

COVID-19 Vaccine for Children Ages 5-11: The Science

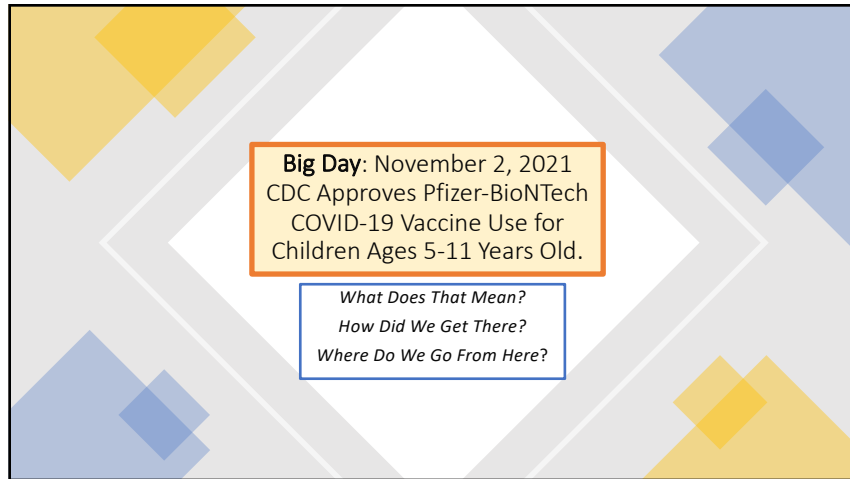
Mary Beth Miotto, MD, MPH, FAAP
November 18, 2021

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Disclosure of Financial Interest

- Dr. Mary Beth Miotto has no financial interests/arrangements/affiliations with any organizations that could be construed as a real or perceived conflict of interest related to the content of this presentation


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Big Day: November 2, 2021
 CDC Approves Pfizer-BioNTech
 COVID-19 Vaccine Use for
 Children Ages 5-11 Years Old.

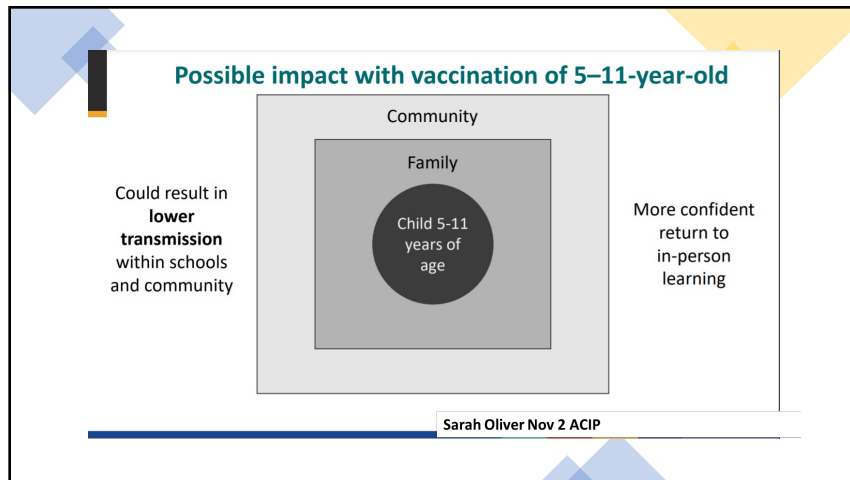
What Does That Mean?
How Did We Get There?
Where Do We Go From Here?

3



Why were vaccine trials
 in elementary age
 children important?

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Kansas records 6th COVID-related child death, uptick in school-based clusters

By Melissa Brunner
Published: Nov. 17, 2021 at 4:34 PM EST |
Updated: 22 hours ago

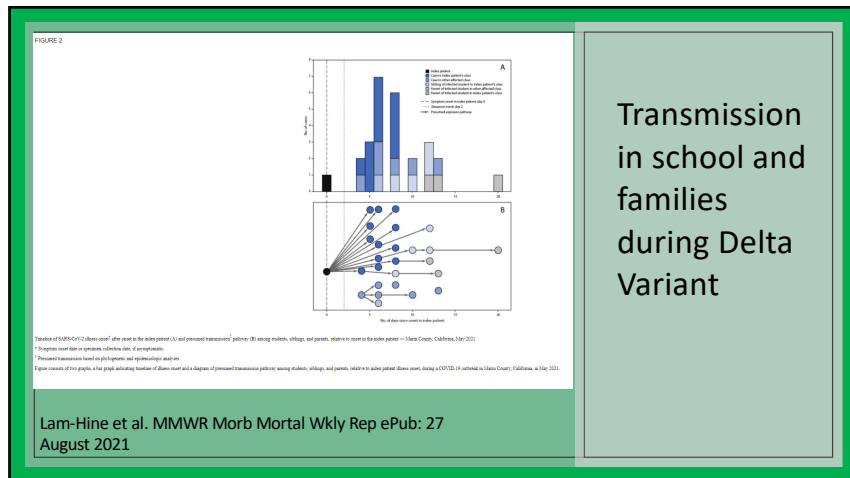
TOPEKA, Kan. (WIBW) - The state of Kansas has recorded a sixth child death related to COVID, as well as an uptick in school-based COVID clusters.

