Supplementary Appendix

This supplementary material is hosted by Eurosurveillance as supporting information alongside the article, "The impact of repeated vaccination using 10-year vaccination history on protection against influenza in older adults: a test-negative design study across the 2010/11 to 2015/16 influenza seasons in Ontario, Canada," on behalf of the authors who remain responsible for the accuracy and appropriateness of the content. The same standards for ethics, copyright, attributions and permissions as for the article apply. Supplements are not edited by Eurosurveillance and Eurosurveillance is not responsible for the maintenance of any links or email addresses provided therein.

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 Table S1. Participating laboratories and research ethics approval numbers

Laboratory	Ethics approval numbers
Children's Hospital of Eastern Ontario	14/124X
London Health Sciences Centre	106495
Mount Sinai Hospital	14-0142-C
North York General Hospital	14-0028
Public Health Ontario	2013-051.04
St. Joseph's Healthcare Hamilton	14-785-C
Sunnybrook Health Sciences Centre	082-2014
University Health Network	14-7887.6
William Osler Health System	14-0014

	<u> </u>		
Characteristic	Subtyped Specimens (n=4,592)	Not Subtyped Specimens (n=4,772)	p-value
Influenza season		· · ·	< 0.001
2010/11	807 (17.6)	331 (6.9)	
2011/12	80 (1.7)	28 (0.6)	
2012/13	999 (21.8)	1,130 (23.7)	
2013/14	371 (8.1)	350 (7.3)	
2014/15	1,787 (38.9)	2,290 (48.0)	
2015/16	548 (11.9)	643 (13.5)	
Age (years), mean ± SD	80.2 ± 8.1	80.5 [`] ± 8.1	0.076
Age group in years			0.24
66-75	1,395 (30.4)	1,411 (29.6)	
76-85	1.886 (41.1)	1,923 (40,3)	
≥ 86	1.311 (28.5)	1,438 (30,1)	
Male sex	2.171 (47.3)	2,218 (46.5)	0.44
Neighbourhood income quintile	_,,	_, (,	0.012
1 (lowest)	1.086 (23.6)	1.087 (22.8)	
2	1.025 (22.3)	944 (19.8)	
3	847 (18.4)	944 (19.8)	
4	807 (17.6)	917 (19.2)	
5 (highest)	804 (17.5)	849 (17.8)	
Missing	23 (0.5)	31 (0.6)	
Received homecare services past 1v	2159(470)	2 143 (44 9)	0.041
Hospitalisations, past 3v, mean + SD	1.3 ± 2.0	1.3 ± 2.0	0.49
Outpatient visits past 1y mean + SD	139 + 111	122+96	< 0.001
Prescription medications, past 1v, mean ± SD	15.8 ± 9.3	15.5 ± 8.9	0.049
Month of influenza testing			< 0.001
November	84 (1.8)	40 (0.8)	0.001
December	1 581 (34 4)	1 149 (24 1)	
January	1 646 (35 8)	1,967 (41.2)	
February	685 (14.9)	889 (18.6)	
March	430 (9.4)	615 (12.9)	
April	130 (2.8)	96 (2 0)	
May	36 (0.8)	16 (0.3)	
Vaccinated against influenza	2 127 (46 3)	2 425 (50 8)	< 0.001

Table S2. Descriptive characteristics of individuals with subtyped and unsubtyped influenza A specimens obtained from community-dwelling adults aged > 65 years, 2010/11 to 2015/16 influenza seasons (n=9,364)

Supplementary Text. Sensitivity analysis involving manual reclassification of past vaccination status based on misclassification of current season vaccination status

For each execution of the misclassification macro developed by Fox et al.,(1) thousands of iterations of exposure re-classification are performed on the observed data, with each iteration using a different combination of sensitivity and specificity values within the pre-specified ranges to calculate an OR. Thus, some individuals could be deemed misclassified in one iteration but not the next. The reported misclassification-corrected adjusted vaccine effectiveness (VE) estimate is based on the median odds ratio (OR) calculated from all iterations.

We modified the macro to retain the re-classified current season vaccination status for each individual from each iteration, which we used to determine the overall proportion vaccinated separately among test-positive cases and test-negative controls for each iteration. After all iterations were completed, we calculated the proportion of iterations for which each individual was re-classified as vaccinated. We also calculated the median overall proportion vaccinated for cases and controls. If an individual's proportion was greater than the median for their case status, their current season vaccination status was set to vaccinated.

For those individuals whose current season vaccination status was re-classified, we created two scenarios to also change their past seasons' vaccination history. In the first scenario, we assumed that for all previous seasons where they were considered to be unvaccinated in the administrative data, we changed them to vaccinated. Consequently, these individuals were re-categorized to the highest past vaccination history group in each respective analysis (e.g., in the one previous season analysis, all were re-categorized into the 'vaccinated in the previous season' group; in the five previous seasons analysis, all were re-categorized to the 'vaccinated in 4-5 previous seasons' group). In the second scenario, we assumed that only some of the previous seasons were misclassified as unvaccinated. To achieve this, we moved these individuals 'up' one past vaccination history category (e.g., for the analysis examining 5-year vaccination history, those initially considered vaccinated in none of the previous five seasons' group). We conducted stratified analyses using these new past vaccination history groups for both scenarios.

