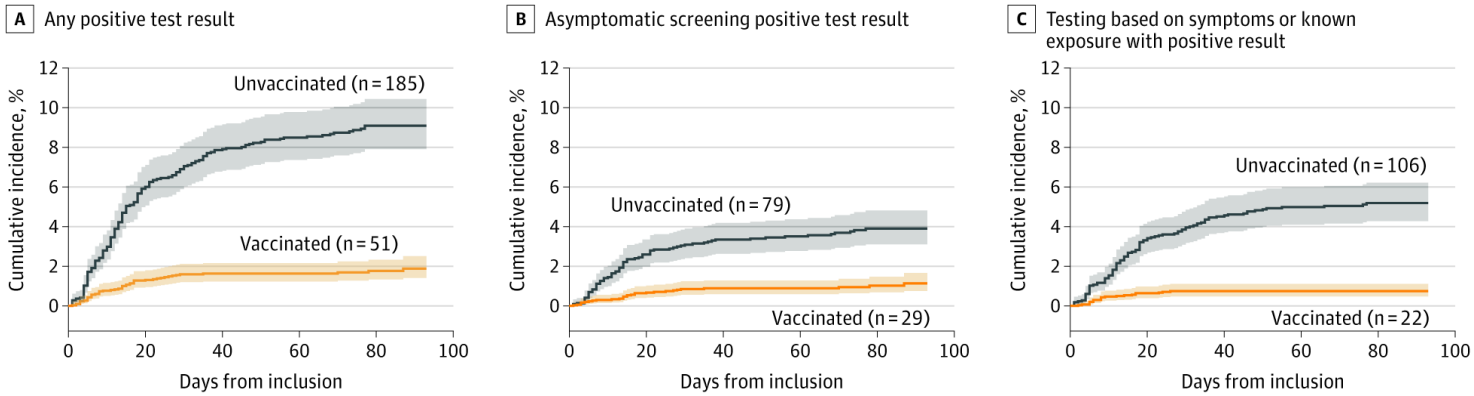


Figure 1. Cumulative Incidence of COVID-19 Against SARS-CoV-2 Infections After the First Dose

QUANTIFYING THE RISK OF SARS-COV-2 REINFECTION OVER TIME

O Murchu E, Byrne P, Carty PG, De Gascun C, Keogan M, O'Neill M, Harrington P, Ryan M.. Rev Med Virol. 2021 May 27:e2260. doi: 10.1002/rmv.2260. Online ahead of print.
Level of Evidence: 2 - Systematic review of surveys that allow matching to local circumstances

BLUF

Researchers at the Health Information and Quality Authority in Ireland. performed a systematic review of of 11 cohort studies including 615,777 patients who recovered from COVID-19 to quantify risk of reinfection with SARS-Cov-2. The median follow-up was 131 days (4.4 months; range of medians: 54–210 days) and with a maximum follow-up of 10 months. They found reinfection rates to be between 0-1% (median PCR-confirmed reinfection rate: 0.27%) with no studies reporting an increase risk of infection with increasing time since recovery.

ABSTRACT

Despite over 140 million SARS-CoV-2 infections worldwide since the beginning of the pandemic, relatively few confirmed cases of SARS-CoV-2 reinfection have been reported. While immunity from SARS-CoV-2 infection is probable, at least in the short term, few studies have quantified the reinfection risk. To our knowledge, this is the first systematic review to synthesise the evidence on the risk of SARS-CoV-2 reinfection over time. A standardised protocol was employed, based on Cochrane methodology. Electronic databases and preprint servers were searched from 1 January 2020 to 19 February 2021. Eleven large cohort studies were identified that estimated the risk of SARS-CoV-2 reinfection over time, including three that enrolled healthcare workers and two that enrolled residents and staff of elderly care homes. Across studies, the total number of PCR-positive or antibody-positive participants at baseline was 615,777, and the maximum duration of follow-up was more than 10 months in three studies. Reinfection was an uncommon event (absolute rate 0%-1.1%), with no study reporting an increase in the risk of reinfection over time. Only one study estimated the population-level risk of reinfection based on whole genome sequencing in a subset of patients; the estimated risk was low (0.1% [95% CI: 0.08-0.11%]) with no evidence of waning immunity for up to 7 months following primary infection. These data suggest that naturally acquired SARS-CoV-2 immunity does not wane for at least 10 months post-infection. However, the applicability of these studies to new variants or to vaccine-induced immunity remains uncertain.

CHARACTERISTICS OF COVID-19 CASES AND OUTBREAKS AT CHILD CARE FACILITIES - DISTRICT OF COLUMBIA, JULY-DECEMBER 2020

Kim C, McGee S, Khuntia S, Elnour A, Johnson-Clarke F, Mangla A, Iyengar P, Nesbitt L.. MMWR Morb Mortal Wkly Rep. 2021 May 21;70(20):744-748. doi: 10.15585/mmwr.mm7020a3.
Level of Evidence: 3 - Local non-random sample

BLUF

In a Morbidity and Mortality Weekly Report from the CDC, researchers discuss their observational study of COVID-19 cases and outbreaks at 469 child care facilities in the District of Colombia from July-December 2020. A total of 319 cases were identified from 112 facilities, 180 of whom were teachers or staff members. 27 facilities had 29 index cases that caused an additional 127 cases, which qualify as an outbreak. These results suggest that outbreaks at child care facilities were relatively low and implementing preventative measures can further decrease transmission.

ABSTRACT

The occurrence of cases of COVID-19 reported by child care facilities among children, teachers, and staff members is correlated with the level of community spread (1,2). To describe characteristics of COVID-19 cases at child care facilities and facility adherence to guidance and recommendations, the District of Columbia (DC) Department of Health (DC Health) and CDC reviewed COVID-19 case reports associated with child care facilities submitted to DC Health and publicly available data from the DC Office of the State Superintendent of Education (OSSE) during July 1-December 31, 2020. Among 469 licensed child care facilities, 112 (23.9%) submitted 269 reports documenting 316 laboratory-confirmed cases and three additional cases identified through DC Health's contact tracers. Outbreaks associated with child care facilities, defined as two or more laboratory-confirmed and epidemiologically linked cases at a facility within a 14-day period (3), occurred in 27 (5.8%) facilities and accounted for nearly one half (156; 48.9%) of total cases. Among the 319 total cases, 180 (56.4%) were among

teachers or staff members. The majority (56.4%) of facilities reported cases to DC Health on the same day that they were notified of a positive test result for SARS-CoV-2, the virus that causes COVID-19, by staff members or parents. Facilities were at increased risk for an outbreak if they had been operating for <3 years, if symptomatic persons sought testing >=3 days after symptom onset, or if persons with asymptomatic COVID-19 were at the facility. The number of outbreaks associated with child care facilities was limited. Continued implementation and maintenance of multiple prevention strategies, including vaccination, masking, physical distancing, cohorting, screening, and reporting, are important to reduce transmission of SARS-CoV-2 in child care facilities and to facilitate a timely public health response to prevent outbreaks. .

INDOOR AIR CHANGES AND POTENTIAL IMPLICATIONS FOR SARS-COV-2 TRANSMISSION

Allen JG, Ibrahim AM.. JAMA. 2021 May 25;325(20):2112-2113. doi: 10.1001/jama.2021.5053.
Level of Evidence: 5 - Guidelines and Recommendations

BLUF

A review article conducted by researchers affiliated with Harvard University, University of Michigan, and HOK Architects in Chicago, Illinois provide rational for increasing the current ventilation and filtration standards for indoor spaces levels closer to hospital standards (eTable), since SARS-CoV-2 outbreaks have been largely associated with time spent indoors and low-level ventilation. Higher ventilation and filtration rates allow for rapid removal of particles from indoor air to lessen the duration of respiratory aerosols and far-field transmission (within same room by beyond 6 feet) among room occupants. Considerations for implementing these strategies include cost, minimal impact on close-contact transmission, use in spaces where masks are not worn all the time, and scale of ventilation/filtration to the amount of occupants in the rooms. Improved ventilation and filtration strategies should be a continued emphasis in buildings even after the pandemic as a holistic risk reduction strategy.

