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Supplementary Materials for

Costs and effectiveness of influenza vaccination: a systematic review

Lucia Sara D'Angiolella, Alessandra Lafranconi, Paolo Angelo Cortesi, Silvia Rota, Giancarlo Cesana and Lorenzo Giovanni Mantovani

Corresponding author:
Lucia Sara D'Angiolella, Centro di Studio e Ricerca sulla Sanità Pubblica (CESP), Università degli Studi di Milano Bicocca, Via G. Pergolesi 33, 20900 Monza, Italy. E- mail: l.dangiolella@campus.unimib.it.

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Table 1
Characteristics of included studies

Reference	Study design	Country	Population	Vaccination strategy	Analysis	Perspective	Costs	Incremental cost	Incremental outcome	ICER
Blommaert et al. 2014	Static model	Belgium	Pregnant women (2nd or 3rd trimester]	Increasing TIV vaccine uptake (0%-50%]	CEA	Health care payer	Direct	€ 383,962	59.00 QALYs	6,763
			Health care workers	Increasing TIV vaccine uptake (35%-50%]				€ 709,133	30.00 QALYs	24,595
			0-14 y	Increasing TIV vaccine uptake (20%-40%]				€ 689,189	33.00 QALYs	22,596
			15-49 y	Increasing TIV vaccine uptake (20%-40%]				€ 2,473,748	101.00 QALYs	25,278
			50-64 y	Increasing TIV vaccine uptake (20%-40%]				€ 1,901,101	133.00 QALYs	14,610
Bellinghen et al. 2014	Markov model	UK	Pt at risk and elderly (65+]	TIV *vs* QIV	CEA	NHS	Direct	190,778,818 GBP	36,002 QALY 37,085 LY	5,299 5,144
Baguelin et al. 2015	Markov model	England and Wales	> 2 y	Exteding vaccination (2-4 y]	CEA	HS and Personal Social Services	Direct	10,473,000 GBP	4,009 QALYs	2,613
				Exteding vaccination (50-64y]				48,813,000 GBP	6,642 QALYs	7,350
				Exteding vaccination (5-16y]				41,527,000 GBP	23,801 QALYs	1,745
				Exteding vaccination (2-4 and 50-64 y]				59,438,000 GBP	10,545 QALYs	5,637
				Exteding vaccination (2-16 y]				52,840,000 GBP	27,115 QALYs	1,949
				Exteding vaccination (2-16 and 50-64 y]				101,976,000 GBP	33,186 QALYs	3,073
				Exteding vaccination (2-64 y]				253,941,000 GBP	50,323 QALYs	5,046
Garcia et al. 2016	Markov model	Spain	Risk and elderly (65+]	TIV *vs* QIV	CEA	NHS	Direct	€ 447,554,791	40,005 QALYs:	11,188
						Societal	Direct + Indirect	€ 349,974,624		8,749
Damm et al. 2014	Age structured dynamic model	Germany	2-17 y	TIV *vs* TIV + LAIV	CEA	Narrow third payer	Direct	€ 398,615,966.62	175,960 QALYs	2,265
						Broad third payer	Direct	€ 216,122,046.12		1,228
						Societal	Direct + indirect	€ 3,403,599,345.84		TIV + LAIV dominates
Clements et al. 2014	Decision tree	USA	All population	TIV *vs* QIV	CEA	Societal	Direct + Indirect	$ 121,912,743	3,596 QALYs	90,301
Joyce You et al. 2015	Decision tree	Hong Kong	All population	TIV *vs* QIV	CEA	HS	Direct	$ 38,877	1.72 QALYs	22,603
						Societal	Direct + Indirect	$ 21,600		12,558
			0.5-4 y			HS	Direct	$ 37,471	20.39 QALYs	1,838
						Societal	Direct + Indirect	$ 194,403		QIV dominates
			5-9 y			HS	Direct	$ 23,194	3.95 QALYs	5,872
						Societal	Direct + Indirect	$ 24,445		QIV dominates
			10-14 y			HS	Direct	$ 30,925	0.79 QALYs	39,146
						Societal	Direct + Indirect	$ 20,845		26,386
			15-64 y			HS	Direct	$ 30,243	0.29 QALYs	104,283
						Societal	Direct + Indirect	$ 27,128		93,545
			65-79 y			HS	Direct	$ 103,172	2.81 QALYs	36,716
						Societal	Direct + Indirect	$ 86,416		30,753
			80+			HS	Direct	$ 60,328	7.48 QALYs	8,065
						Societal	Direct + Indirect	$ 7,248		QIV dominates