Reference

Fox MP, Lash TL, Greenland S. A method to automate probabilistic sensitivity analyses of misclassified binary variables. Int J Epidemiol. 2005 Dec 1;34(6):1370–6.

	N (%	6)	
	Test-Positive	Test-Negative	n-value
Characteristic	(n=11,496)	(n=46,808)	p-value
Influenza season*			< 0.001
2010/11	1,204 (10.5)	4,980 (10.6)	
2011/12	413 (3.6)	3,216 (6.9)	
2012/13	2,253 (19.6)	8,577 (18.3)	
2013/14	1,554 (13.5)	9,665 (20.6)	
2014/15	4,432 (38.6)	12,044 (25.7)	
2015/16	1,640 (14.3)	8,326 (17.8)	
Age* (years), mean ± SD	80.2 ± 8.2	79.4 ± 8.1	< 0.001
Age group in years			< 0.001
66-75	3,601 (31.3)	16,716 (35.7)	
76-85	4,548 (39.6)	18,181 (38.8)	
≥86	3,347 (29.1)	11,911 (25.4)	
Male sex*	5,348 (46.5)	22,446 (48.0)	0.006
Neighbourhood income quintile*			0.036
1 (lowest)	2,630 (22.9)	10,473 (22.4)	
2	2,475 (21.5)	9,909 (21.2)	
3	2,177 (18.9)	8,805 (18.8)	
4	2,088 (18.2)	8,308 (17.7)	
5 (highest)	2,062 (17.9)	9,022 (19.3)	
Missing	64 (0.6)	291 (0.6)	
Medical conditions	()	()	
Cardiovascular disease ^a	7,021 (61.1)	30,293 (64.7)	< 0.001
Chronic obstructive pulmonary disease	5.376 (46.8)	24.378 (52.1)	< 0.001
Diabetes	5.020 (43.7)	19,930 (42.6)	0.034
Cancer	2.877 (25.0)	14,244 (30,4)	< 0.001
Asthma	3.102 (27.0)	13.112 (28.0)	0.027
Anaemia	2,445 (21.3)	11.581 (24.7)	< 0.001
Chronic kidney disease	2 331 (20 3)	10,546 (22,5)	< 0.001
Dementia/frailty	2,505 (21.8)	8.947 (19.1)	< 0.001
Immunocompromised	1 363 (11 9)	6 843 (14 6)	< 0.001
Any of the above medical conditions*	10 806 (94 0)	44 773 (95 7)	< 0.001
Received homecare services [*] past 1v	5 193 (45 2)	23 203 (49 6)	< 0.001
Hospitalisations* past 3v mean + SD	13+19	17+23	< 0.001
Outpatient visits* past 1v mean + SD	13.0 ± 10.4	14.5 + 11.1	< 0.001
Prescription medications* past 1v mean + SD	155+90	168+94	< 0.001
Month of influenza testing*	10.0 ± 0.0	10.0 ± 0.4	< 0.001
November	127 (1 1)	1 284 (2 7)	0.001
December	2 763 (24 0)	6 763 (14 4)	
lanuary	2,703 (24.0)	(14.4)	
February	1 780 (15 5)	8 565 (18 3)	
March	1,700 (15.5)	8 953 (10.3)	
April	1,002 (10.7)	6 503 (14 1)	
-τριπ Μav	291 (2.5)	3 230 (6 0)	
Tested sample from innatient setting	Q 170 (70 Q)	10 605 (86 Q)	< 0.001
Vaccinated against influenza	5,110 (19.0)	-+0,030 (00.3) 25 /20 (5/ 2)	
Vaccinated in prior season	6 177 (53 7)	27,723 (34.3)	< 0.001
	0,177(33.7)	27,000 (37.0)	< 0.00 I

Table S3. Descriptive characteristics of influenza test-positive and influenza testnegative community-dwelling adults aged > 65 years, 2010/11 to 2015/16 influenza seasons (n=58,304)

* Included in multivariable models for estimating vaccine effectiveness

^a Includes acute ischaemic stroke, arrhythmias, congestive heart failure, ischaemic heart disease, and transient ischaemic attack.

