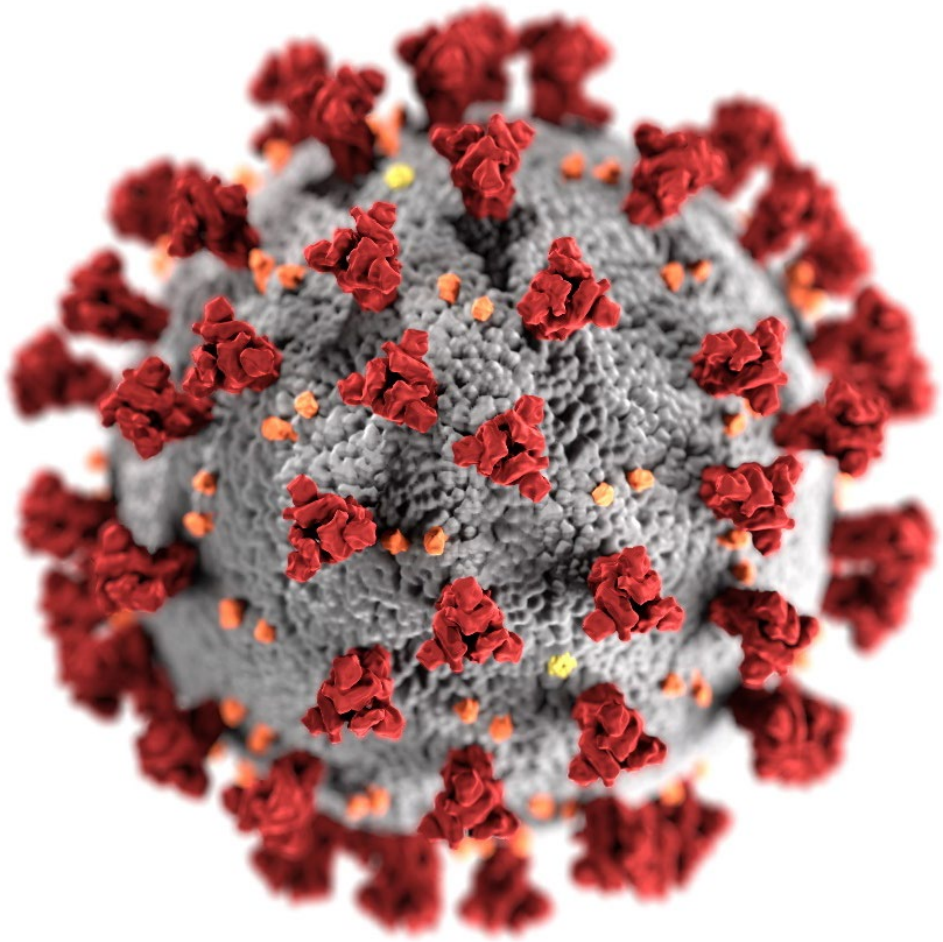
Updates to the Evidence to Recommendation Framework:

2nd COVID-19 booster dose in adults ages 50 years and older and immunocompromised individuals

Sara Oliver, MD, MSPH

ACIP Meeting

April 20, 2022

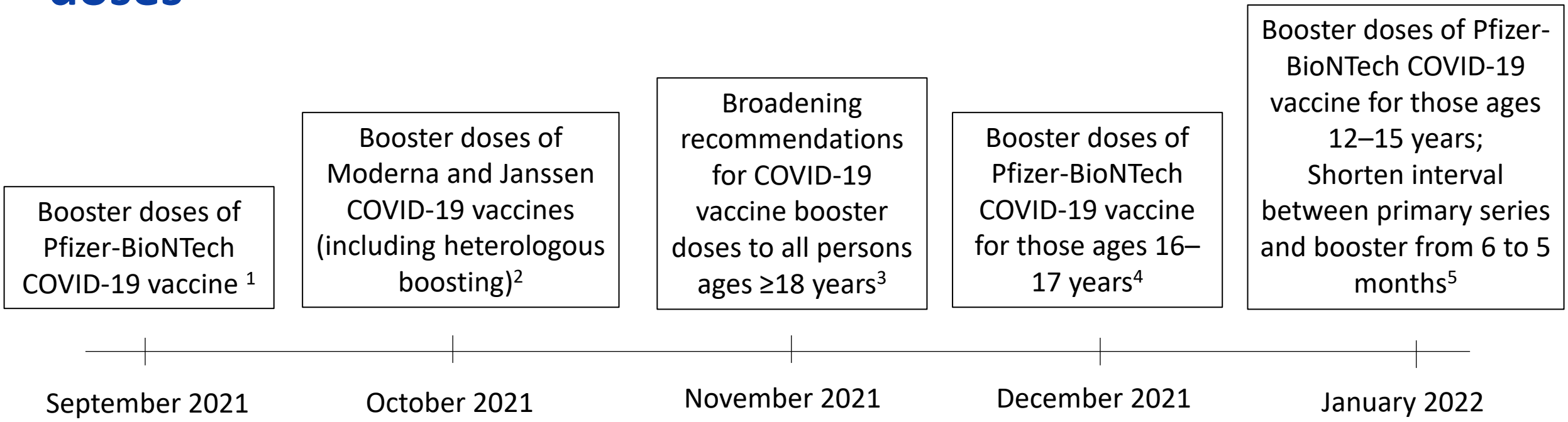


cdc.gov/coronavirus

Policy question

- Do the **balance** of **benefits** and **risks** warrant an update to COVID-19 vaccine policy, allowing adults ages ≥50 years and persons with moderate to severe immunocompromise ages ≥12 years to receive a second booster of an mRNA COVID-19 vaccine?

Timeline of recommendations for COVID-19 vaccine booster doses



1. ACIP Meeting, September 23rd https://www.cdc.gov/vaccines/acip/meetings/slides-2021-09-22-23.html
2. ACIP Meeting, October 21st https://www.cdc.gov/vaccines/acip/meetings/slides-2021-10-20-21.html
3. ACIP Meeting, November 19th https://www.cdc.gov/vaccines/acip/meetings/slides-2021-11-19.html and CDC Director's Memo: https://www.cdc.gov/media/releases/2021/s1129-booster-recommendations.html
4. CDC's Director's Memo: https://www.cdc.gov/media/releases/2021/s1208-16-17-booster.html
5. CDC's Director's Memo: https://www.cdc.gov/media/releases/2022/s0104-Pfizer-Booster.html

Recent updates to COVID-19 vaccine booster policy

- Following FDA's regulatory action on March 29, 2022, CDC updated its COVID-19 vaccination guidance to give some individuals the option to receive a second booster dose using an mRNA COVID-19 vaccine. These individuals include:
  - People ages **50 years and older** who received an initial COVID-19 booster dose (regardless of which vaccine was used) at least 4 months ago
  - People ages **12 years and older** who are **moderately or severely immunocompromised** who received an initial COVID-19 booster dose (regardless of which vaccine was used) at least 4 months ago
  - People ages **18 years and older** who received both a **primary dose** and a **booster dose** of **J&J/Janssen COVID-19 vaccine** at least 4 months ago

Coronavirus (COVID-19) Update: FDA Authorizes Second Booster Dose of Two COVID-19 Vaccines for Older and Immunocompromised Individuals | FDA
CDC Recommends Additional Boosters for Certain Individuals | CDC Online Newsroom | CDC

Summary of recommendations by primary series product and age

People who are not moderate to severely immunocompromised

Everyone in the age group **SHOULD** receive the dose

Some people in the age group **MAY** receive the dose

Pfizer-BioNTech
(ages 5–11 years)

Dose 1 (primary) → 3 weeks → Dose 2 (primary)

Pfizer-BioNTech
(ages 12 years and older)

Dose 1 (primary) → 3-8 weeks → Dose 2 (primary) → At least 5 months → Dose 3 (booster) → At least 4 months → Dose 4 (2nd booster)

Moderna
(ages 18 years and older)

Dose 1 (primary) → 4-8 weeks → Dose 2 (primary) → At least 5 months → Dose 3 (booster) → At least 4 months → Dose 4 (2nd booster)

Janssen (J&J)
(ages 18 years and older)

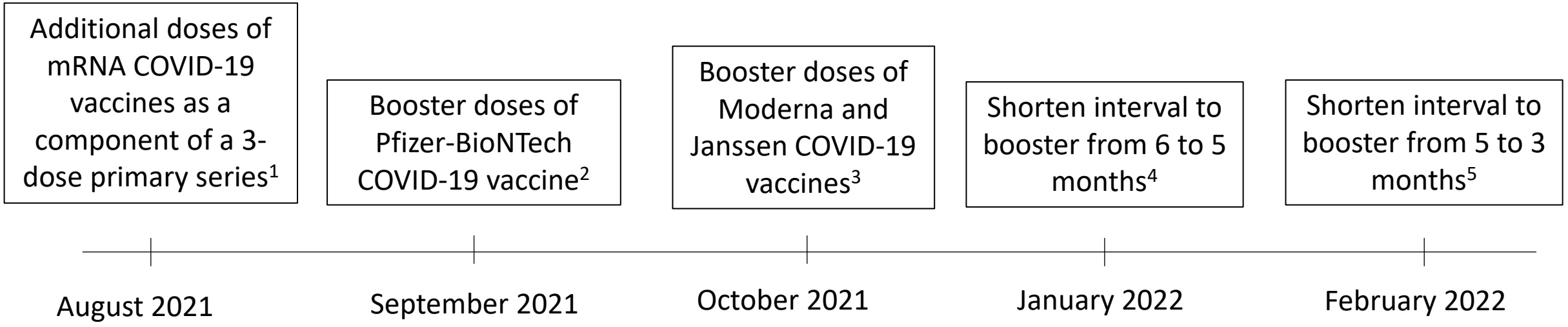
Dose 1 (primary) → At least 2 months → Dose 2 (booster) → At least 4 months → Dose 3 (2nd booster)

People ages 18 years and older who received 2 Janssen doses

People ages 50 years and older

Timeline of recommendations for COVID-19 vaccine doses

Moderate to severely immunocompromised individuals



1. ACIP Meeting, August 13th https://www.cdc.gov/vaccines/acip/meetings/slides-2021-08-13.html
2. ACIP Meeting September 23rd https://www.cdc.gov/vaccines/acip/meetings/slides-2021-09-22-23.html
3. ACIP Meeting, October 21st https://www.cdc.gov/vaccines/acip/meetings/slides-2021-10-20-21.html
4. CDC's Director's Memo: https://www.cdc.gov/media/releases/2022/s0104-Pfizer-Booster.html
5. Interim Clinical Considerations: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html#recommendations

Summary of recommendations by primary series product and age

Persons who are moderate to severely immunocompromised

Everyone in the age group **SHOULD** receive the dose

Some people in the age group **MAY** receive the dose

Pfizer-BioNTech
(ages 5–11 years)

Dose 1 (primary) → 3 weeks → Dose 2 (primary) → At least 4 weeks → Dose 3 (primary)

Pfizer-BioNTech
(ages 12 years and older)

Dose 1 (primary) → 3 weeks → Dose 2 (primary) → At least 4 weeks → Dose 3 (primary) → At least 3 months → Dose 4 (booster) → At least 4 months → Dose 5 (2nd booster)

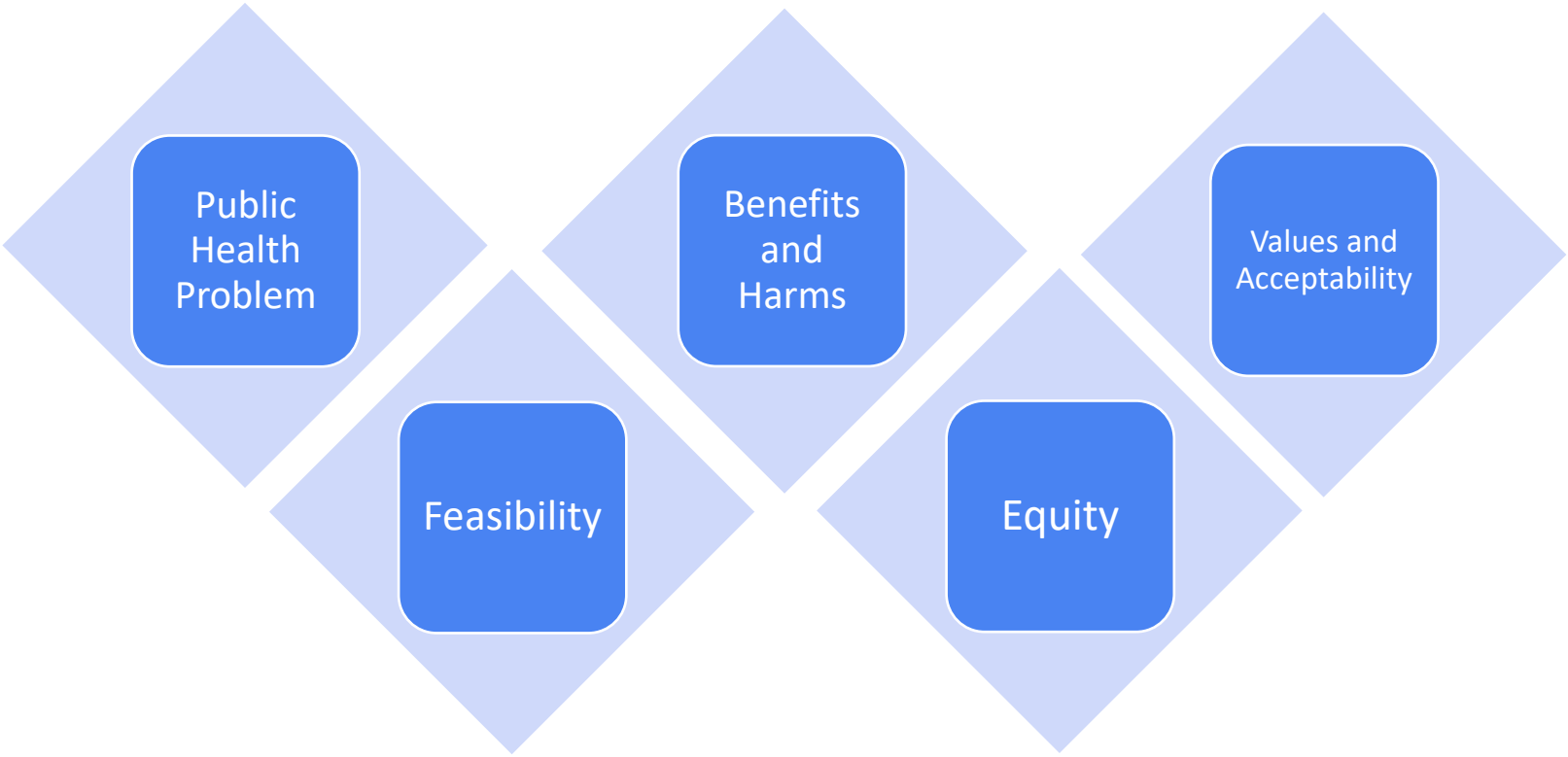
Moderna
(ages 18 years and older)

Dose 1 (primary) → 4 weeks → Dose 2 (primary) → At least 4 weeks → Dose 3 (primary) → At least 3 months → Dose 4 (booster) → At least 4 months → Dose 5 (2nd booster)

Janssen (J&J)
(ages 18 years and older)

Dose 1 (primary) → 4 weeks → Dose 2 (addl. dose) → At least 2 months → Dose 3 (booster) → At least 4 months → Dose 4 (2nd booster)

Evidence to Recommendations (EtR) Framework

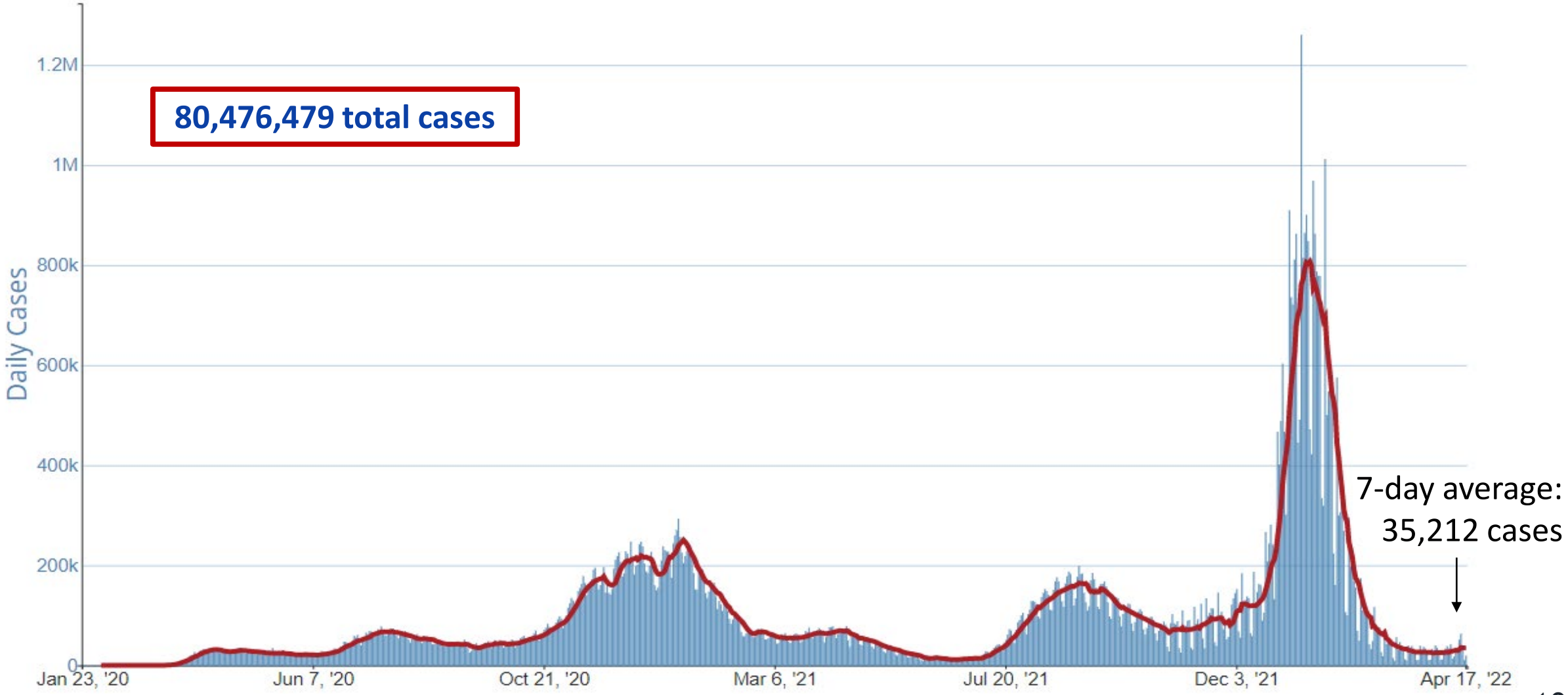


Evidence to Recommendations Framework

Booster doses of COVID-19 vaccines

Daily trends in number of COVID-19 cases, United States

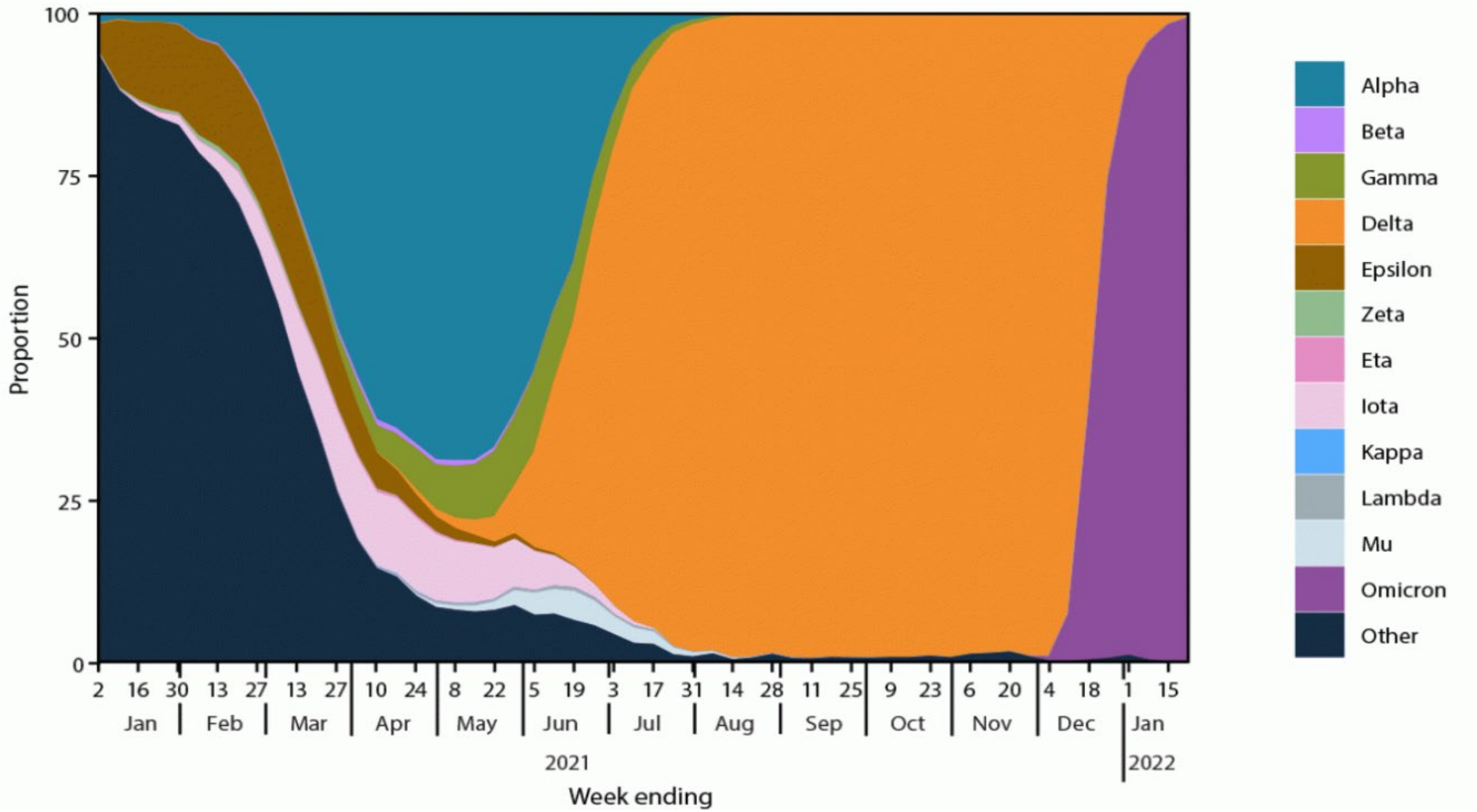
January 23, 2020 – April 17, 2022



CDC COVID Data Tracker. https://covid.cdc.gov/covid-data-tracker/#trends_dailycases Accessed April 19, 2022

