Il vaccino anti-influenzale nell'anziano

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Outline

L’influenza: le reali dimensioni del problema

Le complicanze «non ovvie» dell’influenza

La prevenzione vaccinale: strumenti disponibili

Analisi di costo/efficacia dei vaccini potenziati

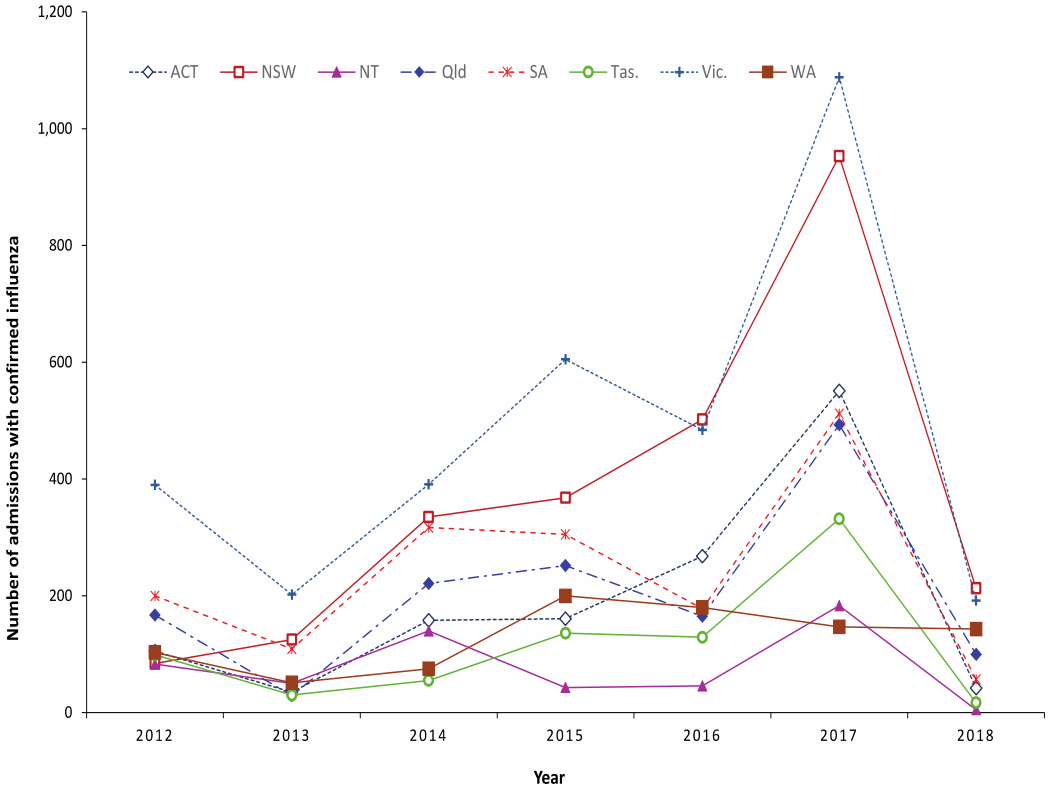
Popolazioni particolari

I limiti delle coperture vaccinali

L’influenza: le reali dimensioni del problema

Dimensioni del problema: da valutare sempre sulla serie storica…

Figure 17: Number of hospital admissions with confirmed influenza in sentinel hospitals in Australia, by state or territory and year, 2012 to 2018[a]



Communicable Diseases Intelligence

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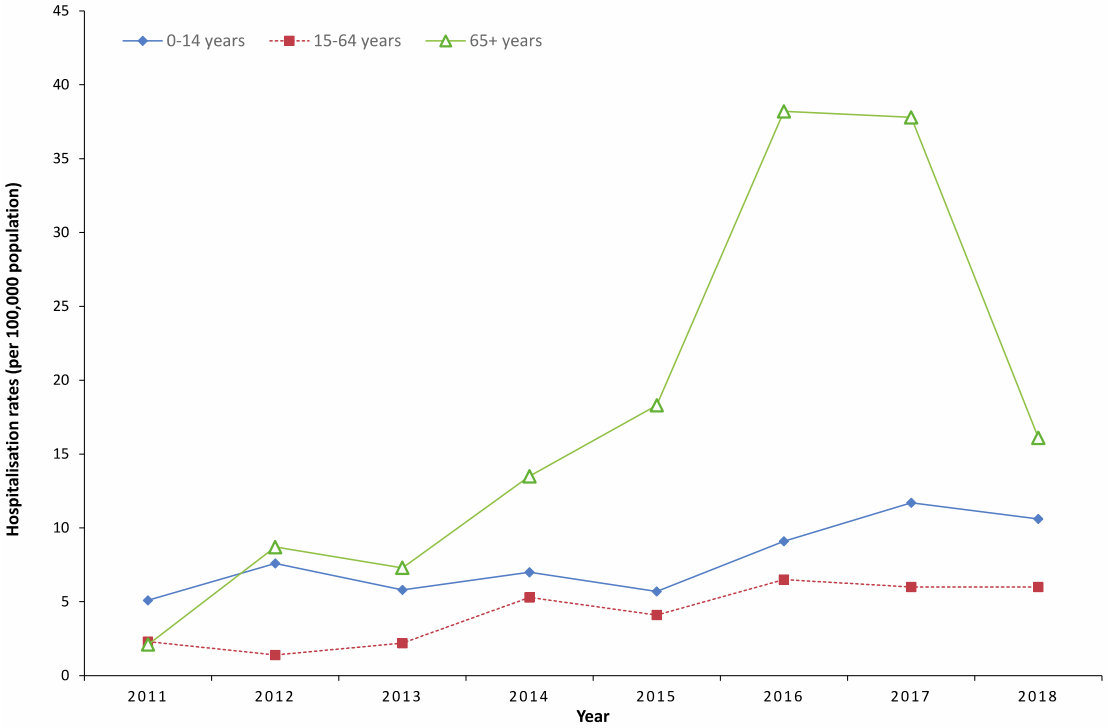
…e da rapportare alla classe di età

Figure 9: Influenza hospitalisation rates in Australia by age group, 2011 to 2018



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Considerare la variabilità eziologica: il caso del 2015, «l'anno B»

Figure 10: Number of isolates tested at the Australian WHOCC site by type/subtype, 2011 to 2018[a,b]

a 2015 data only up to 21 December 2015.

b 2018 data only up to 17 December 2018.

