Benefit and risk assessment for COVID-19 vaccines

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Benefit-risk assessment

- Benefits of COVID-19 vaccine by age for **primary series**
- Incremental benefits of COVID-19 vaccine by age and time since last dose for **bivalent booster dose**
  - Sensitivity analyses model high and low points in the pandemic
- Benefit-risk assessment for bivalent booster dose
  - Focused on ages 12-17 years and 18-49 years

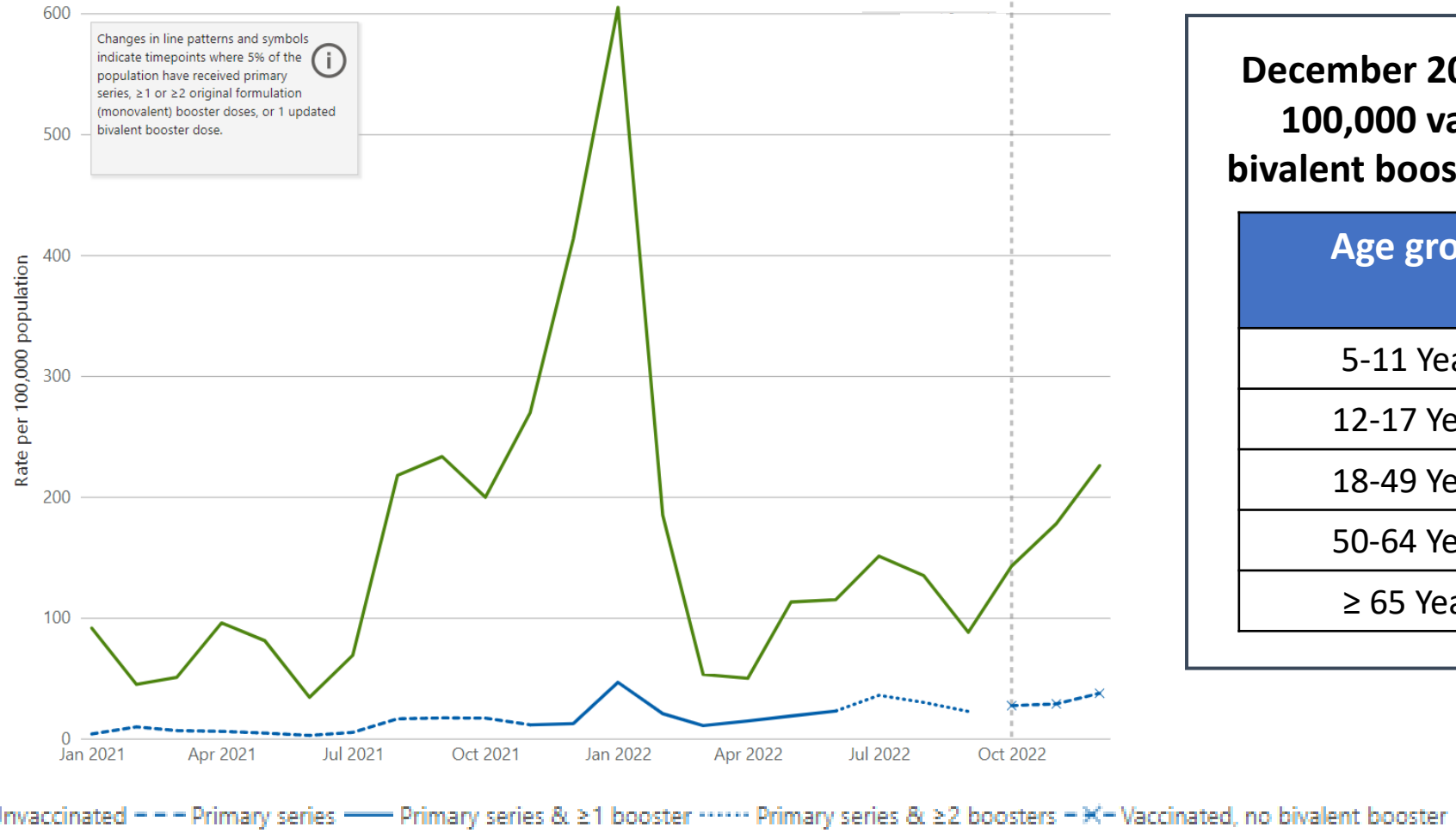
Methods for benefit assessment

Benefits – Calculated per 1 million primary series or bivalent booster doses

- Hospitalization rates[1]: December 2022 COVID-19-associated hospitalization rate among persons aged 5–11, 12–17, 18–49, 50–65, 65+ years, by vaccination status, from COVID-NET
  - Sensitivity analyses model high and low points in the pandemic
- Time horizon[2]: 6 months
- Vaccine Effectiveness: VE estimates from VISION[3] with assumption of waning of effectiveness by 10% each month starting after month 2
  - VE of primary series based on absolute VE for bivalent dose[4]
  - VE of bivalent booster dose based on relative VE by interval from last monovalent dose to bivalent[5]

