Supplementary materials

Clinical impact and cost-effectiveness of updated 2023/24 COVID-19 mRNA vaccination in high-risk populations in the United States

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Table S1. Population size by condition and age group

Age, y	CLD	DM	CVD	IC	CKD
18-29	1,520,407	1,617,426	370,602	729,647	114,131
30-39	1,285,417	1,367,440	546,976	616,874	96,491
40-49	1,182,300	3,653,659	1,003,115	1,006,191	88,751
50-64	11,904,738	9,376,977	4,669,876	2,922,188	885,617
65-74	12,573,728	7,920,487	4,641,925	1,178,233	1,497,944
75-84	6,121,910	3,856,335	3,824,726	442,810	729,320
≥85	2,415,331	1,521,474	1,509,003	139,998	287,745
Total	**37,003,832**	**29,313,799**	**16,566,223**	**7,035,940**	**3,700,000**

CKD: chronic kidney disease; **CLD:** chronic lung disease; **CVD:** cardiovascular disease; **DM:** diabetes mellitus; **IC:** immune-compromised; **y:** year

Table S2. COVID-19 predicted incidence rates 2023-2024 (general population)

Age group	Sep 23	Oct 23	Nov 23	Dec 23	Jan 24	Feb 24	Mar 24	Apr 24	May 24	Jun 24	Jul 24	Aug 24
Base case incidence rates												
18-29y	1.88	2.56	3.05	3.40	3.11	2.31	1.80	1.22	0.88	0.62	0.50	0.43
30-39y	1.88	2.57	3.08	3.46	3.18	2.37	1.84	1.24	0.89	0.62	0.49	0.42
40-49y	1.82	2.49	3.00	3.38	3.12	2.34	1.82	1.22	0.88	0.61	0.48	0.41
50-64y	1.45	2.01	2.47	2.86	2.71	2.07	1.62	1.08	0.77	0.52	0.40	0.33
65-74y	0.86	1.22	1.53	1.84	1.82	1.43	1.14	0.76	0.53	0.35	0.27	0.22
75-84y	0.62	0.89	1.13	1.36	1.36	1.08	0.86	0.58	0.40	0.27	0.20	0.16
≥85y	0.58	0.82	1.04	1.25	1.25	0.99	0.79	0.53	0.37	0.24	0.18	0.15
Scenario: Low incidence												
18-29y	1.85	2.19	2.14	1.95	1.54	1.08	0.84	0.58	0.43	0.30	0.23	0.18
30-39y	1.91	2.27	2.21	2.02	1.60	1.12	0.87	0.60	0.43	0.30	0.23	0.18
40-49y	1.88	2.25	2.22	2.03	1.62	1.14	0.88	0.60	0.44	0.30	0.23	0.18
50-64y	1.67	2.06	2.08	1.96	1.59	1.13	0.87	0.59	0.42	0.28	0.21	0.16
65-74y	1.15	1.47	1.54	1.51	1.27	0.91	0.71	0.48	0.33	0.22	0.16	0.12
75-84y	0.87	1.12	1.19	1.18	1.00	0.72	0.56	0.38	0.27	0.18	0.13	0.10
≥85y	0.80	1.03	1.09	1.08	0.91	0.66	0.51	0.35	0.24	0.16	0.12	0.09
Scenario: High incidence												
18-29y	2.65	3.76	4.62	5.19	4.70	3.48	2.74	1.92	1.48	1.12	0.98	0.93
30-39y	2.57	3.68	4.57	5.20	4.76	3.53	2.78	1.94	1.48	1.11	0.96	0.90
40-49y	2.44	3.49	4.35	4.97	4.57	3.41	2.68	1.87	1.42	1.07	0.92	0.86
50-64y	1.76	2.56	3.26	3.83	3.62	2.75	2.18	1.50	1.13	0.83	0.70	0.64
65-74y	0.90	1.33	1.74	2.12	2.09	1.64	1.31	0.90	0.66	0.48	0.39	0.35
75-84y	0.63	0.93	1.22	1.50	1.49	1.17	0.94	0.65	0.48	0.34	0.28	0.25
≥85y	0.58	0.86	1.13	1.38	1.37	1.07	0.86	0.59	0.44	0.31	0.26	0.23

y: year

The rate of hospitalization given symptomatic COVID-19 infection in the unvaccinated general population (10.54% for adults) was based on claims data [1] and adjusted for high-risk groups by applying a risk ratio (RR) based on hazard ratios (HRs) from data on disease burden in patients with medical conditions [2]. The RRs were estimated as an optimal minimax transformation of HRs [3] (**Table S3**).

For CKD, CLD, CVD and DM patients, the distribution by in-hospital level of care (no ICU or ventilator; ICU only; ventilator) was derived from the CDC COVID-NET hospitalizations tracker in the season 2023-2024 [4]. For patients aged 65 years and older, these estimates were then redistributed by the model age groups, using data provided in CDC Morbidity and Mortality Weekly Report (MMWR) [5]. Due to the lack of condition-specific data, the general population estimates were assumed to be applicable for these populations. The distribution for the IC population was estimated by applying a RR to general population CDC data [4, 5]. The RR for ICU admission (RR of 1.30) was derived by converting the reported OR of 1.40 [6]. The same RR was assumed for the increased risk of ventilator use in IC patients (**Table S3**).

For CVD, DM and IC patients, in-hospital mortality was estimated by applying an RR to the general population mortality due to COVID-19 [4]: RR of 1.23 for DM [7]; RR of 1.62 for CVD [8] ; and RR of 1.74 for IC [6]. For CKD and CLD patients, in-hospital mortality rates were informed by data reported for the general population [4], in line with previous studies [9, 10]. In-hospital mortality for the general population was derived from the CDC COVID-NET hospitalizations tracker in the season 2023-2024 [4]. For patients 65 years and older, these estimates were then redistributed by the model age groups, using CDC data [5] (**Table S3**).

The risk of hospital re-admission by location of care was estimated by applying a RR to general population data [11, 12], with RRs based on converting ORs (**Table S3**).

The risk of post discharge mortality was based on previous estimates from a US economic analysis of COVID-19 [12], due to the lack of data in high-risk patients, and assumed to be the same for ICU only and ventilator (**Table S3**).