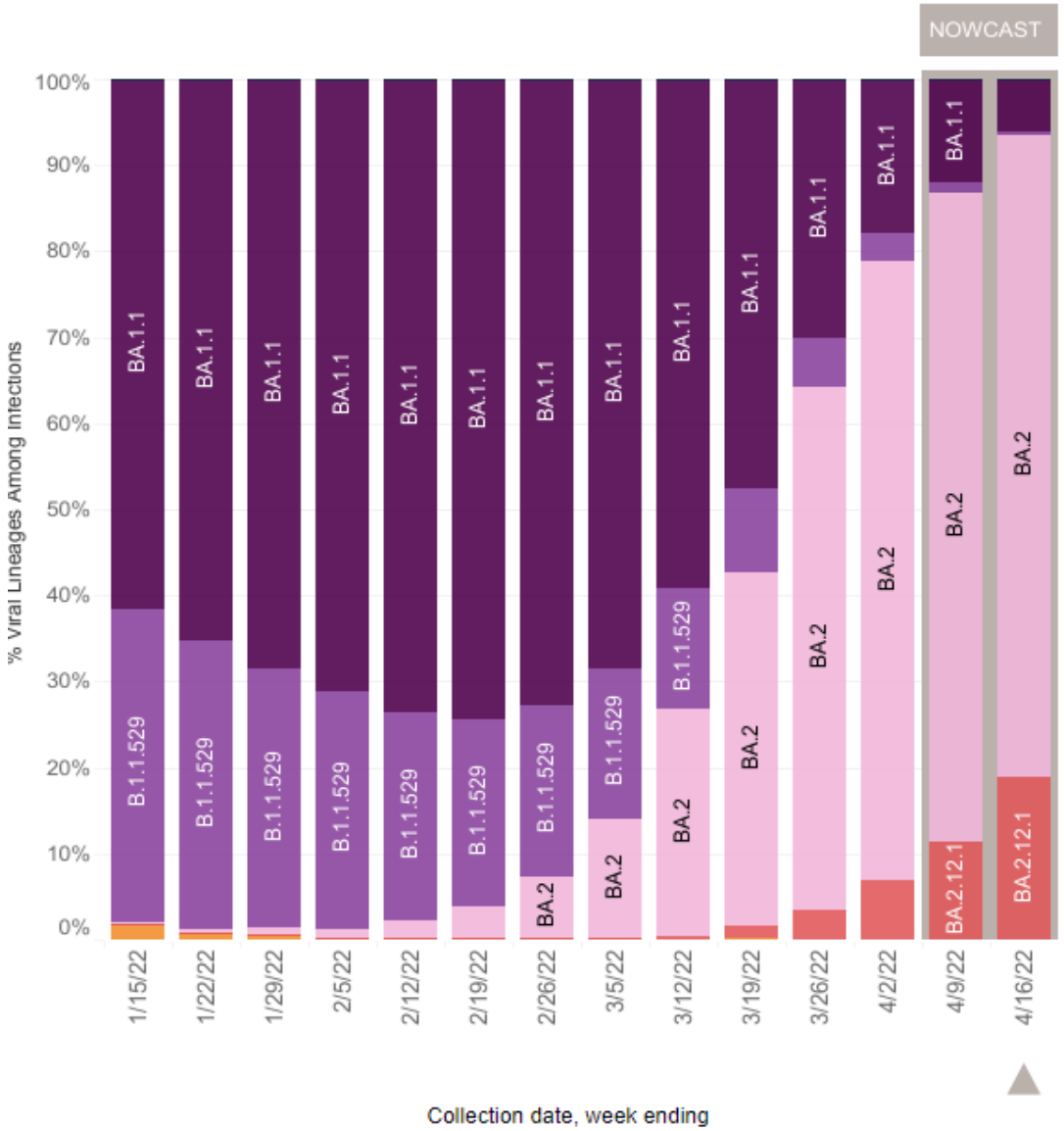
Changing landscape of circulating variants

FIGURE 1. National weekly proportion estimates* of SARS-CoV-2 variants† — United States, January 2, 2021–January 22, 2022



Lambrou et al. Genomic Surveillance for SARS-CoV-2 Variants: Predominance of the Delta (B.1.617.2) and Omicron (B.1.1.529) Variants — United States, June 2021–January 2022 https://www.cdc.gov/mmwr/volumes/71/wr/mm7106a4.htm

Recent trends in weighted variant proportion estimates & Nowcast



USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BA.2	VOC	74.4%	68.3-79.7%
	BA.2.12.1	VOC	19.0%	13.4-26.0%
	BA.1.1	VOC	6.1%	5.1-7.3%
	B.1.1.529	VOC	0.5%	0.3-0.6%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		0.0%	0.0-0.0%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.
** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates
# AY.1-AY.133 and their sublineages are aggregated with B.1.617.2. BA.1, BA.3, BA.4, BA.5 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. For regional data, BA.1.1 and its sublineages are also aggregated with B.1.1.529, as they currently cannot be reliably called in each region. Except BA.2.12.1, BA.2 sublineages are aggreagated with BA.2.

https://covid.cdc.gov/covid-data-tracker/#variant-proportions Accessed April 19, 2022

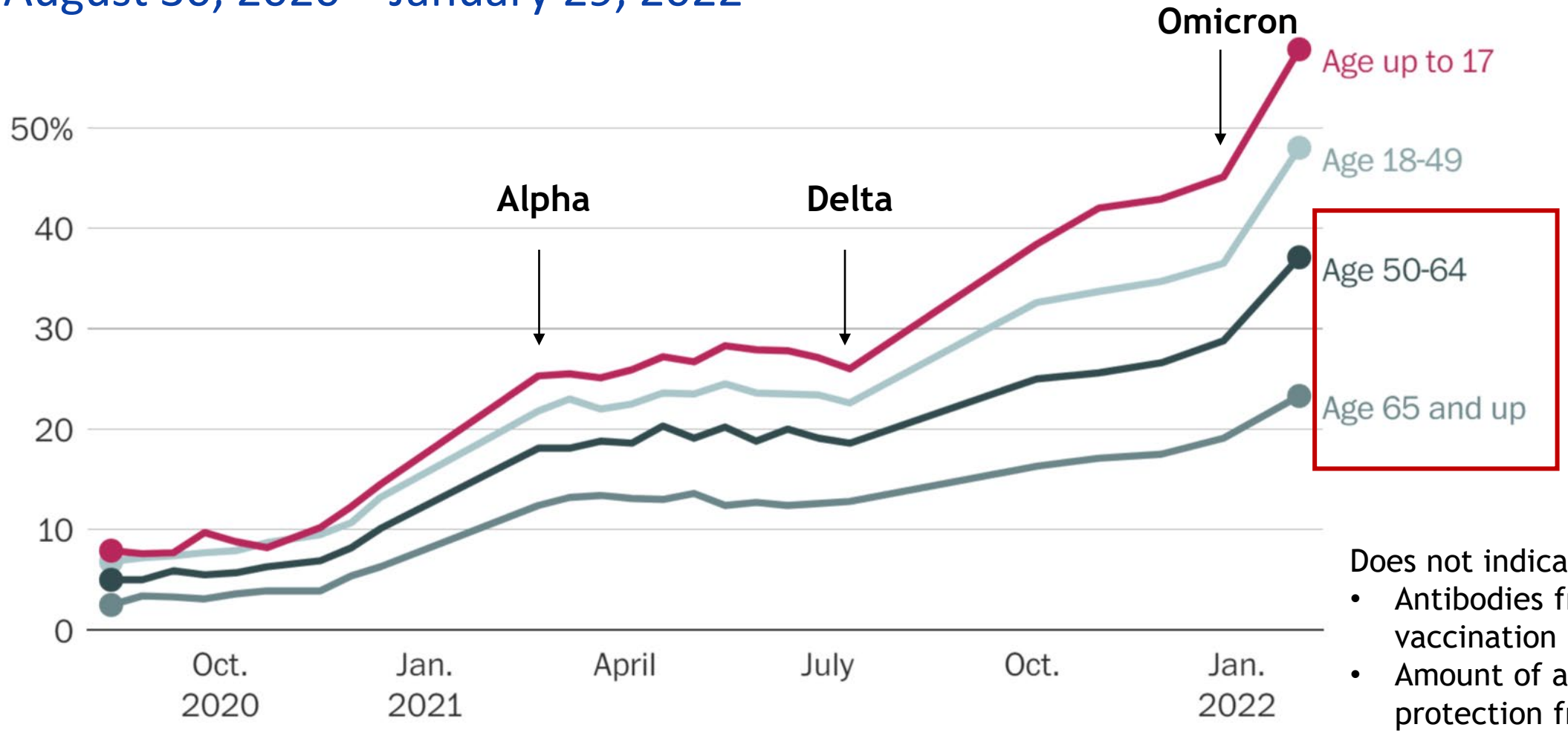
Daily trends in number of COVID-19 cases, United States

January 23, 2020 – April 17, 2022

CDC COVID Data Tracker. https://covid.cdc.gov/covid-data-tracker/#trends_dailycases Accessed April 19, 2022

Percentage of people with antibodies (anti-nucleocapsid) indicating resolving or past infection with SARS-CoV-2, United States

August 30, 2020 – January 29, 2022



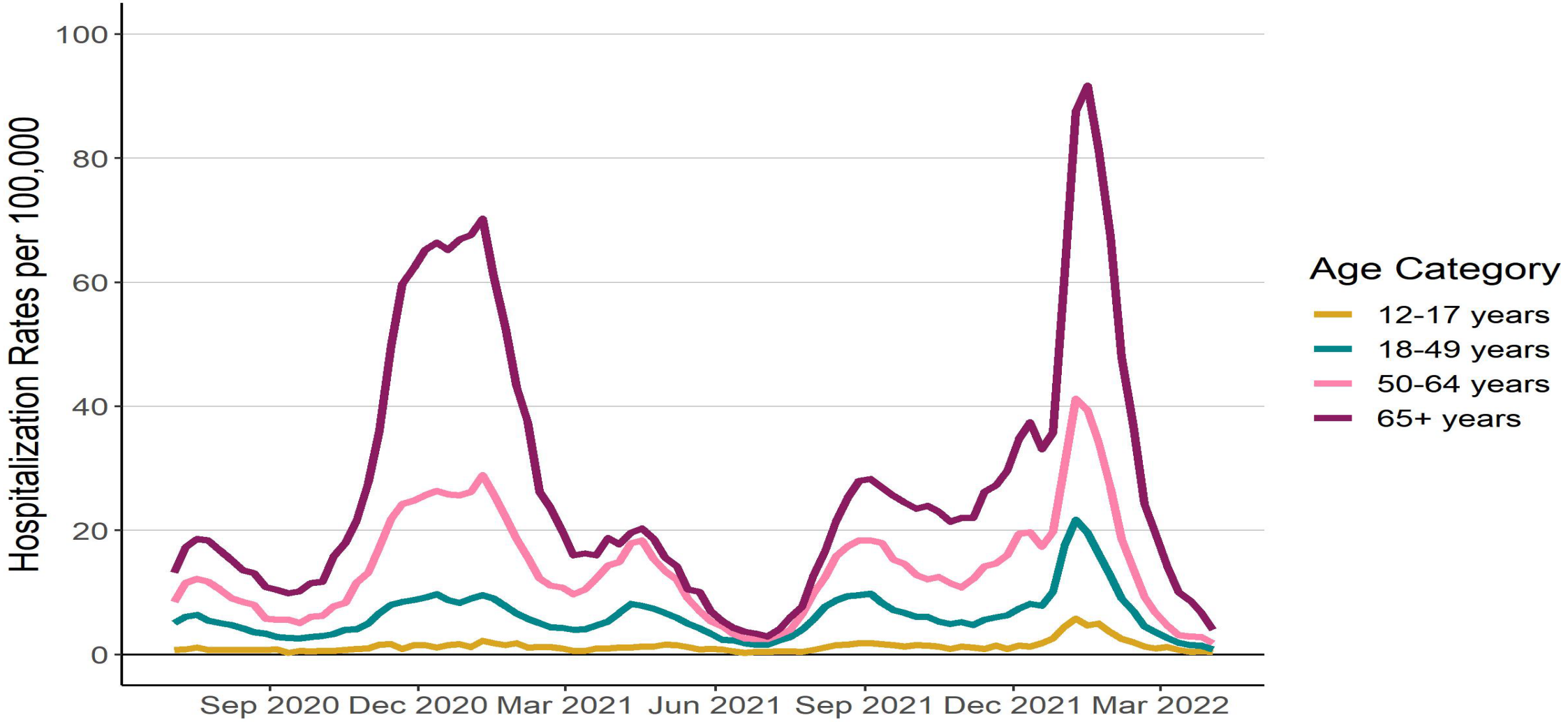
Does not indicate:

- Antibodies from vaccination (anti-spike)
- Amount of antibodies or protection from reinfection

Data Source: CDC COVID Data Tracker: https://covid.cdc.gov/covid-data-tracker/#national-lab

Data Visualization: Dan Keating, Washington Post: https://www.washingtonpost.com/health/2022/02/28/covid-cases-nationwide/

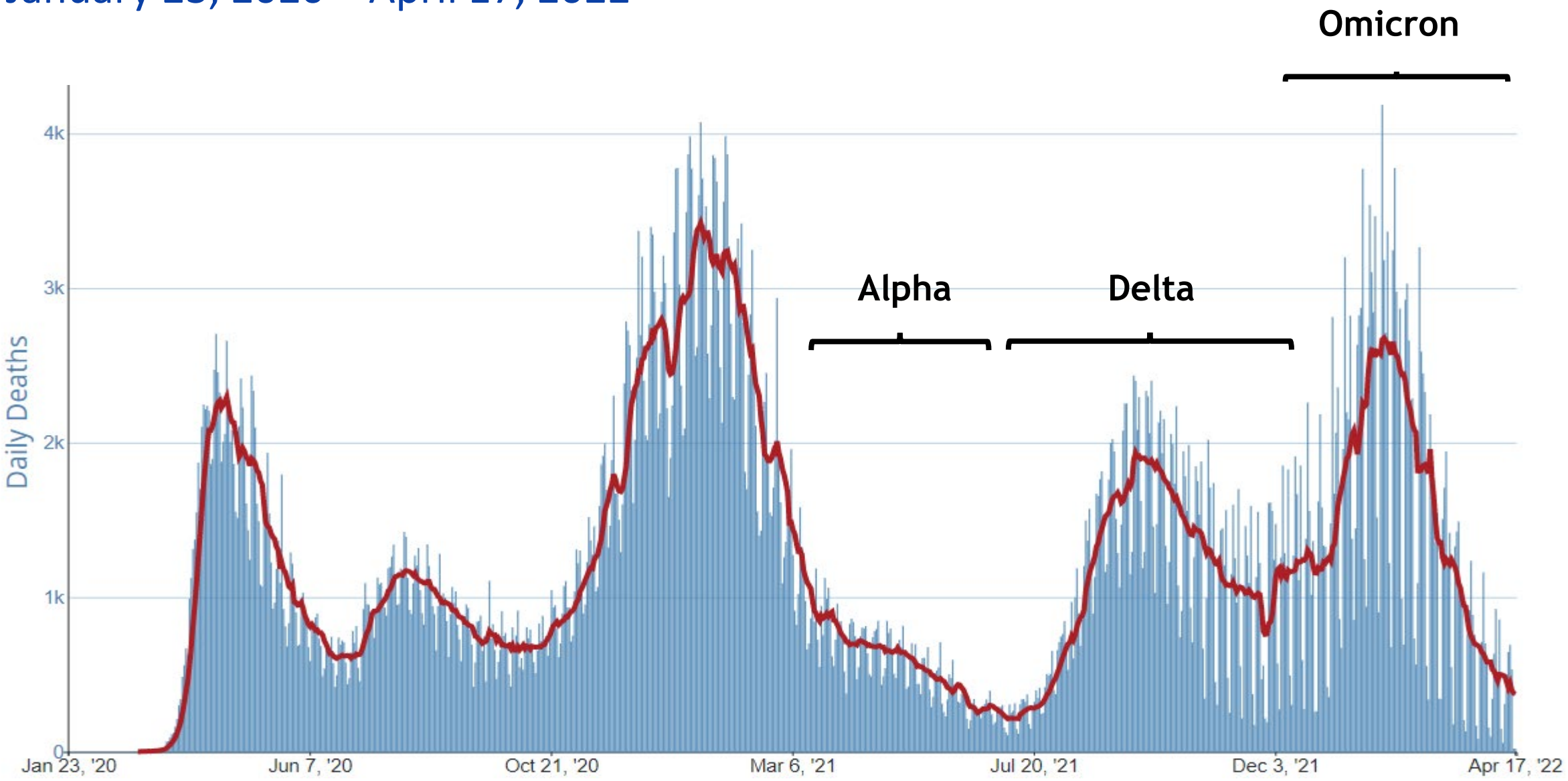
Weekly trends in COVID-19-associated hospitalization rates by age group, United States, July 4, 2020 – April 9, 2022



Source: CDC's COVID-NET, https://covid.cdc.gov/covid-data-tracker/#covidnet-hospitalization-network, Accessed April 19, 2022

Daily trends in number of COVID-19 deaths, United States

January 23, 2020 – April 17, 2022



CDC COVID Data Tracker. https://covid.cdc.gov/covid-data-tracker/#trends_dailydeaths Accessed April 13, 2022

COVID-19 vaccinations in the United States,

As of April 18, 2022

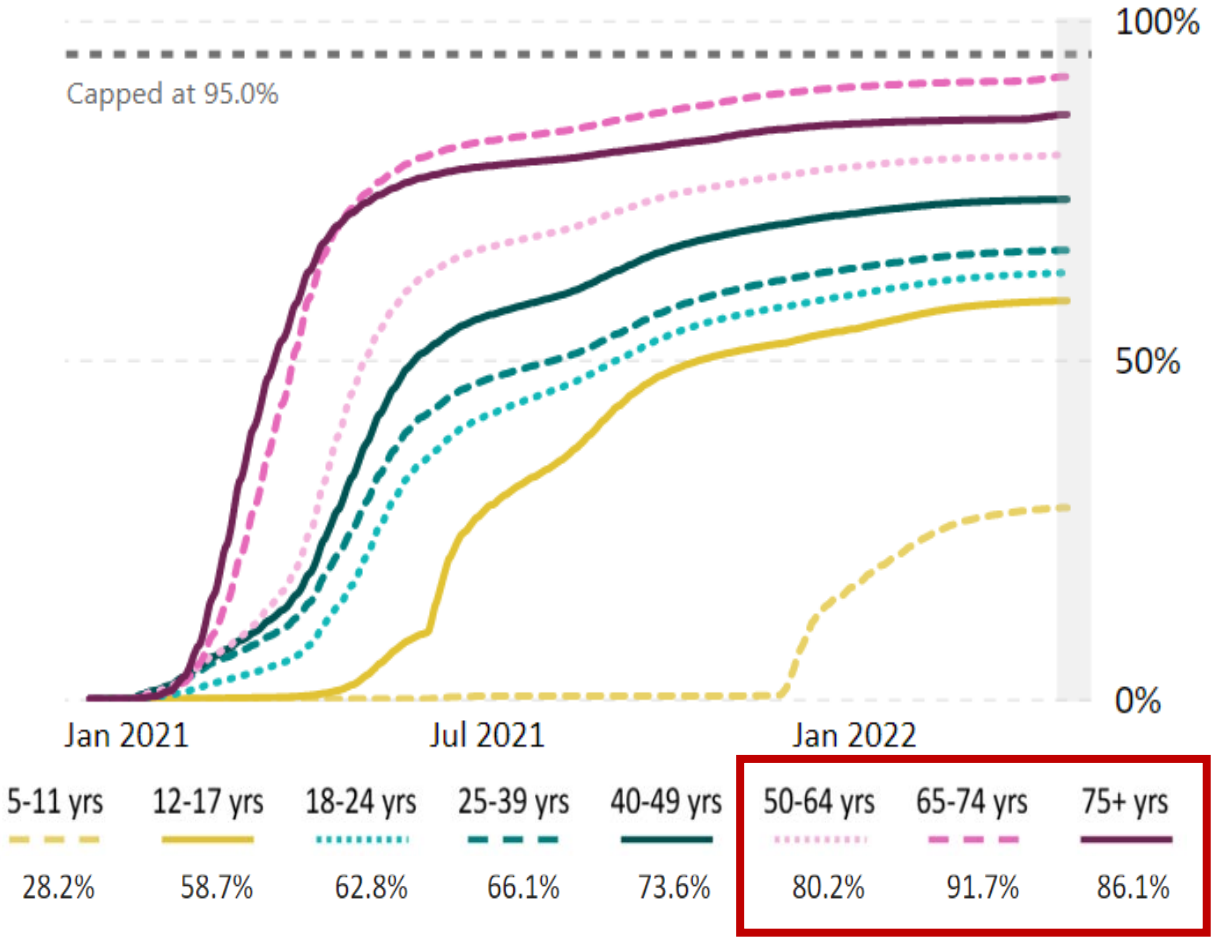
218.9M **People fully vaccinated**	70.1% Population ≥5 Years of Age
99.5M **People received a booster dose***	47.2% Population ≥12 Years of Age