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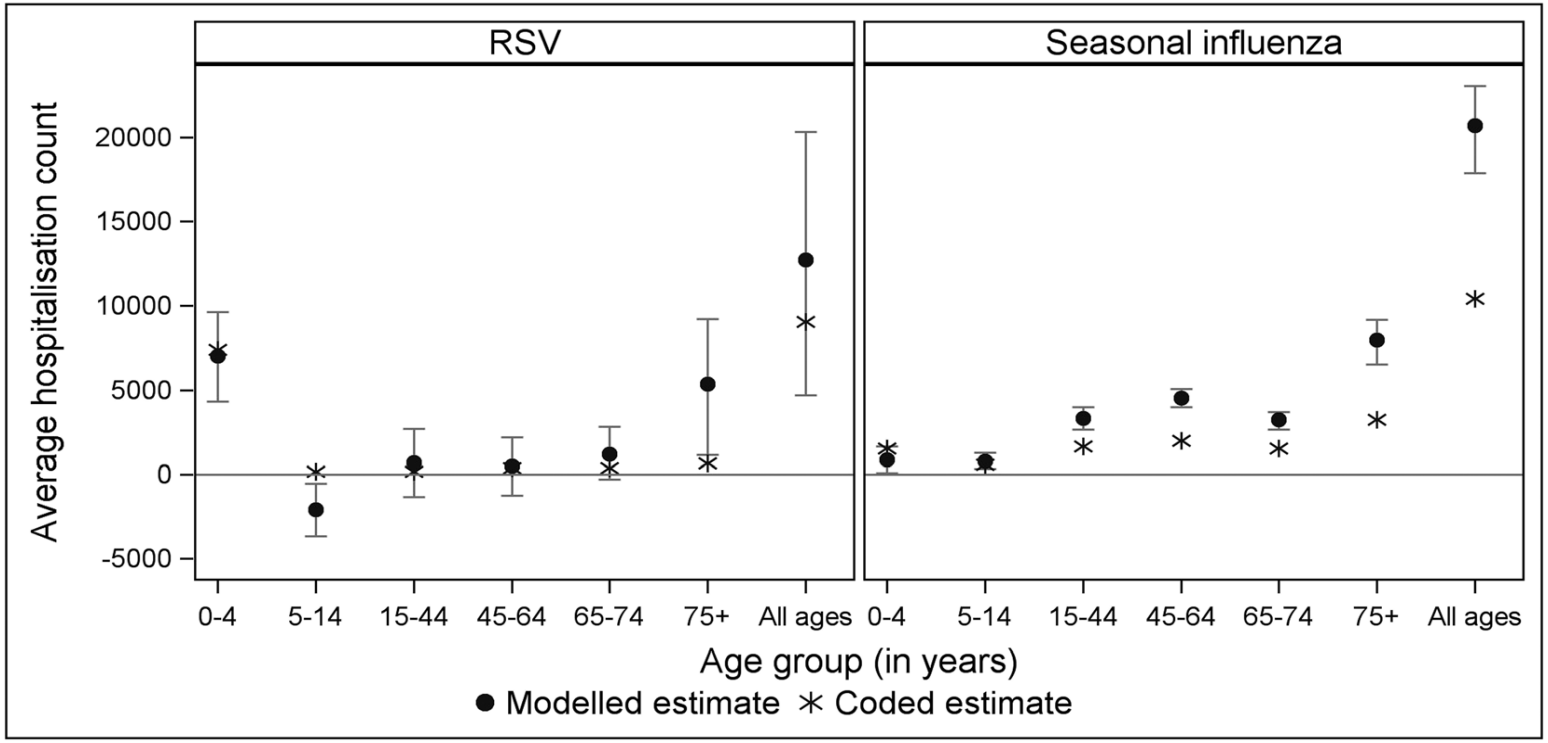
Il rischio di sottostimare il problema (Nazareno AL et al. Influenza Other Respi Viruses. 2022;1)



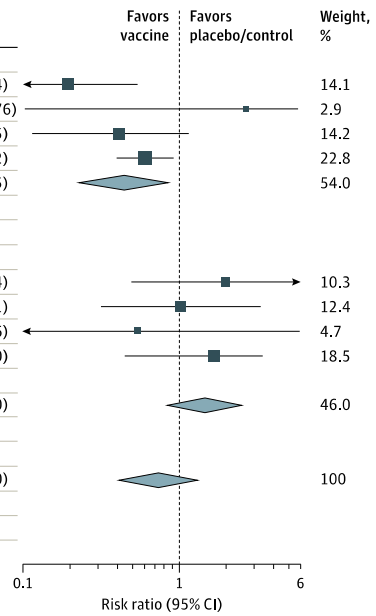
F I G U R E 2 Comparison of the average annual estimate of modelled (attributable) and coded hospitalisations (any diagnosis field) from 2009 to 2017 for RSV and 2010 to 2017 for seasonal influenza, by age group, Australia. RSV, respiratory syncytial virus

Le complicanze «non ovvie» dell'influenza

Il vaccino protegge dalla morte i pazienti recentemente incorsi in sindrome coronarica acuta (follow up=12 mesi) (Behrouzi B et al. *JAMA Network Open.* 2022;5(4):e228873)

Figure 3. Cardiovascular Mortality Comparing Influenza Vaccine vs Control Stratified by History of Recent Acute Coronary Syndrome (ACS)

Study or subgroup	Vaccine Events	Vaccine Total	Placebo/control Events	Placebo/control Total	Risk ratio, (95% CI)	Weight, %
Recent ACS						
Gurfinkel et al,[19] 2004	4	96	21	97	0.19 (0.07-0.54)	14.1
Ciszewski et al,[20] 2008	1	83	0	74	2.68 (0.11-64.76)	2.9
Phrommintikul et al,[21] 2011	5	221	12	218	0.41 (0.15-1.15)	14.2
Frøbert et al,[7] 2021	34	1266	56	1258	0.60 (0.40-0.92)	22.8
Total events	44	1666	89	1647	0.44 (0.23-0.85)	54.0
Heterogeneity: $\tau^2=0.18$; $\chi^2=5.29$, df = 3 ($P=.15$); $I^2=43\%$						
Test for overall effect: z = 2.45 ($P=.01$)						
Stable outpatients						
Govaert et al,[22] 1994	6	927	3	911	1.97 (0.49-7.84)	10.3
Gurfinkel et al,[19] 2004	5	49	5	50	1.02 (0.32-3.31)	12.4
Ciszewski et al,[20] 2008	1	242	2	259	0.54 (0.05-5.86)	4.7
De Villiers et al,[23] 2009	20	1620	12	1622	1.67 (0.82-3.40)	18.5
Frøbert et al,[7] 2021	0	6	0	2	Not estimable	
Total events	32	2844	22	2844	1.45 (0.84-2.50)	46.0
Heterogeneity: $\tau^2=0.00$; $\chi^2=1.35$, df = 3 ($P=.72$); $I^2=0\%$						
Test for overall effect: z = 1.35 ($P=.18$)						
Total events	76	4510	111	4491	0.74 (0.41-1.30)	100
Heterogeneity: $\tau^2=0.33$; $\chi^2=16.55$, df = 7 ($P=.02$); $I^2=58\%$						
Test for overall effect: z = 1.05 ($P=.29$)						
Test for subgroup differences: $\chi^2=7.52$; df = 1 ($P=.006$); $I^2=86.7\%$						



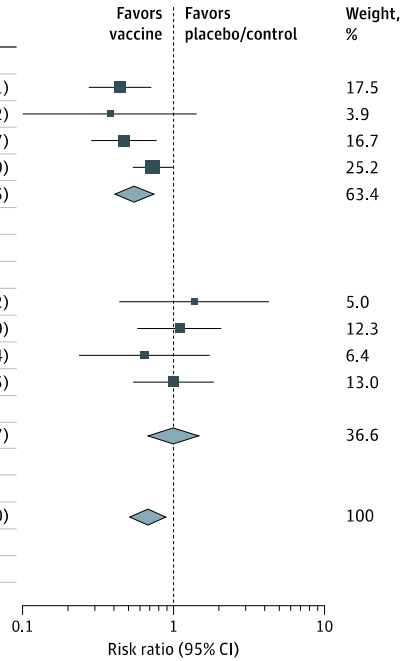
Square data markers represent risk ratios; horizontal lines, the 95% CIs with marker size reflecting the statistical weight of the study using random-effects meta-analysis. Diamond data markers represent each subgroup and overall risk ratio and 95% CIs for the outcome of interest. Evaluated using the random-effects Mantel-Haenszel test. Heterogeneity variance τ^2 calculated using the DerSimonian-Laird estimator.