FIGURES

Building type	Minimum required ACH	ASHRAE guideline[7]
US homes		
Single-family home	0.32[a]	62.1-2019
Multifamily unit	0.35[b]	
Retail[c]	1.7[d]	62.1-2019
Banks	1.3[d]	62.1-2019
Barbershops	1.9[d]	62.1-2019
School classrooms		
Students 5-8 years	2.8[d]	62.1-2019
Students ≥9 years	3.5[d]	
Airplane cabins	7-17[e]	161-2018
Hospitals		
Patient rooms	4-6 total; 2 of outdoor air[f]	170-2017
Emergency examination or treatment rooms	6 total; 2 of outdoor air[f]	
Airborne infection isolation rooms	12 total; 2 of outdoor air[f]	
Operating rooms	20 total; 4 of outdoor air[f]	

eTable. Minimum Air Changes per Hour (ACH) According to Current Design Standards by Building Type
Abbreviations: ASHRAE, American Society of Heating, Refrigerating and Air-Conditioning Engineers; HEPA, high-efficiency particulate air; MERV, minimum efficiency reporting value. aAssumes home size of 2301 square feet, 8-foot ceilings, 3 bedrooms, and default occupancy from ASHRAE.
bAssumes home size of 1350 square feet, 8-foot ceilings, 2 bedrooms, and default occupancy from ASHRAE.
cRetail refers to locations where general sales occur, not including barbershops, beauty and nail salons, coin-operated laundries, mall common areas, pet shops (animal areas), and supermarkets. dAssuming default ceiling height of 8 ft and default occupant densities from ASHRAE.
eTotal air supply consists of outside air and recirculated air through HEPA filters; estimated ACH listed here based on an application of ASHRAE 161-2018 to cabin dimensions and typical and maximum passenger loads of 3 commercial airplanes.
fTotal air refers to outdoor air plus recirculated air, where recirculated air passes through MERV 14 filters.

SAFETY IN THE PRACTICE OF DECONTAMINATING FILTERING FACEPIECE RESPIRATORS: A SYSTEMATIC REVIEW

Gnatta JR, Souza RQ, Lemos CS, Oliveira RA, Martins LR, Moriya GAA, Poveda VB.. Am J Infect Control. 2021 Jun;49(6):825-835. doi: 10.1016/j.ajic.2020.11.022. Epub 2020 Dec 3.
Level of Evidence: 5 - Review / Literature Review

BLUF

A systematic review by a group of PhD's in Brazil aimed to analyze the safety of processing N95 or higher filtration masks for professional use by looking at the outcomes of integrity, filtration, and microbiological safety. 40 Studies that evaluated the decontamination and/or sterilization of Filtering facepiece respirators (FFRs) were included in the review. Due to the diversity of the tested methods and products, the results did not enable generalization but the analysis showed complex relationship between the raw materials of the FFRs and the cycle conditions of the decontamination methods (Table 1).

SUMMARY

* In settings where reuse is inevitable for the continuity of patient care, such as in emergency situations like the COVID-19 pandemic, automated sterilization methods is a safer options due to the possibility of validating specific cycles which are compatible with each type of respirator, as long as they are intact and without any visible dirt.

* Importantly, the maintenance of its functionality must be verified after processing, such as the facial sealing.

* The number of reuses of the FFRs must be controlled and incorporated into the Sterile Processing Department Traceability (or tracking) systems.

ABSTRACT

BACKGROUND: Considering the new SARS-CoV-2 pandemic and the potential scarcity of material resources, the reuse of personal protective equipment such as filtering facepiece respirators (FFRs) for N95 filtering or higher is being discussed, mainly regarding the effectiveness and safety of cleaning, disinfection and sterilization processes. AIM: To analyze the available evidence in the literature on the safety in processing FFRs. METHODS: A systematic review conducted by searching for studies in the following databases: PubMed, CINAHL, LILACS, CENTRAL, EMBASE, Web of Science and Scopus. RESULTS: The disinfectant/sterilizing agents most frequently tested at different concentrations and exposure periods were ultraviolet irradiation, vaporized hydrogen peroxide and steam sterilization. Microbial reduction was assessed in 21 (52.5%) studies. The only disinfectants/sterilizers that did not caused degradation of the material-integrity were alcohol, electric cooker, ethylene oxide and peracetic acid fogging. Exposure to ultraviolet irradiation or microwave generated-steam resulted in a non-significant reduction in filter performance. CONCLUSION: There is a complex relationship between the FFR raw materials and the cycle conditions of the decontamination methods, evidencing the need for validating FFRs by models and manufacturers, as well as the process. Some methods may require additional tests to demonstrate the safety of FFRs for use due to toxicity.

Cleaning/disinfection/ sterilization methods	Viscusi et al. (2007)[7]	Vo et al. (2009)[14]	Viscusi et al. (2009)[19]	Bergman et al. (2010)[16]	Salter et al (2010)[15]	Fisher et al., 2010[24]	Fisher et al. (2011)[17]	Viscusi et al. (2011)[18]	Heimbuch et al. (2011)[5]	Lore et al. (2012)[8]	Heimbuch et al. (2014)[9]	Lin et al. (2017)[10]	Mills et al. (2018)[11]	Lin et al. (2018)[12]	Kumar et al. (2020)[13]	Battelle et al. 2020)[4]	Alijabo et al. (2020)[25]	Andereg et al. (2020)[26]	Bopp et al. (2020)[23]	Cadnum et al. (2020)[27]	Celina et al. (2020)[28]	Czubryt et al. (2020)[29]	Daeschler et al. (2020)[31]	Grinshpun et al. (2020)[31]	Harskamp et al. (2020)[20]	Ibáñez-Cervantes, 2020[32]	Jatta et al. (2020)[33]	Kim et al. (2020)[34]	Lieu et al. (2020)[35]	Lin et al. (2020)[36]	Ludwig et al. (2020)[37]	Ma et al. (2020)[38]	Oh et al. (2020)[39]	Ozog et al. (2020)[40]	Pascoe et al. (2020)[41]	Purschke et al. (2020)[42]	Widmer et al. (2020)[43]	Xiang et al. (2020)[21]	Zhao et al. (2020)[23]	Zulauf et al. (2020)[44]	Total
UV-C/A	X	X	X	X	X	X		X	X	X			X	X						X						X	X				X			X			X		16
VHP	X		X	X	X										X	X										X	X		X		X				X				11
Steam sterilization (Autoclave 121°C)	X											X		X	X		X		X			X		X	X			X		X								11
Sodium hypochlorite	X	X	X	X	X						X	X		X																									8
Microwave-generated steam				X		X	X	X	X	X																									X			X	8
70% Ethanol/70% Isopropyl/100% Isopropyl	X											X		X										X				X		X								6
Moist heat								X	X	X								X				X										X							6
Dry heat	X																			X	X										X					X			5
EtO	X		X	X	X										X																								5
HPGP				X	X										X																								3
Liquid hydrogen peroxide	X			X	X																																		3
Electric cooker												X		X																				X					3
Microwave	X		X																																				2
DMDO					X																																		1
Pasteurization				X																																			1
Soap and water	X																																						1
Antiseptic wipes											X																													1
Peracetic acid dry fogging system															X																									1
High-level disinfection cabinet (Altapure, Mequon: peracetic acid, hydrogen peroxide, acetic acid)																			X																					1
1% Pine-Sol and 1% benzalkonium chloride in Ethanol 70%																					X																			1
Gamma Irradiation																															X									1

HP = vaporized hydrogen peroxide; HPGP = hydrogen peroxide gas plasma.

Table 1. Methods of disinfection/sterilization methods analyzed accordingly the included studies.

ADJUSTING PRACTICE DURING COVID-19

FOR HEALTHCARE PROFESSIONALS

DISPARITIES IN COVID-19 VACCINATION COVERAGE BETWEEN URBAN AND RURAL COUNTIES - UNITED STATES, DECEMBER 14, 2020-APRIL 10, 2021

Murthy BP, Sterrett N, Weller D, Zell E, Reynolds L, Toblin RL, Murthy N, Kriss J, Rose C, Cadwell B, Wang A, Ritchey MD, Gibbs-Scharf L, Qualters JR, Shaw L, Brookmeyer KA, Clayton H, Eke P, Adams L, Zajac J, Patel A, Fox K, Williams C, Stokley S, Flores S, Barbour KE, Harris LQ.. MMWR Morb Mortal Wkly Rep. 2021 May 21;70(20):759-764. doi: 10.15585/mmwr.mm7020e3.
Level of Evidence: 3 - Local non-random sample

BLUF

The CDC reports on a retrospective cohort study from 12/14/2020–4/15/2021 in 49 US states and DC that rural counties had a 38.9% COVID-19 vaccine rate while urban counties had 45.7%, with those over 65 years old and female receiving more vaccines than those under 65 and male. Continued collaboration among community and faith-based organizations, employers, and pharmacies is needed to address vaccine hesitancy and promote equity in vaccine administration.