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Table 1
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Reference	Study design	Country	Population	Vaccination strategy	Analysis	Perspective	Costs	Incremental cost	Incremental outcome	ICER
Akin et al. 2016	Decision analytic model	Turkey	Adults (18+] with DM 2	Increasing vaccination coverage from 9.1% to 20%	CEA	Societal	Direct + Indirect	174,597 TRY	2,743 QALYs	64
						Public payer perspective	Direct			1,158
				Increasing vaccination coverage from 9.1% to 30%-75%		Societal	Direct + Indirect	334,778 TRY	5,258 QALYs	64
Chit et al. 2014	Economic model	US	> 65 y	TIV high dose *vs* TIV standard dose	CEA	Societal	Direct + Indirect	$ 153,790,271	29,023 QALYs	5,299
						Thirdy payer perspective	Direct	$ 300,400,337		10,350
				TIV high dose *vs* QIV standard dose		Societal	Direct + Indirect	$ -16,509,606	27,718 QALYs	TIV dominates
						Thirdy payer perspective	Direct	$122,090,183		4,365
Chit et al. 2015 (A)	Static model	Ontario	All population (6m+]	QIV *vs* TIV	CEA	HS	Direct	7.2 million CAD	76 QALYs	94,248
						Societal	Direct + Indirect	4,784,112 CAD		63,773
			≤ 4y			HS	Direct	NA	2.36 QALYs	112,274
						Societal	Direct + Indirect			112,017
			5-19y			HS	Direct	NA	6.1 QALYs	174,525
						Societal	Direct + Indirect			167,856
			20-49y			HS	Direct	NA	7.0 QALYs	303,851
						Societal	Direct + Indirect			76,351
			50-64y			HS	Direct	NA	8.4 QALYs	217,878
						Societal	Direct + Indirect			146,192
			65+			HS	Direct	NA	52.1 QALYs	36,034
						Societal	Direct + Indirect			32,864
Chit et al. 2015 (B)	Economic model based on single clinical trial	US	65+	TIV high dose *vs* TIV standard dose	CEA	HS	Direct	$ 116 (per participant]	-0.0003 QALYs	Dominated
						Societal	Direct + Indirect	$ 128		Dominated
			Adults with ≥ 1 comorbility			HS	Direct	$ 106	-0.0013 QALYs	Dominated
						Societal	Direct + Indirect	$ 119		Dominated
			75+			HS	Direct	$ 12	-0.0053 QALYs	Dominated
						Societal	Direct + Indirect	$ 22		Dominated
Shim et al. 2016	Age-structured model	US	2-8y	Mixed vaccination strategy: 33.3% LAIV and 66.7% IIV *vs* IIV alone	CEA	HS	Direct	664 million $	NA	LAIV dominates
						Societal	Direct + Indirect	978 million $		LAIV dominates
				Mixed vaccination strategy: 33.3% LAIV and 66.7% IIV *vs* LAIV alone		HS	Direct	664 million $		LAIV was cost-effective 99% of the time
Gregg et al. 2014	RCT	Canada	Children (36 m-15 y]	Vaccinated *vs* non vaccinated	CEA	Societal (school-work]	Direct	$ 36.41	-0.23 influenza cases	164.12
Brydak et al. 2012	Decision-analytic model	Poland	65+	New situation (universal coverage] *vs* Current situation (out of poket]	CEA	Payer perspective	Direct	71.6 PLN million	2,744 QALYs	26,118