***This includes people who received booster doses and people who received additional doses.**

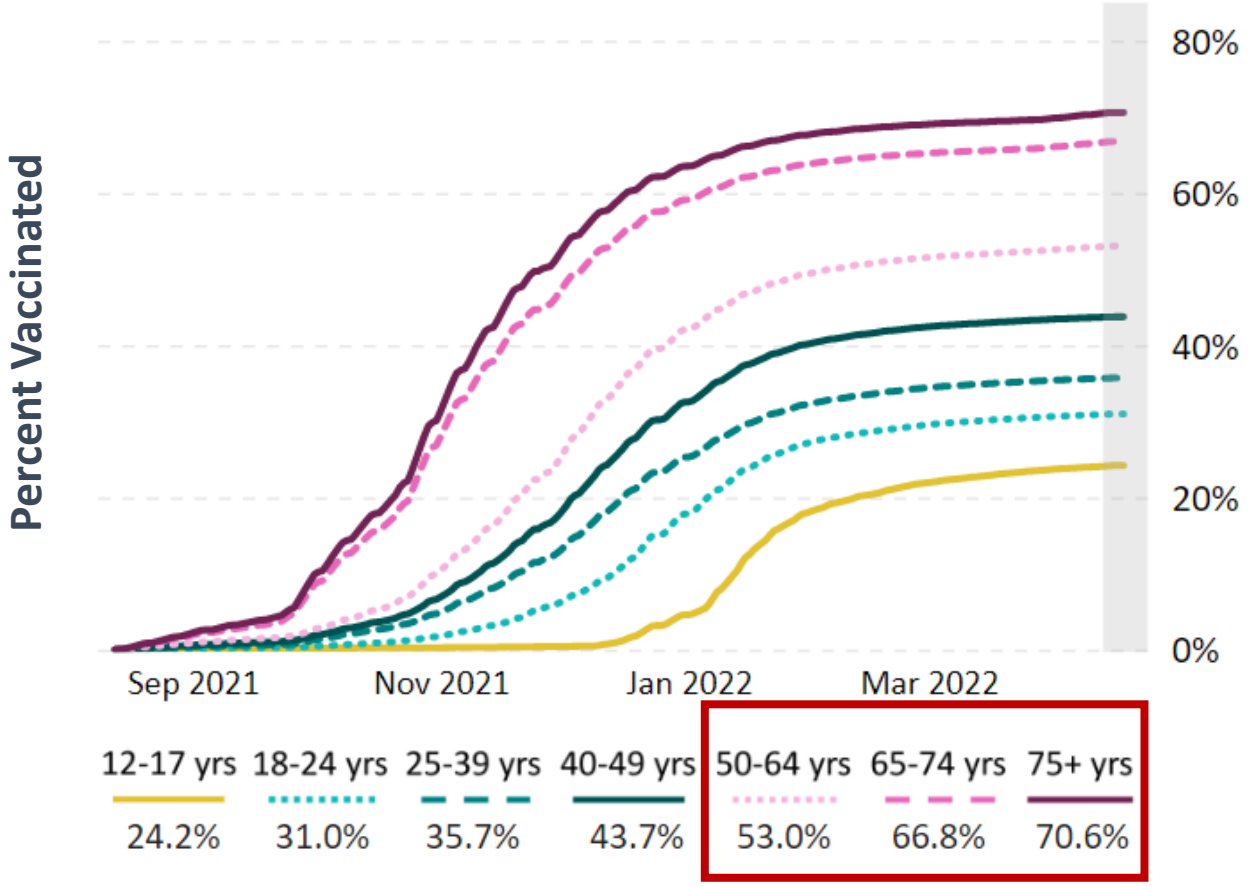
https://covid.cdc.gov/covid-data-tracker/#vaccinations_vacc-total-admin-rate-total Accessed April 19, 2022

Percentage of people vaccinated with at least a primary series or booster dose by age group and date administered, United States

Primary Series



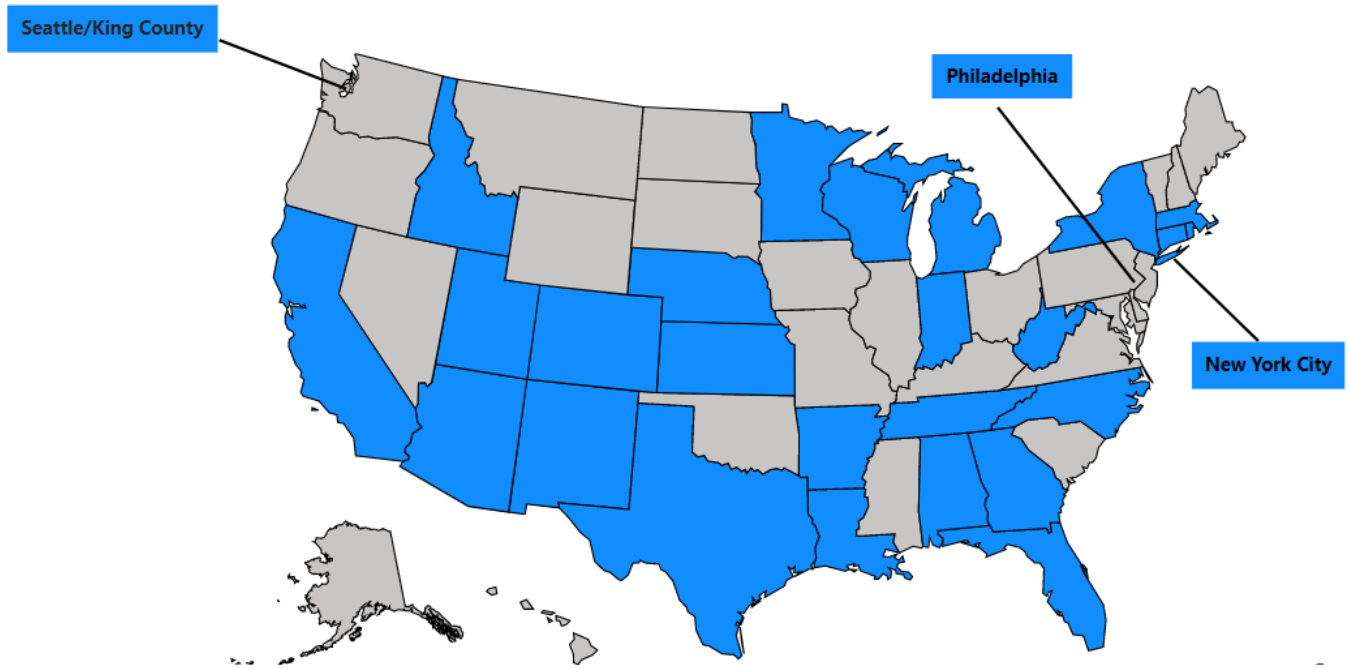
Booster Dose



CDC COVID Data Tracker. https://covid.cdc.gov/covid-data-tracker/#vaccination-demographics-trends Accessed April 19, 2022

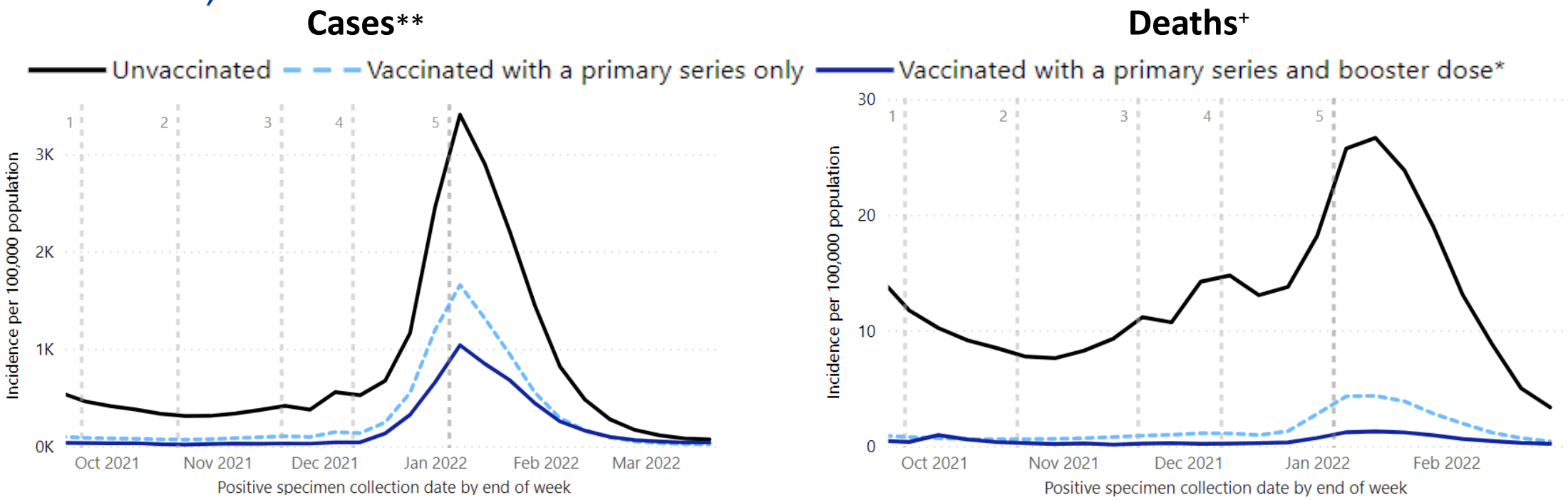
Monitoring rates of cases and deaths by vaccination status

- 29 jurisdictions that routinely link surveillance and immunization data*
  - 67% of total U.S. population
- Report COVID-19 cases and COVID-19 associated deaths by vaccination status
- Weekly rates and incidence rate ratios
  - Unvaccinated vs. fully vaccinated (overall, with or without a booster dose)



*AL, AR, AZ, CA, CO, CT, DC, FL, GA, ID, IN, KS, LA, MA, MI, MN, NC, NE, NM, NY, NY City, Philadelphia, RI, Seattle/King County, TN, TX, UT, WI, WV

Age-adjusted rates of COVID-19 cases & deaths by vaccination status and receipt of booster dose,*



Unvaccinated people aged 12 years and older had:

3.1X *Risk of Testing Positive for COVID-19*	**AND**	**20X** *Risk of Dying from COVID-19*	**in February, and**
2.0X *Risk of Testing Positive for COVID-19*	**in March,**	**compared to people vaccinated with a primary series and a booster dose.**	

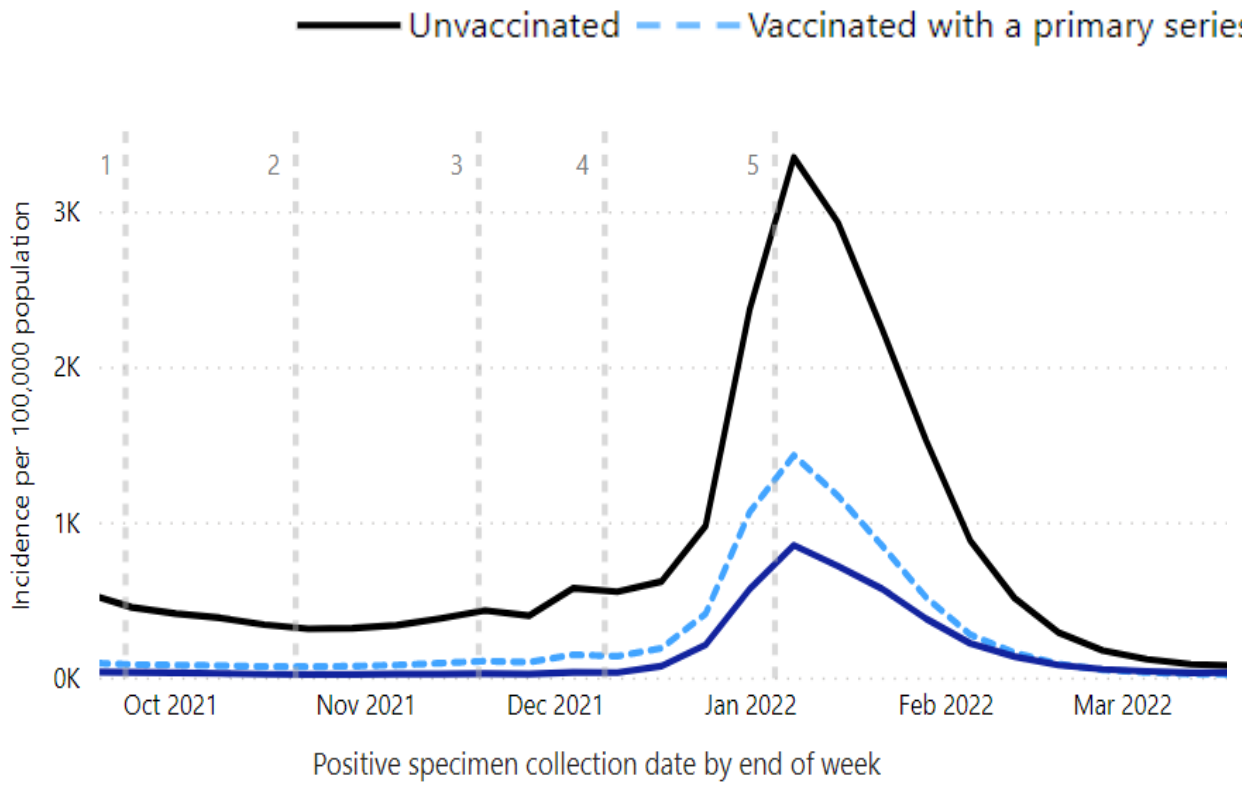
*This includes people who received booster doses and people who received additional doses.

** Data from September 19, 2021 – March 19, 2022 (24 U.S. jurisdictions)

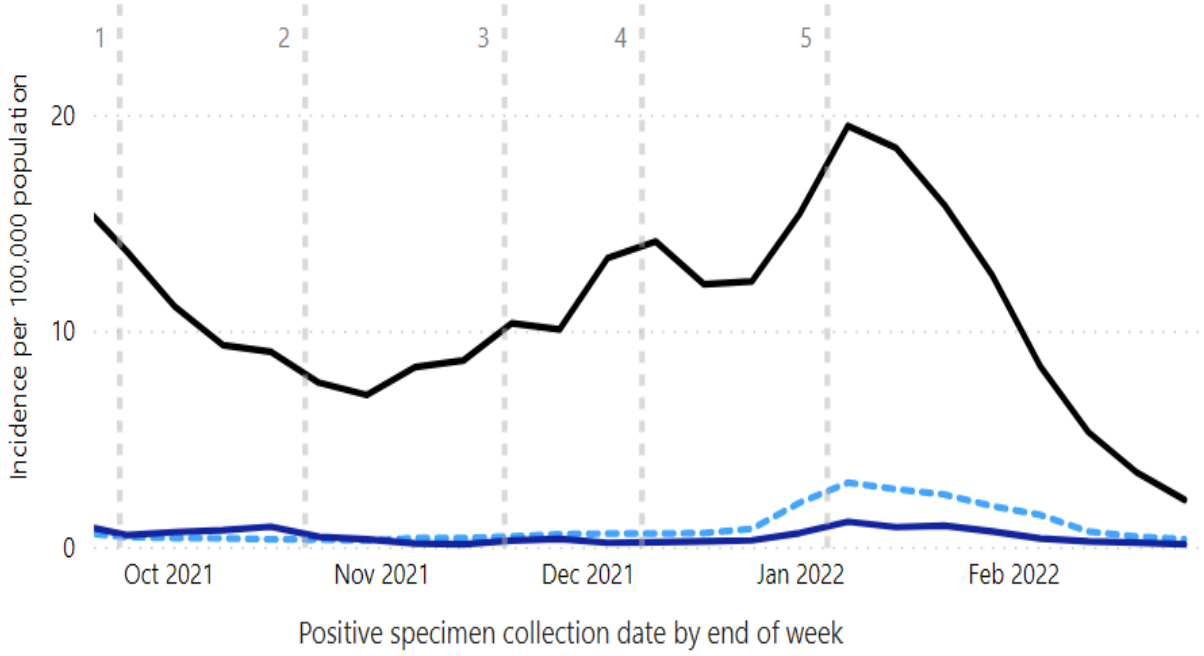
+ Data from September 19, 2021 – February 26, 2022 (23 U.S. jurisdictions)

CDC COVID Data Tracker. https://covid.cdc.gov/covid-data-tracker/#rates-by-vaccine-status Accessed April 19, 2022

Age-adjusted rates of COVID-19 cases & deaths by vaccination status and receipt of booster dose among adults 50-64 years,*



Cases**



Deaths+

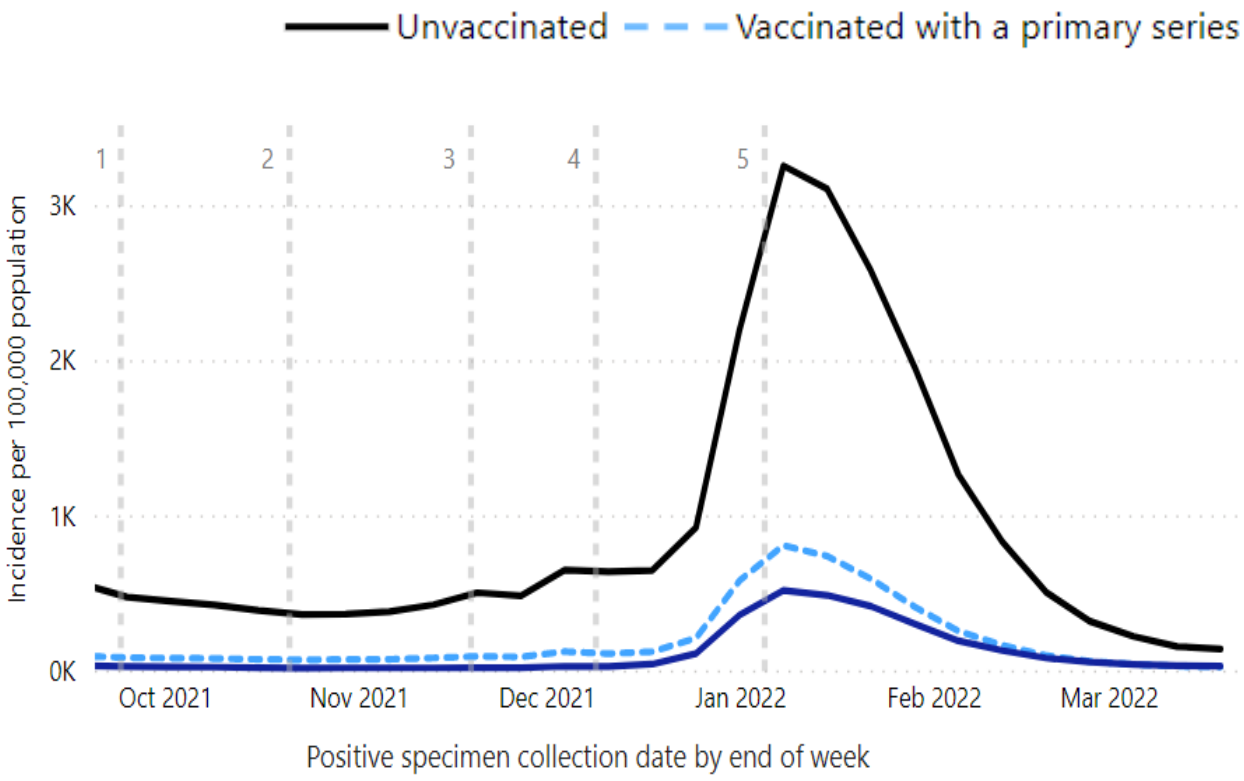
*This includes people who received booster doses and people who received additional doses.