[1]https://covid.cdc.gov/covid-data-tracker/#covidnet-hospitalizations-vaccination. Rates among unvaccinated used for primary series assessment. Rates among those vaccinated with monovalent doses only used for bivalent booster dose assessment.
[2]Period over which benefits of bivalent vaccination accrue
[3]https://www.cdc.gov/mmwr/volumes/71/wr/mm715152e1.htm?s_cid=mm715152e1_w.
[4]Absolute VE of bivalent booster dose (57%) used as the estimated primary series VE. Absolute VE from the bivalent booster was used as an estimate of primary series VE because current VE of monovalent primary series is unknown.
[5]Relative VE of bivalent booster dose used in booster dose assessment (5-7 month interval: 38%; 8-10 month interval: 42%; 11+ month interval 45%). Relative VE for ED/UC visit was used for 2-4 month interval (31%) because VE against hospitalization was not available

Monthly age-adjusted rates of COVID-19-associated hospitalization by vaccination status in patients ≥ 18 years, COVID-NET

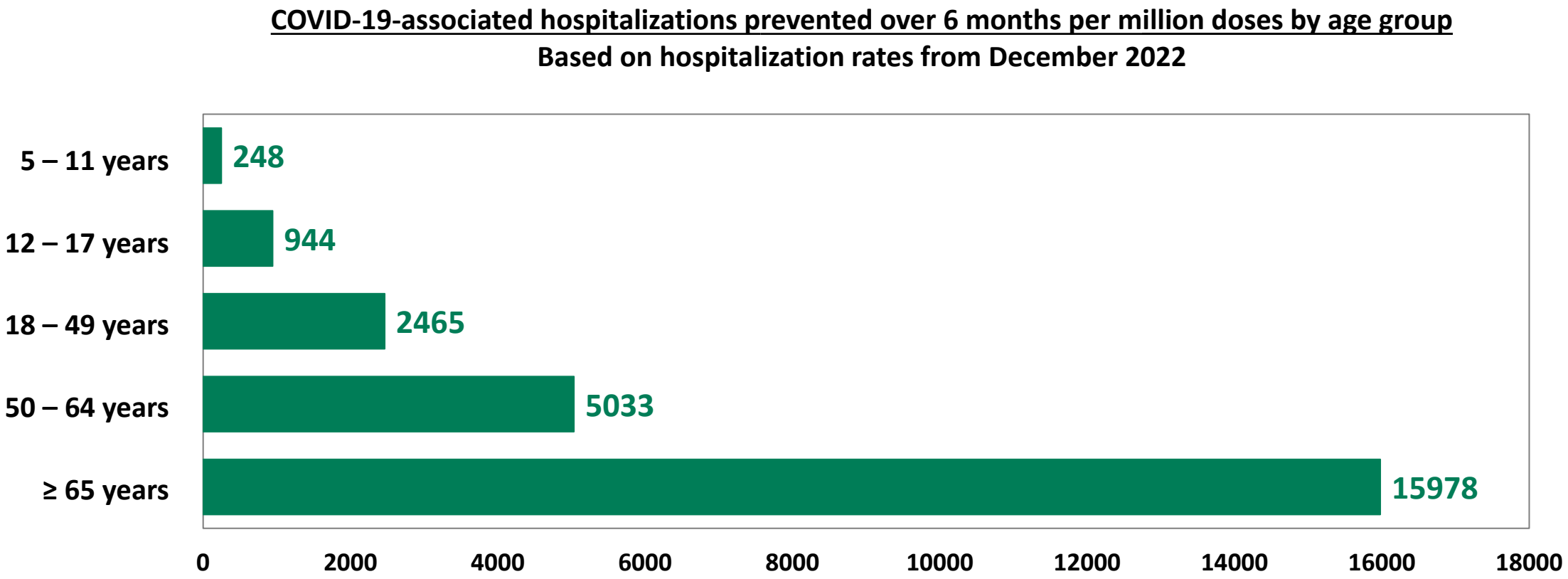


December 2022 hospitalization rates per 100,000 vaccinated persons with no bivalent booster by age group, COVID-NET