Following symptomatic infection, there is an age-dependent risk of myocarditis. A portion of infections are treated in hospital, and the risk of this more severe type of COVID-19 increases with age. Data were from the general population (**Table S4**).

Table S3. Hospitalization rates by high-risk population

	Base case	Scenario: LB for hospitalization rate	Scenario: UB for hospitalization rate
Hospitalization rates, given infection (%)			
All ages, CLD	14.90%	14.56%	28.06%

All ages, DM	19.05%	18.70%	28.82%
All ages, CVD	16.19%	15.72%	33.46%
All ages, IC	12.58%	12.13%	29.31%
All ages, CKD	19.8%	18.5%	49.4%
In-hospital level of care, by age (%) – other reports (general population)			
	No ICU or ventilator	**ICU only**	**Ventilator**
18-49y	80.04%	14.89%	5.07%
50-64y	71.74%	18.83%	9.43%
65-74y	68.24%	21.50%	10.26%
75-84y	84.50%	8.86%	6.64%
≥85y	74.84%	17.50%	7.66%
In-hospital level of care, by age (%) – IC report			
	No ICU or ventilator	**ICU only**	**Ventilator**
18-49y	74.24%	19.21%	6.54%
50-64y	63.53%	24.30%	12.17%
65-74y	59.02%	27.74%	13.24%
75-84y	80.00%	11.43%	8.57%
85+y	67.53%	22.59%	9.88%

Age group	**In-hospital outcomes**				
In-hospital mortality, by age (%), any level of care,					
	CLD (=general population)	**DM**	**CVD**	**IC**	**CKD**
18-49y	1.34%	1.61%	2.09%	2.28%	2.10%
50-64y	5.86%	7.04%	9.14%	9.98%	4.00%
65-74y	9.35%	11.23%	14.59%	15.92%	6.40%
75-84y	7.25%	8.70%	11.31%	12.34%	4.90%
≥85y	7.08%	8.51%	11.05%	12.06%	4.10%
Hospital re-admission rate, by location of care					
	No ICU or ventilator	**ICU only**	**Ventilator**		
All ages, CLD	4.03%	3.86%	2.09%		
All ages, DM	4.65%	4.46%	2.41%		
All ages, CVD	5.08%	4.87%	2.63%		
All ages, IC	4.31%	4.13%	2.24%		
All ages, CKD	8.70%	8.70%	8.70%		
Post discharge mortality, by location of care (%), general population					
	No ICU or ventilator	**ICU only**	**Ventilator**		
All ages	5.36%	10.40%	10.40%		

CKD: chronic kidney disease; **CLD:** chronic lung disease; **CVD:** cardiovascular disease; **DM:** diabetes mellitus; **IC:** immune-compromised; **LB/UB:** lower bound/ upper bound; **y:** year

Table S4. Long COVID and myocarditis (infection-related), general population (and CKD population)

Age group	Proportion with any long COVID	Proportion with severe long COVID (of those with long COVID)	% experiencing myocarditis (infection-related)
18-29y	26.90%	6.9% (13.9% CKD)	0.08%
30-39y	31.70%	6.9% (13.9% CKD)	0.07%
40-49y	32.60%	6.9% (13.9% CKD)	0.09%
50-64y	32.30%	6.9% (13.9% CKD)	0.14%
65-74y	28.00%	6.9% (13.9% CKD)	0.16%
75-84y	22.70%	6.9% (13.9% CKD)	0.21%
≥85y	18.50%	6.9% (13.9% CKD)	0.21%

y: year

Table S5. Direct healthcare costs and indirect costs

Model parameter	Base case	Scenario: LB hospitalization cost	Scenario: UB hospitalization cost	Scenario: Alternative post-infection cost
Vaccination costs				
Spikevax vaccine cost*	$129.50	base case	base case	base case
Comirnaty vaccine cost*	$129.00	base case	base case	base case
Administration cost*	$20.33	base case	base case	base case
Short-term infection: not hospitalized				
Proportion not hospitalized who seek outpatient care*	41.00%	base case	base case	base case
Cost of acute outpatient care*	$460.57	base case	base case	base case
Short-term infection: hospitalized				
No ICU or ventilation *	$15,089.00	$11,316.75	$18,861.25	base case
ICU only *	$27,058.00	$20,293.50	$33,822.50	base case
Ventilator *	$71,367.00	$53,525.25	$89,208.75	base case
Cost of inpatient follow-up (per case)*	$1,075.22	base case	base case	base case
DM -No ICU or ventilation *	$16,150.78	$12,113.08	$20,188.47	base case
DM - ICU only *	$28,962.01	$21,721.50	$36,202.51	base case
DM - Ventilator *	$76,388.92	$57,291.69	$95,486.15	base case
CVD -No ICU or ventilation *	$16,632.48	$12,474.36	$20,790.60	base case
CVD - ICU only *	$29,825.81	$22,369.36	$37,282.26	base case
CVD - Ventilator *	$78,667.26	$59,000.44	$98,334.07	base case
IC -No ICU or ventilation *	$18,734.79	$14,051.09	$23,418.49	base case
IC - ICU only *	$33,595.73	$25,196.80	$41,994.66	base case
IC - Ventilator *	$88,610.63	$66,457.97	$110,763.29	base case
CKD -No ICU or ventilation *	$24,572.75	$18,429.56	$30,715.94	base case
CKD - ICU only *	$44,064.52	$33,048.39	$55,080.65	base case
CKD - Ventilator *	$116,222.65	$87,166.98	$145,278.31	base case
Other costs				
Post-infection, not hospitalized (18-64 years)***	$3,262.00	base case	base case	$504.00
Post-infection, not hospitalized (≥ 65 years)***	$6,930.00	base case	base case	$1,666.00
Post-infection, hospitalized (18-64 years)***	$3,262.00	base case	base case	$504.00
Post-infection, hospitalized (≥ 65 years)***	$6,930.00	base case	base case	$1,666.00
Myocarditis, infection-related*	$14,130.00	base case	base case	base case
Adverse events, grade 3 local (all ages)*	$7.59	base case	base case	base case
Adverse events, grade 3 systemic (all ages)*	$11.49	base case	base case	base case
Adverse events, anaphylaxis (all ages)*	$3,412.81	base case	base case	base case
Adverse events, myocarditis / Pericarditis (applies to ages 18-39 only)*	$3,584.48	base case	base case	base case