** Data from September 19, 2021 – March 19, 2022 (24 U.S. jurisdictions)

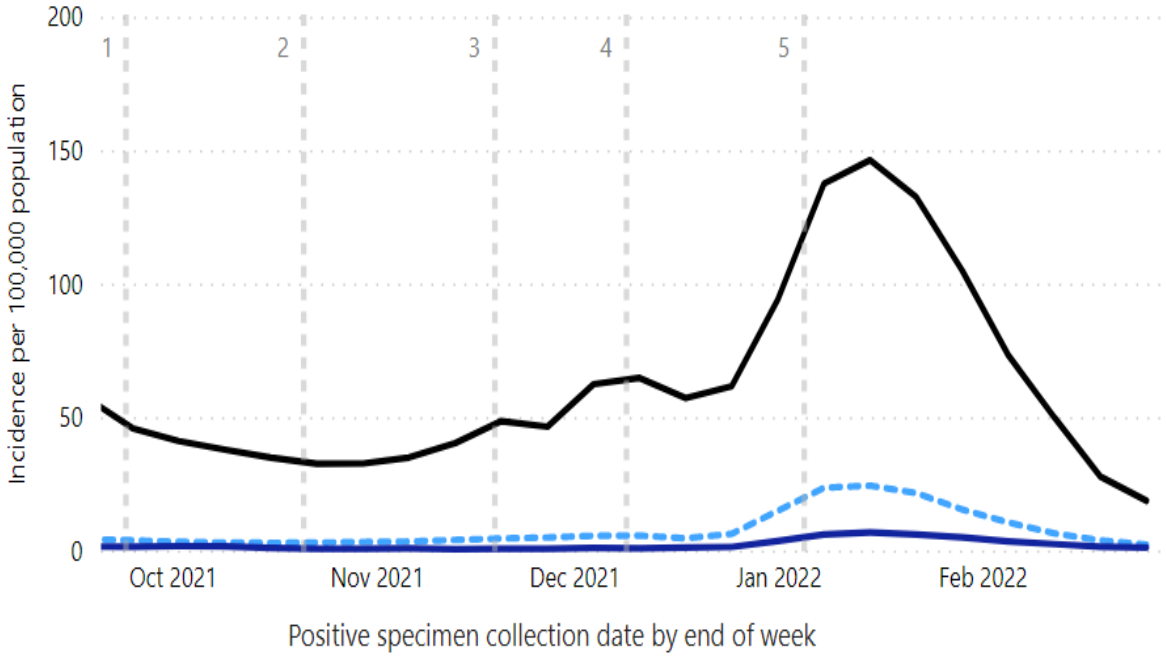
+ Data from September 19, 2021 – February 26, 2022 (23 U.S. jurisdictions)

CDC COVID Data Tracker. https://covid.cdc.gov/covid-data-tracker/#rates-by-vaccine-status Accessed April 19, 2022

Age-adjusted rates of COVID-19 cases & deaths by vaccination status and receipt of booster dose among adults ≥65 years,*



Cases**



Deaths+

*This includes people who received booster doses and people who received additional doses.

** Data from September 19, 2021 – March 19, 2022 (24 U.S. jurisdictions)

+ Data from September 19, 2021 – February 26, 2022 (23 U.S. jurisdictions)

CDC COVID Data Tracker. https://covid.cdc.gov/covid-data-tracker/#rates-by-vaccine-status Accessed April 19, 2022

COVID-19-associated hospitalization surveillance network (COVID-NET)

- **Population-based** surveillance **for laboratory-confirmed** COVID-19-associated **hospitalizations**
- Catchment area: >250 acute care hospitals in 99 counties in 14 states, representing 10% of U.S. population
- **Case definition**: Resident of the surveillance area and positive SARS-CoV-2 test within 14 days prior to or during hospitalization
- **Rates by vaccination status***
  - Linkage to immunization information systems
  - Representative sample of hospitalized cases (>37,000 to date)

*California, Colorado, Connecticut, Georgia, Maryland, Michigan, Minnesota, New Mexico, New York, Ohio, Oregon, Tennessee, and Utah are included in these analyses

COVID-19-associated hospitalizations among vaccinated adults ≥18 years with COVID-19 as primary reason for admission — COVID-NET

January 1, 2021–January 31, 2022

- Fully vaccinated persons with COVID-19-associated hospitalizations **differ** from unvaccinated persons with COVID-19-associated hospitalizations

- Fully vaccinated cases more likely to be:
  - Older
  - Long-term care facility resident
  - DNR/DNI/CMO code
- More underlying medical conditions in fully vaccinated cases

Category	Unvaccinated weighted % N=8,013	Fully vaccinated weighted % N=1,768
Age group (median, IQR)	58 (46-70)	70 (59-80)
18-49 years	31	11
50-64 years	33	16
≥65 years	37	72
LTCF residence	4	12
DNR/DNI/CMO	6	14
≥3 Underlying medical conditions	50	76

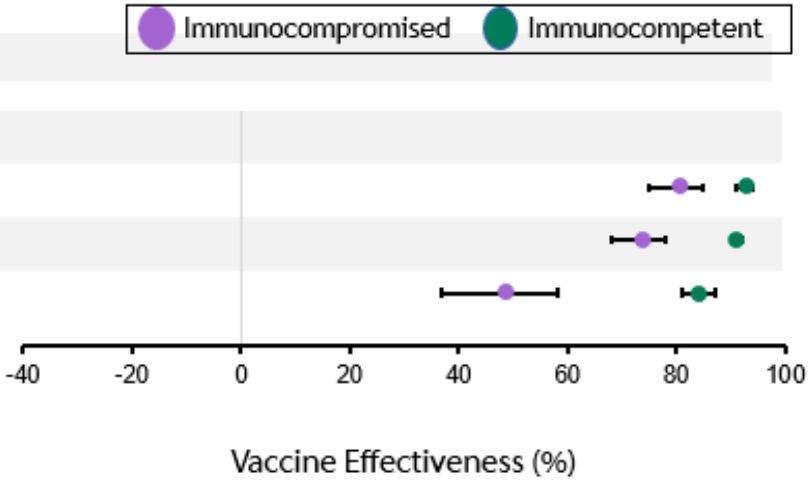
LTCF = long-term care facility; DNR = do not resuscitate; DNI = do not intubate; CMO=comfort measure only

Unpublished data, as described at: https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covid-net/purpose-methods.html

Summary: mRNA VE during Omicron

Persons with moderate to severe immunocompromise

	Adjusted VE% (95% CI)	
Status:	Immunocompromised	Immunocompetent
3 doses		
14-59 days	81 (75-85)	93 (91-94)
60-119 days	74 (68-78)	91 (90-92)
120-179 days	49 (37-58)	84 (81-87)



VISION platform

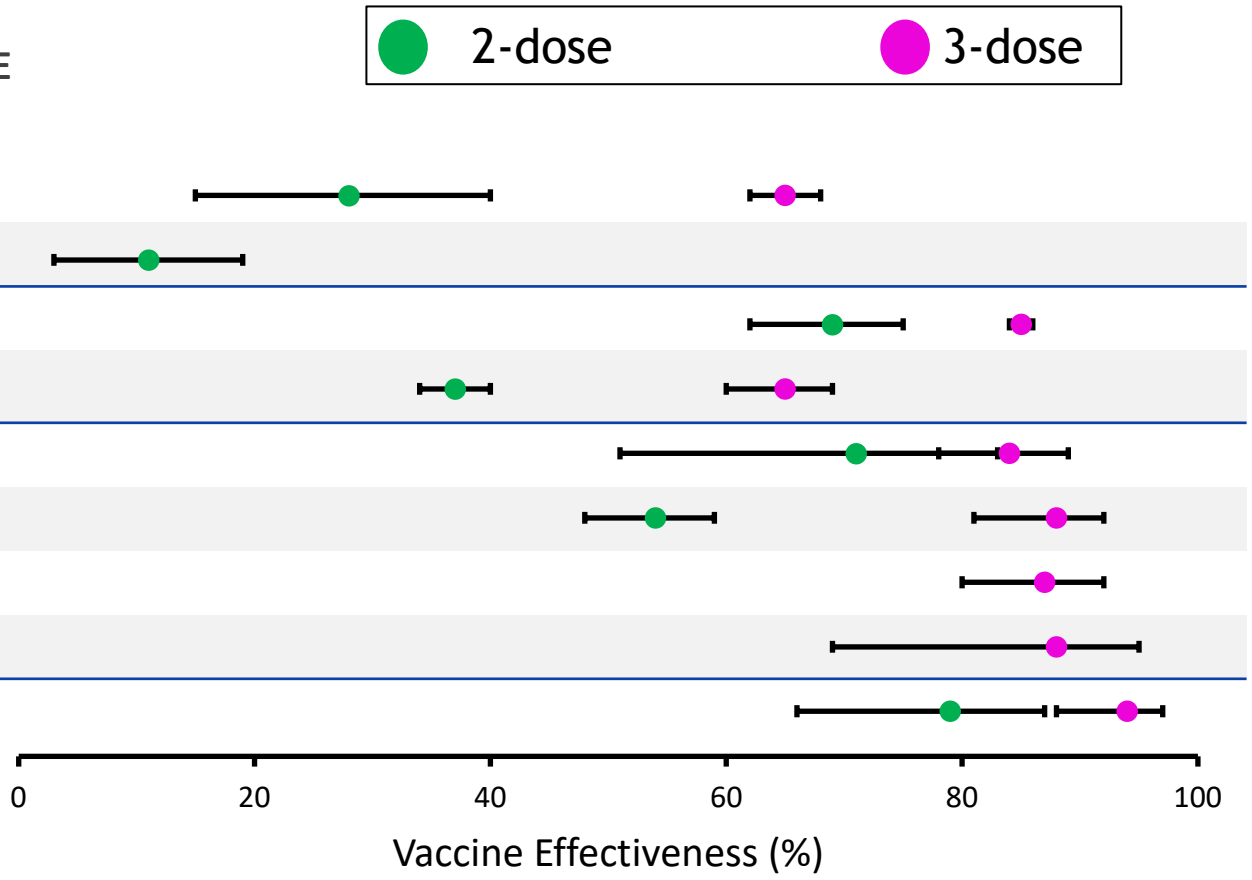
IVY platform

Group	No. of vaccinated case-patients/total case-patients (%)	No. of vaccinated control-patients/ total control-patients (%)	Adjusted* vaccine effectiveness % (95% CI)
3 doses overall	288/909 (32)	508/776 (65)	78 (73–83)
Immunocompromised	153/250 (61)	191/238 (80)	65 (44–78)
7–120 days	89/186 (48)	134/181 (74)	73 (55–84)
>120 days	64/161 (40)	57/104 (55)	54 (16–75)

- More **rapid waning** for 3rd dose with immunocompromised population
- Note that in immunocompromised population, 3rd dose is considered part of **primary series**, and a booster (4th dose) currently recommended

Summary: VE of 2 doses of mRNA vaccine increases with increasing severity of outcome during Omicron in adults ≥18 years; 3rd dose increases VE

		2-dose Adjusted VE % (95% CI)	3-dose Adjusted VE % (95% CI)
Infection	1mo post-last dose, ICATT	28 (15-40)	65 (62-68)
	3mos post-last dose, ICATT	11 (3-19)	--
Emergency department/ urgent care	Last dose <2m ago, VISION	69 (62-75)	85 (84-86)
	Last dose 4-<6m ago, VISION	37 (34-40)	65 (60-69)
Hospitalization	Last dose <2m ago, VISION	71 (51-83)	84 (78-89)*
	Last dose 4-<6m ago, VISION	54 (48-59)	88 (81-92)*
	3rd dose 7-120 days ago, IVY	Not estimated	87 (80-92)*
	3rd dose >120 days ago, IVY	Not estimated	88 (69-95)*
Critical illness/death	2nd dose median 256 days/3rd dose median 60 days ago, IVY	79 (66-87)	94 (88-97)



Booster receipt increases protection across all outcomes.
Booster dose VE remains high among immunocompetent individuals 4-6 months after dose.

*Among immunocompetent individuals ≥65 years of age.

Summary: mRNA VE during Omicron

Persons with moderate to severe immunocompromise

	Immunocompetent	Immunocompromised
2-dose VE against:		
Infection (+/- symptoms)	Limited protection, fast waning	Not estimated
ED/UC	Higher protection, some waning	Not estimated
Hospitalization	Highest protection, some waning	Not estimated
3-dose VE against:		
Infection (+/- symptoms)	Some protection, evidence of waning	Not estimated
ED/UC	Some protection, limited waning	Some protection, clear waning
Hospitalization	Highest protection, limited waning	Highest protection, clear waning
	2-dose primary series + 1st booster	3-dose primary series

Summary

Public Health Problem

- Current 7-day average of COVID-19 cases ~**4%** of peak seen during Omicron surge
- COVID-19 related hospitalization admissions and deaths also continuing to decline from recent winter Omicron surge
- COVID-19 cases, hospitalizations, and deaths **2–20 times higher** in unvaccinated individuals in recent months, compared to vaccinated individuals
- Vaccine effectiveness for 3 doses (primary series + booster) in immunocompetent older adults remains **high**, especially for more severe outcomes

Evidence to Recommendations Framework

Booster doses of COVID-19 vaccines

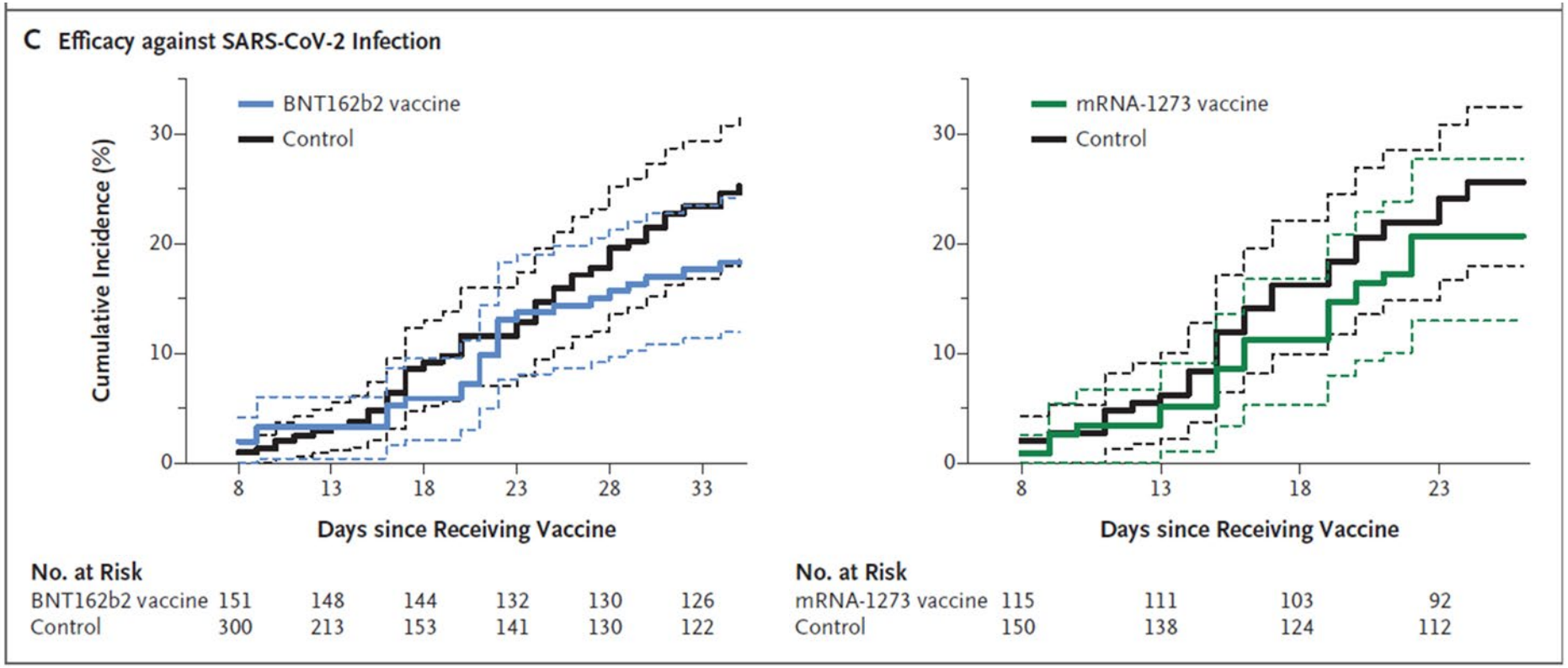
Efficacy of a fourth dose of COVID-19 mRNA vaccine against Omicron among healthcare workers – Israel

- Open-label non-randomized study among healthcare workers
- 4th doses administered 4 months after 3rd dose (Pfizer-BioNTech)
  - 154 received 4th dose of Pfizer-BioNTech
  - 120 received 4th dose of Moderna
  - Two age-matched controls selected for each participant
- After the fourth dose, both vaccines induced IgG antibodies to SARS-CoV-2 receptor-binding domain and increased neutralizing antibody titers to titers that were slightly higher than those achieved after the third dose
- Mild systemic and local reactogenicity reported by majority of recipients

https://www.nejm.org/doi/full/10.1056/NEJMc2202542

Effectiveness of a fourth dose of COVID-19 mRNA vaccine against Omicron among healthcare workers – Israel

- Vaccine efficacy against infection of 4 vs. 3 doses
  - Pfizer-BioNTech: 30% (-9%, 55%); Moderna: 11% (-43%, 44%)



https://www.nejm.org/doi/full/10.1056/NEJMc2202542

Effectiveness of a fourth dose of COVID-19 mRNA vaccine against Omicron among persons ages ≥60 years – Israel

- On January 2, 2022, began administering a 4th dose of Pfizer-BioNTech COVID-19 vaccine to people ages ≥60 years, who had received a 3rd dose of vaccine at least 4 months earlier
- Follow-up from January 10-March 2 for confirmed infection and February 18 for severe illness

	Cases (person-days at risk)		Rate Ratio (95% CI)	Adjusted rate difference per 100,000 person-days at risk (95% CI)
	3rd dose only	Week 4 after 4th dose	3rd dose only vs week 4 after 4th dose	3rd dose only vs. week 4 after 4th dose
Confirmed infections	111,780 (31,000,299)	7,225 (3,883,824)	2.0 (1.9, 2.1)	170 (162, 176)
Severe illness	1210 (24,857,976)	66 (3,639,393)	3.5 (2.7, 4.6)	3.9 (3.4, 4.5)

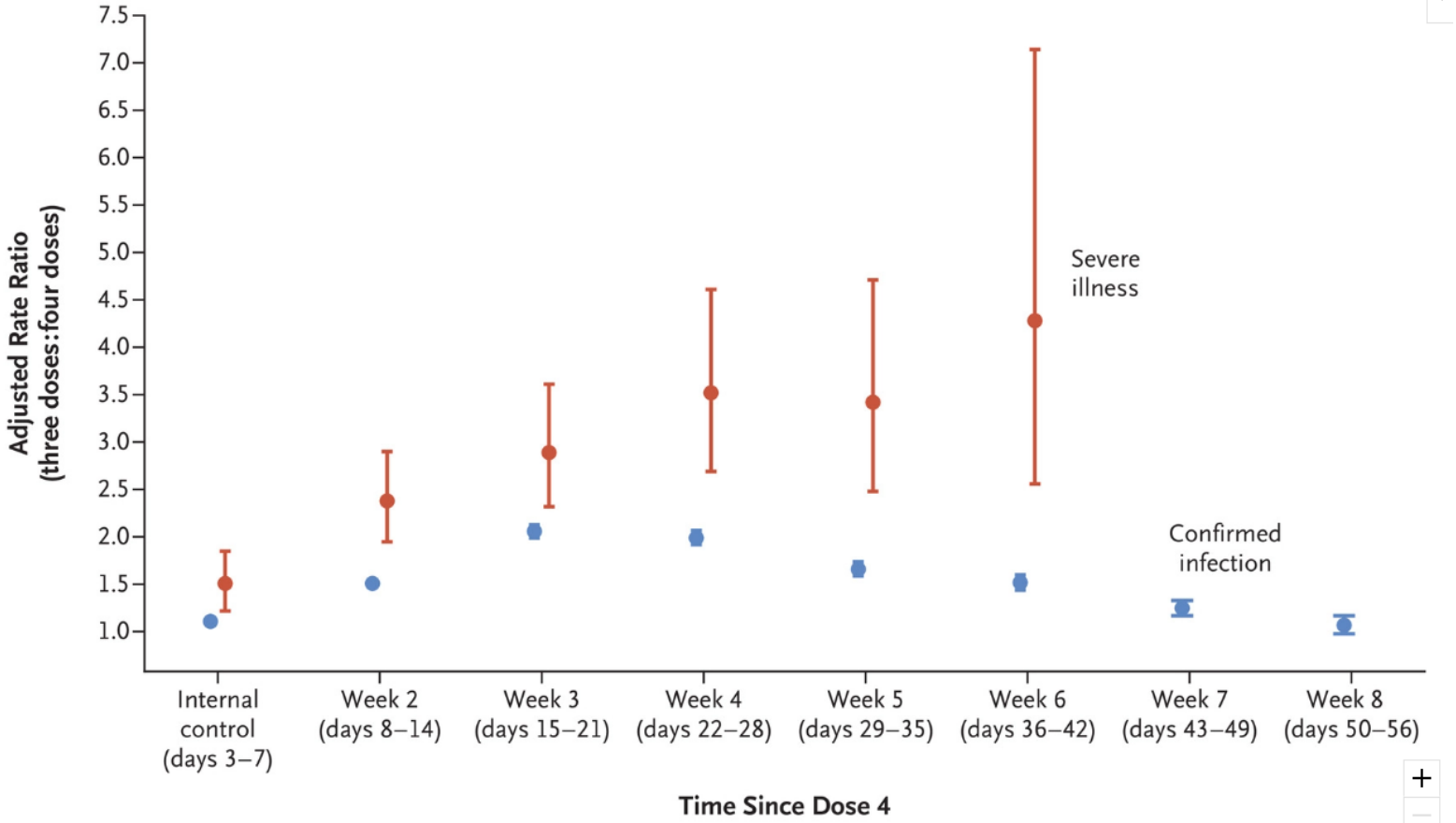
4th dose estimated to prevent additional **3-4 cases** of severe disease per 100,000 person-days compared to 3 doses

https://www.nejm.org/doi/full/10.1056/NEJMoa2201570

Effectiveness of a fourth dose of COVID-19 mRNA vaccine against Omicron among persons ages ≥60 years – Israel

