Pfizer-BioNTech COVID-19 Vaccine Booster:
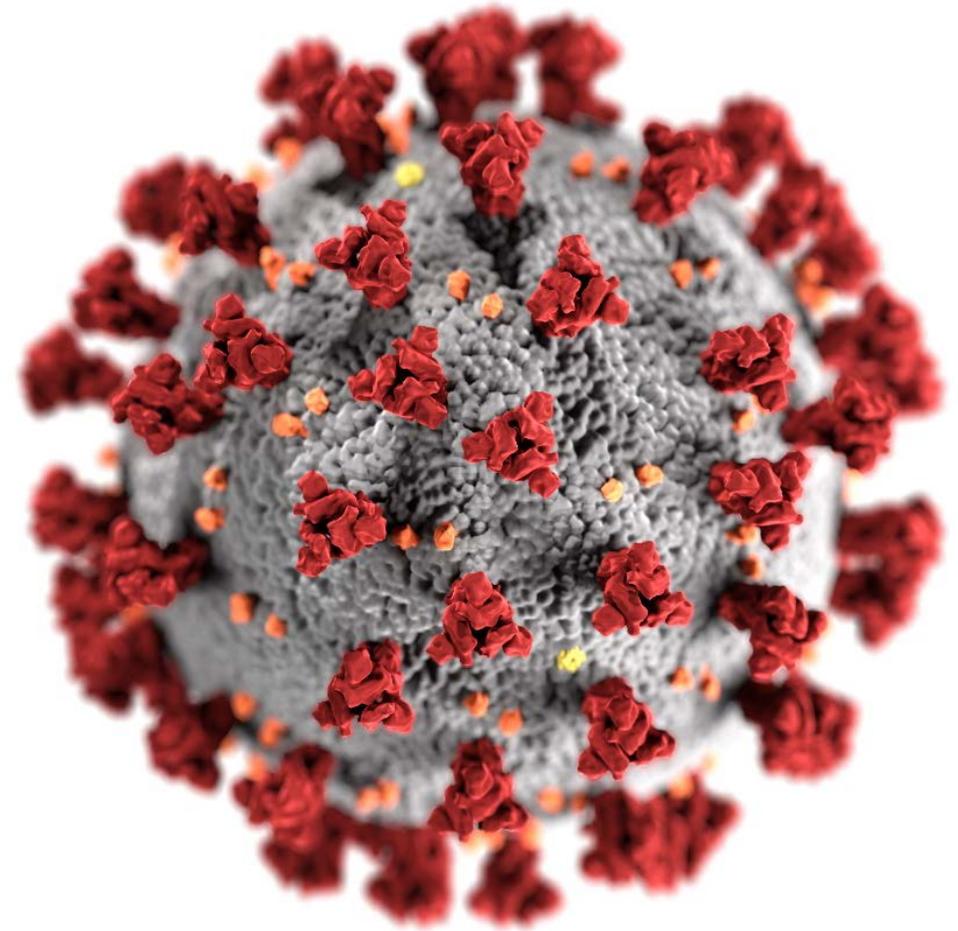## Benefits-Risk Discussion

Megan Wallace, DrPH, MPH
ACIP Meeting
September 23, 2021

Benefits and risks of Pfizer-BioNTech COVID-19 vaccine booster dose

Benefits of Pfizer-BioNTech COVID-19 booster dose

Risks after Pfizer-BioNTech COVID-19 booster dose

Methods for assessment of benefit-risk balance

Benefits — Calculated per 1 million booster doses (Pfizer-BioNTech)

- Age groups: 18 – 29 years, 30 – 49 years, 50 – 64 years, ≥65 years
- Time Horizon: 180-day period

Input	Source
Case Incidence	CDC Data Tracker (Sept 9, 2021)[1]
Hospitalization Incidence	COVID-NET (Aug 21, 2021)[2]
Vaccine Effectiveness (primary series)	Averaged VE estimates from four platforms
Vaccine Effectiveness booster	Assumption (VE post-booster is **unknown**) 95% VE for hospitalization 90% VE for infection

VE: Vaccine Effectiveness
[1]https://covid.cdc.gov/covid-data-tracker/#trends_dailycases
[2]https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html

Current age-specific VE estimates for hospitalization

	VE for hospitalization				
Age Group	COVID-NET, April – August 2021[1]	Scobie *et al.,* June – July 2021[2]	VISION, June – August 2021[3]	IVY Network, July – August 2021[4]	Average VE for base case
18 – 29 years	94.7%	93%	85%	90%	90.7%
30 – 49 years	95.6%	93%	82%		90.2%
50 – 64 years	95.5%	91%	84%	94%	91.1%
≥65 years	95.2%	87%	73%	85%	85.1%

VE = vaccine effectiveness;
[1]https://www.medrxiv.org/content/10.1101/2021.08.27.21262356v1
[2]https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e1.htm?s_cid=mm7037e1_w
[3]https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e2.htm. Using Pfizer specific estimate.
[4]https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e2.htm

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Methods for assessment of benefit-risk balance

- **Harms** — per 1 million booster doses (Pfizer-BioNTech)

Input	Source
Myocarditis incidence following a booster dose	Assumption (myocarditis risk after 3rd dose is **unknown**) Based on Vaccine Adverse Event Reporting System data post dose 2