Six published RCTs comprising a total of 9001 patients were included (mean age,65.5 years; 42.5% women; 52.3% with a cardiac history)

E da nuovi eventi coronarici tutti i pazienti CAD (Behrouzi B et al. *JAMA Network Open.* 2022;5(4):e228873)

Figure 2. Major Adverse Cardiovascular Events Comparing Influenza Vaccine vs Control Stratified by History of Recent Acute Coronary Syndrome (ACS)

Study or subgroup	Vaccine Events	Vaccine Total	Placebo/control Events	Placebo/control Total	Risk ratio, (95% CI)	Weight, %
Recent ACS						
Gurfinkel et al,[19] 2004	18	96	41	97	0.44 (0.28-0.71)	17.5
Ciszewski et al,[20] 2008	3	83	7	74	0.38 (0.10-1.42)	3.9
Phrommintikul et al,[21] 2011	20	221	42	218	0.47 (0.29-0.77)	16.7
Frøbert et al,[7] 2021	67	1266	91	1258	0.73 (0.54-0.99)	25.2
Total events	108	1666	181	1647	0.55 (0.41-0.75)	63.4
Heterogeneity: $\tau^2 = 0.03$; $\chi^2 = 4.50$, df = 3 ($P = .21$); $I^2 = 33\%$						
Test for overall effect: z = 3.78 ($P < .001$)						
Stable outpatients						
Govaert et al,[22] 1994	7	927	5	911	1.38 (0.44-4.32)	5.0
Gurfinkel et al,[19] 2004	14	49	13	50	1.10 (0.58-2.09)	12.3
Ciszewski et al,[20] 2008	6	242	10	259	0.64 (0.24-1.74)	6.4
De Villiers et al,[23] 2009	20	1620	20	1622	1.00 (0.54-1.85)	13.0
Frøbert et al,[7] 2021	0	6	0	2	Not estimable	
Total events	47	2844	48	2844	1.00 (0.68-1.47)	36.6
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 1.14$, df = 3 ($P = .77$); $I^2 = 0\%$						
Test for overall effect: z = 0.02 ($P = .98$)						
Total events	155	4510	229	4491	0.68 (0.52-0.90)	100
Heterogeneity: $\tau^2 = 0.05$; $\chi^2 = 11.27$, df = 7 ($P = .13$); $I^2 = 38\%$						
Test for overall effect: z = 2.73 ($P = .006$)						
Test for subgroup differences: $\chi^2 = 5.65$; df = 1 ($P = .02$); $I^2 = 82.3\%$						

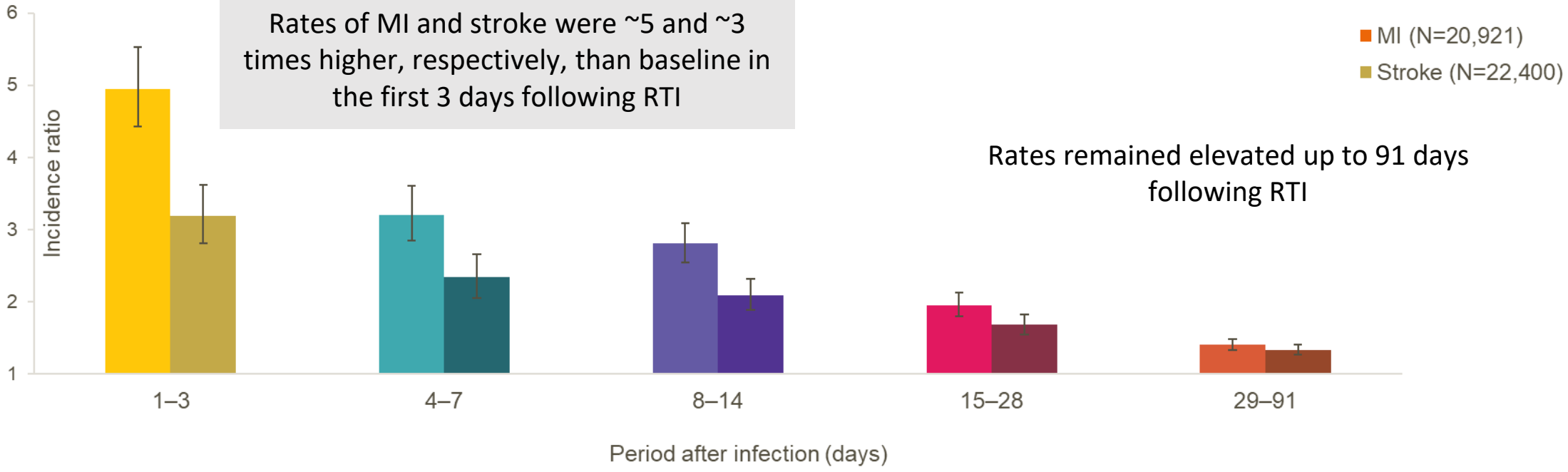


Square data markers represent risk ratios; horizontal lines, the 95% CIs with marker size reflecting the statistical weight of the study using random-effects meta-analysis. Diamond data markers represent each subgroup and overall risk ratio and 95% CIs for the outcome of interest. Evaluated using the random-effects Mantel-Haenszel test. Heterogeneity variance τ^2 calculated using the DerSimonian-Laird estimator.

Respiratory tract infections such as influenza increase the risk of myocardial infarction and stroke in adults

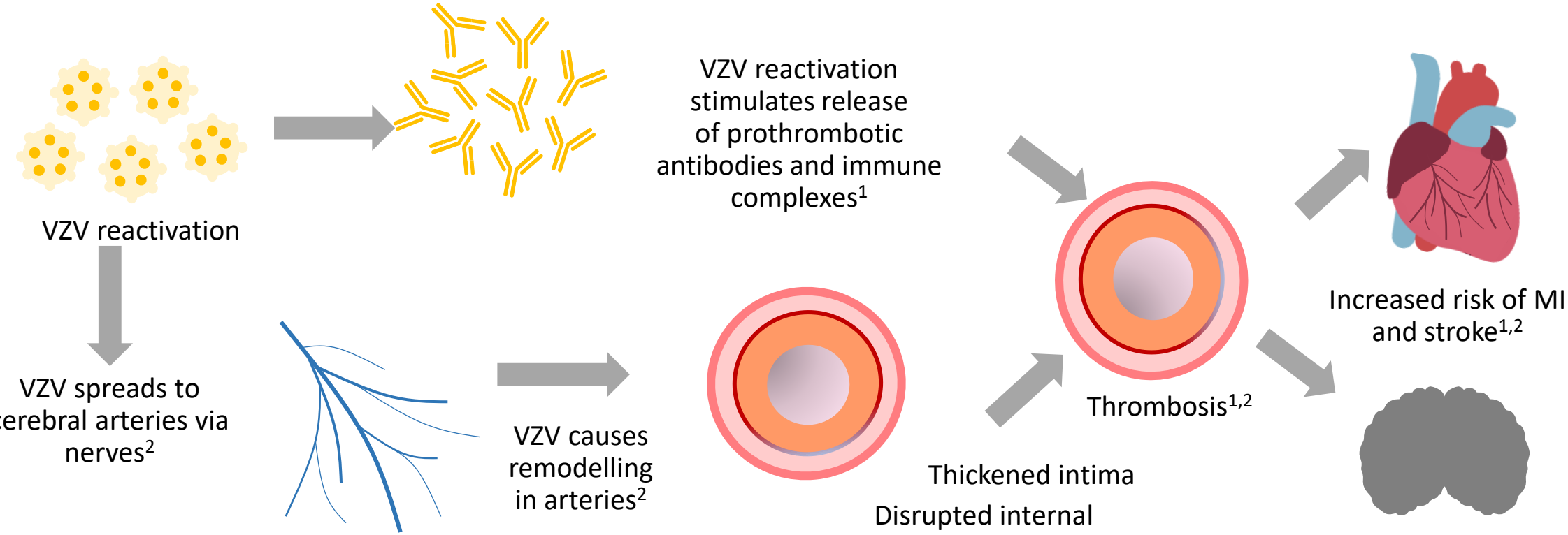
Age-adjusted incidence ratios of a first myocardial infarction or stroke after respiratory tract infection, in adults aged ≥18 years