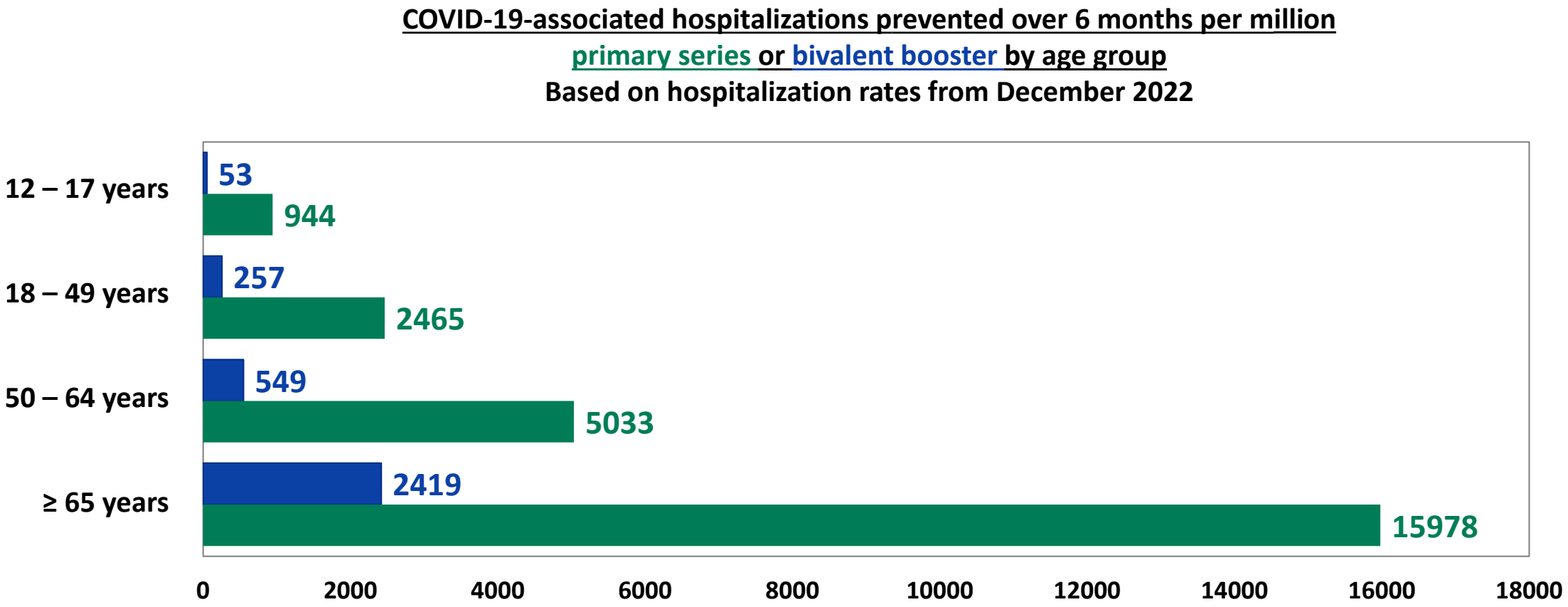
Age group	Rate per 100,000 persons
5-11 Years	2.13
12-17 Years	2.66
18-49 Years	12.89
50-64 Years	27.48
≥ 65 Years	121.10

https://covid.cdc.gov/covid-data-tracker/#covidnet-hospitalizations-vaccination

Estimated COVID-19-associated hospitalizations prevented over 6 months for every million mRNA COVID-19 primary series given



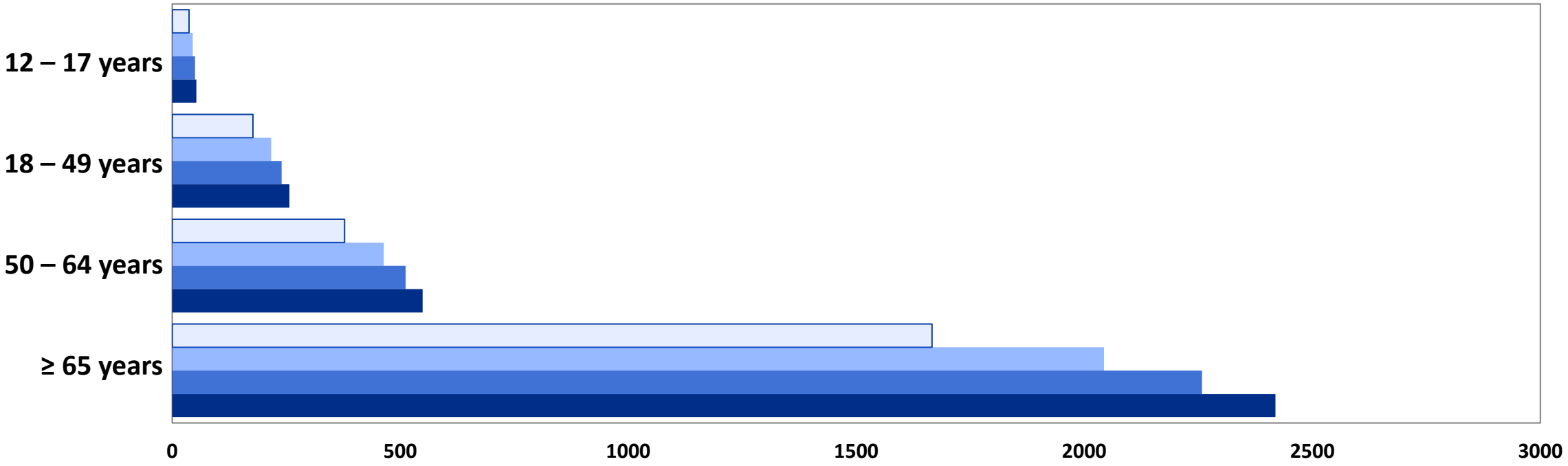
Estimated COVID-19 hospitalizations prevented over 6 months for every million mRNA COVID-19 primary series and bivalent booster doses[1]



