

Supplementary Table 1. Baseline Demographic Characteristics – Unadjusted

Characteristic	QIVc (N=665,047)	QIVe-SD (N=3,062,843)	SMD ¹
Mean Age (years)	41.9	35.8	-0.31
SD	16.5	19.6	
Median	45	38	
Age group (%)			
4-8 years	3.0%	11.0%	0.32
9-17 years	8.1%	16.4%	0.25
18-49 years	47.4%	39.0%	-0.17
50-64 years	41.4%	33.6%	-0.16
Gender (n,%)			
Male	43.4%	44.9%	0.03
Female	56.6%	55.1%	-0.03
Payer type (%)			
Commercial	62.7%	59.9%	-0.06
Medicaid	0.1%	0.9%	0.11
Medicare Advantage	0.0%	0.0%	0.02
Self-Insured	37.2%	39.2%	0.04
Health plan type (%)			
Consumer directed health care	0.0%	0.1%	0.03
HMO	7.6%	8.4%	0.03
POS	4.8%	6.3%	0.07
PPO	87.0%	84.1%	-0.09
Other/Unknown	0.5%	1.1%	0.06
Geographic region (%)			
Northeast	14.4%	17.0%	0.07
Midwest	23.7%	35.4%	0.26
South	51.6%	36.2%	-0.32
West	10.3%	11.5%	0.04
DHHS (U.S. Dept. of Health & Human Services) region (%)			
Region 1: CT, ME, MA, NH, RI, VT	6.7%	6.6%	-0.01
Region 2: NJ, NY, PR, VI	2.6%	3.0%	0.02
Region 3: DE, DC, MD, PA, VA, WV	7.0%	9.5%	0.09
Region 4: AL, FL, GA, KY, MS, NC, SC, TN	35.6%	21.6%	-0.31
Region 5: IL, IN, MI, MN, OH, WI	16.4%	26.2%	0.24
Region 6: AR, LA, NM, OK, TX	14.4%	13.0%	-0.04
Region 7: IA, KS, MO, NE	6.7%	7.8%	0.04
Region 8: CO, MT, ND, SD, UT, WY	1.3%	3.2%	0.13
Region 9: AZ, CA, HI, NV, AS, FS, GU, PU	2.7%	3.3%	0.03
Region 10: AK, ID, OR, WA	6.6%	6.0%	-0.02

¹ SMD (absolute) ≥ 0.1 indicates significance ; HMO = health maintenance organization; POS = point-of-service, PPO = preferred provider organization; QIVc = cell-based quadrivalent influenza vaccine; QIVe-SD = standard-dose egg-based quadrivalent influenza vaccine; SD = standard deviation; SMD = standardized mean difference

Supplementary Table 2. Baseline Clinical Characteristics – Unadjusted

Characteristic	QIVc (N=665,047)	QIVe-SD (N=3,062,843)	SMD ¹
Month of flu vaccine (%)			
August	0.2%	2.0%	0.18
September	13.8%	19.1%	0.14
October	50.2%	46.6%	-0.07
November	20.2%	20.9%	0.02
December	9.5%	7.1%	-0.09
January	6.0%	4.4%	-0.08
Charlson Comorbidity Index (CCI) Score: (%)			
0	81.3%	83.7%	0.06
1	10.5%	9.6%	-0.03
2	5.2%	4.3%	-0.05
3+	2.9%	2.4%	-0.04
Mean CCI	0.3	0.3	-0.07
SD	0.9	0.8	
Median	0	0	
Pre-index comorbid conditions of interest (%)			
Asthma	3.9%	4.2%	0.01
Blood disorders	0.1%	0.1%	0.00
Chronic lung disease	1.9%	1.6%	-0.02
Diabetes	7.8%	6.4%	-0.05
Heart disease	1.8%	1.5%	-0.03
Kidney disorders	1.3%	0.9%	-0.03
Liver disorders	1.8%	1.5%	-0.03
Neurological or neurodevelopmental conditions	1.6%	1.5%	-0.01
Weakened immune system ²	3.0%	2.6%	-0.02
IBD	0.7%	0.6%	-0.01
Composite of the above	18.8%	16.7%	-0.05
Patients with pre-index hospitalization (%)	2.3%	2.1%	-0.01
Number of pre-index hospitalizations			
Mean	0.0	0.0	-0.01
SD	0.2	0.2	
Median	0	0	
Patients with pre-index ER visit (%)	7.4%	7.7%	0.01
Mean number of pre-index ER visits	0.1	0.1	0.01
SD	0.5	0.5	
Median	0	0	
Patients with pre-index outpatient physician office visit (%)	78.0%	76.3%	-0.04
Mean number of pre-index outpatient physician office visits	3.9	3.7	-0.06
SD	6.8	6.6	
Median	2	2	
Mean total pre-index all-cause outpatient pharmacy costs	\$1,411	\$1,268	-0.13
SD	\$7,666	\$8,254	
Median	\$87	\$56	
Total pre-index all-cause medical costs			
Mean inpatient	\$640	\$624	-0.01

