Vaccines and Related Biological Products Advisory Committee Meeting

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mRNA-1273 (Moderna COVID-19 Vaccine) – Request for Emergency Use Authorization in Individuals 6 - 17 Years of Age

ModernaTX, Inc.

Vaccines and Related Biological Products Advisory Committee

June 14, 2022

Introduction

Carla Vinals, PhD
Vice President
Regulatory Affairs Strategy, Infectious Diseases
ModernaTX, Inc.

Approvals, Authorizations and Doses of Moderna COVID-19 Vaccine Administered in Adults

- US BLA approved January 2022 for 100 µg 2-dose primary series
- US EUAs
  - 3rd dose primary series (100 µg) for immunocompromised
  - 1st booster (50 µg) for adults ≥ 18
  - 2nd booster (50 µg) for adults ≥ 50
- Worldwide approvals / authorizations for adults ≥ 18
  - Primary series in 86 countries
  - Booster dose in 48 countries

Adults ≥ 18 Years

>633 Million
Doses administered worldwide

>220 Million
Fully vaccinated worldwide

>120 Million
Received booster worldwide

*Estimated data as of April 15, 2022**

**Data based on estimates from Moderna Bi-Monthly Summary Safety Reports*

Approvals, Authorizations and Use of Moderna COVID-19 Vaccine for Children and Adolescents 6-17 Years

- Worldwide approvals / authorizations
  - Adolescents 12-17 in 42 countries (100 µg 2-dose primary series)
  - Children 6-11 in 40 countries (50 µg 2-dose primary series)

Adolescents 12-17 Years

>6.4 Million

Fully vaccinated worldwide

Children 6-11 Years

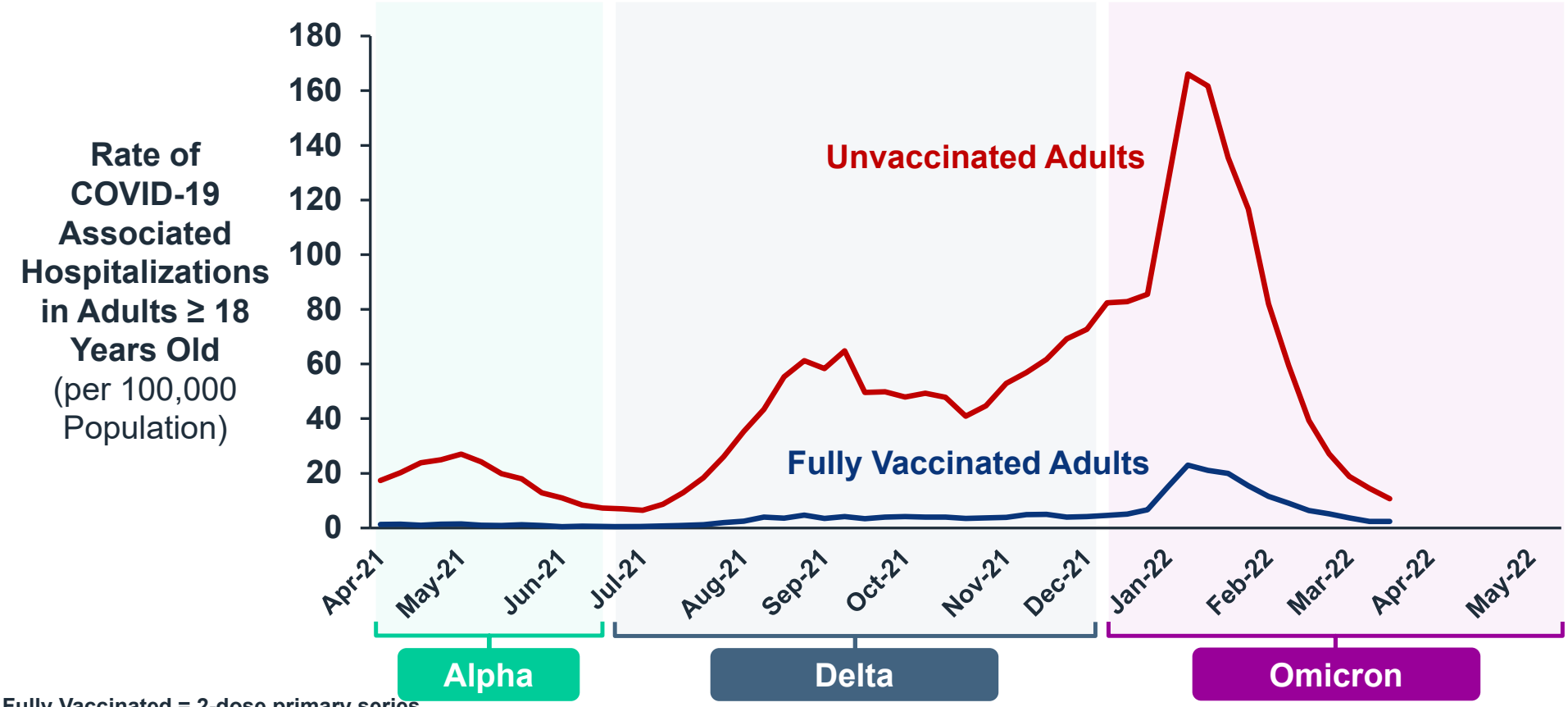
>300,000

Fully vaccinated worldwide

*Estimated data as of April 15, 2022**

***Data based on estimates from Moderna Bi-Monthly Summary Safety Reports**

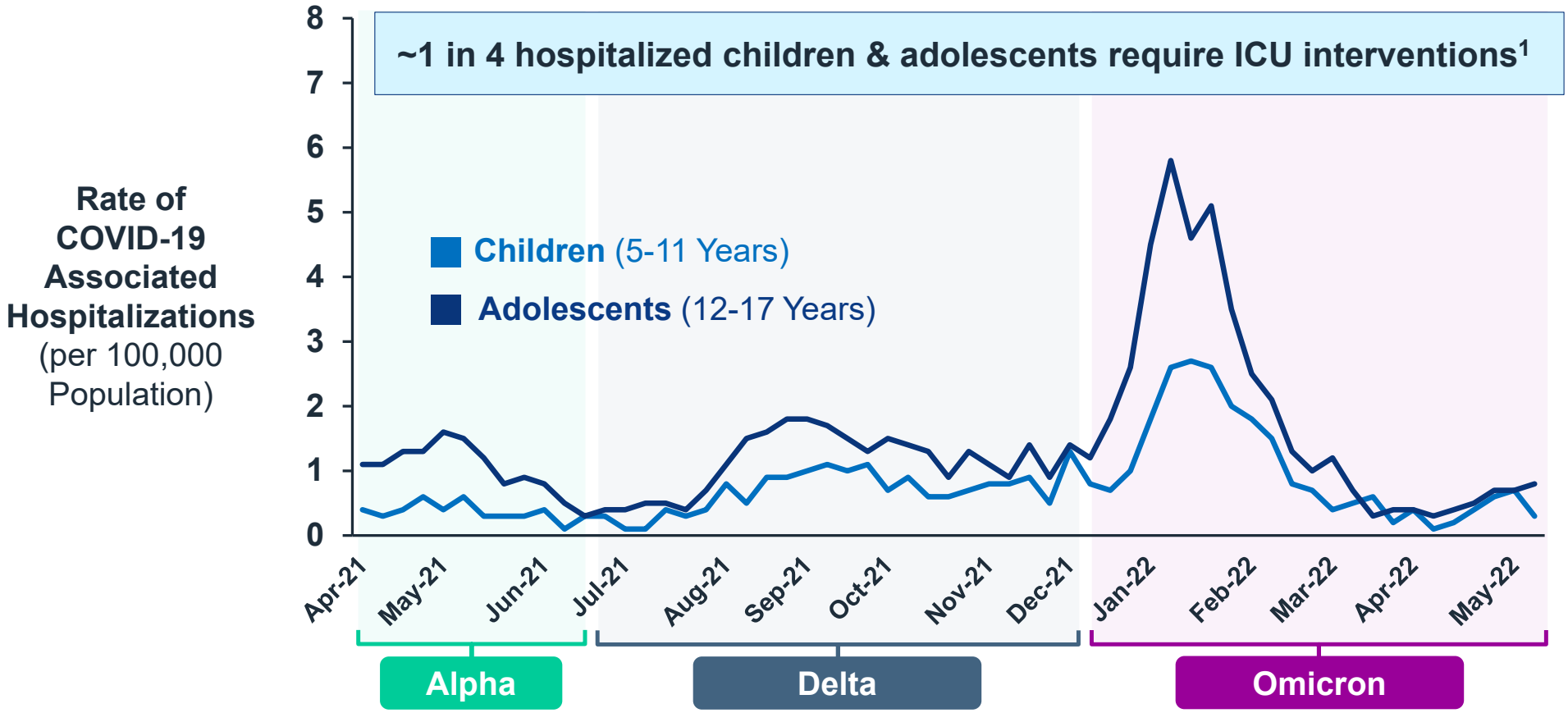
COVID-19 Vaccines Offer Protection Against Severe Disease and Reduce Hospitalizations in Adults ≥ 18



Fully Vaccinated = 2-dose primary series
Data as of May 14, 2022 - https://covid.cdc.gov/covid-data-tracker/#covidnet-hospitalizations-vaccination

Emergence of Highly Transmissible Variants of Concern Increases COVID-19 Hospitalizations

Children and Adolescents, 6-17 Years



Data as of May 14, 2022 - https://gis.cdc.gov/grasp/covidnet/covid19_3.html

1. Delahoy, et al., Clin Infect Dis 20212; 73:336-340. doi: 10.1093/cid/ciac388/6589788

EUA Request for Moderna COVID-19 Vaccine in Children and Adolescents (6 - 17 Years)

Adolescents
12-17 Years

Primary Series
100 µg, 2-Dose

Children
6-11 Years

Primary Series
50 µg, 2-Dose

Proposed Indication: Prevention of COVID-19 caused by SARS-CoV-2

Primary Series: 2-dose, intramuscular administration 1 month apart

Totality of Evidence Supports Benefits of mRNA-1273 in Children & Adolescents Outweigh Potential Risks

Safety (Primary Objective)	▪ mRNA-1273 generally well tolerated ▪ Safety profile consistent with young adults ▪ No new safety concerns have been identified
Immunogenicity (Primary Objective)	▪ Designed to meet FDA recommendations for Emergency Use Authorization for COVID-19 vaccines ▪ Co-primary immunogenicity objectives met for 2-dose primary series
Efficacy (Secondary Objective)	▪ Evidence of vaccine efficacy against COVID-19 with mRNA-1273 ▪ 88% - 100% in children and adolescents (6-17 years)*

*Vaccine efficacy for Children (6-11 Years) based on mITT1 population

Moderna COVID-19 Vaccine Meets FDA Recommendations for EUA for Individuals 6 - 17 Years of Age

1. Clinical trials enrolled >8,000 individuals 6 - 17 years
   - >5,800 participants received ≥ 1 injection of mRNA-1273
   - Median duration of follow-up exceeds 5.6 months
2. Doses selected met pre-specified co-primary immunogenicity objectives compared to young adults 18-25 years of age
3. Vaccine efficacy consistent with efficacy/effectiveness in individuals ≥ 18 years of age
4. Established plans for active safety & effectiveness follow-up post authorization
5. Benefit / risk balance positive in children and adolescents

Unmet Medical Need	**Evan Anderson, MD, FAAP** Associate Professor, Pediatrics and Medicine Emory University School of Medicine
Clinical Development Program	**Jacqueline Miller, MD, FAAP** Senior Vice President Therapeutic Area Head, Infectious Diseases ModernaTX, Inc.
Adolescents (12 - 17 Years)	**Jacqueline Miller, MD, FAAP**
Children (6 - 11 Years)	**Rituparna Das, MD, PhD** Vice President, Clinical Development, COVID-19 Vaccines ModernaTX, Inc.
Benefit-Risk/Conclusions	**Jacqueline Miller, MD, FAAP**

CO-11

The Burden of COVID-19 in Children and Adolescents and the Need for Vaccines

Evan J. Anderson, MD, FAAP, FIDSA, FPIDS
Associate Division Chief for Clinical Research in Pediatric ID
Professor of Pediatrics and Medicine
Attending Physician at Children's Healthcare of Atlanta
Emory University School of Medicine

