The Daily COVID-19 Literature Surveillance Summary

March 19, 2021

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COVID-19 Daily Literature Surveillance

COVID19LST

Bringing you real time, distilled information for guiding best practices during the COVID-19 pandemic

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

- Vaccinating the oldest against COVID-19 saves both the most lives and most years of life. Demographers from University of California, Berkeley and Bucknell University conducted a mathematical analysis of life tables from United States, Germany, and South Korea and found vaccinating the elderly first maximizes both lives saved and years of future life saved. They argue that this finding contradicts the misconception that vaccinating the elderly conflicts with the principle of maximizing the years of future life saved and strongly recommend prioritizing COVID-19 vaccines for the elderly.

- Community-tested cases of SARS-CoV-2 lineage B.1.1.7 may have higher mortality. A team of mathematicians and scientists from the London School of Hygiene's Centre of Mathematical Modelling of Infectious diseases conducted a stratified analysis on the new SARS-CoV-2 lineage B.1.1.7 that emerged in the UK using a dataset of over 2.2 million positive community cases and 17,452 COVID-19 related deaths. Using COX proportional hazard models to control for geographical and temporal differences, researchers identified the estimated hazard of death for the B.1.1.7 to be 1.55 (CI 1.39-1.72) or a 39-72% higher mortality compared to other SARS-CoV-2 strains. Though they acknowledge a number of potential confounding factors, authors suggest the B.1.1.7 variant causes more severe disease compared to other variants.

Management

- Neonates of COVID-19 positive mothers in a 16 hospital study all tested negative and had good clinical outcomes. A retrospective case series from the department of pediatrics at the University of California described the early outcomes and inpatient management of neonates born to women with perinatal SARS-CoV-2 infection. Every infant born to the 70 COVID-19 positive mothers across 16 hospitals were well appearing and tested negative for SARS-CoV-2. The authors note that although clinical outcomes were good overall, clinical management was largely inconsistent with current U.S. Covid-19 guidelines for nursery care, suggesting concerns about the feasibility and acceptability of those recommendations.

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VACCINATING THE OLDEST AGAINST COVID-19 SAVES BOTH THE MOST LIVES AND MOST YEARS OF LIFE

Goldstein JR, Cassidy T, Wachter KW.. Proc Natl Acad Sci U S A. 2021 Mar 16;118(11):e2026322118. doi: 10.1073/pnas.2026322118.
Level of Evidence: 5 - Modeling

BLUF

Demographers from University of California, Berkeley and Bucknell University conducted a mathematical analysis of life tables from United States, Germany, and South Korea and found vaccinating the elderly first maximizes both lives saved and years of future life saved (Figure 1). They argue that this finding contradicts the misconception that vaccinating the elderly conflicts with the principle of maximizing the years of future life saved and strongly recommend prioritizing COVID-19 vaccines for the elderly.

ABSTRACT

Many competing criteria are under consideration for prioritizing COVID-19 vaccination. Two criteria based on age are demographic: lives saved and years of future life saved. Vaccinating the very old against COVID-19 saves the most lives, but, since older age is accompanied by falling life expectancy, it is widely supposed that these two goals are in conflict. We show this to be mistaken. The age patterns of COVID-19 mortality are such that vaccinating the oldest first saves the most lives and, surprisingly, also maximizes years of remaining life expectancy. We demonstrate this relationship empirically in the United States, Germany, and South Korea and with mathematical analysis of life tables. Our age-risk results, under usual conditions, also apply to health risks.