1. Calculated assuming booster dose given ≥11 months from last monovalent vaccine dose

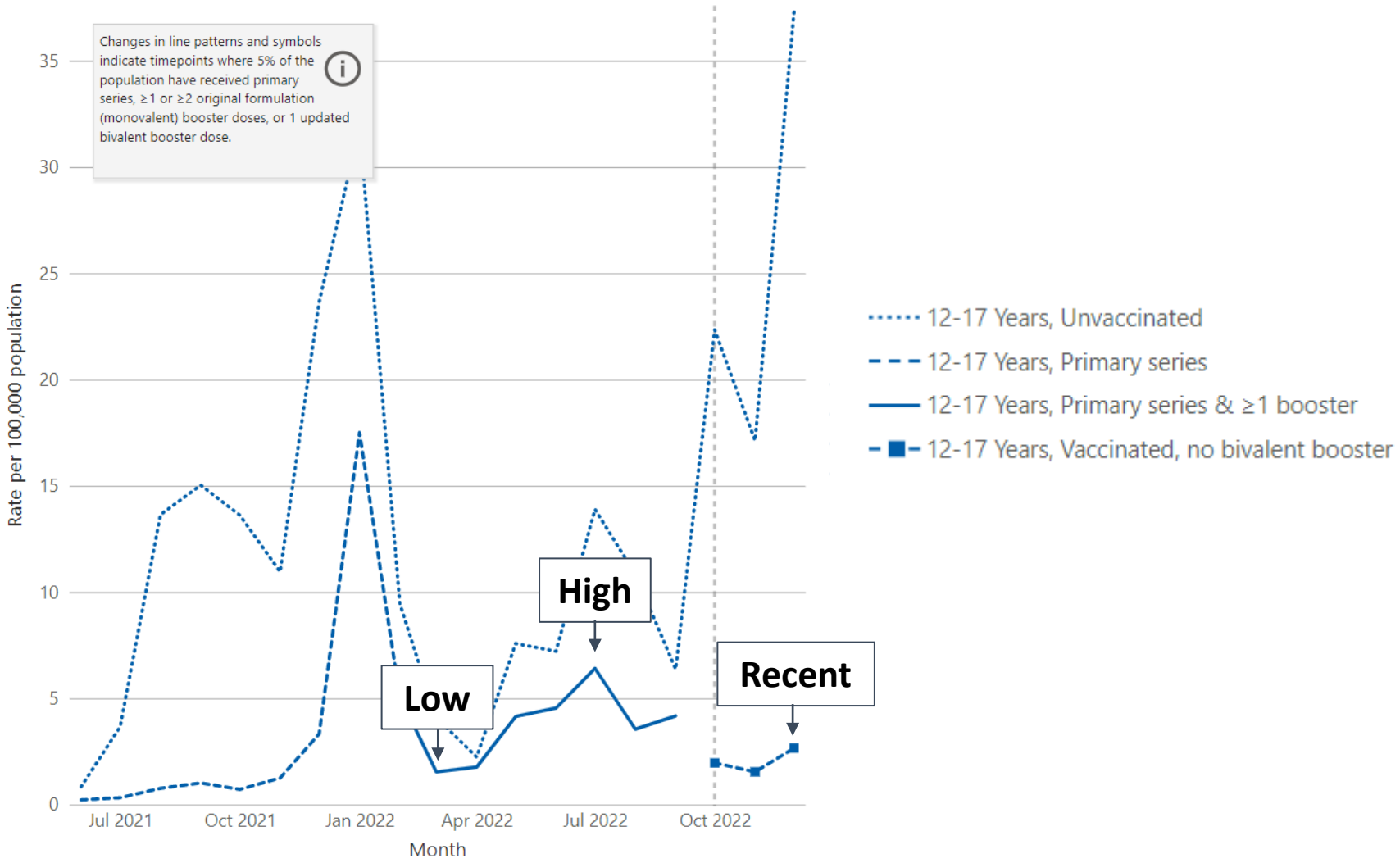
Estimated COVID-19 hospitalizations prevented over 6 months for every million bivalent mRNA COVID-19 booster doses, by age group and dose interval[1]

COVID-19-associated hospitalizations prevented over 6 months per million doses given in
2 – 4 month interval, 5 – 7 month interval, 8 – 10 month interval, ≥11 month interval
Based on hospitalization rates from December 2022



