Economic Analysis of Vaccination with mRNA Booster Dose against COVID-19 Among Adults

University of Michigan

COVID-19 Vaccination Modeling Team

Presentation to ACIP
September 12, 2023

SCHOOL OF PUBLIC HEALTH
UNIVERSITY OF MICHIGAN

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Conflict of interest statement

Authors have no known conflicts of interest.

Objectives

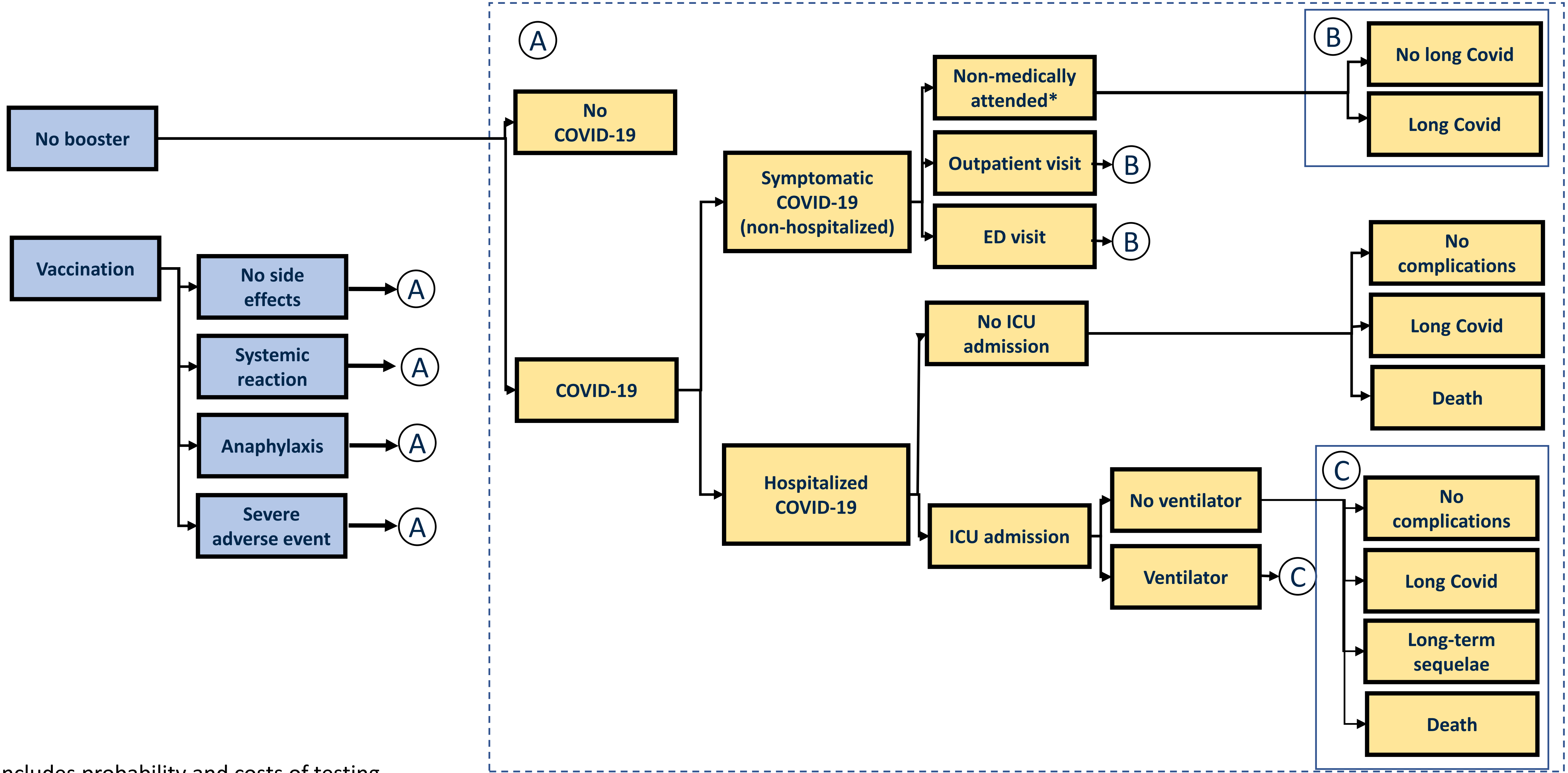
- Estimate annual disease burden and healthcare utilization associated with COVID-19 illness and COVID-19 booster vaccination, including cases of symptomatic illness, hospitalizations, deaths, adverse events, costs, and quality-adjusted life years
- Project cost-effectiveness of an updated mRNA booster against COVID-19-associated illness in persons ages ≥18 years

Methods

- Intervention strategies:
  - Vaccination against COVID-19 illness with an updated “generic” mRNA booster
  - No updated mRNA booster (vaccination against COVID-19 illness with primary series only or primary series plus current booster)
- Target population: all US adults, stratified by age
  - 18-49 y, 50-64 y, 65+ y
  - Pediatric and adolescent age groups excluded from current analysis, insufficient data to incorporate into this first phase analysis
- Time horizon: 1 year*
- Perspective: Societal
- Costing year: 2023$
- Discount rate: 3%

* Costs and QALYs lost due to long-term sequelae and deaths beyond one year are included

Model schematic



*Includes probability and costs of testing
ED= emergency department; ICU= intensive care unit