$\begin{tabular}{ c c c c c } \hline Vaccinated (n=31,004) & Unvaccinated (n=27,300) & p-value \\ \hline Influenza season* & < 0.001 \\ \hline Influenza season* & < 0.001 \\ \hline 2010/11 & 3,049 (9.8) & 3,135 (11.5) \\ 2011/12 & 2,018 (6.5) & 1,611 (5.9) \\ 2012/13 & 5,327 (17.2) & 5,503 (20.2) \\ 2013/14 & 6,079 (19.6) & 5,140 (18.8) \\ 2014/15 & 9,128 (29.4) & 7,348 (26.9) \\ 2015/16 & 5,403 (17.4) & 4,563 (16.7) \\ Age * (years), mean \pm SD & 80.0 \pm 7.9 & 79.0 \pm 8.4 < 0.00166.75 & 9,912 (32.0) & 10,405 (38.1) \\ 76.85 & 12,730 (41.1) & 9,999 (36.6) \\ \geq 86 & 8,362 (27.0) & 6,896 (25.3) \\ Male sex^* & 15,081 (48.6) & 12,713 (46.6) & < 0.001 \\ Neighbourhood income quintile* & < 0.665 (21.5) & 6,438 (23.6) \\ 2 & 6,589 (21.3) & 5,795 (21.2) \\ 3 & 5,860 (18.9) & 5,122 (18.8) \\ 4 & 5,586 (18.0) & 4,810 (17.6) \\ 5 (highest) & 6,147 (19.8) & 4,937 (18.1) \\ Missing & 157 (0.5) & 198 (0.7) \\ \hline \end{tabular}$		N (%)				
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	-	Vaccinated	Unvaccinated			
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Characteristic	(n=31,004)	(n=27,300)	p-value		
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Influenza season*			< 0.001		
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	2010/11	3,049 (9.8)	3,135 (11.5)			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	2011/12	2,018 (6.5)	1,611 (5.9)			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	2012/13	5,327 (17.2)	5,503 (20.2)			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	2013/14	6,079 (19.6)	5,140 (18.8)			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	2014/15	9,128 (29.4)	7,348 (26.9)			
Age* (years), mean \pm SD80.0 \pm 7.979.0 \pm 8.4< 0.001Age group in years9,912 (32.0)10,405 (38.1)< 0.001	2015/16	5.403 (17.4)	4.563 (16.7)			
Age group in years< 0.001 $66-75$ 9,912 (32.0)10,405 (38.1) $76-85$ 12,730 (41.1)9,999 (36.6) ≥ 86 8,362 (27.0)6,896 (25.3)Male sex*15,081 (48.6)12,713 (46.6)Neighbourhood income quintile*< 0.001	Age* (vears), mean ± SD	80.0 ± 7.9	79.0 ± 8.4	< 0.001		
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Age group in years			< 0.001		
$76-85$ $12,730(41.1)$ $9,999(36.6)$ ≥ 86 $8,362(27.0)$ $6,896(25.3)$ Male sex* $15,081(48.6)$ $12,713(46.6)$ < 0.001 Neighbourhood income quintile* $< 0.665(21.5)$ $6,438(23.6)$ 1 (lowest) $6,665(21.3)$ $5,795(21.2)$ 3 $5,860(18.9)$ $5,122(18.8)$ 4 $5,586(18.0)$ $4,810(17.6)$ 5 (highest) $6,147(19.8)$ $4,937(18.1)$ Missing $157(0.5)$ $198(0.7)$	66-75	9,912 (32,0)	10.405 (38.1)			
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	76-85	12.730 (41.1)	9,999 (36.6)			
Male sex* 15,081 (48.6) 12,713 (46.6) < 0.001	≥86	8.362 (27.0)	6.896 (25.3)			
Neighbourhood income quintile* < 0.001	Male sex*	15.081 (48.6)	12.713 (46.6)	< 0.001		
1 (lowest) 6,665 (21.5) 6,438 (23.6) 2 6,589 (21.3) 5,795 (21.2) 3 5,860 (18.9) 5,122 (18.8) 4 5,586 (18.0) 4,810 (17.6) 5 (highest) 6,147 (19.8) 4,937 (18.1) Missing 157 (0.5) 198 (0.7)	Neighbourhood income guintile*	,,	,,	< 0.001		
2 6,589 (21.3) 5,795 (21.2) 3 5,860 (18.9) 5,122 (18.8) 4 5,586 (18.0) 4,810 (17.6) 5 (highest) 6,147 (19.8) 4,937 (18.1) Missing 157 (0.5) 198 (0.7)	1 (lowest)	6.665 (21.5)	6.438 (23.6)			
