From: (b)(4) (b)(4) (x)
Sent: Thu, 27 May 2021 17:54:52 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP); (b)(4) (b)(4) (b)(4) (b)(4)
Subject: (b)(4)
Attachments:

Hi Sara,

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From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Tue, 8 Jun 2021 20:28:37 +0000
To: (b)(4) (b)(4) (x)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: GRADE tables for Moderna
Attachments: ACIP Standard GRADE Tables_Moderna_Adolescent.docx

(b)(4)

Passing along the draft GRADE tables for the adolescent data. Let us know if you have any questions or concerns. In addition- it would be helpful to review the (b)(4)

(b)(4)

Looking forward to potentially receiving the EUA submission fairly soon. We sent the confidentiality agreement Friday- let us know if there is anything else needed from that standpoint as well.

Thanks!

Sara
Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

DRAFT

Please provide complete protocol for the adolescent trial. Make corrections below as needed, especially where highlighted.

Appendix 1

Studies Included in the Review of Evidence

Last name first author, Publication year	Study design	Country (or more detail, if needed)	Age (measure central tendency – mean/SD; range)	Total population	N Intervention	N comparison	Outcomes	Funding source
Phase 2/3 trial	RCT						• Symptomatic laboratory-confirmed COVID-19 • Hospitalization due to COVID-19 • All-cause death • SARS-CoV-2 seroconversion to a non-spike protein • Asymptomatic SARS-CoV-2 infection • Serious adverse events • Reactogenicity grade ≥3	

Table 3a1

Summary of Studies Reporting Symptomatic COVID-19 (PCR-confirmed)

Authors last name, pub year	Age or other characteristic of importance	n/N intervention	n/N comparison	Comparator	Efficacy (95% CI) [100 x (1-IRR)]	
Phase 2/3 trial	Primary[1]: SARS-CoV-2 RT-PCR-positive symptomatic illness[2], in seronegative persons, **≥ 14 days** post second dose			Placebo		
Phase 2/3 trial	SARS-CoV-2 RT-PCR-positive symptomatic illness[1], in *seropositive or seronegative* persons, **≥ 14 days** post second dose			Placebo		
Phase 2/3 trial	SARS-CoV-2 RT-PCR-positive symptomatic illness (according to CDC-defined) symptoms[2]), in seronegative persons, **≥14 days** post second dose			Placebo		
Phase 2/3 trial	SARS-CoV-2 RT-PCR-positive symptomatic illness[2], in seronegative persons **≥ 14 days** post first dose (1 dose VE)			Placebo		
Phase 2/3 trial	SARS-CoV-2 RT-PCR-positive symptomatic illness (according to CDC-defined) symptoms[2]), in seronegative persons **≥ 14 days** post first dose (1 dose VE)			Placebo		

[1] Primary outcome, defined as SARS-CoV-2 RT-PCR-positive symptomatic illness*, in seronegative persons, **≥ 15 days** post second dose. The participant must have experienced at least TWO of the following systemic symptoms: Fever (≥ 38ºC), chills, myalgia, headache, sore throat, new olfactory and taste disorder(s), OR The participant must have experienced at least ONE of the following respiratory signs/symptoms: cough, shortness of breath or difficulty breathing, OR clinical or radiographical evidence of pneumonia; AND The participant must have at least one NP swab, nasal swab, or saliva sample (or respiratory sample, if hospitalized) positive for SARS-CoV-2 by RT-PCR.

[2] The secondary case definition of COVID-19 is defined as the following systemic symptoms: fever (temperature ≥38ºC), or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle aches, or body aches, headache, new loss of taste or smell, sore throat, nasal congestion or rhinorrhea, nausea, or vomiting or diarrhea AND a positive NP swab, nasal swab, or saliva sample (or respiratory sample, if hospitalized) for SARS-CoV-2 by RT-PCR.

Table 3a2

Summary of Studies Reporting Immunogenicity

		Adolescent vaccination (12-15 years)			Young adult vaccination (16-25 years)			
Authors last name, pub year	Age or other characteristic of importance	Sero-positive n/N	Sero-positive %	GMTs (95% CI)	Sero-positive n/N	Sero-positive %	GMTs (95% CI)	GMR[1]
Phase 3 trial	SARS-CoV-2 neutralizing titers in seronegative persons[2] (28 days after receipt of the second dose) of past SARS-CoV-2 infection							

Note: In addition, please provide any other available immunogenicity outcomes, such as T-cell responses.

[1] Estimated by the ratio of the geometric mean of SARS-CoV-2 neutralizing titers in the 2 age groups (12-17 years of age to XXX years of age) 1 month after completion of vaccination. Please provide noninferiority criteria used.

[2] No serological or virological evidence (up to 1 month after receipt of the second dose) of past SARS-CoV-2 infection

Table 3b

Summary of Studies Reporting Hospitalization due to COVID-19

Authors last name, pub year	Age or other characteristic of importance	n/N intervention	n/N comparison	Comparator	Efficacy (95% CI) [100 x (1-IRR)]	
Phase 2/3 trial	Persons aged 12-17			Placebo		

Table 3c

Summary of Studies Reporting All-cause Death[1]

Authors last name, pub year	Age or other characteristic of importance	n/N intervention	n/N comparison	Comparator	Efficacy (95% CI) [100 x (1-IRR)]	

Phase 2/3 trial	Persons aged 12-17			Placebo		

[1]Death from any cause, including COVID-related or SAE.

Table 3d

Summary of Studies Reporting SARS-CoV-2 seroconversion to a non-spike protein[1]

Authors last name, pub year	Age or other characteristic of importance	n/N intervention	n/N comparison	Comparator	% of intervention and placebo groups, p-value	
Phase 2/3 trial	N-binding antibody*, persons aged 12-17			Placebo		

[1]Confirmed seroconversion to SARS-CoV-2 without confirmed COVID-19: positive N-binding antibody result in a participant with a prior negative N-binding antibody result

Table 3e

Summary of Studies Reporting Serial PCRs for Asymptomatic Infection

Authors last name, pub year	Age or other characteristic of importance	n/N intervention	n/N comparison	Comparator	Absolute difference/effect estimate	

Table 3f

Summary of Studies Reporting Serious Adverse Events[1]

Authors last name, pub year	Age or other characteristic of importance	n/N intervention	n/N comparison	Comparator	% (95% CI) of intervention and placebo groups, p-value	

Phase 2/3 trial	Persons aged 12-17			Placebo		

[1]Death, life-threatening event, hospitalization, incapacity to perform normal life functions, medically important event, or congenital anomaly/birth defect

Table 3g

Summary of Studies Reporting Reactogenicity[1]

Authors last name, pub year	Age or other characteristic of importance	n/N intervention	n/N comparison	Comparator	% of intervention and placebo groups, p-value	
Phase 2/3 trial	Local reaction or systemic events [2,3], after either dose			Placebo		
Phase 2/3 trial	Local reaction[2], after either dose			Placebo		
Phase 2/3 trial	Systemic events[3], after either dose			Placebo		
Phase 2/3 trial	Local reaction or systemic events [2,3] post dose 1			Placebo		
Phase 2/3 trial	Local reaction[2], post dose 1			Placebo		
Phase 2/3 trial	Systemic events[3] post dose 1			Placebo		
Phase 2/3 trial	Local reaction or systemic events [2] post dose 2			Placebo		
Phase 2/3 trial	Local reaction[2], post dose 2			Placebo		
Phase 2/3 trial	Systemic events[3], post dose 2			Placebo		

[1]Grade 3 or worse

[2] Grade 3 local reactions include pain at injection site that prevents daily activity or results in use of narcotic pain reliever, erythema/redness > 10 cm, and induration/swelling > 10 cm

[3] Grade 3 systemic events include fever 39.0°C -40.0°C, significant fatigue, chills, myalgia, or arthralgia that prevent daily activity, significant headache that prevents daily activity or results in use of narcotic pain reliever, nausea that prevents daily activity or requires outpatient IV hydration.

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Mon, 5 Apr 2021 15:49:18 +0000
To: (b)(4) (b)(4) T; (b)(4) Mary M.; (b)(4) (b)(4)
Subject: GRADE tables
Attachments: ACIP GRADE Tables_CVWG_Pfizer_BNT162b2_Adolescent_DATAREQUEST.docx

(b)(4) Mary and (b)(4

Hope everyone had a great weekend. I've attached the blank GRADE tables for the adolescent data. We look forward to receiving the data from the EUA amendment submission. Once we receive the data, we can discuss plans around presentations to the WG.

To clarify for our planning (b)(4) (b)(4) There is interest to be able to review that data as well.

Thanks!

Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Co-Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

Appendix 1

Studies Included in the Review of Evidence

Last name first author, Publication year	Study design	Country (or more detail, if needed)	Age (measure central tendency – mean/SD; range)	Total population	N Intervention	N comparison	Outcomes	Funding source
Phase 2/3 trial	RCT						• Symptomatic laboratory-confirmed COVID-19 • Hospitalization due to COVID-19 • All-cause death • SARS-CoV-2 seroconversion to a non-spike protein • Asymptomatic SARS-CoV-2 infection • Serious adverse events • Reactogenicity grade ≥3	

Table 3a1

Summary of Studies Reporting Symptomatic COVID-19 (PCR-confirmed)

Authors last name, pub year	Age or other characteristic of importance	n/N intervention	n/N comparison	Comparator	Efficacy (95% CI) [100 x (1-IRR)]	
Phase 2/3 trial	Primary[1]: SARS-CoV-2 RT-PCR-positive symptomatic illness[2], in seronegative persons, **≥ 7 days** post second dose			Placebo		
Phase 2/3 trial	Secondary: SARS-CoV-2 RT-PCR-positive symptomatic illness[2], in *seropositive or seronegative* persons, **≥ 7 days** post second dose			Placebo		
Phase 2/3 trial	SARS-CoV-2 RT-PCR-positive symptomatic illness[2], in seronegative persons, **≥ 14 days** post second dose			Placebo		
Phase 2/3 trial	Secondary: SARS-CoV-2 RT-PCR-positive symptomatic illness[2], in *seropositive or seronegative* persons, **≥ 14 days** post second dose			Placebo		
Phase 2/3 trial	SARS-CoV-2 RT-PCR-positive symptomatic illness (according to CDC-defined) symptoms[4]), in seronegative persons, **≥ 7 days** post second dose			Placebo		
Phase 2/3 trial	SARS-CoV-2 RT-PCR-positive symptomatic illness (according to CDC-defined symptoms[4]), in seronegative persons, **≥ 14 days** post second dose			Placebo		
Phase 2/3 trial	SARS-CoV-2 RT-PCR-positive symptomatic illness[2], in seronegative persons **≥ 7 days** post first dose (1 dose VE)			Placebo		

[1]Primary outcome, defined as SARS-CoV-2 RT-PCR-positive symptomatic illness, in seronegative adults, **≥ 7 days** post second dose.

[2]Symptomatic illness defined as least one respiratory or other COVID-19-related symptom (Fever, Cough, shortness of breath, chills, muscle pain, loss of taste/smell, sore throat, diarrhea, vomiting), PCR+ during or +/-4 days of symptom onset

[3]Age groups from post-hoc analysis

[4]CDC-defined symptoms include those defining symptomatic illness[2] plus fatigue, headache, nasal congestion, and nausea.

Table 3a2

Summary of Studies Reporting Immunogenicity

		Adolescent vaccination (12-15 years)			Young adult vaccination (16-25 years)			
Authors last name, pub year	Age or other characteristic of importance	Sero-positive n/N	Sero-positive %	GMTs (95% CI)	Sero-positive n/N	Sero-positive %	GMTs (95% CI)	GMR[1]
Phase 2/3 trial	SARS-CoV-2 neutralizing titers in seronegative persons[2] (up to 1 month after receipt of the second dose) of past SARS-CoV-2 infection							

Note: In addition, please provide any other available immunogenicity outcomes, such as T-cell responses.

[1] Estimated by the ratio of the geometric mean of SARS-CoV-2 neutralizing titers in the 2 age groups (12-15 years of age to 16-25 years of age) 1 month after completion of vaccination

[2] No serological or virological evidence (up to 1 month after receipt of the second dose) of past SARS-CoV-2 infection

Table 3b

Summary of Studies Reporting Hospitalization due to COVID-19

Authors last name, pub year	Age or other characteristic of importance	n/N intervention	n/N comparison	Comparator	Efficacy (95% CI) [100 x (1-IRR)]	
Phase 2/3 trial	Persons aged 12-15			Placebo		

Table 3c

Summary of Studies Reporting All-cause Death[1]

Authors last name, pub year	Age or other characteristic of importance	n/N intervention	n/N comparison	Comparator	Efficacy (95% CI) [100 x (1-IRR)]	
Phase 2/3 trial	Persons aged 12-15			Placebo		

[1]Death from any cause, including COVID-related or SAE.

Table 3d

Summary of Studies Reporting SARS-CoV-2 seroconversion to a non-spike protein[1]

Authors last name, pub year	Age or other characteristic of importance	n/N intervention	n/N comparison	Comparator	% of intervention and placebo groups, p-value	
Phase 2/3 trial	N-binding antibody*, persons aged 12-15			Placebo		

[1]Confirmed seroconversion to SARS-CoV-2 without confirmed COVID-19: positive N-binding antibody result in a participant with a prior negative N-binding antibody result

Table 3e

Summary of Studies Reporting Serial PCRs for Asymptomatic Infection

Authors last name, pub year	Age or other characteristic of importance	n/N intervention	n/N comparison	Comparator	Absolute difference/effect estimate	

Table 3f

Summary of Studies Reporting Serious Adverse Events[1]

Authors last name, pub year	Age or other characteristic of importance	n/N intervention	n/N comparison	Comparator	% (95% CI) of intervention and placebo groups, p-value	
Phase 2/3 trial	Persons aged 12-15			Placebo		

[1]Death, life-threatening event, hospitalization, incapacity to perform normal life functions, medically important event, or congenital anomaly/birth defect

Table 3g

Summary of Studies Reporting Reactogenicity[1]

Authors last name, pub year	Age or other characteristic of importance	n/N intervention	n/N comparison	Comparator	% of intervention and placebo groups, p-value	
Phase 2/3 trial	Local reaction or systemic events [2,3], after either dose			Placebo		
Phase 2/3 trial	Local reaction[2], after either dose			Placebo		
Phase 2/3 trial	Systemic events[3], after either dose			Placebo		
Phase 2/3 trial	Local reaction or systemic events [2,3] post dose 1			Placebo		
Phase 2/3 trial	Local reaction[2], post dose 1			Placebo		
Phase 2/3 trial	Systemic events[3] post dose 1			Placebo		
Phase 2/3 trial	Local reaction or systemic events [2] post dose 2			Placebo		
Phase 2/3 trial	Local reaction[2], post dose 2			Placebo		
Phase 2/3 trial	Systemic events[3], post dose 2			Placebo		

[1]Grade 3 or worse

[2] Grade 3 local reactions include pain at injection site that prevents daily activity, redness > 10 cm, and swelling > 10 cm

[3] Grade 3 systemic events include vomiting that requires IV hydration, Diarrhea of 6 or more loose stools in 24 hours, or headache, fatigue/tiredness, chills, new or worsened muscle pain, or new or worsened joint pain that prevent daily routine activity.

From: (b)(4) (b)(4) (x)
Sent: Fri, 2 Jul 2021 13:50:12 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: JCVI Statement - Booster Doses

Hi Sara,
I assume you have seen this statement from the JCVI, but sending just in case.

https://www.gov.uk/government/publications/jcvi-interim-advice-on-a-potential-coronavirus-covid-19-booster-vaccine-programme-for-winter-2021-to-2022/jcvi-interim-advice-potential-covid-19-booster-vaccine-programme-winter-2021-to-2022
(b)(4)

Please consider the environment before printing this email

From: (b)(4) (b)(4) (x)
Sent: Fri, 11 Jun 2021 12:41:04 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: June 18 ACIP Meeting - Moderna Representatives

HI Sara,
Thanks for allowing us to be on the call for the June 18 ACIP meeting to address any questions that might arise for Moderna. I would ask that the following individuals be on the line:
(b)(4) (b)(4) (b)(4)
(b)(4) (b)(4) (b)(4)
Me (b)(4)
I assume we will be sent a separate meeting invite. Thanks very much.
(b)(4)

From: (b)(4) (b)(4) (x)
Sent: Mon, 19 Jul 2021 22:09:02 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Manuscript - Adolescent Study of Moderna COVID-19 Vaccine - CONFIDENTIAL
Attachments: COVID-19 - P203 Adolescent Study - Confidential Embargoed Manuscript with revisions - July 14 CLEAN VERSION (1).pdf

Hi Sara,
The attached manuscript on our adolescent study has been accepted for publication in the *NEJM*. We have yet to receive the proofs, so it may be a while before published, but I wanted to make sure you had a copy.
Please handle this as confidential as it is embargoed by *NEJM*. You may share with your CDC colleagues who are covered under the CDA, but we ask that this not be shared with the WG at this time.
I hope this is helpful.
(b)(4)

Please consider the environment before printing this email

Evaluation of mRNA-1273 SARS-CoV-2 Vaccine in Youths 12 to <18 Years of Age

Authors: Kashif Ali, M.D.[*], Gary Berman, M.D.[*], Honghong Zhou, Ph.D., Weiping Deng, Ph.D., Veronica Faughnan, B.S., Maria Coronado-Voges, M.S., Baoyu Ding, M.S., Jacqueline Dooley, B.A., Bethany Girard, Ph.D., William Hillebrand, M.S., Rolando Pajon, Ph.D., Jacqueline M Miller, M.D., Brett Leav, M.D., Roderick McPhee, M.D., Ph.D.[†]

From DM Clinical Research-Kool Kids Pediatrics, Houston, TX (K.A.); Clinical Research Institute, Minneapolis, MN (G.B.); Moderna, Inc., Cambridge, MA (H.Z., W.D., V.F., M.C.-V., B.D., J.D., B.G., W.H., R.P., J.M.M., B.L., R.M.)

- *Drs. Ali and Berman contributed equally to this article
- [†]Corresponding author: Roderick McPhee, roderick.mcphee@modernatx.com

Abstract

Background

Adolescents 12-17 years of age had an incidence rate of Covid-19 of approximately 900 per 100,000 population from 1April-11June, 2021. The safety, immunogenicity and efficacy data of mRNA-1273 in adolescents was tested.

Methods

This ongoing phase 2/3 observer-blind, placebo-controlled study randomized healthy adolescents 12-<18 years of age 2:1 to receive 2 injections of 100 µg of mRNA-1273 or placebo 28 days apart. The primary objectives were to evaluate the safety of mRNA-1273 and to infer efficacy by demonstrating non-inferior immune responses in adolescents compared with those of young adults (18-≤25 years) from the phase 3 COVE study of mRNA-1273. Secondary endpoints included the efficacy of mRNA-1273 at preventing Covid-19 or asymptomatic infection.

Results

A total of 3,732 participants were randomized to receive mRNA-1273 (n=2,489) or placebo (n=1,243). The most common solicited adverse reactions after the first or second injections were injection site pain (92.4%; 93.1%), headache (44.6%; 70.2%) and fatigue (47.9%; 67.8%). No related serious adverse events were noted. The immune response in adolescents was non-inferior to that in young adults demonstrated by the geometric mean titer ratio of pseudovirus neutralizing antibody (1.08 [95% CI 0.94−1.24]) and the difference in seroresponse rates (0.2% [95% CI -1.8−2.4]). In the mRNA-1273 group, no cases of Covid-19 starting 14 days post-injection 2 were reported compared to four cases in the placebo group.

Conclusions

The mRNA-1273 vaccine was safe in adolescents. The immune response was comparable to that of young adults and the vaccine was efficacious in preventing Covid-19.

Trial registration number: NCT04649151

Introduction

Coronavirus disease 2019 (Covid-19) has resulted in significant global morbidity and mortality.[1] Adolescents 12-17 years of age had a cumulative incidence rate of Covid-19 of approximately 900 per 100,000 population from April 1, 2021 to June 11, 2021.[2] Although Covid-19 illness is generally milder in children than adults, children can experience severe disease requiring hospitalization.[3,4] Approximately one-third of adolescents hospitalized due to Covid-19 were admitted to an intensive care unit and 4.9% required invasive mechanical ventilation.[4] Multisystem inflammatory syndrome (MIS-C) is a serious but rare condition associated with Covid-19 that occurs in children who present with fever, rash, conjunctival injection, and gastrointestinal symptoms.[5] Opening schools may indirectly be associated with a 26% increase in SARS-CoV-2 transmission from children and teenagers.[6] Children continue to be disproportionately impacted by the Covid-19 pandemic in social costs (stressors, school closures, loss of social support, child maltreatment).[7-10]

The mRNA-1273 vaccine is a liquid nanoparticle dispersion containing an mRNA that encodes the SARS-CoV-2 S glycoprotein stabilized in the prefusion conformation. The safety, immunogenicity and efficacy of mRNA-1273 has been evaluated in several ongoing clinical trials in adults.[11-15] The mRNA-1273 vaccine was safe and highly effective in preventing Covid-19 in a large phase 3 trial,[15] which supported the emergency use authorization of mRNA-1273 in adults 18 years of age and older in December 2020.[16] Based on these data, the randomized, observer-blind, placebo-controlled phase 2 study (TeenCOVE) evaluated the safety, immunogenicity and efficacy of 100 µg of mRNA-1273 administered as two injections in an adolescent population aged 12-<18 years.

Methods

Trial design

This phase 2/3 observer-blind, placebo-controlled study, conducted as a two-part study (Parts A [blinded evaluation of safety, immunogenicity, and efficacy] and B [open-label follow-up, implemented once an Emergency Use Authorization had been issued for mRNA-1273 for adolescents to allow the cross-over vaccination of placebo recipients]), randomized healthy adolescents 12-<18 years of age 2:1 to receive 2 injections of 100 µg of mRNA-1273 or placebo 28 days apart (Fig. 1). Interim results from the blinded part of the ongoing study are reported here (NCT04649151). The study was conducted in accordance with the International Council on Harmonization of Good Clinical Practice guidelines and the protocol was approved by regulatory and institutional committees (supplementary protocol). All participants provided informed consent. The study Sponsor, Moderna, was responsible for the overall trial design (with input from the Biomedical Advanced Research and Development Authority), site selection and monitoring, and data analysis. Investigators were responsible for data collection. Two medical writers funded by Moderna assisted in drafting the manuscript for submission. The authors vouch for the accuracy and completeness of the data and for the fidelity of the trial to the protocol.

Participants, randomization and blinding

Males or females, 12-<18 years of age, considered in good general health by the 26 U.S. investigators (see List of Investigators in the Supplementary Appendix), were eligible for enrollment into the study. Exclusion criteria included travel outside of the United States in the 28 days before screening, pregnancy or breastfeeding, acute illness or fever 24 hours before or at screening, prior administration of an investigational CoV vaccine, or current treatment with investigational agents for prophylaxis against Covid-19. This trial did not exclude participants with prior anaphylaxis or serious allergic

reactions to foods/medications other than to a vaccine. Full inclusion and exclusion criteria are provided in the Supplementary Appendix.

Part A participants were randomly assigned to receive two injections of either 100 μg of mRNA-1273 vaccine or placebo (saline) in a 2:1 ratio using a centralized Interactive Response Technology. The investigators and study staff, participants, site monitors, and sponsor personnel (or its designees) were blinded to the study vaccine administered until the end of Part A or the initiation of Part B, except for unblinded pharmacists and vaccine administrators involved in injection preparation and administration and who had no other role in study conduct.

Trial vaccine

The mRNA-1273 vaccine encodes the prefusion stabilized S protein of SARS-CoV-2. The mRNA-1273 vaccine contains 100 μg of mRNA and was formulated in lipid nanoparticles as previously described.[15]

Safety assessments

The primary safety objective was to evaluate the safety and reactogenicity of 100 μg of mRNA-1273 administered in 2 injections 28 days apart (Table S1). Participants recorded solicited local and systemic adverse reactions daily through 7 days after each injection by completing an electronic diary. Unsolicited adverse events from days 1 through 28 after each injection and medically-attended adverse events, adverse events leading to withdrawal, serious adverse events, and MIS-C data were collected until end of study participation. A data safety monitoring board conducted periodic unblinded data reviews.

Efficacy assessments

The primary immunogenicity objective was to infer the efficacy of mRNA-1273 in adolescents by comparing serum antibody responses, as measured by the coprimary endpoints: geometric mean

(GM) and seroresponse rate in adolescents 28 days post-second injection (day 57) in Part A with those of young adult (18- ≤25 years of age) recipients of mRNA-1273 in the efficacy phase 3 trial (COVE) (Table S1). Neutralizing antibody (nAb) titers were measured using a validated lentivirus pseudovirus (D614G) assay with ID50 as the primary endpoint described in the supplementary methods. Binding antibodies specific to the SARS-CoV-2 spike protein measured by a Meso Scale Discovery (MSD) and an enzyme-linked immunsorbent assay (ELISA) were used as supportive analyses.

The secondary endpoints included evaluations of mRNA-1273 compared with placebo on the incidence of SARS-CoV-2 infection, asymptomatic SARS-CoV-2 infection, and Covid-19 (defined as clinical symptoms consistent with SARS-CoV-2 infection and positive RT-PCR for SARS-CoV-2) starting 14 days after the second injection (Table S1). Vaccine efficacy was calculated as 1 minus the ratio of incidence rate per 1,000 person years (mRNA-1273 vs. placebo). Covid-19 was defined in two ways using the primary case definition per the phase 3 COVE study of at least two systemic symptoms OR at least one respiratory symptom AND at least one nasopharyngeal [NP) swab, nasal swab or saliva sample positive for SARS-CoV-2 by RT-PCR. Due to a lower incidence rate and milder symptoms of Covid-19 in adolescents, a secondary case definition based on the CDC criteria of Covid-19 was also evaluated that required one systemic or respiratory symptom AND a positive RT-PCR for SARS-CoV-2.[17] The assessment of vaccine efficacy using the PP Efficacy Set and starting 2 weeks after the second dose was consistent with the analysis set used in the pivotal phase 3 study of mRNA-1273 in adults. The assessment of vaccine efficacy in adolescents using the mITT1 Set and starting 2 weeks after the first dose was more aligned with the epidemiology and pathophysiology of COVID-19 in adolescents and allowed a longer observation period for case occurrence. An analysis of vaccine efficacy starting 14 days after the second dose (mITT1) could not be performed because the mITT1 group excluded those who did not receive the second dose. Asymptomatic infection was a composite

endpoint determined by positive serology against the nucleocapsid antigen (indicating the presence of anti-nucleocapsid antibodies as markers of previous immunologic exposure) or positive RT-PCR for SARS-CoV-2 at scheduled/unscheduled visits post-baseline without any Covid-19 symptoms in participants with negative SARS-CoV-2 serology and negative RT-PCR at baseline.

Statistical methods

Approximately 3,000 participants were planned to be randomized in a 2:1 ratio to receive mRNA-1273 and placebo. With 2,000 participants exposed to mRNA-1273, the study had at least 90% probability to observe at least one adverse event at a true 0.25% adverse event rate. The safety analysis was performed in the safety set which included all participants who received any study injection.

The primary immunogenicity analysis was performed using the per-protocol (PP) immunogenicity subset. An immunogenicity subset was selected to be representative of the overall study adolescents, and an immunogenicity subset was randomly selected from the 18- ≤25 age group in the COVE study. In the phase 3 COVE trial, a random sample of 340 young adults (18 – ≤25 years of age) who had been randomized to receive mRNA-1273 and received at least one dose of mRNA-1273 (Full Analysis Set) with available baseline SARS-CoV-2 status were selected for the comparison/immunogenicity analysis with adolescents 12 to <18 years of age. The selection of these 340 participants from the COVE trial using a random number generator in March 2021was based on the Full Analysis Set from the primary analysis (data snapshot 25-Nov-2020) which supported the Emergency Use Authorization (EUA) in the US for the mRNA-1273 vaccine in adults. The PP immunogenicity subset included participants who received planned injections of study vaccination and immunogenicity blood sampling per schedule, with negative SARS-CoV-2 status at baseline, and had no major protocol deviations. For the primary immunogenicity objective, with approximately 289

adolescents and 289 young adults on mRNA-1273 planned, the study had >90% power to demonstrate non-inferiority of the immune response for adolescents vs. young adults (success criteria for the coprimary endpoints: GM ratio 95% CI lower bound >0.67 using a noninferiority margin of 1.5, and point estimate >0.80; and seroresponse rate difference 95% CI lower bound >-10% using a noninferiority margin of 10%, and point estimate >-5%) as detailed in the Supplementary Appendix.

Results

Trial population

During 09 December 2020 to 28 February 2021, 3732 participants were randomized 2:1 to receive mRNA-1273 (N=2489) or placebo (N=1243) at 25 sites in the U.S. (Figs. 1 and S2). More than 98% of participants received a second injection. The most common reasons for not receiving a second injection were withdrawal of consent (10 participants) and lost to follow-up (8 participants).

Baseline characteristics were generally balanced between the placebo and mRNA-1273 groups. The mean age of the participants was 14.3 years (74% were 12-<16 years), half of the participants were male (51%), most were White (84%), not Hispanic or Latino (88%), and 93% had body mass indices of <30 kg/m2 (Table 1). Approximately 5.8% of participants were positive for SARS-CoV-2 at baseline. The median durations of follow up from randomization and from the second injection were 83 and 53 days, respectively. The demographics of adolescents 12-<18 years were generally similar to those of adults in the phase 3 COVE trial (Supplementary Table S12). Two percent of adults in the COVE trial had a positive SARS-C0V-2 status at baseline compared to 5.8% of adolescents 12-<18 years. The demographics of the Per-protocol Immunogenicity subsets are shown in Supplementary Table S10. The percentages of adolescents 12-<18 years vs. young adults 18-≤25 years were 7.6% vs 26.6% for Hispanic, 1.2% vs. 11.1% for Black or African-Americans, and 78.5% vs. 48.2% for White non-Hispanic, respectively (Supplementary Table S10).

Safety

Solicited local reactions occurred more frequently in the mRNA-1273 group after the first (94.2%) and second (93.4%) injections than placebo (36.8% and 32.6%) and the occurrence of grade 3 events was 6.8% after the first injection and 8.9% after the second injection (Fig. 2 and Table S2). The most common solicited local reaction was injection site pain after the first (93.1%, grade 3: 5.4%) and

second (92.4%, grade 3: 5.1%) injections of mRNA-1273 versus placebo (34.8% and 30.3%). Systemic adverse reactions were 68.5% after the first injection and 86.1% after the second injection as were grade 3 events (4.4% vs 13.7%) in the mRNA-1273 group. The most common systemic reactions were fatigue, headache, myalgia and chills. Grade 3 fever occurred in 1.9% and grade 4 fever in one mRNA-1273 recipient after injection 2 (Fig. 2 and Table S2). Solicited local or systemic reactions generally persisted for approximately 3 days (median, Table S4). Incidences of local reactions that persisted beyond 7 days were numerically higher in the mRNA-1273 group than in the placebo group and were also higher after the first (6.4%) vs second (1.6%) injection in the mRNA-1273 group (Table S5), primarily attributed to axillary swelling or tenderness. The local reactions with onset after day 7 after any injection occurred in 1.3% of mRNA-1273 recipients (erythema 0.7%, swelling 0.4%, and axillary swelling or tenderness 0.4%). The incidences of solicited systemic reactions that persisted beyond 7 days were similar between the mRNA-1273 (3.1%) and placebo groups (2.6%), and those with onset after day 7 following any injection occurred in 0.7% of mRNA-1273 and 0.3% of placebo recipients. Solicited reactions were generally similar between participants aged 12-<16 and those 16-<18 years (Fig. S4). Solicited local reactions in adolescent participants and young adults (18- ≤25 years) were similar between the 2 groups but erythema was higher in adolescents than young adults (Table S8).

Unsolicited adverse events up to 28 days after any injection were more frequent in participants in the mRNA-1273 (20.5%) group than the placebo (15.9%) group (Table S3); most commonly injection site lymphadenopathy (4.3%) and headache (2.4%). Treatment-related adverse events up to 28 days were reported by 12.6% participants in the mRNA-1273 and 5.8% in the placebo groups. One participant experienced a medically-attended adverse event of grade 2 anaphylaxis to tree nuts on day 21 after the second injection of mRNA-1273 that was considered unrelated to vaccine. No deaths,

MIS-C, severe adverse events or adverse events of special interest occurred. No cases of myocarditis or pericarditis have been reported to date.

Immunogenicity

The primary analysis was based on non-inferiority of nAb titers in adolescents in this trial compared with young adults in the COVE study. The GMT ratio (95% CI) for nAbs between adolescents and young adults was 1.08 (0.94−1.24). The levels of antibodies specific for the spike protein are shown in Table S6. In addition, the seroresponse rates were 98.8% in adolescents and 98.6% in young adults, and the differences (95% CI) in seroresponse rates between adolescents and young adults was 0.2% (-1.8%−2.4%). Therefore, the criteria for non-inferiority were met for both co-primary endpoints.

Efficacy

The vaccine efficacy (VE) of mRNA-1273 14 days after the second injection was difficult to assess precisely because of the low incidence of Covid-19 in the study population (4 cases for placebo, none for mRNA-1273) (Fig. 3; Table S7). The VE (95% CI) of mRNA-1273 for the less stringent CDC definition of Covid-19 starting 14 days after the second injection was 93.3% (47.9-99.9%) in the PP set, and 92.7% (67.8−99.2%) for cases starting 14 days after the first injection in the mITT1 set (Fig. 3; Fig. S2 [cumulative incidence curve]). For the secondary endpoints of preventing SARS-CoV-2 infection starting 14 days after the second (PP set) and first (mITT1 set) injections, the VE estimates (95% CI) of mRNA-1273 were 55.7% (16.8−76.4%) and 69.8% (49.9−82.1%), respectively (Fig. 3; Table S7). The VEs (95% CI) of mRNA-1273 were 39.2% (-24.7−69.7%) for asymptomatic infection starting 14 days after the second injection (PP set) and 59.5% (28.4−77.3%) starting 14 days after the first injection (mITT1 set) (Fig. 3; Table S7). The breakdown of asymptomatic cases by RT-PCR and

serology starting 14 days after dose 1 (mITT1 analysis set) were 14 vs. 20 by RT-PCR and 15 vs. 15 by serology against nucleocapsid for mRNA-1273 vs. placebo, respectively (Table S11). The person-years of follow-up were 238-248 (2,856-2,976 person-months) for the placebo group and 513-522 (6,156-6,264 person-months) for mRNA-1273 (Table S7).

Discussion

The results from this TeenCOVE trial in adolescents 12-<18 years of age extend the evidence of safety and efficacy of mRNA-1273 previously demonstrated in adults.[14,15] The primary immunogenicity objective was met, demonstrating the non-inferiority of immune response based on both the GMT and serorespose rate in adolescents 12-<18 years of age compared to young adults 18-≤25 years of age. It is difficult to compare these results with mRNA-1273 with those for BNT162b2 in which the neutralizing antibody titers in adolescents were higher than that in young adults because the neutralizing antibodies for mRNA-1273 were measured in a pseudovirus assay whereas those for BNT162b2 were measured in a live virus neutralization assay.[18] The safety and reactogenicity of mRNA-1273 in adolescents (12-<18 years) was similar to that observed in adults (≥18-65 years) in the phase 2 and phase 3 COVE trials.[14,15] Additionally, the vaccine efficacy in these adolescents was 93% when considering the less stringent CDC case definition.

Several studies have examined transmission of SARS-CoV-2 in children and adolescents and have generally concluded that most infections in this age group result from household exposure rather than from in-person learning.[19-22] While the precise role of adolescents in transmission of SARS-CoV-2 to adults is not known, it seems reasonable that widespread vaccination of this younger age group could further decrease community transmission and potentially contribute to "herd immunity".[23] Therefore, a safe and effective COVID-19 vaccine could reduce COVID-19 related morbidity and mortality. The availability of effective vaccines for this age group is also important to further reduce the reservoir of SARS-CoV-2. The BNT162b2 vaccine was authorized for emergency use in adolescents 12-15 years old.[24,25]

No cases of myocarditis or pericarditis have been reported to date in this trial. The incidence of myocarditis and pericarditis associated with mRNA COVID-19 vaccination reported in young males has been estimated to be in the range of 13 cases per million doses of vaccine and so it is not unexpected that these events have not been detected in this trial.[26] Current post-licensure vaccine surveillance systems, including the Vaccine Adverse Event Reporting System (VAERS) and the Vaccine Safety Data Link (VSD) are robust to detect exceedingly rare events that cannot be identified in clinical trials.

This study has several limitations. The efficacy analyses were secondary objectives of the trial due to milder Covid-19 disease and a lower disease incidence in adolescents compared with adults in the phase 3 COVE trial. However, the inference of efficacy based on non-inferiority comparison of the immunogenicity results combined with the preliminary estimate of efficacy of mRNA-1273 in adolescents in this trial provides support for the idea that the mRNA-1273 vaccine will be effective in adolescents 12-<18 years of age. A relatively limited number of asymptomatic infections resulted in a negative lower bound of the 95% CI for efficacy starting 14 days after a second mRNA-1273 injection; however, the number of asymptomatic cases after the first injection was higher with vaccine efficacy of 59.5% (95% CI:28.4-77.3%). The efficacy of mRNA-1273 for asymptomatic infection in adults also appears to be lower than that for symptomatic disease in adults. However, the latter was based solely on detection of RT-PCR positive swabs in the absence of symptoms.[15] The safety data presented here for mRNA-1273 in adolescents are based on an interim analysis of 83 median days of follow up from randomization and may change over time. Finally, the study population was less diverse compared to the COVE study and, as such, less representative of the US population.

In this interim analysis of the ongoing study, the overall benefit-risk profile of mRNA-1273 was favorable in adolescents. The immunogenicity of mRNA-1273 in adolescents was non-inferior to

that in young adults in the phase 3 COVE study, with a similar safety profile. The number of documented cases of Covid-19 is too small to generate robust assessments of vaccine efficacy. However, it appears that the mRNA-1273 vaccine safely induces levels of antiviral antibody that should be protective against SARS-CoV2 infection.

Acknowledgements

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Tables

Table 1: Demographics and Characteristics In Safety Set

Characteristic n (%)	Placebo N=1240	mRNA-1273 (100 µg) N=2486	Total N=3726
Age (years)			
Mean (SD) yr	14.2 (1.6)	14.3 (1.6)	14.3 (1.6)
16 to <18 years	311 (25)	648 (26)	959 (26)
12 to <16 years	929 (75)	1838 (74)	2767 (74)
Gender			
Male	632 (51)	1283 (52)	1915 (51)
Female	608 (49)	1203 (48)	1811 (49)
Race			
White	1041 (84)	2085 (84)	3126 (84)
Black or African-American	42 (3)	83 (3)	125 (3)
Asian	79 (6)	142 (6)	221 (6)
Native Hawaiian or Other Pacific Islander	0 (0)	2 (<1)	2 (<1)
American Indian or Alaska Native	7 (<1)	12 (<1)	19 (<1)
Multiracial	50 (4)	118 (5)	168 (5)
Other	9 (<1)	27 (1)	36 (1)
Not reported	11 (<1)	11 (<1)	22 (<1)
Unknown	1 (<1)	6 (<1)	7 (<1)
Ethnicity			
Hispanic or Latino	152 (12)	280 (11)	432 (12)
Not Hispanic or Latino	1076 (87)	2188 (88)	3264 (88)
Not reported or Unknown	12 (1)	18 (<1)	30 (<1)
Race and ethnicity group			
White non-Hispanic	912 (74)	1857 (75)	2769 (74)
Communities of Color	325 (26)	625 (25)	950 (26)
Missing	3 (<1)	4 (<1)	7 (<1)
RT-PCR results at baseline			
Positive	9 (<1)	13 (<1)	22 (<1)
Negative	1139 (92)	2308 (93)	3447 (93)
Missing	92 (7)	165 (7)	257 (7)
Serology result against nucleocapsid antigen at baseline			
Positive	63 (5)	139 (6)	202 (5)
Negative	1153 (93)	2299 (92)	3452 (93)
Missing	24 (2)	48 (2)	72 (2)
Positive baseline SARS-CoV-2 status*	69 (6)	147 (6)	216 (6)
Negative baseline SARS-CoV-2 status †	1075 (87)	2167 (87)	3242 (87)
Missing baseline SARS-CoV-2 status	96 (8)	172 (7)	268 (7)
Body Mass Index (kg/m^2)			
< 30	1146 (92)	2316 (93)	3462 (93)
≥ 30	94 (8)	170 (7)	264 (7)
Study duration from randomization to database lock (median [range]) days	82.0 [9, 151]	83.5 [30, 151]	83.0 [9, 151]

Study duration from second injection to database lock (median [range]) days	51.0 (0, 121)	53.0 (0, 121)	53.0 (0, 121)
* Positive if there is immunologic or virologic evidence of prior Covid-19, defined as positive RT-PCR test or positive serology result for the nucleocapsid antigen at Day 1. † Negative is defined as a negative RT-PCR test and negative Elecsys serology result at Day 1. SD=standard deviation.			

Table 2: Immunogenicity of mRNA-1273 in Adolescents and Young Adults

	Adolescents 12 to <18 yrs N=340	**Young Adults 18 to ≤25 yrs N=296**	**Difference***
Seroresponse, % (n) (95% CI)	98.8% (336) (97.0, 99.7)	98.6% (292) (96.6, 99.6)	0.2% (-1.8, 2.4)
	Adolescents 12 to <18 yrs N=340	**Young Adults 18 to ≤25 yrs N=296**	**GMT Ratio (95% CI)**
Pseudovirus neutralizing antibody titer (Geometric Mean Titers, [95% CI])	1401.67 (1276.30, 1539.36)	1301.31 (1176.98, 1438.78)	1.08 (0.94, 1.24)

*Difference is Adolescent's seroresponse rate–Young Adult's seroresponse rate. The ID50 titer of neutralizing antibodies was determined at day 57 (one month after second injection of mRNA-1273) in a pseudovirus (Wuhan-Hu-1 isolate including D614G) assay. Seroresponse for the ID50 of pseudovirus neutralizing antibody was defined as a change from below the lower limit of quantitation (LLOQ) at baseline to equal or above LLOQ, or at least a 3.3-fold rise if baseline is equal to or above LLOQ. Seroresponse rate 95% confidence intervals (CIs) were calculated using the Clopper-Pearson method. 95% CI for the difference was calculated using the Miettinen-Nurminen (score) confidence limits. Neutralizing antibody values reported as below the lower limit of quantification (LLOQ) were replaced by 0.5 x LLOQ. Values greater than the upper limit of quantification (ULOQ) are replaced by the ULOQ if actual values are not available. The log-transformed antibody levels were analyzed using an analysis of covariance (ANCOVA) model with the group variable (adolescents in P203 and young adults in P301) as fixed effect. The resulted Least Square means, the difference of Least Square means, and 95% CI were back transformed to the original scale for presentation.

Figure 1: Trial Profile

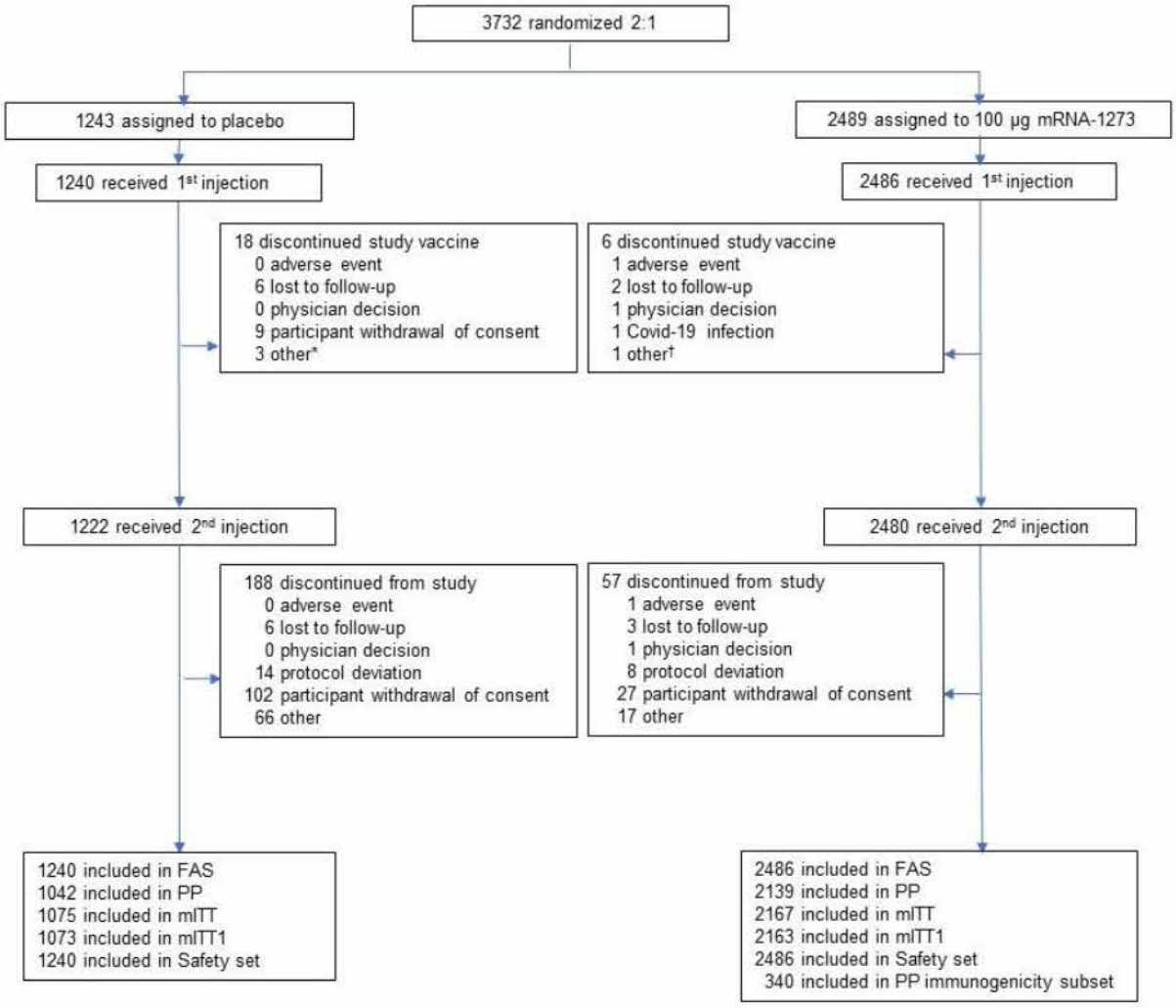

Figure 1. Trial Profile. FAS= Full analysis set, all randomized participants who received at least 1 injection; PP= Per-Protocol for Efficacy, all participants in the FAS who received planned injections of study vaccination, complied with the timing of injection 2, had no immunologic and virologic evidence of prior Covid-19 at baseline, and no major protocol deviations; mITT= Modified Intent-to-Treat Set, all participants in the FAS who had no serologic or virologic evidence of prior SARS-CoV-2 infection before the first injection (both negative RT-PCR test for SARS-CoV-2 and negative serology test based on bAb specific to SARS-CoV-2 nucleocapsid) at baseline; mITT1= all participants in the mITT Set excluding those who received the wrong treatment; Safety set= All randomized participants who received at least 1 injection. The PP Immunogenicity Subset included participants selected for the Immunogenicity Subset who received planned injections of study vaccination per schedule, complied with the timing of injection 2, had no immunologic and virologic evidence of prior Covid-19 at baseline, complied with immunogenicity testing schedule, and had no major protocol deviations that impacted

key or critical data (participants who were seropositive at baseline were excluded from the PP Immunogenicity Subset).

*Two placebo recipients did not receive injection 2 and then discontinued study later with "other" reason [†]One mRNA-1273 recipient did not receive injection 2 and continued study.

Figure 2: Solicited Local and Systemic Adverse Events

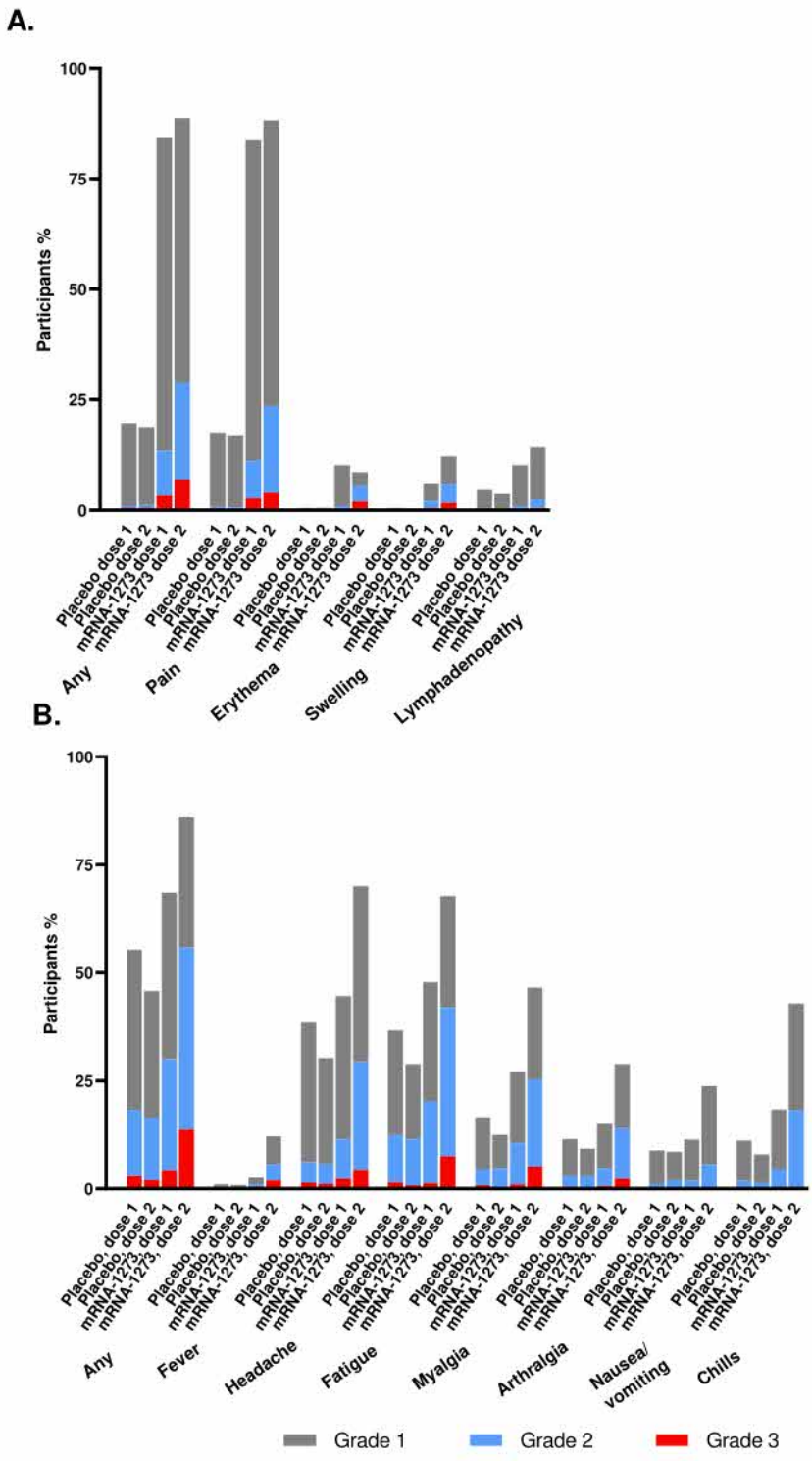

Figure 2. Solicited Local and Systemic Adverse Events: Solicited local (A) and systemic (B) adverse events.

Figure 3: Secondary Analyses of Efficacy

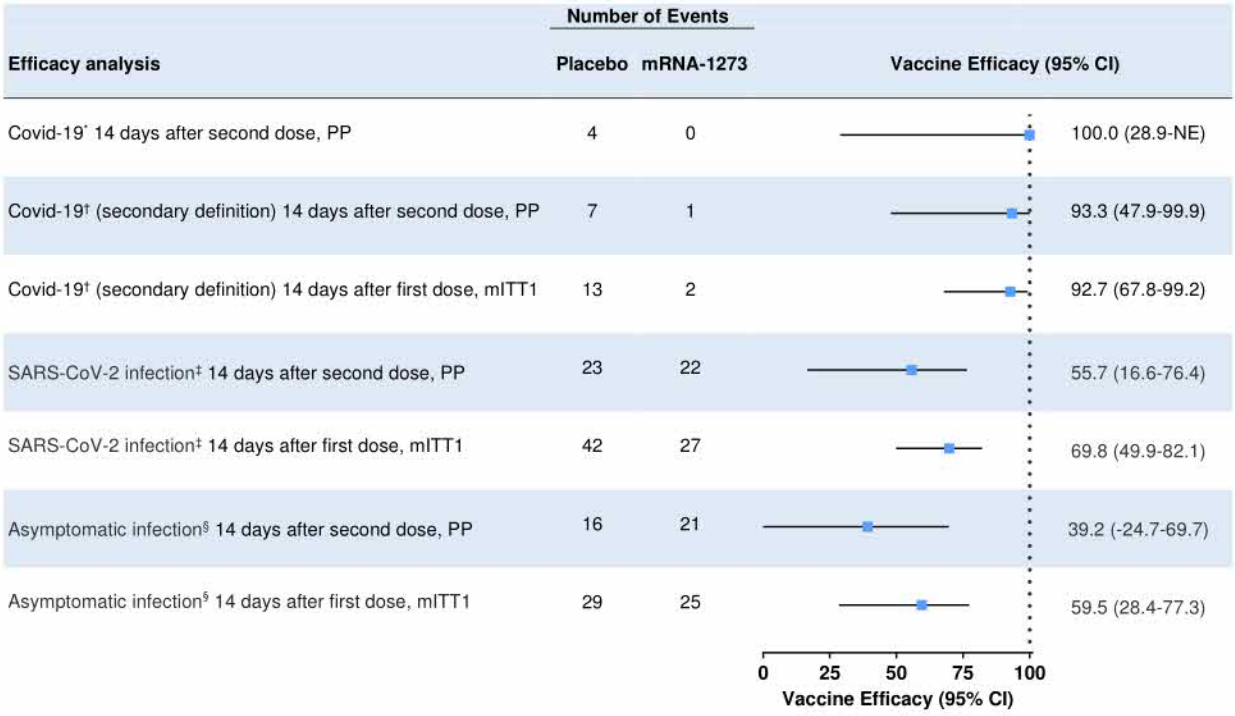

Figure 3. Secondary Analyses of Efficacy. Vaccine efficacy was calculated as 1 minus the ratio of incidence rate per 1,000 person years (mRNA-1273 vs. placebo). *Covid-19 and †Secondary case Covid-19 were defined as described in the Methods section. ‡ SARS-CoV-2 Infection (regardless of symptoms): A combination of post-baseline symptomatic Covid-19 and asymptomatic SARS-CoV-2 infection for participants with negative SARS-CoV-2 status at baseline. §Asymptomatic SARS-CoV-2 infection defined as absence of symptoms and infections detected by post-baseline positive RT-PCR or serology test for participants with negative SARS-CoV-2 status at baseline. NE=Not estimated; PP= Per-Protocol for Efficacy, all participants who received at least one injection and received planned injections of study vaccination, complied with the timing of injection 2, had no immunologic and virologic evidence of prior Covid-19 at baseline, and no major protocol deviations, N=1042 (placebo), N=2139 (mRNA-1273); mITT1= all participants who had no serologic or virologic evidence of prior SARS-CoV-2 infection before the first injection (both negative RT-PCR test for SARS-CoV-2 and negative serology test based on bAb specific to SARS-CoV-2 nucleocapsid) at baseline, and excluding those who received the wrong treatment, N=1073 (placebo), N=2163 (mRNA-1273).

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From: (b)(4) (b)(4) (x)
Sent: Fri, 23 Jul 2021 14:52:20 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Manusript - Preliminary Evaluation of 3rd Dose in Adults - CONFIDENTIAL
Attachments: COVID-19 - P201 Preliminary report_submitted version - PDF.pdf

Hi Sara,
I am attaching a publication that we have just submitted to *Nature Medicine* on the administration of a 3rd dose of vaccine to a small number of adults who previously received 2 doses of mRNA-1273. Subjects received either a single dose of mRNA-1273 (50 µg), modified mRNA-1273.351 (20 or 50 µg) encoding the spike protein of B.1.351, or a multivalent mRNA-1273.211 (a 1:1 mix of mRNA-1273 [25 µg] and mRNA-1273.351 [25 µg]). The manuscript presents the preliminary safety & immunogenicity data from this study.
We would ask that this publication be handled in confidence and not distributed outside of CDC. The publication may be put on a preprint server this week. if so, I will let you know & you could then share with the WG and others.
We would like to present these data as well as an overview of our booster program to the WG in the near future. Could you please let us know if this is possible?
Many thanks.
(b)(4)

Preliminary Analysis of the Safety and Immunogenicity of SARS-CoV-2 Variant mRNA Vaccine Boosters in Adults

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Abstract

The emergence of SARS-CoV-2 variants of concern (VOCs) and interest (VOIs) with decreased susceptibility to neutralization has generated interest in assessments of boosters and variant-specific vaccines. Clinical trial participants who received a primary series of mRNA-1273 ~6 months earlier were enrolled into a phase 2a study to evaluate single booster doses of mRNA-1273 or variant modified boosters, including multivalent mRNA-1273.211 (4 groups, N=20/group). Immediately prior to the booster dose, waning of neutralizing antibody against the wild-type D614G virus was observed and lower or undetectable neutralization was measured versus B.1.351, P.1, and B.1.617.2 variants. mRNA-1273 and the variant modified boosters had acceptable safety profiles. All boosters increased neutralization titers against the wild-type D614G virus and against key VOCs or VOIs, with the multivalent mRNA-1273.211 booster showing higher neutralization titers against the wild-type virus and across a panel of VOCs and VOIs (NCTC04405076).

Several vaccines against severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) targeting the spike (S) protein have been developed[1]. Although these vaccines are highly effective in reducing the symptoms and severe complications of COVID-19, several viral variants with changes in the S protein have arisen, some of which have been identified as variants of concern (VOCs; Alpha [B.1.1.7], Beta [B.1.351], Gamma [P.1], and Delta [B.1.617.2]) [2-4]. Reduction in efficacy has been reported against some COVID-19 vaccines versus B.1.351 [5,6] and more recently B.1.617.2 [7]. Statistical models predict that protection from COVID-19 may be driven by neutralizing antibody levels considerably lower than the neutralizing responses elicited by mRNA vaccines [8,9]. Furthermore, a rapid anamnestic response may be generated upon subsequent exposure to VOCs due to immune memory provided by mRNA vaccines in the form of germinal center memory B-cells and long-lived plasma cells in bone marrow [10]. Despite this, reports of antibody waning following vaccination and the increasing prevalence of SARS-CoV-2 variants warrant further evaluation of the need for and impact of booster vaccines, in particular variant-specific boosters.

mRNA-1273, a lipid nanoparticle-encapsulated messenger RNA vaccine encoding a prefusion stabilized S protein of the Wuhan-Hu-1 isolate, demonstrated anti-SARS-CoV-2 immune responses in phase 1 (NCT04283461) and 2 (NCT04405076) trials in adults, an acceptable safety profile, and 94% efficacy against symptomatic COVID-19 disease in the phase 3 Coronavirus Efficacy (COVE) trial (NCT04470427) in more than 30,000 participants [11-14]. The vaccine received authorization from several global regulatory bodies including the US Food and Drug Administration [15-17].

To monitor if mRNA-1273 was able to neutralize VOCs, neutralizing capacity of sera collected 7 days after the second dose of mRNA-1273 were tested against variants using a

research-grade vesicular stomatitis virus (VSV) pseudovirus neutralization assay (PsVN). Previous studies demonstrated that neutralizing antibody titers measured in sera from 8 mRNA-1273 Phase 1 trial participants were reduced 2.1- to 8.4-fold against the B.1.617.2 , P.1 , and B.1.351 variants [18,19]. Although a neutralizing antibody titer threshold predictive of protection from SARS-CoV-2 infection is unknown in humans, the reduction of in vitro neutralizing antibody titers against some variants relative to the wild-type D614G virus raises the possibility of breakthrough infections and waning efficacy for current SARS-CoV-2 vaccines.

To address this potential risk, modified versions of the prototype mRNA-1273 vaccine that contain the genetic sequence of the variant S protein continue to be developed. These variant vaccines are designed to stimulate an immune response against key sites of neutralization that have been altered on the spike protein of variant virus, and in the case of a multivalent vaccine, simultaneously against the original wild-type strain and variants. Herein we report the preliminary safety and immunogenicity of single booster doses of mRNA-1273 (50 µg), modified mRNA-1273.351 (20 or 50 µg) encoding the spike protein of B.1.351, and multivalent mRNA-1273.211 (a 1:1 mix of mRNA-1273 [25 µg] and mRNA-1273.351 [25 µg]) in a phase 2 trial.

Methods

Study design and trial participants

This phase 2a mRNA-1273 trial (protocol mRNA-1273-P201) was conducted at 8 sites in the United States and consisted of 3 parts: Part A (blinded phase), Part B (open-label intervention phase), and Part C (open-label intervention phase; **Figure 1**). Participants in the Part A and B cohorts were enrolled in the phase 2a mRNA-1273 P201 trial (NCT04405076), while

participants in the Part C cohort were initially enrolled in the phase 3 mRNA-1273-P301 COVE trial (NCT04470427) and rolled over into the phase 2a mRNA-1273 P201 trial (NCT04405076).

In Part A, participants were randomized 1:1:1 to receive 2 injections of 50 µg mRNA-1273, 100 µg mRNA-1273, or placebo and were blinded to treatment assignment. Participants proceeded to the open-label Part B and were eligible to receive the following schedule of injections: participants who received placebo in Part A were offered 2 doses of mRNA-1273 (100 µg) vaccine in Part B; participants who received 1 or 2 doses mRNA-1273 (50 µg or 100 µg) in Part A were offered a single booster dose of mRNA-1273 (50 µg) in Part B. In Part C, a subset of participants enrolled in the phase 3 mRNA-1273-P301 COVE trial were offered a single injection booster of mRNA-1273.351 (20 µg or 50 µg) or mRNA-1273/mRNA-1273.351 mixture (50 µg); enrollment into each booster dose arm was sequential. These individuals previously received 2 doses of mRNA-1273 in the COVE trial.

Eligible participants were healthy adults ≥18 years of age at the time of consent. To be eligible for Part B, participants must have been previously enrolled in Part A of the mRNA-1273 P201 study. To be eligible for Part C, participants must have been enrolled in the mRNA-1273-P301 COVE study and received 2 doses of mRNA-1273, with their second dose ≥6 months prior to enrollment in Part C. Additional inclusion and exclusion criteria are provided in the protocol.

All study materials, including the protocol, amendments, and informed consent, were approved by a central institutional review board (Advarra). All participants provided written informed consent prior to enrollment and participation in study procedures.

Trial vaccines

The mRNA-1273 vaccine encodes for the prefusion stabilized spike protein of the Wuhan-Hu-1 isolate of SARS-CoV-2, while the mRNA-1273.351 vaccine encodes the prefusion stabilized spike protein of the SARS-CoV-2 B.1.351 variant (**Table S1**). mRNA-1273.211 was a 1:1 mix of 25 µg of mRNA-1273 and 25 µg of mRNA-1273.351, for a total dose of 50 µg of mRNA. All vaccines were formulated in lipid nanoparticles as previously described [14].

Safety assessments

Participants completed an electronic diary for 7 days after receiving the booster to record solicited systemic adverse reactions, local adverse reactions (including injection site erythema and swelling/induration), and daily oral body temperatures. Trained site personnel called participants to assess safety every 4 weeks for 6 months after the last dose.

Immunogenicity assessments

For this substudy analysis of 80 participants, samples were collected 28 days post-primary vaccination series, immediately prior to the booster vaccination (Day 1), and at Days 8, 15, 29, 57, and 181 post-booster vaccination. In this preliminary analysis, neutralization results of sera collected 28 days after the primary series, immediately prior to the booster dose, and 15 and 29 days after the booster are reported. A validated lentivirus PsVN assay, used to test the samples from phase 2 and 3 (COVE) trials [20], was used to analyze samples collected immediately prior to the booster (Day 1) and at Day 15 and Day 29. To enable exploratory analysis across a panel of SARS-CoV-2 variants, sera were analyzed for neutralizing antibody titers using a research-grade recombinant VSV-based pseudovirus assay previously used to assess the impact of neutralization from variants against sera collected 7 days after the second dose of mRNA-1273 [18,19]. This assay encodes the S protein of the prototype Wuhan-Hu-1 isolate with the D614G

mutation (wild-type D614G) or the S proteins from variants. For specific mutations in each variant, see **Table S1**. The VSV PsVN neutralization assay demonstrates strong correlation and concordance with the clinically validated lentivirus PsVN assay (**Figure S1**).

Recombinant VSV-based pseudovirus neutralization assay (preclinical assay)

To perform the recombinant VSV-based pseudovirus neutralization assay, codon-optimized full-length spike protein of the D614G and variant sequences (**Table S1**) were cloned into pCAGGS vector. To make SARS-CoV-2 full-length spike pseudotyped recombinant VSV-ΔG-firefly luciferase virus, BHK-21/WI-2 cells (Kerafast, EH1011) were transfected with the spike expression plasmid and subsequently infected with VSVΔG-firefly-luciferase as previously described.[21] For the neutralization assay, serially diluted serum samples were mixed with pseudovirus and incubated at 37°C for 45 minutes. The virus-serum mix was subsequently used to infect A549-hACE2-TMPRSS2 cells for 18 hours at 37 °C before adding ONE-Glo reagent (Promega E6120) for measurement of luciferase signal (relative luminescence unit; RLU). The percentage of neutralization was calculated based on RLU of the virus-only control, and subsequently analyzed using 4-parameter logistic curve (Prism 8). Neutralization against the A.VOI.2 variant, a variant with 3 initial genomes that epidemiologically linked to only 2 basal sequences in the GISAID database [22], was included in the analysis because it contains extensive mutations of concern.

Recombinant lentiviral-based pseudovirus neutralization assay (validated clinical assay)

The quantification of SARS-CoV-2 neutralizing antibodies uses lentivirus particles that express SARS-CoV-2 spike protein (Wuhan-Hu-1 isolate including D614G) or the B.1.351 variant spike protein (L18F-D80A-D215G-ΔL242-ΔA243-ΔL244-K417N-E484K-N501Y-

D614G-A701V) on their surface and contain a firefly luciferase reporter gene for quantitative measurements of infection by RLU. The virus is applied to transduced 293T cells expressing high levels of ACE2 (293T/ACE2 cells), with or without pre-incubation with antibodies (control antibodies or serum samples); the presence of neutralizing antibodies reduces infection and results in lower RLUs. Serial dilution of antibodies or serum samples can be used to produce an injection-response curve. Neutralization is measured as the serum dilution at which the RLU is reduced by 50% (50% inhibitory dilution [ID_{50}]) or 80% (80% inhibitory dilution [ID_{80}]) relative to mean RLU in virus control wells (cells + virus but no control antibody or sample) after subtraction of the mean RLU in cell control wells (cells only).

Statistical analysis

Geometric mean titer (GMT) and geometric mean fold rise (GMFR) were calculated based on log-transformed titers, and 2-sided 95% confidence intervals (CI) based on the *t* distribution of the log-transformed titers or the difference in the log-transformed titers for GMT and GMFR, respectively, then back transformed to the original scale. Analysis of the COVE study participant sera collected 28 days after the primary series was used to establish a GMT benchmark further used to derive GMT ratios after the booster dose. Wilcoxon matched-pairs signed rank test was used to compare results. Spearman nonparametric correlation was used for assay correlation.

Results

Trial population

A total of 600 participants were randomized in Part A (blinded phase) of the phase 2a mRNA-1273 P201 trial, and 558 participants proceeded to Part B (open-label phase; **Figure 1**).

A total of 186 participants received 2 priming doses of mRNA-1273 (100 µg) in Part A and subsequently received 1 mRNA-1273 (50 µg) booster dose in Part B. Of these, 20 participants were randomly selected for inclusion in this preliminary analysis based on visit assessments completed and sample availability of pre-booster sera. In the phase 3 COVE trial, ~30,400 participants were randomized and 14,711 participants received 2 priming doses of mRNA-1273 (100 µg) [14]. Of these, 60 participants were selected to roll over into Part C (open-label phase) of the phase 2a mRNA-1273 P201 trial and received a single booster dose of mRNA-1273.351 (50 µg; cohort 1, n=20), mRNA-1273.211 (total 50 µg; cohort 2, n=20), or mRNA-1273.351 (20 µg; cohort 3, n=20).

The baseline demographic characteristics of the 4 groups of participants who received booster doses of the prototype or the modified mRNA-1273 vaccines were generally similar (**Table 1**). Most of the participants were white and not Hispanic or Latino. The mean age of the participants who received boosters of mRNA-1273 (50 µg), mRNA-1273.351 (20 µg), mRNA-1273.351 (50 µg) or mRNA-1273.211 was 63.8, 47.5, 53.9, and 55.6 years, respectively. The duration (mean [SD]) between the second dose of mRNA-1273 in the primary series and the booster for mRNA-1273 (50 µg), mRNA-1273.351 (20 µg), mRNA-1273.351 (50 µg) or mRNA-1273.211 (50 µg) was 6.7 [0.5], 6.2 [0.3], 6.2 [0.3], and 6.2 [0.4] months, respectively.

Safety

The percentages of participants with solicited local and systemic adverse events were similar between the booster groups (**Figure 2; Table S2**); the majority of solicited local and systemic adverse events were mild (grade 1) or moderate (grade 2). The frequencies of any grade 3 solicited local or systemic adverse events after the booster doses ranged from 10-15%), and there were no grade 4 solicited local or systemic adverse events. The most common local adverse

event was injection site pain. The most common systemic adverse events after the booster doses were fatigue, headache, arthralgia, and myalgia. Fever was reported by 3 participants (15.0%) after the booster dose of mRNA-1273 only. No serious adverse events were reported.

Neutralizing responses to wild-type D614G and B.1.351 immediately prior to and after the booster dose

Wild-type D614G and B.1.351 neutralization were measured in samples collected ~6 months after the primary series of mRNA-1273 immediately before the booster dose (Day 1), and in samples collected on Day 15 or Day 29 after the booster dose in a validated lentivirus PsVN assay. The wild-type D614G virus was neutralized by samples collected prior to the booster from participants in Part B and Part C cohorts 1, 2, and 3 (**Figure 3A**), whereas neutralization of B.1.351 was low or nondetectable prior to the booster dose from participants in Part C cohorts 1, 2, and 3 (**Figure 3B**).

After the booster dose, participant sera were collected on Day 29 from Part B participants (mRNA-1273 booster) or on Days 15 and 29 from Part C cohorts 1, 2, and 3 (50 µg mRNA-1273.351, 50 µg mRNA-1273.211, and 20 µg mRNA-1273.351 boosters, respectively). Neutralization of the wild-type D614G and B.1.351 viruses increased after each booster dose. Against the wild-type D614G virus, 16.7, 11.3, 46.4, and 9.2-fold higher GMTs were measured in the mRNA-1273 (50 µg), mRNA-1273.351 (50 µg), mRNA-1273.211 (50 µg), and mRNA-1273.351 (20 µg) cohorts, respectively, on Day 29. Against the B.1.351 variant, 34.9, 61.6, and 33.7-fold higher GMTs were measured in the mRNA-1273.351 (50 µg), mRNA-1273.211 (50 µg), and mRNA-1273.351 (20 µg) cohorts, respectively, on Day 29. In addition, participants who did not have measurable titers against the wild-type D614G or B.1.351 virus ~6 months

after the primary series, prior to the booster dose, all had considerable titers after the booster dose.

Correlation of the clinically validated lentivirus PsVN assay with a research-grade VSV-based PsVN assay

In order to support exploratory analysis of the Part B and Part C cohort 1 and 2 clinical samples against SARS-CoV-2 variants, participant samples were analyzed in a research-grade VSV-based PsVN assay that has previously been used to evaluate the impact of SARS-CoV-2 variants on mRNA-1273 neutralization [19]. Analysis of the results from the clinically validated and research-grade wild-type D614G and B.1.351 PsVN assays demonstrates significant correlation, with r = 0.9161 against wild-type D614G and 0.9435 against B.1.351 in an analysis of results from Day 1 and Day 15 samples (**Figure S1**).

Exploratory analysis of the kinetics of neutralizing responses to wild-type D614G and VOCs post-primary series vaccination

Exploratory analysis of samples collected after the primary mRNA-1273 vaccination series was performed using the VSV-based PsVN assay. Twenty-eight days after the primary 2-dose series, wild-type D614G neutralizing antibody GMTs were 1210 in the mRNA-1273, 2213 in the mRNA-1273.351, and 1397 in the mRNA-1273.211 cohorts (**Figure 4**), with reductions seen against both B.1.351 (13-14-fold) and P.1 variants (5-6-fold). Approximately 6 months after the second dose of mRNA-1273, neutralizing antibody GMTs decreased in comparison to peak titers measured against the D614G virus 1 month after the primary series. Titers against the wild-type D614G were 6- to 7-fold lower, whereas titers against the B.1.351 and P.1 variants were 24- to 69-fold lower. Approximately 44% and 30% of combined samples from Part B and C cohorts

1 and 2 were below the assay lower limit of quantification (LLOQ) against B.1.351 and P.1 viral variants, respectively.

Similar to B.1.351 and P.1, neutralization of the B.1.617.2 variant, a VOC now circulating globally, was considerably reduced 6 months after completion of the primary series. Sera from a random subset of the Part B cohort collected prior to the booster dose of mRNA-1273 showed a 33 to 40-fold reduction against B.1.617.1 and B.1.617.2 in comparison to peak titers measured against the D614G virus 1 month after the primary series, with neutralization in 5 of 11 samples falling below the assay LLOQ against B.1.617.2 (**Figure 5A**).

Exploratory analysis of neutralizing responses against wild-type D614G virus and VOCs from boosters

Wild-type D614G virus neutralizing titers were measured with the VSV-based PsVN assay to compare titers from samples collected 15 days after the booster dose versus peak titers measured from samples collected 28 days after the second dose of the mRNA-1273 primary series. After the booster dose, wild-type virus neutralization GMTs were 3.8, 1.7, and 4.4-fold higher from the mRNA-1273, mRNA-1273.351, and mRNA-1273.211 boosters, respectively (**Figure 4**). Against VOCs or VOIs, each of the booster strategies increased variant-specific neutralization titers relative to those measured after the primary series. mRNA-1273.211 increased both B.1.351 and P.1 neutralization titers above the GMT level against the D614G strain measured after the primary series, with GMT titers increasing to 1468 against B.1.351 and 1972 against P.1 in the Part C cohort 2 participants 2-weeks after the booster dose.

Exploratory analysis of booster response to VOC compared to a primary series GMT benchmark

The VSV PsVN assay was used to assess COVE study samples collected 28 days after the primary series to establish a GMT benchmark. This benchmark was used to determine whether the boosters reached the same neutralization level shown in the pivotal study where efficacy was demonstrated, ie, to levels seen in the D614G assay where 94% efficacy was measured, indicated by a GMT ratio (GMTr) ≥ 1[14]. Using Day 57 sera from 59 Part C participants from the COVE study, a GMT of 2045 was established as the D614G neutralization benchmark using the VSV-based PsVN assay (**Figure 4 B and C, S2**). GMTs per cohort ranged from 1397-2758.

When samples collected 2 weeks after the respective booster dose were assessed against a panel of variants (**Figure 5B-D**; specific mutations in **Table S1**), each mRNA booster increased variant-specific neutralization against all VOIs or VOCs, including B.1.617.2 and P.1, above peak pre-booster levels with neutralization against some of the variants approaching or exceeding the COVE study wild-type D614G GMT benchmarks. Of the 3 booster vaccines assessed, the multivalent mRNA-1273.211 booster showed the greatest increase in GMTs against the majority of VOCs (**Figures 5D, S3A**).

Compared to the COVE study D614G benchmark, the booster vaccines yielded higher GMTs against the wild-type D614G virus and several VOCs or VOIs based on a GMTr rise ≥ 1 (**Figure 5 B-D**). However, only the multivalent variant vaccine mRNA-1273.211 achieved a GMTr rise ≥ 1 against all VOCs assessed. Of the 3 boosters, the multivalent mRNA-1273.211 50 µg booster also yielded higher variant GMTs versus the Day 57 D614G benchmark and against the largest number of variants including B.1.351, P.1, B.1.427/B.1.429, B.1.526, B.1.617.1, and B.1.617.2. A comparison of the GMT versus the overall COVE GMT D614G benchmark is shown in **Figure S3 A-B**.

Discussion

This preliminary evaluation describes the antibody persistence of mRNA-1273 and administration of booster doses of mRNA-1273, mRNA-1273.351, and mRNA-1273.211 in a subset of 80 participants who had been vaccinated ~6 months previously with the authorized dose and schedule of mRNA-1273. Antibody titers against the wild-type D614G peaked 1 month after the second dose of the primary series and subsequently declined over the 5 months prior to the delivery of the booster dose [19]. These results are consistent with those reported in a study using a lentiviral PsVN assay, in which monitoring of neutralizing antibody levels was performed up to 6 months after the second dose of mRNA-1273 [20]. Reduction of neutralizing antibody was evident 28 days after the primary series vaccination against B.1.351 and P.1 to greater levels than measured against samples collected 7 days after the primary series [19], likely due to further affinity maturation of B-cells and alteration of the available antibody repertoire. Additional reduction or complete loss of detectible levels of neutralizing antibody ~6 months after the primary vaccination was evident against B.1.351, P.1, and B.1.617.2.

The safety profiles following single injections of 50 µg mRNA-1273, 20 or 50 µg mRNA-1273.351, and 50 µg mRNA-1273.211 boosters were generally similar to those observed after a second dose of mRNA-1273 in the previously reported phase 2 and 3 studies. The most common systemic adverse events after the booster doses were fatigue, headache, arthralgia, and myalgia, which occurred at similar-to-lower frequencies for the variant boosters than after receipt of the primary series of 100 µg mRNA-1273.

Booster vaccination with mRNA-1273, mRNA-1273.351, and mRNA-1273.211 induced robust anamnestic responses, confirming that the robust B-cell memory generated by mRNA

vaccines can be quickly and potently boosted [10]. High neutralizing titers were measured against the wild-type D614G strain after a booster dose that were up to 4.4-fold higher than peak titers after the primary series. Increased VSV PsVN titers were measured against variant viruses including the key VOCs B.1.351, P.1, and B.1.617.2, with titers against several variants approaching or exceeding those measured after the primary series against the wild-type D614G virus, particularly after boosting with mRNA-1273.211 (**Figure 4**). Increased titers against the VOCs suggest that further maturation of antibodies is feasible after a 2-dose primary series of mRNA-1273, regardless of the composition of the booster dose. Furthermore, boosting with mRNA-1273.351 and mRNA-1273.211 appeared to be more effective at increasing neutralization against the B.1.351 variant than with mRNA-1273.

For comparison to GMT titers measured in the phase 3 COVE study where efficacy was established, 59 COVE participant samples were evaluated in the VSV PsVN assay with the wild-type D614G assay titers used to support additional analyses. The mRNA boosters each increased variant-specific neutralization against all VOIs or VOCs, including B.1.617.2 and P.1, above peak pre-booster levels with neutralization against some of the variants approaching or exceeding the COVE study benchmark. The multivalent mRNA-1273.211 50 µg booster yielded a GMTr rise ≥1 against all VOCs (**Figure 5D**), indicating that variant neutralization GMTs after the booster exceeded peak wild-type virus GMTs after the primary series in the samples from this cohort, potentially increasing breadth of coverage against VOCs or VOIs.

There are some limitations related to this preliminary analysis. First, the results presented here are based on treatment groups that were not randomized but assigned sequentially, given the different timeframes of availability of the new vaccine formulations. In addition, the sample size was small (N=20 per group) to facilitate rapid initiation of additional studies to support licensure

of a booster to address the evolving pandemic. Although the lentiviral-based PsVN assay used in this evaluation is validated, the VsV-based PsVN assay used in the evaluation of samples against variants is a research-grade assay. The VSV-based PsVN assay has been used consistently to evaluate the impact of variants on neutralization, but has not been validated [19]. Although the data are encouraging, in the absence of a correlate of protection it cannot be definitively determined whether the neutralization titers elicited from mRNA-1273.351 and mRNA-1273.211 would be protective against the B.1.351, P.1, or B.1.617.2 variants. Finally, because the participants in this study were originally enrolled in 2 different clinical trials, comparison of the results from mRNA-1273.211 and mRNA-1273.351 boosting with those of mRNA-1273 should be interpreted with caution.

The emergence of SARS-CoV-2 variants and the ability of the virus to partially overcome natural or vaccine-induced immunity has served as a call to action. Although a correlate of protection has not been established for SARS-CoV-2 infection or COVID-19 disease, lack of detectable neutralization against VOCs after ~6 months in some participants may be indicative of waning protection. However, it should be noted that a rapid anamnestic response upon viral exposure is likely based on the induction of immune memory from the booster dose. The mRNA platform approach against SARS-CoV-2 VOCs in this trial appears to be effective, with boosters increasing neutralizing titers against the wild-type D614G virus and against key VOCs, with numerically higher neutralizing titers measured in participants who received the multivalent mRNA-1273.211 booster. Although this trial evaluated the performance of booster vaccines that encode the original strain or the B.1.351 spike protein, this strategy could be employed in the future to vaccinate against new VOCs through the development of new variant-

specific vaccines. Further research is needed to determine the clinical significance of these preliminary results.

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Author contributions

Concept design, A.C., K.W., L.C., H.B., R.P., J.M.M., B.L., A.C., R.M., D.K.E.; data collection, A.C., M.L., K.W., L.M., A.H., N.N., J.O., H.L., Y.P., B.N.; analysis/interpretation of data, A.C., M.L., K.W., W.H., T.C., B.D., R.P., D.K.E.; write/review/intellectual contribution, A.C., M.L., K.W., W.H., H.B., R.P., J.M.M., B.L., A.C., R.M., D.K.E. All author approved the final version of the manuscript.

Competing interests

K.W., A.C., M.K., L.M., T.C., A.H, N.N., W.H., J.O., H.B., H.L., Y.P., B.N., B.D., R.P., A.C., J.M.M., B.L., R.M., and D.K.E. are employees of Moderna, Inc., and hold stock/stock options in the company.

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Data availability

The authors declare that the data supporting the findings of this study are available within this Article and its Supplementary Information. Source data are provided with this paper.

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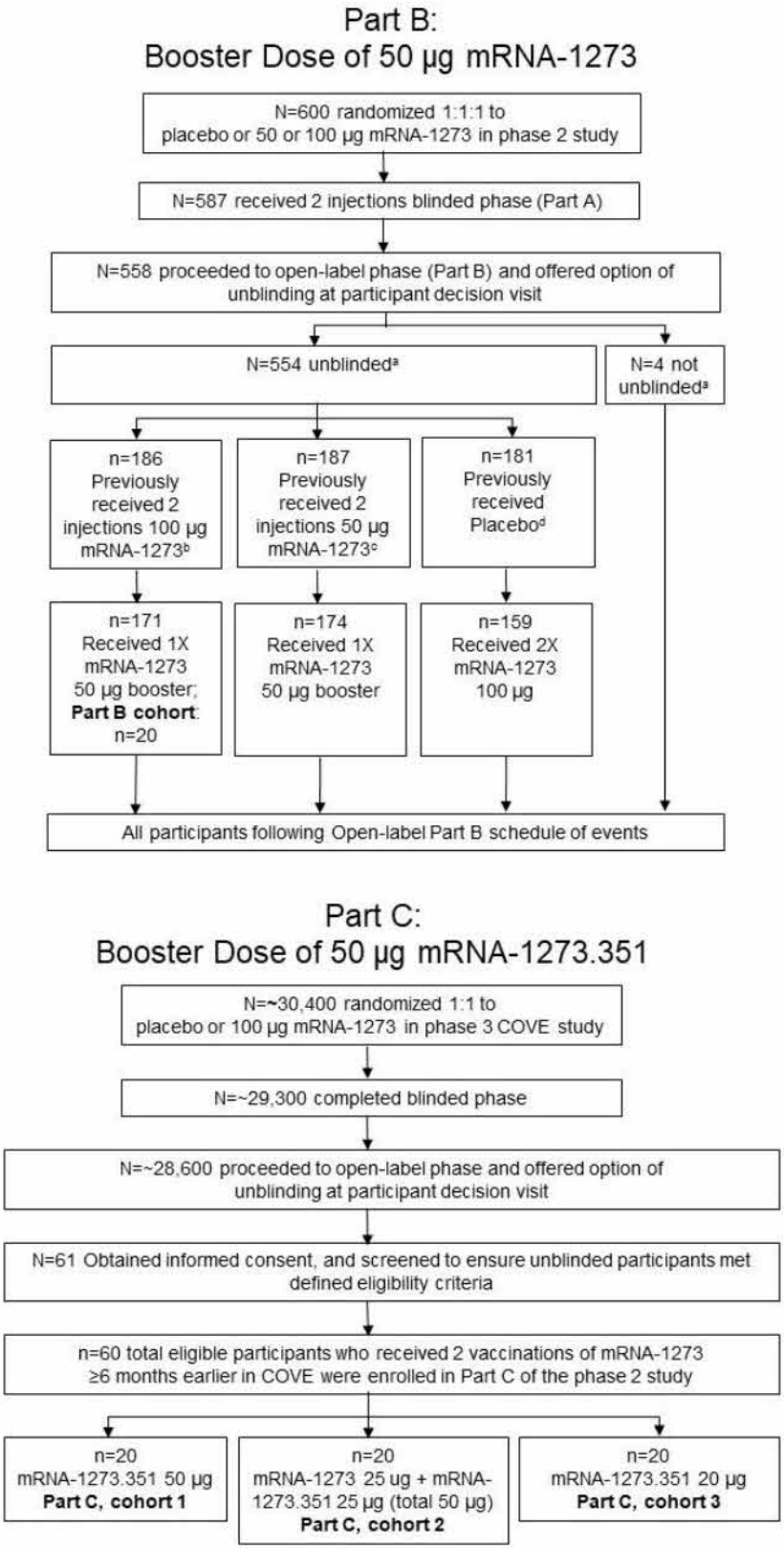
Figure 1. Flow for Parts B and C of the amended phase 2 trial of mRNA-1273.



In Part B, 20 participants who had received 2 injections of 100 µg mRNA-1273, completed the blinded phase (Part A), and went on to receive a single open-label booster dose of 50 µg mRNA-1273 were selected for this preliminary analysis, with selection based on completion of Day 15 visit assessments and immunogenicity sample availability. In Part C, enrollment was site-specific and based on predefined inclusion/exclusion criteria; administration of booster doses occurred in a sequential manner (Part C, cohort C1; Part C, cohort C2; Part C, cohort C3).

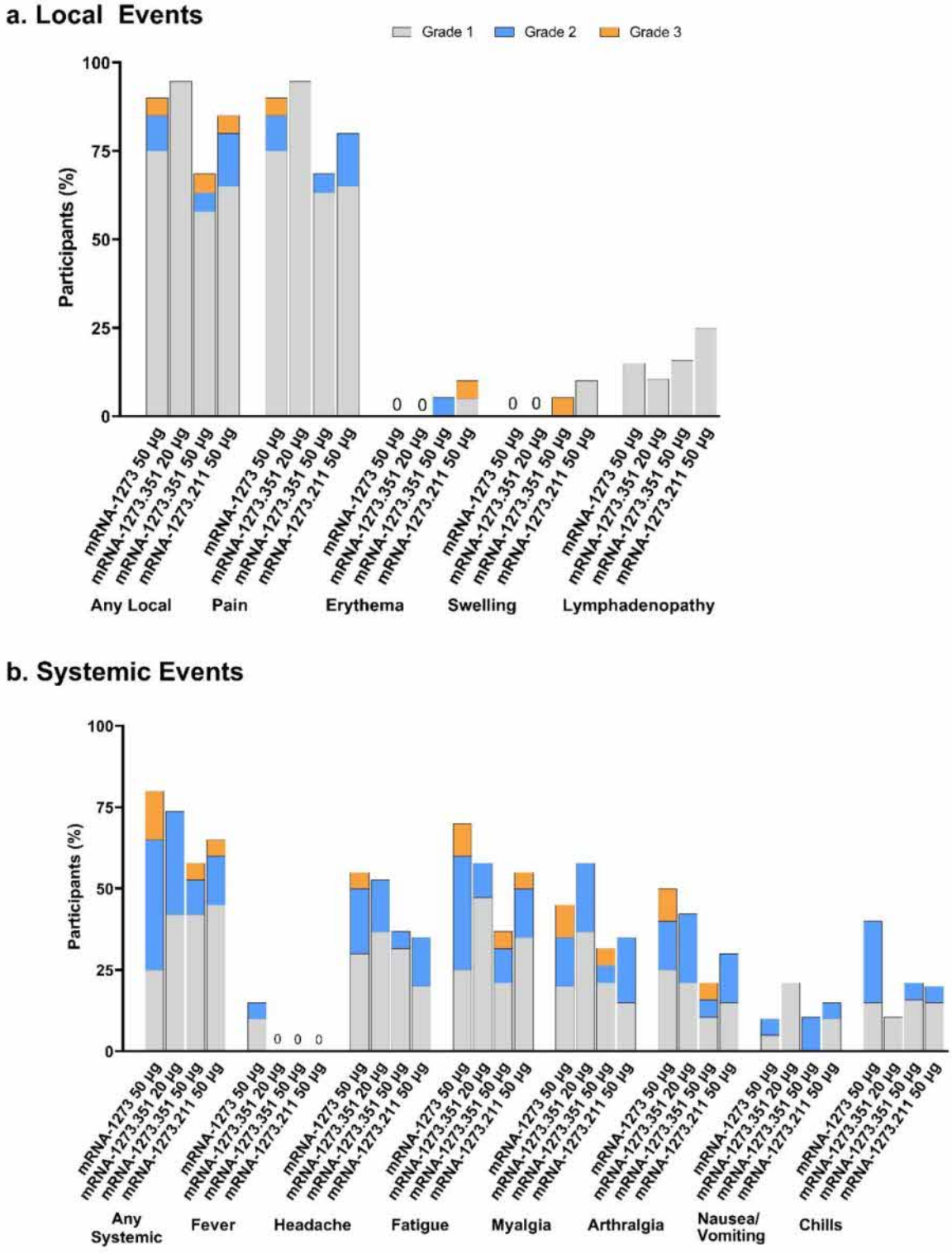
[a]Unblinded or not unblinded to assigned treatment in Part A blinded phase.

[b]15 participants declined to receive a booster.

[c]13 participants declined to receive a booster.

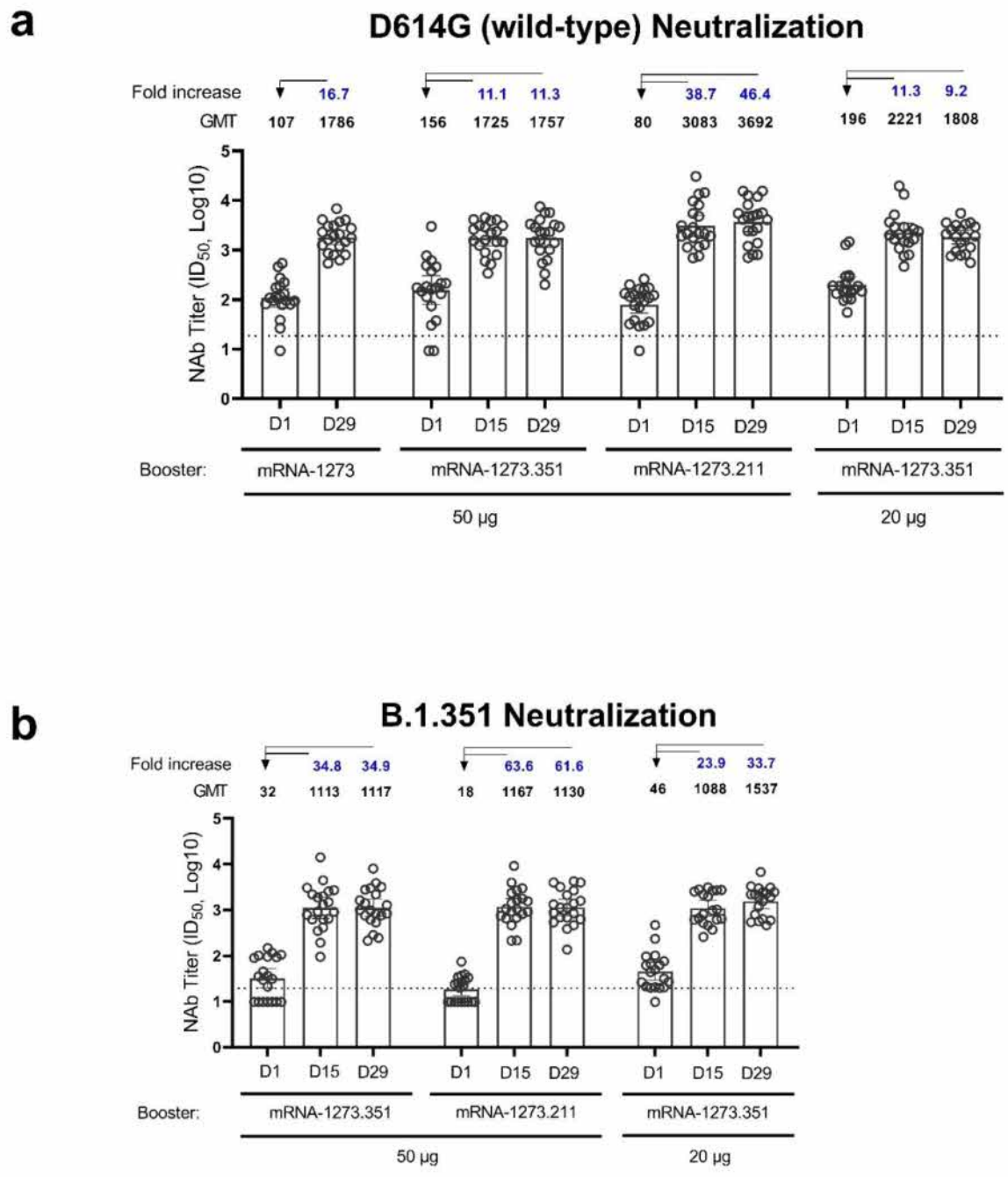
[d]22 participants declined to receive a vaccine in Part B.

Figure 2. Solicited local and systemic adverse events within 7 days following booster dose.



The percentage of participants who reported (A) local and (B) systemic adverse events is shown for 20 participants who received a booster dose of 50 µg of mRNA-1273, 19 participants who received 20 µg of mRNA-1273.351, 19 participants who received a booster dose of 50 µg of mRNA-1273.351, and 20 participants who received 50 µg of mRNA-1273.211. One participant each in the mRNA-1273.351 50 µg and 20 µg groups did not report results for solicited adverse reactions and were excluded from the analysis.

Figure 3. Neutralization of wild-type and B.1.351 lentivirus-based pseudoviruses by participant serum immediately before and after boosters.

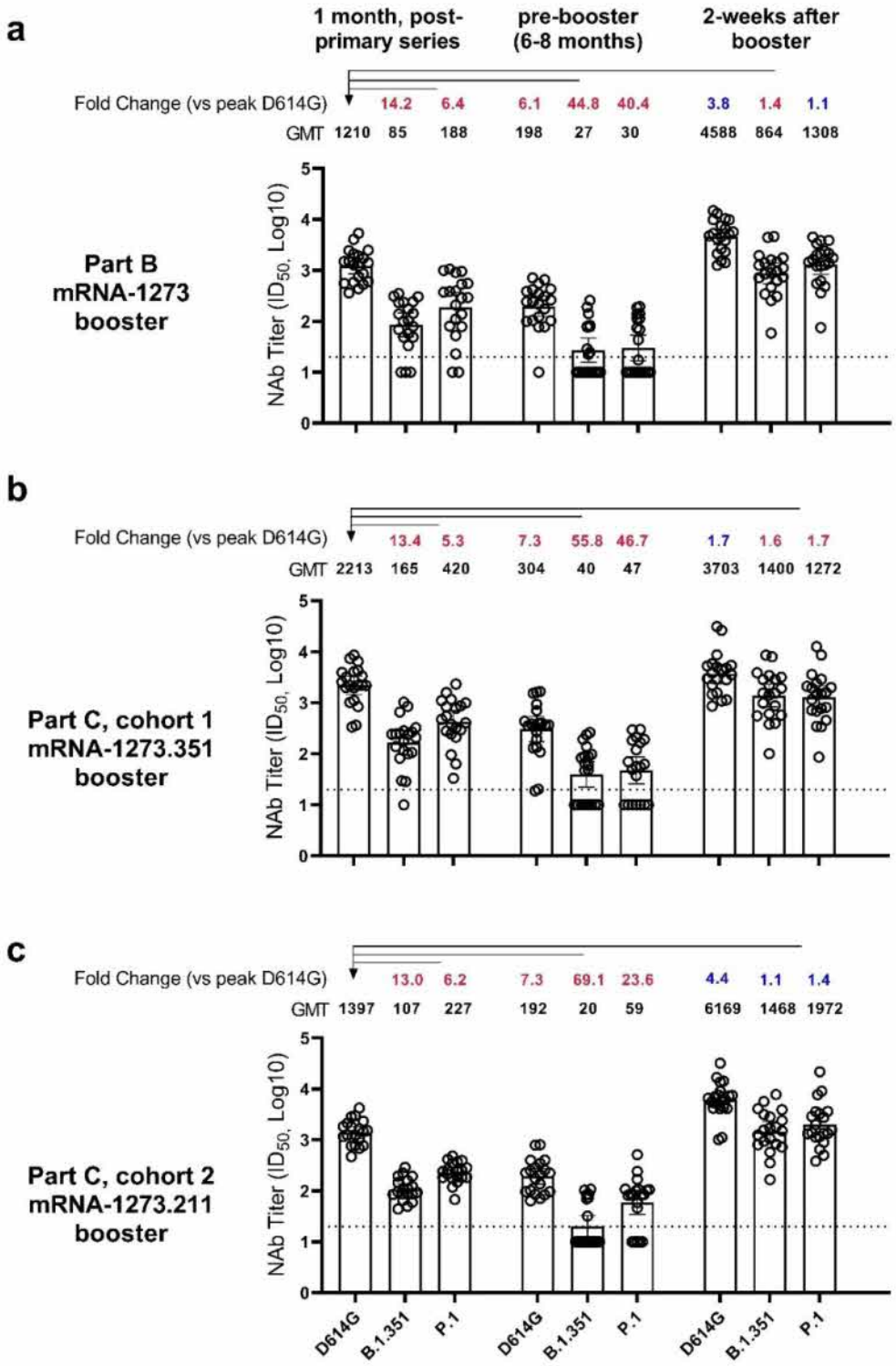


Neutralization in a validated recombinant lentivirus-based SARS-CoV-2 pseudovirus assay (D614G and B.1.351) by serum from participants. Sera were collected immediately prior to

receiving a booster (Day 1) and on Day 15 and Day 29 after the booster dose of 50 µg of mRNA-1273, 50 or 20 µg of mRNA-1273.351, or 50 µg mRNA-1273.211. The geometric mean neutralizing antibody titers with 95% confidence intervals are denoted. The titers for individual participants are shown by the circles. The fold increase versus titers measured versus samples collected prior to the boost are shown. The horizonal dotted lines indicate the lower limit of quantification. N=20 participants per booster cohort.

D, day, GMT, geometric mean titer; ID_{50}, 50% inhibitory dilution; NAb, neutralizing antibody; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2.

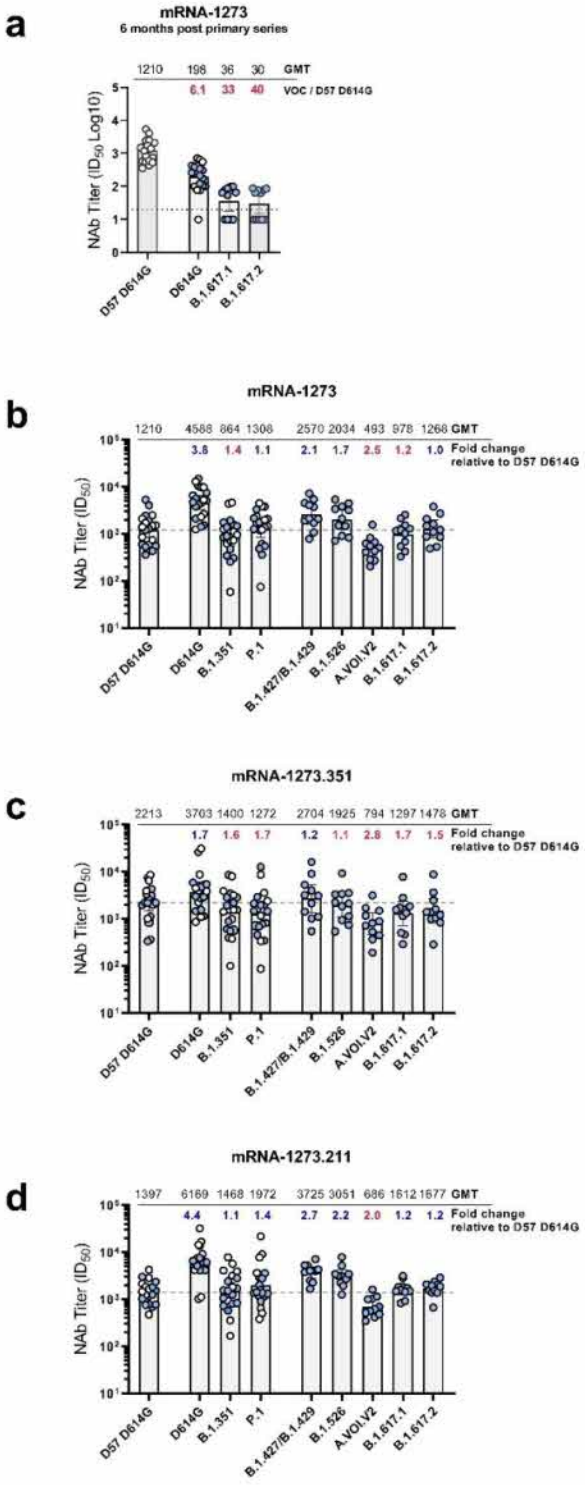
Figure 4. Exploratory analysis of neutralization of wild-type and variants VSV-based pseudoviruses by participant serum.



Neutralization of recombinant VSV-based SARS-CoV-2 pseudoviruses (D614G, B.1.351 and P.1) by serum from participants 1 month after the primary series vaccination with 100 µg mRNA-1273, immediately prior to receiving a booster, and 2 weeks after the booster dose of (**A**) 50 µg of mRNA-1273, (**B**) 50 µg of mRNA-1273.351, or (**C**) 50 µg of mRNA-1273.211. The geometric mean neutralizing antibody titers with 95% confidence intervals are denoted. The titers for individual participants are shown by the circles. The GMT fold change versus the peak titers against the wild-type D614G virus after the primary vaccination series are shown, with red indicating fold drop and blue indicating fold rise. The horizonal dotted lines indicate the lower limit of quantification. N=20 participants per booster cohort.

D, day; GMT, geometric mean titer; ID_{50}, 50% inhibitory dilution; NAb, neutralizing antibody; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; VSV, vesicular stomatitis virus.

Figure 5. B.1.617 impact on neutralization and wild-type D614G and VOCs VSV-based PsVN titers post-boost versus peak D614G titers after the primary series.



Sera was collected from trial participants 1 month after the primary series vaccination with 100 µg mRNA-1273, immediately prior to the booster dose, and 2 weeks after the 50 µg boosters. (**A**) Neutralization of D614G, B.1.617.1, and B.1.617.2 from sera collected from 11 Part B individuals immediately prior to the booster. Sera collected after the primary series or 2 weeks after the boost with (**B**) mRNA-1273, (**C**) mRNA-1273.351, or (**D**) mRNA-1273.211 were analyzed in PsVN assays. The GMT titers against the wild-type virus or variants measured in booster trial participants 2 weeks after the booster were evaluated versus peak titers measured against the wild-type virus after the primary series vaccination, and the fold change for each virus are listed in red (fold drop) or blue (fold rise) text. GMTs for each variant virus are listed above each graph. The Day 57 GMT titers is indicated by the gray line. Results from individual participants are represented as dots on each figure. N=20 for D614G, B.1.351, and P.1 assays. N=11 for B.1.427/B.1.429, B.1.526, A.VOI.V2, B.1.617.1, and B.1.617.2, with blue colored dots indicating these participants and white dots indicating the remaining participants.

D, day; GMT, geometric mean titer; ID50, 50% inhibitory dilution ; NAb, neutralizing antibody; PsVN, pseudovirus neutralization assay;VOC, variants of concern.

Table 1 Demographics and characteristics

Characteristic n (%)	mRNA-1273 (50 µg) N=20	mRNA-1273.351 (20 µg) N=20	mRNA-1273.351 (50 µg) N=20	mRNA-1273.211 (50 µg) N=20
Age, y, mean (range)	63.8 (38-76)	47.5 (26-67)	53.9 (27-70)	55.6 (28-79)
Sex				
Male	8 (40)	5 (25)	11 (55)	12 (60)
Female	12 (60)	15 (75)	9 (45)	8 (40)
Race				
White	20 (100)	20 (100)	19 (95)	19 (95)
Black or African-American	0	0	0	0
Asian	0	0	1 (5)	0
American Indian or Alaska Native	0	0	0	1 (5)
Native Hawaiian or other Pacific Islander, Multiracial, Other, Not reported, Unknown	0	0	0	0
Ethnicity				
Hispanic or Latino	0	1 (5)	0	1 (5)
Not Hispanic or Latino	20 (100)	19 (95)	20 (100)	19 (95)
Not reported or Unknown	0	0	0	0

Time interval between second dose of mRNA-1273 during the primary series and the booster dose				
Mean (SD) (months[a])	6.7 (0.5)	6.2 (0.3)	6.2 (0.3)	6.2 (0.4)
Range (months)	5.9-7.5	5.5-6.6	5.6-6.6	5.4-6.8
Body Mass Index (kg/m^2)				
Mean (SD)	26.2 (2.1)	33.3 (6.6)	30.3 (6.5)[b]	33.0 (7.5)

SD, standard deviation.

[a]Calculated with 30 days/month.

[b]Missing data for 1 participant.

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Sat, 22 May 2021 20:29:06 +0000
To: (b)(4) (b)(4) (x)
Subject: may be a minute or so late

(b)(4)

Just wanted to give you a heads up that we may be a minute or two late. Wrapping up another call and then we will hop over, but didn't want you to worry if we weren't on right at 4:30.

Thanks!
Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: (b)(4) (b)(4) (x)
Sent: Thu, 20 May 2021 20:55:01 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: Moderna Confidentiality Agreement with CDC
Attachments: CDC CDA Contract ID 16732 - Amendment 12.4.20.pdf

Hi Sara,
It was good to talk with you and Jessica today. Can you please take a look at the attached & see what changes you might want to make to this CDA so that we can be more efficient in sharing data for future EUAs related to our COVID-19 vaccine. I will then take to our legal team for their input/review. If you need to add more individuals to the section at the very end, please note that as well.
Thanks.
(b)(4)

Please consider the environment before printing this email

Amendment #01 to Confidentiality Agreement

THIS AMENDMENT #01 TO CONFIDENTIALITY AGREEMENT (this "Amendment #01"), is entered into as of December 4, 2020 (the "Amendment #01 Effective Date"), by and between ModernaTX, Inc. ("Moderna"), and The Centers for Disease Control and Prevention (CDC) ("Recipient" or "CDC"). Each of Moderna and CDC may be referred to herein as a "Party" or together as the "Parties".

WHEREAS, Moderna and CDC are parties to a Confidentiality Agreement dated November 10, 2020 (the "Agreement"); and

WHEREAS, Moderna and CDC desire to continue the Agreement in accordance with and subject to the terms and conditions therein, as more fully described herein.

NOW THEREFORE, for good and valuable consideration, the receipt and sufficiency of which is hereby mutually acknowledged, CDC and Moderna hereby agree as follows. Capitalized terms used but not defined herein shall have the meanings ascribed to such terms in the Agreement.

1. Exhibit A. CDC and Moderna each acknowledge and agree that Exhibit A of the Agreement shall be deleted in its entirety and replaced with the Exhibit A attached to this Amendment #01.

2. General Terms. Except with respect to the amendments as set forth above, the terms and conditions of the Agreement shall remain unchanged. This Amendment #01 shall be construed in accordance with and governed by the same laws that govern the Agreement.

[***Remainder of page intentionally left blank***]

IN WITNESS WHEREOF, CDC and Moderna each has caused this Amendment #01 to be executed by its duly authorized representative.

MODERNATX, INC.

DocuSigned by:
(b)(4)
9368ADE45338401...

By

(b)(4)

Name

(b)(4)

Title

THE CENTERS FOR DISEASE CONTROL AND PREVENTION

Samuel Posner -S
Digitally signed by Samuel Posner -S
Date: 2020.12.05 08:39:56 -05'00'

By

Name

Title

Exhibit A

Recipient (CDC) Representatives

Megan Wallace
Kathryn Curran
Julia Gargano
Sara Oliver
Kathleen Dooling
Karen Broder

From: (b)(4) (b)(4) (x)
Sent: Wed, 14 Apr 2021 12:22:53 +0000
To: Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP); Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Moderna Statement on CVST/Thrombotic Events

HI Tom and Sara,
I thought you would want to know that Moderna issued a statement yesterday regarding a lack of association of our vaccine with CVST or thrombotic events. The link is below.
https://investors.modernatx.com/news-releases/news-release-details/statement-cvst-or-thrombotic-events
(b)(4)

Please consider the environment before printing this email

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Fri, 28 May 2021 20:57:25 +0000
To: (b)(4) (b)(4) (x)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); Mbaeyi, Sarah (CDC/DDID/NCIRD/OD)
Subject: Moderna trial participants
Attachments: 2020-COVID-19-shot-card-3forprinting.pdf

(b)(4)

I wanted to pass this along: We've had discussions around trial participants, especially in light of CDC's guidance for 'fully vaccinated individuals'. Below is the current guidance. Feel free to share and let us know if there are any questions or issues. Also I know that we passed along the "CDC card" already, but I'm including it here as well. I know there are ongoing discussions around getting these into IIS locally but we're happy to facilitate those discussions as well. Also, as mentioned previously- please don't publicly post the card.

Thanks-
Sara

Pfizer, Moderna and Janssen trial participants:

The Pfizer, Moderna and Janssen vaccines are authorized under EUA. In addition, ACIP has independently reviewed the safety and efficacy data from the Phase 3 clinical trials. The "CDC cards" have been provided to the manufacturers. Once it has been confirmed that trial participants received 'active' vaccine and not placebo, the participants can be considered 'fully vaccinated' in terms of CDC guidance, can receive a "CDC card" and can have their vaccine recorded in IIS systems. CDC will work with the manufacturers, PCTs, and states to make sure they are aware of these updates.

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

COVID-19 Vaccination Record Card

Please keep this record card, which includes medical information about the vaccines you have received.

Por favor, guarde esta tarjeta de registro, que incluye información médica sobre las vacunas que ha recibido.

Last Name | First Name | MI

Date of birth | Patient number *(medical record or IIS record number)*

Vaccine	Product Name/Manufacturer Lot Number	Date	Healthcare Professional or Clinic Site
1st Dose COVID-19		____/____/____ *mm dd yy*	
2nd Dose COVID-19		____/____/____ *mm dd yy*	
Other		____/____/____ *mm dd yy*	
Other		____/____/____ *mm dd yy*	

Reminder! Return for a second dose!
¡Recordatorio! ¡Regrese para la segunda dosis!

Vaccine	Date / Fecha
COVID-19 vaccine Vacuna contra el COVID-19	_____/_____/_____ mm dd yy
Other Otra	_____/_____/_____ mm dd yy

Bring this vaccination record to every vaccination or medical visit. Check with your health care provider to make sure you are not missing any doses of routinely recommended vaccines.

For more information about COVID-19 and COVID-19 vaccine, visit **cdc.gov/coronavirus/2019-ncov/index.html**.

You can report possible adverse reactions following COVID-19 vaccination to the Vaccine Adverse Event Reporting System (VAERS) at **vaers.hhs.gov**.

Lleve este registro de vacunación a cada cita médica o de vacunación. Consulte con su proveedor de atención médica para asegurarse de que no le falte ninguna dosis de las vacunas recomendadas.

Para obtener más información sobre el COVID-19 y la vacuna contra el COVID-19, visite **espanol.cdc.gov/coronavirus/2019-ncov/index.html**.

Puede notificar las posibles reacciones adversas después de la vacunación contra el COVID-19 al Sistema de Notificación de Reacciones Adversas a las Vacunas (VAERS) en **vaers.hhs.gov**.

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Wed, 9 Jun 2021 22:04:08 +0000
To: (b)(4) (b)(4) (x)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: Myocarditis update
Attachments: Shimabukuro_VRBPAC_June 2021_CONFIDENTIAL.pdf

(b)(4)

I wanted to pass along a few updates. First- attached is Tom's presentation from the VRBPAC meeting tomorrow. Please keep the slides confidential for now, but he will be giving an update on myocarditis so we wanted to share this with you before tomorrow morning.

In addition- I wanted to let you know that we will be having an ACIP meeting on **June 18th** to discuss myocarditis, including an overall benefit/risk discussion. We will also have a brief discussion around data needed to inform possible future booster dose recommendations. We will likely be announcing this ACIP meeting tomorrow. I will pass along an agenda once it is available.