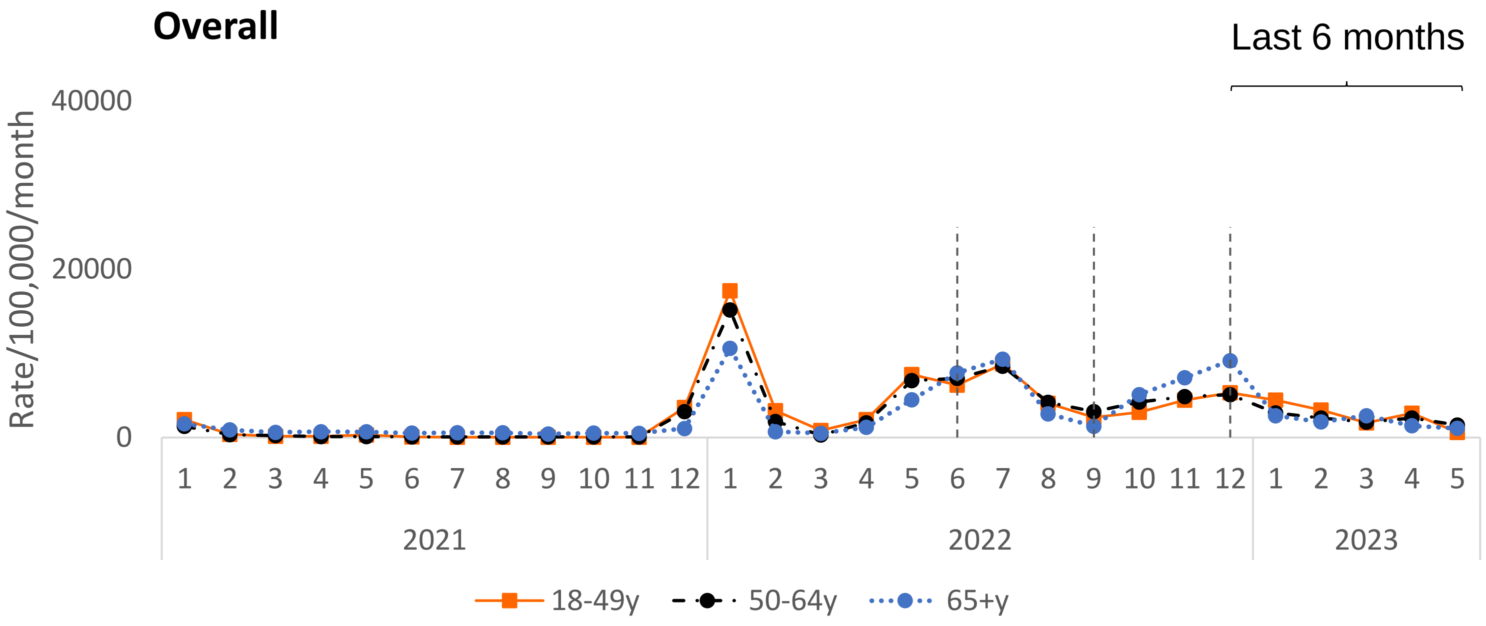
Analysis Plan

- Project health and economic outcomes stratified by intervention strategy and by age subgroups (18-49y, 50-64y, 65+y)
  - Cases
  - Hospitalizations
  - Deaths
  - Costs
  - QALYs
  - Adverse events
- Calculate incremental cost-effectiveness ratios comparing updated mRNA booster to no booster
- Conduct base case and uncertainty analyses (one-way sensitivity and scenario analyses)

****This presentation reports preliminary results from the first phase of an ongoing analysis****

Natural history:
probability of symptomatic infection, outpatient/ED visits, hospitalization, and critical illness

Annual probability of symptomatic infection



Annualized probability based on last 6 months 12/22-5/23	
18-49 y	0.3145
50-64 y	0.2841
65+ y	0.3339

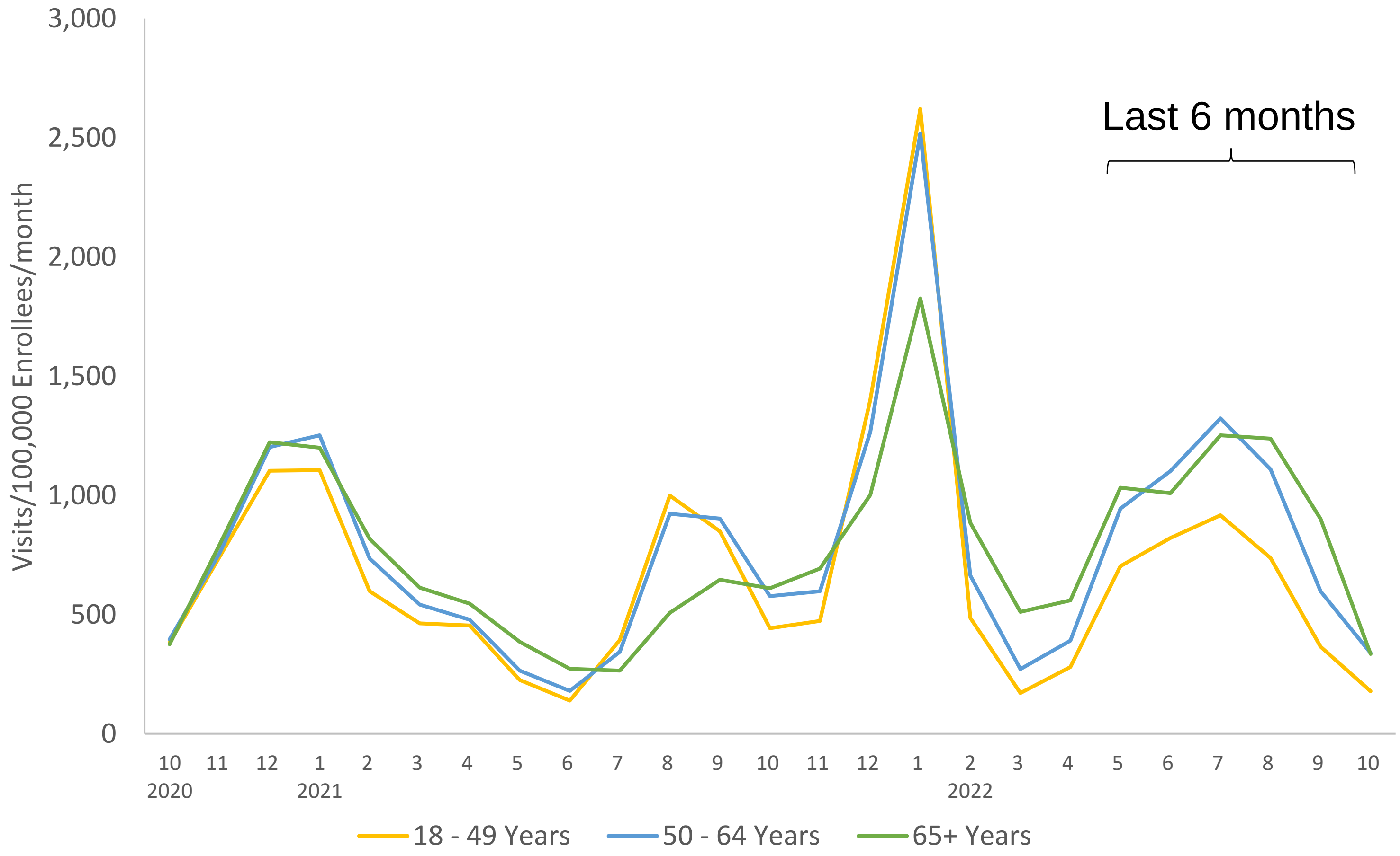
Source: HEROES-RECOVER, unpublished data

Annual probability of symptomatic infection

Annualized probability based on last 6 months 12/22-5/23			
Age group	Base case	Range for sensitivity analysis	
		Low	High
18-49 y	0.3145	0.2858	0.3444
50-64 y	0.2841	0.2438	0.3274
65+ y	0.3339	0.2312	0.4510

Source: HEROES-RECOVER, unpublished data

Probability of an outpatient visit



Annualized Probability based on last 6 months 5/22-10/22			
Age group	Base	Range for sensitivity analysis	
		Low	High
18-49 y	0.075	0.022	0.110
50-64 y	0.106	0.041	0.159
65+ y	0.111	0.040	0.150