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Reference	Study design	Country	Population	Vaccination strategy	Analysis	Perspective	Costs	Incremental cost	Incremental outcome	ICER
Dolk et al. 2016	Dynamic transmission model	Germany	All population	QIV *vs* TIV	CEA	Payer perspective	Direct	57.5 million €	3,975 QALYs	14,461
						Societal	Direct + Indirect	-57.9 million €		QIV dominates
Leung et al. 2016	Decision-analytic model	Hong Kong	65+	IM vaccine *vs* ID vaccine	CEA	Payer perspective	Direct	$ 5.23 (per person]	0.00336 QALYs	14,528
Meeyai et al. 2015	Age-structured decision model	Thailand	Children (2-17 y]	TIV *vs* No vaccination	CEA	Societal	Direct + indirect	218 million $	49,000 DALYs averted	4,445
			Children (2-17 y]	LAIV *vs* No vaccination				91-372 million $ (according to age sub-groups]	45,000-65,000 DALYs averted	1,841- 5,748 (according to age sub-groups]
			Elderly (60+]	TIV *vs* No vaccination				65 million$	23,000 DALYs averted	2,889
Meier 2015	Markov model	UK	At risk adults and elderly (65+]	QIV *vs* TIV	CEA	Payer perspective	Direct	755 million £	51,538 QALYs	14,645
						Societal	Direct + indirect	696 million £		13,497
			Elderly (65+]			Payer perspective	Direct	549 million £	45,753 QALYs	11,998
Nagy et al. 2016	Transmission model	Finland	All population	TIV *vs* No vaccination	CEA	HS	Direct	350 million €	-47 QALYs	Dominated
				QIV *vs* No vaccination				327 million €	62.4 QALYs	5,237
				TIV/Q-LAIV *vs* No vaccination				398 million €	-65 QALYs	Dominated
				QIV/Q-LAIV 50 % *vs* No vaccination				30 million €	5.5 QALYs	5,329
				QIV/Q-LAIV 100 % *vs* No vaccination				30 million €	5.2 QALYs	5,734
				TIV *vs* No vaccination		Societal	Direct + Indirect	238 million €	-47 QALYs	Dominated
				QIV *vs* No vaccination				33 million €-	-62 QALYs	Dominated
				TIV/Q-LAIV *vs* No vaccination				-111 million €	-65 QALYs	Dominated
				QIV/Q-LAIV 50 % *vs* No vaccination				-136 million €	-68 QALYs	Dominated
				QIV/Q-LAIV 100 % *vs* No vaccination				-229 million €	73 QALYs	QIV/Q-LAIV dominates
Newall et al. 2014	Single-year model	Australia	Elderly (65+]	Vaccination *vs* no vaccination	CEA	Payer perspective	Direct	56 million $	1.232 QALYs	45,400
Patterson et al. 2012	Quasi-Markov simulation	US	50+	TIV to 65 *vs* No vaccination	CEA	Payer perspective	Direct	$ 17,375	1.3 Lives saved	13,084
				TIV to 50 *vs* No vaccination (ED]				$ 48,606	1.4 lives saved	34,610
				TIV to 50 *vs* TIV to 65				$ 31,231	0.08 lives saved	408,784