Thanks and let me know if you have any questions-

Sara

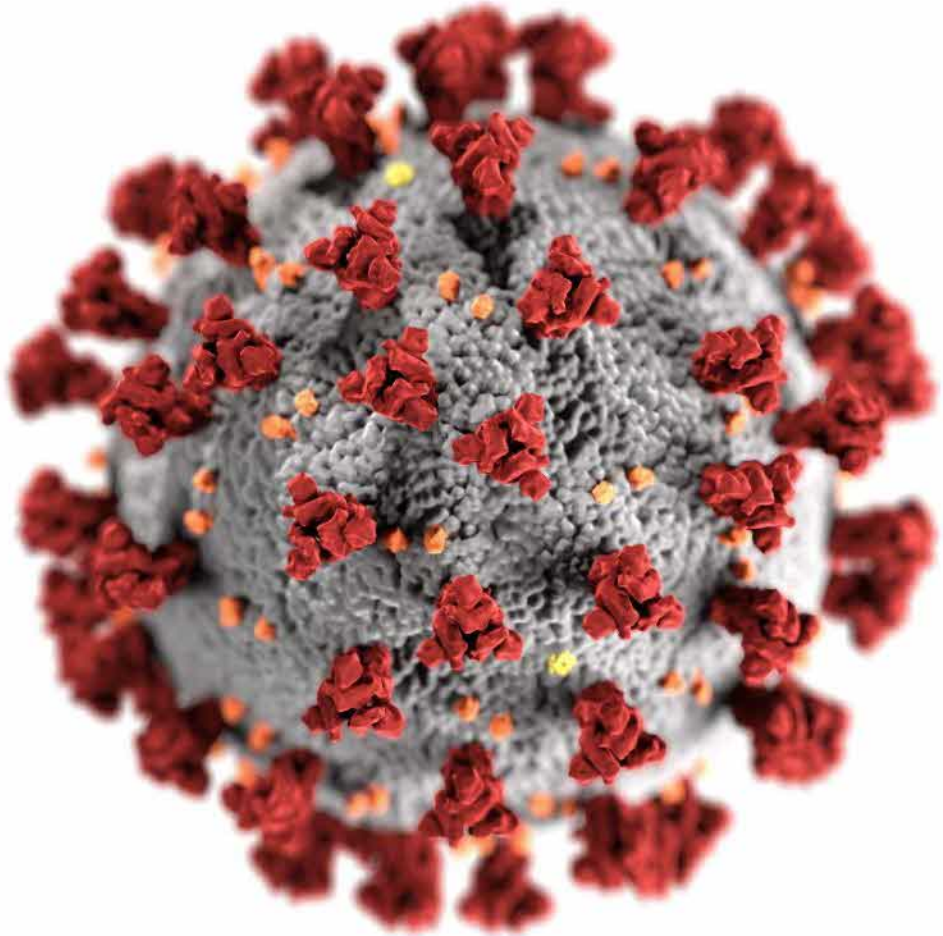
Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

COVID-19 Vaccine Safety Updates

Vaccines and Related Biological Products Advisory Committee (VRBPAC)

June 10, 2021

Tom Shimabukuro, MD, MPH, MBA
Vaccine Safety Team
CDC COVID-19 Vaccine Task Force



cdc.gov/coronavirus

Disclaimer

- The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC) or the U.S. Food and Drug Administration (FDA)
- Mention of a product or company name is for identification purposes only and does not constitute endorsement by CDC or FDA

Topics

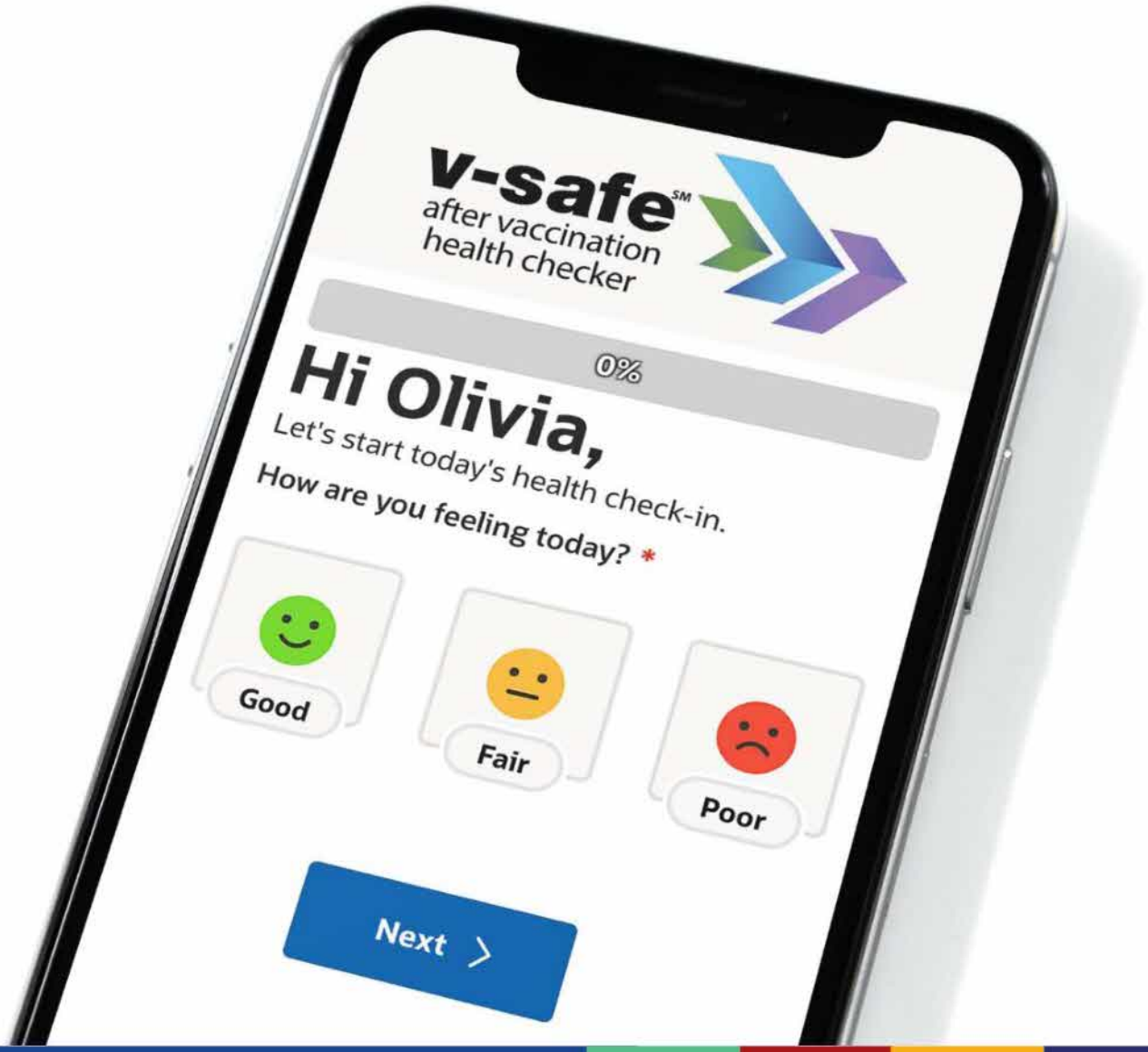
- Early safety data of Pfizer-BioNTech vaccination in persons aged 12–15 years old
- Myocarditis and pericarditis following mRNA vaccination

Early safety data of Pfizer-BioNTech vaccination in persons aged 12–15 years old

Smartphone-based active safety monitoring

v-safe[SM]
after vaccination
health checker

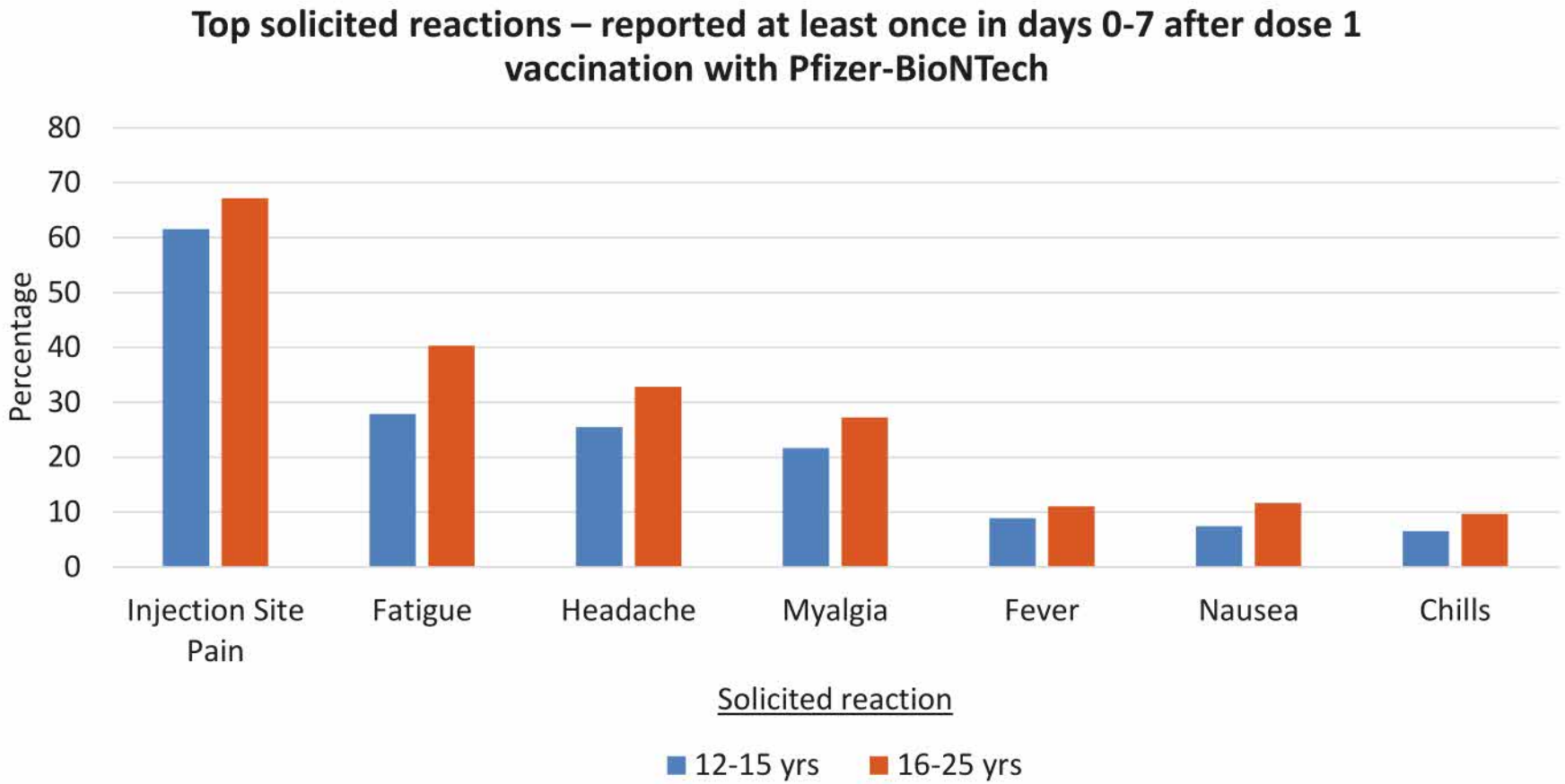
http://cdc.gov/vsafe



Overview of v-safe monitoring of Pfizer-BioNTech COVID-19 vaccine for younger adolescents

- On May 11, 2021, v-safe age limits expanded to allow registration down to 12 years of age at dose 1
- As of May 31 (5 am), 46,533 persons age 12–15 years were registered and submitted at least one health check-in during days 0–7 after dose 1 Pfizer-BioNTech COVID-19 vaccination

Pfizer-BioNTech monitoring in v-safe: Younger adolescents compared to older adolescents/young adults* (data thru May 31, 2021)



* Includes participants who completed at least one survey in the first week after dose 1 of Pfizer-BioNTech COVID-19 vaccine

VAERS is the nation's early warning system for vaccine safety

CDC + FDA

VAERS

Vaccine Adverse Event Reporting System

http://vaers.hhs.gov

VAERS

VAERS accepts all reports from everyone regardless of the plausibility of the vaccine causing the event or the clinical seriousness of the event

key strengths

- Rapidly detects potential safety problems
- Can detect rare adverse events

key limitations

- Inconsistent quality and completeness of information
- Reporting biases
- Generally, cannot determine cause and effect

Reports to VAERS after Pfizer-BioNTech COVID-19 vaccination: persons aged 12–15 years vs. 16–25 years* (data thru May 31, 2021)

Ages	N	Non-serious AEs (%)	Serious AEs‡,§ (%)
12–15 years old	1,497	1,449 (96.8)	48 (3.2)
16–25 years old† (for comparison)	10,095	9,439 (93.5)	656 (6.5)

- 12–15 years old: 3.26 million doses administered (May 10 thru May 31, 2021)
- 16–25 years old: 19.84 million doses administered (December 14, 2020, thru May 31, 2021)

* Data as of June 2, 2021, for reports with vaccination date and receipt date May 10 through May 31, 2021
† Data as of June 2, 2021, for reports with vaccination date and receipt date December 14, 2020, through May 31, 2021
‡ Based on the Code of Federal Regulations if one of the following is reported: death, life-threatening illness, hospitalization or prolongation of hospitalization, permanent disability, congenital anomaly or birth defect
§ Includes 0 reports of death in the 12–15-year-old age group and 14 reports of death in the 16–25-year-old age group

Most commonly reported adverse events to VAERS after Pfizer-BioNTech COVID-19 vaccination* (data thru May 31, 2021)

12–15 years old* (N= 1,497)

Adverse event‡	n (%)
Dizziness	416 (27.8)
Syncope	321 (21.4)
Nausea	192 (12.8)
Pallor	150 (10.0)
Loss of consciousness	142 (9.5)
Headache	134 (9.0)
Hyperhidrosis	132 (8.8)
Vomiting	119 (7.9)
Fatigue	79 (5.3)
Fall	77 (5.1)

16–25 years old† (N= 10,095)

(for comparison)

Adverse event‡	n (%)
Dizziness	2,249 (22.3)
Headache	1,798 (17.8)
Pyrexia	1,585 (15.7)
Nausea	1,577 (15.6)
Fatigue	1,367 (13.5)
Chills	1,307 (12.9)
Pain	1,254 (12.4)
Syncope	980 (9.7)
Hyperhidrosis	726 (7.2)
Vomiting	723 (7.2)

- 12–15 years old: 3.26 million doses administered (May 10 thru May 31, 2021)
- 16–25 years old: 19.84 million doses administered (December 14, 2020, thru May 31, 2021)

* Data as of June 2, 2021, for reports with vaccination date and receipt date May 10 through May 31, 2021

† Data as of June 2, 2021, for reports with vaccination date and receipt date December 14, 2020, through May 31, 2021

‡ Adverse events are not mutually exclusive

Myocarditis and pericarditis following mRNA vaccination

Preliminary myocarditis/pericarditis reports to VAERS following mRNA vaccination with dose number documented (data thru May 31, 2021)

Manufacturer	Myocarditis/pericarditis reports after dose 1	Myocarditis/pericarditis reports after dose 2
Pfizer-BioNTech (488 total reports)	116	372
Moderna (301 total report)	100	201
	216 Total reports after dose 1	573 Total reports after dose 2

- Includes total preliminary reports identified through VAERS database searches for reports with myocarditis/pericarditis MedDRA* codes and pre-screened VAERS reports with signs and symptoms consistent with myocarditis/pericarditis (and with dose number documented)
  - Follow-up, medical record review, application of CDC working case definition, and adjudication is ongoing or pending

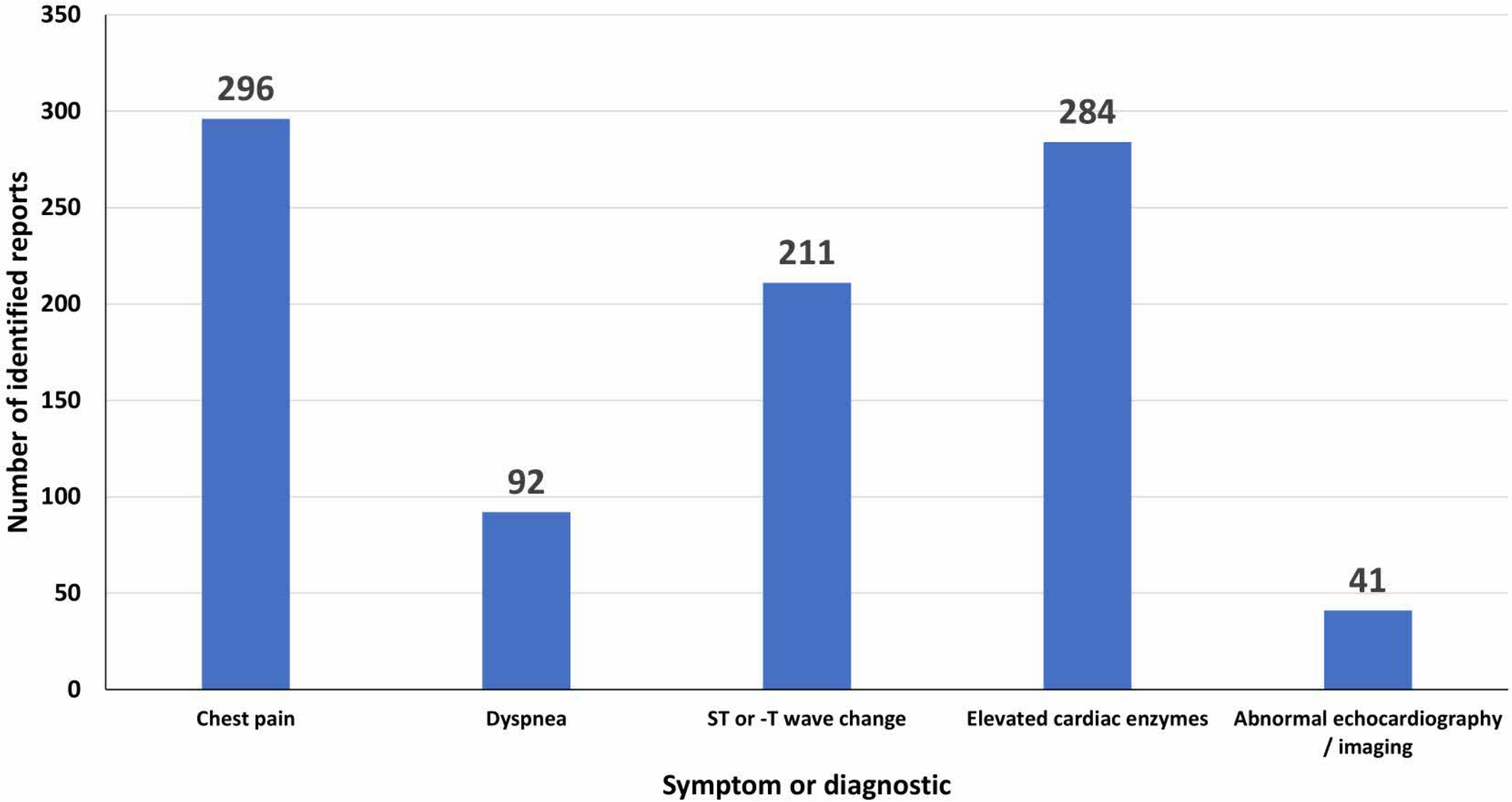
* Medical Dictionary for Regulatory Activities https://www.meddra.org/

Characteristics of preliminary myocarditis/pericarditis reports to VAERS following mRNA vaccination (data thru May 31, 2021)

Characteristics	Dose 1 (n=216)	Dose 2 (n=573)
Median age, years (range)	30 (12–94)	24 (14–87)
Median time to symptom onset, days (range)	3 (0–33)	2 (0–80)
Sex (%)		
Male	140 (65)	455 (79)
Female	73 (34)	113 (20)
Not reported/not available	3 (1)	5 (1)

* Includes total reports identified through VAERS database searches for reports with myocarditis/pericarditis MedDRA codes and pre-screened VAERS reports with signs and symptoms consistent with myocarditis/pericarditis (and with dose number documented); Follow-up, medical record review, application of CDC working case definition, and adjudication is ongoing or pending

Symptoms and diagnostics of preliminary myocarditis/pericarditis reports under review (limited to ≤30 years old) (N=475)



Outcomes of preliminary myocarditis/pericarditis cases reported to VAERS in persons ≤30 years old (N=475) (data thru May 31, 2021)

- 226 (of 475) case reports meet CDC working case definition; follow-up and review are in progress for remaining reports
- 285 (of 475) case reports had known disposition at time of report review
  - 270 discharged; 15 still hospitalized (3 in intensive care unit*)
    - Of 270 discharged
      - 246 (91%) to home
      - 3 to another facility (e.g., rehabilitation facility)
      - 21 did not specify
  - Of 270 discharged, recovery status was known for 221
    - **180 (81%) had full recovery of symptoms**
    - 41 (19%) had ongoing signs or symptoms or unknown status

* One patient with significant comorbidities and BMI>40; one patient with positive stool culture (Campylobacter)

Preliminary myocarditis/pericarditis reports to VAERS following dose 2 mRNA vaccination, Exp. vs. Obs. (data thru May 31, 2021)

Age groups	Doses admin	Crude reporting rate*	Expected†,‡ Myocarditis/ pericarditis cases	Observed† Myocarditis/ pericarditis reports
12–15 yrs	134,041	22.4	0–1	2
16–17 yrs	**2,258,932**	**35.0**	**2–19**	**79**
18–24 yrs	**9,776,719**	**20.6**	**8–83**	**196**
25–39 yrs	26,844,601	5.0	23–228	124
40–49 yrs	19,576,875	3.0	17–166	51
50–64 yrs	36,951,538	1.3	31–314	39
65+ yrs	42,124,078	0.9	36–358	26
NR	—	—	—	11

8.8% of doses admin

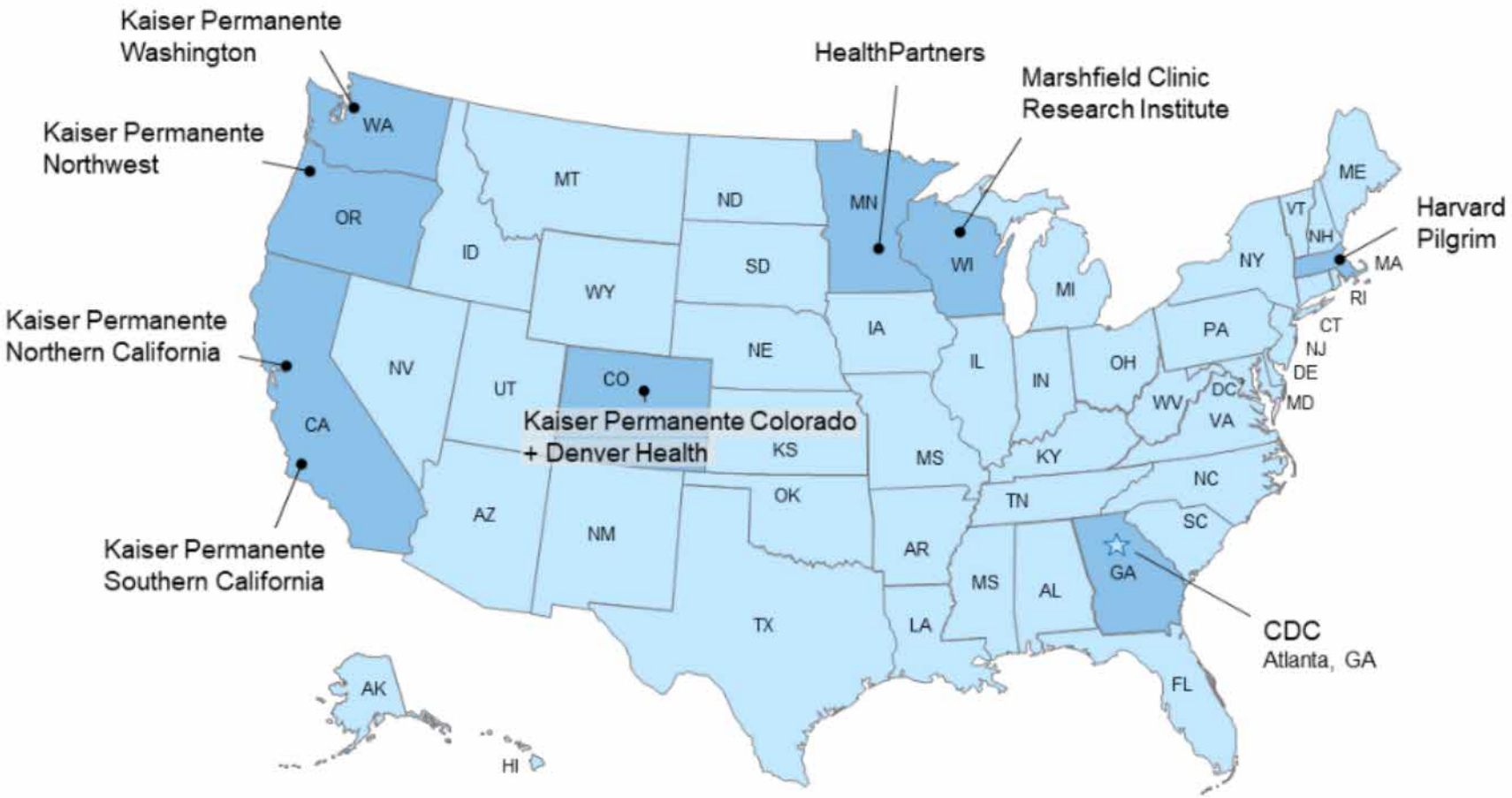
n=277 reports

52.5% of total reports

* Per million doses administered; † Assumes a 31-day post-vaccination observation window; 528 reports with symptom onset within 30 days of vaccination shown; ‡ Based on Gubernot et al. U.S. Population-Based background incidence rates of medical conditions for use in safety assessment of COVID-19 vaccines. Vaccine. 2021 May 14:S0264-410X(21)00578-8.

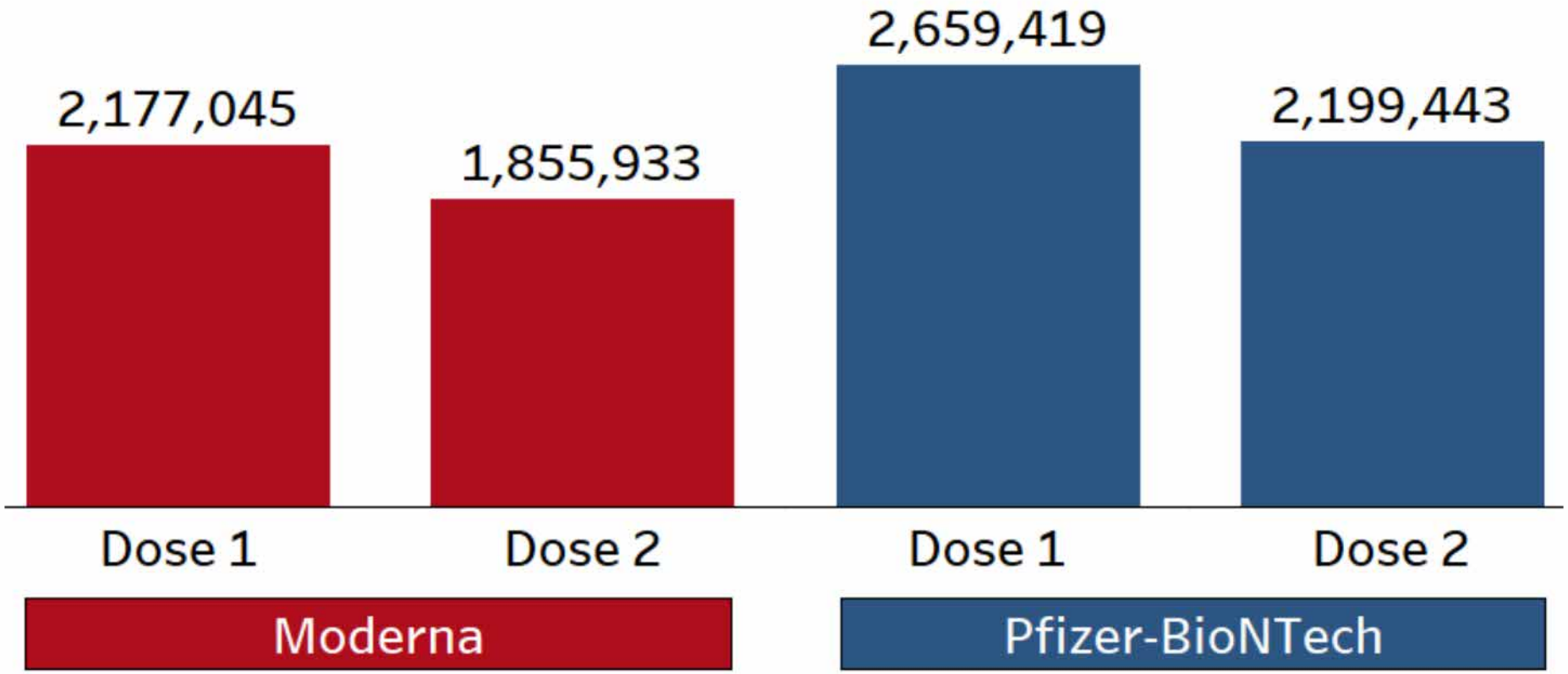
VSD

Vaccine Safety Datalink



- **9** participating integrated healthcare organizations
- Data on over **12 million** persons per year

COVID-19 vaccine doses administered in the VSD
(thru May 29, 2021)



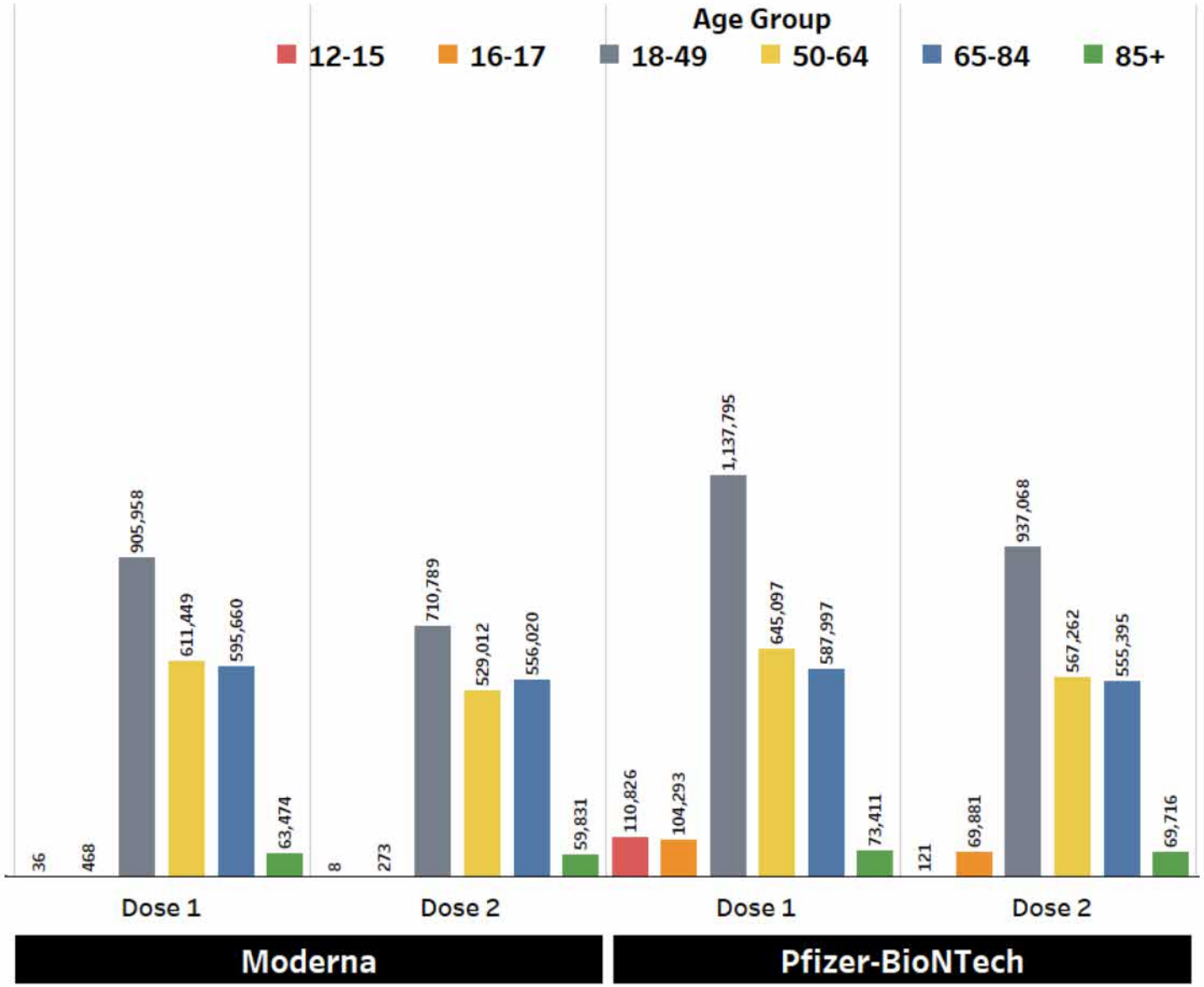
4,032,978
total doses

4,858,862
total doses

COVID-19 vaccine doses administered by age group in the VSD
(thru May 29, 2021)

Pfizer-BioNTech doses

- 12–15-year-olds
  - 110,826 first doses
  - 121 second doses
- 16–17-year-olds
  - 104,293 first doses
  - 69,881 second doses



Outcome events in the VSD in 21-day risk interval after either dose of any mRNA vaccine compared with outcome events in vaccinated comparators on the same calendar days

(thru May 29, 2021)

Pre-specified outcome event	Events in risk interval	Adj Rate Ratio*	95% CI	Signal
Acute disseminated encephalomyelitis	2	.	0.07– .	no
Acute myocardial infarction	560	1.00	0.86–1.17	no
Appendicitis	608	0.82	0.71–0.95	no
Bell's palsy	454	1.02	0.85–1.21	no
Cerebral venous sinus thrombosis	4	1.07	0.17–9.36	no
Disseminated intravascular coagulation	26	0.62	0.33–1.19	no
Encephalitis / myelitis / encephalomyelitis	15	1.06	0.38–3.41	no
Guillain-Barré syndrome	10	0.63	0.20–2.14	no
Stroke, hemorrhagic	224	0.89	0.70–1.14	no
Stroke, ischemic	944	0.97	0.86–1.10	no
Immune thrombocytopenia	43	1.04	0.58–1.92	no
Kawasaki disease	0	0.00	0.00–6.53	no
Myocarditis / pericarditis	**60**	**0.94**	**0.59–1.52**	**no**
Seizures	233	1.01	0.79–1.31	no
Transverse myelitis	2	0.50	0.04–15.32	no
Thrombotic thrombocytopenic purpura	5	2.04	0.33–17.36	no
Thrombosis with thrombocytopenia syndrome (TTS)	60	0.76	0.49–1.18	no
Venous thromboembolism	530	1.06	0.90–1.25	no
Pulmonary embolism	459	1.00	0.84–1.19	no

* Adjusted for VSD site, 5-year age group, sex, race/ethnicity, and calendar date. ne=not estimable

Myocarditis/pericarditis events in VSD in 16-39-year-olds in the 21-day risk interval compared with outcome events in vaccinated comparators on the same calendar days

(thru May 29, 2021)

Vaccine (dose #)	Events in risk interval	Adj Rate Ratio*	95% CI
Pfizer-BioNTech (both doses)	8	0.49	0.15–1.81
Pfizer-BioNTech (dose 1)	1	0.12	0–1.06
Pfizer-BioNTech (dose 2)	7	0.84	0.25–3.01
Moderna (both doses)†	14	4.07	1–27.59
Moderna (dose 1)	3	1.74	0.23–17.27
Moderna (dose 2)	**11**	**ne‡**	**3.61– .**

* Adjusted for VSD site, 5-year age group, sex, race/ethnicity, and calendar date
† Moderna COVID-19 vaccine is not authorized in persons aged <18 years
‡ ne=not estimable

Myocarditis/pericarditis incidence in VSD in 21-day risk interval, ages 16-39 years old (data thru May 29, 2021)

Vaccine(s) (dose #)	Cases	Doses admin	Rate per million doses (95% CI)
mRNA (both doses)	22	2,546,874	8.6 (5.4–13.1)
mRNA (dose 1)	4	1,428,872	2.8 (0.8–7.2)
mRNA (dose 2)	18	1,118,002	16.1 (9.5–25.4)
Pfizer-BioNTech (dose 1)	1	846,765	1.2 (0.0–6.6)
Pfizer-BioNTech (dose 2)	7	671,899	10.4 (4.2–21.5)
Moderna (dose 1)	3	582,107	5.2 (1.1–15.1)
Moderna (dose 2)	11	446,103	24.7 (12.3–44.1)

Summary

Summary (as of May 31, 2021)

- Initial safety findings from Pfizer-BioNTech COVID-19 vaccination of 12-15-year-olds from v-safe and VAERS surveillance are consistent with results from pre-authorization clinical trials
- Analysis of VAERS preliminary reports of myocarditis/pericarditis is in progress, including follow-up to obtain medical records, complete reviews, apply CDC working case definition, and adjudicate cases
- Preliminary findings suggest:
  - Median age of reported patients is younger and median time to symptom onset is shorter among those who developed symptoms after dose 2 vs. dose 1
  - Predominance of male patients in younger age groups, especially after dose 2
  - Observed reports > expected cases after dose 2 (16–24 years of age)
  - Limited outcome data suggest most patients (at least 81%) had full recovery of symptoms
- Early VSD data also suggest more cases after dose 2 vs. dose 1; rate ~16 cases per million 2nd doses
- ACIP meeting scheduled for June 18, 2021: update data, further evaluate myocarditis following mRNA COVID-19 vaccination, and assess benefit-risk balance

CDC educational materials*

Myocarditis and Pericarditis Following mRNA COVID-19 Vaccination

Updated May 27, 2021 Languages Print

What You Need to Know

- More than 165 million people have received at least one dose of COVID-19 vaccine in the United States, and CDC continues to monitor the safety of COVID-19 vaccines for any health problems that happen after vaccination.
- Since April 2021, there have been increased reports to the Vaccine Adverse Event Reporting System (VAERS) of cases of inflammation of the heart—called myocarditis and pericarditis—happening after mRNA COVID-19 vaccination (Pfizer-BioNTech and Moderna) in the United States.
- These reports are rare, given the number of vaccine doses administered, and have been reported after mRNA COVID-19 vaccination (Pfizer-BioNTech and Moderna), particularly in adolescents and young adults.
- CDC and its partners are actively monitoring these reports, by reviewing data and medical records, to learn more about what happened and to see if there is any relationship to COVID-19 vaccination.
- Most patients who received care responded well to medicine and rest and quickly felt better.

Clinical Considerations: Myocarditis and Pericarditis after Receipt of mRNA COVID-19 Vaccines Among Adolescents and Young Adults

Summary

Since April 2021, increased cases of myocarditis and pericarditis have been reported in the United States after mRNA COVID-19 vaccination (Pfizer-BioNTech and Moderna), particularly in adolescents and young adults. There has not been a similar reporting pattern observed after receipt of the Janssen COVID-19 Vaccine (Johnson & Johnson).

In most cases, patients who presented for medical care have responded well to medications and rest and had prompt improvement of symptoms. Reported cases have occurred predominantly in male adolescents and young adults 16 years of age and older. Onset was typically within several days after mRNA COVID-19 vaccination, and cases have occurred more often after the second dose than the first dose. CDC and its partners are investigating these reports of myocarditis and pericarditis following mRNA COVID-19 vaccination.

CDC continues to recommend COVID-19 vaccination for everyone 12 years of age and older given the risk of COVID-19 illness and related, possibly severe complications, such as long-term health problems, hospitalization, and even death.

* CDC: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/myocarditis.html and https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html

Acknowledgments

We wish to acknowledge the contributions of investigators from the following organizations:

Centers for Disease Control and Prevention

COVID-19 Vaccine Task Force
Vaccine Safety Team
Immunization Safety Office
Division of Healthcare Quality Promotion
Clinical Immunization Safety Assessment Project
Vaccine Safety Datalink

Food and Drug Administration

Center for Biologics Evaluation and Research

CDC vaccine safety monitoring

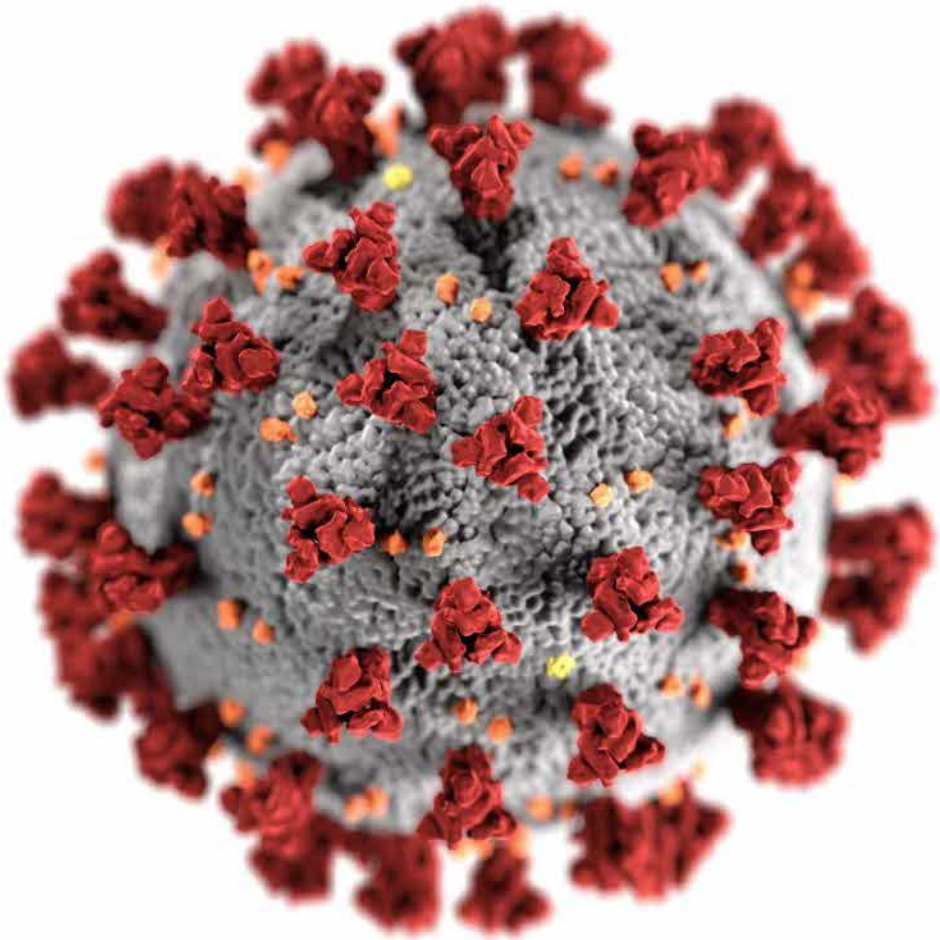
- Authorized COVID-19 vaccines are being administered under **the most intensive vaccine safety monitoring effort in U.S. history**
- Strong, complementary systems are in place—both new and established

v-safe	VAERS	VSD	CISA Project

Full list of U.S. COVID-19 vaccine safety monitoring systems

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety.html

Thank you!



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

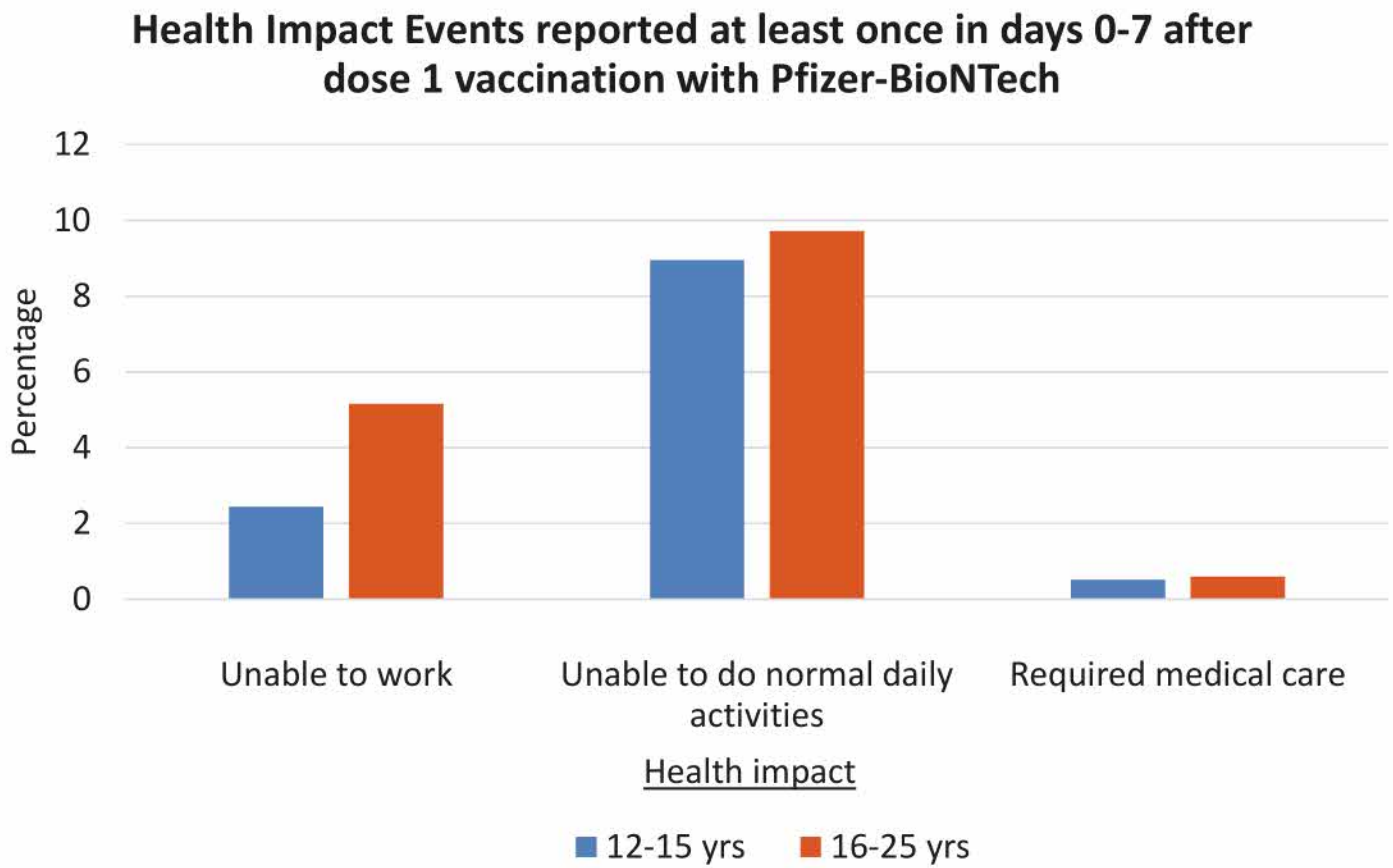
The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Timeline: U.S. adolescent COVID-19 vaccination

- December 2020: FDA issues Emergency Use Authorizations (EUAs) for two COVID-19 vaccines*
  - Pfizer-BioNTech COVID-19 vaccine for persons aged ≥16 years
  - Moderna COVID-19 vaccine for persons aged ≥18 years
- December 2020: CDC publishes ACIP interim recommendations for use of Pfizer-BioNTech and Moderna COVID-19 vaccines for age groups indicated in EUAs†
- February 2021: FDA issues EUA for Janssen COVID-19 vaccines for persons aged ≥18 years*
- March 2021: CDC published ACIP interim recommendations for use of Janssen COVID-19 vaccine for age group indicated in EUA†
- May 2021:
  - FDA expanded the EUA for the Pfizer-BioNTech COVID-19 vaccine to include adolescents aged 12–15 years*
  - ACIP publishes interim recommendations for use of the Pfizer-BioNTech COVID-19 vaccine in adolescents aged 12–15 years†

* FDA: COVID-19 Vaccines https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines
† CDC: COVID-19 ACIP Vaccine Recommendations https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html

Pfizer-BioNTech monitoring in v-safe: Younger adolescents compared to older adolescents/young adults* (data thru May 31, 2021)

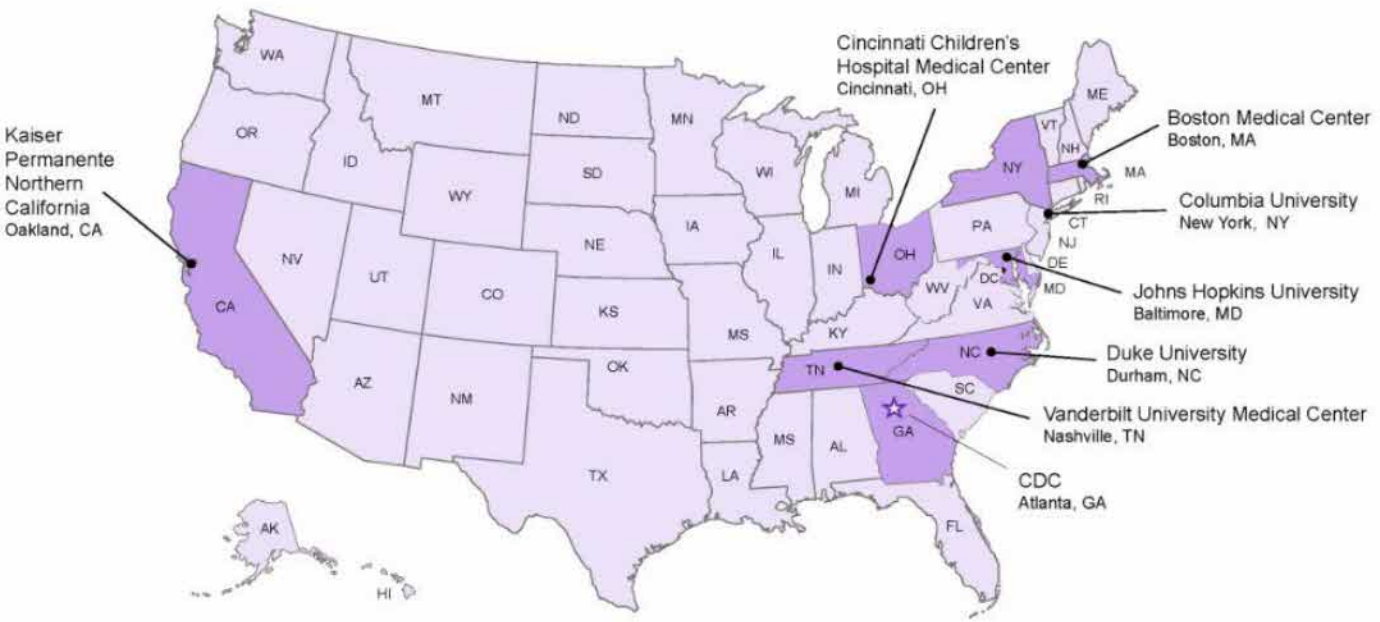


* Includes participants who completed at least one survey in the first week after dose 1 of Pfizer-BioNTech COVID-19 vaccine

CISA

Clinical Immunization Safety Assessment (CISA) Project

7 participating medical research centers with vaccine safety experts



- clinical consult services*
- clinical research

*More information about clinical consults available at http://www.cdc.gov/vaccinesafety/Activities/CISA.html

CDC working case definition for acute myocarditis

Acute Myocarditis

Clinical myocarditis

Probable Case

Presence of at least 1 new or worsening of the following clinical symptoms:

- chest pain/pressure/discomfort
- dyspnea/shortness of breath/pain with breathing, or
- palpitations

OR, infants and children <12 years of age may instead present with at least 2 of:

- irritability
- vomiting
- poor feeding
- tachypnea
- lethargy

AND

At least 1 new finding of:

- troponin level above upper limit of normal (any type of troponin),
- abnormal electrocardiogram (ECG or EKG) or rhythm monitoring findings consistent with myocarditis*, or
- abnormal cardiac function or wall motion abnormalities on echocardiogram or cardiac magnetic resonance imaging (cMRI).†

AND

- No other identifiable cause of the symptoms and findings

Confirmed Case

Presence of at least 1 new or worsening of the following clinical symptoms:

- chest pain/pressure/discomfort
- dyspnea/shortness of breath/pain with breathing, or
- palpitations

OR, infants and children <12 years of age may instead present with at least 2 of:

- irritability
- vomiting
- poor feeding
- tachypnea
- lethargy

AND

Troponin level above upper limit of normal (any type of troponin)

AND

At least one new finding of:

- Histopathologic confirmation of myocarditis§, or
- cMRI findings consistent with myocarditis¶

AND

- No other identifiable cause of the symptoms and findings

CDC working case definition for acute pericarditis

Presence of at least TWO new or worsening of the following clinical features:

- acute chest pain*
- pericardial rub on exam,
- new ST-elevation or PR-depression on EKG, or
- new or worsening pericardial effusion on echocardiogram or MRI

*typically described as pain made worse by lying down, deep inspiration, or cough and relieved by sitting up or leaning forward, although other types of chest pain may occur.

Notes:

1. Autopsy cases may be classified as pericarditis on basis of meeting histopathologic criteria of the pericardium

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Wed, 9 Jun 2021 22:04:17 +0000
To: (b)(4) (b)(4) T; (b)(4) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: Myocarditis updates
Attachments: Shimabukuro_VRBPAC_June 2021_CONFIDENTIAL.pdf

(b)(4) and (b)(4

I wanted to pass along a few updates. First- attached is Tom's presentation from the VRBPAC meeting tomorrow. Please keep the slides confidential for now, but he will be giving an update on myocarditis so we wanted to share this with you before tomorrow morning.

In addition- I wanted to let you know that we will be having an ACIP meeting on **June 18th** to discuss myocarditis, including an overall benefit/risk discussion. We will also have a brief discussion around data needed to inform possible future booster dose recommendations. We will likely be announcing this ACIP meeting tomorrow. I will pass along an agenda once it is available.

Thanks and let me know if you have any questions-

Sara

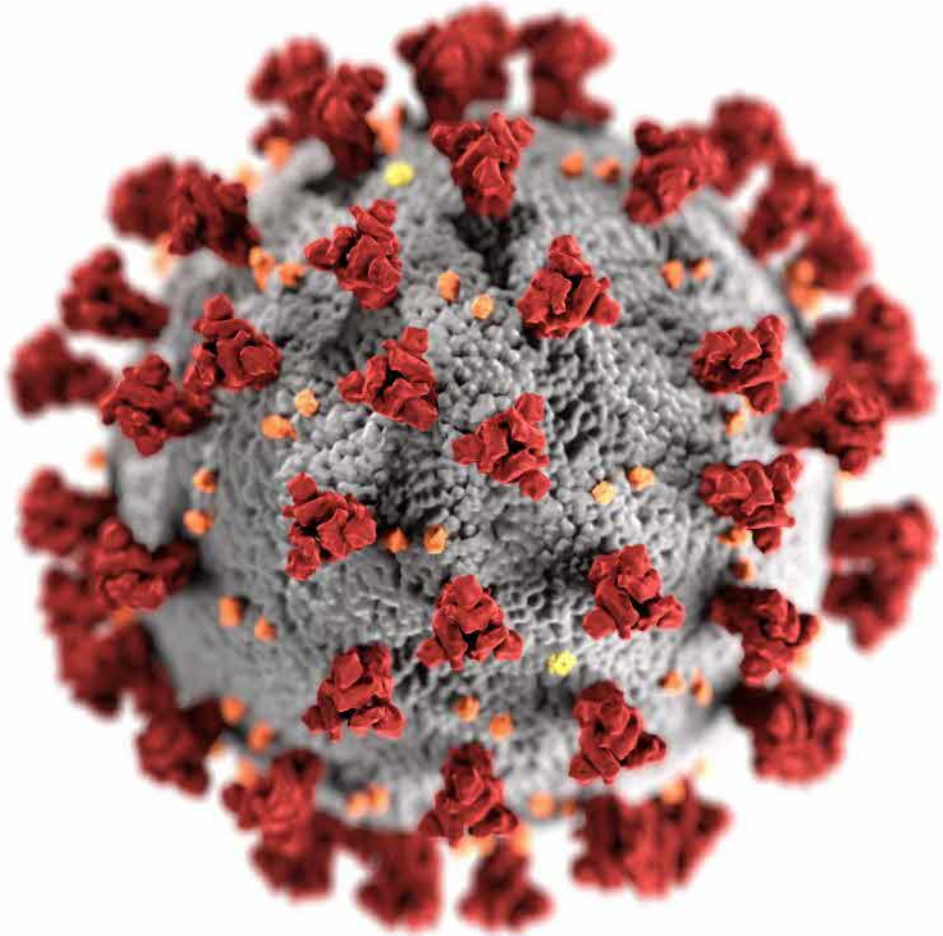
Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

COVID-19 Vaccine Safety Updates

Vaccines and Related Biological Products Advisory Committee (VRBPAC)

June 10, 2021

Tom Shimabukuro, MD, MPH, MBA
Vaccine Safety Team
CDC COVID-19 Vaccine Task Force



cdc.gov/coronavirus

Disclaimer

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- Mention of a product or company name is for identification purposes only and does not constitute endorsement by CDC or FDA

Topics

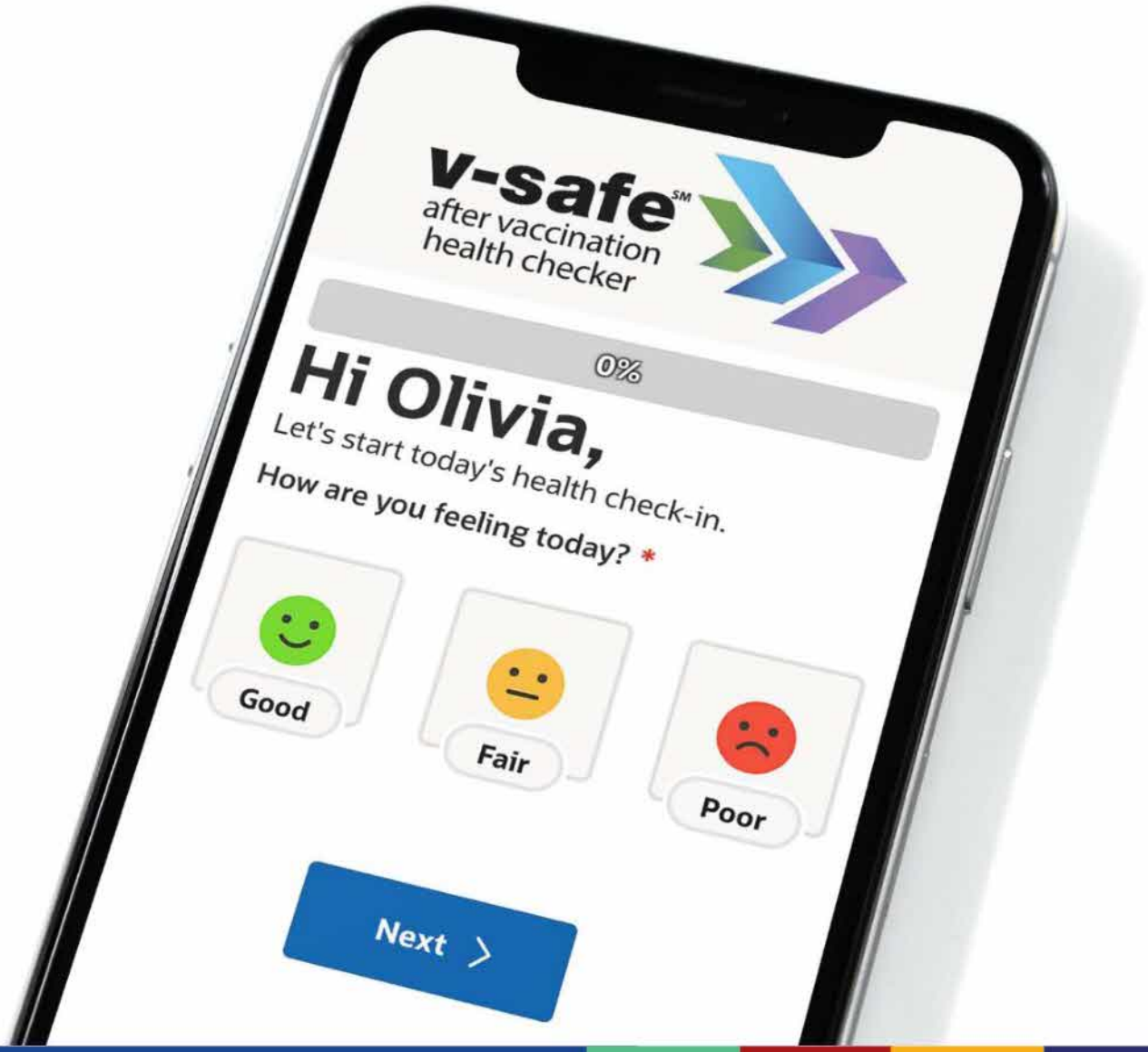
- Early safety data of Pfizer-BioNTech vaccination in persons aged 12–15 years old
- Myocarditis and pericarditis following mRNA vaccination

Early safety data of Pfizer-BioNTech vaccination in persons aged 12–15 years old

Smartphone-based active safety monitoring

v-safe[SM]
after vaccination
health checker

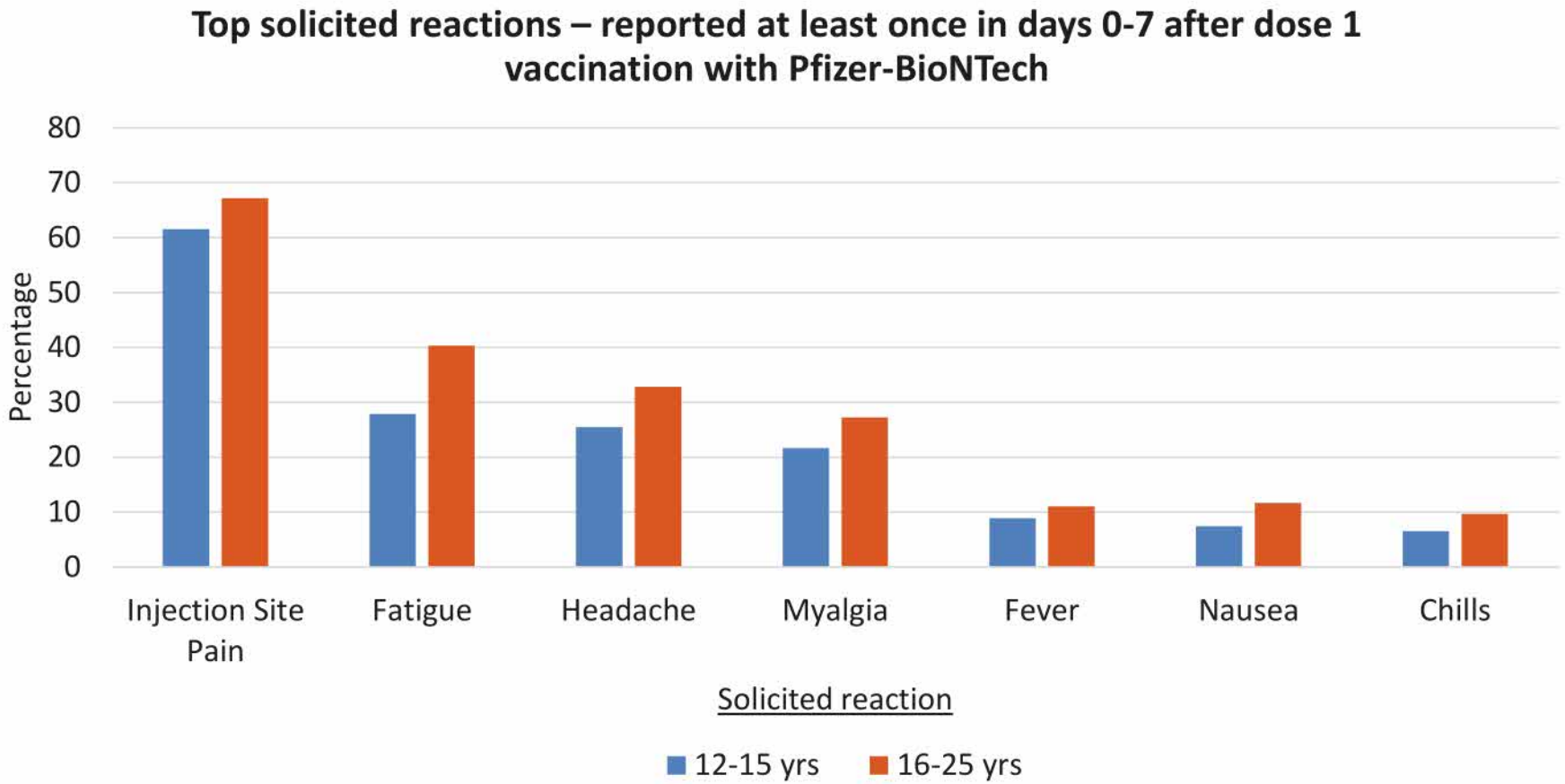
http://cdc.gov/vsafe



Overview of v-safe monitoring of Pfizer-BioNTech COVID-19 vaccine for younger adolescents

- On May 11, 2021, v-safe age limits expanded to allow registration down to 12 years of age at dose 1
- As of May 31 (5 am), 46,533 persons age 12–15 years were registered and submitted at least one health check-in during days 0–7 after dose 1 Pfizer-BioNTech COVID-19 vaccination

Pfizer-BioNTech monitoring in v-safe: Younger adolescents compared to older adolescents/young adults* (data thru May 31, 2021)



* Includes participants who completed at least one survey in the first week after dose 1 of Pfizer-BioNTech COVID-19 vaccine

VAERS is the nation's early warning system for vaccine safety

CDC + FDA

VAERS

Vaccine Adverse Event Reporting System

http://vaers.hhs.gov

VAERS

VAERS accepts all reports from everyone regardless of the plausibility of the vaccine causing the event or the clinical seriousness of the event

key strengths

- Rapidly detects potential safety problems
- Can detect rare adverse events

key limitations

- Inconsistent quality and completeness of information
- Reporting biases
- Generally, cannot determine cause and effect

Reports to VAERS after Pfizer-BioNTech COVID-19 vaccination: persons aged 12–15 years vs. 16–25 years* (data thru May 31, 2021)

Ages	N	Non-serious AEs (%)	Serious AEs‡,§ (%)
12–15 years old	1,497	1,449 (96.8)	48 (3.2)
16–25 years old† (for comparison)	10,095	9,439 (93.5)	656 (6.5)

- 12–15 years old: 3.26 million doses administered (May 10 thru May 31, 2021)
- 16–25 years old: 19.84 million doses administered (December 14, 2020, thru May 31, 2021)

* Data as of June 2, 2021, for reports with vaccination date and receipt date May 10 through May 31, 2021
† Data as of June 2, 2021, for reports with vaccination date and receipt date December 14, 2020, through May 31, 2021
‡ Based on the Code of Federal Regulations if one of the following is reported: death, life-threatening illness, hospitalization or prolongation of hospitalization, permanent disability, congenital anomaly or birth defect
§ Includes 0 reports of death in the 12–15-year-old age group and 14 reports of death in the 16–25-year-old age group

Most commonly reported adverse events to VAERS after Pfizer-BioNTech COVID-19 vaccination* (data thru May 31, 2021)

12–15 years old* (N= 1,497)

Adverse event‡	n (%)
Dizziness	416 (27.8)
Syncope	321 (21.4)
Nausea	192 (12.8)
Pallor	150 (10.0)
Loss of consciousness	142 (9.5)
Headache	134 (9.0)
Hyperhidrosis	132 (8.8)
Vomiting	119 (7.9)
Fatigue	79 (5.3)
Fall	77 (5.1)

16–25 years old† (N= 10,095)

(for comparison)

Adverse event‡	n (%)
Dizziness	2,249 (22.3)
Headache	1,798 (17.8)
Pyrexia	1,585 (15.7)
Nausea	1,577 (15.6)
Fatigue	1,367 (13.5)
Chills	1,307 (12.9)
Pain	1,254 (12.4)
Syncope	980 (9.7)
Hyperhidrosis	726 (7.2)
Vomiting	723 (7.2)

- 12–15 years old: 3.26 million doses administered (May 10 thru May 31, 2021)
- 16–25 years old: 19.84 million doses administered (December 14, 2020, thru May 31, 2021)

* Data as of June 2, 2021, for reports with vaccination date and receipt date May 10 through May 31, 2021

† Data as of June 2, 2021, for reports with vaccination date and receipt date December 14, 2020, through May 31, 2021

‡ Adverse events are not mutually exclusive

Myocarditis and pericarditis following mRNA vaccination

Preliminary myocarditis/pericarditis reports to VAERS following mRNA vaccination with dose number documented (data thru May 31, 2021)

Manufacturer	Myocarditis/pericarditis reports after dose 1	Myocarditis/pericarditis reports after dose 2
Pfizer-BioNTech (488 total reports)	116	372
Moderna (301 total report)	100	201
	216 Total reports after dose 1	573 Total reports after dose 2

- Includes total preliminary reports identified through VAERS database searches for reports with myocarditis/pericarditis MedDRA* codes and pre-screened VAERS reports with signs and symptoms consistent with myocarditis/pericarditis (and with dose number documented)
  - Follow-up, medical record review, application of CDC working case definition, and adjudication is ongoing or pending

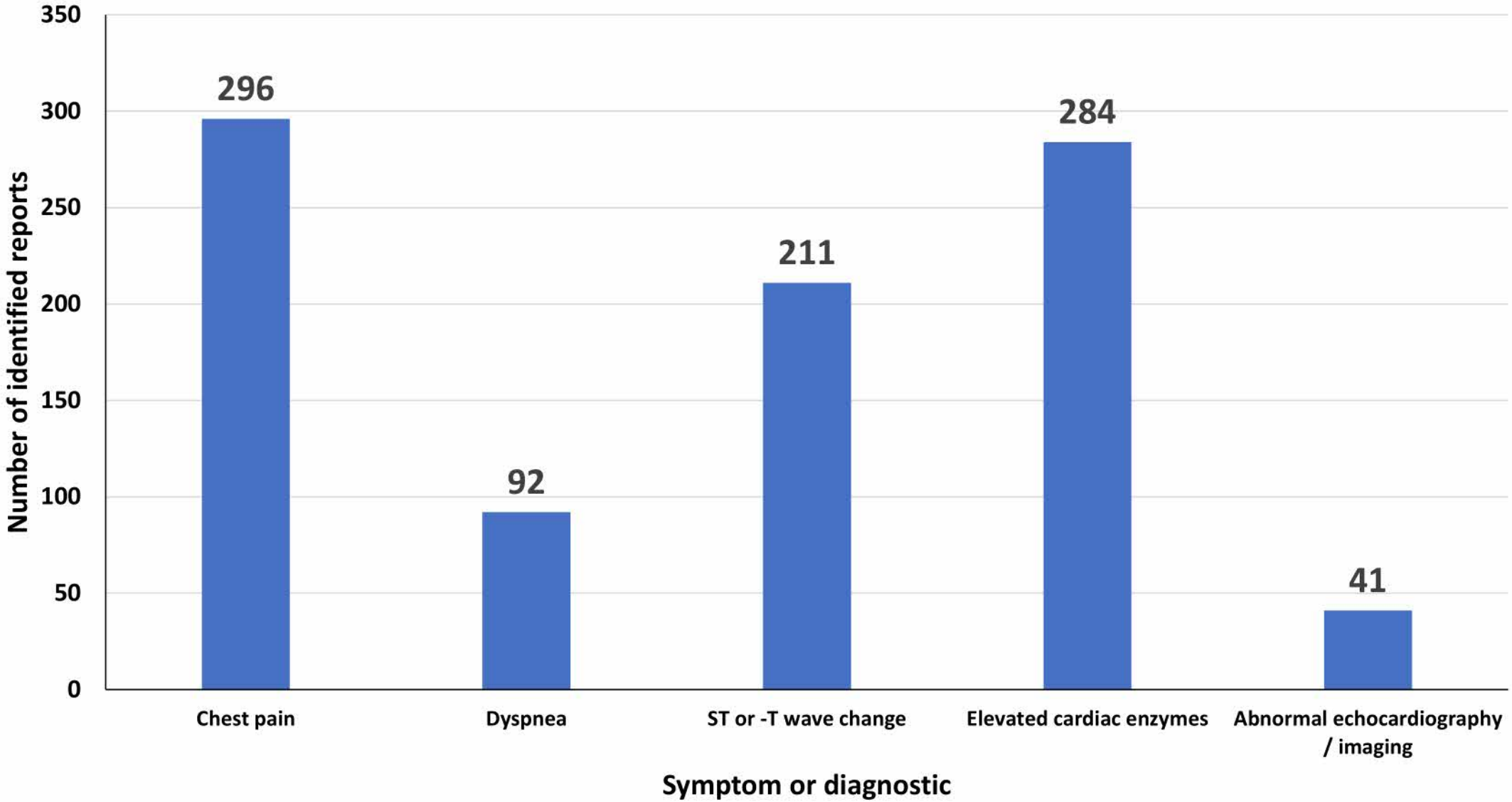
* Medical Dictionary for Regulatory Activities https://www.meddra.org/

Characteristics of preliminary myocarditis/pericarditis reports to VAERS following mRNA vaccination (data thru May 31, 2021)

Characteristics	Dose 1 (n=216)	Dose 2 (n=573)
Median age, years (range)	30 (12–94)	24 (14–87)
Median time to symptom onset, days (range)	3 (0–33)	2 (0–80)
Sex (%)		
Male	140 (65)	455 (79)
Female	73 (34)	113 (20)
Not reported/not available	3 (1)	5 (1)

* Includes total reports identified through VAERS database searches for reports with myocarditis/pericarditis MedDRA codes and pre-screened VAERS reports with signs and symptoms consistent with myocarditis/pericarditis (and with dose number documented); Follow-up, medical record review, application of CDC working case definition, and adjudication is ongoing or pending

Symptoms and diagnostics of preliminary myocarditis/pericarditis reports under review (limited to ≤30 years old) (N=475)



Outcomes of preliminary myocarditis/pericarditis cases reported to VAERS in persons ≤30 years old (N=475) (data thru May 31, 2021)

- 226 (of 475) case reports meet CDC working case definition; follow-up and review are in progress for remaining reports
- 285 (of 475) case reports had known disposition at time of report review
  - 270 discharged; 15 still hospitalized (3 in intensive care unit*)
    - Of 270 discharged
      - 246 (91%) to home
      - 3 to another facility (e.g., rehabilitation facility)
      - 21 did not specify
  - Of 270 discharged, recovery status was known for 221
    - **180 (81%) had full recovery of symptoms**
    - 41 (19%) had ongoing signs or symptoms or unknown status

* One patient with significant comorbidities and BMI>40; one patient with positive stool culture (Campylobacter)

Preliminary myocarditis/pericarditis reports to VAERS following dose 2 mRNA vaccination, Exp. vs. Obs. (data thru May 31, 2021)

Age groups	Doses admin	Crude reporting rate*	Expected†,‡ Myocarditis/ pericarditis cases	Observed† Myocarditis/ pericarditis reports
12–15 yrs	134,041	22.4	0–1	2
16–17 yrs	**2,258,932**	**35.0**	**2–19**	**79**
18–24 yrs	**9,776,719**	**20.6**	**8–83**	**196**
25–39 yrs	26,844,601	5.0	23–228	124
40–49 yrs	19,576,875	3.0	17–166	51
50–64 yrs	36,951,538	1.3	31–314	39
65+ yrs	42,124,078	0.9	36–358	26
NR	—	—	—	11

8.8% of doses admin

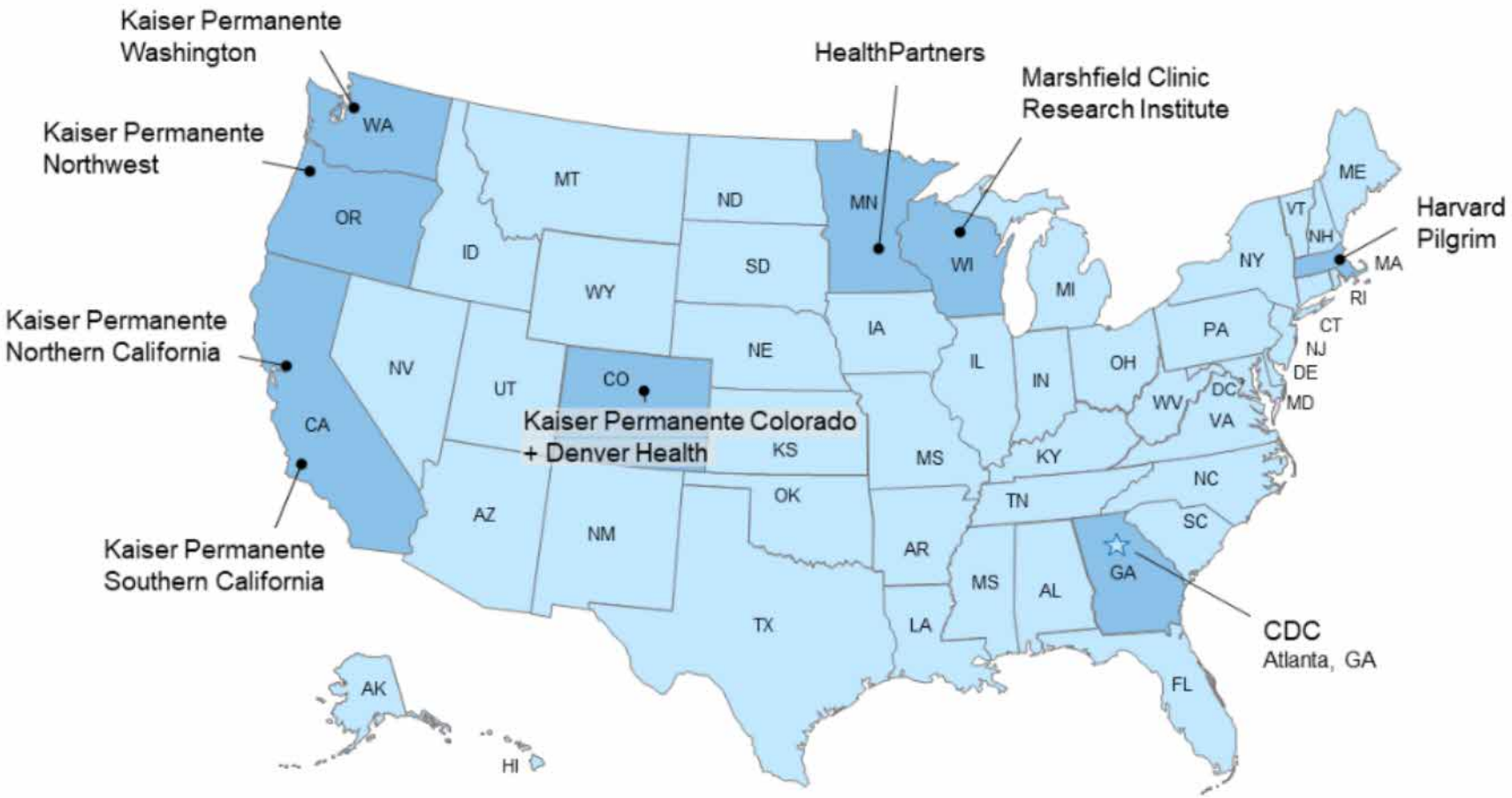
n=277 reports

52.5% of total reports

* Per million doses administered; † Assumes a 31-day post-vaccination observation window; 528 reports with symptom onset within 30 days of vaccination shown; ‡ Based on Gubernot et al. U.S. Population-Based background incidence rates of medical conditions for use in safety assessment of COVID-19 vaccines. Vaccine. 2021 May 14:S0264-410X(21)00578-8.

VSD

Vaccine Safety Datalink



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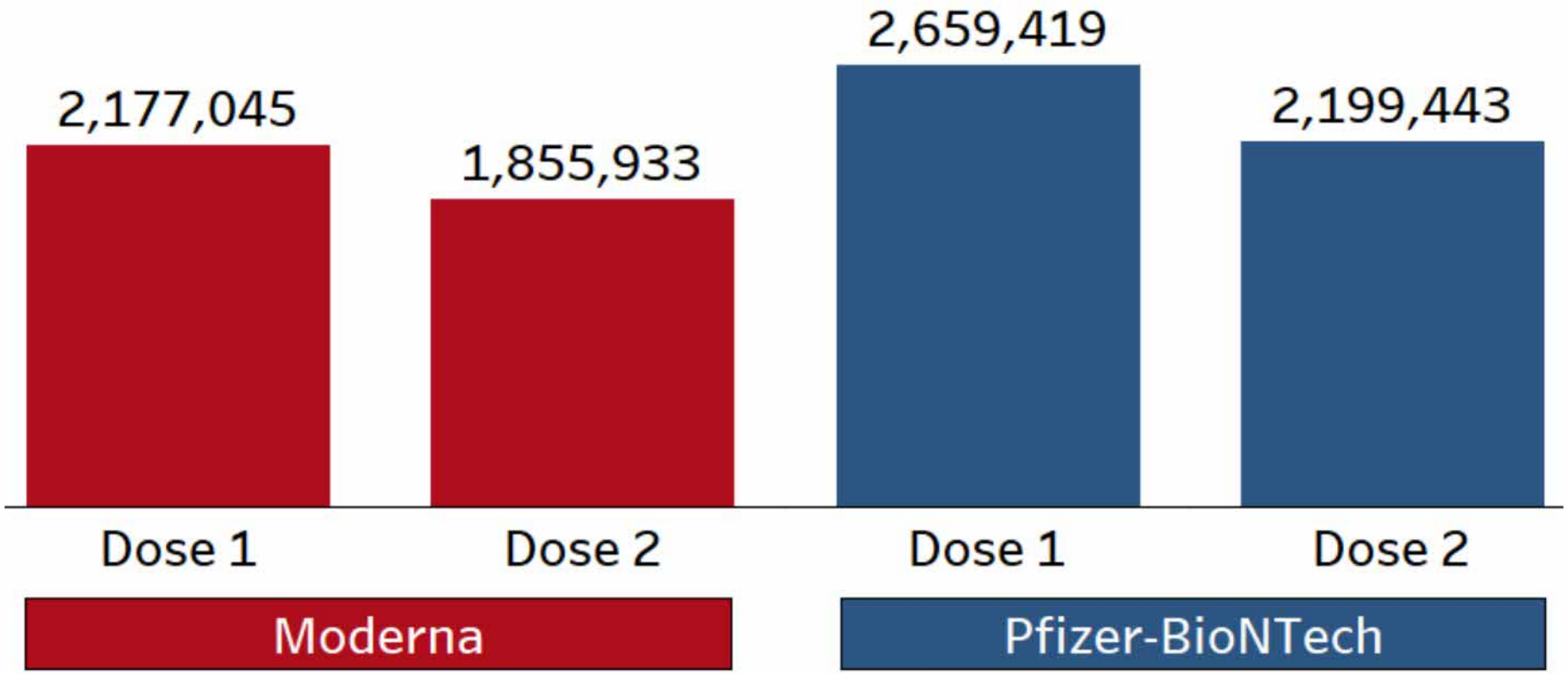
- Data on over **12 million** persons per year

COVID-19 vaccine doses administered in the VSD
(thru May 29, 2021)



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Pfizer-BioNTech doses

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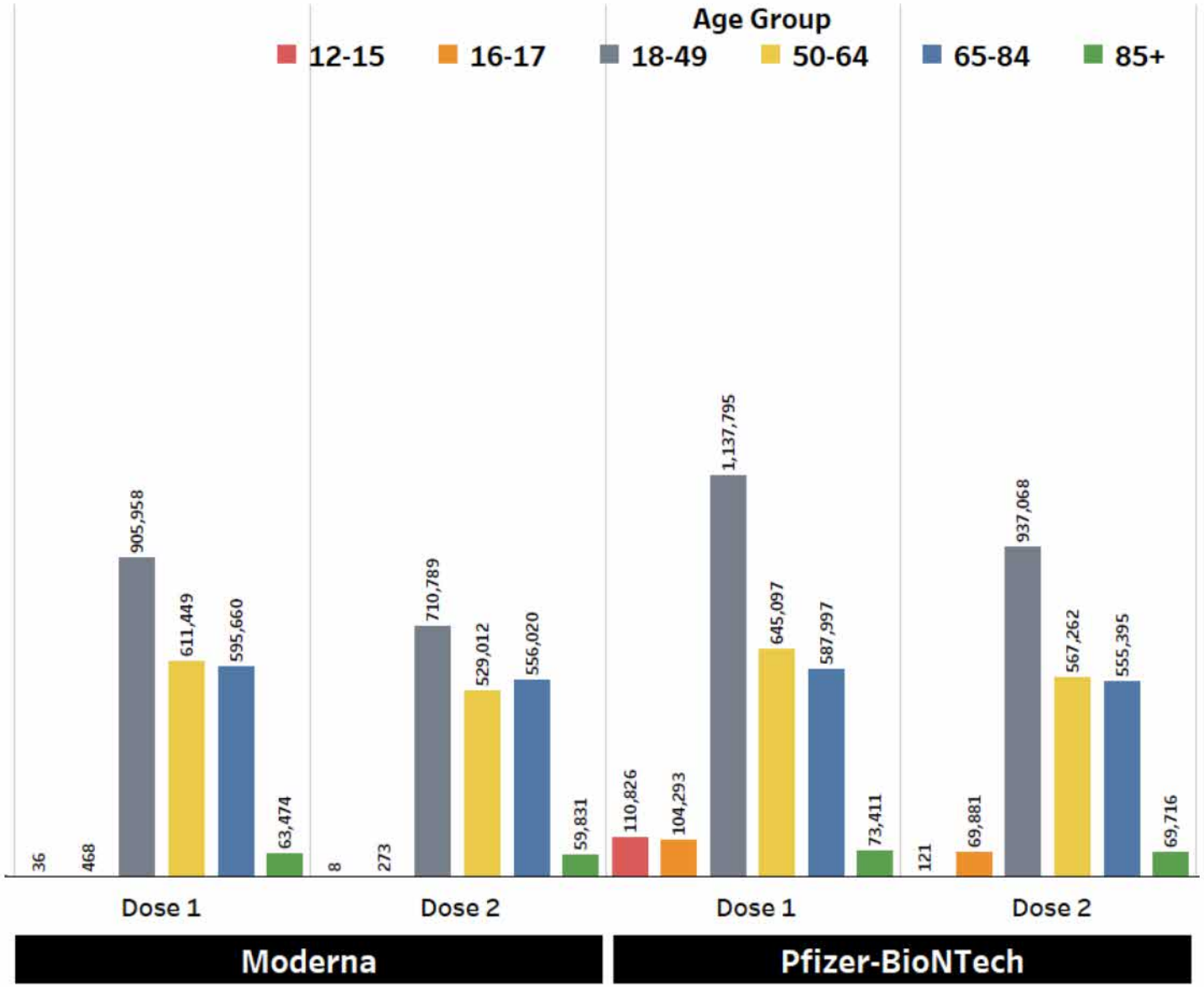
  - 104,293 first doses
  - 69,881 second doses



Outcome events in the VSD in 21-day risk interval after either dose of any mRNA vaccine compared with outcome events in vaccinated comparators on the same calendar days

(thru May 29, 2021)

Pre-specified outcome event	Events in risk interval	Adj Rate Ratio*	95% CI	Signal
Acute disseminated encephalomyelitis	2	.	0.07– .	no
Acute myocardial infarction	560	1.00	0.86–1.17	no
Appendicitis	608	0.82	0.71–0.95	no
Bell's palsy	454	1.02	0.85–1.21	no
Cerebral venous sinus thrombosis	4	1.07	0.17–9.36	no
Disseminated intravascular coagulation	26	0.62	0.33–1.19	no
Encephalitis / myelitis / encephalomyelitis	15	1.06	0.38–3.41	no
Guillain-Barré syndrome	10	0.63	0.20–2.14	no
Stroke, hemorrhagic	224	0.89	0.70–1.14	no
Stroke, ischemic	944	0.97	0.86–1.10	no
Immune thrombocytopenia	43	1.04	0.58–1.92	no
Kawasaki disease	0	0.00	0.00–6.53	no
Myocarditis / pericarditis	**60**	**0.94**	**0.59–1.52**	**no**
Seizures	233	1.01	0.79–1.31	no
Transverse myelitis	2	0.50	0.04–15.32	no
Thrombotic thrombocytopenic purpura	5	2.04	0.33–17.36	no
Thrombosis with thrombocytopenia syndrome (TTS)	60	0.76	0.49–1.18	no
Venous thromboembolism	530	1.06	0.90–1.25	no
Pulmonary embolism	459	1.00	0.84–1.19	no

* Adjusted for VSD site, 5-year age group, sex, race/ethnicity, and calendar date. ne=not estimable

Myocarditis/pericarditis events in VSD in 16-39-year-olds in the 21-day risk interval compared with outcome events in vaccinated comparators on the same calendar days

(thru May 29, 2021)

Vaccine (dose #)	Events in risk interval	Adj Rate Ratio*	95% CI
Pfizer-BioNTech (both doses)	8	0.49	0.15–1.81
Pfizer-BioNTech (dose 1)	1	0.12	0–1.06
Pfizer-BioNTech (dose 2)	7	0.84	0.25–3.01
Moderna (both doses)†	14	4.07	1–27.59
Moderna (dose 1)	3	1.74	0.23–17.27
Moderna (dose 2)	**11**	**ne‡**	**3.61– .**

* Adjusted for VSD site, 5-year age group, sex, race/ethnicity, and calendar date
† Moderna COVID-19 vaccine is not authorized in persons aged <18 years
‡ ne=not estimable

Myocarditis/pericarditis incidence in VSD in 21-day risk interval, ages 16-39 years old (data thru May 29, 2021)

Vaccine(s) (dose #)	Cases	Doses admin	Rate per million doses (95% CI)
mRNA (both doses)	22	2,546,874	8.6 (5.4–13.1)
mRNA (dose 1)	4	1,428,872	2.8 (0.8–7.2)
mRNA (dose 2)	18	1,118,002	16.1 (9.5–25.4)
Pfizer-BioNTech (dose 1)	1	846,765	1.2 (0.0–6.6)
Pfizer-BioNTech (dose 2)	7	671,899	10.4 (4.2–21.5)
Moderna (dose 1)	3	582,107	5.2 (1.1–15.1)
Moderna (dose 2)	11	446,103	24.7 (12.3–44.1)

Summary

Summary (as of May 31, 2021)

- Initial safety findings from Pfizer-BioNTech COVID-19 vaccination of 12-15-year-olds from v-safe and VAERS surveillance are consistent with results from pre-authorization clinical trials
- Analysis of VAERS preliminary reports of myocarditis/pericarditis is in progress, including follow-up to obtain medical records, complete reviews, apply CDC working case definition, and adjudicate cases
- Preliminary findings suggest:
  - Median age of reported patients is younger and median time to symptom onset is shorter among those who developed symptoms after dose 2 vs. dose 1
  - Predominance of male patients in younger age groups, especially after dose 2
  - Observed reports > expected cases after dose 2 (16–24 years of age)
  - Limited outcome data suggest most patients (at least 81%) had full recovery of symptoms
- Early VSD data also suggest more cases after dose 2 vs. dose 1; rate ~16 cases per million 2nd doses
- ACIP meeting scheduled for June 18, 2021: update data, further evaluate myocarditis following mRNA COVID-19 vaccination, and assess benefit-risk balance

CDC educational materials*

Myocarditis and Pericarditis Following mRNA COVID-19 Vaccination

Updated May 27, 2021 Languages Print

What You Need to Know

- More than 165 million people have received at least one dose of COVID-19 vaccine in the United States, and CDC continues to monitor the safety of COVID-19 vaccines for any health problems that happen after vaccination.
- Since April 2021, there have been increased reports to the Vaccine Adverse Event Reporting System (VAERS) of cases of inflammation of the heart—called myocarditis and pericarditis—happening after mRNA COVID-19 vaccination (Pfizer-BioNTech and Moderna) in the United States.
- These reports are rare, given the number of vaccine doses administered, and have been reported after mRNA COVID-19 vaccination (Pfizer-BioNTech and Moderna), particularly in adolescents and young adults.
- CDC and its partners are actively monitoring these reports, by reviewing data and medical records, to learn more about what happened and to see if there is any relationship to COVID-19 vaccination.
- Most patients who received care responded well to medicine and rest and quickly felt better.

Clinical Considerations: Myocarditis and Pericarditis after Receipt of mRNA COVID-19 Vaccines Among Adolescents and Young Adults

Summary

Since April 2021, increased cases of myocarditis and pericarditis have been reported in the United States after mRNA COVID-19 vaccination (Pfizer-BioNTech and Moderna), particularly in adolescents and young adults. There has not been a similar reporting pattern observed after receipt of the Janssen COVID-19 Vaccine (Johnson & Johnson).

In most cases, patients who presented for medical care have responded well to medications and rest and had prompt improvement of symptoms. Reported cases have occurred predominantly in male adolescents and young adults 16 years of age and older. Onset was typically within several days after mRNA COVID-19 vaccination, and cases have occurred more often after the second dose than the first dose. CDC and its partners are investigating these reports of myocarditis and pericarditis following mRNA COVID-19 vaccination.

CDC continues to recommend COVID-19 vaccination for everyone 12 years of age and older given the risk of COVID-19 illness and related, possibly severe complications, such as long-term health problems, hospitalization, and even death.

* CDC: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/myocarditis.html and https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html

Acknowledgments

We wish to acknowledge the contributions of investigators from the following organizations:

Centers for Disease Control and Prevention

COVID-19 Vaccine Task Force
Vaccine Safety Team
Immunization Safety Office
Division of Healthcare Quality Promotion
Clinical Immunization Safety Assessment Project
Vaccine Safety Datalink

Food and Drug Administration

Center for Biologics Evaluation and Research

CDC vaccine safety monitoring

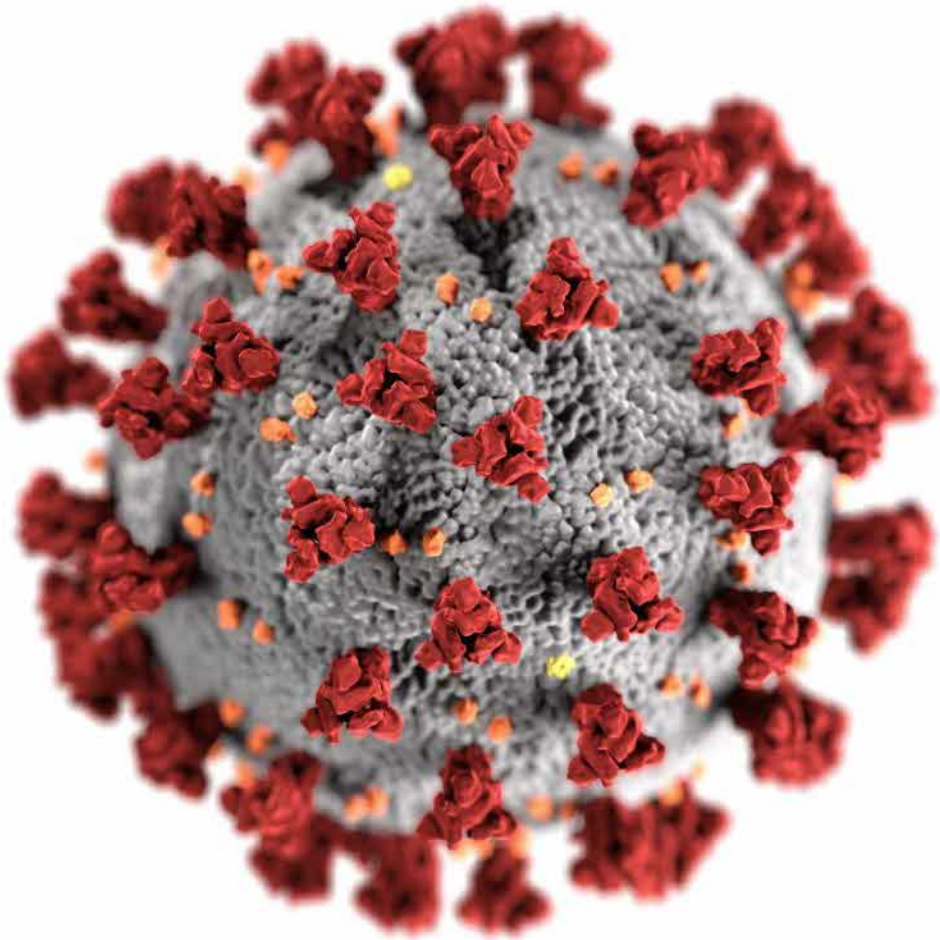
- Authorized COVID-19 vaccines are being administered under **the most intensive vaccine safety monitoring effort in U.S. history**
- Strong, complementary systems are in place—both new and established

v-safe	VAERS	VSD	CISA Project

Full list of U.S. COVID-19 vaccine safety monitoring systems

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety.html

Thank you!



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

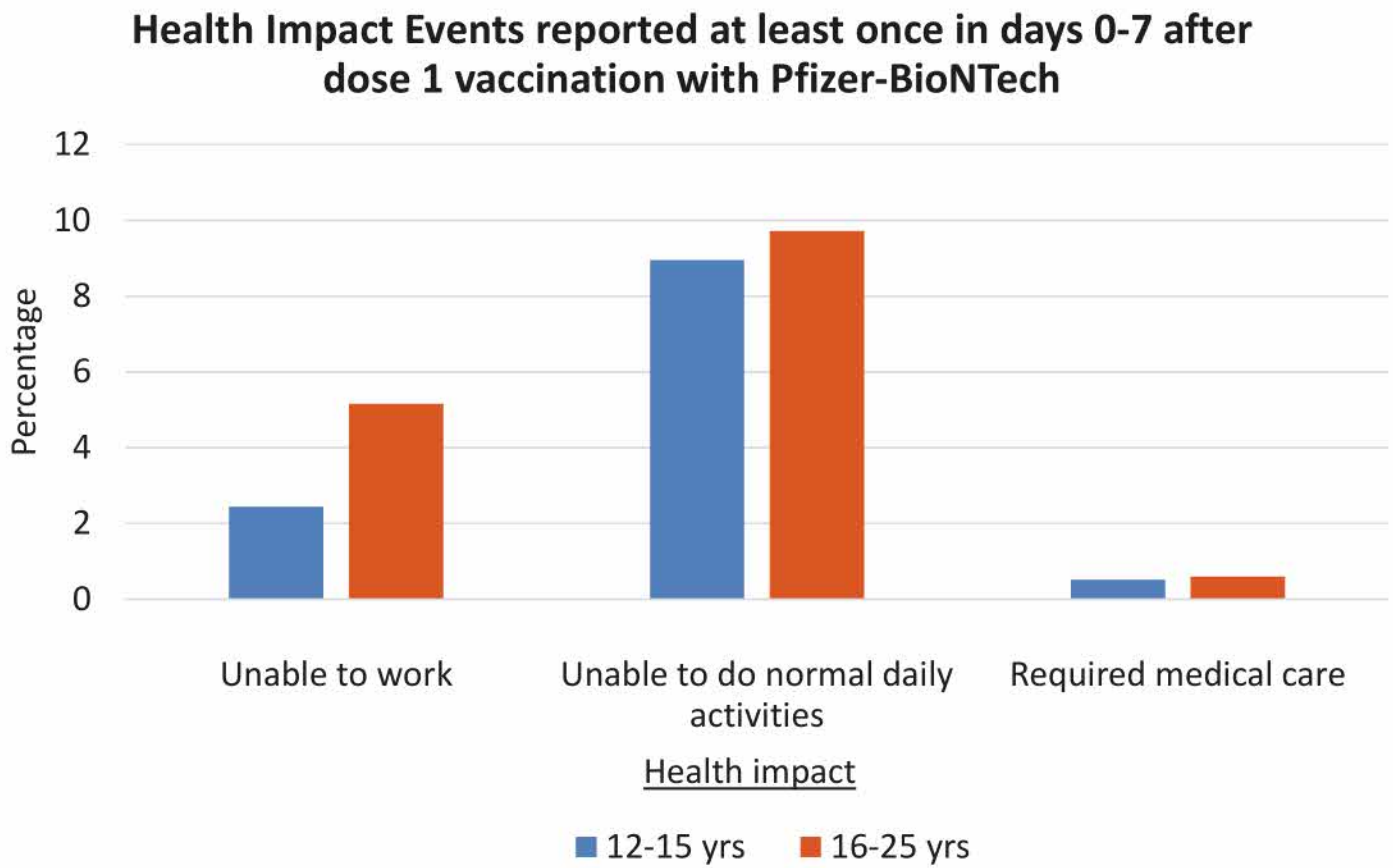
The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Timeline: U.S. adolescent COVID-19 vaccination

- December 2020: FDA issues Emergency Use Authorizations (EUAs) for two COVID-19 vaccines*
  - Pfizer-BioNTech COVID-19 vaccine for persons aged ≥16 years
  - Moderna COVID-19 vaccine for persons aged ≥18 years
- December 2020: CDC publishes ACIP interim recommendations for use of Pfizer-BioNTech and Moderna COVID-19 vaccines for age groups indicated in EUAs†
- February 2021: FDA issues EUA for Janssen COVID-19 vaccines for persons aged ≥18 years*
- March 2021: CDC published ACIP interim recommendations for use of Janssen COVID-19 vaccine for age group indicated in EUA†
- May 2021:
  - FDA expanded the EUA for the Pfizer-BioNTech COVID-19 vaccine to include adolescents aged 12–15 years*
  - ACIP publishes interim recommendations for use of the Pfizer-BioNTech COVID-19 vaccine in adolescents aged 12–15 years†

* FDA: COVID-19 Vaccines https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines
† CDC: COVID-19 ACIP Vaccine Recommendations https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html

Pfizer-BioNTech monitoring in v-safe: Younger adolescents compared to older adolescents/young adults* (data thru May 31, 2021)

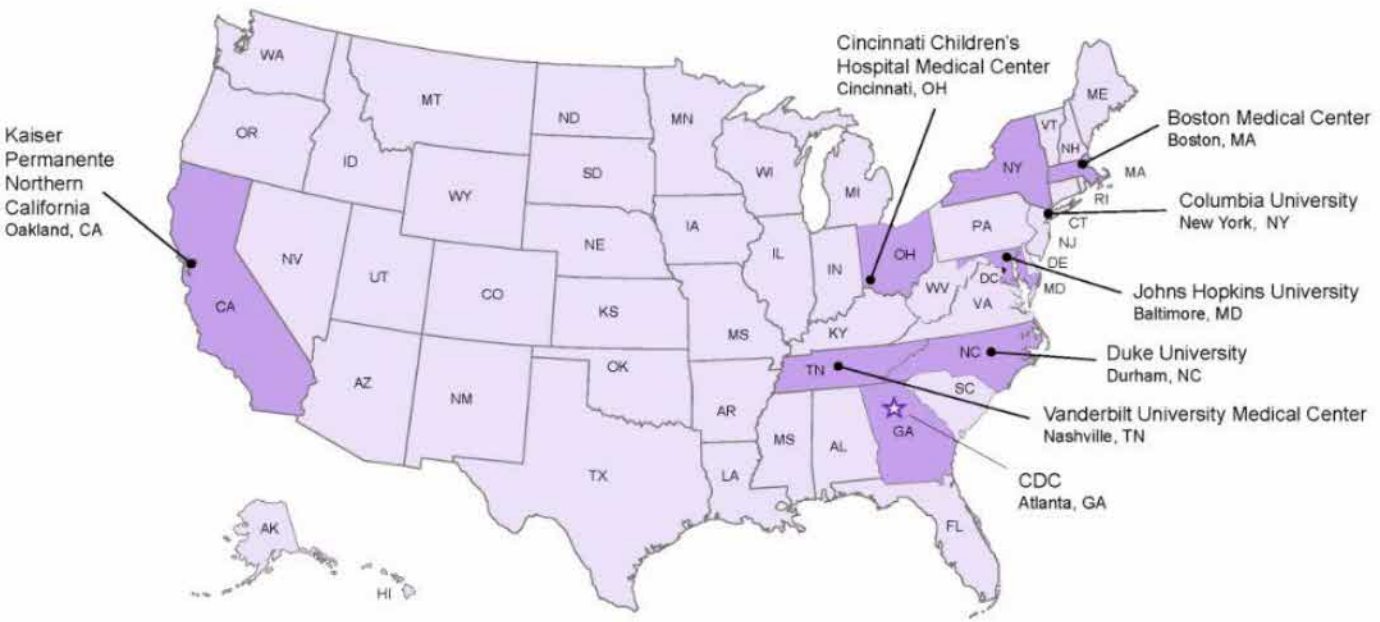


* Includes participants who completed at least one survey in the first week after dose 1 of Pfizer-BioNTech COVID-19 vaccine

CISA

Clinical Immunization Safety Assessment (CISA) Project

7 participating medical research centers with vaccine safety experts



- clinical consult services*
- clinical research

*More information about clinical consults available at http://www.cdc.gov/vaccinesafety/Activities/CISA.html

CDC working case definition for acute myocarditis

Acute Myocarditis

Clinical myocarditis

Probable Case

Presence of at least 1 new or worsening of the following clinical symptoms:

- chest pain/pressure/discomfort
- dyspnea/shortness of breath/pain with breathing, or
- palpitations

OR, infants and children <12 years of age may instead present with at least 2 of:

- irritability
- vomiting
- poor feeding
- tachypnea
- lethargy

AND

At least 1 new finding of:

- troponin level above upper limit of normal (any type of troponin),
- abnormal electrocardiogram (ECG or EKG) or rhythm monitoring findings consistent with myocarditis*, or
- abnormal cardiac function or wall motion abnormalities on echocardiogram or cardiac magnetic resonance imaging (cMRI).†

AND

- No other identifiable cause of the symptoms and findings

Confirmed Case

Presence of at least 1 new or worsening of the following clinical symptoms:

- chest pain/pressure/discomfort
- dyspnea/shortness of breath/pain with breathing, or
- palpitations

OR, infants and children <12 years of age may instead present with at least 2 of:

- irritability
- vomiting
- poor feeding
- tachypnea
- lethargy

AND

Troponin level above upper limit of normal (any type of troponin)

AND

At least one new finding of:

- Histopathologic confirmation of myocarditis§, or
- cMRI findings consistent with myocarditis¶

AND

- No other identifiable cause of the symptoms and findings

CDC working case definition for acute pericarditis

Presence of at least TWO new or worsening of the following clinical features:

- acute chest pain*
- pericardial rub on exam,
- new ST-elevation or PR-depression on EKG, or
- new or worsening pericardial effusion on echocardiogram or MRI

*typically described as pain made worse by lying down, deep inspiration, or cough and relieved by sitting up or leaning forward, although other types of chest pain may occur.

Notes:

1. Autopsy cases may be classified as pericarditis on basis of meeting histopathologic criteria of the pericardium

From: (b)(4) (b)(4) (x)
Sent: Fri, 7 May 2021 12:39:58 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); Cohn, Amanda (CDC/DDID/NCIRD/OD); Mbaeyi, Sarah (CDC/DDID/NCIRD/OD); MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: New Publication - Booster Doses
Attachments: COVID-19 - Wu - Preliminary Analysis of Safety & Immunogenicity of SARS-CoV-2 Variant Vaccine Booster - MedRxix - 2021.pdf

Good morning,
I thought you might be interested in this publication in *MedRxiv* of the early results of a study of a booster dose of Moderna's COVID-19 vaccine or a 1273.351 variant vaccine in healthy adults.
(b)(4)

Please consider the environment before printing this email

Preliminary Analysis of Safety and Immunogenicity of a SARS-CoV-2 Variant Vaccine Booster

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*Contributed equally to the manuscript

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Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causative agent of a global pandemic of coronavirus disease 2019 (COVID-19) that has led to more than 3 million deaths worldwide. Safe and effective vaccines are now available, including the mRNA-1273 prototype vaccine, which encodes for the Wuhan SARS-CoV-2 spike (S) protein stabilized in the prefusion conformation by 2 proline substitutions. This vaccine showed 94% efficacy in prevention of symptomatic COVID-19 disease in a phase 3 clinical study. Recently, SARS-CoV-2 variants have emerged, some of which have shown decreased susceptibility to neutralization by vaccine-induced antibody, most notably the B.1.351 variant, although the overall impact on vaccine efficacy remains to be determined. In addition, recent evidence of waning antibody levels after infection or vaccination point to the need for periodic boosting of immunity. Here we present the preliminary evaluation of a clinical study on the use of the prototype mRNA-1273 or modified COVID-19 mRNA vaccines, designed to target emerging SARS-CoV-2 variants as booster vaccines in participants previously vaccinated approximately 6 months earlier with two doses of the prototype vaccine, mRNA-1273. The modified vaccines include a monovalent mRNA-1273.351 encoding for the S protein found in the B.1.351 variant and multivalent mRNA-1273.211 comprising a 1:1 mix of mRNA-1273 and mRNA-1273.351. As single 50 μg booster vaccinations, both mRNA-1273 and mRNA-1273.351 had acceptable safety profiles and were immunogenic. Antibody neutralization titers against B.1.351 and P.1 variants measured by SARS-CoV-2 pseudovirus neutralization (PsVN) assays before the booster vaccinations, approximately 6 to 8 months after the primary series, were low or below the assay limit of quantification, although geometric mean titers versus the wild-type strain remained above

levels likely to be protective. Two weeks after the booster vaccinations, titers against the wild-type original strain, B.1.351, and P.1 variants increased to levels similar to or higher than peak titers after the primary series vaccinations. Although both mRNA-1273 and mRNA-1273.351 boosted neutralization of the wild-type original strain, and B.1.351 and P.1 variants, mRNA-1273.351 appeared to be more effective at increasing neutralization of the B.1.351 virus versus a boost with mRNA-1273. The vaccine trial is ongoing and boosting of clinical trial participants with the multivalent mRNA-1273.211 is currently being evaluated.

Introduction

Emergence of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) in December 2019 resulted in a pandemic of coronavirus disease 2019 (COVID-19) that has caused millions of deaths globally (1, 2). Vaccines for SARS-CoV-2 targeting the spike (S) protein (mRNA-1273; BNT162b2; AD26.COV2.S; AZD1222) have been developed and administered to over a billion people worldwide (3). Although these vaccines are highly effective in reducing symptoms of COVID-19 and severe disease, several viral variants with changes in the S protein and elsewhere in the viral genome have arisen, some of which have been identified as variants of concern (VOC) due to evidence of increased transmissibility and disease severity, and decreased neutralization by antibodies generated during previous infection or vaccination (B.1.1.7, B.1.351, P.1, B.1.427, and B.1.429) in the United States (US) (4). The B.1.1.7 variant which first emerged in the United Kingdom in September 2020 has become the most prevalent circulating variant in the US and in most other countries (5, 6). The B.1.351 variant is most prevalent in South Africa (~90%) and the P.1 variant is most prevalent in Brazil (>90%) as of late March, 2021 (5). However, the overall impact of variants on vaccine efficacy is being evaluated (7).

mRNA-1273, a novel lipid nanoparticle-encapsulated messenger RNA encoding a prefusion stabilized S protein of the Wuhan-Hu-1 isolate, demonstrated anti-SARS-CoV-2 immune responses in phase 1 (NCT04283461) and 2 (NCT04405076) trials in adults, and 94% efficacy and an acceptable safety profile against symptomatic COVID-19 disease in the phase 3 Coronavirus Efficacy (COVE) (NCT04470427) trial in over 30,000 participants (8-11). The U.S.

Food and Drug Administration granted Emergency Use Authorization (EUA) in December, 2020 for the mRNA-1273 vaccine (12), the European Medicines Agency granted a conditional marketing authorization for the mRNA-1273 vaccine on January 2021 (13), and the World Health Organization has issued Emergency Use Listing for the mRNA-1273 vaccine to prevent COVID-19 in individuals 18 years of age and older on April 2021 (14).

To monitor for VOC, neutralizing capacity of clinical sera is routinely tested against variants. Antibodies from mRNA-1273 vaccinees neutralized the B.1.1.7 variant to a similar extent as the original Wuhan-Hu-1 isolate and the D614G variant; whereas neutralizing antibody titers against the P.1 variant were reduced by 3.5-fold and titers against the B.1.351 variant were reduced by 6.4-fold (15). More recently, data from the ongoing phase 1 trial showed that vaccine antibody responses persisted up to 6 months following the second dose (16). Although a neutralizing antibody titer threshold predictive of protection from SARS-CoV-2 infection is not currently known, the reduction in *in vitro* neutralizing antibody titers against some variants relative to the prototype strain, raises the possibility of breakthrough infections and waning efficacy for current SARS-CoV-2 vaccines. One approach to address variants is to develop new vaccines tailored to the variants. In mice, the initial evaluation of mRNA-1273 vaccines (mRNA-1273.351 and mRNA-1273.211) designed to target emerging SARS-COV-2 variants increased neutralizing titers against variants and showed that a booster dose significantly increased neutralizing titers against the wild-type isolate (D614G) and the variants (17). Both mRNA-1273.351 and mRNA-1273.211 vaccines are currently being evaluated in additional pre-clinical challenge models and in clinical studies. Here we report upon the

preliminary safety and immunogenicity of single booster doses of mRNA-1273 and mRNA-1273.351 in a phase 2 clinical trial.

Methods

Study Design

The phase 2 mRNA-1273-P201 study (NCT04405076) enrolled adult participants ≥18 years of age at 8 sites in the U.S. Preliminary safety and immunogenicity results following two doses of 50 or 100 µg of mRNA-1273 have been previously reported (8, 9). Given that the primary efficacy endpoint for mRNA-1273 against COVID-19 was met in the phase 3 COVE trial and that EUA for the vaccine was granted, both the phase 2 and 3 trial protocols were amended to include open-label interventional phases offering participants in the placebo arm an option to receive mRNA-1273 vaccine at the end of the blinded phases. The phase 2 study offered participants previously primed with two doses of either 50 or 100 ug of mRNA-1273 an option to provide a nasopharyngeal swab for RT-PCR for SARS-CoV-2 and a blood sample for serology and immunogenicity, and to receive a single booster of a 50 µg dose of mRNA-1273. A rollover part was added to the phase 2 study, in which participants from the phase 3 COVE trial who completed a two vaccinations series of 100 ug doses of mRNA-1273 and provided a blood sample for serology and immunogenicity at day 1 received a single booster of either 20 µg or 50 µg doses of mRNA-1273.351 or 50 µg of the multivalent mRNA-1273.211 (Figure 1). In this manuscript, we present the results after a booster dose of 50 µg of mRNA-1273 (Part B) or 50 µg of mRNA-1273.351 (Part C, Cohort 1).

In Part B, all participants in the phase 2 mRNA-1273 study who previously received two doses of 50 ug or 100 µg of mRNA-1273 and provided a written consent to participate in this Part B, were administered a booster dose of 50 µg of mRNA-1273 vaccine at 177 to 226 days (5.9 to 7.5 months) after receiving the second dose of mRNA-1273. Upon enrollment into Part C

of this amended phase 2 study, eligible participants from the COVE study received a single intramuscular injection of mRNA-1273.351 (20 µg or 50 µg) or mRNA-1273.211 (50 µg total) at 168 to 198 days (5.6 to 6.6 months) after receiving the second vaccination of mRNA-1273 (Figure 1). The enrollment and vaccination in each study arm cohort of Part C was sequential. The first 20 participants who gave consent to participate were enrolled and dosed on open-label day 1 (OL-D1) with the 50 µg dose of mRNA-1273.351. Upon completion of the first cohort with 50 µg of mRNA-1273.351, 20 participants were enrolled in the second cohort and received the 50 µg dose of mRNA-1273.211. Following completion of the second cohort, 20 participants were enrolled and dosed with the 20 µg dose of mRNA-1273.351.

mRNA-1273 and mRNA-1273.351 Vaccines

The mRNA-1273.351 vaccine, like mRNA-1273, encodes the prefusion stabilized S protein of SARS-CoV-2 with the key amino acid changes present in the B.1.351 strain of the virus. The amino acid changes in the S protein encoded by mRNA-1273.351 relative to Wuhan-Hu-1 were L18F, D80A, D215G, Δ242-244, R246I, K417N, E484K, N501Y, D614G, and A701V. mRNA-1273.211 is a 1:1 mix of 25 µg of mRNA-1273 and 25 µg of mRNA-1273.351, for a total dose of 50 µg of mRNA. All vaccines were formulated in lipid nanoparticles as previously described (11).

Inclusion and Exclusion Criteria

Eligible participants were adults, 18 years of age, considered by the investigator to be healthy at screening and day 1 of the open-label phase. Part B participants must have been previously enrolled in the mRNA-1273 P201 study. For Part C, participants must have been previously enrolled in the mRNA-1273 COVE study and received two doses of mRNA-1273 in

Part A of that study (i.e., already unblinded and aware of their actual treatment), with their second dose at least 6 months prior to enrollment in Part C and must have been currently enrolled and compliant in that study (i.e., not have withdrawn or discontinued early). Additionally, eligible participants in Part C included healthy adults or adults with pre-existing medical conditions who were in a stable condition (disease not requiring significant change in therapy or hospitalization for worsening disease during the 3 months before enrollment). Participants in the phase 3 mRNA-1273 COVE study must have provided SARS-CoV-2 serology samples at the Participant Decision Visit (OL-D1) and days 29, and 57. Exclusion criteria for Parts B and C included acute illness or febrile (≥38.0°C/100.4°F) 24 hours prior to or at the screening visit (day 0), current treatment with investigational agents for prophylaxis against COVID-19, receipt of systemic immunoglobulins or blood products within 3 months prior to screening, positivity for SARS-CoV-2 by RT-PCR at baseline or at any time during the mRNA-1273 COVE study regardless of the presence or absence of symptoms consistent with COVID-19, or experienced any serious adverse event in the mRNA-1273 COVE study. Pregnant or breastfeeding females, and sexually active males and females unwilling to use adequate contraception for at least 3 months after the second study vaccination were also excluded. See additional eligibility criteria (clinicaltrials.gov NCT04405076).

Assessment of Safety

In order to assess safety, participants completed an electronic diary to record solicited systemic and local adverse reactions, daily oral body temperatures, injection site erythema and swelling/induration. Trained site personnel made telephone calls to the participants to assess safety every 4 weeks.

Assessment of Immunogenicity

For assessment of immunogenicity, serum samples taken from participants on days 1, 8, 15, 29, 57 and 181 were analyzed for serum neutralizing antibody against SARS-CoV-2 as measured with recombinant VSV-based pseudoviruses using the D614G, B.1.351 and P.1 variant sequences of SARS-CoV-2 S protein. For this early report, only data for day 1 and day 15 samples are included. The amino acid changes in the B.1.351 S protein relative to Wuhan-Hu-1 were L18F, D80A, D215G, Δ242-244, R246I, K417N, E484K, N501Y, D614G, and A701V. The 12 amino acid changes in the P.1 S protein relative to Wuhan-Hu-1 were L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, D614G, H655Y, T1027I and V1176F. Of note the key amino acid changes K417T/N, E484K, and N501Y are shared between the B.1.351 and P.1 variants.

Neutralizing Antibody Assay

To perform the recombinant VSV-based pseudovirus neutralization assay, codon-optimized full-length spike protein of the D614G, B.1.351 and P.1 variant sequences were cloned into pCAGGS vector. To make SARS-CoV-2 full-length spike pseudotyped recombinant VSV-ΔG-firefly luciferase virus, BHK-21/WI-2 cells (Kerafast, EH1011) were transfected with the spike expression plasmid and subsequently infected with VSVΔG-firefly-luciferase as previously described (18). For the neutralization assay, serially diluted serum samples were mixed with pseudovirus and incubated at 37°C for 45 minutes. The virus-serum mix was subsequently used to infect A549-hACE2-TMPRSS2 cells for 18 hours at 37 °C before adding ONE-Glo reagent (Promega E6120) for measurement of luciferase signal (relative luminescence unit; RLU). The percentage of neutralization was calculated based on RLU of the virus only control, and subsequently analyzed using four-parameter logistic curve (Prism 8).

Statistical Analysis

Geometric mean titer (GMT) and geometric mean fold rise (GMFR) were calculated based on the log-transformed titers. Calculation of 95% confidence intervals (CI) was based on the t-distribution of the log-transformed titers or the difference in the log-transformed titers for GMT and GMFR, respectively, then back transformed to the original scale.

Wilcoxon matched-pairs signed rank test was used for the participant's sample comparison, such as pre- vs post- booster doses within the same type of assay, and cross assay comparison at the same timepoint.

Results

Disposition of Participants

As described previously, between May 22, 2020 and July 8, 2020, 600 participants were randomized to placebo or 50 or 100 ug of mRNA-1273 administered as two injections in the phase 2 mRNA-1273 trial (9). By April 30, 2021, 188 participants who had received two injections of 100 ug mRNA-1273 completed the blinded phase (Part A) of the study through the participant decision visit or were unblinded or discontinued the study. Of these, 20 who went on to receive a single open-label booster dose of 50 ug mRNA-1273 (Part B) were selected for this preliminary analysis, with selection based on completion of their D15 visit assessments and immunogenicity sample availability. In the previously reported COVE phase 3 trial of mRNA-1273, 14711 (96.9%) participants completed both vaccinations with 100 μg mRNA-1273 in the blinded phase (Part A) of the study (11) and 60 participants at a single site were selected by site based on inclusion/exclusion criteria for Part C, to receive single open-label booster doses of 50 ug of mRNA-1273.351 (Part C, cohort 1) or mRNA-1273.211 (Part C, cohort 2) or 20 ug of mRNA-1273.351 (Part C, cohort 3). Only results for 50 μg booster doses of mRNA-1273 (selected subjects in Part B) or mRNA-1273.351 (Part C cohort 1) are available and reported here.