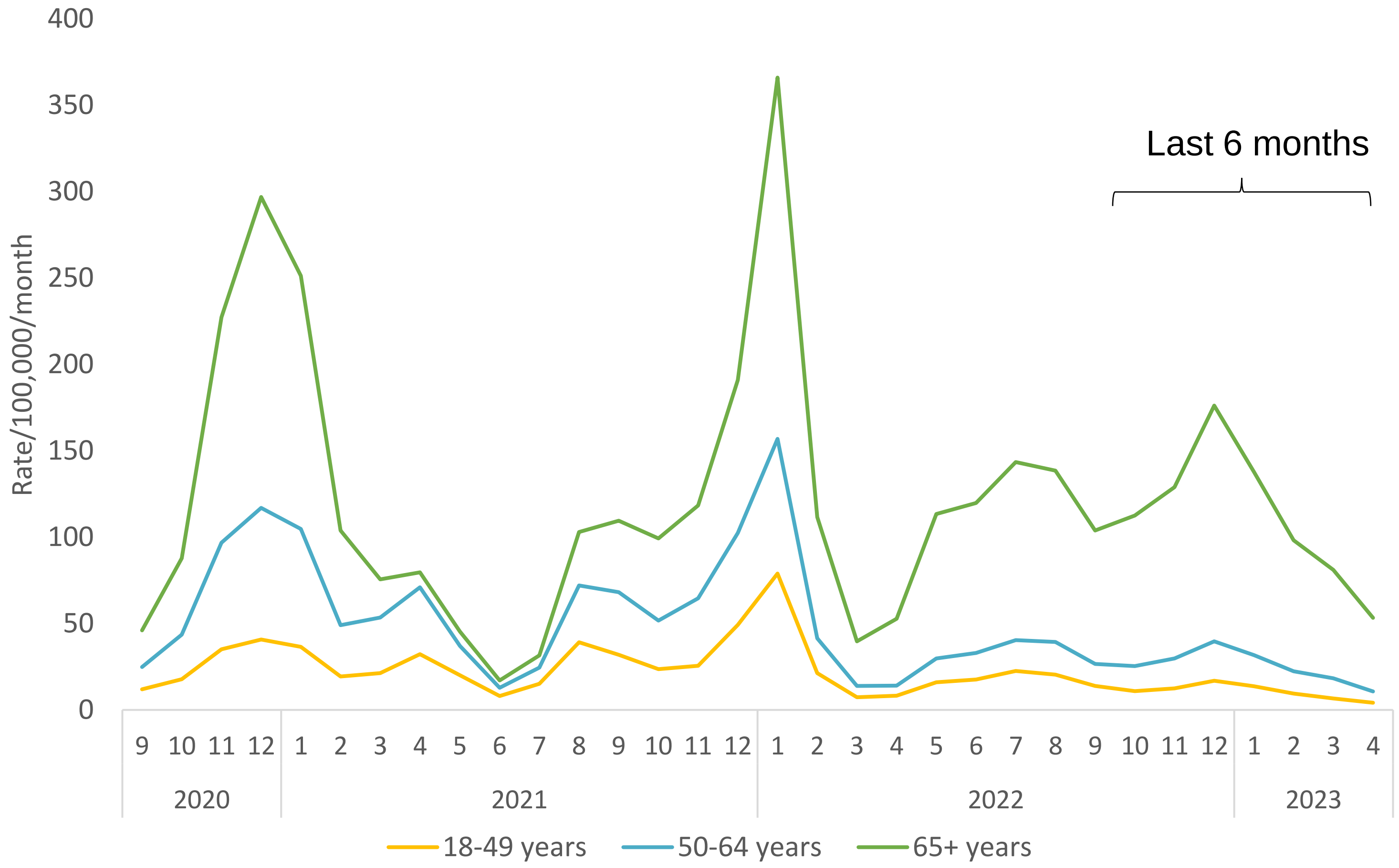
Source: Merative™ MarketScan® Research Database, unpublished data

Probability of outpatient visits and ED visits given symptomatic illness

Age group	Base	Range for sensitivity analysis	
		Low	High
Outpatient visits given symptomatic illness			
18 - 49 y	0.157	0.1483	0.1664
50 - 64 y	0.215	0.1991	0.2335
65+ y	0.244	0.1996	0.3088
Emergency department visits given symptomatic illness			
18 - 49 y	0.0184	0.0172	0.0196
50 - 64 y	0.0191	0.0175	0.0210
65+ y	0.0394	0.0318	0.0505

Source: Derived using probability of an outpatient visit or ED visit from MarketScan data (Merative™ MarketScan® Research Database, unpublished data) and probability of symptomatic illness in the HEROES-RECOVER data, May 2022 - October 2022 (unpublished)

Annual probability of hospitalization



Annualized Probability based on last 6 months 10/22-3/23			
Age group	**Base case**	**Range**	
		Low	**High**
18-49 y	0.00144	0.00080	0.00204
50-64 y	0.00335	0.00216	0.00479
65+ y	0.01453	0.00967	0.02090

Rate/100,000 based on last 6 months 10/22-3/23			
Age group	**Base case per 100,000**	**Range**	
		Low	**High**
18-49 y	144	80	204
50-64 y	335	216	479
65+ y	1453	967	2090

Source: COVID-NET, unpublished data

Probability of critical illness given hospitalization

Probability	Base case	Range for sensitivity analysis (95% CI)	
		Low	High
Probability ICU given hospitalization			
18-49 y	0.123	0.119	0.145
50-64 y	0.200	0.178	0.208
65+ y	0.144	0.138	0.163
Probability ventilator use given ICU			
18-49 y	0.525	0.472	0.577
50-64 y	0.488	0.445	0.532
65+ y	0.386	0.342	0.432

Source: COVID-NET, unpublished data
ICU= intensive care unit

Probability of death given hospitalization

Probability	Base case	Range (95% CI)	
		Low	High
Probability of death given no ICU			
18-49 y	0.006	0.002	0.008
50-64 y	0.009	0.007	0.016
65+ y	0.030	0.022	0.035
Probability of death given ICU without ventilator			
18-49 y	0.024	0.003	0.040
50-64 y	0.047	0.026	0.077
65+ y	0.166	0.144	0.233
Probability of death given ICU with ventilator			
18-49 y	0.284	0.213	0.368
50-64 y	0.379	0.301	0.435
65+ y	0.628	0.476	0.637

Source: COVID-NET, unpublished data
ICU= intensive care unit

Probability of long COVID

Age group	Base case	Range	
		Low	High
18-49 y	0.072	0.058	0.091
50-64 y	0.072	0.058	0.091
65+ y	0.072	0.058	0.091