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Table 1
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Reference	Study design	Country	Population	Vaccination strategy	Analysis	Perspective	Costs	Incremental cost	Incremental outcome	ICER
Pitman et al. 2013	Dinamic influenza transmission model	England and Wales	2-18 y	No Vaccination *vs* Current Policy	CEA	Payer perspective	Direct	£9,164	-20 million QALY	Current Policy dominates
				Current policy + TIV (2-4 y] *vs* Current Policy				£ 192	-1.6 million QALY	Dominated
				Current policy + LAIV (2-4 y] *vs* Current Policy				£ -182	2.0 million QALYs	Current policy + LAIV dominates
				Current policy + TIV (2-10 y] *vs* Current Policy				£ 1,554	-1.8 million QALYs	Dominated
				Current policy + LAIV (2-10 y] *vs* Current Policy				£ 1,152	2.3 million QALYs	506
				Current policy + TIV (2-18 y] *vs* Current Policy				£ 1,218	-1.7 million QALYs	Dominated
				Current policy + LAIV (2-18 y] *vs* Current Policy				£ 699	2.3 million QALYs	298
Raviotta et al. 2016	Markov model	US	65+	No vaccination *vs* TIV	CEA	Societal	Direct+ Indirect	US$ -4.1	0.0011 QALYs	3,693
				No vaccination *vs* QIV				US$ -2.0	0.0001 QALYs	20,939
				No vaccination *vs* High dose TIV				US$ -6.5	0.0002 QALYs	31,214
Smith et al. 2016	Markov model	US	Children (2-8 y]	IIV *vs* LAIV	CEA	Societal	Direct +Indirect	US$8.75	-0.00008 QALYs	Dominated
Thommes et al. 2015	Dynamic model	Canada	Whole population	QIV *vs* TIV	CEA	Payer perspective	Direct	$ 220,036,899	31,791QALYs 22,899 LYs	7,961 11,211
		UK	Whole population	TIV/LAIV *vs* QIV/QLAIV				£ 23,258,257	29,315 QALYs 20,966 LYs	7,234/ 10,364
Thorrington et al. 2015	Dynamic Model	England	2-16 y	No vaccination *vs* vaccination (primary school]	CEA	Payer perspective	Direct	Minimum cost per vaccination per person: £ 9.13 (with 92% coverage]	Maximum QALYs gained 0.0093 (92% coverage]	3,117
				No vaccination versus vaccination (secondary school]				Minimum cost per vaccination per person: £ 11.26 (with 1% coverage]	Maximum QALYs gained as above 0.0063 (12% coverage]	4,280
				No vaccination versus vaccination (primary+secondary school]				Minimum cost per vaccination per person: £ 6.14 (with 44% coverage in primary and 29% in secondary schools]	Maximum QALYs gained as above 0.0128 (45% and 28%]	16,152
Xu et al. 2016	Decision-analytic model	US	Pregnant women	No vaccination *vs* vaccination (moderate intensity]	CEA	Societal	Direct + Indirect	$ -43,040,676	305 QALYs	Vaccination dominates
				No vaccination *vs* vaccination (mild intensity				$ 30,873,253	123 QALYs	250,689
				No vaccination *vs* vaccination (moderately severe intensity]				$ -89,810,994	610 QALYs	Vaccination dominates

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Table 1
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Reference	Study design	Country	Population	Vaccination strategy	Analysis	Perspective	Costs	Incremental cost	Incremental outcome	ICER
Yamin et al. 2014	Retrospective cohort data analysis	Israel	Patients with previous pneumonia, all ages	No vaccination *vs* vaccination (hosp]	CEA	Payer perspective	Direct	$ 656,760	-203.1 QALYs	Vaccination dominates
				No vaccination *vs* vaccination (non-hosp]				$ 680,439	-237.31 QALYs	Vaccination dominates in elderly patients and it is cost-effective (ICER 40.123] in patients with 4-24 years
			65+	No vaccination *vs* vaccination (non hosp]				$ 281,022	-136.04 QALYs	Vaccination dominates
Yao et al. 2012	Decision analysis model	US	Post-partum women	No vaccination *vs* vaccination	CBA	Payer perspective	Direct	US $-13.7		-13.7 US $
						Societal	Direct + indirect	US $ 12.57		12.57 US $
You et al. 2015	Decision tree	Hong Kong	All population	QIV *vs* TIV	CEA	Payer perspective	Direct	$ 38,877	1.72	22,603
						Societal	Direct + indirect	$ 21,600		12,558
You et al. 2014	Epidemiology model	Hong Kong	Elderly (65-79 y] (Year 2007]	QIV *vs* TIV	CEA	Societal	Direct + indirect	$ -266,473	22.826 QALYs	QIV dominates
			(Year 2006]					$ 25,803	2.210 QALYs	103,072
			≥ 80 y (Year 2007]					$ -483,461	27.335 QALYs	QIV dominates
			≥ 80 y (Year 2006]					$ 14,657	0.829 QALYs	78,633
			Elderly (65-79] (Year 2007]					$ 266,473	22.826 QALYs	100,164
			(Year 2006]					$ 25,803	2.21 QALYs	1,135,786
			≥ 80 y (Year 2007]					$ 483,461	27.335 QALYs	13,440
			≥ 80 y (Year 2006]					$ 14,657	0.829 QALYs	945,509

Table 2
Range of costs reported in the selected studies by Region and patients' group