Demographics and Characteristics

The baseline demographics of the group of participants who received the booster dose of the mRNA-1273.351 vaccine were generally similar to that for the group who received the booster dose of the mRNA-1273 vaccine (Table 1). Approximately half of the participants in both groups were male, and most were White and not Hispanic or Latino. The mean (range) age of the participants who received the booster dose of mRNA-1273.351 was 53.9 (27-70) years and for those who received mRNA-1273, 63.8 (38-76) years. The mean (SD) [range]) time between the second dose of mRNA-1273 and the booster dose of mRNA-1273 or mRNA-1273.351 was 201.0 (15.1) [177-226] and 187.1 (9.4 [168-198]) days, respectively.

Safety

With respect to safety, the percentages of participants with solicited local and systemic adverse events were similar in the group who received mRNA-1273.351 as a booster dose compared to those who received mRNA-1273 vaccine as a booster dose (Figure 2). The majority of solicited local and systemic adverse events were mild (grade 1) or moderate (grade 2). The frequency of any grade 3 solicited local or systemic adverse event was 15% (3 of 20 participants) after the booster dose of mRNA-1273 and 10.5% (2 of 19 participants) after the booster dose of mRNA-1273.351. There were no grade 4 solicited local or systemic adverse events. The most common solicited local adverse event was injection site pain after injection in both groups (68.4% for the mRNA-1273.351 vaccine and 90.0% for the mRNA-1273 vaccine) (9, 11). The most common solicited systemic adverse events after the booster dose of the mRNA-1273.351 vaccine were fatigue (36.8%), headache (36.8%), myalgia (31.6%) and arthralgia (21.1%). The most common solicited systemic adverse events after the booster dose of the

mRNA-1273 vaccine were fatigue (70.0%), headache (55.0%), arthralgia (50.0%) and myalgia (45.0%). Fever was reported after the booster dose of mRNA-1273 in 3 of 20 participants (15%) but not after the booster dose of mRNA-1273.351 (0 of 19 participants). There were no serious adverse events reported in this study.

Serum Neutralizing Antibody Titers Against Wild-type and Variant Viruses Prior to Booster Vaccinations

The preclinical SARS-CoV-2 PsVN assay was used to evaluate trial participant sera collected on the same day of vaccination with a booster dose of mRNA-1273 or mRNA-1273.351. While sera collected from these trial participants immediately after the primary series vaccinations have not yet been assessed, previous evaluations of mRNA-1273 vaccinated individuals at similar timepoints post-vaccination demonstrate that peak titers are ~10^3 ID_{50} (1-week post 2nd dose titers). After a mean of 201.0 (15.1) [177-226] and 187.1 (9.4 [168-198]) days between the second dose of mRNA-1273 and the booster dose of mRNA-1273 or mRNA-1273.351 respectively, neutralizing antibody GMT against the original Wuhan-Hu-1 strain with the D614G mutation (referred to as wild-type, D614G throughout the text and figures) in these individuals have decreased to 198 in the Part B cohort and 304 in the Part C cohort 1 (Figure 3 A/C, D1 Pre 3rd dose). However, neutralization of the B.1.351 and P.1 variants was further reduced. GMT levels of neutralizing antibodies of 27 or 40, and 30 or 47 were measured against B.1.351 or P.1 in the Part B and Part C cohort 1 samples respectively. In addition, approximately 50% of samples from both cohorts fell below the assay LLOQ against B.1.351 and P.1 viral variants.

Neutralization after vaccination with a booster dose of mRNA-1273 or mRNA-1273.351 in individuals previously vaccinated with mRNA-1273

To evaluate the ability of mRNA-1273 or mRNA-1273.351 to boost pre-existing immunity and increase neutralization against both the wild-type, B.1.351, and P.1 virus, P201 trial participants were immunized with 50 µg mRNA-1273 (Figure 1, Part B), while participants from P301 were enrolled into P201 Part C and dosed with 50ug mRNA-1273.351 (Figure 1, Part C cohort 1). Sera collection occurred 2 weeks after vaccination with each booster vaccine, and neutralization assessments were performed. Additional arms of this trial are ongoing to evaluate boosting with a multivalent mRNA-1273.211 that contains both mRNA-1273 and mRNA-1273.351 in a 1:1 mix.

Neutralization titers were measured in the D614G, B.1.351, and P.1 preclinical SARS-CoV-2 PsVN assays prior to the boost (D1) and two weeks after (D15). Boosting with mRNA-1273.351 or mRNA-1273 increased neutralization antibody titers (Figure 3). Boosting with mRNA-1273 increased PsVN GMTs to 4508, 864, and 1308 in the respective D614G, B.1.351, and P.1 assays (Figure 3A), representing a 23, 32, and 44-fold rise in neutralization against each respective virus (Figure 3B). Boosting with mRNA-1273.351 increased PsVN neutralizing titers to 3703, 1400, and 1272 (Figure 3C), and represented a 12, 35, and 27-fold increase in neutralization of each respective virus (Figure 3D). Importantly, vaccination with a booster dose of mRNA-1273 or mRNA-1273.351 resulted in the detection of robust neutralization titers against both wild-type and variant viruses after the boost in all participants. In addition, titers against B.1.351 and P.1 assay now approach or exceed 10^3 ID_{50} GMT, the previous peak titers in the wild-type assay (Figure 4E).

A mRNA-1273.351 booster more effectively narrows the gap in neutralizing titers between the wild-type and B.1.351 viruses, versus mRNA-1273

Prior to vaccination with the booster dose, neutralization titers were 7.3 and 7.7-fold reduced versus the B.1.351 virus in the Part B and Part C cohort 1 participants respectively (Figure 4 A, B). Two weeks after the booster dose, a 5.3 and 2.6-fold difference between wild-type and B.1.351 neutralization was measured, and importantly all samples were able to neutralize all viruses (Figure 4 C, D). Importantly, the variant mRNA-1273.351 booster was able to increase titers against the B.1.351 virus to higher levels versus a boost with mRNA-1273 (1400 versus 864 ID_{50} GMT), and was able to further close the gap of neutralization between the two assays to 2.6-fold. Equally important, titers against the variant viruses approach peak titers measured after the primary series vaccination with mRNA-1273, from an analysis of phase 1 trial samples measured in the homologous wild-type assay (Figure 4E) (8).

Discussion

This is a preliminary evaluation of mRNA-1273 and mRNA-1273.351 given as boosters to individuals that had been vaccinated 6.2 to 6.7 months previously with mRNA-1273 in an amended phase 2 clinical trial of mRNA-1273. The safety profiles following single injections of 50 µg of mRNA-1273 (Part B) or mRNA-1273.351 (Part C cohort 1) were evaluated, and although similar to those observed after a second dose of mRNA-1273 in the previously reported phase 2 and phase 3 studies, some differences were seen between the two booster vaccines. Vaccination with both mRNA-1273 and mRNA-1273.351 boosters elicited higher neutralizing titers against the wild-type original strain and comparable titers against the B.1.351 and P.1 variants versus peak titers observed after the primary series vaccinations as measured against the wild-type virus (Figure 4E), suggesting that immune memory was induced by mRNA-1273 priming. Additionally, the mRNA-1273.351 booster appeared to be more effective at increasing neutralization against the B.1.351 variant than a boost with mRNA-1273. The study is ongoing and evaluation of boosting of clinical trial participants with the multivalent mRNA-1273.211 is underway.

In this preliminary report, boosters of 50 µg of mRNA-1273 or mRNA-1273.351 given to individuals who were previously vaccinated with two doses of mRNA-1273 elicited acceptable safety profiles. Solicited local and systemic adverse events after a booster dose of mRNA-1273.351 or mRNA-1273 were similar. The majority of events were mild (grade 1) or moderate (grade 2) in severity, and grade 3 events occurred with a frequency of 15% in Part B and 10% in Part C. No grade 4 events were reported. For both boosters, the most commonly reported

solicited local adverse event was injection site pain and reported systemic events included fatigue, headache, myalgia and arthralgia, consistent with safety profiles seen in the phase 2 and 3 studies (9, 11). It should be noted that limited adverse events of fever post-vaccination were reported in the Part B (mRNA-1273; 15%) but not the Part C (mRNA-1273.351; 0%) participants, similar to those reported after the second mRNA-1273 vaccinations in the phase 2 and phase 3 clinical trials. Importantly, in this small study, the booster dose of mRNA-1273.351 appears to be tolerated (solicited local and systemic adverse events) at least as well if not better than a booster dose of mRNA-1273.

Sera from these participants collected prior to the boost (D1) and two weeks after (D15) were evaluated in a preclinical SARS-CoV-2 PsVN neutralization assay against wild-type virus. Prior to the boost, neutralization titers of 198 and 304 in the Part B and Part C cohorts remained significant, at levels predicted to be protective against the original Wuhan-Hu-1 isolate (19). These results are consistent with those reported in a lentiviral PsVN assay, where monitoring of sera neutralization titers was performed up to 6 months after the second dose of mRNA-1273 (16). In that evaluation, the lentiviral PsVN titer was 57 ID_{50} GMT in participants who were 56 to 70 years old 180 days after the second dose of mRNA-1273.

In our evaluation of Parts B and C participant sera, virus neutralization assays were performed against B.1.351 and P.1 variants. Both are VOCs and contain the key receptor binding domain (RBD) mutations K417T/N, E484K, N501Y present in the mRNA-1273.351 variant vaccine. Significantly reduced levels of neutralization were measured against both the B.1.351 and P.1 variant viruses in samples collected prior to the booster vaccination, with ~50% of titers falling below the assay lower limit of quantification. Although a correlate of protection

has not yet been established for SARS-CoV-2 infection or COVID-19 disease, lack of detectable neutralization against these variants may be indicative of waning immunity, especially against VOCs.

Boosting these trial participants with mRNA-1273 and mRNA-1273.351 both substantially increased neutralization titers against the wild-type, and B.1.351 and P.1 variant viruses (Figure 3). Neutralizing titers against the wild-type virus exceeded the peak titers measured after the primary series in separate studies (15, 16), indicating the induction of immune memory, and titers against the B.1.351 and P.1 viruses increased to a level very similar to those previously measured against the wild-type assay where ~10^3 ID_{50} GMT values were measured (15). Furthermore, all trial participants, including those that had undetectable titers against the variant viruses, had robust neutralization titers in both the wild-type and variant assays two weeks after the booster. A boost with mRNA-1273.351 appeared to be more effective at neutralization of the B.1.351 virus than a boost with mRNA-1273, evidenced by the higher mean GMT levels in the Part C cohort 1 participants (1400) than the GMT Part B participants (864) against the B.1.351 virus. Additionally, the difference between the wild-type and B.1.351 assays at day 1 dropped from 7.7-fold prior to the boost with mRNA-1273.351 to 2.6-fold at 15 days after the boost. Further reductions in the differences between the two assays may be found in samples collected from these participants at later timepoints, as the kinetics of the neutralizing antibody responses to the new epitopes in S-2P.351 protein encoded by mRNA-1273.351 may be different from the epitopes shared between the two immunogens. Strong homologous responses, both in terms of absolute geometric mean titer and geometric mean fold rise, assessed by the same strain in the assay used in the vaccine,

were seen regardless of vaccine strain. Response to the wild-type virus was highest with a boost of mRNA-1273 and response to B.1.351 was highest with mRNA-1273.351. In addition, heterologous responses, against variants when prototype vaccine was used to boost or against prototype after the mRNA-1273.351 booster were also seen. This supports the development of a variant vaccine as a booster dose to prevent infection caused by variant strains.

This phase 2 study is ongoing, and data from additional arms, including an evaluation of a 50 ug booster dose of the multivalent mRNA-1273.211 vaccine comprised of a 1:1 mix of mRNA-1273 and mRNA-1273.351 in Part C cohort 2, will be reported later. This additional arm was designed to evaluate the effectiveness of the multivalent vaccine as a booster and its effectiveness at broadening the immune response to provide better neutralization against both wild-type virus and variants. In addition, sera collected on day 57 after the primary vaccination series from all these trial participants will be analyzed in the preclinical SARS-CoV-2 PsVN assay to allow for direct comparison of peak titers prior to the boost versus neutralizing titers elicited from each booster dose, allowing for better evaluation of the level of waning immunity seen in these participants and further demonstration of the benefit from the booster dose. Global surveillance for the emergence of additional SARS-CoV-2 VOCs and efforts to test the neutralization of VOCs by mRNA-1273 vaccinee sera as well as sera from these boosted trial participants is also ongoing. If additional variants emerge that reduce the neutralization capacity of 2-dose mRNA-1273 or 2-dose mRNA-1273 + booster regimen, alternative mRNA vaccine designs may be developed and evaluated clinically. As variants are likely to emerge and continue to co-circulate globally, it is expected that a multivalent mRNA vaccine design will likely be most effective at increasing cross-variant protection and will also afford the

opportunity to mix and match which variant designs are included in the vaccine to respond to the continued evolution of the SARS-CoV-2 virus and address potentially changing global needs.

There are some limitations related to the preliminary analysis of this study. First, the results presented here are based on a limited sample size. The trial is ongoing, and key evaluations of the multivalent mRNA-1273.211 arm of the trial have not yet been performed. The neutralization assay used in the evaluations of these pre-boost and two-week post-boost samples is a preclinical SARS-CoV-2 PsVN assay, and although this assay has consistently been used to evaluate the impact on neutralization against variant viruses, the assay has not been qualified (16). All samples from this trial will be evaluated in qualified assays and the results will be reported at a later date. As analysis of sera for the trial participants collected on day 57 after the primary series of mRNA-1273 has not yet been performed in this preclinical assay, it cannot yet be definitively determined how the neutralization titers after the 3rd dose will compare to peak measurements after the primary vaccination series. Further, evaluations of the sera collected two weeks after the booster have not yet been performed against other VOC, including B.1.526, B.1.427/B.1.429, or B.1.617; therefore, it remains to be seen if the breadth of protection against other variants has increased after the booster was given. Also, as a correlate of protection for neutralizing antibodies has not yet been established for SARS-CoV-2, it can't be definitively determined from these preliminary results whether the significant neutralization titers elicited from both booster vaccines would be protective against B.1.351 or P.1, although it seems probable. Finally, because the participants in this study were originally enrolled from two different clinical trials (Part B; phase 2 mRNA-1273 study and Part C, Cohort 1; phase 3

mRNA-1273 COVE study), a comparison of the results of a booster dose of mRNA-1273.351 with those of mRNA-1273 should be interpreted with caution.

The emergence of SARS-CoV-2 variants and the ability of the virus to partially overcome natural or vaccine-induced immunity has served as a call to action. Not only are continued vaccination efforts needed to prevent the emergence of future VOCs, but also strategies for SARS-CoV-2 vaccine research and development are needed that can enhance the level of protection against key VOCs, should they arise. The mRNA platform approach against SARS-CoV-2 VOCs in this trial appears to be effective at boosting antibody levels when applied as a booster dose, with mitigation of the reductions in neutralization seen against the B.1.351 and P.1 lineages. The mRNA platform allows for rapid design of vaccine antigens that incorporate key mutations, allowing for faster development of future alternative variant-matched vaccines should they be needed. The vaccine designs evaluated in this clinical study demonstrate the ability to boost immunity to titers that likely exceed those that peak after the primary vaccination series against both the wild-type virus and variants, and also demonstrate the potential of the mRNA-1273.351 booster to close the gap between neutralization of the wild-type virus and the B.1.351 variant. In the future, additional VOC designs can be rapidly developed, evaluated, and deployed if needed to address the evolving SARS-CoV-2 virus.

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Author disclosures

K.W., A.C., M.K., L.M., L.M., A.H, N.N., W.H., J.O., H.B., H.L., Y.P., B.N., B.D., R.P., A.C., J.M., B.L., R.M., and D.E. are employees of Moderna, Inc., and may hold stock/stock options in the company.

Role of the funding source

Employees of the study sponsor, Moderna, Inc., contributed to the study design, data collection, analysis and interpretation, and writing of the report.

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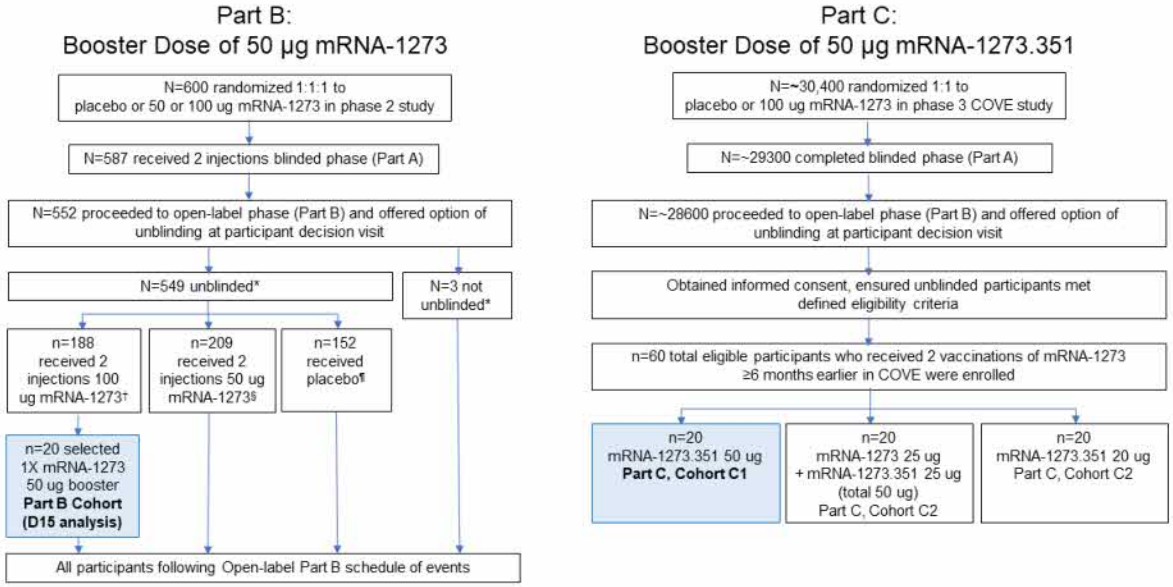
Table 1: Demographics and characteristics

Characteristic n (%)	mRNA-1273.351 N=20	mRNA-1273 N=20
Age (years)		
Mean (range) yr	53.9 (27-70)	63.8 (38-76)
Gender		
Male	11 (55)	8 (40)
Female	9 (45)	12 (60)
Race		
White	19 (95)	20 (100)
Black or African-American	0	0
Asian	1 (5)	0
American Indian or Alaska Native	0	0
Native Hawaiian or other Pacific Islander, Multiracial, Other, Not reported, Unknown	0	0
Ethnicity		
Hispanic or Latino	0	0
Not Hispanic or Latino	20 (100)	20 (100)
Not reported or Unknown	0	0
Time interval between second dose of mRNA-1273 and the booster dose (days)		
Mean (SD)	187.1 (9.4)	201.0 (15.1)
Range	168-198	177-226
Median	189.1	196.0
Q1, Q3	183.0, 194.5	191.5, 217.0
Body Mass Index (kg/m^2)		
Mean (SD)	30.3 (6.5)*	26.2 (2.1)

Legend: SD=standard deviation. *Missing data for 1 participant

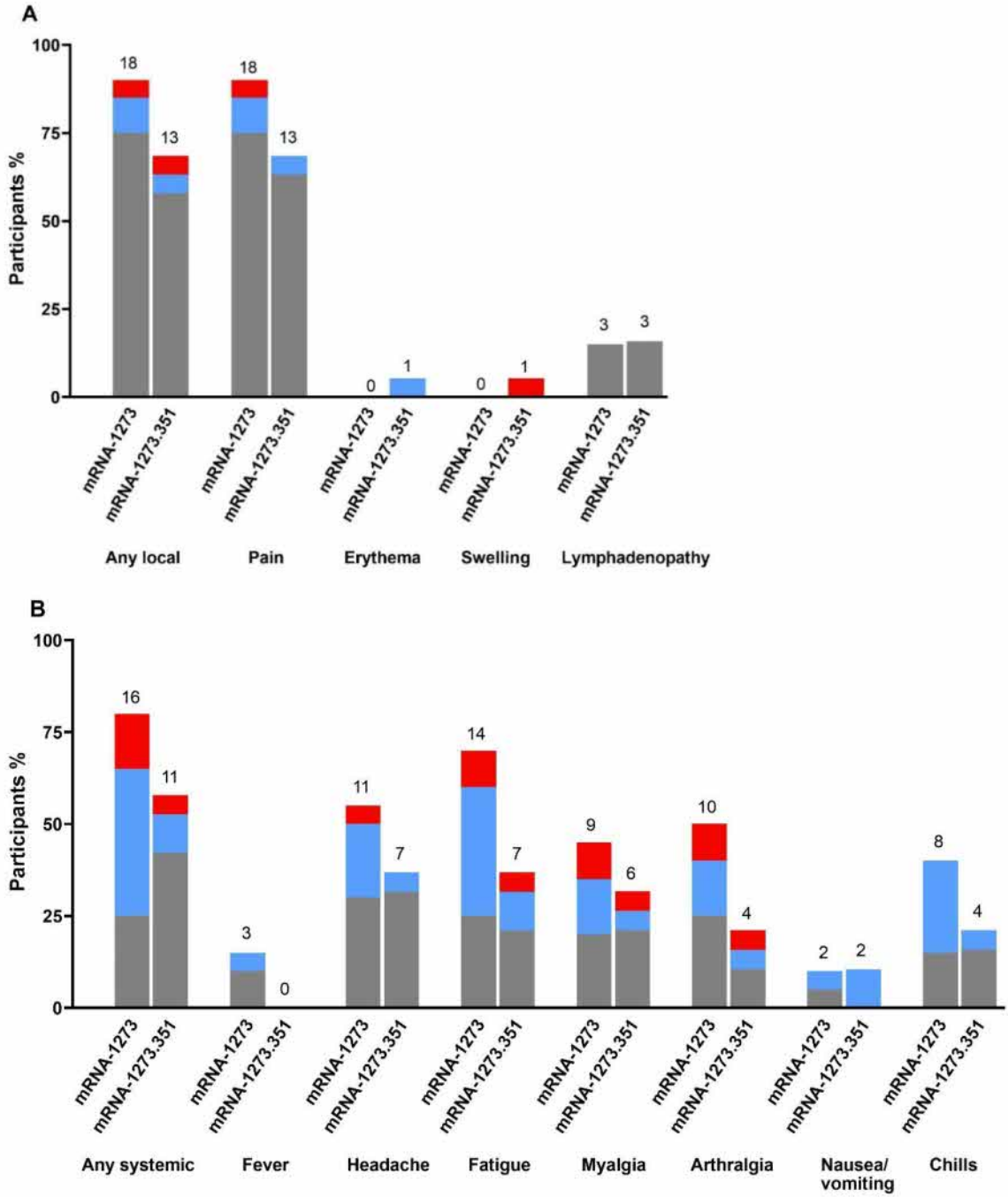
Figures

Figure 1: Open-label Boosting with mRNA-1273 and mRNA-1273.351 (Parts B and C)



Legend: Flow of trial for Parts B and C of the amended phase 2 trial of mRNA-1273. *Unblinded or not unblinded to assigned treatment in Part A blinded phase. †Received 2 injections of 100 ug mRNA-1273 and §50 ug mRNA-1273 during Part A. ¶Received placebo in Part A. participants who had received two injections of 100 ug mRNA-1273 completed the blinded phase (Part A) of the study through the participant decision visit or were unblinded or discontinued the study. In Part B, 20 participants who had received two injections of 100 ug mRNA-1273 and completed the blinded phase (Part A) and went on to receive a single open-label booster dose of 50 ug mRNA-1273 were selected for this preliminary analysis, with selection based on completion of their D15 visit assessments and immunogenicity sample availability. In Part C, enrollment and administration of booster doses in each study arm occurred in a sequential manner. Blue boxes designate cohort data included in this report.

Figure 2: Solicited Local and Systemic Adverse Events Within 7 Days After Vaccination with a Booster Dose of mRNA-1273 or mRNA-1273.351



Legend: The percentage of participants who reported Grade 1 (gray), Grade 2 (blue), or Grade 3 (red) local **(A)** and systemic **(B)** adverse events is shown in the figure for the 20 participants who received a booster dose of mRNA-1273 and the 19 participants who received a booster dose of mRNA-1273.351. One participant who received mRNA-1273.351 did not report any results for solicited adverse reactions and was excluded from the analysis. The number above each bar shows the number of participants who reported the particular adverse event.

Figure 3A and B: Immunogenicity After Boosting with Booster Dose of 50 µg of mRNA-1273

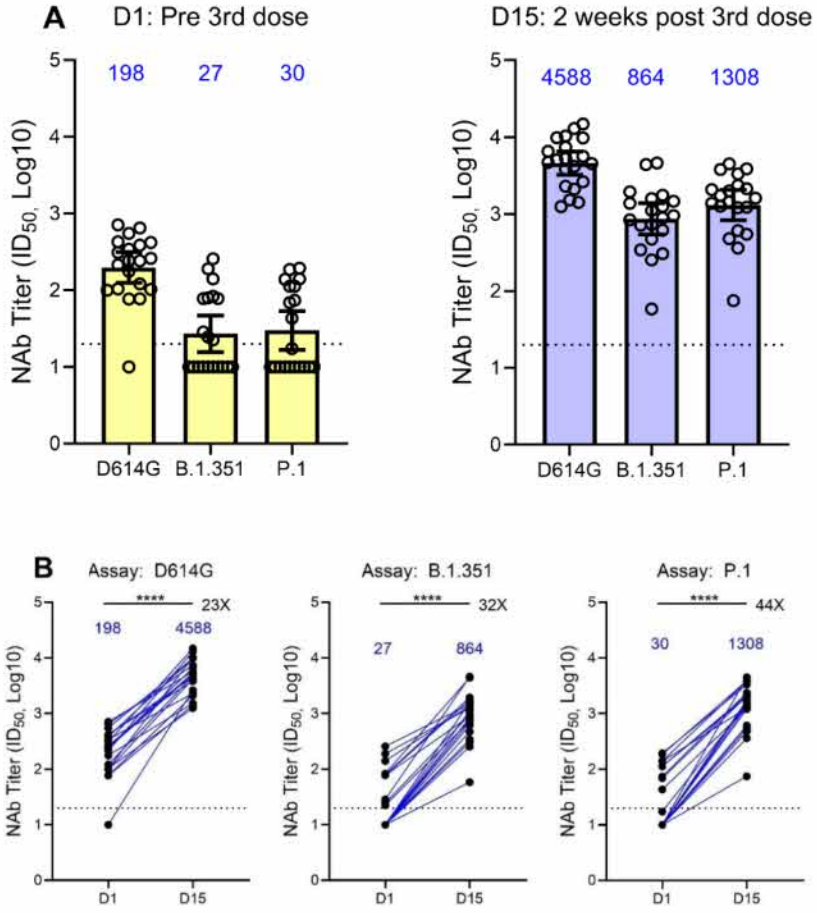
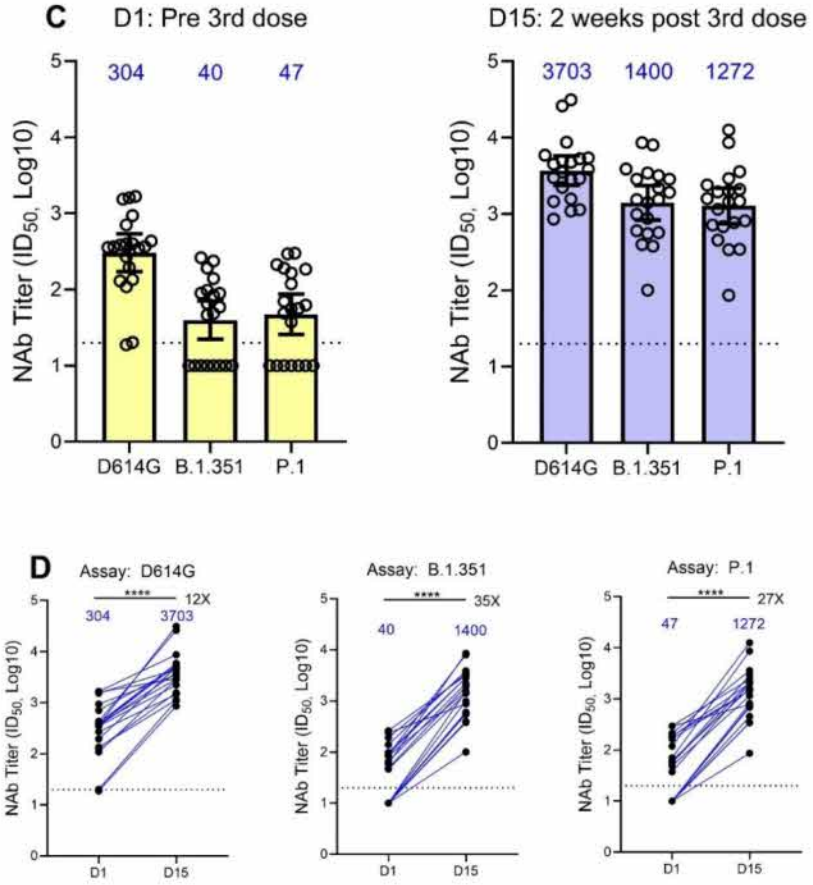
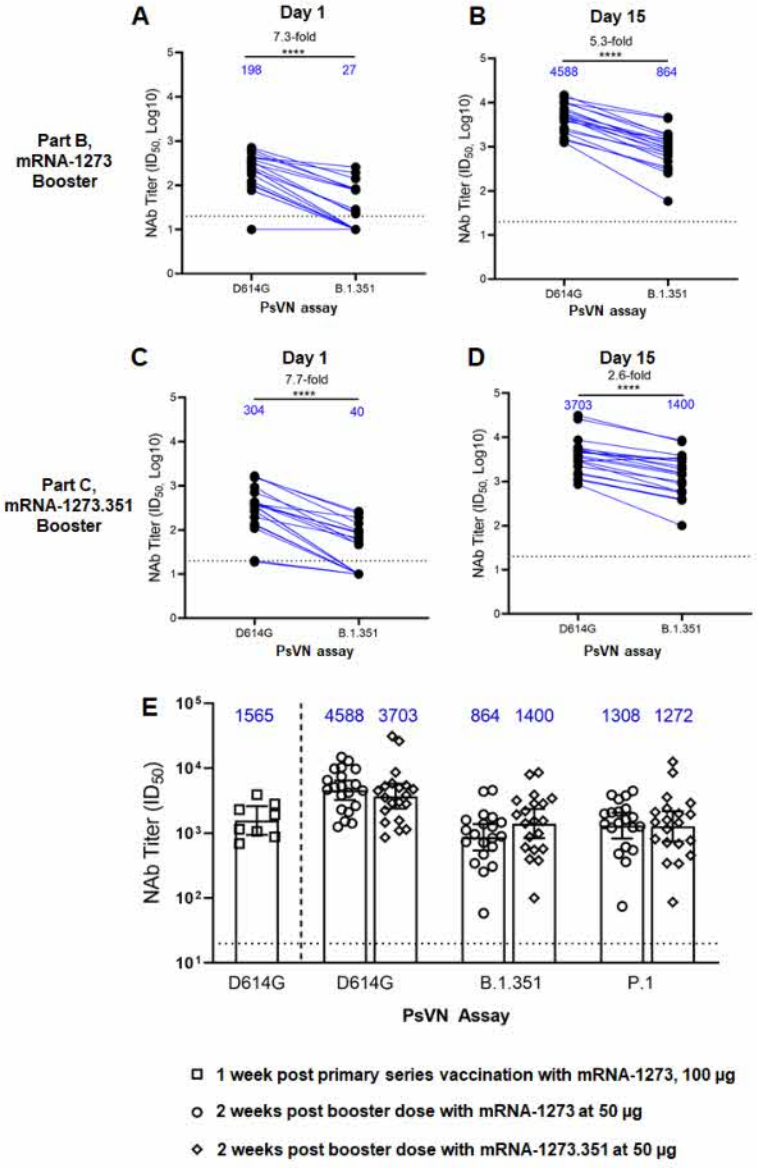


Figure 3C and D: Immunogenicity After Boosting with 50 µg of mRNA-1273.351



Legend: Neutralization of recombinant SARS-CoV-2 VSV-based pseudoviruses (D614G, B.1.351 and P.1) by serum from participants before (D1) and 15 days after boosting (D15) with 50 µg of mRNA-1273 **(A and B)** and mRNA-1273.351 **(C and D)**. The geometric mean neutralizing antibody titer is denoted by the top of the box and the 95% confidence intervals are shown by the brackets. The titers for individual participants are shown by the circles. The fold increases for day 15/day 1 are shown above the bars. The horizonal dotted lines indicate the lower limit of quantification (LLOQ). **** = p<0.0001 by the Wilcoxon matched-pairs signed rank test.

Figure 4: Neutralization of D614G and B.1.351 SARS-CoV-2 pseudoviruses by serum from mRNA-1273 or mRNA-1273.351 boosted trial participants on D1 (pre-boost) and D15 (post-boost)



Legend: Sera was collected from trial participants before and after vaccination with a 50 µg booster dose. mRNA-1273 boosted subjects before (**A**) and after (**B**) the boost. mRNA-1273.351 boosted subjects before (**C**) and after (**D**) the boost. Reference titers in the D614G assay for mRNA-1273 vaccinated subjects after the primary vaccination series of mRNA-1273, versus titers measured in the PsVN assays two weeks after boost with mRNA-1273 or mRNA-1273.351 (**E**). Fold-difference in neutralization between the D614G and B.1.351 VSV PsVN assays are indicated. **** = p<.0001 by the Wilcoxon matched-pairs signed rank test. Blue text indicates the geometric mean titers, which is listed as text above each plot. The horizontal dotted lines indicate the lower limit of quantitation for Nab titer at 10 ID_{50}. Results from individual participants are represented as dots on each figure, with lines connecting the D614G and B.1.351 neutralization titers.

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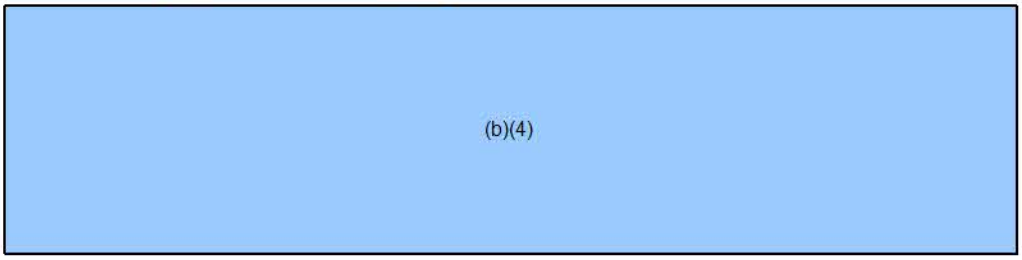
From: (b)(4) (b)(4) (b)
Sent: Tue, 27 Apr 2021 16:33:15 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: (b)(4) (b)(4) (b)(4) (b)(4)
Subject: participants for work group call on thursday

Dear Sara,
Again thank you for your time with us this morning.
Below are the people who will be participating on the COVID work group call on Thursday (in addition to (b)(4 myself and (b)(4) and their emails:



Best regards,
(b)(4)

From: (b)(4) (b)(4) (x)
Sent: Tue, 6 Apr 2021 17:53:44 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); Cohn, Amanda (CDC/DDID/NCIRD/OD); Mbaeyi, Sarah (CDC/DDID/NCIRD/OD)
Subject: Persistence of Antibody - Moderna COVID-19 Vaccine
Attachments: COVID-19 - Doria-Rose - Ab Persistence thru 6 months after 2nd dose of 1273 vaccine - NEJM 2021.pdf

Hi Sara, Amanda, and Sarah,
The attached *Letter to the Editor* was just published today in the *NEJM*. It describes persistence of antibody 6 months after the second dose of Moderna COVID-19 vaccine in the Phase 1 trial. Please feel free to share this with the Work Group.
(b)(4)

CORRESPONDENCE

Antibody Persistence through 6 Months after the Second Dose of mRNA-1273 Vaccine for Covid-19

TO THE EDITOR: Interim results from a phase 3 trial of the Moderna mRNA-1273 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine indicated 94% efficacy in preventing coronavirus disease 2019 (Covid-19).[1] The durability of protection is currently unknown. We describe mRNA1273-elicited binding and neutralizing antibodies in 33 healthy adult participants in an ongoing phase 1 trial,[2-4] stratified according to age, at 180 days after the second dose of 100 μg (day 209).

Antibody activity remained high in all age groups at day 209. Binding antibodies, measured by means of an enzyme-linked immunosorbent assay against SARS-CoV-2 spike receptor–binding domain,[2] had geometric mean end-point titers (GMTs) of 92,451 (95% confidence interval [CI], 57,148 to 149,562) in participants 18 to 55 years of age, 62,424 (95% CI, 36,765 to 105,990) in those 56 to 70 years of age, and 49,373 (95% CI, 25,171 to 96,849) in those 71 years of age or older. Nearly all participants had detectable activity in a pseudovirus neutralization assay,[2] with 50% inhibitory dilution (ID_{50}) GMTs of 80 (95% CI, 40 to 135), 57 (95% CI, 30 to 106), and 59 (95% CI, 29 to 121), respectively. On the more sensitive live-virus focus-reduction neutralization mNeonGreen test,[4] all the participants had detectable activity, with ID_{50} GMTs of 406 (95% CI, 286 to 578), 171 (95% CI, 95 to 307), and 131 (95% CI, 69 to 251), respectively; these GMTs were lower in participants 56 to 70 years of age (P=0.02) and in those 71 years of age or older (P=0.004) than in those 18 to 55 years of age (Fig. 1; also see the Supplementary Appendix, available with the full text of this letter at NEJM.org).

The estimated half-life of binding antibodies after day 43 for all the participants was 52 days (95% CI, 46 to 58) calculated with the use of an exponential decay model, which assumes a steady decay rate over time, and 109 days (95% CI, 92 to 136) calculated with the use of a power-law model (at day 119), which assumes that decay rates decrease over time. The neutralizing antibody half-life estimates in the two models were 69 days (95% CI, 61 to 76) and 173 days (95% CI, 144 to 225) for pseudovirus neutralization and 68 days (95% CI, 61 to 75) and 202 days (95% CI, 159 to 272) for live-virus neutralization. As measured by ΔAIC_c (change in Akaike information criterion, corrected for small sample size), the best fit for binding and neutralization were the exponential decay and power-law models, respectively (see the Supplementary Appendix). These results are consistent with published observations of convalescent patients with Covid-19 through 8 months after symptom onset.[5]

Although the antibody titers and assays that best correlate with vaccine efficacy are not currently known, antibodies that were elicited by mRNA-1273 persisted through 6 months after the second dose, as detected by three distinct serologic assays. Ongoing studies are monitoring immune responses beyond 6 months as well as determining the effect of a booster dose to extend the duration and breadth of activity against emerging viral variants. Our data show antibody persistence and thus support the use of this vaccine in addressing the Covid-19 pandemic.

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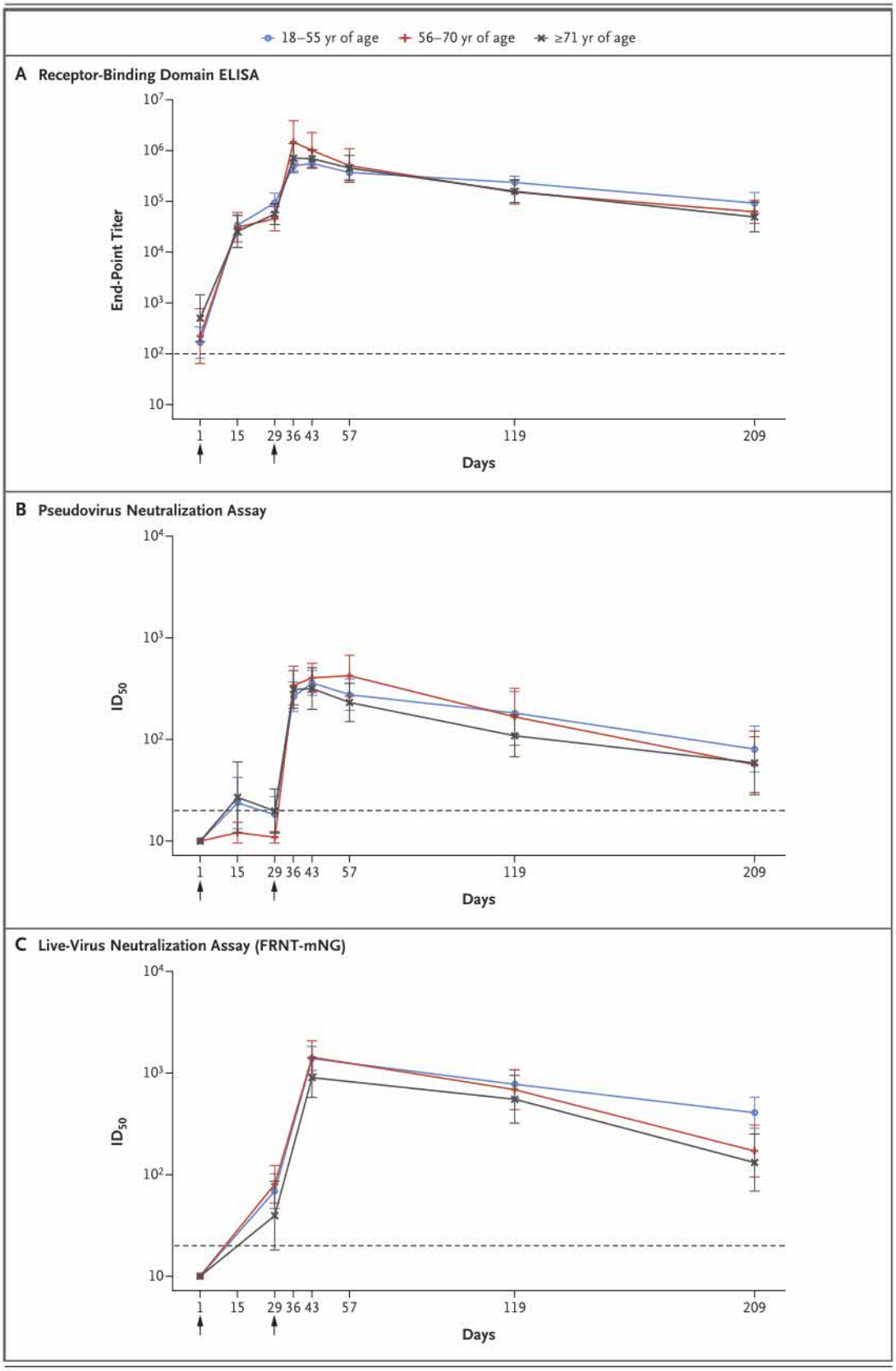

Figure 1 (facing page). Time Course of SARS-CoV-2 Antibody Binding and Neutralization Responses after mRNA-1273 Vaccination.

All the participants received 100 μg of mRNA-1273 on days 1 and 29, indicated by arrows. The numbers of participants in each age group with data available at day 209 are as follows: 18 to 55 years, 15 participants; 56 to 70 years, 9 participants; and 71 years or older, 9 participants. The titers shown are the binding to spike receptor–binding domain protein (the end-point dilution titer) assessed on enzyme-linked immunosorbent assay (ELISA) on days 1, 15, 29, 36, 43, 57, 119, and 209 (Panel A); the 50% inhibitory dilution (ID_{50}) titer on pseudovirus neutralization assay on days 1, 15, 29, 36, 43, 57, 119, and 209 (Panel B); and the ID_{50} titer on the live-virus focus-reduction neutralization mNeonGreen test (FRNT-mNG) on days 1, 29, 43, 119, and 209 (Panel C). Lines show geometric mean titers for each age group; I bars indicate 95% confidence intervals. The dashed line indicates the limit of detection for each assay.

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*The mRNA-1273 Study Group members are listed in the Supplementary Appendix, available with the full text of this letter at NEJM.org.

Drs. Doria-Rose and Suthar contributed equally to this letter.

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Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

This letter was published on April 6, 2021, at NEJM.org.

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From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Fri, 14 May 2021 00:25:30 +0000
To: (b)(4) (b)(4) (b)(4) Mary M.; (b)(4) (b)(4) T
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: Pfizer adolescent MMWR
Attachments: mm7020e1 - ACIP Pfizer adolescents FINAL PROOF.pdf

(b)(4) (b)(and Mary:

I wanted to share the Final Proof with you of the MMWR set to be published tomorrow. It's embargoed until 11am, so please don't distribute, but wanted to shar with you.

Thanks-

Sara

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MMWR
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The Advisory Committee on Immunization Practices' Interim Recommendation for Use of Pfizer-BioNTech COVID-19 Vaccine in Adolescents Aged 12–15 Years — United States, May 2021

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The Pfizer-BioNTech COVID-19 (BNT162b2) vaccine is a lipid nanoparticle–formulated, nucleoside-modified mRNA vaccine encoding the prefusion spike glycoprotein of SARS-CoV-2, the virus that causes COVID-19. Vaccination with the Pfizer-BioNTech COVID-19 vaccine consists of 2 intramuscular doses (30 μg, 0.3 mL each) administered 3 weeks apart. On December 11, 2020, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for use of the Pfizer-BioNTech COVID-19 vaccine (Pfizer, Inc; Philadelphia, Pennsylvania) in persons aged ≥16 years (*1*); on December 12, 2020, the Advisory Committee on Immunization Practices (ACIP) issued an interim recommendation for use of the vaccine in the same age group (*2*). As of May 12, 2021, approximately 141.6 million doses of the Pfizer-BioNTech COVID-19 vaccine had been administered to persons aged ≥16 years.* On May 10, 2021, FDA expanded the EUA for the Pfizer-BioNTech COVID-19 vaccine to include adolescents aged 12–15 years (*1*). On May 12, 2021, ACIP issued an interim recommendation† for use of the Pfizer-BioNTech COVID-19 vaccine in adolescents aged 12–15 years for the prevention of COVID-19. To guide its deliberations regarding the vaccine, ACIP used the Evidence to Recommendation (EtR) Framework,§ using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach.¶ The ACIP recommendation for the use of the Pfizer-BioNTech COVID-19 vaccine in persons aged ≥12 years under an EUA is interim and will be updated as additional information becomes available.

Since June 2020, ACIP has convened 14 public meetings to review data on the epidemiology of COVID-19 and the potential use of COVID-19 vaccines, including the Pfizer-BioNTech COVID-19 vaccine (*3*). The ACIP COVID-19 Vaccines Work Group, comprising experts in infectious diseases, vaccinology, vaccine safety, public health, and ethics, has held weekly meetings to review COVID-19 surveillance data, evidence for vaccine efficacy and safety, and implementation considerations for COVID-19 vaccines. Within the EtR Framework for the Pfizer-BioNTech COVID-19 vaccine for adolescents aged 12–15 years, ACIP considered the importance of COVID-19 as a public health problem, as well as issues of resource use, benefits and harms, patients' and parents' values and preferences, acceptability, feasibility, and equity for use of the vaccine among adolescents. After a systematic review of published and unpublished evidence for benefits and harms, the Work Group used the GRADE approach to assess the certainty of evidence for outcomes related to the vaccine, rated on a scale of 1 (high certainty) to 4 (very low certainty) (*4*). Work Group conclusions regarding the evidence for the Pfizer-BioNTech COVID-19 vaccine were presented to ACIP at a public meeting on May 12, 2021.

The body of evidence for the Pfizer-BioNTech COVID-19 vaccine was primarily guided by one randomized, double-blind, placebo-controlled Phase II/III clinical trial that was expanded

* Accessed May 12, 2021. https://covid.cdc.gov/covid-data-tracker/#vaccinations

† On May 12, 2021, ACIP voted 14–0 (one recusal) in favor of the interim recommendation for use of Pfizer BioNTech COVID-19 vaccine for persons aged 12–15 years. One ACIP member recused herself because of participation in clinical trials and other studies involving companies producing COVID-19 vaccines.

§ https://www.cdc.gov/vaccines/acip/recs/grade/downloads/ACIP-evidence-rec-frame-508.pdf

¶ https://www.cdc.gov/vaccines/acip/recs/grade/about-grade.html

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

to enroll approximately 2,200 participants aged 12–15 years, randomized 1:1 to receive vaccine or saline placebo (*5*). Interim findings from this clinical trial were based on data from participants with a median of 2 months of follow-up. The estimated efficacy of the Pfizer-BioNTech COVID-19 vaccine was supported by two types of evidence: clinical efficacy and immunobridging. In the direct clinical assessment, efficacy was 100% (95% confidence interval [CI] = 75.3%–100%) in preventing symptomatic, laboratory-confirmed COVID-19 in adolescents aged 12–15 years without evidence of previous SARS-CoV-2 infection. Vaccine efficacy was also supported by immunobridging data from vaccine recipients aged 12–15 years compared with those from recipients aged 16–25 years. The immune response to 2 doses of the Pfizer-BioNTech COVID-19 vaccine in adolescents aged 12–15 years without evidence of previous SARS-CoV-2 infection was at least as high as the response observed in persons aged 16–25 years; the geometric mean ratio for 50% neutralizing antibody titer was 1.76 (95% CI = 1.47–2.10), demonstrating statistical noninferiority.** Among adolescent vaccine recipients aged 12–15 years, reactogenicity symptoms, defined as solicited local injection site or systemic reactions during the 7 days after vaccination, were frequent (90.9% of vaccine recipients reported any local reaction, and 90.7% reported any systemic reaction) and mostly mild to moderate. Systemic adverse reactions were more commonly reported after the second dose than after the first dose, had a median onset of 1–4 days after vaccine receipt, and resolved in a median of 1–2 days. Severe local and systemic adverse reactions (grade 3 or higher, defined as interfering with daily activity) occurred more commonly in vaccine recipients than in placebo recipients. Among vaccine recipients, 10.7% reported any reaction of grade 3 or higher; the most common symptoms were fatigue (3.5%), fever (3.0%), headache (2.7%), chills (2.1%), and injection-site pain (1.5%). Overall, reactions of grade 3 or higher were also more commonly reported after the second dose than after the first dose. The frequency of serious adverse events†† was low among all participants; five serious adverse events (0.4%) were reported among vaccine recipients and two (0.2%) among placebo recipients, with no statistically significant difference in frequency observed between the two groups (*5*). These serious adverse events encompassed medical events occurring at a frequency similar to that in the general population aged 12–15 years, with none considered to be related to vaccination (*5*). No specific safety concerns were identified among adolescent vaccine recipients. A detailed summary of safety data, including information on reactogenicity, is available at https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/reactogenicity.html.

From the GRADE evidence assessment, the level of certainty for the benefits of Pfizer-BioNTech COVID-19 vaccination among adolescents aged 12–15 years was type 1 (high certainty) for the prevention of symptomatic COVID-19. Regarding potential harms after vaccination, evidence was type 4 (very low certainty) for serious adverse events and type 1 (high certainty) for reactogenicity. No data were available to assess the other GRADE benefits and harms including prevention of hospitalization due to COVID-19, prevention of multisystem inflammatory syndrome in children (MIS-C), SARS-CoV-2 seroconversion to a nonspike protein, or prevention of asymptomatic SARS-CoV-2 infection.

Data reviewed within the EtR Framework supported the use of the Pfizer-BioNTech COVID-19 vaccine in adolescents aged 12–15 years. ACIP determined that COVID-19 in adolescents is a major public health problem. Adolescents represent a growing proportion of new COVID-19 cases reported to CDC§§ and have been shown to contribute to household transmission (*6*). As of May 1, 2021, the cumulative COVID-19–associated hospitalization rate for adolescents aged 12–17 years was 51.3 per 100,000 population,¶¶ which is higher than the influenza-associated hospitalization rate for the same age group during the 2009 H1N1 influenza pandemic (23.9 per 100,000 population).*** As of May 3, 2021, CDC had received reports of 3,742 cases of MIS-C, a severe hyperinflammatory syndrome occurring several weeks after acute SARS-CoV-2 infection; 21.5% of the MIS-C cases have occurred in adolescents aged 12–17 years.††† ACIP determined that use of the Pfizer-BioNTech COVID-19 vaccine among adolescents is a reasonable and efficient allocation of resources. Whereas there might be uncertainty regarding how different populations value the vaccine, results from several surveys suggest that approximately one half of parents were willing to have their adolescent children vaccinated (range = 46%–60%).§§§ Overall, ACIP determined that the desirable effects clearly outweighed any undesirable effects in most settings. In expanding COVID-19 vaccine access, additional considerations should be given to demographic groups with disproportionate COVID-19 morbidity and mortality, as well as those with barriers to routine health care (e.g., adolescents of certain racial/ethnic groups and those living in a rural or frontier area, experiencing homelessness, having a

** 1.5-fold noninferiority criterion: lower bound of the two-sided 95% CI for geometric mean ratio >0.67.

†† Serious adverse events are defined as any untoward medical occurrence that results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, or results in persistent disability/incapacity.

§§ https://covid.cdc.gov/covid-data-tracker/#demographicsovertime

¶¶ https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html

*** https://gis.cdc.gov/GRASP/Fluview/FluHospRates.html

††† https://www.cdc.gov/mis-c/cases/index.html

§§§ https://www.cdc.gov/vaccines/acip/recs/grade/covid-19-pfizer-biontech-etr-12-15-years.html

disability, or lacking health insurance). Providing rapid and equitable access to COVID-19 vaccine for adolescents will require a stepwise approach, including augmenting existing infrastructure for vaccination, increasing enrollment of providers caring for adolescents into the COVID-19 vaccination program, and applying school-focused strategies to ensure vaccination opportunities for a diverse population. Some aspects of the Pfizer-BioNTech COVID-19 vaccine (e.g., cold-chain storage requirements or large minimum order sizes) might limit access to the vaccine among some populations, which could negatively affect health equity. Advancing health equity, particularly in populations that experience disproportionate COVID-19 morbidity and mortality, requires engagement with community leaders, adolescent health care providers, and parents to identify and remove barriers to COVID-19 vaccination, including those related to vaccine access and vaccine confidence. The GRADE evidence profile and EtR supporting evidence are available at https://www.cdc.gov/vaccines/acip/recs/grade/covid-19-pfizer-biontech-vaccine-12-15-years.html and https://www.cdc.gov/vaccines/acip/recs/grade/covid-19-pfizer-biontech-etr-12-15-years.html.

Before vaccination, the EUA Fact Sheet should be provided to recipients and parents or guardians. There is no federal, legal requirement for caregiver consent for COVID-19 vaccination or any other vaccination; however, COVID-19 vaccine must be administered according to applicable state and territorial vaccination laws. Providers should counsel Pfizer-BioNTech COVID-19 vaccine recipients and parents or guardians about expected systemic and local reactogenicity. Additional clinical considerations are available at https://www.cdc.gov/vaccines/covid-19/info-by-manufacturer/pfizer/clinical-considerations.html. The interim recommendation and clinical considerations are based on use of the Pfizer-BioNTech COVID-19 vaccine under an EUA and might change as more evidence becomes available. ACIP will continue to review additional data as they become available; updates to recommendations or clinical considerations will be posted on the ACIP website (https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html).

Reporting of Vaccine Adverse Events

FDA requires that vaccination providers report vaccination administration errors, serious adverse events, cases of multisystem inflammatory syndrome, and cases of COVID-19 that result in hospitalization or death after administration of COVID-19 vaccine under an EUA (*7*). Adverse events that occur after receipt of any COVID-19 vaccine should be reported to the Vaccine Adverse Events Reporting System (VAERS). Information on how to submit a report to VAERS is available at https://vaers.hhs.gov/index.html or 1-800-822-7967. Any person who administers or receives a COVID-19 vaccine is encouraged to report any clinically significant adverse event, whether or not it is clear that a vaccine caused the adverse event. In addition, CDC has developed a new, voluntary smartphone-based online tool (v-safe) that uses text messaging and online surveys to provide near real-time health check-ins after receipt of a COVID-19 vaccine. Parents or guardians can register their adolescent children in v-safe and complete the health surveys on their behalf. CDC's v-safe call center follows up on reports to v-safe that include possible medically significant health events to collect additional information for completion of a VAERS report. Information on v-safe is available at https://www.cdc.gov/vsafe.

Summary

What is already known about this topic?

On May 10, 2021, the Food and Drug Administration expanded Emergency Use Authorization for the Pfizer-BioNTech COVID-19 vaccine to include adolescents aged 12–15 years.

What is added by this report?

On May 12, 2021, after a systematic review of all available data, the Advisory Committee on Immunization Practices made an interim recommendation for use of the Pfizer-BioNTech COVID-19 vaccine in adolescents aged 12–15 years for the prevention of COVID-19.

What are the implications for public health practice?

The Pfizer-BioNTech COVID-19 vaccine is the first COVID-19 vaccine approved for use in adolescents and has high efficacy against symptomatic COVID-19. Vaccination will be important to protect adolescents against symptomatic COVID-19 disease and to reduce community transmission of SARS-CoV-2.

Acknowledgments

Voting members of the Advisory Committee on Immunization Practices: Kevin A. Ault, University of Kansas Medical Center; Lynn Bahta, Minnesota Department of Health; Henry Bernstein, Zucker School of Medicine at Hofstra/Northwell Cohen Children's Medical Center; Wilbur Chen, University of Maryland School of Medicine; Matthew Daley, Institute for Health Research, Kaiser Permanente Colorado; Sharon E. Frey, Saint Louis University Medical School; Camille Kotton, Harvard Medical School; Sarah Long, Drexel University College of Medicine; Veronica V. McNally, Franny Strong Foundation; Katherine A. Poehling, Wake Forest School of Medicine; Pablo J. Sánchez, The Research Institute at Nationwide Children's Hospital. Members of the Advisory Committee on Immunization Practices COVID-19 Vaccines Work Group: Edward Belongia, Center for Clinical Epidemiology & Population Health, Marshfield Clinic Research Institute; Dayna Bowen Matthew, George Washington University Law School; Oliver Brooks, National Medical Association; Jillian Doss-Walker, Indian Health Service; Marci Drees, Society for Healthcare Epidemiology of America; Jeffrey Duchin, Infectious Diseases Society of America; Kathy Kinlaw,

Center for Ethics, Emory University; Doran Fink, Food and Drug Administration; Sandra Fryhofer, American Medical Association; Jason M. Goldman, American College of Physicians; Michael Hogue, American Pharmacists Association; Denise Jamieson, American College of Obstetricians and Gynecologists; Jeffery Kelman, Centers for Medicare & Medicaid; David Kim, U.S. Department of Health and Human Services; Susan Lett, Council of State and Territorial Epidemiologists; Kendra McMillan, American Nurses Association; Kathleen Neuzil, Center for Vaccine Development and Global Health, University of Maryland School of Medicine; Sean O'Leary, American Academy of Pediatrics; Christine Oshansky, Biomedical Advanced Research and Development Authority; Stanley Perlman, Department of Microbiology and Immunology, University of Iowa; Marcus Plescia, Association of State and Territorial Health Officials; Chris Roberts, National Institutes of Health; William Schaffner, National Foundation for Infectious Diseases; Kenneth Schmader, American Geriatrics Society; Bryan Schumacher, Department of Defense; Rob Schechter, Association of Immunization Managers; Jonathan Temte, American Academy of Family Physicians; Peter Szilagyi, University of California, Los Angeles; Matthew Tunis, National Advisory Committee on Immunization Secretariat, Public Health Agency of Canada; Thomas Weiser, Indian Health Service; Matt Zahn, National Association of County and City Health Officials; Rachel Zhang, Food and Drug Administration.

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All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

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Subject: Pfizer presentation for COVID Work Group

Attachments: CDC COVID-19 Vaccine 12 to 15 EUA FINAL.pdf

Dear Sara,

As promised, please find attached our presentation for tomorrow. We are working on getting the information you requested earlier today.

Thank you for the opportunity to present to the work group and we look forward to the discussion tomorrow. Pease let me know if you need anything else.

Warm regards,

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Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); (b)(4) (b)(4) ; (b)(4) (b)(4)
Subject: Pfizer presentation slides
Attachments: ACIP COVID-19 Vaccine 12 to 15 EUA May 11 2021 Final.pptx

Dear Sara,
Please find attached the (b)(4). We are looking forward to the discussion.

(b)(4)

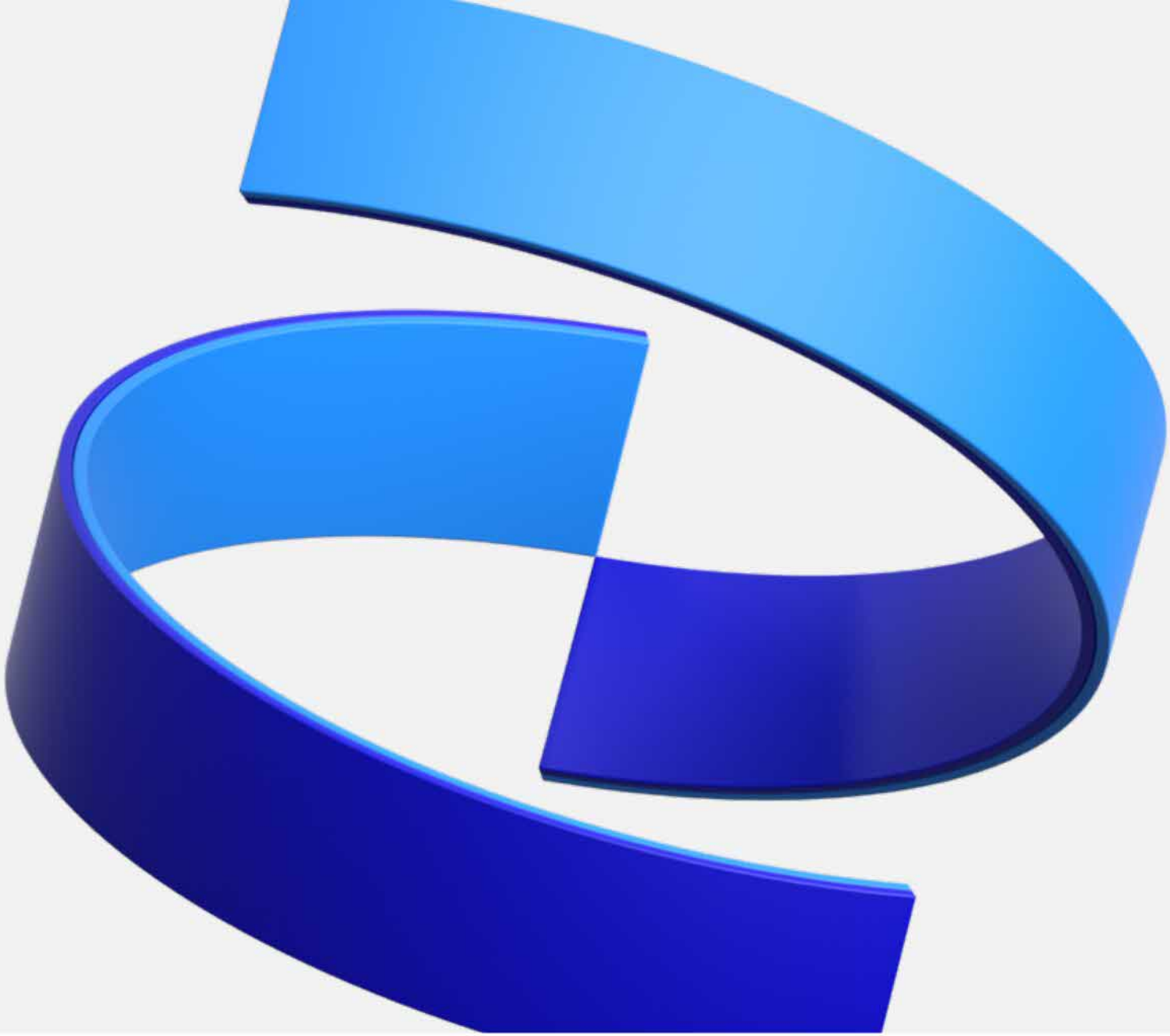
Best regards,
(b)(4) (b)(4) and (b)(

COVID-19 Vaccine BNT162b2

Safety, Immunogenicity, and Efficacy in Subjects 12–15-years-old

Presentation to ACIP
12 May 2021

John L. Perez, MD, MBA, MA



Inclusion of adolescents <16 yrs of age

- C4591001 was initially an adult study (b)(4) that tolerance was acceptable in adults within the original study the protocol was amended to allow inclusion of subjects 16-17 years of age and subsequently 12-15 years of age at the same dose and schedule as adults, without further dose-finding. (b)(4)

(b)(4) Data is from dose 1 to 1 month post dose 2 (12-15- and 16–25-year-olds); and from dose 1 to data cut-off point (13 March 2021) – 12–15-year-oldsData from subjects 16-25 years of age were used for the safety comparisons and immunobridging purposes

Phase 2/3 Safety Schema – Started 27 July, 2020

Vaccination period | **Follow-up period**

Active surveillance
for potential COVID-19 symptoms **TRIGGERING**
telehealth or in-person visit and nasal swab

7 days — **7 days** — **Reactogenicity in subsets for 16 and above; all 12-15 year olds**

One month post dose 2 — **Non-serious AE: all participants**

Six months post dose 2 — **Serious AE: all participants**

Through study — **Deaths: all participants**

- All 12-15 year olds had e-diaries to capture solicited events (N=2260)A random subset of 16-25 year olds had e-diaries (N=1097)Prior history of symptomatic COVID-19/MIS-C were excluded

Demography for 12-15 and 16-25 year olds (Safety population)

		BNT162b2		Placebo	
		12-15 Years(N=1131) n (%)	16-25 Years(N=1867) n (%)	12-15 Years(N=1129) n (%)	16-25 Years(N=1903) n (%)
Sex	Male	567 (50.1)	921 (49.3)	585 (51.8)	882 (46.3)
	Female	564 (49.9)	946 (50.7)	544 (48.2)	1021 (53.7)
Race	White	971 (85.9)	1443 (77.3)	962 (85.2)	1510 (79.3)
	Black or African American	52 (4.6)	189 (10.1)	57 (5.0)	179 (9.4)
	American Indian or Alaska native	4 (0.4)	32 (1.7)	3 (0.3)	18 (0.9)
	Asian	72 (6.4)	108 (5.8)	71 (6.3)	108 (5.7)
	Native Hawaiian or other Pacific Islander	3 (0.3)	10 (0.5)	0	3 (0.2)
	Multiracial	23 (2.0)	76 (4.1)	29 (2.6)	74 (3.9)
	Not reported	6 (0.5)	9 (0.5)	7 (0.6)	11 (0.6)
Racial desig.	Japanese	5 (0.4)	3 (0.2)	2 (0.2	6 (0.3)
Ethnicity	Hispanic/Latino	132 (11.7)	604 (32.4)	130 (11.5)	575 (30.2)
	Non-Hispanic/non-Latino	997 (88.2)	1259 (67.4)	996 (88.2)	1322 (69.5)
	Not reported	2 (0.2)	4 (0.2)	3 (0.3)	6 (0.3)
Country	USA	1131 (100.0)	1333 (71.4)	1129 (100.0)	1364 (71.7)
	Others*	0	534 (28.6)	0	539 (28.3)

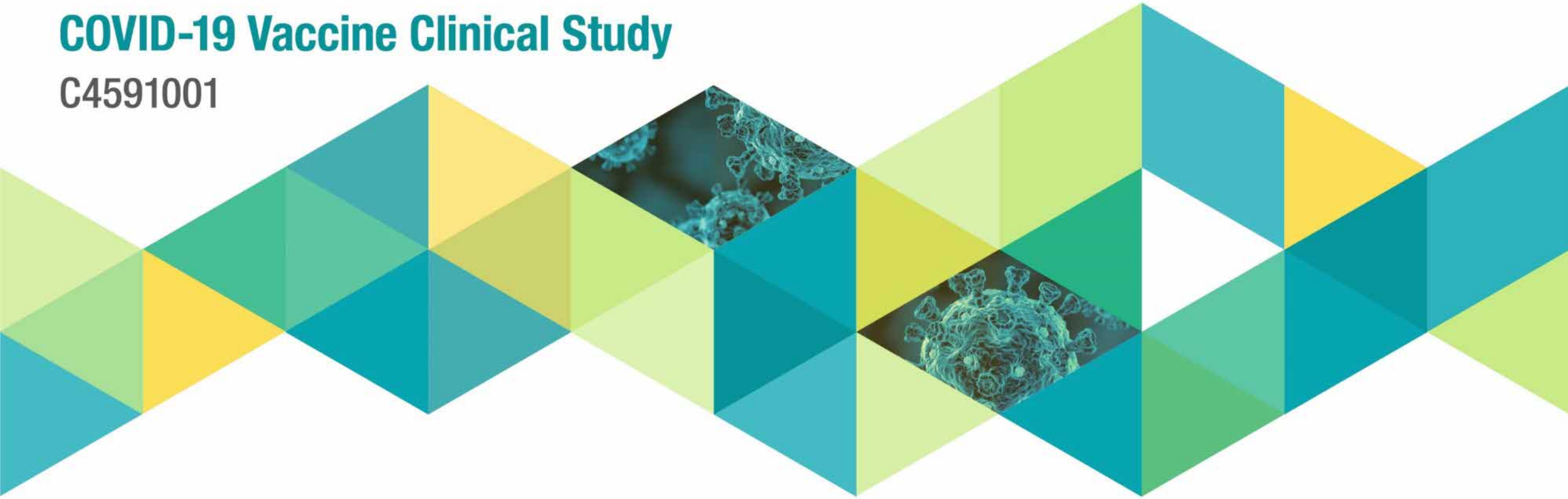
*Argentina, Brazil, Germany, South Africa, Turkey

Note: All 12-15 year olds from the US; ~72% of 16-25 year olds from the US

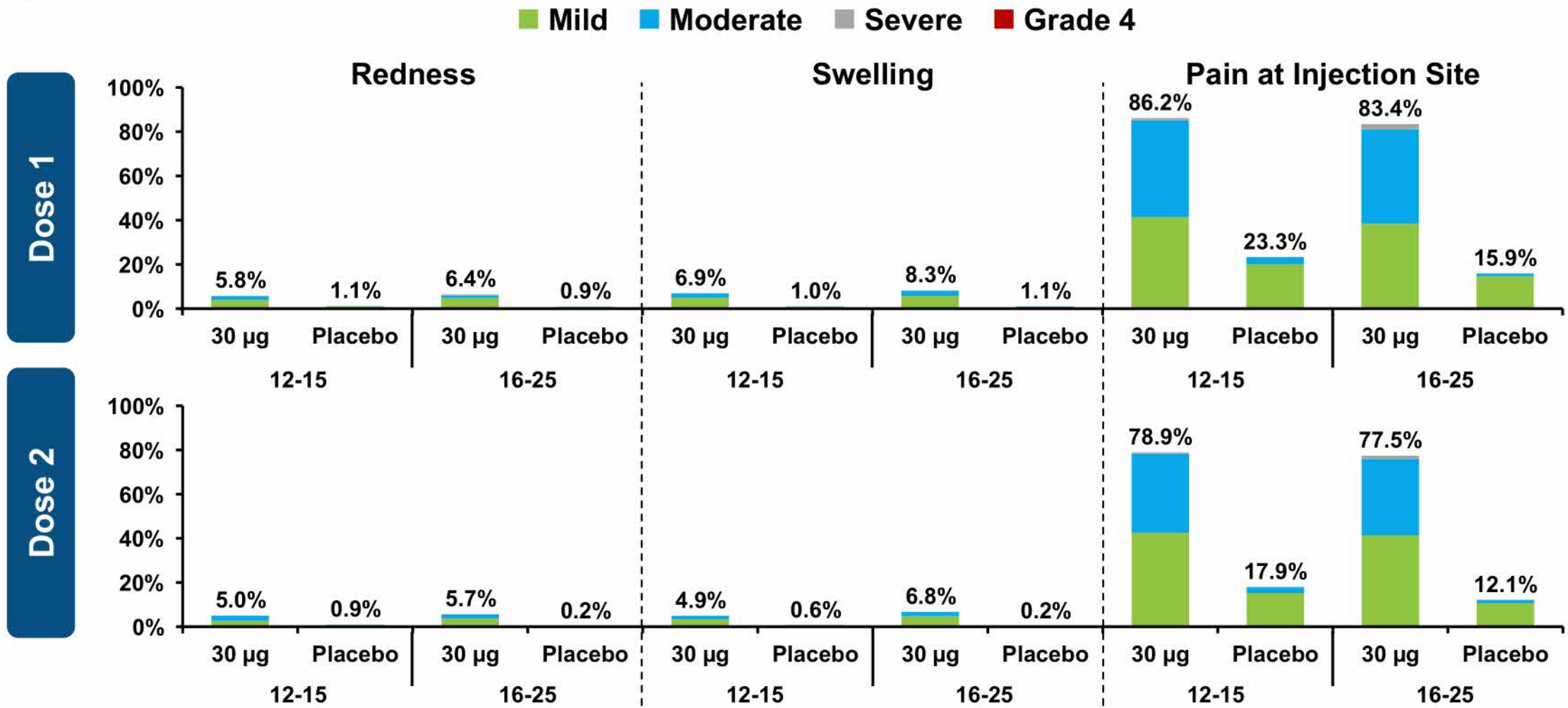
Reactogenicity in 12-15 year olds and 16-25 year olds

COVID-19 Vaccine Clinical Study

C4591001

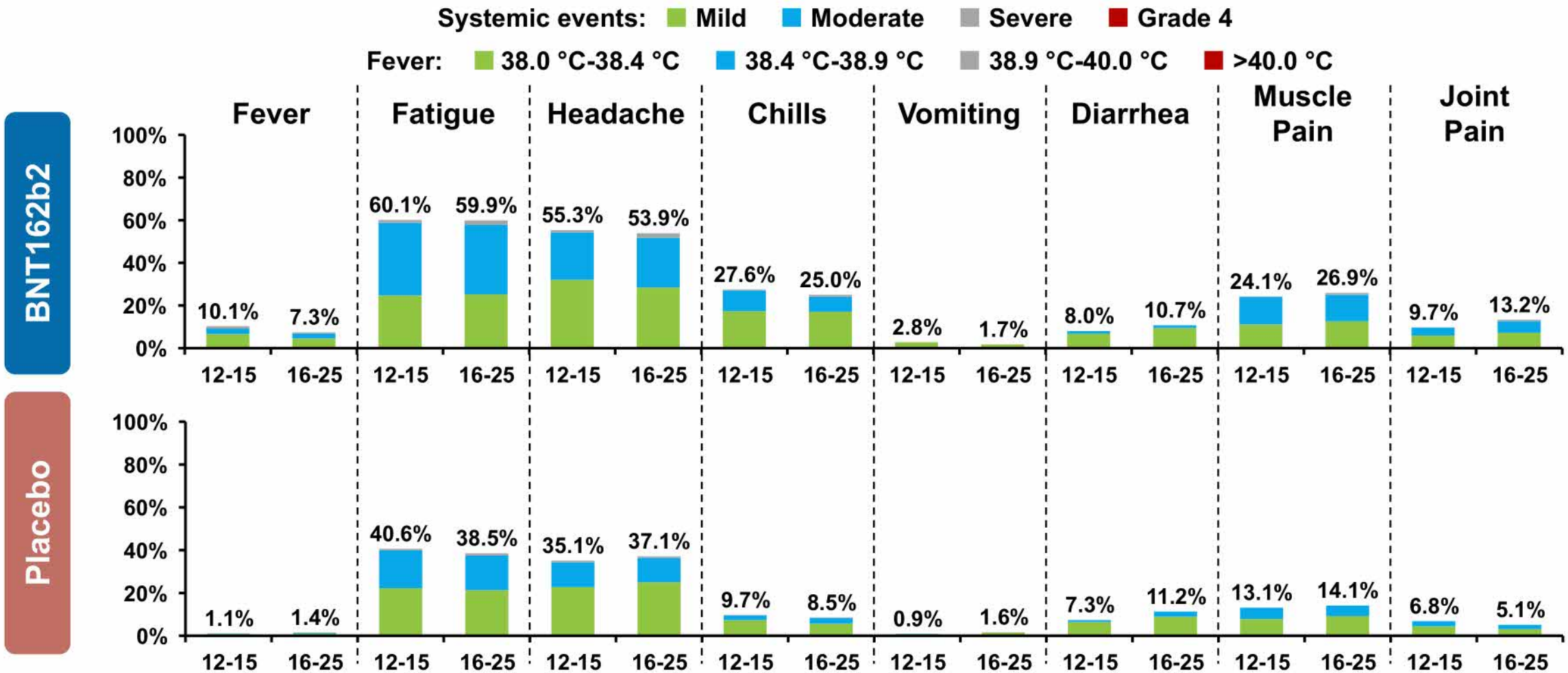


Subjects Reporting Local Reactions, by Maximum Severity, Within 7 Days After Each Dose in 12-15 and 16-25 Year Olds



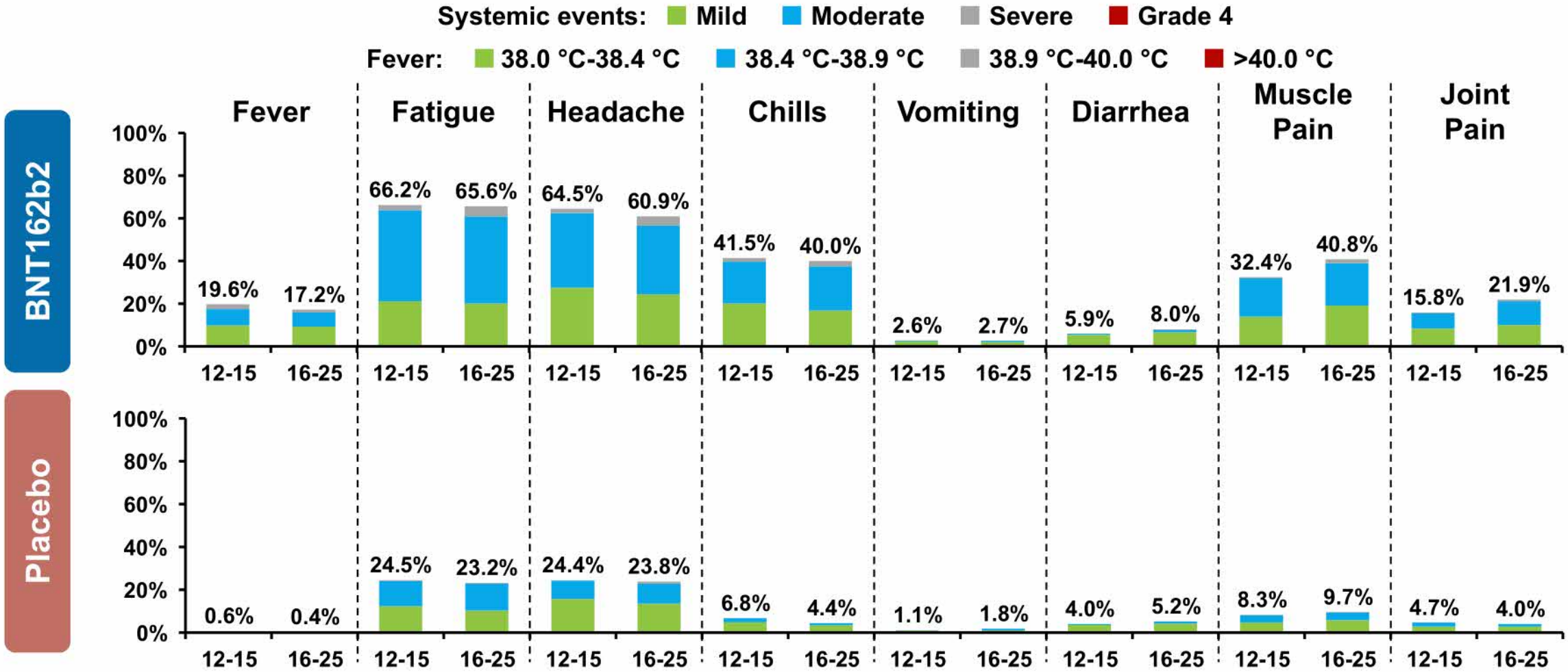
Redness and sweeling severity definition: Mild= >2-5cm, Moderate= >5-10 cm; Severe= >10 cm; Grade 4= necrosis
Pain at injection site severity definition: Mild=no interference; Moderate=some interference; Severe=prevents daily activity; Grade 4=ER visit or hospitalization
Dose 1: 12-15 yrs N=2254; 16-25 yrs N=1084 Dose 2: 12-15 yrs N=2175 16-25 yrs N=984

Subjects Reporting Systemic Events, by Maximum Severity, Within 7 Days After **Dose 1** in 12-15 and 16-25 Year Olds



Fatigue, headache, chills, muscle pain, joint pain severity definition: Mild=no interference; Moderate=some interference; Severe=prevents daily activity; Grade 4=ER visit or hospitalization
Vomiting severity definition: Mild=1-2 time in 24h; Moderate=>2times in 24h; Severe=Requires IV hydration; Grade 4=ER visit or hospitalization
Diarrhea severity definition: Mild=2-3 times in 24h; Moderate=4-5 times in 24h; Severe=6 or more times in 24h; Grade 4=ER visit or hospitalization
Dose 1: 12-15 yrs N=2254; 16-25 yrs N=1084

Subjects Reporting Systemic Events, by Maximum Severity, Within 7 Days After **Dose 2** in 12-15 and 16-25 Year Olds



Fatigue, headache, chills, muscle pain, joint pain severity definition: Mild=no interference; Moderate=some interference; Severe=prevents daily activity; Grade 4=ER visit or hospitalization
Vomiting severity definition: Mild=1-2 time in 24h; Moderate=>2times in 24h; Severe=Requires IV hydration; Grade 4=ER visit or hospitalization
Diarrhea severity definition: Mild=2-3 times in 24h; Moderate=4-5 times in 24h; Severe=6 or more times in 24h; Grade 4=ER visit or hospitalization
Dose 2: 12-15 yrs N=2175 16-25 yrs N=984

Conclusions: Local reactions and systemic events Phase 3 within 7 days of each dose – 12-15 yr olds (N=2254)

- Local reactions were predominantly pain at the injection site – more prominent after the first doseMostly mild to moderateSystemic events were predominantly fatigue, headaches, chills and muscle pain as well as fever and joint pain – more prominent after the second doseMostly mild to moderate

Adverse events in Phase 3 – 12-15 year olds and 16-25 year olds

COVID-19 Vaccine Clinical Study

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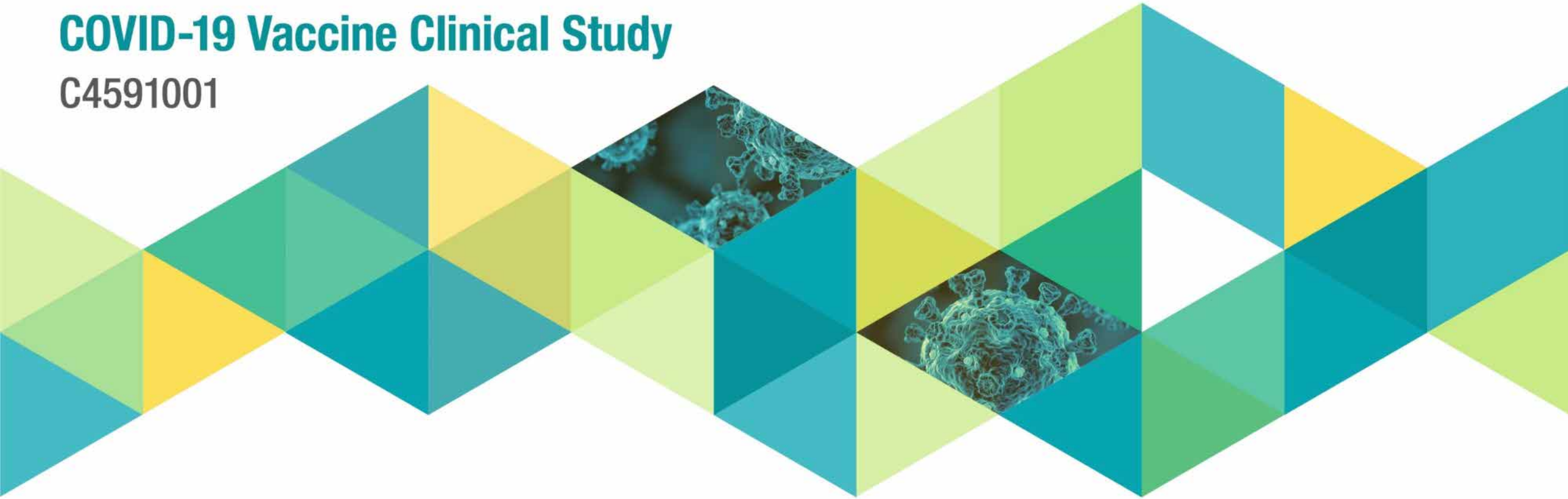
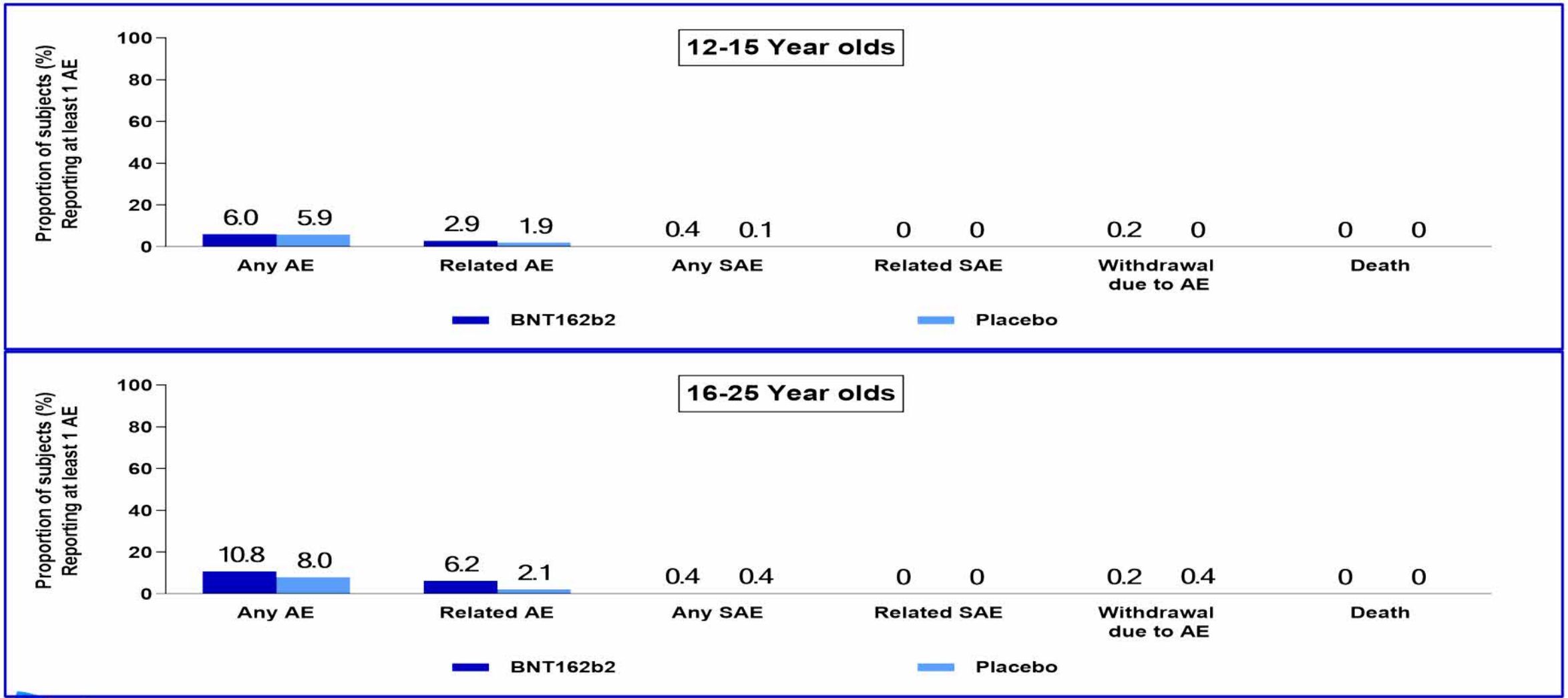
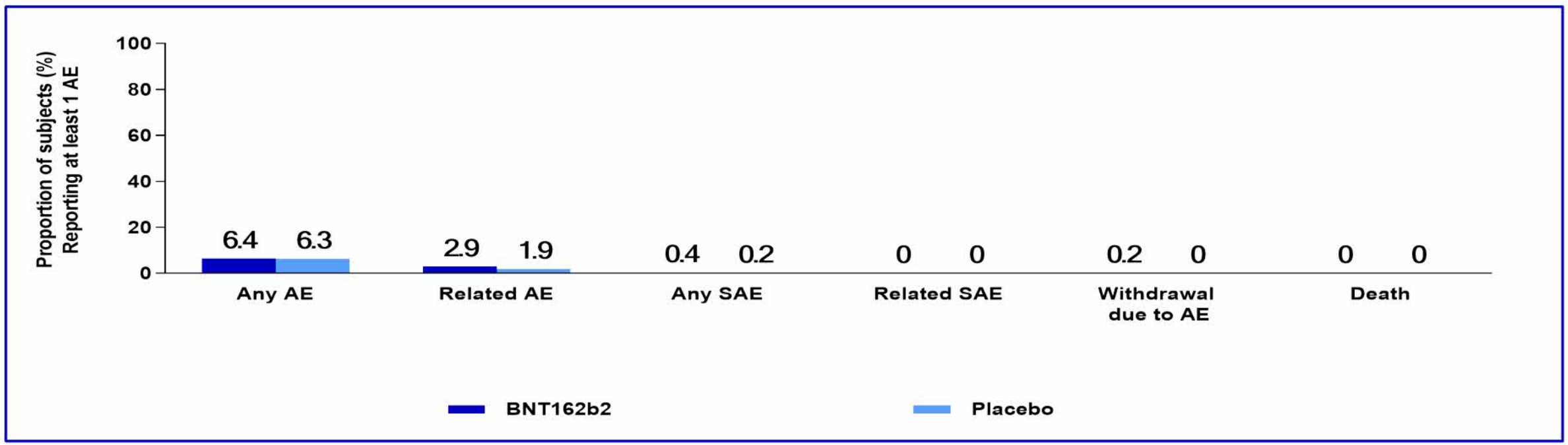


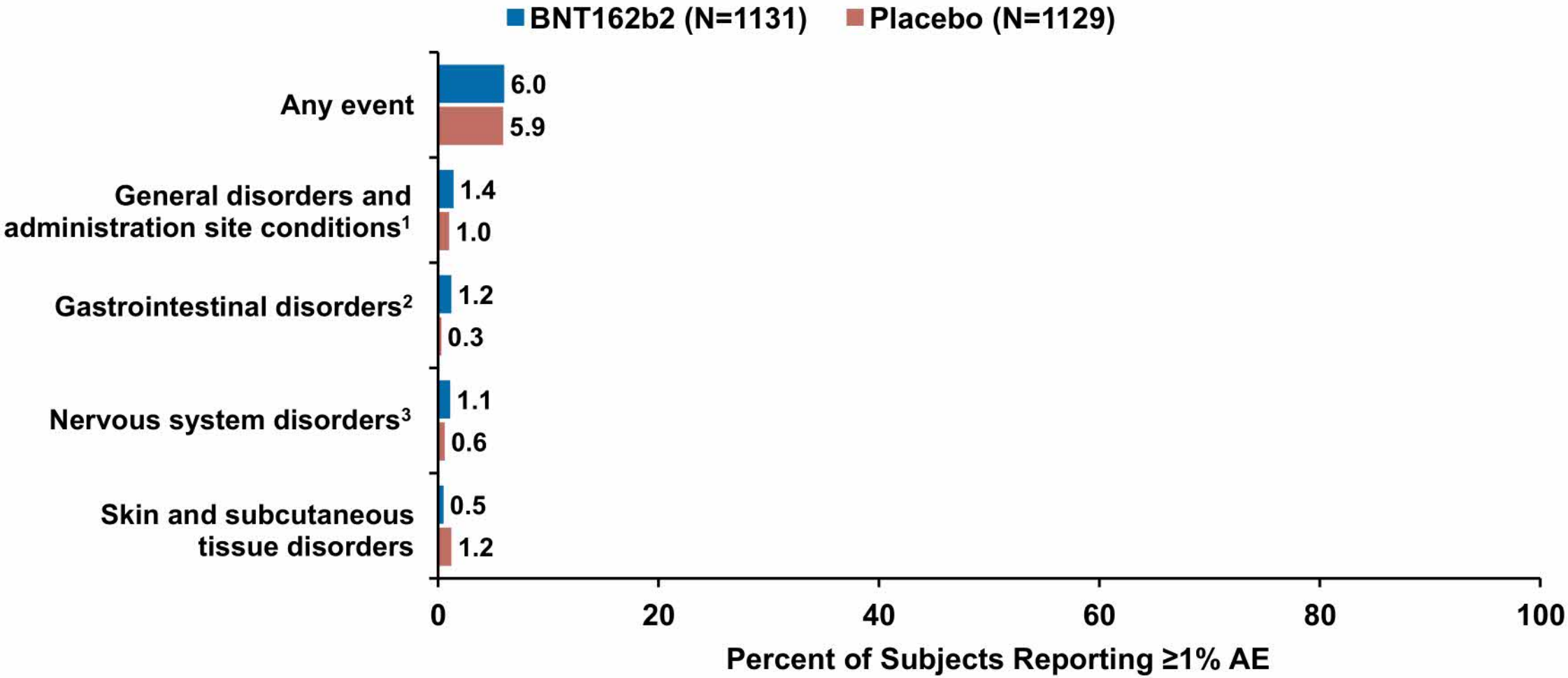
Overall Adverse Events from Dose 1 to 1 Month Post Dose 2
12-15 (N=2260) and 16-25 (Reactogenicity subset N=1097) year olds



Overall Adverse Events from Dose 1 to Data Cut-off Date (13Mar2021) 12-15 year olds (N=2260)

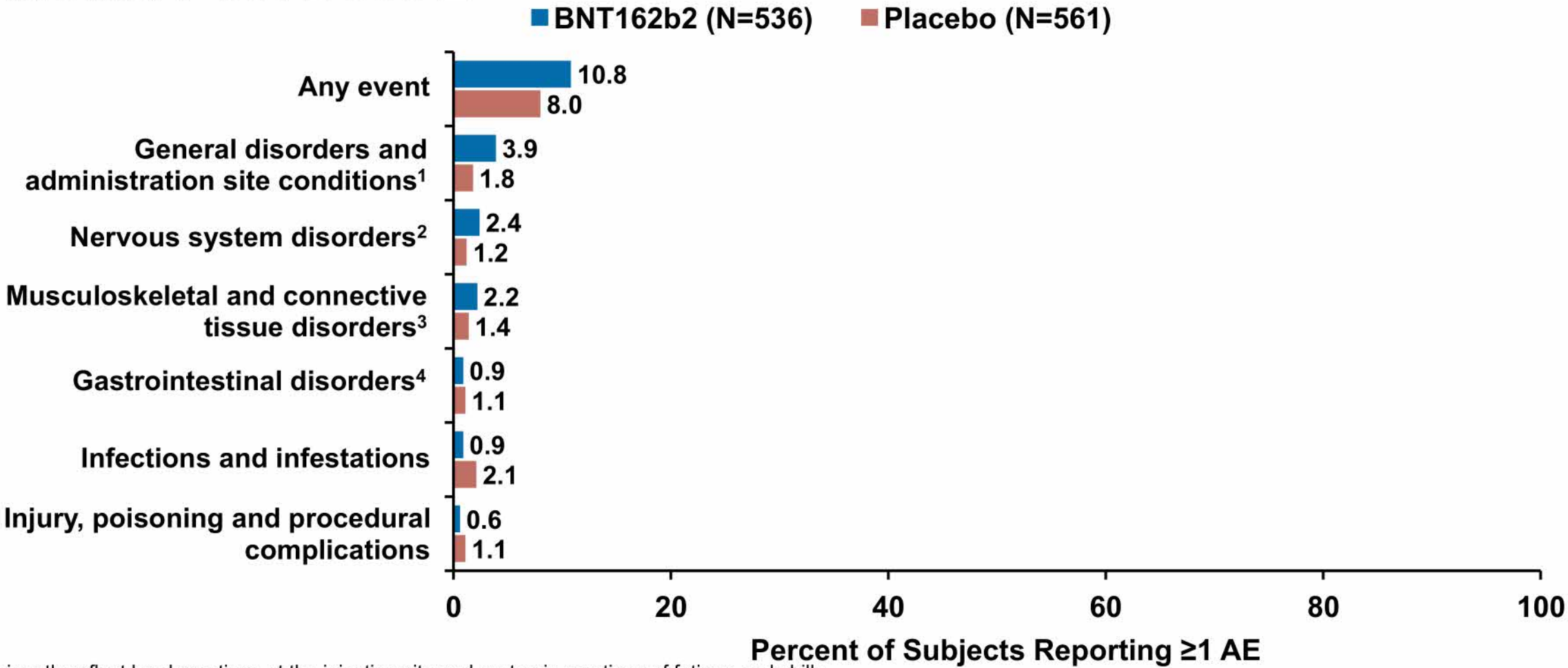


Adverse Events ≥1.0% by System Organ Class for 12-15 year olds 1 Month Post Dose 2



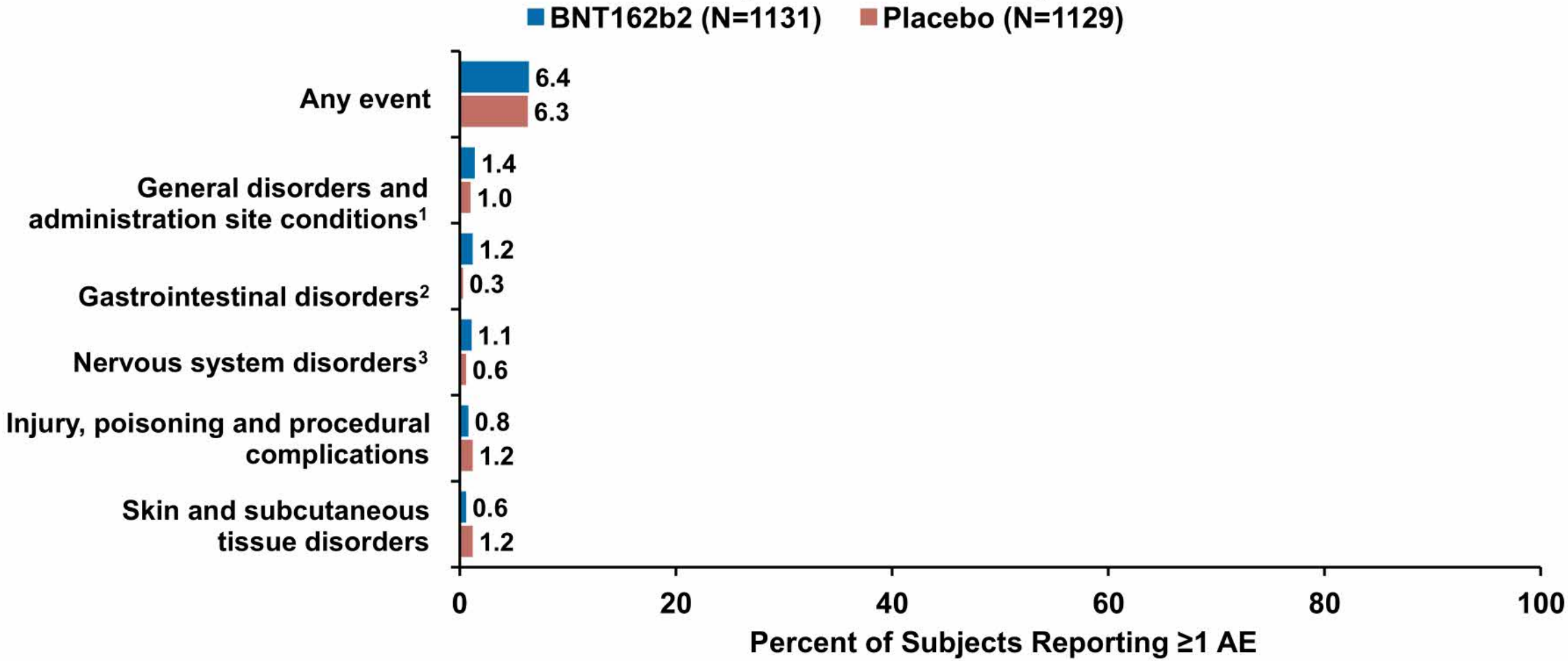
1. Predominantly reflect local reactions at the injection site and systemic reactions of fever and fatigue
2. Predominantly reflect nausea and diarrhea3. Predominantly reflects Headache

Adverse Events ≥1.0% by System Organ Class for 16-25 year olds 1 Month Post Dose 2



1. Predominantly reflect local reactions at the injection site and systemic reactions of fatigue and chills
2. Predominantly reflects Headache 3.. Predominantly reflect myalgias and arthralgia's as part of systemic events4. Predominantly reflects Nausea and Vomiting

Adverse Events ≥1.0% by System Organ Class for 12-15 year olds from Dose 1 to Data Cut-off Date (13 Mar 2021)



1. Predominantly reflect local reactions at the injection site and systemic reactions of fever and fatigue
2. Predominantly reflect nausea and diarrhea3. Predominantly reflects Headache

Lymphadenopathy in 12-15 Year Olds

- 9 cases (0.8%) in BNT162b2 and 2 cases placebo (0.2%)7 (0.6%) were related to vaccination; 1 (0.1%) in the placebo group Primarily Left axillary or Left cervical Onset within 2-10 days after vaccinationDuration 1-10 days where reported (others were ongoing at the time of the data cutoff date).In adults (16-55 years of age), 52 participants (0.4%) in the BNT162b2 group and 2 participants (0.0%) in the placebo group had lymphadenopathy events reported up to the unblinding date and assessed by the investigator as related to study intervention.The majority of these events occurred in the arm and neck region, were reported within 2-4 days after vaccination (usually after Dose 2), and typically resolved within approximately 1 week.

Serious Adverse Events by SOC/PT from Dose 1 to Data Cut-off Date 12-15 year olds

System Organ Class/PT	BNT162b2 (30 µg)(N=1131)		Placebo(N=1129)	
	n	%	n	%
ANY EVENT	5	0.4	2	0.1
GASTROINTESTINAL DISORDERS*ABDOMINAL PAIN*CONSTIPATION	111	0.10.10.1	000	000
INFECTIONS AND INFESTATIONS#APPENDICITIS#FOCAL PERITONITIS	000	000	221	0.20.20.1
NERVOUS SYSTEM DISORDERS*NEURALGIA	11	0.10.1	00	00
PSYCHIATRIC DISORDERSDEPRESSIONANXIETYSUICIDAL IDEATION	4311	0.40.30.10.1	0000	0000

*Abdominal pain, constipation and neuralgia were in the same participant#Appendicitis and focal peritonitis were in the same participant

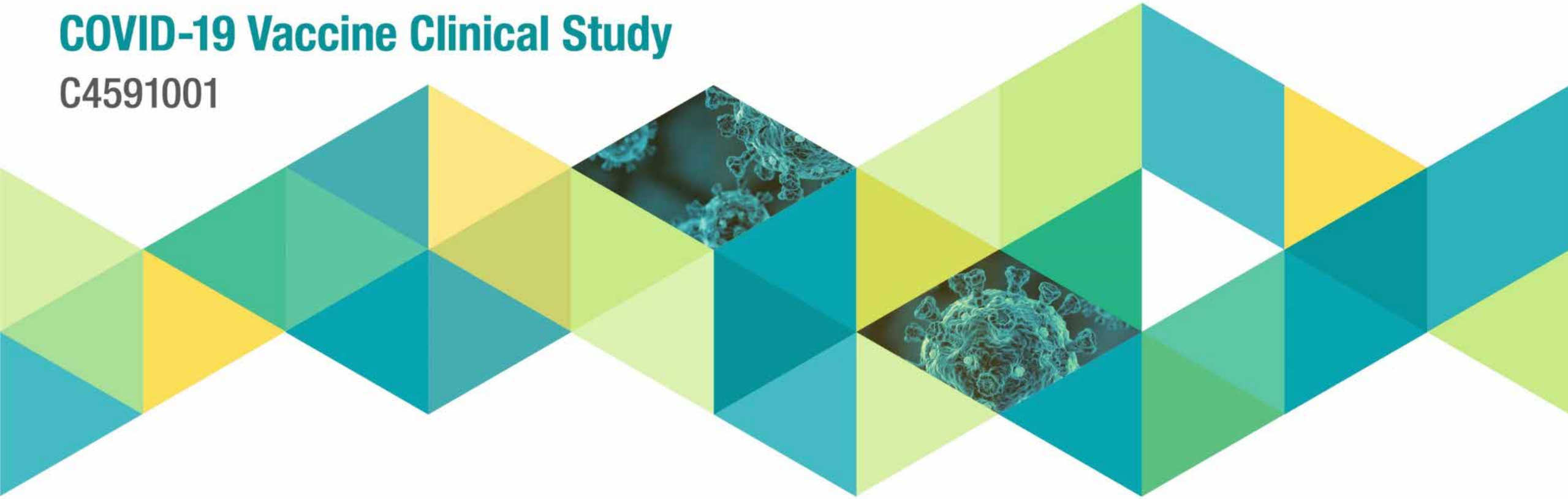
Deaths: 12–15-year-olds

- No deaths

Efficacy and Immunogenicity

COVID-19 Vaccine Clinical Study

C4591001



Follow-up Time After Dose 2: 12-15 year olds – Safety Population

Total exposure from Dose 2 to cut-off date	BNT162b2 (30 µg) (N=1131) n[b](%)	Placebo (N=1129) n (%)	Total (N=2260) n (%)
< 1 Month	13 (1.1)	25 (2.2)	38 (1.7)
≥1 Month to < 2 months	458 (40.5)	456 (40.4)	914 (40.4)
≥2 Months to <3 months	612 (54.1)	599 (53.1)	1211 (53.6)
≥3 Months	48 (4.2)	49 (4.3)	97 (4.3)

Note: 98.3% of subjects had at least 1 month of follow-up time

(b)(4)

Noninferiority Between 12-15 and 16-25 years Of Age Was Met Geometric Mean Ratio (GMR) in Neutralization Titers

(Without prior infection)

		BNT162b2 (30 µg)					
		12-15 year		16-25 years		12-15/16-25 years	
Assay	Dosing/Sampling Time Point	n	GMT (95% CI)	n	GMT (95% CI)	GMR(95% CI)	Met NI (Y/N)
SARS-CoV-2 neutralization assay - NT50 (titer)	2 / 1 Month	190	1239.5(1095.5, 1402.5)	170	705.1(621.4, 800.2)	1.76(1.47, 2.10)	Y

- Noninferiority is declared if the lower bound of the 95% confidence interval is > 0.67LBCI for GMR >1 indicating a statistically greater response in 12-15 that 16-25 year olds

First COVID-19 Occurrence From 7 Days After Dose 2

Subjects 12-15 Years of Age – Evaluable Efficacy Population

Subjects WITHOUT Evidence of Infection Prior to 7 days after Dose 2

	BNT162b2 (30 µg) N=1005		Placebo N=978			
Efficacy Endpoint	**n**	**Surveillance Time (n)**	**n**	**Surveillance Time (n)**	**VE (%)**	**(95% CI)**
First COVID-19 occurrence ≥7 days after Dose 2	**0**	**0.154 (1001)**	**16**	**0.147 (972)**	**100.0**	**(75.3, 100.0)**

- There were no severe COVID-19 cases

Total surveillance time: 1000 person-years for all subjects within each group at risk for the endpoint.The analysis is descriptive; no hypothesis test

First COVID-19 Occurrence From 7 Days After Dose 2

Subjects 12-15 Years of Age – Evaluable Efficacy Population

Subjects WITH or WITHOUT Evidence of Infection Prior to 7 days after Dose 2

	BNT162b2 (30 µg) N=1119		Placebo N=1110			
Efficacy Endpoint	**n**	**Surveillance Time (n)**	**n**	**Surveillance Time (n)**	**VE (%)**	**(95% CI)**
First COVID-19 occurrence ≥7 days after Dose 2	**0**	**0.170 (1109)**	**18**	**0.163 (1094)**	**100.0**	**(78.1, 100.0)**

- There were no severe COVID-19 cases

Total surveillance time: 1000 person-years for all subjects within each group at risk for the endpoint.The analysis is descriptive; no hypothesis test

(b)(4)

- **Reactogenicity: BNT162b2 was well tolerated in subjects 12-15 years old and showed a similar pattern to that seen in 16-25 year olds Pain at the injection site, fatigue, headaches, chills, joint pain and muscle pain were the most predominant as well as feverIncreased systemic events after dose 2 was similar to that seen with 16-25 year oldsAdverse events overall (b)(4) Highest incidence was in the General Disorders and Administration Site Conditions, reflecting local and systemic reactogenicity events Lymphadenopathy was identified as related to vaccinationThere were no related SAEsNo deaths were reported**

(b)(4)

- Immune response to Pfizer-BioNTech COVID-19 Vaccine in SARS-CoV-2 50% neutralizing titers in adolescents 12-15 years of age was noninferior to (and in fact exceeded) the immune response in young adults 16-25 years of age, which provides immunobridging for adolescents in pivotal Study C4591001. In the adolescent group, efficacy analyses based on cases reported from at least 7 days after Dose 2 through the data cutoff date, the observed VE was 100% (95% CI: 75.3%, 100%) for individuals without evidence of prior SARS-CoV-2 infection before and during vaccination regimen, and 100% (2-sided 95% CI: 78.1%, 100%) for those with or without evidence of prior SARS-CoV-2 infection before and during vaccination regimen. No severe cases were reported in the 12-15 years of age group as of the date cutoff date.Overall, these immunogenicity and efficacy data strongly support BNT162b2 use in adolescents 12-15 years of age.

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Fri, 28 May 2021 20:57:19 +0000
To: (b)(4) (b)(4) T; (b)(4) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); Mbaeyi, Sarah (CDC/DDID/NCIRD/OD)
Subject: Pfizer trial participants
Attachments: 2020-COVID-19-shot-card-3forprinting.pdf

(b)(4) and (b)(4

I wanted to pass this along: We've had discussions around trial participants, especially in light of CDC's guidance for 'fully vaccinated individuals'. Below is the current guidance. Feel free to share and let us know if there are any questions or issues. Also I know that we passed along the "CDC card" already, but I'm including it here as well. I know there are ongoing discussions around getting these into IIS locally but we're happy to facilitate those discussions as well. Also, as mentioned previously- please don't publicly post the card.

Thanks-
Sara

Pfizer, Moderna and Janssen trial participants:

The Pfizer, Moderna and Janssen vaccines are authorized under EUA. In addition, ACIP has independently reviewed the safety and efficacy data from the Phase 3 clinical trials. The "CDC cards" have been provided to the manufacturers. Once it has been confirmed that trial participants received 'active' vaccine and not placebo, the participants can be considered 'fully vaccinated' in terms of CDC guidance, can receive a "CDC card" and can have their vaccine recorded in IIS systems. CDC will work with the manufacturers, PCTs, and states to make sure they are aware of these updates.

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

COVID-19 Vaccination Record Card

Please keep this record card, which includes medical information about the vaccines you have received.

Por favor, guarde esta tarjeta de registro, que incluye información médica sobre las vacunas que ha recibido.

Last Name | First Name | MI

Date of birth | Patient number *(medical record or IIS record number)*

Vaccine	Product Name/Manufacturer Lot Number	Date	Healthcare Professional or Clinic Site
1st Dose COVID-19		____/____/____ *mm dd yy*	
2nd Dose COVID-19		____/____/____ *mm dd yy*	
Other		____/____/____ *mm dd yy*	
Other		____/____/____ *mm dd yy*	

Reminder! Return for a second dose!
¡Recordatorio! ¡Regrese para la segunda dosis!

Vaccine	Date / Fecha
COVID-19 vaccine Vacuna contra el COVID-19	_____/_____/_____ mm dd yy
Other Otra	_____/_____/_____ mm dd yy

Bring this vaccination record to every vaccination or medical visit. Check with your health care provider to make sure you are not missing any doses of routinely recommended vaccines.

For more information about COVID-19 and COVID-19 vaccine, visit **cdc.gov/coronavirus/2019-ncov/index.html**.

You can report possible adverse reactions following COVID-19 vaccination to the Vaccine Adverse Event Reporting System (VAERS) at **vaers.hhs.gov**.

Lleve este registro de vacunación a cada cita médica o de vacunación. Consulte con su proveedor de atención médica para asegurarse de que no le falte ninguna dosis de las vacunas recomendadas.

Para obtener más información sobre el COVID-19 y la vacuna contra el COVID-19, visite **espanol.cdc.gov/coronavirus/2019-ncov/index.html**.

Puede notificar las posibles reacciones adversas después de la vacunación contra el COVID-19 al Sistema de Notificación de Reacciones Adversas a las Vacunas (VAERS) en **vaers.hhs.gov**.

From: (b)(4) (b)(4) (x)
Sent: Thu, 17 Jun 2021 14:10:28 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: (b)(4) (b)(4)
Subject: (b)(4)
Attachments:
slides PDF.pdf

Hi Sara,
Here is a PDF of the presentation that Dr. (b)(4) will give today to the COVID-19 Work Group summarizing the results of our COVID-19 vaccine study in adolescents. As always, we would ask that the slides be handled as confidential and not distributed beyond the Work Group.
If OK with you, Dr. (b)(4) will plan to advance her own slides.
Thanks again for the opportunity to present today. Talk to you later!
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From: (b)(4) (b)(4) (b)(

Sent: Thu, 1 Apr 2021 11:51:26 +0000

To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)

Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); (b)(4) (b)(4) (b)(4) (b)(4)

Subject: press release today on 6 month data

Dear Sara,
An additional press release was posted today announcing the 6 months follow up data post dose 2. We can discuss further today on our call.
All the best,
(b)(4) (b)(and (b)(4)

Pfizer Inc. - Pfizer and BioNTech Confirm High Efficacy and No Serious Safety Concerns Through Up to Six Months Following Second Dose in Updated Topline Analysis of Landmark COVID-19 Vaccine Study

From: (b)(4) (b)(4) (b)
Sent: Tue, 22 Jun 2021 02:49:38 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: (b)(4) (b)(4)
Subject: Report attached
Attachments: (b)(4)

Dear Sara,

(b)(4)

Please let us know if you have any questions.
Best regards,
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From: (b)(4) (b)(4) (x)
Sent: Fri, 2 Jul 2021 17:44:05 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Responses to CDC Questions - Adolescent Study

Hi Sara,
I checked with the team here & it looks like we will need more time to finish the responses to the 17 questions that you sent us earlier regarding the adolescent study. It will likely be mid next week before we can send the information.
My apologies for the delay.
Enjoy the long weekend!
(b)(4)

Please consider the environment before printing this email

From: (b)(4) (b)(4) (x)
Sent: Wed, 7 Jul 2021 21:37:42 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); Dooling, Kathleen L. (CDC/DDID/NCIRD/DVD); MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: Responses to Questions - Moderna's Adolescent Study
Attachments: Moderna - Final Responses to CDC - Adolescents - 070721.pdf

Hi everyone,
Attached please find our responses to the 17 questions that CDC asked us to address about our COVID-19 vaccine study in adolescents.
We would appreciate if this information is handled as strictly confidential & only shared with those covered by our CDA with CDC. Note that the responses contain individual subject narratives for which we ask that absolute confidentiality be maintained. It is our understanding that this information will be used in support of your GRADE evaluation.
Please let me know if you have any questions.
(b)(4)

Please consider the environment before printing this email

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From: (b)(4) (b)(4) (b)(

Sent: Tue, 11 May 2021 23:10:27 +0000

To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)

Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); (b)(4) (b)(4)

Subject: REVISED Pfizer presentation slides

Attachments: ACIP COVID-19 Vaccine 12 to 15 EUA May 11 2021 REVISED FINAL.pptx

Importance: High

Dear Sara,
So sorry, we received some last minute revisions from internal colleagues so please use the attached REVISED slides for the meeting tomorrow.

Also, we have a separate question. (b)(4)

(b)(4)

(b)(4) We would appreciate any guidance you could provide us on this.