Indirect costs - Model parameter					Value
Labor force					
	CLD	**DM**	**CVD**	**IC**	**CKD**
18-29y	42.51%	55.50%	52.34%	36.39%	69.8%
30-39y	49.20%	64.23%	60.58%	42.11%	69.8%
40-49y	48.91%	63.86%	60.22%	41.87%	69.8%
50-64y	41.27%	53.88%	50.82%	35.33%	69.8%
65-74y	15.72%	20.52%	19.36%	13.46%	0.0%
≥75y	4.83%	6.31%	5.95%	4.14%	0.0%
Daily wage*					$262.93
Productivity loss (days)					
Time loss for vaccine administration*					0.04
Short-term infection: not hospitalized*					3.57
Short-term infection: hospitalized, No ICU or ventilator*					7.50
Short-term infection: hospitalized, ICU only*					7.50
Short-term infection: hospitalized, Ventilator*					19.75
IC - Short-term infection: hospitalized, No ICU or ventilator**					11.2
IC - Short-term infection: hospitalized, ICU only**					19.9
IC - Short-term infection: hospitalized, Ventilator**					19.9
CKD - Short-term infection: hospitalized, No ICU or ventilator					5.43
CKD - Short-term infection: hospitalized, ICU only					8.55
CKD - Short-term infection: hospitalized, Ventilator					15.05
Hospitalization recovery days lost*					33.43
DM - Post-infection: Additional severe long COVID days lost*					33
CLD - Post-infection: Additional severe long COVID days lost					66
CVD - Post-infection: Additional severe long COVID days lost					85
IC - Post-infection: Additional severe long COVID days lost					42
CKD - Post-infection: Additional severe long COVID days lost					54.89

* General population; *** High-risk population; **CKD:** chronic kidney disease; **CLD:** chronic lung disease; **CVD:** cardiovascular disease; **DM:** diabetes mellitus; **IC:** immune-compromised; **LB/UB:** lower bound/ upper bound; **y:** year

Table S6. Utility inputs, general population

Model parameter	Value
Baseline utility	
18-29 years	0.9205
30-39 years	0.9055
40-49 years	0.8750
50-64 years	0.8490
65-74 years	0.8255
75-84 years	0.7865
≥85 years	0.7530
Utility decrements	
Symptomatic infection, not hospitalized (all ages) *	0.006
Hospitalized, No ICU or ventilator (all ages)	0.027
Hospitalized, ICU only (all ages)	0.027
Hospitalized, ICU with ventilator (all ages)	0.054
Hospital readmission	0.011
Post-infection, not hospitalized (all ages)	0.0277
Post-infection, hospitalized (all ages)	0.1224
Myocarditis, infection-related (all ages)	0.0019
Adverse events, grade 3 local (all ages)	0.0003

Adverse events, grade 3 systemic (all ages)	0.0011
Adverse events, anaphylaxis (all ages)	0.0019
Adverse events, myocarditis / Pericarditis (applies to ages 18-39 only)	0.0019

ICU: Intensive care unit, **QALY**: quality-adjusted life-year; *Regardless of medical attendance

Table S7. Vaccine effectiveness of updated Moderna and updated Pfizer/BioNTech COVID-19 vaccines in high-risk populations

Moderna - Infection		**Moderna - Hospitalization**	
Initial VE	**Waning**	**Initial VE**	**Waning**
Base case: 34.50%	4.75%	58.70%	1.37%
Scenario VE against infection:			
31.20% –37.60%	base case	base case	base case
Scenario VE against hospitalization:			
base case	base case	51.30%–65.00%	base case
Scenario waning of VE against hospitalization:			
base case	base case	base case	0.62%–2.38%
Pfizer/BioNTech - Infection		**Pfizer/BioNTech - Hospitalization**	
Initial VE		**Initial VE**	
CLD - Base case VE (rVE against infection 3.10%; rVE against hospitalization 11.90%)			
32.40% (scenario 30.54–34.24%)		53.10% (scenario 49.51–56.48%)	
DM - Base case VE (rVE against infection 3.70%; rVE against hospitalization 15.10%)			
31.98% (scenario 30.17–33.70%)		51.35% (scenario 47.72–54.76%)	
CVD - Base case VE (rVE against infection 7.40%; rVE against hospitalization 14.70%)			
29.27% (scenario 27.38–31.13%)		51.58% (scenario 48.31–54.62%)	
IC - Base case VE (rVE against infection 4.80%; rVE against hospitalization 15.00%)			
31.20% (scenario 29.04-33.30%)		51.41% (scenario 46.92-55.50%)	
CKD - Base case VE (rVE against infection 7.60%; rVE against hospitalization 8.40%)			
29.11% (scenario 26.40–31.70%)		54.91% (scenario 51.01–58.49%)	

CKD: chronic kidney disease; **CLD:** chronic lung disease; **CVD:** cardiovascular disease; **DM:** diabetes mellitus; **IC:** immune-compromised; **LB/UB:** lower bound/ upper bound

Table S8. Vaccination coverage rates (%) (general population)

Age group	Sep23	Oct23	Nov23	Dec23	Jan24	Feb24	Mar24	Apr24	May24	Jun24	Jul24	Aug24
Base case vaccination coverage												
18-49 y	0.64	3.71	8.20	9.50	12.24	12.50	12.50	12.50	12.50	12.50	12.50	12.50
50-64 y	1.72	9.60	18.36	21.17	23.21	24.80	24.80	24.80	24.80	24.80	24.80	24.80
≥65 y	3.08	17.10	31.64	33.88	38.94	39.80	39.80	39.80	39.80	39.80	39.80	39.80
Scenario: base case +10% coverage												
18-49 y	0.70	4.09	9.02	10.45	13.47	13.75	13.75	13.75	13.75	13.75	13.75	13.75
50-64 y	1.89	10.56	20.19	23.28	25.54	27.28	27.28	27.28	27.28	27.28	27.28	27.28
≥65 y	3.39	18.81	34.81	37.27	42.84	43.78	43.78	43.78	43.78	43.78	43.78	43.78
Scenario: Healthy people target rate of 70%												
18-49 y	3.58	20.80	45.92	53.20	68.56	70.00	70.00	70.00	70.00	70.00	70.00	70.00
50-64 y	4.85	27.09	51.81	59.74	65.52	70.00	70.00	70.00	70.00	70.00	70.00	70.00
≥65 y	5.42	30.08	55.65	59.59	68.49	70.00	70.00	70.00	70.00	70.00	70.00	70.00
Scenario: Two-dose vaccination												
1st dose												
18-49 y	Same as base case											