Reporting rates of myocarditis following Pfizer-BioNTech vaccination (per million doses administered) by age and dose number, 7-day risk period[1]
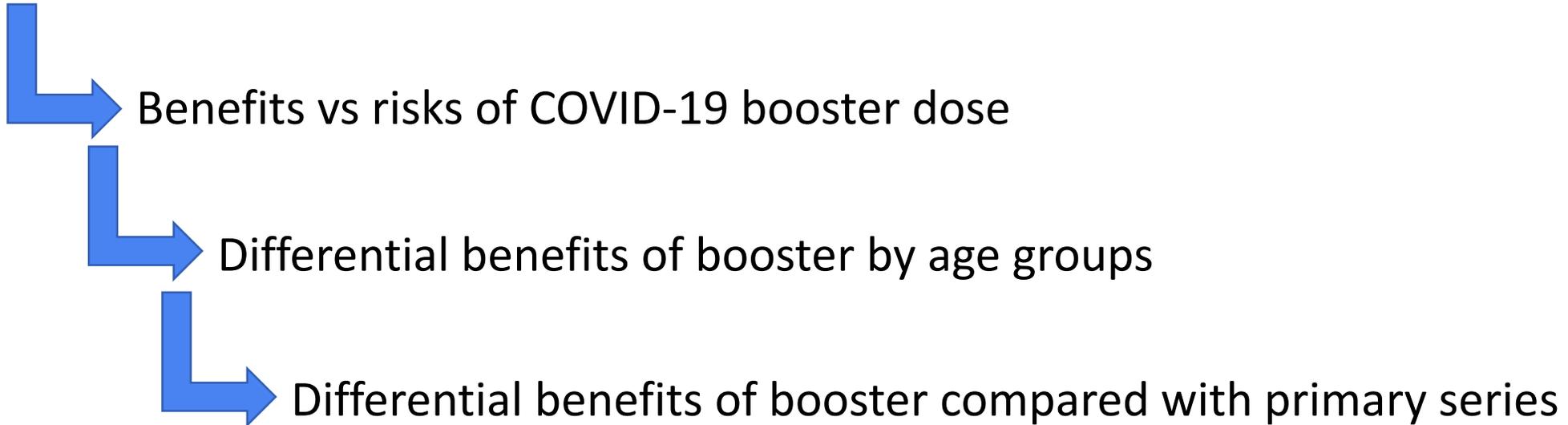
Age group	All		Males		Females	
	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 2
18-29 years old	1.1	12.9	2.1	24.1	0.2	2.0
30-49 years old	0.6	3.1	0.9	5.6	0.4	1.4
50-64 years old	0.2	0.5	0.2	0.5	0.3	0.8
≥65 years old	0.2	0.3	0.2	0.4	0.2	0.4

Sensitivity analysis performed to account for uncertainty

- Varied estimates for how much a booster dose would increase VE

- Varied estimates for what VE is currently
  - Modeled increased VE waning by decreasing current VE estimates by 5% intervals

- Modeled variable risk by considering myocarditis incidence seen after dose 2, and 2x dose 2

Framework for booster dose benefit-risk analysis

Benefits vs risks of COVID-19 booster dose

Differential benefits of booster by age groups

Differential benefits of booster compared with primary series

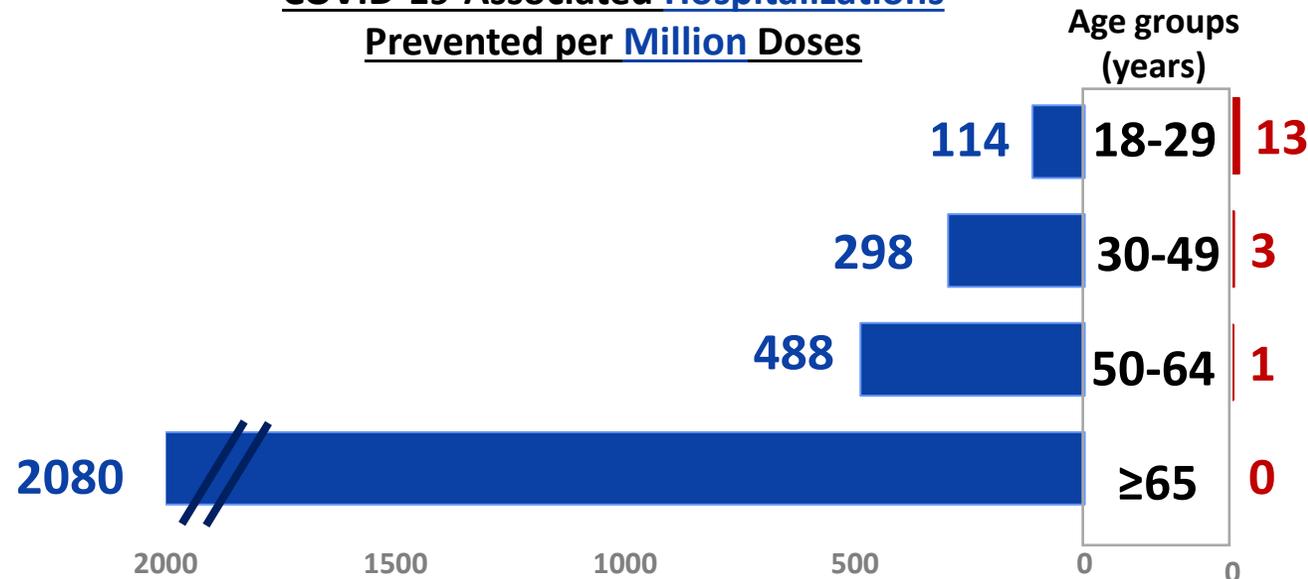# Benefits and risks after Pfizer-BioNTech COVID-19 booster dose

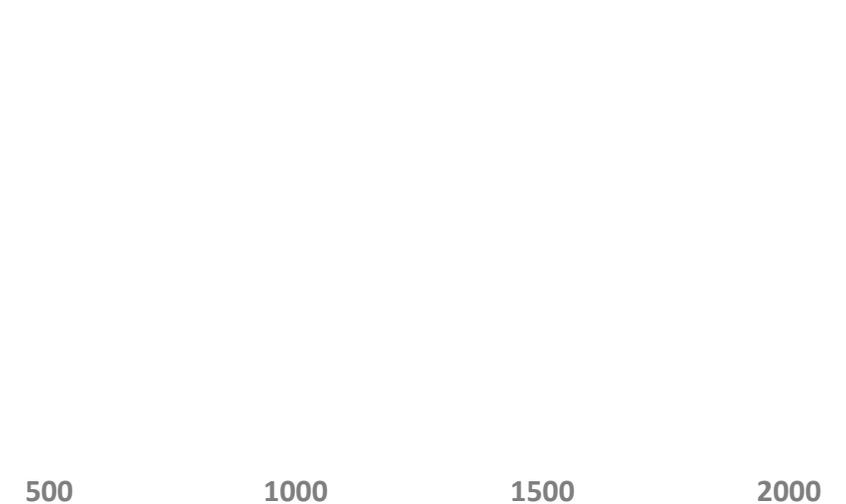*For every **million** doses of vaccine given*

Scenario:
- VE for hospitalization averaged from four platforms
- Boost to 95% VE for hospitalization
- Myocarditis risk equivalent to after 2nd dose

Age Group	VE for hospitalization
18 – 29 years	90.7%
30 – 49 years	90.2%
50 – 64 years	91.1%
≥65 years	85.1%