Rates of MI and stroke were ~5 and ~3 times higher, respectively, than baseline in the first 3 days following RTI



Rates remained elevated up to 91 days following RTI

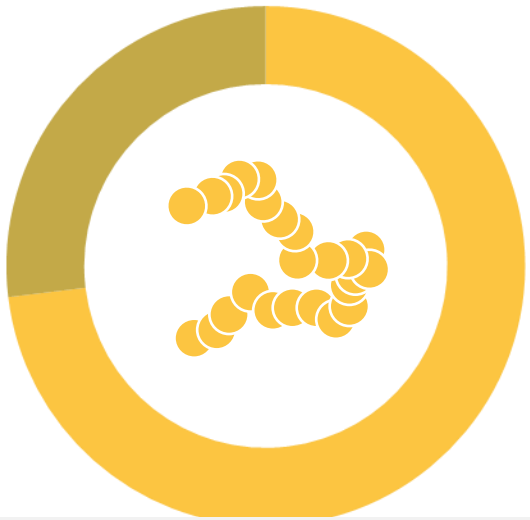
Complicanze vascolari non sono esclusive dell'influenza: il caso dello Zoster

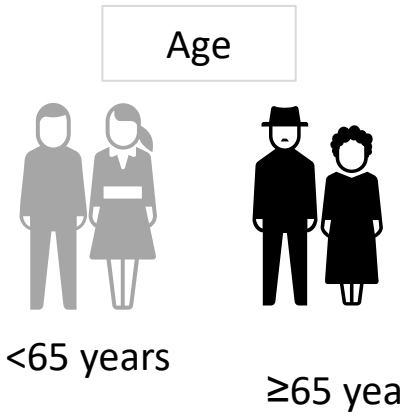


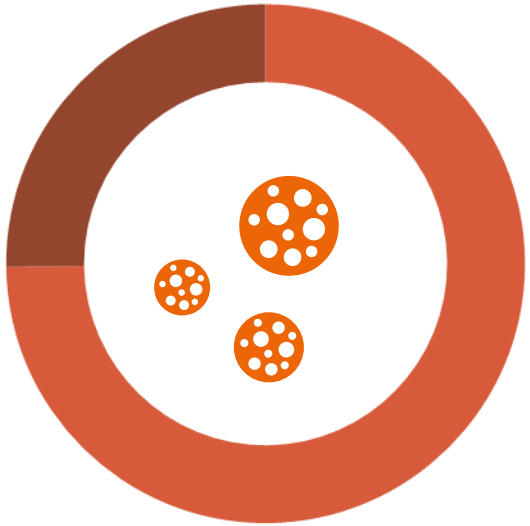
1. Wu PH *et al. J Clin Med* 2019;8: pii: E547; 2. Nagel MA, Gilden D. *Curr Neurol Neurosci Rep* 2015;15:16

Older adults are known to be at higher risk of severe outcomes from infectious diseases than younger individuals

Deaths due to invasive pneumococcal disease, EU, 2018[1]







Almost **75% of deaths** due to influenza and pneumococcal disease occur in adults aged ≥65 years[1,2]

1. European Centre for Disease Prevention and Control (ECDC), 2020. Surveillance atlas of infectious diseases. https://atlas.ecdc.europa.eu/public/index.aspx; 2. Centers for Disease Control and Prevention (CDC), 2020. Estimated influenza illnesses, medical visits, hospitalizations, and deaths in the United States — 2018–2019 influenza season. https://www.cdc.gov/flu/about/burden/2018-2019.html (URLs accessed June 2022)

La prevenzione vaccinale: strumenti disponibili

Vaccini antinfluenzali stagionali e scelta dei vaccini (Circolare ministeriale 2022/23)

18-64 anni	- sub-unità, split quadrivalente (QIV) - quadrivalente su colture cellulari (VIQcc) - quadrivalente a DNA ricombinante (VIQr) - quadrivalente ad alto dosaggio (VIQhd)	- **1** dose (0,50 ml)	QIV, VIQr e VIQcc sono i prodotti utilizzabili Dopo i 60 anni anche VIQhd
≥ 65 anni	- sub-unità, split quadrivalente (QIV) - quadrivalente su colture cellulari (VIQCC) - quadrivalente ad alto dosaggio (HD) - quadrivalente (VIQa) adiuvato con MF59 - quadrivalente a DNA ricombinante (VIQr)	- 1 dose (0,50 ml) - 1 dose (0,50 ml) - 1 dose (0,70 ml) - 1 dose (0,50 ml) - 1 dose (0,50 ml)	QIV, VIQr, VIQcc, VIQa e VIQhd sono i prodotti utilizzabili per gli adulti di età ≥ 65 anni. VIQa e VIQhd sono specificatamente indicati nella popolazione ultra 65enne

Gli obiettivi di copertura, per tutti i gruppi target, sono i seguenti:

- **il 75% come obiettivo minimo perseguibile**
- **il 95% come obiettivo ottimale.**