	All population	Children	Adult	Elderly	Pregnant	High-Risk
Europe (12)	IC with Increasing TIV uptake *vs* No vac.: € 689,687 - € 1,902,263 [8]	No Vac.: 27,468 mln £ Current policy: 18,304 mln £ Increasing LAIV: 18,122-19,973 mln £ Increasing TIV: 18,496-20,493 mln £ [17]	IC with Increasing TIV: 709,703 mln € [8]	TIV £ 7,578,672,042 QIV £ 7,769,450,859 [9]	IC with Increasing TIV: 385,978 mln € [8]	TIV £7,578,672,042 QIV £7,769,450,859 [9]
				No vac.: K£40,664 alternative influenza vac. policies: K£167,425 [10]		
	TIV: £4,114,006,943 QIV: £4,304,813,247 [18]	No Vac.: 188.0 mln £ Vac.: 210.7-226.1 mln £ [19]		TIV: €34,462,064,137-46,363,458,774 QIV: €34,364,483,970-46,713,433,398 [11]		No Vac.: £ k 40,664 Alternative influenza Vac. policies: k £167,425 [10]
	TIV: €798,118,103 -4,066,097,342 QIV: €855,597,200-4,008,204,019 [14]	TIV: €4,089,995,812-15,042,784,059 TIV + LAIV: €4,488,611,779-11,639,184,713 [12]		Current situation: 45.6 mln PLN New Policy: 41.6 mln PLN [13]		TIV: £27,861,559,964 QIV: £28,557,157,397 [15]
	No Vac.: 230-2,828 mln € TIV: 580-3,066 mln € QIV: 556-2,795 mln € [16]					
USA (8)	TIV: $25,769,664,907 QIV: $25,891,577,650 [22]	LAIV: $165.25 IIV: $174.00 (per patient] [26]		No Vac.: $70.52 TIV: $81.73 QIV: $85.83 HD $85.43 (per person] [21]	Vac. was less costly than No vac. [20]	
		LAIV was more costly than IIV [25]		TIV HD 1,377-2,007 US$ TIV SD: 1,493-2,029 US$ (per participant] [23]		
				No vac.: 96.49 $ TIV: 100.62 $ QIV: 102.64 $ TIV HD: 109.10 $ (per person] [5]		
				No vac.: $8,409,289 Vac.: $8,426,664-8,457,895 (per 100,000 persons] [24]	Vac.: $197.6-328.5 No vac.: $ 183.9-341.02 (per mother] [7]	
Canada (3)	TIV: $2,232,166,489 QIV: $2,452,203,389 [18]	Vac.: $69.07 No vac.: $32.66 (per patient] [28]				
	QIV was more costly than TIV [27]					
China (3)	TIV: $44,071-183,235 QIV: $82,948-204,835 (per 100,000] [30]			IM vac.: $47.59 ID vac.: $52.82 (per person] [31]		
				QIV was less costly than TIV [29]		
Turkey (1)						Current situation: 140,517,766 TRY projected situation: 174,597-1,055,590 TRY [32]
Israel (1)						No vac. $ 3,563,543-5,825,904 Vac.: $ 2,906,783-6,506,343 [35]
Thailand (1)		No vac.: 20 mln $ TIV: 237mln $ LAIV: 111-392 mln $[33]				
Australia (1)				IC of Vac. *vs* No vac.: 12-64 mln A$ [34]		

IC: Incremental Costs, No vac.: No vaccination, mln: Million, Vac.: Vaccination, k: Thousand, TIV: Trivalent Inactivated Influenza Vaccine, QIV: Quadrivalent Inactivated Influenza Vaccine, LAIV: live Live Attenuated Influenza Vaccine, IIV: Inactivated Vaccine, HD: High-dose, SD: Standard-dose, IM: Intra-Muscular, ID: Intra-Dermal.