FIGURES

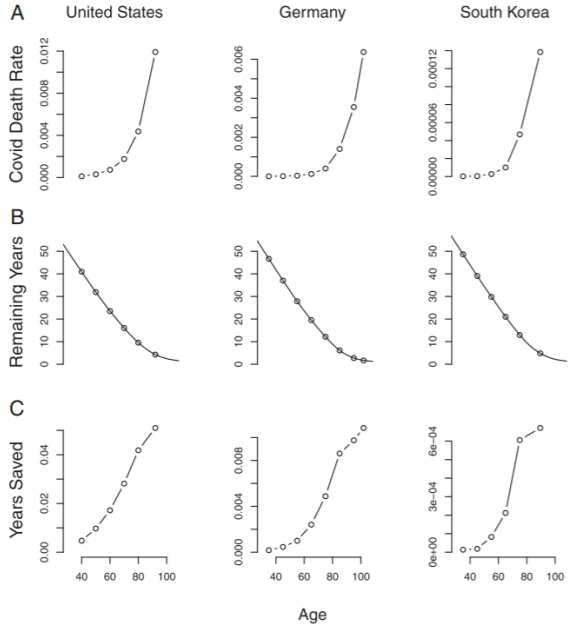

Fig. 1. Age patterns of (*A*) COVID-19 death rates, (*B*) remaining life expectancy, and (*C*) person-years saved per effective vaccination in the United States, Germany, and South Korea. In all three countries, within an age-based framework, vaccination of the oldest group will maximize person-years saved per effective vaccination. (Details are provided in *Materials and Methods*).

ADULTS

INCREASED MORTALITY IN COMMUNITY-TESTED CASES OF SARS-COV-2 LINEAGE B.1.1.7

Davies NG, Jarvis CI; CMMID COVID-19 Working Group, Edmunds WJ, Jewell NP, Diaz-Ordaz K, Keogh RH.. Nature. 2021 Mar 15. doi: 10.1038/s41586-021-03426-1. Online ahead of print.
Level of Evidence: 3 - Cohort study or control arm of randomized trial

BLUF

A team of mathematicians and scientists from the London School of Hygiene's Centre of Mathematical Modelling of Infectious diseases conducted a stratified analysis on the new SARS-CoV-2 lineage B.1.1.7 that emerged in the UK using a dataset of over 2.2 million positive community cases and 17,452 COVID-19 related deaths. Using COX proportional hazard models to control for geographical and temporal differences, researchers identified the estimated hazard of death for the B.1.1.7 to be 1.55 (CI 1.39-1.72)(Table 1) or a 39-72% higher mortality compared to other SARS-CoV-2 strains (Figure 2). Though they acknowledge a number of potential confounding factors, authors suggest the B.1.1.7 variant causes more severe disease compared to other variants.

ABSTRACT

SARS-CoV-2 lineage B.1.1.7, a variant first detected in the UK in September 20201, has spread to multiple countries worldwide. Several studies have established that B.1.1.7 is more transmissible than preexisting variants, but have not identified whether it leads to any change in disease severity2. Here we analyse a dataset linking 2,245,263 positive SARS-CoV-2 community tests and 17,452 COVID-19 deaths in England from 1 September 2020 to 14 February 2021. For 1,146,534 (51%) of these tests, the presence or absence of B.1.1.7 can be identified because of mutations in this lineage preventing PCR amplification of the spike gene target (S gene target failure, SGTF1). Based on 4,945 deaths with known SGTF status, we estimate that the hazard of death associated with SGTF is 55% (95% CI 39-72%) higher after adjustment for age, sex, ethnicity, deprivation, care home residence, local authority of residence and test date. This corresponds to the absolute risk of death for a 55-69-year-old male increasing from 0.6% to 0.9% (95% CI 0.8-1.0%) within 28 days after a positive test in the community. Correcting for misclassification of SGTF and missingness in SGTF status, we estimate a 61% (42-82%) higher hazard of death associated with B.1.1.7. Our analysis suggests that B.1.1.7 is not only more transmissible than preexisting SARS-CoV-2 variants, but may also cause more severe illness.