3,096 new cases since Monday. According to KDHE's online dashboard, the state has seen increased case numbers the past two weeks. However, adult COVID-related hospital admissions continue trending down.

KDHE also shows a new death in the zero-to-nine year old age group. An agency spokesperson says the death was added to the dashboard Friday. He says the child passed away earlier this month, but declined to provide any additional information on the case, including the child's exact age or county of residence.

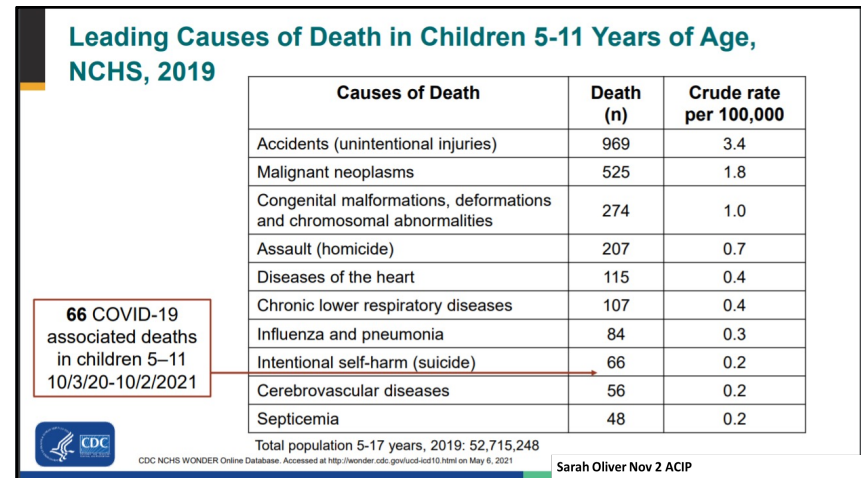
As for clusters, KDHE reports 152 active clusters this week, up from 143 last week. Among the clusters are 54 in K-thru-12 schools, encompassing 694 cases. The number is up from 45 K-thru-12 clusters a week ago.

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Transmission
in school and
families
during Delta
Variant

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Children Aged 5–11 Years Hospitalized with COVID-19— COVID-NET, March 2020–August 2021

- 68% were Black, non-Hispanic or Hispanic
- 32% had no underlying conditions
- Most common underlying medical conditions were chronic lung disease (primarily asthma) and obesity

Demographic and clinical characteristics

	N	(%)
Total	562	(100)
Age (yrs) – median (IQR)*	8	(6–10)
Sex – Male	320	(57)
Race/ethnicity		
Black, non-Hispanic	207	(37)
Hispanic	177	(31)
White, non-Hispanic	124	(22)
Asian, non-Hispanic	23	(4)
Other, non-Hispanic	31	(6)
Severe disease†	200	(36)
≥1 underlying condition	381	(68)



*Interquartile range; †Requiring intensive care unit admission or mechanical ventilation
COVID-NET is a population-based surveillance system that collects data on laboratory-confirmed COVID-19-associated hospitalizations among children and adults through a network of over 250 acute-care hospitals in 14 states. Methods described in: Woodruff RC, et al. Risk factors for Severe COVID-19 in Children. *Pediatrics*. ePub October 2021.

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Clinical Interventions and Outcomes of Children Aged 5-11 Years with COVID-19 or Influenza-Associated Hospitalizations, COVID-NET¹ and FluSurv-NET²

	FluSurv-NET 2017-2018, 2018-2019, and 2019-2020 (N = 1,874), ³ n (%)	COVID-NET March 1, 2020–August 31, 2021 (N = 696), ⁴ n (%)
Hospital length of stay (median, IQR)	2 (1–4)	3 (2–6)
ICU admission	398 (21.2)	222 (31.9)
Invasive mechanical ventilation	87 (4.6)	50 (7.2)
Died during hospitalization	11 (0.6)	4 (0.6)



1 COVID-NET: California, Colorado, Connecticut, Georgia, Iowa, Maryland (entire state), Michigan, Minnesota, New Mexico, New York, Ohio, Oregon, Tennessee, and Utah.
2 FluSurv-NET: California, Colorado, Connecticut, Georgia, Maryland (Baltimore Metropolitan Area), Michigan, Minnesota, New Mexico, New York, Ohio, Oregon, Tennessee, and Utah. Surveillance conducted from October 1–April 30 each season.
3 Includes those with complete clinical data (~97% of pediatric cases) on hospital length of stay, ICU admission, invasive mechanical ventilation, and disposition discharge (i.e., discharged alive or died in-hospital).
4 Includes those with complete clinical data (~90% of pediatric cases) on hospital length of stay, ICU admission, invasive mechanical ventilation, and disposition discharge (i.e., discharged alive or died in-hospital).