Table 3
Range of outcome reported in the selected studies by Region and patients' group

	All popoulation	Children	Adult	Elderly	Pregnant	High-Risk
Europe (12)	Incr. QALYs with Increasing TIV vs No Vac.: 31-132 [8]	No Vac.: 27.7 mln QALYs lost Current policy: 7.7 QALYs lost Current policy + LAIV: 1.1 – 5.7 mln QALYs lost Current policy + TIV: 1.7 – 6.2 mln QALYs lost [17]	Incr. QALYs with Increasing TIV uptake *vs* No Vac.: 29 [8]	TIV 1,190,979,257 QALYs /1,375,979,430 LYs QIV 1,191,015,2591,2 QALYs /1,376,016,515 LYs [9]	Incremental QALYs with Increasing TIV *vs* No Vac.: 58 [8]	TIV 1,190,979,257 QALYs /1,375,979,430 LYs QIV 1,191,015,259 QALYs /1,376,016,515 LYs [9]
				No Vac.: 71,025 QALYs lost Alternative influenza Vac. policies: 54,068 QALYs lost [10]		
	TIV: 998,215 QALYs/496,291 LYs lost QIV:968,900 QALYs/475,295 LYs lost [18]	No Vac.: 38,600 QALYs lost Vac. saves: 38,496 - 37,244 QALYs [19]		TIV: 1,038,585,055 QALYs /1,143,182,206 LYs QIV: 1,038,625,059 QALYs /1,143,233,538 LYs [11]		No Vac.: 71,025 QALYs lost Alternative influenza Vac. policies: 54,068 QALYs lost [10]
	TIV: 78,740 QIV: 74,765 QALYs lost [14]	TIV:449,443 TIV + LAIV: 273,483 QALYs lost [12]		Current situation: 44,143,029 LYs lost/24,490,083 QALYs lost New situation: 44,147,726 LYs/24,492,828 QALYs lost [13]		TIV: 956,326,785 QALYs/1,051,806,914 LYs QIV: 956,378,323 QALYs/1,051,860,14 LYs [15]
	No Vac.: 159 k QALYs lost TIV: 94-112 k QALYs lost QIV: 86-97 k QALYs lost [16]					
USA (8)	TIV: 225,372 LYs/171,428 QALYs lost QIV: 220,560 LYs/167,832 QALYs lost [22]	LAIV: -8.4 E-04 IIV: -9.2 E-04 QALYs [26]		No Vac.: 4.96 QALYs TIV: 4.96 QIV: 4.96 QALYs HD: 4.96 QALY (per person] [21]	Vac. was more efficacious than no vac.[20]	
		LAIV was more efficacious than IIV [25]		TIV HD 8.1187-8.1502 QALYs TIV SD: 8.1134-8.1499 QALYs (per participant] [23]		
				No Vac.: 0.00652 QALYs lost TIV: 0.0054 QALYs lost QIV: 0.0053 QALYs lost HD TIV: 0.0051 QALYs lost (per person] [5]		
				No Vac.: 39.9 deaths Va.: 38.5-38.6 deaths (per 100.000 persons] [24]	Net social benefit value of Vac.: $12.57 (per mother] [7]	
Canada (3)	TIV: 522,596 QALYs/344,912 LYs lost QIV: 490,805 QALYs/322,013 LYs lost [18]	Vac.: 0.04 No Vac.: 0.27 (influenza cases] [28]				
	QIV: 76 QALY/49 LYs [27]					
China (3)	TIV: 13.34 QALYs lost QIV: 11.62 QALYs lost (per 100,000] [30]			IM vac.: 0.00372 QALYs lost ID vac.: 0.00336 QALYs lost (per person] [31]		
				QIV was more efficacious than TIV [29]		
Turkey (1)						Current situation: 91,562,582 QALYs/ 117,155,365 LYs gained Projected situation: Incr. QALYs 2,743-16,580 /Incr. LYs 3,342-20,208 [32]
Israel (1)						QALYs saved with Vac.: 203.71-237.31 [35]
Thailand (1)		No Vac.: 0 DALYs averted TIV: 49 DALYs averted LAIV: 45-65 DALYs averted [33]				
Australia (1)				Incr. QALYs of Vac. *vs* No Vac.: 344-6,324 [34]		

Incr: Incremental, No Vac.: No Vaccination, mln: million, Vac.: Vaccination, k: thousand, TIV: Trivalent Inactivated Influenza Vaccine, QIV: Quadrivalent Inactivated Influenza Vaccine, LAIV: Live Attenuated Influenza Vaccine, IIV: Inactivated Vaccine, HD: High-dose, SD: Standard-dose, IM: Iintra-Muscular, ID: Intra-Dermal, LYs: Life Years, QALYs: Quality Adjusted Life Years, DALYs: Disability Adjusted Life Years.