Thank you and see you tomorrow,
All the best,
(b)(4) and (b)(

(b)(4) (b)(4) (b)(4)

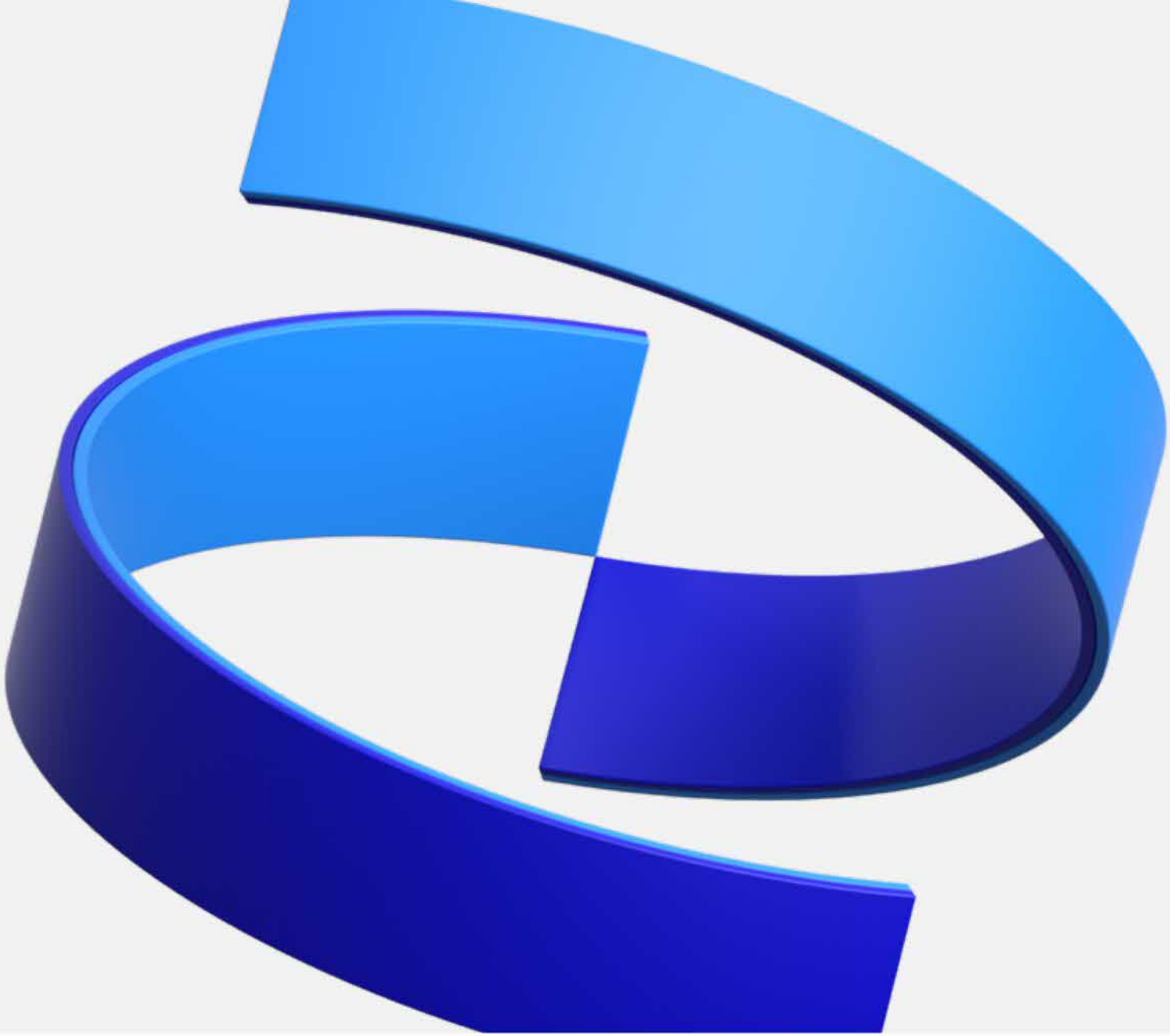
(b)(4)

COVID-19 Vaccine BNT162b2

Safety, Immunogenicity, and Efficacy in Subjects 12–15-years-old

Presentation to ACIP
12 May 2021

John L. Perez, MD, MBA, MA



Inclusion of adolescents <16 yrs of age

- C4591001 was initially an adult studyOnce acceptable tolerance in adults was established within the original study the protocol was amended to allow inclusion of subjects 16-17 years of age and subsequently 12-15 years of age at the same dose and schedule as adults, without further dose-finding. The purpose was to generate data to understand whether people 12-15 years of age could be included in pandemic COVID-19 immunisation programmesData is from dose 1 to 1 month post dose 2 (12-15- and 16–25-year-olds); and from dose 1 to data cut-off point (13 March 2021) – 12–15-year-oldsData from subjects 16-25 years of age were used for the safety comparisons and immunobridging purposes

Phase 2/3 Safety Schema – Started 27 July, 2020

Vaccination period | **Follow-up period**

Active surveillance
for potential COVID-19 symptoms **TRIGGERING**
telehealth or in-person visit and nasal swab

7 days — **7 days** — **Reactogenicity in subsets for 16 and above; all 12-15 year olds**

One month post dose 2 — **Non-serious AE: all participants**

Six months post dose 2 — **Serious AE: all participants**

Through study — **Deaths: all participants**

- All 12-15 year olds had e-diaries to capture solicited events (N=2260)A random subset of 16-25 year olds had e-diaries (N=1097)Prior history of symptomatic COVID-19/MIS-C were excluded

Demography for 12-15 and 16-25 year olds (Safety population)

		BNT162b2		Placebo	
		12-15 Years(N=1131) n (%)	16-25 Years(N=1867) n (%)	12-15 Years(N=1129) n (%)	16-25 Years(N=1903) n (%)
Sex	Male	567 (50.1)	921 (49.3)	585 (51.8)	882 (46.3)
	Female	564 (49.9)	946 (50.7)	544 (48.2)	1021 (53.7)
Race	White	971 (85.9)	1443 (77.3)	962 (85.2)	1510 (79.3)
	Black or African American	52 (4.6)	189 (10.1)	57 (5.0)	179 (9.4)
	American Indian or Alaska native	4 (0.4)	32 (1.7)	3 (0.3)	18 (0.9)
	Asian	72 (6.4)	108 (5.8)	71 (6.3)	108 (5.7)
	Native Hawaiian or other Pacific Islander	3 (0.3)	10 (0.5)	0	3 (0.2)
	Multiracial	23 (2.0)	76 (4.1)	29 (2.6)	74 (3.9)
	Not reported	6 (0.5)	9 (0.5)	7 (0.6)	11 (0.6)
Racial desig.	Japanese	5 (0.4)	3 (0.2)	2 (0.2	6 (0.3)
Ethnicity	Hispanic/Latino	132 (11.7)	604 (32.4)	130 (11.5)	575 (30.2)
	Non-Hispanic/non-Latino	997 (88.2)	1259 (67.4)	996 (88.2)	1322 (69.5)
	Not reported	2 (0.2)	4 (0.2)	3 (0.3)	6 (0.3)
Country	USA	1131 (100.0)	1333 (71.4)	1129 (100.0)	1364 (71.7)
	Others*	0	534 (28.6)	0	539 (28.3)

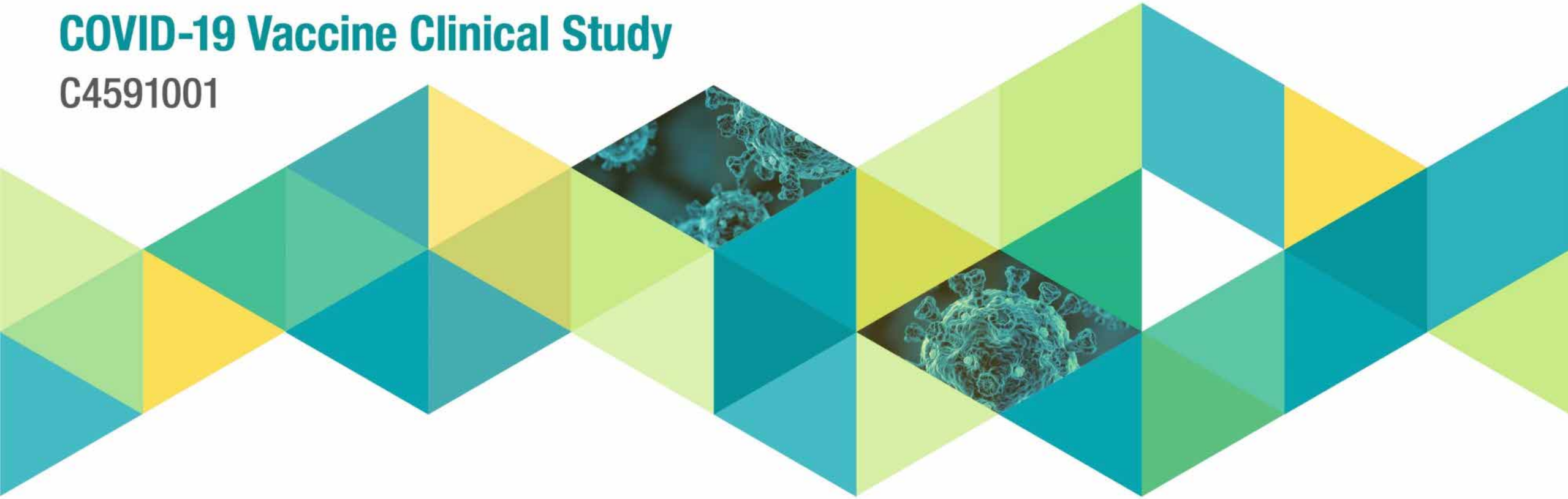
*Argentina, Brazil, Germany, South Africa, Turkey

Note: All 12-15 year olds from the US; ~72% of 16-25 year olds from the US

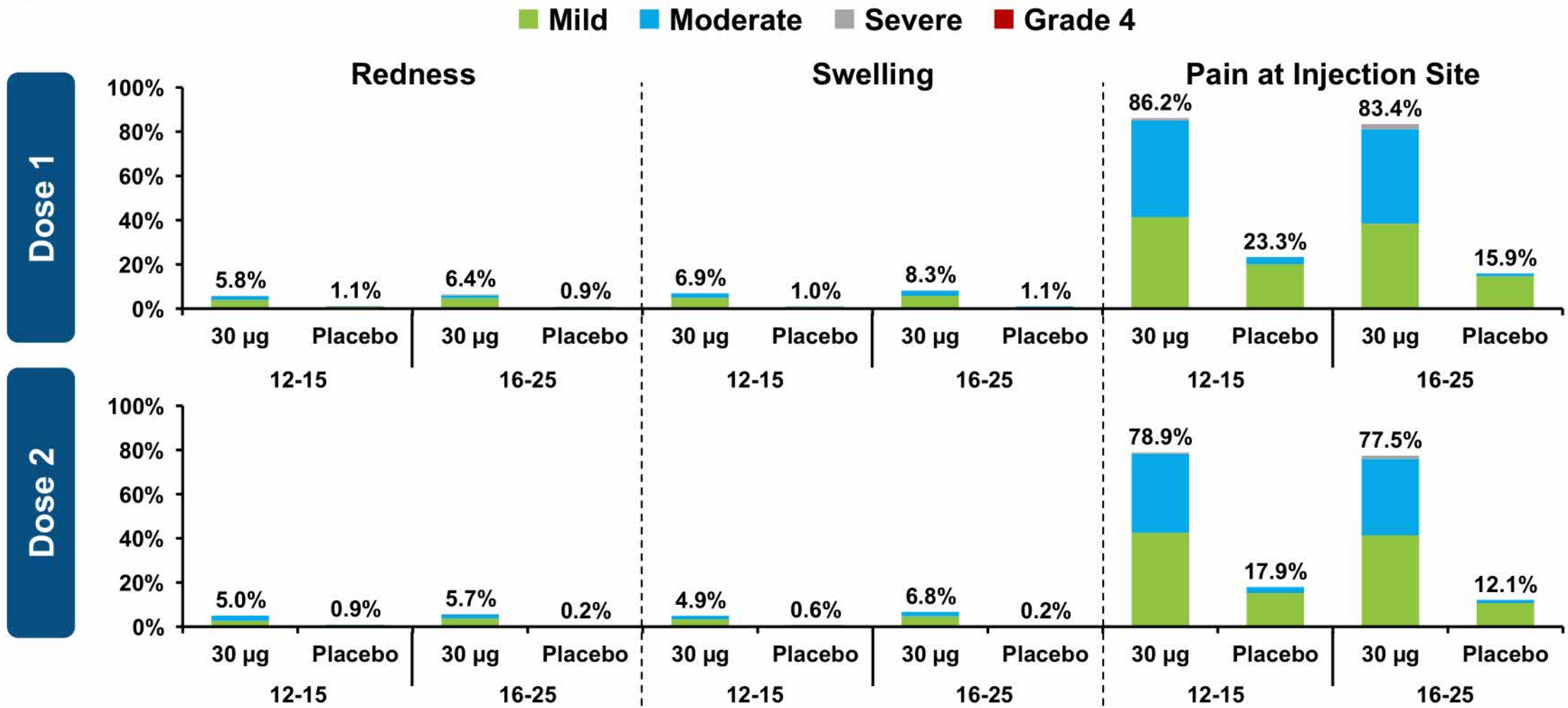
Reactogenicity in 12-15 year olds and 16-25 year olds

COVID-19 Vaccine Clinical Study

C4591001

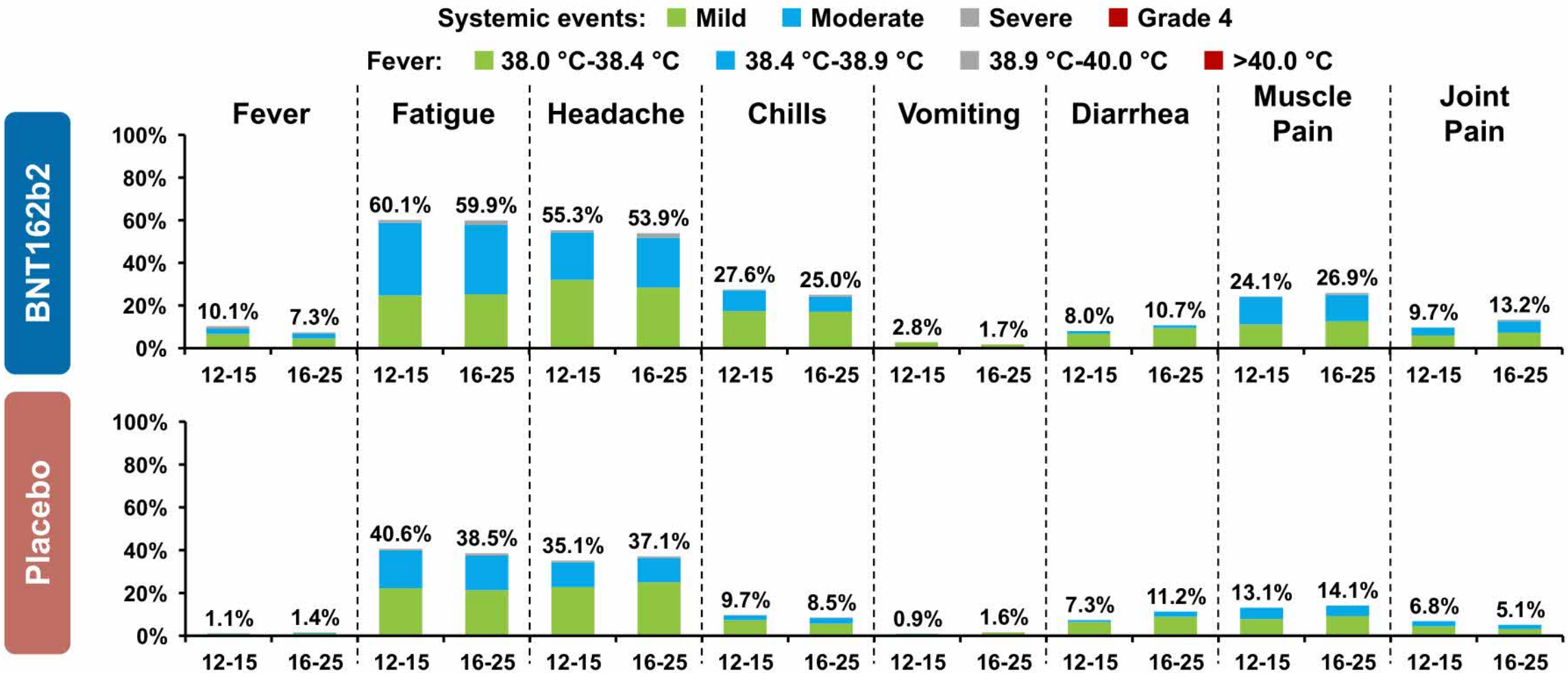


Subjects Reporting Local Reactions, by Maximum Severity, Within 7 Days After Each Dose in 12-15 and 16-25 Year Olds



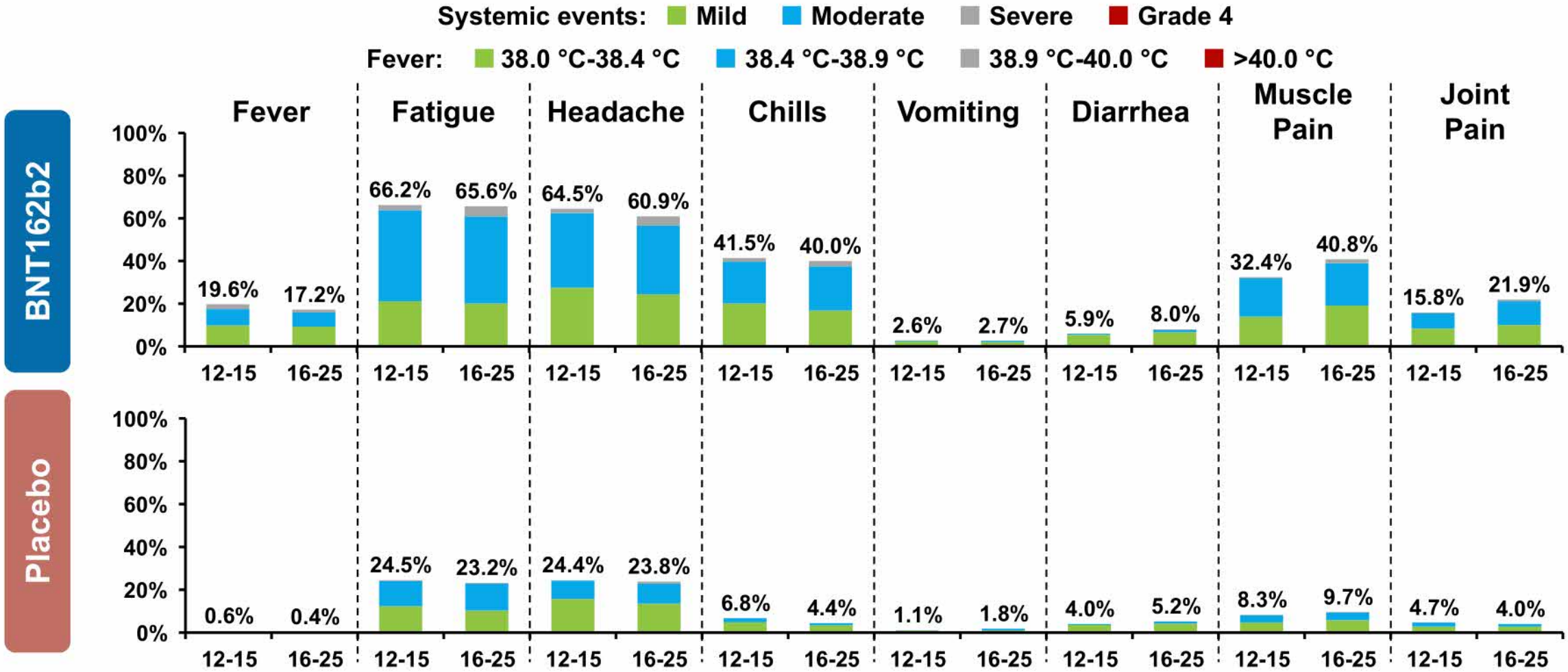
Redness and sweeling severity definition: Mild= >2-5cm, Moderate= >5-10 cm; Severe= >10 cm; Grade 4= necrosis
Pain at injection site severity definition: Mild=no interference; Moderate=some interference; Severe=prevents daily activity; Grade 4=ER visit or hospitalization
Dose 1: 12-15 yrs N=2254; 16-25 yrs N=1084 Dose 2: 12-15 yrs N=2175 16-25 yrs N=984

Subjects Reporting Systemic Events, by Maximum Severity, Within 7 Days After **Dose 1** in 12-15 and 16-25 Year Olds



Fatigue, headache, chills, muscle pain, joint pain severity definition: Mild=no interference; Moderate=some interference; Severe=prevents daily activity; Grade 4=ER visit or hospitalization
Vomiting severity definition: Mild=1-2 time in 24h; Moderate=>2times in 24h; Severe=Requires IV hydration; Grade 4=ER visit or hospitalization
Diarrhea severity definition: Mild=2-3 times in 24h; Moderate=4-5 times in 24h; Severe=6 or more times in 24h; Grade 4=ER visit or hospitalization
Dose 1: 12-15 yrs N=2254; 16-25 yrs N=1084

Subjects Reporting Systemic Events, by Maximum Severity, Within 7 Days After **Dose 2** in 12-15 and 16-25 Year Olds



Fatigue, headache, chills, muscle pain, joint pain severity definition: Mild=no interference; Moderate=some interference; Severe=prevents daily activity; Grade 4=ER visit or hospitalization
Vomiting severity definition: Mild=1-2 time in 24h; Moderate=>2times in 24h; Severe=Requires IV hydration; Grade 4=ER visit or hospitalization
Diarrhea severity definition: Mild=2-3 times in 24h; Moderate=4-5 times in 24h; Severe=6 or more times in 24h; Grade 4=ER visit or hospitalization
Dose 2: 12-15 yrs N=2175 16-25 yrs N=984

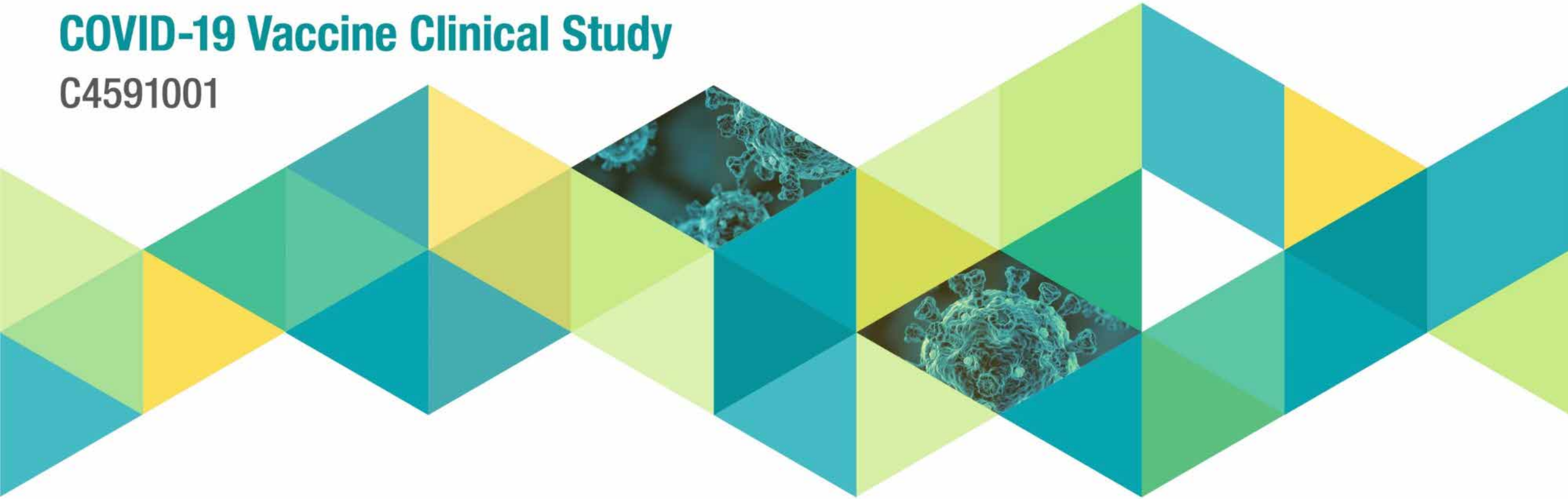
Conclusions: Local reactions and systemic events Phase 3 within 7 days of each dose – 12-15 yr olds (N=2254)

- Local reactions were predominantly pain at the injection site – more prominent after the first doseMostly mild to moderateSystemic events were predominantly fatigue, headaches, chills and muscle pain as well as fever and joint pain – more prominent after the second doseMostly mild to moderate

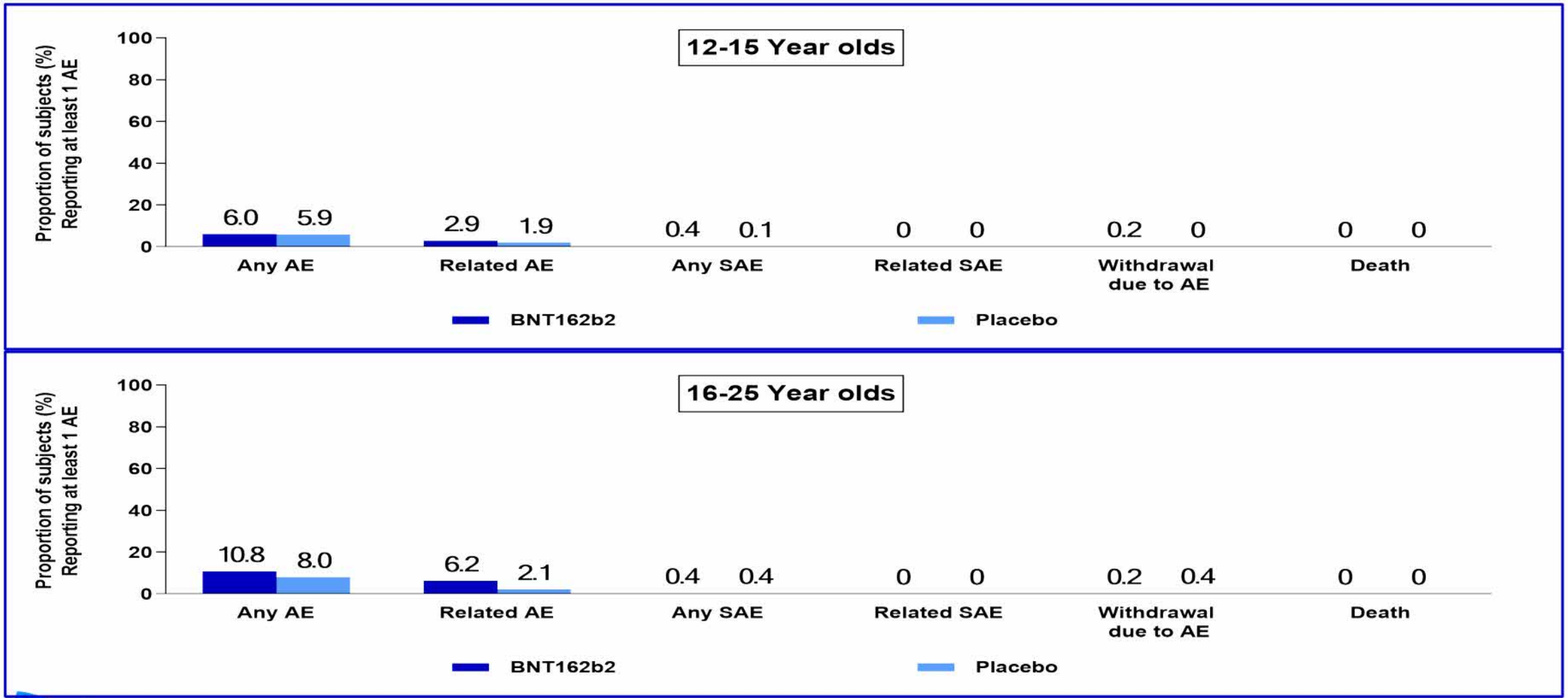
Adverse events in Phase 3 – 12-15 year olds and 16-25 year olds

COVID-19 Vaccine Clinical Study

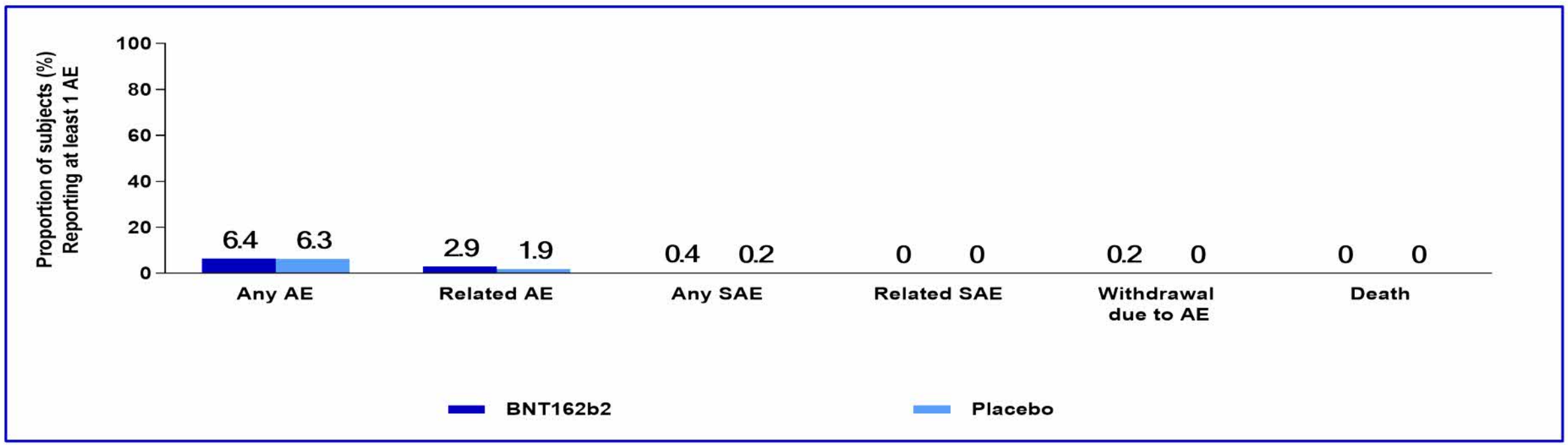
C4591001



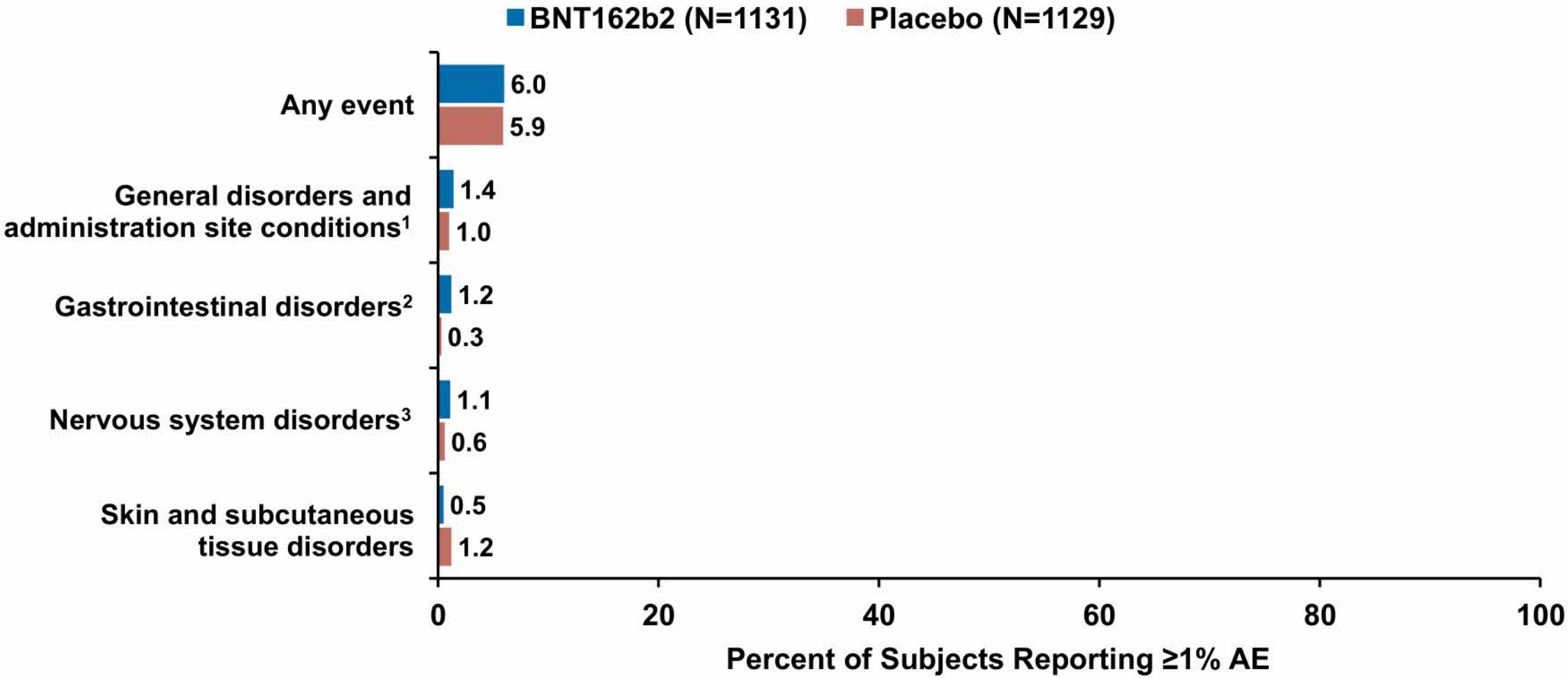
Overall Adverse Events from Dose 1 to 1 Month Post Dose 2
12-15 (N=2260) and 16-25 (Reactogenicity subset N=1097) year olds



Overall Adverse Events from Dose 1 to Data Cut-off Date (13Mar2021) 12-15 year olds (N=2260)

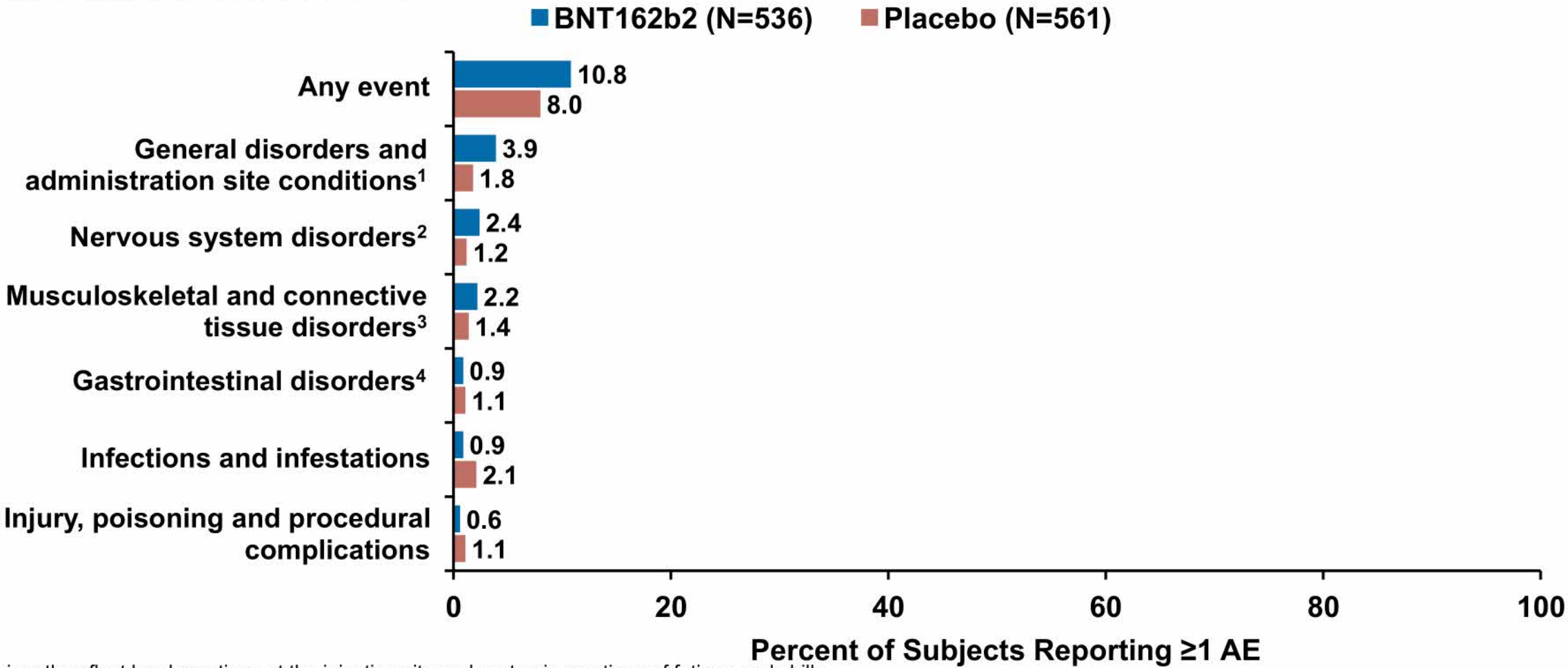


Adverse Events ≥1.0% by System Organ Class for 12-15 year olds 1 Month Post Dose 2



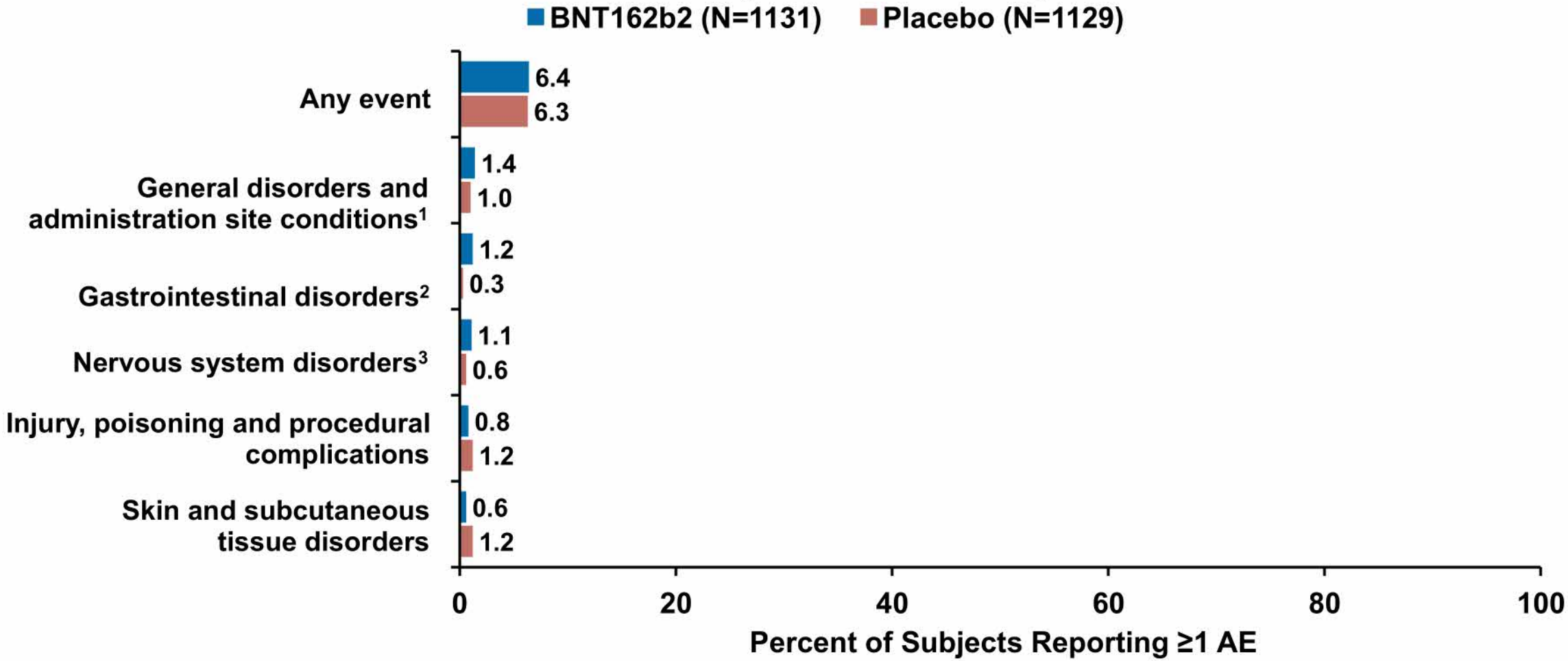
1. Predominantly reflect local reactions at the injection site and systemic reactions of fever and fatigue
2. Predominantly reflect nausea and diarrhea3. Predominantly reflects Headache

Adverse Events ≥1.0% by System Organ Class for 16-25 year olds 1 Month Post Dose 2



1. Predominantly reflect local reactions at the injection site and systemic reactions of fatigue and chills
2. Predominantly reflects Headache 3.. Predominantly reflect myalgias and arthralgia's as part of systemic events4. Predominantly reflects Nausea and Vomiting

Adverse Events ≥1.0% by System Organ Class for 12-15 year olds from Dose 1 to Data Cut-off Date (13 Mar 2021)



1. Predominantly reflect local reactions at the injection site and systemic reactions of fever and fatigue
2. Predominantly reflect nausea and diarrhea3. Predominantly reflects Headache

Lymphadenopathy in 12-15 Year Olds

- 9 cases (0.8%) in BNT162b2 and 2 cases placebo (0.2%)7 (0.6%) were related to vaccination; 1 (0.1%) in the placebo group Primarily Left axillary or Left cervical Onset within 2-10 days after vaccinationDuration 1-10 days where reported (others were ongoing at the time of the data cutoff date).In adults (16-55 years of age), 52 participants (0.4%) in the BNT162b2 group and 2 participants (0.0%) in the placebo group had lymphadenopathy events reported up to the unblinding date and assessed by the investigator as related to study intervention.The majority of these events occurred in the arm and neck region, were reported within 2-4 days after vaccination (usually after Dose 2), and typically resolved within approximately 1 week.

Serious Adverse Events by SOC/PT from Dose 1 to Data Cut-off Date 12-15 year olds

System Organ Class/PT	BNT162b2 (30 µg)(N=1131)		Placebo(N=1129)	
	n	%	n	%
ANY EVENT	5	0.4	2	0.1
GASTROINTESTINAL DISORDERS*ABDOMINAL PAIN*CONSTIPATION	111	0.10.10.1	000	000
INFECTIONS AND INFESTATIONS#APPENDICITIS#FOCAL PERITONITIS	000	000	221	0.20.20.1
NERVOUS SYSTEM DISORDERS*NEURALGIA	11	0.10.1	00	00
PSYCHIATRIC DISORDERSDEPRESSIONANXIETYSUICIDAL IDEATION	4311	0.40.30.10.1	0000	0000

*Abdominal pain, constipation and neuralgia were in the same participant#Appendicitis and focal peritonitis were in the same participant

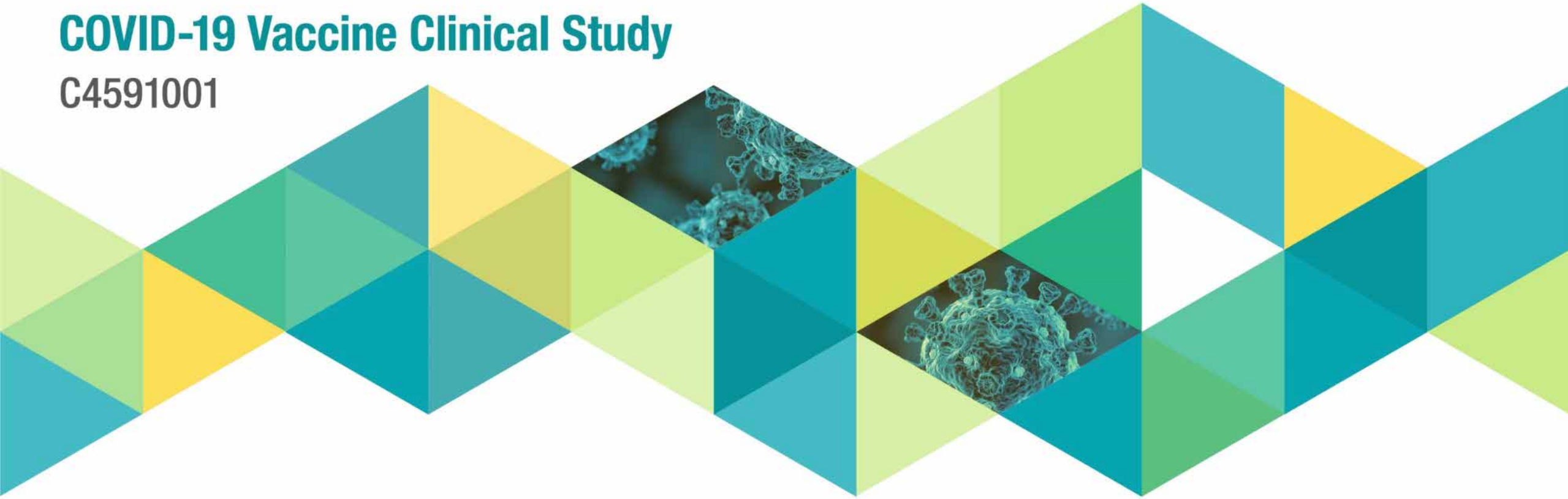
Deaths: 12–15-year-olds

- No deaths

Efficacy and Immunogenicity

COVID-19 Vaccine Clinical Study

C4591001

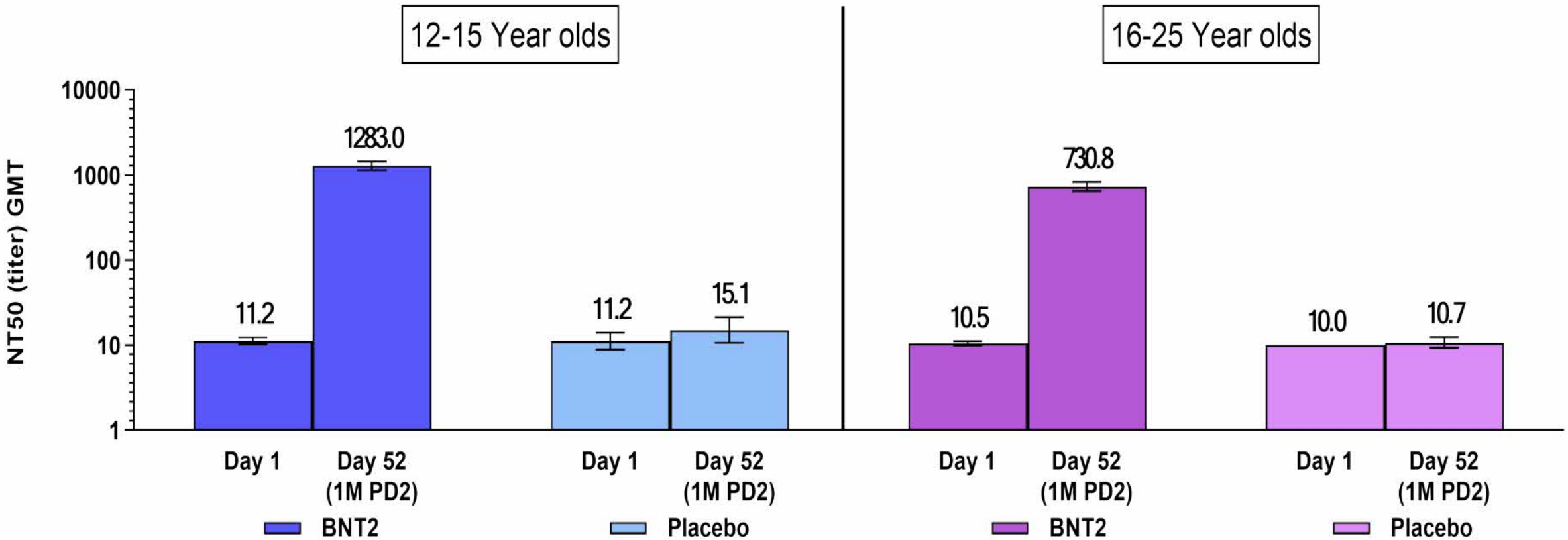


Follow-up Time After Dose 2: 12-15 year olds – Safety Population

Total exposure from Dose 2 to cut-off date	BNT162b2 (30 µg) (N=1131) n[b](%)	Placebo (N=1129) n (%)	Total (N=2260) n (%)
< 1 Month	13 (1.1)	25 (2.2)	38 (1.7)
≥1 Month to < 2 months	458 (40.5)	456 (40.4)	914 (40.4)
≥2 Months to <3 months	612 (54.1)	599 (53.1)	1211 (53.6)
≥3 Months	48 (4.2)	49 (4.3)	97 (4.3)

Note: 98.3% of subjects had at least 1 month of follow-up time

Geometric Mean Titers: SARS-CoV-2 Neutralization Assay – NT50* – Subjects 12-15 and 16-25 Years of Age (Immunogenicity Subset) – Dose 2 Evaluable Immunogenicity Population (All subjects)



*NT50 = 50% neutralizing titers

Noninferiority Between 12-15 and 16-25 years Of Age Was Met Geometric Mean Ratio (GMR) in Neutralization Titers

(Without prior infection)

		BNT162b2 (30 µg)					
		12-15 year		16-25 years		12-15/16-25 years	
Assay	Dosing/Sampling Time Point	n	GMT (95% CI)	n	GMT (95% CI)	GMR(95% CI)	Met NI (Y/N)
SARS-CoV-2 neutralization assay - NT50 (titer)	2 / 1 Month	190	1239.5(1095.5, 1402.5)	170	705.1(621.4, 800.2)	1.76(1.47, 2.10)	Y

- Noninferiority is declared if the lower bound of the 95% confidence interval is > 0.67LBCI for GMR >1 indicating a statistically greater response in 12-15 that 16-25 year olds

First COVID-19 Occurrence From 7 Days After Dose 2

Subjects 12-15 Years of Age – Evaluable Efficacy Population

Subjects WITHOUT Evidence of Infection Prior to 7 days after Dose 2

	BNT162b2 (30 µg) N=1005		Placebo N=978			
Efficacy Endpoint	**n**	**Surveillance Time (n)**	**n**	**Surveillance Time (n)**	**VE (%)**	**(95% CI)**
First COVID-19 occurrence ≥7 days after Dose 2	**0**	**0.154 (1001)**	**16**	**0.147 (972)**	**100.0**	**(75.3, 100.0)**

- There were no severe COVID-19 cases

Total surveillance time: 1000 person-years for all subjects within each group at risk for the endpoint.The analysis is descriptive; no hypothesis test

First COVID-19 Occurrence From 7 Days After Dose 2

Subjects 12-15 Years of Age – Evaluable Efficacy Population

Subjects WITH or WITHOUT Evidence of Infection Prior to 7 days after Dose 2

	BNT162b2 (30 µg) N=1119		Placebo N=1110			
Efficacy Endpoint	**n**	**Surveillance Time (n)**	**n**	**Surveillance Time (n)**	**VE (%)**	**(95% CI)**
First COVID-19 occurrence ≥7 days after Dose 2	**0**	**0.170 (1109)**	**18**	**0.163 (1094)**	**100.0**	**(78.1, 100.0)**

- There were no severe COVID-19 cases

Total surveillance time: 1000 person-years for all subjects within each group at risk for the endpoint.The analysis is descriptive; no hypothesis test

Overall safety conclusions for 12-15 year olds in the Phase 2/3 analysis

- **Reactogenicity: BNT162b2 was well tolerated in subjects 12-15 years old and showed a similar pattern to that seen in 16-25 year olds Pain at the injection site, fatigue, headaches, chills, joint pain and muscle pain were the most predominant as well as feverIncreased systemic events after dose 2 was similar to that seen with 16-25 year oldsAdverse events overall were relatively fewHighest incidence was in the General Disorders and Administration Site Conditions, reflecting local and systemic reactogenicity events Lymphadenopathy was identified as related to vaccinationThere were no related SAEsNo deaths were reported**

Immunogenicity & Efficacy Conclusions for 12-15 year olds in the Phase 2/3 analysis

- Immune response to Pfizer-BioNTech COVID-19 Vaccine in SARS-CoV-2 50% neutralizing titers in adolescents 12-15 years of age was noninferior to (and in fact exceeded) the immune response in young adults 16-25 years of age, which provides immunobridging for adolescents in pivotal Study C4591001. In the adolescent group, efficacy analyses based on cases reported from at least 7 days after Dose 2 through the data cutoff date, the observed VE was 100% (95% CI: 75.3%, 100%) for individuals without evidence of prior SARS-CoV-2 infection before and during vaccination regimen, and 100% (2-sided 95% CI: 78.1%, 100%) for those with or without evidence of prior SARS-CoV-2 infection before and during vaccination regimen. No severe cases were reported in the 12-15 years of age group as of the date cutoff date.Overall, these immunogenicity and efficacy data strongly support BNT162b2 use in adolescents 12-15 years of age.

From: (b)(4) (b)(4) (x)
Sent: Tue, 8 Jun 2021 21:37:00 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Revised Version - Amendment to Confidentiality Agreement - CDC & Moderna
Attachments: CDC - CDA Contract ID 16732 - Amendment 2_effective 08June2021.docx

Hi Sara,
Attached is a revised agreement between CDC and Moderna for the purpose of Moderna sharing confidential clinical data in the future in support of our EUAs in adolescents and children, BLA in persons 18 years of age and older, and any corresponding VRBPAC documents. Note that we have identified this as Amendment 2 and attached Exhibit A with the list of persons allowed to see the data.
Please let us know if this is acceptable. If so, please obtain the appropriate signature at your end, return to me, and I will obtain signature at our end & return a fully executed copy to you. Please destroy the earlier version you sent us.
Thanks.
(b)(4)

Amendment #02 to Confidentiality Agreement

THIS AMENDMENT #02 TO CONFIDENTIALITY AGREEMENT (this "Amendment #02"), is entered into as of June 8, 2021 (the "Amendment #02 Effective Date"), by and between ModernaTX, Inc. ("Moderna"), and The Centers for Disease Control and Prevention (CDC) ("Recipient" or "CDC"). Each of Moderna and CDC may be referred to herein as a "Party" or together as the "Parties".

WHEREAS, Moderna and CDC are parties to a Confidentiality Agreement dated November 10, 2020 (the "Agreement") and Amendment #1 to the Agreement dated December 4, 2020 ("Amendment #1); and

WHEREAS, Moderna and CDC desire to continue the Agreement in accordance with and subject to the terms and conditions therein, as more fully described herein.

NOW THEREFORE, for good and valuable consideration, the receipt and sufficiency of which is hereby mutually acknowledged, CDC and Moderna hereby agree as follows. Capitalized terms used but not defined herein shall have the meanings ascribed to such terms in the Agreement.

1. Section 1 "Purpose". CDC and Moderna each acknowledge and agree that Section 1 of the Agreement shall be deleted in its entirety and replaced with the following:

> **1. Purpose.** This Agreement is made in order for ModernaTX and its Affiliates (collectively, "Moderna") to disclose in confidence to Recipient, during the term of this Agreement, information including: the Clinical Summary (section 2.5) of Moderna's FDA application and its background document for the December 2020 VRBPAC meeting in connection with Moderna's mRNA-1273 Emergency Use Authorization (EUA) submission; the Clinical Summaries in support of Moderna's upcoming EUAs for children and adolescents; and the Biologics License Application (BLA) for persons 18 years and older, as well as any other corresponding background documents submitted for the VRBPAC meeting. CDC will use this information solely for the purpose of developing ACIP recommendations for vaccine use(the "Purpose"). CDC may share these documents in confidence with those employees listed in Exhibit A only. As used herein, the term "Affiliate" means with respect to a given entity any person or legal entity directly or indirectly controlling, controlled by or under common control with such entity, wherecontrol shall mean the direct or indirect ownership of more than fifty percent (50%) of the outstanding voting securities of an entity or such other relationship as results in the actual control over the management,assets, business and affairs of an entity.

2. Exhibit A. CDC and Moderna each acknowledge and agree that Exhibit A of the Agreement shall be deleted in its entirety and replaced with the Exhibit A attached to this Amendment #02.

3. General Terms. Except with respect to the amendments as set forth above, the terms and conditions of the Agreement shall remain unchanged. This Amendment #02 shall be construed in accordance with and governed by the same laws that govern the Agreement.

[***Remainder of page intentionally left blank***]

IN WITNESS WHEREOF, CDC and Moderna each has caused this Amendment #02 to be executed by its duly authorized representative.

MODERNATX, INC.	**THE CENTERS FOR DISEASE CONTROL AND PREVENTION**
_____	_____
By	*By*
_____	_____
Name	*Name*
_____	_____
Title	*Title*
_____	_____
Date	*Date*

Exhibit A

Recipient (CDC) Representatives

Julia Gargano
Danielle Moulia
Hannah Rosenblum
Nicole Reisman
Heather Scobie
Karen Broder
Naomi Tepper
Jessica MacNeil
Sara Oliver

From: (b)(4) (b)(4) (x)
Sent: Sat, 29 May 2021 01:26:15 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: Re: Moderna Confidentiality Agreement with CDC

Hi Sara,
Just a reminder that it would be good to get this document revised next week please. We expect to submit the EUA for adolescents during the week of June 9.
Thanks and have a lovely long weekend!
(b)(4)

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Thursday, May 20, 2021 4:55 PM
To: Sara Oliver <seoliver@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: Moderna Confidentiality Agreement with CDC

Hi Sara,
It was good to talk with you and Jessica today. Can you please take a look at the attached & see what changes you might want to make to this CDA so that we can be more efficient in sharing data for future EUAs related to our COVID-19 vaccine. I will then take to our legal team for their input/review. If you need to add more individuals to the section at the very end, please note that as well.
Thanks.
(b)(4)

From: (b)(4) (b)(4) (x)
Sent: Fri, 2 Apr 2021 13:03:01 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: Dooling, Kathleen L. (CDC/DDID/NCIRD/DVD)
Subject: Re: Vaccination Card

Hi Sara,
I just want to double check on use of the vaccination card. I assume from your note below that study sites can use the standard vaccination card rather than a Moderna card. I am asking again because we received this same question from NIH yesterday in regards to their studies. Many thanks.
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Friday, February 19, 2021 11:10 AM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: Dooling, Kathleen L. (CDC/DDID/NCIRD/DVD) <vic9@cdc.gov>
Subject: Updates

EXTERNAL

(b)(4)

As a follow up for our call earlier this week- attached is the CDC card. Site investigators can use the card if desired. However, our team has asked that it NOT be posted publicly on a website or shared broadly. I'm still working on your question around linking IIS/state registries to those vaccinated in the trials, but will let you know if I hear any answers.

In addition, we're sharing the MMWR that will be published today: the first month of COVID-19 vaccine safety monitoring from our colleagues in vaccine safety.

And finally- we anticipate these dates will be publicly available later today, but we are planning on an ACIP meeting Sunday, Feb 28th and Monday, March 1st. The Sunday ACIP meeting will not discuss the Moderna product so don't anticipate needing anyone online for that day, but the Monday meeting will have broader updates/discussions (vaccine safety, etc). If you would like to have a representative on the line for Monday, let us know and we are happy to coordinate the invitation for that day.

Thanks-

Sara and Kathleen

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service

Co-Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

Please consider the environment before printing this email

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Fri, 28 May 2021 13:17:06 +0000
To: (b)(4) (b)(4) (x)
Subject: RE: ACIP - In Person?

(b)(4)

I agree we're all tired of it! But those discussions happen on a much larger level. At this point we're not even sure when those of us who work at CDC will be back in the office. So the short answer is "I don't know". I think the first step would be bringing in the voting ACIP members into the room, even if the meeting itself is still virtual (that's been Amanda's first goal). So if/when that happens, take it as a good sign, but we aren't even sure when we will be able to do that.

Stay tuned-
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Thursday, May 27, 2021 10:04 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: ACIP - In Person?

Hi Sara,

I forgot to ask you if there is any movement in place to "reopen CDC". I see that the June ACIP meeting is still virtual, but curious if any of you are back in the office routinely and whether there is any discussion of a "live" ACIP meeting for October. I think we are all tired of zoom, webex, Teams, etc.

Thanks for any update you can provide.

(b)(4)

Please consider the environment before printing this email

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Wed, 5 May 2021 17:31:34 +0000
To: (b)(4) (b)(4) T
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: ACIP meeting

Thanks (b)(4) I've updated the agenda. We're working on getting something we could post on the website fairly soon. It's a packed day, but the Pfizer session will be from 11:30-1:30. We break for 'lunch' and public comment, then come back ~2:45 for discussion and vote.

Let me know if there are any questions or issues.

Thanks!
Sara

From: (b)(4) (b)(4) (b) (b)(4)
Sent: Wednesday, May 5, 2021 11:52 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: ACIP meeting

Hello Sara,
Thank you for the heads up on the May 12 ACIP meeting.
Our presenter will be (b)(4) from our (b)(4) and the title is "(b)(4) (b)(4)"

(b)(4)

All the best,
(b)(4) (b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Wednesday, May 5, 2021 10:52 AM
To: (b)(4) (b)(4) (b) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: [EXTERNAL] RE: ACIP meeting

(b)(4) (b)(4) and (b)(4

I wanted to give you guys a quick update. We are working in collaboration with FDA around timing for the ACIP meeting. The ACIP meeting to address the Pfizer adolescent vaccine recs will

now be **Wednesday, May 12**. Time should be the same (~11am-5pm EST). We will work on having a draft agenda posted relatively soon. Happy to update with specific title and presenter from Pfizer as available.

Thanks and let us know if there are any questions!

Sara

From: (b)(4) (b)(4) (b)(4)
Sent: Monday, May 3, 2021 5:36 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: ACIP meeting

Dear Sara,
(b)(4) and the heads up about the potential ACIP meeting next week.
We will get back to you about who our presenter will be for the ACIP meeting and (b)(4) (b)(4) We will do our best to get you the answers to your questions by Thursday.
Best,
(b)(4) (b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, May 3, 2021 2:42 PM
To: (b)(4) (b)(4) (b) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: [EXTERNAL] ACIP meeting

(b)(4) (b)(and (b)(4)

Thank you for your presentation to the WG last week. We have a few follow-up questions, both from the WG call and our data review. The questions are attached here. If you could provide answers by Thurs 5/6, that would be much appreciated.

Next- we haven't publicly announced the ACIP meeting for this, but are working on getting it posted to the website within the next 24 hours. While things can always change, our plan is to have the ACIP meeting **Monday, May 10th**. We are sharing for your internal planning, but please do not share broadly until it is posted on the website. The meeting will likely start at **11am EST**, and while we will need to give a variety of updates in addition to discussing the adolescent data, we plan on discussing the adolescent data first. We would invite Pfizer to present the adolescent data (~20 minute presentation, with time for questions after the

presentation). As we plan the agenda, please let us know who the speaker will be, and if you have a preferred title for the talk.

And finally- our colleagues at BARDA and the group formally known as Operation Warp Speed have asked if they could review the slides from the WG call this past week. I've said our confidentiality agreement with you means that we need to check with you before sharing. Let us know if you would be Ok with us sharing the slides with them, or if you prefer for them to go through you for the data. We are fine either way, but want to preserve the trust and relationship we have with our data agreements.

Thanks!

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Tue, 4 May 2021 12:48:07 +0000
To: (b)(4) (b)(4) (b)(4) (b)(4) (b)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); (b)(4) (b)(4)
Subject: RE: ACIP meeting

Thanks (b)(4)! Appreciate it. We'll use this language (although maybe not the 'filet-o-fish' box… but I do like it ☺).

Thanks-
Sara

From: (b)(4) (b)(4)
Sent: Monday, May 3, 2021 8:27 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>; (b)(4) (b)(4) (b) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4)
Subject: RE: ACIP meeting

Dear Sara,

Here's what we can share:

(b)(4)

As for the analogy for the food container for the 25-pack, here's the closest I can come

but it's just not the same….

Let us know if you need anything else.

Looking forward to Monday!

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, May 3, 2021 6:59 PM
To: (b)(4) (b)(4) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: [EXTERNAL] RE: ACIP meeting

(b)(4) and all:

Great- thanks! I have one more question… as we plan our EtR framework and other aspects for next week, we were curious if the (b)(4) (b)(4) (b)(4) It would be helpful as we think through feasibility for broader implementation with ACIP… but again want to respect confidentiality of information shared with us.

Thanks again!
Sara

From: (b)(4) (b)(4) (b)(4)
Sent: Monday, May 3, 2021 5:36 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: ACIP meeting

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(b)(4) (b)(4)y and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, May 3, 2021 2:42 PM
To: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)

(b)(4) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: [EXTERNAL] ACIP meeting

(b)(4) (b)(and (b)(4)

Thank you for your presentation to the WG last week. We have a few follow-up questions, both from the WG call and our data review. The questions are attached here. If you could provide answers by Thurs 5/6, that would be much appreciated.

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And finally- our colleagues at BARDA and the group formally known as Operation Warp Speed have asked if they could review the slides from the WG call this past week. I've said our confidentiality agreement with you means that we need to check with you before sharing. Let us know if you would be Ok with us sharing the slides with them, or if you prefer for them to go through you for the data. We are fine either way, but want to preserve the trust and relationship we have with our data agreements.

Thanks!

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Fri, 16 Jul 2021 15:22:39 +0000
To: (b)(4) (b)(4) (x)
Subject: RE: ACIP Next Week

(b)(4)

We are still working through the details so I don't want to get ahead of planning too far. It will be building off of what we presented at the last meeting. We will likely use broader language from the Yellow Book to define 'immunocompromised' populations (ie we aren't only talking about solid organ transplant or a singular type of IC).

And- we won't be making any specific ACIP recommendations (no vote). It won't even be guidance because we won't make explicit suggestions for off-EUA use. However, we are all getting FAQs around this and will be highlighting those and the data that are accumulating to inform those discussions.

Hope that helps. As we move closer I may be able to share the slides ahead of the meeting.

Thanks!
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Friday, July 16, 2021 11:07 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: ACIP Next Week

Hi Sara,

I see there is a discussion of considerations for additional doses for immunocompromised persons on the agenda for ACIP. Is there any more background you can provide here? Any particular populations of particular concern? And would this be an off label use?

Thanks.

(b)(4)

From: (b)(4) (b)(4) (x)
Sent: Mon, 26 Jul 2021 03:35:45 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Re: Additional Data - HEROES, VISION, and IVY Studies

Hi Sara,
Kathleen sent the attached response to me when you were on vacation. Is there anything more that you can provide please? We are trying to determine what additional studies we might conduct to assess VE and this information would be helpful.
Thanks.
(b)(4)

From: Dooling, Kathleen L. (CDC/DDID/NCIRD/DVD) <vic9@cdc.gov>
Sent: Wednesday, July 7, 2021 10:02 AM
To: (b)(4) (b)(4) (x) (b)(4) Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>; MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: RE: Additional Data - HEROES, VISION, and IVY Studies

EXTERNAL

Hi (b)(4)

Great questions. I don't know the timing or to what extent breakthrough cases are being sequenced--will have to look into that. The characteristics of the cohorts should be publicly available somewhere… here is the link to the Jan ACIP meeting that laid out the broad vision for VE assessment but it does not describe the cohorts in detail (https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-01/09-COVID-Fleming-Dutra.pdf)

Kathleen

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Tuesday, July 6, 2021 6:04 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>; Dooling, Kathleen L. (CDC/DDID/NCIRD/DVD) <vic9@cdc.gov>; MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: Additional Data - HEROES, VISION, and IVY Studies

Hi everyone,

I am including Kathleen and Jessica on this message as I know that Sara is out this week & she said to direct any questions to you.

At the last ACIP meeting, a slide was shown describing the possibility of obtaining additional data on COVID-19 vaccine effectiveness from the HEROES, VISION, and IVY studies. Might you be able to provide a bit more information on the timing of the results of these studies, age & size of the study population, and whether breakthrough cases will be evaluated for variants?

Any updates you can provide would be much appreciated.

Many thanks.

(b)(4)

Please consider the environment before printing this email

From: (b)(4) (b)(4) (b
Sent: Wed, 28 Apr 2021 20:35:34 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); (b)(4) (b)(4) (b)(4) (b)(4)
M.
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: RE: additional details for SAEs

Dear Sara,

(b)(4)

Best regards,
(b)(4) (b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Wednesday, April 28, 2021 3:53 PM
To: (b)(4) (b)(4) (b) (b)(4) (b)(4) (b)(4) (b)(4)
(b)(4) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: [EXTERNAL] additional details for SAEs

(b)(4) (b)(and (b)(4):

As we review the (b)(4) I had a question I was hoping we may be able to get further information regarding. (I'm sure there will be more after (b)(4), but this is the main question for now.

Do you have case narratives or additional information around the SAEs described in Table 11?

(b)(4)

If there's any information that could be shared before tomorrow, it would be much appreciated. The current GRADE for SAEs highlights this imbalance and we would love to have additional information to put this into context.

Thanks!
Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force

Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: (b)(4) (b)(4) (x)
Sent: Tue, 18 May 2021 19:04:13 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: Re: Additional question

Hi Sara,
I can certainly provide you with a better idea of what data will likely come when. Let me see what I can put together.
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, May 18, 2021 11:57 AM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: Additional question

EXTERNAL

(b)(4)

Sorry for the other additional questions- but now that we've survived the last 1-2 months, we are taking this brief break to plan ahead. This includes many things, but obviously an area of high interest- booster doses.

As we plan for if/when ACIP may recommend booster doses, and possibly in what populations- we are trying to collect what information will be available to inform these discussions. Do you mind sharing a summary of the information that may be available from Moderna? I drafted a table if it is helpful, but feel free to provide additional information or in whatever format would be best. We also have the previous pre-print you shared, but just want to have a larger understanding of what may be available when. We can also discuss this at our upcoming call.

As we plan, it may also be helpful to discuss when and how ACIP will be able to review the data submitted to FDA for a BLA as well, as this will inform both a vote on use of the vaccines under BLA, as well as informing possible booster recommendations as well.

Thanks!
Sara

Vaccine	Interval from primary series	Population (ages, etc)	Endpoint studied (immunogenicity; efficacy)	Time of expected results
mRNA-1273, 100µg	N/A	≥18 years of age N=~30,000	Efficacy (6 months and beyond?) Immunogenicity (IgG, NAb?)	June/July?

	Phase 3 trial, BLA application			
mRNA-1273 50µg	6-8 months	≥18 years of age N=		
mRNA-1273.351 variant-specific booster 20 or 50µg	6-8 months	≥18 years of age N=		
mRNA-1273.211 Multi-valent booster 50µg	6-8 months	≥18 years of age N=		

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: (b)(4) (b)(4)
Sent: Fri, 30 Jul 2021 15:44:10 +0000
To: Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP)
Cc: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: RE: Adolescent MMWR

Thanks Tom!!!
Very much appreciated

Best regards,

(b)(

From: Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP) <ayv6@cdc.gov>
Sent: Friday, July 30, 2021 11:01 AM
To: (b)(4) (b)(4) (b)(4)
Cc: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: [EXTERNAL] Adolescent MMWR
Importance: High

Hi (b)(– This is coming out today. I'm sorry I didn't get it to you sooner.
Tom

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Thu, 10 Jun 2021 20:53:43 +0000
To: (b)(4) (b)(4) (x)
Subject: RE: Background Documents - COVID-19 Vaccine Studies in Adolescents - CONFIDENTIAL

Thanks (b)(4) I'll be in touch tomorrow morning around the ACIP WG call Thursday. Really appreciate it!

Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Thursday, June 10, 2021 4:50 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Background Documents - COVID-19 Vaccine Studies in Adolescents - CONFIDENTIAL

Hi Sara,

Here are some of the documents that we have agreed to share with CDC in confidence regarding our studies in adolescents:

1) The EUA we submitted to FDA
2) The protocol & amendments for the adolescent study

I hope this helps. Please handle as confidential & limit distribution to those identified in our joint confidentiality agreement.

(b)(4)

Please consider the environment before printing this email

From: (b)(4) (b)(4)
Sent: Fri, 30 Jul 2021 22:44:18 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); (b)(4) (b)(4) (b)
Cc: Dooling, Kathleen L. (CDC/DDID/NCIRD/DVD)
Subject: RE: BLA data

Thanks Sara,
I just accepted your invite. If you allow us, we are going to forward it to our regulatory and RU colleagues in order to have a richer conversation.
In the meantime, let us check internally about your request to have the information in advance.

Keep in touch

(b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Friday, July 30, 2021 6:40 PM
To: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) ((b)(4)
Cc: Dooling, Kathleen L. (CDC/DDID/NCIRD/DVD) <vic9@cdc.gov>
Subject: [EXTERNAL] RE: BLA data

(b)(4

It looks like Wednesday at 4pm EST would work for us. I can send a call invitation.

However, while we move forward and plan the next several weeks, we know we need to be working toward review of the BLA data. Would it be possible for us to go ahead and receive the clinical portions of the BLA now so we can begin our review, before the call on Wednesday? I know our team would appreciate even the few extra days. As always, we would keep our review of the data limited to our immediate ACIP data team.

Thanks-
Sara

From: (b)(4) (b)(4) (b)(4)
Sent: Friday, July 30, 2021 5:52 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>; (b)(4) (b)(4) (b)
(b)(4)
Cc: Dooling, Kathleen L. (CDC/DDID/NCIRD/DVD) <vic9@cdc.gov>
Subject: RE: BLA data

Hi Sara,
Sorry for our delayed contact…. It has been a crazy day (another one ☺)

Welcome back Kathleen!!

Monday is a bad day for us, However, I was trying to reach Amanda, to keep her (b)(4)

(b)(4)

Does it work for you?

Thanks again

Have a nice weekend

(b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Friday, July 30, 2021 2:03 PM
To: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Cc: Dooling, Kathleen L. (CDC/DDID/NCIRD/DVD) <vic9@cdc.gov>
Subject: [EXTERNAL] BLA data

(b)(4) and (b)(4

I wanted to see if we could set up a time early next week to chat about the BLA data and plans for that work. We are available to chat from 12-2pm EST, or from 3-4pm on Monday. Would either of those times work? If not, I can look for additional times later in the week but wanted to try for early in the week first.

Thanks!

Sara and Kathleen
(I'm also VERY happy to welcome Kathleen back as well!).

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: (b)(4) (b)(4) (x)
Sent: Thu, 17 Jun 2021 18:01:16 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: Re: Booster presentation Friday

Hi Sara,
We would prefer something like this for your slide on Moderna's booster/variant studies:
Preliminary results for mRNA-1273 (50µg) & mRNA.1273.351 published May 2021
Wu et al. *medRxiv*, doi.org/10.1101/2021.05.05.21256716

Additional data on mRNA-1273 & other variants as boosters expected July-Sept 2021

I hope this helps.
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Wednesday, June 16, 2021 8:08 PM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: Booster presentation Friday

EXTERNAL

(b)(4)

For the booster/additional dose presentation- we are keeping it all very high-level but I was hoping to include 1 bullet point per manufacturer around booster studies that could be shared.

This is what I drafted for a slide entitled "Upcoming studies: Immunogenicity data". Would this be OK to share? Again, not wanting to get terribly detailed, but the overall goal is to lay out timing of when we may have results for ACIP to consider.

- **Moderna: mRNA-1273 (50µg), variant and bi-valent studies: Results ~July/August**

Thanks!
Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

Please consider the environment before printing this email

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Fri, 4 Jun 2021 21:34:35 +0000
To: (b)(4) (b)(4) (x)
Subject: RE: Booster/Variant Data - COVID-19 Vaccines - CONFIDENTIAL
Attachments: CDC CDA Contract ID 16732 - Amendment 12.4.20.pdf, Exhibit A_Updated.pdf

(b)(4)

Attached is the signed Amendment and the updated Exhibit A with our new names for this data review. Let me know if this is sufficient or if anything else is needed.

The WG call will meet from 3:30-5pm EST. We would ask that Moderna join at 3:30 to present the data for ~20-25 minutes, stay for 10 minutes or so of questions and then hop off the call as the WG discusses further. Also- we should have you blank GRADE tables by early next week.

Thanks!
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Friday, June 4, 2021 9:50 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Re: Booster/Variant Data - COVID-19 Vaccines - CONFIDENTIAL

HI Sara,

Thanks for the updates. Can you please remind me what time the WG would meet on June 17? I need to check calendars.

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Friday, June 4, 2021 9:17 AM
To: (b)(4) (b)(4) (x) (b)(4)
Subject: RE: Booster/Variant Data - COVID-19 Vaccines - CONFIDENTIAL

EXTERNAL

OK sounds good. We'll work on getting that back to you ASAP. And I think that's a good plan moving forward- keep the overall agreement in place, but update "exhibit A" with the names each time. Hopefully we will get to the point where we know long-term who will be helping us with this (working on hiring an actual team for COVID vaccine policy!) but right now we're still depending on deployers to the response.

And yes, we can absolutely discuss timing for presentations to the WG. A formal invitation will come once the data are submitted, but happy to share our thoughts for your planning purposes. Our June calls are a bit limited (canceling June 10th for VRBPAC and June 24th for the 'regular' ACIP meeting)… so we were hoping Moderna could present Thurs, 6/17 to the WG. We can also work to get you GRADE tables as well.

Thanks!

Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Thursday, June 3, 2021 10:08 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Re: Booster/Variant Data - COVID-19 Vaccines - CONFIDENTIAL

Hi Sara,

Our preference would be for you to specify the names on this agreement & we can amend as needed.

Can you please send along your suggested changes so we can get this executed soon? We are still planning to submit the EUA for adolescents on June 9 so would like to get you a copy of the clinical section of the filing right after that.

We should also discuss possible dates for a presentation to the WG and what information you will need for GRADE.

Thanks.

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Wednesday, June 2, 2021 9:32 AM
To: (b)(4) (b)(4) (x) (b)(4)
Subject: RE: Booster/Variant Data - COVID-19 Vaccines - CONFIDENTIAL

EXTERNAL

Great- thanks (b)(4)

Also- I'm working on getting you an answer to your school inquiry. That's not something I'm directly tracking but trying to see if we can get you a report or a contact to directly reach out to.

And regarding the confidentiality agreement- we're working on getting a team hired that will be consistent with each of these data reviews, but we're not there yet. So the individuals in "Exhibit A" will need to be updated for future reviews. I know we wanted to make something that would be flexible for future reviews- but if you will need a list of names each time, we may just need to re-do this single page with a new list each time. The other option would be to make it more generic and state something like "only people critical for review of the data". Do you have a preference?

Thanks!
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Tuesday, June 1, 2021 7:33 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Booster/Variant Data - COVID-19 Vaccines - CONFIDENTIAL

Hi Sara,

I hope you had an enjoyable weekend.

As promised, I am sending you some of the slides we discussed recently regarding our studies of booster doses/variants and a rough estimate of the timing for availability of data.

I would appreciate if you would handle this information as Confidential.

Please let me know if you have any questions.

(b)(4)

Amendment #01 to Confidentiality Agreement

THIS AMENDMENT #01 TO CONFIDENTIALITY AGREEMENT (this "Amendment #01"), is entered into as of December 4, 2020 (the "Amendment #01 Effective Date"), by and between ModernaTX, Inc. ("Moderna"), and The Centers for Disease Control and Prevention (CDC) ("Recipient" or "CDC"). Each of Moderna and CDC may be referred to herein as a "Party" or together as the "Parties".

WHEREAS, Moderna and CDC are parties to a Confidentiality Agreement dated November 10, 2020 (the "Agreement"); and

WHEREAS, Moderna and CDC desire to continue the Agreement in accordance with and subject to the terms and conditions therein, as more fully described herein.

NOW THEREFORE, for good and valuable consideration, the receipt and sufficiency of which is hereby mutually acknowledged, CDC and Moderna hereby agree as follows. Capitalized terms used but not defined herein shall have the meanings ascribed to such terms in the Agreement.

1. Exhibit A. CDC and Moderna each acknowledge and agree that Exhibit A of the Agreement shall be deleted in its entirety and replaced with the Exhibit A attached to this Amendment #01.

2. General Terms. Except with respect to the amendments as set forth above, the terms and conditions of the Agreement shall remain unchanged. This Amendment #01 shall be construed in accordance with and governed by the same laws that govern the Agreement.

[***Remainder of page intentionally left blank***]

IN WITNESS WHEREOF, CDC and Moderna each has caused this Amendment #01 to be executed by its duly authorized representative.

MODERNATX, INC.

DocuSigned by:
(b)(4)
9368ADE45338401...

By

(b)(4)

Name

(b)(4)

Title

THE CENTERS FOR DISEASE CONTROL AND PREVENTION

Samuel Posner -S Digitally signed by Samuel Posner -S
Date: 2020.12.05 08:39:56 -05'00'

Samuel Posner -S Digitally signed by Samuel Posner -S
Date: 2021.06.04 17:09:06 -04'00'

By

Name

Title

Exhibit A

Recipient (CDC) Representatives

Megan Wallace
Kathryn Curran
Julia Gargano
Sara Oliver
Kathleen Dooling
Karen Broder

Exhibit A, Updated

Recipient (CDC) Representatives

Julia Gargano
Danielle Moulia
Hannah Rosenblum
Nicole Reisman
Heather Scobie
Karen Broder
Naomi Tepper
Jessica MacNeil
Sara Oliver

From: (b)(4) (b)(4) (b)(
Sent: Mon, 26 Apr 2021 19:57:36 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: brief call on Monday

Sara,
(b)(4) I will let the team here know. (b)(4)
Best,
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, April 26, 2021 3:44 PM
To: (b)(4) (b)(4) (b) (b)(4)
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: [EXTERNAL] RE: brief call on Monday

(b)(4)

Sorry- Yes, pulled in a lot of directions, which leads to incomplete emails. ☺ 10:00 sounds great tomorrow.
(b)(4)
(b)(4) Thanks!

Sara

From: (b)(4) (b)(4) ((b)(4)
Sent: Monday, April 26, 2021 3:36 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: brief call on Monday

Hello Sara,
I can only imagine how crazy its been for you. Tomorrow at 10am would work for us, I will send the appointment.
(b)(4)
Cheers,
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, April 26, 2021 3:20 PM
To: (b)(4) (b)(4) (b) (b)(4)

Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: [EXTERNAL] RE: brief call on Monday

(b)(4)

I'm sorry- today has been beyond crazy. Tomorrow will hopefully be better. I can chat any time before 11 or between 12:30-1:30. Otherwise my Wed afternoon is open.

We can discuss further on a call, but now that we are on the other side of the safety pause, (b)(4) (b)(4) Around 20-25 minutes, with time for questions after.

Thanks!

Sara

From: (b)(4) (b)(4) (b) (b)(4)
Sent: Saturday, April 24, 2021 11:46 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: brief call on Monday

Dear Sara,
First of all congrats on an incredible presentation yesterday. We know you are still very busy but (b)((b)(4) (b)(4) We won't need a lot of time, but we do need to let you know sooner rather than later. Would you be able to spare 30 mins on Monday for us?
Thank you as always,
(b)(4) (b)(and (b)(4)

From: (b)(4) (b)(4) (x)
Sent: Wed, 30 Jun 2021 16:35:23 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Re: Brief Discussion?

Thank you!
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Wednesday, June 30, 2021 12:20 PM
To: (b)(4) (b)(4) (x) (b)(4)
Subject: RE: Brief Discussion?

EXTERNAL

(b)(4)

I could meet at 1:30 tomorrow. I can send a meeting invitation-

Thanks-
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Tuesday, June 29, 2021 11:25 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Brief Discussion?

Hi Sara,

Would you have time for a brief discussion on Thursday, please. I could do any time between 12:30 and 3:30 pm.

Thanks.

(b)(4)

Please consider the environment before printing this email

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Thu, 29 Jul 2021 21:42:05 +0000
To: (b)(4) (b)(4) (x)
Subject: RE: Chat?

Thanks (b)(4) Thankfully have great support here.
Happy to chat Friday, but I'll le you know if that isn't going to work.

Thanks-
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Thursday, July 29, 2021 5:33 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Re: Chat?

Hi Sara,

(b)(6)

If you are up to it, I could talk tomorrow at 4 pm. If not, we can talk Monday.

Many thanks.

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Thursday, July 29, 2021 4:18 PM
To: (b)(4) (b)(4) (x) (b)(4)
Subject: RE: Chat?

EXTERNAL

(b)(4)

Apologies for the delay- (b)(6) I will be available tomorrow (Fri) to chat or Monday. I could meet from 10-12EST or 4-5EST Fri, or from 12-4EST Monday Aug 2nd.

Would any of those times work?

Thanks-

Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Wednesday, July 28, 2021 9:59 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Chat?

Hi Sara,

As we discussed yesterday, it would be good for the 2 of us to have a chat about future presentations to the WG/ACIP. Would you be available at 10, 12 or 2 pm on Thursday?

Let me know please.

Many thanks.

(b)(4)

From: (b)(4) (b)(4) (x)
Sent: Wed, 2 Jun 2021 14:15:17 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Re: Confidentiality Agreement - CONFIDENTIAL

Hi Sara,
I will need to consult Legal on the last point, but suspect names will be preferred.
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Wednesday, June 2, 2021 9:32 AM
To: (b)(4) (b)(4) (x) (b)(4)
Subject: RE: Booster/Variant Data - COVID-19 Vaccines - CONFIDENTIAL

EXTERNAL

Great- thanks (b)(4)

Also- I'm working on getting you an answer to your school inquiry. That's not something I'm directly tracking but trying to see if we can get you a report or a contact to directly reach out to.

And regarding the confidentiality agreement- we're working on getting a team hired that will be consistent with each of these data reviews, but we're not there yet. So the individuals in "Exhibit A" will need to be updated for future reviews. I know we wanted to make something that would be flexible for future reviews- but if you will need a list of names each time, we may just need to re-do this single page with a new list each time. The other option would be to make it more generic and state something like "only people critical for review of the data". Do you have a preference?

Thanks!
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Tuesday, June 1, 2021 7:33 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Booster/Variant Data - COVID-19 Vaccines - CONFIDENTIAL

Hi Sara,

I hope you had an enjoyable weekend.

As promised, I am sending you some of the slides we discussed recently regarding our studies of booster doses/variants and a rough estimate of the timing for availability of data.

I would appreciate if you would handle this information as Confidential.

Please let me know if you have any questions.

(b)(4)

Please consider the environment before printing this email

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Thu, 22 Jul 2021 12:20:18 +0000
To: (b)(4) (b)(4) (x)
Cc: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD)
Subject: RE: contacts on 'speakers line' tomorrow
Attachments: 05 COVID Rosenblum July 2021.pdf, 07 COVID Oliver July 2021.pdf

(b)(4)

Please treat the slides as confidential- but attached are the Benefit/risk slides (05) and the Immunocompromised slides (07).

Thanks-

Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Wednesday, July 21, 2021 4:11 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>
Subject: Re: contacts on 'speakers line' tomorrow

HI Sara,

It would be best if you invite a few persons from our end please.

(b)(4) (b)(4) - (b)(4)
(b)(4)
(b)(4) (b)(4) - (b)(4)
(b)(4)
(b)(4) (b)(4) - (b)(4)

A number of these individuals will be off and on due to other meetings.

Thanks for the invite, the clarity, and for sending the slides when you can.

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Wednesday, July 21, 2021 11:40 AM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>
Subject: RE: contacts on 'speakers line' tomorrow

EXTERNAL

(b)(4)

We aren't planning to address any specific questions to Moderna. But there is the possibility that questions could come to you for either issues, so may be helpful to have someone on to address either? Defer to you on who that may be.

Our slides are still working through CDC clearance but once we have approval, we will share.

Thanks-
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Wednesday, July 21, 2021 11:26 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>
Subject: Re: contacts on 'speakers line' tomorrow

Hi Sara,

Just want to confirm. Are you suggesting we might need to address questions on myocarditis or use of the vaccine in immunocompromised? If so, I will need to identify the right individuals from our end.

And is it still possible to see a draft of the slides for tomorrow please?

Many thanks.

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Wednesday, July 21, 2021 11:18 AM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>
Subject: contacts on 'speakers line' tomorrow

EXTERNAL

(b)(4)

At tomorrow's ACIP meeting, we will be discussing the benefit/risk balance (which includes a

brief update on myocarditis with persons 18+), in addition to a discussion around data with an immunocompromised population.

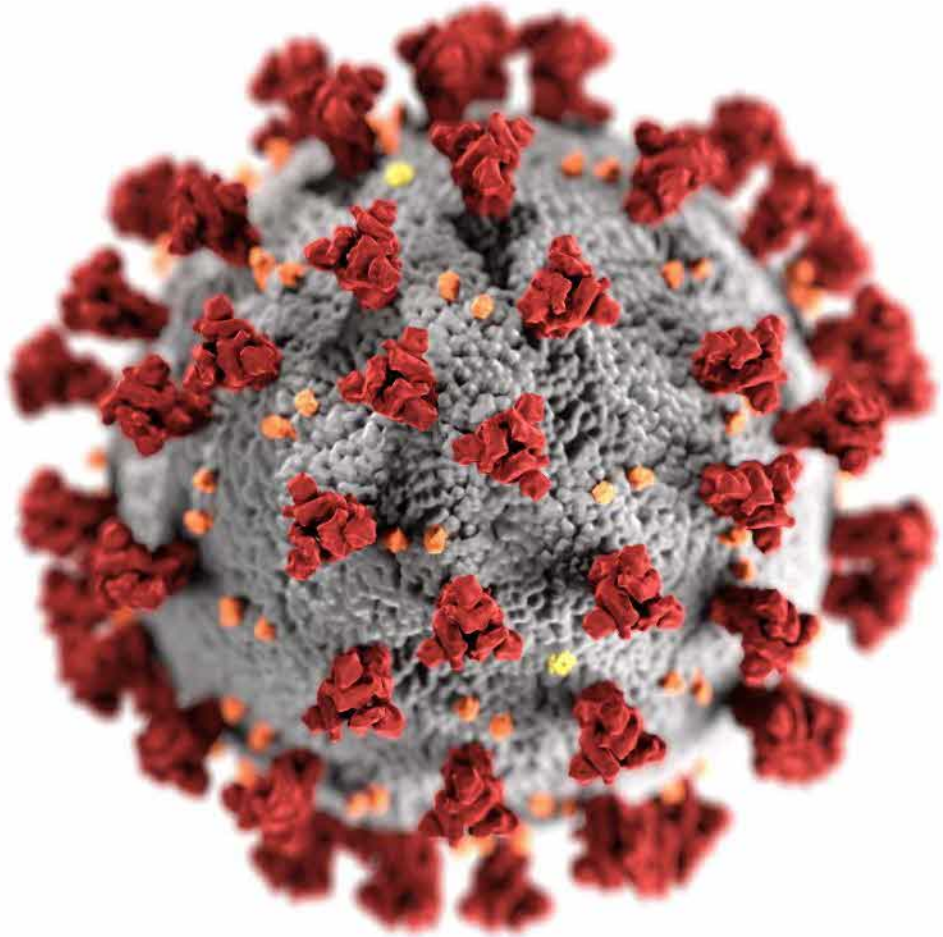
Would Moderna like a few people on the 'speakers line' to address if questions come up for Moderna specifically? We're happy to send a few people the invitation, but wanted to check.

Thanks!
Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

COVID-19 Vaccines in Adults: Benefit-Risk Discussion



Hannah Rosenblum, MD

ACIP Meeting

July 22, 2021

cdc.gov/coronavirus

Current COVID-19 vaccine policy

- Today's discussion will focus on the benefits and harms of COVID-19 vaccines in adults
- Three COVID-19 vaccines are recommended for persons aged 18 years and older in the United States under FDA's Emergency Use Authorization

Benefits and risks by vaccine, age and sex in adults

Benefits of COVID-19 Janssen and mRNA vaccines in adults

Risk after COVID-19 Janssen and mRNA vaccines in adults

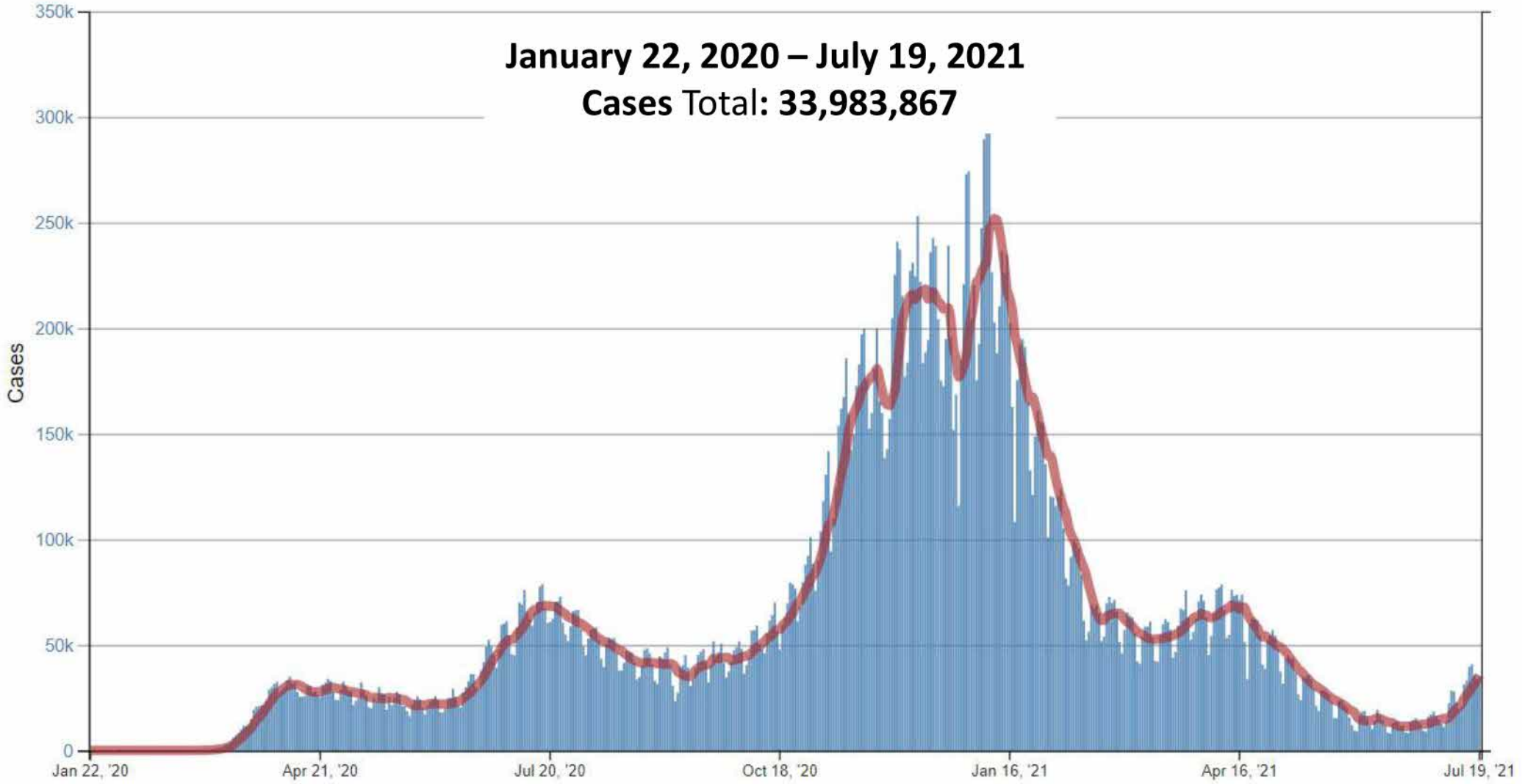
COVID-19 vaccines in adults: Benefit-risk discussion

- Public health problem
  - Recent COVID-19 epidemiology in adults
  - Adverse events reported after vaccination
    - Guillain-Barre Syndrome (GBS)
    - Thrombosis with Thrombocytopenia Syndrome (TTS)
    - Myocarditis

- Benefit/Risk assessment
  - Benefits of Janssen vaccine
  - Risk of GBS after Janssen vaccine
  - Risk of TTS after Janssen vaccine

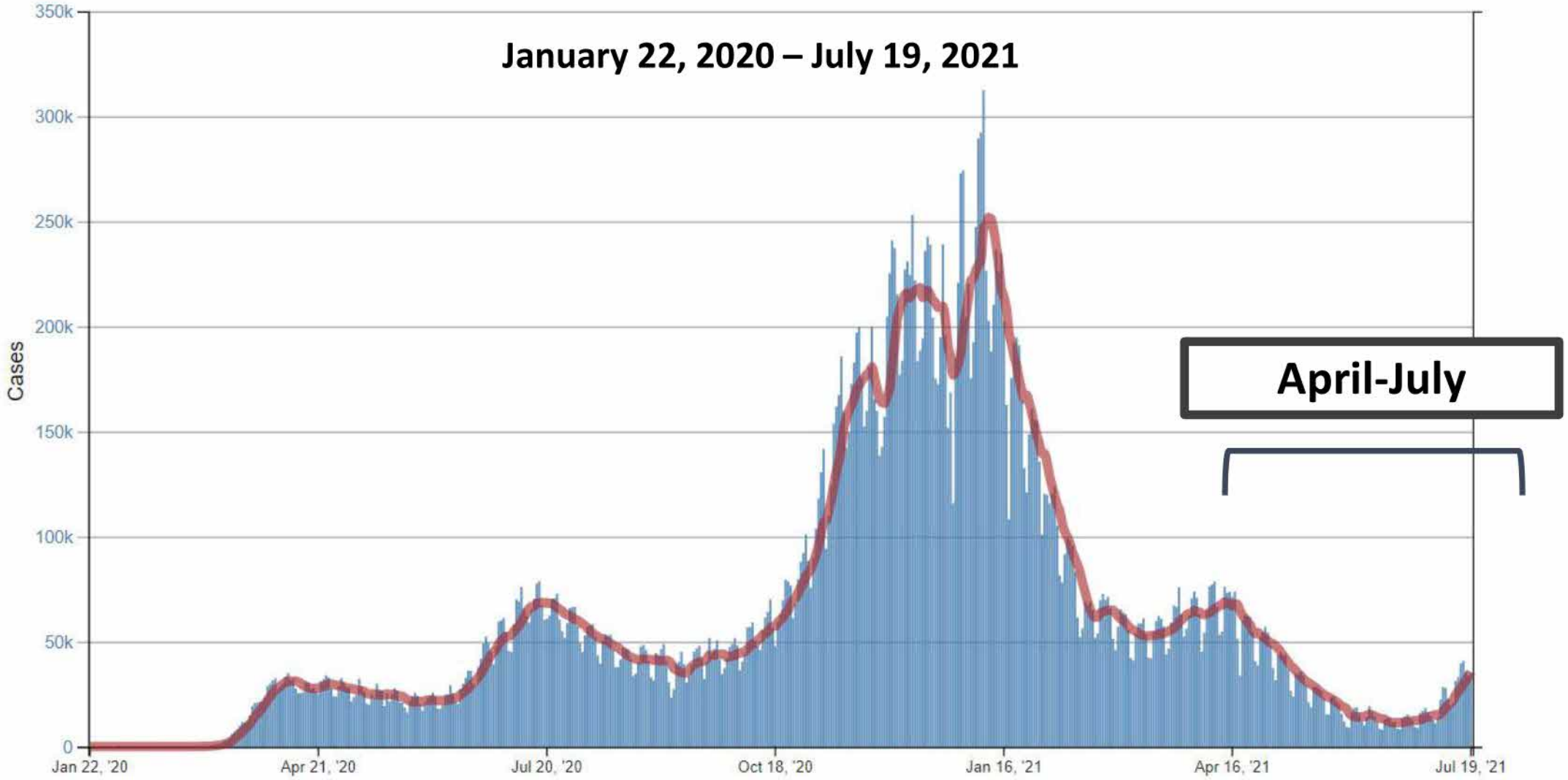
  - Benefits of mRNA vaccines
  - Risk of myocarditis after mRNA vaccines

Trends in number of U.S. COVID-19 cases reported to CDC



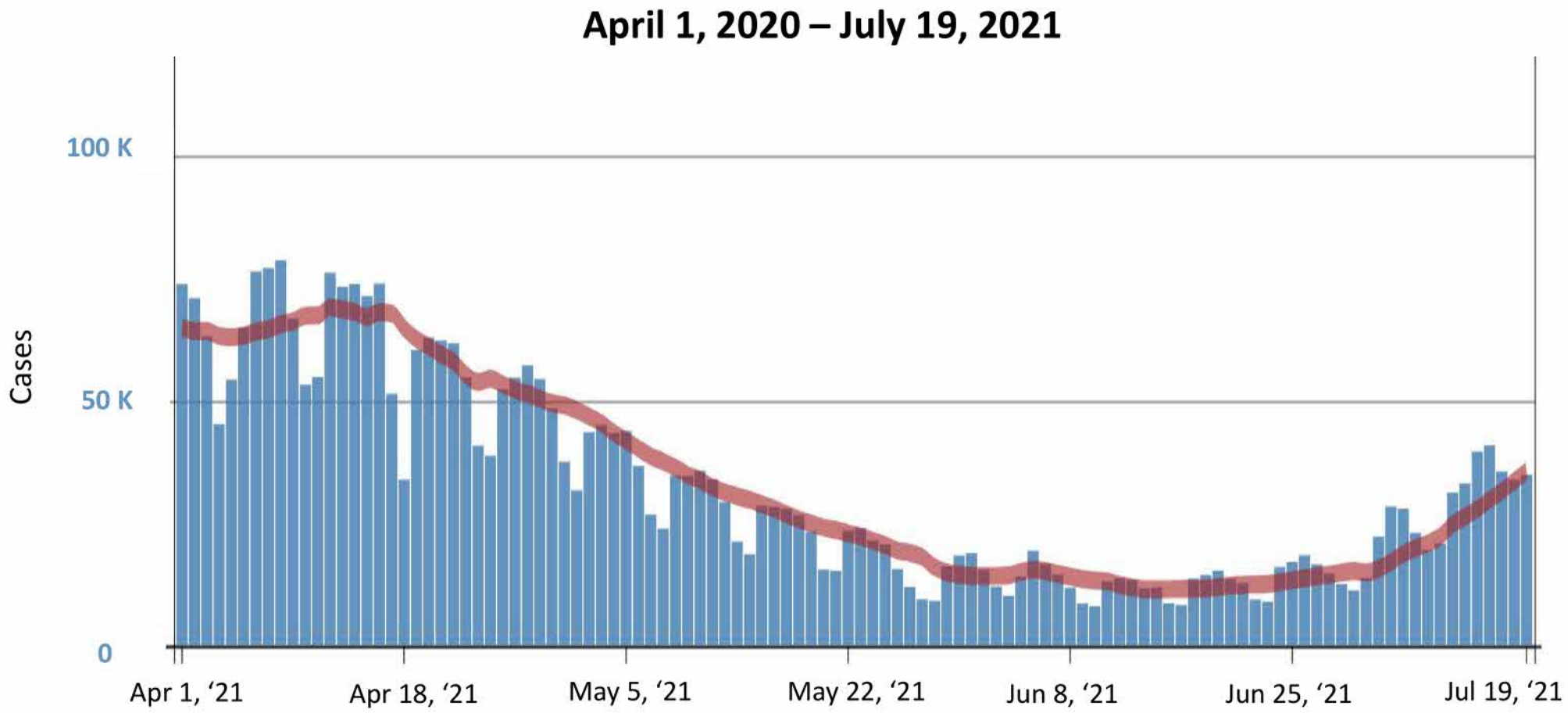
https://covid.cdc.gov/covid-data-tracker/#trends_dailytrendscases; from July 21, 2021

Trends in number of U.S. COVID-19 cases reported to CDC



https://covid.cdc.gov/covid-data-tracker/#trends_dailytrendscases; from July 21, 2021

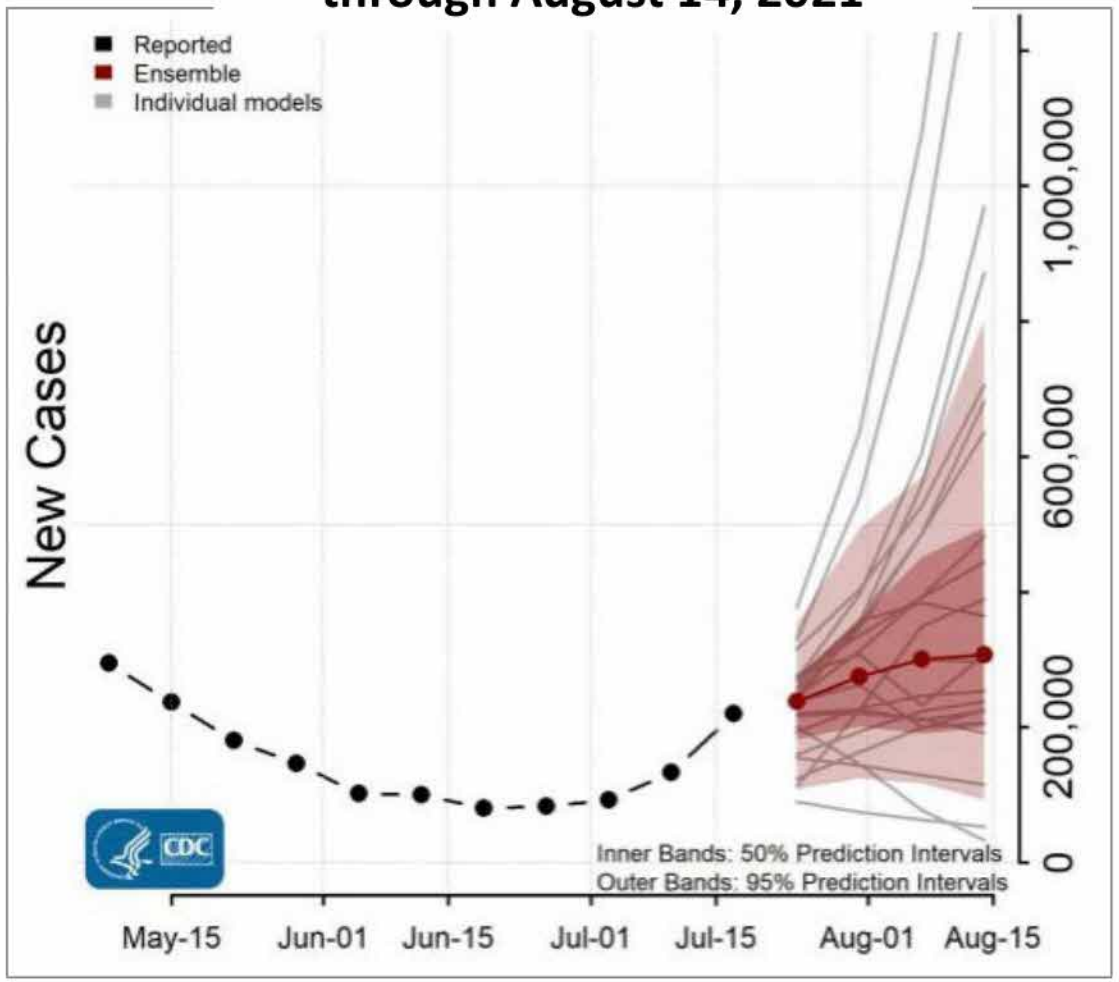
Recent trends in number of U.S. COVID-19 cases



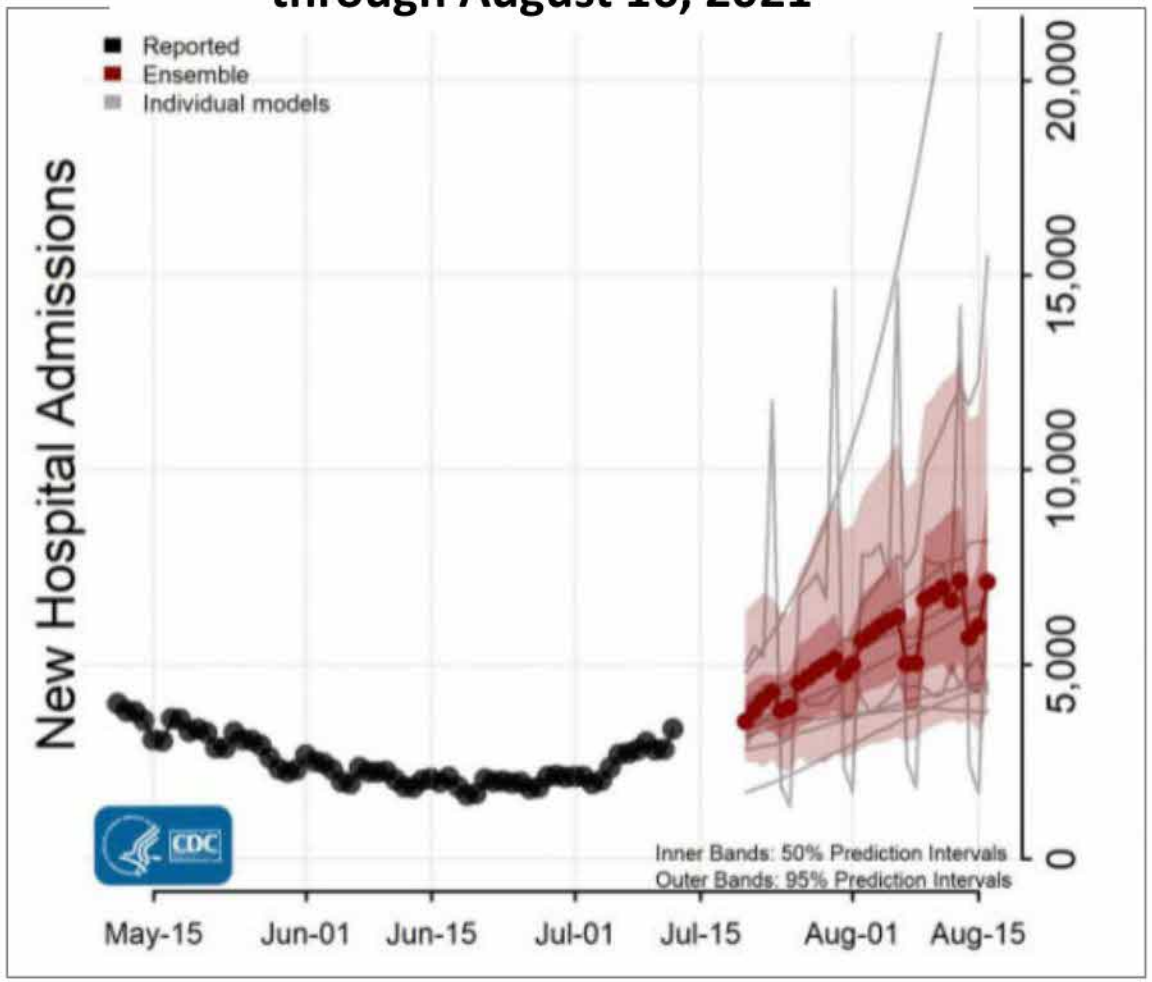
https://covid.cdc.gov/covid-data-tracker/#trends_dailytrendscases; from July 21, 2021

Forecast of cases and hospitalizations for the next four weeks

New COVID-19 cases forecasted through August 14, 2021



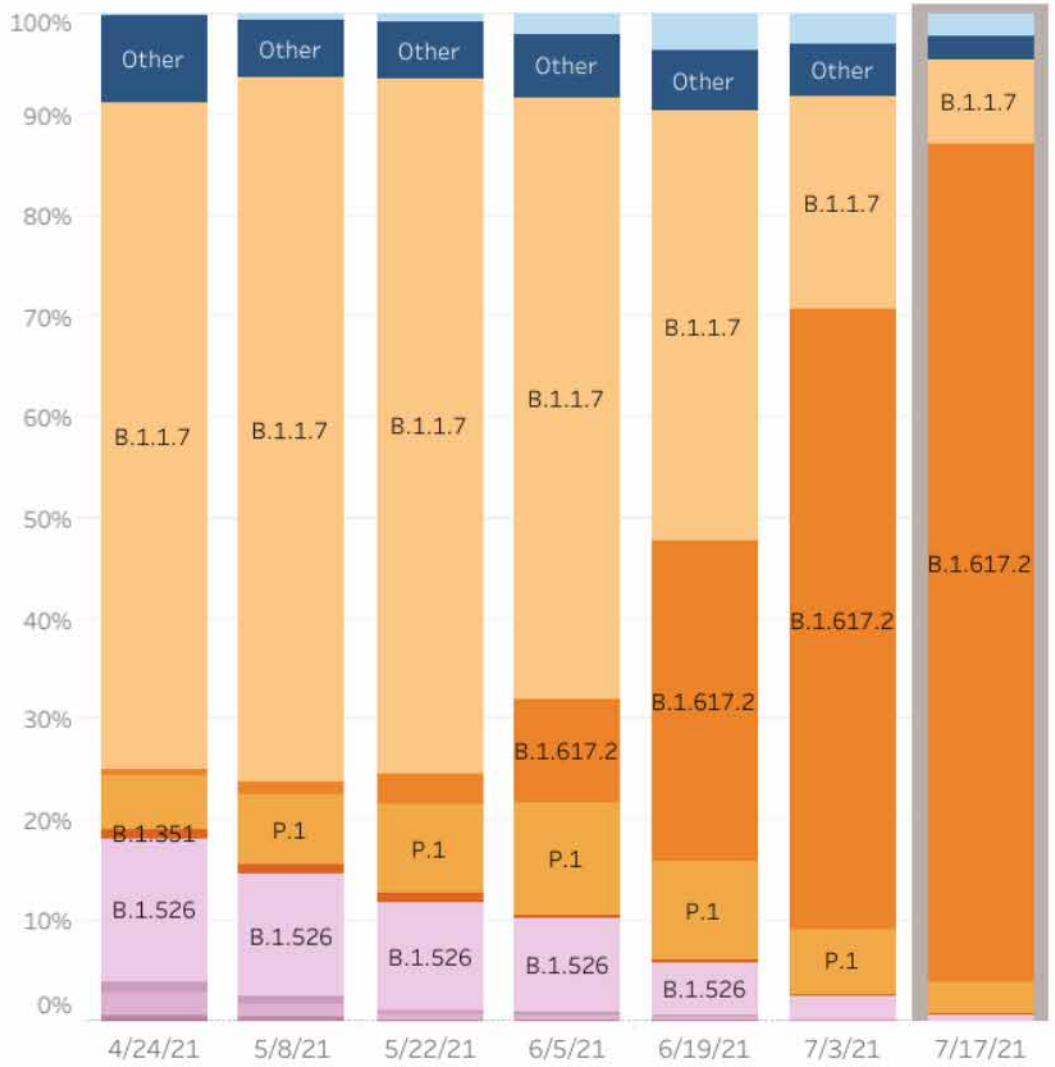
COVID-19 hospitalizations forecasted through August 16, 2021



https://www.cdc.gov/coronavirus/2019-ncov/science/forecasting/forecasts-cases.html; https://www.cdc.gov/coronavirus/2019-ncov/science/forecasting/hospitalizations-forecasts.html

SARS-CoV-2 variants circulating in the United States

April 11 – July 17, 2021



Alpha (B.1.1.7): 8%

Delta (B.1.617.2): 83.2%

Gamma (P.1): 3%

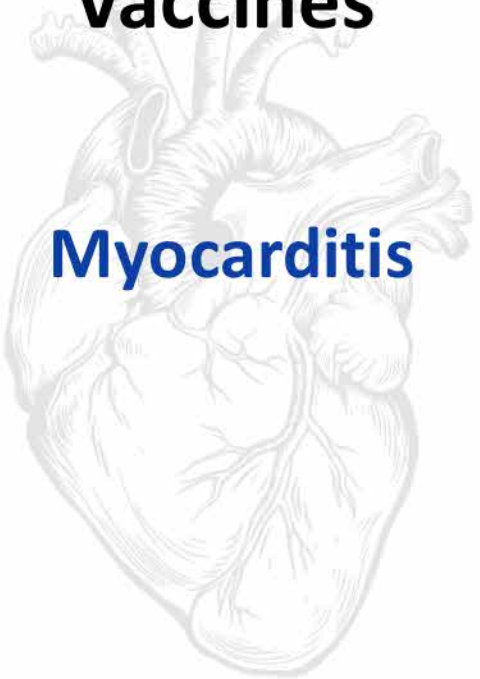
https://covid.cdc.gov/covid-data-tracker/#variant-proportions

Rare serious adverse events reported after COVID-19 vaccination

Janssen vaccine

- Thrombosis with thrombocytopenia syndrome (TTS)
- Guillain-Barré syndrome (GBS)

mRNA vaccines



- Myocarditis

Summary

- After a period of decline, COVID-19 cases and hospitalizations have begun to increase in recent weeks.
  - Variants continue to spread; Delta variant now found in >80% of cases in the United States

- Rare events have been observed after COVID-19 vaccination:
  - Janssen vaccine: TTS & GBS
  - mRNA vaccine: myocarditis

Benefits and Harms of Janssen COVID-19 Vaccine

Methods for assessment of benefit-risk balance – Janssen vaccine

Benefits

- Expected protection provided per 1 million Janssen vaccine doses by age/sex calculated using:
  - Most recent case incidence, COVID-NET hospitalization & severity data (through June 19th)
  - VE (90%) for hospitalization
  - VE (66%) for COVID-19 symptomatic cases
  - 120-day period

VE= Vaccine efficacy

Methods for assessment of benefit-risk balance – Janssen vaccine

Benefits

- Expected protection provided per 1 million Janssen vaccine doses by age/sex calculated using:
  - Most recent case incidence, COVID-NET hospitalization & severity data (through June 19th)
  - VE (90%) for hospitalization
  - VE (66%) for COVID-19 symptomatic cases
  - 120-day period

Potential harms

- Estimated cases of **GBS** per 1 million Janssen vaccine doses, by age/sex using cases from VAERS through June 30, 2021
- Estimated cases of **TTS** per 1 million Janssen vaccine doses, by age/sex using cases reported to VAERS through July 8, 2021

VE= Vaccine efficacy; GBS = Guillain-Barré syndrome; TTS= Thrombosis with thrombocytopenia syndrome; VAERS = Vaccine Adverse Event Reporting System

Benefits of the Janssen COVID-19 vaccine

- The clinical trial demonstrated efficacy against symptomatic, laboratory-confirmed COVID-19. Overall efficacy was **66%**
- Against **severe** outcomes:
  - Vaccine efficacy against COVID-19-associated **hospitalization**: **93%**
  - VE against **deaths** due to COVID-19**: 100%**
- Persistence of antibody response & activity demonstrated against a variety of variants*