COVID-19-Associated Hospitalizations Prevented per Million Doses

Cases of Myocarditis Expected per Million Doses

	Age groups (years)	
114	18-29	13
298	30-49	3
488	50-64	1
2080	≥65	0

2000   1500   1000   500   0   0   500   1000   1500   2000

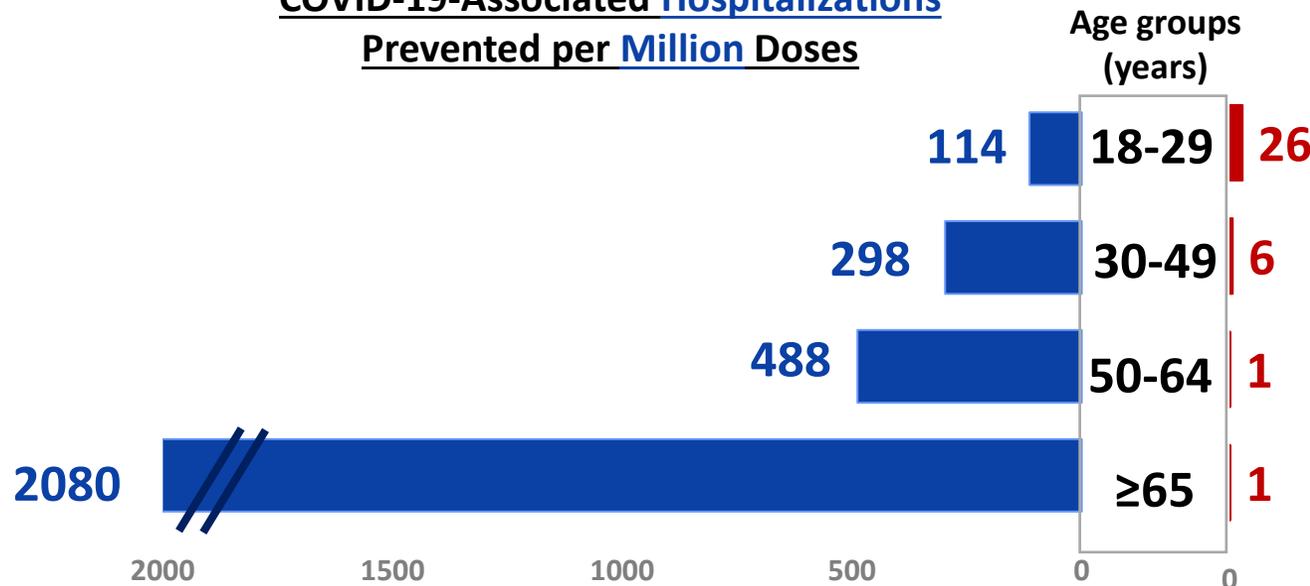# Benefits and risks after Pfizer-BioNTech COVID-19 booster dose

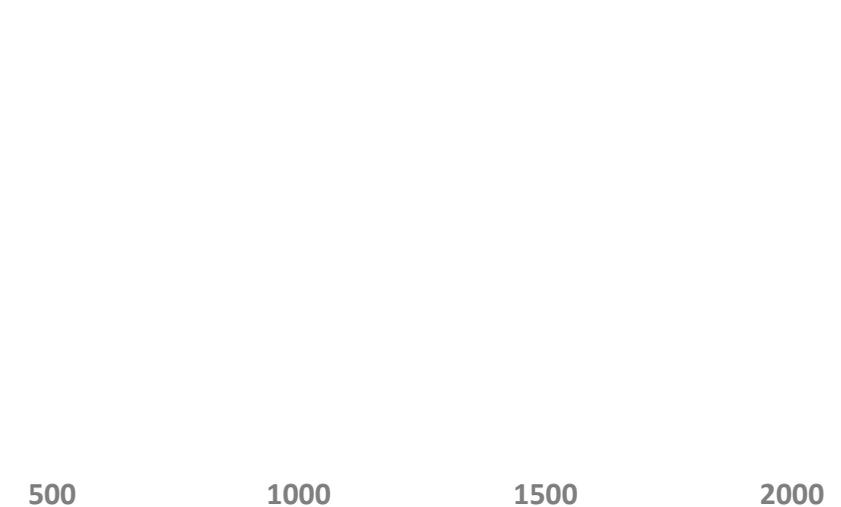*For every **million** doses of vaccine given*

Scenario:
- VE for hospitalization averaged from four platforms
- Boost to 95% VE for hospitalization
- Myocarditis risk equivalent to **2x risk of 2nd dose**

Age Group	VE for hospitalization
18 – 29 years	90.7%
30 – 49 years	90.2%
50 – 64 years	91.1%
≥65 years	85.1%

COVID-19-Associated Hospitalizations Prevented per Million Doses

Age groups (years)

Cases of Myocarditis Expected per Million Doses

	Age groups (years)	
114	18-29	26
298	30-49	6
488	50-64	1
2080	≥65	1

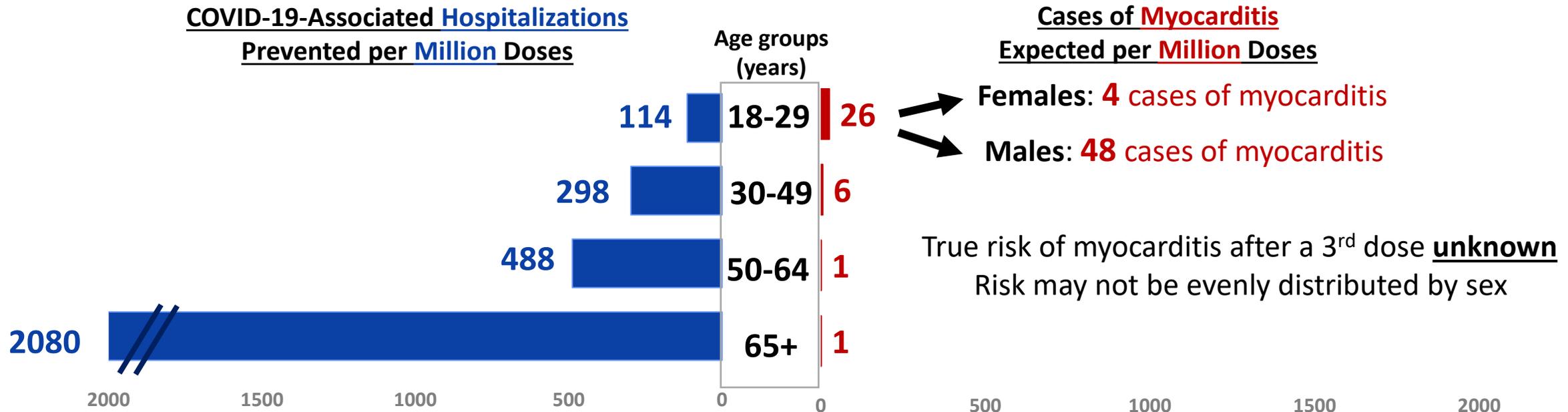2000 1500 1000 500 0   0 500 1000 1500 2000