3 5,860 (18.9) 5,122 (18.8) 4 5,586 (18.0) 4,810 (17.6) 5 (highest) 6,147 (19.8) 4,937 (18.1) Missing 157 (0.5) 198 (0.7)	2	6.589 (21.3)	5.795 (21.2)			
4 5,586 (18.0) 4,810 (17.6) 5 (highest) 6,147 (19.8) 4,937 (18.1) Missing 157 (0.5) 198 (0.7) Medical conditions 157 (0.5) 198 (0.7)	3	5.860 (18.9)	5.122 (18.8)			
5 (highest) 6,147 (19.8) 4,937 (18.1) Missing 157 (0.5) 198 (0.7) Medical conditions 157 (0.5) 198 (0.7)	4	5,586 (18.0)	4.810 (17.6)			
Missing 157 (0.5) 198 (0.7) Medical conditions 157 (0.5) 198 (0.7)	5 (highest)	6,147 (19.8)	4.937 (18.1)			
Medical conditions	Missing	157 (0.5)	198 (0 7)			
	Medical conditions					
Cardiovascular disease ^a 20.258 (65.3) 17.056 (62.5) < 0.001	Cardiovascular disease ^a	20.258 (65.3)	17.056 (62.5)	< 0.001		
Chronic obstructive nulmonary disease $16.561(53.4)$ $13.193(48.3) < 0.001$	Chronic obstructive pulmonary disease	16,561 (53,4)	13 193 (48 3)	< 0.001		
Diabetes $13,595,(43,8)$ $11,355,(41,6) < 0.001$	Diabetes	13 595 (43 8)	11 355 (41 6)	< 0.001		
Cancer 9.290 (30.0) 7.831 (28.7) < 0.001	Cancer	9,290 (30.0)	7.831 (28.7)	< 0.001		
Asthma 9.340 (30.1) 6.874 (25.2) < 0.001	Asthma	9 340 (30 1)	6 874 (25 2)	< 0.001		
Anaemia $7.673(247)$ $6.353(23.3) < 0.001$	Anaemia	7 673 (24 7)	6 353 (23 3)	< 0.001		
Chronic kidney disease 6 874 (22.2) 6 003 (22.0) 0 578	Chronic kidney disease	6 874 (22 2)	6,003 (22,0)	0.578		
Dementia/frailty $5,829(18,8)$ $5,623(20,6)$ < 0.001	Dementia/frailty	5 829 (18 8)	5 623 (20 6)	< 0.001		
Immunocompromised $4599(14.8)$ $3607(13.2) < 0.001$	Immunocompromised	4 599 (14 8)	3 607 (13 2)	< 0.001		
Any of the above medical conditions* $29808(961)$ $25771(944)$ < 0.001	Any of the above medical conditions*	29 808 (96 1)	25 771 (94 4)	< 0.001		
Received homecare services [*] nast 1_{V} 14 523 (46.8) 13 873 (50.8) < 0.001	Received homecare services [*] nast 1v	14 523 (46 8)	13 873 (50 8)	< 0.001		
Hospitalisations* nast 3v mean + SD $15+21$ $17+23$ < 0.001	Hospitalisations* past 3v mean + SD	15+21	17 + 23	< 0.001		
Outpatient visits* past 1y mean + SD $156 + 10.8$ $126 + 10.9$ < 0.001	Outpatient visits* past 1v mean + SD	15.6 + 10.8	126 + 109	< 0.001		
Prescription medications* past 1v mean + SD $172 + 89$ $157 + 96$ < 0.001	Prescription medications* past 1y mean + SD	17 2 + 8 9	157+96	< 0.001		
Month of influenza testing*	Month of influenza testing*	17.2 ± 0.5	10.7 ± 0.0	< 0.001		
November 509 (1.6) 902 (3.3)	November	509 (1.6)	902 (3.3)	0.001		
December $4.674(15.1)$ $4.852(17.8)$	December	4 674 (15 1)	4 852 (17 8)			
$\begin{array}{c} 1 \\ 1 \\ 1 \\ 1 \\ 2 \\ 1 \\ 1 \\ 2 \\ 1 \\ 1 \\$	lanuary	7 919 (25 5)	7 177 (26 3)			
Eebruary $5502(18.0)$ $4,773(17.4)$	February	5 592 (18 0)	A 753 (17 A)			
March 5 969 (19 3) 4 786 (17 5)	March	5,069 (10.0)	4 786 (17.5)			
Δpril (17.3) 4,700 (17.3)	Anril	0,309 (13.0) A 320 (14.0)	3 321 (12 2)			
May 2 0 10 (14.0) 3,321 (12.2)	יוויקר <i>י</i> איפע	2 012 (6 5)	1 500 (5 5)			
Tested sample from inpatient setting 26 592 (95 7) 22 292 (95 2) 0.116	Tested sample from innationt sotting	2,012 (0.3)	23 282 (85 2)	0 1 1 6		
Specimen positive for influenza $5.575(12.0)$ $5.021(21.7)$ -0.001	Specimen positive for influenze	20,303 (03.7) 5 575 (12 0)	5 021 (21 7)			
Vaccinated in prior season $24594(79.3)$ $8651(31.7) < 0.001$	Vaccinated in prior season	24 594 (79 3)	8 651 (31 7)	< 0.001		