EMORY UNIVERSITY SCHOOL OF MEDICINE

Children's Healthcare of Atlanta

POTENTIAL CONFLICTS AND DISCLOSURES

- Financial compensation to Emory for clinical research:
  - Pfizer, Merck, GSK, Sanofi Pasteur, Novavax, Regeneron, PaxVax, MedImmune, Janssen, and Micron unrelated to this talk
  - Pfizer – pediatric COVID-19 vaccine clinical trial
- Consultant for:
  - Medscape, Sanofi Pasteur, Janssen, GSK, Moderna, and Pfizer
- Safety monitoring committees/ Endpoint Adjudication Committee
  - Kentucky BioProcessing, Inc
  - Sanofi Pasteur
  - WCG and ACI Clinical
- NIH funded
  - Local PI for several Moderna mRNA-1273 studies (Phase I & 3 studies in adults, variant study, variant booster studies, and pediatric trial)
  - Local PI for the Janssen Ad26-Spike protein Phase 3 study

Common Misperceptions about COVID-19, Risks and the Need for Vaccination in Children and Adolescents

1) Children and adolescents don't get infected with SARS-CoV-2
2) Children and adolescents don't get hospitalized with COVID-19
3) Children and adolescents don't die with COVID-19
4) Families/children are just inconvenienced by COVID-19

Data demonstrate that these were misperceptions

Common Misperceptions about COVID-19, Risks and the Need for Vaccination in Children and Adolescents

1) **Children and adolescents ~~don't~~ DO get infected with SARS-CoV-2**
2) Children and adolescents don't get hospitalized with COVID-19
3) Children and adolescents don't die with COVID-19
4) Families/children are just inconvenienced by COVID-19

Data demonstrate that these were misperceptions

CO-15

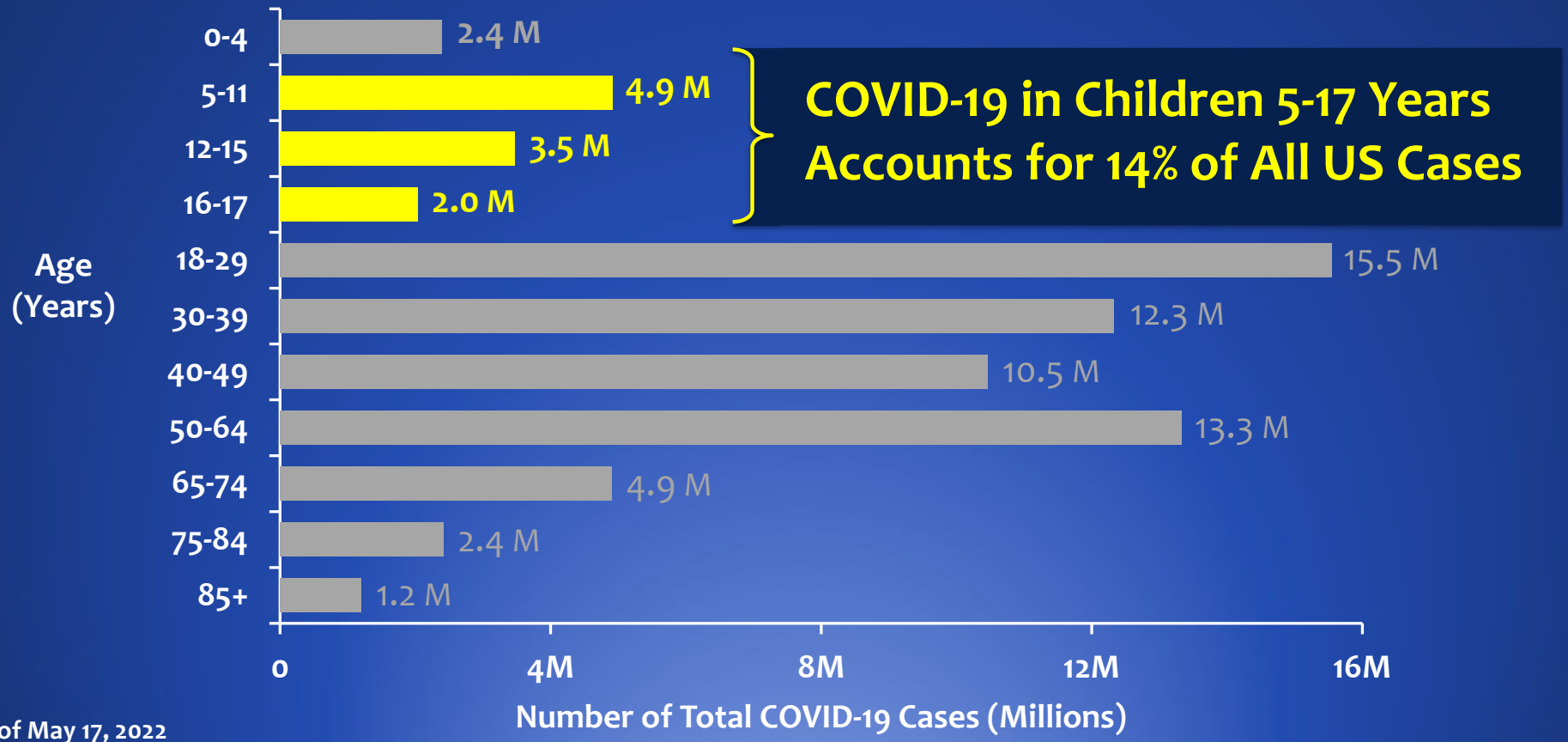
Children and Adolescents Do Get Infected with SARS-CoV-2

Substantial Increase in COVID-19 with New Variants of Concern

Data as of May 14, 2022
https://covid.cdc.gov/covid data tracker/#demographicsovertime

Children and Adolescents Do Get Infected with SARS-CoV-2

~10.4 Million US Children (5-17 Years) Have Been Infected with COVID-19



Data as of May 17, 2022

https://www.statista.com/statistics/1254271/us total number of covid cases by age group/

Common Misperceptions about COVID-19, Risks and the Need for Vaccination in Children and Adolescents

1) Children and Adolescents ~~don't~~ **DO** get infected with SARS-CoV-2

2) Children and Adolescents ~~don't~~ DO get hospitalized with COVID-19

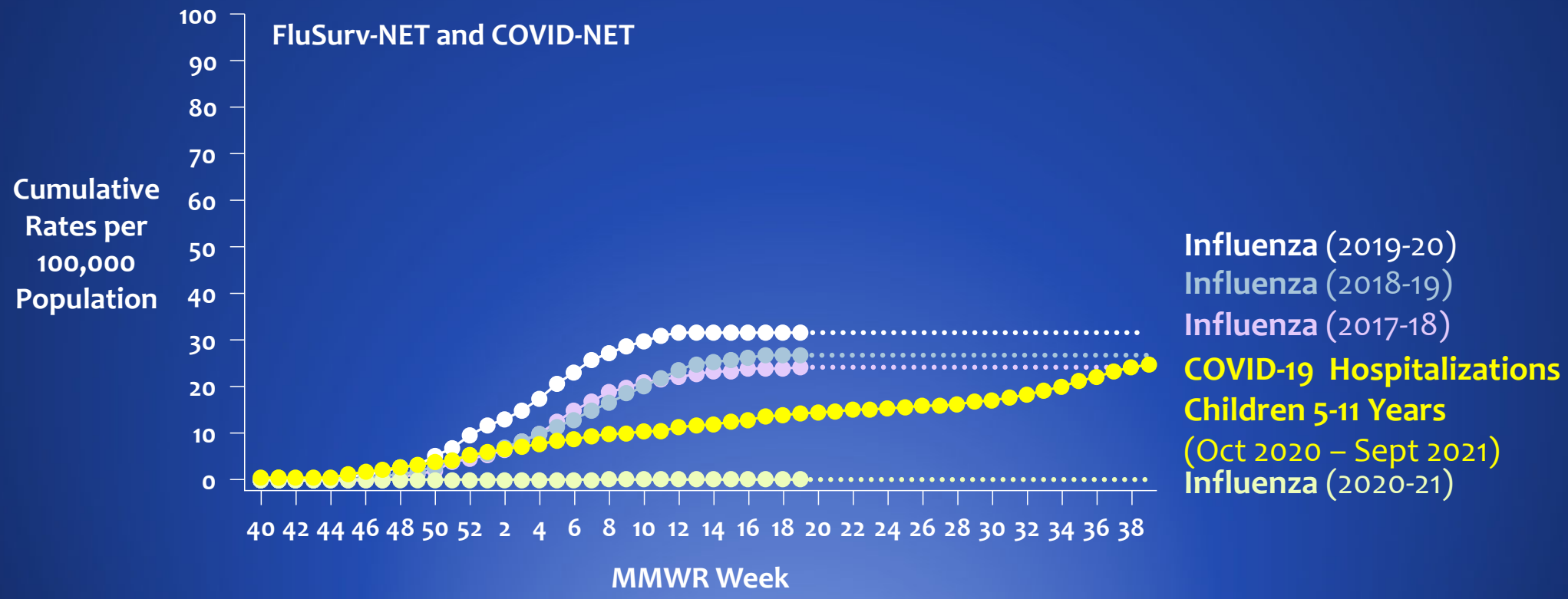
3) Children and adolescents don't die with COVID-19

4) Families/children are just inconvenienced by COVID-19

Data demonstrate that these were misperceptions

Children and Adolescents Do Get Hospitalized with COVID-19

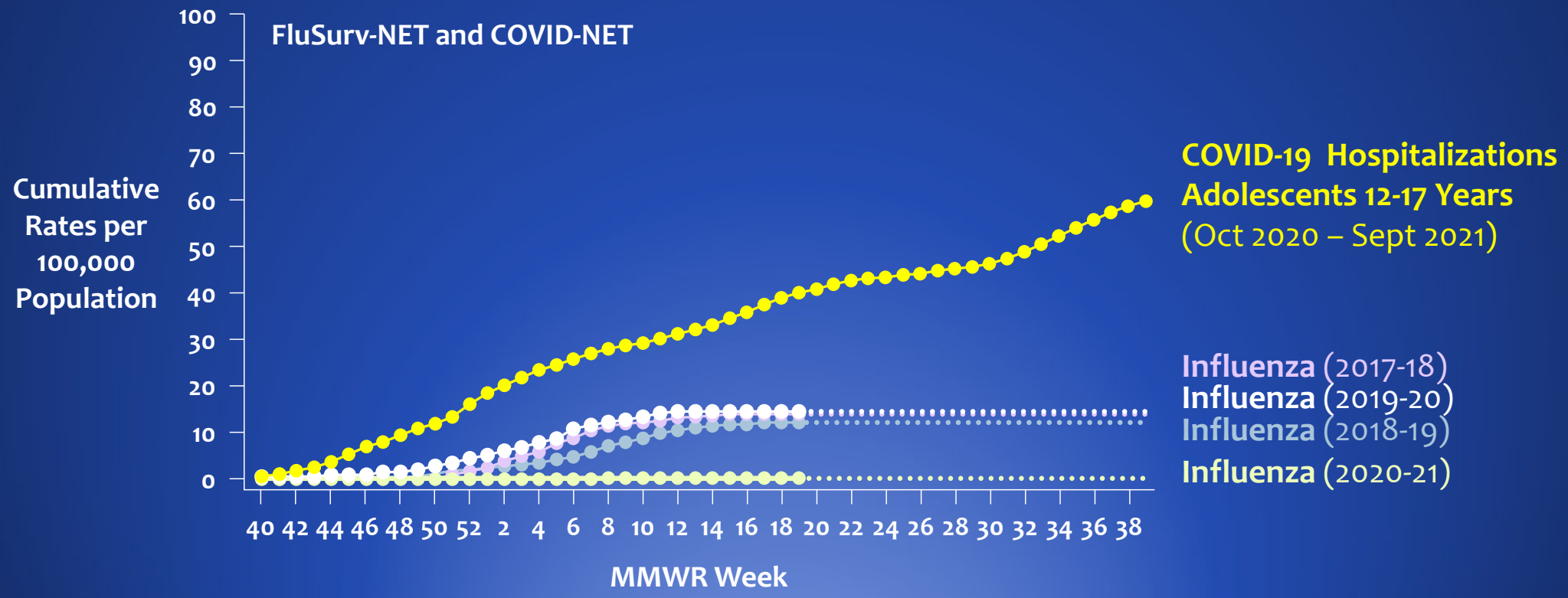
COVID-19 Related Hospitalizations are Comparable to Recent Individual Influenza Seasons (Children 5-11 Years)