- Rapid waning of additional protection against infection

Adjusted rate ratios for confirmed infection and severe illness



https://www.nejm.org/doi/full/10.1056/NEJMoa2201570

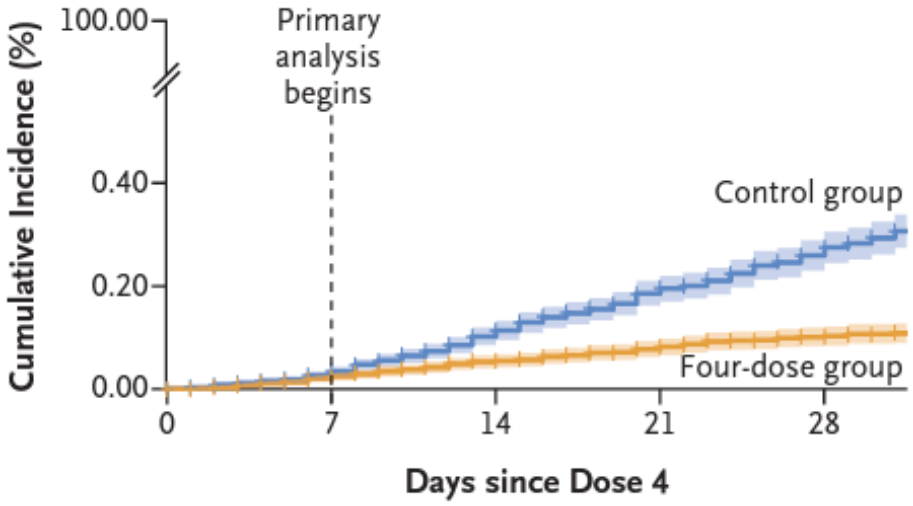
Effectiveness of a fourth dose of COVID-19 mRNA vaccine against Omicron among persons ages ≥60 in a large healthcare organization – Israel

- Included healthcare organization members ages ≥60 years, eligible to receive the fourth vaccine dose, with no previous PCR confirmed SARS-CoV-2 infection
- Matched to eligible persons who had not yet received a fourth dose according to a set of potential confounders
- 182,122 were recruited and matched to controls after receiving dose 4 and were followed for a median of 26 days (interquartile range: 7 to 30)

https://www.nejm.org/doi/pdf/10.1056/NEJMoa2201688?articleTools=true

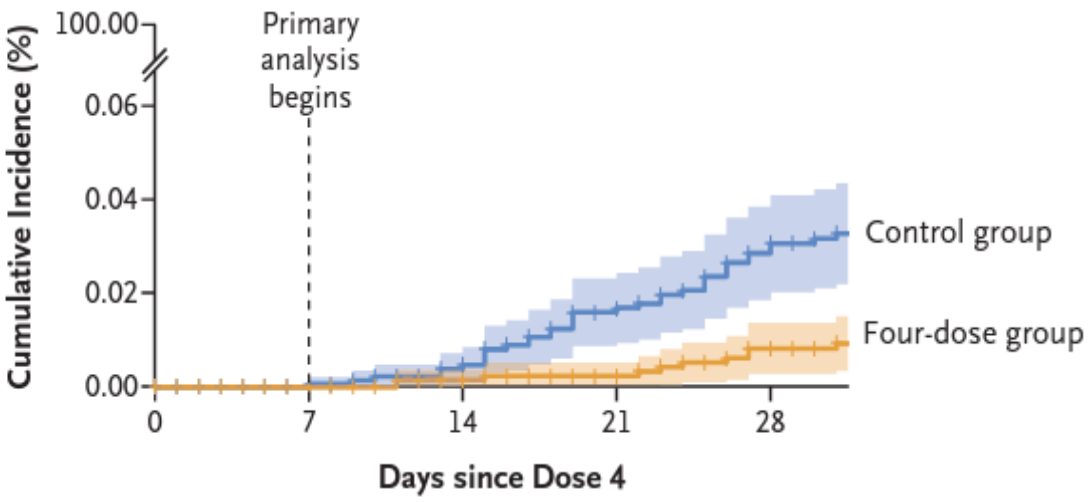
Effectiveness of a fourth dose of COVID-19 mRNA vaccine against Omicron among persons ages ≥60 in a large healthcare organization – Israel

COVID-19-Related Hospitalization



Day 14 to 30 Relative VE: 72% (95% CI: 63% – 79%)

Death from COVID-19



Day 14 to 30 Relative VE: 76% (95% CI: 48% – 91%)

https://www.nejm.org/doi/pdf/10.1056/NEJMoa2201688?articleTools=true

Methods for assessment of benefits

Calculated per 1 million persons with a primary series vaccination, primary series and 1 booster dose, or primary series and 2 booster doses

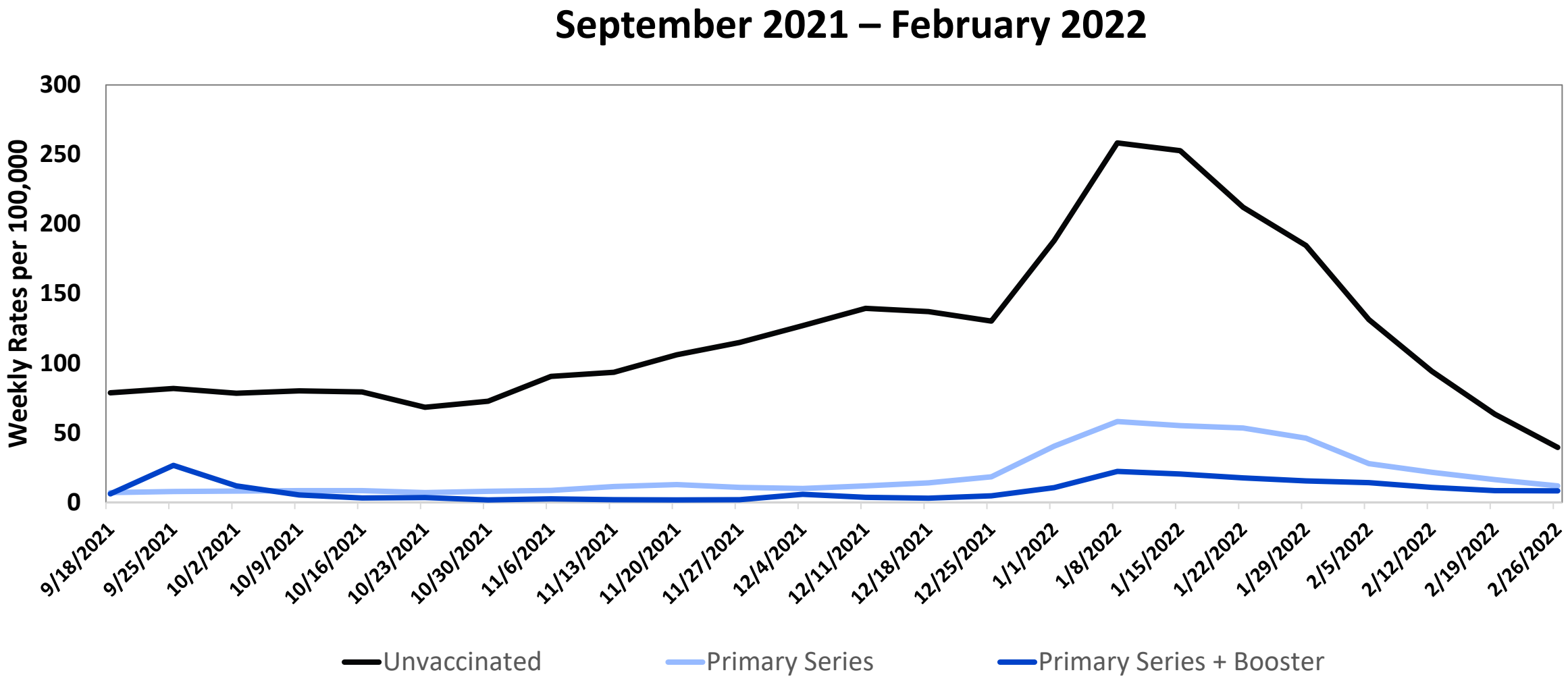
- Age group: 50+ years
- VE against hospitalization estimates
  - Primary series VE estimate of 55%[1]
  - Primary series and one booster dose VE estimate of 88%[1]
  - Primary series and two booster doses VE estimate of 95%[2]
- Age-specific hospitalization rates: COVID-NET rates from the week ending on February 26th, 2022
- Time horizon: 120 days

VE: Vaccine Effectiveness

[1] VE estimate from IVY and VISION: https://covid.cdc.gov/covid-data-tracker/#vaccine-effectiveness

[2] Relative VE estimate for 4th dose: https://www.nejm.org/doi/pdf/10.1056/NEJMoa2201688?articleTools=true

Weekly hospitalization rates by vaccination status among persons ages ≥50 years, COVID-NET



Source: COVID-NET

Benefits after mRNA COVID-19 booster dose among persons ages ≥50 years

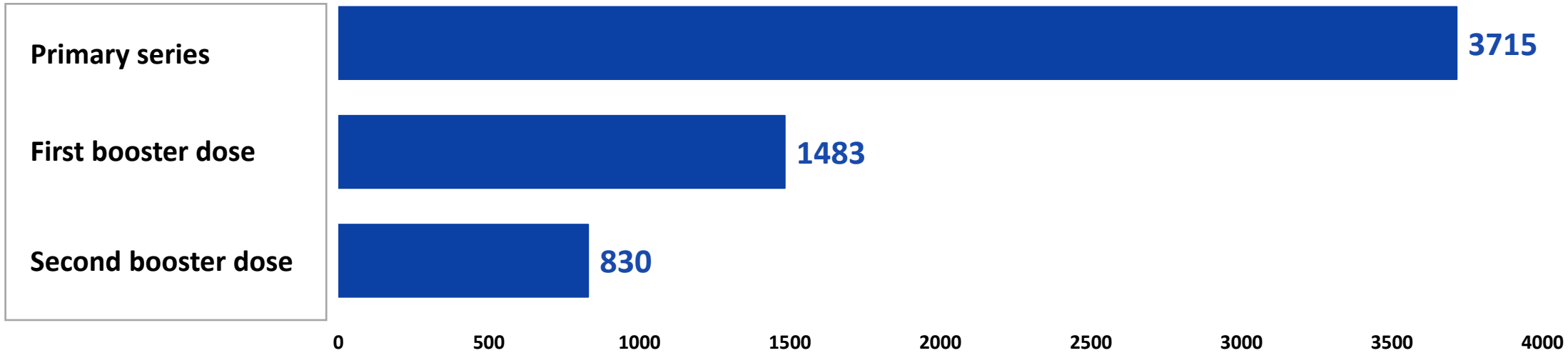
For every million series completed

Scenario:

- 55% VE for primary series[1]
- Boost to 88% VE for single booster[1]
- Assumed boost to 95% VE for second booster[2]

Vaccine series	VE for hospitalization
Primary series	55%
Primary series + one booster dose	88%
Primary series + two booster doses	95%

COVID-19-Associated Hospitalizations Prevented per Million Series Completed



VE: Vaccine Effectiveness; [1] VE estimate from IVY and VISION: https://covid.cdc.gov/covid-data-tracker/#vaccine-effectiveness; [2] Relative VE estimate for 4th dose: https://www.nejm.org/doi/pdf/10.1056/NEJMoa2201688?articleTools=true; COVID-NET hospitalization rates from the week of February 26, 2022

Benefits after mRNA COVID-19 booster dose among persons ages ≥50 years

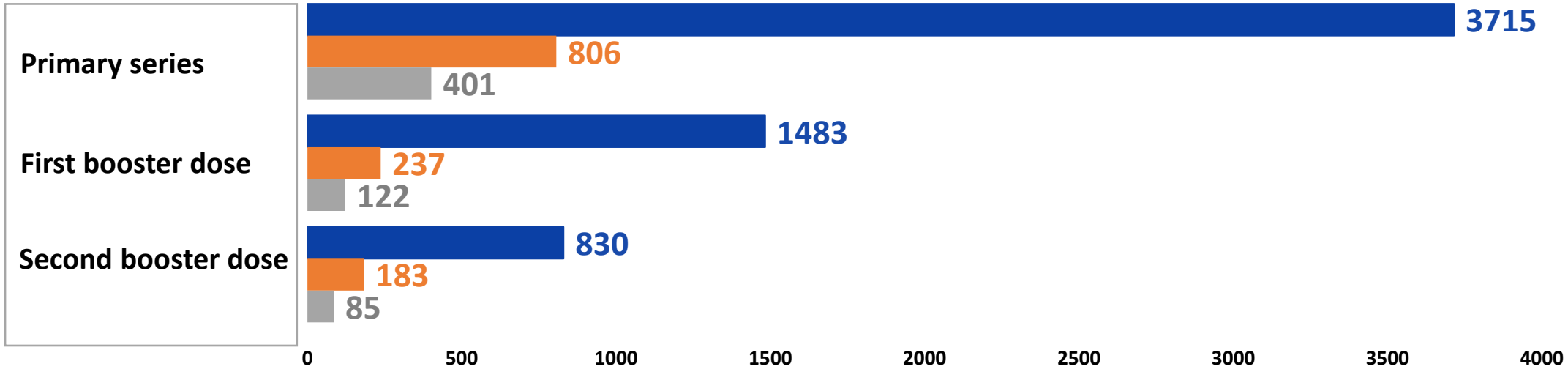
For every million series completed

Scenario:

- 55% VE for primary series[1]
- Boost to 88% VE for single booster[1]
- Assumed boost to 95% VE for second booster[2]

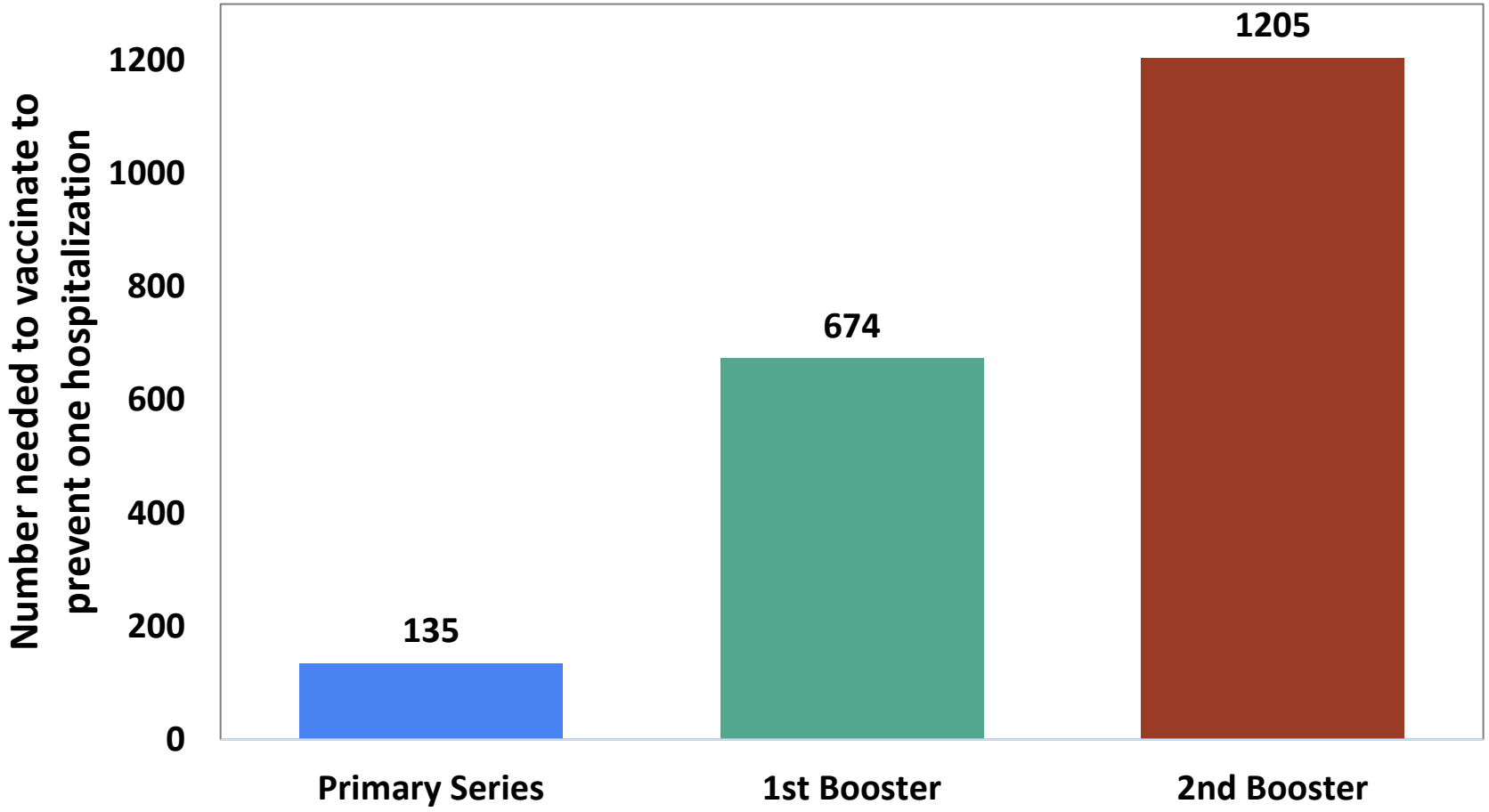
Vaccine series	VE for hospitalization
Primary series	55%
Primary series + booster dose	88%
Primary series + second booster dose	95%

COVID-19-Associated Hospitalizations, ICU Admissions, Deaths Prevented per Million Series Completed



VE: Vaccine Effectiveness; [1] VE estimate from IVY and VISION: https://covid.cdc.gov/covid-data-tracker/#vaccine-effectiveness; [2] Relative VE estimate for 4th dose: https://www.nejm.org/doi/pdf/10.1056/NEJMoa2201688?articleTools=true; COVID-NET hospitalization rates from the week of February 26, 2022

Number needed to vaccinate to prevent one hospitalization over 4 months in persons aged ≥50 years, primary series versus 1st booster versus 2nd booster



To prevent one hospitalization:
Need to vaccinate **5 – 9 times** as many persons with booster doses compared to primary series

Note: Number needed to vaccinate was calculated using the marginal benefit of each additional dose, therefore the number needed to vaccinate for each booster dose considers only the added benefit received from that booster dose

Limitations

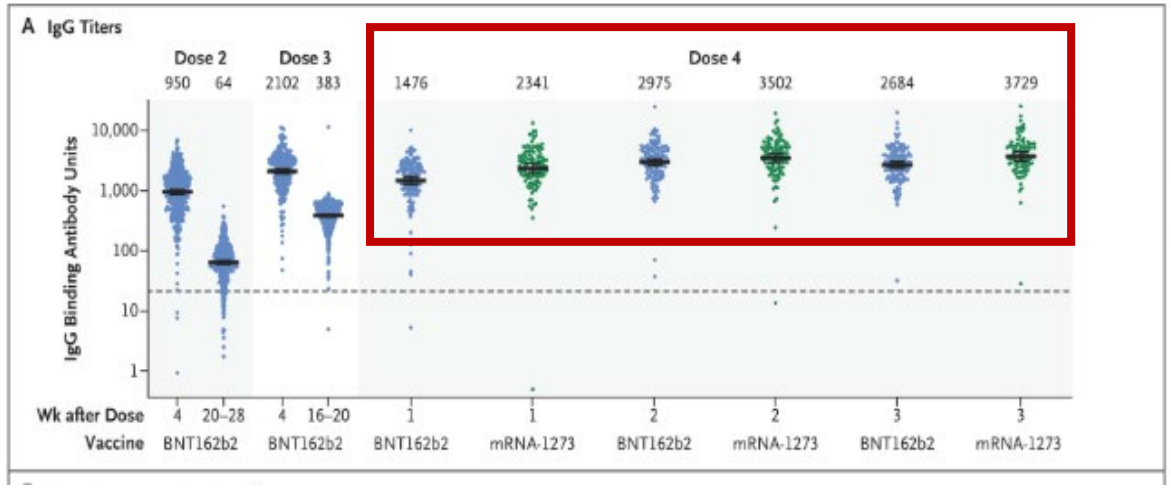
- The model assumes static hospitalization rate over 120 days
  - As rates increase, anticipated benefits also increase. Hospitalization rates among unvaccinated persons tend to have larger increases during times of increased transmission than those seen among vaccinated persons. Therefore, relative benefits of primary series compared to boosters will likely be larger during times of higher transmission.
- Model does not account for prior infection
- Unable to calculate benefits for persons with immunocompromise, however we anticipate that benefits would be greater and risks would be smaller in this population

Other considerations:
Myocarditis and pericarditis

- Risk of myocarditis/pericarditis identified after COVID-19 vaccine booster doses in individuals ages ≥12 years
  - Among those ages **12–39 years**: mostly myocarditis and myopericarditis with onset <7 days after 1st booster; the risk is not as high as after the 2nd dose in primary series
  - Among those ages **≥40 years**: mostly pericarditis, and the small elevated risk is more spread out in the 3 weeks after 1st booster
- Next steps:
  - Evaluate severity and clinical course for pericarditis cases in individuals ages ≥40 years
- Continue to review COVID-19 vaccine booster dose safety data with VaST

Other considerations:
Immune tolerance

- Concern that giving additional doses of COVID-19 vaccine would lead to lower antibody levels (failure to restore antibody levels to what was seen after a previous dose) or T-cell exhaustion
- Data do not suggest this is a concern with COVID-19 vaccines currently
  - Antibody levels (IgG binding antibodies) after a 4th dose in Israel returned to similar levels seen shortly after a 3rd dose
- **Timing** between doses likely an important factor as well
  - When attempting to induce immune tolerance (e.g. allergy shots), must have very frequent (weekly/monthly) exposure
- Continue to closely monitor