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Multisystem Inflammatory Syndrome in Children (MIS-C)

- Severe hyperinflammatory syndrome occurring 2-6 weeks after acute SARS-CoV-2 infection, resulting in a wide range of clinical manifestations and complications
- Incidence has been estimated as 1 MIS-C case in approximately 3,200 SARS-CoV-2 infections
- 60-70% of patients are admitted to intensive care, 1-2% die

• Bowen, et al. Demographic and Clinical Factors Associated With Death Among Persons <21 Years Old With Multisystem Inflammatory Syndrome in Children—United States, February 2020–March 2021. *Open Forum Infectious Diseases*. Volume 8, Issue 8, August 2021. <https://doi.org/10.1093/ofid/ofab388>

• Payne AB, et al. Incidence of Multisystem Inflammatory Syndrome in Children Among US Persons Infected With SARS-CoV-2. *JAMA Netw Open*. 2021;4(6):e2116420. Published 2021 Jun 1. doi:10.1001/jamanetworkopen.2021.16420

• Feldstein LR, et al. Characteristics and Outcomes of US Children and Adolescents With Multisystem Inflammatory Syndrome in Children (MIS-C) Compared With Severe Acute COVID-19. *JAMA*. 2021;325(11):1074-1087. doi:10.1001/jama.2021.2091

• Belay ED, et al. Trends in Geographic and Temporal Distribution of US Children With Multisystem Inflammatory Syndrome During the COVID-19 Pandemic [published online ahead of print. 2021 Apr 6]. *JAMA Pediatr*. 2021;e2119530. doi:10.1001/jamapediatrics.2021.0530

• <https://covid.cdc.gov/covid-data-tracker/#mis-national-surveillance>

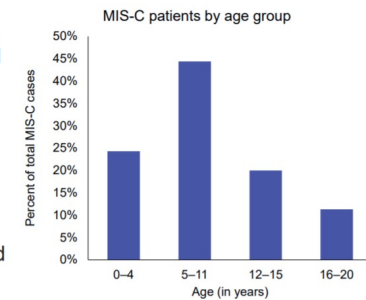


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MIS-C in Children

- 5,217 MIS-C cases reported to national surveillance with date of onset between February 19, 2020–September 23, 2021
 - Median age of 9 years
 - 2,316 (44%) of these cases occurred in children aged 5–11 years
- 61% occurred in children who are Hispanic/Latino or Black, Non-Hispanic
- Among children aged 5–11 years, 9 died (20% of MIS-C deaths)



Bowen, et al. Demographic and Clinical Factors Associated With Death Among Persons <21 Years Old With Multisystem Inflammatory Syndrome in Children—United States, February 2020–March 2021. *Open Forum Infectious Diseases*. Volume 8, Issue 8, August 2021. <https://doi.org/10.1093/ofid/ofab388>

<https://covid.cdc.gov/covid-data-tracker/#mis-national-surveillance>

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Additional Post-COVID Conditions in Children

- **Post-COVID conditions occur in children**
 - Appear to be less common in children than in adults
 - A national survey in the UK found 7-8% of children with COVID-19 reported continued symptoms >12 weeks after diagnosis¹
 - May appear after mild or severe infections, or after MIS-C
- **Most common symptoms:** Similar to adults, and include fatigue, headache, insomnia, trouble concentrating, muscle and joint pain, and cough^{2,3}
- **Impact on quality of life:** Limitations of physical activity, feeling distressed about symptoms, mental health challenges, decreased school attendance/participation²



¹Office for National Statistics United Kingdom. (2021) Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK. Retrieved on September 17, 2021 from Office for National Statistics' website. <https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/prevalenceofongoingsymptomsfollowingcoronaviruscovid19infectionintheuk/1sept2021>

²Buonsenso D, Murdoli D, De Rose C, et al. Preliminary evidence on long COVID in children. *Acta Paediatr*. 2021;110(7):2208-2211. doi:10.1111/apa.15870