Table S4. Descriptive characteristics of vaccinated and unvaccinated communitydwelling adults aged > 65 years, 2010/11 to 2015/16 influenza seasons (n=58,304)

* Included in multivariable models for estimating vaccine effectiveness a Includes acute ischaemic stroke, arrhythmias, congestive heart failure, ischaemic heart disease, and transient ischaemic attack.

Analysis	Test-Positive, No. Vaccinated/Total	Test-Negative, No. Vaccinated/Total	Unadjusted VE% (95% CI)	Adjusted VE% (95% Cl)
2010/11				
Influenza A				
A(H1N1)pdm09	≤ 5 ^b / ≤ 26 ^b	2,561 / 4,980	76 (37, 91)	72 (25, 90)
A(H3N2)	311 / 782	2,561 / 4,980	38 (27, 47)	33 (21, 43)
A(unsubtyped)	144 / 331	2,561 / 4,980	27 (9, 42)	26 (7, 42)
Influenza B	28 / 66	2,561 / 4,980	30 (–14, 57)	35 (–8, 61)
2011/12				
Influenza A				
A(H1N1)pdm09	14 / 33	1,823 / 3,216	44 (–13, 72)	31 (–41, 66)
A(H3N2)	22 / 47	1,823 / 3,216	33 (-20, 62)	40 (-9, 67)
A(unsubtyped)	18 / 28	1,823 / 3,216	-38 (-199, 37)	-47 (-229, 35)
Influenza B	141 / 305	1,823 / 3,216	34 (17, 48)	35 (17, 50)
2012/13			. ,	. ,
Influenza A				
A(H1N1)pdm09	29 / 47	4,339 / 8,577	-57 (-184, 13)	-59 (-191, 14)
A(H3N2)	421 / 953	4,339 / 8,577	23 (12, 32)	20 (7, 30)
A(unsubtyped)	484 / 1,130	4,339 / 8,577	27 (17, 35)	23 (12, 33)
Influenza B	54 / 124	4,339 / 8,577	25 (-8, 47)	28 (-4, 50)
2013/14				
Influenza A				
A(H1N1)pdm09	103 / 269	5,368 / 9,665	50 (36, 61)	44 (28, 57)
A(H3N2)	54 / 103	5,368 / 9,665	12 (-30, 40)	21 (-17, 47)
A(unsubtyped)	160 / 350	5,368 / 9,665	33 (17, 46)	26 (7, 40)
Influenza B	394 / 834	5,368 / 9,665	28 (17, 38)	38 (28, 47)
2014/15				
Influenza A				
A(H1N1)pdm09	≤ 5 [⊳] / ≤ 5 [⊳]	6,712 / 12,044	47 (–217, 91)	31 (–346, 89)
A(H3N2)	926 / 1,783	6,712 / 12,044	14 (5, 22)	17 (7, 25)
A(unsubtyped)	1,302 / 2,290	6,712 / 12,044	-5 (-15, 4)	-5 (-16, 4)
Influenza B	186 / 356	6,712 / 12,044	13 (-7, 30)	18 (–3, 34)
2015/16			. ,	. ,
Influenza A				
A(H1N1)pdm09	194 / 451	4,626 / 8,326	40 (27, 50)	37 (24, 49)
A(H3N2)	46 / 97	4,626 / 8,326	28 (–8, 52)	31 (–3, 54)
A(unsubtyped)	317 / 643	4,626 / 8,326	22 (9, 34)	17 (2, 30)
Influenza B	224 / 453	4,626 / 8,326	22 (5, 35)	22 (6, 36)

Table S5. Influenza vaccine effectiveness estimates for community-dwelling adults aged > 65 years, by influenza type/subtype and influenza season (2010/11 to 2015/16)^a

^a The model adjusted for age, sex, census area-level neighbourhood income quintile, number of hospitalisations in the past 3 years, number of outpatient visits in the past year, receipt of home care services in the past year, number of prescription medications in the past year, comorbidities that increase the risk of influenza complications (anaemia, cancer, cardiovascular disease, dementia, diabetes, frailty, immunodeficiency due to underlying disease and/or therapy, as well as renal disease and respiratory disease), and calendar time.

^b Suppressed due to small cell sizes (direct or by inference), which cannot be reported as per privacy regulations.

Figure S1. Forest plots of (A) current season vaccine effectiveness estimates against influenza A(H3N2) for community-dwelling adults aged > 65 years, taking into account vaccination histories for one, five, and 10 previous seasons and stratifying according to number of vaccinations received, and (B) also correcting for misclassification of current season vaccination status

Analysis	Vaccination History				VE (95% CI)	Trend Test
1 prev. season	Vaccinated prev. season				18% (9, 26)	p=0.252
	Not vaccinated prev. season				24% (13, 33)	
5 prev. seasons	Vaccinated 4-5 of prev. 5 seasons				18% (7, 27)	p=0.107
	Vaccinated 1-3 of prev. 5 seasons		-		29% (19, 38)	
	Vaccinated 0 of prev. 5 seasons				31% (1, 52)	
10 prev. seasons	Vaccinated 9-10 of prev. 10 seasons				11% (-5, 25)	p=0.012
	Vaccinated 7-8 of prev. 10 seasons				24% (8, 37)	
	Vaccinated 4-6 of prev. 10 seasons				33% (19, 44)	
	Vaccinated 1-3 of prev. 10 seasons				33% (12, 50)	
	Vaccinated 0 of prev. 10 seasons			-	41% (-3, 66)	
a		r				
		-50%	0 50%	100%		
			vaccine Ellectivenes	5		
Analysis	Vaccination History				VE (95% CI)	Trend Test
1 prev. season	Vaccinated prev. season		-		32% (24, 40)	p=0.030
	Not vaccinated prev. season		-		43% (36, 49)	
5 prev. seasons	Vaccinated 4-5 of prev. 5 seasons				30% (19, 39)	p=0.239
	Vaccinated 1-3 of prev. 5 seasons				45% (37, 52)	
	Vaccinated 0 of prev. 5 seasons				43% (31, 52)	
10 prev. seasons	Vaccinated 9-10 of prev. 10 seasons				24% (7, 38)	p=0.233
	Vaccinated 7-8 of prev. 10 seasons				41% (28, 52)	
	Vaccinated 4-6 of prev. 10 seasons				41% (28, 52)	
	Vaccinated 1-3 of prev. 10 seasons				48% (34, 58)	
	Vaccinated 0 of prev. 10 seasons				36% (18, 50)	
b		r		1		
		-50%		100%		
			vaccine Effectivenes	5		