Delahoy, et al., *Clin Infect Dis* 20212; 73:336 340. doi: 10.1093/cid/ciac388/6589788
FluSurv NET (October–April 2017–2021) and COVID NET (October 2020–September 2021)

Children and Adolescents Do Get Hospitalized with COVID-19

COVID-19 Related Hospitalizations are Greater than Recent Individual Influenza Seasons (Adolescents 12-17 Years)

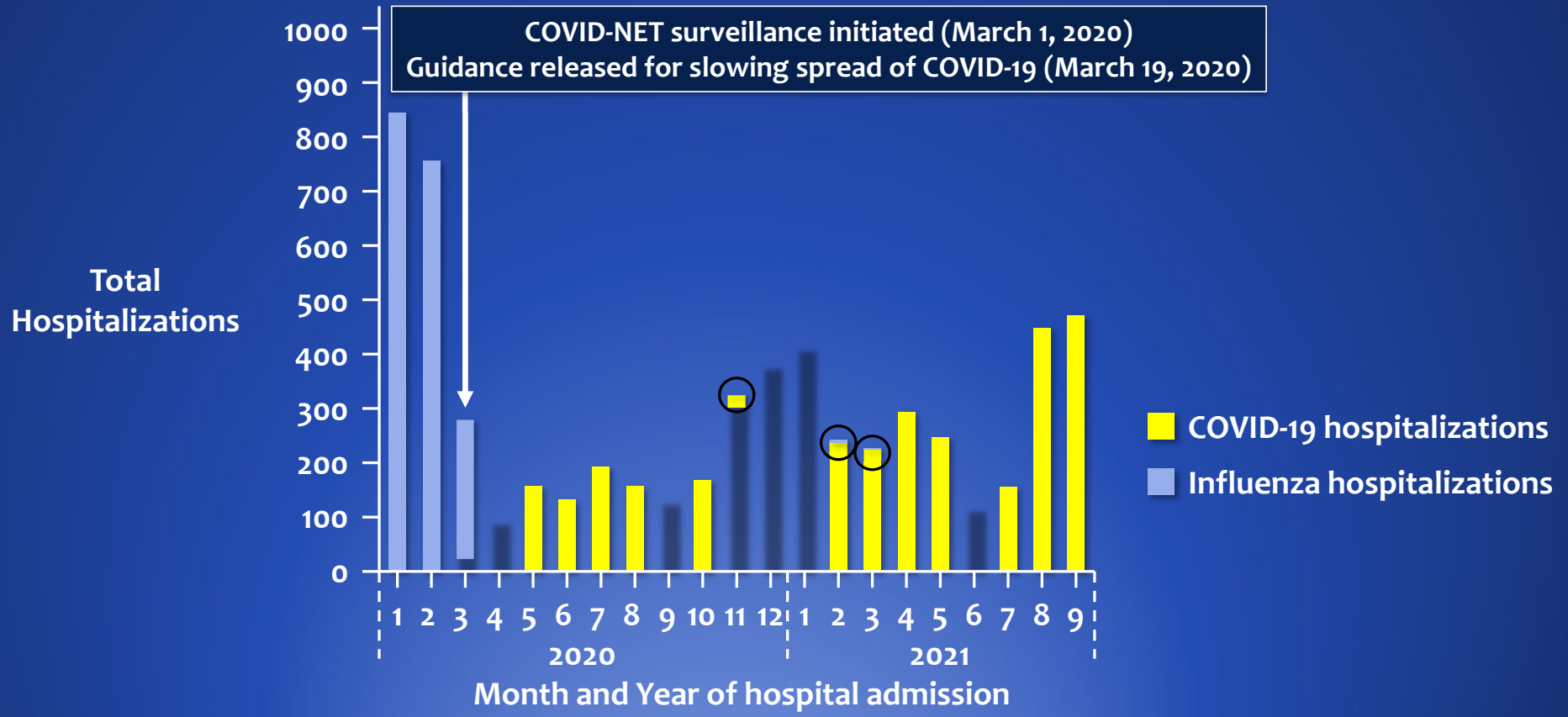


Delahoy, et al., *Clin Infect Dis* 20212; 73:336 340. doi: 10.1093/cid/ciac388/6589788
FluSurv NET (October–April 2017–2021) and COVID NET (October 2020–September 2021)

Children and Adolescents Do Get Hospitalized with COVID-19

CO-20

COVID-19 Hospitalizations Among Children 0-17 Years Despite Social Interventions, 2020-2021



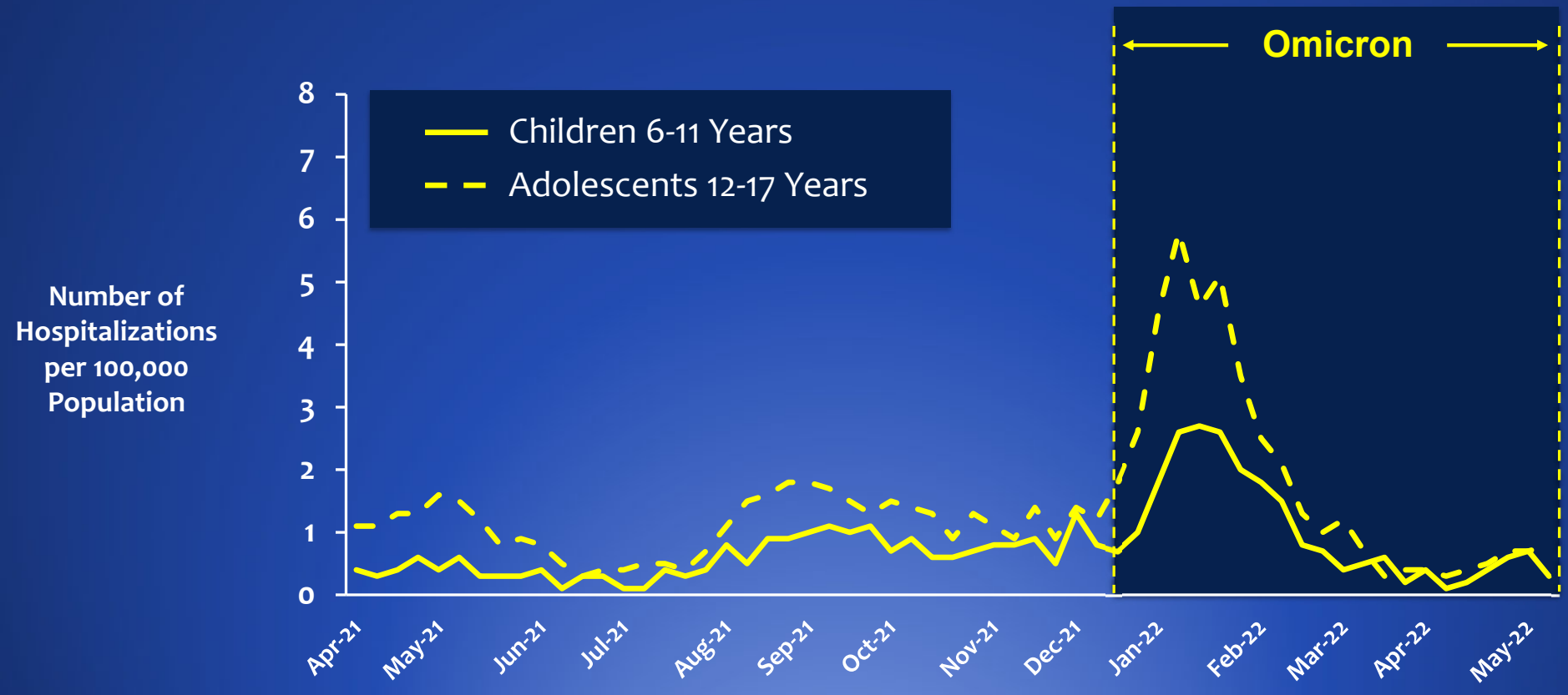
Delahoy, et al., *Clin Infect Dis* 20212; 73:336 340. doi: 10.1093/cid/ciac388/6589788

FluSurv NET (October–April 2017–2021) and COVID NET (October 2020–September 2021)

CO-21

Children and Adolescents Do Get Hospitalized with COVID-19

Marked Surge of COVID-19 Hospitalizations with Omicron



Marks et al. MMWR 2022- COVID-NET
Data as of May 14, 2022 https://gis.cdc.gov/grasp/covidnet/covid19_3.html

Children and Adolescents Do Get Hospitalized with COVID-19

Hospitalizations Occur in Children With & Without Comorbidities

	COVID-NET Oct 2020-Sept 2021		FluSurv-NET Oct-April, 2017-2021	
	5 - 11 Years (N = 698)	12 - 17 Years (N = 1470)	5 - 11 Years (N = 2013)	12 - 17 Years (N =855)
Any Underlying Medical Condition	67%	62%	69%	78%
Obesity	31%	41%	19%	22%
Asthma / Reactive Airway Disease	23%	23%	36%	38%
Neurologic Disorder	22%	14%	21%	25%
Cardiovascular Disease	11%	7%	7%	7%
Immunocompromised Condition	9%	5%	9%	14%
Chronic Lung Disease	5%	3%	7%	8%
Diabetes Mellitus	4%	7%	1%	5%

Delahoy, et al., *Clin Infect Dis* 20212; 73:336 340. doi: 10.1093/cid/ciac388/6589788

FluSurv NET (October–April 2017–2021) and COVID NET (October 2020–September 2021)

Children and Adolescents Do Get Hospitalized with COVID-19

Substantial Disease Burden Associated with COVID-19 Hospitalization

	COVID-NET Oct 2020-Sept 2021		FluSurv-NET Oct-April, 2017-2021	
	5 - 11 Years (N = 698)	12 - 17 Years (N = 1470)	5 - 11 Years (N = 2013)	12 - 17 Years (N =855)
Hospital Length of Stay; median days (IQR)	3 (2-6)	3 (2-6)	2 (1-4)	2 (1-4)
Pneumonia	13%	19%	19%	17%
ICU Admission	29%	28%	21%	27%
Invasive Mechanical Ventilation	7%	6%	5%	6%
ECMO	0.1%	0.6%	0.5%	0.5%

Delahoy, et al., *Clin Infect Dis* 20212; 73:336 340. doi: 10.1093/cid/ciac388/6589788
FluSurv NET (October–April 2017–2021) and COVID NET (October 2020–September 2021)

Children and Adolescents Do Get Hospitalized with COVID-19

Risk of Multisystem Inflammatory Syndrome in Children (MIS-C)

- **8,525 Hospitalizations** in US due to MIS-C
  - Median age 9 years old (range 5-13 years)

- **69 Deaths** due to MIS-C

"Multisystem inflammatory syndrome in children associated with SARS-CoV-2 led to serious and life-threatening illness in previously healthy children and adolescents." - Feldstein LR, New Engl J Med, 2020

Data as of May 31, 2022
https://covid.cdc.gov/covid data tracker/#mis national surveillance

Common Misperceptions about COVID-19, Risks and the Need for Vaccination in Children and Adolescents

1) Children and adolescents ~~don't~~ **DO** get infected with SARS-CoV-2

2) Children and adolescents ~~don't~~ **DO** get hospitalized with COVID-19

3) **Children and adolescents ~~don't~~ DO die with COVID-19**

4) Families/children are just inconvenienced by COVID-19

Data demonstrate that these were misperceptions

Children and Adolescents Do Die from COVID-19

Deaths Involving COVID-19 in US Children & Adolescents 5-17 Years

- **644** total deaths 2020-2022 (as of June 2)
  - **117** Deaths in 2020
  - **364** Deaths in 2021
  - **163** Deaths in 2022 (as of June 2)

Data as of June 2, 2022
https://data.cdc.gov/NCHS/AH Provisional COVID 19 Death Counts by Week Race /siwp yg6m

Children and Adolescents Do Die from COVID-19

COVID-19 is a Leading Cause of Death in US

Rank of COVID-19 Among the Leading Causes of Death in US

Age	Jan 2021	Feb 2021	Mar 2021	Apr 2021	May 2021	June 2021	July 2021	Aug 2021	Sept 2021	Oct 2021	Nov 2021	Dec 2021	Jan 2022
15-24 years	4th	5th	6th	6th	6th	7th	5th	4th	4th	4th	4th	4th	4th
5-14 years	6th	7th	9th	7th	9th	11th	7th	5th	5th	6th	7th	6th	4th