Frailty does not weaken the Antibody response to influenza vaccine…

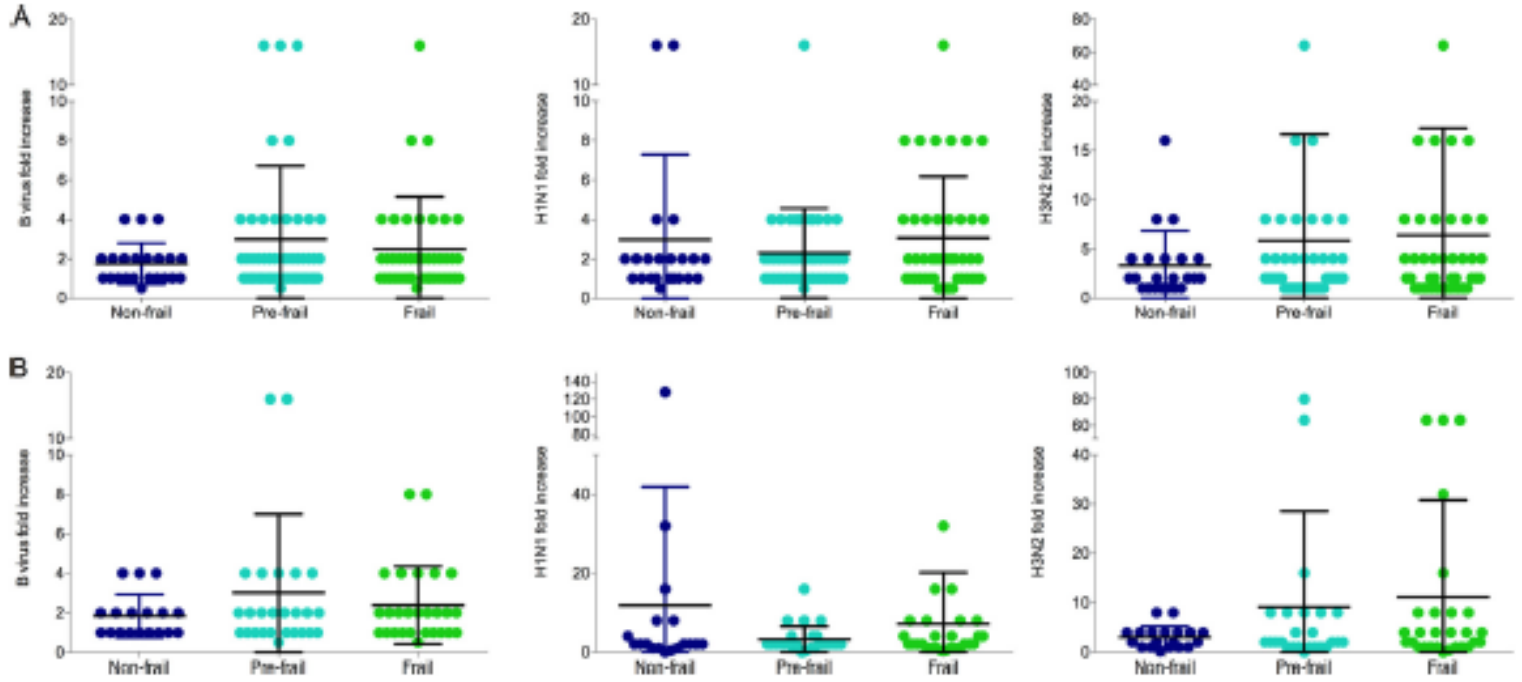


FIG 1 Comparison of hemagglutination inhibition (HI) (A) and microneutralization (MN) (B) postvaccination/prevaccination geometric mean titer (GMT) ratios within frailty groups. No statistically significant differences, as measured by one-way ANOVA, were found between frailty groups. Horizontal black lines represent the mean, and the vertical lines represent 1 standard deviation (SD).

- Frailty does not weaken the Antibody response to influenza vaccine (Van Epps P et al. March 2017 Volume 24 Issue 3 e00498-16 Clinical and Vaccine Immunology)

…, while previous immunization strengthens it (Van Epps P et al. March 2017 Volume 24 Issue 3 e00498-16 Clinical and Vaccine Immunology)

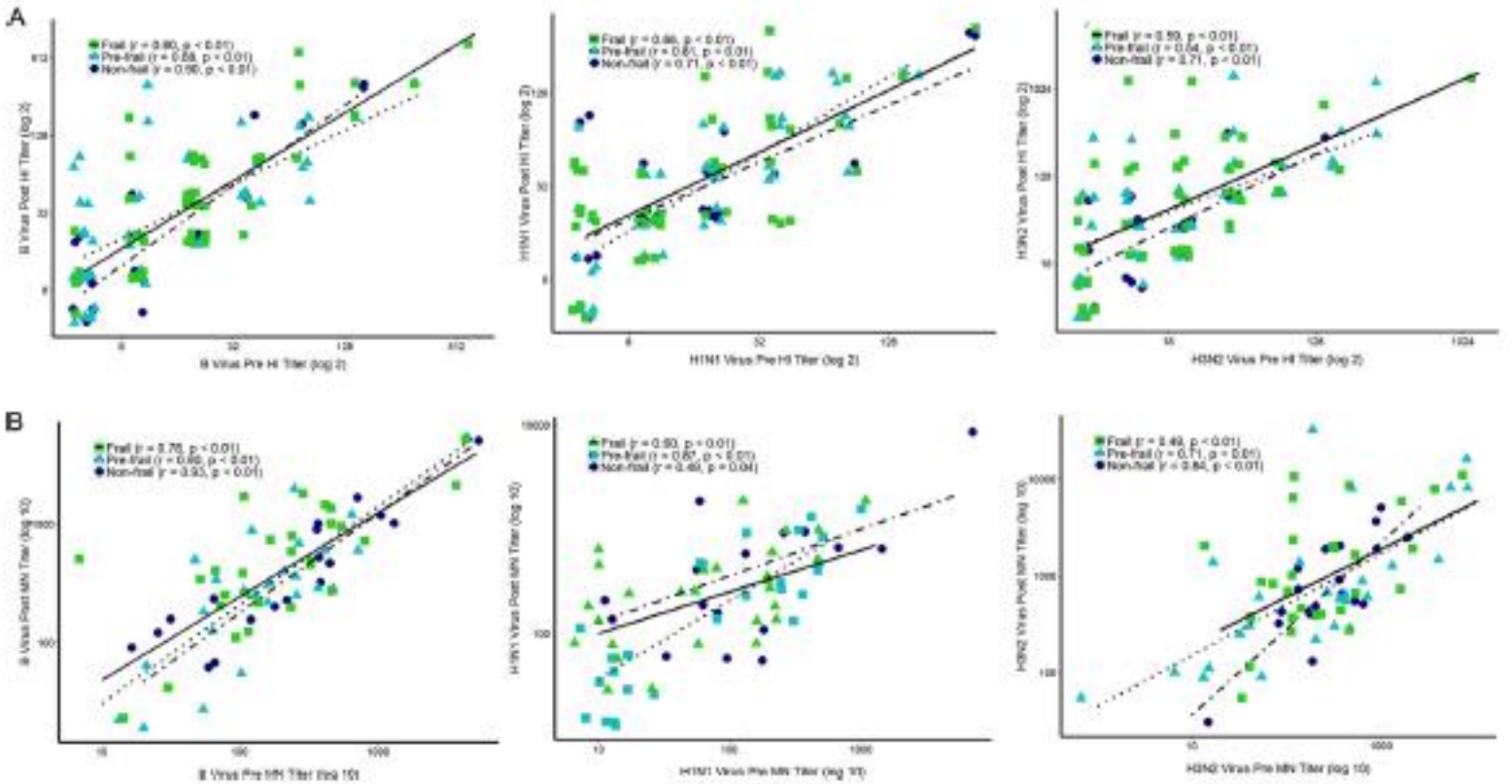
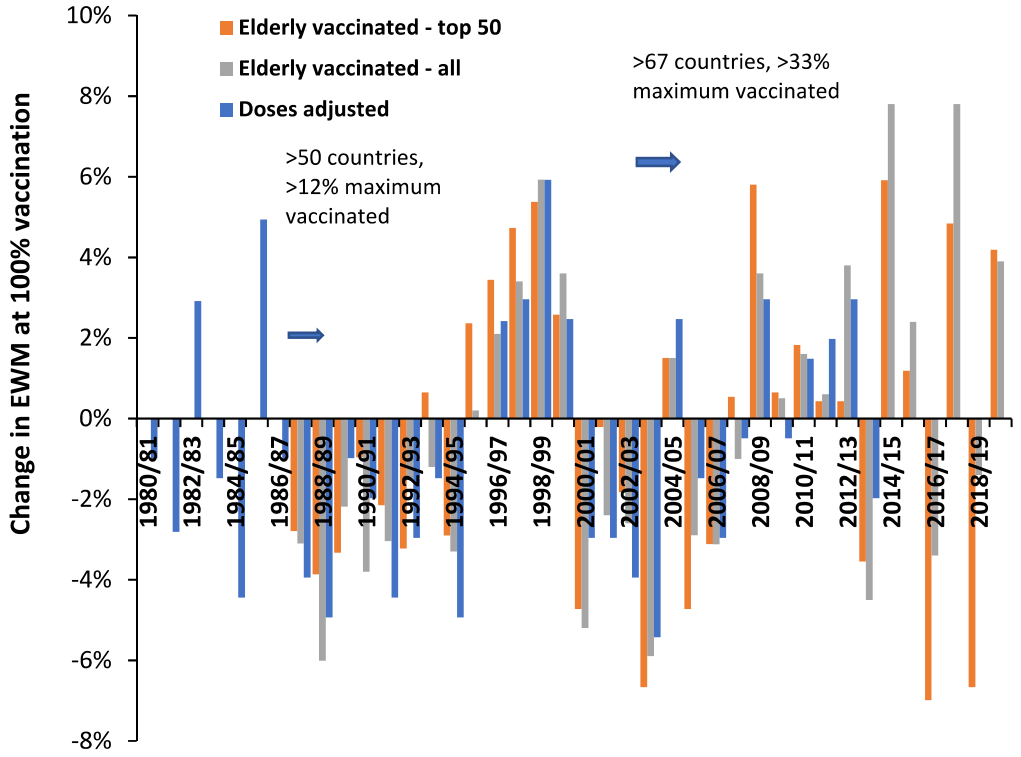