Figure S2. Forest plots of (A) current season vaccine effectiveness estimates against influenza A(H1N1)pdm09 for community-dwelling adults aged > 65 years, taking into account vaccination histories for one, five, and 10 previous seasons and stratifying according to number of vaccinations received, and (B) also correcting for misclassification of current season vaccination status

Analysis	Vaccination History			١	VE (95% CI)	Trend Test
1 prev. season	Vaccinated prev. season			2	20% (-1, 36)	p=0.075
	Not vaccinated prev. season			3	39% (22, 53)	
5 prev. seasons	Vaccinated 4-5 of prev. 5 seasons			C	0% (-37, 27)	p=0.255
	Vaccinated 1-3 of prev. 5 seasons			4	14% (25, 58)	
	Vaccinated 0 of prev. 5 seasons			3	35% (-26, 66)	
10 prev. seasons	Vaccinated 9-10 of prev. 10 seasons			-	-18% (-99, 30)	p=0.834
	Vaccinated 7-8 of prev. 10 seasons			3	32% (-8, 57)	
	Vaccinated 4-6 of prev. 10 seasons			3	35% (2, 58)	
	Vaccinated 1-3 of prev. 10 seasons			1	18% (-37, 51)	
	Vaccinated 0 of prev. 10 seasons	•		-	-58% (-269, 33)	
2		r		_		
a		-50% 0	50%	100%		
		Vaccine E	ffectiveness			
Analysis	Vaccination History			١	VE (95% CI)	Trend Test
1 prev. season	Vaccinated prev. season			4	40% (22, 54)	p=0.304
	Not vaccinated prev. season			4	49% (38, 58)	
5 prev. seasons	Vaccinated 4–5 of prev. 5 seasons			2	27% (-6, 50)	p=0.108
	Vaccinated 1-3 of prev. 5 seasons			4	47% (30, 60)	
	Vaccinated 0 of prev. 5 seasons			5	53% (33, 67)	
10 prev. seasons	Vaccinated 9-10 of prev. 10 seasons			2	2% (-86, 48)	p=0.674
	Vaccinated 7-8 of prev. 10 seasons			3	39% (-3, 63)	
	Vaccinated 4-6 of prev. 10 seasons			4	47% (17, 66)	
	Vaccinated 1-3 of prev. 10 seasons	-		4	47% (16, 66)	
	Vaccinated 0 of prev. 10 seasons			2	20% (-36, 53)	
_		,i		_		
b		-50% 0	50%	100%		
		Vaccine E	ffectiveness			

Figure S3. Forest plots of (A) current season vaccine effectiveness estimates against influenza B for community-dwelling adults aged > 65 years, taking into account vaccination histories for one, five, and 10 previous seasons and stratifying according to number of vaccinations received, and (B) also correcting for misclassification of current season vaccination status

Analysis	Vaccination History					VE (95% CI)	Trend Test
1 prev. season	Vaccinated prev. season		÷			11% (-3, 23)	p<0.001
	Not vaccinated prev. season					42% (32, 51)	
5 prev. seasons	Vaccinated 4-5 of prev. 5 seasons			-		18% (3, 31)	p=0.141
	Vaccinated 1-3 of prev. 5 seasons					20% (4, 33)	
	Vaccinated 0 of prev. 5 seasons					56% (30, 72)	
10 prev. seasons	Vaccinated 9-10 of prev. 10 seasons					29% (9, 44)	p=0.909
	Vaccinated 7-8 of prev. 10 seasons			_		16% (-9, 35)	
	Vaccinated 4-6 of prev. 10 seasons			-		9% (-19, 31)	
	Vaccinated 1-3 of prev. 10 seasons					29% (-1, 50)	
	Vaccinated 0 of prev. 10 seasons			-		48% (-11, 75)	
•		·		1			
a		-50%	0 Maasina Eff	50%	100%		
			vaccine Ene	ectiveness			
Analysis	Vaccination History					VE (95% CI)	Trend Test
1 prev. season	Vaccinated prev. season			-		30% (16, 41)	p=0.002
	Not vaccinated prev. season					51% (44, 57)	
5 prev. seasons	Vaccinated 4-5 of prev. 5 seasons					41% (28, 52)	p=0.460
	Vaccinated 1-3 of prev. 5 seasons		_	-		32% (18, 44)	
	Vaccinated 0 of prev. 5 seasons					53% (42, 62)	
10 prev. seasons	Vaccinated 9-10 of prev. 10 seasons		-	-		44% (25, 58)	p=0.952
	Vaccinated 7-8 of prev. 10 seasons		_	-		37% (16, 53)	
	Vaccinated 4-6 of prev. 10 seasons			-		33% (11, 50)	
	Vaccinated 1-3 of prev. 10 seasons		-			43% (22, 58)	
	Vaccinated 0 of prev. 10 seasons		—	-		41% (20, 56)	
		r		1			
b		-50%	0	50%	100%		
			Vaccine Effe	ectiveness			