50-64 y												
≥65 y												
2nd dose												
18-49 y	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
50-64 y	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
≥65 y	0.00	0.00	0.00	0.00	0.00	0.00	7.10	10.00	10.00	10.00	10.00	10.00

y: year

File S2. Indirect costs and QALYs

Participation in the labor force was calculated from average employment rates in the US general population [13], adjusted to reflect decreased employment rates in high-risk populations. An RR of 0.55 was applied for CLD (based on COPD data [14]); an RR of 0.74 was applied for DM (based on Behavioral Risk Factor Surveillance System Survey (BRFSS) data for 2013 [15]); and a 28% decrease was applied for CVD [16]. The proportion of CKD patients in the labor force was calculated as a weighted average of employment rates [17] in the population with CKD by stage (distribution from USRDS [18]), assuming only stages 3 to 5 were working (i.e., excluding dialysis patients). Due to substantial heterogeneity in the IC population (e.g., employment rates in various IC populations ranged from 22.00% [19] to 77.30% [20]), the employment rate in IC patients was assumed to be 50% lower than in the general population, and this 50% decrease was applied to the age-stratified proportion of individuals in the US labor force[13].

The daily wage was estimated from the mean wage and working days reported for the US in 2023 [21, 22]. Lost productivity due to vaccine administration, outpatient care and hospitalization recovery was based on a previous US economic analysis for COVID-19 [12]. Lost productivity due to hospitalization was based on CDC data on the average length of stay of confirmed COVID-19 inpatient discharges [23]. For the IC population, lost productivity due to hospitalization was based on the average length of stay for the first COVID-19 hospitalization in IC patients [24]; and for CKD, lost productivity due to hospitalization [25] was adjusted to account for increased productivity losses reported in this group [26] (**Table S5**).

The number of working days lost due to severe long COVID was based on the most recent available data in the general population [27, 28]. For CLD, data on absenteeism for working patients with COPD [29] were adjusted by the RR for the number of days lost due to long COVID-19 in CLD patients [30]. For CVD, general population data [22] were adjusted by the decrease in income for CVD patients [16], and relative increase in the number of days lost due to long COVID-19 in patients with CVD [30]. For the IC population, number of working days lost due to severe long COVID was based on data for cancer with active treatment [31], and adjusted by the relative increase in the number of days lost due to long COVID in patients with cancer [30]. For

CKD, additional days lost calculated due to severe long COVID [17, 18, 30] assumed a comparable loss to patients with DM (**Table S5**).

QALYs/ utilities

The model applied baseline utility values [32] stratified by age group. Utility decrements associated with infections and hospitalization were from 5UM-CDC data [33]. Utility decrements associated with hospital re-admission, myocarditis, post-infection period, long COVID, and adverse events were based on a previous US economic analysis of COVID-19 in the general population [12], assumed to apply to high-risk populations due to lack of data (**Table S6**).

File S3. Primary analysis results

Fig S1. A) Total healthcare and societal cost savings ($M), and B) patient-level cost savings ($) and ROI (payer/societal perspectives) with updated Moderna COVID-19 vaccination versus no 2023/24 vaccination

CKD: chronic kidney disease; **CLD:** chronic lung disease; **CVD:** cardiovascular disease; **DM:** diabetes mellitus; **IC:** immuno-compromised; **M:** million; **ROI:** return-on-investment

Table S9. ICERs and ROIs with updated Moderna COVID-19 vaccination versus no 2023/24 vaccination (Healthcare payer and Societal perspectives)

		Updated Moderna COVID-19 vaccine	No 2023/24 vaccination	Difference
CLD	Total QALYs lost	1,267,930	1,428,672	-160,742
	Total costs (Healthcare), $	42,748,683,383	44,728,385,642	-1,979,702,259
	Total costs (Societal), $	46,989,284,107	49,266,941,919	-2,277,657,812

	ICER			**Dominant**
	ROI (patient-level, Healthcare)			1.10
	ROI (patient-level, Societal)			1.30
DM	Total QALYs lost	1,478,263	1,646,133	-167,870
	Total costs (Healthcare), $	40,065,273,678	42,194,428,399	-2,129,154,721
	Total costs (Societal), $	46,060,312,139	48,591,332,536	-2,531,020,397
	ICER			**Dominant**
	ROI (patient-level, Healthcare)			1.70
	ROI (patient-level, Societal)			2.00
CVD	Total QALYs lost	672,410	760,600	-88,191
	Total costs (Healthcare), $	19,943,615,352	20,962,298,340	-1,018,682,988
	Total costs (Societal), $	22,299,388,634	23,478,117,070	-1,178,728,436
	ICER			**Dominant**
	ROI (patient-level, Healthcare)			1.30
	ROI (patient-level, Societal)			1.50
IC	Total QALYs lost	337,257	370,216	-32,959
	Total costs (Healthcare), $	9,287,636,844	9,686,294,772	-398,657,928
	Total costs (Societal), $	10,338,726,629	10,796,130,732	-457,404,103
	ICER			**Dominant**
	ROI (patient-level, Healthcare)			1.50
	ROI (patient-level, Societal)			1.80
CKD	Total QALYs lost	145,973	166,549	-20,577
	Total costs (Healthcare), $	6,025,268,254	6,521,907,134	-496,638,880
	Total costs (Societal), $	6,557,600,514	7,088,580,989	-530,980,475
	ICER			**Dominant**
	ROI (patient-level, Healthcare)			2.60
	ROI (patient-level, Societal)			2.80

Dominant ICER signifies cost savings and QALYs saved with vaccination; **CKD:** chronic kidney disease; **CLD:** chronic lung disease; **CVD:** cardiovascular disease; **DM:** diabetes mellitus; **IC:** immuno-compromised; **ICER:** incremental cost-effectiveness ratio; **QALY:** quality-adjusted life-year; **ROI:** return on investment

Fig S2. Scenario analysis results: Tornado diagram for healthcare cost savings and QALYs saved – DM population