³Molteni E, Sudre CH, Canas LS, et al. Illness duration and symptom profile in symptomatic UK school-aged children tested for SARS-CoV-2. *Lancet Child Adolesc Health*. 2021;5:708-18. [https://www.thelancet.com/action/showPdf?pii=S2352-4642\(21\)0001180-X](https://www.thelancet.com/action/showPdf?pii=S2352-4642(21)0001180-X)

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Summary: COVID-19 Epidemiology in Children Aged 5–11 years

- **Children aged 5–11 years are at least as likely to be infected with SARS-CoV-2 as adults**
 - Over 1.9 million reported cases; seroprevalence estimated to be ~38% in September 2021
 - Seroprevalence data suggests that infections in children less likely to be reported as cases than infections in adults
- **Children aged 5–11 years are at risk of severe illness from COVID-19**
 - >8,300 hospitalizations to date
 - Hospitalization rates are 3x times higher for non-Hispanic Black, non-Hispanic American Indian/Alaska Native, and Hispanic children compared with non-Hispanic White children
 - Hospitalization rates are similar to pre-pandemic influenza-associated hospitalization rates
 - Severity was comparable among children hospitalized with influenza and COVID-19
 - Approximately 1/3 of hospitalized children aged 5–11 years require ICU admission
 - At least 94 COVID-19-associated deaths occurred in children aged 5–11 years
 - MIS-C was most frequent among children aged 5–11 years
 - Post-COVID conditions have been reported in children
 - All might have been more numerous had pandemic mitigation measures not been implemented
- **Secondary transmission from young school-aged children occurs in household and school settings**



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The Journey of Your Child's Vaccine

How a new vaccine is developed, approved and manufactured

PHASE 1
Healthy volunteers
Safety and efficacy
Preliminary efficacy

PHASE 2
Healthy volunteers
Safety and efficacy
Preliminary efficacy

PHASE 3
Healthy volunteers
Safety and efficacy
Preliminary efficacy

FDA reviews the vaccine only if:

- The vaccine is safe
- The vaccine is effective
- The vaccine is of high quality

How a vaccine is added to the U.S. Recommended Immunization Schedule

The Advisory Committee on Immunization Practices (ACIP) is a group of experts who advise the U.S. Department of Health and Human Services (HHS) on the safety and effectiveness of vaccines. The group also advises on the timing and frequency of vaccine administration. The group's recommendations are based on the best available scientific evidence. The group's recommendations are then adopted by the HHS Secretary and the U.S. Department of Health and Human Services.

When making recommendations, ACIP considers:

- The safety and effectiveness of the vaccine
- The number of people who get the disease if there is no vaccine
- How well a vaccine works for people of different ages
- How practical the recommendations are to put into practice

After being added to the U.S. Recommended Immunization Schedule, health care providers are notified by the vaccine manufacturer.

Who makes these decisions?

- FDA: Vaccines and Related Biological Products Advisory Committee (VRBPAC)
- CDC: Advisory Committee on Immunization Practices (ACIP)

https://www.cdc.gov/vaccines/parents/infographics/journey-of-child-vaccine.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fparents%2Finfographics%2Fjourney-of-child-vaccine-text.html

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FDA Approval versus ACIP Recommendations

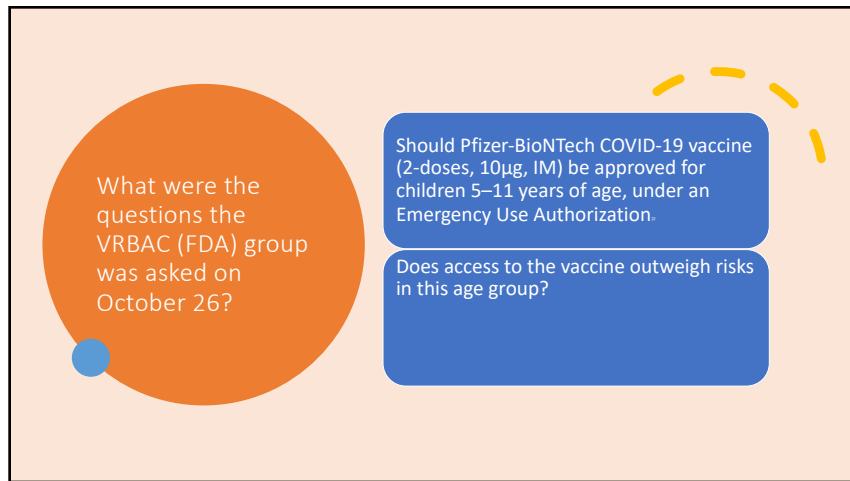
FDA:

- How the vaccine works
- What was the process
- What were the findings at every step of development and testing?
- Efficacy data
- Safety data
- For Whom is the vaccine appropriate to approve?
- "The VRBPAC recommendation is based on the totality of scientific evidence available"

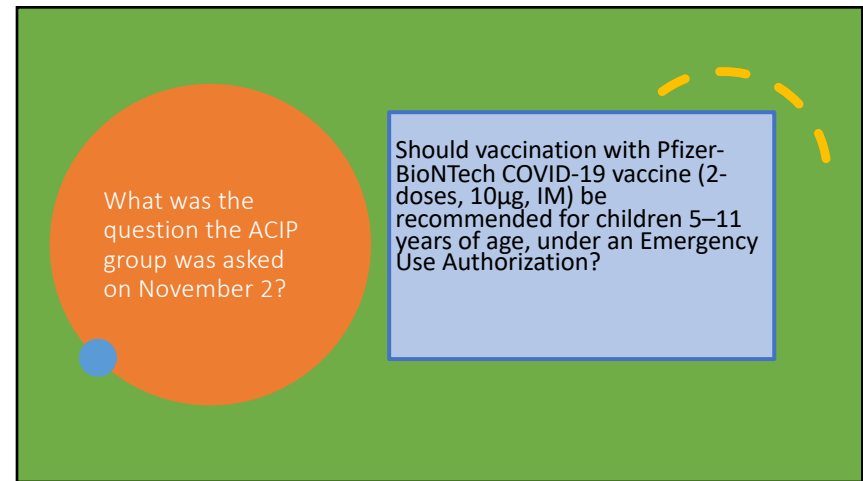
ACIP:

- The safety and effectiveness of the vaccine when given at specific ages. Only vaccines licensed or authorized by FDA are recommended.
- The severity of the disease..
- The number of people who get the disease if there is no vaccine.
- How well a vaccine works for people of different ages.
- How practical the recommendations are to put into practice.

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Evidence to Recommendations (EtR) Framework

EtR Domain	Question(s)
Public Health Problem	<ul style="list-style-type: none"> Is the problem of public health importance?
Benefits and Harms	<ul style="list-style-type: none"> How substantial are the desirable anticipated effects? How substantial are the undesirable anticipated effects? Do the desirable effects outweigh the undesirable effects?
Values	<ul style="list-style-type: none"> Does the target population feel the desirable effects are large relative to the undesirable effects? Is there important variability in how patients value the outcome?
Acceptability	<ul style="list-style-type: none"> Is the intervention acceptable to key stakeholders?
Feasibility	<ul style="list-style-type: none"> Is the intervention feasible to implement?
Resource Use	<ul style="list-style-type: none"> Is the intervention a reasonable and efficient allocation of resources?
Equity	<ul style="list-style-type: none"> What would be the impact of the intervention on health equity?

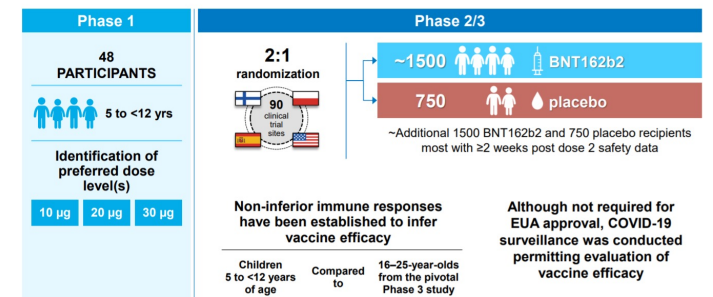
"The intervention" = Pfizer-BioNTech COVID-19 vaccine, given to children aged 5–11 years

"The problem" = COVID-19 among children aged 5–11 years

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Pfizer-BioNTech Pediatric COVID-19 Vaccine BNT162b2: Study Overview: 5 to <12 Years

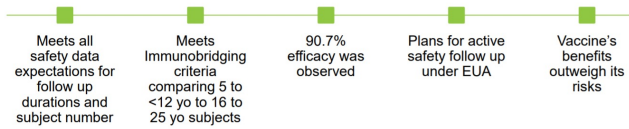


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BNT162b2 – Meets EUA Guidance for 5 to <12 Years of Age