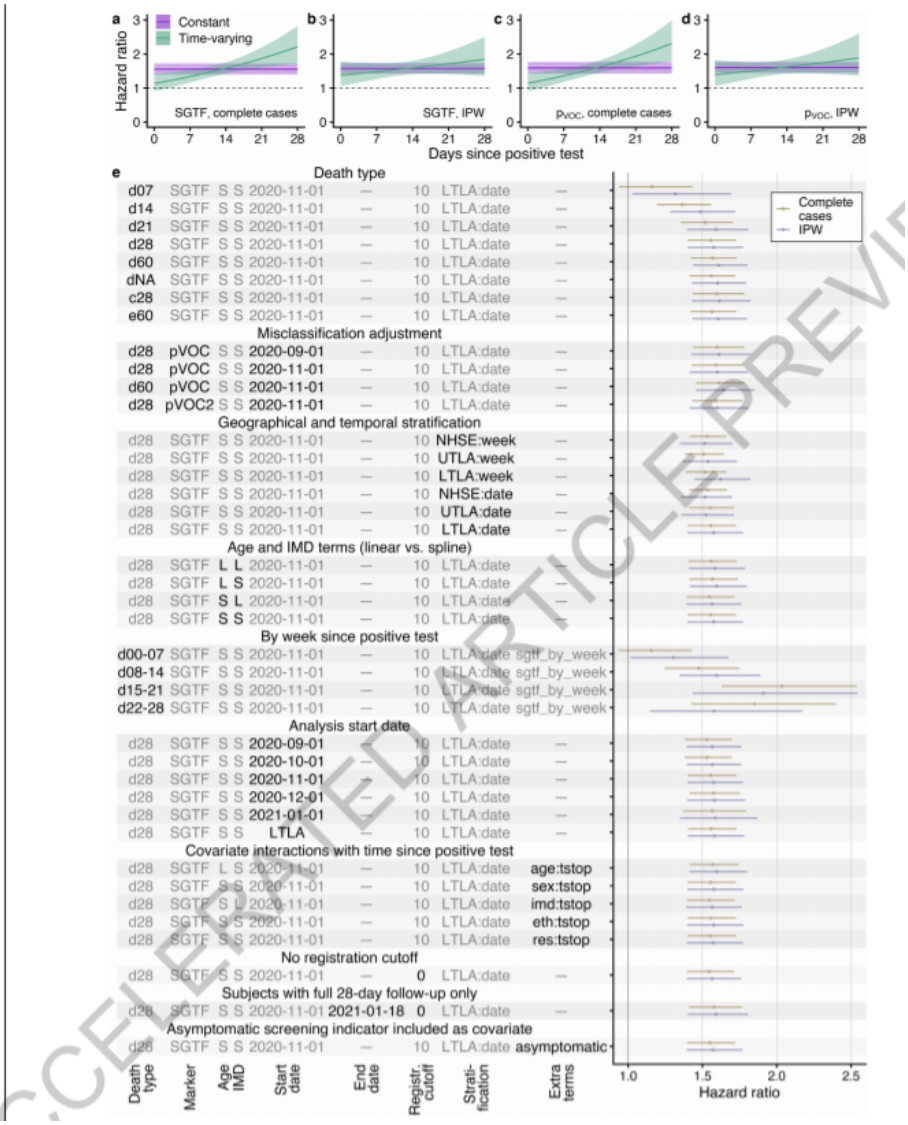

Figure 2. Survival analyses. a–d Estimated hazard ratio of death (mean and 95% CIs) within 28 days of positive test for (a) SGTF, complete-cases analysis; (b) SGTF, IPW analysis; (c) pVOC, complete-cases analysis; and (d) pVOC, IPW analysis, in model stratified by LTLA and specimen date and adjusted for the other covariates. e Estimated hazard ratio of death (point estimates and 95% CIs) across each model investigated. Death types are coded as follows: dX, all deaths within X days of a positive test; c28, death-certificate-confirmed COVID-19 deaths within 28 days; e60, all deaths within 60 days plus all death-certificate confirmed COVID-19 deaths within any time period. S, spline term (for Age or IMD); L, linear term (for Age or IMD); NHSE, NHS England region (n = 7); UTLA, upper-tier local authority (n = 150); LTLA, lower-tier local authority (n = 316). LTLA start date signifies a start date chosen separately for each LTLA (see Methods).

Sex	Age	Baseline	SGTF, complete cases	p_{VOC}, IPW
Female	0–34	0.00069%	0.0011% (0.00096–0.0012%)	0.0011% (0.00097–0.0012%)
	35–54	0.033%	0.050% (0.045–0.056%)	0.052% (0.046–0.059%)
	55–69	0.18%	0.28% (0.25–0.31%)	0.29% (0.26–0.33%)
	70–84	2.9%	4.4% (4.0–4.9%)	4.6% (4.0–5.1%)
	85 and older	13%	19% (17–21%)	20% (18–22%)
Male	0–34	0.0031%	0.0047% (0.0042–0.0052%)	0.0049% (0.0043–0.0055%)
	35–54	0.064%	0.099% (0.089–0.11%)	0.10% (0.090–0.12%)
	55–69	0.56%	0.86% (0.77–0.95%)	0.89% (0.78–1.0%)
	70–84	4.7%	7.2% (6.4–7.9%)	7.4% (6.6–8.3%)
	85 and older	17%	25% (23–27%)	26% (23–29%)

The baseline risk (i.e., for preexisting SARS-CoV-2 variants) is derived using linked deaths within 28 days for all individuals testing positive in the community from 1 August – 31 October 2020. Adjusted risks are presented for the SGTF analysis for complete cases and for the misclassification-adjusted (p_{VOC}) IPW analysis, which yielded the lowest and highest mortality estimates, respectively, of the main models assessed (Fig. 2a–d).