ABSTRACT

Approximately 60 million persons in the United States live in rural counties, representing almost one fifth (19.3%) of the population.* In September 2020, COVID-19 incidence (cases per 100,000 population) in rural counties surpassed that in urban counties (1). Rural communities often have a higher proportion of residents who lack health insurance, live with comorbidities or disabilities, are aged >=65 years, and have limited access to health care facilities with intensive care capabilities, which places these residents at increased risk for COVID-19-associated morbidity and mortality (2,3). To better understand COVID-19 vaccination disparities across the urban-rural continuum, CDC analyzed county-level vaccine administration data among adults aged >=18 years who received their first dose of either the Pfizer-BioNTech or Moderna COVID-19 vaccine, or a single dose of the Janssen COVID-19 vaccine (Johnson & Johnson) during December 14, 2020-April 10, 2021 in 50 U.S. jurisdictions (49 states and the District of Columbia [DC]). Adult COVID-19 vaccination coverage was lower in rural counties (38.9%) than in urban counties (45.7%) overall and among adults aged 18-64 years (29.1% rural, 37.7% urban), those aged >=65 years (67.6% rural, 76.1% urban), women (41.7% rural, 48.4% urban), and men (35.3% rural, 41.9% urban). Vaccination coverage varied among jurisdictions: 36 jurisdictions had higher coverage in urban counties, five had higher coverage in rural counties, and five had similar coverage (i.e., within 1%) in urban and rural counties; in four jurisdictions with no rural counties, the urban-rural comparison could not be assessed. A larger proportion of persons in the most rural counties (14.6%) traveled for vaccination to nonadjacent counties (i.e., farther from their county of residence) compared with persons in the most urban counties (10.3%). As availability of COVID-19 vaccines expands, public health practitioners should continue collaborating with health care providers, pharmacies, employers, faith leaders, and other community partners to identify and address barriers to COVID-19 vaccination in rural areas (2).

MEDICAL SUBSPECIALTIES

CARDIOLOGY

RETURN TO PLAY FOR ATHLETES AFTER COVID-19 INFECTION: THE FOG BEGINS TO CLEAR

Udelson JE, Rowin EJ, Maron BJ.. JAMA Cardiol. 2021 May 27. doi: 10.1001/jamacardio.2021.2079. Online ahead of print.
Level of Evidence: 5 - Guidelines and Recommendations

BLUF

In an editorial, cardiology specialists associated with Tufts Medical Center discuss their recommendations for athletes returning to play after recovering from COVID-19. Before returning to play, the most practical approach of cardiac screening should include basic COVID-19 symptoms in addition to ECG, echocardiography, and troponin levels. Checking for abnormalities in CMR imaging due to myocarditis may be beneficial because of absence of myocarditis symptoms in some

athletes, however the significance is unknown and access to CMR is limited. Overall, these screening recommendations can detect many cases of cardiac involvement post-COVID-19 prior to returning to sports.

HEMATOLOGY AND ONCOLOGY

COVID-19 (SARS-COV-2) INFECTION AND THROMBOTIC CONDITIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Gabbai-Armelin PR, de Oliveira AB, Ferrisse TM, Sales LS, Barbosa ERO, Miranda ML, Salomão KB, Brighenti FL.. Eur J Clin Invest. 2021 Jun;51(6):e13559. doi: 10.1111/eci.13559. Epub 2021 Apr 14.
Level of Evidence: 4 - Systematic review of cross sectional studies with consistently applied reference standard and blinding

BLUF

A systematic review and meta-analysis conducted using PubMed, Web of Science and Scopus databases by researchers in Brazil sought to quantify risk factors for developing thromboembolic events in the setting of COVID-19. They found that D-dimer levels > 3.17 3.17 µg/mL, age over 60, and comorbid diabetes or hypertension were risk factors for thromboembolism whereas no statistically significant associations were seen with levels of platelets, neutrophils, C-reactive protein, lactate dehydrogenase, or ferritin.

ABSTRACT

Covid-19 is an infectious disease caused by SARS-CoV-2 virus associated with hematological manifestations (thrombolytic events). Considering the high prevalence of the thrombotic scenarios associated with Covid-19, the aim of this study was to perform a systematic review of the available literature, concerning the relation of Covid-19 and the thrombotic events, and identify prognostic factors for these events. PubMed, Web of Science and Scopus databases were searched. Independent reviewers conducted all flow diagram steps. For qualitative analysis, Oxford level of evidence and Newcastle-Ottawa scale were used in the eligible articles. For the prognostic factors a meta-analysis was conducted to age, number of neutrophils and platelets, and levels of ferritin, C-reactive protein, lactate dehydrogenase and D-dimer. Publication bias was accessed by funnel plot and by trim-and-fill test. Trim-and-fill test was also applied to evaluate meta-analysis bias. Twenty articles were included in the qualitative analysis and 6 articles were included in the meta-analysis. Case-control studies showed bias related with exposure and the main bias in cohort studies was related with selection and outcome. All articles received score 4 for the level of evidence. Hypertension and diabetes were the comorbidities more frequently associated with thrombolytic events. Significant results were found regarding D-dimer ($p < 0.0001$) and age ($p = 0.0202$) for thrombotic events in patients diagnosed with Covid-19. Patients older than 60 years, with hypertension, diabetes, and D-Dimer values above 3.17 microg/mL can be considered prognostic factors for developing thrombotic events due to Covid-19.

FIGURES

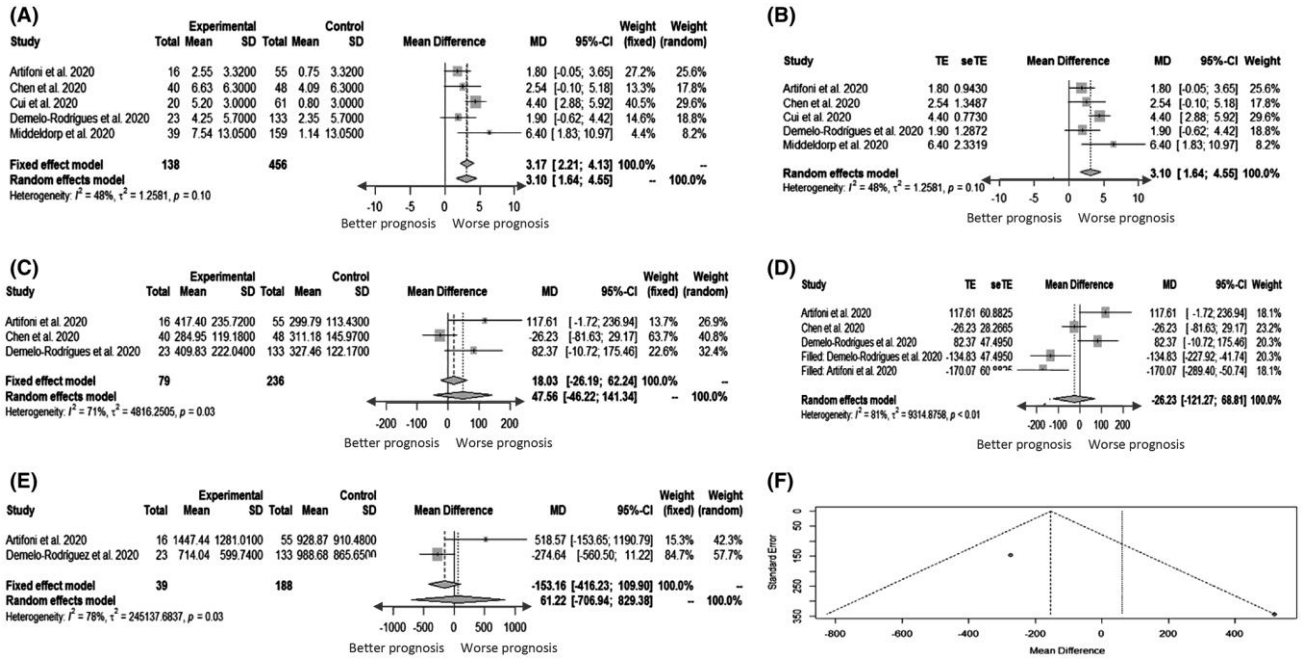


Figure 4. Meta-analysis illustrated in a forest plot showing significant results for D-dimer in fixed effect model (A). Trim-and-fill test illustrated in a forest plot showing significant results in a random effect model and no publication and meta-analysis biases for D-dimer (B). Meta-analysis illustrated in a forest plot showing no significant results for lactate dehydrogenase in fixed effect model (C). Trim-and-fill test illustrated in a forest plot showing that Demelo-Rodrígues et al 2020 and Artifoni et al 2020 are responsible for publication and meta-analysis biases related to lactate dehydrogenase (D). Meta-analysis illustrated in a forest plot showing no significant results for ferritin in fixed effect model (E). Funnel plot showing no publication bias for ferritin (F). Experimental group was formed by patients tested positive for COVID-19 with thrombolytic event. Control group was formed by patients tested positive for COVID-19 without thrombolytic event. CI, confidence interval; MD, mean difference; SD, standard deviation; SeTE, standard error of treatment estimate; TE, estimate of treatment effect. Arrows indicate the direction of the effect