SD	\$7,735	\$8,349	
Median	\$0	\$0	
Mean outpatient	\$1,963	\$1,840	-0.05
SD	\$7,811	\$6,727	
Median	\$485	\$441	
Mean ER	\$133	\$132	0.01
SD	\$931	\$947	
Median	\$0	\$0	
Mean TOTAL pre-index all-cause costs³	\$4,014	\$3,732	-0.08
SD	\$15,476	\$15,391	
Median	\$788	\$674	

¹ SMD (absolute) ≥ 0.1 indicates significance

² Including: HIV/AIDS; metastatic cancer and acute leukemia; lung or upper digestive or other severe cancer; lymphatic, head, neck, brain, or major cancer; breast, prostate, colorectal, or other cancer; and disorders of immunity

³ TOTAL = outpatient pharmacy + inpatient + outpatient medical

CCI = Charlson comorbidity index score; ER = emergency room; IBD = inflammatory bowel diseases (ulcerative colitis and Crohn's disease); IPTW = inverse probability of treatment weighting; QIVc = cell-based quadrivalent influenza vaccine; QIVe-SD = standard-dose egg-based quadrivalent influenza vaccine; SD = standard deviation; SMD = standardized mean difference

Supplementary Table 3. Unadjusted rVEs

<i>Subgroup</i>	Overall (4-64 years)		4-17 years		18-64 years		High-risk (4-64 years)	
	rVE	P- value	rVE	p-value	rVE	p-value	rVE	p-value
All-cause hospitalizations	-6.7%	<.0001	14.5%	0.0004	8.9%	<.0001	1.6%	0.0726
Influenza-related hospitalizations and ER visits	-14.3%	<.0001	6.3%	0.4718	-0.9%	0.6475	-4.7%	0.0867
Respiratory hospitalization / ER events								
Any respiratory hospitalization/ER visit	6.3%	<.0001	22.2%	<.0001	8.1%	<.0001	7.7%	<.0001
Pneumonia hospitalizations/ER visits	-4.5%	0.0553	32.9%	0.0002	3.6%	0.1252	-0.1%	0.9624
Asthma/COPD/bronchial hospitalizations/ER visits	3.4%	0.0043	20.2%	<.0001	10.1%	<.0001	9.0%	<.0001
Influenza-related hospitalizations and ER visits - SA	19.4%	<.0001	21.4%	0.0049	7.8%	0.0430	14.1%	0.0054
UTI hospitalizations/ER visits	6.9%	<.0001	22.4%	<.0001	7.0%	<.0001	6.1%	<.0001

*SA = *Sensitivity Analysis*

Supplementary Table 4. Adjusted Clinical Outcomes Rates (Rates per 1,000)

<i>Age group</i>	Overall		4-17 Years		18-64 years		High-risk	
<i>Study Cohort</i>	QIVc	QIVe-SD	QIVc	QIVe-SD	QIVc	QIVe-SD	QIVc	QIVe-SD
	(N=669,030)	(N=3,062,797)	(N=74,304)	(N=839,744)	(N=590,705)	(N=2,223,435)	(N=142,150)	(N=584,959)
Measure (rate)								
All-cause hospitalizations	35.6	38.7	7.1	8.6	45.3	48.5	100.0	104.1
Influenza-related hospitalizations/ER visits	1.6	1.7	2.3	2.5	1.3	1.4	3.2	3.2
Respiratory hospitalization/ER events								
Any respiratory hospitalization/ER visit	21.8	23.7	16.9	19.8	23.2	25.0	56.0	59.0
Pneumonia hospitalizations/ER visits	3.2	3.4	1.4	1.8	3.8	4.0	9.4	9.7
Asthma/COPD/bronchial hospitalizations/ER visits	11.5	12.8	6.8	8.0	13.0	14.3	36.9	39.2
UTI hospitalizations/ER visits	4.9	5.0	1.8	2.0	6.0	6.0	11.5	11.6

Rate = events (first event only) per 1,000 vaccinated-subject seasons