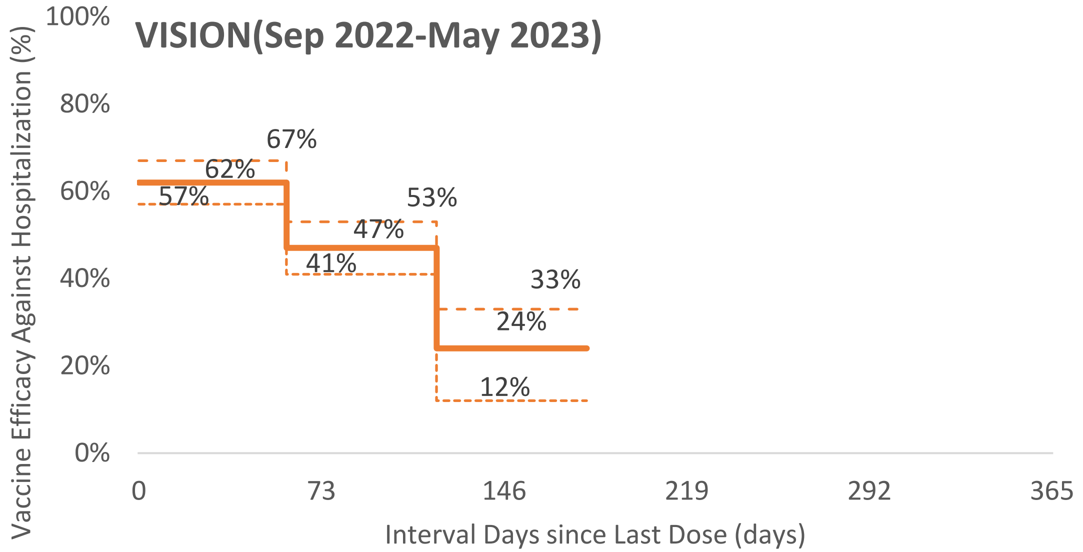
Assumptions:

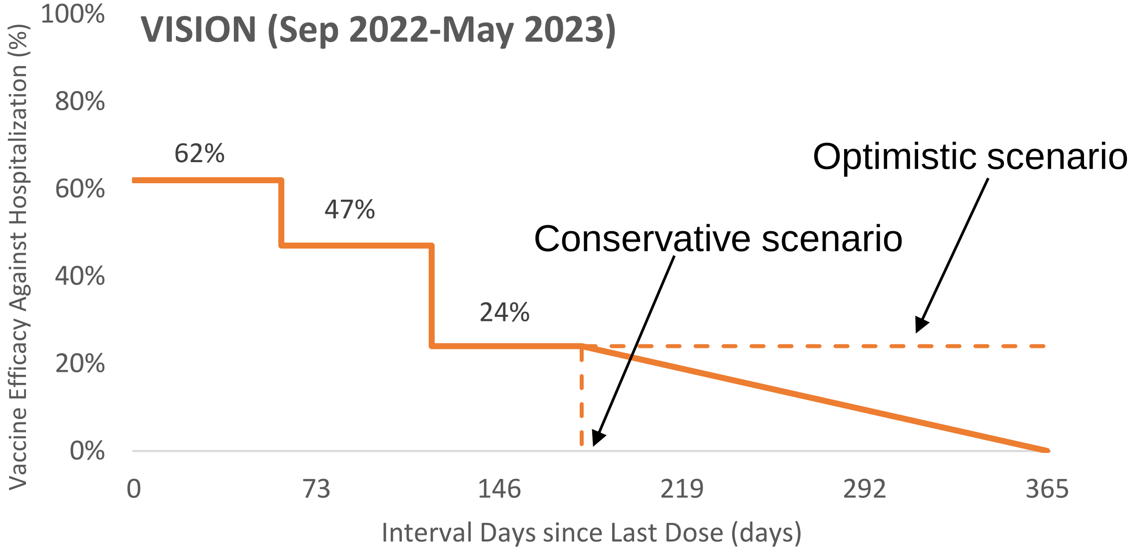
- Derived to reflect 5-month median duration of episode of long covid for individuals who experience symptoms for 3+ months
- Average prevalence of HEENT, constitutional, pulmonary, musculoskeletal, cognitive, and fatigue symptoms at 5 months
- Current estimates do not reflect higher risk associated with age or with severity of illness

Source: Montoy JCC et al. Prevalence of Symptoms ≤12 Months After Acute Illness, by COVID-19 Testing Status Among Adults — United States, December 2020–March 2023. MMWR 2023; 72 (32): 859- 865.

Vaccine effectiveness & adverse events

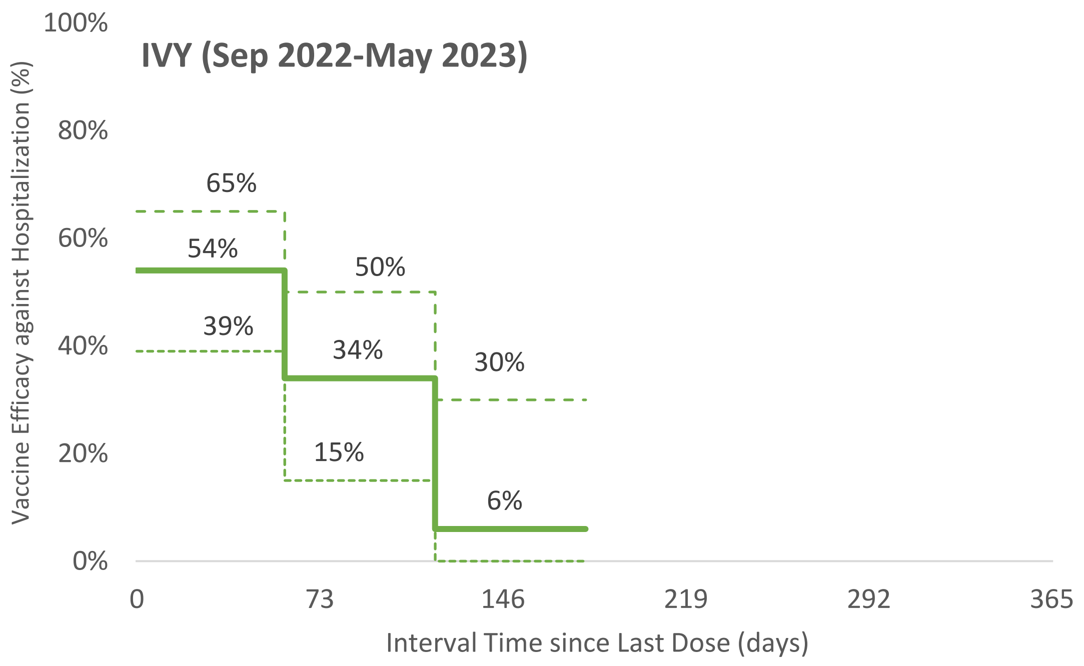
Vaccine effectiveness: hospitalization, 18+ y