*Durable humoral and cellular immune responses months after Ad26.COV2.S vaccination NEJM https://www.nejm.org/doi/full/10.1056/NEJMc2108829?query=featured_home

Potential Harms of the Janssen COVID-19 vaccine:
Guillain-Barré Syndrome

- 12.6 million vaccine doses administered* and 98 GBS cases as of June 30, 2021

	Females n= 37			Males n=61		
Age group	Cases	Doses admin	Reporting rate†	Cases	Doses admin	Reporting rate†
18-29 years old	1	1,037,996	1.0 per million	3	1,258,963	2.4 per million
30-49 years old	13	1,957,663	6.6 per million	18	2,407,430	7.5 per million
50-64 years old	14	1,888,715	7.4 per million	**33**	**2,115,411**	**15.6 per million**
65+ years old	9	1,037,996	8.7 per million	7	932,764	7.5 per million

* Source of doses administered: FDA, through June 30, 2021; Some age- and sex-specific dose administered data were imputed

† Reporting rate = GBS cases per 1 million Janssen COVID-19 vaccine doses administered

GBS = Guillain-Barré Syndrome

Potential Harms of the Janssen COVID-19 vaccine:
Thrombosis with Thrombocytopenia Syndrome

- 12.5 million vaccine doses administered* and 38 confirmed TTS cases as of July 8, 2021

	Females n= 28			Males n=10		
Age group	Cases	Doses admin	Reporting rate†	Cases	Doses admin	Reporting rate†
18-29 years old	4	946,358	4.2 per million	3	1,281,479	2.3 per million
30-49 years old	**17**	**1,934,574**	**8.8 per million**	4	2,440,773	1.6 per million
50-64 years old	7	1,865,372	3.8 per million	3	2,130,473	1.4 per million
65+ years old	0	1,028,190	0.0 per million	0	943,098	0.0 per million

* Source of doses administered: https://covid.cdc.gov/covid-data-tracker/#vaccinations through July 8, 2021; Some age- and sex-specific doses administered data were imputed

† Reporting rate = TTS cases per 1 million Janssen COVID-19 vaccine doses administered

TTS=Thrombosis with Thrombocytopenia Syndrome

Estimated predicted COVID-19 cases prevented vs. GBS cases for every million Janssen vaccinations over 120 days

Females 18–29 Years

8,900 COVID-19 cases prevented

700 hospitalizations prevented

50 ICU admissions prevented

5 deaths prevented

1 GBS case

Males 18–29 Years

6,600 COVID-19 cases prevented

300 hospitalizations prevented

60 ICU admissions prevented

3 deaths prevented

2 GBS cases

Hospitalizations, ICU admissions and deaths based on data for week of June 19, 2021; GBS = Guillain-Barré Syndrome

Estimated predicted COVID-19 cases prevented vs. GBS & TTS cases for every million Janssen vaccinations over 120 days

Females 18–29 Years

8,900 COVID-19 cases prevented

700 hospitalizations prevented

50 ICU admissions prevented

5 deaths prevented

1 GBS case
4-5 TTS cases

Males 18–29 Years

6,600 COVID-19 cases prevented

300 hospitalizations prevented

60 ICU admissions prevented

3 deaths prevented

2 GBS cases
2-3 TTS cases

Hospitalizations, ICU admissions and deaths based on data for week of June 19, 2021; GBS = Guillain-Barré Syndrome; TTS= Thrombosis with Thrombocytopenia Syndrome

Estimated predicted COVID-19 cases prevented vs. GBS & TTS cases for every million Janssen vaccinations over 120 days

Females 30–49 Years

10,100 COVID-19 cases prevented

900 hospitalizations prevented

140 ICU admissions prevented

20 deaths prevented

6-7 GBS cases
8-10 TTS cases

Males 30–49 Years

7,600 COVID-19 cases prevented

650 hospitalizations prevented

150 ICU admissions prevented

25 deaths prevented

7-8 GBS cases
1-2 TTS cases

Hospitalizations, ICU admissions and deaths based on data for week of June 19, 2021; GBS = Guillain-Barré Syndrome; TTS= Thrombosis with Thrombocytopenia Syndrome

Estimated predicted COVID-19 cases prevented vs. GBS & TTS cases for every million Janssen vaccinations over 120 days

Females 50–64 Years

12,100 COVID-19 cases prevented

1,600 hospitalizations prevented

350 ICU admissions prevented

120 deaths prevented

7-8 GBS cases
3-4 TTS cases

Males 50–64 Years

10,100 COVID-19 cases prevented

1,800 hospitalizations prevented

480 ICU admissions prevented

140 deaths prevented

14-17 GBS cases
1-2 TTS cases

Hospitalizations, ICU admissions and deaths based on data for week of June 19, 2021; GBS = Guillain-Barré Syndrome; TTS= Thrombosis with Thrombocytopenia Syndrome

Estimated predicted COVID-19 cases prevented vs. GBS & TTS cases for every million Janssen vaccinations over 120 days

Females 65+ Years

29,000 COVID-19 cases prevented

5,900 hospitalizations prevented

1,250 ICU admissions prevented

840 deaths prevented

8-10 GBS cases
0 TTS cases

Males 65+ Years

36,600 COVID-19 cases prevented

11,800 hospitalizations prevented

3,300 ICU admissions prevented

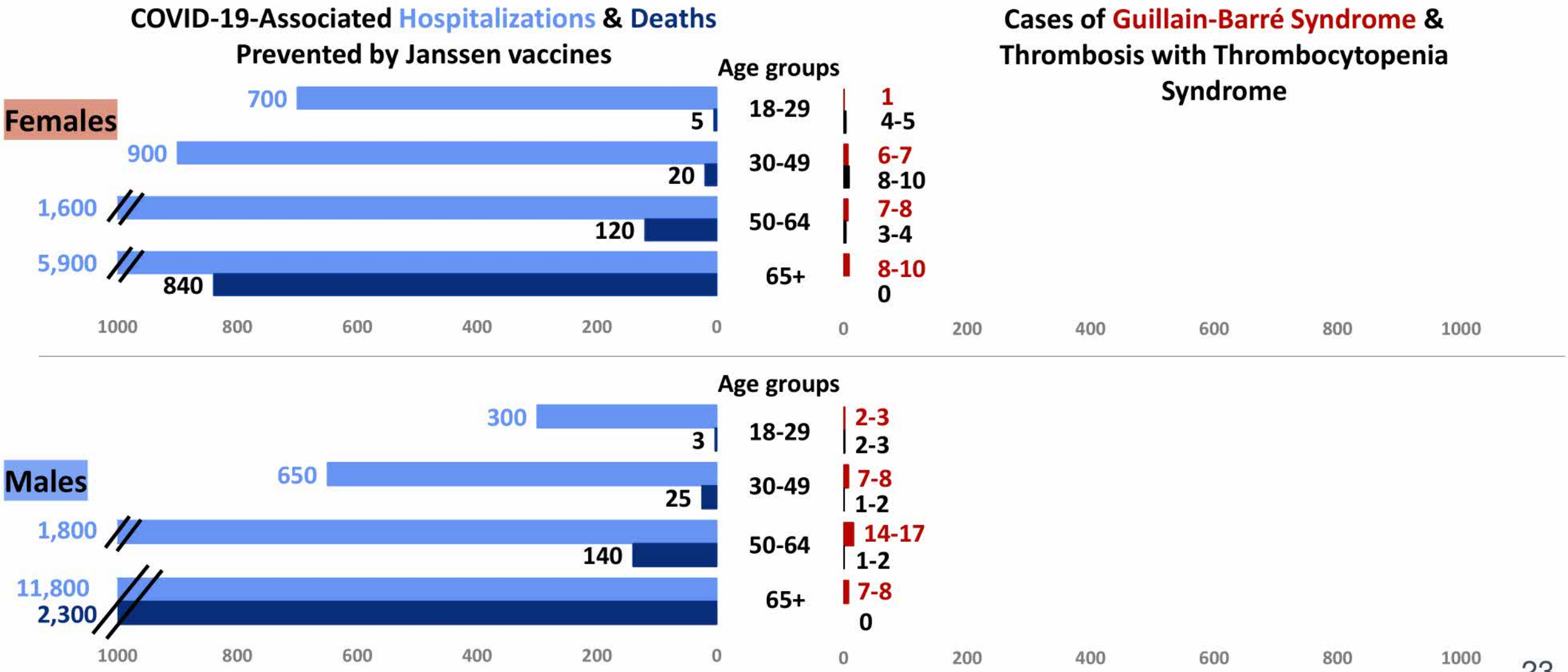
2,300 deaths prevented

7-8 GBS cases
0 TTS cases

Hospitalizations, ICU admissions and deaths based on data for week of June 19, 2021; GBS = Guillain-Barré Syndrome; TTS= Thrombosis with Thrombocytopenia Syndrome

Benefits and risks after Janssen vaccine, by age group & sex

For every million doses of vaccine given with US exposure risk and hospitalization rates from June 19, 2021



Benefits and Harms of mRNA COVID-19 Vaccines

Methods for assessment of benefit-risk balance – mRNA COVID-19 vaccines in adults

Benefits

- Expected protection provided per 1 million mRNA vaccine doses using:
  - Most recent case incidence, COVID-NET hospitalization and severity data (through June 19th)
  - VE for hospitalization (95%)
  - VE for COVID-19 symptomatic cases (95%)
  - 120-day period

Potential harms

- Estimated cases of **myocarditis** per 1 million second doses of mRNA COVID-19 vaccine, by age/sex using data from VAERS through June 30, 2021

VE= Vaccine efficacy; VAERS = Vaccine Adverse Event Reporting System

Benefits of mRNA vaccines

- Clinical trial data demonstrated high efficacy against symptomatic, laboratory-confirmed COVID-19 among adults with both mRNA vaccines (Pfizer-BioNTech and Moderna)
  - Overall efficacy was **94-95%**
  - Vaccine efficacy against COVID-19 associated hospitalization was **89-100%**

- Persistence of antibody response & activity demonstrated against a variety of variants*

Polack FP et al. N Engl J Med 2020; DOI: 10.1056/NEJMoa2034577; Frenck RW et al. N Engl J Med 2021; DOI: 10.1056/NEJMoa2107456;
Baden LR et al. N Engl J Med 2021; DOI: 10.1056/NEJMoa2035389
*https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html

Potential Harms of the mRNA COVID-19 vaccines:
Myocarditis

- 141 million 2nd mRNA vaccine doses administered* and 497 myocarditis cases as of June 30, 2021 in age 18+

	Females n= 105			Males n= 392		
Age group	**Cases**	**Doses admin**	**Reporting rate†**	**Cases***	**Doses admin**	**Reporting rate†**
18-29 years old§	34	10,491,212	3.2 per million	**248**	**10,212,647**	**24.3 per million**
30-49 years old	38	20,875,708	1.8 per million	117	20,154,577	5.8 per million
50-64 years old	23	19,714,915	1.2 per million	15	18,514,388	0.8 per million
65+ years old	10	22,274,470	0.4 per million	12	19,518,324	0.6 per million

*Source of doses administered: https://covid.cdc.gov/covid-data-tracker/#vaccinations; some age- and sex-specific doses administered data were imputed

†Reporting rate = myocarditis cases per 1 million mRNA COVID-19 mRNA second vaccine doses administered

§Myocarditis cases in 18-29-year-olds are confirmed cases meeting CDC's case definition

Estimated predicted COVID-19 cases prevented vs. myocarditis cases for every million mRNA vaccinations over 120 days

Females 18-29 Years

12,800 COVID-19 cases prevented

750 hospitalizations prevented

50 ICU admissions prevented

5 deaths prevented

3-4 myocarditis cases

Males 18-29 Years

9,600 COVID-19 cases prevented

300 hospitalizations prevented

60 ICU admissions prevented

3 deaths prevented

22-27 myocarditis cases

Hospitalizations, ICU admissions and deaths based on data for week of June 19, 2021

Estimated predicted COVID-19 cases prevented vs. myocarditis cases for every million mRNA vaccinations over 120 days

Females 30-49 Years

14,600 COVID-19 cases prevented

950 hospitalizations prevented

140 ICU admissions prevented

20 deaths prevented

1-2 myocarditis cases

Males 30-49 Years

11,000 COVID-19 cases prevented

700 hospitalizations prevented

160 ICU admissions prevented

25 deaths prevented

5-6 myocarditis cases

Hospitalizations, ICU admissions and deaths based on data for week of June 19, 2021

Estimated predicted COVID-19 cases prevented vs. myocarditis cases for every million mRNA vaccinations over 120 days

Females 50-64 Years

17,500 COVID-19 cases prevented

1,700 hospitalizations prevented

375 ICU admissions prevented

125 deaths prevented

1 myocarditis case

Males 50-64 Years

14,700 COVID-19 cases prevented

1,900 hospitalizations prevented

500 ICU admissions prevented

150 deaths prevented

1 myocarditis case

Hospitalizations, ICU admissions and deaths based on data for week of June 19, 2021

Estimated predicted COVID-19 cases prevented vs. myocarditis cases for every million mRNA vaccinations over 120 days

Females 65+ Years

32,000 COVID-19 cases prevented

6,200 hospitalizations prevented

1,300 ICU admissions prevented

900 deaths prevented

<1 myocarditis case

Males 65+ Years

52,700 COVID-19 cases prevented

12,500 hospitalizations prevented

3,500 ICU admissions prevented

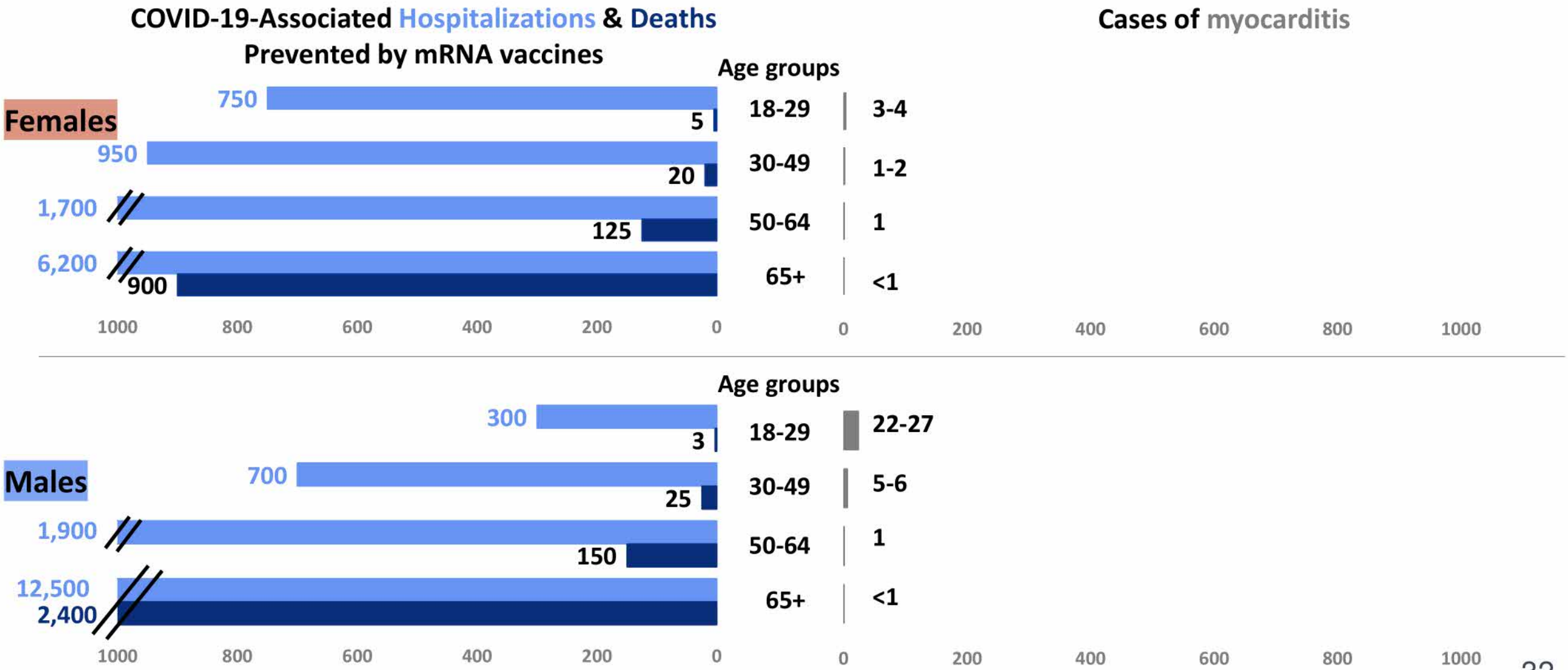
2,400 deaths prevented

<1 myocarditis case

Hospitalizations, ICU admissions and deaths based on data for week of June 19, 2021

Benefits and risks after mRNA vaccine, by age group & sex

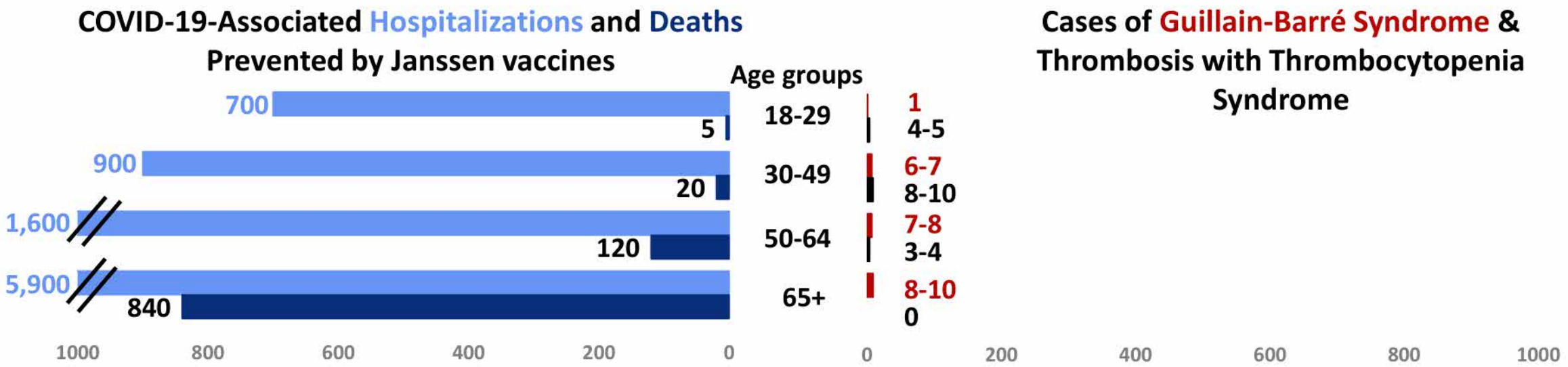
For every million doses of vaccine given with US exposure risk and hospitalization rates from June 19, 2021

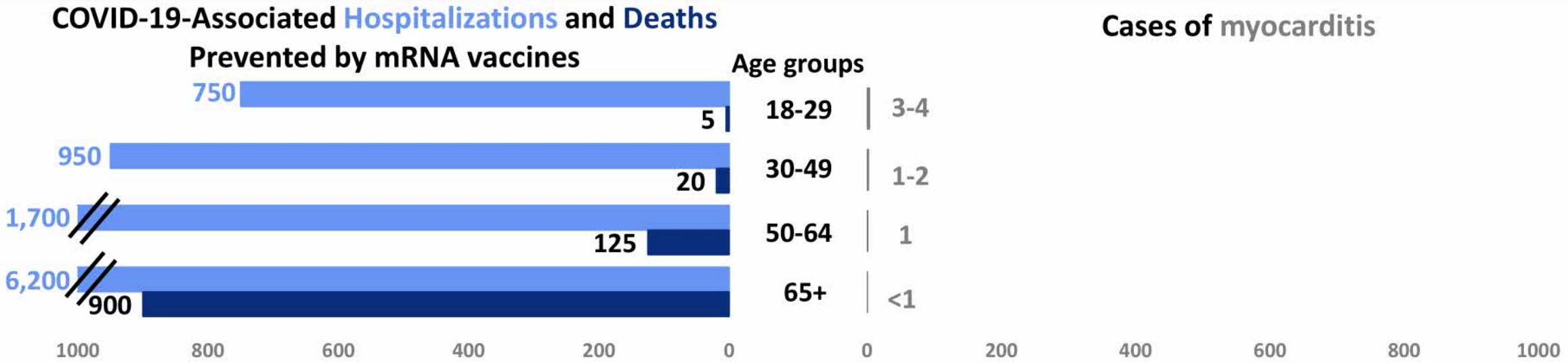


Summary

Benefits and risks after COVID-19 vaccine, by age group- females

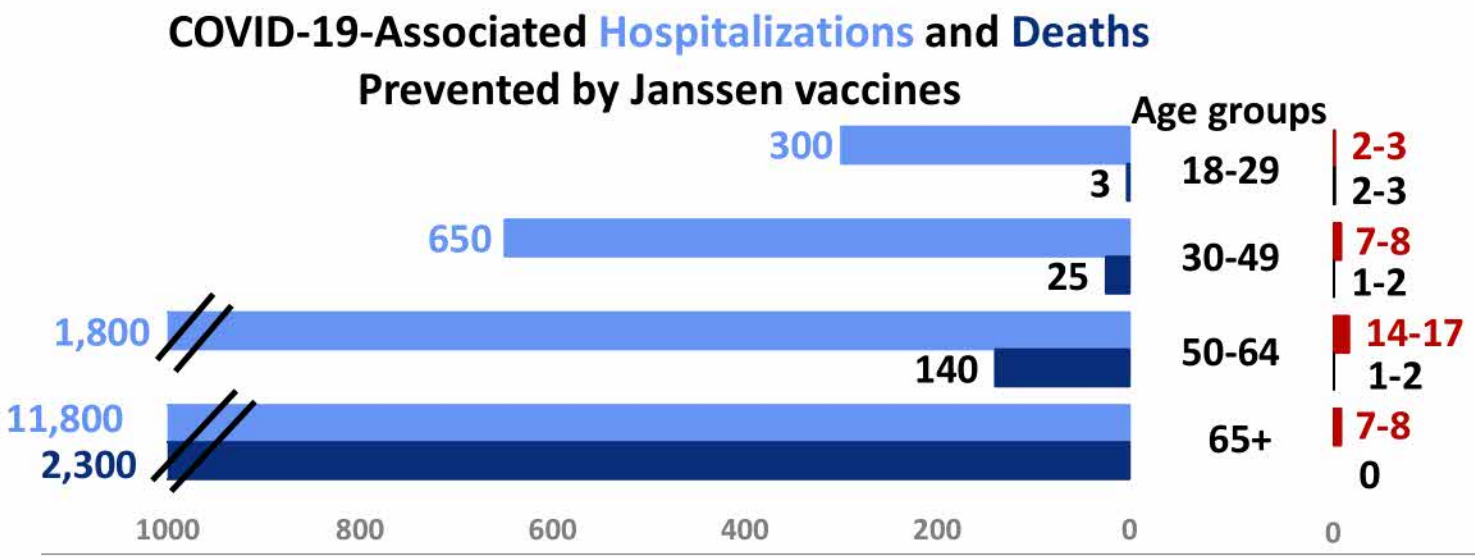
For every million doses of vaccine given with US exposure risk and hospitalization rates from June 19, 2021

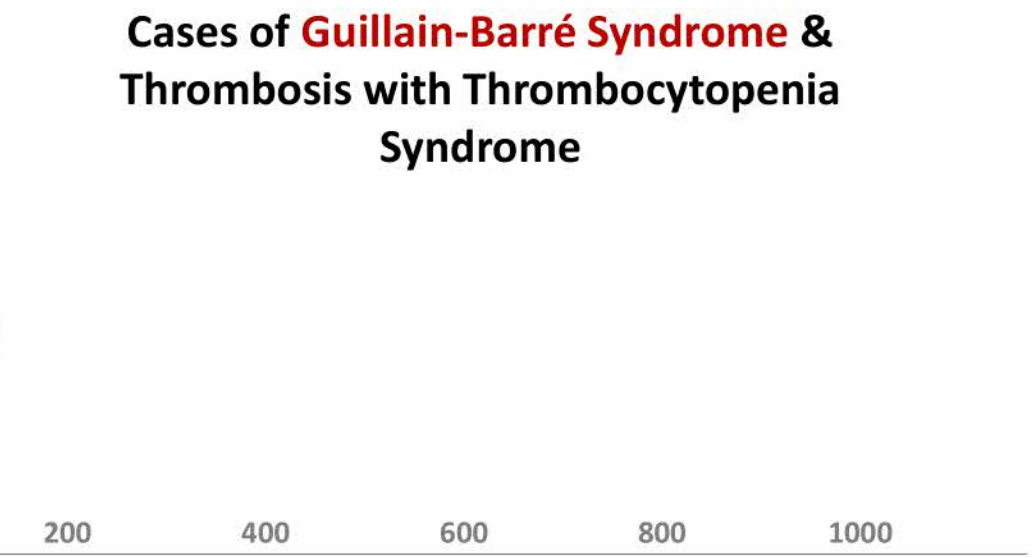


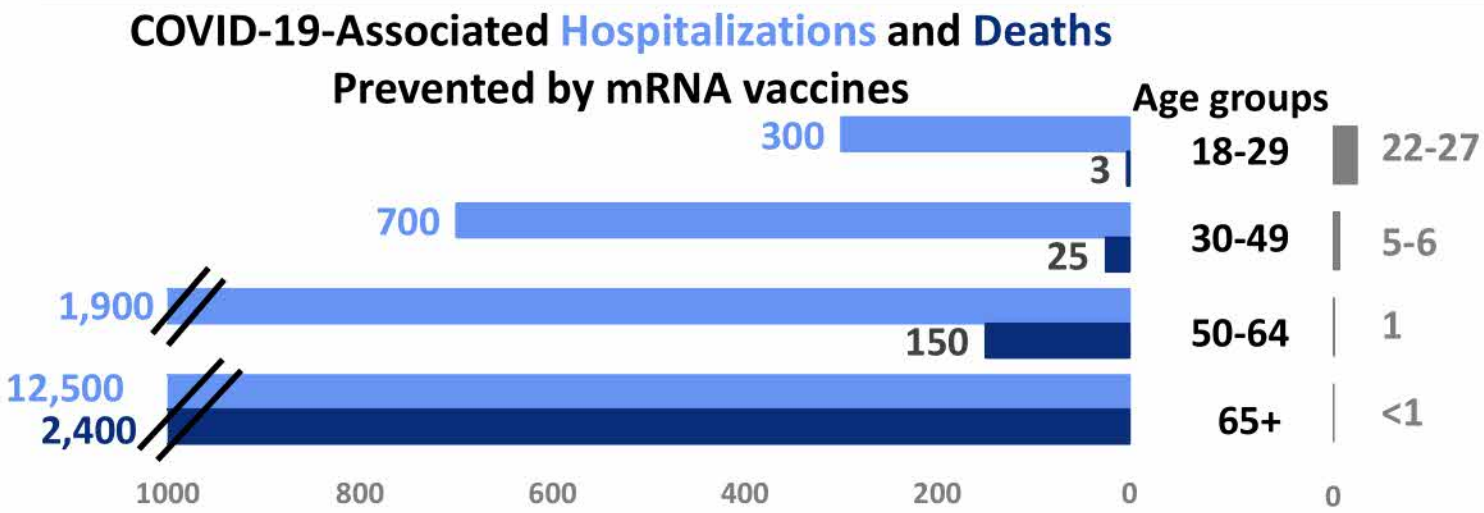


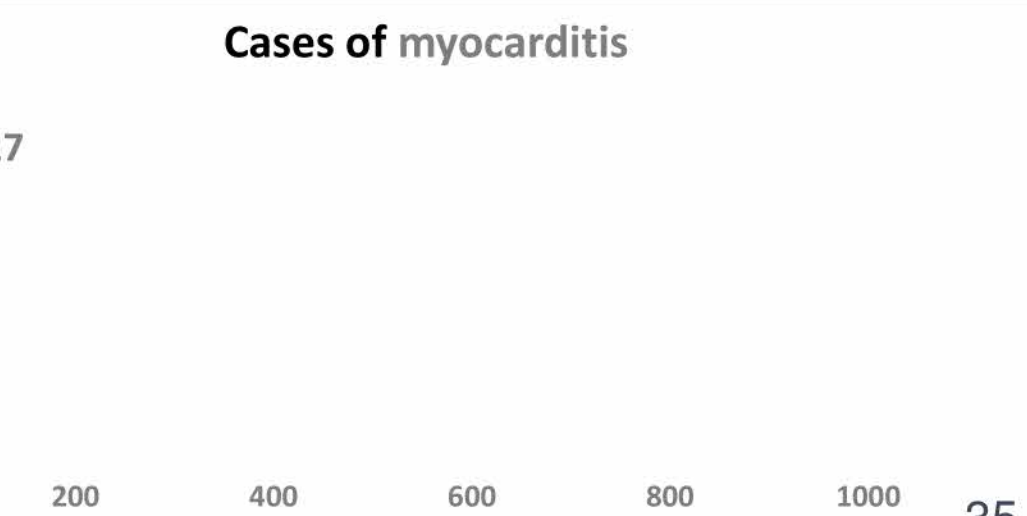
Benefits and risks after COVID-19 vaccine, by age group- males

For every million doses of vaccine given with US exposure risk and hospitalization rates from June 19, 2021









Benefits and risks after COVID-19 vaccine, by age group & sex

For every million doses of vaccine given with US exposure risk and hospitalization rates from June 19, 2021

Age	Janssen COVID-19 vaccine					mRNA COVID-19 vaccines			
	Prevented COVID-19 Outcomes			GBS Cases	TTS Cases	Prevented COVID-19 Outcomes			Myocarditis Cases
	Hospitalization	ICU	Death			Hospitalization	ICU	Death	
FEMALES									
18-29 years	700	50	5	1	4-5	750	50	5	3-4
30-49 years	900	140	20	6-7	8-10	950	140	20	1-2
50-64 years	1600	350	120	7-8	3-4	1,700	375	125	1
65+ years	5,900	1250	840	8-10	0	6,200	1300	900	<1
MALES									
18-29 years	300	60	3	2	2-3	300	60	3	22-27
30-49 years	650	150	25	7-8	1-2	700	160	25	5-6
50-64 years	1,800	480	140	14-17	1-2	1,900	500	150	1
65+ years	11,800	3300	2300	7-8	0	12,500	3500	2400	<1

Potential harms reported overall after COVID-19 vaccination

Janssen vaccine

Thrombosis with thrombocytopenia syndrome:

3.0 cases per million doses among adults

Guillain-Barré syndrome:

7.8 cases per million doses among adults

mRNA vaccines

Myocarditis:

3.5 cases per million doses among adults

- Risk for each potential harm varies by age and by sex

Limitations of benefit-risk estimates

- Benefits of vaccination likely even greater than shown
  - Model uses current case estimates; does not account for underreporting or rising case counts
  - Benefits are estimated over 120 days following vaccination, but protection likely lasts longer
  - Does not account for post-COVID-19 conditions

- Some hospitalizations (COVID-NET) may be related to diagnoses other than COVID-19
- Vaccine efficacy from clinical trials rather than real-world data
- Crude numbers of potential harms were used for some estimates

Benefit-risk interpretation and summary

- An assessment of the individual benefits and individual risks of vaccination is an important tool to help inform vaccination policy

- **This assessment demonstrates that the benefits of COVID-19 vaccination far outweigh the potential risks**

- The relative balance of benefits-risks varies by age/sex

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- Melinda Wharton
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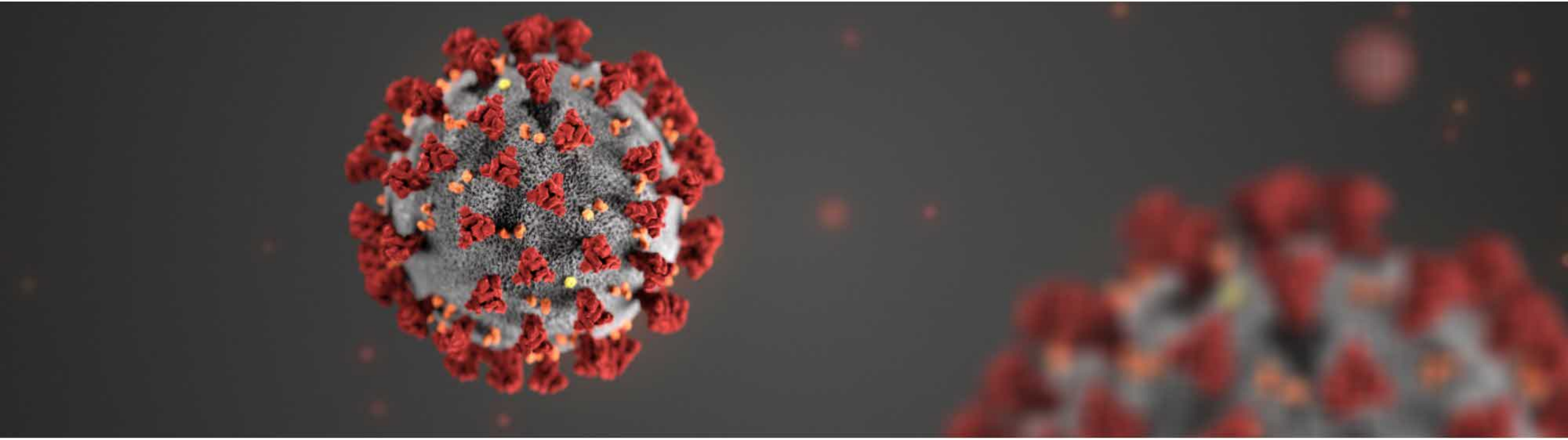
- Epidemiology and Surveillance Task Force
- Vaccine Task Force



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Thank you

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Extra slides

Rare serious adverse events reported after COVID-19 vaccination

Janssen COVID-19 vaccine

- **Guillain-Barré Syndrome:**
  - Cases largely reported ~ 2 weeks after vaccination and mostly in men, 50 years and older.
- **Thrombosis with thrombocytopenia syndrome**
  - Rare, but clinically serious and potentially life-threatening adverse event
  - Most cases in females aged 18-49 years old
  - Janssen vaccine was paused in April 2021, and ACIP discussed the benefit-risk balance before resumption of vaccine administration (benefits outweighed risks)

mRNA COVID-19 vaccines

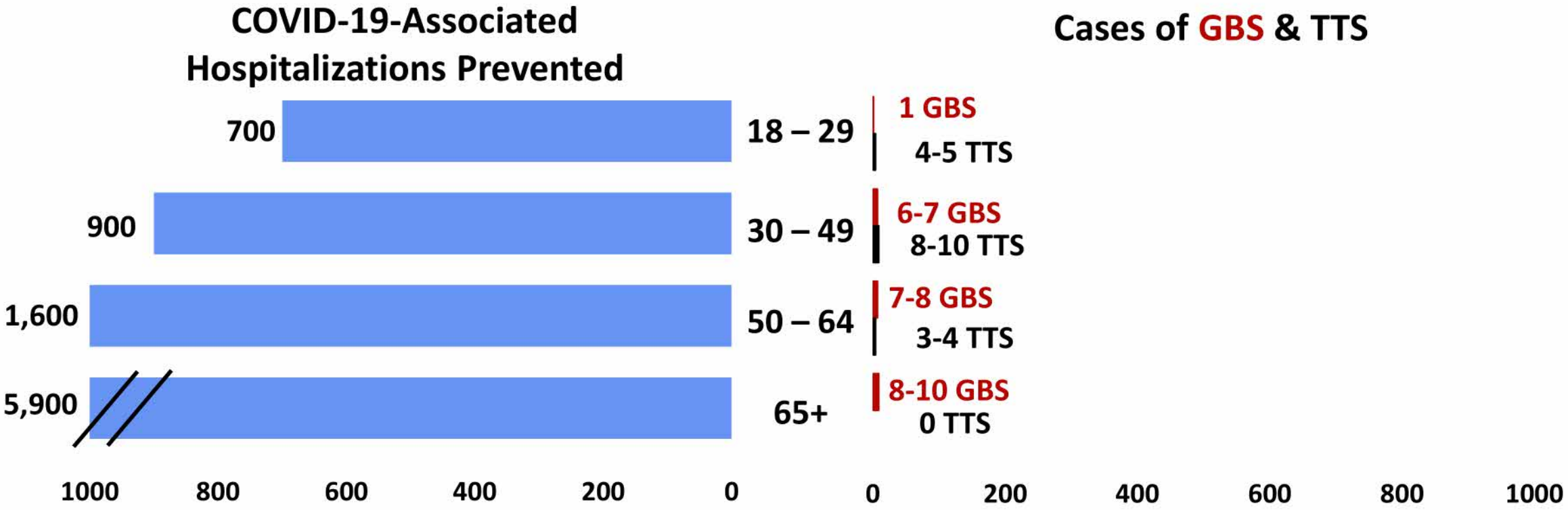
- **Myocarditis:**
  - Rare event most commonly been observed in males, <age 30 years, within a few days after 2nd dose
  - Benefit-risk assessment presented for adolescents and young adults in June 2021; benefits outweigh risks

MacNeil JR, Su JR, Broder KR, et al. Updated Recommendations from the Advisory Committee on Immunization Practices for Use of the Janssen (Johnson & Johnson) COVID-19 Vaccine After Reports of Thrombosis with Thrombocytopenia Syndrome Among Vaccine Recipients — United States, April 2021. MMWR Morb Mortal Wkly Rep 2021;70:651-656. DOI: http://dx.doi.org/10.15585/mmwr.mm7017e4external icon

Gargano JW, Wallace M, Hadler SC, et al. Use of mRNA COVID-19 Vaccine After Reports of Myocarditis Among Vaccine Recipients: Update from the Advisory Committee on Immunization Practices — United States, June 2021. MMWR Morb Mortal Wkly Rep 2021;70:977–982. DOI: http://dx.doi.org/10.15585/mmwr.mm7027e2external icon

Benefits and risks after Janssen, by age group- females

For every **million** doses of Janssen vaccine given with US exposure risk*

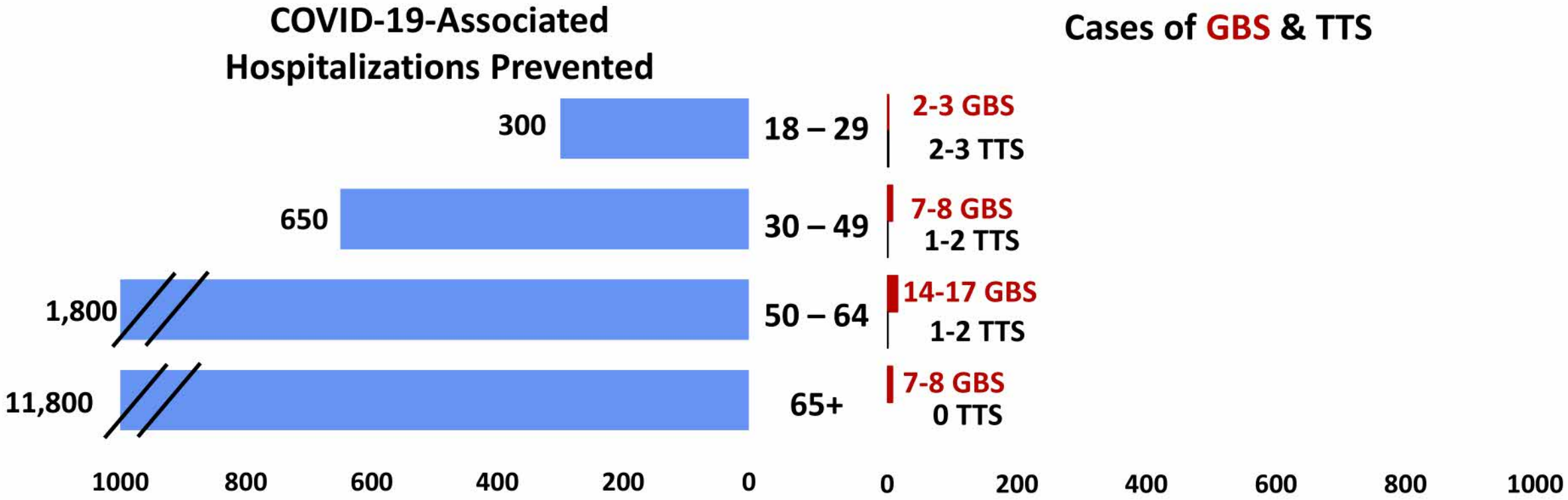


* Hospitalizations based on data for week of June 19, 2021.

GBS = Guillain-Barré Syndrome; TTS= Thrombosis with Thrombocytopenia Syndrome

Benefits and risks after Janssen, by age group- males

For every **million** doses of Janssen vaccine given with US exposure risk*

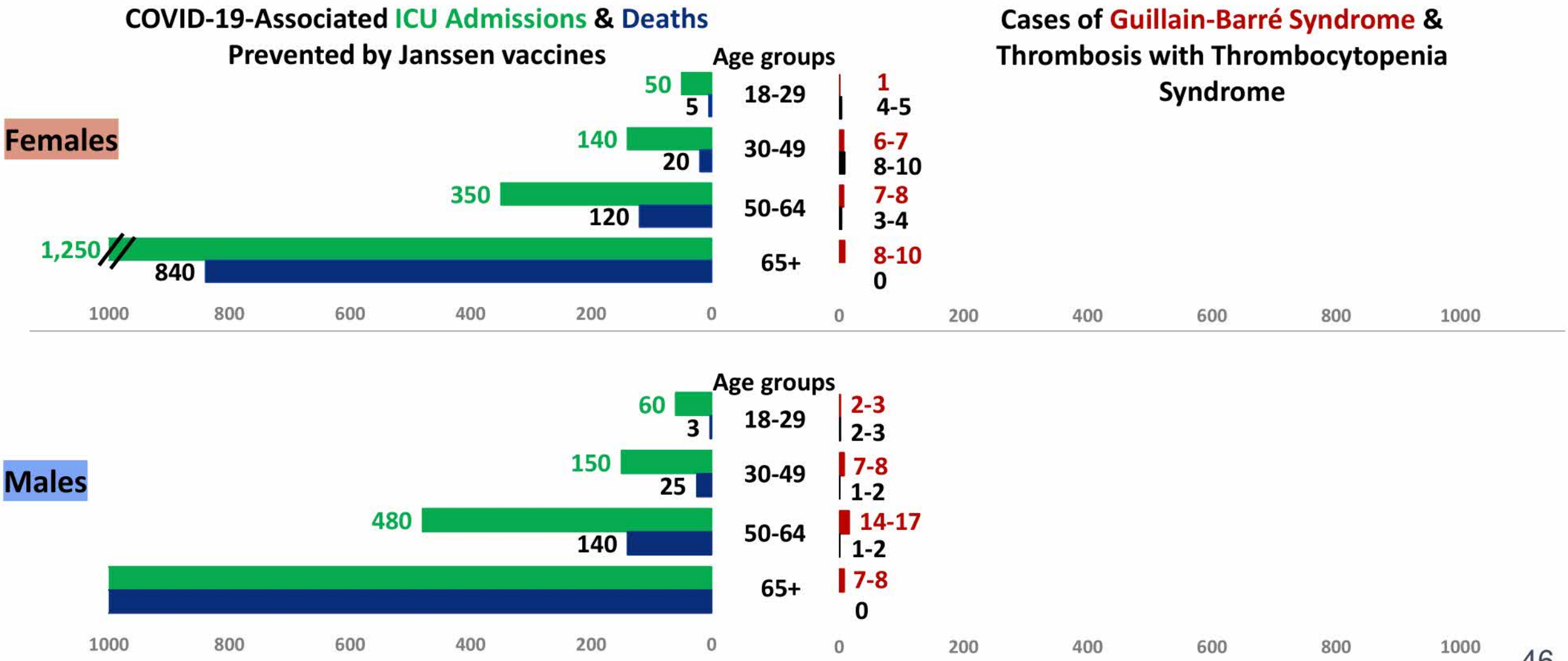


* Hospitalizations based on data for week of June 19, 2021.

GBS = Guillain-Barré Syndrome; TTS= Thrombosis with Thrombocytopenia Syndrome

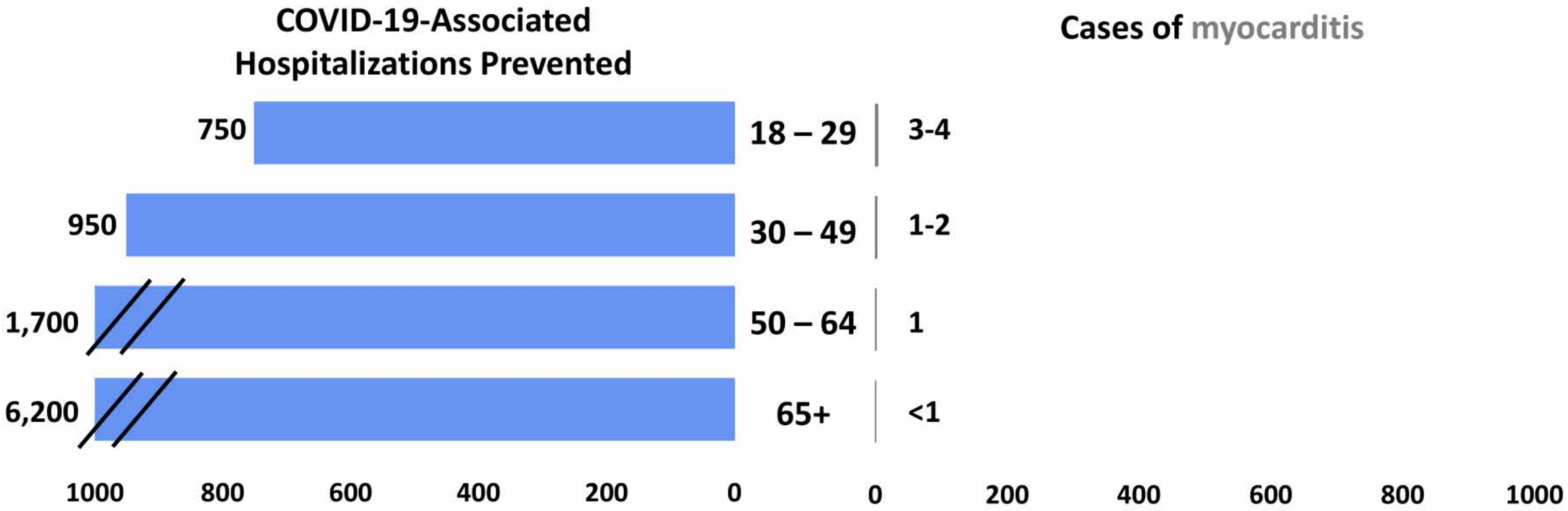
Benefits and risks after Janssen vaccine, by age group

For every million doses of vaccine given with US exposure risk and hospitalization rates from June 19, 2021



Benefits and risks after mRNA vaccine, by age group- females

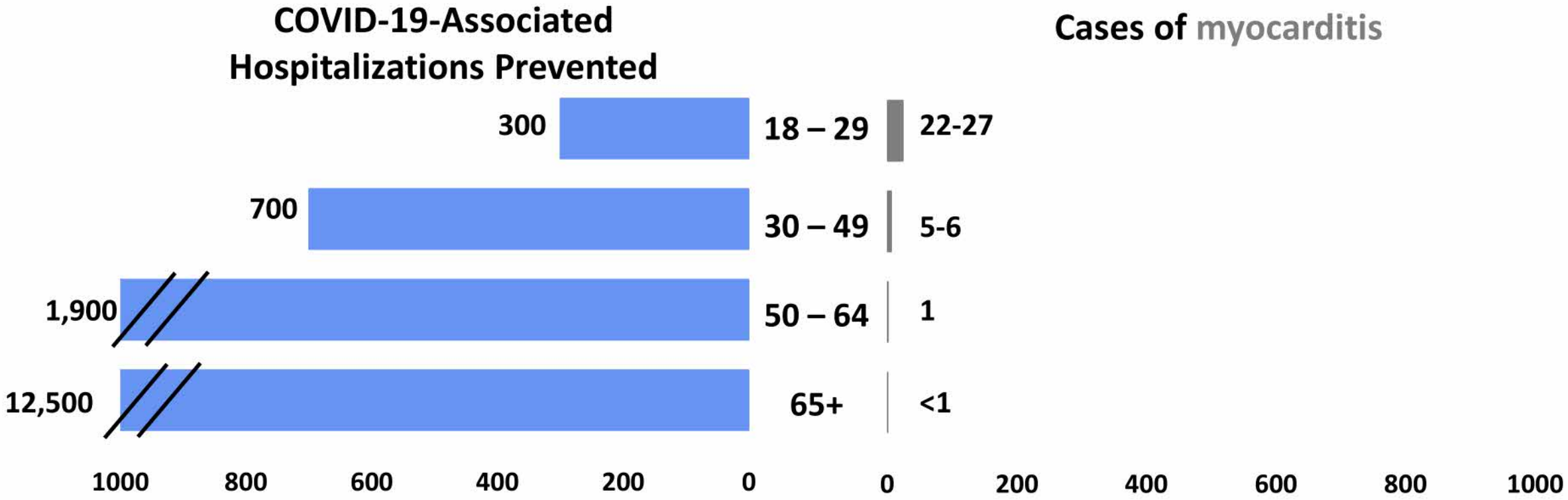
For every **million** doses of mRNA vaccine given with US exposure risk*



*Hospitalizations based on data for week of June 19, 2021.

Benefits and risks after mRNA vaccine, by age group- males

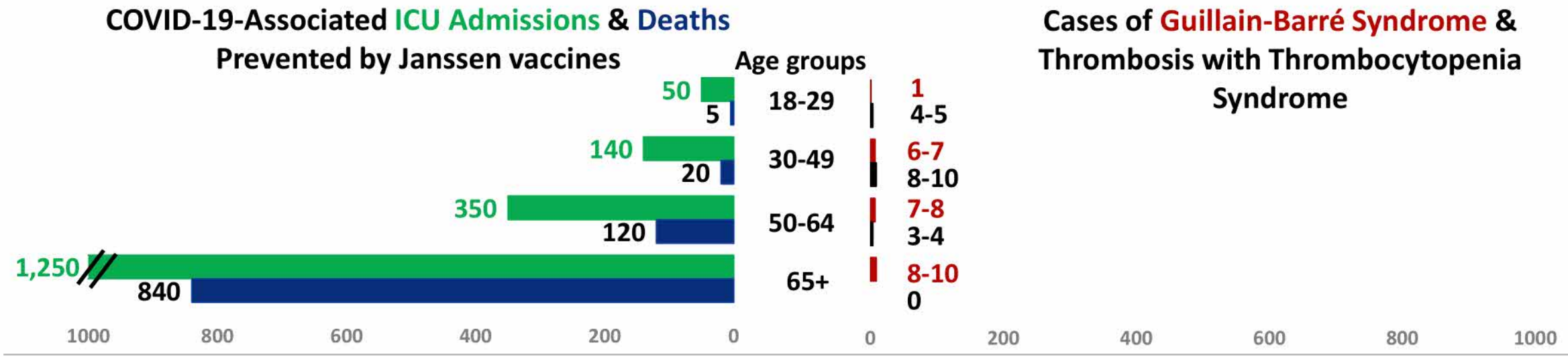
For every **million** doses of mRNA vaccine given with US exposure risk*



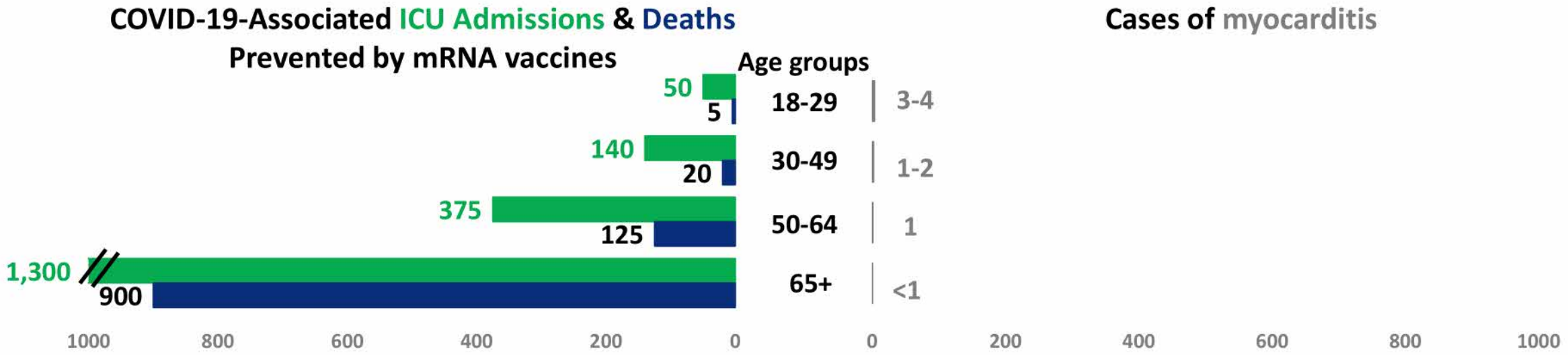
*Hospitalizations based on data for week of June 19, 2021.

Benefits and risks after COVID-19 vaccine, by age group- females

For every million doses of vaccine given with US exposure risk and hospitalization rates from June 19, 2021



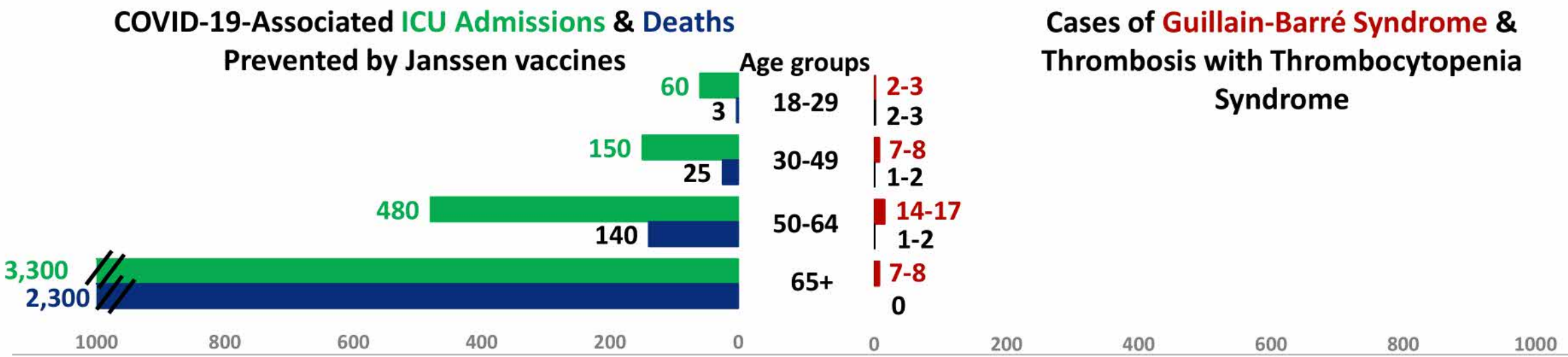
Cases of Guillain-Barré Syndrome & Thrombosis with Thrombocytopenia Syndrome

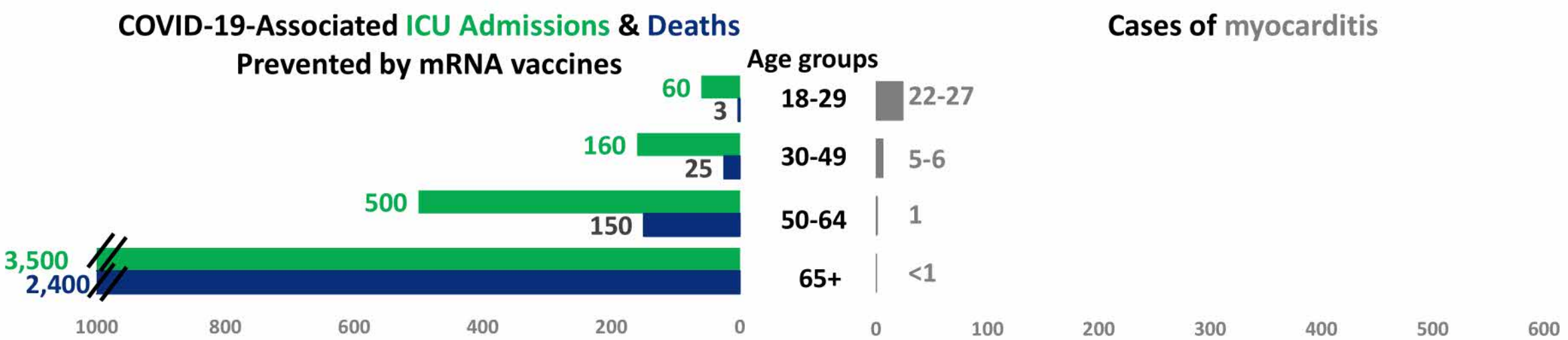


Cases of myocarditis

Benefits and risks after COVID-19 vaccine, by age group- males

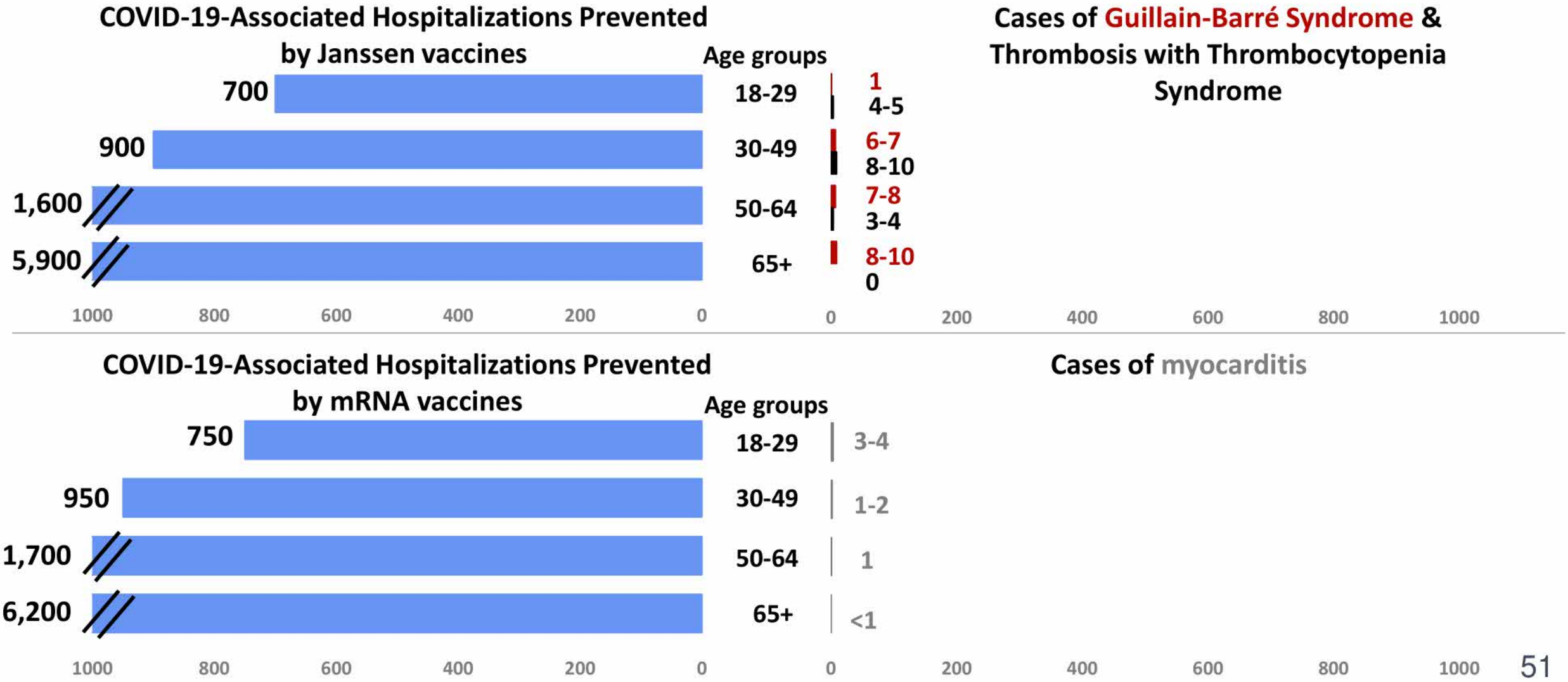
For every million doses of vaccine given with US exposure risk and hospitalization rates from June 19, 2021





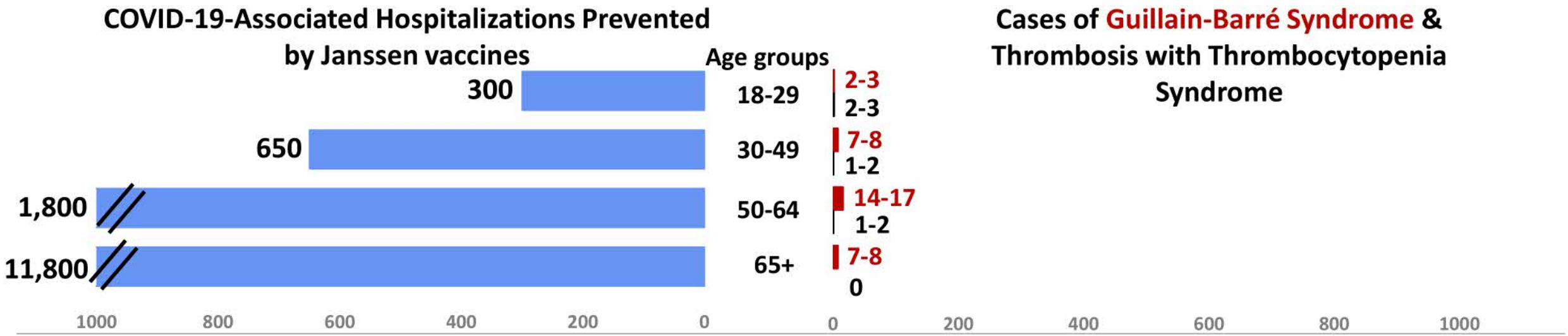
Benefits and risks after COVID-19 vaccine, by age group- females

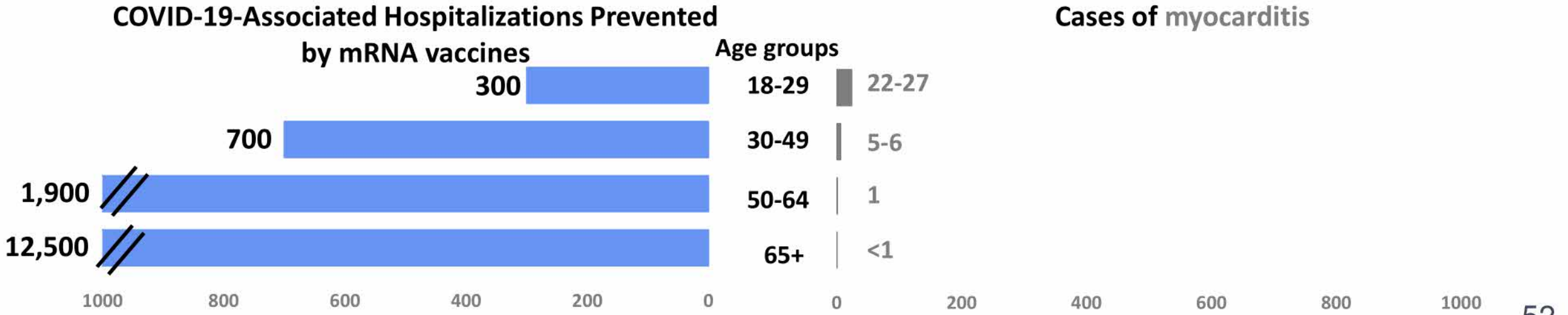
For every million doses of vaccine given with US exposure risk and hospitalization rates from June 19, 2021



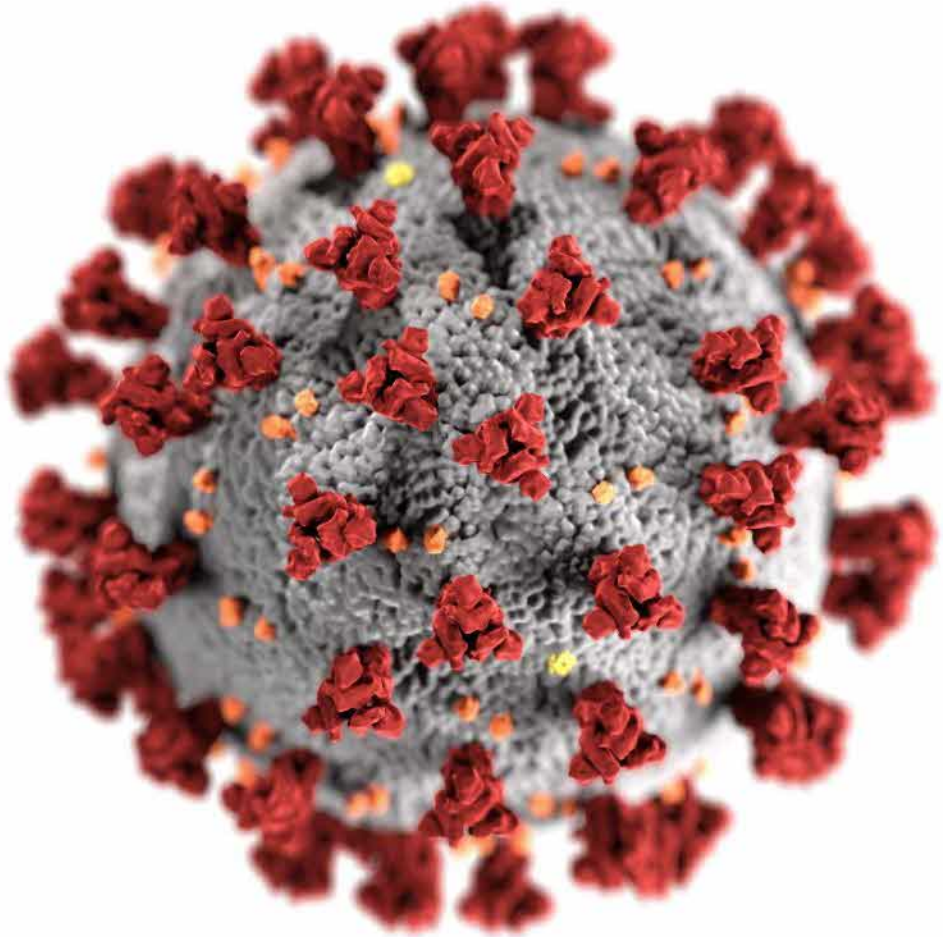
Benefits and risks after COVID-19 vaccine, by age group- males

For every million doses of vaccine given with US exposure risk and hospitalization rates from June 19, 2021





Data and clinical considerations for additional doses in immunocompromised people



Sara Oliver MD, MSPH
ACIP Meeting
July 22, 2021

cdc.gov/coronavirus

Outline

1) COVID-19 vaccine response among immunocompromised people

2) Response to an additional dose of COVID-19 vaccine among immunocompromised people

3) Frequently asked questions about vaccination of immunocompromised people

Additional doses in immunocompromised people

EUA= Emergency Use Authorization; BLA= Biologics License Application

Additional doses in immunocompromised people

EUA= Emergency Use Authorization; BLA= Biologics License Application

COVID-19 vaccine response in immunocompromised people:

What do we know now?

Immunocompromised people and SARS-CoV-2 infection

- Immunocompromised people comprise ~2.7% of U.S. adults[1]
  - Solid tumor and hematologic malignancies
  - Receipt of solid-organ or hematopoietic stem cell transplant
  - Severe primary immunodeficiencies
  - Persons living with HIV
  - Treatment with immunosuppressive medications such as cancer chemotherapeutic agents, TNF blockers, certain biologic agents (e.g., rituximab), and high-dose corticosteroids

1. Harpaz et al. Prevalence of Immunosuppression Among U.S. Adults, 2013. JAMA 2016

Immunocompromised people and SARS-CoV-2 infection

- More likely to get severely ill from COVID-19[1,2]
- Higher risk for:
  - Prolonged SARS-CoV-2 infection and shedding[3-7 14-16]
  - Viral evolution during infection and treatment (hospitalized patients)[3,6,8-10,14,17]
  - Low antibody/neutralization titers to SARS-CoV-2 variants[12]
- More likely to transmit SARS-CoV-2 to household contacts[11]
- More likely to have breakthrough infection:
  - **44%** of hospitalized breakthrough cases are immunocompromised people in US study[13]
  - **40%** of hospitalized breakthrough cases are immunocompromised people in Israeli study[18]

See reference slide at end

mRNA vaccine effectiveness (VE) studies among immunocompromised populations

- VE: 7-27 days after 2nd dose of Pfizer-BioNTech vaccine[1]
  - **71%** (CI 37-87%) among immunosuppressed* people vs. **90%** (CI 83-96%) overall: **SARS-CoV-2 infection**
  - **75%** (CI 44-88%) among immunosuppressed people vs. **94%** (CI 87-97%) overall: **symptomatic COVID-19**

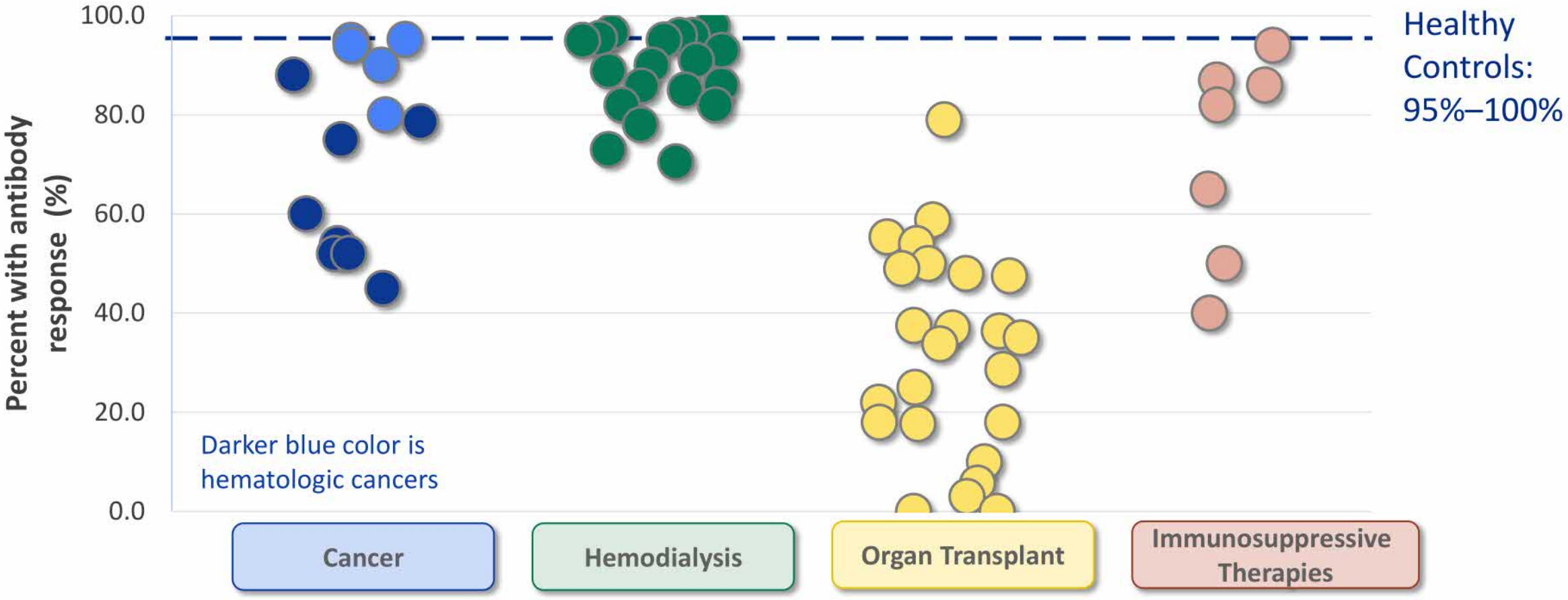
- VE: ≥7 days after 2nd dose of mRNA vaccine[2]
  - **80%** among people with inflammatory bowel disease on immunosuppressive meds: **SARS-CoV-2 infection**
  - VE of **25%** was noted after 1st dose of mRNA vaccine for **SARS-CoV-2 infection**

- VE: ≥14 days after 2nd dose of mRNA vaccine[3]
  - **59%** (CI 12-81%) among immunocompromised people vs. **91%** (CI 86-95%) without immunocompromise: **COVID-19 hospitalization**[3]

*Immunocompromised conditions (e.g., recipients of hematopoietic cell or solid organs transplant, patients under immunosuppressive therapy, asplenia, and chronic renal failure: advanced kidney disease, dialysis, or nephrotic syndrome)

1. Chodick et al. *Clinical Infectious Diseases*, ciab438, https://doi.org/10.1093/cid/ciab438; **2.** Khan et al. Gastroenterology (2021). https://www.gastrojournal.org/article/S0016-5085(21)03066-3/pdf; **3.** Tenforde et al. medRxiv preprint: https://doi.org/10.1101/2021.07.08.21259776

Percent of subjects with antibody response after two mRNA vaccine doses by immunocompromising condition and study (n=63)



- Studies that compared response after 1st and 2nd dose demonstrated poor response to dose 1
- Antibody measurement and threshold levels vary by study protocol

See reference list at end

Response to an additional dose of COVID-19 vaccine in immunocompromised people:

The emerging data

Comparing evidence 3rd mRNA COVID-19 vaccine dose in immunosuppressed people with seropositive response

Study	Patient Population	2nd Dose			3rd Dose Seronegative after 2nd dose		
		Sample Size	Seronegative N (%)	Seropositive N (%)	Sample Size	Seronegative N (%)	Seropositive N (%)
Kamar et al.	Recipients of solid-organ transplant	99	59 (60)	40 (40)	59	33 (56)	**26 (44)**
Werbel et al.*	Recipients of solid-organ transplant	30	24 (80)	6 (20)	24	16 (67)	**8 (33)**
Longlune et al.	Patients on hemodialysis	82	13 (16)	69 (84)	12	7 (58)	**5 (42)**
Maxime et al.	Patients on hemodialysis	106	66 (62)	40 (38)	12	6 (50)	**6 (50)**

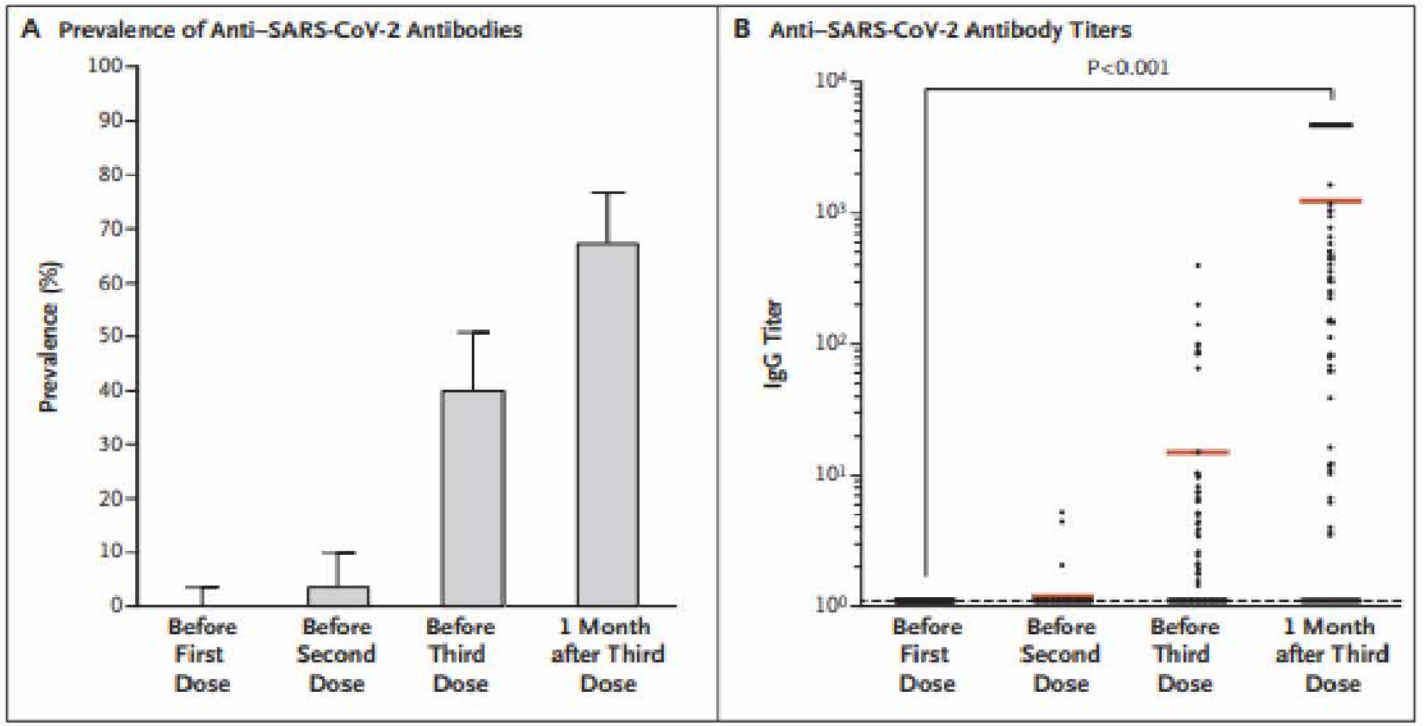
* Recipients received homologous mRNA prime followed by either a single Moderna, Pfizer, or Janssen boost

- Among those who had **no detectable antibody** response to an initial mRNA vaccine series,

33-50% developed an antibody response to an additional dose

See references list at end

Three doses of an mRNA COVID-19 vaccine in solid-organ transplant recipients

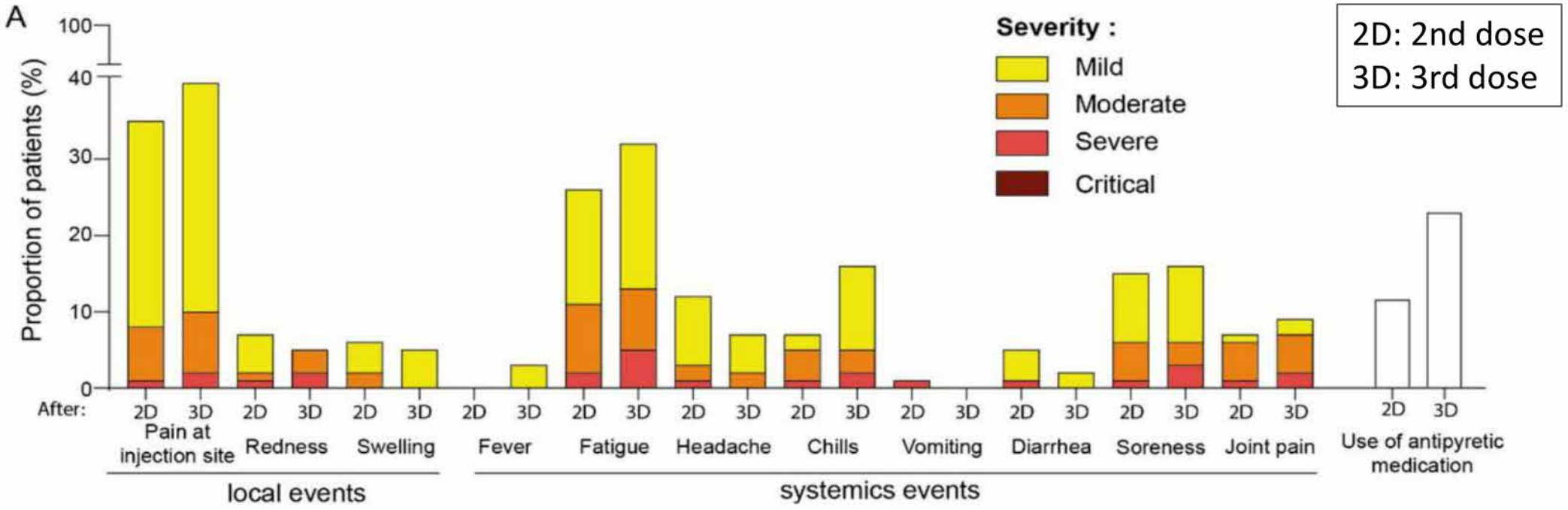


- No serious adverse events were reported after administration of the 3rd dose, and no acute rejection episodes occurred (n=99)

Kamar et al. (2021) NEJM Three Doses of an mRNA Covid-19 Vaccine in Solid-Organ Transplant Recipients (nejm.org)

Reactogenicity of 3rd mRNA vaccine dose in cohort of patients on hemodialysis (n=63*)

- No patients developed critical side effects requiring hospitalization
- Symptoms reported were consistent with previous doses and the intensity of the symptoms was mostly mild or moderate



*Sample included patients who had an optimal and suboptimal antibody response to primary mRNA series and chose to receive a 3rd dose

Maxime et al. (2021) medRxiv doi: https://doi.org/10.1101/2021.07.02.21259913

International policies on additional doses for immunocompromised people

- France[1] (Announced April 11, 2021)
  - 3rd dose 4 weeks after the 2nd dose for patients who are “severely immunocompromised”
  - Could be extended at a later date to include a larger immunocompromised population

- United Kingdom[2] (Announced July 1, 2021)
  - Proposal for an additional dose for immunocompromised people ≥16 years (among others), to be implemented between 6 September and 17 December 2021
  - Decision pending

- Israel[3] (Announced July 11, 2021)
  - People living with organ or stem cell transplants, blood cancer, autoimmune disease and treatment with specific immunosuppressive medications
  - People with breast, lung, or colon cancer do not qualify

1.dgs_urgent_n43_vaccination_modalites_d_administration_des_rappels.pdf (solidarites-sante.gouv.fr), 2. C1327-covid-19-vaccination-autumn-winter-phadvicease-3-planning.pdf
3.https://govextra.gov.il/media/30095/meeting-summary-15122020.pdf

Summary

- Immunocompromised people are at increased risk of poor outcomes from COVID-19
- Studies indicate a reduced antibody response in immunocompromised people following a primary vaccine series, compared to healthy vaccine recipients
- Emerging data suggest that an additional COVID-19 vaccine dose in immunocompromised people enhances antibody response and increases the proportion who respond
- In small studies, the reactogenicity of the 3rd dose of mRNA vaccine was similar to prior doses

Frequently asked questions about vaccination of immunocompromised people

Which immunocompromised groups should be considered for an additional dose as allowed by regulatory mechanisms?

- Conditions and treatments associated with *moderate to severe* immune compromise*
  - Active or recent treatment for solid tumor and hematologic malignancies
  - Receipt of solid-organ or recent hematopoietic stem cell transplant
  - Severe primary immunodeficiency
  - Advanced or untreated HIV infection
  - Treatment with immunosuppressive medications such as cancer chemotherapeutic agents, TNF blockers, certain biologic agents (e.g., rituximab), and high-dose corticosteroids
- Chronic conditions associated with *varying* degrees of immune deficit, such as asplenia and chronic renal disease*
- Different medical conditions and treatments can result in widely varying degrees of immunosuppression. A patient's clinical team is best able to assess the degree of altered immunocompetence and optimal timing of vaccination

*General Best Practice Guidelines for Immunization and CDC Yellow Book can be consulted for detailed information

Should immunocompromised people undergo antibody testing following COVID-19 vaccination?

- Utility of serologic testing or cellular immune testing to assess immune response to COVID-19 vaccination has not been established
- Exact correlation between antibody level and protection from COVID-19 remains unclear
- Commercial antibody and cellular immune testing may not be consistent across laboratories
- Serologic (antibody) testing or cellular immune testing outside of the context of research studies is **not recommended in the United States at this time**

Are there data to support mixed-dose series in immunocompromised people: for example, Janssen followed by mRNA COVID-19 vaccine?

- Studies from Europe have assessed heterologous primary series (AstraZeneca and Pfizer-BioNTech) in the general adult population and found immunogenicity to be at least equivalent to homologous series [1-5]
  - Large UK trial (Com-COV) found that one dose of AstraZeneca + one dose of Pfizer-BioNTech resulted in superior immunogenicity compared with two doses of AstraZeneca vaccine but lower antibodies than 2 doses of Pfizer-BioNTech; increase in systemic reactogenicity observed with heterologous schedules[5]
- Evidence is needed regarding the safety and immunogenicity of using a mixed-dose approach for Janssen (FDA-authorized adenoviral vector vaccine) + mRNA vaccine in immunocompromised people

1. Borobia et al. Reactogenicity and Immunogenicity of BNT162b2 in Subjects Having Received a First Dose of ChAdOx1s: Initial Results of a Randomized, Adaptive, Phase 2 Trial (CombiVacS). Available at SSRN: https://ssrn.com/abstract=3854768 **2**. Shaw et al. Heterologous prime-boost COVID-19 vaccination: initial reactogenicity data, ISSN 0140-6736, https://doi.org/10.1016/S0140-6736(21)01115-6. **3.** Hillus et al. Safety, reactogenicity, and immunogenicity of homologous and heterologous prime-boost immunization with ChAdOx1-nCoV19 and BNT162b2: a prospective cohort study. medRxiv; 2021. DOI: 10.1101/2021.05.19.21257334. **4.** Schmidt et al. medRxiv preprint (June 15 2021): https://doi.org/10.1101/2021.06.13.21258859 Click to add text **5.** Liu et al. Lancet preprint (June 25, 2021): http://dx.doi.org/10.2139/ssrn.3874014

Following COVID-19 vaccination, what infection prevention measures should immunocompromised people maintain?

- Immunocompromised people should be counseled about potential for reduced immune responses to COVID-19 vaccination and need to follow prevention measures*
  - Wear a mask
  - Stay 6 feet apart from others they don't live with
  - Avoid crowds and poorly ventilated indoor spaces until advised otherwise by their healthcare provider
- Close contacts of immunocompromised people should be encouraged to be vaccinated against COVID-19

* https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html

Is there a role for monoclonal antibody use in immunocompromised people?

- Monoclonal antibodies are currently authorized by FDA for emergency use in persons with SARS-CoV-2 infection who are at high risk for progressing to severe COVID-19 and/or hospitalization

- Monoclonal antibodies are not yet authorized for SARS-CoV-2 infection prevention

https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap#dashboard

What are the implications of the Emergency Use Authorizations (EUAs) for the COVID-19 vaccines, with respect to considerations for an additional dose in immunocompromised persons?

- FDA has authorized mRNA vaccines as a 2-dose series and Janssen COVID-19 vaccine as a single dose
- At this time, we are not aware of data submitted to FDA to support an amendment to the EUA for this population
- CDC/ACIP will closely monitor any updates to data and regulatory mechanisms

EUA= Emergency Use Authorization; BLA= Biologics License Application

Additional doses in immunocompromised people

Review data:
Assess safety, immunogenicity, and implementation

FDA

Regulatory allowance:
EUA amendment would allow recommendations under EUA

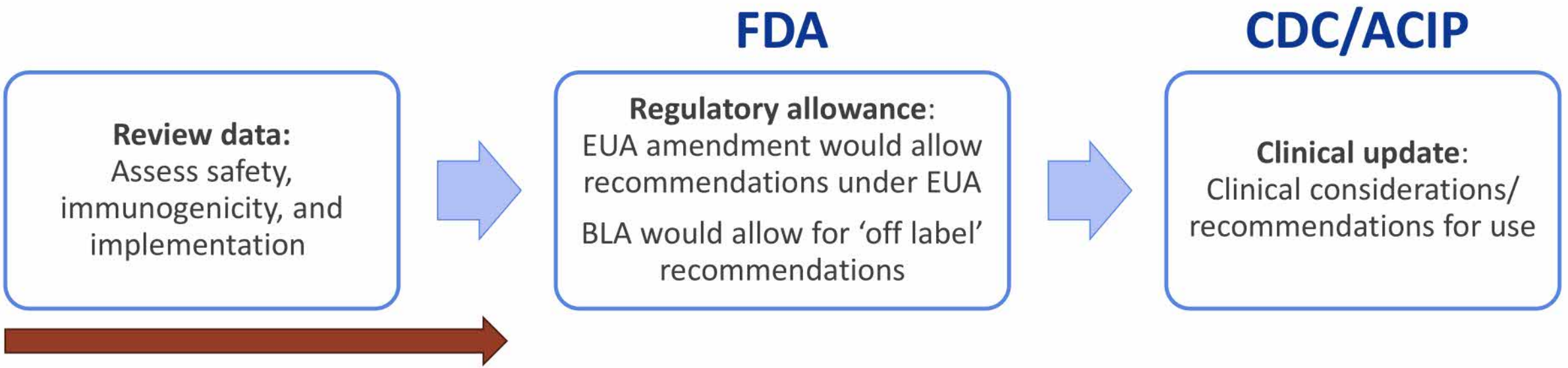
BLA would allow for 'off label' recommendations

CDC/ACIP

Clinical update:
Clinical considerations/ recommendations for use

EUA= Emergency Use Authorization; BLA= Biologics License Application

Additional doses in immunocompromised people



Now:

Immunocompromised people should continue to **follow infection prevention measures**:

Wear a mask, stay 6 feet apart from others, avoid crowds and poorly ventilated spaces

Close contacts (≥12 years) of immunocompromised people should be **vaccinated against COVID-19**

Early treatment with **monoclonal antibodies** may be beneficial in this population

EUA= Emergency Use Authorization; BLA= Biologics License Application

Additional COVID-19 vaccine dose in immunocompromised people: Next steps

- Assess additional studies of safety and immunogenicity of additional dose in immunocompromised people
- Assess additional studies and expert opinion regarding the subpopulations of immunocompromised people who may benefit most from an additional dose
- Determine acceptable intervals and mix and match schedules
- Await regulatory allowance (e.g. FDA amendment of EUA or BLA) for an additional dose of COVID-19 vaccine

EUA= Emergency Use Authorization; BLA= Biologics License Application

Questions for ACIP

Questions for ACIP

1. What additional data do ACIP need to inform these discussions?

2. Thoughts on the focus of “moderate to severe” immunocompromised populations, once authorized/approved?

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- Vaccine Task Force
- Epi Task Force
- Respiratory Viruses Branch

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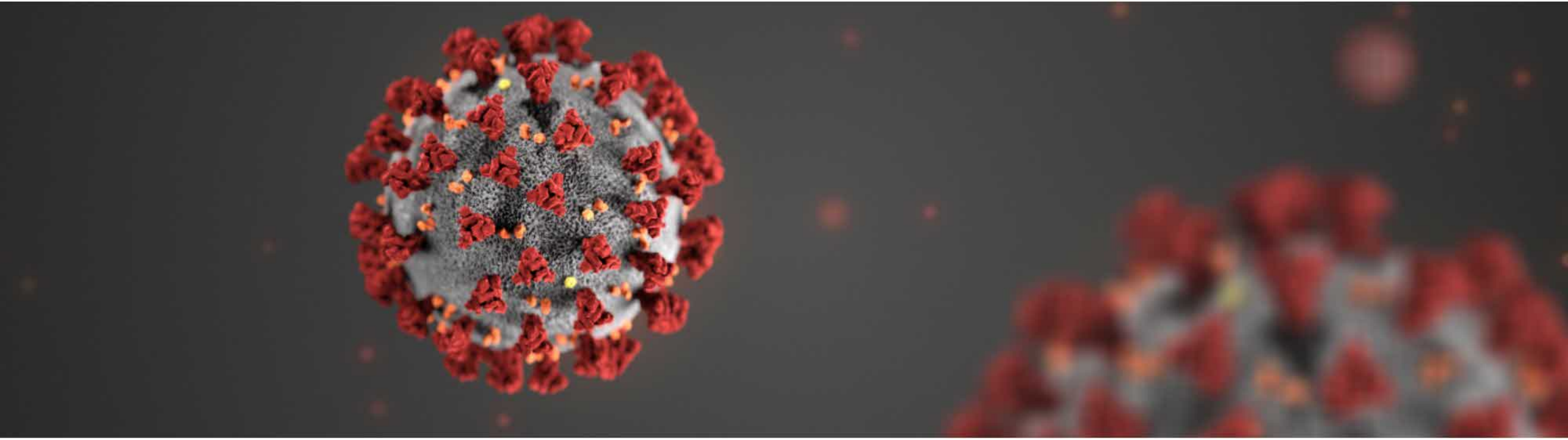

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

From: (b)(4) (b)(4) (b)(
Sent: Thu, 22 Jul 2021 12:48:07 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD); (b)(4) (b)(4)
Subject: RE: contacts on the 'speaker line' tomorrow

Thank you so much Sara, we appreciate it!

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Thursday, July 22, 2021 8:20 AM
To: (b)(4) (b)(4) (b (b)(4)
Cc: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>; (b)(4) (b)(4)
(b)(4)
Subject: [EXTERNAL] RE: contacts on the 'speaker line' tomorrow

(b)(and (b)(4)

Thanks for this. In addition, I've attached relevant slides for today as an FYI. Please treat the slides as confidential- but attached are the Benefit/risk slides (05) and the Immunocompromised slides (07).

Thanks-

Sara

From: (b)(4) (b)(4) ((b)(4)
Sent: Wednesday, July 21, 2021 7:57 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>; (b)(4) (b)(4)
(b)(4)
Subject: RE: contacts on the 'speaker line' tomorrow

Dear Sara,
The following people can be available on the speakers line for questions from the ACIP tomorrow

(b)(4)

(b)((b)(4) (b)(4) and myself
(b)(4)
(b)(4)
(b)(4)

Thank you for the opportunity to a (b)(4)
Warm regards,
(b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Wednesday, July 21, 2021 11:19 AM
To: (b)(4) (b)(4) (b) (b)(4) (b)(4) (b)(4) (b)(4)
Cc: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>
Subject: [EXTERNAL] contacts on the 'speaker line' tomorrow

(b)(4) and (b)(4

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Thanks!
Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: (b)(4) (b)(4) (b)
Sent: Wed, 21 Jul 2021 16:32:50 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); (b)(4) (b)(4)
Cc: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD)
Subject: RE: contacts on the 'speaker line' tomorrow

Of course Sara, we totally understand and sorry we certainly didn't mean to pile on to everything else you have on your plate!!!!
Best,
(b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Wednesday, July 21, 2021 12:03 PM
To: (b)(4) (b)(4) (b) (b)(4) (b)(4) (b)(4) (b)(4)
Cc: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>
Subject: [EXTERNAL] RE: contacts on the 'speaker line' tomorrow

(b)(4)

Thanks!
Acknowledge the VE email. In all honestly- our team hasn't had the bandwidth this week to tackle broader booster discussions. But I know that CDC has several contacts within the Israeli MOH so I think we feel comfortable with our ability to review their VE data. Once we survive this week, I will definitely be reaching out on all things BLA and boosters.

Thanks!

Sara

From: (b)(4) (b)(4) (b) (b)(4)
Sent: Wednesday, July 21, 2021 11:57 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>; (b)(4) (b)(4) (b)(4)
Cc: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>
Subject: RE: contacts on the 'speaker line' tomorrow

Hi Sara,
Thank you for this message, I am checking with internal colleagues and will get back to you on who can be available to be on the line tomorrow.
Best,
(b)(4) and (b)(

PS just checking that you saw my email yesterday afternoon on more recent VE data coming in from Israel

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Wednesday, July 21, 2021 11:19 AM
To: (b)(4) (b)(4) (b) (b)(4) (b)(4) (b)(4) (b)(4)
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Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Thu, 22 Jul 2021 12:20:28 +0000
To: (b)(4) (b)(4) (b
Cc: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD); (b)(4) (b)(4)
Subject: RE: contacts on the 'speaker line' tomorrow
Attachments: 05 COVID Rosenblum July 2021.pdf, 07 COVID Oliver July 2021.pdf

(b)(and (b)(4)

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(b)(4)
Subject: RE: contacts on the 'speaker line' tomorrow

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Warm regards,
(b)(4) and (b)(

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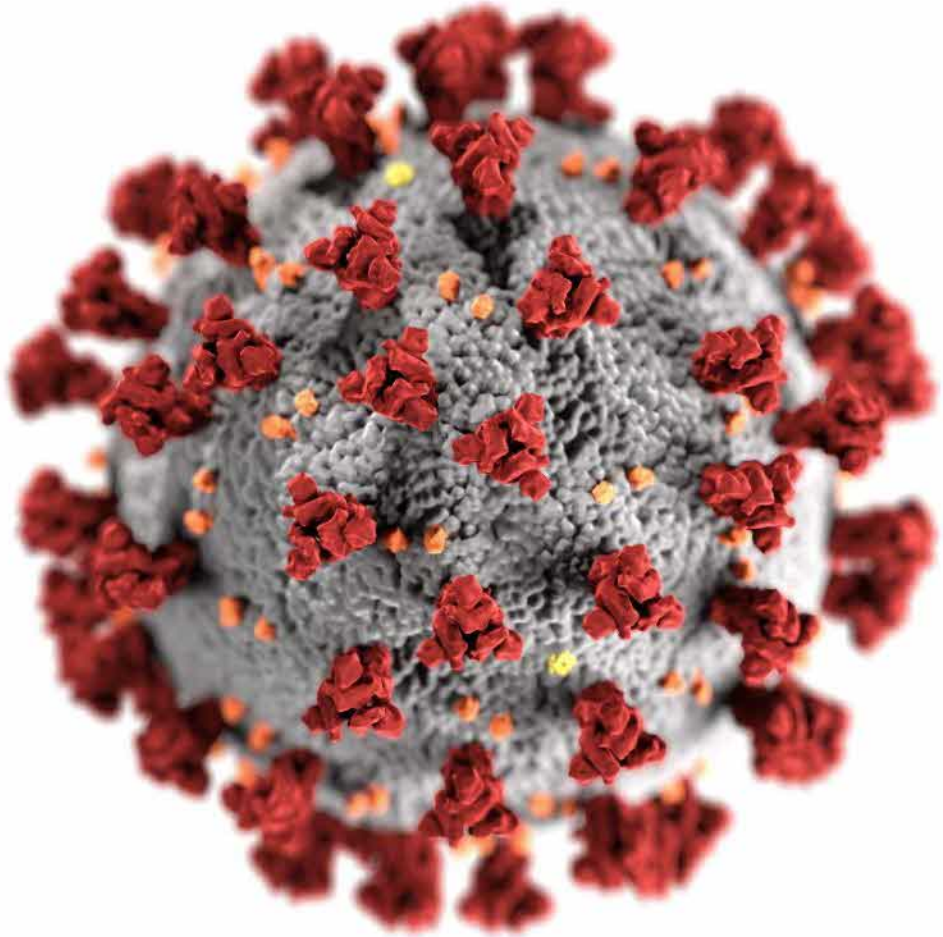
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

COVID-19 Vaccines in Adults: Benefit-Risk Discussion



Hannah Rosenblum, MD

ACIP Meeting

July 22, 2021

cdc.gov/coronavirus

Current COVID-19 vaccine policy

- Today's discussion will focus on the benefits and harms of COVID-19 vaccines in adults
- Three COVID-19 vaccines are recommended for persons aged 18 years and older in the United States under FDA's Emergency Use Authorization

Benefits and risks by vaccine, age and sex in adults

Benefits of COVID-19 Janssen and mRNA vaccines in adults

Risk after COVID-19 Janssen and mRNA vaccines in adults

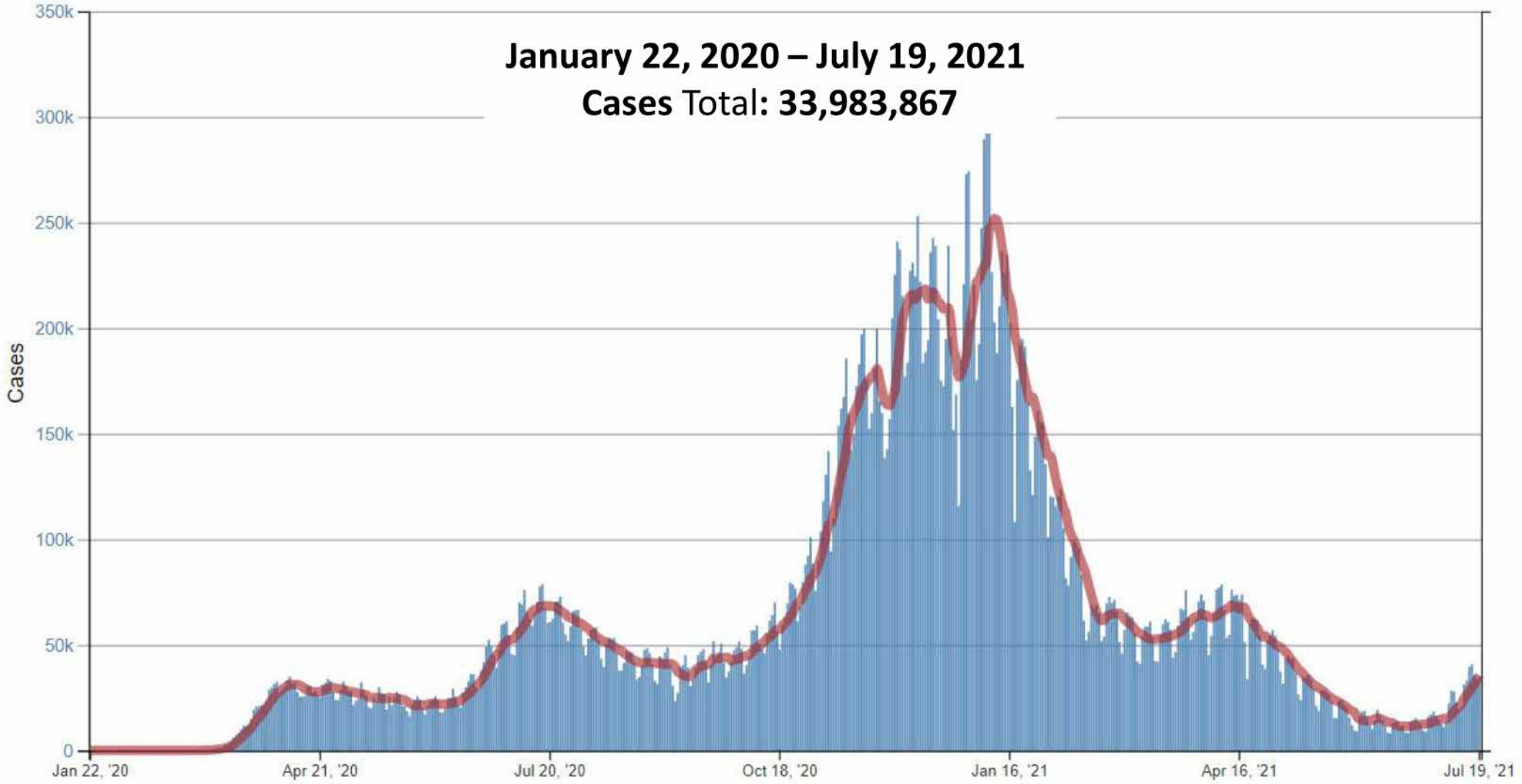
COVID-19 vaccines in adults: Benefit-risk discussion

- Public health problem
  - Recent COVID-19 epidemiology in adults
  - Adverse events reported after vaccination
    - Guillain-Barre Syndrome (GBS)
    - Thrombosis with Thrombocytopenia Syndrome (TTS)
    - Myocarditis

- Benefit/Risk assessment
  - Benefits of Janssen vaccine
  - Risk of GBS after Janssen vaccine
  - Risk of TTS after Janssen vaccine

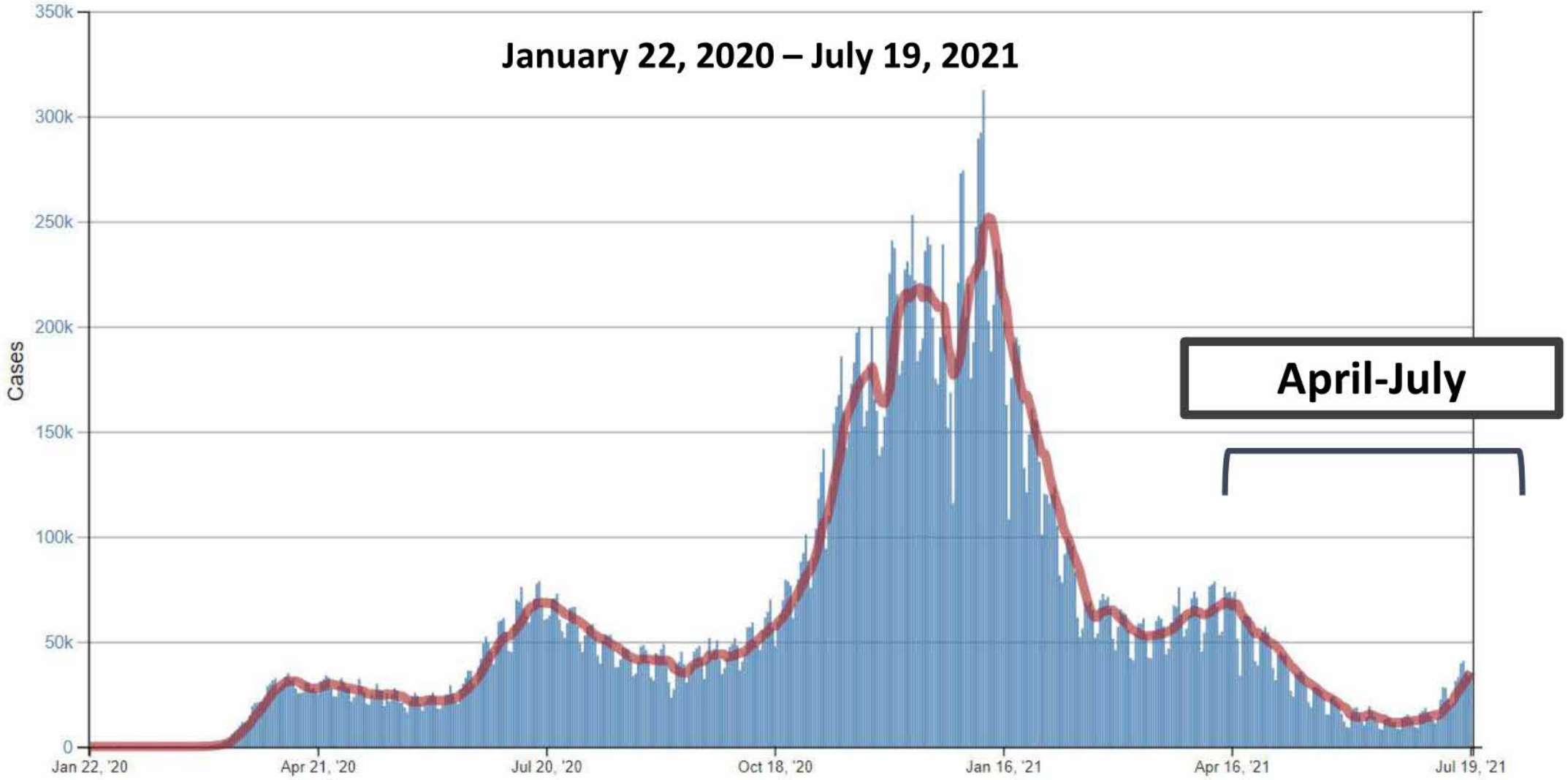
  - Benefits of mRNA vaccines
  - Risk of myocarditis after mRNA vaccines

Trends in number of U.S. COVID-19 cases reported to CDC



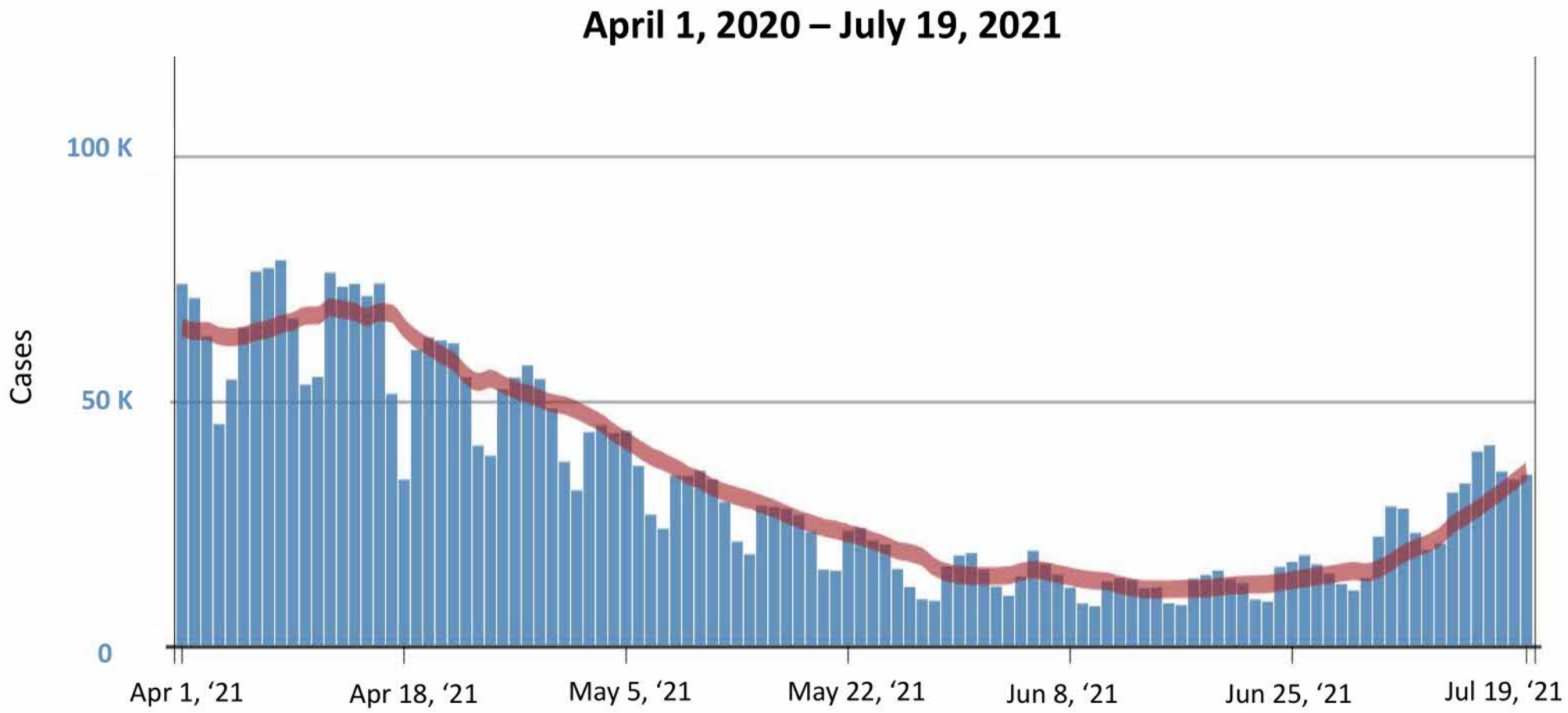
https://covid.cdc.gov/covid-data-tracker/#trends_dailytrendscases; from July 21, 2021

Trends in number of U.S. COVID-19 cases reported to CDC



https://covid.cdc.gov/covid-data-tracker/#trends_dailytrendscases; from July 21, 2021

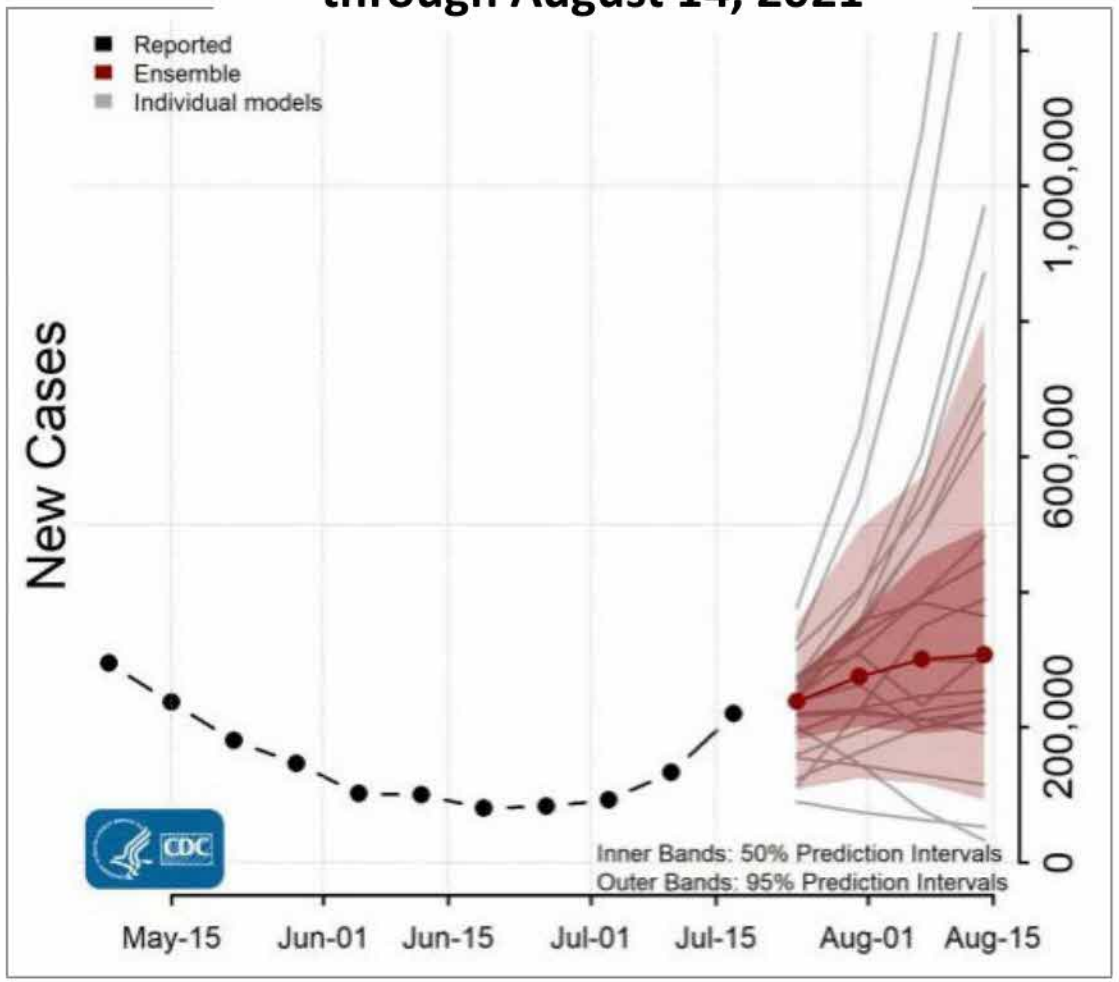
Recent trends in number of U.S. COVID-19 cases



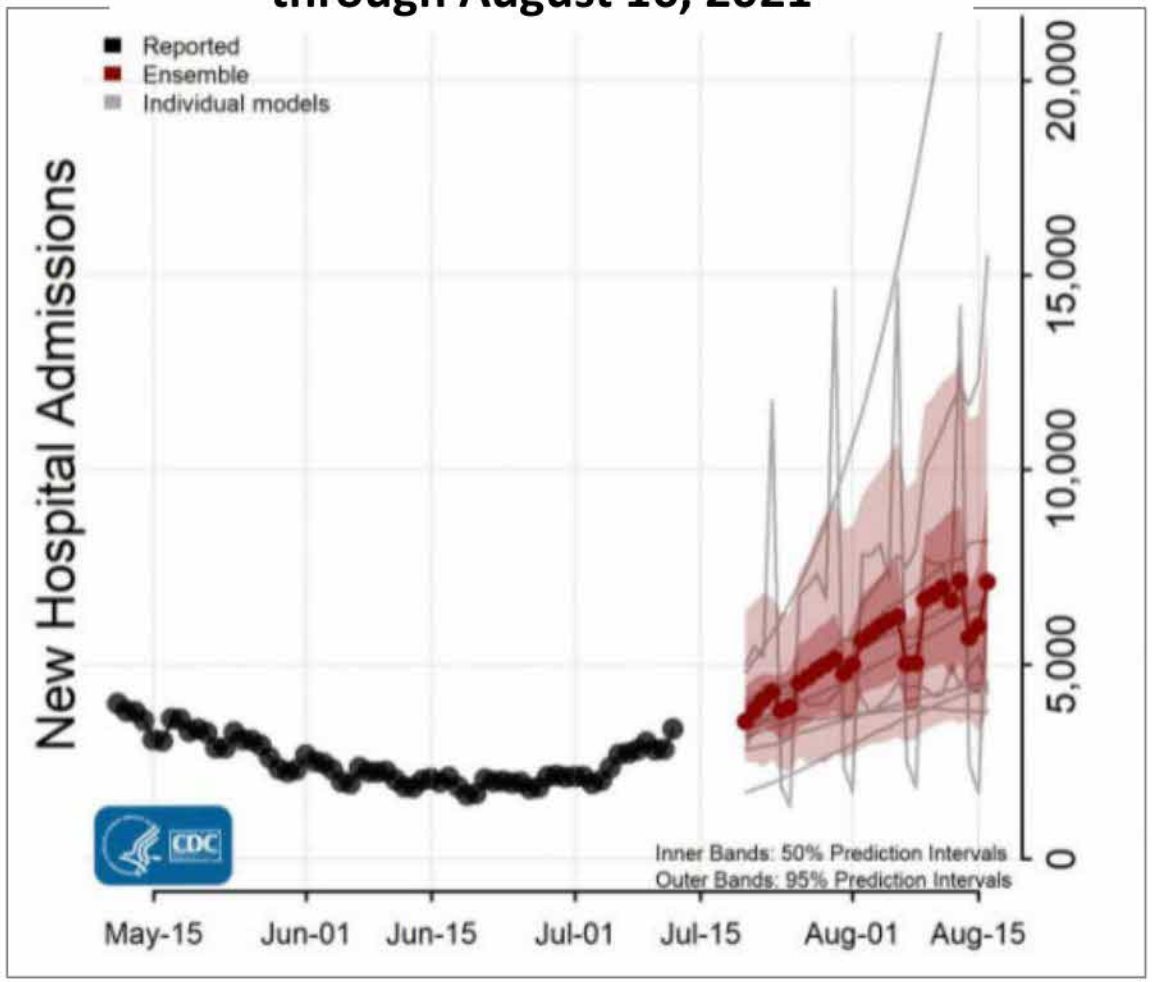
https://covid.cdc.gov/covid-data-tracker/#trends_dailytrendscases; from July 21, 2021