Benefits and risks after Pfizer-BioNTech COVID-19 booster

*For every **million** doses of vaccine given*

Scenario:
- VE for hospitalization averaged from four platforms
- Boost to 95% VE for hospitalization
- Myocarditis risk equivalent to **2x risk of 2nd dose**

Age Group	VE for hospitalization
18 – 29 years	90.7%
30 – 49 years	90.2%
50 – 64 years	91.1%
≥65 years	85.1%

COVID-19-Associated Hospitalizations Prevented per Million Doses

Age groups (years)

Cases of Myocarditis Expected per Million Doses

Hospitalizations Prevented	Age group	Myocarditis cases
114	18-29	26
298	30-49	6
488	50-64	1
2080	65+	1

Females: **4** cases of myocarditis

Males: **48** cases of myocarditis

True risk of myocarditis after a 3rd dose **unknown**
Risk may not be evenly distributed by sex

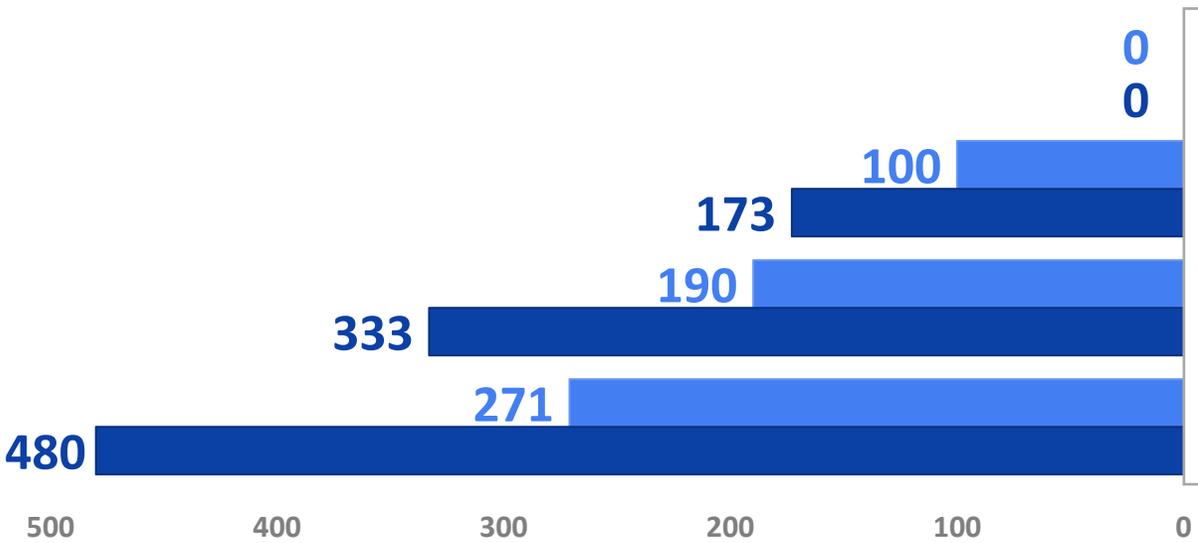2000 1500 1000 500 0 0 500 1000 1500 2000

Benefits and risks after Pfizer-BioNTech COVID-19 booster for persons aged 18 – 29 years with varying pre-booster VE, by sex
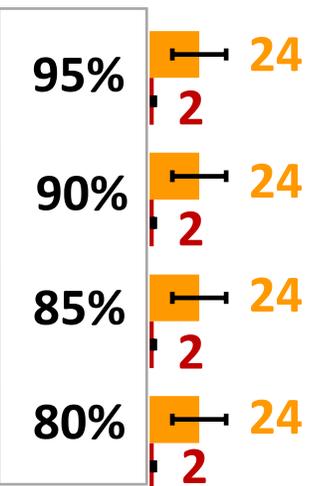
*For every **million** doses of vaccine given*

Scenario:
- **Hypothetical, varied pre-booster VE for hospitalization**
- **COVID-19 hospitalization rates stratified by sex**
- Boost to 95% VE for hospitalization
- Myocarditis risk equivalent to **risk after 2nd dose, by sex**
  - **Range: risk in 25–29-year-olds – risk in 18–24-year-olds**

COVID-19-Associated Hospitalizations Among Males & Females Prevented per Million Doses

Pre-Booster VE

Cases of Myocarditis Among Males & Females Expected per Million Doses

	Pre-Booster VE	Males	Females
0 / 0	95%	24	2
100 / 173	90%	24	2
190 / 333	85%	24	2
271 / 480	80%	24	2

500 400 300 200 100 0   0   100 200 300 400 500

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Benefits and risks after Pfizer-BioNTech COVID-19 booster for persons aged 18 – 29 years with varying pre-booster VE, by sex

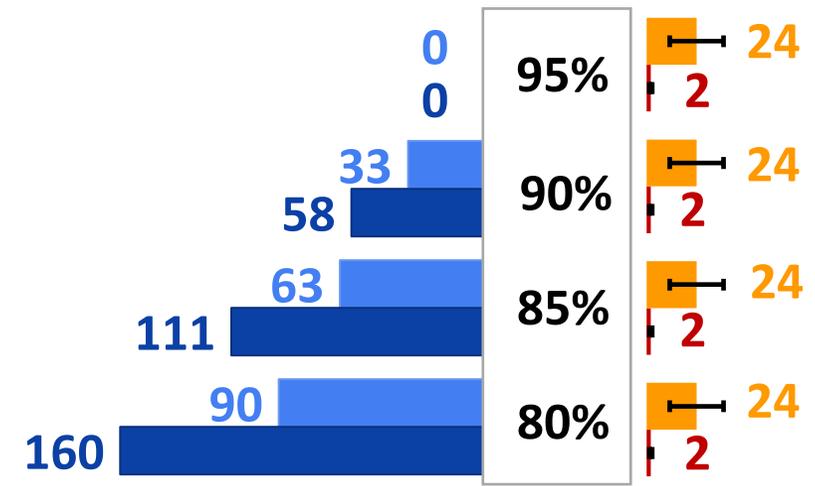*For every **million** doses of vaccine given*