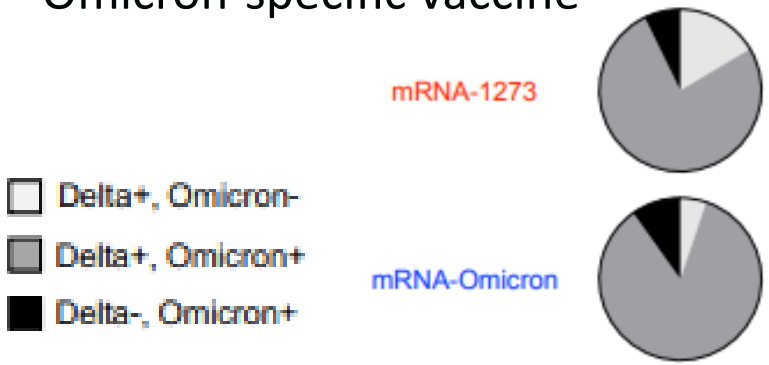


Efficacy of a Fourth Dose of Covid-19 mRNA Vaccine against Omicron | NEJM

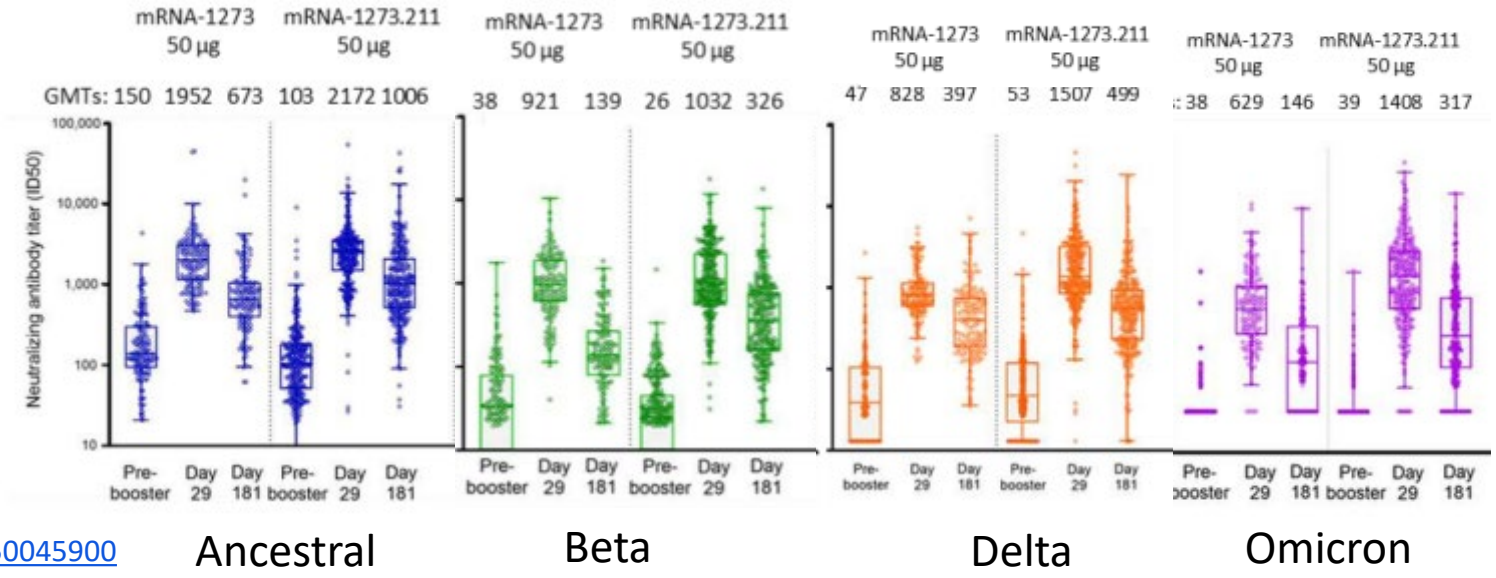
Other considerations:
Imprinting

- Concern that initial exposure to one virus strain primes B-cell memory and limits the development of memory B cells and neutralizing antibodies against new strains
- Data suggest a diverse response obtained after priming with current vaccines

In animal study, majority of memory B-cell responses after a booster were cross-reactive to multiple variants (dark grey) after both ancestral vaccine and Omicron-specific vaccine[1]



After being primed with ancestral SARS-CoV-2 containing vaccine, boost with ancestral or Beta-variant vaccine elicited neutralizing antibody titers to variety of variants[2]



1. https://www.biorxiv.org/content/10.1101/2022.02.03.479037v1.full.pdf
2. https://assets.researchsquare.com/files/rs-1555201/v1_covered.pdf?c=1650045900

Benefit and risk balance for COVID-19 vaccine booster doses

Benefits

Known

Prevention of COVID-19 associated hospitalization, ICU and death

Possible

Prevention of post-COVID conditions

Prevention of COVID-19 transmission

Risks

Known

Rare vaccine-associated myo-pericarditis

Theoretical

Immune tolerance

Imprinting

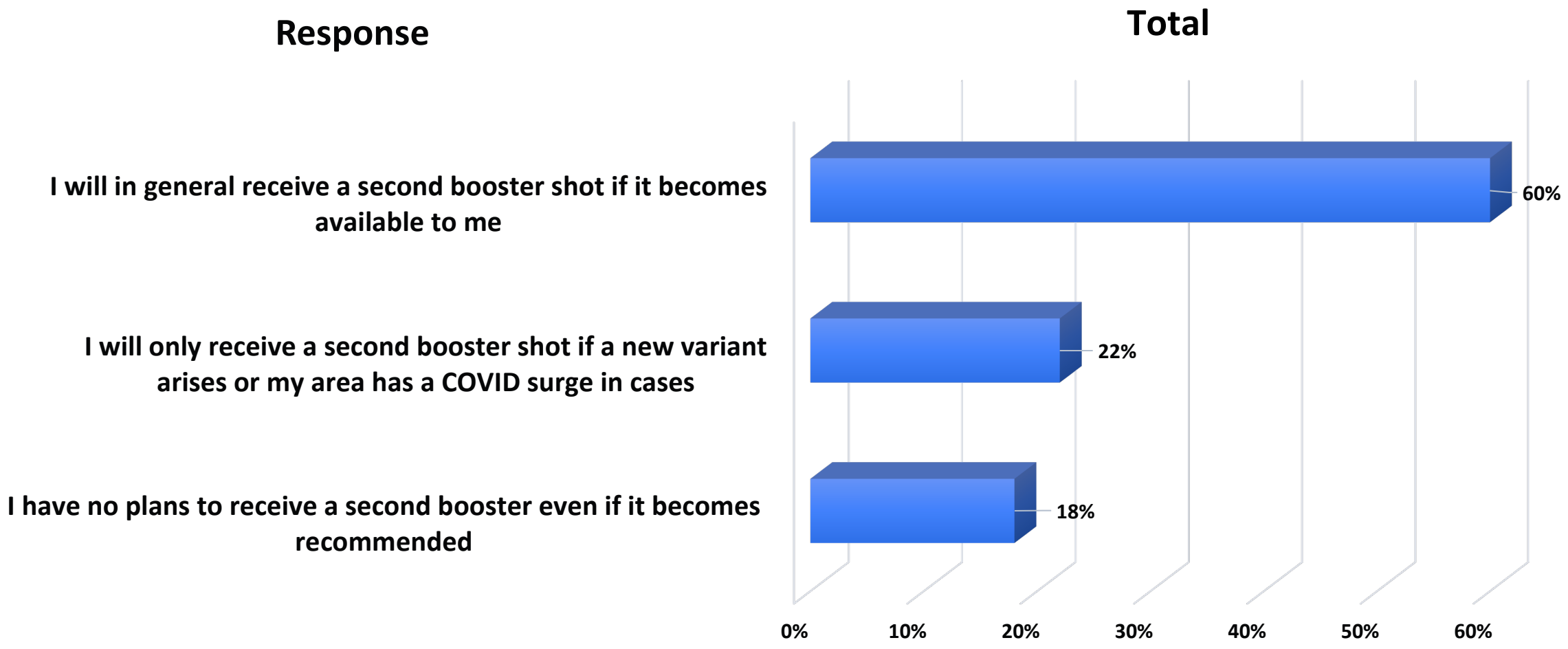
Summary
Benefits and Harms

- Data from Israel demonstrate increased immune response after fourth dose
  - Higher rates of infection and severe illness seen in 3-dose recipients compared to 4-dose recipients
- Greatest benefit from vaccination is achieved from receipt of **primary series** and **first booster dose**
  - Additional benefits may be achieved through receipt of a second booster dose
- Known and possible **benefits outweigh risks** (including theoretical risks)
  - Individual factors that influence magnitude of benefits for second booster
  - Monitor additional data to inform theoretical risks

Evidence to Recommendations Framework

Booster doses of COVID-19 vaccines

Survey on attitudes toward receiving a second booster shot among US adults, March 25 – 27, 2022 (N=2,028)



STAT+. STAT-Harris Poll: Most Americans would get a COVID-19 booster shot if recommended. https://www.statnews.com/pharmalot/2022/04/06/covid19-vaccine-mask-booster-harris-poll/. Accessed April 12, 2022

Survey on attitudes toward receiving a second booster shot March 25 – 27, 2022 (N=2,028)

- Additionally, **73%** of Baby Boomers – those 57 years and older – plan to get a booster, if recommended, compared with **48%** of Gen Z'ers, who are between 18 and 24 years old
- Among those polled, **54%** of Black, non-Hispanic respondents and **43%** of Hispanic individuals would get another booster, compared with **73%** of Asian, non-Hispanic individuals and **65%** of White, non-Hispanic respondents

STAT+. STAT-Harris Poll: Most Americans would get a COVID-19 booster shot if recommended. https://www.statnews.com/pharmalot/2022/04/06/covid19-vaccine-mask-booster-harris-poll/. Accessed April 12, 2022

Attitudes and intentions for additional COVID-19 vaccine doses among "boosted" U.S. adults aged 50 years and older (N=1,412)

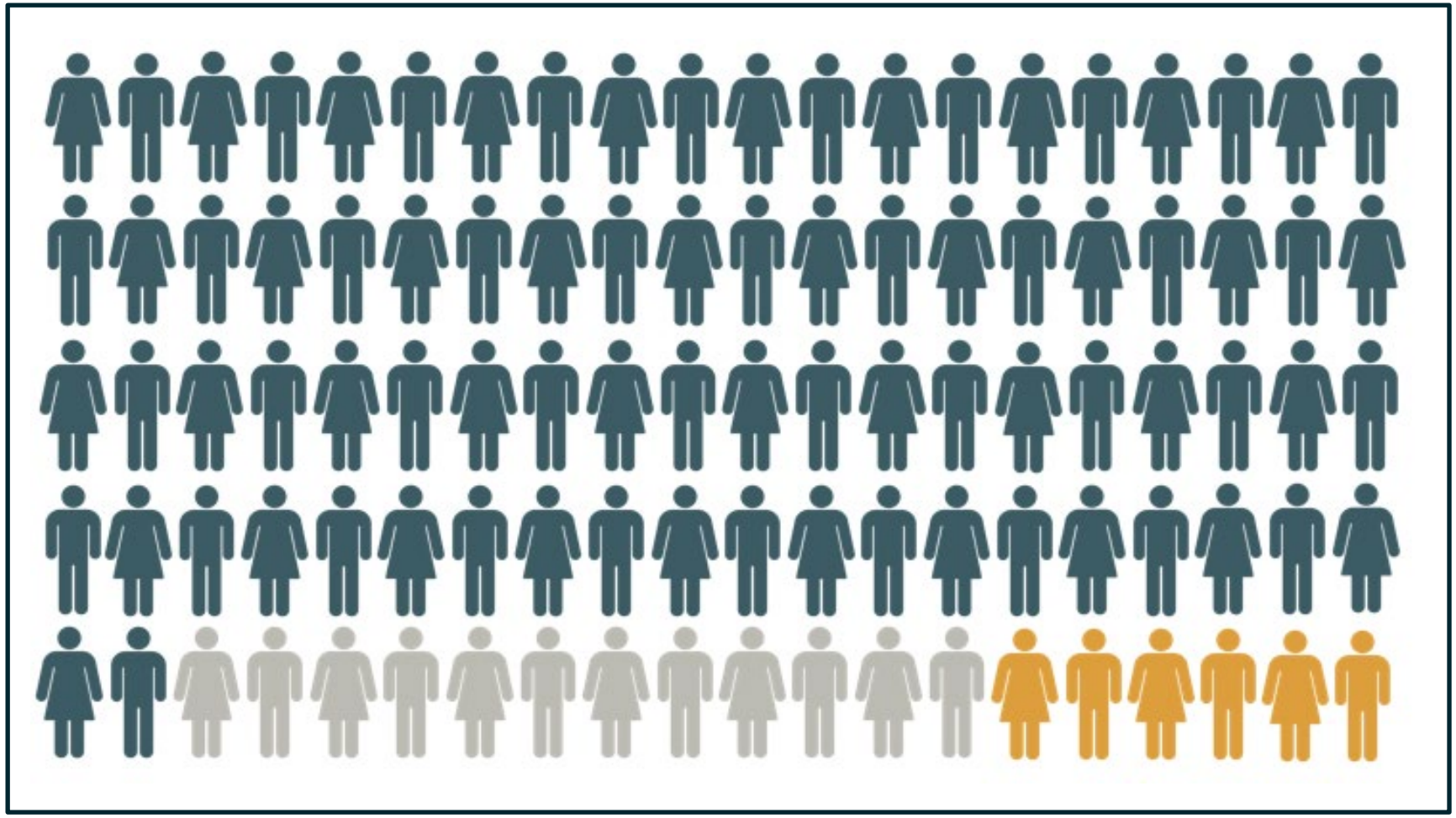
PURPOSES OF CONDUCTING THIS SURVEY

1) Assess vaccination intentions for a 2nd COVID booster in the next 4 months among boosted, U.S. adults aged ≥50 years
2) Assess barriers towards receiving a 2nd booster
3) Assess vaccination intentions for receiving another COVID vaccine dose now and again in the Fall

CDC and University of Iowa/RAND survey, unpublished

SECOND COVID-19 VACCINE BOOSTER DOSE

82% of respondents “definitely” or “probably” will get a 2nd booster dose in the next 4 months



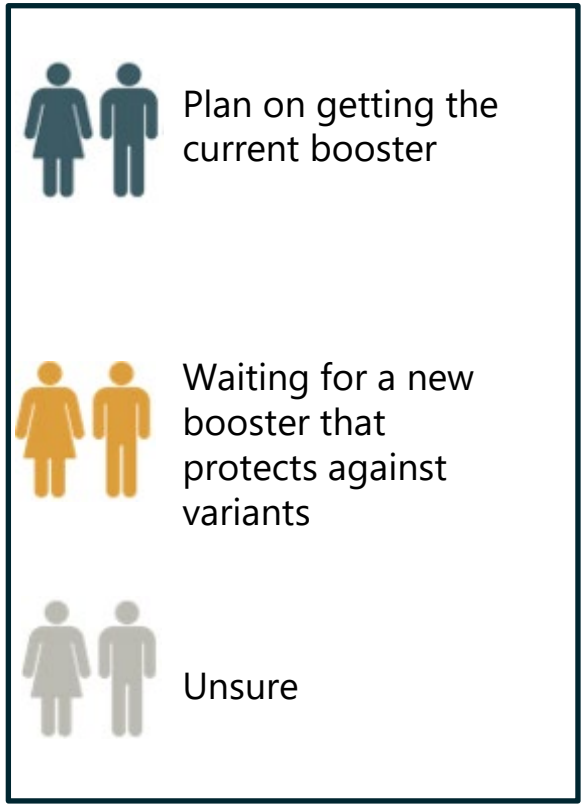
‘Probably’ or ‘Definitely’ will get a 2nd booster

Unsure

‘Probably’ or ‘Definitely’ will not get a 2nd booster

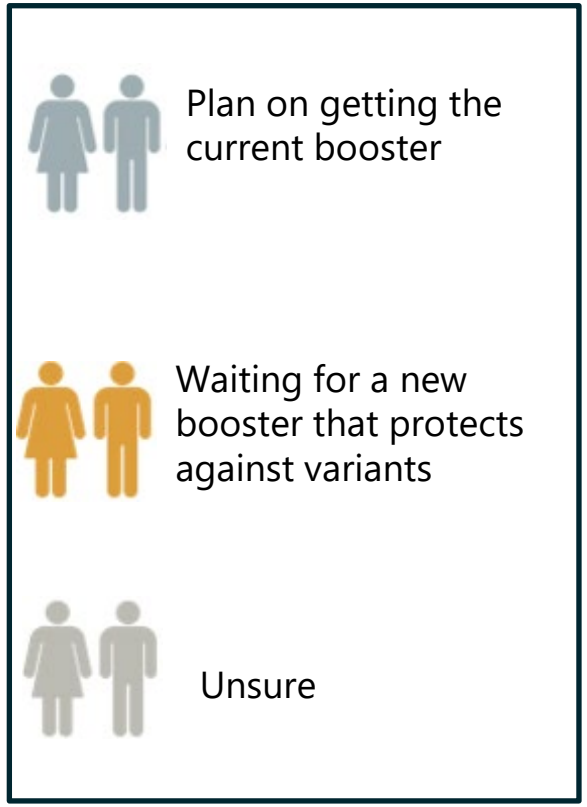
CDC and University of Iowa/RAND survey, unpublished

68% of respondents intending to get a 2nd booster reported they would get the currently available booster



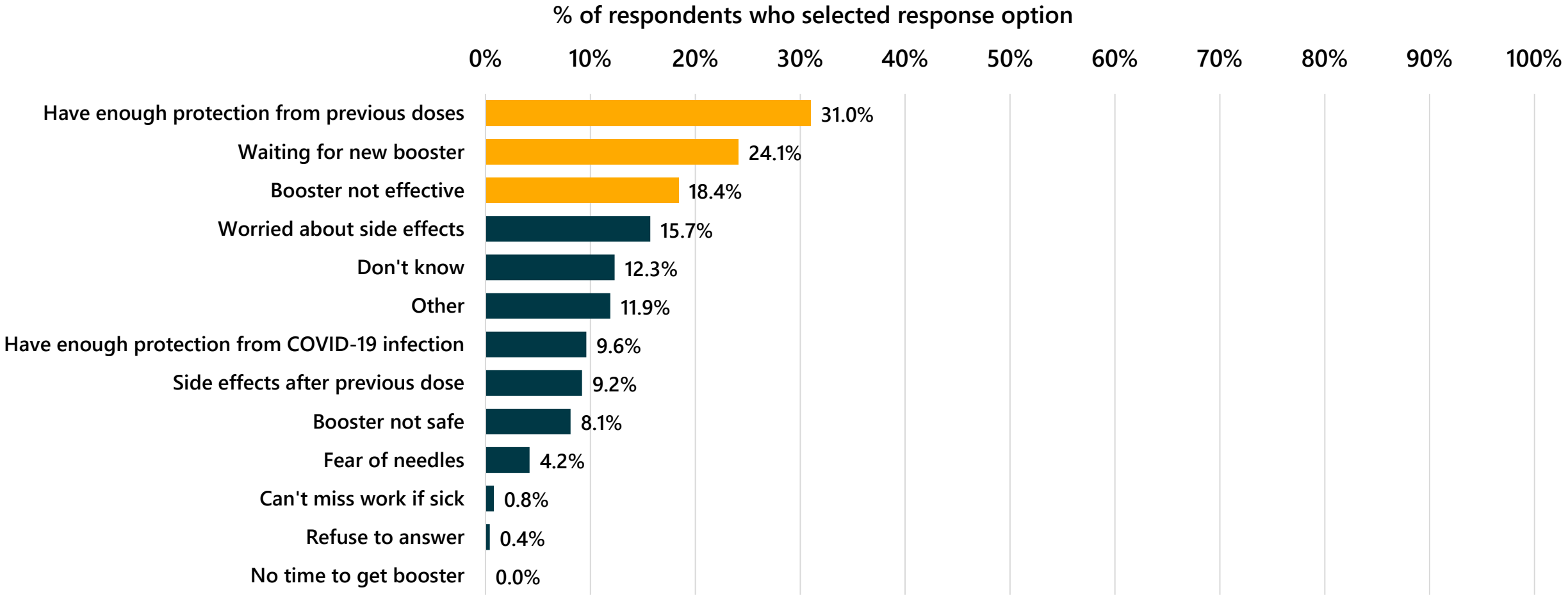
CDC and University of Iowa/RAND survey, unpublished

19% of respondents intending to get a 2nd booster reported they would wait for a new booster that protects against variants