FIG 2 Correlation of preexisting immunity with postvaccination responses, as measured by hemagglutination inhibition (HI) (A) and microneutralization (MN) (B) assays. Antibody levels were plotted within frailty groups, and correlations were calculated to determine the effect of preexisting immunity on postvaccination antibody titers. The Spearman correlation coefficient and *P* value are presented for each frailty group.

Effetto del vaccino antiinfluenzale non va equiparato all'eccesso di mortalità invernale (Jones RP et al. *Infect. Dis. Rep.* **2022**, *14*, 287–309)



I fattori condizionanti l'eccesso di mortalità invernale (Jones RP et al. *Infect. Dis. Rep.* 2022, *14*, 287–309)

1. human immune variability which includes gender, chronological and immune age, individual history of host-virus and host-antigen interactions, ethnicity, persistent pathogens, genetic mutations, epigenetic factors, psychological stress, and metabolic health [2–8],
2. the role of meteorological variables on influenza (and other respiratory pathogen) survival and transmission [9–14],
3. influenza virus evolution [15,16],
4. the variable spatiotemporal spread and distribution of influenza strains and mutations (clades) each year [17,18].
5. the pathogenicity of influenza being the result of a complex system of interactions between the influenza viruses, other viruses, the host, anthropogenic interventions, and secondary infections [19–21].
6. the totality of winter pathogen-induced deaths which is a composite of (co)infection by multiple pathogens [22–25].

Efficacia del vaccino in funzione del matching vaccino-ceppo (2006 si) e della comorbilità (Liang C-Y, et al. BMJ Open 2022;**12**:e050594)

Table 4 ORs for the risk of community-acquired pneumonia hospitalisation in Non-admitted individuals during the influenza period using stratified analysis

	Non-admitted group*			
	2006-vaccinated		2007-vaccinated	
	OR (95% CI)	P value	OR (95% CI)	P value
Age group (years)				
65–74	0.74 (0.60 to 0.91)	0.003	0.97 (0.78 to 1.22)	0.820
75–84	0.74 (0.61 to 0.89)	0.001	1.08 (0.86 to 1.33)	0.536
≥85	0.61 (0.42 to 0.89)	0.012	1.41 (0.93 to 2.08)	0.104
Gender				
Male	0.69 (0.58 to 0.83)	<0.001	1.16 (0.96 to 1.41)	0.128
Female	0.77 (0.63 to 0.93)	0.009	0.94 (0.76 to 1.19)	0.648
CCI score†				
0	0.73 (0.54 to 0.90)	0.041	1.08 (0.79 to 1.49)	0.629
1	0.76 (0.64 to 0.92)	0.043	1.07 (0.88 to 1.32)	0.492
2	0.62 (0.47 to 0.82)	0.001	1.16 (0.85 to 1.59)	0.346
3	0.75 (0.49 to 1.15)	0.192	0.70 (0.39 to 1.27)	0.241

*In the two consecutive years, the elderly who were not hospital admitted with pneumonia during the pre-vaccination period.
†CCI, Charlson Comorbidity Index.

Dare il giusto peso alle differenze: negli ultra75enni i ricoveri calano del 29% dopo quadrivalente inattivato (Mimura W et al. Vaccine 2022)

Table 2
Influenza vaccine effectiveness against hospitalization.

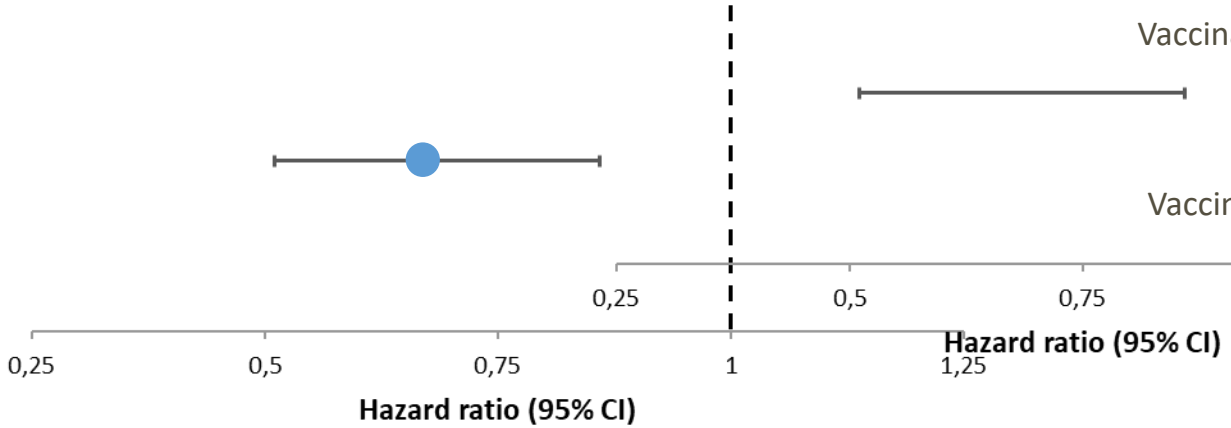
	Vaccinated (N = 30,881)			Unvaccinated (N = 30,881)			Hazard ratio		Vaccine effectiveness	
	Events n (%)	Person-days	Incidence rate (/100,000 person-days)	Events n (%)	Person-days	Incidence rate (/100,000 person-days)	Unadjusted (95% CI)	Adjusted[a] (95% CI)	Unadjusted % (95% CI)	Adjusted[a] % (95% CI)
Hospitalization for pneumonia, influenza, or any other acute lower respiratory infection	587 (1.9)	3,751,399	15.6	644 (2.1)	3,713,328	17.3	0.903 (0.808 to 1.01)	0.711 (0.606 to 0.834)	9.7 (−0.9 to 19.2)	28.9 (16.6 to 39.4)
Hospitalization for pneumonia	402 (1.3)	3,768,951	10.7	457 (1.5)	3,732,168	12.2	0.872 (0.763 to 0.996)	0.680 (0.565 to 0.819)	12.8 (0.4 to 23.7)	32.0 (18.1 to 43.5)
Hospitalization for influenza	259 (0.8)	3,776,889	6.9	277 (0.9)	3,745,058	7.4	0.928 (0.784 to 1.099)	0.831 (0.656 to 1.053)	7.2 (−9.9 to 21.6)	16.9 (−5.3 to 34.4)
Hospitalization for any other acute lower respiratory infection	56 (0.2)	3,798,059	1.5	58 (0.2)	3,767,432	1.5	0.958 (0.663 to 1.384)	0.665 (0.370 to 1.196)	4.2 (−38.4 to 33.7)	33.5 (−19.6 to 63.0)