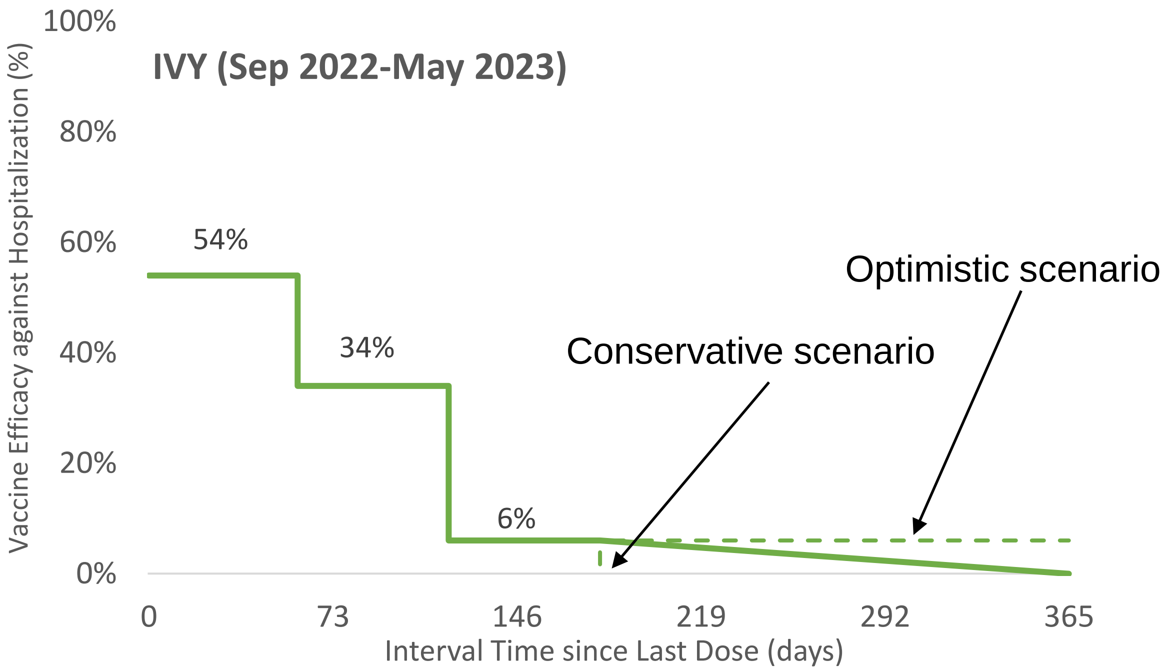




Source: VISION, bivalent booster, Sept 2022- May 2023. Link-Gelles R. Monovalent and bivalent VE against hospitalization among adults aged ≥18 years. Paper presented at: Advisory Committee on Immunization Practices. June 2023

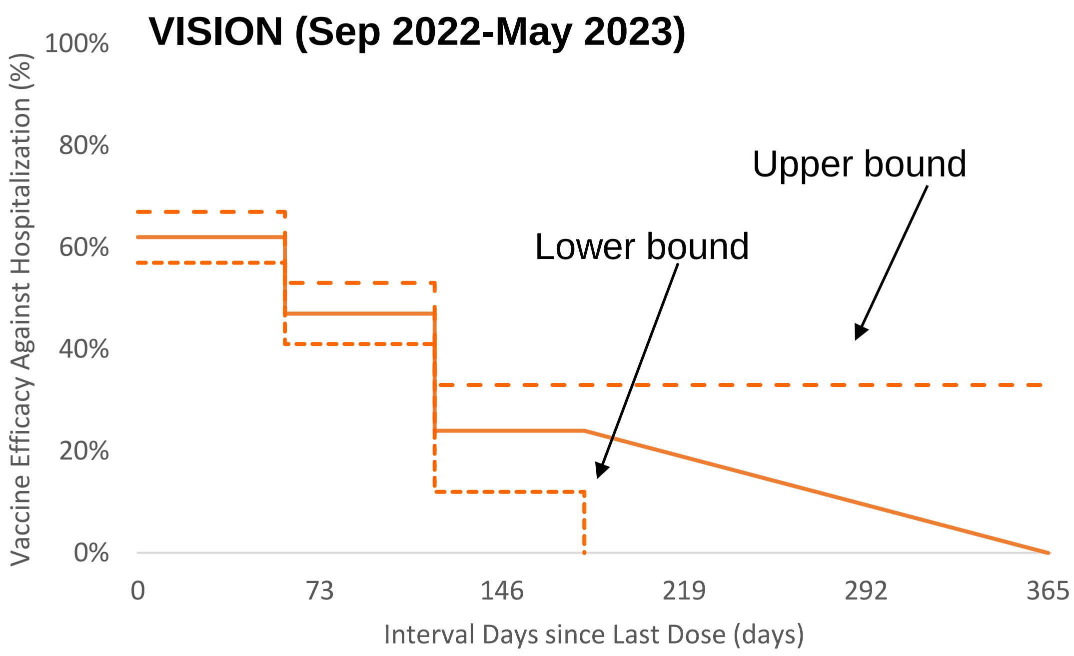
Vaccine effectiveness: hospitalization, 18+ y