Delta and Omicron Periods

From Jan 2021 – Jan 2022, COVID-19 ranked 4th - 11th among the leading causes of death per month in individuals, 5-24 years of age in the US

Kaiser analysis of CDC Provisional Data from Wonder Database

Children and Adolescents Do Die from COVID-19

Deaths due to COVID-19 Higher than Other Vaccine Preventable Diseases

Disease	Deaths (Per Year)	Date Range	Age (Years)
COVID-19	117-364	2020-2022	5-17
Influenza	76-112	2018-2020	5-17
Varicella	50	1970-1994 (pre-vaccine)	< 15
Rubella	17	1966-1968 (pre-vaccine)	All
Hepatitis A	3	1990-1995 (pre-vaccine)	< 20
Rotavirus	20-60	1999-2007 (pre-vaccine)	< 5

Anderson EJ, et al. *Clin Infect Dis* 2021; 73:336 340. doi: 10.1093/cid/ciaa1425.
https://gis.cdc.gov/grasp/fluview/pedfludeath.html
https://data.cdc.gov/NCHS/Provisional COVID 19 Deaths by Week Sex and Age/vsak wrfu and https://gis.cdc.gov/grasp/fluview/pedfludeath.html

Common Misperceptions about COVID-19, Risks and the Need for Vaccination in Children and Adolescents

1) Children and adolescents ~~don't~~ **DO** get infected with SARS-CoV-2

2) Children and adolescents ~~don't~~ **DO** get hospitalized with COVID-19

3) Children and adolescents ~~don't~~ **DO** die with COVID-19

4) Families/children are NOT just inconvenienced by COVID-19

Data demonstrate that these were misperceptions

Families/Children are Not Just Inconvenienced by COVID-19

Impacts on Children's Mental Health, Home and School Life

- **40%** with low health-related Quality of Life[1]
  - Compared with **15.3%** pre-pandemic
- **67-70%** experienced mental health deterioration during pandemic[2]
- **66%** found it difficult to complete their schoolwork[3]
  - National test scores showed progress slowed, gap widened in math and reading for millions of US students

AAP, AACAP and CHA have declared a national emergency in children's mental health, citing serious toll of COVID-19 Pandemic[4]

1. Ravens Siebere U, et al. European Child & Adolescent Psychiatry. 2021. https://doi.org/10.1007/s00787 021 01726 5.
2. Cost KT, et al. European Child & Adolescent Psychiatry. 2021. https://doi.org/10.1007/s00787 021 01744 3.
3. Krause KH, et al. *MMWR*. 2022;71(3):28 34 and https://www.nber.org/papers/w29497 DOI 10.3386/w29497
4. https://www.aap.org/en/advocacy/child and adolescent healthy mental development/aap aacap cha declaration of a national emergency in child and adolescent mental health/

COVID-19 is Important in Children and Adolescents, and a Safe and Effective Vaccine is Needed

1) Children and adolescents DO get infected with SARS-CoV-2

- ~10.4 million diagnosed cases in US children, 14% of US cases

2) Children and adolescents DO get hospitalized with COVID-19

- Similar to or greater than recent pre-pandemic influenza seasons despite social interventions

3) Children and adolescents DO die with COVID-19

- Mortality far exceeds that of many other pre-vaccine pathogens

4) Families/children are NOT just inconvenienced by COVID-19

- Developmental, educational, extracurricular activities, and mental health

Overview of Clinical Trials Supporting EUA of mRNA-1273 for Individuals 6 – 17 Years

Jacqueline Miller, MD, FAAP

Senior Vice President

Therapeutic Area Head, Infectious Diseases

ModernaTX, Inc.

> 5,800 Children & Adolescents (6-17 Years Old) Received ≥ 1 Dose of mRNA-1273

Study 203 and 204 (Safety Set)

Study	Age Range	Dose Selected	Participants Receiving ≥ 1 Injection		
			mRNA-1273	Placebo	Total
203	12-17 years	100 µg	2,486	1,240	3,726
204	6-11 years	50 µg	3,387	995	4,382
		Total	5,873	2,235	8,108

Median Safety Follow-Up Exceeds FDA Recommendations

Study 203 and 204

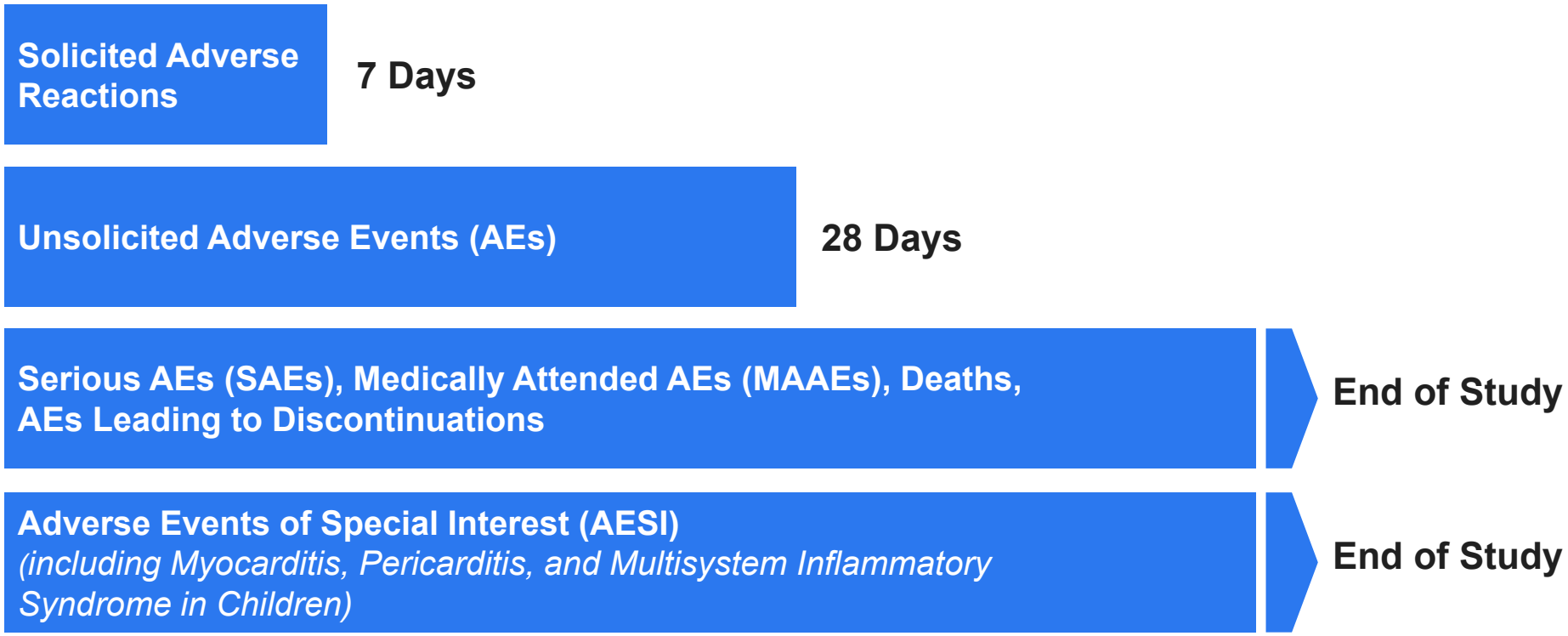
Study	Age Range	Part	Dose	mRNA-1273 (N)	Median Follow-Up Post-Dose 2 (Months)
203	12-17 years	Blinded, Randomized	100 µg	2,486	11.1
204	6-11 years	Dose-Ranging	50 µg	380	8.9
			100 µg	371	8.7
		Blinded, Randomized	50 µg	3,007	5.6

1 month = 28 days

Primary Safety Objective: Endpoints and Duration of Follow-up

Study 203 and 204

Active Surveillance



Robust Evaluation of Myocarditis and Pericarditis in Clinical Trials of Infants, Toddlers, Children & Adolescents

- Fact Sheets, Investigator Brochures, and Informed Consent Forms updated to increase awareness
- Included as AESIs to enhance detection and standardized follow-up
- Actively queried symptoms suggestive of myocarditis / pericarditis based on CDC case definition during safety follow-up calls
- Clinical database reviewed for participant-reported symptoms
- Potential events independently adjudicated by Cardiac Event Adjudication Committee (CEAC)

Identification of Potential Subclinical Myocarditis and Pericarditis in Clinical Trials of Infants, Toddlers, Children & Adolescents

- Two methods were used to query the clinical database for potential, subclinical cases of myocarditis
  1. Standard MedDRA queries were applied for myocarditis and pericarditis
  2. Specific algorithm was developed to identify clinical signs and symptoms in the CDC working case definitions for myocarditis and pericarditis
- Ongoing post-authorization safety studies continue to capture myocarditis and pericarditis as AESIs

Primary Effectiveness Objective

Study 203 and 204

Immunogenicity

- GMT of serum antibody and seroresponse rate (day 57) compared to 18-25-year-olds in pivotal efficacy Study 301
  - GMT Ratio lower 95% CI ≥ 0.67 and point estimate ≥ 0.8
    - FDA requested point estimate ≥ 1.0 if doses < 100 µg selected
  - Difference in seroresponse rate lower 95% CI > -10% and point estimate > -5%
- Effectiveness is inferred by immunobridging