Table 1. Absolute 28-day mortality risk associated with B.1.1.7, as expressed by case fatality ratio (%) among individuals testing positive in the community

PROLONGED SARS-COV-2 INFECTION IN A CAR T-CELL THERAPY RECIPIENT

Abbasi J.. JAMA. 2021 Mar 9;325(10):924. doi: 10.1001/jama.2021.2493.
Level of Evidence: 5 - Review / Literature Review

BLUF

A health writer reflects on a case report of a 73-year-old immunocompromised male infected with SARS-CoV-2 receiving chimeric antigen receptor T-cell therapy. His endotracheal aspirate originally had SARS-CoV-2 particles present that were similar to the strains in his community. Over 72 days, SARS-CoV-2 particles were still found to be present, indicating infectious potential, and new strains found in the UK and South Africa were identified within the patient. This finding suggests a longer need of isolation in individuals who are immunocompromised and supports the thought that the virus can evolve within patients.

TRANSMISSION & PREVENTION

COVID-19 VACCINATION IN PREGNANT AND LACTATING WOMEN

Adhikari EH, Spong CY.. JAMA. 2021 Mar 16;325(11):1039-1040. doi: 10.1001/jama.2021.1658.
Level of Evidence: 5 - Opinion

BLUF

Obstetrician-gynecologists from The University of Texas Southwestern Medical Center discuss the lack of evidence on COVID-19 vaccine safety in pregnant and lactating females who are at higher risk for severe COVID-19. Because the World Health Organization has recommended pregnant women with high risk of exposure should be vaccinated, authors encourage physicians to educate pregnant women on the benefits and risks of COVID-19 vaccine to allow them to make informed choices regarding vaccination.

DEVELOPMENTS IN TRANSMISSION & PREVENTION

COVID-19 VACCINES VS VARIANTS-DETERMINING HOW MUCH IMMUNITY IS ENOUGH

Rubin R.. JAMA. 2021 Mar 17. doi: 10.1001/jama.2021.3370. Online ahead of print.
Level of Evidence: 5 - Review / Literature Review

BLUF

A JAMA medical writer cites several studies to discuss whether the current COVID-19 vaccines are efficient against SARS-CoV-2 virus variants. Some previous studies indicate that the Pfizer-BioNTech and Moderna vaccines have decreased neutralization titers for the B.1.351 spike protein in comparison to the Wuhan-Hu-1 spike protein. This article suggests there is a lack of information regarding these new variants and more studies are needed to determine whether the addition of a booster shot against variants can be effective.

SARS-COV-2 VACCINE CHADOX1 NCOV-19 INFECTION OF HUMAN CELL LINES REVEALS LOW LEVELS OF VIRAL BACKBONE GENE TRANSCRIPTION ALONGSIDE VERY HIGH LEVELS OF SARS-COV-2 S GLYCOPROTEIN GENE TRANSCRIPTION

Almuqrin A, Davidson AD, Williamson MK, Lewis PA, Heesom KJ, Morris S, Gilbert SC, Matthews DA.. Genome Med. 2021 Mar 15;13(1):43. doi: 10.1186/s13073-021-00859-1.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

A recent laboratory study conducted by cellular and molecular medicine researchers associated with the University of Bristol assessed the efficacy of the COVID-19 ChAdOx1 nCoV-19 recombinant adenovirus vaccine as a vector by analyzing RNA sequences of the transcript expression. Some key results are that the coding transcript for SARS-CoV-2 predominated in all cell lines (Table 2) and that in the A549 continuous line lung epithelial cells, there was some adenoviral gene expression and proteins found (Table 4). The implication of this data is that with regards to various cell lines, the vaccine's vector transcriptome is functioning as was intended.

ABSTRACT

BACKGROUND: ChAdOx1 nCoV-19 is a recombinant adenovirus vaccine against SARS-CoV-2 that has passed phase III clinical trials and is now in use across the globe. Although replication-defective in normal cells, 28 kbp of adenovirus genes is delivered to the cell nucleus alongside the SARS-CoV-2 S glycoprotein gene. METHODS: We used direct RNA sequencing to analyse transcript expression from the ChAdOx1 nCoV-19 genome in human MRC-5 and A549 cell lines that are non-permissive for vector replication alongside the replication permissive cell line, HEK293. In addition, we used quantitative proteomics to study over time the proteome and phosphoproteome of A549 and MRC5 cells infected with the ChAdOx1 nCoV-

19 vaccine. RESULTS: The expected SARS-CoV-2 S coding transcript dominated in all cell lines. We also detected rare S transcripts with aberrant splice patterns or polyadenylation site usage. Adenovirus vector transcripts were almost absent in MRC-5 cells, but in A549 cells, there was a broader repertoire of adenoviral gene expression at very low levels. Proteomically, in addition to S glycoprotein, we detected multiple adenovirus proteins in A549 cells compared to just one in MRC5 cells. CONCLUSIONS: Overall, the ChAdOx1 nCoV-19 vaccine's transcriptomic and proteomic repertoire in cell culture is as expected. The combined transcriptomic and proteomics approaches provide a detailed insight into the behaviour of this important class of vaccine using state-of-the-art techniques and illustrate the potential of this technique to inform future viral vaccine vector design.

FIGURES

Table 2 List of ORFs searched for and the transcript frequency for each ORF

From: SARS-CoV-2 vaccine ChAdOx1 nCoV-19 infection of human cell lines reveals low levels of viral backbone gene transcription alongside very high levels of SARS-CoV-2 S glycoprotein gene transcription

	MRC-5 cells						A549 cells						293 cells	
Feature	Count 24 h	Percent of total at 24 h	Count 48 h	Percent of total at 48 h	Count 72 h	Percent of total at 72 h	Count 24 h	Percent of total at 24 h	Count 48 h	Percent of total at 48 h	Count 72 h	Percent of total at 72 h	Count 24 h	Percent of total at 24 h
Total of all reads	4443	100.00	9201	100.00	6849	100.00	2070	100.00	1937	100.00	1811	100.00	62,281	100.00
SARS_CoV_2_S_protein	4156	93.54	8570	93.14	6453	94.22	1536	74.20	1447	74.70	1645	90.83	10,586	17.00
None from list	148	3.33	278	3.02	214	3.12	92	4.44	112	5.78	53	2.93	4138	6.64
pIX	21	0.47	27	0.29	23	0.34	14	0.68	13	0.67	2	0.11	909	1.46
DBP(E2A)	1	0.02	3	0.03	0	0.00	205	9.90	95	4.90	13	0.72	5198	8.35
fibre(L5)	0	0.00	0	0.00	0	0.00	2	0.10	9	0.46	2	0.11	6011	9.65
hexon(L3)	0	0.00	0	0.00	0	0.00	16	0.77	20	1.03	3	0.17	3990	6.41
33K_full_length(L4)	0	0.00	0	0.00	0	0.00	10	0.48	20	1.03	7	0.39	3217	5.17
preVII(L2)	0	0.00	0	0.00	0	0.00	12	0.58	7	0.36	2	0.11	3212	5.16
100K(L4)	0	0.00	0	0.00	0	0.00	11	0.53	25	1.29	7	0.39	2212	3.55
i_leader_protein	0	0.00	0	0.00	0	0.00	18	0.87	46	2.37	11	0.61	1969	3.16
IVa2	0	0.00	0	0.00	0	0.00	6	0.29	14	0.72	3	0.17	1676	2.69
pV(L2)	0	0.00	0	0.00	0	0.00	4	0.19	3	0.15	0	0.00	1373	2.20
52/55K(L1)	0	0.00	0	0.00	0	0.00	20	0.97	28	1.45	6	0.33	1345	2.16
22K(L4)	0	0.00	0	0.00	0	0.00	9	0.43	9	0.46	2	0.11	1193	1.92
preX(L2)	0	0.00	0	0.00	0	0.00	6	0.29	8	0.41	4	0.22	1180	1.89
E4_orf2	0	0.00	2	0.02	0	0.00	0	0.00	1	0.05	2	0.11	1040	1.67
E4_orf3	0	0.00	1	0.01	0	0.00	13	0.63	8	0.41	3	0.17	1011	1.62
preVI(L3)	0	0.00	0	0.00	0	0.00	8	0.39	7	0.36	1	0.06	821	1.32
preVIII(L4)	0	0.00	0	0.00	0	0.00	1	0.05	2	0.10	1	0.06	821	1.32
penton_base(L2)	0	0.00	0	0.00	0	0.00	1	0.05	2	0.10	1	0.06	631	1.01
Ad5_E1b_19K	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	506	0.81
E4_orf1	0	0.00	0	0.00	0	0.00	1	0.05	0	0.00	0	0.00	286	0.46
prellla(L1)	0	0.00	0	0.00	0	0.00	5	0.24	3	0.15	0	0.00	239	0.38
E4_orf4	0	0.00	0	0.00	0	0.00	2	0.10	2	0.10	0	0.00	187	0.30
UXP	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	159	0.26
Ad5_E1a_13S	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	97	0.16
E4_orf6_7	0	0.00	0	0.00	0	0.00	1	0.05	0	0.00	1	0.06	79	0.13
23K_protease(L3)	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	70	0.11
Ad5_E1a_12S	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	26	0.04
preTP(E2B)	0	0.00	0	0.00	0	0.00	1	0.05	0	0.00	0	0.00	23	0.04
Ad5_pIX	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	10	0.02
pol(E2B)	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	4	0.01
Ad5_E1a_10S(171R)	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	3	0.00
E4_orf6	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	3	0.00
Ad5_E1b_13S(E1b-84R)	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	2	0.00
Ad5_E1b_22S(E1b 55 K)	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	2	0.00
Ad5_E1a_9S	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	1	0.00
Ad5_E1a_11S(217R)	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Ad5_E1b_14.5S(E1b-93R)	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Ad5_E1b_14S(E1b-156R)	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Ad5_E1b_novel-84R	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00