Forecast of cases and hospitalizations for the next four weeks

New COVID-19 cases forecasted through August 14, 2021



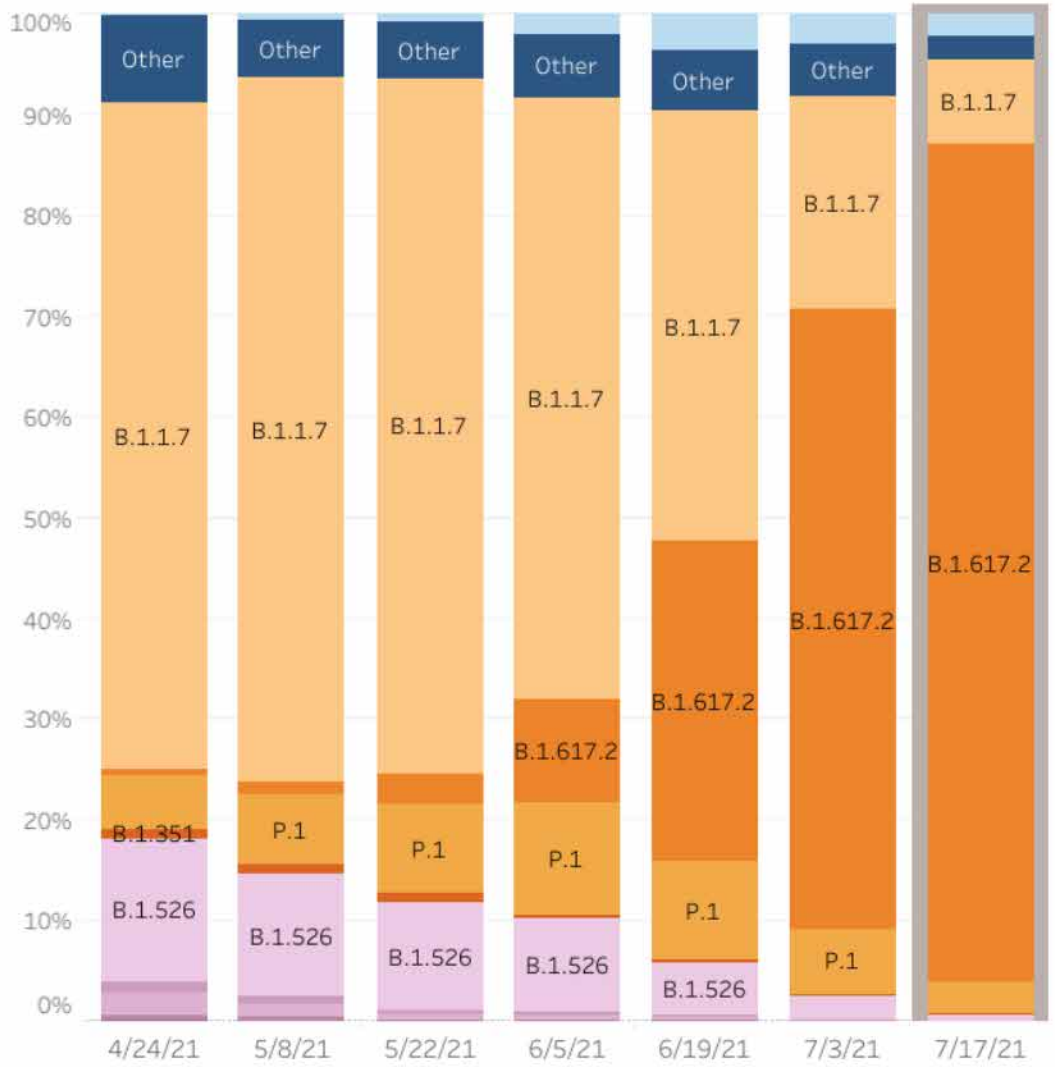
COVID-19 hospitalizations forecasted through August 16, 2021



https://www.cdc.gov/coronavirus/2019-ncov/science/forecasting/forecasts-cases.html; https://www.cdc.gov/coronavirus/2019-ncov/science/forecasting/hospitalizations-forecasts.html

SARS-CoV-2 variants circulating in the United States

April 11 – July 17, 2021



Alpha (B.1.1.7): 8%

Delta (B.1.617.2): 83.2%

Gamma (P.1): 3%

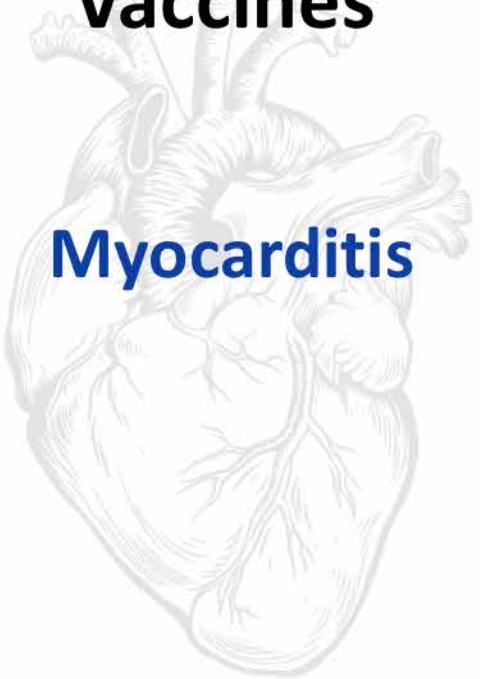
https://covid.cdc.gov/covid-data-tracker/#variant-proportions

Rare serious adverse events reported after COVID-19 vaccination

Janssen vaccine

- Thrombosis with thrombocytopenia syndrome (TTS)
- Guillain-Barré syndrome (GBS)

mRNA vaccines



- Myocarditis

Summary

- After a period of decline, COVID-19 cases and hospitalizations have begun to increase in recent weeks.
  - Variants continue to spread; Delta variant now found in >80% of cases in the United States

- Rare events have been observed after COVID-19 vaccination:
  - Janssen vaccine: TTS & GBS
  - mRNA vaccine: myocarditis

Benefits and Harms of Janssen COVID-19 Vaccine

Methods for assessment of benefit-risk balance – Janssen vaccine

Benefits

- Expected protection provided per 1 million Janssen vaccine doses by age/sex calculated using:
  - Most recent case incidence, COVID-NET hospitalization & severity data (through June 19th)
  - VE (90%) for hospitalization
  - VE (66%) for COVID-19 symptomatic cases
  - 120-day period

VE= Vaccine efficacy

Methods for assessment of benefit-risk balance – Janssen vaccine

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- Expected protection provided per 1 million Janssen vaccine doses by age/sex calculated using:
  - Most recent case incidence, COVID-NET hospitalization & severity data (through June 19th)
  - VE (90%) for hospitalization
  - VE (66%) for COVID-19 symptomatic cases
  - 120-day period

Potential harms

- Estimated cases of **GBS** per 1 million Janssen vaccine doses, by age/sex using cases from VAERS through June 30, 2021
- Estimated cases of **TTS** per 1 million Janssen vaccine doses, by age/sex using cases reported to VAERS through July 8, 2021

VE= Vaccine efficacy; GBS = Guillain-Barré syndrome; TTS= Thrombosis with thrombocytopenia syndrome; VAERS = Vaccine Adverse Event Reporting System

Benefits of the Janssen COVID-19 vaccine

- The clinical trial demonstrated efficacy against symptomatic, laboratory-confirmed COVID-19. Overall efficacy was **66%**
- Against **severe** outcomes:
  - Vaccine efficacy against COVID-19-associated **hospitalization**: **93%**
  - VE against **deaths** due to COVID-19**: 100%**
- Persistence of antibody response & activity demonstrated against a variety of variants*

*Durable humoral and cellular immune responses months after Ad26.COV2.S vaccination NEJM https://www.nejm.org/doi/full/10.1056/NEJMc2108829?query=featured_home

Potential Harms of the Janssen COVID-19 vaccine:
Guillain-Barré Syndrome

- 12.6 million vaccine doses administered* and 98 GBS cases as of June 30, 2021

	Females n= 37			Males n=61		
Age group	Cases	Doses admin	Reporting rate†	Cases	Doses admin	Reporting rate†
18-29 years old	1	1,037,996	1.0 per million	3	1,258,963	2.4 per million
30-49 years old	13	1,957,663	6.6 per million	18	2,407,430	7.5 per million
50-64 years old	14	1,888,715	7.4 per million	**33**	**2,115,411**	**15.6 per million**
65+ years old	9	1,037,996	8.7 per million	7	932,764	7.5 per million

* Source of doses administered: FDA, through June 30, 2021; Some age- and sex-specific dose administered data were imputed

† Reporting rate = GBS cases per 1 million Janssen COVID-19 vaccine doses administered

GBS = Guillain-Barré Syndrome

Potential Harms of the Janssen COVID-19 vaccine:
Thrombosis with Thrombocytopenia Syndrome

- 12.5 million vaccine doses administered* and 38 confirmed TTS cases as of July 8, 2021

	Females n= 28			Males n=10		
Age group	Cases	Doses admin	Reporting rate†	Cases	Doses admin	Reporting rate†
18-29 years old	4	946,358	4.2 per million	3	1,281,479	2.3 per million
30-49 years old	**17**	**1,934,574**	**8.8 per million**	4	2,440,773	1.6 per million
50-64 years old	7	1,865,372	3.8 per million	3	2,130,473	1.4 per million
65+ years old	0	1,028,190	0.0 per million	0	943,098	0.0 per million

* Source of doses administered: https://covid.cdc.gov/covid-data-tracker/#vaccinations through July 8, 2021; Some age- and sex-specific doses administered data were imputed

† Reporting rate = TTS cases per 1 million Janssen COVID-19 vaccine doses administered

TTS=Thrombosis with Thrombocytopenia Syndrome

Estimated predicted COVID-19 cases prevented vs. GBS cases for every million Janssen vaccinations over 120 days

Females 18–29 Years

8,900 COVID-19 cases prevented

700 hospitalizations prevented

50 ICU admissions prevented

5 deaths prevented

1 GBS case

Males 18–29 Years

6,600 COVID-19 cases prevented

300 hospitalizations prevented

60 ICU admissions prevented

3 deaths prevented

2 GBS cases

Hospitalizations, ICU admissions and deaths based on data for week of June 19, 2021; GBS = Guillain-Barré Syndrome

Estimated predicted COVID-19 cases prevented vs. GBS & TTS cases for every million Janssen vaccinations over 120 days

Females 18–29 Years

8,900 COVID-19 cases prevented

700 hospitalizations prevented

50 ICU admissions prevented

5 deaths prevented

1 GBS case
4-5 TTS cases

Males 18–29 Years

6,600 COVID-19 cases prevented

300 hospitalizations prevented

60 ICU admissions prevented

3 deaths prevented

2 GBS cases
2-3 TTS cases

Hospitalizations, ICU admissions and deaths based on data for week of June 19, 2021; GBS = Guillain-Barré Syndrome; TTS= Thrombosis with Thrombocytopenia Syndrome

Estimated predicted COVID-19 cases prevented vs. GBS & TTS cases for every million Janssen vaccinations over 120 days

Females 30–49 Years

10,100 COVID-19 cases prevented

900 hospitalizations prevented

140 ICU admissions prevented

20 deaths prevented

6-7 GBS cases
8-10 TTS cases

Males 30–49 Years

7,600 COVID-19 cases prevented

650 hospitalizations prevented

150 ICU admissions prevented

25 deaths prevented

7-8 GBS cases
1-2 TTS cases

Hospitalizations, ICU admissions and deaths based on data for week of June 19, 2021; GBS = Guillain-Barré Syndrome; TTS= Thrombosis with Thrombocytopenia Syndrome

Estimated predicted COVID-19 cases prevented vs. GBS & TTS cases for every million Janssen vaccinations over 120 days

Females 50–64 Years

12,100 COVID-19 cases prevented

1,600 hospitalizations prevented

350 ICU admissions prevented

120 deaths prevented

7-8 GBS cases
3-4 TTS cases

Males 50–64 Years

10,100 COVID-19 cases prevented

1,800 hospitalizations prevented

480 ICU admissions prevented

140 deaths prevented

14-17 GBS cases
1-2 TTS cases

Hospitalizations, ICU admissions and deaths based on data for week of June 19, 2021; GBS = Guillain-Barré Syndrome; TTS= Thrombosis with Thrombocytopenia Syndrome

Estimated predicted COVID-19 cases prevented vs. GBS & TTS cases for every million Janssen vaccinations over 120 days

Females 65+ Years

29,000 COVID-19 cases prevented

5,900 hospitalizations prevented

1,250 ICU admissions prevented

840 deaths prevented

8-10 GBS cases
0 TTS cases

Males 65+ Years

36,600 COVID-19 cases prevented

11,800 hospitalizations prevented

3,300 ICU admissions prevented

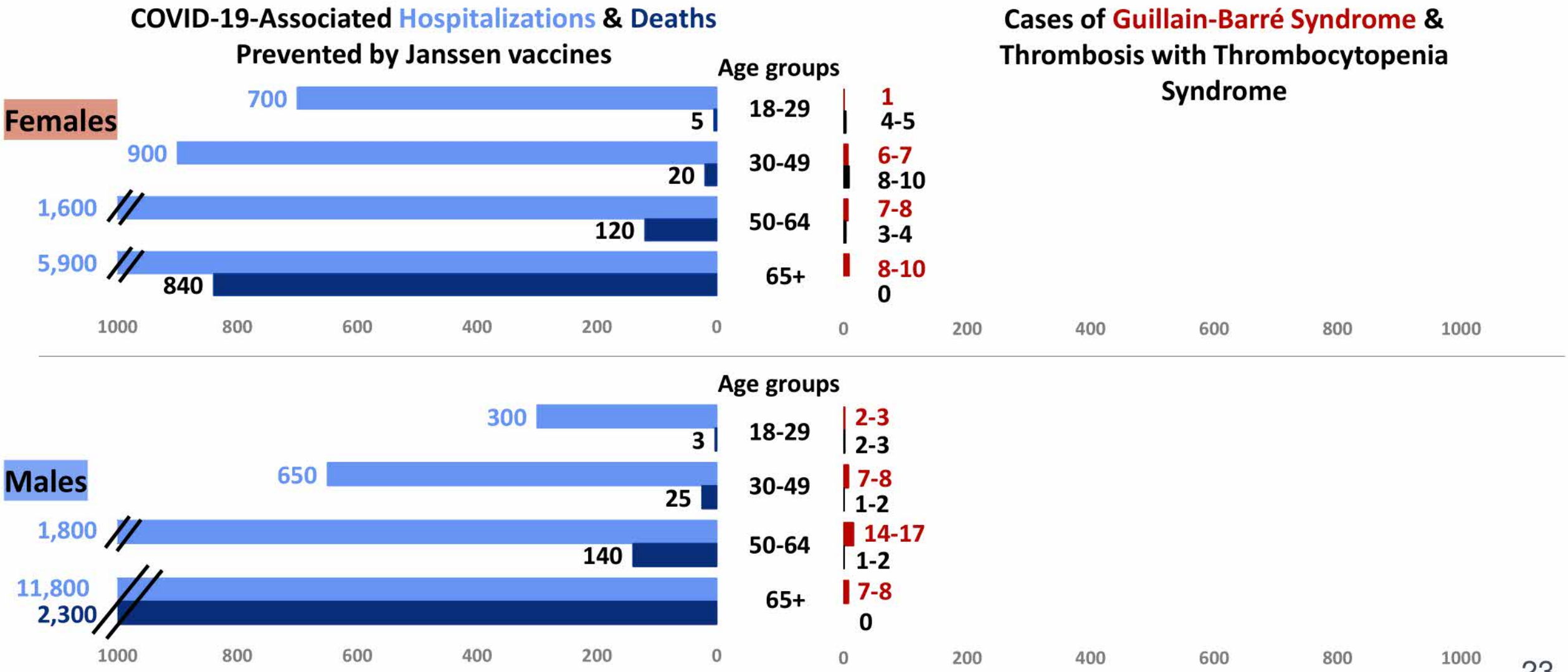
2,300 deaths prevented

7-8 GBS cases
0 TTS cases

Hospitalizations, ICU admissions and deaths based on data for week of June 19, 2021; GBS = Guillain-Barré Syndrome; TTS= Thrombosis with Thrombocytopenia Syndrome

Benefits and risks after Janssen vaccine, by age group & sex

For every million doses of vaccine given with US exposure risk and hospitalization rates from June 19, 2021



Benefits and Harms of mRNA COVID-19 Vaccines

Methods for assessment of benefit-risk balance – mRNA COVID-19 vaccines in adults

Benefits

- Expected protection provided per 1 million mRNA vaccine doses using:
  - Most recent case incidence, COVID-NET hospitalization and severity data (through June 19th)
  - VE for hospitalization (95%)
  - VE for COVID-19 symptomatic cases (95%)
  - 120-day period

Potential harms

- Estimated cases of **myocarditis** per 1 million second doses of mRNA COVID-19 vaccine, by age/sex using data from VAERS through June 30, 2021

VE= Vaccine efficacy; VAERS = Vaccine Adverse Event Reporting System

Benefits of mRNA vaccines

- Clinical trial data demonstrated high efficacy against symptomatic, laboratory-confirmed COVID-19 among adults with both mRNA vaccines (Pfizer-BioNTech and Moderna)
  - Overall efficacy was **94-95%**
  - Vaccine efficacy against COVID-19 associated hospitalization was **89-100%**

- Persistence of antibody response & activity demonstrated against a variety of variants*

Polack FP et al. N Engl J Med 2020; DOI: 10.1056/NEJMoa2034577; Frenck RW et al. N Engl J Med 2021; DOI: 10.1056/NEJMoa2107456;
Baden LR et al. N Engl J Med 2021; DOI: 10.1056/NEJMoa2035389
*https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html

Potential Harms of the mRNA COVID-19 vaccines:
Myocarditis

- 141 million 2nd mRNA vaccine doses administered* and 497 myocarditis cases as of June 30, 2021 in age 18+

	Females n= 105			Males n= 392		
Age group	**Cases**	**Doses admin**	**Reporting rate†**	**Cases***	**Doses admin**	**Reporting rate†**
18-29 years old§	34	10,491,212	3.2 per million	**248**	**10,212,647**	**24.3 per million**
30-49 years old	38	20,875,708	1.8 per million	117	20,154,577	5.8 per million
50-64 years old	23	19,714,915	1.2 per million	15	18,514,388	0.8 per million
65+ years old	10	22,274,470	0.4 per million	12	19,518,324	0.6 per million

*Source of doses administered: https://covid.cdc.gov/covid-data-tracker/#vaccinations; some age- and sex-specific doses administered data were imputed

†Reporting rate = myocarditis cases per 1 million mRNA COVID-19 mRNA second vaccine doses administered

§Myocarditis cases in 18-29-year-olds are confirmed cases meeting CDC's case definition

Estimated predicted COVID-19 cases prevented vs. myocarditis cases for every million mRNA vaccinations over 120 days

Females 18-29 Years

12,800 COVID-19 cases prevented

750 hospitalizations prevented

50 ICU admissions prevented

5 deaths prevented

3-4 myocarditis cases

Males 18-29 Years

9,600 COVID-19 cases prevented

300 hospitalizations prevented

60 ICU admissions prevented

3 deaths prevented

22-27 myocarditis cases

Hospitalizations, ICU admissions and deaths based on data for week of June 19, 2021

Estimated predicted COVID-19 cases prevented vs. myocarditis cases for every million mRNA vaccinations over 120 days

Females 30-49 Years

14,600 COVID-19 cases prevented

950 hospitalizations prevented

140 ICU admissions prevented

20 deaths prevented

1-2 myocarditis cases

Males 30-49 Years

11,000 COVID-19 cases prevented

700 hospitalizations prevented

160 ICU admissions prevented

25 deaths prevented

5-6 myocarditis cases

Hospitalizations, ICU admissions and deaths based on data for week of June 19, 2021

Estimated predicted COVID-19 cases prevented vs. myocarditis cases for every million mRNA vaccinations over 120 days

Females 50-64 Years

17,500 COVID-19 cases prevented

1,700 hospitalizations prevented

375 ICU admissions prevented

125 deaths prevented

1 myocarditis case

Males 50-64 Years

14,700 COVID-19 cases prevented

1,900 hospitalizations prevented

500 ICU admissions prevented

150 deaths prevented

1 myocarditis case

Hospitalizations, ICU admissions and deaths based on data for week of June 19, 2021

Estimated predicted COVID-19 cases prevented vs. myocarditis cases for every million mRNA vaccinations over 120 days

Females 65+ Years

32,000 COVID-19 cases prevented

6,200 hospitalizations prevented

1,300 ICU admissions prevented

900 deaths prevented

<1 myocarditis case

Males 65+ Years

52,700 COVID-19 cases prevented

12,500 hospitalizations prevented

3,500 ICU admissions prevented

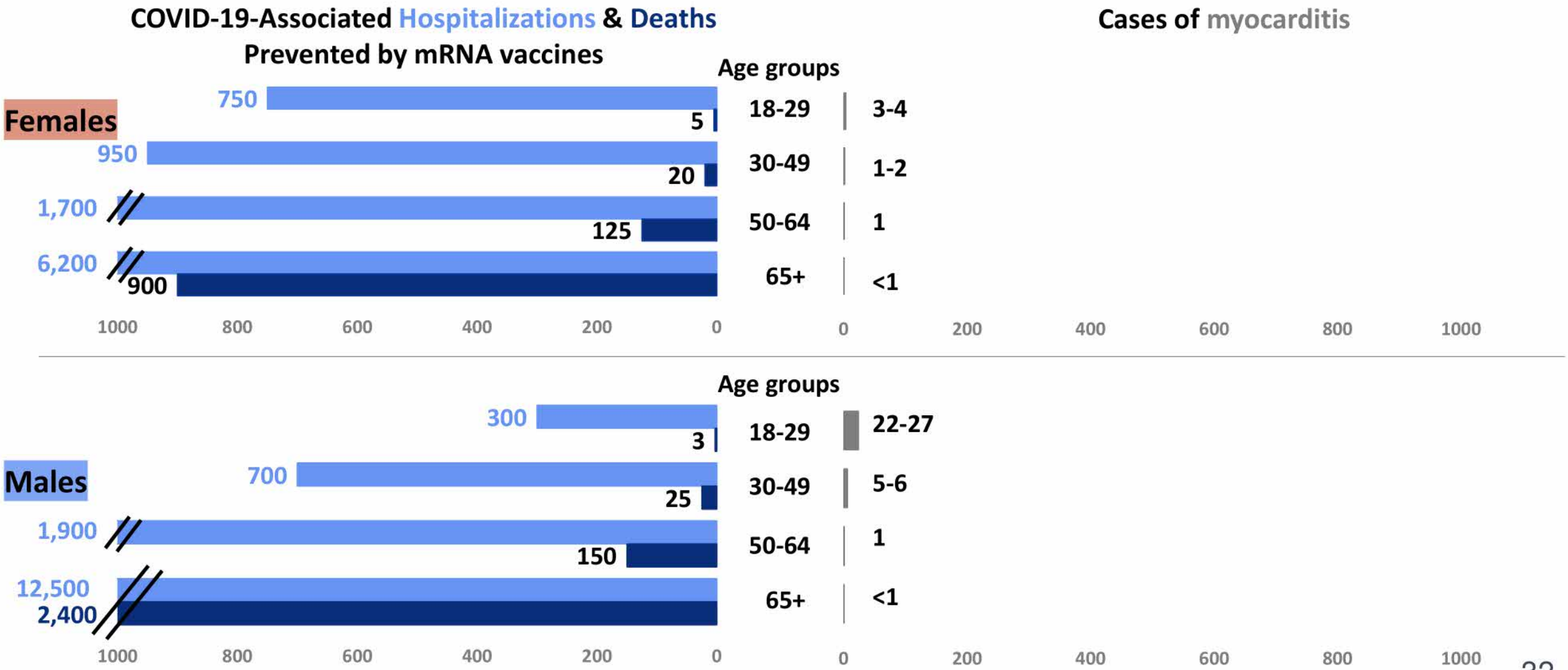
2,400 deaths prevented

<1 myocarditis case

Hospitalizations, ICU admissions and deaths based on data for week of June 19, 2021

Benefits and risks after mRNA vaccine, by age group & sex

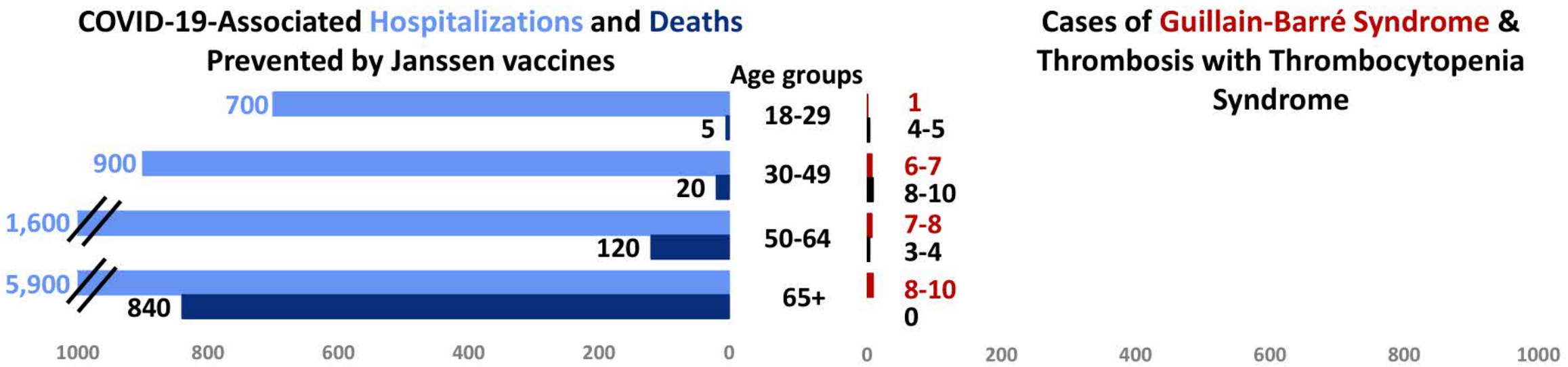
For every million doses of vaccine given with US exposure risk and hospitalization rates from June 19, 2021

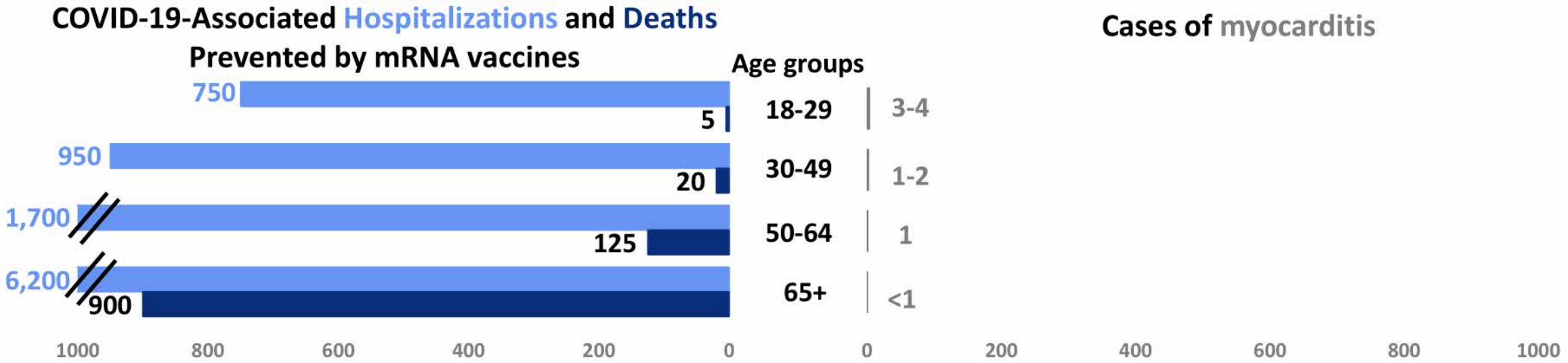


Summary

Benefits and risks after COVID-19 vaccine, by age group- females

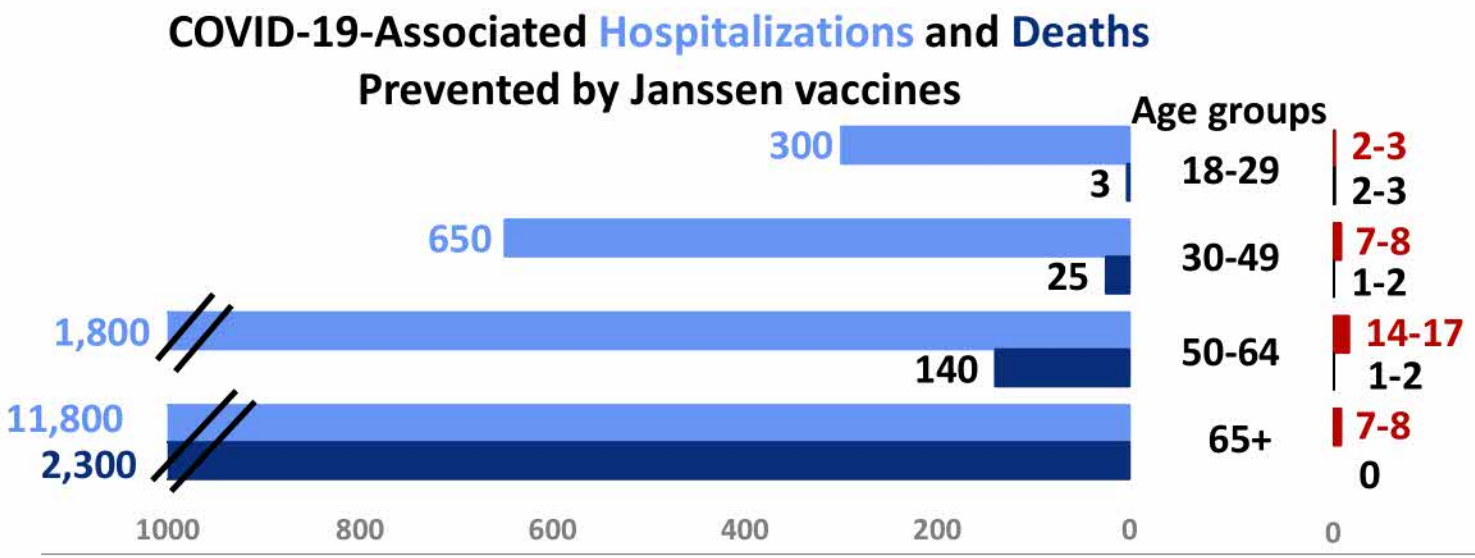
For every million doses of vaccine given with US exposure risk and hospitalization rates from June 19, 2021

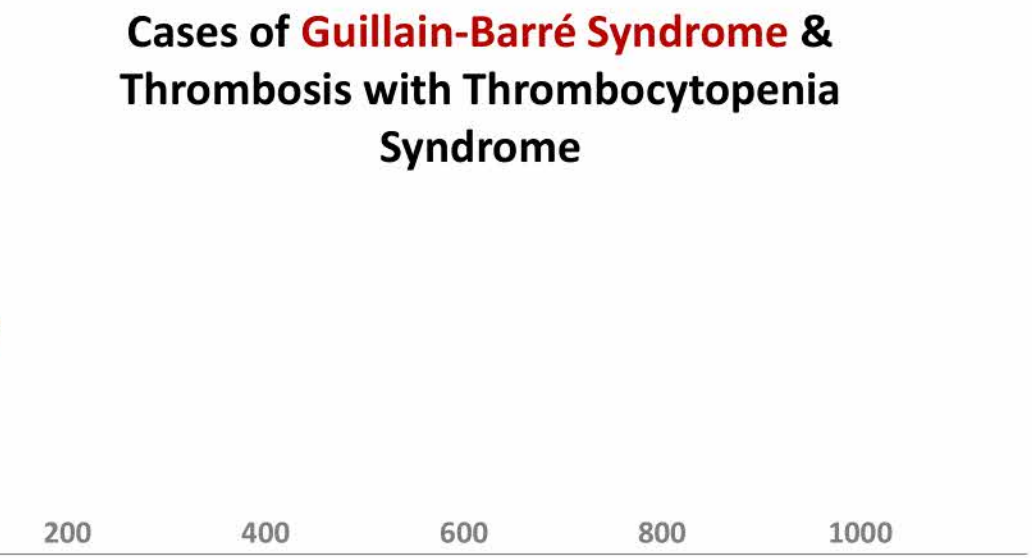


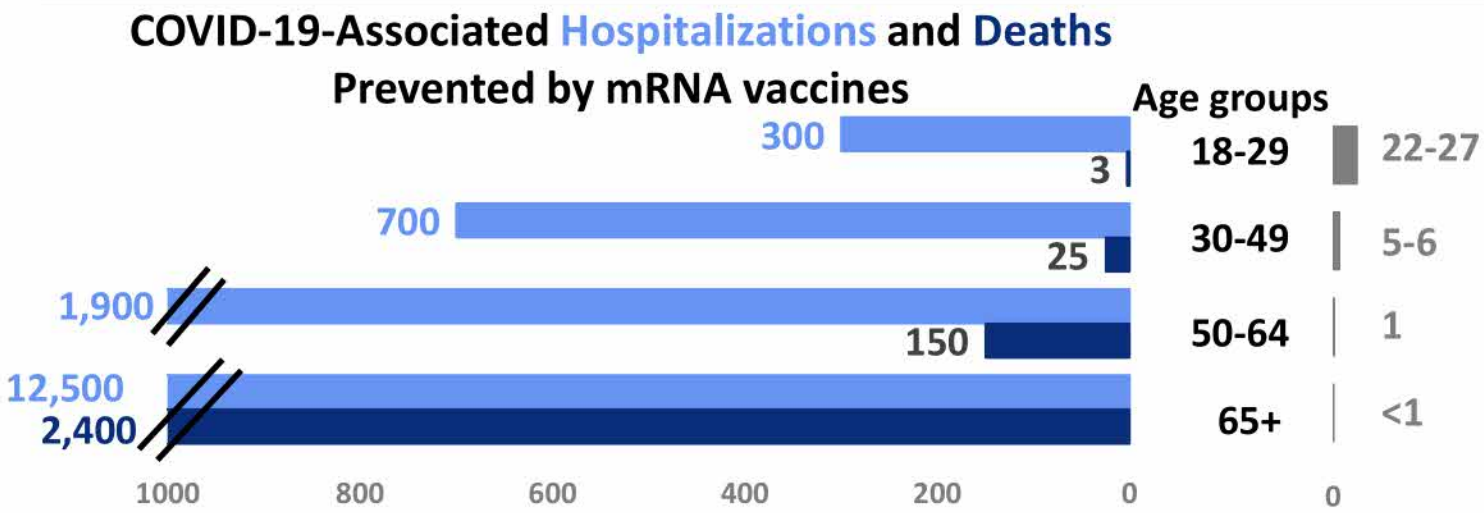


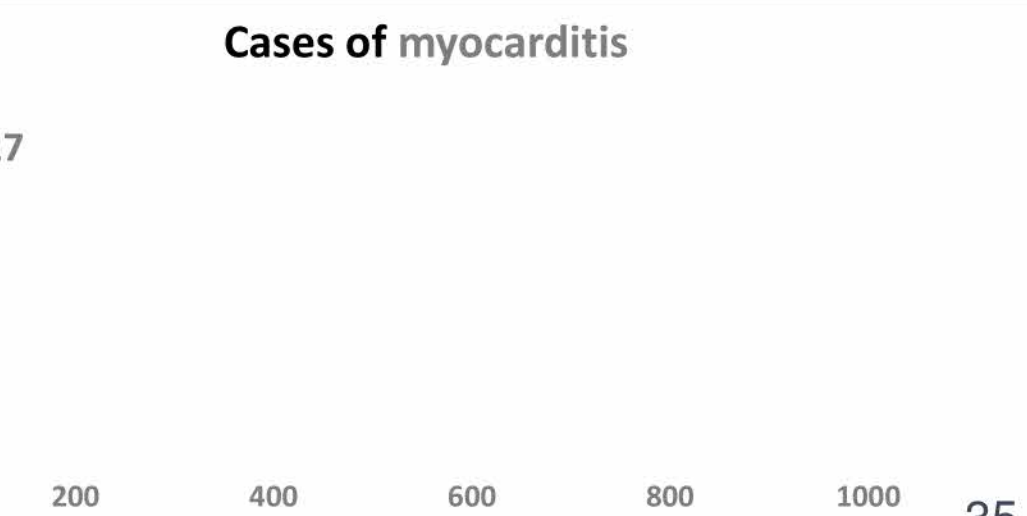
Benefits and risks after COVID-19 vaccine, by age group- males

For every million doses of vaccine given with US exposure risk and hospitalization rates from June 19, 2021









Benefits and risks after COVID-19 vaccine, by age group & sex

For every million doses of vaccine given with US exposure risk and hospitalization rates from June 19, 2021

Age	Janssen COVID-19 vaccine					mRNA COVID-19 vaccines			
	Prevented COVID-19 Outcomes			GBS Cases	TTS Cases	Prevented COVID-19 Outcomes			Myocarditis Cases
	Hospitalization	ICU	Death			Hospitalization	ICU	Death	
FEMALES									
18-29 years	700	50	5	1	4-5	750	50	5	3-4
30-49 years	900	140	20	6-7	8-10	950	140	20	1-2
50-64 years	1600	350	120	7-8	3-4	1,700	375	125	1
65+ years	5,900	1250	840	8-10	0	6,200	1300	900	<1
MALES									
18-29 years	300	60	3	2	2-3	300	60	3	22-27
30-49 years	650	150	25	7-8	1-2	700	160	25	5-6
50-64 years	1,800	480	140	14-17	1-2	1,900	500	150	1
65+ years	11,800	3300	2300	7-8	0	12,500	3500	2400	<1

Potential harms reported overall after COVID-19 vaccination

Janssen vaccine

Thrombosis with thrombocytopenia syndrome:

3.0 cases per million doses among adults

Guillain-Barré syndrome:

7.8 cases per million doses among adults

mRNA vaccines

Myocarditis:

3.5 cases per million doses among adults

- Risk for each potential harm varies by age and by sex

Limitations of benefit-risk estimates

- Benefits of vaccination likely even greater than shown
  - Model uses current case estimates; does not account for underreporting or rising case counts
  - Benefits are estimated over 120 days following vaccination, but protection likely lasts longer
  - Does not account for post-COVID-19 conditions

- Some hospitalizations (COVID-NET) may be related to diagnoses other than COVID-19
- Vaccine efficacy from clinical trials rather than real-world data
- Crude numbers of potential harms were used for some estimates

Benefit-risk interpretation and summary

- An assessment of the individual benefits and individual risks of vaccination is an important tool to help inform vaccination policy

- **This assessment demonstrates that the benefits of COVID-19 vaccination far outweigh the potential risks**

- The relative balance of benefits-risks varies by age/sex

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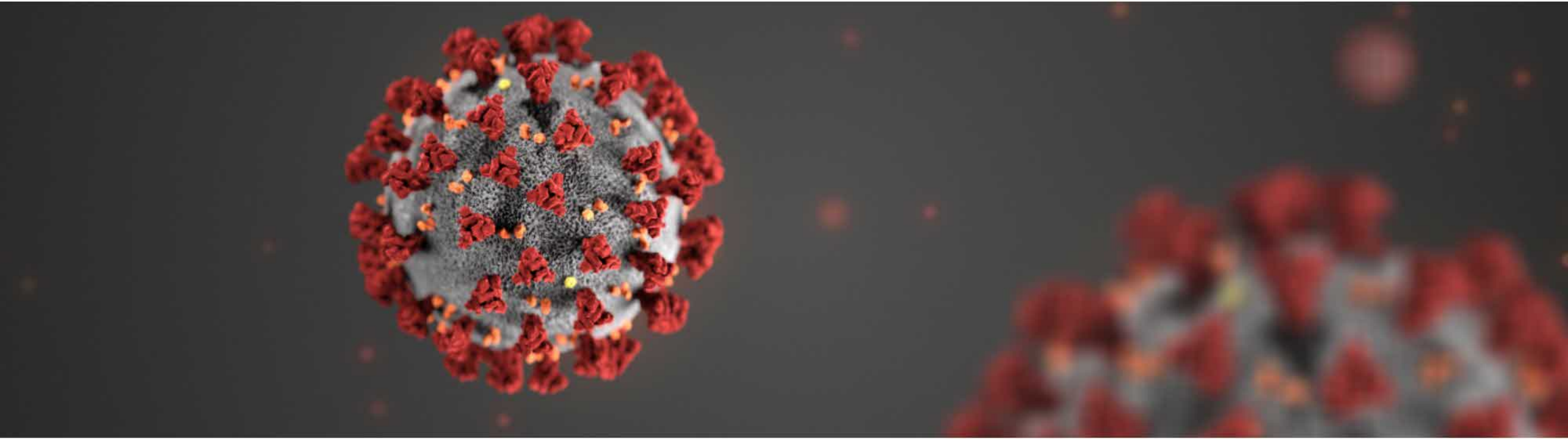
- Vaccine Task Force



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Thank you

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Extra slides

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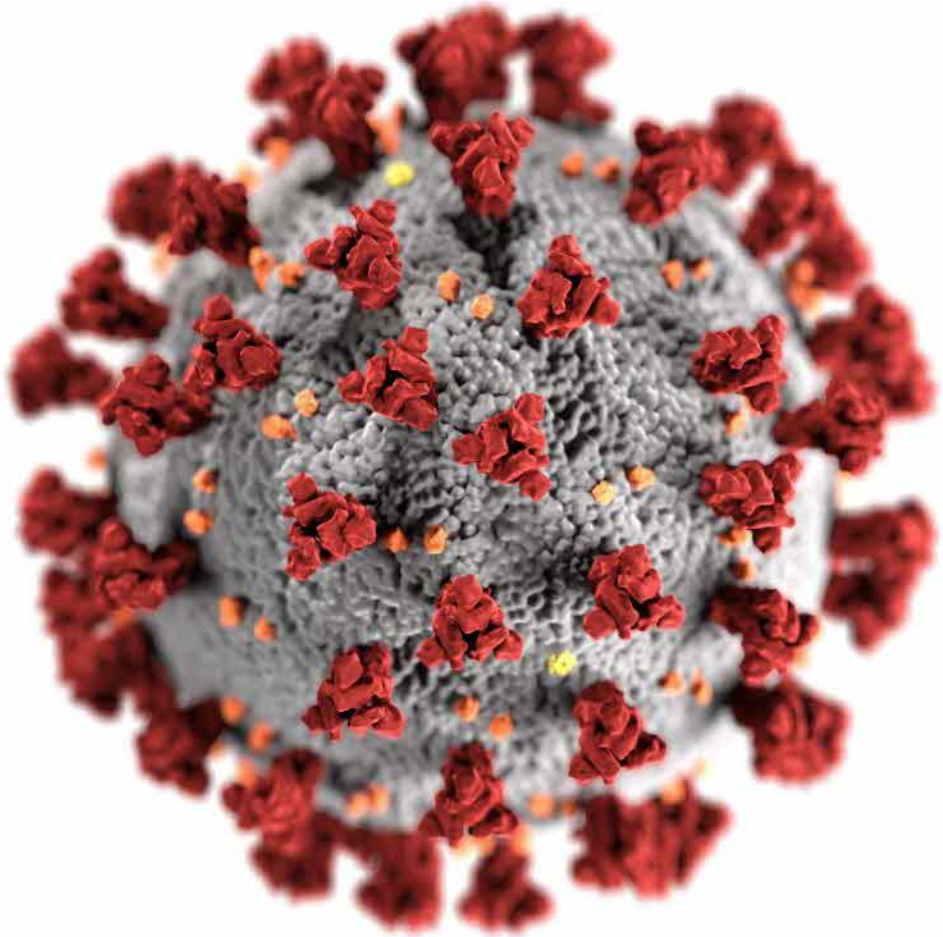
Data and clinical considerations for additional doses in immunocompromised people



Sara Oliver MD, MSPH
ACIP Meeting
July 22, 2021

cdc.gov/coronavirus

Outline

1) COVID-19 vaccine response among immunocompromised people

2) Response to an additional dose of COVID-19 vaccine among immunocompromised people

3) Frequently asked questions about vaccination of immunocompromised people

Additional doses in immunocompromised people

EUA= Emergency Use Authorization; BLA= Biologics License Application

Additional doses in immunocompromised people

EUA= Emergency Use Authorization; BLA= Biologics License Application

COVID-19 vaccine response in immunocompromised people:

What do we know now?

Immunocompromised people and SARS-CoV-2 infection

- Immunocompromised people comprise ~2.7% of U.S. adults[1]
  - Solid tumor and hematologic malignancies
  - Receipt of solid-organ or hematopoietic stem cell transplant
  - Severe primary immunodeficiencies
  - Persons living with HIV
  - Treatment with immunosuppressive medications such as cancer chemotherapeutic agents, TNF blockers, certain biologic agents (e.g., rituximab), and high-dose corticosteroids

1. Harpaz et al. Prevalence of Immunosuppression Among U.S. Adults, 2013. JAMA 2016

Immunocompromised people and SARS-CoV-2 infection

- More likely to get severely ill from COVID-19[1,2]
- Higher risk for:
  - Prolonged SARS-CoV-2 infection and shedding[3-7 14-16]
  - Viral evolution during infection and treatment (hospitalized patients)[3,6,8-10,14,17]
  - Low antibody/neutralization titers to SARS-CoV-2 variants[12]
- More likely to transmit SARS-CoV-2 to household contacts[11]
- More likely to have breakthrough infection:
  - **44%** of hospitalized breakthrough cases are immunocompromised people in US study[13]
  - **40%** of hospitalized breakthrough cases are immunocompromised people in Israeli study[18]

See reference slide at end

mRNA vaccine effectiveness (VE) studies among immunocompromised populations

- VE: 7-27 days after 2nd dose of Pfizer-BioNTech vaccine[1]
  - **71%** (CI 37-87%) among immunosuppressed* people vs. **90%** (CI 83-96%) overall: **SARS-CoV-2 infection**
  - **75%** (CI 44-88%) among immunosuppressed people vs. **94%** (CI 87-97%) overall: **symptomatic COVID-19**

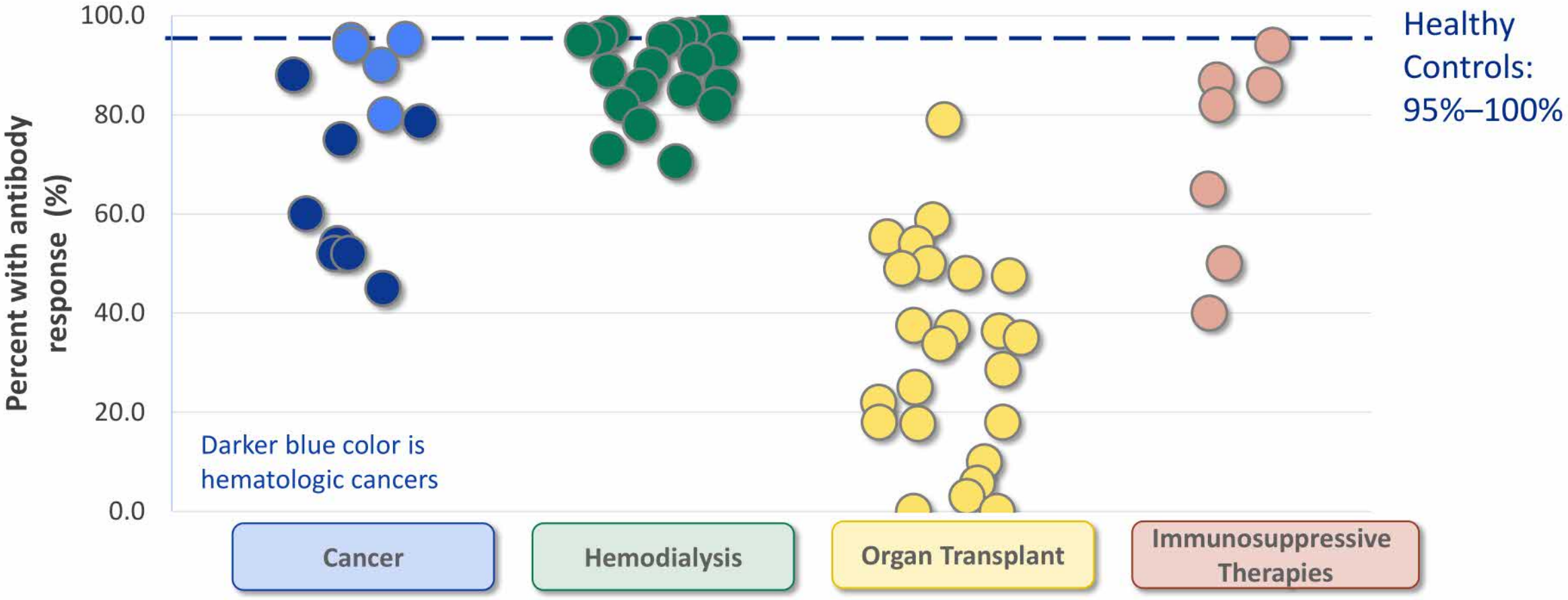
- VE: ≥7 days after 2nd dose of mRNA vaccine[2]
  - **80%** among people with inflammatory bowel disease on immunosuppressive meds: **SARS-CoV-2 infection**
  - VE of **25%** was noted after 1st dose of mRNA vaccine for **SARS-CoV-2 infection**

- VE: ≥14 days after 2nd dose of mRNA vaccine[3]
  - **59%** (CI 12-81%) among immunocompromised people vs. **91%** (CI 86-95%) without immunocompromise: **COVID-19 hospitalization**[3]

*Immunocompromised conditions (e.g., recipients of hematopoietic cell or solid organs transplant, patients under immunosuppressive therapy, asplenia, and chronic renal failure: advanced kidney disease, dialysis, or nephrotic syndrome)

1. Chodick et al. *Clinical Infectious Diseases*, ciab438, https://doi.org/10.1093/cid/ciab438; **2.** Khan et al. Gastroenterology (2021). https://www.gastrojournal.org/article/S0016-5085(21)03066-3/pdf; **3.** Tenforde et al. medRxiv preprint: https://doi.org/10.1101/2021.07.08.21259776

Percent of subjects with antibody response after two mRNA vaccine doses by immunocompromising condition and study (n=63)



- Studies that compared response after 1st and 2nd dose demonstrated poor response to dose 1
- Antibody measurement and threshold levels vary by study protocol

See reference list at end

Response to an additional dose of COVID-19 vaccine in immunocompromised people:

The emerging data

Comparing evidence 3rd mRNA COVID-19 vaccine dose in immunosuppressed people with seropositive response

Study	Patient Population	2nd Dose			3rd Dose Seronegative after 2nd dose		
		Sample Size	Seronegative N (%)	Seropositive N (%)	Sample Size	Seronegative N (%)	Seropositive N (%)
Kamar et al.	Recipients of solid-organ transplant	99	59 (60)	40 (40)	59	33 (56)	**26 (44)**
Werbel et al.*	Recipients of solid-organ transplant	30	24 (80)	6 (20)	24	16 (67)	**8 (33)**
Longlune et al.	Patients on hemodialysis	82	13 (16)	69 (84)	12	7 (58)	**5 (42)**
Maxime et al.	Patients on hemodialysis	106	66 (62)	40 (38)	12	6 (50)	**6 (50)**

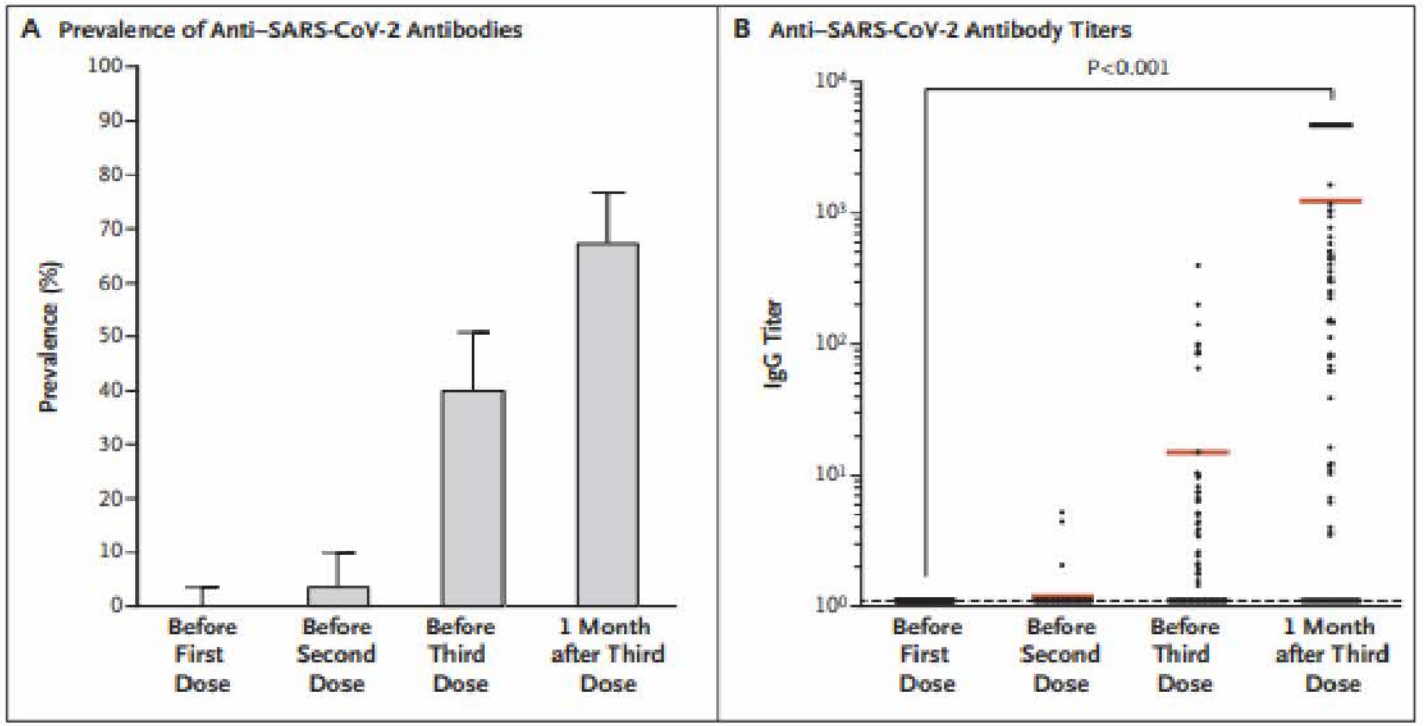
* Recipients received homologous mRNA prime followed by either a single Moderna, Pfizer, or Janssen boost

- Among those who had **no detectable antibody** response to an initial mRNA vaccine series,

33-50% developed an antibody response to an additional dose

See references list at end

Three doses of an mRNA COVID-19 vaccine in solid-organ transplant recipients

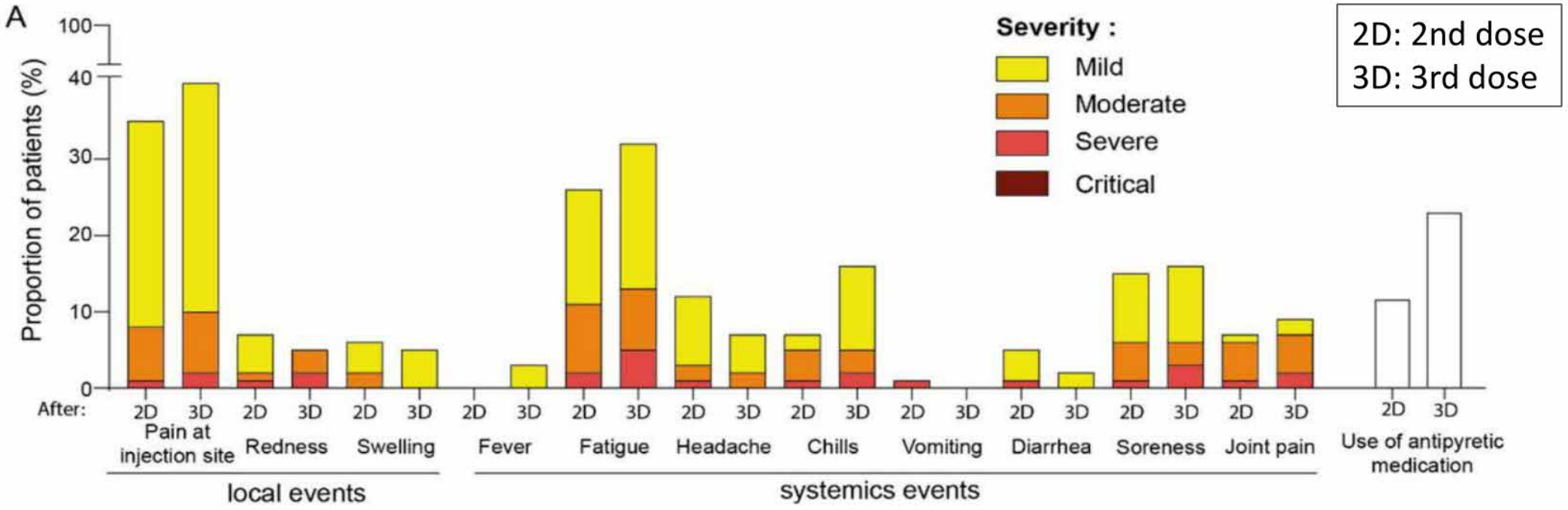


- No serious adverse events were reported after administration of the 3rd dose, and no acute rejection episodes occurred (n=99)

Kamar et al. (2021) NEJM Three Doses of an mRNA Covid-19 Vaccine in Solid-Organ Transplant Recipients (nejm.org)

Reactogenicity of 3rd mRNA vaccine dose in cohort of patients on hemodialysis (n=63*)

- No patients developed critical side effects requiring hospitalization
- Symptoms reported were consistent with previous doses and the intensity of the symptoms was mostly mild or moderate



*Sample included patients who had an optimal and suboptimal antibody response to primary mRNA series and chose to receive a 3rd dose

Maxime et al. (2021) medRxiv doi: https://doi.org/10.1101/2021.07.02.21259913

International policies on additional doses for immunocompromised people

- France[1] (Announced April 11, 2021)
  - 3rd dose 4 weeks after the 2nd dose for patients who are “severely immunocompromised”
  - Could be extended at a later date to include a larger immunocompromised population

- United Kingdom[2] (Announced July 1, 2021)
  - Proposal for an additional dose for immunocompromised people ≥16 years (among others), to be implemented between 6 September and 17 December 2021
  - Decision pending

- Israel[3] (Announced July 11, 2021)
  - People living with organ or stem cell transplants, blood cancer, autoimmune disease and treatment with specific immunosuppressive medications
  - People with breast, lung, or colon cancer do not qualify

1.dgs_urgent_n43_vaccination_modalites_d_administration_des_rappels.pdf (solidarites-sante.gouv.fr), 2. C1327-covid-19-vaccination-autumn-winter-phadvicease-3-planning.pdf
3.https://govextra.gov.il/media/30095/meeting-summary-15122020.pdf

Summary

- Immunocompromised people are at increased risk of poor outcomes from COVID-19
- Studies indicate a reduced antibody response in immunocompromised people following a primary vaccine series, compared to healthy vaccine recipients
- Emerging data suggest that an additional COVID-19 vaccine dose in immunocompromised people enhances antibody response and increases the proportion who respond
- In small studies, the reactogenicity of the 3rd dose of mRNA vaccine was similar to prior doses

Frequently asked questions about vaccination of immunocompromised people

Which immunocompromised groups should be considered for an additional dose as allowed by regulatory mechanisms?

- Conditions and treatments associated with *moderate to severe* immune compromise*
  - Active or recent treatment for solid tumor and hematologic malignancies
  - Receipt of solid-organ or recent hematopoietic stem cell transplant
  - Severe primary immunodeficiency
  - Advanced or untreated HIV infection
  - Treatment with immunosuppressive medications such as cancer chemotherapeutic agents, TNF blockers, certain biologic agents (e.g., rituximab), and high-dose corticosteroids
- Chronic conditions associated with *varying* degrees of immune deficit, such as asplenia and chronic renal disease*
- Different medical conditions and treatments can result in widely varying degrees of immunosuppression. A patient's clinical team is best able to assess the degree of altered immunocompetence and optimal timing of vaccination

*General Best Practice Guidelines for Immunization and CDC Yellow Book can be consulted for detailed information

Should immunocompromised people undergo antibody testing following COVID-19 vaccination?

- Utility of serologic testing or cellular immune testing to assess immune response to COVID-19 vaccination has not been established
- Exact correlation between antibody level and protection from COVID-19 remains unclear
- Commercial antibody and cellular immune testing may not be consistent across laboratories
- Serologic (antibody) testing or cellular immune testing outside of the context of research studies is **not recommended in the United States at this time**

Are there data to support mixed-dose series in immunocompromised people: for example, Janssen followed by mRNA COVID-19 vaccine?

- Studies from Europe have assessed heterologous primary series (AstraZeneca and Pfizer-BioNTech) in the general adult population and found immunogenicity to be at least equivalent to homologous series [1-5]
  - Large UK trial (Com-COV) found that one dose of AstraZeneca + one dose of Pfizer-BioNTech resulted in superior immunogenicity compared with two doses of AstraZeneca vaccine but lower antibodies than 2 doses of Pfizer-BioNTech; increase in systemic reactogenicity observed with heterologous schedules[5]
- Evidence is needed regarding the safety and immunogenicity of using a mixed-dose approach for Janssen (FDA-authorized adenoviral vector vaccine) + mRNA vaccine in immunocompromised people

1. Borobia et al. Reactogenicity and Immunogenicity of BNT162b2 in Subjects Having Received a First Dose of ChAdOx1s: Initial Results of a Randomized, Adaptive, Phase 2 Trial (CombiVacS). Available at SSRN: https://ssrn.com/abstract=3854768 **2**. Shaw et al. Heterologous prime-boost COVID-19 vaccination: initial reactogenicity data, ISSN 0140-6736, https://doi.org/10.1016/S0140-6736(21)01115-6. **3.** Hillus et al. Safety, reactogenicity, and immunogenicity of homologous and heterologous prime-boost immunization with ChAdOx1-nCoV19 and BNT162b2: a prospective cohort study. medRxiv; 2021. DOI: 10.1101/2021.05.19.21257334. **4.** Schmidt et al. medRxiv preprint (June 15 2021): https://doi.org/10.1101/2021.06.13.21258859 Click to add text **5.** Liu et al. Lancet preprint (June 25, 2021): http://dx.doi.org/10.2139/ssrn.3874014

Following COVID-19 vaccination, what infection prevention measures should immunocompromised people maintain?

- Immunocompromised people should be counseled about potential for reduced immune responses to COVID-19 vaccination and need to follow prevention measures*
  - Wear a mask
  - Stay 6 feet apart from others they don't live with
  - Avoid crowds and poorly ventilated indoor spaces until advised otherwise by their healthcare provider
- Close contacts of immunocompromised people should be encouraged to be vaccinated against COVID-19

* https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html

Is there a role for monoclonal antibody use in immunocompromised people?

- Monoclonal antibodies are currently authorized by FDA for emergency use in persons with SARS-CoV-2 infection who are at high risk for progressing to severe COVID-19 and/or hospitalization

- Monoclonal antibodies are not yet authorized for SARS-CoV-2 infection prevention

https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap#dashboard

What are the implications of the Emergency Use Authorizations (EUAs) for the COVID-19 vaccines, with respect to considerations for an additional dose in immunocompromised persons?

- FDA has authorized mRNA vaccines as a 2-dose series and Janssen COVID-19 vaccine as a single dose
- At this time, we are not aware of data submitted to FDA to support an amendment to the EUA for this population
- CDC/ACIP will closely monitor any updates to data and regulatory mechanisms

EUA= Emergency Use Authorization; BLA= Biologics License Application

Additional doses in immunocompromised people

Review data:
Assess safety, immunogenicity, and implementation

FDA

Regulatory allowance:
EUA amendment would allow recommendations under EUA

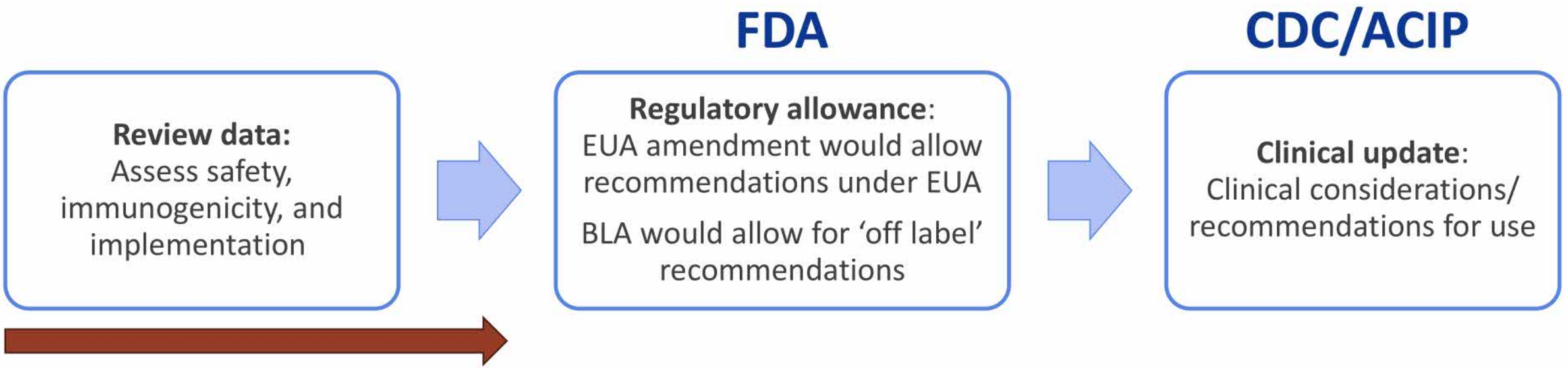
BLA would allow for 'off label' recommendations

CDC/ACIP

Clinical update:
Clinical considerations/ recommendations for use

EUA= Emergency Use Authorization; BLA= Biologics License Application

Additional doses in immunocompromised people



Now:

Immunocompromised people should continue to **follow infection prevention measures**:

Wear a mask, stay 6 feet apart from others, avoid crowds and poorly ventilated spaces

Close contacts (≥12 years) of immunocompromised people should be **vaccinated against COVID-19**

Early treatment with **monoclonal antibodies** may be beneficial in this population

EUA= Emergency Use Authorization; BLA= Biologics License Application

Additional COVID-19 vaccine dose in immunocompromised people: Next steps

- Assess additional studies of safety and immunogenicity of additional dose in immunocompromised people
- Assess additional studies and expert opinion regarding the subpopulations of immunocompromised people who may benefit most from an additional dose
- Determine acceptable intervals and mix and match schedules
- Await regulatory allowance (e.g. FDA amendment of EUA or BLA) for an additional dose of COVID-19 vaccine

EUA= Emergency Use Authorization; BLA= Biologics License Application

Questions for ACIP

Questions for ACIP

1. What additional data do ACIP need to inform these discussions?

2. Thoughts on the focus of “moderate to severe” immunocompromised populations, once authorized/approved?

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- Eddie Shanley
- Hannah Rosenblum
- Monica Godfrey

- Vaccine Task Force
- Epi Task Force
- Respiratory Viruses Branch

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References for slide 7: Immunocompromised people and SARS-CoV-2 infection

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16. Nakajima, Yukiko et al. *Prolonged viral shedding of SARS-CoV-2 in an immunocompromised patient.* Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy doi:10.1016/j.jiac.2020.12.001
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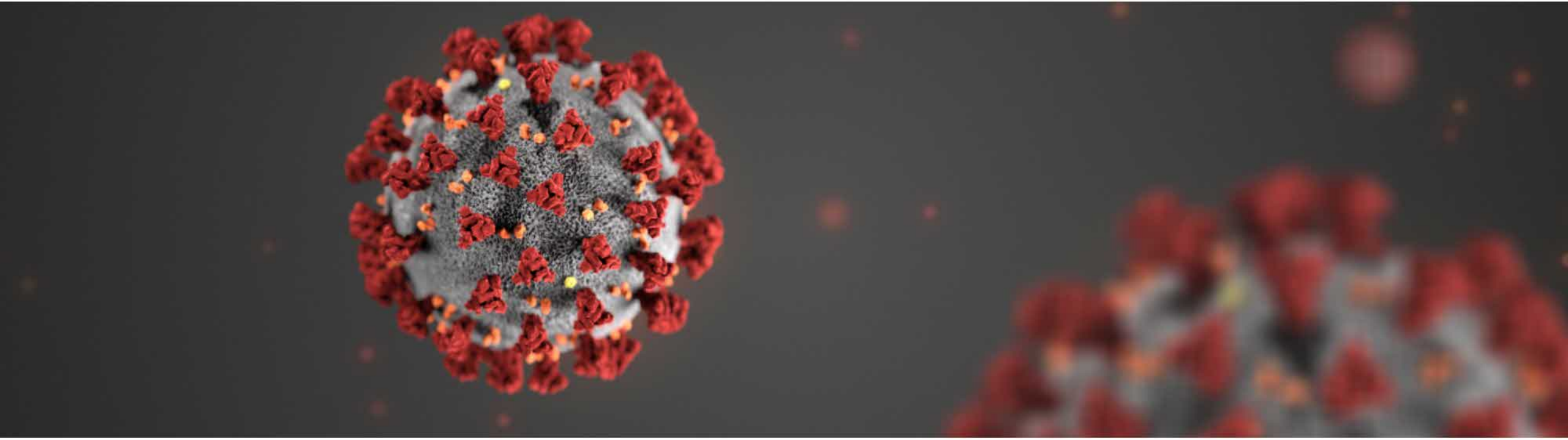

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

From: (b)(4) (b)(4) (b
Sent: Tue, 22 Jun 2021 20:41:49 +0000
To: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); (b)(4) (b)(4)
Cc: Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP); Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: RE: COVID slides

Thank you Jessica and Sara, very much appreciated!

From: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Sent: Tuesday, June 22, 2021 4:10 PM
To: (b)(4) (b)(4) (b (b)(4) (b)(4) (b)(4) (b)(4)
Cc: Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP) <ayv6@cdc.gov>; Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: [EXTERNAL] COVID slides

Hello (b)(4) and (b)(

Attached are draft slides for presentation during tomorrow's ACIP meeting. These versions will likely change before presentation tomorrow, but we wanted to share for your awareness.

Thank you,
Jessica

Jessica MacNeil, MPH
Deputy Executive Secretary, Advisory Committee on Immunization Practices
Currently supporting CDC COVID-19 Response on the Vaccine Task Force
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention
Email: jmacneil@cdc.gov

From: (b)(4) (b)(4)
Sent: Tue, 22 Jun 2021 23:38:51 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: RE: COVID slides

I'll call you now!
Thanks Sara!!!

(b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, June 22, 2021 7:38 PM
To: (b)(4) (b)(4) (b)(4)
Cc: (b)(4) (b)(4) (b) (b)(4) (b)(4) (b)(4)
Subject: [EXTERNAL] RE: COVID slides

Sure- sorry- long story but I was traveling a bit today so out of pocket but I'm back on now. Let me know if you want it to be a meeting invitation- or you can just call my work phone: 404-639-1204.

Thanks!

sara

From: (b)(4) (b)(4) (b)(4)
Sent: Tuesday, June 22, 2021 6:17 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: (b)(4) (b)(4) (b) (b)(4) (b)(4) (b)(4)
Subject: RE: COVID slides

Hi Sarah,
Thank you very much !!

I know you are so busy preparing tomorrow's presentation. I wanted to know if I can call you 5 minutes for a short call.
Please let me know

Thanks in advance (again)

(b)(

From: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Sent: Tuesday, June 22, 2021 4:10 PM

To: (b)(4) (b)(4) T (b)(4) (b)(4) (b)(4) (b)(4)
Cc: Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP) <ayv6@cdc.gov>; Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
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Jessica MacNeil, MPH
Deputy Executive Secretary, Advisory Committee on Immunization Practices
Currently supporting CDC COVID-19 Response on the Vaccine Task Force
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention
Email: jmacneil@cdc.gov

From: (b)(4) (b)(4)
Sent: Tue, 22 Jun 2021 21:55:14 +0000
To: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); (b)(4) (b)(4) (x)
Cc: Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP); Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: RE: COVID slides

Dear Jessica,

Thank you so much for sharing these materials I advance- most appreciated, and we acknowledge that the final presentations may change.

Best regards,
(b)(4)

From: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Sent: Tuesday, June 22, 2021 4:12 PM
To: (b)(4) (b)(4) (x) (b)(4) (b)(4) (b)(4) (b)(4)
Cc: Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP) <ayv6@cdc.gov>; Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: COVID slides

EXTERNAL

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Thank you,
Jessica

Jessica MacNeil, MPH
Deputy Executive Secretary, Advisory Committee on Immunization Practices
Currently supporting CDC COVID-19 Response on the Vaccine Task Force
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention
Email: jmacneil@cdc.gov

From: (b)(4) (b)(4) (x)
Sent: Mon, 21 Jun 2021 22:29:36 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Re: COVID-19 Discussion at ACIP This Week

Thank you!
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, June 21, 2021 2:15 PM
To: (b)(4) (b)(4) (x) (b)(4)
Subject: RE: COVID-19 Discussion at ACIP This Week

EXTERNAL

This is the agenda to the best of my knowledge right now. It's draft and subject to change, but hopefully Wednesday (the COVID-focused day) is pretty set.

Thanks-

Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Monday, June 21, 2021 2:08 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: COVID-19 Discussion at ACIP This Week

Hi Sara,

I hope you had some weekend!

I am just checking in to see if you have any further update on the date and time for the ACIP discussion of COVID-19 vaccines, please. We are trying to reschedule some meetings in order to make sure we have the right people available for the call.

Any update you can provide would be much appreciated.

Thanks.

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Mon, 21 Jun 2021 18:15:58 +0000
To: (b)(4) (b)(4) (x)
Subject: RE: COVID-19 Discussion at ACIP This Week
Attachments: Draft_Meeting Agenda_June 23_25 2021_6-21.pdf

This is the agenda to the best of my knowledge right now. It's draft and subject to change, but hopefully Wednesday (the COVID-focused day) is pretty set.

Thanks-

Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Monday, June 21, 2021 2:08 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: COVID-19 Discussion at ACIP This Week

Hi Sara,

I hope you had some weekend!

I am just checking in to see if you have any further update on the date and time for the ACIP discussion of COVID-19 vaccines, please. We are trying to reschedule some meetings in order to make sure we have the right people available for the call.

Any update you can provide would be much appreciated.

Thanks.

(b)(4)

Draft - June 21, 2021

MEETING OF THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES (ACIP)

Centers for Disease Control and Prevention
Atlanta, Georgia 30329
June 23-25, 2021

		PRESIDER/PRESENTER(s)
Wednesday, June 23, 2021		
11:00	**Welcome & Introductions**	Dr. José Romero (ACIP Chair) Dr. Amanda Cohn (ACIP Executive Secretary, CDC)
11:30	**Coronavirus Disease 2019 (COVID-19) Vaccines**	
	Introduction	Dr. Matthew Daley (ACIP, WG Chair)
	Overview of myocarditis and pericarditis	Dr. Matthew Oster (CDC/NCBDDD)
	Update on COVID-19 vaccine safety, including myocarditis after mRNA vaccines	Dr. Tom Shimabukuro (CDC/NCEZID)
	VaST assessment	Dr. Grace Lee (ACIP, VaST Co-chair)
12:45	***Break***	
1:00	COVID-19 mRNA vaccines in adolescents and young adults: benefit-risk	Dr. Megan Wallace (CDC/NCIRD)
	Discussion	
2:15	***Break***	
2:30	**Public Comment**	
3:00	Overview of data to inform recommendations for additional doses of COVID-19 vaccines	Dr. Sara Oliver (CDC/NCIRD)
	Discussion	
4:00	**Adjourn**	

Thursday, June 24, 2021		
10:00	**Welcome & Introductions**	Dr. José Romero (ACIP Chair) Dr. Amanda Cohn (ACIP Executive Secretary, CDC)
10:30	**Dengue Vaccine**	
	Introduction	Dr. Wilbur Chen (ACIP, WG Co-Chair)
	Acceptability of dengue vaccine in Puerto Rico	Dr. Ines Esquilin (University of Puerto Rico, School of Medicine)
	Implementation of dengue vaccine in Puerto Rico	Dr. Iris Cardona (Department of Health, Puerto Rico)
	Dengue vaccine draft recommendations using the evidence to recommendation framework	Dr. Gabriela Paz-Bailey (CDC/NCEZID)
	Dengue VFC Resolution	Dr. Jeanne Santoli (CDC/NCIRD)
12:20	***Break***	
12:30	**Influenza Vaccines**	
	Introduction	Dr. Keipp Talbot (ACIP, WG Chair)
	Flucelvax Quadrivalent (ccIIV4) Phase III Randomized Controlled Trial—Immunogenicity and Safety in Children 6 through 47 months	Dr. Gregg Sylvester (Seqirus)
	Work group considerations and proposed recommendations for the 2021-22 Influenza Season	Dr. Lisa Grohskopf (CDC/NCIRD)
	Updates to Influenza VFC Resolution	Dr. Jeanne Santoli (CDC/NCIRD)
2:10	***Break***	
2:20	**Rabies Vaccines**	
	Introduction	Dr. Sharon Frey (ACIP, WG Chair)
	Rabies immune globulin	Dr. Agam Rao (CDC/NCEZID)
	Rabies post-exposure prophylaxis schedule	Dr. Agam Rao (CDC/NCEZID)
	Rabies pre-exposure prophylaxis: GRADE/EtR summary	Dr. Agam Rao (CDC/NCEZID)
3:40	***Break***	
3:45	**Public Comment**	
4:15	***Break***	
4:20	**Votes and VFC Votes**	
	Dengue Vaccine	Dr. Gabriela Paz-Bailey (CDC/NCEZID)
	Dengue Vaccine (VFC)	Dr. Jeanne Santoli (CDC/NCIRD)
	Influenza Vaccines	Dr. Lisa Grohskopf (CDC/NCIRD)
	Influenza Vaccine (VFC)	Dr. Jeanne Santoli (CDC/NCIRD)
	Rabies Vaccines	Dr. Agam Rao (CDC/NCEZID)
5:15	**Adjourn**	

Friday, June 25, 2021

10:00	**Welcome & Introductions**	Dr. José Romero (ACIP Chair) Dr. Amanda Cohn (ACIP Executive Secretary, CDC)
10:15	**Zoster Vaccines**	
	Introduction	Dr. Grace Lee (ACIP, WG Chair)
	Burden of herpes zoster in immunocompromised adults	Dr. Tara Anderson (CDC/NCIRD)
	Use of recombinant zoster vaccine in immunocompromised populations: overview of clinical program	Ms. Robyn Widenmaier (GSK)
11:05	**Pneumococcal Vaccines**	
	Introduction	Dr. Kathy Poehling (ACIP, WG Chair)
	Updates on epidemiology of invasive pneumococcal disease in U.S. adults	Mr. Ryan Gierke (CDC/NCIRD)
	Cost effectiveness of PCV15 and PCV20 use in U.S. adults	Dr. Charles Stoecker (Tulane University)
	GRADE for age-based PCV15 and PCV20 use in U.S. adults	Ms. Jennifer Farrar (CDC/NCIRD)
	EtR summary of age-based PCV15 and PCV20 use in U.S. adults	Dr. Miwako Kobayashi (CDC/NCIRD)
	Summary and Timeline	Dr. Miwako Kobayashi (CDC/NCIRD)
1:00	**Adjourn**	

Acronyms

CDC	Centers for Disease Control and Prevention
CMS	Centers for Medicare and Medicaid Services
COVID-19	Coronavirus Disease 2019
EtR	Evidence to Recommendations Framework
FDA	Food and Drug Administration
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HRSA	Health Resources and Services Administration
IHS	Indian Health Service
NCHHSTP	National Center for HIV, Hepatitis, STD and TB Prevention [of CDC/DDID]
NCIRD	National Center for Immunization & Respiratory Diseases [of CDC/DDID]
NCEZID	National Center for Emerging and Zoonotic Diseases [of CDC/DDID]
NIAID	National Institute of Allergy and Infectious Diseases
OIDP	Office of Infectious Disease and HIV/AIDS Policy
PCV15	15-Valent Pneumococcal Conjugate Vaccine
PCV20	20-Valent Pneumococcal Conjugate Vaccine
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
WG	Work Group
WHO	World Health Organization
VE	Vaccine Effectiveness

From: (b)(4) (b)(4) (x)
Sent: Mon, 26 Apr 2021 22:22:00 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Re: Discussion This Week

Oh no, I forgot about the MMWRs - you deserve a medal or two!
I sent a request for Friday at 11 am.
Thanks.
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, April 26, 2021 6:10 PM
To: (b)(4) (b)(4) (x) (b)(4)
Subject: RE: Discussion This Week

EXTERNAL

(b)(4)

Thanks- no weekend off unfortunately. Getting these MMWRs out in a matter of days requires a substantial amount of work. But hopefully rest and days off at some point!

Yes- happy to talk. Friday at 11 sound good.

Thanks!
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Monday, April 26, 2021 4:08 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Discussion This Week

Hi Sara,

I hope you got some rest this weekend and took the weekend off!

I wanted to ask if I could please talk with you for 15-20 minutes this week to give you an update on some of our studies and filings. Is Friday at 11 am or 3 pm a possibility for you?

Let me know, please.

Thanks.

(b)(4)

Please consider the environment before printing this email

From: (b)(4) (b)(4) (x)
Sent: Tue, 27 Jul 2021 14:34:06 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Re: Discussion Today

Thanks. It will just be me from our end. Totally understand that you may need to reach out to others - no problem.
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, July 27, 2021 9:39 AM
To: (b)(4) (b)(4) (x) (b)(4)
Subject: RE: Discussion Today

EXTERNAL

I can meet from 2-2:30. I'll see if we can pull in others but I may just have to check in with others if there are questions I can't address. I'll send a meeting invitation.

Thanks-
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Tuesday, July 27, 2021 8:40 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Discussion Today

Hi Sara,

Would it be possible for us to talk today please? I would like to continue our conversation of yesterday.

I am available between 1 pm and 2:30 pm. Would that work for you please?

Let me know.

Many thanks.

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Mon, 17 May 2021 17:25:35 +0000
To: (b)(4) (b)(4) (x)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: RE: EUA Filing & Concomitant Use Studies

(b)(4)

Thanks for letting us know- and happy to have a quick call. Below are times I'm available (and potentially Jessica as well)- all EST.

Tues 5/18: 12-1
Wed 5/19: 10-11:30; 2-2:30
Thurs 5/20: 12:30-2

In addition- we have requests from other manufacturers regarding how to handle people who received vaccines in clinical trials that were not the dose/schedule where efficacy was demonstrated (if they are considered 'fully vaccinated' or need additional vaccine doses, etc). As a part of these discussions, we are trying to determine the number of people and type of vaccines this may represent. Do you mind providing a list of the different vaccines people received (dose, schedule and type), as well as the number of people it may involve (estimates are OK- just an idea of the scale) outside of the 100µg dose? The plan is once we have an idea of what may be involved, we can hopefully make a more informed decision that would apply to participants from all clinical trials. Happy to briefly talk about this at our call as well.

Thanks-

Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Monday, May 17, 2021 1:06 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: EUA Filing & Concomitant Use Studies

Hi Sara,

I wanted to let you know that our latest estimate is that we will file the EUA for 12-17 year olds during the first week in June. I would ask that you handle this information in confidence, but thought it was important to keep you updated. I assume, as we discussed, that you would want us to present to the WG shortly thereafter.

I also wanted to better understand some of the discussion that occurred at the last ACIP meeting where you mentioned that you were pursuing multiple avenues to obtain coadministration data. Could we please have a quick call to talk about this? We are discussing what needs to be done to support this from our end & it would be good to understand what data is most helpful.

Thanks.

(b)(4)

Please consider the environment before printing this email

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Thu, 10 Jun 2021 13:32:57 +0000
To: Cohn, Amanda (CDC/DDID/NCIRD/OD); (b)(4) (b)(4) (x); MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: RE: EUA Filing - Adolescents

Yes congrats! I will say that the sooner we can receive the data- the better. Our team is now preparing a benefit/risk analysis for myocarditis and mRNA vaccines, in addition to the Moderna GRADE analysis so any additional time will be helpful.

Is it possible to share the protocol, prior to the data? We have the Phase 3 adult protocol, but it doesn't go into the adolescent details, such as immunogenicity testing performed or non-inferiority criteria used.

Thanks!
Sara

From: Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>
Sent: Thursday, June 10, 2021 8:46 AM
To: (b)(4) (b)(4) (x) (b)(4) Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>; MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: RE: EUA Filing - Adolescents

Great news, thanks!

Amanda

From: (b)(4) (b)(4) (x) (b)(4) @modernatx.com>
Sent: Thursday, June 10, 2021 8:34 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>; MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>
Subject: EUA Filing - Adolescents

Hi Sara, Jessica, and Amanda,

This is just a quick note to let you know that we have now filed our EUA for adolescents, 12-17 years of age. Here is the press release.

https://investors.modernatx.com/news-releases/news-release-details/moderna-files-emergency-use-authorization-its-covid-19-vaccine

We should be able to share data with you in the next day or so & the GRADE tables are in the works.

(b)(4)

Please consider the environment before printing this email

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Fri, 18 Jun 2021 21:53:06 +0000
To: (b)(4) (b)(4) (x)
Subject: RE: Followup from Presentation
Attachments: Questions for Moderna regarding adolescents.docx

(b)(4)

Attached are questions from the WG, our safety team, and the data/GRADE team.

Thanks!

Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Thursday, June 17, 2021 5:30 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Followup from Presentation

Hi Sara,

Thanks for allowing us to present today.

I wanted to check back in to see if there are any additional questions that we can answer for the WG on our adolescent data or should be prepared to address when we present the data to the ACIP.

And I am also curious if you can share any more information on the presentation tomorrow afternoon on the overview of data to inform recommendations for additional vaccine doses. Can you give us some idea of what will be covered please?

Many thanks.

(b)(4)

Questions for Moderna regarding adolescents

1. Were any adolescents with comorbidities (other than obesity as detailed in EUA table 3) included? What proportion of vaccine and placebo arms had comorbidities other than obesity?
2. Why were 7.2% of participants missing baseline SARS-CoV-2 status?
3. In the EUA document, Table 22, last row, the numbers with asymptomatic infection were 21/2162 in vaccine group and 16/1073 in placebo group, but GRADE Table 3e has 14/2163 and 20/1073. We believe the difference in the numerators is due to the EUA including seroconversion and the GRADE table 3e only including PCR. However, the denominators are different. Please explain the differences in these numbers.
4. Lymphadenopathy p. 35

   How do we reconcile the report "Injection site lymphadenopathy (unsolicited TEAE to 28 days, MedDRA codes) = 4.3%, but "lymphadenopathy (unsolicited TEAE to 28 days, MedDRA codes, most axilla, supraclavicular, or cervical) was reported as 0.7%
5. Please provide clinical narratives for solicited grade 4 reactions, and if possible, include if these participants had prior SARS-CoV-2 infection.
6. Axillary swelling was higher in SARS-CoV2 positive compared to negative at baseline- do you have this data for the young adults (18-25)?
7. Could the sponsor please provide more information on the hypersensitivity events considered related to the vaccine and which were medically attended vs. severe- were some of these events counted more than once? There were 5 who had MAAEs of "potential hypersensitivity" and 49 who had "hypersensitivity" by MedDRA codes. Can the sponsor clarify whether there was overlap between these groups and particularly describe which events were considered related to vaccine? Also, patient who was wheezing- more clinical details available? History of asthma or anaphylaxis?
8. In your presentation to the ACIP WG, the N for total population randomized was 3726, but we had been given 3725. Could you please clarify which is correct?
9. Could you provide more information on patient with DILI and patient with appendicitis, diarrhea, vomiting and post-procedural fever (timing of clinical courses)
10. SAEs- 9 (?) events in 6 participants- please provide more clinical details/narrative on each of the 6 participants (more than is provided on page 36) and the tables in the EUA.
11. Clinical narrative on peripheral neuropathy (p. 42-43)
12. Please provide more detail on syncope and more details on dyspnea cases.
13. Please provide number of person-years for the full analysis and efficacy sets.
14. How was the immunogenicity population selected for the 12-17-year-olds? Was it randomly as was specified for the 18-25-year-olds?
15. The proportion experiencing axillary swelling or tenderness among ages 12-17 is reported by baseline SARS-CoV-2 status. Is there information on the proportion that experienced axillary swelling among ages 18-25 by baseline SARS-CoV-2 status, for comparison?
16. Could you provide GMTs by sex in the 12-17 year olds?
17. Could you please provide the data for the table below for the 18-25 age group? You provided this data for the 12-17-year-olds previously.

Authors last name, pub year	Age or other characteristic of importance	n/N intervention	n/N comparison	Comparator	% of intervention and placebo groups, p-value	
Phase 2/3 trial	Local reaction or systemic events [2,3], after either dose			Placebo		
Phase 2/3 trial	Local reaction[2], after either dose			Placebo		
Phase 2/3 trial	Systemic events[3], after either dose			Placebo		
Phase 2/3 trial	Local reaction or systemic events [2,3] post dose 1			Placebo		
Phase 2/3 trial	Local reaction[2], post dose 1			Placebo		
Phase 2/3 trial	Systemic events[3] post dose 1			Placebo		
Phase 2/3 trial	Local reaction or systemic events [2] post dose 2			Placebo		
Phase 2/3 trial	Local reaction[2], post dose 2			Placebo		
Phase 2/3 trial	Systemic events[3], post dose 2			Placebo		

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Wed, 30 Jun 2021 12:33:36 +0000
To: (b)(4) (b)(4) (x)
Subject: RE: Followup from Presentation

That sounds great- thanks!

Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Tuesday, June 29, 2021 9:13 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Re: Followup from Presentation

HI Sara,

We are still working on them. If we get them to you this week, is that OK?

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, June 29, 2021 8:55 PM
To: (b)(4) (b)(4) (x) (b)(4)
Subject: RE: Followup from Presentation

EXTERNAL

(b)(4)

Just anted to follow up if there were any available answers to the questions asked by the WG and our team.

Thanks!
Sara

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Friday, June 18, 2021 5:53 PM
To: (b)(4) (b)(4) (x) (b)(4)
Subject: RE: Followup from Presentation

(b)(4)

Attached are questions from the WG, our safety team, and the data/GRADE team.

Thanks!

Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Thursday, June 17, 2021 5:30 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Followup from Presentation

Hi Sara,

Thanks for allowing us to present today.

I wanted to check back in to see if there are any additional questions that we can answer for the WG on our adolescent data or should be prepared to address when we present the data to the ACIP.

And I am also curious if you can share any more information on the presentation tomorrow afternoon on the overview of data to inform recommendations for additional vaccine doses. Can you give us some idea of what will be covered please?

Many thanks.

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Fri, 18 Jun 2021 19:50:48 +0000
To: (b)(4) (b)(4) (x)
Subject: RE: Followup from Presentation

We're still working on an agenda. It's likely that we will end up just having the entire day Wednesday, but I'll pass along an agenda once we have it.

Thanks-
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Thursday, June 17, 2021 7:59 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Re: Followup from Presentation

Hi Sara,

Thanks for the important updates. I am glad we are observing an important holiday tomorrow.

By chance do you know if the COVID-19 session will be on the morning or the afternoon of the June 23 meeting?

I will look forward to seeing your updated slides next week.

And I I hope this give you just a little breathing room & can enjoy the weekend !

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Thursday, June 17, 2021 5:33 PM
To: (b)(4) (b)(4) (x) (b)(4)
Subject: RE: Followup from Presentation

EXTERNAL

(b)(4)

Thanks for the presentation today- the WG really appreciated the data. There were a few additional questions and we will get back to you with those. They won't require an additional WG presentation, but can just be clarified via email with us (we will share with the WG) and then potentially for the ACIP presentation.

I did want to let you know about something urgently though. Tomorrow has now officially been declared a federal holiday for Juneteenth. To allow everyone to recognize this important day, we are postponing the ACIP meeting. The current plan is that we will hold our COVID ACIP meeting next Wednesday (during the planned ACIP meeting). We are working through an overall agenda and will share as soon as we have it. But we will NOT be having the ACIP meeting tomorrow.

This extra time will give us a little bit longer to prep slides, so we will plan on sharing the slides with you shortly before the meeting.

Thanks and let me know if there are any follow-up questions.

Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Thursday, June 17, 2021 5:30 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Followup from Presentation

Hi Sara,

Thanks for allowing us to present today.

I wanted to check back in to see if there are any additional questions that we can answer for the WG on our adolescent data or should be prepared to address when we present the data to the ACIP.

And I am also curious if you can share any more information on the presentation tomorrow afternoon on the overview of data to inform recommendations for additional vaccine doses. Can you give us some idea of what will be covered please?

Many thanks.

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Sun, 23 May 2021 22:00:27 +0000
To: (b)(4) (b)(4) (x)
Subject: RE: Followup Questions - Discussion of Myocarditis

(b)(4)

I'll do the best I can to answer what I know. The most recent version of what I've seen included a discussion of myocarditis and pericarditis. Regarding a 'possible causal relationship'- my current understanding is that it isn't necessarily a defined mechanism, but that we've seen very similar/consistent findings where mRNA vaccines have been used all occurring within days of receipt of an mRNA vaccine (although it could be that systemic inflammation plays a role). And VSD updates all of the numbers weekly for all the pre-specified outcomes, so they have been (and will be) constantly evaluating for signals. We don't have an ACIP meeting planned to discuss this but will let you know if/when that occurs.

Thanks-
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Saturday, May 22, 2021 5:40 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Followup Questions - Discussion of Myocarditis

Hi Sara,

Thanks so much for taking the time to talk with us today.

We realized we had a few more questions after the call. Could you kindly address the following:

1. Will the communication you will be sending on Monday cover myocarditis only or myocarditis + pericarditis?
2. There was mention that a "possible causal relationship" may exist between vaccination and myocarditis. Can you please share your thoughts on a possible mechanism of action with an mRNA vaccine?
3. Will there be a more formal evaluation thru VSD (as was presented at the March 1 ACIP meeting where no association was identified for myocarditis/pericarditis)? Assuming this will be done, any idea of timing please?

Many thanks & we look forward to seeing the communication you plan to send out on Monday.

Enjoy the rest of your weekend.

(b)(4)

Please consider the environment before printing this email

From: (b)(4) (b)(4) (x)
Sent: Fri, 11 Jun 2021 20:08:24 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: Re: GRADE tables for Moderna
Attachments: ACIP - Adolescents - Standard GRADE Tables_Moderna FINAL to CDC 061121.docx

Hi Sara,
Here are the completed GRADE tables for the adolescent study.
Please let me know if you have any questions on the data.
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, June 8, 2021 4:28 PM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: GRADE tables for Moderna

EXTERNAL

(b)(4)

Passing along the draft GRADE tables for the adolescent data. Let us know if you have any questions or concerns. In addition- it would be helpful to review the Phase 3 protocol used for the adolescent trial as we undergo our GRADE/data review.

Looking forward to potentially receiving the EUA submission fairly soon. We sent the confidentiality agreement Friday- let us know if there is anything else needed from that standpoint as well.

Thanks!

Sara
Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

DRAFT

Please provide complete protocol for the adolescent trial. Make corrections below as needed, especially where highlighted.

Commented [BK(1]: Protocol provided to CDC in confidence on 6/10/21

Appendix 1

Studies Included in the Review of Evidence

Last name first author, Publication year	Study design	Country (or more detail, if needed)	Age (measure central tendency – mean/SD; range)	Total population	N Intervention	N comparison	Outcomes	Funding source
Phase 2/3 trial (unpublished data)	RCT	US	14.3 (1.60); 12-17 years	3732	2489	1243	• Symptomatic laboratory-confirmed COVID-19 • Hospitalization due to COVID-19 • All-cause death • SARS-CoV-2 seroconversion to a non-spike protein • Asymptomatic SARS-CoV-2 infection • Serious adverse events • Reactogenicity grade ≥3	Moderna, BARDA

Table 3a1

Summary of Studies Reporting Symptomatic COVID-19 (PCR-confirmed)

Authors last name, pub year	Age or other characteristic of importance	n/N intervention	n/N comparison	Comparator	Efficacy (95% CI) [100 x (1-IRR)]	
Phase 2/3 trial	Primary[1]: SARS-CoV-2 RT-PCR-positive symptomatic illness[1], in seronegative persons, **≥ 14 days** post second dose	0/2139	4/1042	Placebo	100% (28.9, NE)	
Phase 2/3 trial	SARS-CoV-2 RT-PCR-positive symptomatic illness[1], in *seropositive or seronegative* persons, **≥ 14 days** post second dose	0/2486	5/1240	Placebo	100% (47.6, NE)	
Phase 2/3 trial	SARS-CoV-2 RT-PCR-positive symptomatic illness (according to CDC-defined) symptoms[2]), in seronegative persons, **≥14 days** post second dose	1/2139	7/1042	Placebo	93.3% (47.9, 99.9)	
Phase 2/3 trial	SARS-CoV-2 RT-PCR-positive symptomatic illness[1], in seronegative persons **≥ 14 days** post first dose (1 dose VE)	0/2163	6/1073	Placebo	100% (59.6, NE)	
Phase 2/3 trial	SARS-CoV-2 RT-PCR-positive symptomatic illness (according to CDC-defined) symptoms[2]), in seronegative persons **≥ 14 days** post first dose (1 dose VE)	2/2163	13/1073	Placebo	92.7% (67.8, 99.2)	

Commented [BK(2]: These numbers are based on an ad hoc analysis performed by our Stat group – not in the EUA

Commented [BK(3]: Same here – these are based on an ad hoc analysis – not in the EUA

[1] Primary outcome, defined as SARS-CoV-2 RT-PCR-positive symptomatic illness*, in seronegative persons, **≥ 14 days** post second dose. The participant must have experienced at least TWO of the following systemic symptoms: Fever (≥ 38ºC), chills, myalgia, headache, sore throat, new olfactory and taste disorder(s), OR The participant must have experienced at least ONE of the following respiratory signs/symptoms: cough, shortness of breath or difficulty breathing, OR clinical or radiographical evidence of pneumonia; AND The participant must have at least one NP swab, nasal swab, or saliva sample (or respiratory sample, if hospitalized) positive for SARS-CoV-2 by RT-PCR.

[2] The CDC case definition of COVID-19 is defined as the following systemic symptoms: fever (temperature ≥38ºC), or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle aches, or body aches, headache, new loss of taste or smell, sore throat, nasal congestion or rhinorrhea, nausea, or vomiting or diarrhea AND a positive NP swab, nasal swab, or saliva sample (or respiratory sample, if hospitalized) for SARS-CoV-2 by RT-PCR.

NE = not estimable

Table 3a2

Summary of Studies Reporting Immunogenicity

		Adolescent vaccination (12-17 years)			Young adult vaccination (18-25 years)				
Authors last name, pub year	Age or other characteristic of importance	Sero-positive n/N	Sero-positive %	GMTs (95% CI)	Sero-positive n/N	Sero-positive %	GMTs (95% CI)	GMR[1a] (95% CI)	Seroresponse (Sero-positive) Rate Difference[1b] % (95% CI)
Phase 3 trial	SARS-CoV-2 neutralizing titers in seronegative persons[2] (28 days after receipt of the second dose) of past SARS-CoV-2 infection)	336/340	98.8	1401.670 (1276.3, 1539.4	292/296	98.6	1301.312 (1177.0, 1439.0)	1.077 (0.9, 1.2)	0.2 (-1.8, 2.4)

Note: In addition, please provide any other available immunogenicity outcomes, such as T-cell responses.

[1a] Estimated by the ratio of the geometric mean of SARS-CoV-2 neutralizing titers in the 2 age groups (12-17 years of age to 18-25 years of age) 1 month after completion of vaccination.

[1b] Estimated by the difference of the seroresponse (sero-positive) rates of SARS-CoV-2 neutralizing antibody for 12-17 years of age vs. 18-25 years of age at 1 month after completion of vaccination.

Noninferiority criteria:

- Coprimary endpoint GMT at 1 month after the 2nd dose, success criteria: the lower bound of the 95% CI of the GM ratio (GMR) rules out 0.67 (lower bound > 0.67) using a noninferiority margin of 1.5 (or 0.67), and the GMR point estimate > 0.8.
- Coprimary endpoint seroresponse rate at 1 month after the 2nd dose, success criteria: the lower bound of the 95% CI of the seroresponse rate difference rules out -10% (i.e. lower bound > -10%) using a noninferiority margin of 10%, and the seroresponse rate difference point estimate > -5%.

[2] No serological or virological evidence of prior SARS-CoV-2 infection at baseline

Table 3b

Summary of Studies Reporting Hospitalization due to COVID-19

Authors last name, pub year	Age or other characteristic of importance	n/N intervention	n/N comparison	Comparator	Efficacy (95% CI) [100 x (1-IRR)]	
Phase 2/3 trial	Persons aged 12-17	0/2486	0/1240	Placebo	N/A	No hospitalizations due to COVID-19

Table 3c

Summary of Studies Reporting All-cause Death[1]

Authors last name, pub year	Age or other characteristic of importance	n/N intervention	n/N comparison	Comparator	Efficacy (95% CI) [100 x (1-IRR)]	
Phase 2/3 trial	Persons aged 12-17	0/2486	0/1240	Placebo	N/A	No deaths in this study

[1]Death from any cause, including COVID-related or SAE.

Table 3d

Summary of Studies Reporting SARS-CoV-2 seroconversion to a non-spike protein without confirmed COVID-19 (aymptomatic infection)[1]

Authors last name, pub year	Age or other characteristic of importance	n/N intervention	n/N comparison	Comparator	Efficacy (95% CI) [100 x (1-IRR)]	
Phase 2/3 trial	N-binding antibody[1], persons aged 12-17	15/2163	15/1073	Placebo	52.5% (-4.3, 78.4)	

[1]Confirmed seroconversion to SARS-CoV-2 without confirmed COVID-19: positive N-binding antibody result in a participant with negative SARS-CoV-2 at baseline

Table 3e

Summary of Studies Reporting Serial PCRs for Asymptomatic Infection

Authors last name, pub year	Age or other characteristic of importance	n/N intervention	n/N comparison	Comparator	Efficacy (95% CI) [100 x (1-IRR)]	
Phase 2/3 trial	Positive PCR[1], persons aged 12-17	14/2163	20/1073	Placebo	66.9% (31.2, 84.5)	

[1] Positive PCR without confirmed COVID-19 in a participant with negative SARS-CoV-2 at baseline

Table 3f

Summary of Studies Reporting Serious Adverse Events[1]

Authors last name, pub year	Age or other characteristic of importance	n/N intervention	n/N comparison	Comparator	% of intervention and placebo groups	
Phase 2/3 trial	Persons aged 12-17	6/2486	2/1240	Placebo	0.2 vs. 0.2	

[1]Death, life-threatening event, hospitalization, incapacity to perform normal life functions, medically important event, or congenital anomaly/birth defect

Table 3g

Summary of Studies Reporting Grade 3 or above Reactogenicity[1]

Authors last name, pub year	Age or other characteristic of importance	n/N intervention	n/N comparison	Comparator	% of intervention and placebo groups	
Phase 2/3 trial	Local reaction or systemic events [2,3], after either dose, persons aged 12-17	629/2485	60/1240	Placebo	25.3 vs. 4.8	
Phase 2/3 trial	Local reaction[2], after either dose, persons aged 12-17	344/2485	4/1240	Placebo	13.8 vs. 0.3	
Phase 2/3 trial	Systemic events[3], after either dose, persons aged 12-17	414/2485	58/1240	Placebo	16.7 vs. 4.7	
Phase 2/3 trial	Local reaction or systemic events [2,3] post dose 1, persons aged 12-17	233/2482	36/1238	Placebo	9.4 vs. 2.9	
Phase 2/3 trial	Local reaction[2], post dose 1, persons aged 12-17	170/2482	1/1238	Placebo	6.8 vs. <0.1	
Phase 2/3 trial	Systemic events[3] post dose 1, persons aged 12-17	108/2482	36/1238	Placebo	4.4 vs. 2.9	
Phase 2/3 trial	Local reaction or systemic events [2] post dose 2, persons aged 12-17	486/2478	29/1220	Placebo	19.6 vs. 2.4	
Phase 2/3 trial	Local reaction[2], post dose 2, persons aged 12-17	220/2478	3/1220	Placebo	8.9 vs. 0.2	
Phase 2/3 trial	Systemic events[3], post dose 2, persons aged 12-17	343/2478	26/1220	Placebo	13.8 vs. 2.1	

[1]Grade 3 or worse

[2] Grade 3 local reactions include pain at injection site that prevents daily activity or results in use of prescription pain reliever, erythema/redness > 10 cm, and induration/swelling > 10 cm

[3] Grade 3 systemic events include fever 39.0°C -40.0°C, significant fatigue, chills, myalgia, or arthralgia that prevent daily activity, significant headache that prevents daily activity or results in use of prescription pain reliever, nausea that prevents daily activity or requires outpatient IV hydration.

From: (b)(4) (b)(4) (x)
Sent: Sat, 12 Jun 2021 00:53:08 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: Re: GRADE tables for Moderna

Hi Sara,
Thanks for the information.
I will get you the names for the WG call early next week. (b)(4) (b)(4) will present.
We are under the impression there will not be a VRBPAC meeting since there was no meeting for Pfizer for this age range.
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Friday, June 11, 2021 8:05 PM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: RE: GRADE tables for Moderna

EXTERNAL

(b)(4)

Thanks for this! The team really appreciates the prompt response. We will let you know if there are any questions.

We would also invite you to present this data to the WG this week: **Thurs 6/17** from ~3:30-4:15. We will ask for ~20-25 minute presentation focusing on the safety, efficacy and immunogenicity in the 12-17 year old population, and then have time for questions. If you can get us names, we will work on getting the call invitation sent out.

Regarding an ACIP meeting for this- we will have to wait until FDA issues the EUA to hold the ACIP meeting. Without a VRBPAC meeting, it's tough to know exactly when that will be, but we will let you know when we having anything tentatively scheduled.

Thanks! Let me know if there are any questions or issues.

Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Friday, June 11, 2021 4:08 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: Re: GRADE tables for Moderna

Hi Sara,

Here are the completed GRADE tables for the adolescent study.

Please let me know if you have any questions on the data.

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, June 8, 2021 4:28 PM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: GRADE tables for Moderna

EXTERNAL

(b)(4)

Passing along the draft GRADE tables for the adolescent data. Let us know if you have any questions or concerns. In addition- it would be helpful to review the Phase 3 protocol used for the adolescent trial as we undergo our GRADE/data review.

Looking forward to potentially receiving the EUA submission fairly soon. We sent the confidentiality agreement Friday- let us know if there is anything else needed from that standpoint as well.

Thanks!

Sara
Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: (b)(4) (b)(4) (x)
Sent: Tue, 8 Jun 2021 21:28:06 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Re: GRADE tables for Moderna

This will be tight, but I think I can send the agreement in a few minutes.
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, June 8, 2021 5:16 PM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: RE: GRADE tables for Moderna

EXTERNAL

(b)(4)

For a presentation on 6/17, we will really need to see the data by the end of this week. We will need to be able to do our prelim GRADE review to accompany the Moderna presentation. Happy to sign additional agreements- apologies for the missed communication around what was needed. In addition, we would appreciate the draft GRADE tables by 6/16, so we could make sure we are using the appropriate data before the 6/17 GRADE/data review.

Thanks!
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Tuesday, June 8, 2021 5:06 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: Re: GRADE tables for Moderna

Hi Sara,

Thanks for the GRADE tables. Can you give me an idea as to when you will need the input please? Like you, we have many competing priorities.

The confidentiality agreement is being revised by our Legal dept. Unfortunately, there was no mention of which documents are being shared in the version you sent us so we are revising.

The EUA should be filed late tomorrow or early Thursday with FDA. Please handle as confidential for now. I will try to get the document to you as soon as the agreement is signed. Our best "guess" is that we hope to have approval before July 4.

When you are able, please send the call-in information for the WG meeting on June 17.

Thanks for the homework!

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, June 8, 2021 4:28 PM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: GRADE tables for Moderna

EXTERNAL

(b)(4)

Passing along the draft GRADE tables for the adolescent data. Let us know if you have any questions or concerns. In addition- it would be helpful to review the Phase 3 protocol used for the adolescent trial as we undergo our GRADE/data review.

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Thanks!

Sara
Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Thu, 17 Jun 2021 14:04:54 +0000
To: (b)(4) (b)(4) (x)
Subject: RE: GRADE tables for Moderna

Wanted to check and see if you thought you would be able to have slides ready to send out to the WG by 12-1EST today?

They appreciate the ability to have a heads up on the data, and refer to the slides if there are any questions.

Thanks!
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Saturday, June 12, 2021 12:41 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Re: GRADE tables for Moderna

Hi Sara,

The Moderna attendees will be:

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(b)(4)

Me

If you send me the invite, I can send to them.

Thanks.

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Friday, June 11, 2021 8:05 PM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: RE: GRADE tables for Moderna

EXTERNAL

(b)(4)

Thanks for this! The team really appreciates the prompt response. We will let you know if there are any questions.

We would also invite you to present this data to the WG this week: **Thurs 6/17** from ~3:30-4:15. We will ask for ~20-25 minute presentation focusing on the safety, efficacy and immunogenicity in the 12-17 year old population, and then have time for questions. If you can get us names, we will work on getting the call invitation sent out.

Regarding an ACIP meeting for this- we will have to wait until FDA issues the EUA to hold the ACIP meeting. Without a VRBPAC meeting, it's tough to know exactly when that will be, but we will let you know when we having anything tentatively scheduled.

Thanks! Let me know if there are any questions or issues.

Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Friday, June 11, 2021 4:08 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: Re: GRADE tables for Moderna

Hi Sara,

Here are the completed GRADE tables for the adolescent study.

Please let me know if you have any questions on the data.

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, June 8, 2021 4:28 PM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: GRADE tables for Moderna

EXTERNAL

(b)(4)

Passing along the draft GRADE tables for the adolescent data. Let us know if you have any questions or concerns. In addition- it would be helpful to review the Phase 3 protocol used for the adolescent trial as we undergo our GRADE/data review.

Looking forward to potentially receiving the EUA submission fairly soon. We sent the confidentiality agreement Friday- let us know if there is anything else needed from that standpoint as well.

Thanks!

Sara
Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: (b)(4) (b)(4) (b)
Sent: Sun, 11 Apr 2021 14:32:28 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: (b)(4) (b)(4) (b)(4) (b)(4)
Subject: (b)(4)
Attachments: (b)(4)

Dear Sara,
Thank you, we are very excited about this new milestone. (b)(4)

(b)(4)

Let us know if you have any questions!
All the best,
(b)(4) (b)(and (b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Friday, April 9, 2021 5:27 PM
To: (b)(4) (b)(4) (b (b)(4)
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: [EXTERNAL] RE: (b)(4)

(b)(4) (b)(4) and (b)(4

Congrats on the submission to FDA! When you're able to share the EUA submission, we're happy to get started with our GRADE process, while we wait on the completed GRADE tables.

Thanks!
Sara

From: (b)(4) (b)(4) (b (b)(4)
Sent: Monday, April 5, 2021 1:16 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: GRADE tables

Dear Sara,

(b)(4)

All the best,
(b)(4) (b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, April 5, 2021 11:49 AM
To: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
(b)(4) (b)(4) (b)(4)
Subject: [EXTERNAL] (b)(4)

(b)(4) (b)(4) and (b)(4)

Hope everyone had a great weekend. I've attached the blank GRADE tables for the adolescent data. We look forward to receiving the data from the EUA amendment submission. Once we receive the data, (b)(4)

(b)(4)

Thanks!

Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Co-Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

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From: (b)(4) (b)(4) (b)(
Sent: Thu, 27 May 2021 18:06:40 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); (b)(4) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: RE: (b)(4)

Hi Sara,
Yes individuals with stable HIV, HBV and HCV were included in the phase 3 trial.

(b)(4)

All the best,
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Thursday, May 27, 2021 12:58 PM
To: (b)(4) (b)(4) (b) (b)(4) (b)(4) (b)(4) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: [EXTERNAL] RE: (b)(4)

(b)(4)

Thanks for this- will you remind me if individuals with HIV were included in the Phase 3 trial?

Thanks!
Sara

From: (b)(4) (b)(4) ((b)(4)
Sent: Monday, May 24, 2021 8:03 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>; (b)(4) (b)(4) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: RE: (b)(4)

Hello Sara,
Thanks, we certainly would appreciate any updates you can give us!

(b)(4)

All the best,
(b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, May 24, 2021 6:59 PM
To: (b)(4) (b)(4) (b) (b)(4) (b)(4) (b)(4) (b)(4)

Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: [EXTERNAL] (b)(4)

(b)(4) and (b)(4

I don't have any updates for myocarditis- but will share when we do!

I have another quick question though. As we plan for data to inform the booster discussions, we've had several questions around what data may be available in immunocompromised individuals. Is Pfizer doing any studies looking at VE or immunogenicity in immunocompromised individuals? And if so, do you know when data may be available?

Thanks!

Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Thu, 10 Jun 2021 15:29:01 +0000
To: (b)(4) (b)(4) (x)
Subject: RE: June 18 ACIP meeting

The current plan is for 11am-3:15pm EST (end time obviously subject to change based on the discussion). We won't be asking for any presentations by manufacturers, but are happy to extend a 'speakers line' invitation to a small number of people from Moderna to address questions as needed.

Thanks-
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Thursday, June 10, 2021 11:09 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: June 18 ACIP meeting

Hi Sara,

Two quick questions regarding the June 18 ACIP meeting please:

1) What time is the meeting
2) Any need for us to make any presentations?

Thanks.

(b)(4)

Please consider the environment before printing this email

From: (b)(4) (b)(4)
Sent: Wed, 23 Jun 2021 00:35:00 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); Thomas, Stephanie B. (CDC/DDID/NCIRD/OD)
Subject: RE: June 23, 2021 ACIP Meeting

Yes…apparently there are 2 of us here! ….as if!

The email below is correct. Thank you, Sara!

Best,
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, June 22, 2021 8:05 PM
To: Thomas, Stephanie B. (CDC/DDID/NCIRD/OD) <hkp4@cdc.gov>
Cc: (b)(4) (b)(4)
Subject: [EXTERNAL] RE: June 23, 2021 ACIP Meeting

It seems to have a '2' after it:

(b)(4) (b)(4)

Thanks!

From: Thomas, Stephanie B. (CDC/DDID/NCIRD/OD) <hkp4@cdc.gov>
Sent: Tuesday, June 22, 2021 12:02 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: FW: June 23, 2021 ACIP Meeting

Do you have an updated email for (b)(4)?

Stephanie Thomas
ACIP

From: Microsoft Outlook
<MicrosoftExchange329e71ec88ae4615bbc36ab6ce41109e@cdc.onmicrosoft.com>
Sent: Tuesday, June 22, 2021 11:59 AM
To: Thomas, Stephanie B. (CDC/DDID/NCIRD/OD)
Subject: Undeliverable: June 23, 2021 ACIP Meeting

Delivery has failed to these recipients or groups:

(b)(4)

Your message wasn't delivered because the recipient's email provider rejected it.