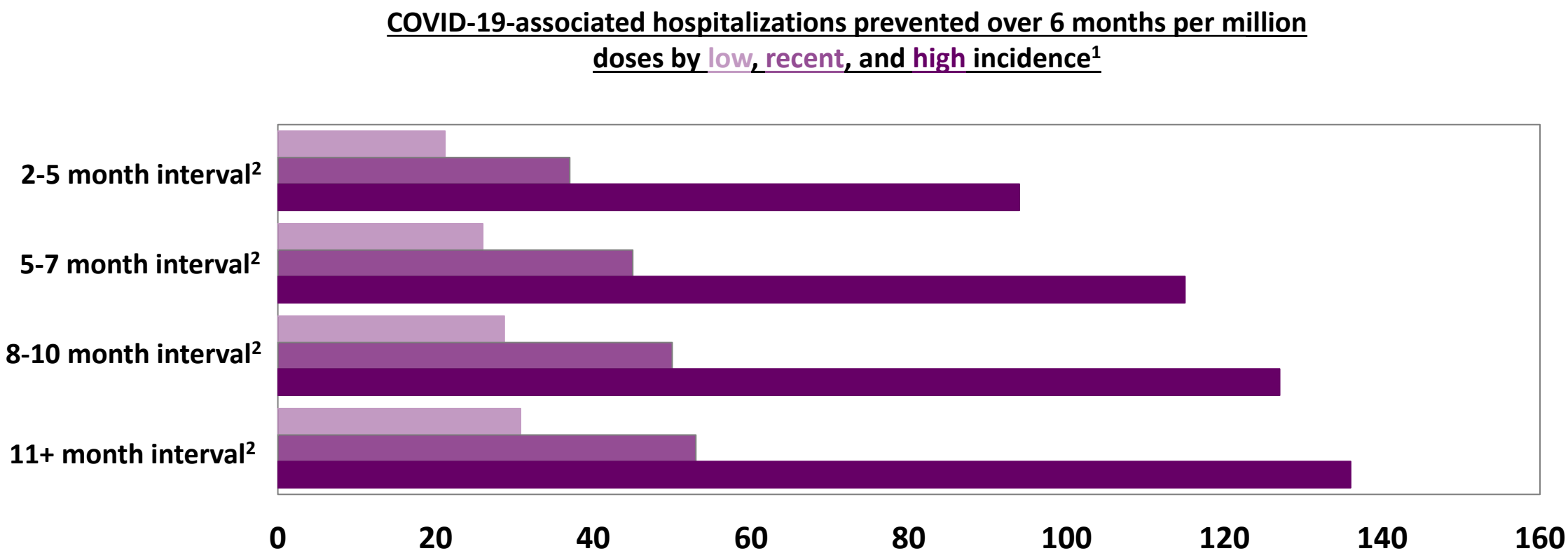
[1]Interval refers to the time between the most recent monovalent dose and a bivalent dose.

Monthly age-adjusted rates of COVID-19-associated hospitalization by vaccination status in patients 12 – 17 years, COVID-NET



https://covid.cdc.gov/covid-data-tracker/#covidnet-hospitalizations-vaccination

Estimated COVID-19 hospitalizations prevented over 6 months for every million bivalent mRNA COVID-19 booster doses, 12 – 17-year-olds



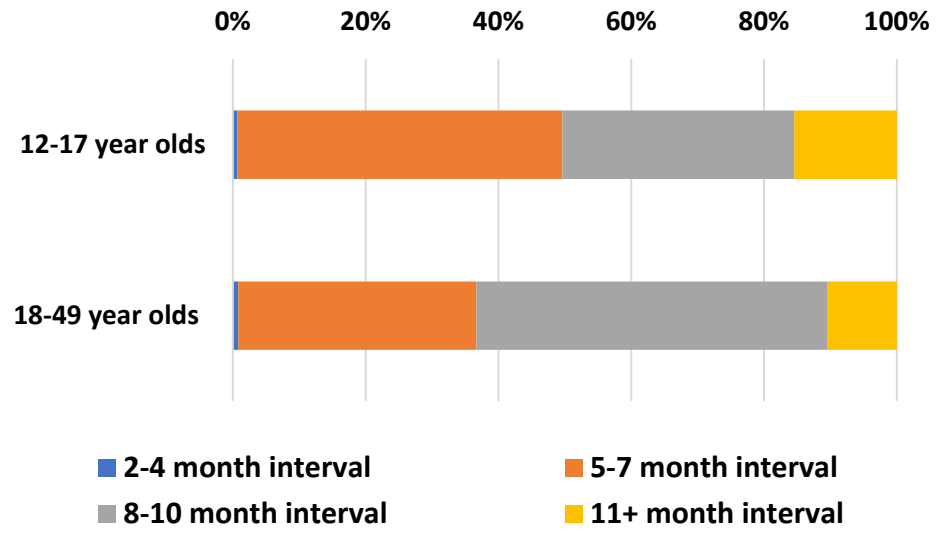
[1]Low incidence scenario uses hospitalization rate from March 2022, recent incidence scenario uses hospitalization rate from December 2022, and high incidence scenario uses hospitalization rate from July 2022

[2]Interval refers to the time between the most recent monovalent dose and a bivalent dose.

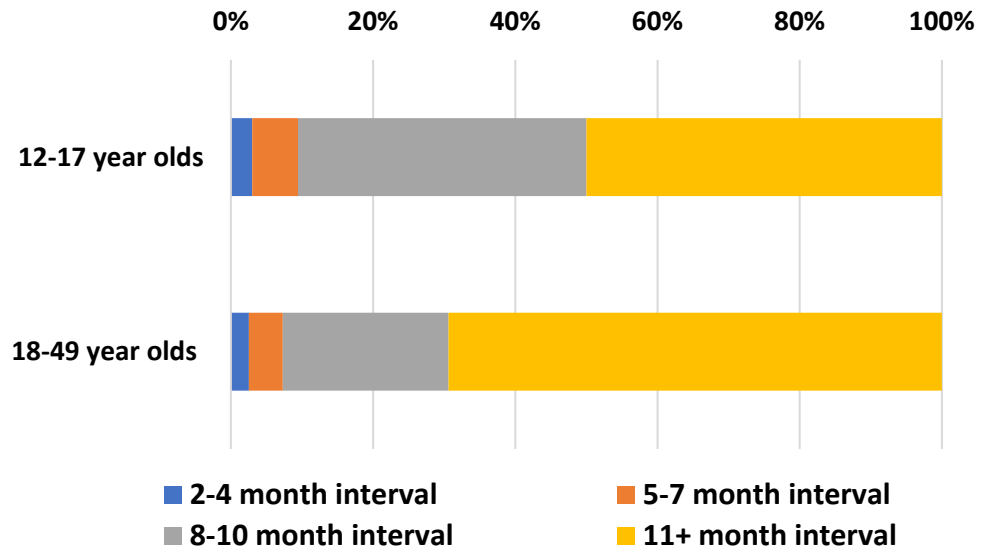
Dosing intervals for monovalent booster and bivalent booster, by age group

- Among adolescents who received a monovalent booster, nearly **half** received the monovalent booster at an interval <8 months after their primary series
- Over **90%** of adolescents received a bivalent booster ≥8 months after their previous dose

Interval between completion of the primary series and monovalent booster



Interval between completion of the most recent monovalent dose* and bivalent booster

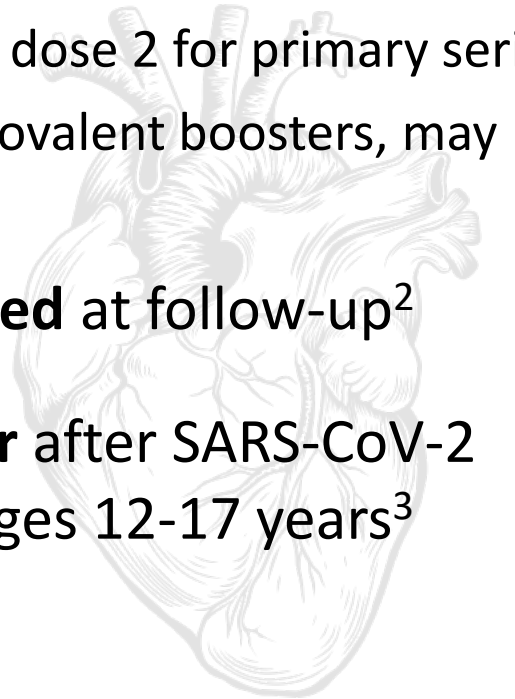


IZ Data Lake: Accessed 2/7/2023

* Primary series or monovalent booster

Myocarditis and COVID-19 vaccines

- Limited data to inform myocarditis risk after bivalent COVID-19 vaccine booster dose
  - Preliminary VSD myocarditis rates following **bivalent booster dose** in adolescent and young adult males **lower** than first monovalent boosters, but limited by small numbers of doses administered
- Myocarditis risk **lower** with **longer time between doses**
  - Rates of myocarditis **lower** with **extended interval** between dose 1 and dose 2 for primary series[1]
  - Longer interval between doses for bivalent boosters, compared to monovalent boosters, may also impact myocarditis rates
- Most individuals with myocarditis/pericarditis have **fully recovered** at follow-up[2]
- The risk of adverse cardiac outcomes were **1.8 – 5.6 times higher** after SARS-CoV-2 infection than after mRNA COVID-19 vaccination among males ages 12-17 years[3]



[1] https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-02-04/11-COVID-Moulia-508.pdf [2]https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-02-04/04-COVID-Kracalic-508.pdf [3]https://www.cdc.gov/mmwr/volumes/71/wr/mm7114e1.htm?s_cid=mm7114e1_w

VSD incidence rates of verified myocarditis or pericarditis in the 0-7 days after Pfizer-BioNTech vaccination in people 12 – 39 years[1]

	Dose 2 Primary Series Pfizer-BioNTech			1st Monovalent Booster Dose Pfizer-BioNTech			Bivalent Booster Dose Pfizer-BioNTech		
Age & Sex	Cases	Dose 2 Total	Incidence rate/ million doses (95% CI)	Cases	1st Booster Total	Incidence rate/ million doses (95% CI)	Cases	Bivalent Booster Total	Incidence rate/ million doses (95% CI)
12-17 Years Males Females	45 6	308,046 311,247	146.1 (106.6 – 195.5) 19.3 (7.1 – 42.0)	14 2	129,487 139,118	108.1 (59.1 – 181.4) 14.4 (1.7 – 51.9)	0 0	48,066 49,725	0.0 (0.0 – 62.3) 0.0 (0.0 – 60.2)
18-29 Years Males Females	27 2	331,889 400,321	81.4 (53.6 – 118.4) 5.0 (0.6 – 18.0)	7 1	166,973 240,226	41.9 (16.9 – 86.4) 4.2 (0.1 – 23.2)	1 0	50,687 80,211	19.7 (0.5 – 53.1) 0.0 (0.0 – 37.3)
30-39 Years Males Females	5 3	341,527 410,713	14.6 (4.8 – 34.2) 7.3 (1.5 – 21.3)	3 1	197,554 268,412	15.2 (3.1 – 44.4) 3.7 (0.1 – 20.8)	0 0	82,191 115,014	0.0 (0.0 – 36.4) 0.0 (0.0 – 26.0)

[1] Primary series and 1st monovalent booster data through August 20, 2022, bivalent booster data through January 29, 2023; Source: Kristin Goddard, Kayla E. Hanson, Ned Lewis, et al. Incidence of Myocarditis/Pericarditis Following mRNA COVID-19 Vaccination Among Children and Younger Adults in the United States. Ann Intern Med. [Epub 4 October 2022]. doi:10.7326/M22-2274

VSD incidence rates of verified myocarditis or pericarditis in the 0–7 days after Moderna vaccination in people ages 18–39 years[1]

	Dose 2 primary series Moderna			1st monovalent booster dose Moderna			Bivalent booster dose Moderna		
Age/sex	Cases	Dose 2 total	Incidence rate/ million doses (95% CI)	Cases	1st booster total	Incidence rate/ million doses (95% CI)	Cases	Bivalent booster total	Incidence rate/ million doses (95% CI)
18–29 years Males Females	19 0	195,809 243,560	97.0 (58.4 – 151.5) 0.0 (0.0 – 12.3)	7 1	109,337 156,707	64.0 (25.7 – 131.9) 6.4 (0.2 – 35.6)	0 0	18,499 29,561	0.0 (0.0–161.9) 0.0 (0.0–101.3)
30–39 years Males Females	8 1	216,583 259,780	36.9 (15.9 – 72.8) 3.9 (0.1 – 21.4)	1 2	149,468 191,765	6.7 (0.2 – 37.3) 10.4 (1.3 – 37.7)	0 0	35,318 47,620	0.0 (0.0–84.8) 0.0 (0.0–62.9)

[1] Primary series and 1st monovalent booster data through August 20, 2022, bivalent booster data through January 29, 2023; source: Goddard K, et al. Incidence of Myocarditis/Pericarditis Following mRNA COVID-19 Vaccination Among Children and Younger Adults in the United States. Ann Intern Med. 2022;175:1169-1771.

Estimated COVID-19 hospitalizations prevented vs. potential myocarditis cases for every million bivalent mRNA COVID-19 booster doses: 12 – 17-year-olds

Per million doses in 12 – 17-year-olds over 6 months[1]

31 – 136 hospitalizations prevented

9 – 40 ICU admissions prevented

0 – 1 death prevented

0 myocarditis[2] cases in 48,066 **males** with a bivalent booster

0 myocarditis[2] cases in 49,725 **females** with a bivalent booster

[1]Ranges presented for benefits are based on the high and low incidence scenarios presented on slides 7 and 8

[2]Based on preliminary Pfizer-BioNTech bivalent booster safety data from VSD (incident rate/million doses): **0 (95% CI: 0-62)** in males and **0 (95% CI: 0-60)** in females

Estimated COVID-19 hospitalizations prevented vs. potential myocarditis cases for every million bivalent mRNA COVID-19 booster doses: 12 – 17-year-olds

Accounting for potential incidental SARS-CoV-2 infections among hospitalized patients[1]

Per million doses in 12 – 17-year-olds over 6 months[2]

17 – 75 hospitalizations prevented

5 – 22 ICU admissions prevented

0 – 1 death prevented

0 myocarditis[3] cases in 48,066 **males** with a bivalent booster

0 myocarditis[3] cases in 49,725 **females** with a bivalent booster

[1] Results were adjusted to account for potential incidental findings of SARS-CoV-2 infection by multiplying the estimated hospitalizations, ICU admissions, and deaths prevented by the estimated percent of COVID-NET hospitalizations that are likely due to COVID-19 among 12 – 17-year-olds during on Omicron BA.5 predominant period (55%)

[2] Ranges presented for benefits are based on the high and low incidence scenarios presented on slides 7 and 8