Scenario:
- Hypothetical, varied pre-booster VEs
- Hospitalization rates stratified by sex
- Boost to 95% VE for hospitalization
- Myocarditis risk equivalent to risk 2nd dose
  - Range: risk in 25–29-year-olds – risk in 18 – 25-year-olds
- **Decreased hospitalization rate to 1/3 of current rate, similar to rates seen in June/July 2021**

COVID-19-Associated Hospitalizations Among Males & Females Prevented per Million Doses	Pre-Booster VE	Cases of Myocarditis Among Males & Females Expected per Million Doses
0 / 0	95%	24 / 2
33 / 58	90%	24 / 2
63 / 111	85%	24 / 2
90 / 160	80%	24 / 2

500 400 300 200 100 0   0 100 200 300 400 500

https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e1.htm?s_cid=mm7037e1_w.

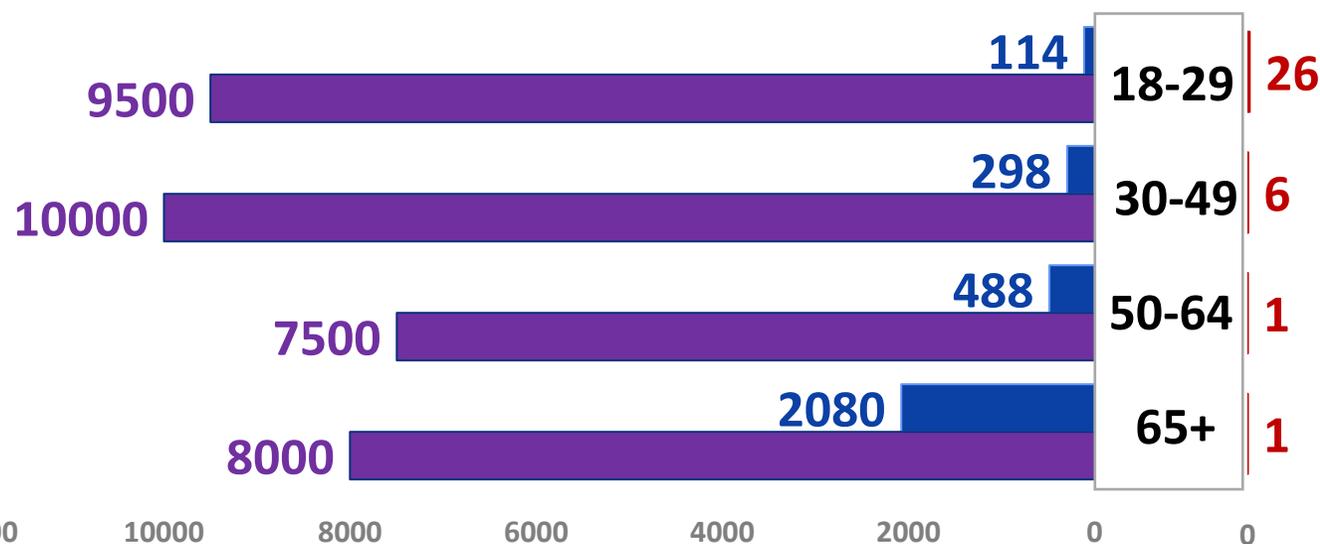# Benefits and risks after Pfizer-BioNTech COVID-19 booster

*For every **million** doses of vaccine given*
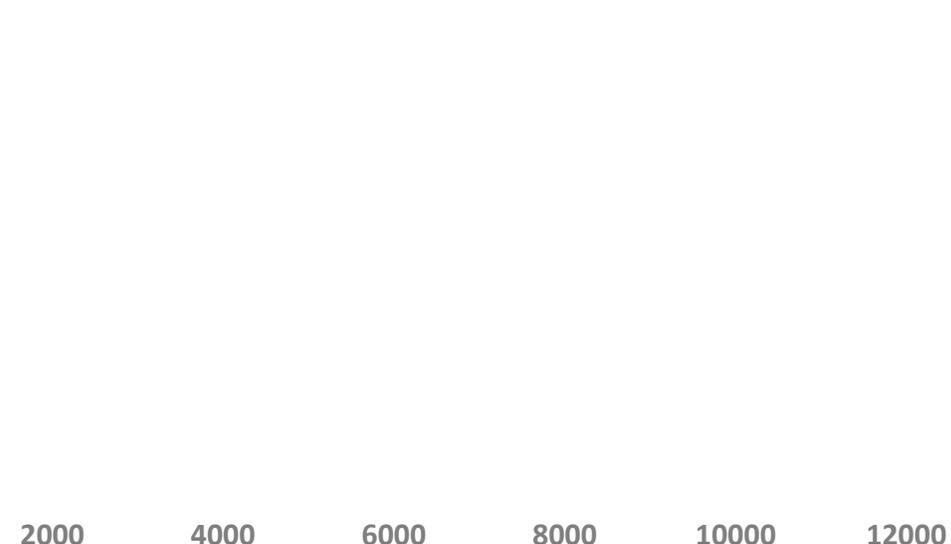
Scenario:
- VE for hospitalization averaged from four platforms
- **VE for infection estimates from Scobie et al.[1]**
- Boost to 95% VE for hospitalization, **90% VE for infection**
- Myocarditis risk equivalent to **2x risk of 2nd dose**

Age Group	VE for hospitalization	VE for infection
18 – 29 years	90.9%	78%
30 – 49 years	90.2%	78%
50 – 64 years	90.2%	80%
≥65 years	85.1%	78%

**COVID-19-Associated Hospitalizations &
COVID-19 Cases Prevented per Million Doses**

**Cases of Myocarditis Expected per
Million Doses**

Age groups (years)

Age group	Hospitalizations prevented	Cases prevented	Myocarditis cases
18-29	114	9500	26
30-49	298	10000	6
50-64	488	7500	1
65+	2080	8000	1

[1]https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e1.htm?s_cid=mm7037e1_w.
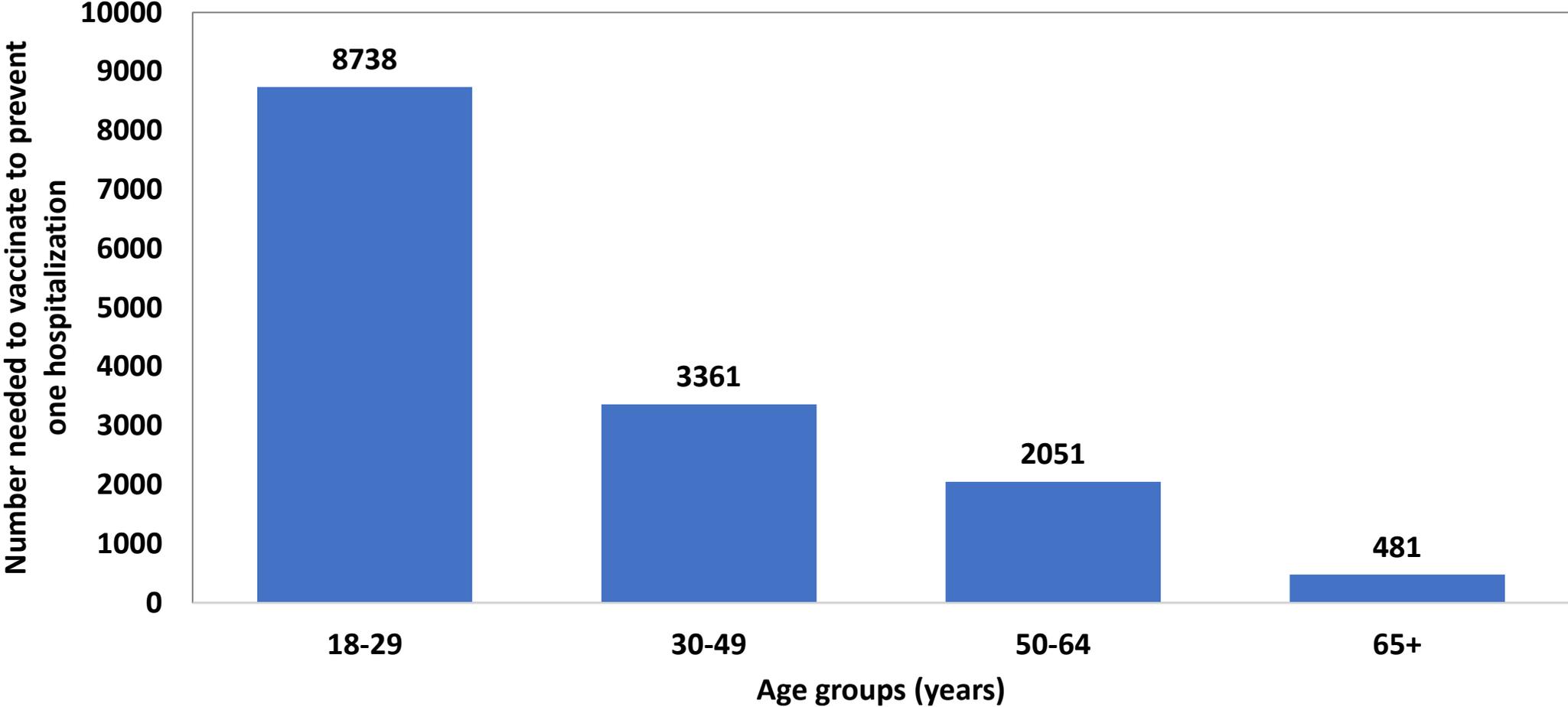
Benefits and risks after Pfizer-BioNTech COVID-19 booster in persons aged 18-29 years and 65+ years

*Variation by booster effectiveness against hospitalization*
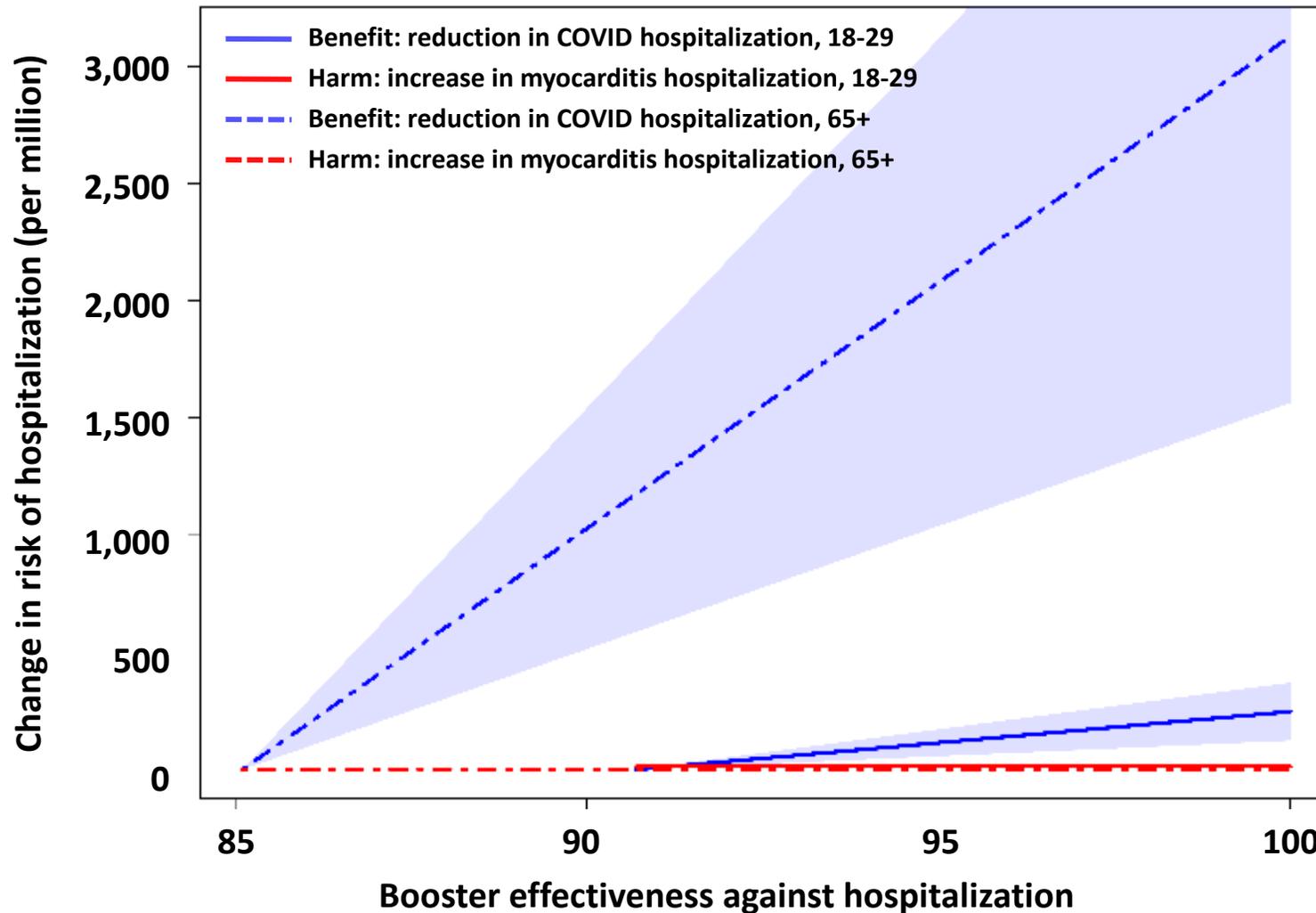
Age Group	VE for hospitalization
18 – 29 years	90.7%
≥65 years	85.1%