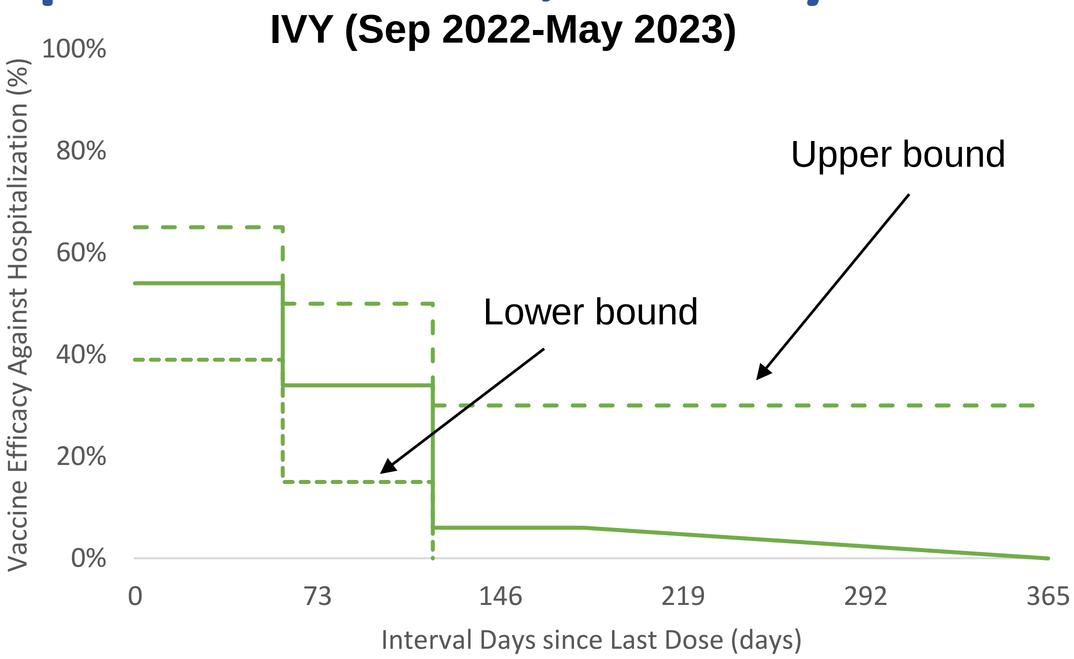


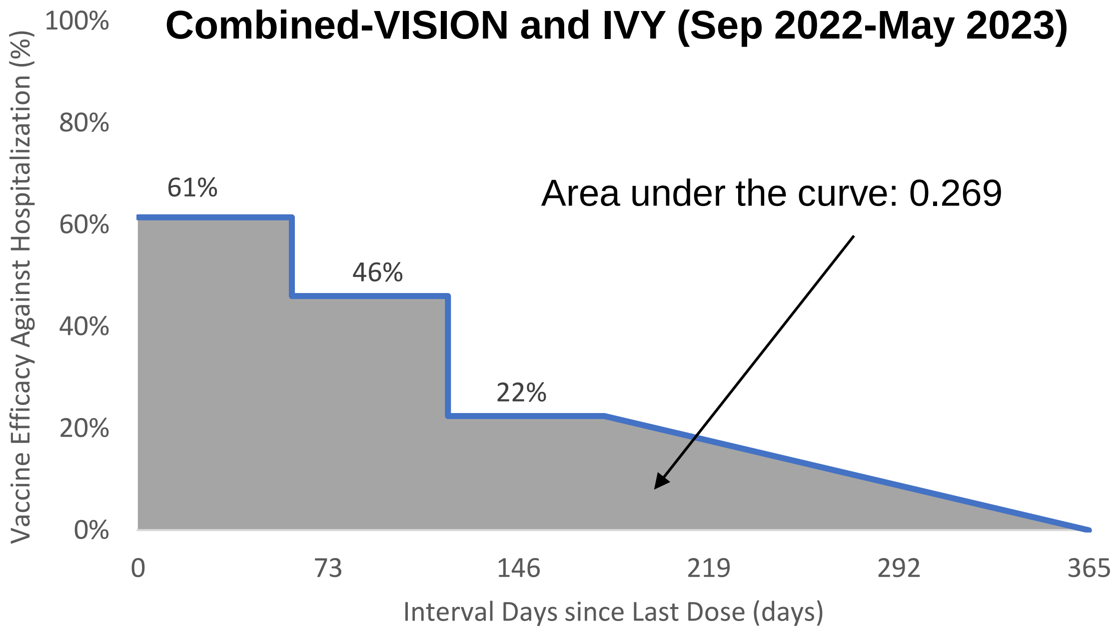


Source: IVY, bivalent booster, Sept 2022- May 2023. Link-Gelles R. Monovalent and bivalent VE against hospitalization among adults aged ≥18 years. Paper presented at: Advisory Committee on Immunization Practices. June 2023

Vaccine effectiveness: hospitalization, 18+ y







Source: VISION and IVY, bivalent vaccination, Sept 2022- May 2023. Link-Gelles R. Monovalent and bivalent VE against hospitalization among adults aged ≥18 years. Paper presented at: Advisory Committee on Immunization Practices. June 2023

Vaccine effectiveness, hospitalization, 18+ y

	Linear waning	Conservative	Optimistic
VISION			
Base case	0.278	0.217	0.339
Lower bound	0.210	0.180	0.240
Upper bound	0.334	0.250	0.418
IVY			
Base case	0.168	0.153	0.183
Lower bound	0.088	0.088	0.088
Upper bound	0.313	0.237	0.389
Base Case*	**0.269**	**0.088**	**0.418**

* Base case includes a weighted average of the area under the vaccine effectiveness (VE) curve with the assumption that VE wanes linearly after 180 days. Ranges were selected by taking the minimum and maximum of the individual dataset VEs, applying a conservative approach (assuming VE drops to 0 at 180 days) for the lower bound and an optimistic approach for the upper bound (assuming VE at 365 days=VE at 180 days)

Summary, vaccine effectiveness

	Base case	Low	High
Symptomatic illness (non-hospitalized)*			
Hospitalization, uncomplicated	0.269	0.088	0.418
Hospitalization, critical illness**	0.403	0.191	0.671
Death	0.403	0.191	0.671

* Non-medically attended illness, illness that includes an outpatient or ED visit
** Intensive care unit with or without mechanical ventilation

Source: VISION and IVY, Link-Gelles R. Monovalent and bivalent VE against hospitalization among adults aged ≥18 years. Paper presented at: Advisory Committee on Immunization Practices. June 2023

Summary, vaccine effectiveness

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Probability of adverse events

	Base case	Range for sensitivity analysis		Source
		Low	High	
Systemic reaction				
18-49 y	0.106	0.073	0.148	1,2
50-64 y	0.106	0.073	0.148	
≥65 y	0.137	0.107	0.171	
Anaphylaxis (all ages)	0.00000495	0.0000032	0.0000074	3
Death given anaphylaxis	0	0	0.00966	Assumption, 4
Myocarditis				
18 - 29 y	0.0000238	0.0000085	0.0000838	5
30-39 y	0.0000087	0.0000008	0.0000375	5
40+ y	0	0	0	Assumption
Death given myocarditis	0.0005	0	0.001	Expert opinion

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4. Su JR, Moro PL, Ng CS, Lewis PW, Said MA, Cano MV. Anaphylaxis after vaccination reported to the Vaccine Adverse Event Reporting System, 1990-2016. *J Allergy Clin Immunol.* 2019;143(4):1465-1473.
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Costs: Direct medical costs and productivity losses

Direct medical costs

Variable	Base case	Range for sensitivity analysis		Source
		Low	High	
Testing				
Test cost	$8	$8	$62	1,2
Probability of testing	0.05	0.02	0.20	3
Recipient time (hours)	0.50	0.25	1.50	Assumption
Outpatient visit				
18-49 y	$372	$370	$375	4
50-64 y	$380	$377	$384	
65+ y	$391	$386	$396	
Long Covid	$1091	$1018	$1165	5

1. Justin Lo CC, Krutika Amin, Imani Telesford, Lindsey Dawson, and Jennifer Kates. Prices for COVID-19 testing. 2023; https://www.healthsystemtracker.org/brief/prices-for-covid-19-testing/#Prices%20for%20COVID-19%20tests%20in%20the%20outpatient%20setting,%20among%20people%20with%20large%20employer%20health%20coverage,%202021.
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5. Pike J et al. Direct Medical Costs Associated With Post–COVID-19 Conditions Among Privately Insured Children and Adults. Prev Chronic Dis. 2023;20 (6)

Direct medical costs, cont.