CI, confidence interval. [a]The analysis adjusted for age, sex, comorbidities (chronic pulmonary disease, cardiovascular disease, cerebrovascular disease, rheumatic disease, diabetes, renal disease, liver disease, dementia, and cancer), influenza vaccination in the previous season, PPSV23 vaccination in the last 3 years, certified LTC needs level, number of clinic/hospital visits in the past year, pneumonia-associated hospitalization during the past year, and influenza infection during the previous season.

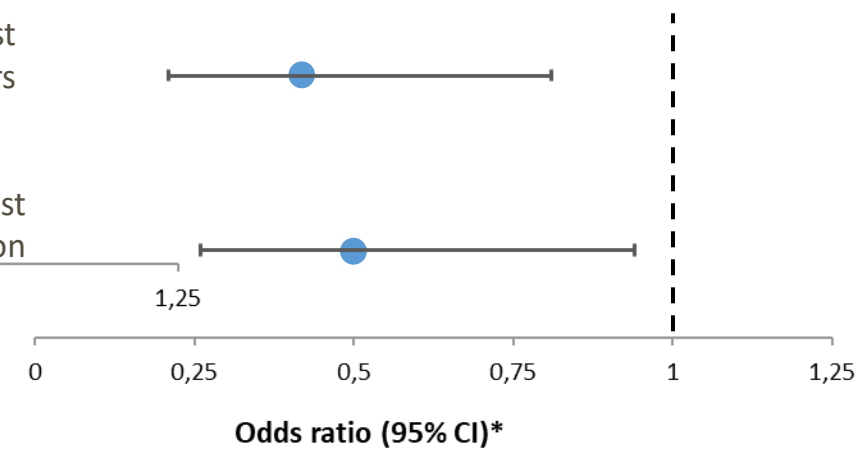
The primary outcome was a composite outcome of hospitalization for pneumonia, influenza, or any other acute lower respiratory infection.

The risk of major cardiovascular and cerebrovascular events was significantly reduced following influenza vaccination

Risk of major adverse CV event in influenza-vaccinated subjects with ACS aged >50 years (n = 221) vs unvaccinated (n = 218)[1]



Risk of brain infarction in influenza-vaccinated subjects aged ≥60 years vs unvaccinated[2]



Influenza vaccination significantly reduced the risk of major adverse cardiovascular events **by 33%**

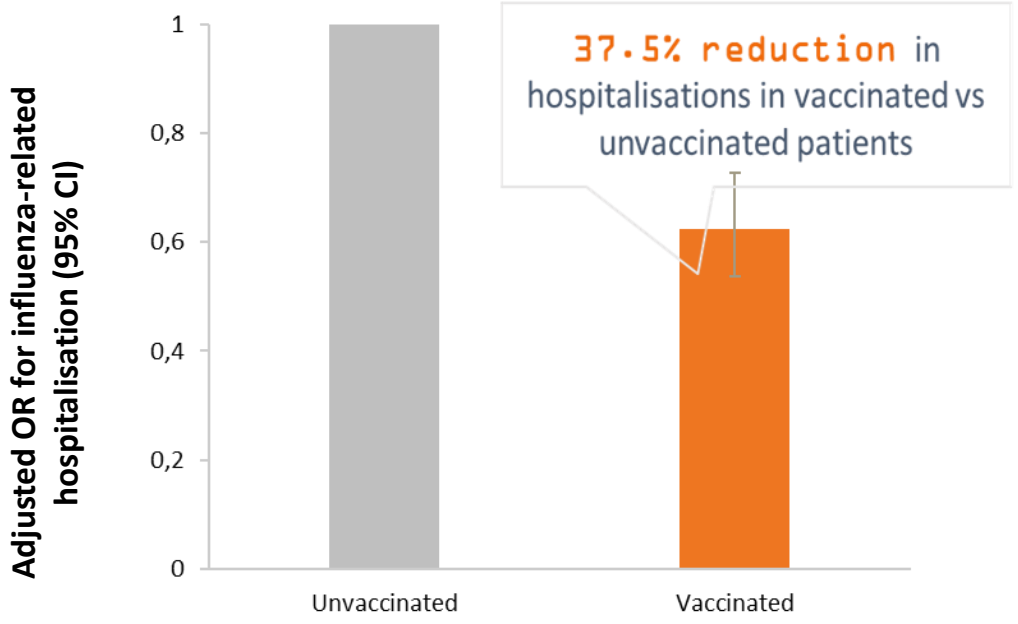
Influenza vaccination **significantly reduced** the risk of brain infarction regardless of time since vaccination

ACS, acute coronary syndrome; CI, confidence interval; CV, cardiovascular; *adjusted for age, sex, diabetes, hypertension, body mass index, current smoking, cholesterol and use of antibiotics in the last 3 months.

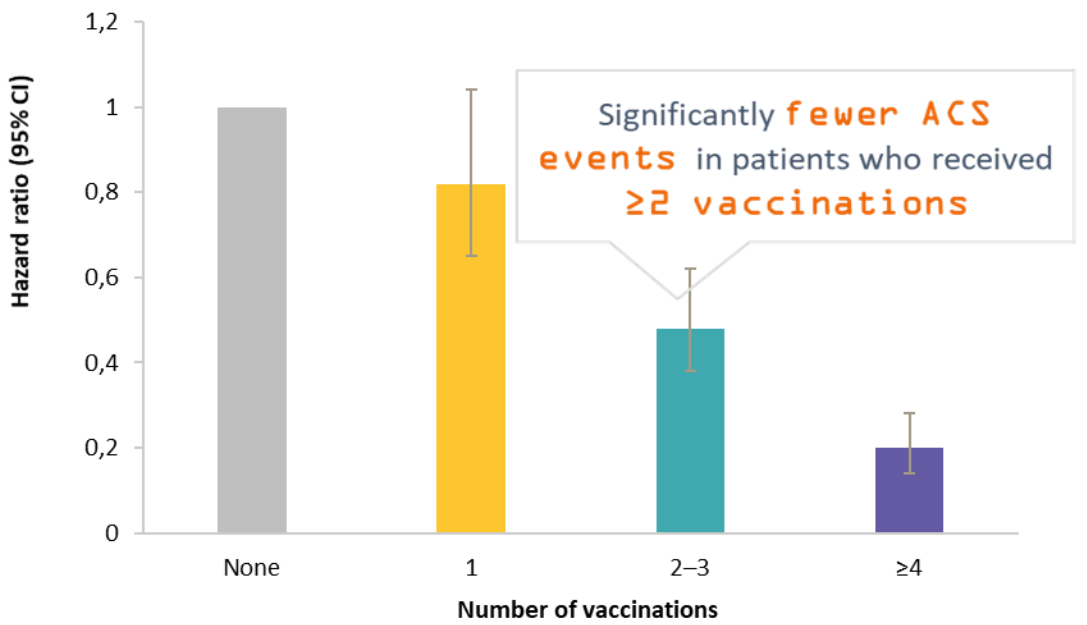
1. Phrommintikul A *et al. Eur Heart J* 2011;32:1730–1735: 2. Lavallee *et al. Stroke* 2002;33:513–518