This table details how many transcripts would code for each indicated ORF from the ChAdOx1 nCoV-19 genome or ORFs coded by the region of Ad5 integrated into the HEK293 cell line. The “total of all reads” row indicates how many transcripts map to either the ChAdOx nCoV-19 genome or the region of human Ad5 integrated into the HEK 293 genome. The “none from list” row indicates how many transcripts did map but the pipeline was unable to correlate the 5′ most ORF on that transcript with any of the known ORFs from the genomes under consideration

Table 2. List of ORFs searched for and the transcript frequency for each ORF. This table details how many transcripts would code for each indicated ORF from the ChAdOx1 nCoV-19 genome or ORFs coded by the region of Ad5 integrated into the HEK293 cell line. The “total of all reads” row indicates how many transcripts map to either the ChAdOx nCoV-19 genome or the region of human Ad5 integrated into the HEK 293 genome. The “none from list” row indicates how many transcripts did map but the pipeline was unable to correlate the 5′ most ORF on that transcript with any of the known ORFs from the genomes under consideration

Table 4 Peptides identified as derived from ChAdOx1 nCoV-19 in each cell line used

From: SARS-CoV-2 vaccine ChAdOx1 nCoV-19 infection of human cell lines reveals low levels of viral backbone gene transcription alongside very high levels of SARS-CoV-2 S glycoprotein gene transcription

	A549 total proteome analysis—number of unique peptides identified	A549 phosphoproteome analysis—number of unique phospho sites identified	MRC5 total proteome analysis—number of unique peptides identified	MRC5 phosphoproteome analysis—number of unique phospho sites identified
SARS-CoV-2 S glycoprotein	39	1	43	1
ChAdv DBP	16	4	ND	ND
ChAdv Hexon	2	ND	ND	ND
ChAdv E4 ORF3	3	ND	2	ND
mRNA#962	1	ND	1	ND

The table lists the number of unique peptides identified and unique phosphorylation sites identified for the proteins listed. ND indicates that none was detected in that sample, ChAdv indicates a protein from the ChAdOx1 viral vector backbone and mRNA#962 indicates the truncated S glycoprotein coded by this single transcript