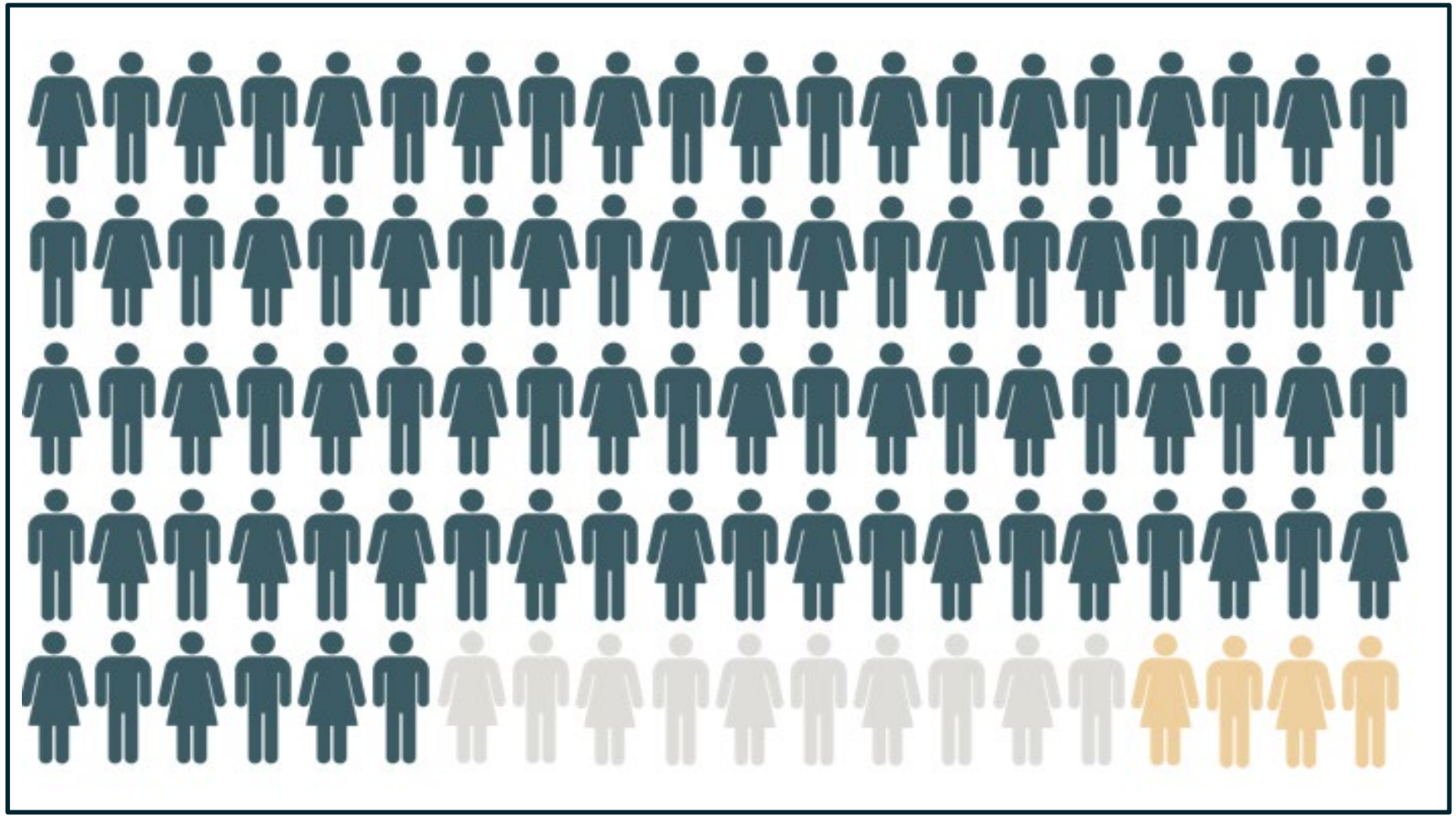
CDC and University of Iowa/RAND survey, unpublished

Beliefs related to another dose of the currently available vaccines not providing additional protection were the top reasons given for not wanting a 2nd COVID-19 booster



CDC and University of Iowa/RAND survey, unpublished

86% of respondents “definitely” or “probably” would get a 2nd booster dose if a new COVID vaccine that protects against variants became available



‘Probably’ or ‘Definitely’ would get the new booster

Unsure

‘Probably’ or ‘Definitely’ would not get the new booster

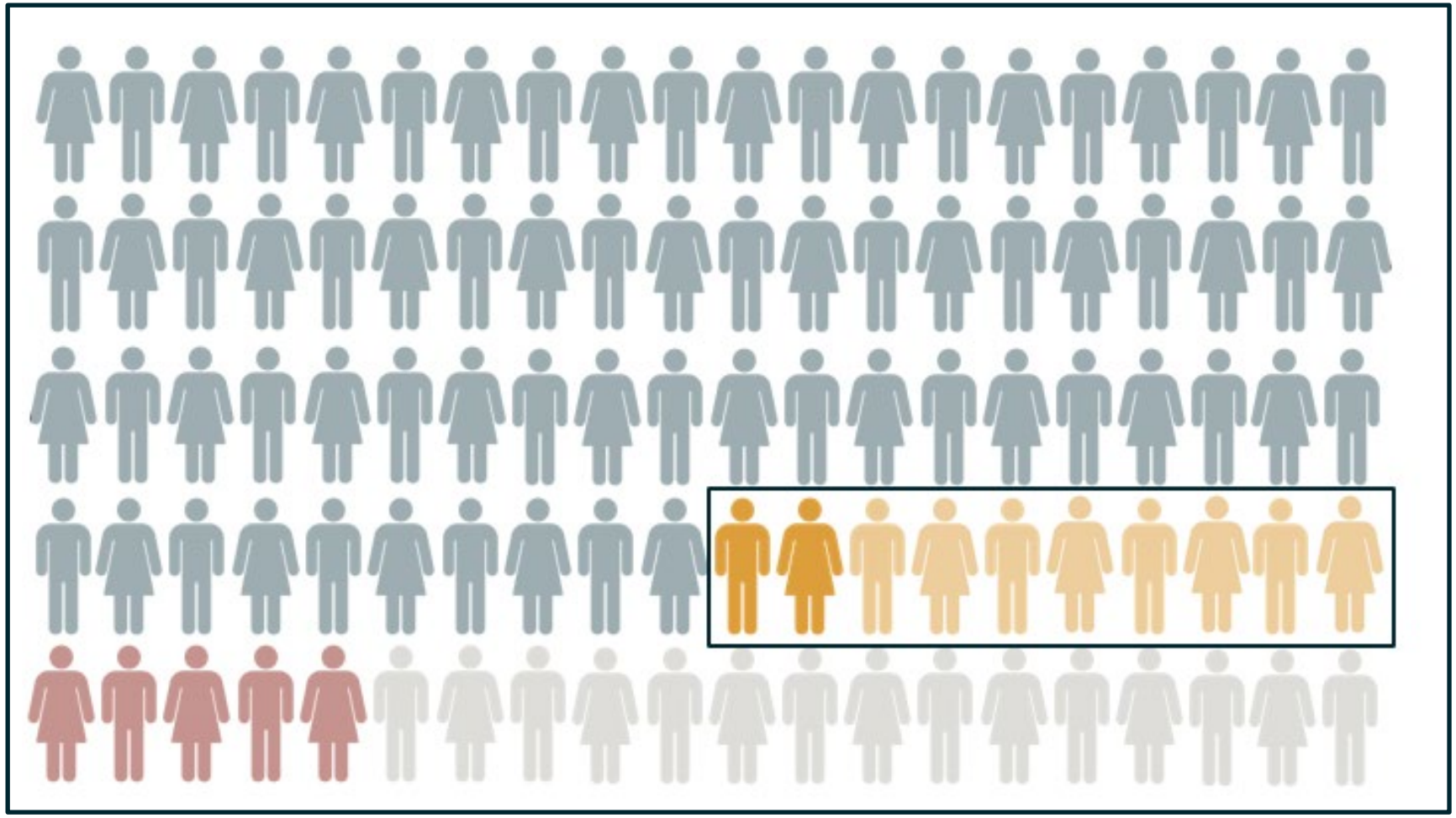
CDC and University of Iowa/RAND survey, unpublished

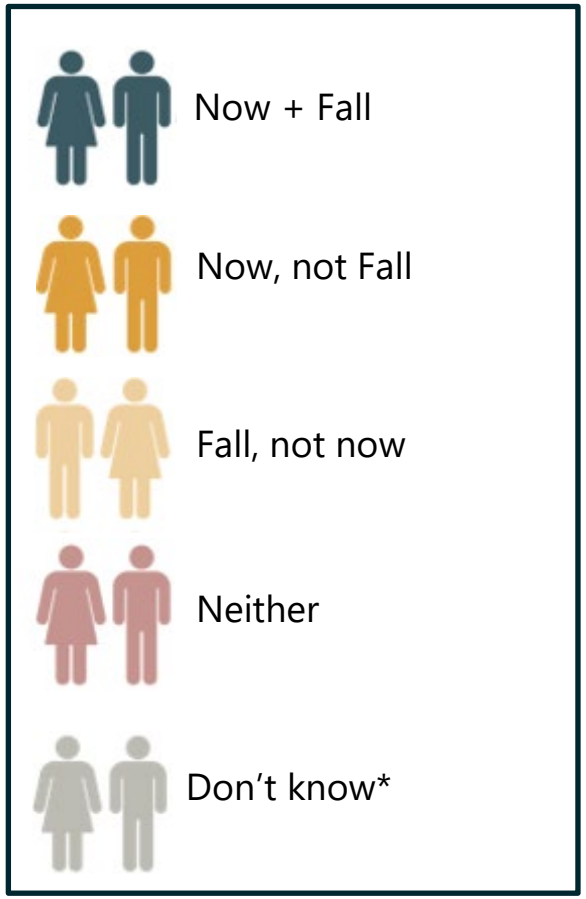
COVID-19 BOOSTERS NOW + FALL

70% of respondents said they would get a COVID booster now and again in the Fall

CDC and University of Iowa/RAND survey, unpublished

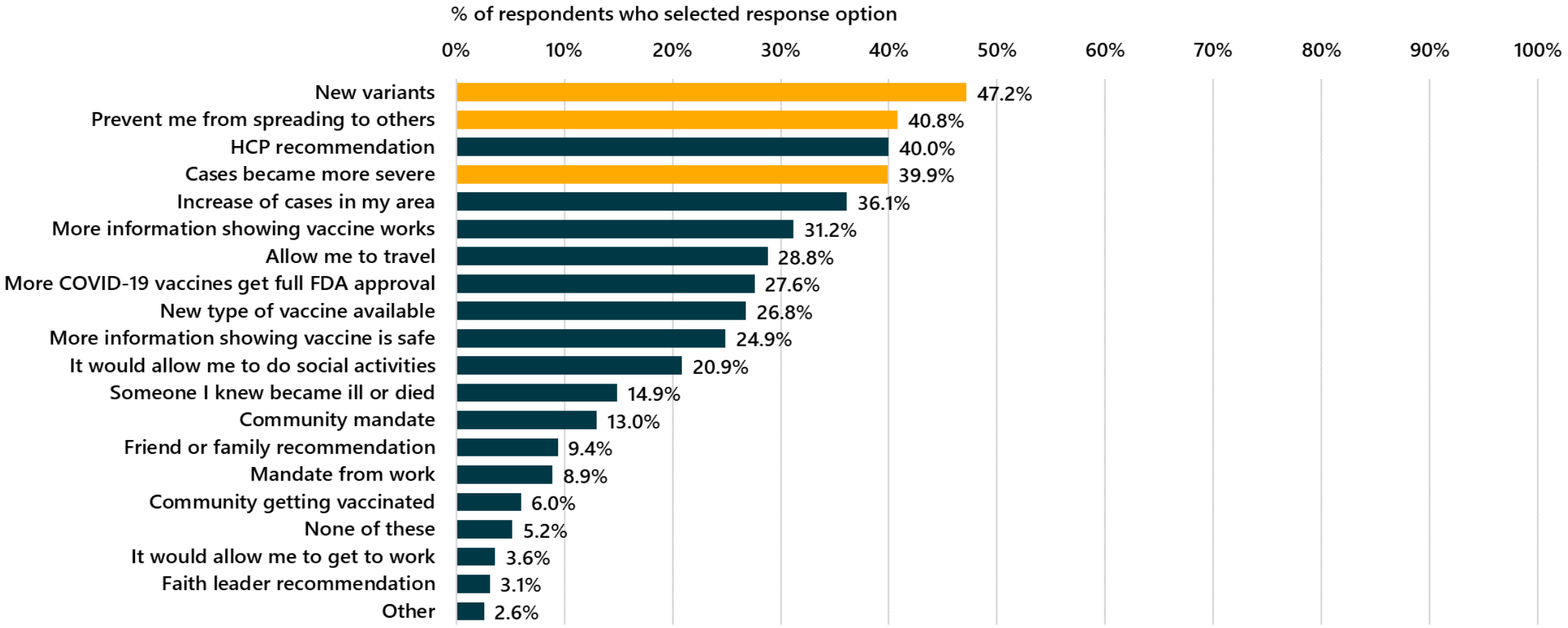
10% of respondents said they would get a COVID booster either now or in the Fall





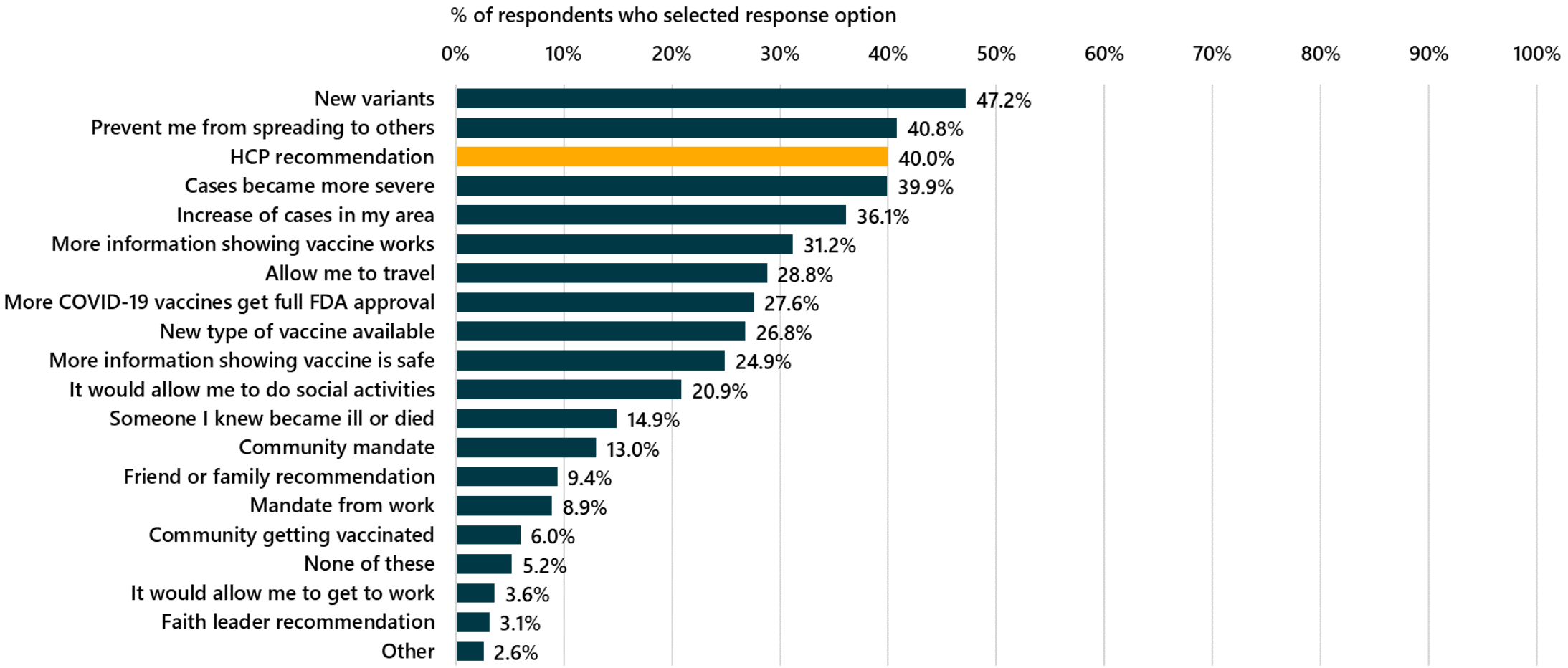
CDC and University of Iowa/RAND survey, unpublished

The emergence of new variants, preventing spread, and increased severity were top reasons given for getting boosted again now and in the Fall…



CDC and University of Iowa/RAND survey, unpublished

…so was a strong health care provider recommendation



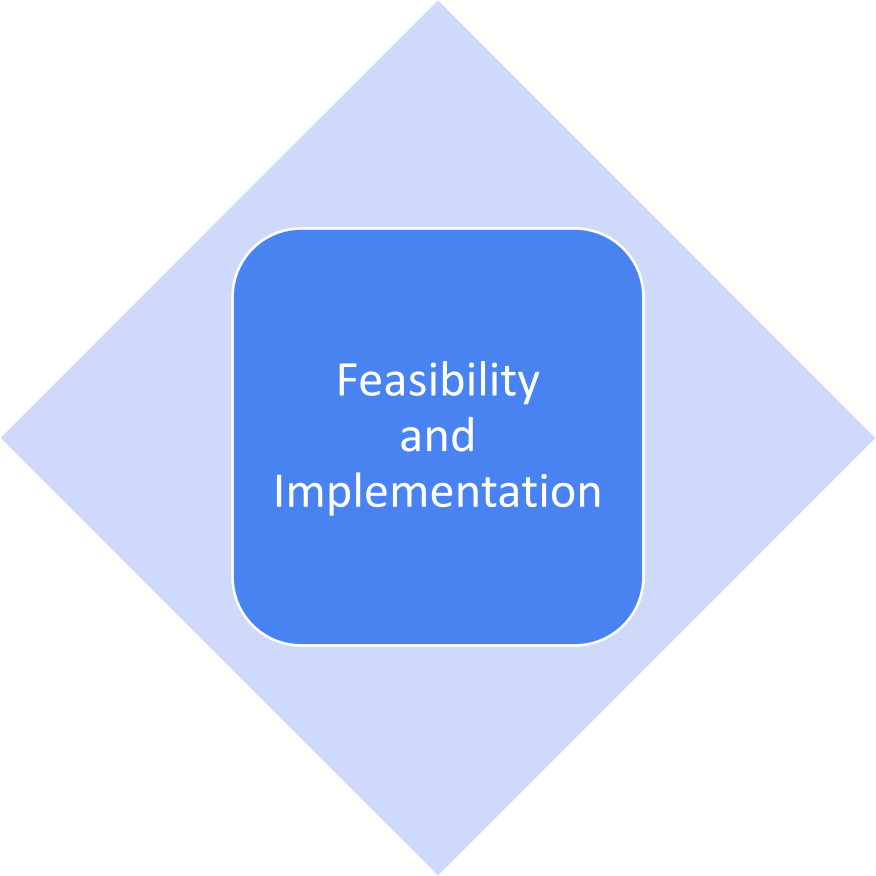
CDC and University of Iowa/RAND survey, unpublished

Summary
Values and Acceptability

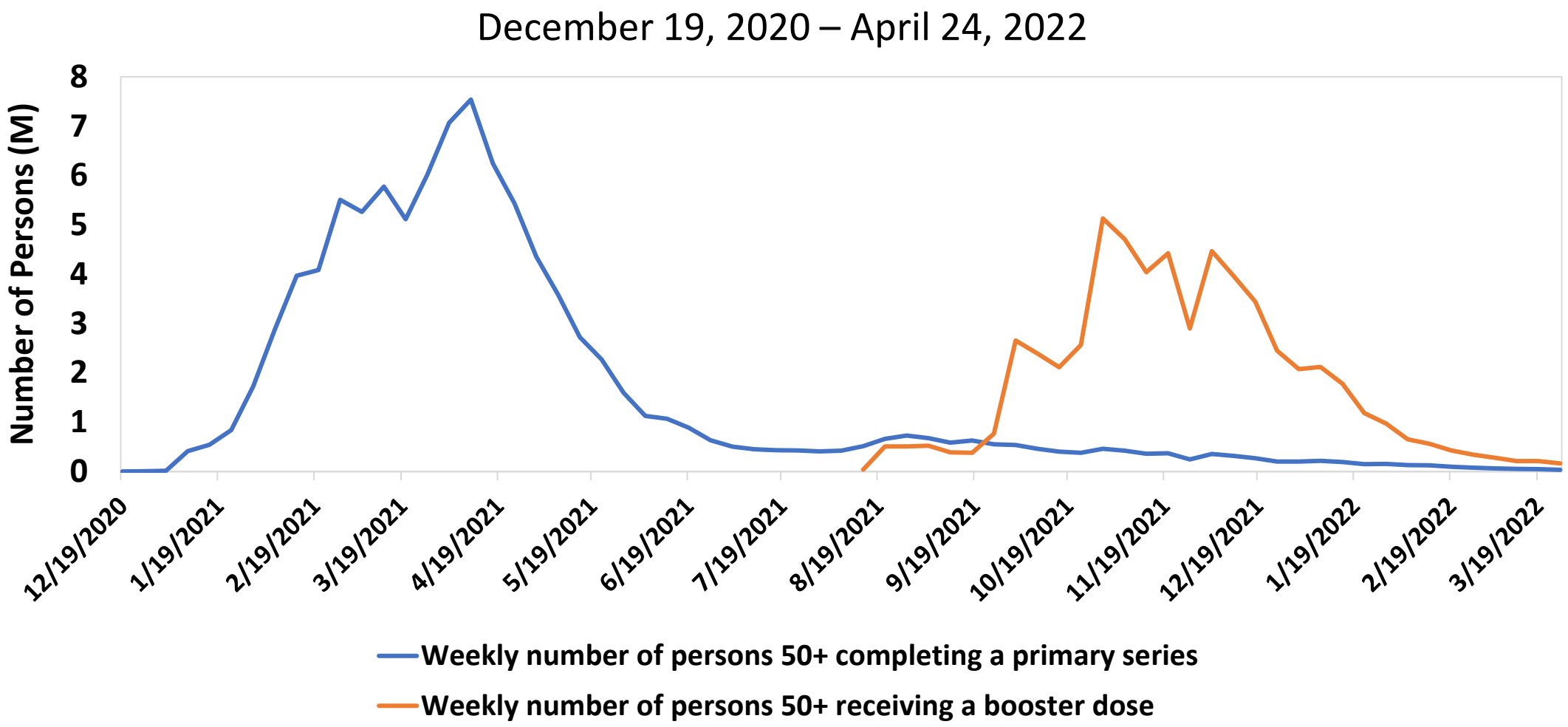
- Majority of adults (60-80%) state they may get a second booster dose
  - Varies by age and race/ethnicity
- ~20% of boosted adults ages 50 and over would prefer a vaccine focused on new variants, and 10% state they would either get a vaccine now + fall, but not both
- Strong healthcare provider recommendation influential in decision to receive additional COVID-19 vaccine doses

Evidence to Recommendations Framework

Booster doses of COVID-19 vaccines



Weekly trends in completed COVID-19 primary series and booster doses among persons ages ≥50 years, United States



Source: CDC IZ Data Lake. 3/28/2022

Eligible population for second COVID-19 vaccine booster doses

- Among people who are fully vaccinated, approximately **52**% of people ages 50-64 years and **67**% of people ages ≥65 years have received a COVID-19 vaccine booster dose
- At the time of authorization, ~**30** million people eligible (at least 4 months after their previous dose)
  - ~10 million eligible individuals ages 50-64 years
  - ~20 million eligible individuals ages ≥65 years
- Based on the timing of recommendations, people with immunocompromised conditions would not be eligible for second booster (5th total dose) until May 13th at the earliest

Uptake of second COVID-19 vaccine booster doses

- The number of people reportedly getting vaccinated has nearly tripled since authorization of second booster doses, to an average of 447,000 per day in the week ending April 8th, compared with 160,000 per day in the week ending March 29th.[1,2]

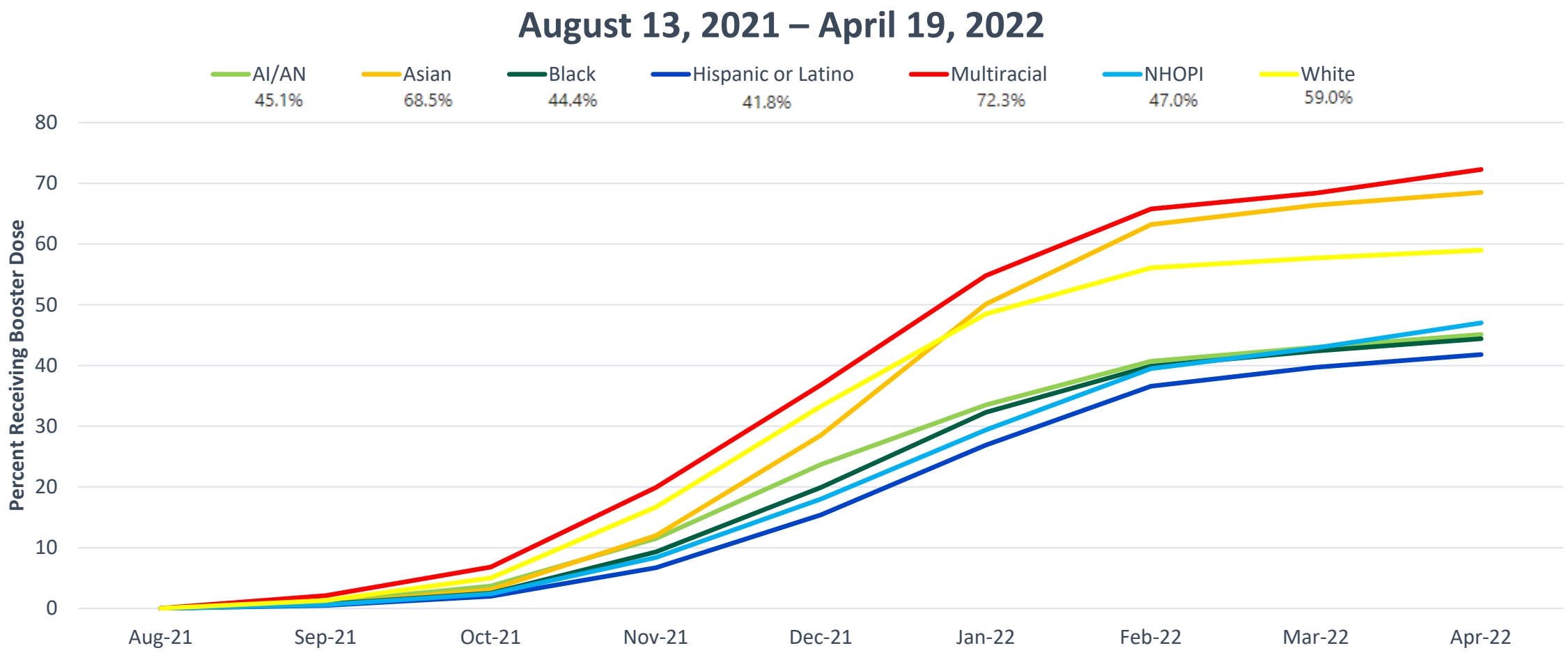
- As of April 19, 2022, approximately **1.1 million** second COVID-19 vaccine booster doses given in adults ages 50–64 years and **3.2 million** second booster doses given in adults ages ≥65 years since authorization

1. SEAN COVID-19 Survey Summary: April 15, 2022. https://www.langerresearch.com/wp-content/uploads/SEAN-COVID-19-Survey-Summary_4-15-22.pdf. Accessed April 15, 2022
2. CDC COVID Data Tracker. Trends in Number of COVID-19 Vaccinations in the US. https://covid.cdc.gov/covid-data-tracker/#vaccination-trends_vacctrends-total-daily. Accessed April 15, 2022
3. Data Source: IZDL All Admin

Evidence to Recommendations Framework

Booster doses of COVID-19 vaccines

Booster vaccination trends by race or ethnicity among fully vaccinated people in the United States



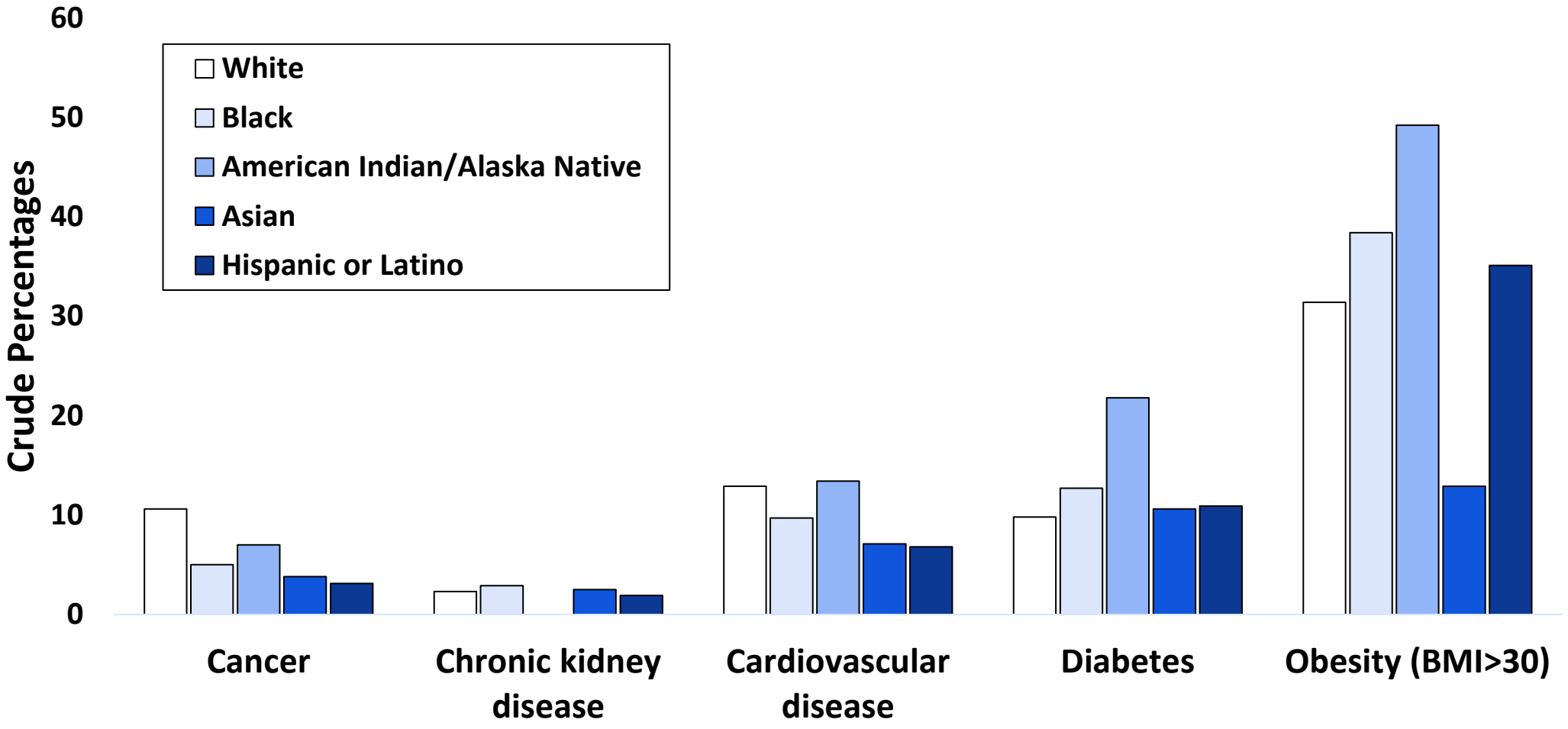
CDC COVID Data Tracker. Trends in Demographic Characteristics of People Receiving COVID-29 Vaccinations in the United States. https://covid.cdc.gov/covid-data-tracker/#vaccination-demographics-trends. Accessed April 19, 2022

Population ages ≥65 years, by race and ethnicity

Race or Ethnicity	Total Population	65 yrs and older
Hispanic or Latino	17.8%	8.0%
Not Hispanic or Latino	82.2%	92.0%
White	61.1%	77.3%
Black	12.3%	8.9%
AI/AN	0.7%	0.5%
Asian	5.4%	4.2%
NH/PI	0.2%	0.1%
Two or more races	2.4%	0.9%

https://www.census.gov/library/publications/2018/acs/acs-38.html

Prevalence of selected underlying conditions that increase risk for severe COVID-19 disease, by race and ethnicity

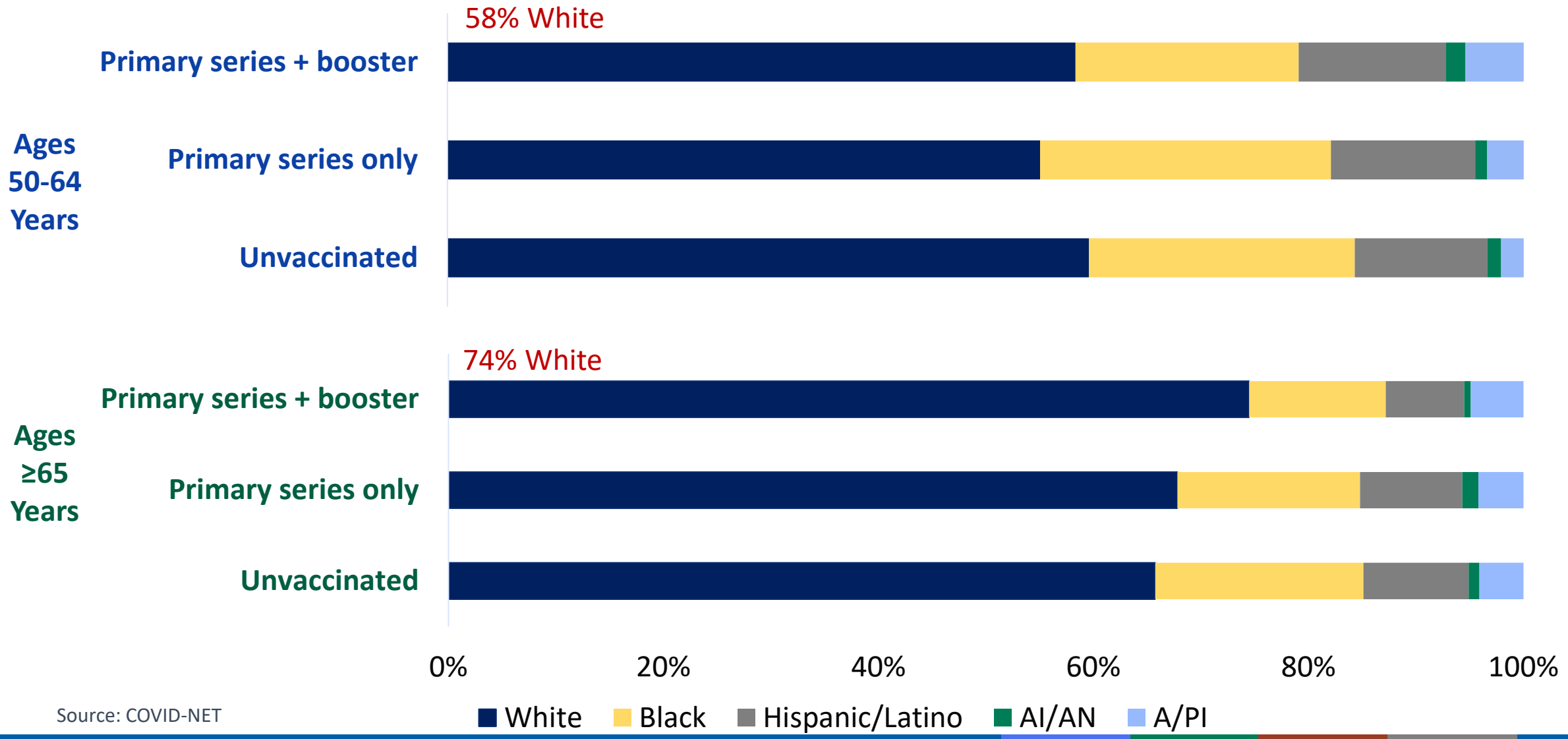


Presented to ACIP September 22, 2020 https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2020-09/COVID-07-Dooling-508.pdf

Source: National Center for Health Statistics, National Health Interview Survey, 2018

Estimates were not available for Hawaiian/other Pacific Islanders or for chronic kidney disease among American Indian/Alaska Native

COVID-19-associated hospitalizations among adults ages 50 years and older by race and ethnicity



Source: COVID-NET

Summary

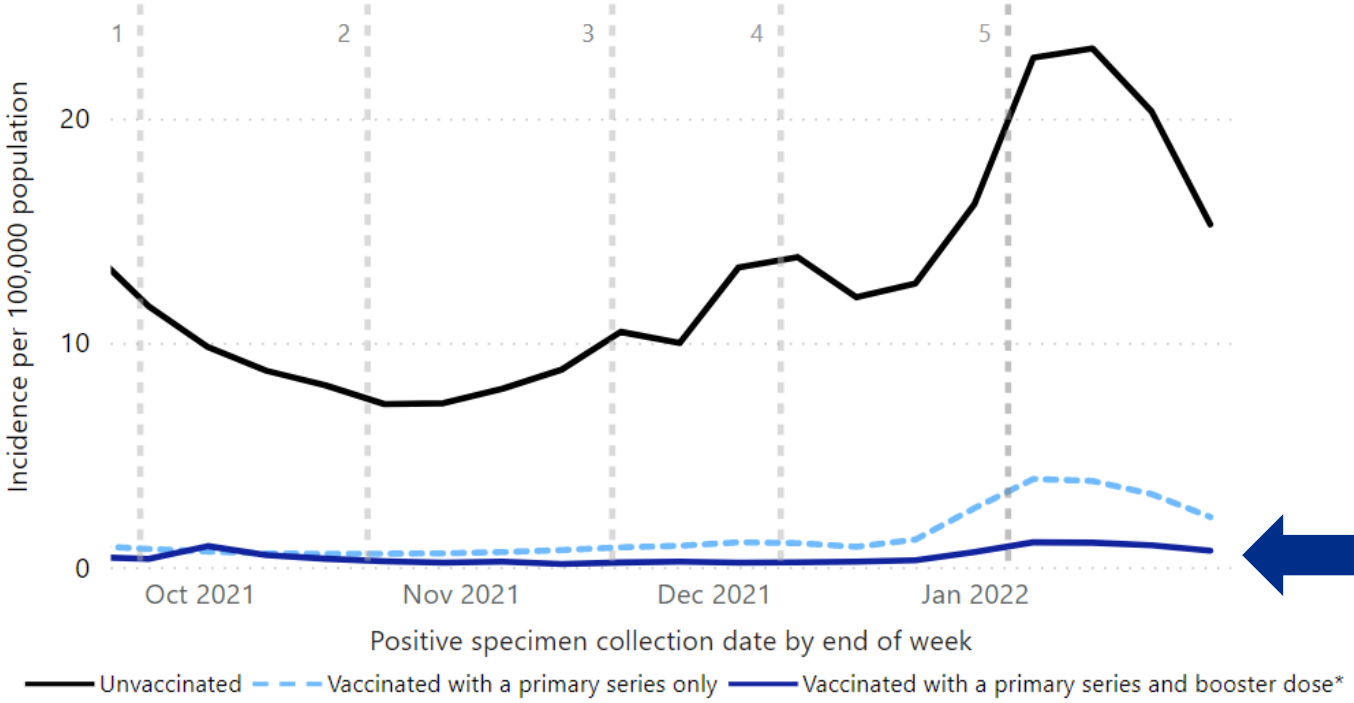
Equity

- Racial and ethnic minority groups are under-represented in the population ages ≥65 years, both overall and among COVID-19-associated hospitalizations
  - COVID-19-associated hospitalizations among adults ages 50-64 years are more consistent with underlying population
- Underlying medical conditions more prevalent in racial and ethnic minority groups
- A second booster recommendation for adults ages ≥50 years may prevent COVID-19 among persons from racial and ethnic minority groups and persons with underlying medical conditions

Summary

Summary

- Top priority remains **vaccination** of **unvaccinated individuals**
  - **Benefits** of COVID-19 vaccine primary series **largest** across all sex and age groups
  - Additional benefits to receiving first COVID-19 booster dose



Current policy question focused on the population with COVID-19 vaccine primary series and booster, with lowest rates of severe disease currently

Age-Adjusted Rates of COVID-19 Deaths by Vaccination Status and Receipt of Booster Dose, September 19 – January 29, 2022 (26 U.S. Jurisdictions) CDC COVID Data Tracker. https://covid.cdc.gov/covid-data-tracker/#rates-by-vaccine-status

Work Group Interpretation

Goals of COVID-19 vaccines:

- Primary goal: Prevention of **severe disease**
- Secondary goals:
  - Maintaining workforce and healthcare capacity
  - Reduce infection rates and risk of transmission
  - Improved mental health with more social interactions
  - Prevention of post-COVID conditions

Work Group Interpretation

Goals of COVID-19 vaccines:

- Primary goal: Prevention of **severe disease**
- Secondary goals:
  - Maintaining workforce and healthcare capacity
  - Reduce infection rates and risk of transmission
  - Improved mental health with more social interactions
  - Prevention of post-COVID conditions
- COVID-19 vaccines continue to offer **high levels** of protection against severe disease- especially for individuals who have received a booster dose
- Vaccines are a critical aspect of protection against severe COVID-19; monoclonal antibodies and antivirals are also essential
- Continued research into vaccines that may also have prolonged protection against SARS-CoV-2 infection (e.g. mucosal vaccines) important

Work Group Interpretation

Adults ages 50 years and older

- The risk of COVID-19 increase with age; a 2nd booster (4th total dose) for older adults can help ensure those at risk are protected from severe disease
- Current VE data shows limited waning for immunocompetent adults after a 3rd dose
- Lower COVID-19 case counts and hospitalization rates currently
- May have recommendations for additional COVID-19 vaccines in the future
- Work Group supported recommendation that adults ages 50 and over may receive a 2nd COVID-19 vaccine booster dose

Work Group Interpretation

Immunocompromised individuals ages 12 years and older

- Earliest eligibility for this 2nd booster (5th dose) would be mid-May, based on timing of previous recommendations
- Currently available VE data from 3rd dose in primary series; no VE data from the currently recommended 1st booster (4th dose)
- Lower COVID-19 case counts and hospitalization rates currently; however, immunocompromised individuals likely remain at higher risk for severe outcomes
- Important that immunocompromised individuals receive **all** doses of primary series (including additional doses) and 1st booster dose
- Work Group supported recommendation that immunocompromised individuals ages 12 and over may receive a 2nd COVID-19 vaccine booster dose

Work Group Interpretation

- Recommendations that individuals **may receive** a COVID-19 vaccine 2nd booster reflect **current conditions** in the pandemic:
  - Wide availability of COVID-19 vaccines
  - High protection against severe disease from primary series and first booster dose
  - Low rates of COVID-19 cases and hospitalizations
  - Use of antivirals and monoclonal antibodies for SARS-CoV-2
- As the 2nd booster is already authorized and available, can rapidly adjust recommendations if COVID-19 epi changes in the future
- Current recommendation allows for **flexibility**, giving patients and providers **access** to this vaccine dose and the ability to decide based on individual factors and timing

Work Group Interpretation

- BREAK FOR CLINICAL CONSIDERATIONS PRESENTATION

Summary

- Additional booster doses of COVID-19 vaccines likely be needed in the future
- Important to **optimize** vaccine recommendations based on current conditions, while maintaining **flexibility** to update recommendations as needed if epidemiology changes

Question to ACIP

- What are the factors that would influence the benefit/risk discussion for patients and providers regarding second booster doses of COVID-19 vaccines?

Acknowledgments

- Megan Wallace
- Monica Godfrey
- Danielle Moulia
- Susan Goldstein
- Mary Chamberland
- Lauren Roper
- Jack Gersten
- Jefferson Jones
- Eddie Shanley
- Stephen Hadler
- Tara Anderson
- Alfonso Hernandez-Romieu
- Adriana Lopez
- Sarah Meyer
- Valerie Morelli
- JoEllen Wolicki
- Elisha Hall
- Tamara Pilishvili
- Ruth Link-Gelles
- Heather Scobie
- VTF ACIP WG Team and CMO
- ACIP COVID-19 Vaccines Work Group
- Vaccine Task Force
- Epi Task Force
- Data Analytics and Visualization Task Force
- Respiratory Viruses Branch