Vaccination against influenza reduces the risk of hospitalisation in individuals with underlying disease such as COPD

Influenza-related hospitalisations in patients with COPD, 2011-2015 (N = 4198)1



Risk of ACS in patients with COPD aged ≥55 years receiving influenza vaccination compared with unvaccinated patients; Taiwan, 2000-2007 (N = 7722; 3027 vaccinated)2

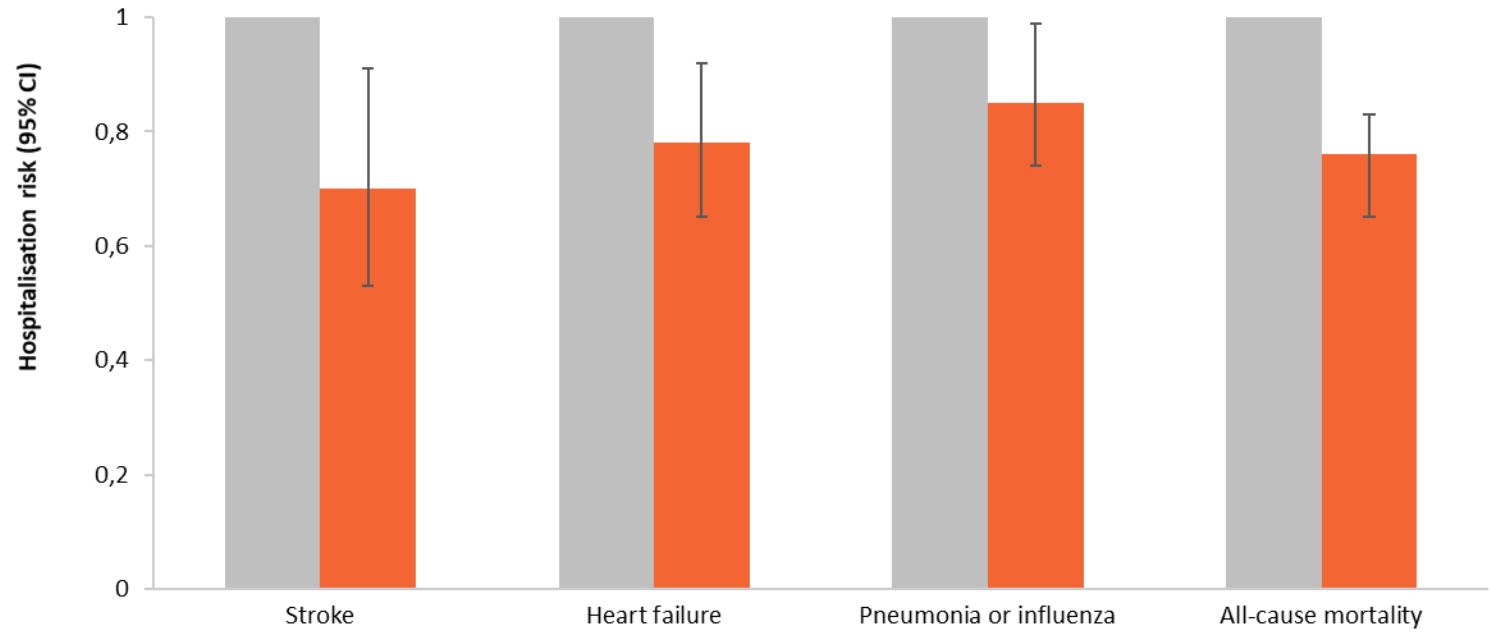


ACS, acute coronary syndrome; CI, confidence interval; COPD, chronic obstructive pulmonary disease; OR, odds ratio

1. Mulpuru S *et al. Chest* 2019;155:69–78; 2. Sung LC *et al. Vaccine* 2014;32:3843–3849

In those with diabetes, influenza vaccination reduces the risk of not only hospitalisation, but also cardiovascular events and death

Risk of hospitalisation for acute CV and respiratory conditions and all-cause death in adults aged ≥18 years with T2DM vaccinated against influenza compared with unvaccinated, 2003/04 to 2009/10 (N = 124,503)



Risk of death from any cause was reduced by >20% in those with diabetes vaccinated against influenza

Vamos EP *et al. CMAJ* 2016;188:E342–E351

In CHF patients, vaccine did not achieve the main outcomes, …(Loeb M et al. *Lancet Glob Health* 2022; 10: e1835–44)

The vaccine reduced all-cause hospitalisation by 16% and community-acquired pneumonia by 42%. The reduction in all-cause hospitalisation was largely due to the effect of the vaccine reducing heart failure hospitalisations and pneumonia.

	Number of events		Hazard ratio (95% CI)	p value
	Influenza vaccine group (n=2560)	Placebo group (n=2569)		
First events				
First co-primary outcome of cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke	380 (14·8%)	410 (16·0%)	0·93 (0·81–1·07)	0·30
Second co-primary outcome of cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke, hospitalisation for heart failure	524 (20·5%)	570 (22·2%)	0·92 (0·81–1·03)	0·15
Secondary outcomes				
Death—all cause	427 (16·7%)	473 (18·4%)	0·90 (0·79–1·03)	0·13
Death—cardiovascular	334 (13·0%)	374 (14·6%)	0·89 (0·77–1·04)	0·13
Death—non-cardiovascular	93 (3·6%)	99 (3·9%)	0·94 (0·71–1·25)	0·68
Non-fatal myocardial infarction	21 (0·8%)	23 (0·9%)	0·91 (0·50–1·65)	0·76
Non-fatal stroke	47 (1·8%)	43 (1·7%)	1·10 (0·73–1·66)	0·66
Hospitalisation—all causes	388 (15·2%)	455 (17·7%)	0·84 (0·74–0·97)	0·013
Hospitalisation—for heart failure	245 (9·6%)	277 (10·8%)	0·88 (0·74–1·05)	0·15
Pneumonia	61 (2·4%)	104 (4·0%)	0·58 (0·42–0·80)	0·0006
Recurrent events				
Second co-primary outcome of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, or hospitalisation for heart failure	754 (29·5%)	819 (31·9%)	0·92 (0·84–1·02)	0·12
Secondary outcomes				
Hospitalisation—all causes	557 (21·8%)	671 (26·1%)	0·84 (0·75–0·94)	0·0022
Hospitalisation—for heart failure	346 (13·5%)	377 (14·7%)	0·92 (0·80–1·07)	0·28

Data are n (%) or hazard ratio (95% CI). Excludes events during the 2-week period following vaccination and events occurring after administrative censoring; for the first co-primary outcomes, 20 events in the influenza group and 10 in the placebo group were excluded; for recurrent events, 82 events in the influenza group and 79 in the placebo group were excluded. