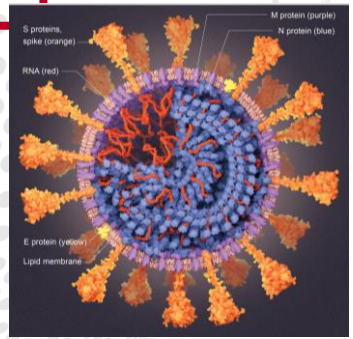
COVID-19

When Will We Have Vaccines for Children and Other Frequently Asked Questions

MDAAP Annual Meeting
September 11, 2021



James Campbell, MD, MS
Division of Infectious Diseases and Tropical Pediatrics
Center for Vaccine Development and Global Health
University of Maryland School of Medicine
11 September 2021

UNIVERSITY of MARYLAND
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CENTER FOR VACCINE DEVELOPMENT AND GLOBAL HEALTH


PRICE $3.50
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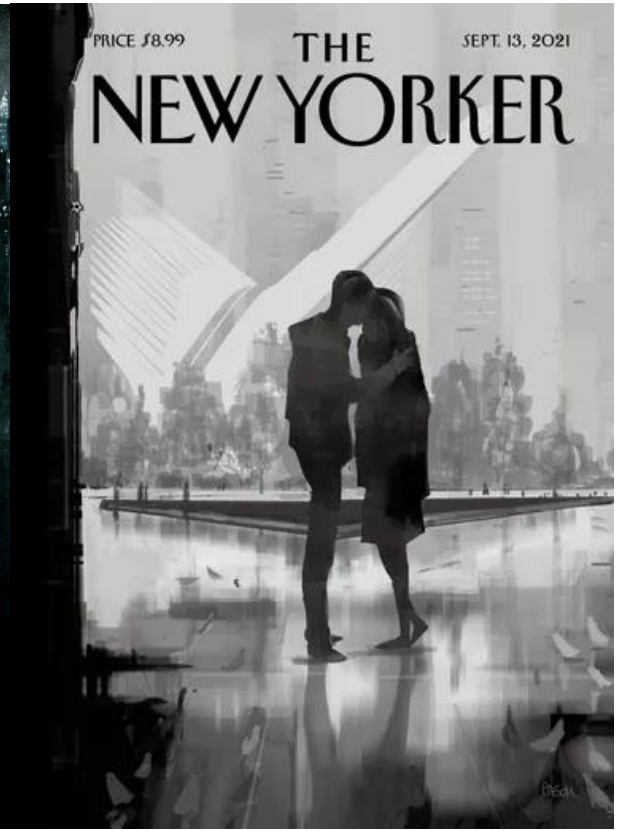
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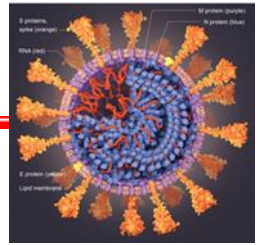
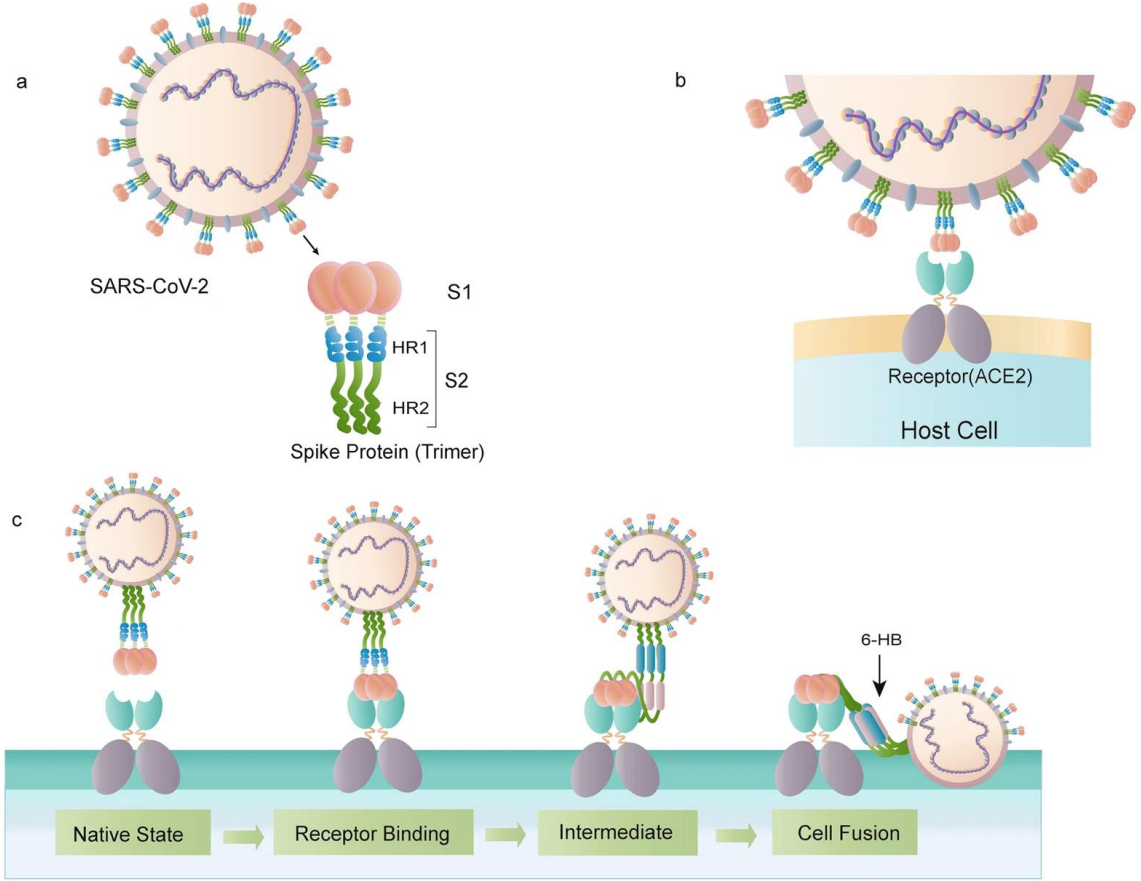
It’s All About the Spike Protein





When will we have COVID-19 vaccines for children under 12?

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When will we have COVID-19 vaccines for children under 12?

Pfizer
BIONTECH

- *12 and up- 30 mcg*
- *5-11y- 10 mcg*
- *6m-5y- 3 mcg*

- **Trial of 5-11 yo** fully enrolled
  - Data expected to be submitted to the FDA late Sept/Oct
- **Trial of 2-5 yo** is enrolling
  - Data expected to be submitted to the FDA by the end of 2021
- **Trial of under 2s**
  - Late 2021/early 2022?

When will we have COVID-19 vaccines for children under 12?

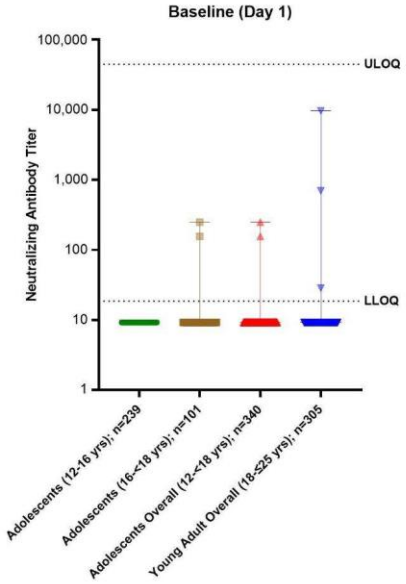
moderna

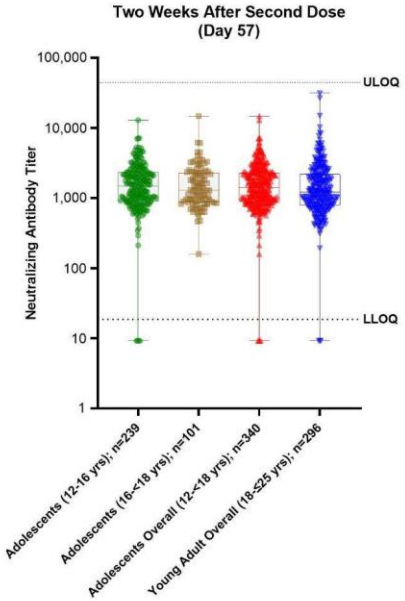
- *12 and up- 100 mcg*
- *6-11y- 50 mcg*
- *6m-5y- likely 25 mcg*

- **Teens:** VE 100%, better nAb than adults, safe
  - Filed for EUA, under review
- **Trial of 6-11 yo** fully enrolled – 4000, 3:1 vaccine
  - Second doses just begun, D57 is primary, 6 months=Jan
- **Trial of 2-5 yo** is expected to begin early Oct- 4000, 3:1
  - 6 months is April 2022
- **Trial of under 2s**
  - Could start late 2021, 6 months spring of 2022

When will we have COVID-19 vaccines for children under 12?

moderna





The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Evaluation of mRNA-1273 SARS-CoV-2 Vaccine in Adolescents

Kashif Ali, M.D., Gary Berman, M.D., Honghong Zhou, Ph.D.,

DOI: 10.1056/NEJMoa2109522

- 0 cases in vaccinees
- 4 cases in placebos

When will we have COVID-19 vaccines for children under 12?

- *Adults:* 5×10^{10} *virus particles*
- *Teens and children: ?*

- 12-17 year olds- expected to start Fall 2021
- Younger ages- unknown, perhaps 2022

When will we have COVID-19 vaccines for children under 12?

NOVAVAX

Creating Tomorrow's Vaccines Today

- *All ages: 5 mcg spike, 50 mcg M Matrix antigen*

- **Adult data**: safe and effective, 2 doses 21d interval
  - 100% protection against moderate and severe illness, and 93% VE against variants of concern and of interest
  - >65 years or underlying conditions or who work in high-risk occupations—91% VE
  - Submitting to FDA very soon (been "very soon" for a while)
- **Teens**: just completed the double-blind crossover
  - Data cleaning and interim analysis is happening
- **Younger children-** hopefully later in 2021

AAP President Interview with NPR: Sept 7,2021

- CHANG: And just to be clear, in this letter that you wrote, you argue that the FDA will have, very soon, the data it will need to authorize the vaccine for children, right? Can you just explain, what is that data that the FDA will have quite soon?

- SAVIO BEERS: Our understanding from what we're hearing from the clinical trial sites and from the manufacturers is that **their trials are fully enrolled** and that the - at least one of the manufacturers expects to have **data available to submit to the FDA, hopefully by the end of September, perhaps early in October**. And so what that means is that once that data is submitted, the FDA will have a chance to look at it to determine the safety and effectiveness of the vaccine and consider the risk-benefit for children.

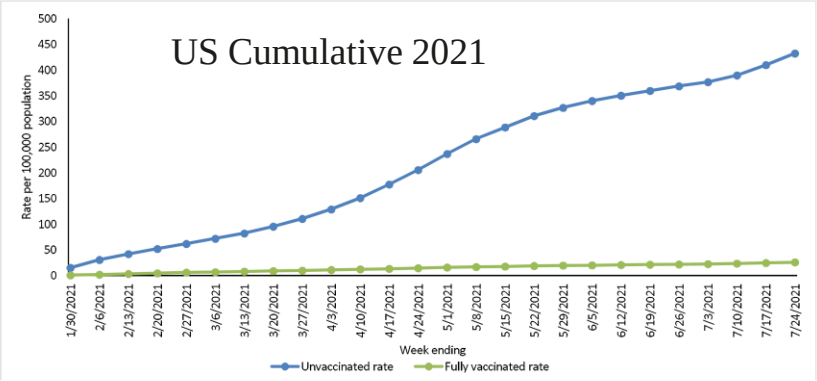
- CHANG: OK, but the FDA wants six months of data. Why is that? Can you explain that discrepancy? And how important is that discrepancy?

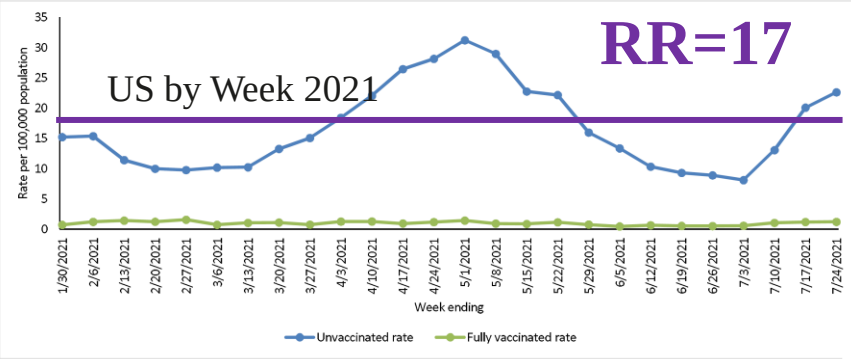
- SAVIO BEERS: Yes, absolutely. You know, and this is actually something that we've seen with the emergency use authorization of the vaccine in adults. **The emergency use authorization came after two months because the FDA really felt and believed that the benefit of approving the vaccine because of the public health emergency was great enough** that they could rely on the very strong safety data at two months. And the final approval came at six months, which is an important landmark but a cautious one. **And we really believe that the same situation applies for children.** So we absolutely believe that we have enough data to determine the safety and efficacy of the vaccine for emergency use authorization in children after two months.

Does Vaccination Prevent Hospitalization?

Figure 2. Age-adjusted population-based rates[a] of COVID-19-associated hospitalizations among unvaccinated and fully vaccinated ≥18 years admitted January 24–July 24, 2021,[b] A) cumulative and B) by week of admission — COVID-NET, 13 States[c]

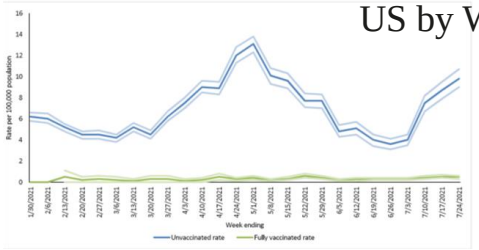
A)

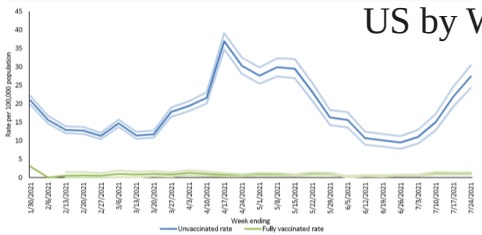


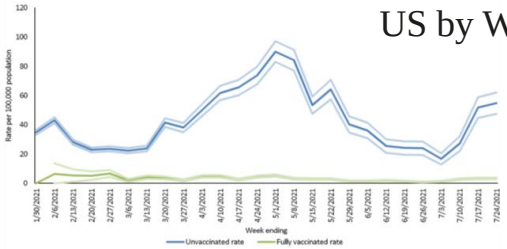


Preprint Aug 29, 2021

3. Age-specific population-based rates[a] of COVID-19-associated hospitalizations among unvaccinated and fully vaccinated adults ars admitted January 24–July 24, 2021,[b] by week of admission and aged A) 18–49 years B) 50–64 years and C) ≥65 years — COVIE es[c]. Rates are shown with 95% confidence intervals.







COVID-19-associated hospitalizations among vaccinated and unvaccinated adults ≥18 years – COVID-NET, 13 states, January 1 – July 24, 2021

Do Children Get "Long Haul" COVID?

- Switzerland- observational cohort 55 schools
- In person school except 6 weeks lockdown March – May, 2020
- Parent survey about child symptoms comparing seropositives to seronegatives
- Symptom >12 wk: 4% v 2%
- Symptom >4 wk: 9% v 10%
- Similar proportions reported excellent or good health (94 v 96%)

RESEARCH LETTER

Long-term Symptoms After SARS-CoV-2 Infection in Children and Adolescents

Published Online: July 15, 2021. doi:10.1001/jama.2021.11880

Table. Participant Characteristics, Most Frequently Reported Symptoms After Serologic Testing (October 2020 Through March-April 2021), and Self-rated Health Among Seropositive and Seronegative Children

	No. (%)	
	Seropositive (n = 109)	Seronegative (n = 1246)
Female sex	58 (53)	669 (54)
Age, y		
6-11	66 (61)	703 (56)
12-16	43 (39)	543 (44)
≥1 Symptom lasting >12 wk	4 (4)	28 (2)
Tiredness	3 (3)	10 (1)
Difficulty concentrating	2 (2)	8 (1)
Increased need for sleep	2 (2)	0
Congested or runny nose	1 (1)	3 (<1)
Stomachache	1 (1)	3 (<1)
Chest tightness	1 (1)	0
≥1 Symptom lasting >4 wk	10 (9)	121 (10)
Tiredness	7 (6)	51 (4)
Headache	5 (5)	39 (3)
Congested or runny nose	3 (3)	40 (3)
Stomachache	3 (3)	18 (1)
Sleep disturbances	3 (3)	14 (1)
Cough	3 (3)	15 (1)
Self-rated health[a]		
Excellent	43 (41)	497 (41)
Good	56 (53)	680 (55)
Fair	5 (5)	48 (4)
Poor	2 (2)	2 (<1)

[a] The item self-rated health was assessed with the Health Behavior in School-Aged Children–Survey Instrument (eMethods in the Supplement). Self-rated health was not reported for 3 seropositive and 19 seronegative children.

Do Children Get "Long Haul" COVID?

- Melbourne, Australia
- 171 children diagnosed with COVID-19
  - March 2020 to March 2021
- 151 (88%) completed standard survey
- 12 children (8%) had persistent symptoms
  - All had been symptomatic with acute disease
  - Most common were cough (3-8 wks), fatigue (6-8 wks)
  - By March 2021- all back to baseline
- No controls

	Children (n=12)
Sex	..
Male	7 (58%)
Female	5 (42%)
Age, years	..
Mean	3·7 (3·5)
Median	2 (1–7)
Age group, years	..
0–2	8 (67%)
6–12 years	4 (33%)
13–18 years	0
Comorbidities	3 (25%)
Congenital cardiac disease	1 (8%)
Chronic respiratory condition	2 (17%)
Symptom duration, days	..
Mean	14·6 (12·8)
Median	11·5 (3·5–25·5)
Acute disease severity	..
Asymptomatic	0
Mild disease	11 (92%)
Moderate disease	0
Severe disease	1 (8%)
Admitted to hospital*	6 (50%)
For observation	2 (17%)
For fluid rehydration	1 (8%)
Received intensive care unit care*	3 (25%)
Post-acute COVID-19 symptoms	..
Post-viral cough	6 (50%)
Fatigue	3 (25%)
Both cough and fatigue	1 (8%)
Inflammatory conditions	2 (17%)

Data are n (%), mean (SD), or median (IQR). *All hospital admissions were for acute COVID-19 illness except for two children who were admitted to the intensive care unit due to post-acute inflammatory conditions.

Table: **Demographic and clinical characteristics of children with post-acute COVID-19 symptoms**

www.thelancet.com/child-adolescent Vol 5 June 2021

Post-acute COVID-19 outcomes in children with mild and asymptomatic disease

Published Online April 20, 2021 https://doi.org/10.1016/S2352-4642(21)00124-3

Do Children Get "Long Haul" COVID?

- German children 5-18 years
- August 2020 to March 2021
- Compared 73 children with COVID-19 to 45 without COVID-19 but some of whom had had other infections
- Pulmonary tests performed
  - Including multiple-breath washout, body plethysmography, and diffusion capacity testing
  - Average time for PFTs after COVID-19: 2.6 months
- No significant differences in frequency of abnormal PFTs of any test
- But, children with severe infection (COVID-19 or others) had reduced FVC compared to those with mild or no infection
  - *Mogensen Ida. Abstract OA4053. Presented at: European Respiratory Society International Congress; Sept. 5-8, 2021 (virtual meeting).*

Are Children More Likely to Get COVID-19 in School?

Morbidity and Mortality Weekly Report

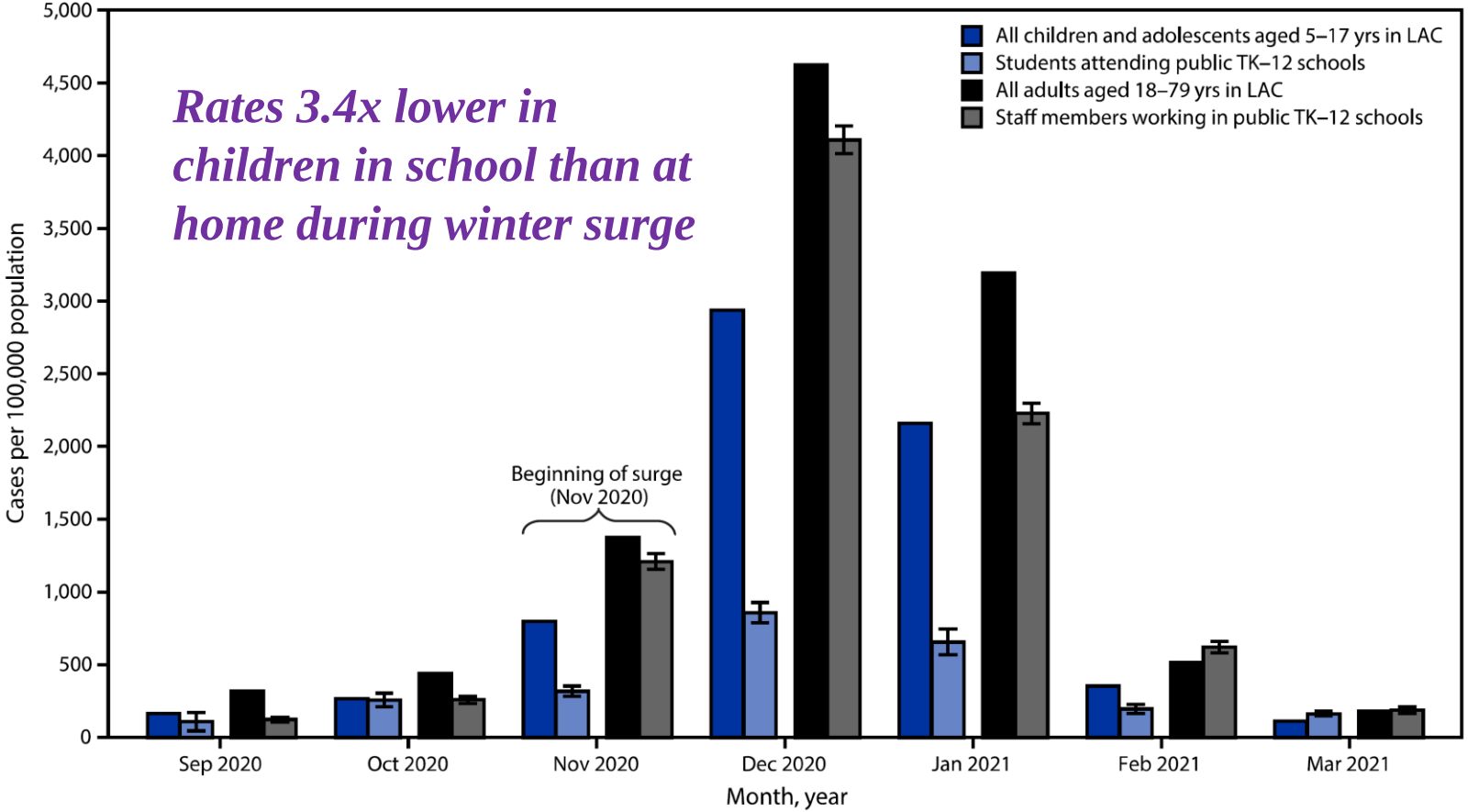
COVID-19 Case Rates in Transitional Kindergarten Through Grade 12 Schools and in the Community — Los Angeles County, California, September 2020–March 2021

Sherry Yin, MPH[1]; Kaitlin Barnes, MBA[2]; Rebecca Fisher, MPH[1]; Dawn Terashita, MD[1]; Andrea A. Kim, PhD[1]

MMWR / September 3, 2021 / Vol. 70 / No. 35 US Department of Health and Human Services/Centers for Disease Control and Prevention

- LA County is the nation's largest; 1.7M children 5-17 yo
- Study compares rates of TK-12 who attended school vs community
  - September 2020 to March 2021
  - 5-17 yo, and 18 and up
  - 463 students and 3927 staff had school-based infections
- Not adjusted for potential confounders

FIGURE. COVID-19 case rates* among children, adolescents, and adults† in transitional kindergarten through grade 12 schools and in the community, by month — Los Angeles County, California, September 2020–March 2021



Abbreviations: LAC = Los Angeles County; TK–12 = transitional kindergarten through grade 12.

* New cases per month per 100,000 persons; standard error bars shown for school case rates.

Do Children Get and Give COVID-19 in Households?

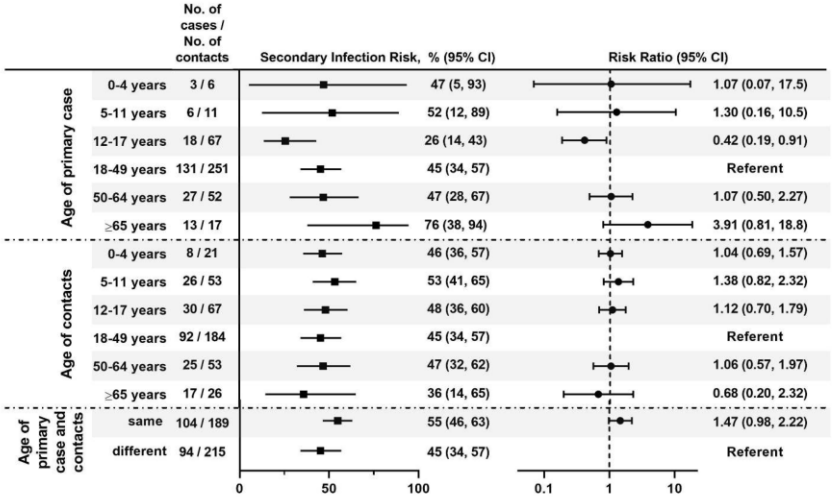
- Wisconsin and Tennessee: 577 households, unvaccinated
- 226 primary cases with 198 secondary cases among 404 HHCs
  - 49% secondary infection rate overall (all ages)
  - Range when divided into age groups: 36-53%- no differences by age
  - No difference in secondary infections when different v same age group
- No difference in asymptomatic infection by age group- 12 to 27%
- Both adults and children can transmit and are susceptible to SARS-CoV-2 household infections

Household Transmission and Clinical Features of SARS-CoV-2 Infections by Age in 2 US Communities

Huong Q. McLean, PhD, MPH,[a] Carlos G. Grijalva, MD, MPH,[b] Kayla E. Hanson, MPH,[a]

medRxiv preprint doi: https://doi.org/10.1101/2021.08.16.21262121; this version posted August 20, 2021.

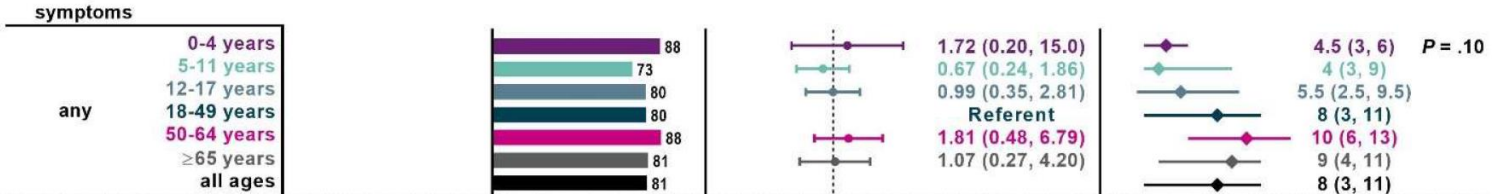
Figure 2. Estimated transmission risk from the primary case and infection risk among household contacts by age — Prospective study of SARS-CoV-2 household transmission, Tennessee and Wisconsin, April 2020–April 2021.



- **About ½ of contacts are infected**
- **No difference by age**

- **About 80% have symptoms**
- **No difference by age**

Figure 4. Reported symptoms, timing, and duration of symptoms by age group among persons with SARS-CoV-2 infection in a prospective study of SARS-CoV-2 household transmission — Tennessee and Wisconsin, April 2020–April 2021.



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What % of the US population has been infected?

Seroprevalence Estimate

20.6%

95% Confidence Interval: 20.2%-21.1%

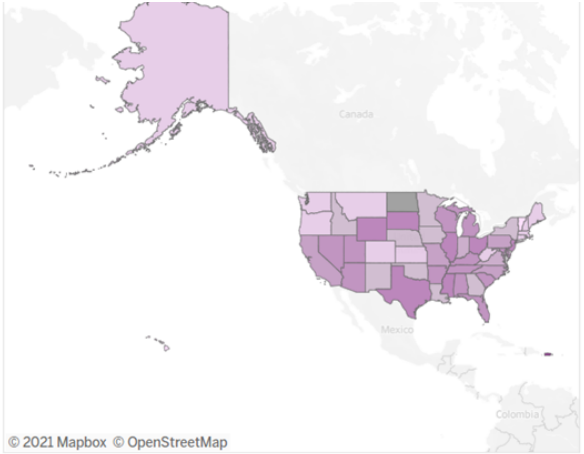
Number of Estimated Infections

66,518,000

95% Confidence Interval: 65,130,000-67,971,000

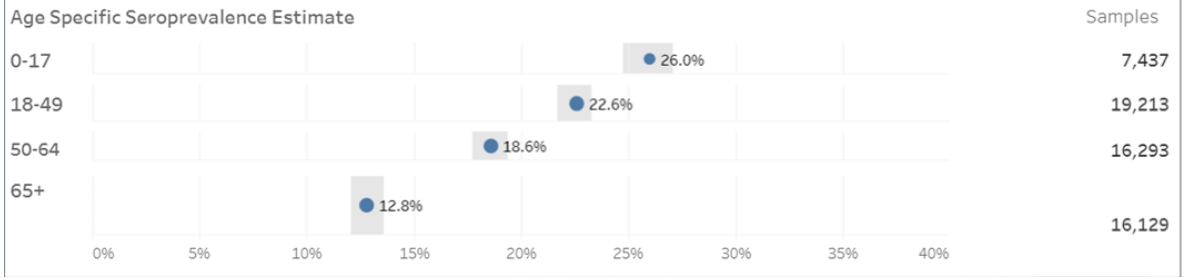
Antigen target:

Mix of Nucleocapsid and Spike (Mix of % infected and % infected or vaccinated)



Catchment Area: **50 States & DC**

Number of Samples Tested: **59,072**



- **About 20% of the US has been infected**
- **About a quarter of US children**

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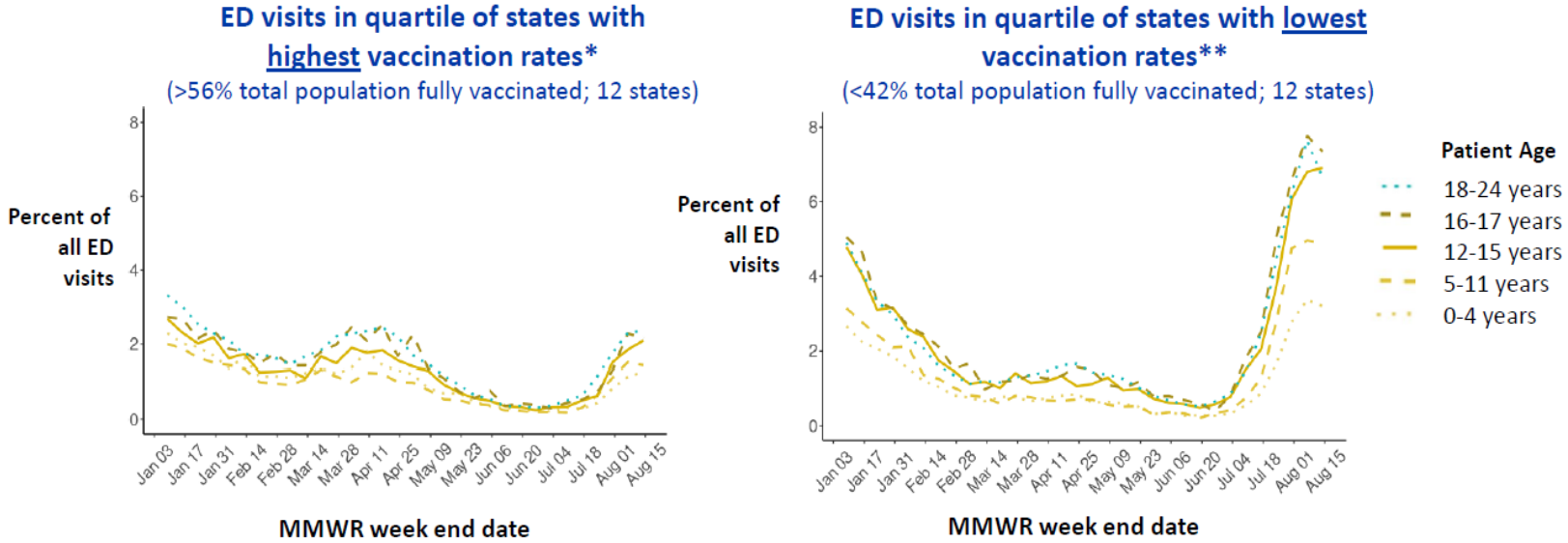
Do children benefit if adults/teens are vaccinated?

U.S. Emergency Department (ED) Visits for COVID-19 in Children and Young Adults, by State Vaccination Rate; Jan 9–Aug 14, 2021



Data Source: ED visits from the National Syndromic Surveillance Program (NSSP). Fewer than 50% of facilities in CA, HI, IA, MN, OK, and OH report to NSSP.

* Highest vaccination states: VT, MA, ME, CT, RI, MD, NJ, NH, WA, NM, NY, OR.

** Lowest vaccination states: AL, MS, WY, AR, LA, ID, GA, WV, TN, ND, OK, SC. Two states; WY and OK excluded because they did not have consistent data.

Newest on myo/pericarditis after SARS-CoV-2 vaccination? VAERS

- 2,574 reports of myopericarditis or pericarditis to VAERS (as of August 18, 2021)
  - 1,903 myopericarditis, 671 pericarditis
- Epidemiology of myopericarditis following COVID-19 vaccination similar to previously reported updates
  - Primarily in younger males, after dose 2 mRNA vaccination, symptom onset clustering within several days of vaccination,
- Limited follow-up information in VAERS case reports suggests most patients (77%) recovered from symptoms at time of report or follow-up
- Observed vs. Expected analysis with VAERS reports
  - Males: Observed > Expected in age groups through 49 years
  - Females: Observed > Expected in age groups through 29 years
- Enhanced surveillance for myocarditis outcomes after mRNA COVID-19 vaccination in VAERS case reports is ongoing

CDC ACIP Meeting Aug 30, 2021

Newest on myo/pericarditis after SARS-CoV-2 vaccination? VSD

Confirmed Myocarditis/Pericarditis, among 12–17-year-olds (Pfizer only) in the 0-7 and 0-21 Day Risk Interval by Dose

Compared with Outcome Events in Vaccinated Comparators on the Same Calendar Days

				Analysis			
Vaccine	Dose	Events in Risk Interval	Events in Comparison Interval[1]	Adjusted Rate Ratio[2]	95% Confidence Interval	2-Sided P-value	Excess Cases in Risk Period per 1 Million Doses
Days 0-21	**Both Doses**	**18**	**0**	**NE**	**3.07 - NE**	**<.001**	**20.9**
	Dose 1	3	0	NE	0.39 - NE	0.172	6.6
	Dose 2	**11**	**0**	**NE**	**4.22 – NE**	**<.001**	**37.0**
Days 0-7	**Both Doses**	**15**	**0**	**NE**	**8.19 – NE**	**<.001**	**16.7**
	Dose 1	1	0	NE	0.02 - NE	0.706	2.1
	Dose 2	**10**	**0**	**NE**	**13.53 - NE**	**<.001**	**33.7**

NE= not estimable
[1]**Comparison interval** is 22–42 days after either dose.
[2]**Adjusted** for VSD site, 5-year age group, sex, race/ethnicity, and calendar date.

CDC ACIP Meeting Aug 30, 2021

Is the Delta variant causing more severe disease in children?

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 70
September 3, 2021

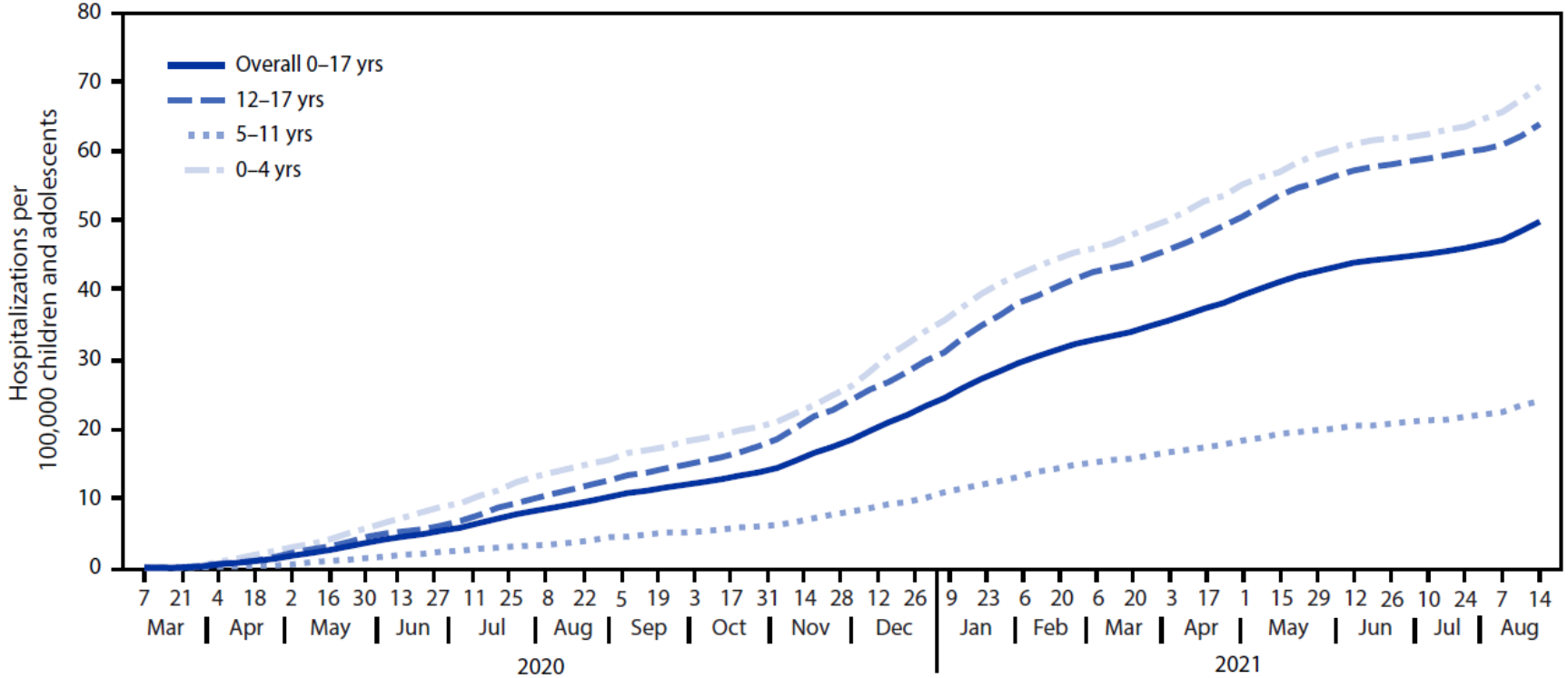
Hospitalizations Associated with COVID-19 Among Children and Adolescents — COVID-NET, 14 States, March 1, 2020–August 14, 2021

Miranda J. Delahoy, PhD[1,2]; Dawud Ujamaa, MS[1,3]; Michael Whitaker, MPH[1]; Alissa O'Halloran, MSPH[1]; Onika Anglin, MPH[1,3]; Erin Burns[1];

- Used COVID-NET: 99 counties in 14 states (Maryland is the only state with 100% of the population included!)
- In June and July, hospitalization rate among unvaccinated 12-17 yo was 10x higher than among vaccinated
  - 64 (94%) of 68 adolescents hospitalized in Delta era were unvaccinated
- Severity indicators same pre-Delta and during-Delta

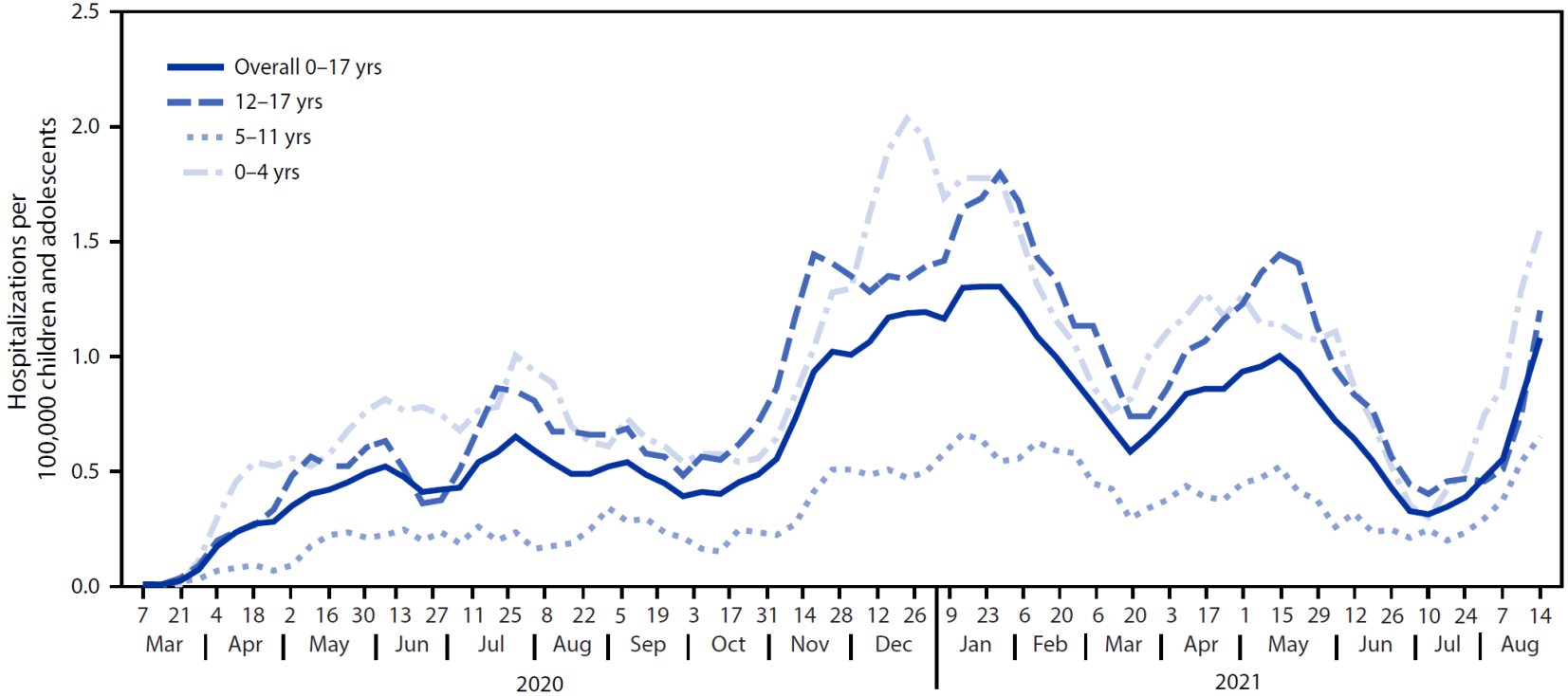
Is the Delta variant causing more severe disease in children?

