The Weekly COVID-19 Literature Surveillance Summary

May 07, 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

- Trends in Patient Characteristics and COVID-19 In-Hospital Mortality in the United States During the COVID-19 Pandemic: Cardiologists from multiple American universities conducted a retrospective cohort study of 20,736 adults with COVID-19 admitted to 107 acute care hospitals between March and November 2020. They found in-hospital deaths were significantly lower in May through November compared to March and April even after adjustment for confounding variables. Though the study methodology precludes causal inferences, authors suggest rapid implementation of new isolation procedures and new techniques such as high flow nasal oxygen and prone positioning may have contributed to improved survival rates as providers gained knowledge.

- Severe SARS-CoV-2 placenta infection can impact neonatal outcome in the absence of vertical transmission: Molecular biologists and neonatologists from several institutions in Milan, Italy analyzed the placentas and clinical outcomes of 37 pregnant women who delivered between March 12 and April 23, 2020. While there was no observed evidence of vertical transmission of the virus in neonates, the virus was detected in the placental tissue of one-half of the total women (n=21) who were positive with the virus in their third trimester. In one case with high placental viral load there was extensive placental necrosis, and the infant had seizures and hypoxia requiring mechanical ventilation and oxygen supplementation for three days after birth. Authors suggest that while the relatively low viral tissue load found in the majority of placentas did not induce a harmful inflammatory response, in some situations high SARS-CoV-2 viral loads could impair neonatal development and impact outcomes in absence of vertical transmission.

- Association of Maternal SARS-CoV-2 Infection in Pregnancy With Neonatal Outcomes: Neonatologists and women's health experts from the Karolinska Institutet in Sweden studied a prospective cohort of 88,159 infants delivered to mothers who tested positive for SARS-CoV-2 between March 2020 and January 2021 using Swedish patient registries. Compared to infants born to healthy mothers in the same time frame, these infants were more likely to be admitted to the neonatal intensive care unit (11.7 vs 8.4%; odds ratio [OR], 1.47; 95%CI, 1.26-1.70) or have respiratory distress syndrome (1.2 vs 0.5%; OR, 2.40; 95%CI, 1.50-3.84), any neonatal respiratory disorder (2.8 vs 2.0%; OR, 1.42; 95%CI, 1.07-1.90), and hyperbilirubinemia (3.6 vs 2.5%; OR, 1.47; 95%CI, 1.13-1.90). Authors suggest neonates born to SARS-CoV-2 mothers are at higher risk for complications, though due to limitations in the data (imbalanced testing, heterogeneity of maternal disease severity) recommend further research into virally-altered prognosis and outcomes for newborns.

Understanding the Pathology

- Viral genomic, metagenomic and human transcriptomic characterization and prediction of the clinical forms of COVID-19: Researchers from Hôpitaux Universitaires Henri Mondor in Créteil, France used shotgun metagenomics to characterize genomic, metagenomic, and transcriptomic features of nasopharyngeal swabs from 104 COVID-19 patients. Overexpression of transcripts activating the CXCR2 pathway was seen in patients with severe pneumonia, while a T helper "Th1-Th17" profile was seen in patients with benign disease. Overall, this suggests that patients with severe COVID-19 have prolonged inflammation due to neutrophil accumulation, suggesting possible treatments such as CXCR2 antagonists and IL-8 antagonists.

Transmission & Prevention

- SARS-CoV-2 Vaccine-Induced Immune Thrombotic Thrombocytopenia: Professors from the department of pathology and laboratory medicine from the University of Pennsylvania discuss 3 independent studies describing 39 cases of thrombosis and thrombocytopenia associated with the ChAdOx1 nCoV-19 (AstraZeneca) COVID-19 vaccine. They found most patients were women under the age of 50, and that thromboses formed at unusual sites on the body with a death rate of 40%. High levels of platelet factor 4 (PF4) were detected in almost all patients. Authors suggest there is a rare link between AstraZeneca vaccination and thrombosis, and recommend future research focus on the potential role of PF4, identify patients at higher risk, and guide management.

- Pathologic Antibodies to Platelet Factor 4 after ChAdOx1 nCoV-19 Vaccination: Hematologists from University College London Hospitals NHS Foundation Trust, among others, present cases of vaccine induced thrombosis and thrombocytopenia (VITT) 6 to 24 days after the first dose of ChAdOx1 nCoV-19 vaccination (AstraZeneca) in 23 patients with no prethrombotic history (except 1 patient with DVT) and in absence of heparin. They found 22 patients developed both thrombosis and thrombocytopenia while 1 had only thrombocytopenia with bruising. Anti-PF4 antibody ELISA was positive in 22/23 patients. Authors suggest providers monitor for VITT after AstraZeneca COVID-19 vaccination and propose an algorithm to help in its diagnosis and management.

TABLE OF CONTENTS

NAVIGATING ATTACKS AGAINST HEALTH CARE WORKERS IN THE COVID-19 ERA

Larkin H.. JAMA. 2021 Apr 21. doi: 10.1001/jama.2021.2701. Online ahead of print.
Level of Evidence: 5 - Opinion

BLUF

A science journalist writing for the Journal of the American Medical Association reports on the perceived increase in physical and verbal attacks against healthcare workers (HCW) during the COVID-19 pandemic, which had been rising prior to the pandemic (Figure). The author reviews potential strategies to protect HCWs including timely reporting, technological safeguards (panic buttons, cameras, weapon detectors), minimizing access to potential weapons (i.e. IV poles, needles), safe furniture arrangement, and de-escalation training for both in-person and online interactions to help prevent future attacks.

FIGURES

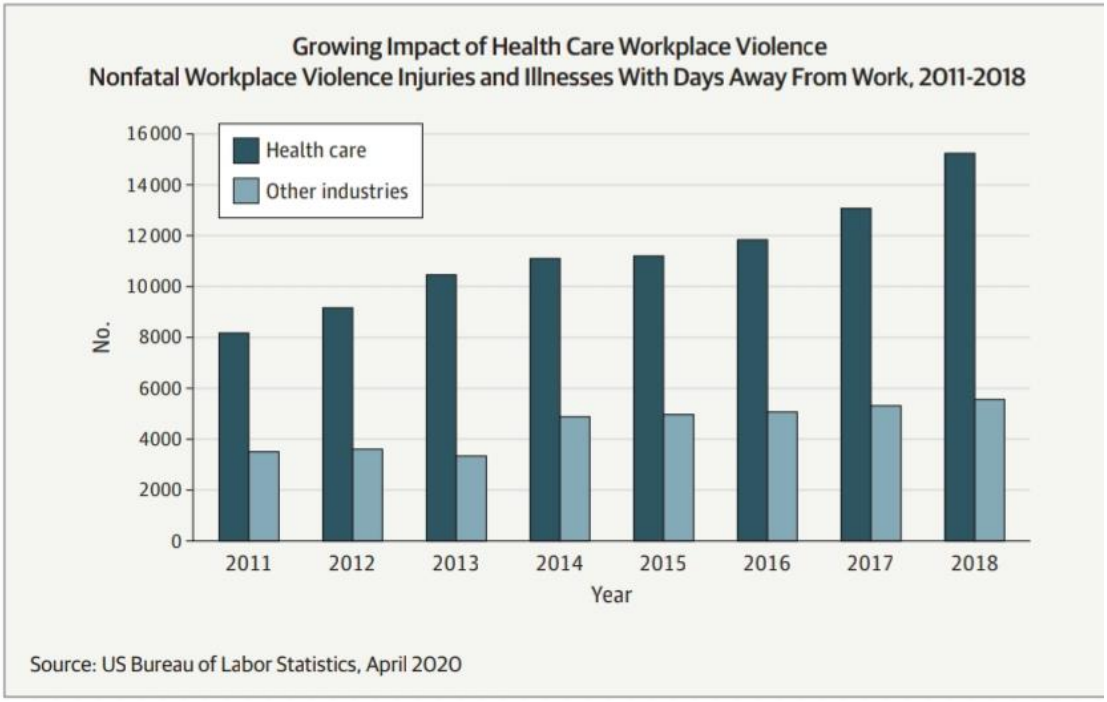


Figure: "Growing Impact of Health Care Workplace Violence
Nonfatal Workplace Violence Injuries and Illnesses With Days Away From Work, 2011-2018".

TEMPORAL DYNAMICS OF VIRAL LOAD AND FALSE NEGATIVE RATE INFLUENCE THE LEVELS OF TESTING NECESSARY TO COMBAT COVID-19 SPREAD

Jarvis KF, Kelley JB.. Sci Rep. 2021 Apr 28;11(1):9221. doi: 10.1038/s41598-021-88498-9.
Level of Evidence: 5 - Modeling

BLUF

Molecular biologists from the University of Maine created a stochastic agent-based Susceptible-Exposed-Infectious-Recovered (SEIR) model to investigate the impact of viral load on spread of SARS-CoV-2. In 100 independent runs of a simulation with 10,000 individuals running daily for 120 days, authors found non-uniform dynamics of viral spread and false negative rates significantly influenced the degree of testing required to decrease spread (Figures 1, 5). Authors suggest non-uniform dynamics must be accounted for in models of testing programs due to their observed effect on transmission.

ABSTRACT

Colleges and other organizations are considering testing plans to return to operation as the COVID-19 pandemic continues. Pre-symptomatic spread and high false negative rates for testing may make it difficult to stop viral spread. Here, we develop a stochastic agent-based model of COVID-19 in a university sized population, considering the dynamics of both viral load and false negative rate of tests on the ability of testing to combat viral spread. Reported dynamics of SARS-CoV-2 can lead to an apparent false negative rate from ~ 17 to ~ 48%. Nonuniform distributions of viral load and false negative rate lead to higher requirements for frequency and fraction of population tested in order to bring the apparent Reproduction number (Rt) below 1. Thus, it is important to consider non-uniform dynamics of viral spread and false negative rate in order to model effective testing plans.

FIGURES

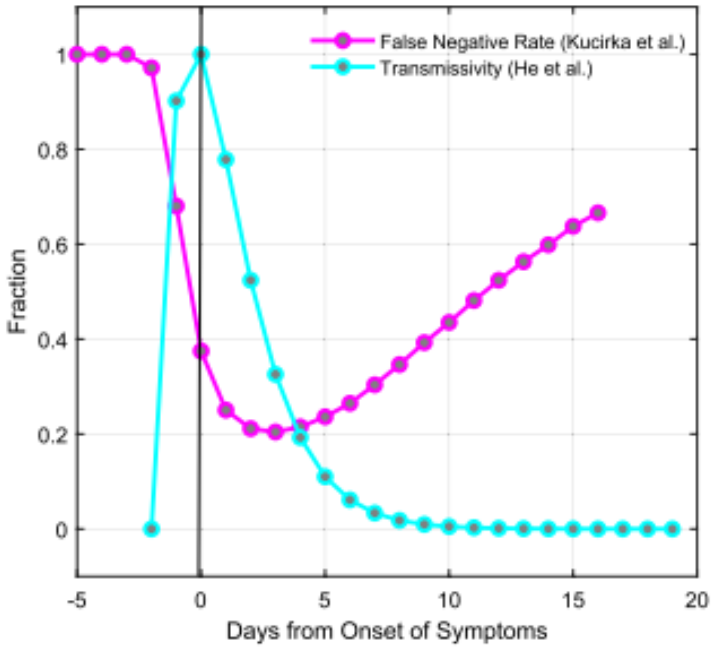


Figure 1. Viral transmission data and test false negative rate data both suggest that SARS-CoV-2 is undetectable until ~2 days prior to symptom onset. Shown in cyan is the viral load data by day from onset of symptoms from He et al.6. Shown in magenta is the false negative rate of tests by day from Kucirka et al.7. Transmission probability begins increasing~2 days before symptom onset, at the same time that the false negative rate of tests begins dropping

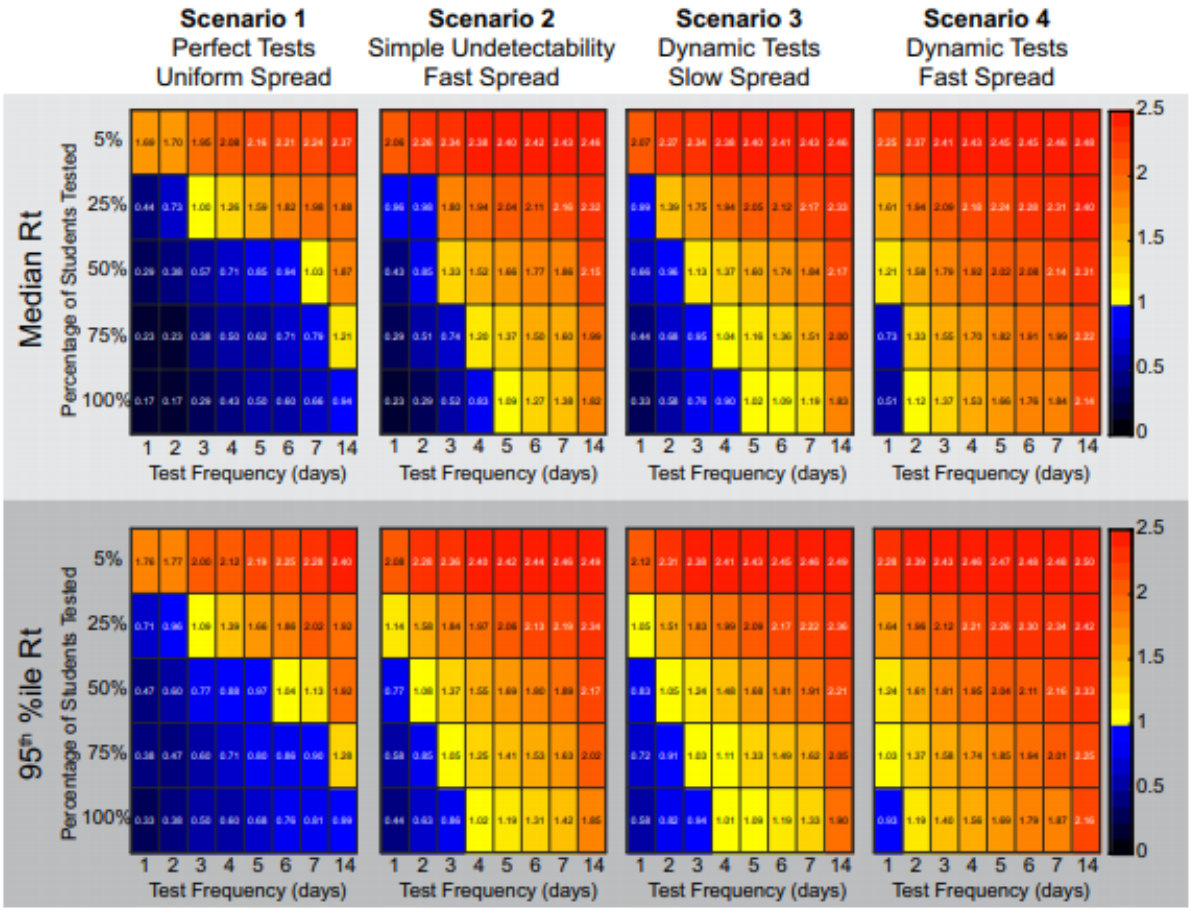


Figure 5. High asymptomatic transmission and dynamic false negative rate lead to a requirement for more testing to bring the viral spread under control. Heatmaps show the efective Reproduction number (Rt) from 100 simulations run with the given proportion of the population tested at the indicated frequency. Te top row of matrices shows the median Rt, while the bottom row of matrices shows the value of the upper 95th percentile (i.e. conditions that will work in 19 out of 20 situations). While the scenario 1 perfect tests suggest testing the entire population every two weeks may work to stop spread of the virus, using scenario 4 parameters predicts that testing the entire population daily was necessary.

SYMPTOMS AND CLINICAL PRESENTATION

ADULTS

TRENDS IN PATIENT CHARACTERISTICS AND COVID-19 IN-HOSPITAL MORTALITY IN THE UNITED STATES DURING THE COVID-19 PANDEMIC

Roth GA, Emmons-Bell S, Alger HM, Bradley SM, Das SR, de Lemos JA, Gakidou E, Elkind MSV, Hay S, Hall JL, Johnson CO, Morrow DA, Rodriguez F, Rutan C, Shakil S, Sorensen R, Stevens L, Wang TY, Walchok J, Williams J, Murray C.. JAMA Netw Open. 2021 May 3;4(5):e218828. doi: 10.1001/jamanetworkopen.2021.8828.
Level of Evidence: 3 - Local non-random sample

BLUF

Cardiologists from multiple American universities conducted a retrospective cohort study of 20,736 adults with COVID-19 admitted to 107 acute care hospitals between March and November 2020. They found in-hospital deaths were significantly lower in May through November compared to March and April even after adjustment for confounding variables (Figure 1). Though the study methodology precludes causal inferences, authors suggest rapid implementation of new isolation procedures and new techniques such as high flow nasal oxygen and prone positioning may have contributed to improved survival rates as providers gained knowledge.

ABSTRACT

Importance: In-hospital mortality rates from COVID-19 are high but appear to be decreasing for selected locations in the United States. It is not known whether this is because of changes in the characteristics of patients being admitted. Objective: To describe changing in-hospital mortality rates over time after accounting for individual patient characteristics. Design, Setting, and Participants: This was a retrospective cohort study of 20 736 adults with a diagnosis of COVID-19 who were included in the US American Heart Association COVID-19 Cardiovascular Disease Registry and admitted to 107 acute care hospitals in 31 states from March through November 2020. A multiple mixed-effects logistic regression was then used to estimate the odds of in-hospital death adjusted for patient age, sex, body mass index, and medical history as well as vital signs, use of supplemental oxygen, presence of pulmonary infiltrates at admission, and hospital site. Main Outcomes and Measures: In-hospital death adjusted for exposures for 4 periods in 2020. Results: The registry included 20 736 patients hospitalized with COVID-19 from March through November 2020 (9524 women [45.9%]; mean [SD] age, 61.2 [17.9] years); 3271 patients (15.8%) died in the hospital. Mortality rates were 19.1% in March and April, 11.9% in May and June, 11.0% in July and August, and 10.8% in September through November. Compared with March and April, the adjusted odds ratios for in-hospital death were significantly lower in May and June (odds ratio, 0.66; 95% CI, 0.58-0.76; P < .001), July and August (odds ratio, 0.58; 95% CI, 0.49-0.69; P < .001), and September through November (odds ratio, 0.59; 95% CI, 0.47-0.73). Conclusions and Relevance: In this cohort study, high rates of in-hospital COVID-19 mortality among registry patients in March and April 2020 decreased by more than one-third by June and remained near that rate through November. This difference in mortality rates between the months of March and April and later months persisted even after adjusting for age, sex, medical history, and COVID-19 disease severity and did not appear to be associated with changes in the characteristics of patients being admitted.

FIGURES

Months and ages, y	No. of deaths/ total No. (%)	Unadjusted OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
May and June					
All ages	488/4116 (11.9)	0.57 (0.53-0.62)	<.001	0.66 (0.58-0.76)	<.001
41-50	27/557 (4.8)	0.65 (0.48-0.88)	<.01	0.73 (0.43-1.24)	.24
51-60	59/730 (8.1)	0.59 (0.48-0.72)	<.001	0.62 (0.43-0.90)	.01
61-70	104/804 (12.9)	0.64 (0.54-0.75)	<.001	0.67 (0.51-0.88)	<.01
71-80	131/660 (19.8)	0.60 (0.52-0.70)	<.001	0.57 (0.44-0.74)	<.001
≥81	141/610 (23.1)	0.51 (0.44-0.56)	<.001	0.56 (0.42-0.73)	<.001
July and August					
All ages	292/2709 (11.0)	0.52 (0.48-0.58)	<.001	0.58 (0.49-0.69)	<.001
41-50	16/325 (4.9)	0.66 (0.45-0.97)	.03	0.51 (0.26-0.98)	.04
51-60	36/509 (7.1)	0.51 (0.39-0.66)	<.001	0.50 (0.32-0.79)	<.01
61-70	67/547 (12.2)	0.60 (0.49-0.73)	<.001	0.58 (0.41-0.81)	<.01
71-80	86/494 (17.4)	0.51 (0.43-0.61)	<.001	0.52 (0.37-0.71)	<.001
≥81	73/336 (21.7)	0.47 (0.39-0.57)	<.001	0.48 (0.34-0.70)	<.001
September, October, and November					
All ages	217/2010 (10.8)	0.51 (0.46-0.57)	<.001	0.59 (0.47-0.73)	<.001
41-50	15/233 (6.4)	0.88 (0.59-1.31)	.53	0.76 (0.37-1.57)	.45
51-60	22/322 (6.8)	0.49 (0.36-0.67)	<.001	0.48 (0.27-0.86)	.01
61-70	45/472 (9.5)	0.45 (0.36-0.57)	<.001	0.54 (0.36-0.82)	<.01
71-80	69/395 (17.5)	0.51 (0.42-0.62)	<.001	0.51 (0.35-0.74)	<.001
≥81	58/284 (20.4)	0.44 (0.35-0.54)	<.001	0.47 (0.30-0.72)	<.001

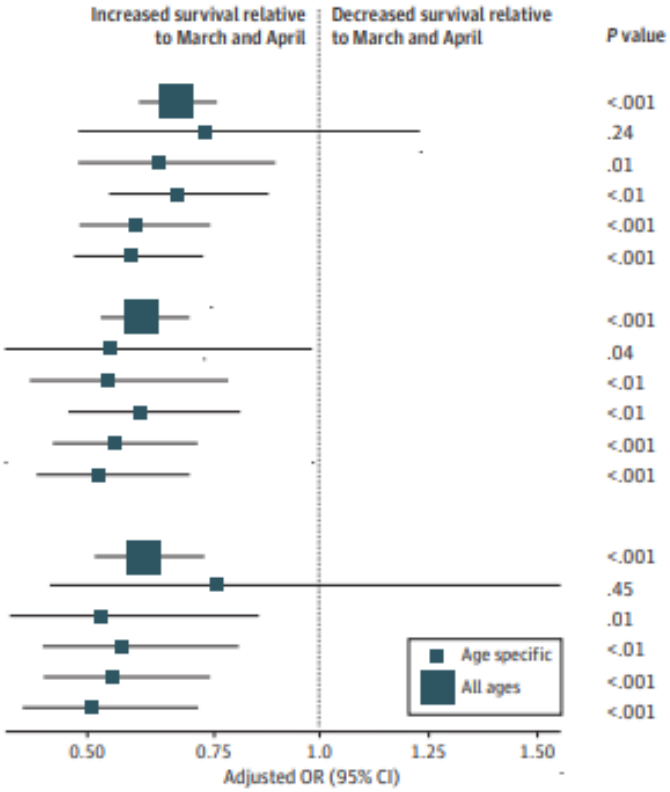


Figure. Unadjusted and Adjusted Odds of Inpatient Death in May and June, July and August, and September Through November Compared With March and April, 2020

PREGNANT PERSONS

SEVERE SARS-COV-2 PLACENTA INFECTION CAN IMPACT NEONATAL OUTCOME IN THE ABSENCE OF VERTICAL TRANSMISSION

Cribiù FM, Erra R, Pugni L, Rubio-Perez C, Alonso L, Simonetti S, Croci GA, Serna G, Ronchi A, Pietrasanta C, Lunghi G, Fagnani AM, Piñana M, Matter MS, Tzankov A, Terracciano L, Anton A, Ferrazzi E, Ferrero S, Iurlaro E, Seoane J, Nuciforo P.. J Clin Invest. 2021 Jan 26:145427. doi: 10.1172/JCI145427. Online ahead of print.
Level of Evidence: 4 - Case-series

BLUF

Molecular biologists and neonatologists from several institutions in Milan, Italy analyzed the placentas and clinical outcomes of 37 pregnant women who delivered between March 12 and April 23, 2020. While there was no observed evidence of vertical transmission of the virus in neonates, the virus was detected in the placental tissue of one-half of the total women (n=21) who were positive with the virus in their third trimester (Figure 2). In one case with high placental viral load there was extensive placental necrosis (Figure 1), and the infant had seizures and hypoxia requiring mechanical ventilation and oxygen supplementation for three days after birth. Authors suggest that while the relatively low viral tissue load found in the majority of placentas did not induce a harmful inflammatory response, in some situations high SARS-CoV-2 viral loads could impair neonatal development and impact outcomes in absence of vertical transmission.

ABSTRACT

The effect of SARS-CoV-2 infection on the pathophysiology of the placenta and its impact on pregnancy outcome has not yet been fully elucidated. Here, we present a comprehensive clinical, morphological, and molecular analysis of placental tissues from pregnant women with and without SARS-CoV-2 infection. SARS-CoV-2 could be detected in half of placental tissues from SARS-CoV-2-positive women. The presence of the virus was not associated with any distinctive pathological, maternal or neonatal outcome features. SARS-CoV-2 tissue load was low in all but one patient which exhibited severe placental damage leading to neonatal neurological manifestations. The placental transcriptional response induced by high viral load of SARS-CoV-2 showed an immunopathology phenotype similar to autopsy lung tissues from patients with severe COVID-19. This finding contrasted with the lack of inflammatory response in placental tissues from SARS-CoV-2-positive women with low viral tissue load and from SARS-CoV-2-negative women. Importantly, no evidence of vertical transmission of SARS-CoV-2 was found in any newborns, suggesting that the placenta may be an effective maternal-neonatal barrier against the virus even in the presence of severe infection. Our observations suggest that severe placental damage induced by the virus may be detrimental for the neonate independently of vertical transmission.

FIGURES

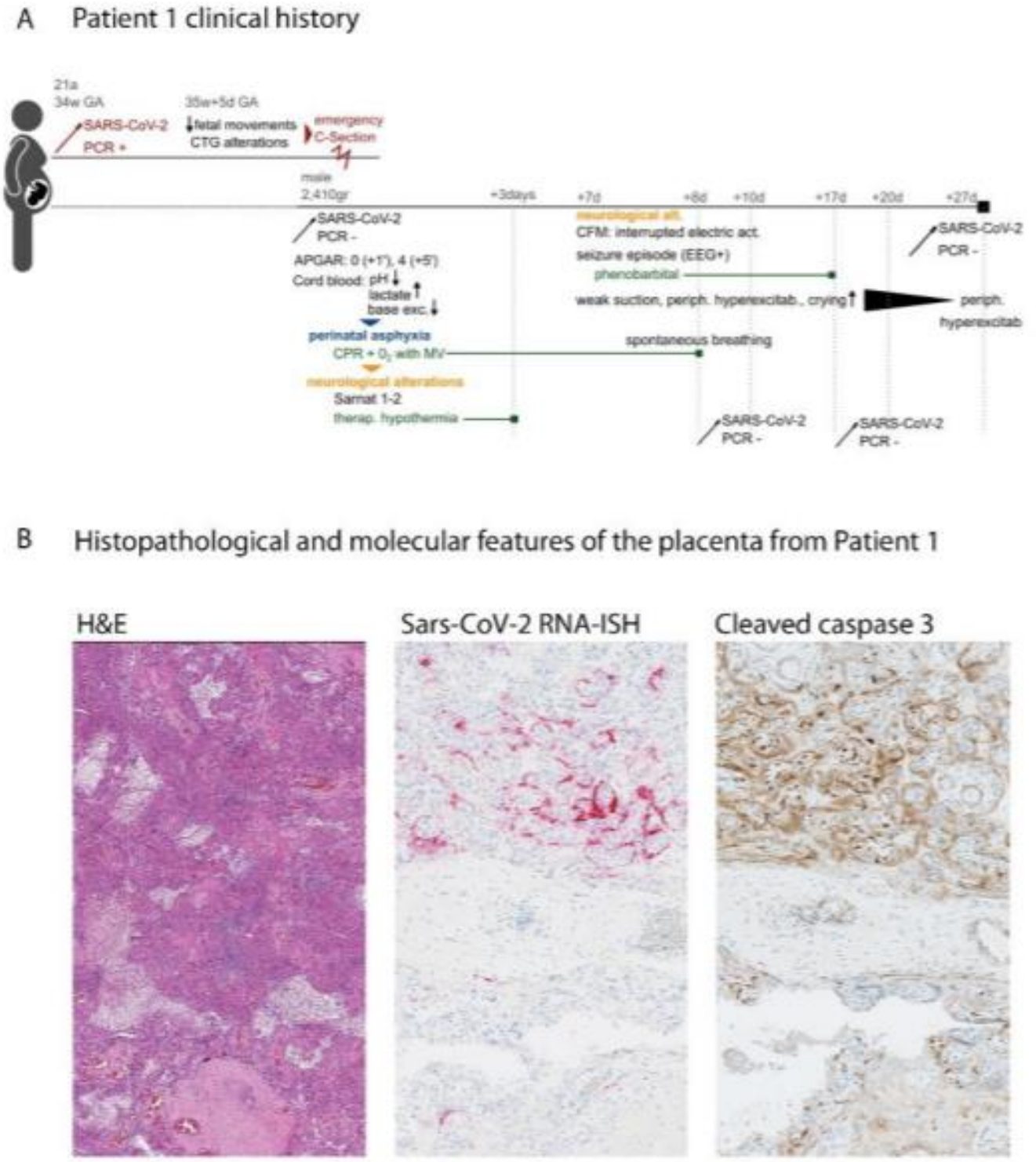


Figure 1. Examination of SARS-CoV-2 in Patient 1. (A) Case timeline. (B) Histopathological and molecular features of the placenta with severe injury. Massive fibrin deposition associated with syncytiotrophoblast layer necrosis and ghost villi (left, Hematoxylin-eosin staining. Original magnification, 10x. See also Supplementary Figure S1). Placental SARS-CoV-2 in situ hybridization reveals an intense positivity (red staining) of peri-villous trophoblastic cells (middle, RNA-ISH). Marked peri-villous trophoblastic cells apoptosis outlined by cleaved caspase-3 brown staining (right, immunohistochemistry). Scale bar: 100 um.

PEDIATRICS

ASSOCIATION OF MATERNAL SARS-COV-2 INFECTION IN PREGNANCY WITH NEONATAL OUTCOMES

Norman M, Navér L, Söderling J, Ahlberg M, Hervius Askling H, Aronsson B, Byström E, Jonsson J, Sengpiel V, Ludvigsson JF, Håkansson S, Stephansson O.. JAMA. 2021 Apr 29. doi: 10.1001/jama.2021.5775. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Neonatologists and women's health experts from the Karolinska Institutet in Sweden studied a prospective cohort of 88,159 infants delivered to mothers who tested positive for SARS-CoV-2 between March 2020 and January 2021 using Swedish patient registries. Compared to infants born to healthy mothers in the same time frame, these infants were more likely to be admitted to the neonatal intensive care unit (11.7 vs 8.4%; odds ratio [OR], 1.47; 95%CI, 1.26-1.70) or have respiratory distress syndrome (1.2 vs 0.5%; OR, 2.40; 95%CI, 1.50-3.84), any neonatal respiratory disorder (2.8 vs 2.0%; OR, 1.42; 95%CI, 1.07-1.90), and hyperbilirubinemia (3.6 vs 2.5%; OR, 1.47; 95%CI, 1.13-1.90)(Figure 2). Authors suggest neonates born to SARS-CoV-2 mothers are at higher risk for complications, though due to limitations in the data (imbalanced testing, heterogeneity of maternal disease severity) recommend further research into virally-altered prognosis and outcomes for newborns.

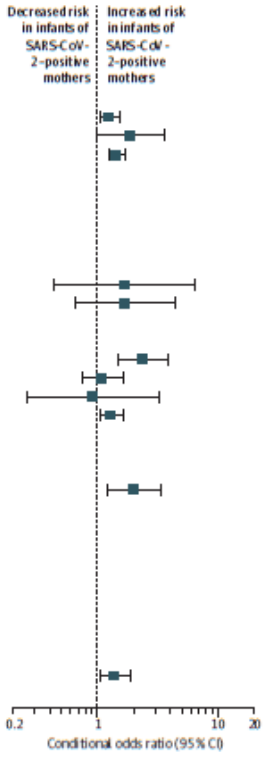
ABSTRACT

Importance: The outcomes of newborn infants of women testing positive for SARS-CoV-2 in pregnancy is unclear. Objective: To evaluate neonatal outcomes in relation to maternal SARS-CoV-2 test positivity in pregnancy. Design, Setting, and Participants: Nationwide, prospective cohort study based on linkage of the Swedish Pregnancy Register, the Neonatal Quality Register, and the Register for Communicable Diseases. Ninety-two percent of all live births in Sweden between March 11, 2020, and January 31, 2021, were investigated for neonatal outcomes by March 8, 2021. Infants with malformations were excluded. Infants of women who tested positive for SARS-CoV-2 were matched, directly and using propensity scores, on maternal characteristics with up to 4 comparator infants. Exposures: Maternal test positivity for SARS-CoV-2 in pregnancy. Main Outcomes and Measures: In-hospital mortality; neonatal resuscitation; admission for neonatal care; respiratory, circulatory, neurologic, infectious, gastrointestinal, metabolic, and hematologic disorders and their treatments; length of hospital stay; breastfeeding; and infant test positivity for SARS-CoV-2. Results: Of 88 159 infants (49.0% girls), 2323 (1.6%) were delivered by mothers who tested positive for SARS-CoV-2. The mean gestational age of infants of SARS-CoV-2-positive mothers was 39.2 (SD, 2.2) weeks vs 39.6 (SD, 1.8) weeks for comparator infants, and the proportions of preterm infants (gestational age <37 weeks) were 205/2323 (8.8%) among infants of SARS-CoV-2-positive mothers and 4719/85 836 (5.5%) among comparator infants. After matching on maternal characteristics, maternal SARS-CoV-2 test positivity was significantly associated with admission for neonatal care (11.7% vs 8.4%; odds ratio [OR], 1.47; 95% CI, 1.26-1.70) and with neonatal morbidities such as respiratory distress syndrome (1.2% vs 0.5%; OR, 2.40; 95% CI, 1.50-3.84), any neonatal respiratory disorder (2.8% vs 2.0%; OR, 1.42; 95% CI, 1.07-1.90), and hyperbilirubinemia (3.6% vs 2.5%; OR, 1.47; 95% CI, 1.13-1.90). Mortality (0.30% vs 0.12%; OR, 2.55; 95% CI, 0.99-6.57), breastfeeding rates at discharge (94.4% vs 95.1%; OR, 0.84; 95% CI, 0.67-1.05), and length of stay in neonatal care (median, 6 days in both groups; difference, 0 days; 95% CI, -2 to 7 days) did not differ significantly between the groups. Twenty-one infants (0.90%) of SARS-CoV-2-positive mothers tested positive for SARS-CoV-2 in the neonatal period; 12 did not have neonatal morbidity, 9 had diagnoses with unclear relation to SARS-CoV-2, and none had congenital pneumonia. Conclusions and Relevance: In a nationwide cohort of infants in Sweden, maternal SARS-CoV-2 infection in pregnancy was significantly associated with small increases in some neonatal morbidities. Given the small numbers of events for many of the outcomes and the large number of statistical comparisons, the findings should be interpreted as exploratory.

FIGURES

Figure 2. Neonatal Outcomes (Resuscitation at Birth, Admission to Neonatal Unit, Admission Hypothermia, Neurologic Disorders, and Respiratory Disorders and Treatments) Among Infants Born in Sweden (March 11, 2020–January 31, 2021) by Maternal SARS-CoV-2 Test Status in Pregnancy (Assessed as of March 8, 2021)

Neonatal outcomes	Infants of SARS-CoV-2–positive mothers (n = 2323)	All infants of non-SARS-CoV-2–positive mothers (n = 85 836)	Matched infants of non-SARS-CoV-2–positive mothers (n = 9275)	Risk difference per 100 infants or median difference (95% CI)[a]	Conditional odds ratio (95% CI)
Resuscitation at birth					
Assisted ventilation (by mask or CPAP)	148 (6.4)	4232 (4.9)	470 (5.1)	1.3 (0.2 to 2.4)	1.28 (1.05 to 1.55)
Intubated at birth	14 (0.6)	251 (0.3)	29 (0.3)	0.3 (−0.0 to 0.6)	1.90 (1.00 to 3.59)
Admission to neonatal unit[b]	271 (11.7)	7351 (8.6)	776 (8.4)	3.3 (1.9 to 4.7)	1.47 (1.26 to 1.70)
Postterm	6/39 (15.4)	146/2042 (7.1)	16/268 (6.0)	9.4 (−2.3 to 21.1)	
Term or near-term	177/2194 (8.1)	5516/82 052 (6.7)	589/8830 (6.7)	1.4 (0.1 to 2.6)	
Preterm	88/90 (97.8)	1691/1742 (97.1)	171/177 (96.6)	1.2 (−2.9 to 5.2)	
Very preterm	38/38 (100)	650/675 (96.3)	61/66 (92.4)	7.6 (1.2 to 14.0)	
Admission hypothermia[c]	4/38 (10.5)	18/675 (2.7)	5/66 (7.6)	3.0 (−8.7 to 14.6)	
Neurologic disorders					
Hypoxic-ischemic encephalopathy stage 2-3[d]	3 (0.1)	82 (0.1)	7 (0.1)	0.1 (−0.1 to 0.2)	1.71 (0.44 to 6.63)
Neonatal convulsions	6 (0.3)	173 (0.2)	14 (0.2)	0.1 (−0.1 to 0.3)	1.71 (0.66 to 4.46)
Severe brain injury[e]	1/38 (2.6)	45/675 (6.7)	4/66 (6.1)	−3.4 (−11.1 to 4.3)	
Respiratory disorders and treatments					
Respiratory distress syndrome	29 (1.2)	508 (0.6)	50 (0.5)	0.7 (0.2 to 1.2)	2.40 (1.50 to 3.84)
Transient tachypnea of the newborn	33 (1.4)	893 (1.0)	117 (1.3)	0.2 (−0.4 to 0.7)	1.12 (0.76 to 1.65)
Meconium aspiration	3 (0.1)	117 (0.1)	13 (0.1)	−0.0 (−0.2 to 0.2)	0.92 (0.26 to 3.24)
CPAP	113 (4.9)	2985 (3.5)	348 (3.8)	1.1 (0.2 to 2.1)	1.32 (1.06 to 1.64)
Duration, d					
Median (IQR)	2 (1-4)	2 (1-3)	2 (1-2)	0 (0 to 0)	
Range	1-78	1-161	1-101		
Mechanical ventilation	23 (1.0)	435 (0.5)	46 (0.5)	0.5 (0.1 to 0.9)	2.04 (1.22 to 3.39)
Duration, d					
Median (IQR)	7 (2-8)	4 (2-9)	4 (2-8)	3 (∞ to 6)	
Range	1-23	1-70	1-70		
Surfactant administration[f]	16/38 (42.1)	283/675 (41.9)	28/66 (42.4)	−0.3 (−20.0 to 19.4)	
No. of administrations					
Median (IQR)	1 (1-2)	1 (1-2)	1 (1-2)	0 (0 to 0)	
Range	1-4	1-5	1-4		
Postnatal corticosteroids for lung disease[g]	2/38 (5.3)	62/675 (9.2)	7/66 (10.6)	−5.3 (−15.6 to 4.9)	
Need for oxygen at 28 d of postnatal age	0/38 (0)	11/675 (1.6)	3/66 (4.5)	−4.5 (−9.6 to 0.5)	
Any respiratory disorder[h]	65 (2.8)	1557 (1.8)	184 (2.0)	0.8 (0.1 to 1.5)	1.42 (1.07 to 1.90)



Data are No. (%) unless otherwise indicated. CPAP indicates continuous positive airway pressure.

[a] Between infants of SARS-CoV-2–positive mothers vs matched infants of mothers without a positive test result.

[b] Admission to a unit with capacity to treat and care for ill or preterm infants. Very preterm indicates <32 weeks; preterm, <35 weeks; near-term, 35 to 36 weeks; term, 37 to 41 weeks; and postterm, ≥42 weeks.

[c] Defined as <35.5 °C in infants <32 weeks of gestational age.

[d] Stage 2 to 3 is moderate to severe encephalopathy.[27]

[e] Defined as intraventricular hemorrhage grade 3 to 4 (grade 4 is most severe, with hemorrhage from the ventricles extending into the surrounding brain) or cystic periventricular leukomalacia (last stage of white-matter brain injury with cystic scaring) among infants <32 weeks of gestational age.

[f] In infants <32 weeks of gestational age.

[g] Respiratory distress syndrome, transient tachypnea of the newborn, meconium aspiration, or pneumonia.

Figure 3. Neonatal Outcomes (Infections; Circulatory, Metabolic, Hematologic, and Gastrointestinal Problems; In-Hospital Mortality; Length of Hospital Stay; Breastfeeding; and Infant SARS-CoV-2 Test Status) Among Infants Born in Sweden (March 11, 2020–January 31, 2021) by Maternal SARS-CoV-2 Test Status in Pregnancy

CORONAVIRUS INFECTION IN NEONATES: A SYSTEMATIC REVIEW

Trevisanuto D, Cavallin F, Cavicchiolo ME, Borellini M, Calgaro S, Baraldi E.. Arch Dis Child Fetal Neonatal Ed. 2021 May;106(3):330-335. doi: 10.1136/archdischild-2020-319837. Epub 2020 Sep 17.
Level of Evidence: 4 - Case-series or case-control studies, or poor quality prognostic cohort study

BLUF

Neonatologists from the University of Padova in Italy conducted a systematic review of 26 case reports and case series regarding clinical outcomes of neonates with COVID-19 published between December 2019 and May 2020 (Figure 1). In 44 newborns with confirmed SARS-CoV-2 infections, they found neonates were diagnosed at a median of five days from birth, with 25% presenting asymptomatically and the rest presenting with mild symptoms. Symptoms resolved in all after 10 days of hospitalization (Table 3). Based on these early findings, authors suggest SARS-COV-2 infection in neonates is generally mild but emphasize the need for larger rigorous studies in this area.

ABSTRACT

OBJECTIVE: To summarise currently reported neonatal cases of SARS-CoV-2 infection. METHODS: A search strategy was designed to retrieve all articles published from 1 December 2019 to 12 May 2020, by combining the terms 'coronavirus' OR 'covid' OR 'SARS-CoV-2') AND ('neonat*' OR 'newborn') in the following electronic databases: MEDLINE/Pubmed, Scopus, Web of Science, MedRxiv, the Cochrane Database of Systematic Review and the WHO COVID-19 database, with no language restrictions. Quality of studies was evaluated by using a specific tool for assessment of case reports and/or case series.

RESULTS: Twenty-six observational studies (18 case reports and 8 case series) with 44 newborns with confirmed SARS-CoV-2 infection were included in the final analysis. Studies were mainly from China and Italy. Half of neonates had a documented contact with the infected mother and one out of three infected neonates was admitted from home. Median age at diagnosis was 5 days. One out of four neonates was asymptomatic, and the remaining showed mild symptoms typical of acute respiratory infections and/or gastrointestinal symptoms. The majority of neonates were left in spontaneous breathing (room air) and had good prognosis after a median duration of hospitalisation of 10 days. CONCLUSIONS: Most neonates with SARS-CoV-2 infection were asymptomatic or presented mild symptoms, generally were left in spontaneous breathing and had a good prognosis after median 10 days of hospitalisation. Large epidemiological and clinical cohort studies, as well as the implementation of collaborative networks, are needed to improve the understanding of the impact of SARS-CoV-2 infection in neonates.

FIGURES

Table 3 Clinical characteristics, treatment and outcome of neonates with SARS-CoV-2 infection

	n/N neonates (%) or median (IQR)
Symptoms	
Symptomatic neonates	26/38 (68)
Onset of symptoms, days	10 (2–19)
Fever	17/34 (50)
Gastrointestinal symptoms (diarrhoea and vomiting)	9/34 (26)
Hypoxia	7/35 (20)
Cough	7/34 (20)
Tachycardia	3/34 (9)
Shortening of breathing	3/34 (9)
Rhinorrhoea	2/34 (6)
Seizures	1/34 (3)
Skin lesions	0/34 (0)
Conjunctivitis	0/34 (0)
Therapy	
Respiratory management:	
Spontaneous breathing (room air)	27/36 (75)
Oxygen supplementation	3/36 (8)
Non-invasive respiratory support	2/36 (6)
Mechanical ventilation	4/36 (11)
Complications*	2/35 (6)
Antibiotics	7/35 (20)
Antiviral drugs	0/35 (0)
Nutrition	
Breast feeding	8/28 (28)
Pump milk	3/28 (11)
Formula	17/28 (61)
Outcome	
Length of hospital stay, days	10 (6–14)†
Mortality	0/44 (0)

*Both neonates had pneumothorax.
†Data available in 24 neonates.

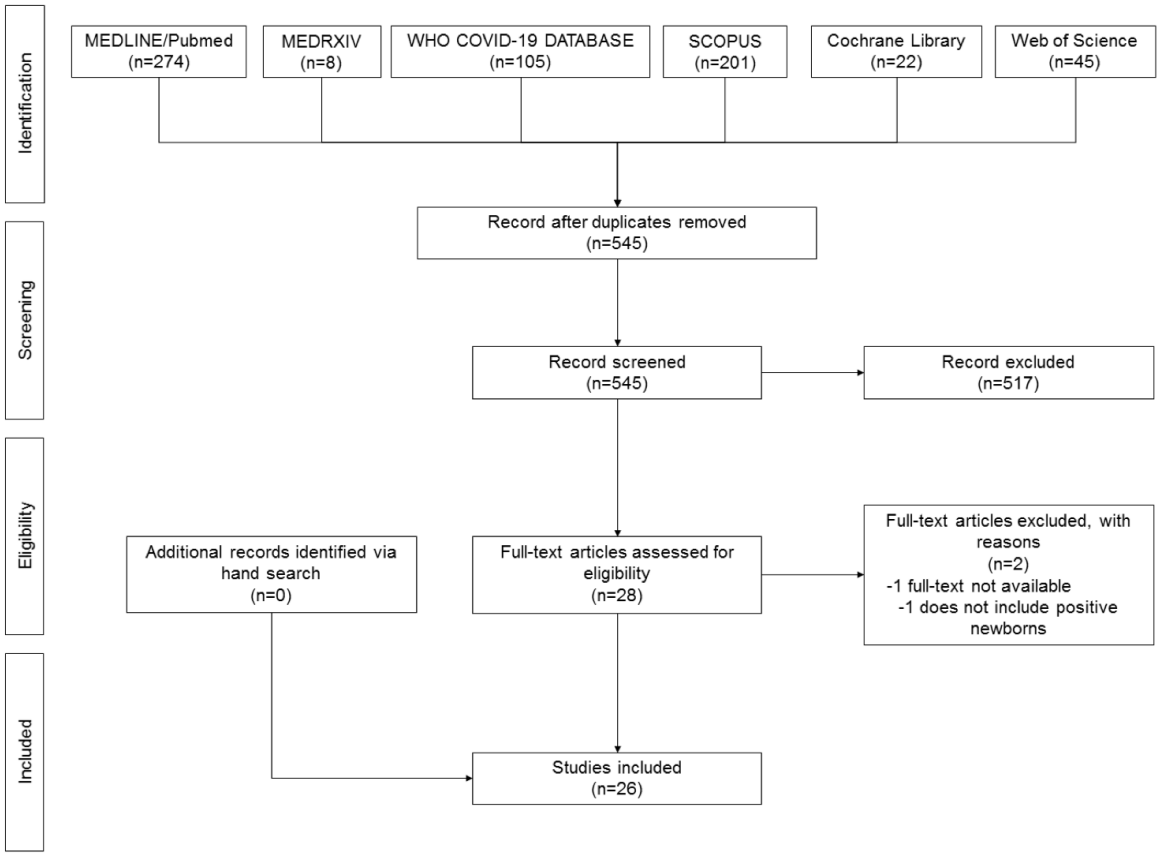


Figure 1 Flow chart of included studies.

ASYMPTOMATIC TRANSMISSION AND THE INFECTION FATALITY RISK FOR COVID-19: IMPLICATIONS FOR SCHOOL REOPENING

Vermund SH, Pitzer VE.. Clin Infect Dis. 2021 May 4;72(9):1493-1496. doi: 10.1093/cid/ciaa855.
Level of Evidence: 5 - Opinion

BLUF

An epidemiologist and pediatrician from Yale review data regarding asymptomatic SARS-CoV-2 infection, COVID-19 fatality risk, and how these factors should influence school reopening. They found now-ubiquitous prevention measures (physical distancing, wearing masks, personal hygiene) appear to minimize asymptomatic infections. Using case fatality risk rather than infection fatality risk, authors argue mortality from influenza is consistently lower in school-aged populations and that reopening schools can occur safely with the implementation of strict adherence to infection prevention protocols to minimize asymptomatic transmission.

ABSTRACT

Asymptomatic infection occurs for numerous respiratory viral diseases, including influenza and COVID-19. We seek to clarify confusion in three areas: age-specific risks of transmission and/or disease; various definitions for the COVID-19 "mortality rate", each useful for specific purposes; and implications for student return strategies from pre-school through university settings.

VIRAL GENOMIC, METAGENOMIC AND HUMAN TRANSCRIPTOMIC CHARACTERIZATION AND PREDICTION OF THE CLINICAL FORMS OF COVID-19

Rodriguez C, de Prost N, Fourati S, Lamoureux C, Gricourt G, N'debi M, Canoui-Poitrine F, Désveaux I, Picard O, Demontant V, Trawinski E, Lepeule R, Surgers L, Vindrios W, Lelièvre JD, Mongardon N, Langeron O, Cohen JL, Mekontso-Dessap A, Woerther PL, Pawlotsky JM.. PLoS Pathog. 2021 Mar 29;17(3):e1009416. doi: 10.1371/journal.ppat.1009416. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

Researchers from Hôpitaux Universitaires Henri Mondor in Créteil, France used shotgun metagenomics to characterize genomic, metagenomic, and transcriptomic features of nasopharyngeal swabs from 104 COVID-19 patients (Table 1). Overexpression of transcripts activating the CXCR2 pathway was seen in patients with severe pneumonia, while a T helper "Th1-Th17" profile was seen in patients with benign disease (Figure 3). Overall, this suggests that patients with severe COVID-19 have prolonged inflammation due to neutrophil accumulation, suggesting possible treatments such as CXCR2 antagonists and IL-8 antagonists.

ABSTRACT

COVID-19 is characterized by respiratory symptoms of various severities, ranging from mild upper respiratory signs to acute respiratory failure/acute respiratory distress syndrome associated with a high mortality rate. However, the pathophysiology of the disease is largely unknown. Shotgun metagenomics from nasopharyngeal swabs were used to characterize the genomic, metagenomic and transcriptomic features of patients from the first pandemic wave with various forms of COVID-19, including outpatients, patients hospitalized not requiring intensive care, and patients in the intensive care unit, to identify viral and/or host factors associated with the most severe forms of the disease. Neither the genetic characteristics of SARS-CoV-2, nor the detection of bacteria, viruses, fungi or parasites were associated with the severity of pulmonary disease. Severe pneumonia was associated with overexpression of cytokine transcripts activating the CXCR2 pathway, whereas patients with benign disease presented with a T helper "Th1-Th17" profile. The latter profile was associated with female gender and a lower mortality rate. Our findings indicate that the most severe cases of COVID-19 are characterized by the presence of overactive immune cells resulting in neutrophil pulmonary infiltration which, in turn, could enhance the inflammatory response and prolong tissue damage. These findings make CXCR2 antagonists, in particular IL-8 antagonists, promising candidates for the treatment of patients with severe COVID-19.

FIGURES

Patient characteristics	*Outpatients (N = 42)*	*Hospitalized patients (N = 17)*	*ICU patients (N = 45)*	*P-value*[*]
Demographic parameters				
Age, median [range], year (N = 104)	50 [19–87]	61 [31–82]	68 [33–90]	<0.01
Female- n/N (%) (N = 104)	30/42 (71.4)	7/17 (41.2)	8/45 (17.8)	<0.01
Risk factors				
Current smokers- n|N (%) (N = 92)	4/34 (11.8)	1/14 (7.1)	3/44 (6.8)	0.73
BMI, kg/m^2 median [range] (N = 87)	25.6 [16.9–34.0]	28.1 [19.8–39.0]	28.0 [21.0–43.3]	0.02
Chronic underlying conditions, n|N (%)				
Chronic obstructive pulmonary disease (N = 92)	2/34 (5.8)	1/14 (7.1)	2/44 (4.5)	0.16
Asthma (N = 92)	7/34 (20.6)	2/14 (14.3)	1/44 (2.3)	0.03
Diabetes (N = 92)	1/34 (2.9)	4/14 (28.6)	14/44 (31.8)	<0.01
Hypertension (N = 92)	7/34 (20.6)	8/14 (57.1)	24/44 (54.6)	<0.01
Cardiac disease (N = 92)	2/34 (5.9)	2/14 (14.3)	10/44 (22.7)	0.12
Chronic renal disease (N = 92)	1/34 (2.9)	0/14 (0)	3/44 (6.8)	0.17
Cancer (N = 92)	2/34 (5.9)	0/14 (0)	1/44 (2.3)	0.28
Immunodeficiency (Transplant, HIV) (n = 92)	0/34 (0)	2/14 (14.3)	4/44 (9.1)	0.33
COVID treatments *n|N (%)*				
Antibiotics (N = 93)	11/34 (32.4)	9/15 (60.0)	38/44 (86.4)	<0.01
Corticosteroids (N = 93)	1/34 (2.9)	2/15 (13.3)	1/44 (2.3)	0.17
NSAIDs (N = 93)	9/34 (26.5)	1/15 (6.7)	5/44 (11.4)	0.11
Chronic immunosuppressive treatment n|N (%) *(N = 93)*	0/34 (0)	2/15 (13.3)	4/44 (9.1)	0.33
COVID-19 Disease				
Interval from symptoms to NSP, median [range], *days*	4 [0–14]	7 [2–14]	6 [0–19]	<0.01
Blood neutrophil counts, median [range], G/L		4.9 [2.4–11.0]	5.6 [2.3–16.4]	0.32
Blood lymphocyte counts, median [range], G/L		1.1 [0.6–3.2]	0.7 [0.2–1.6]	0.01
Ventilation, n|N (%)				
Oxygen	0/42 (0)	12/16 (75.0)	45/45 (100)	<0.01
Non-invasive ventilation/C-PAP			21/45 (46.7)	
Mechanical ventilation			19/45 (42.3)	
SOFA score ≥6, n|N (%)			23/43 (53.5)[*]	
Death at day-15, n/N (%) (N = 104)	0/42 (0)	2/17 (11.8)	17/45 (37.8)	<0.01

BMI, body mass index; NSAIDs, non-steroidal anti-inflammatory drugs; C-PAP, continuous positive airway pressure.

[*] Chi-Square test for categorial data, ANOVA One Way test for quantitative data.

[*]Blood Pressure was not available for two patients.

Table 1. Patient characteristics at the time of nasopharyngeal swab sampling.

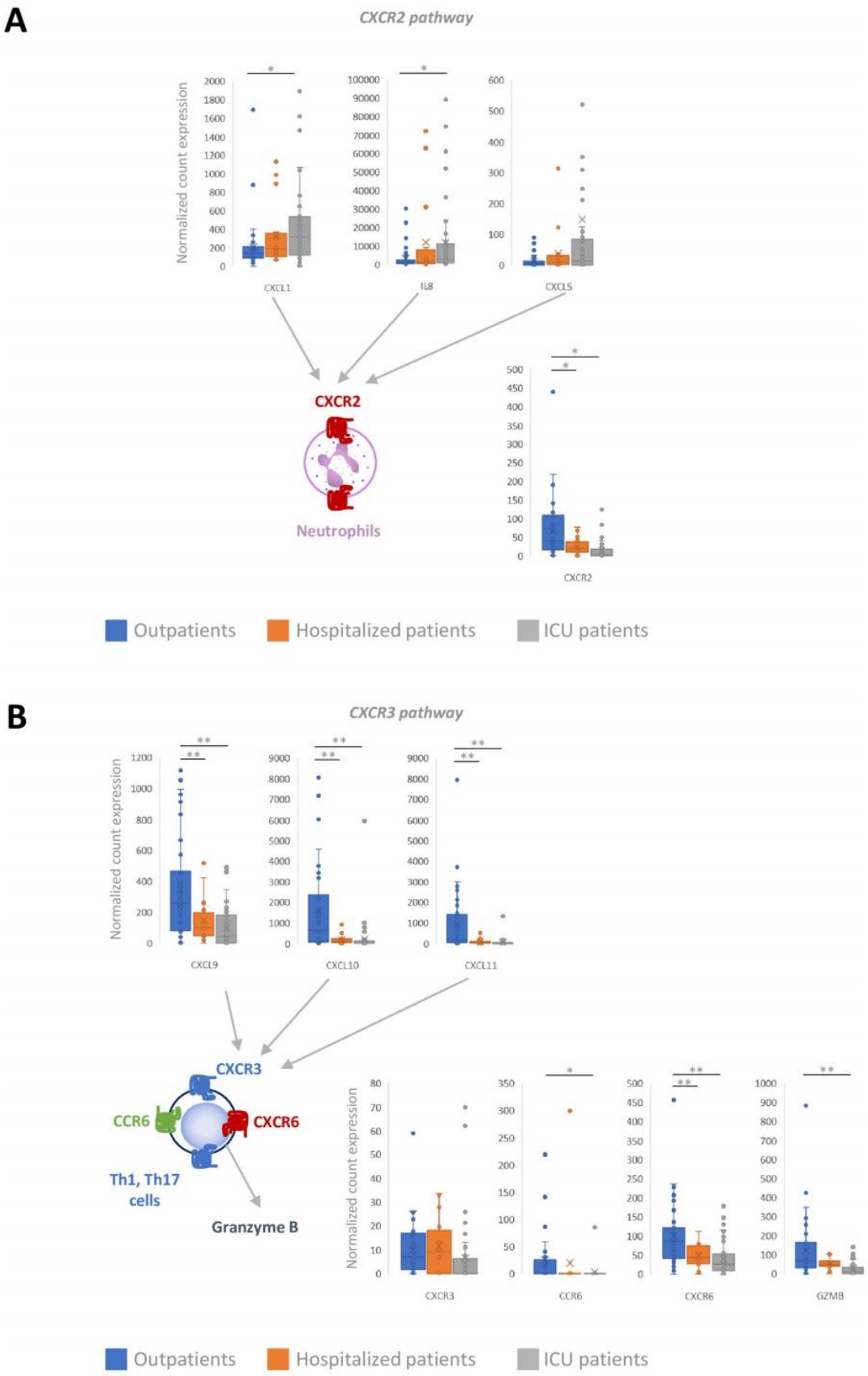


Fig 3. Relationship between naso-pharyngeal swab transcriptomics and the severity of COVID-19 disease.

(A) CXCR2 receptor pathway. (B) CXCR3/CCR6 pathway. *p<0.05; **p<0.01.

SARS-COV-2 IGG SEROPOSITIVITY AND ACUTE ASYMPTOMATIC INFECTION RATE AMONG FIREFIGHTER FIRST RESPONDERS IN AN EARLY OUTBREAK COUNTY IN CALIFORNIA

Newberry JA, Gautreau M, Staats K, Carrillo E, Mulkerin W, Yang S, Kohn MA, Matheson L, Boyd SD, Pinsky BA, Blomkalns AL, Strehlow MC, D'Souza PA.. Prehosp Emerg Care. 2021 Apr 5:1-10. doi: 10.1080/10903127.2021.1912227. Online ahead of print.

Level of Evidence: 3 - Local non-random sample

BLUF

Researchers from Stanford School of Medicine conducted a cross-sectional study to determine the rates of SARS-CoV-2 IgG seropositivity and RT-PCR swab positivity in 983 firefighters cross-trained as paramedics or EMTs in Santa Clara County, CA in June-August 2020. Results showed that only 25 participants (2.54%, 95% CI 1.65-3.73) tested positive for IgG antibodies, 10 of whom were asymptomatic (Table 1). Additionally, 9 firefighters (0.92%, 95% CI 0.42-1.73) tested positive for SARS-CoV-2 by RT-PCR, 8 of whom were asymptomatic (Table 1). These findings suggest that despite being first responders in a county with an early COVID-19 outbreak, firefighters had a significantly low SARS-CoV-2 seroprevalence, but the reason for this is still unclear.

ABSTRACT

Objective: Firefighter first responders and other emergency medical services (EMS) personnel have been among the highest risk healthcare workers for illness during the SARS-CoV-2 pandemic. We sought to determine the rate of seropositivity for SARS-CoV-2 IgG antibodies and of acute asymptomatic infection among firefighter first responders in a single county with early exposure in the pandemic.Methods: We conducted a cross-sectional study of clinically active firefighters cross-trained as paramedics or EMTs in the fire departments of Santa Clara County, California. Firefighters without current symptoms were tested between June and August 2020. Our primary outcomes were rates of SARS-CoV-2 IgG antibody seropositivity and SARS-CoV-2 RT-PCR swab positivity for acute infection. We report cumulative incidence, participant characteristics with frequencies and proportions, and proportion positive and associated relative risk (with 95% confidence intervals).Results: We enrolled 983 out of 1339 eligible participants (response rate: 73.4%). Twenty-five participants (2.54%, 95% CI 1.65-3.73) tested positive for IgG antibodies and 9 (0.92%, 95% CI 0.42-1.73) tested positive for SARS-CoV-2 by RT-PCR. Our cumulative incidence, inclusive of self-reported prior positive PCR tests, was 34 (3.46%, 95% CI 2.41-4.80).Conclusion: In a county with one of the earliest outbreaks in the United States, the seroprevalence among firefighter first responders was lower than that reported by other studies of frontline health care workers, while the cumulative incidence remained higher than that seen in the surrounding community.

FIGURES

Table 1: Characteristics of Study Participants and Proportion with IgG Antibodies or SARS-CoV-2

		Total	IgG Positive			SARS-CoV-2 PCR Positive		
		N (%)	n (% of N)	Relative Risk (95% CI)	p-value	n (% of N)	Relative Risk (95% CI)	p-value
	Total	**983**	25 (2.5)			9 (0.9)		
Age, years								
	18-34	206 (21)	2 (1)	reference	-	2 (1)	reference	-
	35-49	556 (56.6)	17 (3.1)	3.15 (0.73–13.51)	0.123	3 (0.5)	0.56 (0.09–3.3)	0.518
	50 or older	221 (22.5)	6 (2.7)	2.8 (0.57–13.7)	0.205	4 (1.8)	1.86 (0.35–10.07)	0.469
Race/ethnicity*								
	White (non-Hispanic)	594 (60.4)	8 (1.3)	reference	-	6 (1)	reference	-
	Hispanic	192 (19.5)	9 (4.7)	3.48 (1.36–8.9)	0.009	3 (1.6)	1.55 (0.39–6.13)	0.534
	Asian or Pacific Islander (non-Hispanic)	78 (7.9)	3 (3.8)	2.86 (0.77–10.54)	0.115	0	-	-
	Black (non-Hispanic)	26 (2.6)	1 (3.8)	2.86 (0.37–21.99)	0.314	0	-	-
	Other or did not answer	93 (9.5)	4 (4.3)	3.19 (0.98–10.39)	0.054	0	-	-
Number of people living in home†								
	1	45 (4.6)	2 (4.4)	reference	-	0	-	-
	2+	929 (94.5)	23 (2.5)	0.56 (0.13–2.27)	0.410	9 (1)	-	-
Living with children								
	No	317 (32.2)	7 (2.2)	reference	-	3 (0.9)	reference	-
	Yes	666 (67.8)	18 (2.7)	1.22 (0.52–2.9)	0.646	6 (0.9)	0.95 (0.24–3.78)	0.944
Non-work-related exposures to COVID-19								
	0 people	896 (91.1)	20 (2.2)	reference	-	9 (1)	-	-
	1 person	43 (4.4)	2 (4.7)	2.08 (0.5–8.63)	0.311	0	-	-
	2+ people	44 (4.5)	3 (6.8)	3.05 (0.94–9.89)	0.063	0	-	-
Domestic or international trips since 11/1/2019**								
	No	706 (71.8)	16 (2.3)	reference	-	7 (1)	reference	-
	Yes	277 (28.2)	9 (3.2)	1.43 (0.64–3.21)	0.380	2 (0.7)	0.73 (0.15–3.48)	0.691
Number of PCR tests (prior to study)								
	No prior PCR tests	675 (68.7)	12 (1.8)	reference	-	3 (0.4)	reference	-
	1 prior PCR test	226 (23)	6 (2.7)	1.49 (0.57–3.93)	0.417	2 (0.9)	1.99 (0.33–11.84)	0.449
	2+ prior PCR tests	82 (8.3)	7 (8.5)	4.8 (1.95–11.85)	0.001	4 (4.9)	10.98 (2.5–48.18)	0.002
Positive PCR result (prior to study)								
	No	971 (98.8)	17 (1.8)	reference	-	6 (0.6)	reference	-
	Yes	12 (1.2)	8 (66.7)	38.08 (20.52–70.65)	<.0001	3 (25)	40.46 (11.44–143.15)	<.0001
Do you think you have had COVID-19?‡								
	No, I do NOT think so	528 (54.4)	5 (0.9)	reference	-	3 (0.6)	reference	-
	No, I think it is somewhat UNLIKELY	91 (9.4)	2 (2.2)	2.32 (0.46–11.78)	0.310	1 (1.1)	1.93 (0.2–18.39)	0.566
	I am UNSURE if had COVID-19	186 (19.2)	3 (1.6)	1.7 (0.41–7.06)	0.463	0	-	-
	Yes, I think it is somewhat LIKELY	142 (14.6)	5 (3.5)	3.72 (1.09–12.67)	0.036	2 (1.4)	2.48 (0.42–14.69)	0.317
	Yes, I DEFINITELY think so	24 (2.5)	2 (8.3)	8.8 (1.8–43.07)	0.007	0	-	-

* Race/ethnicity categories defined by investigators and included because infection rates may vary by race/ethnicity.
** Domestic trips defined as trips within the continental U.S (excludes Hawaii and U.S terriorites or possessions).
† Number includes self.
‡ Only if no prior positive PCR test

Table 1: Characteristics of Study Participants and Proportion with IgG Antibodies or SARS-CoV-2

SARS-COV-2 VACCINE-INDUCED IMMUNE THROMBOTIC THROMBOCYTOPENIA

Cines DB, Bussel JB.. N Engl J Med. 2021 Apr 16. doi: 10.1056/NEJMe2106315. Online ahead of print.
Level of Evidence: 4 - Case-series, case-control, or historically controlled studies

BLUF

Professors from the department of pathology and laboratory medicine from the University of Pennsylvania discuss 3 independent studies describing 39 cases of thrombosis and thrombocytopenia associated with the ChAdOx1 nCoV-19 (AstraZeneca) COVID-19 vaccine. They found most patients were women under the age of 50, and that thromboses formed at unusual sites on the body with a death rate of 40%. High levels of platelet factor 4 (PF4) were detected in almost all patients. Authors suggest there is a rare link between AstraZeneca vaccination and thrombosis, and recommend future research focus on the potential role of PF4, identify patients at higher risk, and guide management.

PATHOLOGIC ANTIBODIES TO PLATELET FACTOR 4 AFTER CHADOX1 NCOV-19 VACCINATION

Scully M, Singh D, Lown R, Poles A, Solomon T, Levi M, Goldblatt D, Kotoucek P, Thomas W, Lester W.. N Engl J Med. 2021 Apr 16. doi: 10.1056/NEJMoa2105385. Online ahead of print.
Level of Evidence: 4 - Case-series, case-control, or historically controlled studies

BLUF

Hematologists from University College London Hospitals NHS Foundation Trust, among others, present cases of vaccine induced thrombosis and thrombocytopenia (VITT) 6 to 24 days after the first dose of ChAdOx1 nCoV-19 vaccination (AstraZeneca) in 23 patients with no prethrombotic history (except 1 patient with DVT) and in absence of heparin. They found 22 patients developed both thrombosis and thrombocytopenia while 1 had only thrombocytopenia with bruising. Anti-PF4 antibody ELISA was positive in 22/23 patients (Figures 1). Authors suggest providers monitor for VITT after AstraZeneca COVID-19 vaccination and propose an algorithm to help in its diagnosis and management (Figure 2).

ABSTRACT

BACKGROUND: The mainstay of control of the coronavirus disease 2019 (Covid-19) pandemic is vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Within a year, several vaccines have been developed and millions of doses delivered. Reporting of adverse events is a critical postmarketing activity. METHODS: We report findings in 23 patients who presented with thrombosis and thrombocytopenia 6 to 24 days after receiving the first dose of the ChAdOx1 nCoV-19 vaccine (AstraZeneca). On the basis of their clinical and laboratory features, we identify a novel underlying mechanism and address the therapeutic implications. RESULTS: In the absence of previous prothrombotic medical conditions, 22 patients presented with acute thrombocytopenia and thrombosis, primarily cerebral venous thrombosis, and 1 patient presented with isolated thrombocytopenia and a hemorrhagic phenotype. All the patients had low or normal fibrinogen levels and elevated d-dimer levels at presentation. No evidence of thrombophilia or causative precipitants was identified. Testing for antibodies to platelet factor 4 (PF4) was positive in 21 patients, negative in 1 patient, and equivocal in 1 patient. On the basis of the pathophysiological features observed in these patients, we recommend that treatment with platelet transfusions be avoided because of the risk of progression in thrombotic symptoms and that the administration of a nonheparin anticoagulant agent and intravenous immune globulin be considered for the first occurrence of these symptoms. CONCLUSIONS: Vaccination against SARS-CoV-2 remains critical for control of the Covid-19 pandemic. A pathogenic PF4-dependent syndrome, unrelated to the use of heparin therapy, can occur after the administration of the ChAdOx1 nCoV-19 vaccine. Rapid identification of this rare syndrome is important because of the therapeutic implications.

FIGURES

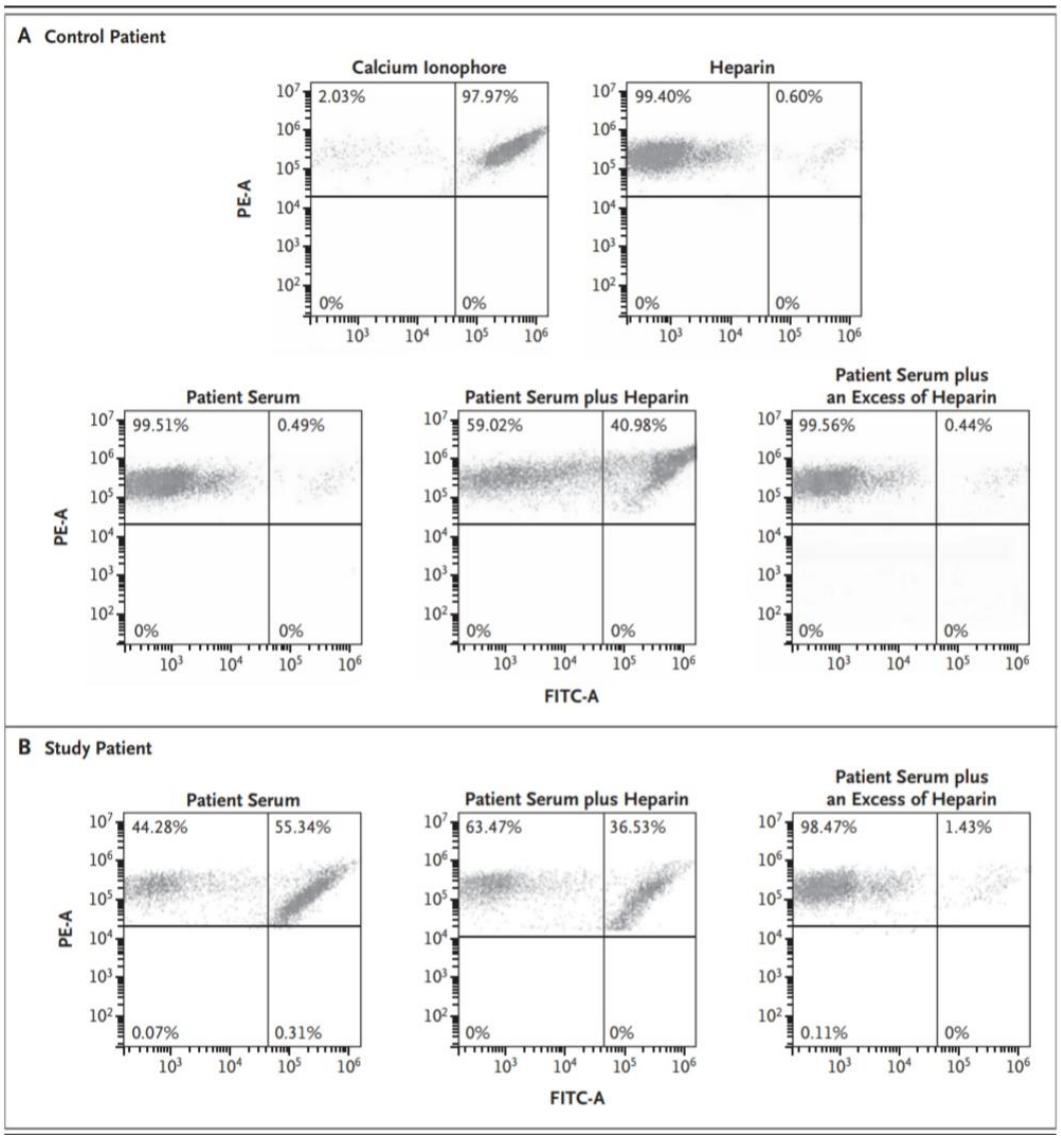


Figure 1: " Flow Cytometric Analysis of Results of a Functional HIT Assay in a Control Patient and a Patient in the Study. Shown is the flow cytometric analysis of results of a functional heparin-induced thrombocytopenia (HIT) assay (HITAlert, Diapharma) performed on a serum sample from a control patient with a confirmed diagno-sis of HIT (Panel A) and on a serum sample from a pa-tient included in the study (Panel B). Platelets from a volunteer donor with group O blood are incubated in five tubes containing the following substances: calcium ionophore, heparin (0.3 U per milliliter), patient serum, patient serum plus heparin (0.3 U per milliliter), and patient serum plus an excess of heparin (100 U per mil-liliter). In the analysis of the control sample (Panel A), donor platelets show reactivity in the presence of calcium ionophore, with 98% of platelets positive for both anti–CD41 PE and anti–annexin V–FITC conjugated antibodies (data are shown in the upper right quadrant of each plot); reduced reactivity in the presence of heparin (0.3 U per milliliter), with only 0.6% of CD41-positive platelets also positive for annexin V; reduced reactivity in the presence of patient serum, with only 0.5% of platelets activated; reactivity in the presence of patient serum plus heparin (0.3 U per milliliter), with 41% of platelets activated; and reduced reactivity in the presence of patient serum plus an excess of heparin (100 U per milliliter), with 0.4% of platelets activated, as compared with 41% with patient serum plus heparin in a physiologic dose. In the analysis of the study sample (Panel B), donor platelets show reactivity in the presence of patient serum, with 55% of platelets activated; reactivity in the presence of patient serum plus heparin (0.3 U per milliliter), with 37% of platelets activated; and reduced reactivity in the presence of patient serum plus an excess of heparin (100 U per milliliter), with 1% of platelets activated. FITC denotes fluorescein isothiocyanate, and PE phycoerythrin".

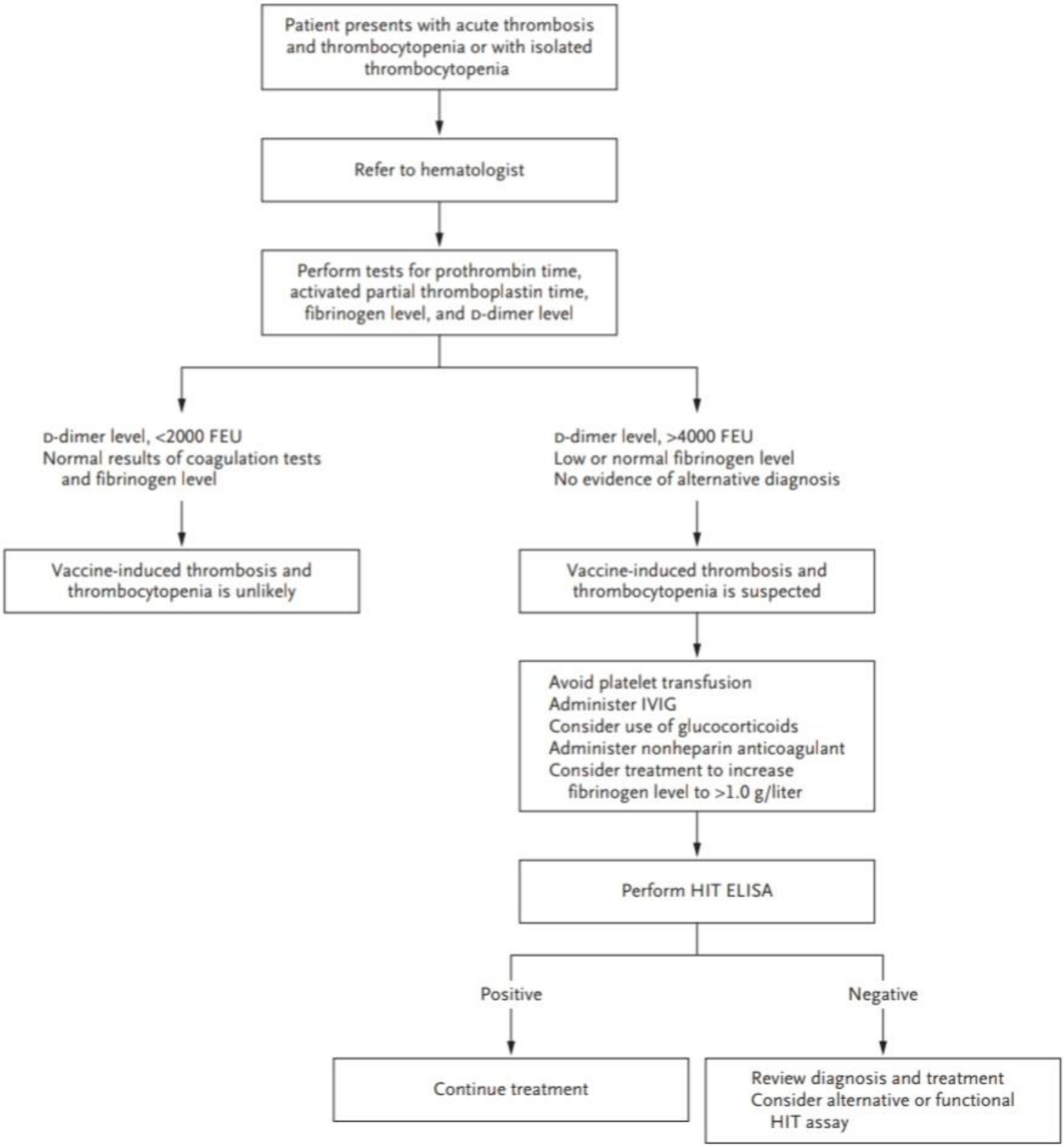


Figure 2: "Suggested Algorithm for Testing and Treatment of Patients Presenting with Thrombosis and Thrombocyto-penia 5 to 30 Days after Vaccination.
The HemosIL AcuStar HIT IgG assay is not recommended for the evaluation of suspected vaccine-induced thrombosis and thrombocytopenia. ELISA denotes enzyme-linked immunosorbent assay, FEU fibrinogen-equivalent units, HIT heparin-induced thrombosis, and IVIG intravenous immune globulin".

A GUIDELINE TO LIMIT INDOOR AIRBORNE TRANSMISSION OF COVID-19

Bazant MZ, Bush JWM.. Proc Natl Acad Sci U S A. 2021 Apr 27;118(17):e2018995118. doi: 10.1073/pnas.2018995118.
Level of Evidence: 5 - Modeling

BLUF

A chemical engineer and mathematician from the Massachusetts Institute of Technology created an airborne-disease transmission model to explore indoor transmission of SARS-CoV-2. Using the oft-cited well-mixed room model (see summary), their simulations demonstrated a higher rate of infectiousness compared to SARS-CoV (Figure 2) and suggests the "six-foot rule" in indoor spaces is inadequate (Figure 3). Authors use their findings to create a calculator for safe indoor occupancy after an infected person enters a space (see summary for link).

SUMMARY

The well mixed room model accounts for:
- speed of ambient air circulation
- the low density and radius of infectious droplets
- the deterioration of droplets relative to temperature, droplet size, and humidity.

The authors' calculator can be accessed here:
https://indoor-covid-safety.herokuapp.com

ABSTRACT

The current revival of the American economy is being predicated on social distancing, specifically the Six-Foot Rule, a guideline that offers little protection from pathogen-bearing aerosol droplets sufficiently small to be continuously mixed through an indoor space. The importance of airborne transmission of COVID-19 is now widely recognized. While tools for risk assessment have recently been developed, no safety guideline has been proposed to protect against it. We here build on models of airborne disease transmission in order to derive an indoor safety guideline that would impose an upper bound on the "cumulative exposure time," the product of the number of occupants and their time in an enclosed space. We demonstrate how this bound depends on the rates of ventilation and air filtration, dimensions of the room, breathing rate, respiratory activity and face mask use of its occupants, and infectiousness of the respiratory aerosols. By synthesizing available data from the best-characterized indoor spreading events with respiratory drop size distributions, we estimate an infectious dose on the order of 10 aerosol-borne virions. The new virus (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]) is thus inferred to be an order of magnitude more infectious than its forerunner (SARS-CoV), consistent with the pandemic status achieved by COVID-19. Case studies are presented for classrooms and nursing homes, and a spreadsheet and online app are provided to facilitate use of our guideline. Implications for contact tracing and quarantining are considered, and appropriate caveats enumerated. Particular consideration is given to respiratory jets, which may substantially elevate risk when face masks are not worn.

FIGURES

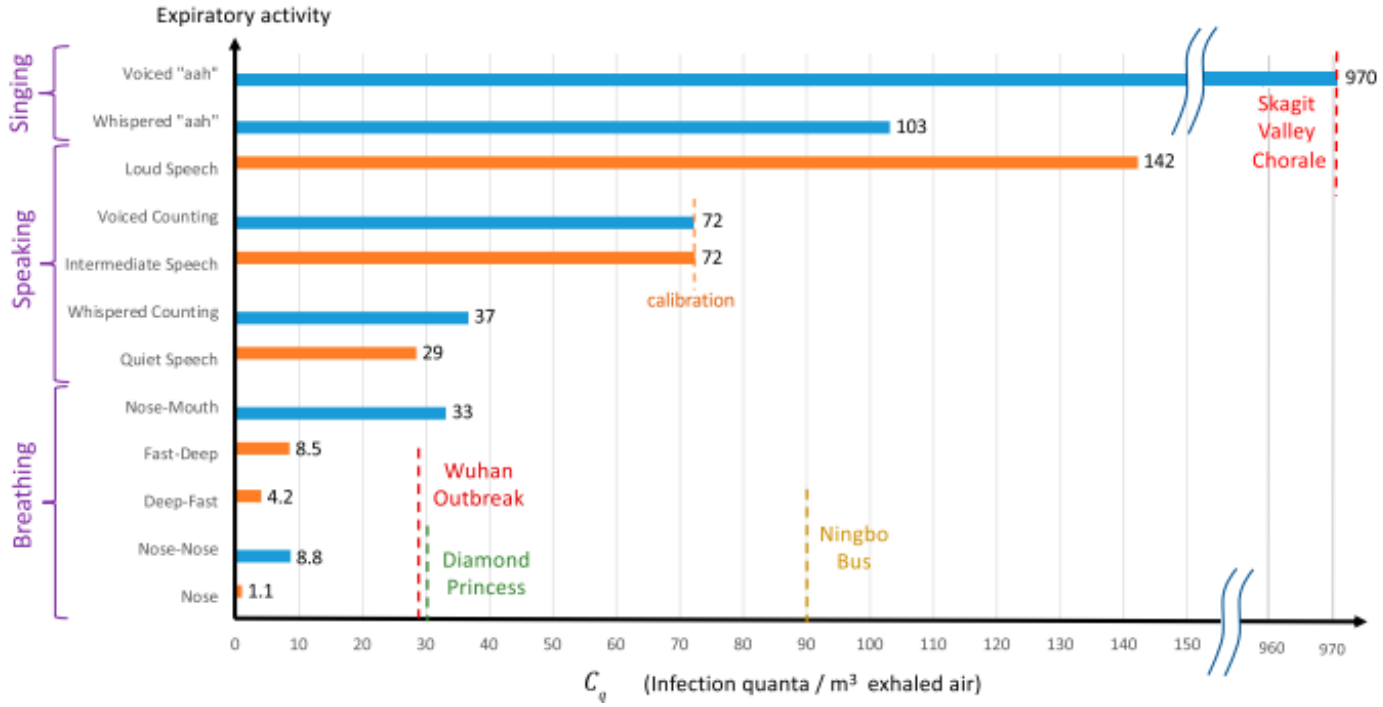


Fig. 2. Estimates of the "infectiousness" of exhaled air, Cq, defined as the peak concentration of COVID-19 infection quanta in the breath of an infected person, for various respiratory activities. Values are deduced from the drop size distributions reported by Morawska et al. (11) (blue bars) and Asadi et al. (39) (orange bars). The only value reported in the epidemiological literature, Cq = 970 quanta/m3 , was estimated (25) for the Skagit Valley Chorale superspreading event (27), which we take as a baseline case (sr = 1) of elderly individuals exposed to the original strain of SARS-CoV-2. This value is rescaled by the predicted infectious aerosol volume fractions, φ1 = R rc 0 φs(r)dr, obtained by integrating the steady-state size distributions reported in Fig. 1 for different expiratory activities (11). Aerosol volume fractions calculated for various respiratory activities from figure 5 of Asadi et al. (39) are rescaled so that the value Cq = 72 quanta/m3 for "intermediate speaking" matches that inferred from Morawska et al.'s (11) for "voiced counting." Estimates of Cq for the outbreaks during the quarantine period of the Diamond Princess (26) and the Ningbo bus journey (28), as well as the initial outbreak in Wuhan City (2, 81), are also shown (see SI Appendix for details).

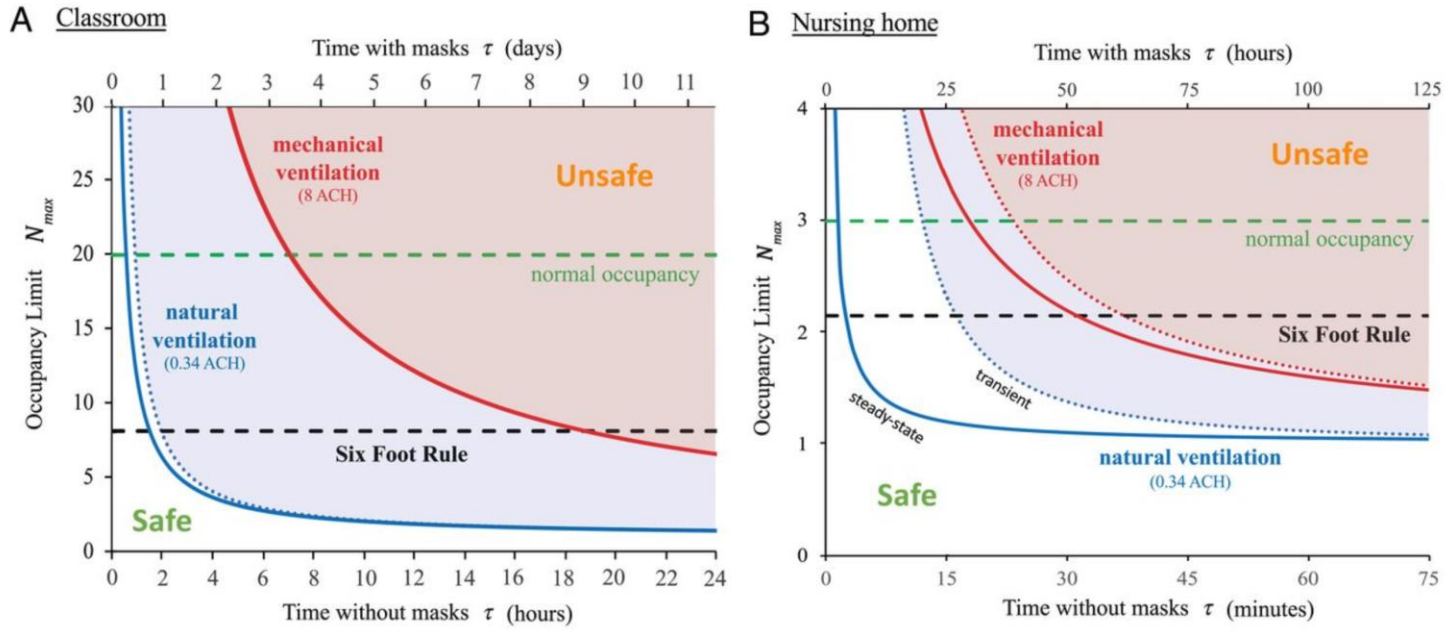


Figure 3. The COVID-19 indoor safety guideline would limit the cumulative exposure time (CET) in a room with an infected individual to lie beneath the curves shown. Solid curves are deduced from the pseudo-steady formula, Eq. 5, for both natural ventilation (λa=0.34/h; blue curve) and mechanical ventilation (λa=8.0/h; red curve). Horizontal axes denote occupancy times with and without masks. Evidently, the Six-Foot Rule (which limits occupancy to Nmax=A−−√/(6 ft)) becomes inadequate after a critical time, and the Fifteen-Minute Rule becomes inadequate above a critical occupancy. (A) A typical school classroom: 20 persons share a room with an area of 900 ft2 and a ceiling height of 12 ft (A=83.6 m2, V=301 m3). We assume low relative transmissibility (sr=25%), cloth masks (pm=30%), and moderate risk tolerance (ϵ=10%) suitable for children. (B) A nursing home shared room (A=22.3 m2, V=53.5 m3) with a maximum occupancy of three elderly persons (sr=100%), disposable surgical or hybrid-fabric masks (pm=10%), and a lower risk tolerance (ϵ=1%) to reflect the vulnerability of the community. The transient formula, SI Appendix, Eq. S8, is shown with dotted curves. Other parameters are Cq=30 quanta/m3, λv=0.3/h, Qb=0.5 m3/h, and r¯¯=0.5 μm.

PREVENTION IN THE COMMUNITY

REVIEW OF COVID-19 MRNA VACCINES: BNT162B2 AND MRNA-1273

Teo SP.. J Pharm Pract. 2021 Apr 12:8971900211009650. doi: 10.1177/08971900211009650. Online ahead of print.
Level of Evidence: 5 - Review / Literature Review

BLUF

A geriatrician from Raja Isteri Pengiran Anak Saleha Hospital in Brunei reviews the mechanisms of mRNA COVID-19 vaccines (BNT126b2 [Pfizer-BioNTech] and mRNA-1273 [Moderna]) and currently available clinical trial data. They found recent phase 3 studies showed high efficacy (95% for Pfizer-BioNTech and 94.5% for Moderna)(Table 1) and suggest this, coupled with low rates of adverse effects, makes both vaccines promising for large-scale vaccination programs. Due to the practical challenges of 2-dose administrations and emergence of new variants, the author emphasizes that more work in distribution planning and understanding the S protein remains.

ABSTRACT

The United States Food and Drug Administration recently issued emergency use authorization for 2 mRNA vaccines for preventing COVID-19 disease caused by SARS-CoV-2 virus infections. BNT162b2 from Pfizer-BioNTech and mRNA-1273 by Moderna are planned for use in mass-immunization programs to curb the pandemic. A brief overview of COVID-19 mRNA vaccines is provided, describing the SARS-CoV-2 RNA, how mRNA vaccines work and the advantages of mRNA over other vaccine platforms. The Pfizer-BioNTech collaboration journey to short-list mRNA vaccine candidates and finally selecting BNT162b2 based on safety data is outlined, followed by the Phase 3 study of BNT162b2 demonstrating 95% efficacy in preventing COVID-19 infections. Studies regarding mRNA-1273 (Moderna) are described, including extended immunogenicity data up to 119 days. The Phase 3 COVE study of mRNA-1273 eventually showed vaccine efficacy of 94.5%. Recommendations

for future mRNA vaccine development are provided, including ongoing safety surveillance, evaluation in under-represented groups in previous studies and improving mRNA vaccine thermostability. Finally, further logistical considerations are required for manufacturing, storing, distribution and implementing mass vaccination programs to curb the pandemic.

FIGURES

Table 1. Comparison of BNT162b2 and mRNA-1273 Phase 3 Trial Outcomes.[14,22]

	BNT162b2	mRNA-1273
Age of participants	Age 16 years and above	Age 18 and above
Number of participants	43448 participants (21720 with BNT162b2; 21728 with placebo)	30351 participants (15181 with mRNA-1273; 15170 with placebo)
Injection Received	Vaccine: 30µg BNT162b2 (0.3mL per dose); Placebo: saline	Vaccine: 100 µg mRNA-1273 (0.5mL per dose); Placebo: saline
Dose	Two injections 21 days apart	Two injections 28 days apart
Efficacy	95% (8 cases in BNT162b2 group; 162 cases in placebo group)	94.1% (11 cases in mRNA-1273 group; 185 cases in placebo group)
Characterization of Main Adverse Events	Short-term, mild-to-moderate pain at injection site, fatigue and headache. Low rate of serious adverse events.	Short-term, mild-to-moderate pain at injection site, fatigue and headache. Low rate of serious adverse events.
Death (does not indicate causality to vaccine / placebo received)	Death: 2 BNT162b2; 4 placebo	Death: 2 mRNA-1273; 3 placebo

Table 1. Comparison of BNT162b2 and mRNA-1273 Phase 3 Trial Outcomes.

PREVENTION IN THE HOSPITAL

FIRST DOSE OF BNT162B2 MRNA VACCINE IN A HEALTH CARE WORKER COHORT IS ASSOCIATED WITH REDUCED SYMPTOMATIC AND ASYMPTOMATIC SARS-COV-2 INFECTION

Lillie PJ, O'Brien P, Lawtie M, Jessop S, Easom NJW, Patmore R.. Clin Infect Dis. 2021 Apr 24:ciab351. doi: 10.1093/cid/ciab351. Online ahead of print.
Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

An infection prevention and vaccine deployment team from Hull Teaching Hospitals in the United Kingdom compared staff SARS-CoV-2 testing data during the first 2 months of a staff vaccination program with the Pfizer-Biontech (BNT162b2) vaccine. In the first week of January, with 8.3% of staff vaccinated with their first dose, there were 120 NAAT-proven SARS-CoV-2 infections compared to 10 cases during the last week of February with 82.5% of staff vaccinated with a first dose ($p<0.005$, Figure 1). Authors suggest a single dose of the Pfizer-Biontech vaccine reduces SARS-CoV-2 incidence in hospital staff, though acknowledge limitations in data collection due to under-reporting and changes in testing behaviors.

ABSTRACT

Over the first 2 months of 2021 vaccination coverage of staff at Hull Teaching Hospitals withBNT162b2 increased from 8.3% to 82.5%, and was associated with a significant reduction in symptomatic and asymptomatic SARS-CoV-2 cases. The proportion of positive lateral flow tests from asymptomatic screening was maintained over this period.

FIGURES

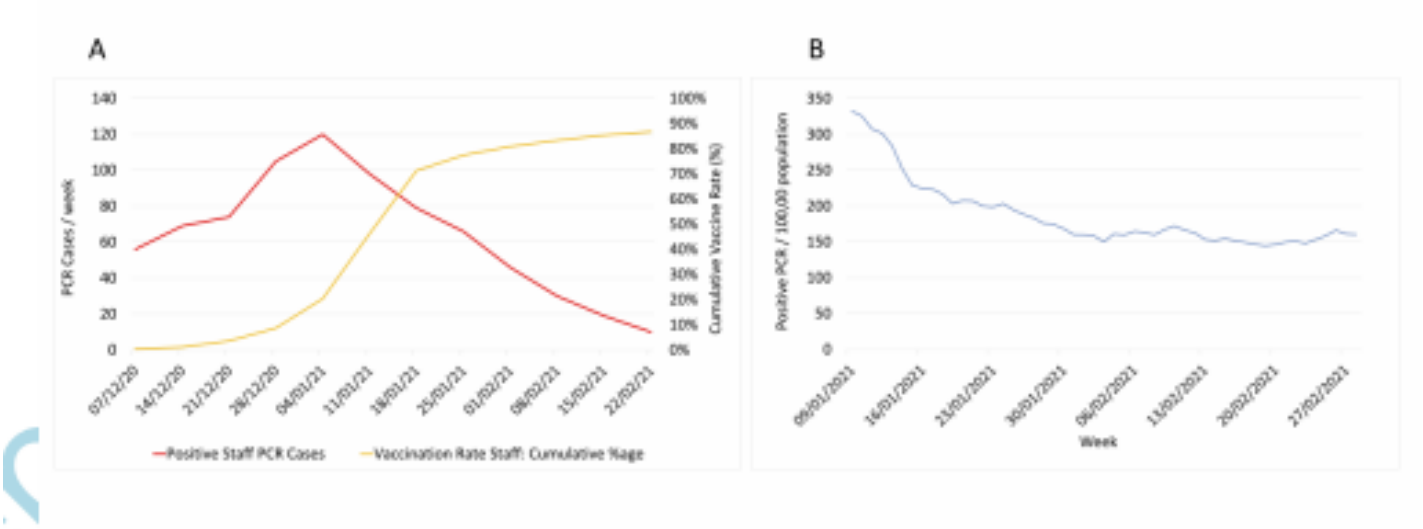


Figure 1a– Vaccination coverage and PCR positive test numbers

CRITICAL CARE

TREATMENT OF SEVERE HYPERTRIGLYCERIDEMIA WITH INSULIN INFUSIONS IN SEVERE COVID-19: A CASE SERIES

Thomas CM, Vicent M, Moore S, Ali F, Wooten L, Louzon PR.. J Pharm Pract. 2021 Apr 22:8971900211010473. doi: 10.1177/08971900211010473. Online ahead of print.
Level of Evidence: 4 - Case-series, case-control studies, or historically controlled studies

BLUF

Pharmacists and critical care physicians from AdventHealth in Orlando, Florida present a case series of 5 critically ill COVID-19 patients on mechanical ventilation who received continuous insulin infusion to treat severe hypertriglyceridemia (TG>1000mg/dl) between March 22 and April 15, 2020 (Table 1). They found hypertriglyceridemia resolved in all patients while on insulin infusion plus standard oral lipid lowering medications and discontinuation of propofol. None developed pancreatitis or hypoglycemia (Figure1). Though findings are limited without a comparison group, authors suggest insulin may activate lipoprotein lipase and lower TG levels in COVID-19 patients with hypertriglyceridemia but encourage more rigorous studies to clarify its benefits.

SUMMARY

Case 1: 36-year-old male with a history of hypertension and diabetes admitted to ICU with 10 day history of worsening flu-like symptoms and contact with COVID-19 patient. On day 2, he was started on propofol and day 5, TG levels were 1494mg/dl and propofol discontinued. On day 6, insulin drip (5.3units/hr) started along with omega 3 PUFA 2mg twice daily. On day 7, TG 1172mg/dL, insulin increased to 21units/hr. Insulin was titrated according to TG levels and on day 34, TG reduced to 332mg/dl on insulin drip 41.4units/hr.

Case 2: 44-year-old male presented to ED and admitted to ICU with COVID-19. On day 2, propofol started. On day 3 TG started increasing, on day 6 TG peaked to 1349mg/dl and propofol discontinued. Insulin drip 6.2units/hr iniatiated to reduce TG levels. TG gradually declined and on day 18, TG was 101mg/dl and given long acting insulin injection on day 19.

Case 3: 79-year-old caucasian female admitted to ICU with COVID-19. Given propofol on admission. On day 3, TG peaked to 1093mg/dl and propofol was discontinued, an insulin drip started 3units/hr with 10% dextrose in water to ensure normoglycemia. On day 5 TG decreased to 248mg/dl and insulin drip was discontinued.

Case 4: 66-year-old male admitted to ICU on day 2 and started on propofol. On day 5, TG peaked to 1042mg/dl, propofol discontinued and insulin drip 3 units/hr started. On day 7 TG 1602mg/dl and insulin 5units/hr. On day 10, insulin drip was 8units/hr and day 11, fenofibrate 200mg daily and atorvastatin 40mg bedtime were added. On day 13, TG decreased to <500mg/dl and on day 23, it was <200mg/dl.

Case 5: 72-year-old female was admitted in ICU and on propofol. On day 3 TG peaked to 1263mg/dl, propofol discontinued and insulin drip 5.8units/hr started. Fenofibrate increased to 200mg daily, niacin 500mg daily and atorvastatin 20mg daily given. On day 6 TG decreased to 405mg/dl.

ABSTRACT

PURPOSE: Rapid onset of severe hypertriglyceridemia was quickly recognized in critical COVID-19 patients. Associated causes have been due to secondary hemophagocytic lymphohystiocytosis (HLH) syndrome, medication-induced, or acute liver failure. Statins, omega-3 polyunsaturated acids, niacin, and fibrates are common oral lipid lowering therapy options in patients at risk for hypertriglyceridemia. The severity of hypertriglyceridemia in COVID-19 patients with triglyceride values reaching greater than 1,000 mg/dL put them at a heightened risk of pancreatitis and therefore an essential need to acutely lower their levels. We present a case series of 5 patients who achieved rapid triglyceride lowering through continuous insulin infusion therapy. METHODS: A retrospective chart review of 48 critical COVID-19 patients who were admitted from March 22 to April 15, 2020 was conducted. Inclusion criteria consisted of mechanical ventilation and continuous insulin infusion to treat severe

hypertriglyceridemia resulting with 5 eligible patients in this case report. RESULTS AND CONCLUSION: In addition to standard oral lipid lowering therapies, continuous insulin infusion successfully treated severe hypertriglyceridemia in critically ill COVID-19 patients. None of the patients experienced pancreatitis or hypoglycemia necessitating cessation of insulin. Further studies are needed to show the optimum dose and duration of insulin infusion as monotherapy and in combination with oral therapies.

FIGURES

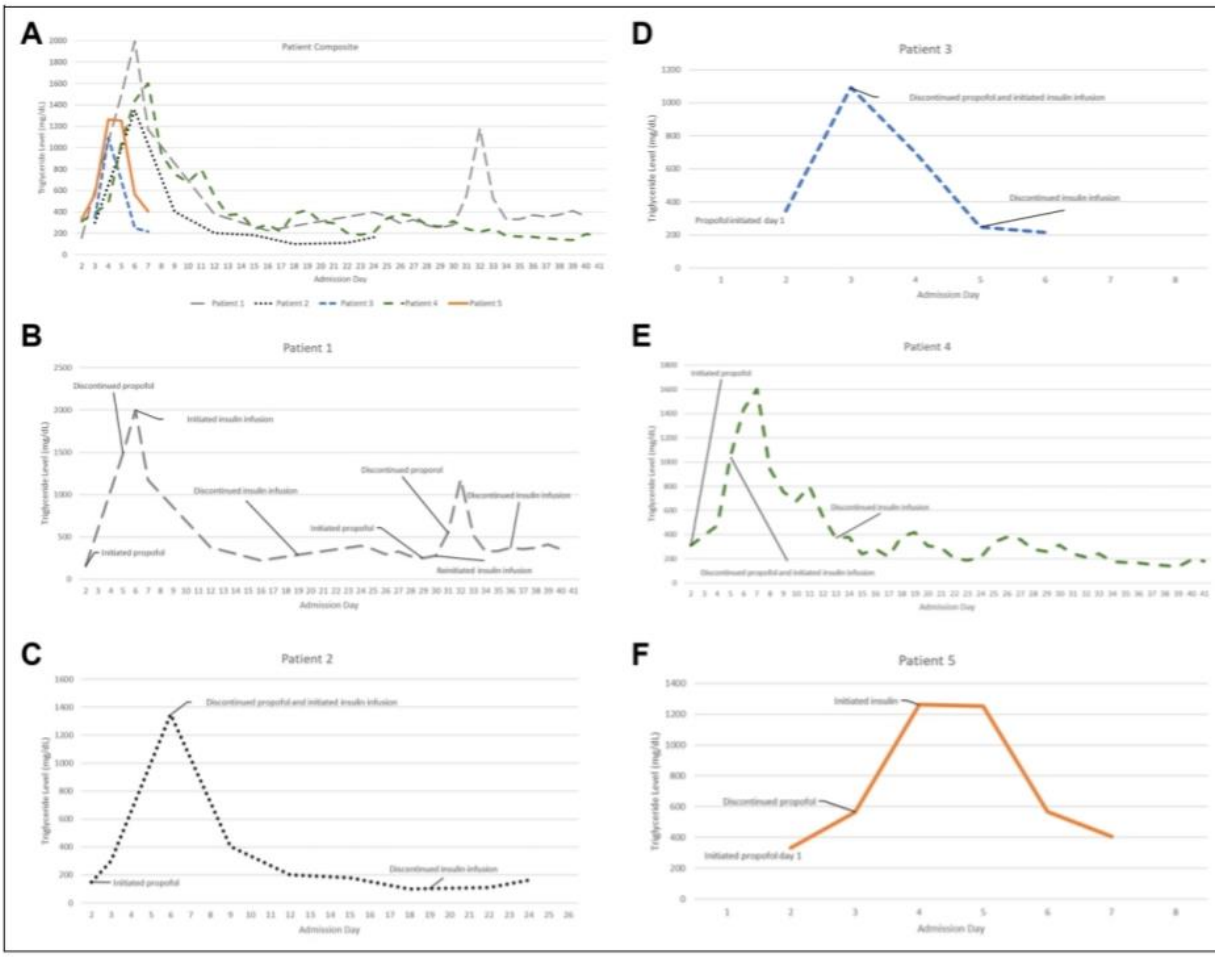


Figure 1: "Composite of patient triglycerde levels over the course of admission (A), patient 1 medication intervention by admission day (B), patient 2 medication intervention by admission day (C), patient 3 medication intervention by admission day (D), patient 4 medication intervention by admission day (E), patient 5 medication intervention by admission day (F)".

Table 1. Baseline Characteristics.

Parameters	Case 1	Case 2	Case 3	Case 4	Case 5
Age (years)/Gender	36/M	44/M	79/F	66/M	72/F
Weight (kg)	122.9	110.0	64.8	92.3	100.0
BMI (kg/m2)	37.7	35.7	26.1	30.9	40.2
HbA1c (%)	11.4	11.9	6.2	6.5	7.0
History of Diabetes	Yes	Yes	No	No	Yes
History of Dyslipidemia	No	No	No	Yes	Yes
Antidiabetic drugs at baseline	Metformin 1 g/day	None	None	None	Insulin glargine 60 units/day Insulin aspart 90 units/day Semaglutide 0.5 mg/week
Antilipidemic drugs at baseline	None	None	Rosuvastatin 20 mg/d Omega-3 polyunsaturated fatty acids 1.5 g/day	None	Fenofibrate 160 mg/day
Days of symptoms prior to hospitalization	10	10	14	5	8

Abbreviations: BMI, body mass index; M, male; F, female; HbA1c, glycated hemoglobin.

ENDOCRINOLOGY

NEW-ONSET DIABETES IN "LONG COVID"

Sathish T, Anton MC, Sivakumar T.. J Diabetes. 2021 Apr 23. doi: 10.1111/1753-0407.13187. Online ahead of print.
Level of Evidence: 5 - Opinion

BLUF

Experts in endocrinology and population health from Canada and India highlight literature reporting the increased risk of new onset diabetes in "long COVID" in multiple retrospective cohort studies and discuss possible mechanisms (i.e. sympathoadrenal axis activation, catalysis of pancreatic beta cells, steroid-induced). Authors suggest this risk warrants attention in patients with long COVID and recommend diabetes screening in this population.

GASTROENTEROLOGY

THE IMPACT OF VEDOLIZUMAB ON COVID-19 OUTCOMES AMONG ADULT IBD PATIENTS IN THE SECURE-IBD REGISTRY

Agrawal M, Zhang X, Brenner EJ, Ungaro RC, Kappelman MD, Colombel JF.. J Crohns Colitis. 2021 Apr 22:jjab071. doi: 10.1093/ecco-jcc/jjab071. Online ahead of print.
Level of Evidence: 4 - Case-series, case-control, or historically controlled studies

BLUF

Gastroenterologists and pediatricians from Icahn School of Medicine in New York evaluated COVID-19 outcomes among 457 patients with inflammatory bowel disease (IBD) managed with vedolizumab using data from an international registry of IBD patients (SECURE-IBD). They found no difference in outcomes in COVID-19 patients on vedolizumab compared to all other medications used to treat IBD (Table 2). Authors suggest that use of the vedolizumab appears to be safe in IBD patients with COVID-19, but recommend future studies to confirm this association due to limitations in their dataset.

ABSTRACT

INTRODUCTION: The impact of immune-modifying therapies on outcomes of Coronavirus disease of 2019 (COVID-19) is variable. The purpose of this study was to determine the impact of vedolizumab (VDZ), a gut-selective anti-integrin, on COVID-19 outcomes in inflammatory bowel disease (IBD) patients. METHODS: Using data from the Surveillance of Coronavirus Under Research Exclusion for IBD (SECURE-IBD), an international registry of IBD patients with confirmed COVID-19, we studied the impact of VDZ on COVID-19 hospitalization and severe COVID-19 (intensive care unit stay, mechanical ventilation and/or death). RESULTS: Of 3,647 adult patients on any IBD medication in the registry, 457 (12.5%) patients were on VDZ. On multivariable analyses using backward selection of covariates, VDZ use was not associated with hospitalization or severe COVID-19 when comparing to patients on all other medications [adjusted odds ratio (aOR) 0.87; 95% confidence interval (CI) 0.71, 1.1 and aOR 0.95; 95% CI 0.53; 1.73, respectively]. On comparing VDZ monotherapy to anti-TNF monotherapy, the odds for hospitalization, but not severe COVID-19, were higher (aOR CI 1.39; 95% CI 1.001, 1.90 and aOR 2.92; 95% CI 0.98, 8.71, respectively). In an exploratory analysis, VDZ monotherapy, compared to anti-TNF monotherapy, was associated with new-onset GI symptoms at the time of COVID-19, especially among patients whose IBD was in remission. CONCLUSIONS: COVID-19 outcomes among IBD patients on VDZ are comparable to those on all other therapies. Hospitalization, but not severe COVID-19, is more likely with VDZ monotherapy than with anti-TNF monotherapy. Overall, VDZ appears to be safe in IBD patients with COVID-19.

FIGURES

Manuscript Doi: 10.1093/ecco-jcc/jjab071

Table 2: Multivariable regression analyses with backward selection of covariates for COVID-19 outcomes by medication class from adult cases in the SECURE-IBD registry

Outcome	Adjusted OR (95% CI)	P value
Hospitalization		
VDZ vs. all other IBD therapies[#]	0.87 (0.72, 1.06)	0.17
VDZ monotherapy vs. anti-TNF monotherapy[##]	**1.38 (1.001, 1.90)**	**0.049**
Severe COVID-19		
VDZ vs. all other IBD therapies*	0.95 (0.53, 1.73)	0.88
VDZ monotherapy vs. anti-TNF monotherapy**	2.92 (0.98, 8.71)	0.055

Table 2: Multivariable regression analyses with backward selection of covariates for COVID19 outcomes by medication class from adult cases in the SECURE-IBD registry

CLINICAL ADJUSTMENTS DURING COVID-19 FOR OUTPATIENT SUBSTANCE USE TREATMENT IN A SAMPLE OF MEN WHO HAVE SEX WITH MEN

Arnold T, Rogers BG, Schierberl Scherr A, Pinkston M, Chan PA.. Public Health Rep. 2021 Mar 25:333549211006984. doi: 10.1177/00333549211006984. Online ahead of print.
Level of Evidence: 5 - Review / Literature Review

BLUF

Psychologists from Brown University in Providence, RI describe their Substance Abuse and Mental Health Services Administration (SAMHSA)-funded treatment program and how it changed during the COVID-19 pandemic. 80 men who have sex with men (MSM) with substance use disorder (SUD) were enrolled in the program, which consisted of psychotherapy sessions to reduce substance use and stressors. Due to the COVID-19 pandemic, many participants had more relapses in substance use due to increased feelings of loneliness, guilt, and anxiety, and several adjustments to the program were made such as transitioning to telehealth, increasing the number of sessions, and tailoring treatment to relapse prevention.

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