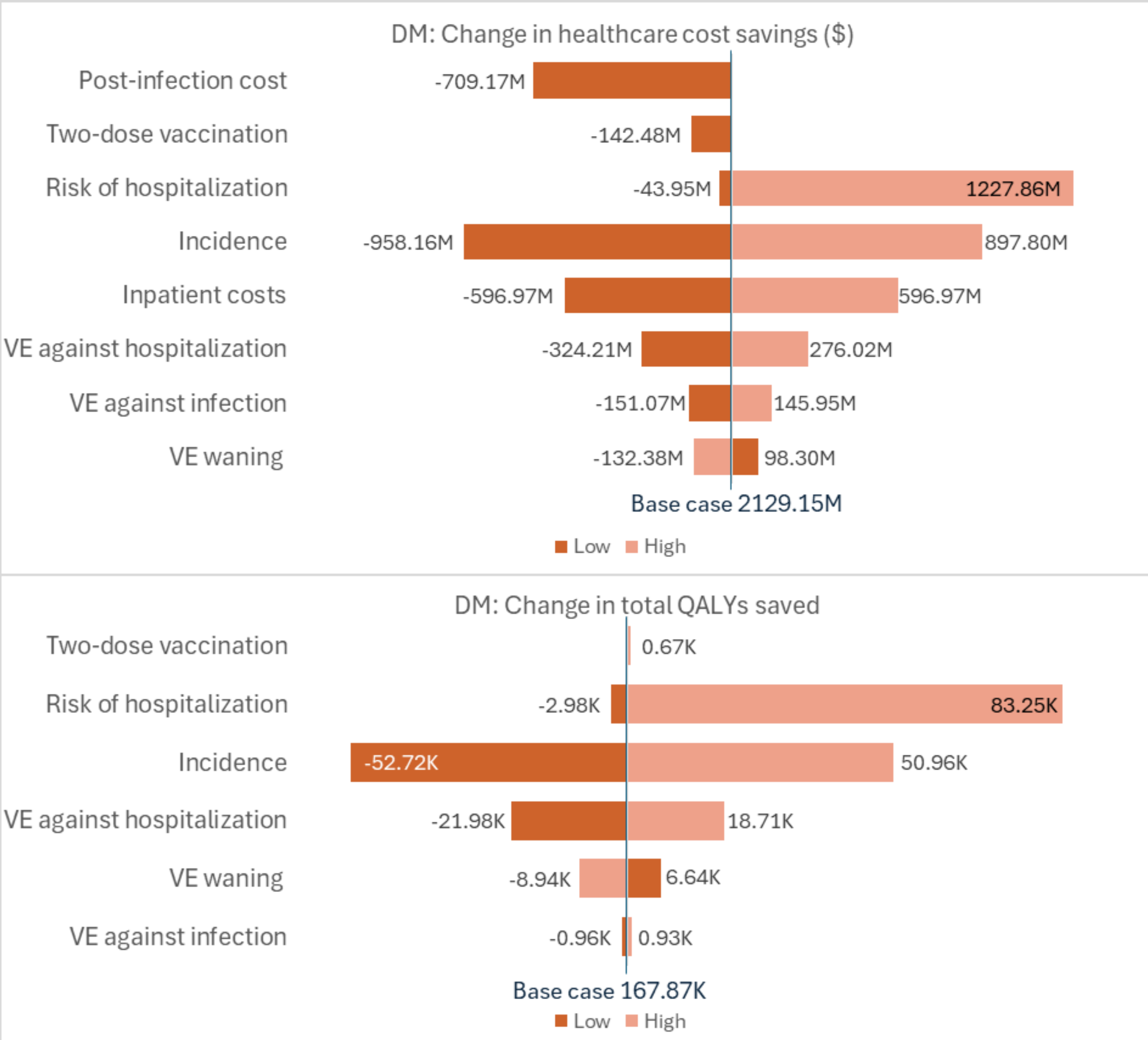

DM: Change in healthcare cost savings ($)
Post-infection cost
Two-dose vaccination
Risk of hospitalization
Incidence
Inpatient costs
VE against hospitalization
VE against infection
VE waning
-709.17M
-142.48M
-43.95M
1227.86M
-958.16M
897.80M
-596.97M
596.97M
-324.21M
276.02M
-151.07M
145.95M
-132.38M
98.30M
Base case 2129.15M
Low
High
DM: Change in total QALYs saved
Two-dose vaccination
Risk of hospitalization
Incidence
VE against hospitalization
VE waning
VE against infection
0.67K
-2.98K
83.25K
-52.72K
50.96K
-21.98K
18.71K
-8.94K
6.64K
-0.96K
0.93K
Base case 167.87K
Low
High

Fig S3. Scenario analysis results: Tornado diagram for healthcare cost savings and QALYs saved – CVD population