Figure S4. Forest plots of (A) current season vaccine effectiveness estimates against any influenza restricted to community-dwelling adults aged ≥ 75 years, taking into account vaccination histories for one, five, and 10 previous seasons and stratifying according to number of vaccinations received, and (B) also correcting for misclassification of current season vaccination status

Analysis	Vaccination History					VE (95% CI)	Trend Test
1 prev. season	Vaccinated prev. season		-			7% (0, 14)	p=0.001
	Not vaccinated prev. season		-	-		23% (16, 30)	
5 prev. seasons	Vaccinated 4-5 of prev. 5 seasons		-			8% (0, 16)	p=0.008
	Vaccinated 1-3 of prev. 5 seasons		-	-		20% (12, 27)	
	Vaccinated 0 of prev. 5 seasons		_			29% (11, 44)	
10 prev. seasons	Vaccinated 9-10 of prev. 10 seasons		-			7% (-4, 16)	p=0.001
	Vaccinated 7-8 of prev. 10 seasons		-	-		13% (2, 22)	
	Vaccinated 4-6 of prev. 10 seasons		-	-		24% (15, 33)	
	Vaccinated 1-3 of prev. 10 seasons		-	-		26% (13, 37)	
_	Vaccinated 0 of prev. 10 seasons		—			34% (9, 52)	
а		r		1			
		-50%	0	50%	100%		
			Vaccine E	ffectiveness			
Analysis	Vaccination History					VE (95% CI)	Trend Test
1 prev. season	Vaccinated prev. season			-		27% (20, 33)	p<0.001
	Not vaccinated prev. season			+		42% (37, 46)	
5 prev. seasons	Vaccinated 4-5 of prev. 5 seasons			-		30% (22, 36)	p=0.003
	Vaccinated 1-3 of prev. 5 seasons			-		38% (31, 43)	
	Vaccinated 0 of prev. 5 seasons			-		44% (37, 50)	
10 prev. seasons	Vaccinated 9-10 of prev. 10 seasons		-	-		26% (15, 35)	p=0.013
	Vaccinated 7-8 of prev. 10 seasons					35% (26, 43)	
	Vaccinated 4-6 of prev. 10 seasons					39% (31, 46)	
	Vaccinated 1-3 of prev. 10 seasons					46% (38, 53)	
	Vaccinated 0 of prev. 10 seasons					39% (30, 48)	
b		r					
		-50%	0	50%	100%		
			Vaccine E	ffectiveness			

Figure S5. Forest plots of current season vaccine effectiveness estimates against any influenza for community-dwelling adults aged > 65 years, taking into account vaccination histories for one, five, and 10 previous seasons and stratifying according to number of vaccinations received and, based on misclassification of current season vaccination status, (A) manually reclassifying vaccination status from unvaccinated to vaccinated for all previous seasons, and (B) moving individuals 'up' a single category

Analysis	Vaccination History					VE (95% CI)	Trend Test
1 prev. season	Vaccinated prev. season			-		29% (23, 34)	p=<0.001
	Not vaccinated prev. season			-		45% (40, 49)	
5 prev. seasons	Vaccinated 4-5 of prev. 5 seasons			+		32% (26, 38)	p=0.039
	Vaccinated 1-3 of prev. 5 seasons					36% (30, 42)	
	Vaccinated 0 of prev. 5 seasons					51% (40, 61)	
10 prev. seasons	Vaccinated 9-10 of prev. 10 seasons					29% (20, 38)	p=0.010
	Vaccinated 7-8 of prev. 10 seasons					33% (23, 41)	
	Vaccinated 4-6 of prev. 10 seasons		1			39% (30, 47)	
	Vaccinated 1-3 of prev. 10 seasons					44% (33, 52)	
	Vaccinated 0 of prev. 10 seasons					48% (27, 62)	
а		-50%	0 Vaccine	50% Effectiveness	100%		
Analysis	Vaccination History					VE (95% CI)	Trend Test
1 prev. season	Vaccinated prev. season			-		29% (23, 34)	p=<0.001
	Not vaccinated prev. season			+		45% (40, 49)	
5 prev. seasons	Vaccinated 4-5 of prev. 5 seasons			+		32% (26, 38)	p=0.046
	Vaccinated 1-3 of prev. 5 seasons			-		36% (30, 41)	
	Vaccinated 0 of prev. 5 seasons					51% (40, 61)	
10 prev. seasons	Vaccinated 9-10 of prev. 10 seasons					28% (17, 36)	p=0.011
	Vaccinated 7-8 of prev. 10 seasons					34% (25, 42)	
	Vaccinated 4-6 of prev. 10 seasons					41% (33, 48)	
	Vaccinated 1-3 of prev. 10 seasons					40% (31, 47)	
	Vaccinated 0 of prev. 10 seasons					48% (27, 62)	
b		-50%	0	50%	100%		
-			Vaccine	Effectiveness			