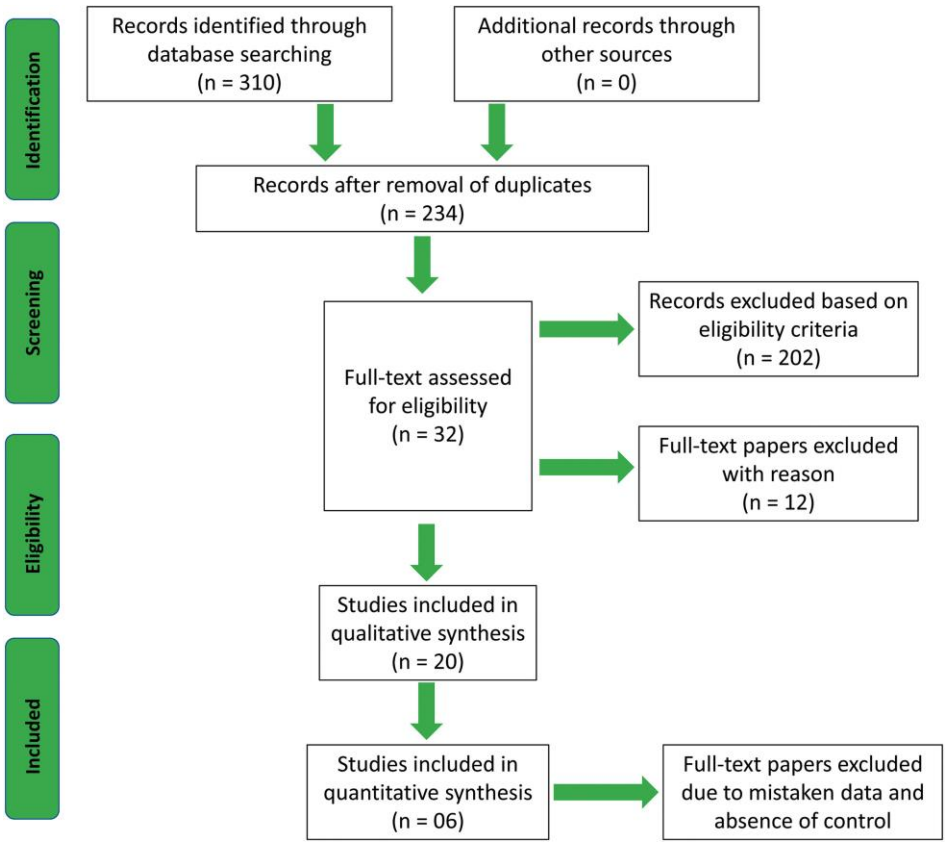


Figure 1. Flow diagram for the systematic review according to PRISMA Guidelines

S-GENE TARGET FAILURE AS A MARKER OF VARIANT B.1.1.7 AMONG SARS-COV-2 ISOLATES IN THE GREATER TORONTO AREA, DECEMBER 2020 TO MARCH 2021

Brown KA, Gubbay J, Hopkins J, Patel S, Buchan SA, Daneman N, Goneau LW.. JAMA. 2021 May 25;325(20):2115-2116. doi: 10.1001/jama.2021.5607.
Level of Evidence: 3 - Local non-random sample

BLUF

A research letter written by researchers at Public Health Ontario discussed that through performing RT-PCR on 20,051 nasopharyngeal swab samples from December 2020 to February 2021 in the Greater Toronto area, 4,692 had detectable S-gene deletion (SGTF) in amino acids 69 and 70 (Figure 1). The SGTF prevalence increased from 2% in December 2020 to 75% by the end of March 2021 with an estimated weekly growth rate 1.49 times greater than non-SGTF samples (Figure 2). Validation with whole genome sequencing led the researchers to conclude that SGTF is a reliable marker for the B.1.1.7 variant, which is rapidly increasing in prevalence globally.

FIGURES

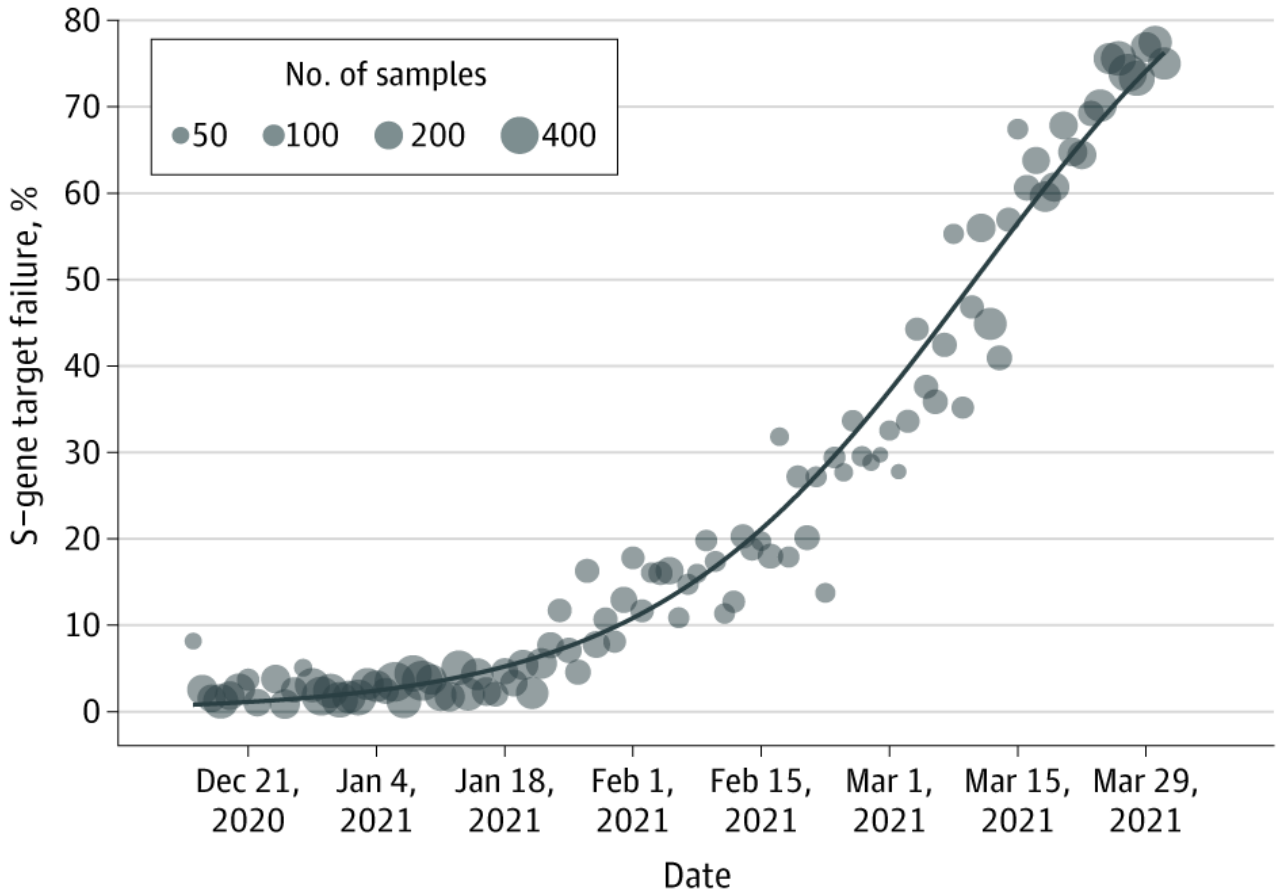


Figure 1. Percentage of Samples Positive for SARS-CoV-2 With S-Gene Target Failure

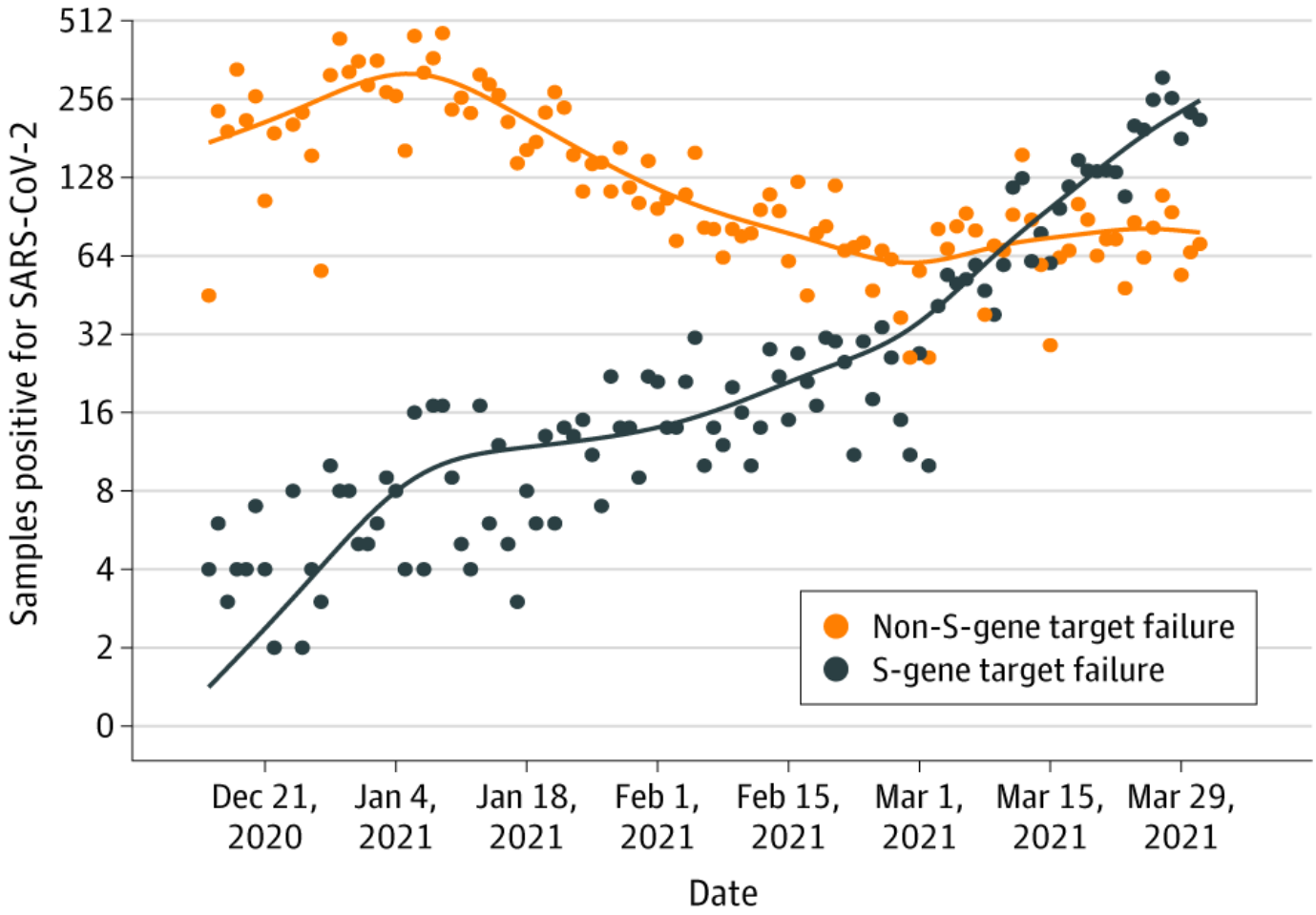


Figure 2. Daily Counts of SGTF (n = 4692) vs Non-SGTF Samples (n = 15 359)

DYNAMICS OF ANTI-SARS-COV-2 IGG ANTIBODIES POST-COVID-19 IN A BRAZILIAN AMAZON POPULATION

Bichara CDA, da Silva Graça Amoras E, Vaz GL, da Silva Torres MK, Queiroz MAF, do Amaral IPC, Vallinoto IMVC, Bichara CNC, Vallinoto ACR.. BMC Infect Dis. 2021 May 15;21(1):443. doi: 10.1186/s12879-021-06156-x.
Level of Evidence: 3 - Local non-random sample

BLUF

An observational cohort study conducted at the Federal University of Pará in Brazil followed 125 anti-SARS-CoV-2 antibody positive volunteers for 90 days following COVID-19 diagnosis to assess the persistence of antibodies. They found that persistence was detected after 90 days in 87 participants (69.6%) (Table 3) with symptoms lasting longer in those with persistent IgG response (greater than or equal to 21 days, compared to less than or equal to 7 days) (Table 2). The findings suggest a potentially high rate of immunity loss in this population.

ABSTRACT

BACKGROUND: In this study, the prevalence and persistence of anti-SARS-CoV-2 (severe acute respiratory syndrome-coronavirus) IgG was evaluated in volunteers 90 days after COVID-19 (coronavirus disease 2019) diagnosis by correlating response dynamics with clinical conditions, epidemiological characteristics, and disease severity. METHODS: The study recruited 200 volunteers aged 18 years or older of both sexes diagnosed with COVID-19. Of the 200 volunteers initially selected, the 135 individuals who underwent serological testing for anti-SARS-CoV-2 antibodies on the first visit to the laboratory, were invited to return, after 90 days, and provide a new blood sample for a second assessment of the presence of anti-SARS-CoV-2 IgG antibody. Disease severity and longevity of symptoms were evaluated for each individual and associated with the serological profile. RESULTS: Among the 135 individuals who underwent a previous serological test for anti-SARS-CoV-2 antibody, 125 showed reactivity to IgG (92.6%). Of the 125 individuals with detectable IgG in the first test, 87 (69.6%) showed persistence of this antibody after 90 days and 38 (30.4%) lost IgG reactivity in the second evaluation. The frequency of all reported symptoms was higher in individuals who maintained IgG persistence after 90 days of symptoms. Symptom

manifestations lasted >=21 days in the group with a persistent IgG response (39.6%) and <= 7 days in the group with a nonpersistent IgG response (50.0%). The length of hospital stay and supplemental oxygen use were higher in individuals with a persistent IgG response. CONCLUSIONS: The results of the present study show a high frequency of loss of anti-SARS-CoV-2 IgG antibodies within 3 months after COVID-19 diagnosis in the Brazilian Amazon.

FIGURES

Table 3

The frequency and persistence of SARS-CoV-2-reactive IgG in the study population 90 days after diagnosis

1st IgG test	2nd IgG test		*p**
	Reactive (*n* = 93) n (%)	Nonreactive (*n* = 42) n (%)	
Reactive (*n* = 125)	87 (69.6)	38 (30.4)	0.7846
Nonreactive (*n* = 10)	06 (60.0)	04 (40.0)	

*G test

Table 2

The frequency of symptoms in individuals with and without SARS-CoV-2-reactive IgG at the time of diagnosis and the time of symptom onset

Symptoms	N	1st IgG test		*p**
		Reactive *n* = 125 n (%)	Nonreactive *n* = 10 n (%)	
Fever	84	76 (60.8)	7 (70.0)	0.7405
Headache	94	88 (70.4)	6 (60.0)	0.4911
Coryza	62	59 (47.2)	3 (30.0)	0.3422
Cough	85	79 (63.2)	6 (60.0)	0.9994
Sore throat	73	66 (52.8)	7 (70.0)	0.3422
Body pain	94	89 (71.2)	5 (50.0)	0.2818
Abdominal pain	32	32 (25.6)	0 (0.0)	0.1165
Diarrhea	62	58 (46.4)	4 (40.0)	0.7532
Vomiting	16	16 (12.8)	0 (0.0)	0.3681
Nausea	37	37 (29.6)	0 (0.0)	0.0614
Anosmia	95	90 (72.0)	5 (50.0)	0.1640
Ageusia	91	86 (68.8)	5 (50.0)	0.2939
Shortness of breath	60	58 (46.4)	2 (20.0)	0.1843
Hair loss	47	44 (35.2)	3 (30.0)	1.0000
Duration of symptoms				
≤ 7 days	43	40 (32.0)	3 (30.0)	1.0000
15 days	43	39 (31.2)	4 (40.0)	0.7253
≥ 21 days	46	44 (35.2)	2 (20.0)	0.4936
No symptoms	03	2 (1.6)	1 (10.0)	0.2073

*Fisher's exact test

BAMLANIVIMAB FOR PREVENTION OF COVID-19

Kuritzkes DR.. JAMA. 2021 Jun 3. doi: 10.1001/jama.2021.7515. Online ahead of print.
Level of Evidence: 2 - Randomized trial or observational study with dramatic effect

BLUF

An editorial article written by a researcher affiliated with Harvard Medical School discusses a randomized, double-blind, placebo-controlled trial in 74 skilled nursing and assisted living facilities with 966 total participants to evaluate single IV 4200 mg dose of Bamlanivimab (a SARS-CoV-2 neutralizing monoclonal antibody) in COVID-19 prophylaxis. They found a significant reduction in incidence of symptomatic COVID-19 compared with placebo (8.5% vs. 15.2%, OR 0.43, 95% CI 0.28-0.68) as well as moderate to severe COVID-19 by day 57 (8.3% vs. 14.1%, OR 0.46, 95% CI 0.29-0.73). They additionally found significant decreases in viral loads in the Bamlanivimab group compared with placebo (2.44 vs. 3.64) and no COVID-19 related deaths among those in the treatment groups versus 5 deaths in the control. These findings suggest that passive immune prophylaxis with Bamlanivimab could abort outbreaks and reduce transmission in similar residential facilities.