Diagnostic information for administrators:

Generating server: DM8PR09MB6856.namprd09.prod.outlook.com

(b)(4)

Remote Server returned '550 5.7.0 Local Policy Violation'

Original message headers:


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DKIM-Signature: v=1; a=rsa-sha256; c=relaxed/relaxed; d=CDC.GOV; s=selector2;
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 by DM8PR09MB6856.namprd09.prod.outlook.com (2603:10b6:5:2ed::20) with
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 2021 15:59:23 +0000
Received: from DM8PR09MB6502.namprd09.prod.outlook.com
 ([fe80::cc6e:7cb5:8d5c:a01a]) by DM8PR09MB6502.namprd09.prod.outlook.com
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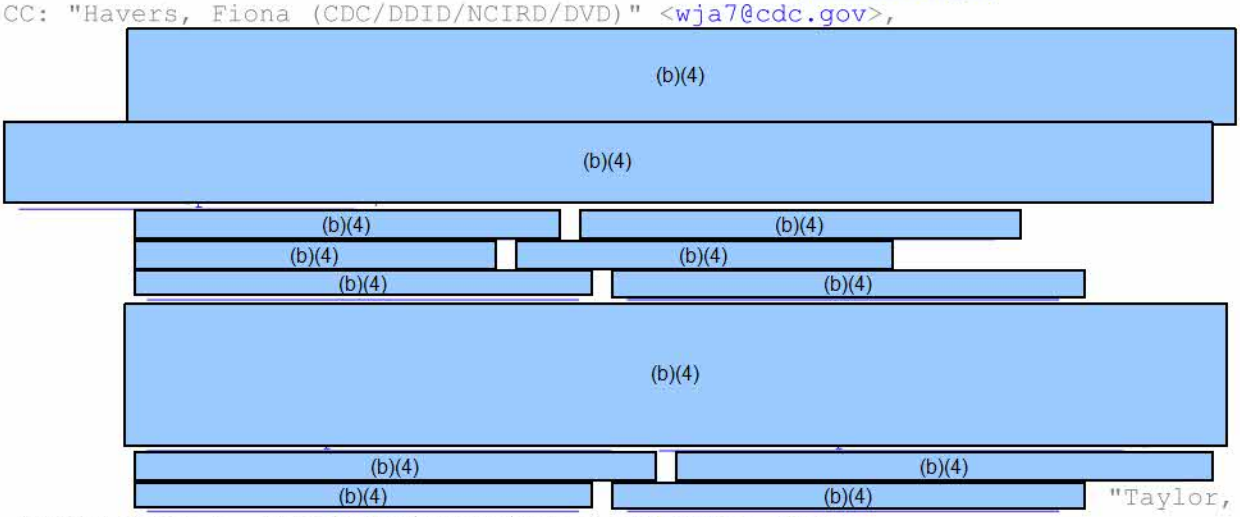
15:59:23 +0000
From: "Thomas, Stephanie B. (CDC/DDID/NCIRD/OD)" <hkp4@cdc.gov>
To: "Oster, Matt (CDC/DDNID/NCBDDD/DBDID) (CTR)" <IGP8@cdc.gov>
CC: "Havers, Fiona (CDC/DDID/NCIRD/DVD)" <wja7@cdc.gov>,



"Taylor, Christopher A. (CDC/DDID/NCIRD/DVD)" <iyq3@cdc.gov>
Subject: June 23, 2021 ACIP Meeting
Thread-Topic: June 23, 2021 ACIP Meeting
Thread-Index: Addnf48IcU8X3pQKQkKITLyS7kNRVg==
Date: Tue, 22 Jun 2021 15:59:23 +0000
Message-ID:
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Accept-Language: en-US
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X-MS-Has-Attach: yes
X-MS-TNEF-Correlator:
x-ms-publictraffictype: Email
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From: (b)(4) (b)(4)
Sent: Wed, 23 Jun 2021 14:42:13 +0000
To: Thomas, Stephanie B. (CDC/DDID/NCIRD/OD)
Cc: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: June 23, 2021 ACIP Meeting

Thanks Stephanie!!

Best

(b)(

From: Thomas, Stephanie B. (CDC/DDID/NCIRD/OD) <hkp4@cdc.gov>
Sent: Wednesday, June 23, 2021 10:41 AM
To: (b)(4) (b)(4) (b)(4)
Cc: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>; (b)(4) (b)(4) (b)((b)(4) (b)(4)
Subject: [EXTERNAL] RE: June 23, 2021 ACIP Meeting

Yes, adding now.

Stephanie Thomas
ACIP

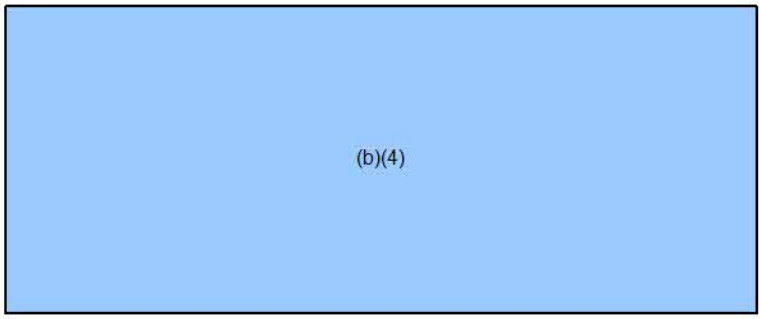
From: (b)(4) (b)(4) (b)(4)
Sent: Wednesday, June 23, 2021 8:38 AM
To: Thomas, Stephanie B. (CDC/DDID/NCIRD/OD) <hkp4@cdc.gov>
Cc: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>; (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: June 23, 2021 ACIP Meeting

Dear Stephanie,

I hope you are doing well.
One of my colleagues (b)(4) has not received this invite to join the Zoom call with others Pfizer participants and his participation would be important. Can you send an invitation to him ((b)(4))

Thanks in advance

(b)(4)



-----Original Appointment-----
From: Thomas, Stephanie B. (CDC/DDID/NCIRD/OD) <hkp4@cdc.gov>
Sent: Tuesday, June 22, 2021 12:00 PM
To: Thomas, Stephanie B. (CDC/DDID/NCIRD/OD); Oster, Matt (CDC/DDNID/NCBDDD/DBDID) (CTR)
Cc: Havers, Fiona (CDC/DDID/NCIRD/DVD); (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) Taylor, Christopher A. (CDC/DDID/NCIRD/DVD)
Subject: June 23, 2021 ACIP Meeting
When: Wednesday, June 23, 2021 11:00 AM-4:00 PM (UTC-05:00) Eastern Time (US & Canada).
Where: Via Zoom

The June 23rd ACIP Meeting time is 11:00pm – 4:00pm ET.

Login available as early as 10:30am ET, in hopes of staggering logins and not overwhelming the system.

Please Read:

- Please edit your Name/ID in the name field. **Last Name, First Name** so that we can see your name and find you easily

- MUTE your lines at all times until you're called on for discussion

- If you're dialing in by telephone EMAIL me and let me know the number you're calling from. You will be in the waiting room until we ID the number.

- When Dr. Romero opens the meeting for discussion, please virtually raise your hand

- Invited guests should be in listen only mode unless specifically called on by the ACIP Chair to speak.
- **Please no chat in the Zoom chat feature**
- Please disable your Video (a profile picture is fine, just no live video)

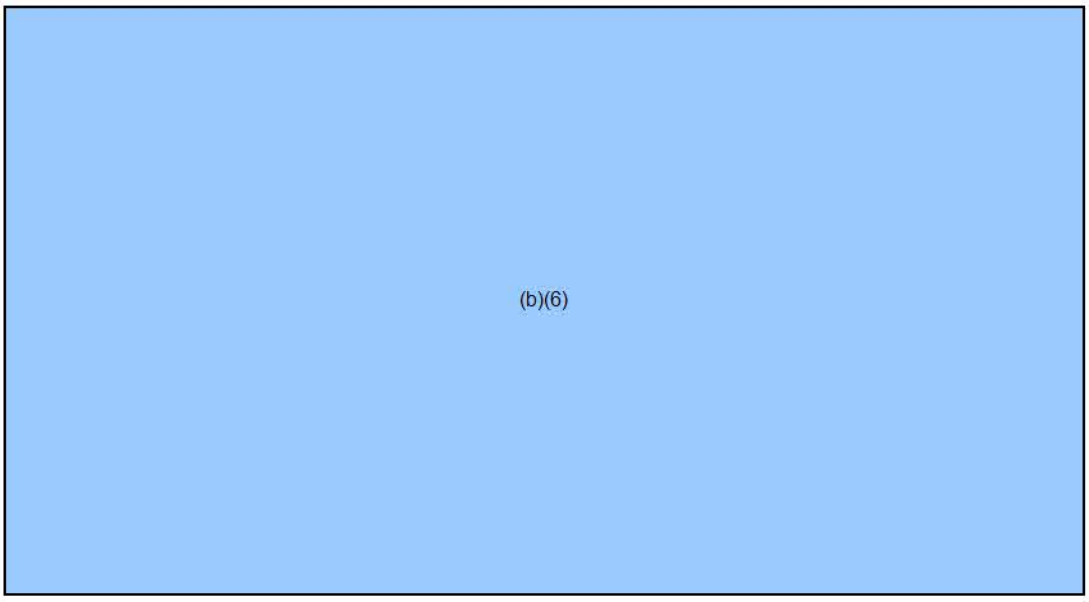
- Do not forward or share the Zoom login link with those not approved to join the Zoom call by the ACIP Secretariat.
- The webcast link is for the public or anyone that you want to invite to the meeting. Weblink can be found here: https://www.cdc.gov/vaccines/acip/index.html

Zoom tutorials: https://support.zoom.us/hc/en-us/articles/206618765-Zoom-Video-Tutorials

ACIP CDC is inviting you to a scheduled ZoomGov meeting.

Join ZoomGov Meeting

(b)(6)



From: (b)(4) (b)(4)
Sent: Fri, 21 May 2021 23:59:46 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); (b)(4) (b)(4) (b)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP)
Subject: RE: Meeting for tomorrow

Hi Sarah,

Thanks for your contact.
We will be waiting for your confirmation to jump into a call at your best convenience.

Best regards,

(b)(and (b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Friday, May 21, 2021 7:44 PM
To: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP) <ayv6@cdc.gov>
Subject: [EXTERNAL] Meeting for tomorrow

(b)(and (b)(4)

I was reaching out to see if you would be available for a call around noon tomorrow. I know it's a weekend and late notice, but we wanted to make sure you were aware before anything was made public. You may be aware, but there have been concerns for myocarditis seen in adolescents and young adults after receipt of the mRNA vaccines. Thankfully, the cases appear relatively mild, but there is concern that we need to make providers aware of this issue. CDC is discussing communication options, and we may have more information tomorrow. Would you be available around noon EST tomorrow (Sat 5/22)? (Waiting to confirm another meeting, and then we can formally schedule).

Thanks-
Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: (b)(4) (b)(4)
Sent: Sat, 22 May 2021 01:46:51 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP); (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: Meeting for tomorrow
Attachments: (b)(4)

Hi Sara,

(b)(4)

Please feel free to share it with your team before our conversation

Best regards,

(b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Friday, May 21, 2021 7:44 PM
To: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP) <ayv6@cdc.gov>
Subject: [EXTERNAL] Meeting for tomorrow

(b)(and (b)(4)

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Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force

Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

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From: (b)(4) (b)(4) (x)
Sent: Sat, 22 May 2021 13:51:05 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP)
Subject: Re: Meeting for tomorrow

Thanks Sara. I will await the invite.
(b)(4)
Get Outlook for iOS
From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Saturday, May 22, 2021 9:49:32 AM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP) <ayv6@cdc.gov>
Subject: RE: Meeting for tomorrow

EXTERNAL

(b)(4)

Sorry- waiting to see how a few things were scheduled here. Turns out it will be better for us for later afternoon EST time. I'll send a meeting invitation out for 4:30. Feel free to invite (b)(4) or anyone from the safety team.

Thanks!
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Saturday, May 22, 2021 9:39 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP) <ayv6@cdc.gov>
Subject: Re: Meeting for tomorrow

Hi Sara,

Any update for us please?

Thanks.

(b)(4)

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Friday, May 21, 2021 7:50 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP) <ayv6@cdc.gov>
Subject: Re: Meeting for tomorrow

Hi Sara, o can certainly be available tomorrow, but think others from Moderna should join as well. I would likely invite (b)(4) and (b)(4) (b)(4) from our Safety team. Is that OK?

(b)(4)

Get Outlook for iOS

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Friday, May 21, 2021 7:45:17 PM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP) <ayv6@cdc.gov>
Subject: Meeting for tomorrow

EXTERNAL

(b)(4)

I was reaching out to see if you would be available for a call around noon tomorrow. I know it's a weekend and late notice, but we wanted to make sure you were aware before anything was made public. You may be aware, but there have been concerns for myocarditis seen in adolescents and young adults after receipt of the mRNA vaccines. Thankfully, the cases appear relatively mild, but there is concern that we need to make providers aware of this issue. CDC is discussing communication options, and we may have more information tomorrow. Would you be available around noon EST tomorrow (Sat 5/22)? (Waiting to confirm another meeting, and then we can formally schedule).

Thanks-
Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

Please consider the environment before printing this email

From: (b)(4) (b)(4) (x)
Sent: Thu, 20 May 2021 17:37:58 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: Re: Meeting Now

Sorry - yes, I thought I had responded that 1:30 worked for me. But I did not set up a Webex & now I cannot get in.
Can you set this up on Teams or should I just call you? If so, let me know the best number.
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Thursday, May 20, 2021 1:36 PM
To: (b)(4) (b)(4) (x) (b)(4) MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: RE: Meeting Now

EXTERNAL

(b)(4)

Are we meeting right now? I didn't know we had set up a specific time- but I tried to go to the meeting and it says that you haven't joined??
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Thursday, May 20, 2021 1:33 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>; MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: Meeting Now

Hi,

I just sent a webex for our discussion now.

(b)(4)

Please consider the environment before printing this email

From: (b)(4) (b)(4) (x)
Sent: Thu, 17 Jun 2021 19:23:41 +0000
To: Shanley, Edwin (CDC/DDID/NCIRD/OD); Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Re: Moderna Attendees - Call with WG

Many thanks for the rapid response.
(b)(4)

From: Shanley, Edwin (CDC/DDID/NCIRD/OD) <ets5@cdc.gov>
Sent: Thursday, June 17, 2021 3:22 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>; (b)(4) (b)(4) (x)
(b)(4)
Subject: RE: Moderna Attendees - Call with WG

EXTERNAL

Hi (b)(4)
You can still forward the meeting invitation I sent you. My apologies for the confusing text.

I verified the individuals listed below are on the invitation.

Best regards,
Eddie

Edwin Shanley III, MPH
Ops Coordinator | ACIP Work Group
Vaccine Task Force
COVID-19 Response
Centers for Disease Control and Prevention (CDC)
ets5@cdc.gov

www.cdc.gov/COVID19

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Thursday, June 17, 2021 3:09 PM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: Shanley, Edwin (CDC/DDID/NCIRD/OD) <ets5@cdc.gov>
Subject: RE: Moderna Attendees - Call with WG

I ***think*** you should be able to forward, but am including Eddie so he can clarify. We would also ask that that everyone from Moderna identify themselves with (Moderna) after their name as they join.

Thanks-
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Thursday, June 17, 2021 3:02 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Moderna Attendees - Call with WG

Several additional persons may join the call today.

Can I just send them the invite or does it have to come from CDC? The instructions I received sounded like I could not forward.

Here is our entire list. If the invite needs to come from CDC, can you please send to the following persons.

(b)(4) (b)(4) (b)(4)

(b)(4)

(b)(4) (b)(4) (b)(4)

(b)(4) (b)(4) (b)(4)

Many thanks!

(b)(4)

Please consider the environment before printing this email

From: (b)(4) (b)(4) (x)
Sent: Wed, 9 Jun 2021 22:30:33 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: Re: Myocarditis update

Hi Sara,
Thanks so much for the updates.
(b)(4)
From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Wednesday, June 9, 2021 6:04 PM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: Myocarditis update

EXTERNAL

(b)(4)

I wanted to pass along a few updates. First- attached is Tom's presentation from the VRBPAC meeting tomorrow. Please keep the slides confidential for now, but he will be giving an update on myocarditis so we wanted to share this with you before tomorrow morning.

In addition- I wanted to let you know that we will be having an ACIP meeting on **June 18th** to discuss myocarditis, including an overall benefit/risk discussion. We will also have a brief discussion around data needed to inform possible future booster dose recommendations. We will likely be announcing this ACIP meeting tomorrow. I will pass along an agenda once it is available.

Thanks and let me know if you have any questions-

Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: (b)(4) (b)(4) (b)(4)
Sent: Wed, 9 Jun 2021 22:49:58 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); (b)(4) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: RE: Myocarditis updates

Thank you for the heads up Sara!
Best,
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Wednesday, June 9, 2021 6:04 PM
To: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: [EXTERNAL] Myocarditis updates

(b)(4) and (b)(4)

I wanted to pass along a few updates. First- attached is Tom's presentation from the VRBPAC meeting tomorrow. Please keep the slides confidential for now, but he will be giving an update on myocarditis so we wanted to share this with you before tomorrow morning.

In addition- I wanted to let you know that we will be having an ACIP meeting on **June 18th** to discuss myocarditis, including an overall benefit/risk discussion. We will also have a brief discussion around data needed to inform possible future booster dose recommendations. We will likely be announcing this ACIP meeting tomorrow. I will pass along an agenda once it is available.

Thanks and let me know if you have any questions-

Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: (b)(4) (b)(4) (b)(4)
Sent: Fri, 14 May 2021 12:51:08 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: RE: Pfizer adolescent MMWR

Thank you Sara we appreciate it
And as always congrats on your fantastic presentations at ACIP
Best,
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Thursday, May 13, 2021 8:26 PM
To: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4);
(b)(4) (b)(4) (b)(4) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: [EXTERNAL] Pfizer adolescent MMWR

(b)(4) (b)(and (b)(4)

I wanted to share the Final Proof with you of the MMWR set to be published tomorrow. It's embargoed until 11am, so please don't distribute, but wanted to shar with you.

Thanks-

Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: (b)(4) (b)(4)
Sent: Fri, 14 May 2021 00:52:54 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); (b)(4) (b)(4) (b)(4) (b)(4) (b)(
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: RE: Pfizer adolescent MMWR

Thank you very much Sara

Best

(b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Thursday, May 13, 2021 8:26 PM
To: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4); (b)(4) (b)(4) ((b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: [EXTERNAL] Pfizer adolescent MMWR

(b)(4) (b)(and M (b)(4)

I wanted to share the Final Proof with you of the MMWR set to be published tomorrow. It's embargoed until 11am, so please don't distribute, but wanted to shar with you.

Thanks-

Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: (b)(4) (b)(4) (b)
Sent: Wed, 16 Jun 2021 21:02:24 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Cc: (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: Pfizer attendees for June 18 ACIP meeting

Dear Sara and Jessica,
My apologies, I forgot one name for our list, could you please also include our (b)(4)
(b)(4)
Thank you so much!
Best regards,
(b)(4)

From: (b)(4) (b)(4) (b)(
Sent: Tuesday, June 15, 2021 8:08 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DBD) <yxo4@cdc.gov>; MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: Pfizer attendees for June 18 ACIP meeting

Dear Sara and Jessica,
Please find below the Pfizer attendees for the ACIP meeting on Friday June 18.

(b)(4)

Many thanks as always,
(b)(4) (b)(4) and (b)(

From: (b)(4) (b)(4) (b)
Sent: Mon, 10 May 2021 20:41:25 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: Pfizer attendees for May 12 ACIP meeting

Thanks Sara, understood, we will to condense our presentation down to 21-22 minutes. We will send you the slides by tomorrow afternoon for sure. Also I left one name off our attendee list, could you please also include (b)(4) from our (b)(4)
Thank you.
Warm regards,
(b)(4) (b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, May 10, 2021 3:00 PM
To: (b)(4) (b)(4) ((b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4)
(b)(4) (b)(4) (b)(4)
Subject: [EXTERNAL] RE: Pfizer attendees for May 12 ACIP meeting

(b)(4)

Thanks- I'll get these email address to ACIP so they can receive a speaker-line invitation.

Regarding the time for the presentation- the agenda is really packed so we would prefer to keep the presentations succinct. We could accommodate an extra minute or two if needed, but need to make sure we allow sufficient time for discussions.

Regarding the slides- if you could get us slides by tomorrow afternoon, that would be great. We can have a PPT version with back-up slides as needed, and then a PDF for only the presentation slides to post.

Thanks!
Sara

From: (b)(4) (b)(4) (b) (b)(4)
Sent: Monday, May 10, 2021 9:25 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4)
(b)(4) (b)(4) (b)(4)
Subject: Pfizer attendees for May 12 ACIP meeting

Dear Sara,

I hope you had a nice weekend and Mother's Day. I wanted to provide you with the list of the Pfizer attendees for the Zoom appointment for the ACIP meeting on Wednesday. I also wanted to follow up on our request to please be allowed 25 minutes for our presentation.
Thank you!

Attendees in addition to (b)(4) myself and (b)(4)

(b)(4)

Best regards,
(b)(4) (b)(4) and (b)(

From: (b)(4)
Sent: Tue, 13 Jul 2021 19:49:10 +0000
To: (b)(4)
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4); Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); Mbaeyi, Sarah (CDC/DDID/NCIRD/OD); (b)(4) (b)(4)
Subject: (b)(4)

Yes (b)(4) There are a few new slides from today's TC in Israel but the clinical slides are the same. I will manage the slide deck from my computer.
(b)(4)

Sent from my iPhone

On Jul 13, 2021, at 15:43, (b)(4) wrote:

Thanks, (b)(4) (b)(4) for forwarding. I assume we are sharing the same slides as yesterday at Kessler+NIH, CDC, FDA meeting, and we will divide up presentation in same way. Please send me latest version we plan to present. Best, (b)(4)

(b)(4)

-----Original Appointment-----
From: (b)(4) (b)(4) (b)(4)
Sent: Tuesday, July 13, 2021 3:31 PM
To: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); Mbaeyi, Sarah (CDC/DDID/NCIRD/OD); (b)(4) (b)(4)
Subject: (b)(4)
When: Tuesday, July 13, 2021 4:00 PM-5:00 PM (UTC-05:00) Eastern Time (US & Canada).
Where: webex

-----Original Appointment-----
From: (b)(4) (b)(4) (b)(4)
Sent: Tuesday, July 13, 2021 10:52 AM
To: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4); Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); Mbaeyi, Sarah (CDC/DDID/NCIRD/OD); (b)(4) (b)(4)

Subject: (b)(4)
When: Tuesday, July 13, 2021 4:00 PM-5:00 PM (UTC-05:00) Eastern Time (US & Canada).
Where: webex

Thank you all for your flexibility to attend this meeting today

-- Do not delete or change any of the following text. --

1. Click to Join the Meeting

IMPORTANT NOTICE: Please note that this Webex service allows audio and other information sent during the session to be recorded, which may be discoverable in a legal matter. By joining this session, you automatically consent to such recordings. If you do not consent to being recorded, discuss your concerns with the host or do not join the session.

2. Join the Audio

- From a Pfizer office - select Call Me (and have it call your office or conference phone)
- Not working in a Pfizer office or using a mobile phone?
    - From a **computer** with a good Internet connection, select **Call Using Computer+**
    - From a **mobile device** with Wi-Fi access, select **Connect Using Internet+**
    - If no Internet or data connection is available, see below for dial-in details

+ Use a headset or mobile phone earbuds for the best quality sound

WebEx Meeting and Support Details
Meeting number: (b)(6) Meeting password: (b)(6)

No Internet or data connection?
If you are located in a different country than the one shown, find your country's dial-in number using the **Global call-in numbers** link below - please use the **TOLL number**, if available:

Join by phone
(b)(6) Call-in toll number (US/Canada)
Access code: (b)(6)
Global call-in numbers | Toll-free calling restrictions

Attend a video meeting from a Pfizer conference room device, via the touch panel or remote - dial ***88** and enter the **10-digit meeting number**. If you are the Host, enter your Host PIN when prompted.

Join from a video conferencing system or application
Dial (b)(6)
You can also dial (b)(6) and enter your meeting number.

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Thu, 17 Jun 2021 14:12:21 +0000
To: (b)(4) (b)(4) (x)
Cc: (b)(4) (b)(4)
Subject: RE: Presentation to CDC COVID-19 Work Group - Adolescent Study

Great- thanks. Will do!

Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Thursday, June 17, 2021 10:10 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: (b)(4) (b)(4) (b)(4)
Subject: Presentation to CDC COVID-19 Work Group - Adolescent Study

Hi Sara,

Here is a PDF of the presentation that Dr. (b)(4) will give today to the COVID-19 Work Group summarizing the results of our COVID-19 vaccine study in adolescents. As always, we would ask that the slides be handled as confidential and not distributed beyond the Work Group.

If OK with you, Dr. (b)(4) will plan to advance her own slides.

Thanks again for the opportunity to present today. Talk to you later!

(b)(4)

Please consider the environment before printing this email

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Fri, 2 Apr 2021 15:40:38 +0000
To: (b)(4) (b)(4) (x)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: RE: Presentations/Discussions

Thanks (b)(4) We did bring the VE work to our VE leads. Ultimately they are still working out details around interactions with manufacturers. We did let them know you were interested in discussions so we will pass along anything they let us know about.
Regarding studies on the variants: the WG is very interested in this. However- I think the WG will be consumed with pressing policy issues over the next 1-2 months so we may not be able to accommodate presentations that aren't directly leading to a vote. Once we get through this 'late-spring' push, we will definitely let you know.

I know in 'normal' times this would all be discussed with the WG regularly- we appreciate any updates and I pass them along. In these crazy times we're balancing this with these emergency ACIP meetings and votes. But will hopefully get back to more 'normal' times relatively soon.

Thanks-

Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Friday, April 2, 2021 11:23 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Presentations/Discussions

HI Sara,

I am just following up on our recent call. Can you tell when you would like us to present:

1) Our plans for our real world effectiveness study _ I think you said you wanted to check with another group about such a presentation - can probably be done in 15 inutes
2) Our plans/status of studies of variants - assume this would be to the Work Group - might warrant 30 minutes?

Let me know please. Happy to discuss via phone if that is easier.

Thanks!

(b)(4)

Please consider the environment before printing this email

From: (b)(4) (b)(4)
Sent: Tue, 27 Jul 2021 01:29:11 +0000
To: Cohn, Amanda (CDC/DDID/NCIRD/OD); (b)(4) (b)(4) (b) (b)(4) (b)(4)
Cc: (b)(4) Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); Yu, Patricia A. (CDC/DDID/NCEZID/DPEI); Yu, Yon C. (CDC/DDID/NCEZID/DPEI)
Subject: RE: Proposed CDC sponsored eIND

Hi Amanda,

Thanks for your note.

We understand the situation and the urgency of this situation. (b)(4)
(b)(4)

Please let us know if it makes sense to you

Best regards,

(b)(4) (b)(4) and (b)(

From: Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>
Sent: Monday, July 26, 2021 8:46 PM
To: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) T (b)(4)
(b)(4) (b)(4)
Cc: (b)(4) Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>; Yu, Patricia A. (CDC/DDID/NCEZID/DPEI) <pby7@cdc.gov>; Yu, Yon C. (CDC/DDID/NCEZID/DPEI) <fkb8@cdc.gov>
Subject: [EXTERNAL] Proposed CDC sponsored eIND

Dear (b)((b)(4) and (b)(4)

I apologize for missing the call earlier! I hope you are doing well.

I wanted to follow-up on Pfizer's willingness to support the proposed CDC-sponsored EA-IND. I heard there were some questions and concerns raised, but we are hoping that the company will consider aligning with this effort to provide an opportunity for the severely immunocompromised to receive an additional dose of an mRNA COVID vaccine through an approved regulatory mechanism as a bridge to an approved BLA or an EUA amendment. In the setting of high disease transmission, especially in those living in states with low vaccination coverage, CDC intends to rapidly develop and submit a protocol for review by FDA.

Could you confirm if Pfizer is willing or unwilling to provide CDC a cross reference authorization to data contained in the Pfizer IND and MF, if applicable, for Pfizer COvI-19 vaccine? If it is possible to have an answer by tomorrow, that would be ideal as we move forward with planning.

Best,

Amanda

Amanda Cohn, MD
CAPT, USPHS
Chief Medical Officer
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

From: (b)(4) (b)(4) (x)
Sent: Tue, 25 May 2021 15:03:08 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Re: Publication - Myocarditis

Thanks, Sara. That is very helpful.
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, May 25, 2021 10:29 AM
To: (b)(4) (b)(4) (x) (b)(4)
Subject: RE: Publication - Myocarditis

EXTERNAL

I haven't heard plans for an MMWR yet. There's just not enough data yet so an MMWR wouldn't make sense at this point. I would anticipate as we have additional data and more formal analyses, there may be an MMWR, but not right now.

The pros and cons of an official HAN are what the main discussions are right now. I think it's likely to be a HAN since that is CDC's primary method of communications to clinicians and public health departments, but people don't want to appear alarmist either.

I am not trying to be vague on purpose- I really don't know. If I had to guess, I would think it's likely to be a HAN, but can't say for sure yet. I anticipate there will be firm decisions within the next 24 hours so I'll let you know.

Thanks-
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Tuesday, May 25, 2021 10:24 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Re: Publication - Myocarditis

Hi Sara,

Thanks for your note. Can I just ask what are the possible options where this might be published?

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, May 25, 2021 10:20 AM

To: (b)(4) (b)(4) (x) (b)(4)
Subject: RE: Publication - Myocarditis

EXTERNAL

(b)(4)

Apologies that there hasn't been more solid communication on this. Unfortunately, I still don't have a firm update to share. Things have been changing rapidly here. As we know more, I will share.

Thanks-
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Tuesday, May 25, 2021 9:45 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Publication - Myocarditis

Hi Sara,

I am just checking in to see if you have decided where you will publish your statement on myocarditis. Will it be the MMWR or somewhere else please? And if you have any update on timing, that would be a big help.

We hope to send CDC the report that we are submitting to PRAC sometime this week.

Many thanks.

(b)(4)

From: (b)(4) (b)(4) (b)(
Sent: Mon, 17 May 2021 17:49:09 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); (b)(4) (b)(4)
Subject: RE: question

Dear Sara,
I am very glad to hear you were able to get a little rest!!!
We will ask our research unit colleagues for the info you requested. We will get back to you as soon as we hear from them.
Cheers,
(b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, May 17, 2021 1:25 PM
To: (b)(4) (b)(4) (b) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4)
(b)(4)
Subject: [EXTERNAL] RE: question

(b)(4) and (b)(4

Thanks for this. I did get a bit of a break over the weekend which was nice! (3 ACIP meetings in the last 5 weeks didn't leave time for much rest previously!).

We are still having discussions around this issue. It is obviously easier to make a decision around those who received the vaccine in a clinical trial, but at the same dose/interval, etc where efficacy was demonstrated- but harder for those other vaccines. We are also trying to determine the number of people and type of vaccines this may represent. Do you mind providing a list of the different vaccines people received (dose, schedule and type), as well as the number of people it may involve (estimates are OK- just an idea of the scale). The plan is once we have an idea of what may be involved, we can hopefully make a more informed decision.

Thanks-

Sara

From: (b)(4) (b)(4) ((b)(4)
Sent: Monday, May 17, 2021 12:49 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4)
(b)(4)
Subject: RE: question

Hello Sara,
I hope you had a nice weekend, dare I hope that maybe you got to rest a bit after the marathon ACIP, MMWR and clinical considerations updates last week!
I was just following up on the question we asked below regarding using the vaccination cards to record experimental vaccines in our trials (see below email)
Thank you in advance for any guidance you can provide us.
Best regards,
(b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, May 11, 2021 7:47 PM
To: (b)(4) (b)(4) (b (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4)
Subject: [EXTERNAL] RE: REVISED Pfizer presentation slides

(b)(4)

Thanks- passed your updated slides along. I'll also check on your question as well. Can't promise we'll have an answer by tomorrow, but we'll get back to you.

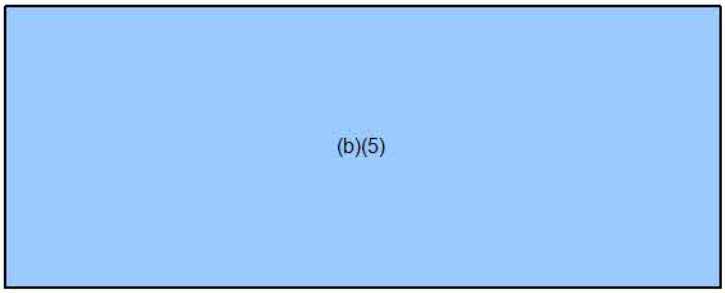
Thanks!
Sara

From: (b)(4) (b)(4) (b (b)(4)
Sent: Tuesday, May 11, 2021 7:10 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4)
Subject: REVISED Pfizer presentation slides
Importance: High

Dear Sara,
So sorry, we received some last minute revisions from internal colleagues so please use the attached REVISED slides for the meeting tomorrow.

Also, we have a separate question. (b)(4) (b)(4) (b)(4). Some guidance was received suggesting that it would be appropriate to do so and to include such vaccines on the card (as long as their precise nature and investigational status is recorded) but that such individuals should not feel at will to follow the current CDC recommendations for fully vaccinated individuals. We would appreciate any guidance you could provide us on this.

Thank you and see you tomorrow,
All the best,
(b)(4) and (b)(



From: (b)(4) (b)(4) (b
Sent: Mon, 14 Jun 2021 17:39:40 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); (b)(4) (b)(4) (b)(4) (b)(5)
Subject: RE: question

Thank you so much Sara, much appreciated!
Also, I will be getting back to you later today with the names and emails of the Pfizer representatives for the ACIP meeting on Friday.
Best regards,
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, June 14, 2021 12:42 PM
To: (b)(4) (b)(4) T (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4)
(b)(4) (b)(4) (b)(4)
Subject: [EXTERNAL] RE: question

(b)(4) and all:

Apologies but took a minute to get the final version of the Trial Participant card. It is attached here. Similar to the standard CDC card, we would ask that you not post it publicly on a website or anything else public facing.

Regarding the B.1.351 variant- we would actually be OK with those individuals receiving the 'standard' CDC card. Based on the preliminary data from Moderna's 1.351 variant-specific vaccine that provided very similar antibody levels for the D614G 'wild type' SARS-CoV-2 virus and other variants, we aren't anticipating a meaningful difference in VE for most variants. (However, let us know if you have any data that may suggest otherwise!).

Thanks and let me know if there are any other questions.

Sara

From: (b)(4) (b)(4) (b (b)(4)
Sent: Thursday, June 10, 2021 9:22 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4)
(b)(4) (b)(4) (b)(4)
Subject: RE: question

Good morning Sara,

(b)(4)

(b)(4)

(b)(4) We look forward to receiving copies of the CDC Clinical Trial Participant card.

Best,

(b)(4) (b)(4) and (b)(

From: (b)(4) (b)(4) (b)

Sent: Wednesday, June 9, 2021 12:38 PM

To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>

Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)

Subject: RE: question

Great minds!

Thank you for this response Sara.

I will send out an appointment shortly for Friday 3-3:30pm, thank you again for your time and flexibility.

All the best,

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>

Sent: Wednesday, June 9, 2021 12:24 PM

To: (b)(4) (b)(4) (b) (b)(4)

Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)

Subject: [EXTERNAL] RE: question

(b)(4)

I was literally typing the response on the vaccination cards as I received your email- apologies for the delay!!

We've discussed internally and feel that those who received the lyophilized formulation study could receive a "Clinical Trial Participant" CDC card- we drafted it for trial participants for non-EUA authorized vaccines and are happy to share for these individuals. It looks similar to the regular "CDC card"- but acknowledges that FDA and ACIP have not reviewed data on this specific vaccine.

For the others:

- Anyone who received a 2-dose primary series of BNT162b2 can receive the standard "CDC card". A 3rd dose could be recorded, but it's the receipt of the initial 2 doses that count for the 'fully vaccinated' guidance (and implications of 'the card').
- Individuals who received 2 doses of 20mcg can receive the standard "CDC card". Per our guidance, the dose can 'count' if it is at least half the original dose.

- Individuals who received the 'ready to use' formulation can receive the standard "CDC card".

I *__think__* that should cover it, but let us know if there are other questions we didn't address. I will get the "Clinical Trial Participant" card and share it with you ASAP.

We can be available from 3-3:30 on Friday. Happy to chat about booster dose studies.

Thanks!
Sara

From: (b)(4) (b)(4) (b) (b)(4)
Sent: Wednesday, June 9, 2021 12:07 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: question

Dear Sara,
I hope you are well.
Two things: I wanted to follow up on the pending question below regarding the use of the vaccination cards in our trials using mixed doses of COVID vaccine.
The second is we would like to give you a quick update and get your insights on our booster studies and timelines. We won't need more than a half hour. Would you have any availability this Friday between 2pm-3:30pm EDT?
Thank you as always!
Best,
(b)(4) (b)(4) and (b)(

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Sent: Tuesday, June 1, 2021 9:17 AM
To: 'Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)' <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4)
Subject: RE: question

Thank you Sara, we know you are extremely busy and we so appreciate your insights and assistance.
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Subject: [EXTERNAL] RE: question

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Thanks and sorry this has taken so long!!!

Sara

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Subject: [EXTERNAL] RE: REVISED Pfizer presentation slides

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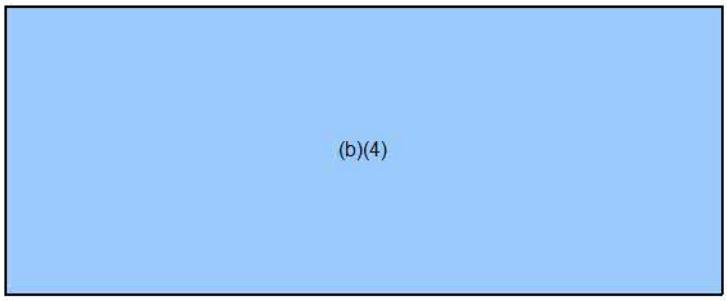


From: (b)(4) (b)(4) (b)(
Sent: Fri, 21 May 2021 14:06:17 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); (b)(4) (b)(4)
Subject: RE: question

Dear Sara,
We have added the information you requested into the table below (b)(4)
(b)(4)
(b)(4) As always, please let us know if you have any other questions.

(b)(4)

All the best,
(b)(4) and (b)(

From: (b)(4) (b)(4) (b)(
Sent: Tuesday, May 18, 2021 8:12 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4)
(b)(4)
Subject: RE: question

Thank you Sara, we appreciate it.
Regarding your questions on (b)(4) we will work with our research unit colleagues to get you the requested information.
Warm regards,
(b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, May 18, 2021 11:57 AM
To: (b)(4) (b)(4) ((b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4)
(b)(4)
Subject: [EXTERNAL] RE: question

(b)(4) and (b)(4

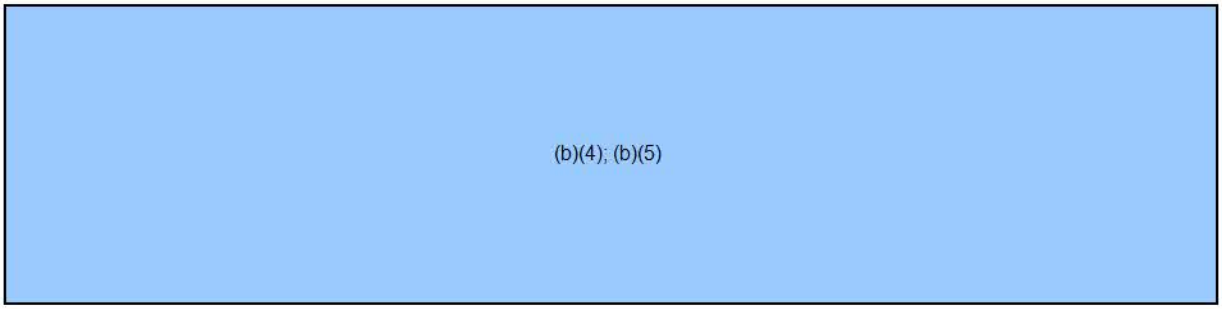
Thanks- this information is helpful. We will discuss here internally and I'll let you know what is discussed/decided.

Sorry for the other additional questions- but now that we've survived the last 1-2 months, we are taking this brief break to plan ahead. This includes many things, but obviously an area of high interest- booster doses.

As we plan for if/when ACIP may recommend booster doses, and possibly in what populations- we are trying to collect what information will be available to inform these discussions. Do you mind sharing a summary of the information that may be available from Pfizer? I drafted a table if it is helpful, but feel free to provide additional information or in whatever format would be best. We are also happy to have a call to discuss this information.

As we plan, it may also be helpful to discuss when and how ACIP will be able to review the data submitted to FDA for a BLA as well, as this will inform both a vote on use of the vaccines under BLA, as well as informing possible booster recommendations as well.

Thanks!
Sara



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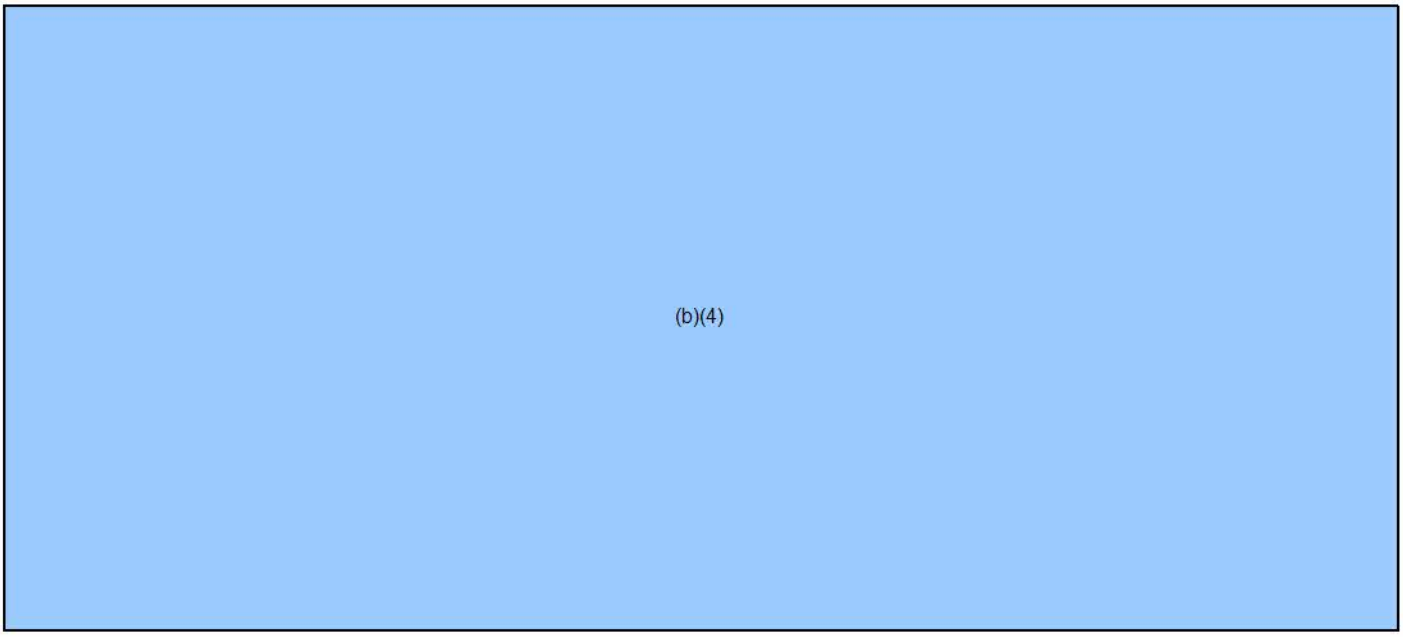

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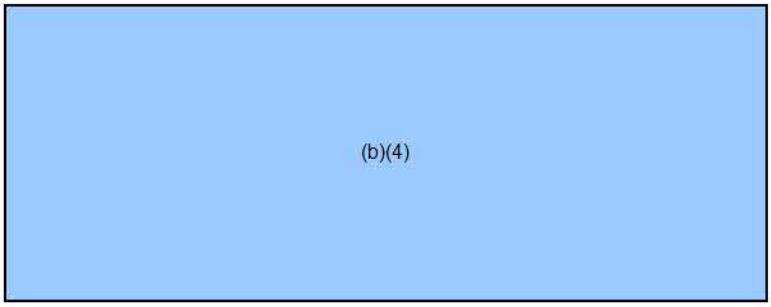

From: (b)(4) (b)(4) (b)
Sent: Tue, 1 Jun 2021 21:28:22 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); (b)(4) (b)(4)
Subject: RE: question

Hi Sara,
I am in the process of getting you some information on this. Hope to have something for you soon.
Best,
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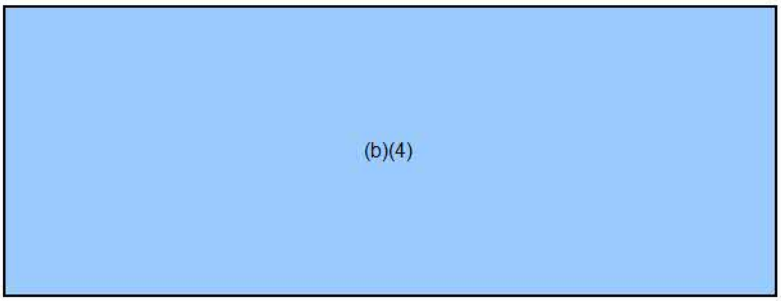

From: (b)(4) (b)(4) (b
Sent: Wed, 2 Jun 2021 13:39:40 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); (b)(4) (b)(4) (b)(4) (b)(4)
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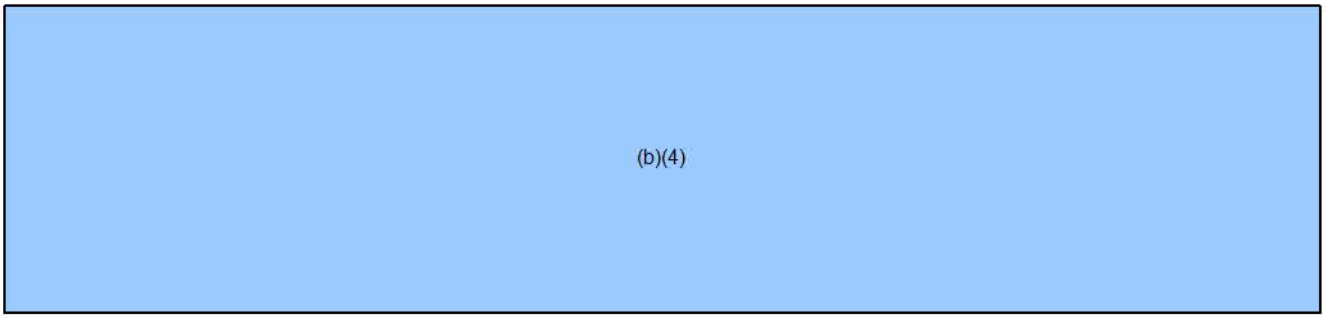

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We are still having discussions around this issue. It is obviously easier to make a decision around those who received the vaccine in a clinical trial, but at the same dose/interval, etc where efficacy was demonstrated- but harder for those other vaccines. We are also trying to determine the number of people and type of vaccines this may represent. Do you mind providing a list of the different vaccines people received (dose, schedule and type), as well as the number of people it may involve (estimates are OK- just an idea of the scale). The plan is once we have an idea of what may be involved, we can hopefully make a more informed decision.

Thanks-

Sara

From: (b)(4) (b)(4) (b) (b)(4)
Sent: Monday, May 17, 2021 12:49 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4)
Subject: RE: question

Hello Sara,
I hope you had a nice weekend, dare I hope that maybe you got to rest a bit after the marathon ACIP, MMWR and clinical considerations updates last week!
I was just following up on the question we asked below regarding using the vaccination cards to record experimental vaccines in our trials (see below email)
Thank you in advance for any guidance you can provide us.
Best regards,
(b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, May 11, 2021 7:47 PM
To: (b)(4) (b)(4) ((b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4)
Subject: [EXTERNAL] RE: REVISED Pfizer presentation slides

(b)(4)

Thanks- passed your updated slides along. I'll also check on your question as well. Can't promise we'll have an answer by tomorrow, but we'll get back to you.

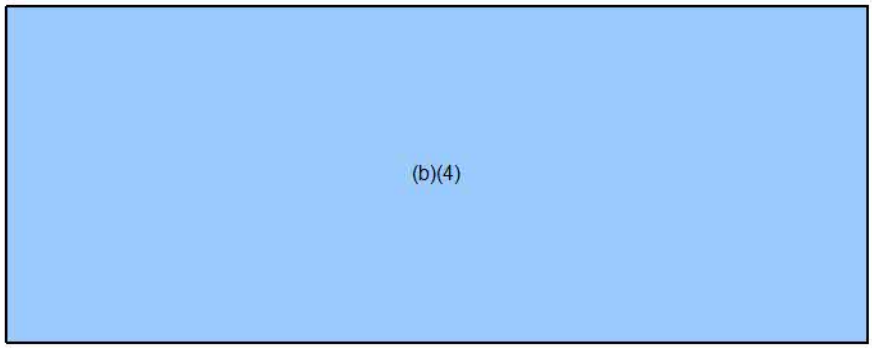
Thanks!
Sara

From: (b)(4) (b)(4) (b (b)(4)
Sent: Tuesday, May 11, 2021 7:10 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4)
Subject: REVISED Pfizer presentation slides
Importance: High

Dear Sara,
So sorry, we received some last minute revisions from internal colleagues so please use the attached REVISED slides for the meeting tomorrow.

Also, we have a separate question. (b)(4) (b)(4) (b)(4). Some guidance was received suggesting that it would be appropriate to do so and to include such vaccines on the card (as long as their precise nature and investigational status is recorded) but that such individuals should not feel at will to follow the current CDC recommendations for fully vaccinated individuals. We would appreciate any guidance you could provide us on this.

Thank you and see you tomorrow,
All the best,
(b)(4) and (b)(



From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Mon, 14 Jun 2021 16:42:23 +0000
To: (b)(4) (b)(4) (b)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: question
Attachments: 2021-COVID-19-vaccine-participant-record-print.pdf

(b)(4) and all:

Apologies but took a minute to get the final version of the Trial Participant card. It is attached here. Similar to the standard CDC card, we would ask that you not post it publicly on a website or anything else public facing.

Regarding the B.1.351 variant- we would actually be OK with those individuals receiving the 'standard' CDC card. Based on the preliminary data from Moderna's 1.351 variant-specific vaccine that provided very similar antibody levels for the D614G 'wild type' SARS-CoV-2 virus and other variants, we aren't anticipating a meaningful difference in VE for most variants. (However, let us know if you have any data that may suggest otherwise!).

Thanks and let me know if there are any other questions.

Sara

From: (b)(4) (b)(4) (b) (b)(4)
Sent: Thursday, June 10, 2021 9:22 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: question

Good morning Sara,

(b)(4)

(b)(4) We look forward to receiving copies of the CDC Clinical Trial Participant card.

Best,

(b)(4) (b)(4) and (b)(

From: (b)(4) (b)(4) (b
Sent: Wednesday, June 9, 2021 12:38 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4)

(b)(4) (b)(4) (b)(4)
Subject: RE: question

Great minds!
Thank you for this response Sara.
I will send out an appointment shortly for Friday 3-3:30pm, thank you again for your time and flexibility.
All the best,
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Wednesday, June 9, 2021 12:24 PM
To: (b)(4) (b)(4) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4)
(b)(4) (b)(4) (b)(4)
Subject: [EXTERNAL] RE: question

(b)(4)

I was literally typing the response on the vaccination cards as I received your email- apologies for the delay!!

We've discussed internally and feel that those who received the (b)(4) study could receive a "Clinical Trial Participant" CDC card- we drafted it for trial participants for non-EUA authorized vaccines and are happy to share for these individuals. It looks similar to the regular "CDC card"- but acknowledges that FDA and ACIP have not reviewed data on this specific vaccine.

For the others:

- Anyone who received a 2-dose primary series of BNT162b2 can receive the standard "CDC card". A 3rd dose could be recorded, but it's the receipt of the initial 2 doses that count for the 'fully vaccinated' guidance (and implications of 'the card').
- Individuals who received 2 doses of 20mcg can receive the standard "CDC card". Per our guidance, the dose can 'count' if it is at least half the original dose.
- Individuals who received the 'ready to use' formulation can receive the standard "CDC card".

I ***think*** that should cover it, but let us know if there are other questions we didn't address. I will get the "Clinical Trial Participant" card and share it with you ASAP.

We can be available from 3-3:30 on Friday. Happy to chat about booster dose studies.

Thanks!
Sara

From: (b)(4) (b)(4) (b)((b)(4)
Sent: Wednesday, June 9, 2021 12:07 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: question

Dear Sara,
I hope you are well.
Two things: I wanted to follow up on the pending question below regarding the use of the vaccination cards in our trials using mixed doses of COVID vaccine.
The second is we would like to give you a quick update and get your insights on our booster studies and timelines. We won't need more than a half hour. Would you have any availability this Friday between 2pm-3:30pm EDT?
Thank you as always!
Best,
(b)(4) (b)(4) and (b)(

From: (b)(4) (b)(4) (b)(4
Sent: Tuesday, June 1, 2021 9:17 AM
To: 'Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)' <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4)
Subject: RE: question

Thank you Sara, we know you are extremely busy and we so appreciate your insights and assistance.
Best,
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, June 1, 2021 9:07 AM
To: (b)(4) (b)(4) (b) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4)
Subject: [EXTERNAL] RE: question

(b)(4)

Thanks for staying on top of this. When we started trying to answer this question- it led us down the road for "well first we need to figure out what to do with all the Phase 3 trial participants". Now that we've decided that clearly, we can hopefully make an informed decision on this issue. I've sent draft responses to our leadership. As soon as I get their approval I'll send it back to you.

Thanks and sorry this has taken so long!!!

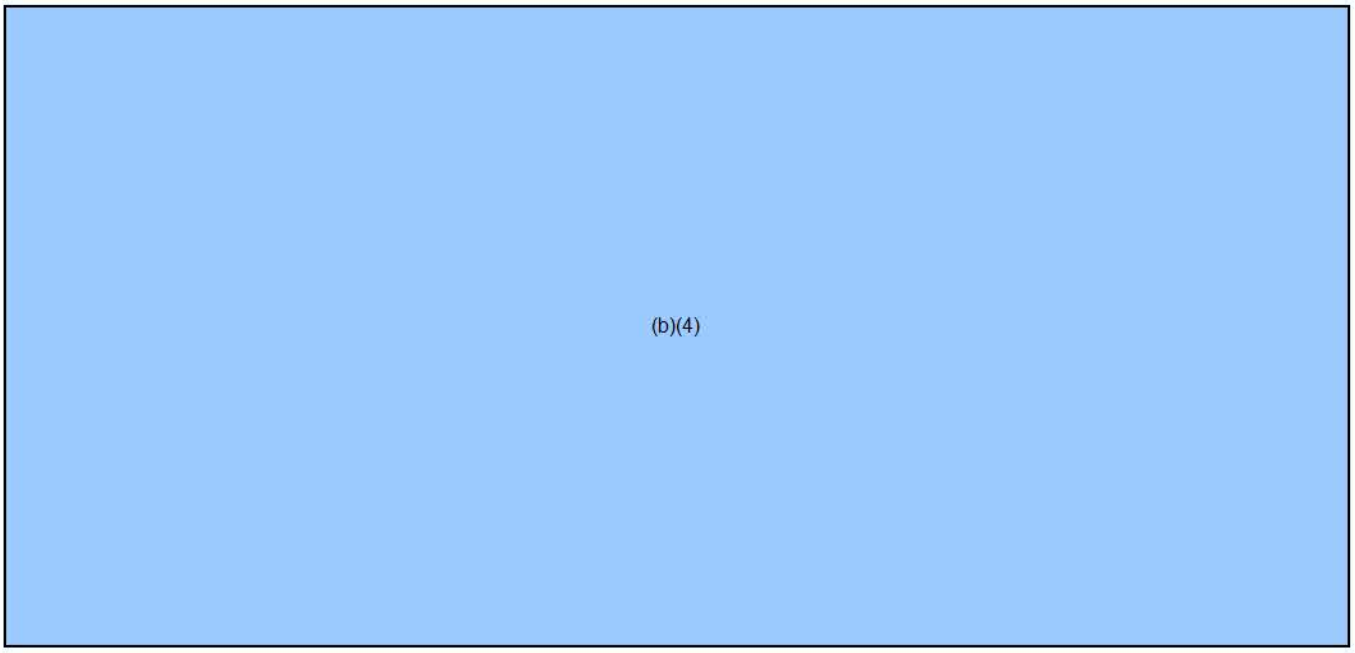
Sara

From: (b)(4) (b)(4) (b) (b)(4)
Sent: Tuesday, June 1, 2021 8:42 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4)
Subject: RE: question

Dear Sara,
I hope you had a nice holiday (and hopefully better weather than here is the northeast, it was miserable!!!!)
I just wanted to follow up with you on this questions from our clinical trial colleagues.
Best regards,
(b)(4) and (b)(

From: (b)(4) (b)(4) (b)
Sent: Monday, May 17, 2021 8:56 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4)
Subject: RE: question

Dear Sara,
We received the following information from our research colleagues regarding approximately how many people have received what formulations and schedules in the trials thus far:



Hopefully this is helpful. Please let us know if you have any other questions.

Best,
(b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, May 17, 2021 1:25 PM
To: (b)(4) (b)(4) (b (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4)
Subject: [EXTERNAL] RE: question

(b)(4) and (b)(4

Thanks for this. I did get a bit of a break over the weekend which was nice! (3 ACIP meetings in the last 5 weeks didn't leave time for much rest previously!).

We are still having discussions around this issue. It is obviously easier to make a decision around those who received the vaccine in a clinical trial, but at the same dose/interval, etc where efficacy was demonstrated- but harder for those other vaccines. We are also trying to determine the number of people and type of vaccines this may represent. Do you mind providing a list of the different vaccines people received (dose, schedule and type), as well as the number of people it may involve (estimates are OK- just an idea of the scale). The plan is once we have an idea of what may be involved, we can hopefully make a more informed decision.

Thanks-

Sara

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Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4)
Subject: RE: question

Hello Sara,
I hope you had a nice weekend, dare I hope that maybe you got to rest a bit after the marathon ACIP, MMWR and clinical considerations updates last week!
I was just following up on the question we asked below regarding using the vaccination cards to record experimental vaccines in our trials (see below email)
Thank you in advance for any guidance you can provide us.
Best regards,
(b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, May 11, 2021 7:47 PM
To: (b)(4) (b)(4) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4)
Subject: [EXTERNAL] RE: REVISED Pfizer presentation slides

(b)(4)

Thanks- passed your updated slides along. I'll also check on your question as well. Can't promise we'll have an answer by tomorrow, but we'll get back to you.

Thanks!
Sara

From: (b)(4) (b)(4) (b)(4)
Sent: Tuesday, May 11, 2021 7:10 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4)
Subject: REVISED Pfizer presentation slides
Importance: High

Dear Sara,
So sorry, we received some last minute revisions from internal colleagues so please use the attached REVISED slides for the meeting tomorrow.

Also, we have a separate question. (b)(4)

(b)(4)

(b)(4) We would appreciate any guidance you could provide us on this.

Thank you and see you tomorrow,
All the best,
(b)(4) and (b)(

(b)(4)

(b)(4)

COVID-19 Vaccine Trial Participant

Vaccines recorded on this card were received through participation in a clinical trial. The individual can be considered "fully vaccinated" for public health purposes. However, this does not imply that the vaccine has been authorized by the FDA, or is recommended by CDC or ACIP.

Last Name First Name MI

Date of birth Patient number *(medical record or IIS record number)*

Vaccine	**Product Name/Manufacturer** **Lot Number**	**Date**	**Healthcare Professional or Clinic Site**
1st Dose COVID-19		____/____/____ *mm dd yy*	
2nd Dose COVID-19		____/____/____ *mm dd yy*	
Other		____/____/____ *mm dd yy*	
Other		____/____/____ *mm dd yy*	

Reminder! Keep this card!

Bring this vaccination record to every vaccination or medical visit. Check with your health care provider to make sure you are not missing any doses of routinely recommended vaccines.

For more information about COVID-19 and COVID-19 vaccine, visit **cdc.gov/coronavirus/2019-ncov/index.html**.

You can report possible adverse reactions following COVID-19 vaccination to the Vaccine Adverse Event Reporting System (VAERS) at **vaers.hhs.gov**.

Lleve este registro de vacunación a cada cita médica o de vacunación. Consulte con su proveedor de atención médica para asegurarse de que no le falte ninguna dosis de las vacunas recomendadas.

Para obtener más información sobre el COVID-19 y la vacuna contra el COVID-19, visite **espanol.cdc.gov/coronavirus/2019-ncov/index.html**.

Puede notificar las posibles reacciones adversas después de la vacunación contra el COVID-19 al Sistema de Notificación de Reacciones Adversas a las Vacunas (VAERS) en **vaers.hhs.gov**.

From: (b)(4) (b)(4) (b)(
Sent: Tue, 13 Jul 2021 14:27:55 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: (b)(4) (b)(4) Mbaeyi, Sarah (CDC/DDID/NCIRD/OD)
Subject: RE: quick update call tomorrow?

No worries Sara, I will check schedules again here for any flexibility and get back to you ASAP. And many thanks for your flexibility in all this!

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, July 13, 2021 10:08 AM
To: (b)(4) (b)(4) ((b)(4)
Cc: (b)(4) (b)(4) (b)(4) Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>
Subject: [EXTERNAL] RE: quick update call tomorrow?

(b)(4)

My apologies- when I sent the available times, I didn't have it on my work calendar that I have an appointment for my son at 5pm this afternoon. I'm happy to join the first part of the call and then catch up with Sarah M later, or we can reschedule. We are still open tomorrow morning. Again- apologies… the 'life' calendar didn't sync with the 'work' calendar!

Thanks-

Sara

From: (b)(4) (b)(4) (b) (b)(4)
Sent: Monday, July 12, 2021 5:59 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: (b)(4) (b)(4) (b)(4) Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>
Subject: RE: quick update call tomorrow?

Hello Sara and Sarah,
Sorry for the delay on my response! I was checking with the internal colleagues and tomorrow from 4:30-5:30pm EDT would work best for us. Is that still an ok time for you all?
Best,
(b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, July 12, 2021 11:51 AM
To: (b)(4) (b)(4) (b (b)(4)
Cc: (b)(4) (b)(4) (b)(4) Mbaeyi, Sarah (CDC/DDID/NCIRD/OD)

<vif6@cdc.gov>
Subject: [EXTERNAL] RE: quick update call tomorrow?

(b)(4)

Sorry- I was out last week. Back now and catching up on all the craziness.

We would love to hear the data you have available. Is this the data being presented to CDC, FDA and HHS this afternoon?

Also- would be interested in discussing ACIP reviewing the data submitted to FDA for a BLA as well. We're working out exactly how that will work with ACIP, but as our initial votes were specifically 'under an EUA', we will likely need to re-review the additional data.

I am including Sarah M in the meeting because she's been helping coordinate booster information as well. We could be available:
Tues from 1-1:30 or any time after 2pm. We could also meet Wednesday from 9:30-12 (all times EST).

Thanks!
Sara

From: (b)(4) (b)(4) (b)((b)(4)
Sent: Thursday, July 8, 2021 10:21 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: (b)(4) (b)(4) (b)(4)
Subject: quick update call tomorrow?

Dear Sara,
I hope you had a nice holiday weekend. (b)(4)

(b)(4)

Would you be able to get on a call with us tomorrow, no more than an hour or 45 mins?
Thank you!
All the best,
(b)(4) and (b)(

From: (b)(4) (b)(4) (b)(
Sent: Tue, 13 Jul 2021 14:37:42 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: (b)(4) (b)(4) Mbaeyi, Sarah (CDC/DDID/NCIRD/OD)
Subject: RE: quick update call tomorrow?

Hello again,
We can adjust and make it 4-5pm today, I will send the appointment shortly.
Thank you again!

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, July 13, 2021 10:08 AM
To: (b)(4) (b)(4) (b (b)(4)
Cc: (b)(4) (b)(4) (b)(4) Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>
Subject: [EXTERNAL] RE: quick update call tomorrow?

(b)(4)

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Thanks-

Sara

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Cc: (b)(4) (b)(4) (b)(4) Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>
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Hello Sara and Sarah,
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Best,
(b)(4) and (b)(

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To: (b)(4) (b)(4) ((b)(4)
Cc: (b)(4) (b)(4) (b)(4) Mbaeyi, Sarah (CDC/DDID/NCIRD/OD)

<vif6@cdc.gov>
Subject: [EXTERNAL] RE: quick update call tomorrow?

(b)(4)

Sorry- I was out last week. Back now and catching up on all the craziness.

We would love to hear the data you have available. Is this the data being presented to CDC, FDA and HHS this afternoon?

Also- would be interested in discussing ACIP reviewing the data submitted to FDA for a BLA as well. We're working out exactly how that will work with ACIP, but as our initial votes were specifically 'under an EUA', we will likely need to re-review the additional data.

I am including Sarah M in the meeting because she's been helping coordinate booster information as well. We could be available:
Tues from 1-1:30 or any time after 2pm. We could also meet Wednesday from 9:30-12 (all times EST).

Thanks!
Sara

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Sent: Thursday, July 8, 2021 10:21 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: (b)(4) (b)(4) (b)(4)
Subject: quick update call tomorrow?

Dear Sara,
I hope you had a nice holiday weekend. (b)(4)
(b)(4)
Would you be able to get on a call with us tomorrow, no more than an hour or 45 mins?
Thank you!
All the best,
(b)(4) and (b)(

From: (b)(4) (b)(4) (b)(
Sent: Tue, 22 Jun 2021 20:20:35 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: (b)(4) (b)(4)
Subject: RE: Report attached

Dear Sara,
I know you must be swamped but I just wanted to make sure you received this email and the report that was attached.
Of course, we would greatly appreciate it if you can share the presentations for tomorrow when available.
Thank you as always,
(b)(4) and (b)(

From: (b)(4) (b)(4) (b)
Sent: Monday, June 21, 2021 10:50 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: (b)(4) (b)(4) (b)(4)
Subject: Report attached

Dear Sara,
Our research and safety colleagues have compiled the attached report (b)(4) and we thought it might also be of interest to you and Tom.
Please let us know if you have any questions.
Best regards,
(b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Fri, 11 Jun 2021 21:59:04 +0000
To: (b)(4) (b)(4) (x)
Cc: Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP); Markowitz, Lauri (CDC/DDID/NCIRD/DVD)
Subject: RE: Review of Myocarditis/Pericarditis Data

(b)(4)

We won't be able to accommodate a presentation from Moderna this week, at either VaST or the Work Group. However- if you have a summary document you want us to share with the WG and ACIP members as 'background material' before the 6/18 ACIP meeting, I would be happy to do that. I'll defer to Lauri if it may be helpful to have a presentation on this at a future VaST meeting.

Regarding the definitions- our safety group hasn't been using the Brighton Collaboration definition specifically. Others are working to set up a meeting between Moderna and the safety group, so maybe that would be the best time to get into the definitions. But I'm sure we can work out sharing the definition.

Thanks!

Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Friday, June 11, 2021 8:05 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Review of Myocarditis/Pericarditis Data

Hi Sara,

Would it be possible for Moderna to present its summary of myocarditis to the VaST or COVID-19 Work Group? We thought it might be useful to share what we have done. And do you know if the VAERS/VSD data have been analyzed using the Brighton Collaboration definition or will be soon?

Let me know please.

Thanks.

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Wed, 12 May 2021 12:09:19 +0000
To: (b)(4) (b)(4) (b)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); (b)(4) (b)(4)
Subject: RE: REVISED Pfizer presentation slides

(b)(4)

We are going to need to discuss this with Amanda. Especially since our meetings are virtual now, we have been posting all slides during the meeting. This is how we've handled it with all the votes and all the manufacturers, and is very important in the transparency of the process. We won't post them until I've discussed with Amanda and we can let you know what her thoughts are.

Thanks-
Sara

From: (b)(4) (b)(4) (b)(4)
Sent: Wednesday, May 12, 2021 7:13 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4)
Subject: RE: REVISED Pfizer presentation slides

Thank you Sara, we understand!
Also just re-confirming the presentation cannot be posted yet.
Many thanks
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, May 11, 2021 7:47 PM
To: (b)(4) (b)(4) (b) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4)
Subject: [EXTERNAL] RE: REVISED Pfizer presentation slides

(b)(4)

Thanks- passed your updated slides along. I'll also check on your question as well. Can't promise we'll have an answer by tomorrow, but we'll get back to you.

Thanks!
Sara

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Sent: Tuesday, May 11, 2021 7:10 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; (b)(4) (b)(4) (b)(4)
Subject: REVISED Pfizer presentation slides
Importance: High

Dear Sara,
So sorry, we received some last minute revisions from internal colleagues so please use the attached REVISED slides for the meeting tomorrow.

Also, we have a separate question. (b)(4) (b)(4) (b)(4) Some guidance was received suggesting that it would be appropriate to do so and to include such vaccines on the card (as long as their precise nature and investigational status is recorded) but that such individuals should not feel at will to follow the current CDC recommendations for fully vaccinated individuals. We would appreciate any guidance you could provide us on this.

Thank you and see you tomorrow,
All the best,
(b)(4) and (b)(

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Tue, 8 Jun 2021 21:45:12 +0000
To: (b)(4) (b)(4) (x)
Subject: RE: Revised Version - Amendment to Confidentiality Agreement - CDC & Moderna

Thanks (b)(4) We will work on getting this back to you ASAP.

Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Tuesday, June 8, 2021 5:37 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Revised Version - Amendment to Confidentiality Agreement - CDC & Moderna

Hi Sara,

Attached is a revised agreement between CDC and Moderna for the purpose of Moderna sharing confidential clinical data in the future in support of our EUAs in adolescents and children, BLA in persons 18 years of age and older, and any corresponding VRBPAC documents. Note that we have identified this as Amendment 2 and attached Exhibit A with the list of persons allowed to see the data.

Please let us know if this is acceptable. If so, please obtain the appropriate signature at your end, return to me, and I will obtain signature at our end & return a fully executed copy to you. Please destroy the earlier version you sent us.

Thanks.

(b)(4)

Please consider the environment before printing this email

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Wed, 9 Jun 2021 15:21:06 +0000
To: (b)(4) (b)(4) (x)
Subject: RE: Revised Version - Amendment to Confidentiality Agreement - CDC & Moderna
Attachments: CDC - CDA Contract ID 16732 - Amendment 2_effective 08June2021_CDC SIGNED.docx

(b)(4)

Thanks- we've signed the attached confidentiality agreement. Let me know if there's anything else you need.

Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Tuesday, June 8, 2021 5:37 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Revised Version - Amendment to Confidentiality Agreement - CDC & Moderna

Hi Sara,

Attached is a revised agreement between CDC and Moderna for the purpose of Moderna sharing confidential clinical data in the future in support of our EUAs in adolescents and children, BLA in persons 18 years of age and older, and any corresponding VRBPAC documents. Note that we have identified this as Amendment 2 and attached Exhibit A with the list of persons allowed to see the data.

Please let us know if this is acceptable. If so, please obtain the appropriate signature at your end, return to me, and I will obtain signature at our end & return a fully executed copy to you. Please destroy the earlier version you sent us.

Thanks.

(b)(4)

Please consider the environment before printing this email

Amendment #02 to Confidentiality Agreement

THIS AMENDMENT #02 TO CONFIDENTIALITY AGREEMENT (this "Amendment #02"), is entered into as of June 8, 2021 (the "Amendment #02 Effective Date"), by and between ModernaTX, Inc. ("Moderna"), and The Centers for Disease Control and Prevention (CDC) ("Recipient" or "CDC"). Each of Moderna and CDC may be referred to herein as a "Party" or together as the "Parties".

WHEREAS, Moderna and CDC are parties to a Confidentiality Agreement dated November 10, 2020 (the "Agreement") and Amendment #1 to the Agreement dated December 4, 2020 ("Amendment #1); and

WHEREAS, Moderna and CDC desire to continue the Agreement in accordance with and subject to the terms and conditions therein, as more fully described herein.

NOW THEREFORE, for good and valuable consideration, the receipt and sufficiency of which is hereby mutually acknowledged, CDC and Moderna hereby agree as follows. Capitalized terms used but not defined herein shall have the meanings ascribed to such terms in the Agreement.

1. Section 1 "Purpose". CDC and Moderna each acknowledge and agree that Section 1 of the Agreement shall be deleted in its entirety and replaced with the following:

> **1. Purpose.** This Agreement is made in order for ModernaTX and its Affiliates (collectively, "Moderna") to disclose in confidence to Recipient, during the term of this Agreement, information including: the Clinical Summary (section 2.5) of Moderna's FDA application and its background document for the December 2020 VRBPAC meeting in connection with Moderna's mRNA-1273 Emergency Use Authorization (EUA) submission; the Clinical Summaries in support of Moderna's upcoming EUAs for children and adolescents; and the Biologics License Application (BLA) for persons 18 years and older, as well as any other corresponding background documents submitted for the VRBPAC meeting. CDC will use this information solely for the purpose of developing ACIP recommendations for vaccine use(the "Purpose"). CDC may share these documents in confidence with those employees listed in Exhibit A only. As used herein, the term "Affiliate" means with respect to a given entity any person or legal entity directly or indirectly controlling, controlled by or under common control with such entity, wherecontrol shall mean the direct or indirect ownership of more than fifty percent (50%) of the outstanding voting securities of an entity or such other relationship as results in the actual control over the management,assets, business and affairs of an entity.

2. Exhibit A. CDC and Moderna each acknowledge and agree that Exhibit A of the Agreement shall be deleted in its entirety and replaced with the Exhibit A attached to this Amendment #02.

3. General Terms. Except with respect to the amendments as set forth above, the terms and conditions of the Agreement shall remain unchanged. This Amendment #02 shall be construed in accordance with and governed by the same laws that govern the Agreement.

[***Remainder of page intentionally left blank***]

IN WITNESS WHEREOF, CDC and Moderna each has caused this Amendment #02 to be executed by its duly authorized representative.

MODERNATX, INC.	**THE CENTERS FOR DISEASE CONTROL AND PREVENTION**
	(b)(6)
By	*By*
	Samuel Posner
Name	*Name*
	Acting Director, NCIRD
Title	*Title*
	June 9, 2021
Date	*Date*

Exhibit A

Recipient (CDC) Representatives

Julia Gargano
Danielle Moulia
Hannah Rosenblum
Nicole Reisman
Heather Scobie
Karen Broder
Naomi Tepper
Jessica MacNeil
Sara Oliver

From: (b)(4) (b)(4) (x)
Sent: Tue, 13 Jul 2021 17:04:15 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Re: RE: ACIP July 22

Thanks. That is helpful. We are still hoping to hear something later this week or early next week. I will keep you posted.
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, July 13, 2021 12:50 PM
To: (b)(4) (b)(4) (x) (b)(4)
Subject: RE: RE: ACIP July 22

EXTERNAL

No- that meeting is already scheduled for a full day. Once authorized, we will need to have a separate ACIP meeting. We've let the WG and ACIP members know that could happen, but don't think we could add it all in for 1 single meeting.

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Tuesday, July 13, 2021 12:47 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Re: RE: ACIP July 22

Thanks . Might that also be a slot for us to present our adolescent data if authorized by then?

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, July 13, 2021 12:26 PM
To: (b)(4) (b)(4) (x) (b)(4)
Subject: RE:

EXTERNAL

(b)(4)

Thanks- it was nice but not nearly long enough!

We're working on getting an agenda posted ASAP. But the current plan is to discuss the GBS safety signal, update our benefit/risk analyses, and updates to clinical considerations.

Thanks-
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Tuesday, July 13, 2021 12:23 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject:

Hi Sara,

I hope you had a good vacation.

I wanted to ask about the July 22 ACIP meeting that has just been called. Can you provide any more details please?

Thanks.

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Thu, 3 Jun 2021 13:23:47 +0000
To: (b)(4) (b)(4) (x)
Subject: RE: School Impact - COVID-19

Yes- my 'inside source' tells me that they use several inputs to model- and that the estimate they get is within the range of those two sources. Unfortunately their isn't one standard number/approach, but it seems if you use those as a high and low estimate for a range, it may work.

Sorry that there isn't a better way to look at that, but it varies how it is reported and collected (as all things in the US!)

Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Wednesday, June 2, 2021 10:13 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Re: School Impact - COVID-19

Hi Sara,

Many thanks for this information. At first glance, it appears that the data are quite different between the 2 sources, but perhaps I should review in more detail.

Thanks again

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Wednesday, June 2, 2021 5:15 PM
To: (b)(4) (b)(4) (x) (b)(4)
Subject: RE: School Impact - COVID-19

EXTERNAL

(b)(4)

To follow up on this request- I was able to find two sources that you could publicly cite. CDC is working on broader modeling on this, but we don't have results that are ready to be shared publicly, but hopefully these sources can be helpful.

- MCH: Stay informed of the rapid school district changes with the below resources - MCH Data

- IES: Dept. of ED survey, which collects data on a monthly basis. Monthly School Survey Dashboard (ed.gov)

Thanks-
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Friday, May 28, 2021 7:38 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: School Impact - COVID-19

Hi Sara,

In looking at the impact of COVID-19 on children, have you come across any data describing how many children have either not gone to school or used virtual schooling? Any information you have on this would be most helpful as we start to talk about the value of vaccinating children.

Many thanks!

(b)(4)

From: (b)(4) (b)(4)
Sent: Fri, 11 Jun 2021 19:36:11 +0000
To: Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP)
Cc: Nair, Narayan (FDA/CBER); Hicks, Lauri (CDC/DDID/NCEZID/DHQP); Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); Destefano, Frank (CDC/DDID/NCEZID/DHQP)
Subject: RE: Technical specifications for VRBPAC presentation

Dear Tom,

Many thanks for the quick response.

Let me propose the following times – and we can see what is most convenient:

Week of June 14-18

Monday 9-10 AM
Tuesday 1-6 PM
Wednesday 7 AM- 12 noon

If folks could respond with workable times, we can finalize one.

Best,

(b)(4)

From: Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP) <ayv6@cdc.gov>
Sent: Friday, June 11, 2021 3:24 PM
To: (b)(4) (b)(4) (b)(4)
Cc: Nair, Narayan (FDA/CBER) <Narayan.Nair@fda.hhs.gov>; Hicks, Lauri (CDC/DDID/NCEZID/DHQP) <auq3@cdc.gov>; Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>; Destefano, Frank (CDC/DDID/NCEZID/DHQP) <fxd1@cdc.gov>
Subject: RE: Technical specifications for VRBPAC presentation

EXTERNAL

Dear (b)(4)

Nice to hear from you and I hope you are well. We would be happy to have a call with you and your Moderna colleagues. I would ask that our FDA partners be invited too. Would you please include the folks on the Cc line. Thanks.

Regards,

Tom

From: (b)(4) (b)(4) (b)(4)
Sent: Friday, June 11, 2021 10:09 AM
To: Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP) <ayv6@cdc.gov>; Destefano, Frank (CDC/DDID/NCEZID/DHQP) <fxd1@cdc.gov>
Subject: Technical specifications for VRBPAC presentation

Dear Tom and Frank,

As you can imagine, there is great interest in the material presented at yesterday's VRBPAC.

Would it be possible to arrange a brief call between CDC and Moderna so that we can better understand the data sources and methods used to derive the results presented at yesterday's VRBPAC?

This would be helpful as we continue to assess the myocarditis/pericarditis signal at Moderna.

With best regards,

(b)(4)

(b)(4) (b)(4) (b)(4)
(b)(4)

moderna

From: (b)(4) (b)(4) (b)(
Sent: Fri, 16 Jul 2021 11:12:51 +0000
To: (b)(4) (b)(4) Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: (b)(4) (b)(4)
Subject: RE: thank you and another request!

Thank you Sara!

From: (b)(4) (b)(4) (b)(4)
Sent: Thursday, July 15, 2021 8:19 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>; (b)(4) (b)(4) (b)(4)
Cc: (b)(4) (b)(4)
Subject: RE: thank you and another request!

Thanks Sara!
It works!

Best

(b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Thursday, July 15, 2021 8:18 PM
To: (b)(4) (b)(4) (b) (b)(4)
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: [EXTERNAL] RE: thank you and another request!

OK sounds good. Sent an invitation for noon on Monday. It was the only time I could find, so hopefully it works.

Thanks-
Sara

From: (b)(4) (b)(4) ((b)(4)
Sent: Thursday, July 15, 2021 3:46 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: thank you and another request!

Thanks for this message Sara. We won't need to take any of your time today or tomorrow, we will wait to hear back from you on possible times for a call on Monday.
Thank you so much,
(b)(4) (b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Thursday, July 15, 2021 1:59 PM
To: (b)(4) (b)(4) (b)(4)
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: [EXTERNAL] RE: thank you and another request!

(b)(4)

I wanted to let you know I received this and have been working on it. I'll be bringing in Tom, someone from FDA working on myocarditis, and someone else within our Vaccine Task Force who have done more of the work with the myocarditis longer term follow up. However, it will be Monday before we can bring in the right people. I'm happy to chat with you today/tomorrow, but it will definitely be a more beneficial conversation if we are able to bring in the people working on myocarditis.

Thanks!
Sara

From: (b)(4) (b)(4) (b)(4)
Sent: Wednesday, July 14, 2021 11:02 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: thank you and another request!

Dear Sara,
Thank you again for your time yesterday, we appreciate it very much.

(b)(4)

(b)(6) Could we set something up in the next day or two?
Thank you as always!
Best,
(b)(4) (b)(6) and (b)(

From: (b)(4) (b)(4) (b)(
Sent: Mon, 26 Jul 2021 21:15:38 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: Cohn, Amanda (CDC/DDID/NCIRD/OD); (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: touch base soon

Thanks! Will do

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, July 26, 2021 5:03 PM
To: (b)(4) (b)(4) ((b)(4)
Cc: Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>; (b)(4) (b)(4)
(b)(4) (b)(4) (b)(4)
Subject: [EXTERNAL] RE: touch base soon

I'll send a Teams invitation for 5:30- feel free to forward as needed.

Thanks!
Sara

From: (b)(4) (b)(4) (b (b)(4)
Sent: Monday, July 26, 2021 2:36 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>; (b)(4) (b)(4)
(b)(4) (b)(4) (b)(4)
Subject: RE: touch base soon

Dear Sara,
Today at 5:30pm EDT works for our Pfizer colleagues. Would you like to send the appt or shall I?
Best,
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, July 26, 2021 1:48 PM
To: (b)(4) (b)(4) (b (b)(4) (b)(4) (b)(4) (b)(4)
(b)(4) (b)(4)
Cc: Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>
Subject: [EXTERNAL] touch base soon

(b)(4) (b)(and (b)(4):

Wanted to reach out to you about something quickly. As I am sure you are aware after this last ACIP meeting, there is substantial desire to move forward with additional doses in immunocompromised populations. We have had a recent development in these discussions and wanted to touch base with you about this. Things are moving rather quickly so was

wondering if you would be able to touch base either late this afternoon/evening, or sometime tomorrow.

I'm trying to find a time our regulatory colleagues at CDC can join so there may be a few details around regulatory points, if that helps you with any additional people on the call.

We could meet after 5pm this evening, or 9:30-10:30 or 12-1 EST tomorrow morning.

Thanks-
Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: (b)(4) (b)(4) (b)
Sent: Mon, 26 Jul 2021 17:57:38 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); (b)(4) (b)(4) (b)(4) (b)(4)
M.
Cc: Cohn, Amanda (CDC/DDID/NCIRD/OD)
Subject: RE: touch base soon

Dear Sara,
Thank you for your note. I will check schedules internally and see what times work best.
I will get back to you as soon as possible
Best,
(b)(4) (b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, July 26, 2021 1:48 PM
To: (b)(4) (b)(4) (b) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Cc: Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>
Subject: [EXTERNAL] touch base soon

(b)(4) (b)(and (b)(4)

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Thanks-
Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Mon, 26 Jul 2021 22:00:47 +0000
To: (b)(4) (b)(4) (x)
Subject: RE: touch base soon

(b)(4)

FYI our call at 5:30 is running over. Will join as soon as we can.

Thanks!
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Monday, July 26, 2021 5:04 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>
Subject: Re: touch base soon

What time please? 6 pm?

Thanks.

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, July 26, 2021 5:02 PM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>
Subject: RE: touch base soon

EXTERNAL

Yes- please do. I'll send a meeting invitation, feel free to forward as needed.

Thanks
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Monday, July 26, 2021 2:02 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>
Subject: Re: touch base soon

Hi Sara,

Thanks for reaching out. I would be happy to talk at 6 pm tonight or either time tomorrow.

May I invite one of our regulatory colleagues and (b)(4) (b)(4) to join the call as well?

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, July 26, 2021 1:48 PM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>
Subject: touch base soon

EXTERNAL

(b)(4)

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I'm trying to find a time our regulatory colleagues at CDC can join so there may be a few details around regulatory points, if that helps you with any additional people on the call.

We could meet after 5pm this evening, or 9:30-10:30 or 12-1 EST tomorrow morning.

Thanks-
Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Mon, 26 Jul 2021 21:06:36 +0000
To: (b)(4) (b)(4) (x)
Cc: Cohn, Amanda (CDC/DDID/NCIRD/OD)
Subject: RE: touch base soon

Yes- just sent a meeting invitation for 6pm EST.

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Monday, July 26, 2021 5:04 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>
Subject: Re: touch base soon

What time please? 6 pm?

Thanks.

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, July 26, 2021 5:02 PM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>
Subject: RE: touch base soon

EXTERNAL

Yes- please do. I'll send a meeting invitation, feel free to forward as needed.

Thanks
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Monday, July 26, 2021 2:02 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>
Subject: Re: touch base soon

Hi Sara,

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May I invite one of our regulatory colleagues and (b)(4) (b)(4) to join the call as well?

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, July 26, 2021 1:48 PM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>
Subject: touch base soon

EXTERNAL

(b)(4)

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I'm trying to find a time our regulatory colleagues at CDC can join so there may be a few details around regulatory points, if that helps you with any additional people on the call.

We could meet after 5pm this evening, or 9:30-10:30 or 12-1 EST tomorrow morning.

Thanks-
Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: (b)(4) (b)(4)
Sent: Tue, 27 Jul 2021 00:48:04 +0000
To: Cohn, Amanda (CDC/DDID/NCIRD/OD); (b)(4) (b)(4) (x); (b)(4)
Cc: Yu, Patricia A. (CDC/DDID/NCEZID/DPEI); Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); Yu, Yon C. (CDC/DDID/NCEZID/DPEI)
Subject: RE: Touch Base: CDC and Moderna

Hi Amanda,

(b)(4) has already sent an e-mail to key team members to solicit additional questions, but please let me reassure you that there is definite interest on our part to figure out how to help, which was confirmed by my manager earlier this evening. (b)(4) will be getting back to you tomorrow.

Best regards,
(b)(4)

From: Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>
Sent: Monday, July 26, 2021 8:46 PM
To: (b)(4) (b)(4) (x) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Cc: Yu, Patricia A. (CDC/DDID/NCEZID/DPEI) <pby7@cdc.gov>; Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>; Yu, Yon C. (CDC/DDID/NCEZID/DPEI) <fkb8@cdc.gov>
Subject: RE: Touch Base: CDC and Moderna

EXTERNAL

Dear (b)(4) (b)(4) and (b)(4)

I wanted to follow-up on Moderna's willingness to support the proposed CDC-sponsored EA-IND. You raised some great questions on the call that we are working through, but we are hoping that the company will consider aligning with this effort to provide an opportunity for the severely immunocompromised to receive an additional dose of an mRNA vaccine through an approved regulatory mechanism as a bridge to an approved BLA or an EUA amendment. In the setting of high disease transmission, especially in those living in states with low vaccination coverage, CDC intends to rapidly develop and submit a protocol for review by FDA.

Could you confirm if Moderna is willing or unwilling to provide CDC a cross reference authorization to data contained in the Moderna IND and MF, if applicable, for Moderna COvI-19 vaccine? If it is possible to have an answer by tomorrow, that would be ideal as we move forward with planning.

Thank you!

Amanda

Amanda Cohn, MD
CAPT, USPHS

Chief Medical Officer
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

Please consider the environment before printing this email

From: (b)(4) (b)(4) (x)
Sent: Thu, 10 Jun 2021 19:46:53 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: Re: Upcoming Meetings

HI Sara,
That is most helpful - thank you!
(b)(4)
From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Thursday, June 10, 2021 3:45 PM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: RE: Upcoming Meetings

EXTERNAL

(b)(4)

We will have a separate WG call next week to discuss myocarditis, prior to the ACIP meeting on the 18th. I can't promise that someone wouldn't ask a question around myocarditis since that is on everyone's mind as it relates to mRNA vaccine and adolescents, but we are anticipating the WG call on the 17th will focus on the Moderna adolescent data for EUA.

Then- we are anticipating we will hold an ACIP meeting to discuss the data shortly after FDA issues an EUA. It is difficult for us to estimate timing when there isn't a set VRBPAC meeting date, but (similar to the Pfizer adolescent data)- we are planning on having a data presentation and vote at the same meeting shortly after an EUA.

Thanks- let me know if there are additional questions.

Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Thursday, June 10, 2021 3:32 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Upcoming Meetings

Hi Sara,

Two more questions for you, please:

1) Should Moderna be prepared to discuss myocarditis at the June 17 WG meeting or is this just about the adolescent data?
2) Is CDC still planning to have a discussion of our adolescent data at the full ACIP once we have an EUA? Or will you present the data beforehand and then have a vote once the EUA is issued?

If you can address these questions, that would be most helpful.

Many thanks.

(b)(4)

Please consider the environment before printing this email

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Fri, 23 Jul 2021 16:21:05 +0000
To: (b)(4) (b)(4) (x)
Subject: RE: Update on EUA - Adolescents

(b)(4)

We aren't sure, but will let you know as soon as we hear anything

Thanks!
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Friday, July 23, 2021 12:08 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Update on EUA - Adolescents

Hi Sara,

I promised to keep you updated on our EUA for adolescents. The latest we heard is that it is likely to be early next week. If any thing changes, I will let you know.

It was mentioned at ACIP yesterday that there might be an Emergency meeting in early August Have all of you set a possible date?

Thanks.

(b)(4)

Please consider the environment before printing this email

From: (b)(4) (b)(4) (x)
Sent: Thu, 27 May 2021 15:45:07 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); Mbaeyi, Sarah (CDC/DDID/NCIRD/OD)
Subject: Re: update on myocarditis

Thanks so much. Tom sent us the near final language to us.
Please send the links when they become live.
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Thursday, May 27, 2021 11:17 AM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>
Subject: update on myocarditis

EXTERNAL

(b)(4)

Wanted to let you know an update on myocarditis. The (current) plan is to release web content describing the reports of myocarditis/pericarditis and clinical considerations, but not a formal HAN. This will be combined with targeted clinician outreach as well. The goal is to have these web updates posted this afternoon. I'll send them on when they are posted.

The language is still being finalized, but a few highlights are below (language is still draft until it's posted, but wanted you to have an idea of what it may say).

- More than 165 million people have received at least one dose of COVID-19 vaccine in the United States, and CDC continues to monitor the safety of COVID-19 vaccines for any health problems that happen after vaccination.
- In April and May of 2021, there have been increased reports to the Vaccine Adverse Event Reporting System (VAERS) of cases of inflammation of the heart—called myocarditis and pericarditis—happening after mRNA COVID-19 vaccination (Pfizer-BioNTech and Moderna) in the United States.
- These reports are rare, given the number of vaccine doses administered, and have been reported after mRNA COVID-19 vaccination (Pfizer-BioNTech and Moderna), particularly in adolescents and young adults.
- CDC and its partners are actively monitoring these reports, by reviewing data and medical records, to learn more about what happened and to see if there is any relationship to COVID-19 vaccination.

As all things CDC, this may change, but I wanted to let you know what our current understanding of the communications plan is.

Thanks-
Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

Please consider the environment before printing this email

From: (b)(4) (b)(4) (b)(4)
Sent: Thu, 27 May 2021 15:26:39 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); (b)(4) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); Mbaeyi, Sarah (CDC/DDID/NCIRD/OD)
Subject: RE: update on myocarditis

Dear Sara,
Thank you so much for this update, it is very helpful. Tom was kind enough to send us a draft of the web content earlier this morning. We would greatly appreciate it if you let us know when it is actually posted and if possible on which webpages so we can direct people to them as appropriate.
Again, we so appreciate your transparency and kindness in keeping us updated.
Best regards,
(b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Thursday, May 27, 2021 11:17 AM
To: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>
Subject: [EXTERNAL] update on myocarditis

(b)(4) and (b)(4

Wanted to let you know an update on myocarditis. The (current) plan is to release web content describing the reports of myocarditis/pericarditis and clinical considerations, but not a formal HAN. This will be combined with targeted clinician outreach as well. The goal is to have these web updates posted this afternoon. I'll send them on when they are posted.

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As all things CDC, this may change, but I wanted to let you know what our current understanding of the communications plan is.

Thanks-
Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: (b)(4) (b)(4) (x)
Sent: Mon, 28 Jun 2021 15:48:43 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Re: Updated Clinical Guidance - Myocarditis/Pericarditis

Thank you!
From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, June 28, 2021 11:48 AM
To: (b)(4) (b)(4) (x) (b)(4)
Subject: RE: Updated Clinical Guidance - Myocarditis/Pericarditis

EXTERNAL

(b)(4)

The language is working its way through CDC clearance. The plan is to post as soon as it is cleared- I'll let you know as soon as we have cleared language to share.

Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Sunday, June 27, 2021 10:33 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Subject: Re: Updated Clinical Guidance - Myocarditis/Pericarditis

Hi Sara,

I am just checking in again. I looked at the Clinical Guidance on myocarditis/pericarditis on the CDC website, but did not see any changes. Has anything changed in the last few days or will anything change in the near future?

Thanks.

(b)(4)

From: (b)(4) (b)(4) (x)
Sent: Thursday, June 24, 2021 4:28 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DBD) <yxo4@cdc.gov>
Subject: Updated Clinical Guidance - Myocarditis/Pericarditis

Hi Sara,

As I am sure you know, we have been asked to update our Fact Sheets today for Moderna's COVID-19 vaccine to include new language on myocarditis/pericarditis. There is a reference in the text to the updated Clinical Guidance from CDC. Do you know when that updated link will go live, please?

Thanks, and nice job yesterday (as always!),

(b)(4)

Please consider the environment before printing this email

From: (b)(4) (b)(4) (b)
Sent: Sat, 29 May 2021 00:44:16 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: (b)(4) (b)(4) MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); Mbaeyi, Sarah (CDC/DDID/NCIRD/OD)
Subject: Re: [EXTERNAL] Pfizer trial participants

Thank you Sara!
Hope you all have a lovely, and hopefully restful, holiday weekend!
Cheers,
(b)(4) and (b)(4

On May 28, 2021, at 5:01 PM, Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov> wrote:

(b)(4) and (b)(4

I wanted to pass this along: We've had discussions around trial participants, especially in light of CDC's guidance for 'fully vaccinated individuals'. Below is the current guidance. Feel free to share and let us know if there are any questions or issues. Also I know that we passed along the "CDC card" already, but I'm including it here as well. I know there are ongoing discussions around getting these into IIS locally but we're happy to facilitate those discussions as well. Also, as mentioned previously- please don't publicly post the card.

Thanks-
Sara

Pfizer, Moderna and Janssen trial participants:

The Pfizer, Moderna and Janssen vaccines are authorized under EUA. In addition, ACIP has independently reviewed the safety and efficacy data from the Phase 3 clinical trials. The "CDC cards" have been provided to the manufacturers. Once it has been confirmed that trial participants received 'active' vaccine and not placebo, the participants can be considered 'fully vaccinated' in terms of CDC guidance, can receive a "CDC card" and can have their vaccine recorded in IIS systems. CDC will work with the manufacturers, PCTs, and states to make sure they are aware of these updates.

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

<2020-COVID-19-shot-card-3forprinting.pdf>

From: (b)(4) (b)(4) (b)(
Sent: Mon, 21 Jun 2021 18:53:15 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: (b)(4) (b)(4) (b)(4) (b)(4); MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: RE: [EXTERNAL] RE: Booster presentation Friday

Thank you so much for this Sara, it is very helpful!

I also have a revised attendee list for the Wednesday COVID sessions:

(b)(4)

Thank you and as always let us know if you need anything from us!
All the best,
(b)(4) (b)(and (b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, June 21, 2021 2:20 PM
To: (b)(4) (b)(4) (b) (b)(4)
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: RE: [EXTERNAL] RE: Booster presentation Friday

(b)(4) and crew:

This is the current agenda for the upcoming ACIP meeting. It is draft and subject to change, but hopefully Wednesday (the COVID-focused day) is relatively set.

Thanks!
Sara

From: (b)(4) (b)(4) (b) (b)(4)
Sent: Friday, June 18, 2021 4:57 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: Re: [EXTERNAL] RE: Booster presentation Friday

Thank you so much!

On Jun 18, 2021, at 4:48 PM, Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov> wrote:

I'll let you know as soon as we have it. Still trying to work out some of the details. It is likely that the COVID-day will become Wednesday. But I'll let you know once we have it.

Thanks!
Sara

From: (b)(4) (b)(4) (b) (b)(4)
Sent: Friday, June 18, 2021 4:44 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: Re: [EXTERNAL] RE: Booster presentation Friday

Hi Sara,
Yes that would be fine!
Quick question, do you know when the new agenda will be coming out?
Thank you!
(b)(4)

On Jun 18, 2021, at 4:00 PM, Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov> wrote:

(b)(4)

Thanks- Are you OK if I replace 'Q3' with July-Sept 2021. Just trying to make it less 'jargon-y', but according to my math, that should be Q3.

Thanks!
Sara

From: (b)(4) (b)(4) (b) (b)(4)
Sent: Thursday, June 17, 2021 8:36 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>; (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: RE: Booster presentation Friday

Good morning Sara,

(b)(4)

Thank you!
All the best,

(b)(4) (b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Wednesday, June 16, 2021 8:08 PM
To: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: [EXTERNAL] Booster presentation Friday

(b)(4) (b)(and (b)(4)

For the booster/additional dose presentation- we are keeping it all very high-level but I was hoping to include 1 bullet point per manufacturer around booster studies that could be shared.

This is what I drafted for a slide entitled "Upcoming studies: Immunogenicity data". Would this be OK to share? Again, not wanting to get terribly detailed, but the overall goal is to lay out timing of when we may have results for ACIP to consider. (Also I wasn't sure if you had publicly shared about working on a 1.351 variant vaccine- happy to add that but only want to share what you are OK with us sharing).

- **Pfizer: BNT162b2 (30µg): Results ~July**

Thanks!
Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Mon, 21 Jun 2021 18:19:35 +0000
To: (b)(4) (b)(4) (b)
Cc: (b)(4) (b)(4) (b)(4) (b)(4); MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: RE: [EXTERNAL] RE: Booster presentation Friday
Attachments: Draft_Meeting Agenda_June 23_25 2021_6-21.pdf

(b)(4) and crew:

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Thanks!
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From: (b)(4) (b)(4) (b) (b)(4)
Sent: Friday, June 18, 2021 4:57 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4); (b)(5)
MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: Re: [EXTERNAL] RE: Booster presentation Friday

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Thanks!
Sara

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Sent: Thursday, June 17, 2021 8:36 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>; (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: RE: Booster presentation Friday

Good morning Sara,
We have received permission for you to say that we expect results from our BNT162b2 (30µg) and variant booster studies during **Q3** of this year.
Thank you!
All the best,
(b)(4) (b)(4); and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Wednesday, June 16, 2021 8:08 PM
To: (b)(4) (b)(4) (b (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: [EXTERNAL] Booster presentation Friday

(b)(4) (b)(and (b)(4)

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timing of when we may have results for ACIP to consider. (Also I wasn't sure if you had publicly shared about working on a 1.351 variant vaccine- happy to add that but only want to share what you are OK with us sharing).

- **Pfizer: BNT162b2 (30µg): Results ~July**

Thanks!
Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

Draft - June 21, 2021

MEETING OF THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES (ACIP)

Centers for Disease Control and Prevention
Atlanta, Georgia 30329
June 23-25, 2021

		PRESIDER/PRESENTER(s)
Wednesday, June 23, 2021		
11:00	**Welcome & Introductions**	Dr. José Romero (ACIP Chair) Dr. Amanda Cohn (ACIP Executive Secretary, CDC)
11:30	**Coronavirus Disease 2019 (COVID-19) Vaccines**	
	Introduction	Dr. Matthew Daley (ACIP, WG Chair)
	Overview of myocarditis and pericarditis	Dr. Matthew Oster (CDC/NCBDDD)
	Update on COVID-19 vaccine safety, including myocarditis after mRNA vaccines	Dr. Tom Shimabukuro (CDC/NCEZID)
	VaST assessment	Dr. Grace Lee (ACIP, VaST Co-chair)
12:45	***Break***	
1:00	COVID-19 mRNA vaccines in adolescents and young adults: benefit-risk	Dr. Megan Wallace (CDC/NCIRD)
	Discussion	
2:15	***Break***	
2:30	**Public Comment**	
3:00	Overview of data to inform recommendations for additional doses of COVID-19 vaccines	Dr. Sara Oliver (CDC/NCIRD)
	Discussion	
4:00	**Adjourn**	

Thursday, June 24, 2021		
10:00	**Welcome & Introductions**	Dr. José Romero (ACIP Chair) Dr. Amanda Cohn (ACIP Executive Secretary, CDC)
10:30	**Dengue Vaccine**	
	Introduction	Dr. Wilbur Chen (ACIP, WG Co-Chair)
	Acceptability of dengue vaccine in Puerto Rico	Dr. Ines Esquilin (University of Puerto Rico, School of Medicine)
	Implementation of dengue vaccine in Puerto Rico	Dr. Iris Cardona (Department of Health, Puerto Rico)
	Dengue vaccine draft recommendations using the evidence to recommendation framework	Dr. Gabriela Paz-Bailey (CDC/NCEZID)
	Dengue VFC Resolution	Dr. Jeanne Santoli (CDC/NCIRD)
12:20	***Break***	
12:30	**Influenza Vaccines**	
	Introduction	Dr. Keipp Talbot (ACIP, WG Chair)
	Flucelvax Quadrivalent (ccIIV4) Phase III Randomized Controlled Trial—Immunogenicity and Safety in Children 6 through 47 months	Dr. Gregg Sylvester (Seqirus)
	Work group considerations and proposed recommendations for the 2021-22 Influenza Season	Dr. Lisa Grohskopf (CDC/NCIRD)
	Updates to Influenza VFC Resolution	Dr. Jeanne Santoli (CDC/NCIRD)
2:10	***Break***	
2:20	**Rabies Vaccines**	
	Introduction	Dr. Sharon Frey (ACIP, WG Chair)
	Rabies immune globulin	Dr. Agam Rao (CDC/NCEZID)
	Rabies post-exposure prophylaxis schedule	Dr. Agam Rao (CDC/NCEZID)
	Rabies pre-exposure prophylaxis: GRADE/EtR summary	Dr. Agam Rao (CDC/NCEZID)
3:40	***Break***	
3:45	**Public Comment**	
4:15	***Break***	
4:20	**Votes and VFC Votes**	
	Dengue Vaccine	Dr. Gabriela Paz-Bailey (CDC/NCEZID)
	Dengue Vaccine (VFC)	Dr. Jeanne Santoli (CDC/NCIRD)
	Influenza Vaccines	Dr. Lisa Grohskopf (CDC/NCIRD)
	Influenza Vaccine (VFC)	Dr. Jeanne Santoli (CDC/NCIRD)
	Rabies Vaccines	Dr. Agam Rao (CDC/NCEZID)
5:15	**Adjourn**	

Friday, June 25, 2021

10:00	**Welcome & Introductions**	Dr. José Romero (ACIP Chair) Dr. Amanda Cohn (ACIP Executive Secretary, CDC)
10:15	**Zoster Vaccines**	
	Introduction	Dr. Grace Lee (ACIP, WG Chair)
	Burden of herpes zoster in immunocompromised adults	Dr. Tara Anderson (CDC/NCIRD)
	Use of recombinant zoster vaccine in immunocompromised populations: overview of clinical program	Ms. Robyn Widenmaier (GSK)
11:05	**Pneumococcal Vaccines**	
	Introduction	Dr. Kathy Poehling (ACIP, WG Chair)
	Updates on epidemiology of invasive pneumococcal disease in U.S. adults	Mr. Ryan Gierke (CDC/NCIRD)
	Cost effectiveness of PCV15 and PCV20 use in U.S. adults	Dr. Charles Stoecker (Tulane University)
	GRADE for age-based PCV15 and PCV20 use in U.S. adults	Ms. Jennifer Farrar (CDC/NCIRD)
	EtR summary of age-based PCV15 and PCV20 use in U.S. adults	Dr. Miwako Kobayashi (CDC/NCIRD)
	Summary and Timeline	Dr. Miwako Kobayashi (CDC/NCIRD)
1:00	**Adjourn**	

Acronyms

CDC	Centers for Disease Control and Prevention
CMS	Centers for Medicare and Medicaid Services
COVID-19	Coronavirus Disease 2019
EtR	Evidence to Recommendations Framework
FDA	Food and Drug Administration
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HRSA	Health Resources and Services Administration
IHS	Indian Health Service
NCHHSTP	National Center for HIV, Hepatitis, STD and TB Prevention [of CDC/DDID]
NCIRD	National Center for Immunization & Respiratory Diseases [of CDC/DDID]
NCEZID	National Center for Emerging and Zoonotic Diseases [of CDC/DDID]
NIAID	National Institute of Allergy and Infectious Diseases
OIDP	Office of Infectious Disease and HIV/AIDS Policy
PCV15	15-Valent Pneumococcal Conjugate Vaccine
PCV20	20-Valent Pneumococcal Conjugate Vaccine
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
WG	Work Group
WHO	World Health Organization
VE	Vaccine Effectiveness

From: (b)(4) (b)(4) (b)(
Sent: Fri, 16 Apr 2021 19:07:43 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: [EXTERNAL] RE: GRADE tables
Attachments: ACIP GRADE

(b)(4)

Hi Sara,
I was just about to send you an email with the tables! (see attached)
We completely understand, everything is a moving target and moving so fast. We will as always await your word and guidance on next steps for the data presentation for (b)(4)

(b)(4)

All the best,
(b)(4) (b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Friday, April 16, 2021 3:03 PM
To: (b)(4) (b)(4) (b) (b)(4)
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: [EXTERNAL] RE: GRADE tables

(b)(4) and all:

Apologies to do this again, but we are going to have to post-pone again. We have announced an ACIP meeting Friday April 23rd to discuss the safety concerns again, so the WG call on the 22nd will need to focus on those policy discussions.

Adolescent vaccines remain important to the WG and ACIP so I will follow up with you as soon as we can reschedule a Pfizer presentation to the WG. Thanks again so much for your patience. In addition, we will still need the GRADE tables for several of the outcomes, particularly reactogenicity- as the data in the EUA submission is slightly different than how we will need to present it.

Thanks again! (and sorry!)

Sara

From: (b)(4) (b)(4) (b) (b)(4)
Sent: Monday, April 12, 2021 9:01 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: Re: [EXTERNAL] RE: GRADE tables

Hi Sara,
We totally understand. We will await your confirmation about next week. We will still plan to get you the GRADE tables this week. Please let us know if we can be of any assistance.
Best regards,
(b)(4) (b)(and (b)(4)

On Apr 12, 2021, at 8:32 PM, Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov> wrote:

(b)(4) (b)(and (b)(4)

Apologies for this, but we are going to need to postpone this WG call for a week. We've had an urgent issue arise that we will need to deal with this week. We still look forward to hearing from Pfizer on this issue- but think we will need to tentatively postpone until Thurs the 22nd. I will confirm that timing early next week.

Again- apologies for the postponement!

Sara

From: (b)(4) (b)(4) (b) (b)(4)
Sent: Monday, April 12, 2021 8:28 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: GRADE tables

Dear Sara,
Thank you for inviting us to present to the COVID work group on Thursday, we will be happy to provide the presentation you requested. (b)(4) will be our presenter. We will also have other Pfizer colleagues on the call from (b)(4) (b)(4) and myself.)
(b)(4)
Best regards,
(b)(4) (b)(and (b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Sunday, April 11, 2021 11:14 AM
To: (b)(4) (b)(4) (b) (b)(4)
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: [EXTERNAL] RE: GRADE tables

(b)(4) (b)(and (b)(4)

Thanks for this- we look forward to reading through the data. As previously, we will keep access to the EUA submission very limited and only for those on our 'data team' conducting the GRADE analyses.

We would also invite you to present this data to the WG this week: Thurs 4/15 from ~3:30-4:15. We will ask for ~20-25 minute presentation focusing on the safety, efficacy and immunogenicity in the 12-15 year old population, and then have time for questions.

Given that there won't be a VRBPAC briefing document this time, let us know if you would be OK with sharing portions of the EUA submission with the WG after the call (and potentially the voting ACIP members prior to an ACIP meeting). Previously, we've shared the VRBPAC briefing document; we want to make sure people have the data needed prior to a vote, but want to keep the data confidential per your request. (We can continue to discuss this as we move forward as well).

Thanks!
Sara

From: (b)(4) (b)(4) (b) (b)(4)
Sent: Sunday, April 11, 2021 10:32 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: GRADE tables

Dear Sara,
Thank you, we are very excited about this new milestone. (b)(4)

(b)(4)

Let us know if you have any questions!
All the best,
(b)(4) (b)(and (b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Friday, April 9, 2021 5:27 PM
To: (b)(4) (b)(4) (b) (b)(4)
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: [EXTERNAL] RE: GRADE tables

(b)(4) (b)(4) and (b)(4

Congrats on the submission to FDA! When you're able to share the EUA submission, we're happy to get started with our GRADE process, while we wait on the completed GRADE tables.

Thanks!
Sara

From: (b)(4) (b)(4) (b)(4) (b)(4)
Sent: Monday, April 5, 2021 1:16 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: RE: GRADE tables

Dear Sara,
Thanks for the tables, we will start work on them right away.
(b)(4) We will work internally to be able to provide you the data.
All the best,
(b)(4) (b)(4) and (b)(

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, April 5, 2021 11:49 AM
To: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
(b)(4) (b)(4) (b)(4)
Subject: [EXTERNAL] GRADE tables

(b)(4) (b)(4) and (b)(4

Hope everyone had a great weekend. I've attached the blank GRADE tables for the adolescent data. We look forward to receiving the data from the EUA amendment submission. Once we receive the data, we can discuss plans around presentations to the WG.

To clarify for our planning: the 'comparison' data on the 16-25 year olds: including safety data- that will be included in the EUA submission, correct? There is interest to be able to review that data as well.

Thanks!

Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Co-Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204

email: yxo4@cdc.gov

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

From: (b)(4) (b)(4)
Sent: Sat, 22 May 2021 22:19:40 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: (b)(4) (b)(4) (b)(
Subject: Re: [EXTERNAL] RE: Quick question
Attachments: image001.png

Thanks Sara!!
Keep in touch
Best regards,
(b)(

On May 22, 2021, at 18:03, Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov> wrote:

(b)(

Thanks! Although today my role was mostly 'party host'! The FDA colleague was Narayan Nair. He's with CBER at FDA- the Division Director for Epi.

Hope that helps- let me know if there are other questions!

Sara

From: (b)(4) (b)(4) (b)(4)
Sent: Saturday, May 22, 2021 5:27 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: (b)(4) (b)(4) (b) (b)(4)
Subject: Quick question

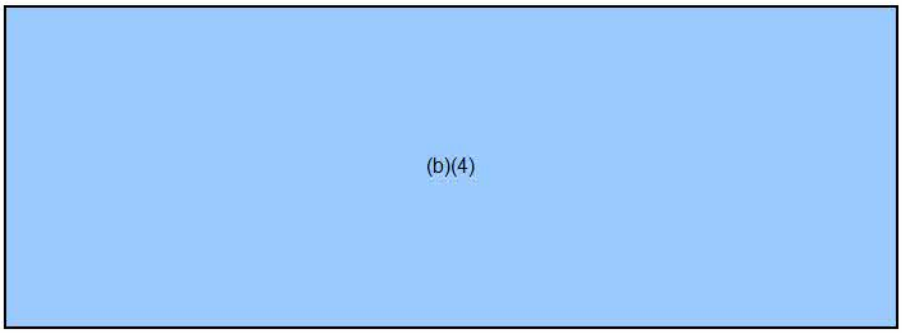
Hi Sara,

Thanks again for your work, we know you don't need our opinion or recognition but you are doing a fantastic job! Thank you very much!!!

I have one question, do you have the name of the person representing FDA in the call that we just had, I could not recognized him and my colleagues are asking for that info. Can you share his name and role with us?

Thanks

(b)(4) and (b)(


(b)(4)

From: (b)(4) (b)(4)
Sent: Wed, 16 Jun 2021 18:22:02 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD); (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) Sarah Elizabeth
Subject: Re: [EXTERNAL] RE: revaccination at NY Times Square vaccination center
Attachments: image002.png

Thanks a lot, Sara. It's a mystery! (b)(4)

(b)(4)

Thanks again.

(b)(4)

Sent from my iPhone

On Jun 16, 2021, at 1:45 PM, Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov> wrote:

(b)(4)

This is the information I was able to track down. Hope it's helpful. Let me know if there are additional questions, and I'm happy to check back in with our crew.

Thanks-
Sara

The NYC team provided further details. The expired vaccine had been in the freezer for longer than 2 weeks and the BUD had passed. (b)(4)

(b)(4) (b)(4)

(b)(4) They have already contacted all 899 people impacted. Per the guidance in Appendix A, this was not escalated to CDC for further guidance.

From: (b)(4) (b)(4)
Sent: Tuesday, June 15, 2021 7:26 PM
To: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>; Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)

(b)(4)

Subject: revaccination at NY Times Square vaccination center

Dear Sara(h)s, ☺

(b)(4)

Can you please tell me if you have any awareness of this or if CDC possibly communicated with the site and advised to re-vaccinate?

If I should address this question with someone else, please advise.

Hope you're both well.

Best,

(b)(4)

<image002.png>

From: (b)(4) (b)(4)
Sent: Thu, 17 Jun 2021 19:52:56 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD); (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
(b)(4)
Subject: RE: [EXTERNAL] RE: revaccination at NY Times Square vaccination center

Well thank them profusely from the Pfizer team!
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Thursday, June 17, 2021 3:52 PM
To: (b)(4) (b)(4)
Cc: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>; (b)(4) (b)(4) (b)
(b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
(b)(4)
Subject: RE: [EXTERNAL] RE: revaccination at NY Times Square vaccination center

No problem. I was mostly the sender-of-a-few-emails. The actual detective work was handled by our stellar Clinical Education team!

From: (b)(4) (b)(4)
Sent: Thursday, June 17, 2021 3:51 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>; (b)(4) (b)(4) (b)
(b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
(b)(4)
Subject: RE: [EXTERNAL] RE: revaccination at NY Times Square vaccination center

Dear Sara,

Thank you very much. (I know that you have better things to do and sorry that we couldn't identify the on this end.)

Talk soon,

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Thursday, June 17, 2021 3:43 PM
To: (b)(4) (b)(4)
Cc: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>; (b)(4) (b)(4) (b)(
(b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
(b)(4)
Subject: RE: [EXTERNAL] RE: revaccination at NY Times Square vaccination center

(b)(4)

We were able to collect this information- she also provided 2 documents (attached). Hope this helps solve the mystery!

Sara

The NYC POC would be Melissa Mickle-Hope (mmickle@health.nyc.gov). She spoke to (b)(4) at Pfizer, and the case number is (b)(4) The vaccine in question was kept in the freezer for longer than the three day grace period that Pfizer allows (it was more like 12 days).

From: (b)(4) (b)(4)
Sent: Wednesday, June 16, 2021 2:22 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>; (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: Re: [EXTERNAL] RE: revaccination at NY Times Square vaccination center

Thanks a lot, Sara. It's a mystery! (b)(4) (b)(4)

Thanks again.

(b)(4)

Sent from my iPhone

On Jun 16, 2021, at 1:45 PM, Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov> wrote:

(b)(4)

This is the information I was able to track down. Hope it's helpful. Let me know if there are additional questions, and I'm happy to check back in with our crew.

Thanks-
Sara

The NYC team provided further details. The expired vaccine had been in the freezer for longer than 2 weeks and the BUD had passed. (b)(4) (b)(4) (b)(4) (b)(4) They have already contacted all 899 people impacted. Per the guidance in Appendix A, this was not escalated to CDC for further guidance.

From: (b)(4) (b)(4)
Sent: Tuesday, June 15, 2021 7:26 PM
To: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>; Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: revaccination at NY Times Square vaccination center

Dear Sara(h)s,

(b)(4)

Can you please tell me if you have any awareness of this or if CDC possibly communicated with the site and advised to re-vaccinate?

If I should address this question with someone else, please advise.

Hope you're both well.

Best,

(b)(4)

<image002.png>

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Thu, 17 Jun 2021 19:43:02 +0000
To: (b)(4) (b)(4)
Cc: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD); (b)(4) (b)(4) (b) (b)(4) (b)(4) (b)(4)
Subject: RE: [EXTERNAL] RE: revaccination at NY Times Square vaccination center
Attachments: Fulfillment for Interaction (b)(4) pdf, Revaccination after Administration of Invalid Dose (v12.pdf

(b)(4)

We were able to collect this information- she also provided 2 documents (attached). Hope this helps solve the mystery!

Sara

The NYC POC would be Melissa Mickle-Hope (mmickle@health.nyc.gov). She spoke to (b)(4) at Pfizer, and the case number is (b)(4) The vaccine in question was kept in the freezer for longer than the three day grace period that Pfizer allows (it was more like 12 days).

From: (b)(4) (b)(4)
Sent: Wednesday, June 16, 2021 2:22 PM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>; (b)(4) (b)(4) (b) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: Re: [EXTERNAL] RE: revaccination at NY Times Square vaccination center

Thanks a lot, Sara. It's a mystery! (b)(4) (b)(4)

Thanks again.

(b)(4)

Sent from my iPhone

On Jun 16, 2021, at 1:45 PM, Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov> wrote:

(b)(4)

This is the information I was able to track down. Hope it's helpful. Let me know if there are additional questions, and I'm happy to check back in with our crew.

Thanks-
Sara

The NYC team provided further details. The expired vaccine had been in the freezer for longer than 2 weeks and the BUD had passed. (b)(4) (b)(4) (b)(4) (b)(4). They have already contacted all 899 people impacted. Per the guidance in Appendix A, this was not escalated to CDC for further guidance.

From: (b)(4) (b)(4)
Sent: Tuesday, June 15, 2021 7:26 PM
To: Mbaeyi, Sarah (CDC/DDID/NCIRD/OD) <vif6@cdc.gov>; Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) (b)(4)
Subject: revaccination at NY Times Square vaccination center

Dear Sara(h)s,

(b)(4)

Can you please tell me if you have any awareness of this or if CDC possibly communicated with the site and advised to re-vaccinate?