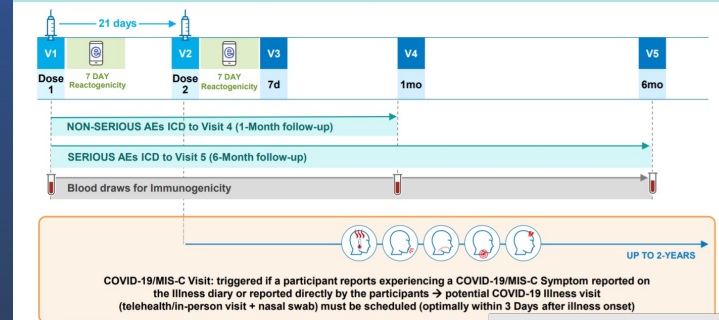
Clear and Compelling Data



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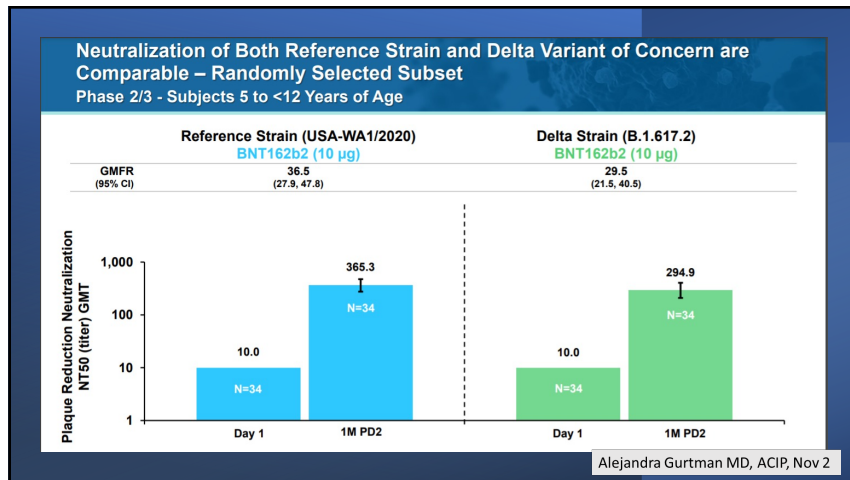
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Phase 2/3 Timelines of Participants 5 to <12 Years of Age Through 6 Months Post-dose 2

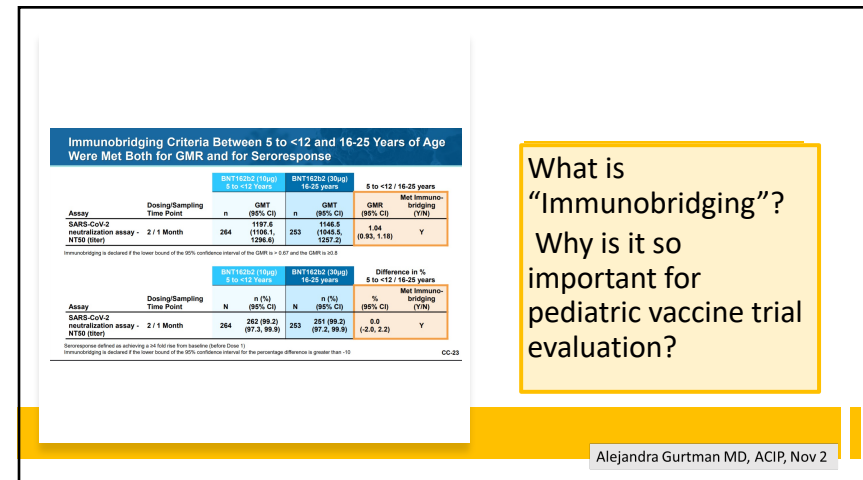


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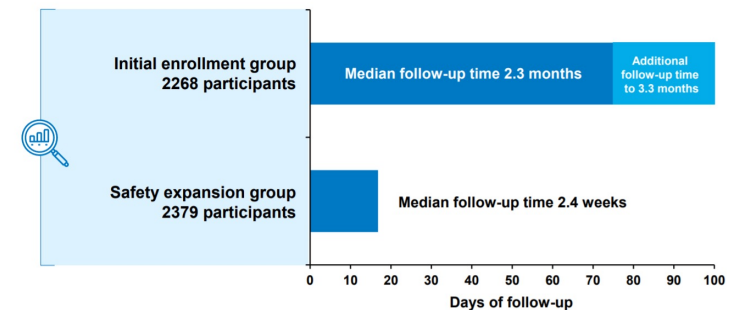
Immunogenicity and Efficacy Conclusions

- Immunobridging success criteria were met for 5 to <12 year olds at 10 µg dose level
- BNT162b2-immune sera effectively neutralized both USA-WA1/2020 (reference strain) and the highly transmissible B.1.617.2 (Delta) variant of concern
- BNT162b2 as a two dose series is highly protective against COVID-19 in 5 to <12 year olds when Delta variant was prominent

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Safety Data for 5 to <12 Year Olds to Support EUA Application