EFFICACY OF NVX-COV2373 COVID-19 VACCINE AGAINST THE B.1.351 VARIANT

Shinde V, Bhikha S, Hoosain Z, Archary M, Bhorat Q, Fairlie L, Lalloo U, Masilela MSL, Moodley D, Hanley S, Fouche L, Louw C, Tameris M, Singh N, Goga A, Dheda K, Grobbelaar C, Kruger G, Carrim-Ganey N, Baillie V, de Oliveira T, Lombard Koen A, Lombaard JJ, Mngqibisa R, Bhorat AE, Benadé G, Lalloo N, Pitsi A, Vollgraaff PL, Luabeya A, Esmail A, Petrick FG, Oommen-Jose A, Foulkes S, Ahmed K, Thombrayil A, Fries L, Cloney-Clark S, Zhu M, Bennett C, Albert G, Faust E, Plested JS, Robertson A, Neal S, Cho I, Glenn GM, Dubovsky F, Madhi SA; 2019nCoV-501 Study Group.. N Engl J Med. 2021 May 5. doi: 10.1056/NEJMoa2103055. Online ahead of print.
Level of Evidence: 2 - Randomized trial or observational study with dramatic effect

BLUF

Researchers from South Africa conducted a multicenter, randomized, placebo-controlled trial enrolling 6324 participants between August 17, 2020-November 25, 2020 to assess the efficacy and safety of NVX-CoV2373 vaccine against the B.1.351 SARS-CoV-2 variant. They found 49.4% overall vaccine efficacy and 60.1% in HIV-negative participants. Genome sequencing showed 38 out of 41 COVID-19 cases were caused by the B.1.351 variant (Figure 1, 2), and post hoc analysis showed 51% efficacy among HIV-negative participants against B.1.351. Safety analysis revealed higher reactogenicity in the vaccine group than the placebo group and few adverse events in either group, suggesting the NVX-CoV2373 vaccine is safe and effective against the B.1.351 SARS-CoV-2 variant.

SUMMARY

Participants were randomly assigned to receive either 2 doses of NVX-CoV2373 vaccine or placebo given 21 days apart. Among the participants, 30% were seropositive at baseline.

Primary endpoints of the study:
- Efficacy: mild, moderate, severe COVID-19, 7 days post-second dose against B.1.351 in previously SARS-CoV-2 uninfected participants.
- Safety: solicited local and systemic adverse events for 7 days following each vaccination and solicited adverse events through day 35.

They found (Figures 1, 2):
- Among 2684 seronegative participants at baseline, 15 in the vaccine and 29 in the placebo group developed mild or moderate COVID-19.
- The vaccine group developed mild to moderate and higher local and systemic reactogenicity like headache (20–25%), muscle pain (17%-20%) and fatigue (12%-16%) than the placebo group.

ABSTRACT

BACKGROUND: The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants threatens progress toward control of the coronavirus disease 2019 (Covid-19) pandemic. In a phase 1-2 trial involving healthy adults, the NVX-

CoV2373 nanoparticle vaccine had an acceptable safety profile and was associated with strong neutralizing-antibody and antigen-specific polyfunctional CD4+ T-cell responses. Evaluation of vaccine efficacy was needed in a setting of ongoing SARS-CoV-2 transmission. METHODS: In this phase 2a-b trial in South Africa, we randomly assigned human immunodeficiency virus (HIV)-negative adults between the ages of 18 and 84 years or medically stable HIV-positive participants between the ages of 18 and 64 years in a 1:1 ratio to receive two doses of either the NVX-CoV2373 vaccine (5 mug of recombinant spike protein with 50 mug of Matrix-M1 adjuvant) or placebo. The primary end points were safety and vaccine efficacy against laboratory-confirmed symptomatic Covid-19 at 7 days or more after the second dose among participants without previous SARS-CoV-2 infection. RESULTS: Of 6324 participants who underwent screening, 4387 received at least one injection of vaccine or placebo. Approximately 30% of the participants were seropositive for SARS-CoV-2 at baseline. Among 2684 baseline seronegative participants (94% HIV-negative and 6% HIV-positive), predominantly mild-to-moderate Covid-19 developed in 15 participants in the vaccine group and in 29 in the placebo group (vaccine efficacy, 49.4%; 95% confidence interval [CI], 6.1 to 72.8). Vaccine efficacy among HIV-negative participants was 60.1% (95% CI, 19.9 to 80.1). Of 41 sequenced isolates, 38 (92.7%) were the B.1.351 variant. Post hoc vaccine efficacy against B.1.351 was 51.0% (95% CI, -0.6 to 76.2) among the HIV-negative participants. Preliminary local and systemic reactogenicity events were more common in the vaccine group; serious adverse events were rare in both groups. CONCLUSIONS: The NVX-CoV2373 vaccine was efficacious in preventing Covid-19, with higher vaccine efficacy observed among HIV-negative participants. Most infections were caused by the B.1.351 variant. (Funded by Novavax and the Bill and Melinda Gates Foundation; ClinicalTrials.gov number, NCT04533399.).

FIGURES

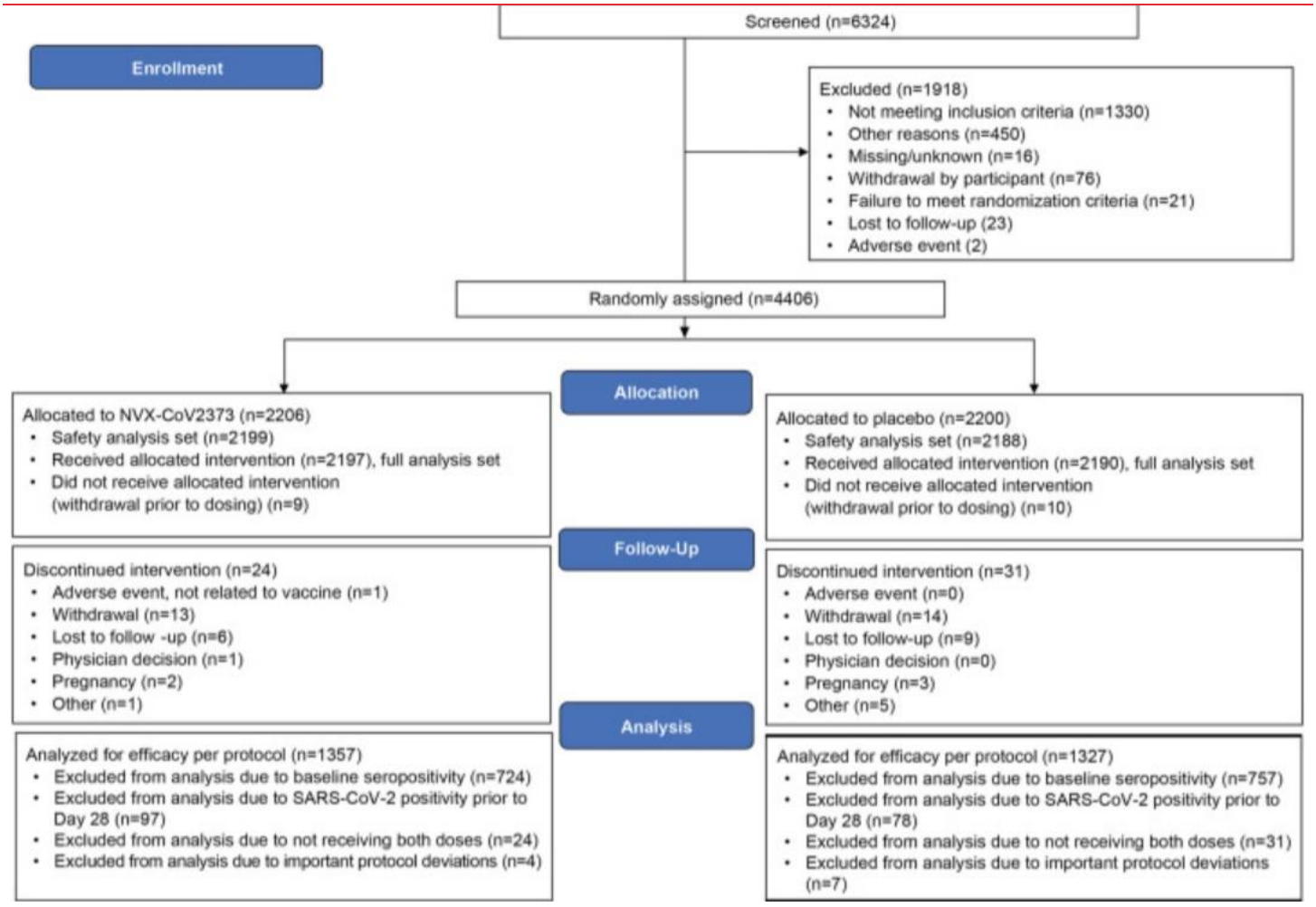


Figure 1: "Disposition of Participants in the Trial.
The full analysis set included all participants who were randomly assigned to treatment and received at least one dose, regardless of protocol violations or missing data, and are analyzed according to the trial vaccine group as randomized.