Secondary Efficacy Endpoints, COVID-19 Case Definitions

Study 203 and 204

Two COVID-19 Definitions

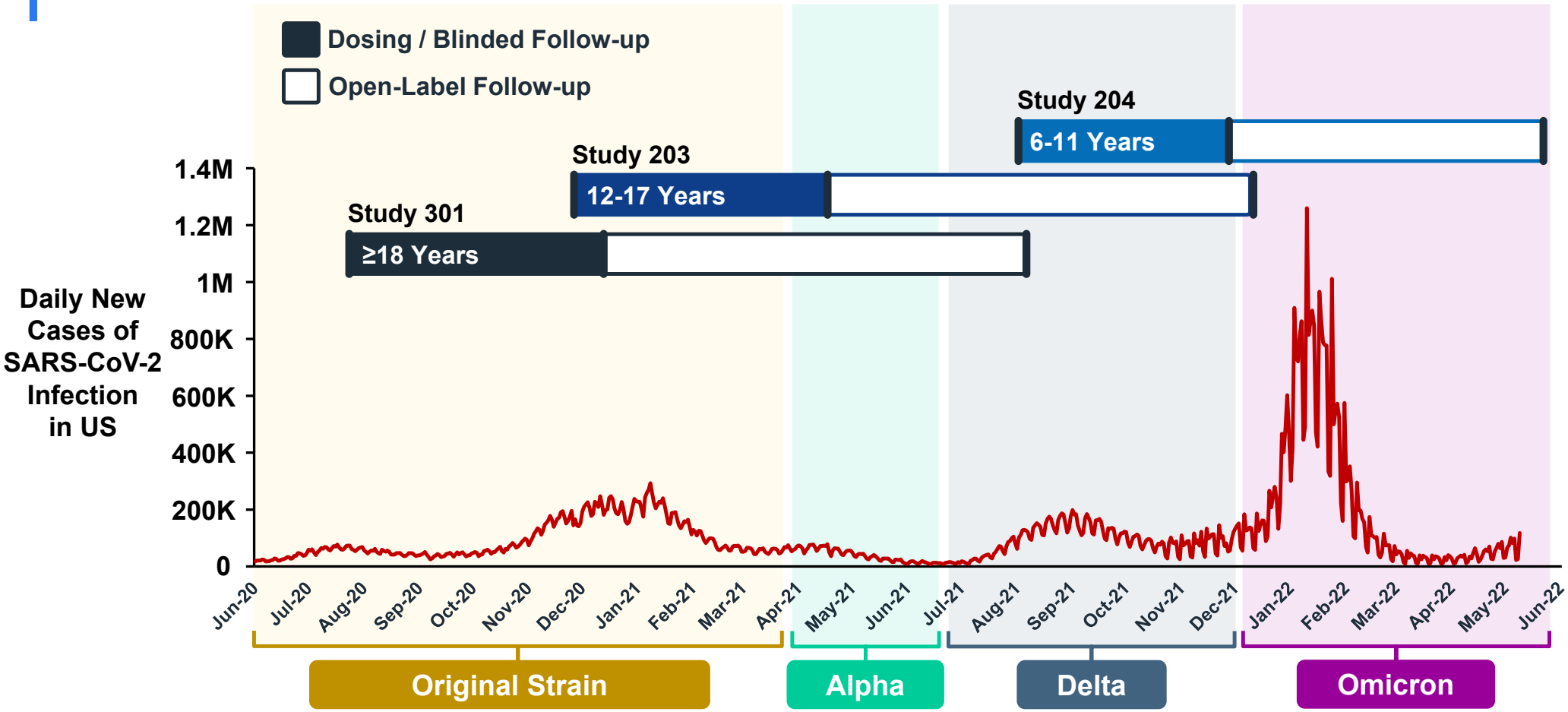
CDC Case Definition

1 systemic symptom or 1 respiratory symptom + a positive RT-PCR

Efficacy (Study 301) Case Definition

2 systemic symptoms or 1 respiratory symptom + a positive RT-PCR

Clinical Studies Conducted During Different Periods of COVID-19 Pandemic



https://covid.cdc.gov/covid-data-tracker/#trends_dailycases

Safety, Immunogenicity, and Efficacy in Adolescents 12 - 17 Years of Age

Jacqueline Miller, MD, FAAP

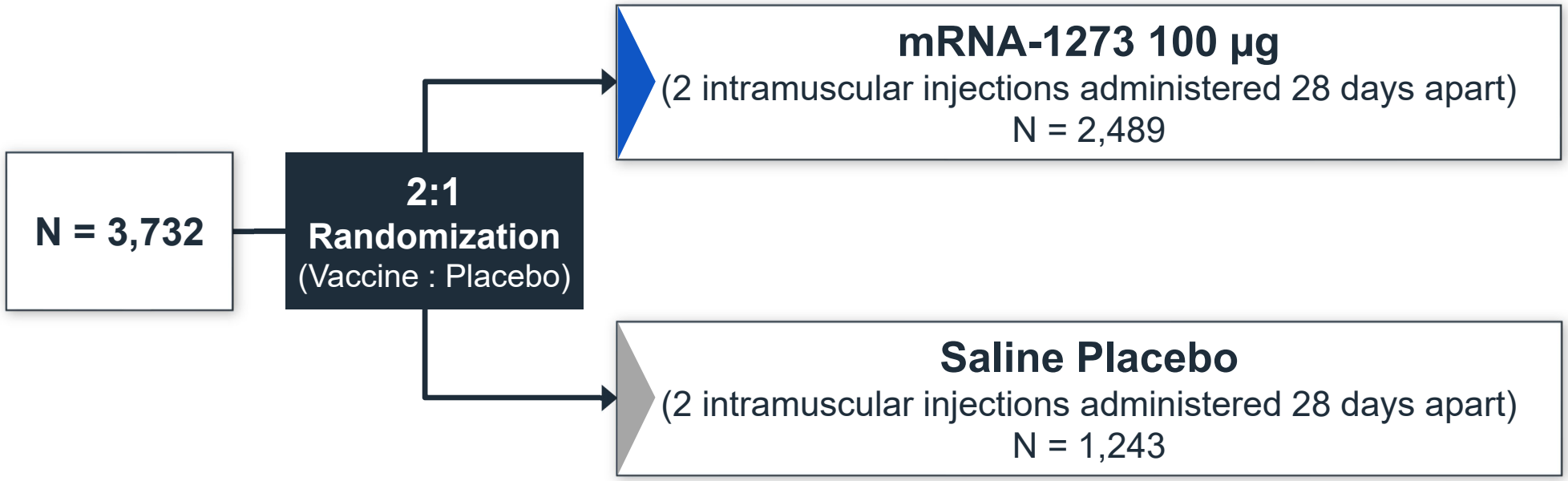
Senior Vice President

Therapeutic Area Head, Infectious Diseases

ModernaTX, Inc.

Pivotal, Randomized, Placebo-Controlled Evaluation of Safety, Immunogenicity, and Efficacy

Study 203: Adolescents (12-17 Years)



- **Planned follow-up:** 12-months after last dose

Ali et al., *NEJM* 2021

Demographics

Study 203: Adolescents (12-17 Years), Safety Set

		mRNA-1273 N = 2,486	Placebo N = 1,240
Age (years)	Mean	14.3	14.2
	12-15	74%	75%
	16-18	26%	25%
Gender	Female	48%	49%
Race	White	84%	84%
	Black or African American	3%	3%
	Asian	6%	6%
	American Indian or Alaska Native	0.5%	0.6%
	Multiracial	5%	4%
Ethnicity	Hispanic or Latino	11%	12%
	Not Hispanic or Latino	88%	87%

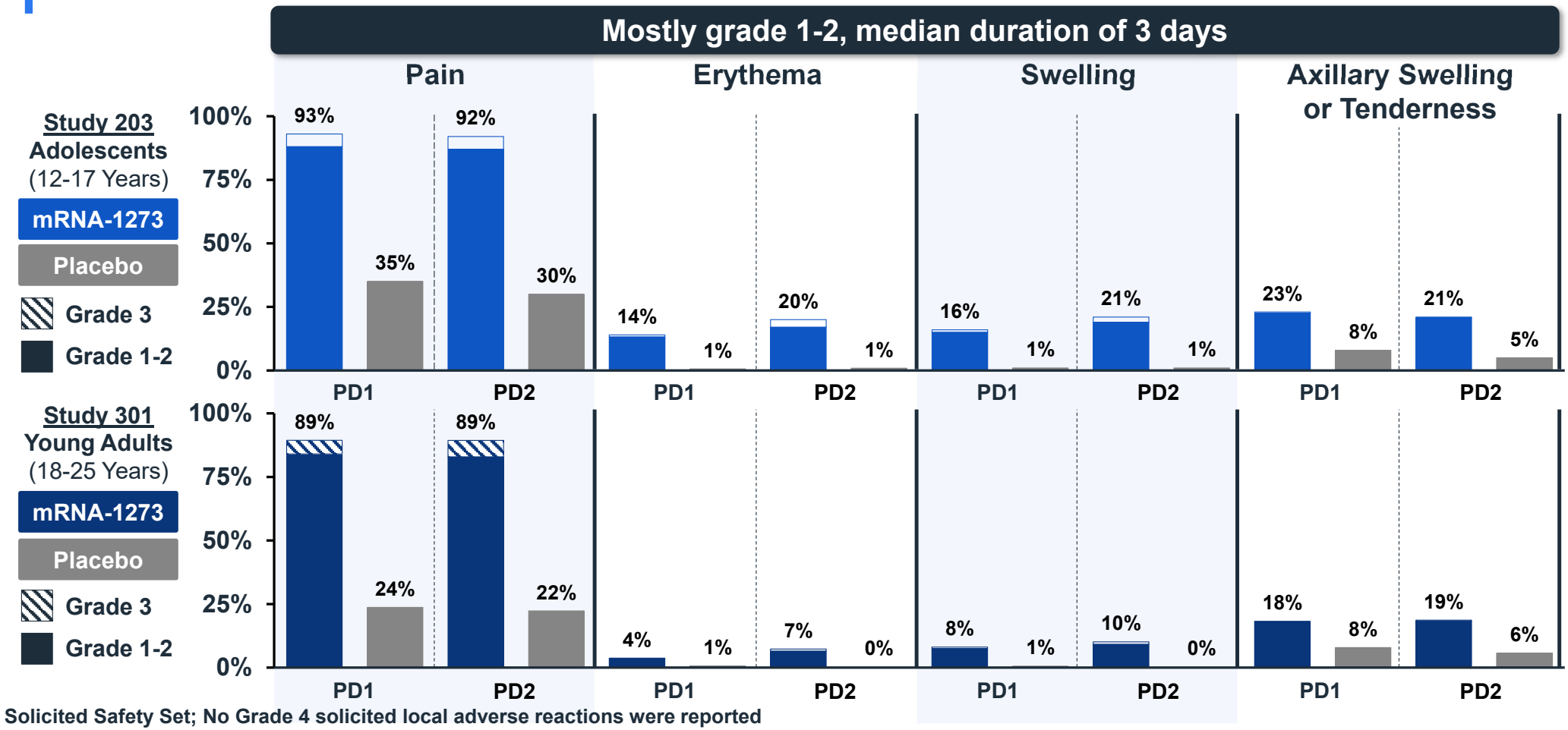
Ali et al., *NEJM* 2021

Safety

Primary Objective

Solicited Local Adverse Reactions within 7 Days After Dose 1 & 2

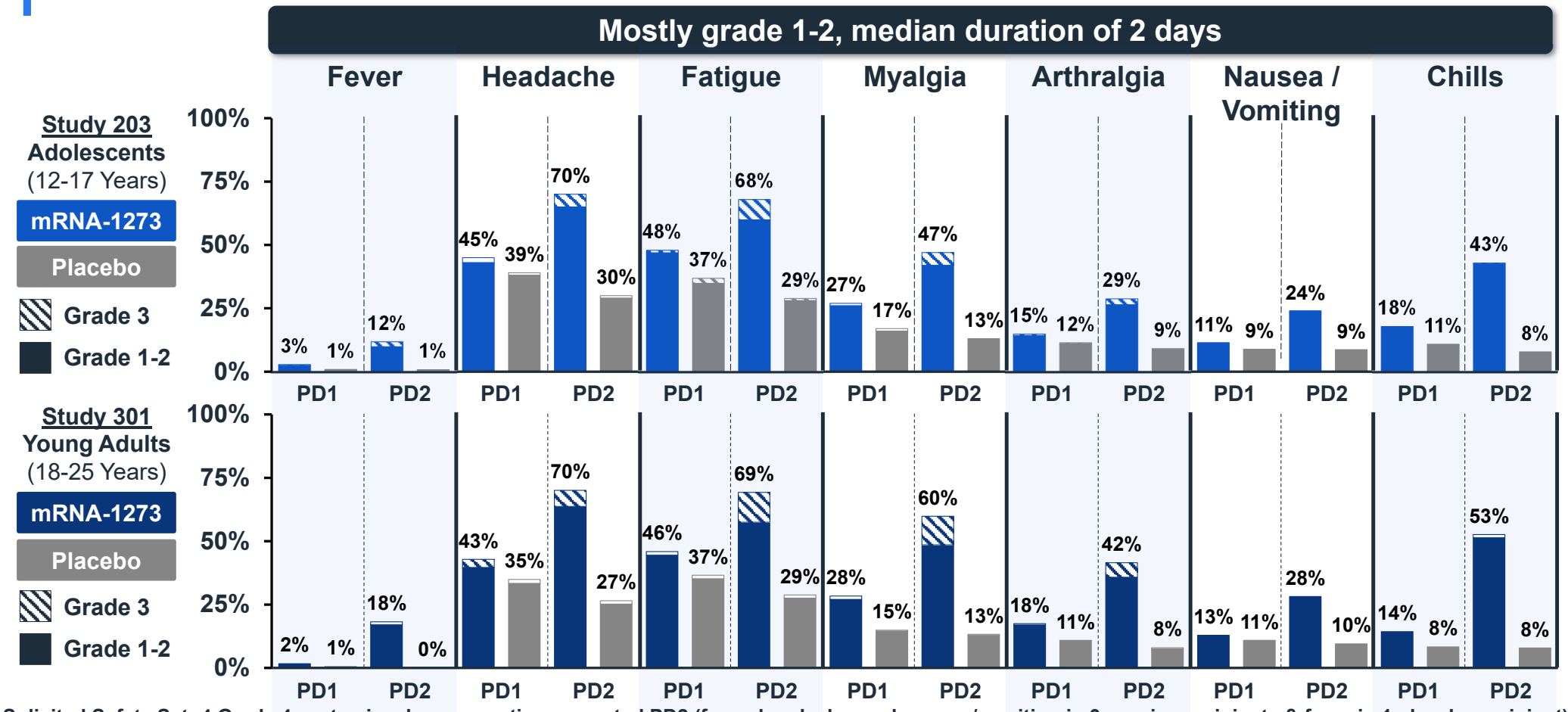
Study 203: Adolescents (12-17 Years) vs Study 301: Young Adults (18-25 Years)



Solicited Safety Set; No Grade 4 solicited local adverse reactions were reported

Solicited Systemic Adverse Reactions within 7 Days After Dose 1 & 2

Study 203: Adolescents (12-17 Years) vs Study 301: Young Adults (18-25 Years)