Number needed to vaccinate with booster dose to prevent one hospitalization over 6 months

Chart showing number needed to vaccinate to prevent one hospitalization by age group:
- 18-29: 8738
- 30-49: 3361
- 50-64: 2051
- 65+: 481

Y-axis: Number needed to vaccinate to prevent one hospitalization (0 to 10000)
X-axis: Age groups (years)

Number needed to vaccinate with booster dose to prevent one hospitalization or infection over 6 months
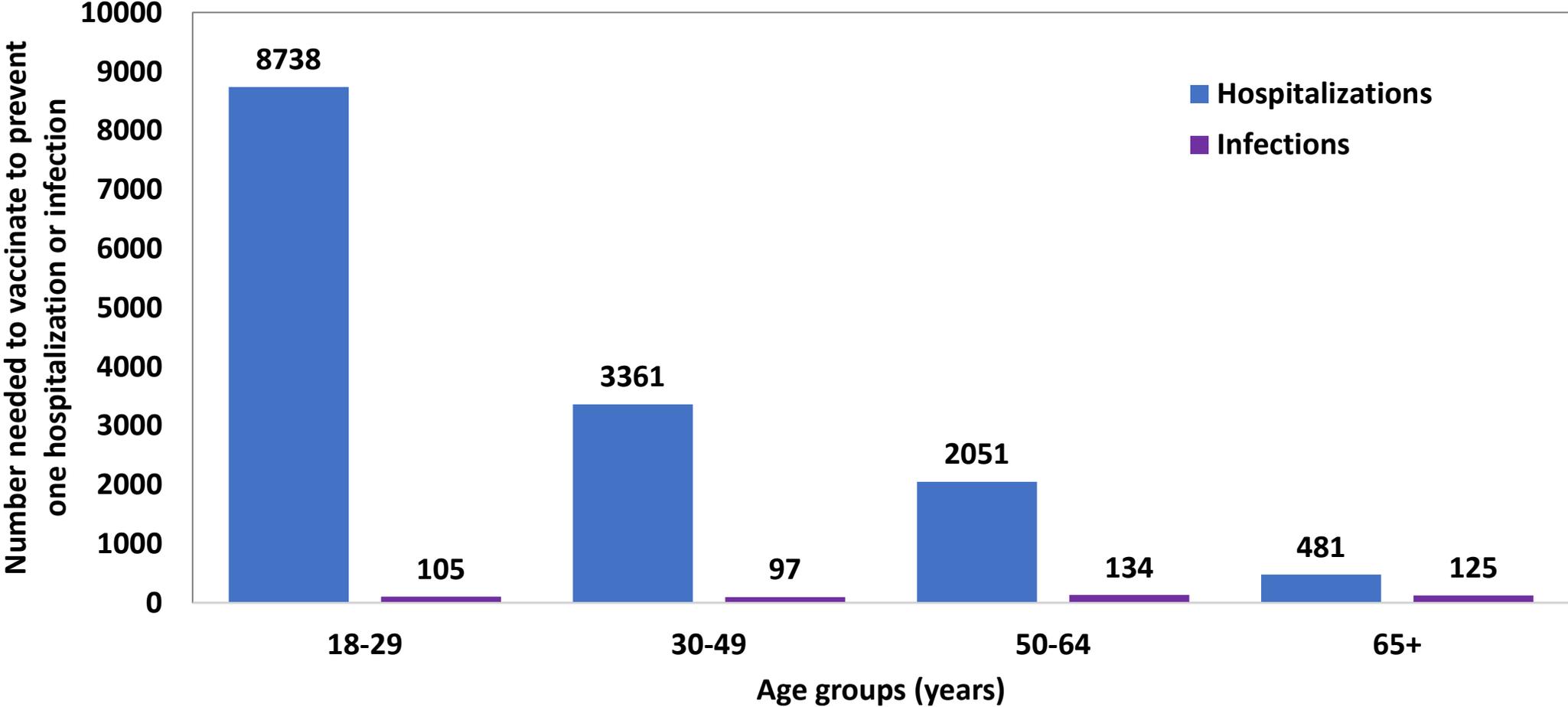
Relative benefits of booster dose vs primary series vaccination with Pfizer-BioNTech COVID-19 Vaccine

Scenario:

- VE for hospitalization averaged from four platforms

- VE for infection estimates from Scobie et al.[1]