Variable	Base case	Range for Sensitivity Analysis	
		Low	High
Hospitalization episode			
18-49 y	$32,514	$28,505	$36,523
50-64 y	$32,854	$31,450	$34,258
65+ y	$20,648	$20,295	$21,000
ICU episode (no ventilator)			
18-49 y	$37,159	$30,116	$44,203
50-64 y	$46,727	$40,269	$53,186
65+ y	$23,220	$22,408	$24,032
ICU (with ventilator) episode			
18-49 y	$245,432	$168,362	$322,503
50-64 y	$169,189	$140,250	$198,129
65+ y	$55,257	$50,705	$59,809

Source: Merative™ MarketScan® Research Database, unpublished data

ICU= Intensive care unit

Medication costs

Variable	Base case	Range for Sensitivity Analysis		Source
		Low	High	
Over the counter medication*	$4.12	-	-	1
Probability of nirmatrelvir-r prescription given an outpatient visit				
18-49 years	0.1751	0.10	0.30	2,3, Assumption
50-64 years	0.2696	0.10	0.50	
65+ years	0.2739	0.10	0.50	
Cost, nirmatrelvir-r	$530	$530	$1200	4, 5

*5 days of generic cold/flu medicine

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2. HealthVerity, Inc. COVID-19 database licensed by CDC, unpublished data
3. Merative™ MarketScan® Research Database, unpublished data
4. Recht H. Paxlovid Has Been Free So Far. Next Year, Sticker Shock Awaits. 2022; https://kffhealthnews.org/news/article/paxlovid-covid-sticker-shock-insurance/#:~:text=The%20U.S.%20government%20has%20so,in%20a%20July%20earnings%20call.
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Vaccine receipt, costs

Variable	Base case	Range for Sensitivity Analysis		Source
		Low	High	
mRNA monovalent booster, per dose*	$120	$30	$200	1, expert opinion
Administration, per dose**	$20.33	$18.07	$26.58	2
Vaccination setting				
Proportion, pharmacy	0.644	0.625	0.663	3
Proportion, physician office visit	0.256	0.221	0.294	3
Proportion, mass vaccination	0.100	0.075	0.155	3
Recipient time by vaccination setting (hours)				
Pharmacy	0.25	0.083	0.50	4, expert opinion
Physician office	1.19	0.17	2	4
Mass vaccination	0.195	0	0.390	4
Mean hourly earnings	$33.74	$23.98	$50.16	5

*Lower bound reflects current price of COVID-19 boosters

**CPT 90471

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3. CDC national survey data, 2/10/23-5/1/23, unpublished
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Vaccination-associated adverse events, costs

Variable	Base case	Range for Sensitivity Analysis		Source
		Low	High	
Systemic reaction				
Physician visit	$90.82	$82.72	$115.84	1
Productivity loss (days)	1	-	-	Assumption
Anaphylaxis				
Hospitalization	$5035			2*
Productivity loss (days)	1	1	3	3
Myocarditis/pericarditis				
Hospitalization	$75,927			4**
Productivity loss (days)	4	0	14	5, 6, Expert opinion

* HCUP-NIS 2012 estimates (mean LOS = 4.9 days) adjusted to 1 days LOS

** HCUP-NIS 2014 estimates (mean LOS = 7.4 days) adjusted to 4 days LOS

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Quality adjustments

QALY losses, COVID-19 illness

Variable	Base Case	Range for Sensitivity Analysis		QALDs lost
		Low	High	
Symptomatic illness*	0.006	0.004	0.008	2.2 (1.5 - 2.9)
Hospitalization	0.027	-	-	9.9
Critical illness**	0.054	-	-	19.7
Long COVID	0.067	0.038	0.088	24.3 (13.7 - 31.9)

* Non-medically attended and outpatient illness

** Intensive care unit with mechanical ventilation. Derived by applying the ratio of ICU to hospitalization QALY loss (2x) to the hospitalization QALY loss from SARS CoV-2 EQ5D Study. The model also includes a health state for ICU care without ventilator use for which QALY loss is interpolated using QALY loss for hospitalization and critical illness

Source: Coronavirus Household Evaluation and Respiratory Testing (C-HEaRT) and Prospective Assessment of COIVD-19 in a Community (PACC), unpublished data

QALY loss, vaccination-associated AEs

Variable	Base Case	Range for Sensitivity Analysis		QALDs lost	Source
		Low	High		
Systemic reaction (QALY loss)*					
All ages	0.0004	0.0003	0.0005	0.15 (0.11 - 0.18)	Assumption
Anaphylaxis (QALY loss)					
All ages	0.0137	0.0135	0.0139	5.0 (0.93 - 5.08)	1
Myocarditis/pericarditis (QALY loss)					
Acute illness**	0.010	0.0086	0.0112	3.65 (3.14 - 4.09)	2

* QALY loss equal to one day of COVID-19 illness
** Derived from health utility for COVID-19 related myocarditis. Assumed 2-week illness
QALY= Quality-adjusted life year; QALD= Quality-adjusted life day

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Results

preliminary estimates

Disaggregated results, per 100,000
preliminary estimates

Age group	Strategy	Cases				Cases Averted			
		Cases	Hosp	ICU	Deaths	Cases	Hosp	ICU	Deaths
18-49 y	No booster	31,450	144	17.7	3.6	-	-	-	-
	Booster dose	22,990	105	10.6	2.2	8,460	39	7.1	1.4
50-64y	No booster	28,410	335	67.1	16.4	-	-	-	-
	Booster dose	20,768	245	40.0	9.9	7,642	90	27.0	6.6
65+ y	No booster	33,390	1,453	209.3	109.4	-	-	-	-
	Booster dose	24,408	1,062	124.9	66.0	8,982	391	84.3	43.4

Incremental cost-effectiveness ratios, societal perspective, per 1000 *preliminary estimates*

Age group	Strategy	Projected Costs	Incremental Costs	Projected QALYs	Incremental QALYs	$/QALY
18-49 y	No booster	$192,335	-	20207.0670	-	**-**
	Booster vaccination	$293,503	$101,168	20207.9423	0.8752	**$115,588**
50-64y	No booster	$385,752	-	12275.8345	-	**-**
	Booster vaccination	$421,249	$35,498	12277.2111	1.3766	**$25,787**
65+ y	No booster	$642,488	-	6519.9466	-	**-**
	Booster vaccination	$598,857	-$43,630	6523.5511	3.6046	**Cost-saving**