Solicited Safety Set; 4 Grade 4 systemic adverse reactions reported PD2 (fever, headache, and nausea/vomiting in 3 vaccine recipients & fever in 1 placebo recipient)

Unsolicited Adverse Events

Study 203: Adolescents (12-17 Years), Safety Set, Up to 28 Days After Any Injection

2:1 Randomization (mRNA-1273:Placebo)	mRNA-1273 N = 2,486		Placebo N = 1,240	
	Any AE	Related to Vaccination	Any AE	Related to Vaccination
All	21%	13%	16%	6%
SAE	<0.1%	0	<0.1%	0
Fatal	0	0	0	0
Medically Attended AEs	6.3%	0.8%	6.5%	0.4%
Leading to Discontinuation - Vaccine	0	0	0	0
Leading to Discontinuation - Study	<0.1%	0	0	0
Severe	0.2%	0	<0.1%	0
AESI of MIS-C	0	0	0	0

2 AESIs retrospectively identified at 31 Jan 2022 data cut following 27 Jul 2021 protocol amendment

- Events were appendicitis (N=1) and injection site hypersensitivity (N=1)

Serious Adverse Event (SAE), Multisystem Inflammatory Syndrome in Children (MIS-C), Adverse Event of Special Interest (AESI)

Long-Term Safety – 11.1 Months Median Duration of Follow-Up After Dose 2

Study 203: Adolescents (12-17 Years), Safety Set

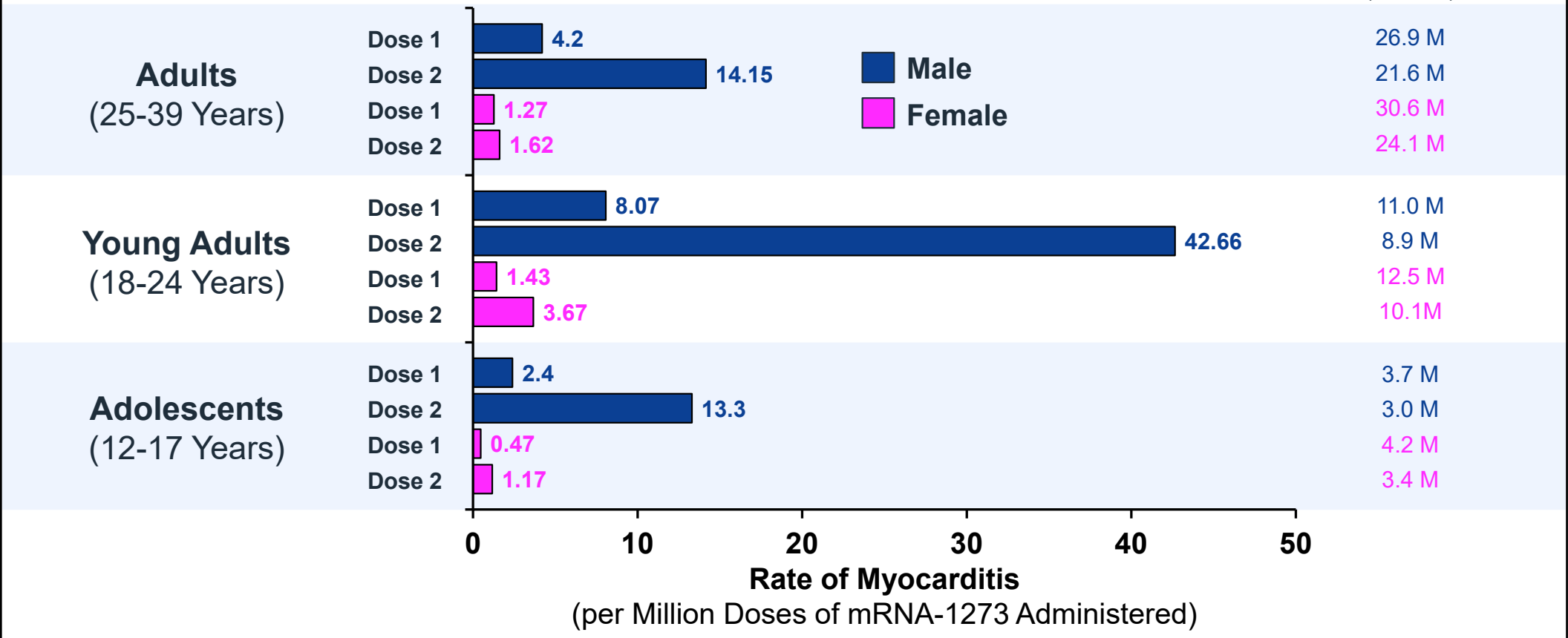
	mRNA-1273 N = 2,486			
	Any AE		Related to Vaccination	
	n	%	n	%
SAE	21	0.8%	0	-
Fatal	0	-	0	-
Medically Attended AEs	980	39.4%	25	1.0%
Leading to Discontinuation - Vaccine	3	0.1%	1	<0.1%
Leading to Discontinuation - Study	0	-	0	-
AESI – Any	13	0.5%	1	<0.1%
AESI of MIS-C	0	-	0	-
AESI of Other	13	0.5%	1	<0.1%

1 SAE in mRNA-1273 participant, reported within 28 days, identified at 31 Jan 2022 data cut

Serious Adverse Event (SAE), Multisystem Inflammatory Syndrome in Children (MIS-C), Adverse Event of Special Interest (AESI)

Myocarditis Reporting Rates with mRNA-1273 in Post Licensure Follow-up

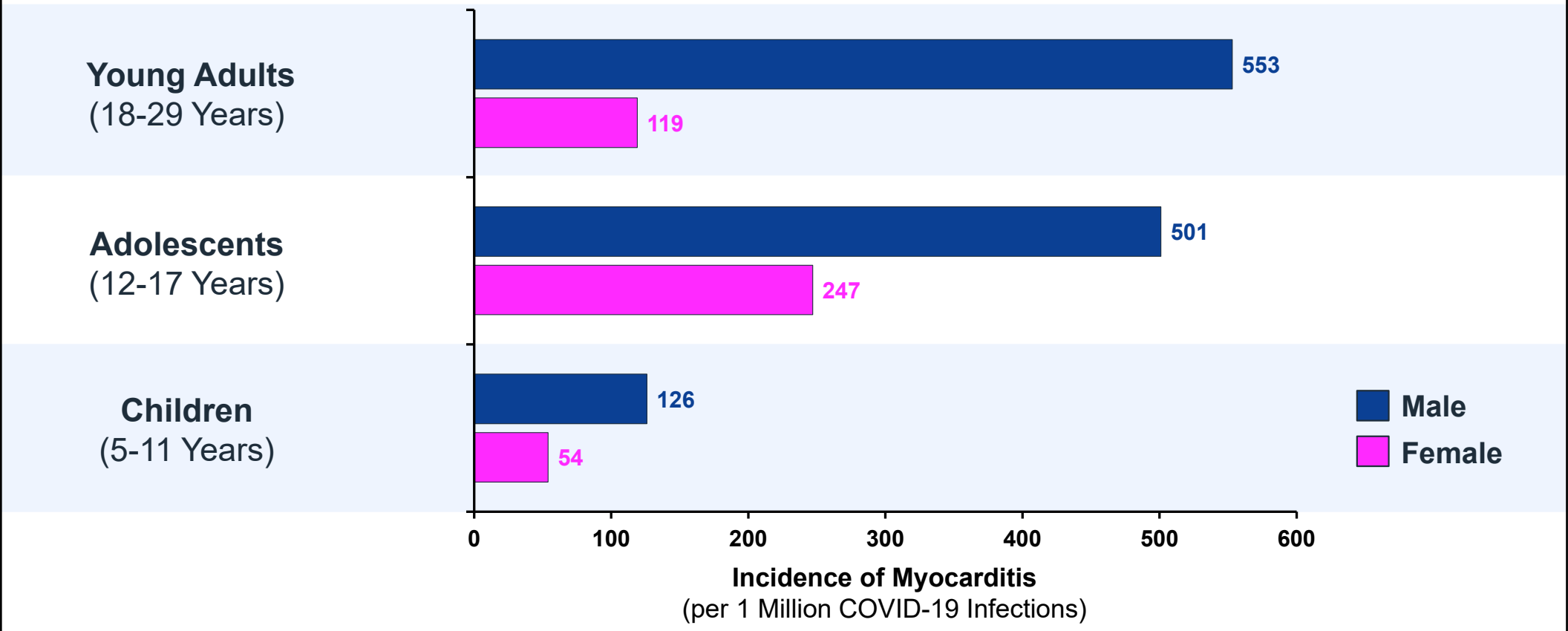
Moderna Global Safety Database (as of April 15, 2022)



*Numbers vaccinated estimated from April 15, 2022 Moderna Bi-Monthly Summary Safety Reports

Myocarditis Reporting Rates Associated with SARS-CoV-2 Infections

PCORnet United States, Jan 2021 – Jan 2022



Block, J. P. et al. Cardiac Complications After SARS-CoV-2 Infection and mRNA COVID-19 Vaccination — PCORnet, United States, January 2021–January 2022. Mmwr Morbidity Mortal Wkly Rep 71, (2022).

Immunogenicity Objectives of GMT Ratio and Seroresponse Rate

Primary Objective

Co-Primary Immunogenicity Objectives of GMT Ratio and Seroresponse Rate were Met

Study 203: Adolescents (12-17 Years), Per Protocol Immunogenicity Subset

Day 57 Analysis PsVNA	Study 203 **Adolescents** (12-17 Years) **mRNA-1273 (100 µg)** N = 340	Study 301 **Young Adults** (18-25 Years) **mRNA-1273 (100 µg)** N = 296
GMT (Geometric Mean Titer) 95% CI	**1401.7** (1276.3, 1539.4)	**1301.3** (1177.0, 1438.8)
GMT Ratio (Study 203 vs 301) 95% CI	**1.1** (0.9, 1.2)	
Seroresponse, n/N (%) 95% CI	**336 (98.8%)** (97.0, 99.7)	**292 (98.6%)** (96.6, 99.6)
Difference (Study 203 vs 301) 95% CI	**0.2%** (-1.8, 2.4)	

Success Criteria Met

GMT Ratio: Lower 95% CI ≥ 0.67 & Point Estimate ≥ 0.8

Difference in Seroresponse Rate: 95% CI > -10% & Point Estimate > -5%

Efficacy

Secondary Endpoints

Vaccine Efficacy in Blinded Phase (through May 31, 2021)

Study 203: Adolescents (12-17 Years), Per Protocol Set, COVID-19 Cases Starting 14 Days After Dose 2

	mRNA-1273 100 µg	Placebo
CDC case definition of COVID-19		
Cases, n/N (%)	1 / 2,139 (<0.1)	7 / 1,042 (0.7)
Incidence rate per 1000 person-years (95% CI)	1.9 (0.0, 10.8)	29.0 (11.7, 59.7)
VE (%) based on incidence rate (95% CI)	**93.3% (47.9, 99.9)**	
301 case definition of COVID-19		
Cases, n/N (%)	0 / 2,139 (0)	4 / 1,042 (0.4)
Incidence rate per 1000 person-years (95% CI)	0 (NE, 7.1)	16.5 (4.5, 42.3)
VE (%) based on incidence rate (95% CI)	**100% (28.9, NE)**	

CDC case definition: 1 systemic or 1 respiratory symptom + positive RT-PCR
301 case definition: 2 systemic or 1 respiratory symptom + positive RT-PCR

Ali et al, *NEJM*, 2021

Summary of Moderna COVID-19 Vaccine

Study 203: Adolescents (12-17 Years)

Safety (Primary Endpoint)	▪ mRNA-1273 was well tolerated ▪ Solicited adverse reactions mostly grade 1-2, median duration of 2-3 days ▪ No SAEs reported within 28 days were considered vaccine-related ▪ No deaths, myocarditis/pericarditis through 11.1 months median follow-up
Immunogenicity (Primary Objective)	▪ Co-primary immunogenicity objectives met for 2-dose primary series ▪ GMTs and seroresponse rates non-inferior to young adults (18-25 years) ▪ GMT Ratio = 1.1; Difference in seroresponse rate 0.2% ▪ Vaccine effectiveness successfully inferred based on immunobridging
Efficacy (Secondary Objective)	▪ 93.3% - 100% vaccine efficacy of mRNA-1273 against COVID-19 infection

Study 204: Safety, Immunogenicity, and Efficacy of mRNA-1273 in Children, 6 - 11 Years of Age

Rituparna Das, MD, PhD

Vice President, Clinical Development, COVID-19 Vaccines

ModernaTX, Inc.