This diagram represents the disposition of participants in the trial. Among participants excluded for not meeting inclusion/exclusion criteria: approximately 32% tested HIV-positive on screening, 18% had a history of suspected or diagnosed Covid-19, 11% had an exclusionary chronic disease condition, 9% had exclusionary high or low BMI, 7% could not provide informed consent, and 5% had acute or ongoing illness. Among participants excluded for “other” reasons: approximately 69% were otherwise eligible but had missed the time window for enrollment into a particular stage or

cohort; and 23% of “other” did not meet inclusion/exclusion criteria but were recorded under the free text category of “other” (these had a similar distribution of exclusion criteria as those recorded under “not meeting inclusion/exclusion criteria”). The data cutoff date for the primary efficacy analysis was January 8, 2021, which represented a median follow-up of 66 and 45 days after first and second vaccination, respectively. The data cutoff date for the primary safety analysis was January 25, 2021, which included safety data through 35 days after first vaccination in all 968 Stage 1 participants (889 HIV-negative and 79 PLWH). The safety analysis set included all participants who received at least one dose of NVX-CoV2373 or placebo, with participants analyzed according to the treatment actually received. The per-protocol efficacy analysis set (PP-EFF) included baseline seronegative (by anti-spike IgG) participants who received both injection of NVX-CoV2373 or placebo as assigned, had no evidence of SARS-CoV-2 infection (by NAAT or anti-spike IgG) within 7 days after the second vaccination (ie, before Day 28), and had no major protocol deviations affecting the primary efficacy outcome. A second per-protocol efficacy analysis set (PP-EFF-2) was defined in a similar fashion except without the exclusion of baseline seropositive participants to allow for analysis of efficacy in seropositive or all participants, regardless of serostatus.

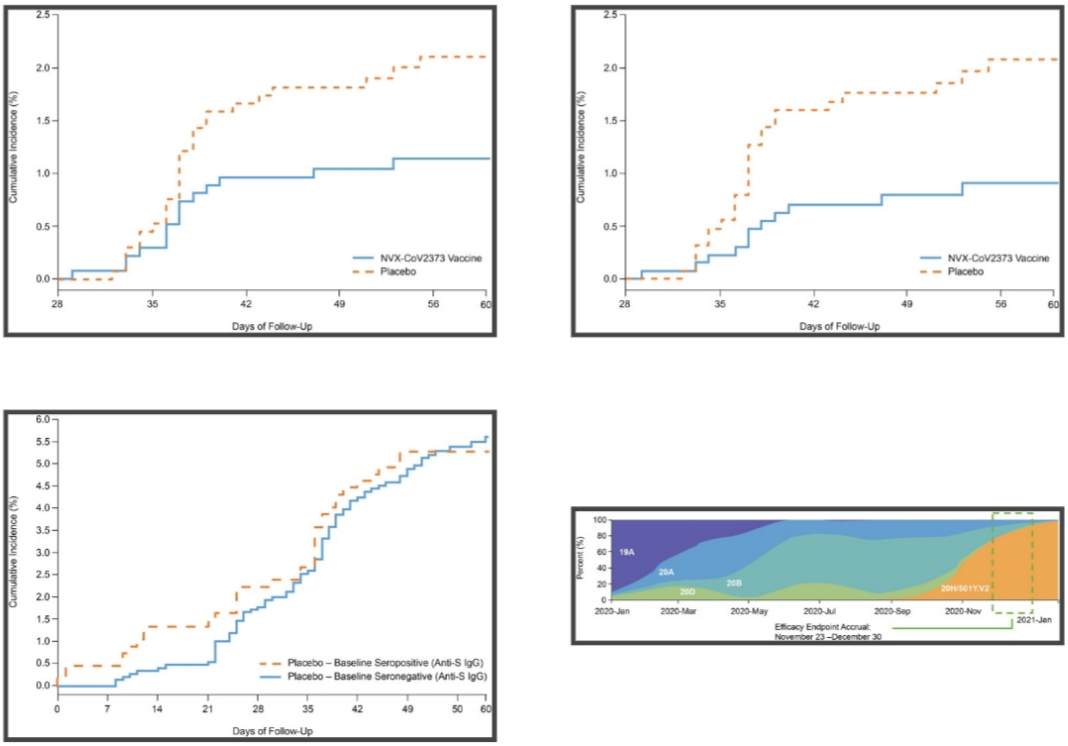


Figure 2: "Kaplan-Meyer Plots of Efficacy of NVX-CoV2373 Against Symptomatic Covid-19, Risk of Symptomatic Covid-19 in Seropositive versus Seronegative Placebo Recipients, and Timing of Endpoint Accrual.

Shown is the cumulative incidence of symptomatic Covid-19. The time period for surveillance of per-protocol symptomatic Covid-19 cases was from at least 7 days after the second dose (ie, Day 28) of NVX-CoV2373 or placebo through the first 2 months of follow-up. Data shown are for the per-protocol efficacy analysis sets (PP-EFF or PP-EFF-2), unless otherwise indicated. A) All participants (HIV-negative and PLWH), baseline seronegative; B) HIV-negative participants, baseline seronegative; C) Placebo participants, baseline seronegative vs baseline seropositive, in the full analysis set (FAS) from Day 0 onwards. The FAS included all participants who were randomly assigned to treatment and receive at least 1 dose, regardless of protocol violations or missing data. D) Per protocol efficacy endpoint accrual relative to distribution of variant as reported in Nextstrain.org.

A. All participants (baseline seronegative): primary efficacy endpoint from 7 days after second dose (Day 28) in the per-protocol analysis set

B. HIV-negative participants (baseline seronegative): primary efficacy endpoint from 7 days after second dose (Day 28) in the per-protocol analysis set

C. Placebo participants ONLY (baseline seronegative placebo versus baseline seropositive placebo): primary efficacy endpoint from Day 0 onwards in the full analysis set

D. Accrual of Primary Efficacy Endpoints Relative to B.1.351 (501Y.V2) Variant Circulation in South Africa by Time".

INCREASES IN NALOXONE ADMINISTRATIONS BY EMERGENCY MEDICAL SERVICES PROVIDERS DURING THE COVID-19 PANDEMIC: RETROSPECTIVE TIME SERIES STUDY

Khoury D, Preiss A, Geiger P, Anwar M, Conway KP.. JMIR Public Health Surveill. 2021 May 27;7(5):e29298. doi: 10.2196/29298.
Level of Evidence: 3 - Local non-random sample

BLUF

A retrospective time series study conducted by researchers affiliated with Research Triangle Institute International, North Carolina A & T State University, and the National Institute of Mental Health compared the 29-week period before (9/1/19–3/9/20) and after (3/10–9/30/20) the COVID-19 state of emergency declaration in North Carolina to data from each similar 29-week period dating back to 2014 and found increases in weekly mean number of opioid-related EMS runs (25.6) (Figure 2), naloxone administrations (22.3) (Figure 3), and multiple naloxone administrations (5.0) (Figure 4), resulting in proportional comparative increases of 37.4%, 57.8%, and 84.8%, respectively. As the first study to report increases in both occurrence and severity of opioid overdoses during this time, the findings suggest an exacerbation of the opioid crisis during the pandemic.