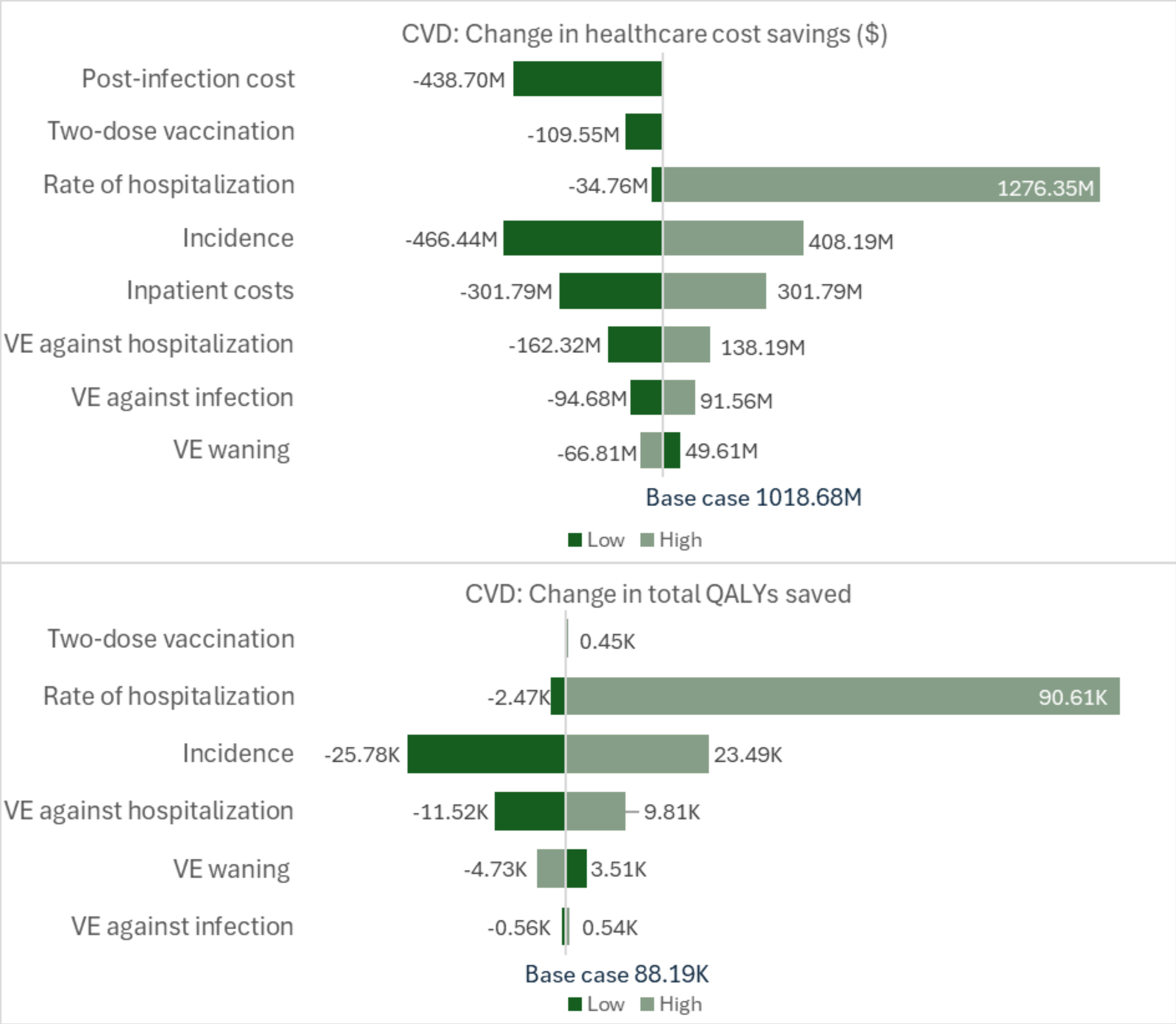


Fig S4. Scenario analysis results: Tornado diagram for healthcare cost savings and QALYs saved – IC population