Figure S6. Forest plots of (A) current season vaccine effectiveness estimates against any influenza for community-dwelling adults aged > 65 years, taking into account vaccination histories for one, five, and 10 previous seasons, using the standard approach of a common reference group (i.e., patients who were not vaccinated in the current or any previous seasons under consideration), and (B) also correcting for misclassification of current season vaccination status

Analysis	Vaccination History			VE (95% CI)	Trend Test
1 prev. season	Vacc. prev. season + current		+	25% (22, 29)	Current: p=0.308
	Vacc. prev. season + no current		+	18% (13, 23)	No current: p<0.001
	Not vacc. prev. season + current		-	29% (23, 34)	
	Not vacc. prev. season + no current		+	Reference	
5 prev. seasons	Vacc. 4-5 of prev. 5 seasons + current		+	26% (20, 30)	Current: p=0.007
	Vacc. 4-5 of prev. 5 seasons + no current		-	17% (10, 24)	No current: p<0.001
	Vacc. 1-3 of prev. 5 seasons + current		-	31% (25, 36)	
	Vacc. 1-3 of prev. 5 seasons + no current		-	13% (6, 19)	
	Vacc. 0 of prev. 5 seasons + current			36% (22, 48)	
	Vacc. 0 of prev. 5 seasons + no current		+	Reference	
10 prev. seasons	Vacc. 9-10 of prev. 10 seasons + current			22% (14, 29)	Current: p<0.001
	Vacc. 9-10 of prev. 10 seasons + no current			16% (6, 26)	No current: p<0.001
	Vacc. 7-8 of prev. 10 seasons + current		-	26% (18, 33)	
	Vacc. 7-8 of prev. 10 seasons + no current			14% (4, 24)	
	Vacc. 4-6 of prev. 10 seasons + current			31% (22, 38)	
	Vacc. 4-6 of prev. 10 seasons + no current			9% (-2, 18)	
	Vacc. 1-3 of prev. 10 seasons + current			33% (22, 43)	
	Vacc. 1-3 of prev. 10 seasons + no current		++-	9% (-2, 18)	
	Vacc. 0 of prev. 10 seasons + current			33% (8, 51)	
а	Vacc. 0 of prev. 10 seasons + no current		•	Reference	
u			i .		
		-50%	0 50%	100%	
		Va	ccine Effectiveness		

Analysis	Vaccination History			VE (95% CI)	Trend Test
1 prev. season	Vacc. prev. season + current		+	44% (41, 47)	Current: p=0.363
	Vacc. prev. season + no current		-	22% (15, 28)	No current: p<0.001
	Not vacc. prev. season + current		+	45% (42, 49)	
	Not vacc. prev. season + no current		•	Reference	
5 prev. seasons	Vacc. 4-5 of prev. 5 seasons + current		+	44% (40, 48)	Current: p=0.079
	Vacc. 4-5 of prev. 5 seasons + no current			20% (10, 28)	No current: p<0.001
	Vacc. 1-3 of prev. 5 seasons + current		+	48% (44, 52)	
	Vacc. 1-3 of prev. 5 seasons + no current		-	16% (8, 24)	
	Vacc. 0 of prev. 5 seasons + current		+	47% (42, 53)	
	Vacc. 0 of prev. 5 seasons + no current		+	Reference	
10 prev. seasons	Vacc. 9-10 of prev. 10 seasons + current			37% (30, 44)	Current: p<0.001
	Vacc. 9-10 of prev. 10 seasons + no current			16% (2, 29)	No current: p=0.005
	Vacc. 7-8 of prev. 10 seasons + current		-	42% (34, 48)	
	Vacc. 7-8 of prev. 10 seasons + no current		++-	10% (-5, 22)	
	Vacc. 4-6 of prev. 10 seasons + current		-	44% (36, 50)	
	Vacc. 4-6 of prev. 10 seasons + no current			8% (-6, 20)	
	Vacc. 1-3 of prev. 10 seasons + current		-	48% (40, 55)	
	Vacc. 1-3 of prev. 10 seasons + no current			2% (-13, 15)	
	Vacc. 0 of prev. 10 seasons + current			39% (30, 48)	
	Vacc. 0 of prev. 10 seasons + no current		+	Reference	
		Γ	-i		
b		-50%	0 50%	100%	
		١	/accine Effectiveness		