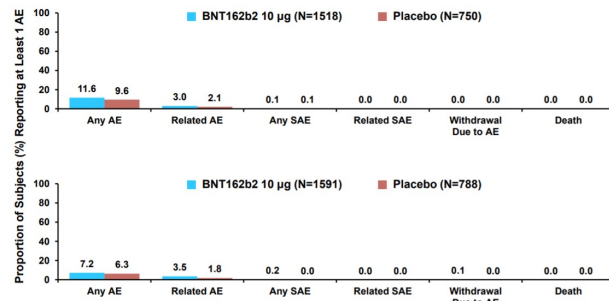
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Overall Adverse Events from Dose 1 to Data Cutoff Date: 5 to <12 Year Olds

Initial enrollment group:
Median follow-up time 2.3 months
Cutoff date
September 6, 2021

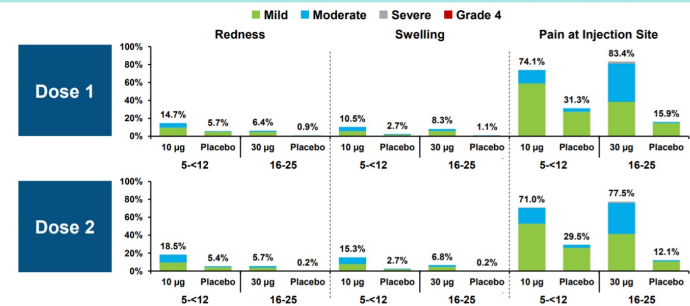
Safety expansion group:
Median follow-up time 2.4 weeks
Cutoff date
October 8, 2021



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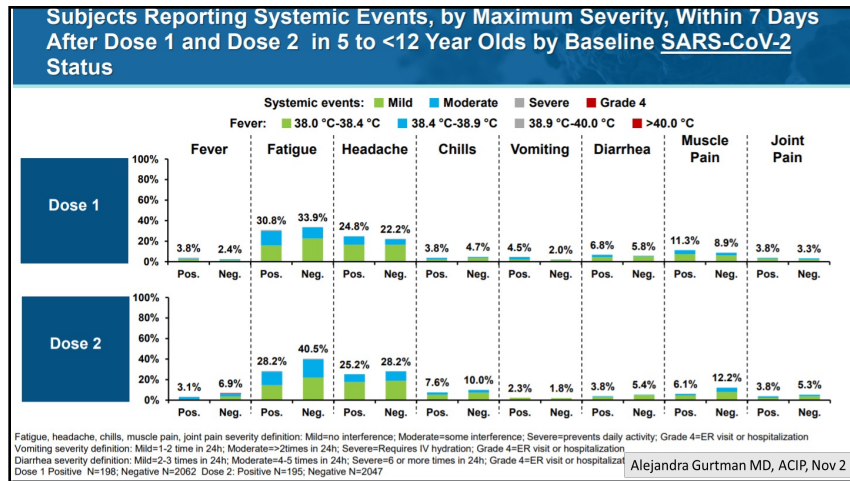
Local Reactions, by Maximum Severity, Within 7 Days After Each Dose in 5 to <12 and 16-25 Year Olds



Redness and swelling severity definition: Mild= >2.5cm, Moderate= >5-10 cm; Severe= >10 cm; Grade 4= necrosis
Pain at injection site severity definition: Mild=no interference, Moderate=some interference, Severe=prevents daily activity, Grade 4=ER visit or hospital
Dose 1: 5-12yrs N=2280, 16-25 yrs N=1064 Dose 2: 5-12 yrs N=2242 16-25 yrs N=884

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Safety Conclusions for 5 to <12 Year Olds

- Reactogenicity was mostly mild to moderate, and short lived
- Observed mild to moderate local reactions (redness, swelling) captured by diary were more common and systemic reactions (including fever) less common than those in 16-25 year olds
- The observed AE profile in this study did not suggest any safety concerns for BNT162b2 vaccination in children 5 to <12 years of age

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Plans for post-authorization monitoring of COVID-19 vaccine effectiveness among children 5-11 years of age

Platform name	Platform details	Outcomes studied					
		Immunogenicity	Household transmission	Infection	Outpatient	Emergency department/urgent care	Hospitalization MIS-C
PROTECT	Weekly swabbing of 2,000 kids	✓		✓			
CASCADIA	Weekly swabbing of 715 kids			✓			
PACC	Weekly swabbing of 400 kids	✓					
RVTN	Case-ascertained transmission study of 1,500 households		✓	✓			
ICATT	National pharmacy testing data			✓			
VISION*	Electronic health records at 458 pediatric hospitals, ED/UCs				✓	✓	✓
Overcoming COVID	30-40 pediatric hospitals						✓

First VE estimates may occur as early as 60-90 days after authorization; timelines will depend on vaccine coverage and background rates of disease

PROTECT = Pediatric Research Observing Trends and Exposures in COVID-19 Timelines; PACC = Prospective Assessment of COVID-19 in the Community; RVTN = Respiratory Virus Transmission Network; UCSF = University of California, San Francisco; ICATT = Increasing Community Access To Testing partnership
* A cohort design is currently being assembled in a subset of VISION sites.