Dose Selection (Part 1) Followed by Randomized, Placebo-Controlled Study (Part 2)

Study 204: Children (6-11 Years)

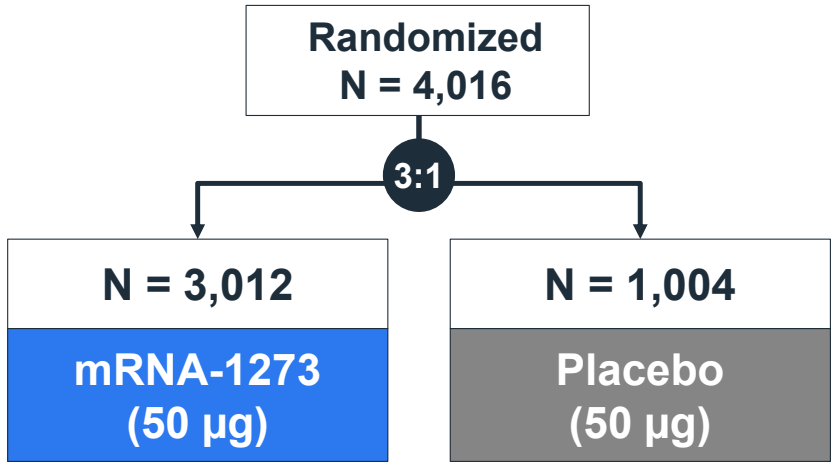
Open-Label, Dose Selection

N = 371	N = 380
mRNA-1273 (100 µg)	mRNA-1273 (50 µg)

Dose Selected

- Showed acceptable tolerability profile
- High likelihood of meeting immunogenicity criteria
- External DSMB agreed with 50 µg dose

Randomized, Placebo-Controlled



- Randomized 3:1 (mRNA-1273:Placebo)
- 12-month planned follow-up after last dose

Demographics

Study 204 (Part 2): Children (6-11 Years), Safety Set

		mRNA-1273 (50 µg) N = 3,007	Placebo N = 995
Age	Mean (Years)	8.5	8.5
	6-8 Years	50%	49%
	9-11 Years	50%	51%
Gender	Female	48%	52%
Race	White	65%	67%
	Black or African American	10%	9%
	Asian	10%	10%
	American Indian or Alaska Native	< 1%	< 1%
	Multiracial	11%	10%
Ethnicity	Hispanic or Latino	19%	18%
	Not Hispanic or Latino	80%	81%

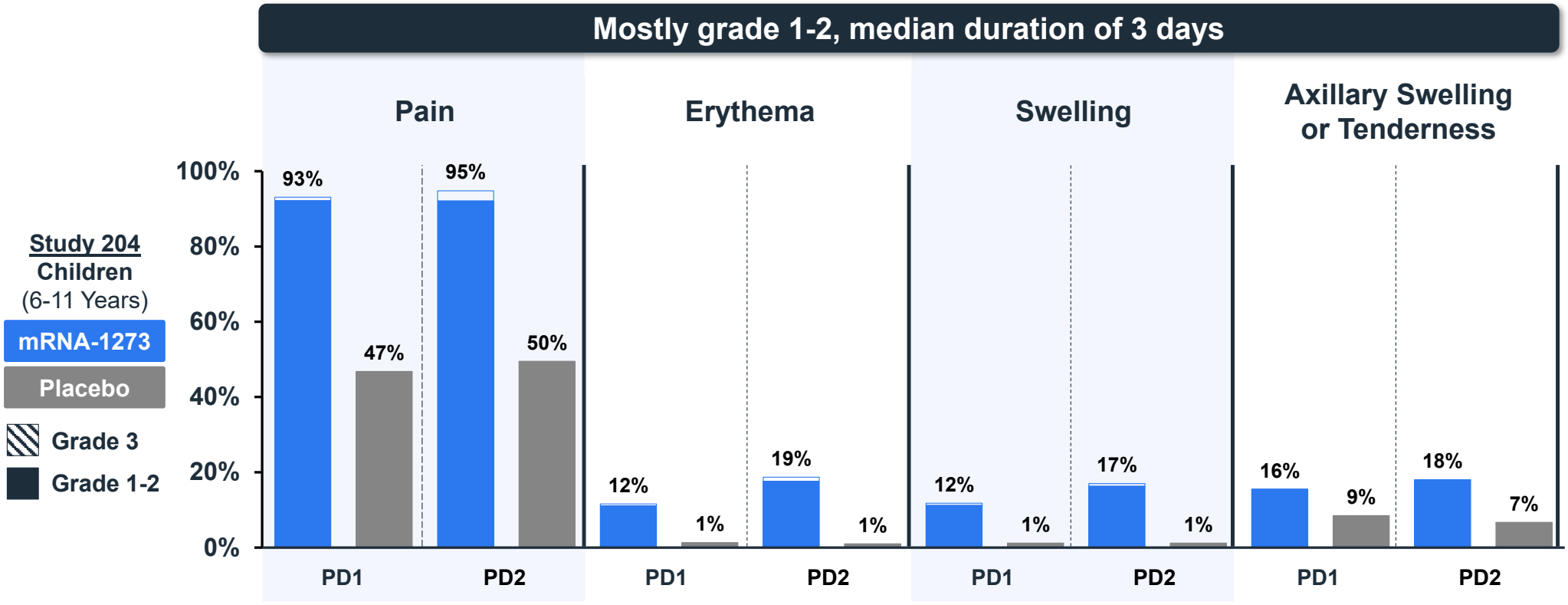
Creech et al., *NEJM*, 2022

Safety

Local Reactions

Solicited Local Reactions within 7 Days After Dose 1 & 2

Study 204: Children (6-11 Years)

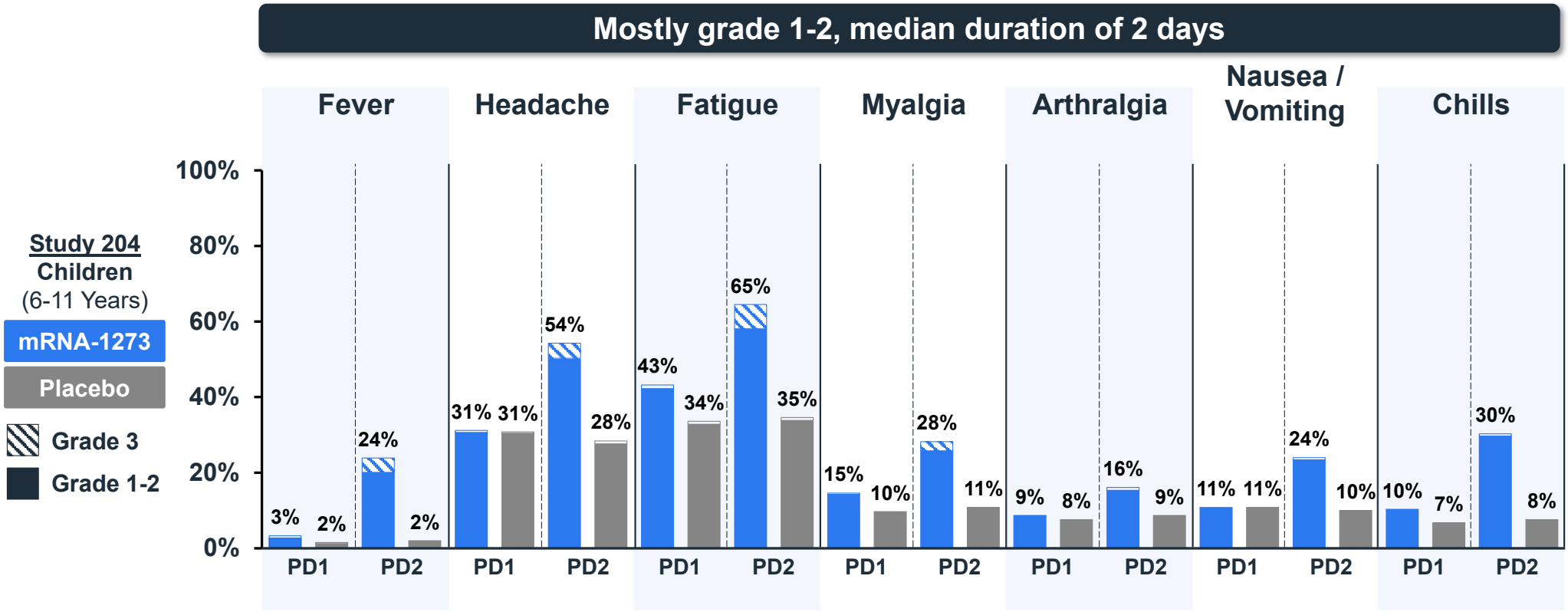


Solicited Safety Set; SARS-CoV2 negative at baseline; No Grade 4 local reactions reported

Creech et al., *NEJM*, 2022

Solicited Systemic Reactions within 7 Days After Dose 1 & 2

Study 204: Children (6-11 Years)



Solicited Safety Set; SARS-CoV2 negative at baseline; No Grade 4 systemic reactions reported

Creech et al., *NEJM*, 2022

Safety

Unsolicited Adverse Events

Unsolicited Adverse Events

Study 204: Children (6-11 Years), Safety Set (Part 2), Up to 28 Days After Any Injection

3:1 Randomization (mRNA-1273:Placebo)	mRNA-1273 N = 3,007		Placebo N = 995	
	Any AE	Related to Vaccination	Any AE	Related to Vaccination
All	30%	11%	25%	5%
SAE	<0.1%	0	0.2%	0
Fatal	0	0	0	0
Medically Attended AEs	13%	1%	14%	0.4%
Leading to Discontinuation - Vaccine	<0.1%	0	0	0
Leading to Discontinuation - Study	<0.1%	0	0	0
Severe	0.4%	0.3%	0.2%	0.1%
AESI – Any	<0.1%	0	0.2%	0
AESI of MIS-C	0	0	0	0
AESI of Myocarditis/Pericarditis	0	0	0	0

Serious Adverse Event (SAE), Multisystem Inflammatory Syndrome in Children (MIS-C), Adverse Event of Special Interest (AESI)

Long-Term Safety – 5.6 Months Median Duration of Follow-Up After Dose 2

Study 204: Children (6-11 Years), Safety Set (Part 2)

	mRNA-1273 N = 3,007			
	Any AE		Related to Vaccination	
	n	%	n	%
All	1517	50%	364	12%
SAE	15	0.5%	0*	0
Fatal	0	0	0	0
Medically Attended AEs	1028	34%	38	1.3%
Leading to Discontinuation - Vaccine	3	<0.1%	1	<0.1%
Leading to Discontinuation - Study	1	<0.1%	0	0
Severe	23	0.8%	11	0.4%
AESI – Any	12	0.4%	1	<0.1%
AESI of MIS-C	0	0	0	0
AESI of Myocarditis/Pericarditis	0	0	0	0

1 related SAE of ileus reported in participant from placebo cross-over group with a complex GI medical history

Serious Adverse Event (SAE), Multisystem Inflammatory Syndrome in Children (MIS-C), Adverse Event of Special Interest (AESI)

Immunogenicity

Primary Objective

Prespecified Co-Primary Immunogenicity Objectives of GMT Ratio and Seroresponse Were Met

Study 204 (Part 2): Children (6-11 Years), Per Protocol Immunogenicity Subset

Day 57 Analysis, Part 2 PsVNA	Study 204 **Children** (6-11 Years) **mRNA-1273 (50 µg)** N = 320	Study 301 **Young Adults** (18-25 Years) **mRNA-1273 (100 µg)** N = 295
GMT (Geometric Mean Titer) 95% CI	**1610** (1457, 1780)	**1300** (1171, 1443)
GMT Ratio (Study 204 vs. 301) 95% CI	**1.2** (1.1, 1.4)	
Seroresponse, n/N (%) 95% CI	**313/316 (99.1%)** (97.3, 99.8)	**292/295 (99.0%)** (97.1, 99.8)
Difference (Study 204 vs. 301) 95% CI	**0.1%** (-1.9, 2.1)	