- Boost to 95% VE for hospitalization and 90% VE for infection

- Primary series assumes 1,000,000 doses used to provide 500,000 primary series

  - Primary series provides 95% VE for hospitalization and 90% VE for infection

- Presented as number needed to vaccinate

Number needed to vaccinate to prevent one **hospitalization** over 6 months, booster versus **primary series**
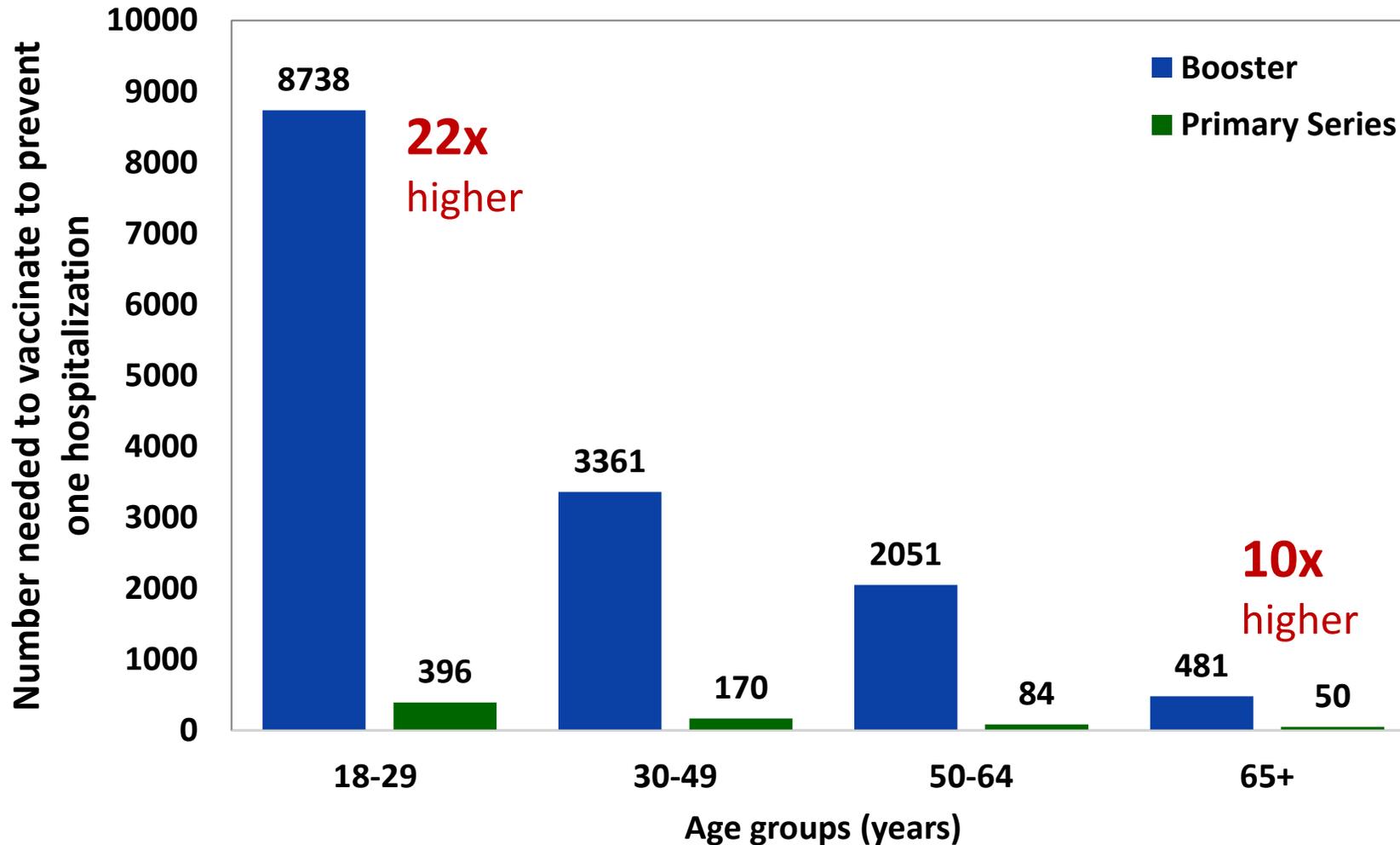
Limitations

- Benefit-risk analyses very sensitive to pre-booster vaccine effectiveness and effectiveness data for Delta variant are limited
  - Available age specific U.S. data based on month of COVID-19 onset, not on duration since vaccination
  - Preferred pre-booster data would measure effectiveness by duration since 2nd dose (e.g., 6 months, 8 months)

- Post-booster effectiveness and post-booster myocarditis risk are unknown and based on available evidence from the primary series

- Model assumes static incidence and VE over a 6-month period

Summary of benefit-risk balance for Pfizer-BioNTech COVID-19 booster and myocarditis

- Direct benefit-risk assessment for Pfizer-BioNTech COVID-19 vaccine booster & myocarditis
  - Considers individual benefits of vaccination vs. individual risks

- Using current VE estimates, benefit/risk balance **most favorable** for **adults ≥65 years of age**
  - Current estimates show smaller benefits for population <65 years of age

- Benefits **increase** in scenarios with lower VE for prevention of hospitalization and cases

- Risks of myocarditis after a 3rd dose of mRNA vaccines may **vary** by age and sex
  - Highest rates of myocarditis after the 2nd dose seen in younger males

Benefits and risks of Pfizer-BioNTech COVID-19 Vaccine booster dose by age

Benefits
of providing a
Pfizer-BioNTech
COVID-19
booster dose

Risks
of providing a
Pfizer-BioNTech
COVID-19
booster dose

Prevention of COVID-19 cases, hospitalizations and deaths
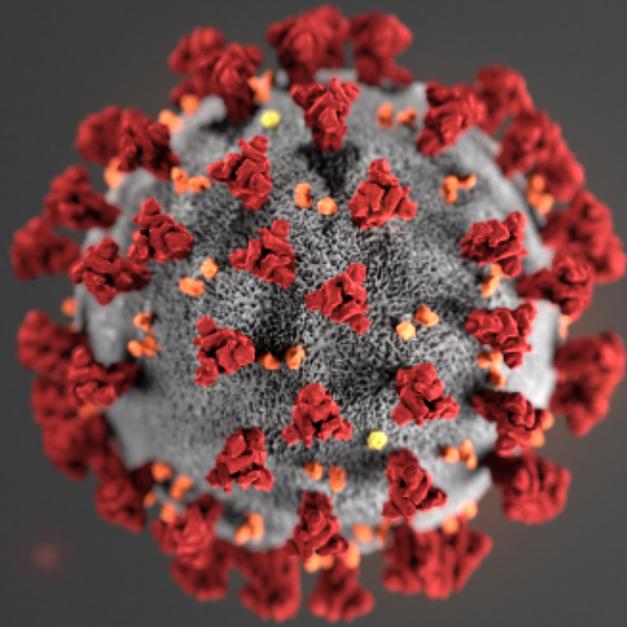
Possible prevention of transmission

Myocarditis or other rare events after mRNA vaccines

Short-term reactogenicity

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Acknowledgements

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.