Table 4. Peptides identified as derived from ChAdOx1 nCoV-19 in each cell line used. The table lists the number of unique peptides identified and unique phosphorylation sites identified for the proteins listed. ND indicates that none was detected in that sample, ChAdv indicates a protein from the ChAdOx1 viral vector backbone and mRNA#962 indicates the truncated S glycoprotein coded by this single transcript

MANAGEMENT AND EARLY OUTCOMES OF NEONATES BORN TO WOMEN WITH SARS-COV-2 IN 16 U.S. HOSPITALS

Congdon JL, Kair LR, Flaherman VJ, Wood KE, LoFrumento MA, Nwaobasi-Iwuh E, Phillipi CA; Better Outcomes through Research for Newborns (BORN) Network.. Am J Perinatol. 2021 Mar 15. doi: 10.1055/s-0041-1726036. Online ahead of print.
Level of Evidence: 4 - Case-series

BLUF

A retrospective case series from the department of pediatrics at the University of California described the early outcomes and inpatient management of neonates born to women with perinatal SARS-CoV-2 infection. Every infant born to the 70 COVID-19 positive mothers across 16 hospitals were well appearing and tested negative for SARS-CoV-2. The authors note that although clinical outcomes were good overall, clinical management was largely inconsistent with current U.S. Covid-19 guidelines for nursery care, suggesting concerns about the feasibility and acceptability of those recommendations (Summary).

SUMMARY

- Despite being recommended by both AAP and CDC, rates of indirect breastfeeding were exceedingly low (Table 3). This calls into the question the feasibility and acceptability of indirect breastfeeding in the first days of life to parents and or providers of neonates with SARS-CoV-2 positive mothers. This information raises serious concerns about the unintended consequences of separation on breastfeeding rates.

- The authors note the urgent need for longitudinal studies to assess the benefits and harms of current practices to inform evidence-based clinical care and aid shared decision-making.

ABSTRACT

Objective: There is a paucity of evidence to guide the clinical care of late preterm and term neonates born to women with perinatal severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The objective of this case series is to describe early neonatal outcomes and inpatient management in U.S. hospitals.

Study design: We solicited cases of mother-infant dyads affected by novel coronavirus disease 2019 (COVID-19) from the Better Outcomes through Research for Newborns (BORN) Network members. Using a structured case template, participating sites contributed deidentified, retrospective birth hospitalization data for neonates ≥35 weeks of gestation at birth with mothers who tested positive for SARS-CoV-2 before delivery. We describe demographic and clinical characteristics, clinical management, and neonatal outcomes.

Results: Sixteen U.S. hospitals contributed 70 cases. Birth hospitalizations were uncomplicated for 66 (94%) neonates in which 4 (6%) required admission to a neonatal intensive care unit. None required evaluation or treatment for infection, and all who were tested for SARS-CoV-2 were negative (n = 57). Half of the dyads were colocated (n = 34) and 40% directly breastfed (n = 28). Outpatient follow-up data were available for 13 neonates, all of whom remained asymptomatic.

Conclusion: In this multisite case series of 70 neonates born to women with SARS-CoV-2 infection, clinical outcomes were overall good, and there were no documented neonatal SARS-CoV-2 infections. Clinical management was largely inconsistent with contemporaneous U.S. COVID-19 guidelines for nursery care, suggesting concerns about the acceptability and feasibility of those recommendations. Longitudinal studies are urgently needed to assess the benefits and harms of current practices to inform evidence-based clinical care and aid shared decision-making.

Method of feeding	Full sample ($n = 70$) *n* (%)	Colocated ($n = 34$) *n* (%)	Roomed separately ($n = 36$) *n* (%)
Direct breastfeeding exclusively	21 (30)	21 (64)	–
Direct breastfeeding + supplementation[a]	7 (10)	7 (21)	–
Expressed breastmilk exclusively	1 (1)	–	1 (3)
Expressed breastmilk + supplementation[a]	4 (6)	–	4 (11)
Formula or donor milk exclusively	37 (53)	6 (18)	31 (84)

Table 3. Method of feeding for neonates born to women with SARS-CoV-2 infection (n=70)

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CONTRIBUTORS

Ankita Dharmendran
Ashia Hackett
Brad Mott
Krithika Kumarasan
Michael Wang
Nicolas Longobardi
Zainab Awan

EDITORS

Julia Ghering
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