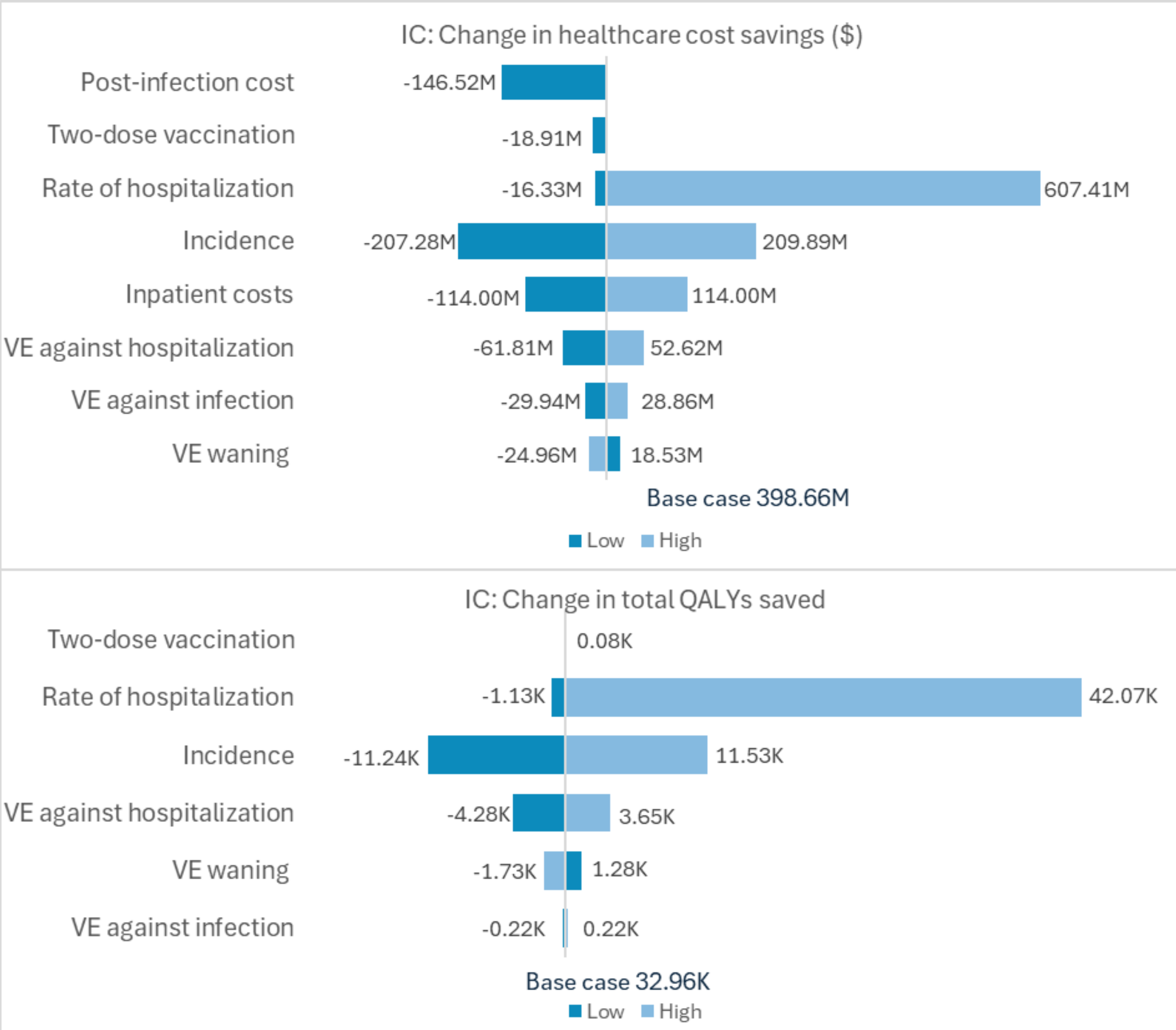
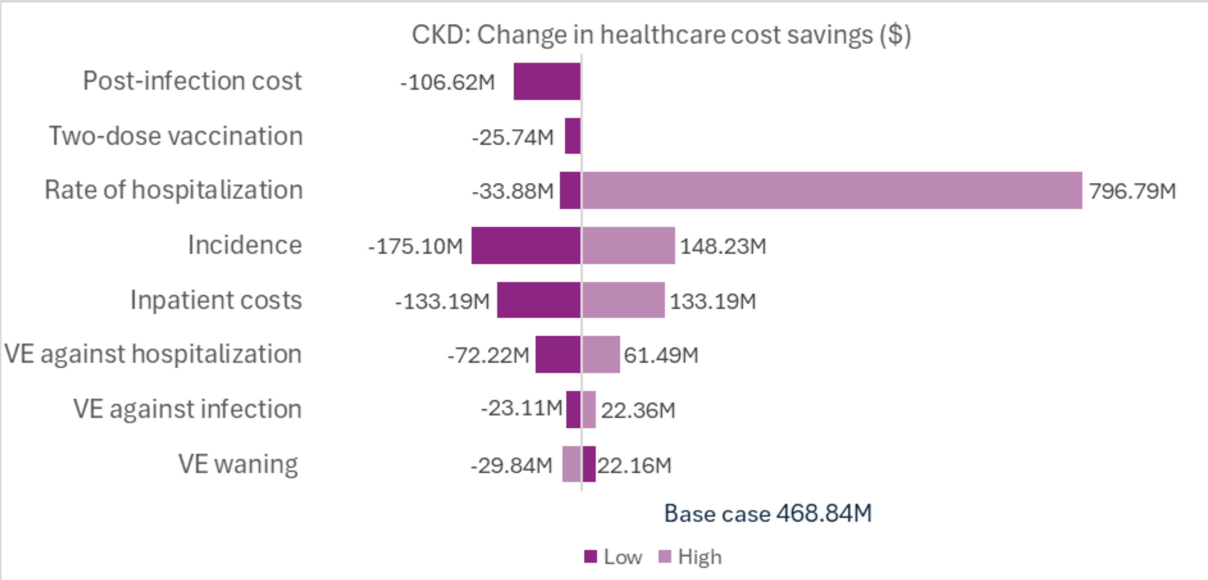
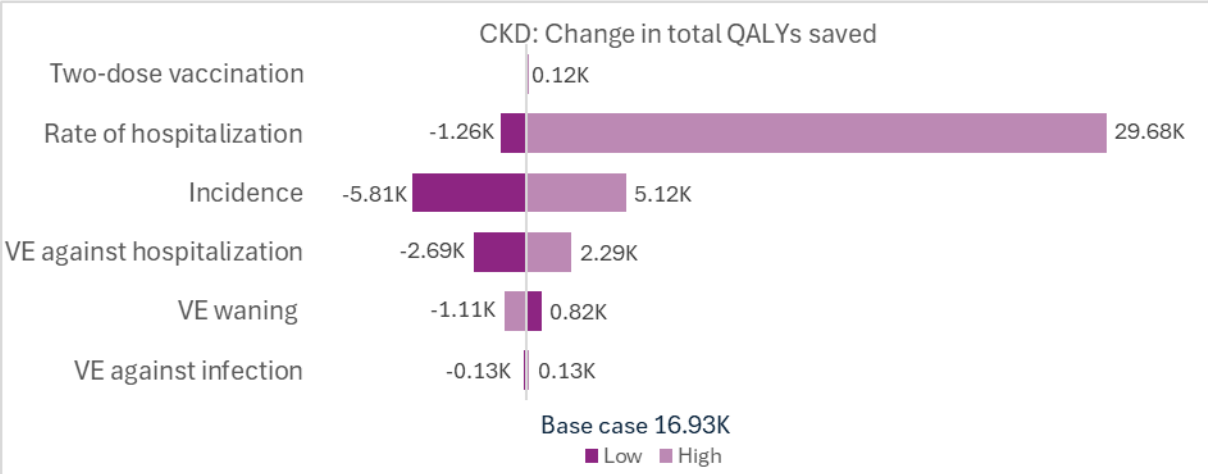


Fig S5. Scenario analysis results: Tornado diagram for healthcare cost savings and QALYs saved – CKD population





File S4. Secondary analysis results

Results for Moderna's versus Pfizer/BioNTech's updated vaccination

Table S10. ICERs with Moderna's versus Pfizer/BioNTech's updated COVID-19 vaccination (Healthcare payer and Societal perspectives)

		Updated Moderna COVID-19 vaccine	Updated Pfizer/BioNTech COVID-19 vaccine	Difference
CLD	Total QALYs lost	1,267,930	1,284,419	-16,489
	Total costs (Healthcare), $	42,748,683,383	43,118,842,484	-370,159,101
	Total costs (Societal), $	46,989,284,107	47,393,625,182	-404,341,074
	ICER			**Dominant**
DM	Total QALYs lost	1,478,263	1,500,829	-22,567
	Total costs (Healthcare), $	40,065,273,678	40,498,847,181	-433,573,503
	Total costs (Societal), $	46,060,312,139	46,552,299,237	-491,987,099
	ICER			**Dominant**
CVD	Total QALYs lost	672,410	684,372	-11,963
	Total costs (Healthcare), $	19,943,615,352	20,246,610,149	-302,994,797
	Total costs (Societal), $	22,299,388,634	22,630,627,166	-331,238,533
	ICER			**Dominant**
IC	Total QALYs lost	337,257	341,697	-4,440
	Total costs (Healthcare), $	9,287,636,844	9,377,607,912	-89,971,068
	Total costs (Societal), $	10,338,726,629	10,437,794,549	-99,067,920
	ICER			**Dominant**
CKD	Total QALYs lost	145,973	147,560	-1,588
	Total costs (Healthcare), $	6,025,268,254	6,099,232,025	-73,963,771
	Total costs (Societal), $	6,557,600,514	6,635,638,923	-78,038,409
	ICER			**Dominant**

Dominant ICER signifies cost savings and QALYs saved with vaccination; **CKD:** chronic kidney disease; **CLD:** chronic lung disease; **CVD:** cardiovascular disease; **DM:** diabetes mellitus; **IC:** immuno-compromised; **ICER:** incremental cost-effectiveness ratio; **QALY:** quality-adjusted life-year

For the comparison against Pfizer/BioNTech's updated vaccine, scenarios assessed the impact of varying the rVE estimates, and of increasing coverage.