Success Criteria Met

GMT Ratio: Lower 95% CI ≥ 0.67 & Point Estimate ≥ 0.8

Difference in Seroresponse Rate: 95% CI > -10% & Point Estimate > -5%

Efficacy

Secondary Objective

Availability of an EUA Vaccine for 6-11 Year Age Group Limited Efficacy Follow-up During Blinded Period

- Participants unblinded to allow placebo recipients to either:
  - Cross-over to receive mRNA-1273 and remain in study
  - Withdraw from study to receive authorized vaccine
- Loss of placebo comparator group limited efficacy follow-up during blinded period (1.8 months median post-dose 2)
- Analysis conducted in mITT1 using cases accrued 14 days post-dose 1

Efficacy of mRNA-1273 During Delta Period

Study 204 (Part 2): Children (6-11 Years), mITT1 Starting 14 Days After Dose 1

	mRNA-1273 50 µg	Placebo
CDC case definition of COVID-19		
Cases, n/N (%)	7 / 2,680 (0.3%)	18 / 875 (2.1%)
Incidence rate per 1000 person-years (95% CI)	14 (6, 29)	117 (69, 185)
VE (%) based on incidence rate (95% CI)	**88.0%** (70.0, 95.8)	
301 case definition of COVID-19		
Cases, n/N (%)	4 / 2,681 (0.1%)	15 / 877 (1.7%)
Incidence rate per 1000 person-years (95% CI)	8 (2, 20)	97 (54, 160)
VE (%) based on incidence rate (95% CI)	**91.8%** (74.2, 98.0)	

CDC case definition: 1 systemic or 1 respiratory symptom + positive RT-PCR
301 case definition: 2 systemic or 1 respiratory symptom + positive RT-PCR

Creech et al., *NEJM*, 2022

Summary of Moderna COVID-19 Vaccine

Study 204: Children (6 - 11 Years)

Safety (Primary Endpoint)	▪ mRNA-1273 was well tolerated ▪ Solicited adverse reactions mostly grade 1-2, median duration of 2-3 days ▪ No related SAEs within 28 days ▪ No deaths, myocarditis/pericarditis through 5.6 months of follow-up
Immunogenicity (Primary Objective)	▪ Co-primary immunogenicity objectives met for 2-dose primary series ▪ GMTs and seroresponse rates non-inferior to young adults (18-25 years) ▪ GMT Ratio = 1.2; Difference in seroresponse rate 0.1% ▪ Vaccine effectiveness successfully inferred based on immunobridging
Efficacy (Secondary Objective)	▪ 88% - 92% vaccine efficacy against COVID-19 infection (mITT1)

Summary

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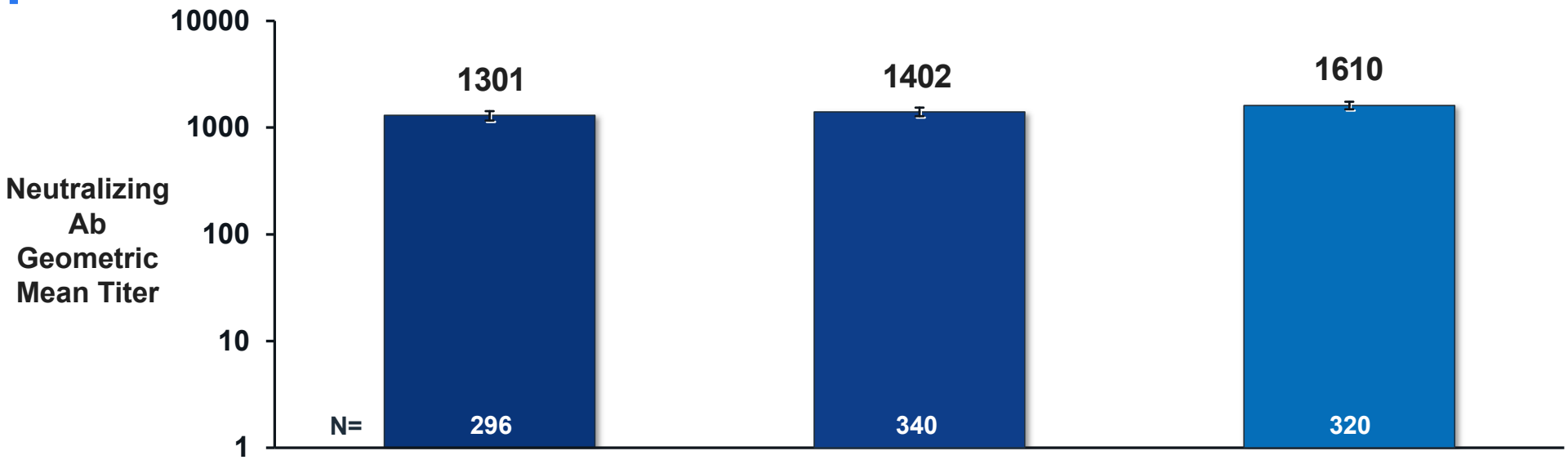
Senior Vice President
Therapeutic Area Head, Infectious Diseases
ModernaTX, Inc.

Immunogenicity of mRNA-1273 Demonstrated in Children and Adolescents



	Study 301 Young Adults (18-25 Years)	Study 203 Adolescents (12-17 Years)	Study 204 Children (6-11 Years)
Dose	**100 µg**	**100 µg**	**50 µg**
Geometric Mean Ratio (vs Young Adults)		**1.1**	**1.2**

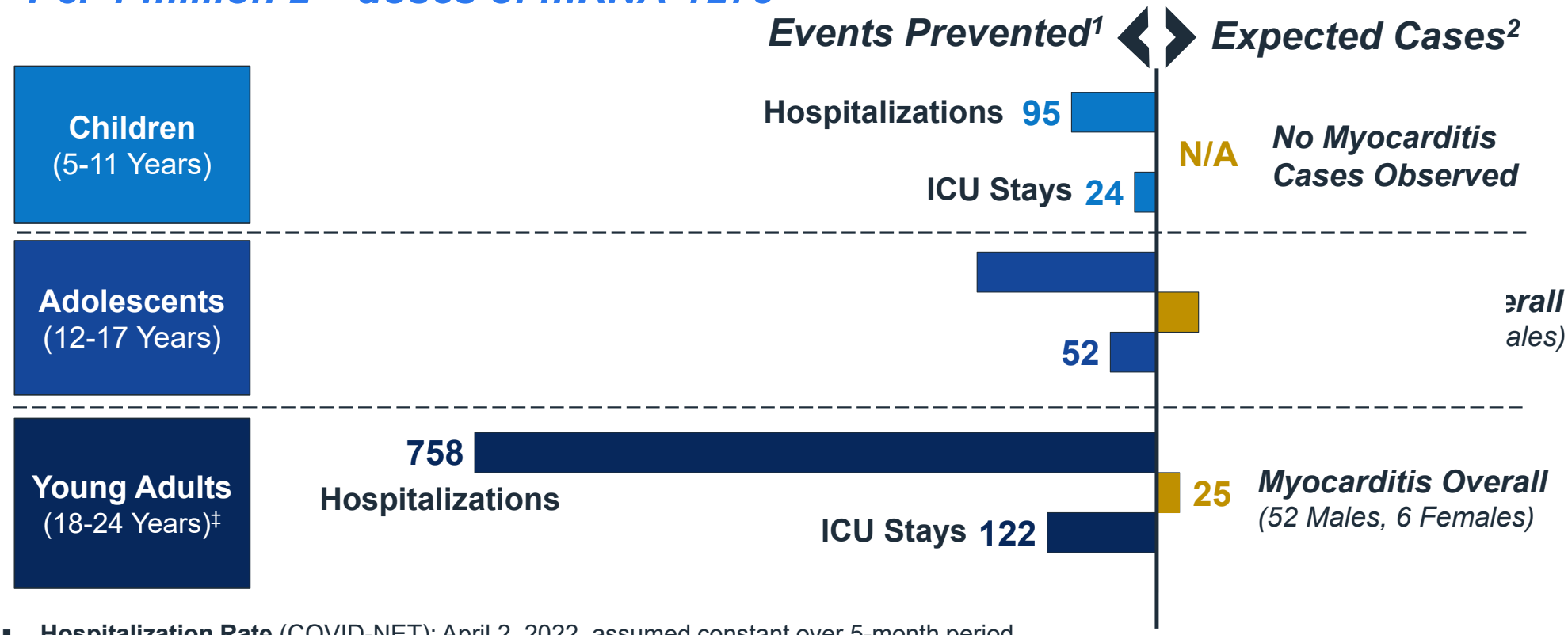
88% - 100% Vaccine Efficacy of mRNA-1273 in Children and Adolescents (6 – 17 Years)

	Per Protocol Analysis (Starting 14 Days PD2)		mITT1 Analysis (Starting 14 Days PD1)	
	mRNA-1273 (100 µg)	**Placebo**	**mRNA-1273** (50 µg)	**Placebo**
CDC case definition of COVID-19				
VE (%) based on incidence rate (95% CI)	**93.3%** (47.9, 99.9)		**88.0%** (70.0, 95.8)	
301 case definition of COVID-19				
VE (%) based on incidence rate (95% CI)	**100%** (28.9, NE)		**91.8%** (74.2, 98.0)	

Ali et al. *NEJM*, 2021; Creech et al. *NEJM*, 2022

Benefit-Risk Assessment: Hospitalizations and ICU Stays Prevented and Expected Myocarditis Cases

Per 1 million 2nd doses of mRNA-1273



- **Hospitalization Rate** (COVID-NET): April 2, 2022, assumed constant over 5-month period
- **Vaccine Effectiveness[3]:** 72% against hospitalization (during Omicron)

1. CDC Wonder; COVID Data Tracker; COVID-NET ; 2. Moderna US PASS – query May 09, 2022 (HealthVerity); 3. UK Health Security Agency, 2021
‡ COVID-NET hospitalization rates cover ages 18-29

Moderna's Ongoing Commitment to Long-Term Evaluation of Safety and Effectiveness of mRNA-1273

Pre-authorization clinical trials

- Administration of booster doses ≥4 months post 2nd dose
- Long-term safety follow-up through 12 months post last dose

Post-authorization observational studies

- 4 ongoing studies to evaluate myocarditis postvaccination in various populations
- 2 PASS assessing vaccine safety, different populations (US & EU) & age groups
- Kaiser Permanente vaccine effectiveness study in different age groups

PASS – Postauthorization Safety Study

Totality of Evidence Supports Benefits of mRNA-1273 in Children & Adolescents Outweigh Potential Risks

Safety (Primary Objective)	▪ mRNA-1273 generally well tolerated ▪ Safety profile consistent with young adults ▪ No new safety concerns have been identified
Immunogenicity (Primary Objective)	▪ Designed to meet FDA recommendations for Emergency Use Authorization for COVID-19 vaccines ▪ Co-primary immunogenicity objectives met for 2-dose primary series
Efficacy (Secondary Objective)	▪ Evidence of vaccine efficacy against COVID-19 with mRNA-1273 ▪ 88% - 100% in children and adolescents (6-17 years)*

*Vaccine efficacy for Children (6-11 Years) based on mITT1 population

Moderna COVID-19 Vaccine Meets FDA Recommendations for EUA for Individuals 6 - 17 Years of Age

1. Clinical trials enrolled >8,000 individuals 6 - 17 years
   - >5,800 participants received ≥ 1 injection of mRNA-1273
   - Median duration of follow-up exceeds 5.6 months
2. Doses selected met pre-specified co-primary immunogenicity objectives compared to young adults 18-25 years of age
3. Vaccine efficacy consistent with efficacy/effectiveness in individuals ≥ 18 years of age
4. Established plans for active safety & effectiveness follow-up post authorization
5. Benefit / risk balance positive in children and adolescents

EUA Request for Moderna COVID-19 Vaccine in Children and Adolescents (6 - 17 Years)

Adolescents
12-17 Years

Primary Series
100 µg, 2-Dose

Children
6-11 Years

Primary Series
50 µg, 2-Dose

Proposed Indication: Prevention of COVID-19 caused by SARS-CoV-2

Primary Series: 2-dose, intramuscular administration 1 month apart

THANK YOU to Our Study Collaborators, Investigators, and Participants

- All investigators
- Study site personnel
- BARDA
- NIH & COV-PN
- Most importantly, the infants, toddlers, children, and adolescents who participated in these trials & their families