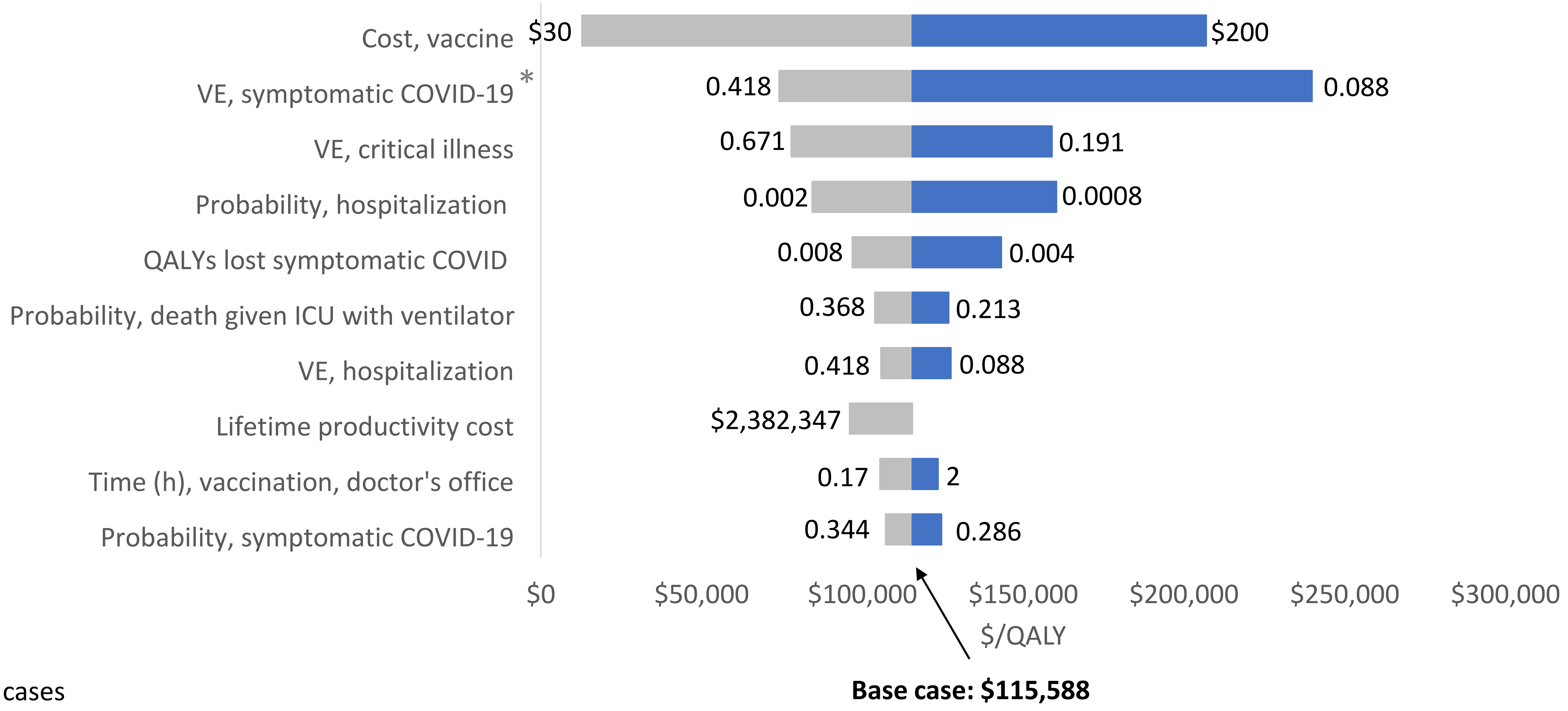
QALY= quality-adjusted life year

Incremental cost-effectiveness ratios, societal perspective, per 1000 *preliminary estimates, w/pooled 18+*

Age group	Booster Dose, $/QALY
18-49 y	$115,588
50-64 y	$25,787
65+ y	Cost-saving
18+ y	**$33,437**

QALY= quality-adjusted life year

One way sensitivity analyses, 18-49 y *preliminary estimates*



*Non-hospitalized cases
Note: Numbers next to bars indicate input values for sensitivity analysis
VE=vaccine effectiveness; QALY=Quality-adjusted life year

VE scenario analyses
preliminary estimates

	Base case	Scenario 1	Scenario 2	Scenario 4	Scenario 5
VE inputs					
Symptomatic illness	**0.269**	0.088	0.418	0.269	0.403
Hospitalization, uncomplicated	**0.269**	0.088	0.418	0.269	0.403
Hospitalization, critical illness	**0.403**	0.191	0.671	0.269	0.403
Death	**0.403**	0.191	0.671	0.269	0.403
$/QALY					
18-49 y	**$115,588**	$435,886	$45,376	$141,155	$70,928
50-64 y	**$25,787**	$199,830	Cost-saving	$51,792	$3,001
65+ y	**Cost-saving**	$51,782	Cost-saving	Cost-saving	Cost-saving

VE= vaccine effectiveness; QALY= quality-adjusted life year

Scenario analyses: probability of symptomatic illness, non-hospitalized* *preliminary estimates*

Age group	Base case	0.1	0.2	0.3	0.4	0.5
18-49 y	$115,588	$229,724	$160,000	$120,013	$94,082	$75,905
50-64 y	$25,787	$48,937	$34,724	$24,324	$16,384	$10,123
65+ y	Cost-saving	Cost-saving	Cost-saving	Cost-saving	Cost-saving	Cost-saving

QALY=Quality-adjusted life year
*One-way sensitivity analysis of non-hospitalized symptomatic illness varied separately from hospitalization and critical illness; base case probability of symptomatic illness: 18-49 y, 0.3145; 50-64 y, 0.2841; 65+ y, 0.3339

Scenario analysis: probability of hospitalization *preliminary estimates*

Age group	Base case*	2x base case	3x base case	4x base case
18-49 y	$115,588	$51,978	$14,541	Cost-saving
50-64 y	$25,787	Cost-saving	Cost-saving	Cost-saving
65+ y	Cost-saving	Cost-saving	Cost-saving	Cost-saving

QALY=Quality-adjusted life year

*Base case probability of hospitalization 18-49 y- 0.00144; 50-64 y-0.00335; 65+ - 0.01453

Scenario analysis: probability of critical care *preliminary estimates*

Age group	Probability of ICU given hospitalization			
	Base case*	**2x**	**3x**	**4x**
18-49 y	$115,588	$71,487	$42,307	$21,570
50-64 y	$25,787	Cost-saving	Cost-saving	Cost-saving
65+ y	Cost-saving	Cost-saving	Cost-saving	Cost-saving

QALY=Quality-adjusted life year; ICU= Intensive care unit

* Base case probability of ICU given hospitalization: 18-49 y- 0.123; 50-64 y- 0.200, 65+ y- 0.144

Scenario analysis: vaccine setting *preliminary estimates*

Age group	Base case*	100% pharmacy	100% physician office	100% mass vaccination
18-49 y	$115,588	$106,523	$142,759	$104,403
50-64 y	$25,787	$20,024	$43,063	$18,676
65+ y	Cost-saving	Cost-saving	Cost-saving	Cost-saving

QALY=Quality-adjusted life year

* Base case: Physician office visit- 0.256, Pharmacy- 0.644, Mass vaccination- 0.100

Limitations

- Unpublished data used to derive key parameters in the model: vaccine effectiveness, symptomatic illness, probabilities of hospitalization and critical illness
- Data sources vary in representativeness, generalizability
- VE estimates derived from data on bivalent booster
- Hospitalization rates may overestimate cases due to COVID-19 for younger age groups
- MarketScan data for ages 65+ only includes those with supplemental insurance
- Evidence base for long covid is especially scarce – future analyses will incorporate adjustments to reflect differences in probability and duration of long covid by age and severity of illness
- Cost estimates for long covid may not reflect current practice patterns or rates of HC utilization

Summary - *preliminary estimates*

- Vaccination averts substantial morbidity and mortality as demonstrated through estimated disaggregated outcomes
- ICERs for 50-64y and 65+ age groups are robust to changes in parameter inputs across plausible ranges in all but one scenario (<$51,800 or cost-saving)
- ICERs for 18-49y are sensitive to changes in parameter inputs; more favorable for higher VE, higher risk of hospitalization and critical illness