FIGURE 1. COVID-19–associated cumulative hospitalizations per 100,000 children and adolescents,* by age group — COVID-NET, 14 states,† March 1, 2020–August 14, 2021



Is the Delta variant causing more severe disease in children?

FIGURE 2. COVID-19–associated weekly hospitalizations per 100,000 children and adolescents,* by age group — COVID-NET, 14 states,† March 1, 2020–August 14, 2021 (3-week smoothed running averages)§



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Is the Delta variant causing more severe disease in children?

TABLE. Clinical interventions and outcomes among children and adolescents aged 0-17 years during COVID-19–associated hospitalizations — COVID-NET, 14 states,* March 1, 2020–June 19, 2021 and June 20–July 31, 2021

Interventions and outcomes	Children and adolescents hospitalized, No. (%) March 1, 2020–June 19, 2021 (N = 3,116)†	June 20–July 31, 2021 (N = 164)†	p-value§
Hospital length of stay, median (interquartile range)	3 (2–5)	2 (1–4)	0.01
Outcome			
Died during hospitalization	21 (0.7)	3 (1.8)	0.12
ICU admission	827 (26.5)	38 (23.2)	0.34
Vasopressor support	233 (7.5)	13 (7.9)	0.83
Highest level of respiratory support¶			
High flow nasal cannula	162 (5.2)	13 (7.9)	0.13
BiPAP/CPAP	131 (4.2)	6 (3.7)	0.73
Invasive mechanical ventilation	190 (6.1)	16 (9.8)	0.06

So far, Delta is causing more cases and hospitalizations, but those hospitalized do not have more severe disease

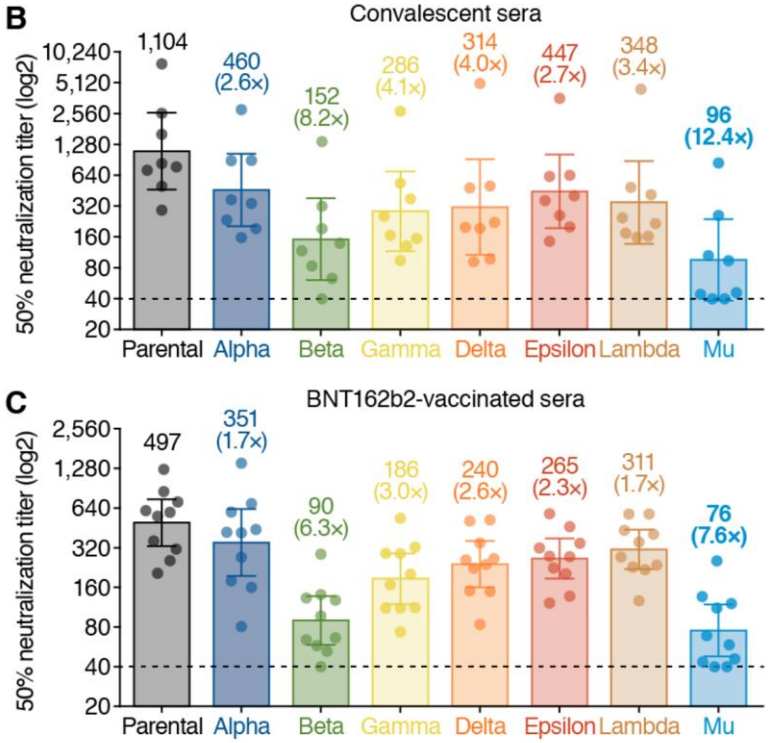
- LOS: 2-3 days
- Died: ~1%
- ICU: ~25%
- Pressors: ~8%
- Ventilated: ~8%

What do we know about the mu variant?

- aka B.1.621.1
- A variant of interest per WHO
- Follows alpha (UK), beta (So Afr), gamma (Brazil), and delta (India)
- First seen in Colombia in January 2021, now 100% of Colombia strains
- 2500 (0.2%) US cases, incl MD
- Reduced neutralizing antibodies

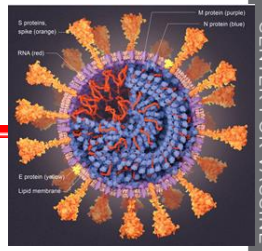
Ineffective neutralization of the SARS-CoV-2 Mu variant by convalescent and vaccine sera

Keiya Uriu[1#], Izumi Kimura[1#], Kotaro Shirakawa[2], Akifumi Takaori-Kondo[2], Taka-aki



bioRxiv preprint doi: https://doi.org/10.1101/2021.09.06.459005; this version posted September 7, 2021.

Take Home Points



- When will we have COVID-19 vaccines for children under 12y? November
- Does vaccination prevent hospitalization? Definitely!
- Do children get long haul COVID-19? Yes, but very infrequently and not forever.
- Are children more likely to get COVID-19 in school? No, risk is higher at home
- Do children get and give COVID-19 in households? Yes, similar to adults.
- What % of the US population has been infected? Estimate is 20 to 25%
- Do children benefit if adults and teen are vaccinated? Yes, fewer ED visits.
- Is myocarditis after COVID-19 vaccine real? Yes, but rare & typically mild/transient
- Is Delta causing more severe disease? No, just more disease overall
- Is Mu even worse? Not likely, but we have our eye on it

Thank You

UNIVERSITY of MARYLAND
SCHOOL OF MEDICINE
CENTER FOR VACCINE DEVELOPMENT
AND GLOBAL HEALTH