If I should address this question with someone else, please advise.

Hope you're both well.

Best,

(b)(4)

<image002.png>

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

From: (b)(4) (b)(4) (b)(4)
Sent: Thu, 17 Jun 2021 21:58:07 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: (b)(4) (b)(4) (b)(4) (b)(4); MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: Re: [EXTERNAL] Update for tomorrow

Thank you for the heads up Sara!

On Jun 17, 2021, at 5:33 PM, Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov> wrote:

(b)(4) (b)(4) and (b)(4)

I wanted to give you an update. Tomorrow has now officially been declared a federal holiday for Juneteenth. To allow everyone to recognize this important day, we are postponing the ACIP meeting. The current plan is that we will hold our COVID ACIP meeting next Wednesday (during the planned ACIP meeting). We are working through an overall agenda and will share as soon as we have it. But we will NOT be having the ACIP meeting tomorrow.

Thanks and let me know if there are any follow-up questions.

Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

From: (b)(4) (b)(4) (b)
Sent: Fri, 2 Jul 2021 20:54:00 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: (b)(4) (b)(4) (b)(4) (b)(4); MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: Re: [EXTERNAL] updates

Thank you Sara, we appreciate the heads up.
Hope you all have a nice holiday weekend!
Warm regards,
(b)(4) (b)(4 and (b)(4)

On Jul 2, 2021, at 4:39 PM, Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov> wrote:

(b)(4 (b)(4) and (b)(4)

Few updates- first, the ACIP myocarditis MMWR is planned to be released July 6th. Attached is the final proof as FYI. It is obviously confidential at this point, but wanted you to be aware of what is upcoming.

Then- the clinical considerations finally made it through clearance and they were just published: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fcovid-19%2Finfo-by-product%2Fclinical-considerations.html

Thanks-

Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

<mm7027e2 - ACIP myocarditis FINAL PROOF.pdf>

From: (b)(4) (b)(4) (x)
Sent: Tue, 22 Jun 2021 19:34:49 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Slides - Tomorrow's ACIP Meeting

Hi Sara,
You mentioned in your email last week that you might be able to share the slides that are being presented in the COVID-19 session tomorrow. Is anything available that we might be able to see at this point (even a draft, please)? We will certainly handle as confidential. It is helpful for us to know what questions might arise.
Many thanks.
(b)(4)

From: (b)(4)
Sent: Thu, 13 May 2021 14:15:41 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Survey of Parents - intent to have children vaccinated

Hi Sara,

Thank you for the wonderful slide presentation yesterday I enjoyed the meeting ACIP meeting.
I found your slides regarding " Survey of Parents (intent to have children vaccinated)"extremely valuable.

Appreciate the hard work you were doing!
Best Regards,

(b)(4)

moderna

From: (b)(4) (b)(4) (x)
Sent: Thu, 17 Jun 2021 16:39:07 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Timing for EUA for Adolescents

HI Sara,
I just wanted to let you know that our best estimate for the EUA authorization for use of Moderna's COVID-19 vaccine in adolescents is shortly before the July 4th holiday. We do not have an exact date from FDA, but assume it will be around that time based on their previous reviews.
Please handle this information as confidential.
I will let you know when we hear a more definitive date.
Thanks.
(b)(4)

From: (b)(4) (b)(4) (x)
Sent: Tue, 25 May 2021 13:56:43 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); Cohn, Amanda (CDC/DDID/NCIRD/OD)
Subject: Update - Study of Moderna COVID-19 Vaccine in Adolescents

Hi Sara, Jessica, and Amanda,
I wanted to share the press release that was issued this morning describing the results of Moderna's COVID-19 trial in adolescents, 12-17 years of age. I know that you wanted to know when the data would be available.
https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-teencove-study-its-covid-19-vaccine
The study enrolled >3700 individuals (2:1 randomization vaccine:placebo). The standard dose (100 mcg) was well tolerated in this age group and the vaccine was highly efficacious after the first and second doses.
We hope to file for EUA for this population in early June. Please let me know when you would like us to engage with the WG and/or ACIP.
(b)(4)

From: (b)(4) (b)(4) (x)
Sent: Mon, 28 Jun 2021 23:34:47 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Update on Adolescent EUA - Moderna

Hi Sara,
I wanted to keep you posted on the timing for our EUA for adolescents. FDA just informed us that the earliest authorization is now July 15.
So perhaps we can all have a relaxing holiday!
(b)(4)

Please consider the environment before printing this email

From: (b)(4) (b)(4) (b)(4)
Sent: Tue, 20 Jul 2021 21:54:08 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: (b)(4) (b)(4) (b)(4)
Subject: updated data

Dear Sara,
Thank you for your time with us yesterday.

(b)(4)

Alternatively, since you already have contacts with the MoH you can reach them directly. Please let us know your preference and we'd be happy to set anything up.
Thank you as always,
(b)(4) and (b)(

From: (b)(4) (b)(4) (x)
Sent: Fri, 2 Apr 2021 20:25:47 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); Mbaeyi, Sarah (CDC/DDID/NCIRD/OD); MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: Updated Fact Sheets -- Moderna COVID-19 Vaccine
Attachments: Moderna - EUA fact-sheet-providers 033121 Final.pdf, Moderna - EUA fact-sheet-recipients 033121 Final.pdf

Hi everyone,
I wanted to let you know that the Fact Sheets for Moderna's COVID-19 vaccine were updated yesterday to reflect both the 11 and 15 dose vials as well as some of the changes I mentioned in our recent call related to storage & handling. Attached are copies of both the Fact Sheet for HCPs & for vaccine recipients.
These documents are also posted on the Moderna website at https://www.modernatx.com/covid19vaccine-eua/
Happy weekend!
(b)(4)

Please consider the environment before printing this email

FACT SHEET FOR HEALTHCARE PROVIDERS ADMINISTERING VACCINE (VACCINATION PROVIDERS)
EMERGENCY USE AUTHORIZATION (EUA) OF THE MODERNA COVID-19 VACCINE TO PREVENT CORONAVIRUS DISEASE 2019 (COVID-19)

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved product, **MODERNA COVID-19 VACCINE**, for active immunization to prevent COVID-19 in individuals 18 years of age and older.

SUMMARY OF INSTRUCTIONS FOR COVID-19 VACCINATION PROVIDERS
Vaccination providers enrolled in the federal COVID-19 Vaccination Program must report all vaccine administration errors, all serious adverse events, cases of Multisystem Inflammatory Syndrome (MIS) in adults, and cases of COVID-19 that result in hospitalization or death following administration of the Moderna COVID-19 Vaccine. See "MANDATORY REQUIREMENTS FOR MODERNA COVID-19 VACCINE ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION" for reporting requirements.

The Moderna COVID-19 Vaccine is a suspension for intramuscular injection administered as a series of two doses (0.5 mL each) 1 month apart.

See this Fact Sheet for instructions for preparation and administration. This Fact Sheet may have been updated. For the most recent Fact Sheet, please see www.modernatx.com/covid19vaccine-eua.

For information on clinical trials that are testing the use of the Moderna COVID-19 Vaccine for active immunization against COVID-19, please see www.clinicaltrials.gov.

DESCRIPTION OF COVID-19
Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the novel coronavirus, SARS-CoV-2, that appeared in late 2019. It is predominantly a respiratory illness that can affect other organs. People with COVID-19 have reported a wide range of symptoms, ranging from mild symptoms to severe illness. Symptoms may appear 2 to 14 days after exposure to the virus. Symptoms may include: fever or chills; cough; shortness of breath; fatigue; muscle and body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; nausea or vomiting; diarrhea.

DOSAGE AND ADMINISTRATION

Storage and Handling
The information in this Fact Sheet supersedes the information on the vial and carton labels.

During storage, minimize exposure to room light.

The Moderna COVID-19 Vaccine multiple-dose vials are stored frozen between -50º to -15ºC (-58º to 5ºF). Store in the original carton to protect from light.

Do not store on dry ice or below -50ºC (-58ºF). Use of dry ice may subject vials to temperatures colder than -50°C (-58°F).

Vials may be stored refrigerated between 2° to 8°C (36° to 46°F) for up to 30 days prior to first use.

Vials may be stored between 8° to 25°C (46° to 77°F) for a total of 24 hours.

After the first dose has been withdrawn, the vial should be held between 2° to 25°C (36° to 77°F). Vials should be discarded 12 hours after the first puncture.

Thawed vials can be handled in room light conditions.

Do not refreeze once thawed.

Transportation of Thawed Vials at 2° to 8°C (35° to 46°F)

If transport at -50° to -15°C (-58° to 5°F) is not feasible, available data support transportation of one or more thawed vials for up to 12 hours at 2° to 8°C (35° to 46°F) when shipped using shipping containers which have been qualified to maintain 2° to 8°C (35° to 46°F) and under routine road and air transport conditions with shaking and vibration minimized. Once thawed and transported at 2° to 8°C (35° to 46°F), vials should not be refrozen and should be stored at 2° to 8°C (35° to 46°F) until use.

Dosing and Schedule
The Moderna COVID-19 Vaccine is administered intramuscularly as a series of two doses (0.5 mL each) 1 month apart.

There are no data available on the interchangeability of the Moderna COVID-19 Vaccine with other COVID-19 vaccines to complete the vaccination series. Individuals who have received one dose of the Moderna COVID-19 Vaccine should receive a second dose of the Moderna COVID-19 Vaccine to complete the vaccination series.

Dose Preparation
- The Moderna COVID-19 Vaccine multiple-dose vials contain a frozen suspension that does not contain a preservative and must be thawed prior to administration.
- Remove the required number of vial(s) from storage and thaw each vial before use following the instructions below.

Vial	Thaw in Refrigerator	Thaw at Room Temperature
Maximum 11-Dose Vial (range: 10-11 doses)	Thaw in refrigerated conditions between 2° to 8°C for 2 hours and 30 minutes. Let each vial stand at room temperature for 15 minutes before administering.	Alternatively, thaw at room temperature between 15° to 25°C for 1 hour.
Maximum 15-Dose Vial (range: 13-15 doses)	Thaw in refrigerated conditions between 2° to 8°C for 3 hours. Let each vial stand at room temperature for 15 minutes before administering.	Alternatively, thaw at room temperature between 15° to 25°C for 1 hour and 30 minutes.

- After thawing, do not refreeze.
- Swirl vial gently after thawing and between each withdrawal. **Do not shake.** Do not dilute the vaccine.
- The Moderna COVID-19 Vaccine is a white to off-white suspension. It may contain white or translucent product-related particulates. Visually inspect the Moderna COVID-19 Vaccine vials for other particulate matter and/or discoloration prior to administration. If either of these conditions exists, the vaccine should not be administered.
- The Moderna COVID-19 Vaccine is supplied in two multiple-dose vial presentations:
    - A multiple-dose vial containing a maximum of 11 doses: range 10-11 doses (0.5 mL each).
    - A multiple-dose vial containing a maximum of 15 doses: range 13-15 doses (0.5 mL each).
- Depending on the syringes and needles used for each dose, there may not be sufficient volume to extract more than 10 doses from the maximum of 11 doses vial or more than 13 doses from the maximum of 15 doses vial. Irrespective of the type of syringe and needle:
    - Each dose must contain 0.5 mL of vaccine.
    - If the amount of vaccine remaining in the vial cannot provide a full dose of 0.5 mL, discard the vial and contents. Do not pool excess vaccine from multiple vials.
    - Pierce the stopper at a different site each time.
- After the first dose has been withdrawn, the vial should be held between 2° to 25°C (36° to 77°F). Record the date and time of first use on the Moderna COVID-19 Vaccine vial label. Discard vial after 12 hours. Do not refreeze.

Administration

Visually inspect each dose of the Moderna COVID-19 Vaccine in the dosing syringe prior to administration. The white to off-white suspension may contain white or translucent product-related particulates. During the visual inspection,

- verify the final dosing volume of 0.5 mL.
- confirm there are no other particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains other particulate matter.

Administer the Moderna COVID-19 Vaccine intramuscularly.

CONTRAINDICATION
Do not administer the Moderna COVID-19 Vaccine to individuals with a known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the Moderna COVID-19 Vaccine *(see Full EUA Prescribing Information)*.

WARNINGS
Appropriate medical treatment to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of the Moderna COVID-19 Vaccine.

Monitor Moderna COVID-19 Vaccine recipients for the occurrence of immediate adverse reactions according to the Centers for Disease Control and Prevention guidelines (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/managing-anaphylaxis.html).

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the Moderna COVID-19 Vaccine.

The Moderna COVID-19 Vaccine may not protect all vaccine recipients.

ADVERSE REACTIONS
Adverse reactions reported in a clinical trial following administration of the Moderna COVID-19 Vaccine include pain at the injection site, fatigue, headache, myalgia, arthralgia, chills, nausea/vomiting, axillary swelling/tenderness, fever, swelling at the injection site, and erythema at the injection site. *(See Full EUA Prescribing Information)*

Severe allergic reactions, including anaphylaxis, have been reported following administration of the Moderna COVID-19 Vaccine during mass vaccination outside of clinical trials.

Additional adverse reactions, some of which may be serious, may become apparent with more widespread use of the Moderna COVID-19 Vaccine.

USE WITH OTHER VACCINES
There is no information on the co-administration of the Moderna COVID-19 Vaccine with other vaccines.

INFORMATION TO PROVIDE TO VACCINE RECIPIENTS/CAREGIVERS
As the vaccination provider, you must communicate to the recipient or their caregiver, information consistent with the "Fact Sheet for Recipients and Caregivers" (and provide a copy or direct the individual to the website www.modernatx.com/covid19vaccine-eua to obtain the Fact Sheet) prior to the individual receiving each dose of the Moderna COVID-19 Vaccine, including:

- FDA has authorized the emergency use of the Moderna COVID-19 Vaccine, which is not an FDA-approved vaccine.
- The recipient or their caregiver has the option to accept or refuse the Moderna COVID-19

Vaccine.
- The significant known and potential risks and benefits of the Moderna COVID-19 Vaccine, and the extent to which such risks and benefits are unknown.
- Information about available alternative vaccines and the risks and benefits of those alternatives

For information on clinical trials that are evaluating the use of the Moderna COVID-19 Vaccine to prevent COVID-19, please see www.clinicaltrials.gov.

Provide a vaccination card to the recipient or their caregiver with the date when the recipient needs to return for the second dose of Moderna COVID-19 Vaccine.

Provide the **v-safe** information sheet to vaccine recipients/caregivers and encourage vaccine recipients to participate in **v-safe**. **V-safe** is a new voluntary smartphone-based tool that uses text messaging and web surveys to check in with people who have been vaccinated to identify potential side effects after COVID-19 vaccination. **V-safe** asks questions that help CDC monitor the safety of COVID-19 vaccines. **V-safe** also provides second-dose reminders if needed and live telephone follow-up by CDC if participants report a significant health impact following COVID-19 vaccination. For more information, visit: www.cdc.gov/vsafe.

MANDATORY REQUIREMENTS FOR MODERNA COVID-19 VACCINE ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION

In order to mitigate the risks of using this unapproved product under EUA and to optimize the potential benefit of the Moderna COVID-19 Vaccine, the following items are required. Use of unapproved Moderna COVID-19 Vaccine for active immunization to prevent COVID-19 under this EUA is limited to the following (all requirements **must** be met):

1. The Moderna COVID-19 Vaccine is authorized for use in individuals 18 years of age and older.

2. The vaccination provider must communicate to the individual receiving the Moderna COVID-19 Vaccine or their caregiver information consistent with the "Fact Sheet for Recipients and Caregivers" prior to the individual receiving the Moderna COVID-19 Vaccine.

3. The vaccination provider must include vaccination information in the state/local jurisdiction's Immunization Information System (IIS) or other designated system.

4. The vaccination provider is responsible for mandatory reporting of the following to the Vaccine Adverse Event Reporting System (VAERS):
    - vaccine administration errors whether or not associated with an adverse event,
    - serious adverse events* (irrespective of attribution to vaccination),
    - cases of Multisystem Inflammatory Syndrome (MIS) in adults, and
    - cases of COVID-19 that result in hospitalization or death.

    Complete and submit reports to VAERS online at https://vaers.hhs.gov/reportevent.html.

For further assistance with reporting to VAERS, call 1-800-822-7967. The reports should include the words "Moderna COVID-19 Vaccine EUA" in the description section of the report.

5. The vaccination provider is responsible for responding to FDA requests for information about vaccine administration errors, adverse events, cases of MIS in adults, and cases of COVID-19 that result in hospitalization or death following administration of the Moderna COVID-19 Vaccine to recipients.

*Serious adverse events are defined as:

- Death;
- A life-threatening adverse event;
- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- A congenital anomaly/birth defect;
- An important medical event that based on appropriate medical judgement may jeopardize the individual and may require medical or surgical intervention to prevent one of the outcomes listed above.

OTHER ADVERSE EVENT REPORTING TO VAERS AND MODERNATX, INC.
Vaccination providers may report to VAERS other adverse events that are not required to be reported using the contact information above.

To the extent feasible, report adverse events to ModernaTX, Inc. using the contact information below or by providing a copy of the VAERS form to ModernaTX, Inc.

Email	Fax number	Telephone number
ModernaPV@modernatx.com	1-866-599-1342	1-866-MODERNA (1-866-663-3762)

ADDITIONAL INFORMATION
For general questions, visit the website or call the telephone number provided below.

To access the most recent Moderna COVID-19 Vaccine Fact Sheets, please scan the QR code or visit the website provided below.

Website	Telephone number
www.modernatx.com/covid19vaccine-eua 	1-866-MODERNA (1-866-663-3762)

AVAILABLE ALTERNATIVES
There is no approved alternative vaccine to prevent COVID-19. There may be clinical trials or availability under EUA of other COVID-19 vaccines.

FEDERAL COVID-19 VACCINATION PROGRAM
This vaccine is being made available for emergency use exclusively through the CDC COVID-19 Vaccination Program (the Vaccination Program). Healthcare providers must enroll as providers in the Vaccination Program and comply with the provider requirements. Vaccination providers may not charge any fee for the vaccine and may not charge the vaccine recipient any out-of-pocket charge for administration. However, vaccination providers may seek appropriate reimbursement from a program or plan that covers COVID-19 vaccine administration fees for the vaccine recipient (private insurance, Medicare, Medicaid, HRSA COVID-19 Uninsured Program for non-insured recipients). For information regarding provider requirements and enrollment in the CDC COVID-19 Vaccination Program, see https://www.cdc.gov/vaccines/covid-19/provider-enrollment.html.

Individuals becoming aware of any potential violations of the CDC COVID-19 Vaccination Program requirements are encouraged to report them to the Office of the Inspector General, U.S. Department of Health and Human Services, at 1-800-HHS-TIPS or TIPS.HHS.GOV.

AUTHORITY FOR ISSUANCE OF THE EUA
The Secretary of the Department of Health and Human Services (HHS) has declared a public health emergency that justifies the emergency use of drugs and biological products during the COVID-19 Pandemic. In response, the FDA has issued an EUA for the unapproved product, Moderna COVID-19 Vaccine, for active immunization to prevent COVID-19 in individuals 18 years of age and older.

FDA issued this EUA, based on ModernaTX, Inc.'s request and submitted data.

Although limited scientific information is available, based on the totality of the scientific evidence available to date, it is reasonable to believe that the Moderna COVID-19 Vaccine may be effective for the prevention of COVID-19 in individuals as specified in the *Full EUA Prescribing Information*.

This EUA for the Moderna COVID-19 Vaccine will end when the Secretary of HHS determines that the circumstances justifying the EUA no longer exist or when there is a change in the

approval status of the product such that an EUA is no longer needed.

For additional information about Emergency Use Authorization, visit FDA at: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization.

COUNTERMEASURES INJURY COMPENSATION PROGRAM

The Countermeasures Injury Compensation Program (CICP) is a federal program that has been created to help pay for related costs of medical care and other specific expenses to compensate people injured after use of certain medical countermeasures. Medical countermeasures are specific vaccines, medications, devices, or other items used to prevent, diagnose, or treat the public during a public health emergency or a security threat. For more information about CICP regarding the vaccines to prevent COVID-19, visit http://www.hrsa.gov/cicp, email cicp@hrsa.gov, or call: 1-855-266-2427.

Moderna US, Inc.
Cambridge, MA 02139

Patent(s): www.modernatx.com/patents
Revised: Mar/31/2021

END SHORT VERSION FACT SHEET
Long Version (Full EUA Prescribing Information) Begins On Next Page

FULL EMERGENCY USE AUTHORIZATION (EUA)
PRESCRIBING INFORMATION

MODERNA COVID-19 VACCINE

FULL EUA PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed

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FULL EMERGENCY USE AUTHORIZATION (EUA) PRESCRIBING INFORMATION

1 AUTHORIZED USE

Moderna COVID-19 Vaccine is authorized for use under an Emergency Use Authorization (EUA) for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 18 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

2.1 Preparation for Administration

- The Moderna COVID-19 Vaccine multiple-dose vials contain a frozen suspension that does not contain a preservative and must be thawed prior to administration.
- Remove the required number of vial(s) from storage and thaw each vial before use following the instructions below.

Vial	Thaw in Refrigerator	Thaw at Room Temperature
Maximum 11-Dose Vial (range: 10-11 doses)	Thaw in refrigerated conditions between 2° to 8°C for 2 hours and 30 minutes. Let each vial stand at room temperature for 15 minutes before administering.	Alternatively, thaw at room temperature between 15° to 25°C for 1 hour.
Maximum 15-Dose Vial (range: 13-15 doses)	Thaw in refrigerated conditions between 2° to 8°C for 3 hours. Let each vial stand at room temperature for 15 minutes before administering.	Alternatively, thaw at room temperature between 15° to 25°C for 1 hour and 30 minutes.

- After thawing, do not refreeze.
- Swirl vial gently after thawing and between each withdrawal. **Do not shake.** Do not dilute the vaccine.
- The Moderna COVID-19 Vaccine is a white to off-white suspension. It may contain white or translucent product-related particulates. Visually inspect the Moderna COVID-19 Vaccine vials for other particulate matter and/or discoloration prior to administration. If either of these conditions exists, the vaccine should not be administered.
- The Moderna COVID-19 Vaccine is supplied in two multiple-dose vial presentations:
    - A multiple-dose vial containing a maximum of 11 doses: range 10-11 doses (0.5 mL each).
    - A multiple-dose vial containing a maximum of 15 doses: range 13-15 doses (0.5 mL each).
- Depending on the syringes and needles used for each dose, there may not be sufficient volume to extract more than 10 doses from the maximum of 11 doses vial or more than 13 doses from the maximum of 15 doses vial. Irrespective of the type of syringe and needle:
    - Each dose must contain 0.5 mL of vaccine.
    - If the amount of vaccine remaining in the vial cannot provide a full dose of 0.5 mL, discard the vial and contents. Do not pool excess vaccine from multiple vials.
    - Pierce the stopper at a different site each time.
- After the first dose has been withdrawn, the vial should be held between 2° to 25°C (36° to 77°F). Record the date and time of first use on the Moderna COVID-19 Vaccine vial label. Discard vial after 12 hours. Do not refreeze.

2.2 Administration

Visually inspect each dose of the Moderna COVID-19 Vaccine in the dosing syringe prior to administration. The white to off-white suspension may contain white or translucent product-related particulates. During the visual inspection,

- verify the final dosing volume of 0.5 mL.
- confirm there are no other particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains other particulate matter.

Administer the Moderna COVID-19 Vaccine intramuscularly.

2.3 Dosing and Schedule

The Moderna COVID-19 Vaccine is administered intramuscularly as a series of two doses (0.5 mL each) 1 month apart.

There are no data available on the interchangeability of the Moderna COVID-19 Vaccine with other COVID-19 vaccines to complete the vaccination series. Individuals who have received one dose of Moderna COVID-19 Vaccine should receive a second dose of Moderna COVID-19 Vaccine to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

Moderna COVID-19 Vaccine is a suspension for intramuscular injection. A single dose is 0.5 mL.

4 CONTRAINDICATIONS

Do not administer the Moderna COVID-19 Vaccine to individuals with a known history of severe allergic reaction (e.g., anaphylaxis) to any component of the Moderna COVID-19 Vaccine *[see Description (13)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of the Moderna COVID-19 Vaccine.

Monitor Moderna COVID-19 Vaccine recipients for the occurrence of immediate adverse reactions according to the Centers for Disease Control and Prevention guidelines (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/managing-anaphylaxis.html).

5.2 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressive therapy, may have a diminished response to the Moderna COVID-19 Vaccine.

5.3 Limitations of Vaccine Effectiveness

The Moderna COVID-19 Vaccine may not protect all vaccine recipients.

6 OVERALL SAFETY SUMMARY

It is MANDATORY for vaccination providers to report to the Vaccine Adverse Event Reporting System (VAERS) all vaccine administration errors, all serious adverse events, cases of Multi-inflammatory Syndrome (MIS) in adults, and hospitalized or fatal cases of

COVID-19 following vaccination with the Moderna COVID-19 Vaccine. To the extent feasible, provide a copy of the VAERS form to ModernaTX, Inc. Please see the REQUIREMENTS AND INSTRUCTIONS FOR REPORTING ADVERSE EVENTS AND VACCINE ADMINISTRATION ERRORS section for details on reporting to VAERS and ModernaTX, Inc.

In clinical studies, the adverse reactions in participants 18 years of age and older were pain at the injection site (92.0%), fatigue (70.0%), headache (64.7%), myalgia (61.5%), arthralgia (46.4%), chills (45.4%), nausea/vomiting (23.0%), axillary swelling/tenderness (19.8%), fever (15.5%), swelling at the injection site (14.7%), and erythema at the injection site (10.0%).

Severe allergic reactions, including anaphylaxis, have been reported following administration of the Moderna COVID-19 Vaccine during mass vaccination outside of clinical trials.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared with rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

Overall, 15,419 participants aged 18 years and older received at least one dose of Moderna COVID-19 Vaccine in three clinical trials (NCT04283461, NCT04405076, and NCT04470427).

The safety of Moderna COVID-19 Vaccine was evaluated in an ongoing Phase 3 randomized, placebo-controlled, observer-blind clinical trial conducted in the United States involving 30,351 participants 18 years of age and older who received at least one dose of Moderna COVID-19 Vaccine (n=15,185) or placebo (n=15,166) (NCT04470427). At the time of vaccination, the mean age of the population was 52 years (range 18-95); 22,831 (75.2%) of participants were 18 to 64 years of age and 7,520 (24.8%) of participants were 65 years of age and older. Overall, 52.7% were male, 47.3% were female, 20.5% were Hispanic or Latino, 79.2% were White, 10.2% were African American, 4.6% were Asian, 0.8% were American Indian or Alaska Native, 0.2% were Native Hawaiian or Pacific Islander, 2.1% were other races, and 2.1% were Multiracial. Demographic characteristics were similar among participants who received Moderna COVID-19 Vaccine and those who received placebo.

Solicited Adverse Reactions

Data on solicited local and systemic adverse reactions and use of antipyretic medication were collected in an electronic diary for 7 days following each injection (i.e., day of vaccination and the next 6 days) among participants receiving Moderna COVID-19 Vaccine (n=15,179) and participants receiving placebo (n=15,163) with at least 1 documented dose. Solicited adverse reactions were reported more frequently among vaccine participants than placebo participants.

The reported number and percentage of the solicited local and systemic adverse reactions by age group and dose are presented in Table 1 and Table 2, respectively.

Table 1: Number and Percentage of Participants With Solicited Local and Systemic Adverse Reactions Within 7 Days* After Each Dose in Participants 18-64 Years (Solicited Safety Set, Dose 1 and Dose 2)

	Moderna COVID-19 Vaccine		Placebo[a]	
	Dose 1 (N=11,406) n (%)	**Dose 2** (N=10,985) n (%)	**Dose 1** (N=11,407) n (%)	**Dose 2** (N=10,918) n (%)
Local Adverse Reactions				
Pain	9,908 (86.9)	9,873 (89.9)	2,177 (19.1)	2,040 (18.7)
Pain, Grade 3[b]	366 (3.2)	506 (4.6)	23 (0.2)	22 (0.2)
Axillary swelling/tenderness	1,322 (11.6)	1,775 (16.2)	567 (5.0)	470 (4.3)
Axillary swelling/tenderness, Grade 3[b]	37 (0.3)	46 (0.4)	13 (0.1)	11 (0.1)
Swelling (hardness) ≥25 mm	767 (6.7)	1,389 (12.6)	34 (0.3)	36 (0.3)
Swelling (hardness), Grade 3[c]	62 (0.5)	182 (1.7)	3 (<0.1)	4 (<0.1)
Erythema (redness) ≥25 mm	344 (3.0)	982 (8.9)	47 (0.4)	43 (0.4)
Erythema (redness), Grade 3[c]	34 (0.3)	210 (1.9)	11 (<0.1)	12 (0.1)
Systemic Adverse Reactions				
Fatigue	4,384 (38.4)	7,430 (67.6)	3,282 (28.8)	2,687 (24.6)
Fatigue, Grade 3[d]	120 (1.1)	1,174 (10.7)	83 (0.7)	86 (0.8)
Fatigue, Grade 4[e]	1 (<0.1)	0 (0)	0 (0)	0 (0)
Headache	4,030 (35.3)	6,898 (62.8)	3,304 (29.0)	2,760 (25.3)
Headache, Grade 3[f]	219 (1.9)	553 (5.0)	162 (1.4)	129 (1.2)
Myalgia	2,699 (23.7)	6,769 (61.6)	1,628 (14.3)	1,411 (12.9)
Myalgia, Grade 3[d]	73 (0.6)	1,113 (10.1)	38 (0.3)	42 (0.4)
Arthralgia	1,893 (16.6)	4,993 (45.5)	1,327 (11.6)	1,172 (10.7)
Arthralgia, Grade 3[d]	47 (0.4)	647 (5.9)	29 (0.3)	37 (0.3)
Arthralgia, Grade 4[e]	1 (<0.1)	0 (0)	0 (0)	0 (0)
Chills	1,051 (9.2)	5,341 (48.6)	730 (6.4)	658 (6.0)

	Moderna COVID-19 Vaccine		Placebo[a]	
	Dose 1 (N=11,406) n (%)	**Dose 2** (N=10,985) n (%)	**Dose 1** (N=11,407) n (%)	**Dose 2** (N=10,918) n (%)
Chills, Grade 3[g]	17 (0.1)	164 (1.5)	8 (<0.1)	15 (0.1)
Nausea/vomiting	1,068 (9.4)	2,348 (21.4)	908 (8.0)	801 (7.3)
Nausea/vomiting, Grade 3[h]	6 (<0.1)	10 (<0.1)	8 (<0.1)	8 (<0.1)
Fever	105 (0.9)	1,908 (17.4)	37 (0.3)	39 (0.4)
Fever, Grade 3[i]	10 (<0.1)	184 (1.7)	1 (<0.1)	2 (<0.1)
Fever, Grade 4[j]	4 (<0.1)	12 (0.1)	4 (<0.1)	2 (<0.1)
Use of antipyretic or pain medication	2,656 (23.3)	6,292 (57.3)	1,523 (13.4)	1,248 (11.4)

* 7 days included day of vaccination and the subsequent 6 days. Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary).
[a] Placebo was a saline solution.
[b] Grade 3 pain and axillary swelling/tenderness: Defined as any use of prescription pain reliever; prevents daily activity.
[c] Grade 3 swelling and erythema: Defined as >100 mm / >10 cm.
[d] Grade 3 fatigue, myalgia, arthralgia: Defined as significant; prevents daily activity.
[e] Grade 4 fatigue, arthralgia: Defined as requires emergency room visit or hospitalization.
[f] Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.
[g] Grade 3 chills: Defined as prevents daily activity and requires medical intervention.
[h] Grade 3 nausea/vomiting: Defined as prevents daily activity, requires outpatient intravenous hydration.
[i] Grade 3 fever: Defined as ≥39.0° – ≤40.0°C / ≥102.1° – ≤104.0°F.
[j] Grade 4 fever: Defined as >40.0°C / >104.0°F.

Table 2: Number and Percentage of Participants With Solicited Local and Systemic Adverse Reactions Within 7 Days* After Each Dose in Participants 65 Years and Older (Solicited Safety Set, Dose 1 and Dose 2)

	Moderna COVID-19 Vaccine		Placebo[a]	
	Dose 1 (N=3,762) n (%)	**Dose 2** (N=3,692) n (%)	**Dose 1** (N=3,748) n (%)	**Dose 2** (N=3,648) n (%)
Local Adverse Reactions				
Pain	2,782 (74.0)	3,070 (83.2)	481 (12.8)	437 (12.0)
Pain, Grade 3[b]	50 (1.3)	98 (2.7)	32 (0.9)	18 (0.5)
Axillary swelling/tenderness	231 (6.1)	315 (8.5)	155 (4.1)	97 (2.7)
Axillary swelling/tenderness, Grade 3[b]	12 (0.3)	21 (0.6)	14 (0.4)	8 (0.2)

	Moderna COVID-19 Vaccine		Placebo[a]	
	Dose 1 (N=3,762) n (%)	**Dose 2** (N=3,692) n (%)	**Dose 1** (N=3,748) n (%)	**Dose 2** (N=3,648) n (%)
Swelling (hardness) ≥25 mm	165 (4.4)	400 (10.8)	18 (0.5)	13 (0.4)
Swelling (hardness), Grade 3[c]	20 (0.5)	72 (2.0)	3 (<0.1)	7 (0.2)
Erythema (redness) ≥25 mm	86 (2.3)	275 (7.5)	20 (0.5)	13 (0.4)
Erythema (redness), Grade 3[c]	8 (0.2)	77 (2.1)	2 (<0.1)	3 (<0.1)
Systemic Adverse Reactions				
Fatigue	1,251 (33.3)	2,152 (58.3)	851 (22.7)	716 (19.6)
Fatigue, Grade 3[d]	30 (0.8)	254 (6.9)	22 (0.6)	20 (0.5)
Headache	921 (24.5)	1,704 (46.2)	723 (19.3)	650 (17.8)
Headache, Grade 3[e]	52 (1.4)	106 (2.9)	34 (0.9)	33 (0.9)
Myalgia	742 (19.7)	1,739 (47.1)	443 (11.8)	398 (10.9)
Myalgia, Grade 3[d]	17 (0.5)	205 (5.6)	9 (0.2)	10 (0.3)
Arthralgia	618 (16.4)	1,291 (35.0)	456 (12.2)	397 (10.9)
Arthralgia, Grade 3[d]	13 (0.3)	123 (3.3)	8 (0.2)	7 (0.2)
Chills	202 (5.4)	1,141 (30.9)	148 (4.0)	151 (4.1)
Chills, Grade 3[f]	7 (0.2)	27 (0.7)	6 (0.2)	2 (<0.1)
Nausea/vomiting	194 (5.2)	437 (11.8)	166 (4.4)	133 (3.6)
Nausea/vomiting, Grade 3[g]	4 (0.1)	10 (0.3)	4 (0.1)	3 (<0.1)
Nausea/vomiting, Grade 4[h]	0 (0)	1 (<0.1)	0 (0)	0 (0)
Fever	10 (0.3)	370 (10.0)	7 (0.2)	4 (0.1)
Fever, Grade 3[i]	1 (<0.1)	18 (0.5)	1 (<0.1)	0 (0)
Fever, Grade 4[j]	0 (0)	1 (<0.1)	2 (<0.1)	1 (<0.1)
Use of antipyretic or pain medication	673 (17.9)	1,546 (41.9)	477 (12.7)	329 (9.0)

* 7 days included day of vaccination and the subsequent 6 days. Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary).

[a] Placebo was a saline solution.

[b] Grade 3 pain and axillary swelling/tenderness: Defined as any use of prescription pain reliever; prevents daily activity.
[c] Grade 3 swelling and erythema: Defined as >100 mm / >10 cm.
[d] Grade 3 fatigue, myalgia, arthralgia: Defined as significant; prevents daily activity.
[e] Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.
[f] Grade 3 chills: Defined as prevents daily activity and requires medical intervention.
[g] Grade 3 Nausea/vomiting: Defined as prevents daily activity, requires outpatient intravenous hydration.
[h] Grade 4 Nausea/vomiting: Defined as requires emergency room visit or hospitalization for hypotensive shock.
[i] Grade 3 fever: Defined as ≥39.0° – ≤40.0°C / ≥102.1° – ≤104.0°F.
[j] Grade 4 fever: Defined as >40.0°C / >104.0°F.

Solicited local and systemic adverse reactions reported following administration of Moderna COVID-19 Vaccine had a median duration of 1 to 3 days.

Grade 3 solicited local adverse reactions were more frequently reported after Dose 2 than after Dose 1. Solicited systemic adverse reactions were more frequently reported by vaccine recipients after Dose 2 than after Dose 1.

Unsolicited Adverse Events

Participants were monitored for unsolicited adverse events for up to 28 days following each dose and follow-up is ongoing. Serious adverse events and medically attended adverse events will be recorded for the entire study duration of 2 years. As of November 25, 2020, among participants who had received at least 1 dose of vaccine or placebo (vaccine=15,185, placebo=15,166), unsolicited adverse events that occurred within 28 days following each vaccination were reported by 23.9% of participants (n=3,632) who received Moderna COVID-19 Vaccine and 21.6% of participants (n=3,277) who received placebo. In these analyses, 87.9% of study participants had at least 28 days of follow-up after Dose 2.

Lymphadenopathy-related events that were not necessarily captured in the 7-day e-diary were reported by 1.1% of vaccine recipients and 0.6% of placebo recipients. These events included lymphadenopathy, lymphadenitis, lymph node pain, vaccination-site lymphadenopathy, injection-site lymphadenopathy, and axillary mass, which were plausibly related to vaccination. This imbalance is consistent with the imbalance observed for solicited axillary swelling/tenderness in the injected arm.

Hypersensitivity adverse events were reported in 1.5% of vaccine recipients and 1.1% of placebo recipients. Hypersensitivity events in the vaccine group included injection site rash and injection site urticaria, which are likely related to vaccination. Delayed injection site reactions that began >7 days after vaccination were reported in 1.2% of vaccine recipients and 0.4% of placebo recipients. Delayed injection site reactions included pain, erythema, and swelling and are likely related to vaccination.

Throughout the same period, there were three reports of Bell's palsy in the Moderna COVID-19 Vaccine group (one of which was a serious adverse event), which occurred 22, 28, and 32 days after vaccination, and one in the placebo group which occurred 17 days after vaccination. Currently available information on Bell's palsy is insufficient to determine a causal relationship with the vaccine.

There were no other notable patterns or numerical imbalances between treatment groups for specific categories of adverse events (including other neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to Moderna COVID-19 Vaccine.

Serious Adverse Events

As of November 25, 2020, serious adverse events were reported by 1.0% (n=147) of participants who received Moderna COVID-19 Vaccine and 1.0% (n=153) of participants who received placebo, one of which was the case of Bell's palsy which occurred 32 days following receipt of vaccine.

In these analyses, 87.9% of study participants had at least 28 days of follow-up after Dose 2, and the median follow-up time for all participants was 9 weeks after Dose 2.

There were two serious adverse events of facial swelling in vaccine recipients with a history of injection of dermatological fillers. The onset of swelling was reported 1 and 2 days, respectively, after vaccination and was likely related to vaccination.

There was one serious adverse event of intractable nausea and vomiting in a participant with prior history of severe headache and nausea requiring hospitalization. This event occurred 1 day after vaccination and was likely related to vaccination.

There were no other notable patterns or imbalances between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to Moderna COVID-19 Vaccine.

8 REQUIREMENTS AND INSTRUCTIONS FOR REPORTING ADVERSE EVENTS AND VACCINE ADMINISTRATION ERRORS

See Overall Safety Summary (Section 6) for additional information.

The vaccination provider enrolled in the federal COVID-19 Vaccination Program is responsible for the MANDATORY reporting of the listed events following Moderna COVID-19 Vaccine to the Vaccine Adverse Event Reporting System (VAERS)

- Vaccine administration errors whether or not associated with an adverse event
- Serious adverse events* (irrespective of attribution to vaccination)
- Cases of multisystem inflammatory syndrome (MIS) in adults
- Cases of COVID-19 that results in hospitalization or death

*Serious Adverse Events are defined as:

- Death;
- A life-threatening adverse event;
- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant incapacity or substantial disruption of the ability to conduct

normal life functions;
- A congenital anomaly/birth defect;
- An important medical event that based on appropriate medical judgement may jeopardize the individual and may require medical or surgical intervention to prevent one of the outcomes listed above.

Instructions for Reporting to VAERS

The vaccination provider enrolled in the federal COVID-19 Vaccination Program should complete and submit a VAERS form to FDA using one of the following methods:
- Complete and submit the report online: https://vaers.hhs.gov/reportevent.html, or
- If you are unable to submit this form electronically, you may fax it to VAERS at 1-877-721-0366. If you need additional help submitting a report, you may call the VAERS toll-free information line at 1-800-822-7967 or send an email to info@vaers.org.

IMPORTANT: When reporting adverse events or vaccine administration errors to VAERS, please complete the entire form with detailed information. It is important that the information reported to FDA be as detailed and complete as possible. Information to include:
- Patient demographics (e.g., patient name, date of birth)
- Pertinent medical history
- Pertinent details regarding admission and course of illness
- Concomitant medications
- Timing of adverse event(s) in relationship to administration of Moderna COVID-19 Vaccine
- Pertinent laboratory and virology information
- Outcome of the event and any additional follow-up information if it is available at the time of the VAERS report. Subsequent reporting of follow-up information should be completed if additional details become available.

The following steps are highlighted to provide the necessary information for safety tracking:
1. In Box 17, provide information on Moderna COVID-19 Vaccine and any other vaccines administered on the same day; and in Box 22, provide information on any other vaccines received within one month prior.
2. In Box 18, description of the event:
    a. Write "Moderna COVID-19 Vaccine EUA" as the first line
    b. Provide a detailed report of vaccine administration error and/or adverse event. It is important to provide detailed information regarding the patient and adverse event/medication error for ongoing safety evaluation of this unapproved vaccine. Please see information to include listed above.
3. Contact information:
    a. In Box 13, provide the name and contact information of the prescribing healthcare provider or institutional designee who is responsible for the report.
    b. In Box 14, provide the name and contact information of the best doctor/healthcare professional to contact about the adverse event.

c. In Box 15, provide the address of the facility where vaccine was given (NOT the healthcare provider's office address).

Other Reporting Instructions

Vaccination providers may report to VAERS other adverse events that are not required to be reported using the contact information above.

To the extent feasible, report adverse events to ModernaTX, Inc. using the contact information below or by providing a copy of the VAERS form to ModernaTX, Inc.

Email	Fax number	Telephone number
(b)(4)	1-866-599-1342	1-866-MODERNA (1-866-663-3762)

10 DRUG INTERACTIONS

There are no data to assess the concomitant administration of the Moderna COVID-19 Vaccine with other vaccines.

11 USE IN SPECIFIC POPULATIONS

11.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Moderna COVID-19 Vaccine during pregnancy. Women who are vaccinated with Moderna COVID-19 Vaccine during pregnancy are encouraged to enroll in the registry by calling 1-866-MODERNA (1-866-663-3762).

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on Moderna COVID-19 Vaccine administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

In a developmental toxicity study, 0.2 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (100 mcg) and other ingredients included in a single human dose of Moderna COVID-19 Vaccine was administered to female rats by the intramuscular route on four occasions: 28 and 14 days prior to mating, and on gestation days 1 and 13. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

11.2 Lactation

Risk Summary

Data are not available to assess the effects of Moderna COVID-19 Vaccine on the breastfed infant or on milk production/excretion.

11.3 Pediatric Use

Safety and effectiveness have not been assessed in persons less than 18 years of age. Emergency Use Authorization of Moderna COVID-19 Vaccine does not include use in individuals younger than 18 years of age.

11.4 Geriatric Use

Clinical studies of Moderna COVID-19 Vaccine included participants 65 years of age and older receiving vaccine or placebo, and their data contribute to the overall assessment of safety and efficacy. In an ongoing Phase 3 clinical study, 24.8% (n=7,520) of participants were 65 years of age and older and 4.6% (n=1,399) of participants were 75 years of age and older. Vaccine efficacy in participants 65 years of age and older was 86.4% (95% CI 61.4, 95.2) compared to 95.6% (95% CI 90.6, 97.9) in participants 18 to <65 years of age *[see Clinical Trial Results and Supporting Data for EUA (18)]*. Overall, there were no notable differences in the safety profiles observed in participants 65 years of age and older and younger participants *[*see *Overall Safety Summary (6.1)]*.

13 DESCRIPTION

Moderna COVID-19 Vaccine is provided as a white to off-white suspension for intramuscular injection. Each 0.5 mL dose of Moderna COVID-19 Vaccine contains 100 mcg of nucleoside-modified messenger RNA (mRNA) encoding the pre-fusion stabilized Spike glycoprotein (S) of SARS-CoV-2 virus.

Each dose of the Moderna COVID-19 Vaccine contains the following ingredients: a total lipid content of 1.93 mg (SM-102, polyethylene glycol [PEG] 2000 dimyristoyl glycerol [DMG], cholesterol, and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC]), 0.31 mg tromethamine, 1.18 mg tromethamine hydrochloride, 0.043 mg acetic acid, 0.20 mg sodium acetate trihydrate, and 43.5 mg sucrose.

Moderna COVID-19 Vaccine does not contain a preservative.

The vial stoppers are not made with natural rubber latex.

14 CLINICAL PHARMACOLOGY

14.1 Mechanism of Action

The nucleoside-modified mRNA in the Moderna COVID-19 Vaccine is formulated in lipid particles, which enable delivery of the nucleoside-modified mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

18 CLINICAL TRIAL RESULTS AND SUPPORTING DATA FOR EUA

A Phase 3 randomized, placebo-controlled, observer-blind clinical trial to evaluate the efficacy, safety, and immunogenicity of the Moderna COVID-19 Vaccine in participants 18 years of age and older is ongoing in the United States (NCT04470427). Randomization was stratified by age and health risk: 18 to <65 years of age without comorbidities (not at risk for progression to severe COVID-19), 18 to <65 years of age with comorbidities (at risk for progression to severe COVID-19), and 65 years of age and older with or without comorbidities. Participants who were immunocompromised and those with a known history of SARS-CoV-2 infection were excluded from the study. Participants with no known history of SARS-CoV-2 infection but with positive laboratory results indicative of infection at study entry were included. The study allowed for the inclusion of participants with stable pre-existing medical conditions, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 3 months before enrollment, as well as participants with stable human immunodeficiency virus (HIV) infection. A total of 30,420 participants were randomized equally to receive 2 doses of the Moderna COVID-19 Vaccine or saline placebo 1 month apart. Participants will be followed for efficacy and safety until 24 months after the second dose.

The primary efficacy analysis population (referred to as the Per-Protocol Set) included 28,207 participants who received two doses (at 0 and 1 month) of either Moderna COVID-19 Vaccine (n=14,134) or placebo (n=14,073), and had a negative baseline SARS-CoV-2 status. In the Per-Protocol Set, 47.4% were female, 19.7% were Hispanic or Latino; 79.5% were White, 9.7% were African American, 4.6% were Asian, and 2.1% other races. The median age of participants was 53 years (range 18-95) and 25.3% of participants were 65 years of age and older. Of the study participants in the Per-Protocol Set, 18.5% were at increased risk of severe COVID-19 due to at least one pre-existing medical condition (chronic lung disease, significant cardiac disease, severe obesity, diabetes, liver disease, or HIV infection) regardless of age. Between participants who received Moderna COVID-19 Vaccine and those who received placebo, there were no notable differences in demographics or pre-existing medical conditions.

Efficacy Against COVID-19

COVID-19 was defined based on the following criteria: The participant must have experienced at least two of the following systemic symptoms: fever (≥38ºC), chills, myalgia, headache, sore throat, new olfactory and taste disorder(s); or the participant must have experienced at least one of the following respiratory signs/symptoms: cough, shortness of breath or difficulty breathing, or clinical or radiographical evidence of pneumonia; and the participant must have at least one

NP swab, nasal swab, or saliva sample (or respiratory sample, if hospitalized) positive for SARS-CoV-2 by RT-PCR. COVID-19 cases were adjudicated by a Clinical Adjudication Committee.

The median length of follow up for efficacy for participants in the study was 9 weeks post Dose 2. There were 11 COVID-19 cases in the Moderna COVID-19 Vaccine group and 185 cases in the placebo group, with a vaccine efficacy of 94.1% (95% confidence interval of 89.3% to 96.8%).

Table 3: Primary Efficacy Analysis: COVID-19* in Participants 18 Years of Age and Older Starting 14 Days After Dose 2 per Adjudication Committee Assessments – Per-Protocol Set

Moderna COVID-19 Vaccine			Placebo			% Vaccine Efficacy (95% CI)†
Participants (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 per 1,000 Person-Years	Participants (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 per 1,000 Person-Years	
14,134	11	3.328	14,073	185	56.510	94.1 (89.3, 96.8)

* COVID-19: symptomatic COVID-19 requiring positive RT-PCR result and at least two systemic symptoms or one respiratory symptom. Cases starting 14 days after Dose 2.
† VE and 95% CI from the stratified Cox proportional hazard model.

The subgroup analyses of vaccine efficacy are presented in Table 4.

Table 4: Subgroup Analyses of Vaccine Efficacy: COVID-19* Cases Starting 14 Days After Dose 2 per Adjudication Committee Assessments – Per- Protocol Set

Age Subgroup (Years)	Moderna COVID-19 Vaccine			Placebo			% Vaccine Efficacy (95% CI)*
	Participants (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 per 1,000 Person-Years	Participants (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 per 1,000 Person-Years	
18 to <65	10,551	7	2.875	10,521	156	64.625	95.6 (90.6, 97.9)
≥65	3,583	4	4.595	3,552	29	33.728	86.4 (61.4, 95.2)

* COVID-19: symptomatic COVID-19 requiring positive RT-PCR result and at least two systemic symptoms or one respiratory symptom. Cases starting 14 days after Dose 2.
† VE and 95% CI from the stratified Cox proportional hazard model.

Severe COVID-19 was defined based on confirmed COVID-19 as per the primary efficacy endpoint case definition, plus any of the following: Clinical signs indicative of severe systemic illness, respiratory rate ≥30 per minute, heart rate ≥125 beats per minute, SpO2 ≤93% on room

air at sea level or PaO2/FIO2 <300 mm Hg; or respiratory failure or ARDS (defined as needing high-flow oxygen, non-invasive or mechanical ventilation, or ECMO), evidence of shock (systolic blood pressure <90 mmHg, diastolic BP <60 mmHg or requiring vasopressors); or significant acute renal, hepatic, or neurologic dysfunction; or admission to an intensive care unit or death.

Among all participants in the Per-Protocol Set analysis, which included COVID-19 cases confirmed by an adjudication committee, no cases of severe COVID-19 were reported in the Moderna COVID-19 Vaccine group compared with 30 cases reported in the placebo group (incidence rate 9.138 per 1,000 person-years). One PCR-positive case of severe COVID-19 in a vaccine recipient was awaiting adjudication at the time of the analysis.

19 HOW SUPPLIED/STORAGE AND HANDLING

Moderna COVID-19 Vaccine Suspension for Intramuscular Injection Multiple-Dose Vials are supplied as follows:

NDC 80777-273-99	Carton of 10 multiple-dose vials, each vial containing a maximum of 11 doses: range 10-11 doses (0.5 mL)
NDC 80777-273-98	Carton of 10 multiple-dose vials, each vial containing a maximum of 15 doses: range 13-15 doses (0.5 mL)

During storage, minimize exposure to room light.

Store frozen between -50º to -15ºC (-58º to 5ºF). Store in the original carton to protect from light.

Do not store on dry ice or below -50ºC (-58ºF). Use of dry ice may subject vials to temperatures colder than -50°C (-58°F).

Vials may be stored refrigerated between 2° to 8°C (36° to 46°F) for up to 30 days prior to first use. Do not refreeze.

Vials may be stored between 8° to 25°C (46° to 77°F) for a total of 24 hours.

After the first dose has been withdrawn, the vial should be held between 2° to 25°C (36° to 77°F). Vials should be discarded 12 hours after the first puncture.

Thawed vials can be handled in room light conditions.

Do not refreeze once thawed.

<u>Transportation of Thawed Vials at 2°C to 8°C (35°F to 46°F)</u>

If transport at -50° to -15°C (-58° to 5°F) is not feasible, available data support transportation of one or more thawed vials for up to 12 hours at 2° to 8°C (35° to 46°F) when shipped using

shipping containers which have been qualified to maintain 2° to 8°C (35° to 46°F) and under routine road and air transport conditions with shaking and vibration minimized. Once thawed and transported at 2° to 8°C (35° to 46°F), vials should not be refrozen and should be stored at 2° to 8°C (35° to 46°F) until use.

20 PATIENT COUNSELING INFORMATION

Advise the recipient or caregiver to read the Fact Sheet for Recipients and Caregivers.

The vaccination provider must include vaccination information in the state/local jurisdiction's Immunization Information System (IIS) or other designated system. Advise recipient or caregiver that more information about IISs can be found at:
https://www.cdc.gov/vaccines/programs/iis/about.html.

21 CONTACT INFORMATION

For general questions, send an email or call the telephone number provided below.

Email	Telephone number
medinfo@modernatx.com	1-866-MODERNA (1-866-663-3762)

This EUA Prescribing Information may have been updated. For the most resent Full EUA Prescribing Information, please visit www.modernatx.com/covid19vaccine-eua.

Moderna US, Inc.
Cambridge, MA 02139

Patent(s): www.modernatx.com/patents
Revised: Mar/31/2021

FACT SHEET FOR RECIPIENTS AND CAREGIVERS
EMERGENCY USE AUTHORIZATION (EUA) OF THE MODERNA COVID-19 VACCINE TO PREVENT CORONAVIRUS DISEASE 2019 (COVID-19) IN INDIVIDUALS 18 YEARS OF AGE AND OLDER

You are being offered the Moderna COVID-19 Vaccine to prevent Coronavirus Disease 2019 (COVID-19) caused by SARS-CoV-2. This Fact Sheet contains information to help you understand the risks and benefits of the Moderna COVID-19 Vaccine, which you may receive because there is currently a pandemic of COVID-19.

The Moderna COVID-19 Vaccine is a vaccine and may prevent you from getting COVID-19. There is no U.S. Food and Drug Administration (FDA) approved vaccine to prevent COVID-19.

Read this Fact Sheet for information about the Moderna COVID-19 Vaccine. Talk to the vaccination provider if you have questions. It is your choice to receive the Moderna COVID-19 Vaccine.

The Moderna COVID-19 Vaccine is administered as a 2-dose series, 1 month apart, into the muscle.

The Moderna COVID-19 Vaccine may not protect everyone.

This Fact Sheet may have been updated. For the most recent Fact Sheet, please visit www.modernatx.com/covid19vaccine-eua.

WHAT YOU NEED TO KNOW BEFORE YOU GET THIS VACCINE

WHAT IS COVID-19?
COVID-19 is caused by a coronavirus called SARS-CoV-2. This type of coronavirus has not been seen before. You can get COVID-19 through contact with another person who has the virus. It is predominantly a respiratory illness that can affect other organs. People with COVID-19 have had a wide range of symptoms reported, ranging from mild symptoms to severe illness. Symptoms may appear 2 to 14 days after exposure to the virus. Symptoms may include: fever or chills; cough; shortness of breath; fatigue; muscle or body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; nausea or vomiting; diarrhea.

WHAT IS THE MODERNA COVID-19 VACCINE?
The Moderna COVID-19 Vaccine is an unapproved vaccine that may prevent COVID-19. There is no FDA-approved vaccine to prevent COVID-19.

The FDA has authorized the emergency use of the Moderna COVID-19 Vaccine to prevent COVID-19 in individuals 18 years of age and older under an Emergency Use Authorization (EUA).

For more information on EUA, see the "**What is an Emergency Use Authorization (EUA)?**" section at the end of this Fact Sheet.

WHAT SHOULD YOU MENTION TO YOUR VACCINATION PROVIDER BEFORE YOU GET THE MODERNA COVID-19 VACCINE?

Tell your vaccination provider about all of your medical conditions, including if you:

- have any allergies
- have a fever
- have a bleeding disorder or are on a blood thinner
- are immunocompromised or are on a medicine that affects your immune system
- are pregnant or plan to become pregnant
- are breastfeeding
- have received another COVID-19 vaccine

WHO SHOULD GET THE MODERNA COVID-19 VACCINE?

FDA has authorized the emergency use of the Moderna COVID-19 Vaccine in individuals 18 years of age and older.

WHO SHOULD NOT GET THE MODERNA COVID-19 VACCINE?

You should not get the Moderna COVID-19 Vaccine if you:

- had a severe allergic reaction after a previous dose of this vaccine
- had a severe allergic reaction to any ingredient of this vaccine

WHAT ARE THE INGREDIENTS IN THE MODERNA COVID-19 VACCINE?

The Moderna COVID-19 Vaccine contains the following ingredients: messenger ribonucleic acid (mRNA), lipids (SM-102, polyethylene glycol [PEG] 2000 dimyristoyl glycerol [DMG], cholesterol, and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC]), tromethamine, tromethamine hydrochloride, acetic acid, sodium acetate trihydrate, and sucrose.

HOW IS THE MODERNA COVID-19 VACCINE GIVEN?

The Moderna COVID-19 Vaccine will be given to you as an injection into the muscle.

The Moderna COVID-19 Vaccine vaccination series is 2 doses given 1 month apart.

If you receive one dose of the Moderna COVID-19 Vaccine, you should receive a second dose of the same vaccine 1 month later to complete the vaccination series.

HAS THE MODERNA COVID-19 VACCINE BEEN USED BEFORE?

The Moderna COVID-19 Vaccine is an unapproved vaccine. In clinical trials, approximately 15,400 individuals 18 years of age and older have received at least 1 dose of the Moderna COVID-19 Vaccine.

WHAT ARE THE BENEFITS OF THE MODERNA COVID-19 VACCINE?

In an ongoing clinical trial, the Moderna COVID-19 Vaccine has been shown to prevent COVID-19 following 2 doses given 1 month apart. The duration of protection against COVID-19 is currently unknown.

WHAT ARE THE RISKS OF THE MODERNA COVID-19 VACCINE?
There is a remote chance that the Moderna COVID-19 Vaccine could cause a severe allergic reaction. A severe allergic reaction would usually occur within a few minutes to one hour after getting a dose of the Moderna COVID-19 Vaccine. For this reason, your vaccination provider may ask you to stay at the place where you received your vaccine for monitoring after vaccination. Signs of a severe allergic reaction can include:

- Difficulty breathing
- Swelling of your face and throat
- A fast heartbeat
- A bad rash all over your body
- Dizziness and weakness

Side effects that have been reported in a clinical trial with the Moderna COVID-19 Vaccine include:

- Injection site reactions: pain, tenderness and swelling of the lymph nodes in the same arm of the injection, swelling (hardness), and redness
- General side effects: fatigue, headache, muscle pain, joint pain, chills, nausea and vomiting, and fever

Side effects that have been reported during post-authorization use of the Moderna COVID-19 Vaccine include:

- Severe allergic reactions

These may not be all the possible side effects of the Moderna COVID-19 Vaccine. Serious and unexpected side effects may occur. The Moderna COVID-19 Vaccine is still being studied in clinical trials.

WHAT SHOULD I DO ABOUT SIDE EFFECTS?
If you experience a severe allergic reaction, call 9-1-1, or go to the nearest hospital.

Call the vaccination provider or your healthcare provider if you have any side effects that bother you or do not go away.

Report vaccine side effects to **FDA/CDC Vaccine Adverse Event Reporting System (VAERS)**. The VAERS toll-free number is 1-800-822-7967 or report online to https://vaers.hhs.gov/reportevent.html. Please include "Moderna COVID-19 Vaccine EUA" in the first line of box #18 of the report form.

In addition, you can report side effects to ModernaTX, Inc. at 1-866-MODERNA (1-866-663-3762).

You may also be given an option to enroll in **v-safe. V-safe** is a new voluntary smartphone-based tool that uses text messaging and web surveys to check in with people who have been vaccinated to identify potential side effects after COVID-19 vaccination. **V-safe** asks questions that help CDC monitor the safety of COVID-19 vaccines. **V-safe** also provides second-dose reminders if

needed and live telephone follow-up by CDC if participants report a significant health impact following COVID-19 vaccination. For more information on how to sign up, visit: www.cdc.gov/vsafe.

WHAT IF I DECIDE NOT TO GET THE MODERNA COVID-19 VACCINE?
It is your choice to receive or not receive the Moderna COVID-19 Vaccine. Should you decide not to receive it, it will not change your standard medical care.

ARE OTHER CHOICES AVAILABLE FOR PREVENTING COVID-19 BESIDES MODERNA COVID-19 VACCINE?
Currently, there is no FDA-approved alternative vaccine available for prevention of COVID-19. Other vaccines to prevent COVID-19 may be available under Emergency Use Authorization.

CAN I RECEIVE THE MODERNA COVID-19 VACCINE WITH OTHER VACCINES?
There is no information on the use of the Moderna COVID-19 Vaccine with other vaccines.

WHAT IF I AM PREGNANT OR BREASTFEEDING?
If you are pregnant or breastfeeding, discuss your options with your healthcare provider.

WILL THE MODERNA COVID-19 VACCINE GIVE ME COVID-19?
No. The Moderna COVID-19 Vaccine does not contain SARS-CoV-2 and cannot give you COVID-19.

KEEP YOUR VACCINATION CARD
When you receive your first dose, you will get a vaccination card to show you when to return for your second dose of the Moderna COVID-19 Vaccine. Remember to bring your card when you return.

ADDITIONAL INFORMATION
If you have questions, visit the website or call the telephone number provided below.

To access the most recent Fact Sheets, please scan the QR code provided below.

Moderna COVID-19 Vaccine website	Telephone number
www.modernatx.com/covid19vaccine-eua	1-866-MODERNA (1-866-663-3762)

HOW CAN I LEARN MORE?

- Ask the vaccination provider
- Visit CDC at https://www.cdc.gov/coronavirus/2019-ncov/index.html
- Visit FDA at https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization
- Contact your state or local public health department

WHERE WILL MY VACCINATION INFORMATION BE RECORDED?

The vaccination provider may include your vaccination information in your state/local jurisdiction's Immunization Information System (IIS) or other designated system. This will ensure that you receive the same vaccine when you return for the second dose. For more information about IISs, visit: https://www.cdc.gov/vaccines/programs/iis/about.html.

CAN I BE CHARGED AN ADMINISTRATION FEE FOR RECEIPT OF THE COVID-19 VACCINE?

No. At this time, the provider cannot charge you for a vaccine dose and you cannot be charged an out-of-pocket vaccine administration fee or any other fee if only receiving a COVID-19 vaccination. However, vaccination providers may seek appropriate reimbursement from a program or plan that covers COVID-19 vaccine administration fees for the vaccine recipient (private insurance, Medicare, Medicaid, HRSA COVID-19 Uninsured Program for non-insured recipients).

WHERE CAN I REPORT CASES OF SUSPECTED FRAUD?

Individuals becoming aware of any potential violations of the CDC COVID-19 Vaccination Program requirements are encouraged to report them to the Office of the Inspector General, U.S. Department of Health and Human Services, at 1-800-HHS-TIPS or TIPS.HHS.GOV.

WHAT IS THE COUNTERMEASURES INJURY COMPENSATION PROGRAM?

The Countermeasures Injury Compensation Program (CICP) is a federal program that may help pay for costs of medical care and other specific expenses of certain people who have been seriously injured by certain medicines or vaccines, including this vaccine. Generally, a claim must be submitted to the CICP within one (1) year from the date of receiving the vaccine. To learn more about this program, visit www.hrsa.gov/cicp/ or call 1-855-266-2427.

WHAT IS AN EMERGENCY USE AUTHORIZATION (EUA)?

The United States FDA has made the Moderna COVID-19 Vaccine available under an emergency access mechanism called an EUA. The EUA is supported by a Secretary of Health and Human Services (HHS) declaration that circumstances exist to justify the emergency use of drugs and biological products during the COVID-19 pandemic.

The Moderna COVID-19 Vaccine has not undergone the same type of review as an FDA-approved or cleared product. FDA may issue an EUA when certain criteria are met, which includes that there are no adequate, approved, and available alternatives. In addition, the FDA decision is based on the totality of the scientific evidence available showing that the product may be effective to prevent COVID-19 during the COVID-19 pandemic and that the known and potential benefits of the product outweigh the known and potential risks of the product. All of

these criteria must be met to allow for the product to be used during the COVID-19 pandemic.

The EUA for the Moderna COVID-19 Vaccine is in effect for the duration of the COVID-19 EUA declaration justifying emergency use of these products, unless terminated or revoked (after which the products may no longer be used).

Moderna US, Inc.
Cambridge, MA 02139

Patent(s): www.modernatx.com/patents
Revised: Mar/26/2021

Scan to capture that this Fact Sheet was provided to vaccine recipient for the electronic medical records/immunization information systems.

Barcode Date: 04/2021

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Fri, 2 Jul 2021 20:32:41 +0000
To: (b)(4) (b)(4) (b)(4) (b)(4) T; (b)(4) Mary M.
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: updates
Attachments: mm7027e2 - ACIP myocarditis FINAL PROOF.pdf

(b)(4) (b)(4) and Mary:

Few updates- first, the ACIP myocarditis MMWR is planned to be released July 6th. Attached is the final proof as FYI. It is obviously confidential at this point, but wanted you to be aware of what is upcoming.

Then- the clinical considerations finally made it through clearance and they were just published: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fcovid-19%2Finfo-by-product%2Fclinical-considerations.html

Thanks-

Sara

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Centers for Disease Control and Prevention
MMWR
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Use of mRNA COVID-19 Vaccine After Reports of Myocarditis Among Vaccine Recipients: Update from the Advisory Committee on Immunization Practices — United States, June 2021

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In December 2020, the Food and Drug Administration (FDA) issued Emergency Use Authorizations (EUAs) for the Pfizer-BioNTech COVID-19 (BNT162b2) vaccine and the Moderna COVID-19 (mRNA-1273) vaccine,[†] and the Advisory Committee on Immunization Practices (ACIP) issued interim recommendations for their use in persons aged ≥16 years and ≥18 years, respectively.[§] In May 2021, FDA expanded the EUA for the Pfizer-BioNTech COVID-19 vaccine to include adolescents aged 12–15 years; ACIP recommends that all persons aged ≥12 years receive a COVID-19 vaccine. Both Pfizer-BioNTech and Moderna vaccines are mRNA vaccines encoding the stabilized prefusion spike glycoprotein of SARS-CoV-2, the virus that causes COVID-19. Both mRNA vaccines were authorized and recommended as a 2-dose schedule, with second doses administered 21 days (Pfizer-BioNTech) or 28 days (Moderna) after the first dose. After reports of myocarditis and pericarditis in mRNA vaccine recipients,[¶] which predominantly occurred in young males after the second dose, an ACIP meeting was rapidly convened to review reported cases of myocarditis and pericarditis and discuss the benefits and risks of mRNA COVID-19 vaccination in the United States. Myocarditis is an inflammation of the heart muscle; if it is accompanied by pericarditis, an inflammation of the thin tissue surrounding the heart (the pericardium), it is referred to as myopericarditis. Hereafter, myocarditis is used to refer to myocarditis, pericarditis, or myopericarditis. On June 23, 2021, after reviewing available evidence including that for risks of myocarditis, ACIP determined that the benefits of using mRNA COVID-19 vaccines under the FDA's EUA clearly outweigh the risks in all populations, including adolescents and young adults. The EUA has been modified to include information on myocarditis after receipt of mRNA COVID-19 vaccines. The EUA fact sheets should be provided before vaccination; in addition, CDC has developed patient and provider education materials about the possibility of myocarditis and symptoms of concern, to ensure prompt recognition and management of myocarditis.

Since June 2020, ACIP has convened 15 public meetings to review data on COVID-19 epidemiology and use of COVID-19 vaccines. The ACIP COVID-19 Vaccines Work Group, comprising experts in infectious diseases, vaccinology, vaccine safety, public health, and ethics, has held weekly meetings since April 2020 to review COVID-19 surveillance data, evidence for vaccine efficacy and safety, and implementation considerations for COVID-19 vaccination programs. After reports of myocarditis, the work group met twice to review clinical trial and postauthorization safety data for myocarditis after receipt of mRNA COVID-19 vaccines. The work group also reviewed a benefit-risk assessment of myocarditis events after receipt of mRNA COVID-19 vaccines, considering recent epidemiology of COVID-19 and sequelae of COVID-19, including myocarditis and multisystem inflammatory syndrome in children (MIS-C).[**] The ACIP COVID-19 Vaccines

* These authors contributed equally to this work.
† All EUA documents for COVID-19 vaccines, including fact sheets, are available at https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines.
§ ACIP recommendations for all COVID-19 vaccines are available at https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html.
¶ COVID-19 Vaccine Safety Technical Work Group Reports are available at https://www.cdc.gov/vaccines/acip/work-groups-vast/index.html.
** https://www.cdc.gov/mis/hcp/index.html

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Safety Technical (VaST) Work Group, comprising independent vaccine safety expert consultants, had also reviewed safety data on myocarditis after receipt of mRNA COVID-19 vaccines at its weekly meetings. The findings from the VaST and the ACIP COVID-19 Vaccines Work Group assessments, including a summary of the data reviewed, were presented to ACIP during its meeting on June 23, 2021.

Myocarditis typically occurs more commonly in males than in females, and incidence is highest among infants, adolescents, and young adults (*1*,*2*). The clinical presentation and severity of myocarditis vary among patients. Symptoms typically include chest pain, dyspnea, or palpitations, although other symptoms might be present, especially in younger children (*3*). Diagnostic evaluation might reveal an elevated troponin level or abnormal findings on electrocardiogram, echocardiogram, or cardiac magnetic resonance imaging (Table 1). Supportive therapy is a mainstay of treatment, with targeted cardiac medications or interventions as needed. Current guidelines from the American Heart Association and American College of Cardiology recommend exercise restriction until the heart recovers.[††]

As of June 11, 2021, approximately 296 million doses of mRNA COVID-19 vaccines had been administered in the United States, with 52 million administered to persons aged 12–29 years; of these, 30 million were first and 22 million were second doses. Within the Vaccine Adverse Event Reporting System (VAERS) (*4*), the national vaccine safety passive monitoring system, 1,226 reports of myocarditis after mRNA vaccination were received during December 29, 2020–June 11, 2021. Among persons with reported myocarditis after mRNA vaccination, the median age was 26 years (range = 12–94 years), with median symptom onset interval of 3 days after vaccination (range = 0–179). Among 1,194 reports for which patient age was known, 687 were among persons aged <30 years and 507 were among persons aged ≥30 years; of 1,212 with sex reported, 923 were male, and 289 were female.[§§] Among 1,094 patients with number of vaccine doses received reported, 76% occurred after receipt of dose 2 of mRNA vaccine; cases were reported after both Pfizer-BioNTech and Moderna vaccines. Informed by early reports, CDC prioritized rapid review of myocarditis in persons aged <30 years reported during May 1–June 11, 2021; the 484 patient records in this subset were evaluated by physicians at CDC, and several reports were also reviewed with Clinical Immunization Safety Assessment Project investigators,[¶¶] including cardiologists. At the time of this report, 323 of these 484 cases were determined to meet

TABLE 1. Case definitions of probable and confirmed myocarditis, pericarditis, and myopericarditis

Condition	Definition	
Acute myocarditis	**Probable case**	**Confirmed case**
	Presence of ≥1 new or worsening of the following clinical symptoms:*	Presence of ≥1 new or worsening of the following clinical symptoms:*
	• chest pain, pressure, or discomfort • dyspnea, shortness of breath, or pain with breathing • palpitations • syncope	• chest pain, pressure, or discomfort • dyspnea, shortness of breath, or pain with breathing • palpitations • syncope
	OR, infants and children aged <12 years might instead have ≥2 of the following symptoms: • irritability • vomiting • poor feeding • tachypnea • lethargy	OR, infants and children aged <12 years might instead have ≥2 of the following symptoms: • irritability • vomiting • poor feeding • tachypnea • lethargy
	AND ≥1 new finding of • troponin level above upper limit of normal (any type of troponin) • abnormal electrocardiogram (ECG or EKG) or rhythm monitoring findings consistent with myocarditis[§] • abnormal cardiac function or wall motion abnormalities on echocardiogram • cMRI findings consistent with myocarditis[¶]	AND ≥1 new finding of • Histopathologic confirmation of myocarditis[†] • cMRI findings consistent with myocarditis[¶] in the presence of troponin level above upper limit of normal (any type of troponin)
	AND • No other identifiable cause of the symptoms and findings	AND • No other identifiable cause of the symptoms and findings
Acute pericarditis**	Presence of ≥2 new or worsening of the following clinical features: • acute chest pain[††] • pericardial rub on exam • new ST-elevation or PR-depression on EKG • new or worsening pericardial effusion on echocardiogram or MRI	
Myopericarditis	This term may be used for patients who meet criteria for both myocarditis and pericarditis.	

Abbreviations: AV = atrioventricular; cMRI = cardiac magnetic resonance imaging; ECG or EKG = electrocardiogram.

* Persons who lack the listed symptoms but who meet other criteria may be classified as subclinical myocarditis (probable or confirmed).

† Using the Dallas criteria (Aretz HT, Billingham ME, Edwards WD, et al. Myocarditis. A histopathologic definition and classification. Am J Cardiovasc Pathol 1987; 1:3–14). Autopsy cases may be classified as confirmed clinical myocarditis on the basis of meeting histopathologic criteria if no other identifiable cause.

§ To meet the ECG or rhythm monitoring criterion, a probable case must include at least one of 1) ST-segment or T-wave abnormalities; 2) Paroxysmal or sustained atrial, supraventricular, or ventricular arrhythmias; or 3) AV nodal conduction delays or intraventricular conduction defects.

¶ Using either the original or the revised Lake Louise criteria. https://www.sciencedirect.com/science/article/pii/S0735109718388430?via%3Dihub

** https://academic.oup.com/eurheartj/article/36/42/2921/2293375

†† Typically described as pain made worse by lying down, deep inspiration, or cough, and relieved by sitting up or leaning forward, although other types of chest pain might occur.

†† https://www.ahajournals.org/doi/10.1161/CIR.0000000000000239?url_ver = Z39.88-2003&rfr_id = ori:rid:crossref.org&rfr_dat = cr_pub%20%200pubmed#d3e785

§§ Age was not reported for 32 patients, and sex was not reported for 14 patients.

¶¶ https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/cisa/index.html

criteria in CDC's case definitions for myocarditis, pericarditis, or myopericarditis by provider interview or medical record review (Table 1). The median age of the 323 patients with confirmed myocarditis was 19 years (range = 12–29 years); 291 were male, and 32 were female. The median interval from vaccination to symptom onset was 2 days (range = 0–40 days); 92% of patients experienced onset of symptoms within 7 days of vaccination. Of the 323 persons with confirmed cases, 309 (96%) were hospitalized. Acute clinical courses were generally mild; among 304 hospitalized patients with known clinical outcomes, 95% had been discharged at time of review, and none had died. Treatment data in VAERS are preliminary and incomplete; however, many patients have experienced resolution of symptoms with conservative treatment, such as receipt of nonsteroidal antiinflammatory drugs. Follow-up is ongoing to identify and understand longer-term outcomes after myocarditis occurring after COVID-19 vaccination.

Using myocarditis cases reported to VAERS with onset within 7 days after dose 2 of an mRNA vaccine, crude reporting rates (i.e., using confirmed and unconfirmed cases) per million second dose recipients were calculated using national COVID-19 vaccine administration data as of June 11, 2021. Myocarditis reporting rates were 40.6 cases per million second doses of mRNA COVID-19 vaccines administered to males aged 12–29 years and 2.4 per million second doses administered to males aged ≥30 years; reporting rates among females in these age groups were 4.2 and 1.0 per million second doses, respectively.*** The highest reporting rates were among males aged 12–17 years and those aged 18–24 years (62.8 and 50.5 reported myocarditis cases per million second doses of mRNA COVID-19 vaccine administered, respectively). Myocarditis rates from Vaccine Safety Datalink (VSD), based on electronic health records, were also evaluated. Although numbers were too small to show rates in all subgroups by age, VSD data indicated increased risk of myocarditis in the 7 days after receipt of dose 1 or dose 2 of an mRNA COVID-19 vaccine compared with the risk 22–42 days after the second dose, particularly among younger males after dose 2 (*5*).

To assess the benefit-risk balance of mRNA vaccines in adolescents and young adults, ACIP reviewed an individual-level assessment that compared the benefits (i.e., COVID-19 infections and severe disease prevented) to the risks (number of cases of myocarditis) of vaccination, using methods similar to those described previously.††† Specifically, the benefits per million second doses administered (i.e., the benefits of being fully vaccinated in accordance with the FDA EUA) were assessed, including 1) COVID-19 cases prevented based on rates the week of May 29, 2021§§§; 2) COVID-19 hospitalizations prevented based on rates the week of May 22, 2021¶¶¶; and 3) COVID-19 intensive care unit (ICU) admissions and deaths prevented based on the proportion of hospitalized patients who were admitted to the ICU or died.**** The risks were assessed as the number of myocarditis patients reported to VAERS that occurred within 7 days of receipt of a second dose of an mRNA COVID-19 vaccine per million second doses administered through the week of June 11, 2021.†††† The benefit-risk assessment was stratified by age group and sex. The analysis assumed 95% vaccine effectiveness§§§§ of 2 doses of a mRNA COVID-19 vaccine in preventing COVID-19 cases and hospitalization and assessed outcomes for a 120-day period. The 120-day period was selected because 1) no alternative vaccine options currently exist for persons aged <18 years or are expected to be available during this period, and 2) inputs regarding community transmission have high uncertainty beyond this period, particularly in the context of circulating variants.¶¶¶¶

The benefits (prevention of COVID-19 disease and associated hospitalizations, ICU admissions, and deaths) outweighed the risks (expected myocarditis cases after vaccination) in all populations for which vaccination has been recommended. However, the balance of risks and benefits varied by age and sex because cases of myocarditis were primarily identified among males aged <30 years, and the risks of poor outcomes related to COVID-19 increase with age. Per million second doses of mRNA COVID-19 vaccine administered to males aged 12–29 years, 11,000 COVID-19 cases, 560 hospitalizations, 138 ICU admissions, and six deaths due to COVID-19 could be prevented, compared with 39–47 expected myocarditis cases after COVID-19 vaccination (Table 2). Among males aged ≥30 years, 15,300 COVID-19 cases, 4,598 hospitalizations, 1,242 ICU admissions, and 700 deaths could be prevented, compared with three to four expected myocarditis cases after COVID-19 vaccination. This analysis did not include the potential benefit of preventing post-COVID-19 conditions, such as prolonged symptoms and MIS-C (*6*,*7*).

*** Data collection for race/ethnicity of myocarditis cases is ongoing

††† https://www.cdc.gov/vaccines/covid-19/info-by-product/janssen/risk-benefit-analysis.html

§§§ https://covid.cdc.gov/covid-data-tracker/#demographicsovertime. Data were used for the most recent week not subject to reporting delays prior to the ACIP meeting.

¶¶¶ https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html. Data were used for the most recent week not subject to reporting delays prior to the ACIP meeting.

**** https://gis.cdc.gov/grasp/COVIDNet/COVID19_5.html

†††† Because of uncertainty in the accuracy of myocarditis reporting, given that reviews are ongoing, and some cases might not have been reported yet, myocarditis reporting rates are presented as a range of values, calculated as ±10% of the observed reporting rates.

§§§§ https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html

¶¶¶¶ https://covid.cdc.gov/covid-data-tracker/#variant-proportions

TABLE 2. Individual-level estimated number of COVID-19 cases and COVID-19–associated hospitalizations, intensive care unit admissions, and deaths prevented after use of 2-dose mRNA COVID-19 vaccine for 120 days and number of myocarditis cases expected per million second mRNA vaccine doses administered, by sex and age group* — United States, 2021

	No. per million vaccine doses administered in each age group (yrs)†				
Sex/Benefits and harms from mRNA vaccination	**12–29**	**12–17**	**18–24**	**25–29**	**≥30**
Male					
Benefit					
COVID-19 cases prevented§	11,000	5,700	12,100	15,200	15,300
Hospitalizations prevented	560	215	530	936	4,598
ICU admissions prevented	138	71	127	215	1,242
Deaths prevented	6	2	3	13	700
Harms					
Myocarditis cases expected¶	39–47	56–69	45–56	15–18	3–4
Female					
Benefit					
COVID-19 cases prevented§	12,500	8,500	14,300	14,700	14,900
Hospitalizations prevented	922	183	1,127	1,459	3,484
ICU admissions prevented	73	38	93	87	707
Deaths prevented	6	1	13	4	347
Harm					
Myocarditis cases expected¶	4–5	8–10	4–5	2	1

Abbreviations: ICU = intensive care unit; VAERS = Vaccine Adverse Event Reporting System.
* This analysis evaluated direct benefits and harms, per million second doses of mRNA COVID-19 vaccine given in each age group, over 120 days. The numbers of events per million persons aged 12–29 years are the averages of numbers per million persons aged 12–17 years, 18–24 years, and 25–29 years.
† Receipt of 2 doses of mRNA COVID-19 vaccine, compared with no vaccination.
§ Case numbers have been rounded to the nearest hundred.
¶ Ranges calculated as ±10% of crude VAERS reporting rates. Estimates include cases of myocarditis, pericarditis, and myopericarditis.

ACIP also reviewed population-level considerations regarding vaccination. No alternatives to mRNA COVID-19 vaccines for adolescents will be available for the foreseeable future, and vaccination of adolescents offers protection against COVID-19 that can be important for returning to educational, social, and extracurricular activities. Higher levels of vaccination coverage can reduce community transmission, which can protect against development and circulation of emerging variants. Regarding health equity considerations, racial and ethnic minority groups have higher rates of COVID-19 and severe disease*****; potential changes in vaccine policy, or anything that would affect vaccination coverage for adolescents or young adults, might disproportionately affect those groups with the highest rates of poor COVID-19 outcomes.

The ACIP discussion concluded that 1) the benefits of vaccinating all recommended age groups with mRNA COVID-19 vaccine clearly outweigh the risks of vaccination, including the risk of myocarditis after vaccination; 2) continuing to monitor outcomes of myocarditis cases after COVID-19 vaccination is important; and 3) providers and the public should be informed about these myocarditis cases and the use of COVID-19 vaccines. Based on ACIP's conclusion regarding the benefit-risk assessment on June 23, 2021, COVID-19 vaccination continues to be recommended for all persons aged ≥12 years under the FDA's EUA. ACIP emphasized the importance of informing vaccination providers and the public about the benefits and the risks, including the risk for myocarditis after COVID-19 vaccination, particularly for males aged 12–29 years.

CDC has provided guidance regarding evaluation and management of myocarditis after mRNA COVID-19 vaccine (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html), as well as considerations for a second vaccine dose in persons who develop myocarditis after a first dose (https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html). FDA has added information to the Pfizer-BioNTech†††† and Moderna§§§§§ COVID-19 vaccine EUA and fact sheets regarding myocarditis cases that have been reported among vaccine recipients. In addition, CDC has updated patient education and communication materials reflecting this information for the Pfizer-BioNTech¶¶¶¶¶ and Moderna****** COVID-19 vaccines; these are important to ensure that vaccine recipients, especially males aged 12–29 years, are aware of increased risk for myocarditis and to seek care if they develop symptoms of myocarditis. The vaccine product-specific EUA fact sheet should be provided to all vaccine recipients and their caregivers before vaccination with any authorized COVID-19 vaccine.

***** https://covid.cdc.gov/covid-data-tracker/#demographics

†††† https://www.fda.gov/media/144413/download
§§§§§ https://www.fda.gov/media/144637/download
¶¶¶¶¶ https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/index.html
****** https://www.cdc.gov/vaccines/covid-19/info-by-product/moderna/index.html

CDC and FDA will continue to closely monitor reports of myocarditis after receipt of the mRNA COVID-19 vaccines and will bring any additional data to ACIP for consideration. The benefit-risk analysis can be updated as needed to reflect changes in the COVID-19 pandemic and additional information on the risk for and outcomes of myocarditis after COVID-19 vaccination. The ACIP recommendation for use of mRNA COVID-19 vaccines under an EUA is interim and will be updated as additional information becomes available.

Reporting of Vaccine Adverse Events

FDA requires that vaccine providers report to VAERS vaccination administration errors, serious adverse events,[††††††] cases of multisystem inflammatory syndrome, and cases of COVID-19 that result in hospitalization or death after administration of a COVID-19 vaccine under an EUA. CDC also encourages reporting of any additional clinically significant adverse event, even if it is not clear whether a vaccination caused the event. Information on how to submit a report to VAERS is available at https://vaers.hhs.gov/index.html or 1-800-822-7967. In addition, CDC has developed a voluntary smartphone-based online tool (v-safe) that uses text messaging and online surveys to provide near real-time health check-ins after receipt of a COVID-19 vaccine. In cases of v-safe reports that include possible medically attended health events, CDC's v-safe call center follows up with the vaccine recipient to collect additional information for completion of a VAERS report. Information on v-safe is available at https://www.cdc.gov/vsafe.

[††††††] https://vaers.hhs.gov/faq.html

Summary

What is already known about this topic?

An elevated risk for myocarditis among mRNA COVID-19 vaccinees has been observed, particularly in males aged 12–29 years.

What is added by this report?

On June 23, 2021, the Advisory Committee on Immunization Practices concluded that the benefits of COVID-19 vaccination to individual persons and at the population level clearly outweighed the risks of myocarditis after vaccination.

What are the implications for public health practice?

Continued use of mRNA COVID-19 vaccines in all recommended age groups will prevent morbidity and mortality from COVID-19 that far exceed the number of cases of myocarditis expected. Information regarding the risk for myocarditis with mRNA COVID-19 vaccines should be disseminated to providers to share with vaccine recipients.

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Lisa Jackson, Kaiser Permanente Washington Health Research Institute; Jennifer Nelson: Kaiser Permanente Washington Health Research Institute; Laura Riley, American College of Obstetricians and Gynecologists; Patricia Whitley-Williams, National Medical Association; Tatiana Beresnev, National Institutes of Health; Karen Farizo, Food and Drug Administration; Hui Lee Wong, Food and Drug Administration; Judith Steinberg, U.S. Department of Health and Human Services; Matthew Clark, Indian Health Service; Mary Rubin, Health Resources & Services Administration; Fran Cunningham, Veterans Administration; Limone Collins, Department of Defense.

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From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Fri, 2 Jul 2021 20:32:40 +0000
To: (b)(4) (b)(4) (x)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: updates
Attachments: mm7027e2 - ACIP myocarditis FINAL PROOF.pdf

(b)(4)

Few updates- first, the ACIP myocarditis MMWR is planned to be released July 6th. Attached is the final proof as FYI. It is obviously confidential at this point, but wanted you to be aware of what is upcoming.

Then- the clinical considerations finally made it through clearance and they were just published: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fcovid-19%2Finfo-by-product%2Fclinical-considerations.html

Also saw your email around it taking a little bit longer for the questions- I think that's fine since we will have a bit longer for the ACIP meeting, but we will need to share the info back with the WG eventually.

Thanks-

Sara

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Use of mRNA COVID-19 Vaccine After Reports of Myocarditis Among Vaccine Recipients: Update from the Advisory Committee on Immunization Practices — United States, June 2021

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In December 2020, the Food and Drug Administration (FDA) issued Emergency Use Authorizations (EUAs) for the Pfizer-BioNTech COVID-19 (BNT162b2) vaccine and the Moderna COVID-19 (mRNA-1273) vaccine,[†] and the Advisory Committee on Immunization Practices (ACIP) issued interim recommendations for their use in persons aged ≥16 years and ≥18 years, respectively.[§] In May 2021, FDA expanded the EUA for the Pfizer-BioNTech COVID-19 vaccine to include adolescents aged 12–15 years; ACIP recommends that all persons aged ≥12 years receive a COVID-19 vaccine. Both Pfizer-BioNTech and Moderna vaccines are mRNA vaccines encoding the stabilized prefusion spike glycoprotein of SARS-CoV-2, the virus that causes COVID-19. Both mRNA vaccines were authorized and recommended as a 2-dose schedule, with second doses administered 21 days (Pfizer-BioNTech) or 28 days (Moderna) after the first dose. After reports of myocarditis and pericarditis in mRNA vaccine recipients,[¶] which predominantly occurred in young males after the second dose, an ACIP meeting was rapidly convened to review reported cases of myocarditis and pericarditis and discuss the benefits and risks of mRNA COVID-19 vaccination in the United States. Myocarditis is an inflammation of the heart muscle; if it is accompanied by pericarditis, an inflammation of the thin tissue surrounding the heart (the pericardium), it is referred to as myopericarditis. Hereafter, myocarditis is used to refer to myocarditis, pericarditis, or myopericarditis. On June 23, 2021, after reviewing available evidence including that for risks of myocarditis, ACIP determined that the benefits of using mRNA COVID-19 vaccines under the FDA's EUA clearly outweigh the risks in all populations, including adolescents and young adults. The EUA has been modified to include information on myocarditis after receipt of mRNA COVID-19 vaccines. The EUA fact sheets should be provided before vaccination; in addition, CDC has developed patient and provider education materials about the possibility of myocarditis and symptoms of concern, to ensure prompt recognition and management of myocarditis.

Since June 2020, ACIP has convened 15 public meetings to review data on COVID-19 epidemiology and use of COVID-19 vaccines. The ACIP COVID-19 Vaccines Work Group, comprising experts in infectious diseases, vaccinology, vaccine safety, public health, and ethics, has held weekly meetings since April 2020 to review COVID-19 surveillance data, evidence for vaccine efficacy and safety, and implementation considerations for COVID-19 vaccination programs. After reports of myocarditis, the work group met twice to review clinical trial and postauthorization safety data for myocarditis after receipt of mRNA COVID-19 vaccines. The work group also reviewed a benefit-risk assessment of myocarditis events after receipt of mRNA COVID-19 vaccines, considering recent epidemiology of COVID-19 and sequelae of COVID-19, including myocarditis and multisystem inflammatory syndrome in children (MIS-C).[**] The ACIP COVID-19 Vaccines

* These authors contributed equally to this work.
† All EUA documents for COVID-19 vaccines, including fact sheets, are available at https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines.
§ ACIP recommendations for all COVID-19 vaccines are available at https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html.
¶ COVID-19 Vaccine Safety Technical Work Group Reports are available at https://www.cdc.gov/vaccines/acip/work-groups-vast/index.html.
** https://www.cdc.gov/mis/hcp/index.html

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Safety Technical (VaST) Work Group, comprising independent vaccine safety expert consultants, had also reviewed safety data on myocarditis after receipt of mRNA COVID-19 vaccines at its weekly meetings. The findings from the VaST and the ACIP COVID-19 Vaccines Work Group assessments, including a summary of the data reviewed, were presented to ACIP during its meeting on June 23, 2021.

Myocarditis typically occurs more commonly in males than in females, and incidence is highest among infants, adolescents, and young adults (*1*,*2*). The clinical presentation and severity of myocarditis vary among patients. Symptoms typically include chest pain, dyspnea, or palpitations, although other symptoms might be present, especially in younger children (*3*). Diagnostic evaluation might reveal an elevated troponin level or abnormal findings on electrocardiogram, echocardiogram, or cardiac magnetic resonance imaging (Table 1). Supportive therapy is a mainstay of treatment, with targeted cardiac medications or interventions as needed. Current guidelines from the American Heart Association and American College of Cardiology recommend exercise restriction until the heart recovers.[††]

As of June 11, 2021, approximately 296 million doses of mRNA COVID-19 vaccines had been administered in the United States, with 52 million administered to persons aged 12–29 years; of these, 30 million were first and 22 million were second doses. Within the Vaccine Adverse Event Reporting System (VAERS) (*4*), the national vaccine safety passive monitoring system, 1,226 reports of myocarditis after mRNA vaccination were received during December 29, 2020–June 11, 2021. Among persons with reported myocarditis after mRNA vaccination, the median age was 26 years (range = 12–94 years), with median symptom onset interval of 3 days after vaccination (range = 0–179). Among 1,194 reports for which patient age was known, 687 were among persons aged <30 years and 507 were among persons aged ≥30 years; of 1,212 with sex reported, 923 were male, and 289 were female.[§§] Among 1,094 patients with number of vaccine doses received reported, 76% occurred after receipt of dose 2 of mRNA vaccine; cases were reported after both Pfizer-BioNTech and Moderna vaccines. Informed by early reports, CDC prioritized rapid review of myocarditis in persons aged <30 years reported during May 1–June 11, 2021; the 484 patient records in this subset were evaluated by physicians at CDC, and several reports were also reviewed with Clinical Immunization Safety Assessment Project investigators,[¶¶] including cardiologists. At the time of this report, 323 of these 484 cases were determined to meet

TABLE 1. Case definitions of probable and confirmed myocarditis, pericarditis, and myopericarditis

Condition	Definition	
Acute myocarditis	**Probable case**	**Confirmed case**
	Presence of ≥1 new or worsening of the following clinical symptoms:*	Presence of ≥1 new or worsening of the following clinical symptoms:*
	• chest pain, pressure, or discomfort • dyspnea, shortness of breath, or pain with breathing • palpitations • syncope	• chest pain, pressure, or discomfort • dyspnea, shortness of breath, or pain with breathing • palpitations • syncope
	OR, infants and children aged <12 years might instead have ≥2 of the following symptoms: • irritability • vomiting • poor feeding • tachypnea • lethargy	OR, infants and children aged <12 years might instead have ≥2 of the following symptoms: • irritability • vomiting • poor feeding • tachypnea • lethargy
	AND ≥1 new finding of • troponin level above upper limit of normal (any type of troponin) • abnormal electrocardiogram (ECG or EKG) or rhythm monitoring findings consistent with myocarditis[§] • abnormal cardiac function or wall motion abnormalities on echocardiogram • cMRI findings consistent with myocarditis[¶]	AND ≥1 new finding of • Histopathologic confirmation of myocarditis[†] • cMRI findings consistent with myocarditis[¶] in the presence of troponin level above upper limit of normal (any type of troponin)
	AND • No other identifiable cause of the symptoms and findings	AND • No other identifiable cause of the symptoms and findings
Acute pericarditis**	Presence of ≥2 new or worsening of the following clinical features: • acute chest pain[††] • pericardial rub on exam • new ST-elevation or PR-depression on EKG • new or worsening pericardial effusion on echocardiogram or MRI	
Myopericarditis	This term may be used for patients who meet criteria for both myocarditis and pericarditis.	

Abbreviations: AV = atrioventricular; cMRI = cardiac magnetic resonance imaging; ECG or EKG = electrocardiogram.

* Persons who lack the listed symptoms but who meet other criteria may be classified as subclinical myocarditis (probable or confirmed).

† Using the Dallas criteria (Aretz HT, Billingham ME, Edwards WD, et al. Myocarditis. A histopathologic definition and classification. Am J Cardiovasc Pathol 1987; 1:3–14). Autopsy cases may be classified as confirmed clinical myocarditis on the basis of meeting histopathologic criteria if no other identifiable cause.

§ To meet the ECG or rhythm monitoring criterion, a probable case must include at least one of 1) ST-segment or T-wave abnormalities; 2) Paroxysmal or sustained atrial, supraventricular, or ventricular arrhythmias; or 3) AV nodal conduction delays or intraventricular conduction defects.

¶ Using either the original or the revised Lake Louise criteria. https://www.sciencedirect.com/science/article/pii/S0735109718388430?via%3Dihub

** https://academic.oup.com/eurheartj/article/36/42/2921/2293375

†† Typically described as pain made worse by lying down, deep inspiration, or cough, and relieved by sitting up or leaning forward, although other types of chest pain might occur.

†† https://www.ahajournals.org/doi/10.1161/CIR.0000000000000239?url_ver = Z39.88-2003&rfr_id = ori:rid:crossref.org&rfr_dat = cr_pub%20%200pubmed#d3e785

§§ Age was not reported for 32 patients, and sex was not reported for 14 patients.

¶¶ https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/cisa/index.html

criteria in CDC's case definitions for myocarditis, pericarditis, or myopericarditis by provider interview or medical record review (Table 1). The median age of the 323 patients with confirmed myocarditis was 19 years (range = 12–29 years); 291 were male, and 32 were female. The median interval from vaccination to symptom onset was 2 days (range = 0–40 days); 92% of patients experienced onset of symptoms within 7 days of vaccination. Of the 323 persons with confirmed cases, 309 (96%) were hospitalized. Acute clinical courses were generally mild; among 304 hospitalized patients with known clinical outcomes, 95% had been discharged at time of review, and none had died. Treatment data in VAERS are preliminary and incomplete; however, many patients have experienced resolution of symptoms with conservative treatment, such as receipt of nonsteroidal antiinflammatory drugs. Follow-up is ongoing to identify and understand longer-term outcomes after myocarditis occurring after COVID-19 vaccination.

Using myocarditis cases reported to VAERS with onset within 7 days after dose 2 of an mRNA vaccine, crude reporting rates (i.e., using confirmed and unconfirmed cases) per million second dose recipients were calculated using national COVID-19 vaccine administration data as of June 11, 2021. Myocarditis reporting rates were 40.6 cases per million second doses of mRNA COVID-19 vaccines administered to males aged 12–29 years and 2.4 per million second doses administered to males aged ≥30 years; reporting rates among females in these age groups were 4.2 and 1.0 per million second doses, respectively.*** The highest reporting rates were among males aged 12–17 years and those aged 18–24 years (62.8 and 50.5 reported myocarditis cases per million second doses of mRNA COVID-19 vaccine administered, respectively). Myocarditis rates from Vaccine Safety Datalink (VSD), based on electronic health records, were also evaluated. Although numbers were too small to show rates in all subgroups by age, VSD data indicated increased risk of myocarditis in the 7 days after receipt of dose 1 or dose 2 of an mRNA COVID-19 vaccine compared with the risk 22–42 days after the second dose, particularly among younger males after dose 2 (*5*).

To assess the benefit-risk balance of mRNA vaccines in adolescents and young adults, ACIP reviewed an individual-level assessment that compared the benefits (i.e., COVID-19 infections and severe disease prevented) to the risks (number of cases of myocarditis) of vaccination, using methods similar to those described previously.††† Specifically, the benefits per million second doses administered (i.e., the benefits of being fully vaccinated in accordance with the FDA EUA) were assessed, including 1) COVID-19 cases prevented based on rates the week of May 29, 2021§§§; 2) COVID-19 hospitalizations prevented based on rates the week of May 22, 2021¶¶¶; and 3) COVID-19 intensive care unit (ICU) admissions and deaths prevented based on the proportion of hospitalized patients who were admitted to the ICU or died.**** The risks were assessed as the number of myocarditis patients reported to VAERS that occurred within 7 days of receipt of a second dose of an mRNA COVID-19 vaccine per million second doses administered through the week of June 11, 2021.†††† The benefit-risk assessment was stratified by age group and sex. The analysis assumed 95% vaccine effectiveness§§§§ of 2 doses of a mRNA COVID-19 vaccine in preventing COVID-19 cases and hospitalization and assessed outcomes for a 120-day period. The 120-day period was selected because 1) no alternative vaccine options currently exist for persons aged <18 years or are expected to be available during this period, and 2) inputs regarding community transmission have high uncertainty beyond this period, particularly in the context of circulating variants.¶¶¶¶

The benefits (prevention of COVID-19 disease and associated hospitalizations, ICU admissions, and deaths) outweighed the risks (expected myocarditis cases after vaccination) in all populations for which vaccination has been recommended. However, the balance of risks and benefits varied by age and sex because cases of myocarditis were primarily identified among males aged <30 years, and the risks of poor outcomes related to COVID-19 increase with age. Per million second doses of mRNA COVID-19 vaccine administered to males aged 12–29 years, 11,000 COVID-19 cases, 560 hospitalizations, 138 ICU admissions, and six deaths due to COVID-19 could be prevented, compared with 39–47 expected myocarditis cases after COVID-19 vaccination (Table 2). Among males aged ≥30 years, 15,300 COVID-19 cases, 4,598 hospitalizations, 1,242 ICU admissions, and 700 deaths could be prevented, compared with three to four expected myocarditis cases after COVID-19 vaccination. This analysis did not include the potential benefit of preventing post-COVID-19 conditions, such as prolonged symptoms and MIS-C (*6*,*7*).

*** Data collection for race/ethnicity of myocarditis cases is ongoing

††† https://www.cdc.gov/vaccines/covid-19/info-by-product/janssen/risk-benefit-analysis.html

§§§ https://covid.cdc.gov/covid-data-tracker/#demographicsovertime. Data were used for the most recent week not subject to reporting delays prior to the ACIP meeting.

¶¶¶ https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html. Data were used for the most recent week not subject to reporting delays prior to the ACIP meeting.

**** https://gis.cdc.gov/grasp/COVIDNet/COVID19_5.html

†††† Because of uncertainty in the accuracy of myocarditis reporting, given that reviews are ongoing, and some cases might not have been reported yet, myocarditis reporting rates are presented as a range of values, calculated as ±10% of the observed reporting rates.

§§§§ https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html

¶¶¶¶ https://covid.cdc.gov/covid-data-tracker/#variant-proportions

TABLE 2. Individual-level estimated number of COVID-19 cases and COVID-19–associated hospitalizations, intensive care unit admissions, and deaths prevented after use of 2-dose mRNA COVID-19 vaccine for 120 days and number of myocarditis cases expected per million second mRNA vaccine doses administered, by sex and age group* — United States, 2021

	No. per million vaccine doses administered in each age group (yrs)†				
Sex/Benefits and harms from mRNA vaccination	**12–29**	**12–17**	**18–24**	**25–29**	**≥30**
Male					
Benefit					
COVID-19 cases prevented§	11,000	5,700	12,100	15,200	15,300
Hospitalizations prevented	560	215	530	936	4,598
ICU admissions prevented	138	71	127	215	1,242
Deaths prevented	6	2	3	13	700
Harms					
Myocarditis cases expected¶	39–47	56–69	45–56	15–18	3–4
Female					
Benefit					
COVID-19 cases prevented§	12,500	8,500	14,300	14,700	14,900
Hospitalizations prevented	922	183	1,127	1,459	3,484
ICU admissions prevented	73	38	93	87	707
Deaths prevented	6	1	13	4	347
Harm					
Myocarditis cases expected¶	4–5	8–10	4–5	2	1

Abbreviations: ICU = intensive care unit; VAERS = Vaccine Adverse Event Reporting System.
* This analysis evaluated direct benefits and harms, per million second doses of mRNA COVID-19 vaccine given in each age group, over 120 days. The numbers of events per million persons aged 12–29 years are the averages of numbers per million persons aged 12–17 years, 18–24 years, and 25–29 years.
† Receipt of 2 doses of mRNA COVID-19 vaccine, compared with no vaccination.
§ Case numbers have been rounded to the nearest hundred.
¶ Ranges calculated as ±10% of crude VAERS reporting rates. Estimates include cases of myocarditis, pericarditis, and myopericarditis.

ACIP also reviewed population-level considerations regarding vaccination. No alternatives to mRNA COVID-19 vaccines for adolescents will be available for the foreseeable future, and vaccination of adolescents offers protection against COVID-19 that can be important for returning to educational, social, and extracurricular activities. Higher levels of vaccination coverage can reduce community transmission, which can protect against development and circulation of emerging variants. Regarding health equity considerations, racial and ethnic minority groups have higher rates of COVID-19 and severe disease*****; potential changes in vaccine policy, or anything that would affect vaccination coverage for adolescents or young adults, might disproportionately affect those groups with the highest rates of poor COVID-19 outcomes.

The ACIP discussion concluded that 1) the benefits of vaccinating all recommended age groups with mRNA COVID-19 vaccine clearly outweigh the risks of vaccination, including the risk of myocarditis after vaccination; 2) continuing to monitor outcomes of myocarditis cases after COVID-19 vaccination is important; and 3) providers and the public should be informed about these myocarditis cases and the use of COVID-19 vaccines. Based on ACIP's conclusion regarding the benefit-risk assessment on June 23, 2021, COVID-19 vaccination continues to be recommended for all persons aged ≥12 years under the FDA's EUA. ACIP emphasized the importance of informing vaccination providers and the public about the benefits and the risks, including the risk for myocarditis after COVID-19 vaccination, particularly for males aged 12–29 years.

CDC has provided guidance regarding evaluation and management of myocarditis after mRNA COVID-19 vaccine (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html), as well as considerations for a second vaccine dose in persons who develop myocarditis after a first dose (https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html). FDA has added information to the Pfizer-BioNTech†††† and Moderna§§§§§ COVID-19 vaccine EUA and fact sheets regarding myocarditis cases that have been reported among vaccine recipients. In addition, CDC has updated patient education and communication materials reflecting this information for the Pfizer-BioNTech¶¶¶¶¶ and Moderna****** COVID-19 vaccines; these are important to ensure that vaccine recipients, especially males aged 12–29 years, are aware of increased risk for myocarditis and to seek care if they develop symptoms of myocarditis. The vaccine product-specific EUA fact sheet should be provided to all vaccine recipients and their caregivers before vaccination with any authorized COVID-19 vaccine.

***** https://covid.cdc.gov/covid-data-tracker/#demographics

†††† https://www.fda.gov/media/144413/download
§§§§§ https://www.fda.gov/media/144637/download
¶¶¶¶¶ https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/index.html
****** https://www.cdc.gov/vaccines/covid-19/info-by-product/moderna/index.html

CDC and FDA will continue to closely monitor reports of myocarditis after receipt of the mRNA COVID-19 vaccines and will bring any additional data to ACIP for consideration. The benefit-risk analysis can be updated as needed to reflect changes in the COVID-19 pandemic and additional information on the risk for and outcomes of myocarditis after COVID-19 vaccination. The ACIP recommendation for use of mRNA COVID-19 vaccines under an EUA is interim and will be updated as additional information becomes available.

Reporting of Vaccine Adverse Events

FDA requires that vaccine providers report to VAERS vaccination administration errors, serious adverse events,[††††††] cases of multisystem inflammatory syndrome, and cases of COVID-19 that result in hospitalization or death after administration of a COVID-19 vaccine under an EUA. CDC also encourages reporting of any additional clinically significant adverse event, even if it is not clear whether a vaccination caused the event. Information on how to submit a report to VAERS is available at https://vaers.hhs.gov/index.html or 1-800-822-7967. In addition, CDC has developed a voluntary smartphone-based online tool (v-safe) that uses text messaging and online surveys to provide near real-time health check-ins after receipt of a COVID-19 vaccine. In cases of v-safe reports that include possible medically attended health events, CDC's v-safe call center follows up with the vaccine recipient to collect additional information for completion of a VAERS report. Information on v-safe is available at https://www.cdc.gov/vsafe.

[††††††] https://vaers.hhs.gov/faq.html

Summary

What is already known about this topic?

An elevated risk for myocarditis among mRNA COVID-19 vaccinees has been observed, particularly in males aged 12–29 years.

What is added by this report?

On June 23, 2021, the Advisory Committee on Immunization Practices concluded that the benefits of COVID-19 vaccination to individual persons and at the population level clearly outweighed the risks of myocarditis after vaccination.

What are the implications for public health practice?

Continued use of mRNA COVID-19 vaccines in all recommended age groups will prevent morbidity and mortality from COVID-19 that far exceed the number of cases of myocarditis expected. Information regarding the risk for myocarditis with mRNA COVID-19 vaccines should be disseminated to providers to share with vaccine recipients.

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From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Sent: Mon, 3 May 2021 18:41:36 +0000
To: (b)(4) (b)(4) T; (b)(4) (b)(4) (b)(4) Mary M.
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: ACIP meeting
Attachments: FollowUp_Questions.docx

(b)(4) (b)(and Mary:

Thank you for your presentation to the WG last week. We have a few follow-up questions, both from the WG call and our data review. The questions are attached here. If you could provide answers by Thurs 5/6, that would be much appreciated.

Next- we haven't publicly announced the ACIP meeting for this, but are working on getting it posted to the website within the next 24 hours. While things can always change, our plan is to have the ACIP meeting **Monday, May 10th**. We are sharing for your internal planning, but please do not share broadly until it is posted on the website. The meeting will likely start at **11am EST**, and while we will need to give a variety of updates in addition to discussing the adolescent data, we plan on discussing the adolescent data first. We would invite Pfizer to present the adolescent data (~20 minute presentation, with time for questions after the presentation). As we plan the agenda, please let us know who the speaker will be, and if you have a preferred title for the talk.

And finally- our colleagues at BARDA and the group formally known as Operation Warp Speed have asked if they could review the slides from the WG call this past week. I've said our confidentiality agreement with you means that we need to check with you before sharing. Let us know if you would be Ok with us sharing the slides with them, or if you prefer for them to go through you for the data. We are fine either way, but want to preserve the trust and relationship we have with our data agreements.

Thanks!

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force
Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

Questions for Pfizer

1. Please provide narratives for the 5 serious adverse events observed in the vaccine arm, including timing of the events relative to the two vaccine doses.
2. Were data collected on psychiatric conditions among adolescents at study enrollment? Were conditions such as ADHD, depression, and anxiety balanced between vaccine and placebo arms after randomization?
3. Please provide the raw numbers for reactogenicity that were used to create Figure 1 and Figure 2.
4. Were persons with prior MIS-C excluded from the trial due to prior known SARS-CoV-2 infection?
5. Please provide a safety profile stratified by baseline SARS-COV-2 serostatus, including those that were seropositive or PCR+ at baseline. Were safety outcomes different among the ~4% of adolescents that were positive for SARS-CoV-2 at baseline? Did reactogenicity differ by serostatus? Where any of the participants with SAEs seropositive?
6. Please provide information on SAEs for all trial participants aged 16-25.
7. Please share more information about the individual who had an anaphylactoid reaction after unblinding. Did the individual have true anaphylaxis? What was the clinical course and did the individual recover?
8. Please share more information about the individual who had a Grade 4 fever. Was this individual positive for SARS-CoV-2 at baseline?
9. Please explain the differences in the number of subjects included comparing table 23 to table 25 and comparing table 24 to table 27.

From: (b)(4) (b)(4) (x)
Sent: Tue, 13 Apr 2021 15:07:00 +0000
To: Shimabukuro, Tom (CDC/DDID/NCEZID/DHQP); Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: ACIP Tomorrow

Hi Tom and Sara,
I understand that there will be an emergency ACIP tomorrow to discuss the rare event of blood clots after the J& J COVID-19 vaccine.
Two questions for you please:

1. Do you have similar data for the other manufacturers' vaccines that you will be presenting?
2. Should Moderna be prepared to discuss our safety findings, if asked, at the meeting? If so, do you want to open a line for a representative from Moderna? Or will you cover this in your presentation?

Many thanks.
(b)(4)

Please consider the environment before printing this email

From: (b)(4) (b)(4) (b)(

Sent: Thu, 6 May 2021 16:54:05 +0000

To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)

Cc: (b)(4) (b)(4) (b)(4) (b)(4).; MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)

Subject: Answers for work group questions

Attachments: May 6 2021_ COVID-19 Vaccine US CDC Response (12-15 EUA amendment).pdf, CDC COVID-19 Vaccine 12 to 15 EUA May 5 2021 Final.pdf

Dear Sara,

Please find attached our responses to the questions you sent us from the work group. We added some of the answers where it made sense into the presentation document dated May 5 (in red font so you can find them easily). The other document dated May 6 has the answers to some of the questions where it made sense to have more of a narrative. We hope the work group finds these useful.

We do have a request for you. (b)(4) has done our presentation now to several groups and it is always closer to 25 mins. Would it be possible to have 25 mins for our presentation at the full ACIP? If not we will need to remove some slides in order to get it down to 20 mins. Thank you for your consideration of this request.

Best regards,

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From: (b)(4) (b)(4) (x)
Sent: Thu, 10 Jun 2021 20:49:32 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Background Documents - COVID-19 Vaccine Studies in Adolescents - CONFIDENTIAL
Attachments: EUA US Adolescent Request_04June2021 (1).pdf, Moderna - Adolescent Protocol - mRNA-1273-P203 CSP_signed_published.pdf, Moderna - Adolescent Study Amendment - mRNA-1273-P203_Amendment 1_Final - Signed Version.pdf

Hi Sara,
Here are some of the documents that we have agreed to share with CDC in confidence regarding our studies in adolescents:
1) The EUA we submitted to FDA
2) The protocol & amendments for the adolescent study
I hope this helps. Please handle as confidential & limit distribution to those identified in our joint confidentiality agreement.
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From: (b)(4) (b)(4) (b)(4)
Sent: Fri, 7 May 2021 14:22:06 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); (b)(4) (b)(4) (b)(4) (b)(4)
Subject: BLA submission for 16+

Dear Sara,
Just wanted to send you today's press release regarding our BLA submission to FDA for BNT162b2 in ages 16+ that we had mentioned last time we spoke.
Pfizer Inc. - Pfizer and BioNTech Initiate Rolling Submission of Biologics License Application for U.S. FDA Approval of Their COVID-19 Vaccine

As always, please let us know if you have any questions.
Best regards,
(b)(4) (b)(4) and (b)(4)

From: (b)(4) (b)(4) (x)
Sent: Tue, 1 Jun 2021 23:33:22 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Booster/Variant Data - COVID-19 Vaccines - CONFIDENTIAL
Attachments: CDC - Update on Availability of New Data.pptx

Hi Sara,
I hope you had an enjoyable weekend.
As promised, I am sending you some of the slides we discussed recently regarding our studies of booster doses/variants and a rough estimate of the timing for availability of data.
I would appreciate if you would handle this information as Confidential.
Please let me know if you have any questions.
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From: (b)(4) (b)(4) (x)
Sent: Thu, 10 Jun 2021 19:24:26 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Confidentiality Agreement - CDC & Moderna

Hi Sara,
Here is the fully executed confidentiality agreement.
Now that we have this, I can send you the documents for adolescents (EUA filing + protocol).
(b)(4)

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From: (b)(4) (b)(4) (x)
Sent: Fri, 23 Apr 2021 23:22:23 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Congratulations!

Hi Sara,
I just wanted to send my congratulations on an excellent presentation today & a superb handling of "all things COVID-19" of late. BRAVO !!!
The health of the US has truly made a leap forward thanks to your remarkable talents and dedication to public health.
Now go and get some well-deserved sleep!
All the best,
(b)(4)

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From: (b)(4) (b)(4) (x)
Sent: Wed, 26 May 2021 15:00:31 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Subject: Data on Variants/Boosters

Hi Sara,
I will send you the slide in the next day or so. I am going to add a column showing the dates & I want to double check with the team before I do so.
I assume no update on the communication on myocarditis yet?
(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Tuesday, May 25, 2021 11:55 AM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: RE: immunocompromised?

EXTERNAL

(b)(4)

This information is very helpful- thanks so much.

Do you have a copy of the slides you showed us on the call as well? I'm trying to put all the 'info to inform booster dose discussions' in one document for my sanity and I want to make sure the notes I took on the call are correct!

Thanks-
Sara

From: (b)(4) (b)(4) (x) (b)(4)
Sent: Tuesday, May 25, 2021 9:51 AM
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: Re: immunocompromised?

Hi Sara,

Moderna is conducting 2 studies that include immunocompromised subjects.

1. Our P304 trials includes solid organ transplant recipients (kidney & lung). Total N is 220, but enrollment is a bit slow, so we are adding sites. I cannot project study completion at this time.

2. Our P901 large scale effectiveness study at Kaiser Southern is enrolling 0.5-1 million persons by year end. (This is the study I suggested we should present to all of you.) A secondary objective will be to assess effectiveness in patients who are immunocompromised (HIV, cancer, transplant, immunosuppressive medications). We hope to have an initial look at some data in 3Q 2021, but not sure if that will include this secondary objective.

We also enrolled 92 HIV patients in the pivotal efficacy trial (study 301). Those data were presented by Dr. (b)(4) to ACIP at the time of the EUA. Let me know if you need me to send you those slides.

I also know that Anna Giuliano has vaccinated >600 patients with cancer at the Moffitt Cancer Center. She can certainly provide you with more information.

I hope this helps.

(b)(4)

From: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD) <yxo4@cdc.gov>
Sent: Monday, May 24, 2021 6:58 PM
To: (b)(4) (b)(4) (x) (b)(4)
Cc: MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>
Subject: immunocompromised?

EXTERNAL

(b)(4)

I don't have any updates for myocarditis- but will share when we do!

I have another quick question though. As we plan for data to inform the booster discussions, we've had several questions around what data may be available in immunocompromised individuals. Is Moderna doing any studies looking at VE or immunogenicity in immunocompromised individuals? And if so, do you know when data may be available?

Thanks!

Sara

Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Lead, ACIP COVID-19 Vaccine Work Group
Vaccine Task Force

Centers for Disease Control and Prevention
phone: 404-639-1204
email: yxo4@cdc.gov

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From: (b)(4) (b)(4) (x)
Sent: Fri, 25 Jun 2021 19:39:32 +0000
To: Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD)
Subject: Discussion of Booster/Variant Studies with COVID-19 Work Group

Hi Sara,
I wanted to let you know that we have some safety and immunogenicity data from the pilot study that we have conducted with our variant vaccines as boosters, including mRNA-1273.211 (which includes both mRNA-1273 + mRNA.1273.351). The data are preliminary and based on a small N, but might be of interest nonetheless. Would the WG like to hear an overview of our studies of boosters and variants vaccines? If so, please suggest some possible dates. (b)(4) would present.
I realize we may be presenting the adolescent data to the full ACIP before presenting these data to the WG, but wanted you to know that we now have additional data.
Let me know your thoughts please. And have a wonderful weekend!
(b)(4)