Table S11. Scenario analyses: Healthcare cost savings, QALYs saved, and ICERs with Moderna's versus Pfizer/BioNTech's updated COVID-19 vaccination (Healthcare payer perspective)

CLD	**Moderna**	**Pfizer/BioNTech**	**Difference**
Scenario +10% increase in VCR			
Total QALYs lost	1,251,856	1,269,994	-18,138
Total costs (Healthcare), $	42,550,713,157	42,957,888,168	-407,175,012
ICER, $ per QALY / Conclusion			**Dominant**

Scenario VCR 70%			
Total QALYs lost	1,030,360	1,071,153	-40,793
Total costs (Healthcare), $	40,031,764,231	40,877,477,422	-845,713,191
ICER, $ per QALY / Conclusion			**Dominant**
Scenario Lower bound of 95%CI for rVE estimate			
Total QALYs lost	1,267,930	1,274,267	-6,338
Total costs (Healthcare), $	42,748,683,383	42,855,215,986	-106,532,604
ICER, $ per QALY / Conclusion			**Dominant**
Scenario Higher bound of 95%CI for rVE estimate			
Total QALYs lost	1,267,930	1,295,270	-27,340
Total costs (Healthcare), $	42,748,683,383	43,393,054,237	-644,370,854
ICER, $ per QALY / Conclusion			**Dominant**
DM	**Moderna**	**Pfizer/BioNTech**	**Difference**
Scenario +10% increase in VCR			
Total QALYs lost	1,461,476	1,486,299	-24,824
Total costs (Healthcare), $	39,852,358,206	40,329,289,059	-476,930,853
ICER, $ per QALY / Conclusion			**Dominant**
Scenario VCR 70%			
Total QALYs lost	1,181,176	1,243,580	-62,404
Total costs (Healthcare), $	36,487,255,738	37,610,926,891	-1,123,671,153
ICER, $ per QALY / Conclusion			**Dominant**
Scenario Lower bound of 95%CI for rVE estimate			
Total QALYs lost	1,478,263	1,490,202	-11,940
Total costs (Healthcare), $	40,065,273,678	40,271,096,269	-205,822,591
ICER, $ per QALY / Conclusion			**Dominant**
Scenario Higher bound of 95%CI for rVE estimate			
Total QALYs lost	1,478,263	1,512,131	-33,868
Total costs (Healthcare), $	40,065,273,678	40,739,798,307	-674,524,629
ICER, $ per QALY / Conclusion			**Dominant**
CVD	**Moderna**	**Pfizer/BioNTech**	**Difference**
Scenario +10% increase in VCR			
Total QALYs lost	663,591	676,749	-13,159
Total costs (Healthcare), $	19,841,747,054	20,175,041,330	-333,294,277
ICER, $ per QALY / Conclusion			**Dominant**
Scenario VCR 70%			
Total QALYs lost	544,717	573,921	-29,204
Total costs (Healthcare), $	18,530,923,511	19,212,137,622	-681,214,110
ICER, $ per QALY / Conclusion			**Dominant**
Scenario Lower bound of 95%CI for rVE estimate			
Total QALYs lost	672,410	679,329	-6,920
Total costs (Healthcare), $	19,943,615,352	20,127,092,216	-183,476,864
ICER, $ per QALY / Conclusion			**Dominant**
Scenario Higher bound of 95%CI for rVE estimate			
Total QALYs lost	672,410	689,764	-17,355
Total costs (Healthcare), $	19,943,615,352	20,369,442,608	-425,827,256
ICER, $ per QALY / Conclusion			**Dominant**
IC	**Moderna**	**Pfizer/BioNTech**	**Difference**
Scenario +10% increase in VCR			
Total QALYs lost	333,961	338,845	-4,884
Total costs (Healthcare), $	9,247,771,052	9,346,739,226	-98,968,174
ICER, $ per QALY / Conclusion			**Dominant**
Scenario VCR 70%			
Total QALYs lost	267,831	281,603	-13,772
Total costs (Healthcare), $	8,457,680,341	8,726,082,269	-268,401,929

ICER, $ per QALY / Conclusion			**Dominant**
Scenario Lower bound of 95%CI for rVE estimate			
Total QALYs lost	337,257	339,190	-1,934
Total costs (Healthcare), $	9,287,636,844	9,324,570,633	-36,933,789
ICER, $ per QALY / Conclusion			**Dominant**
Scenario Higher bound of 95%CI for rVE estimate			
Total QALYs lost	337,257	344,437	-7,181
Total costs (Healthcare), $	9,287,636,844	9,434,407,244	-146,770,400
ICER, $ per QALY / Conclusion			**Dominant**
CKD	**Moderna**	**Pfizer/BioNTech**	**Difference**
Scenario +10% increase in VCR			
Total QALYs lost	143,915	145,661	-1,746
Total costs (Healthcare), $	5,975,604,366	6,056,964,514	-81,360,148
ICER, $ per QALY / Conclusion			**Dominant**
Scenario VCR 70%			
Total QALYs lost	119,028	122,675	-3,647
Total costs (Healthcare), $	5,425,902,930	5,582,147,902	-156,244,973
ICER, $ per QALY / Conclusion			**Dominant**
Scenario Lower bound of 95%CI for rVE estimate			
Total QALYs lost	145,973	146,159	-186
Total costs (Healthcare), $	6,025,268,254	6,046,327,448	-21,059,194
ICER, $ per QALY / Conclusion			**Dominant**
Scenario Higher bound of 95%CI for rVE estimate			
Total QALYs lost	145,973	149,077	-3,104
Total costs (Healthcare), $	6,025,268,254	6,155,051,184	-129,782,930
ICER, $ per QALY / Conclusion			**Dominant**

Dominant ICER signifies cost savings and QALYs saved; **CI:** confidence interval; **CKD:** chronic kidney disease; **CLD:** chronic lung disease; **CVD:** cardiovascular disease; **DM:** diabetes mellitus; **IC:** immuno-compromised; **ICER:** incremental cost-effectiveness ratio; **QALY:** quality-adjusted life-year; **rVE:** relative vaccine efficacy

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