[3] Based on preliminary Pfizer-BioNTech bivalent booster safety data from VSD (incident rate/million doses): **0 (95% CI: 0-62)** in males and **0 (95% CI: 0-60)** in females

Estimated COVID-19 hospitalizations prevented vs. potential myocarditis cases for every million bivalent mRNA COVID-19 booster doses: 18 – 49-year-olds

Per million doses in 18 – 49-year-olds over 6 months[1]

117 – 376 hospitalizations prevented

21 – 69 ICU admissions prevented

4 – 11 deaths prevented

1 myocarditis[2] case in 186,695 **males** with a bivalent booster

0 myocarditis[2] cases in 272,406 **females** with a bivalent booster

[1]Ranges presented for benefits are based on the high and low incidence scenarios presented on slide 7

[2]Based on preliminary bivalent booster safety data from VSD among persons ages 18-39 years. Among Pfizer-BioNTech recipients, rates per million doses were: **20 (95% CI: 1–53)** in males ages 18–29 years; **0 (95% CI: 0– 37)** in females ages 18–29 years; **0 (95% CI: 0–36)** in males ages 30–39 years and **0 (95% CI: 0–26)** in females ages 30–39 years. Among Moderna recipients, rates per million doses were: **0 (95% CI: 0–162)** in males ages 18–29 years; **0 (95% CI: 0– 101)** in females ages 18–29 years; **0 (95% CI: 0– 85)** in males ages 30–39 years and **0 (95% CI: 0–63)** in females ages 30–39 years.

Estimated COVID-19 hospitalizations prevented vs. potential myocarditis cases for every million bivalent mRNA COVID-19 booster doses: 18 – 49-year-olds

Accounting for potential incidental SARS-CoV-2 infections among hospitalized patients[1]

Per million doses in 18 – 49-year-olds over 6 months[2]

81 – 259 hospitalizations prevented

15 – 48 ICU admissions prevented

3 – 8 deaths prevented

1 myocarditis[3] case in 186,695 **males** with a bivalent booster

0 myocarditis[3] cases in 272,406 **females** with a bivalent booster

[1] Results were adjusted to account for potential incidental findings of SARS-CoV-2 infection by multiplying the estimated hospitalizations, ICU admissions, and deaths prevented by the estimated percent of COVID-NET hospitalizations that are likely due to COVID-19 among 18 – 49-year-olds during on Omicron BA.5 predominant period (69%)

[2] Ranges presented for benefits are based on the high and low incidence scenarios presented on slides 7 and 8

[3]Based on preliminary bivalent booster safety data from VSD among persons ages 18-39 years. Among Pfizer-BioNTech recipients, rates per million doses were: **20 (95% CI: 1–53)** in males ages 18–29 years; **0 (95% CI: 0– 37)** in females ages 18–29 years; **0 (95% CI: 0–36)** in males ages 30–39 years and **0 (95% CI: 0–26)** in females ages 30–39 years. Among Moderna recipients, rates per million doses were: **0 (95% CI: 0–162)** in males ages 18–29 years; **0 (95% CI: 0– 101)** in females ages 18–29 years; **0 (95% CI: 0– 85)** in males ages 30–39 years and **0 (95% CI: 0–63)** in females ages 30–39 years.

Limitations

- Benefits of vaccination may continue to accrue beyond time horizon used
- Stable hospitalization rates were assumed for the duration of the time horizon
- Underlying complexity of vaccine histories and previous infections could not be accounted for
- COVID-NET hospitalization rates include hospitalizations for which COVID-19 was not a primary reason for admission
- Current COVID-19 epidemiology, including hospitalization rates used in assessment, reflects impact of both prior vaccination and prior infection
  - Cannot account for possible future increases in COVID-19 hospitalization rates or new variant
- Myocarditis rates following bivalent booster dose are uncertain. Studies are underway to assess the long-term impact of vaccine-associated myocarditis

Summary of benefit-risk balance for bivalent mRNA COVID-19 vaccination

- **Benefits** continue to **outweigh risks** for primary series vaccination in all age groups
- Benefits of bivalent booster dose vary by **age, time since last dose**, and COVID-19 **incidence**
- Risk of myocarditis after COVID-19 vaccines likely **reduced** by **longer interval** since last dose
  - Additional data can better define risk after bivalent vaccines, but current data encouraging
- Changes in COVID-19 hospitalization rates would impact the benefit assessment
- Additional **benefits** of COVID-19 vaccines unable to be quantified in benefit-risk assessment
  - Likely prevention of post-COVID conditions, possible reduction in transmission, increased confidence in social interactions
- Benefit risk assessment will continue to be monitored as new data are available
- **Receipt of primary series** continues to be important in all ages
- **Boosters** remain an **important option** to improve protection against severe COVID-19, especially for **higher-risk populations**

Acknowledgements

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Thank you

For more information, contact CDC
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TTY: 1-888-232-6348 www.cdc.gov