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v-safeSM
after vaccination
health checker



<https://vsafe.cdc.gov/>

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Evidence to Recommendations Framework

Summary: Work Group Interpretations

Balance of consequences	Undesirable consequences <i>clearly outweigh</i> desirable consequences in most settings	Undesirable consequences <i>probably outweigh</i> desirable consequences in most settings	The balance between desirable and undesirable consequences is <i>closely balanced</i> or <i>uncertain</i>	Desirable consequences <i>probably outweigh</i> undesirable consequences in most settings	Desirable consequences <i>clearly outweigh</i> undesirable consequences in most settings	There is insufficient evidence to determine the balance of consequences
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Summary

Since beginning of the COVID-19 pandemic, among U.S. children 5-11 years of age, there have been

1.9 million cases

8,300 hospitalizations

2,316 MIS-C cases

94 deaths

COVID-19 is now
vaccine preventable

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Tip #1

Dosages are determined by age, **not** a child's size or weight. Some children may be 11 years old when they get their first dose and 12 at the time of their second dose. They should receive a dose based on their age on the day of vaccination, according to the CDC.



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Tip #2

The COVID-19 vaccine can be given at the same times as other routine vaccines but should be done in a different injection site.



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Tip #3

The CDC and AAP also recommend children with prior COVID-19 infection get vaccinated.

This includes children who have a history of multisystem inflammatory syndrome in children (MIS-C) if they have clinically recovered, if 90 days have passed since their diagnosis and they are in an area of high or substantial community transmission or otherwise have increased risk for exposure to the virus.

Even if they don't meet all the criteria post-MIS-C, the CDC said vaccination may be considered.



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Tip 4: Who should NOT get an mRNA vaccine?

Individuals who had an anaphylactic reaction to the first dose of mRNA COVID vaccine

Individuals with a prior anaphylactic or other immediate allergic reaction to components of the mRNA COVID vaccine (Polysorbate)

Are currently ill with COVID infection (finish isolation first)

Are currently ill with another moderate to severe acute illness

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Tip #5

Get your children VACCINATED as soon as possible.

2.6 million children under age 12 have received the vaccine in the US so far.

As of November 18, 2021, around 443 million COVID-19 vaccine doses had been administered in the United States to all ages.

Every step in the vaccine development and testing process was followed and completed.

Children are still getting infected....but not vaccinated children.



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- From the World Health Organization: https://www.who.int/news-room/feature-stories/detail/how-are-vaccines-developed?acid=C0KCGiAhMOM8hDhARisAPVml-GFpH0hUhzlvu7RV8bxiXEOaQUoiAdHez-lmz966e68GQNNsonp7DaaAID7EALw_wc8
- AHA Greater Impact Toolkit: <https://www.aha.org/joining-hands-greater-impact>
- <https://publications.gap.org/gapnews/news/15461/Answers-to-lingering-questions-about-vaccinating-5>
- <https://healthychildren.org/English/health-issues/conditions/COVID-19/Pages/The-Science-Behind-the-COVID-19-Vaccine-Parent-FAQs.aspx>
- https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/children-teens.html?CDC_AA_relvale=https%3A%2F%2Fwww.cdc.gov%2Fncov%2Fvaccines%2Frecommendations%2Fadolescents.html
- What are the Long-Term Side Effects of the COVID Vaccine? <https://www.youtube.com/watch?v=F1YRdE91x5Q>
- <https://www.chop.edu/health-resources/supporting-your-school-age-child-during-and-after-covid-19-vaccination>

More resources on vaccine science, vaccine trials, and the vaccine approval process for kids

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Acknowledgements

I offer thanks to the CDC and specifically to Jefferson Jones, Sarah Oliver and Alejandra Gurtman who presented the evidence surrounding COVID in children at the ACIP meeting of November 2, 2021.

<https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-11-2-3/03-COVID-Jefferson-508.pdf>

I'm grateful to the American Academy of Pediatrics for its advocacy and strong science communication on COVID in children.

Finally, I appreciate the collaboration of NEUSHA Directors Jenny Gormley and Kathy Hassey, who have been helping to build bridges between pediatricians and school nurses since before the pandemic. We are powerful partners!