ABSTRACT

BACKGROUND: The opioid crisis in the United States may be exacerbated by the COVID-19 pandemic. Increases in opioid use, Emergency Medical Service (EMS) runs for opioid-related overdoses, and opioid-overdose deaths have been reported. No study has examined changes in multiple naloxone administrations, an indicator of overdose severity, during the COVID-19 pandemic. OBJECTIVE: This study examined changes in the occurrence of naloxone administrations (NAs) and multiple naloxone administrations (MNAs) during EMS runs for opioid-related overdoses during the COVID-19 pandemic in Guilford County, North Carolina (NC). METHODS: Using a period-over-period approach, we compared the occurrence of opioid-related EMS runs, NAs, and MNAs during the 29-week period before (September 1, 2019 to March 9, 2020) and after NC's COVID-19 state-of-emergency declaration (i.e., the 'COVID-19 period' of 3/10/2020 to 9/30/2020). Furthermore, historical data were used to generate a quasi-control distribution of period-over-period changes to compare the occurrence of each outcome during the COVID-19 period to each 29-week period back to January 1, 2014. RESULTS: All outcomes increased during the COVID-19 period. Compared to the previous 29 weeks, the COVID-19 period experienced increases in the weekly mean number of opioid-related EMS runs (25.6 versus 18.6, p<.001), NAs (22.3 versus 14.1, p<.001), and MNAs (5.0 versus 2.7, p<.001) corresponding to proportional increases of 37.4%, 57.8%, and 84.8%, respectively. Additionally, the increases during the COVID-19 period were greater than 91% of all historical 29-week periods analyzed. CONCLUSIONS: The occurrence of EMS runs for opioid-related overdoses as well as NAs and MNAs during EMS runs increased during the COVID-19 pandemic in Guilford County, NC. For a host of reasons that need to be explored, the COVID-19 pandemic appears to exacerbate the opioid crisis. CLINICALTRIAL:

FIGURES

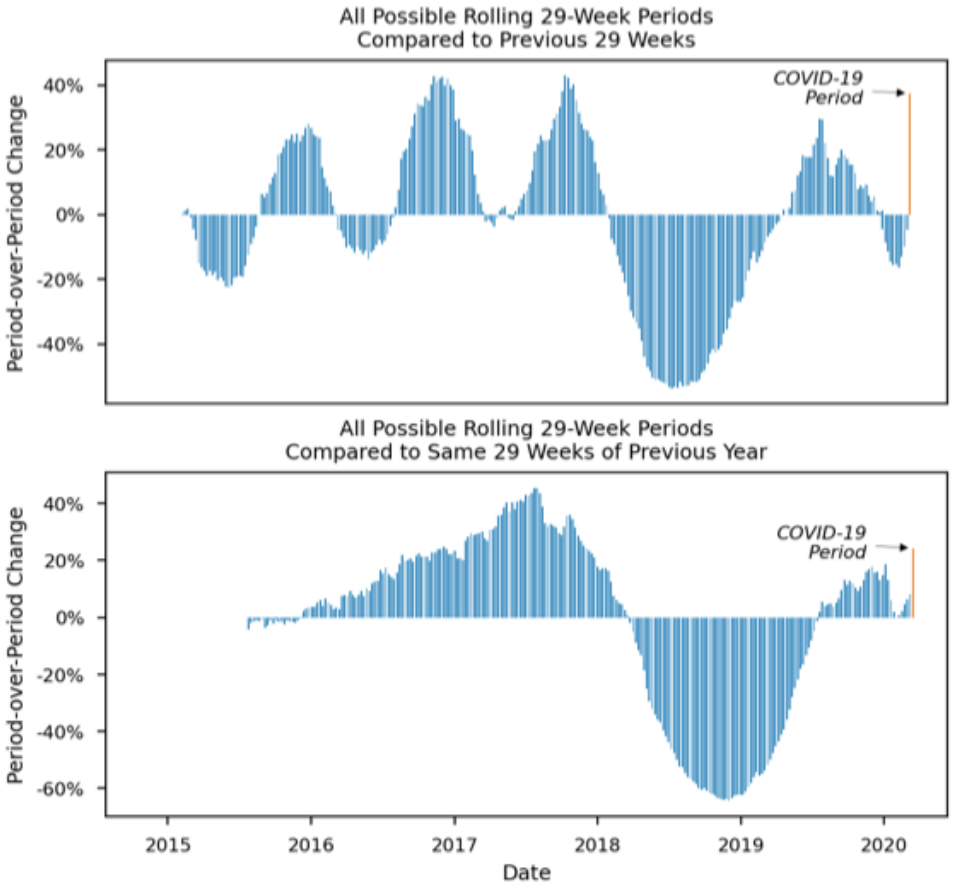


Figure 2. Historical period-over-period change in emergency medical services runs involving opioid overdoses in Guilford County, North Carolina before and after the COVID-19 state of emergency declaration.

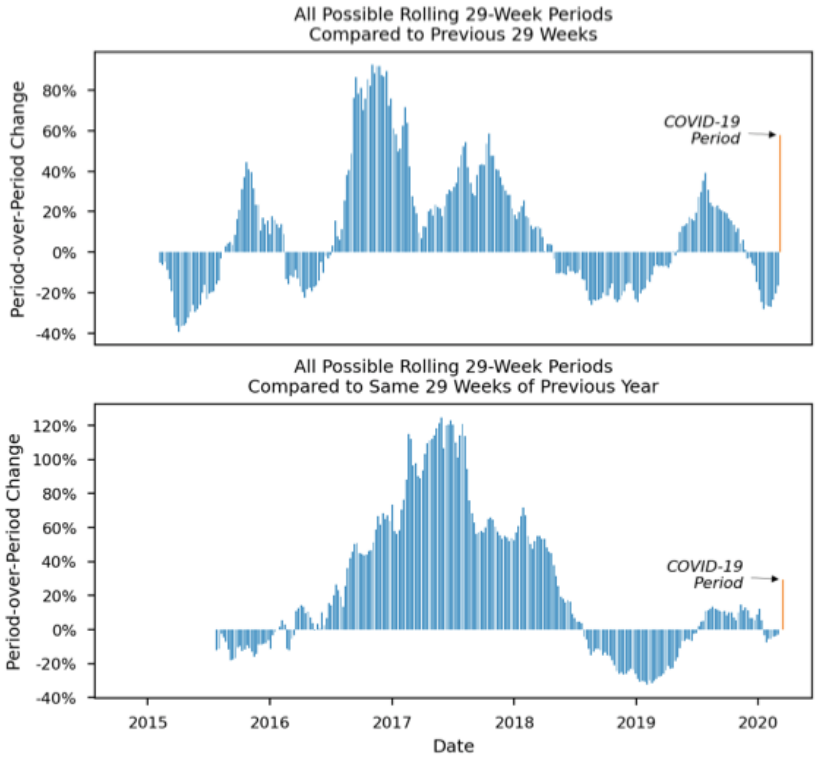


Figure 3. Historical period-over-period change in emergency medical services runs involving naloxone administrations in Guilford County, North Carolina before and after the COVID-19 state of emergency declaration.

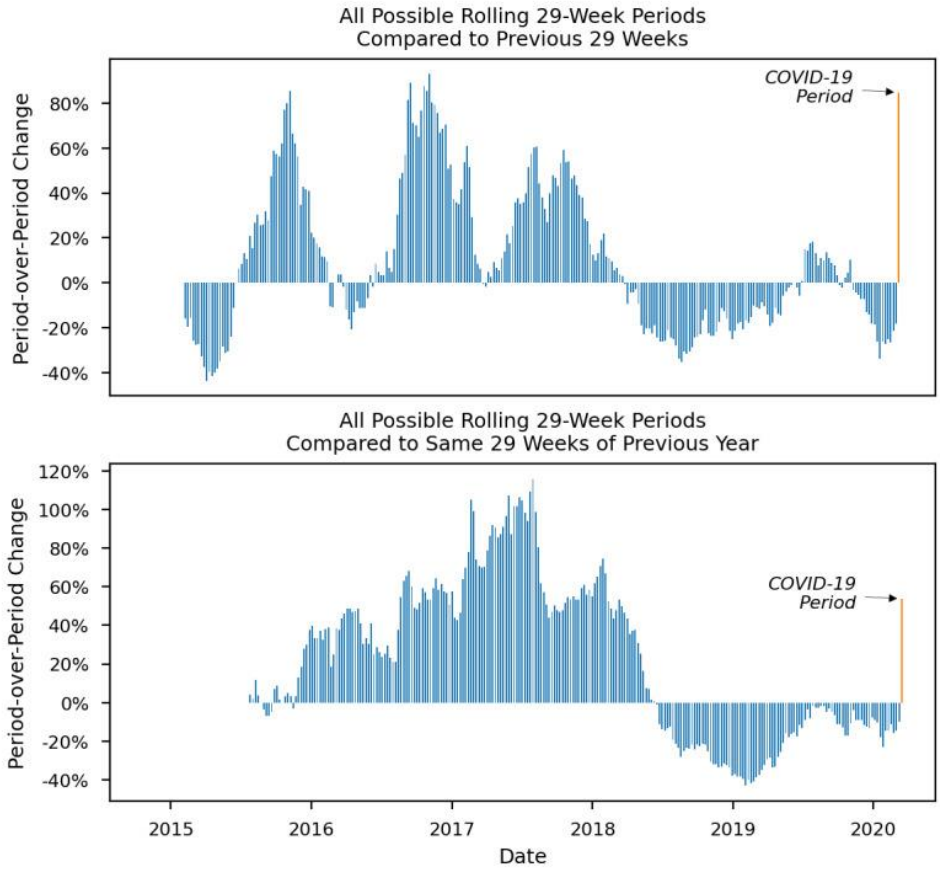


Figure 4. Historical period-over-period change in emergency medical services runs involving multiple naloxone administrations in Guilford County, North Carolina before and after the COVID-19 state of emergency declaration.

ACKNOWLEDGEMENTS

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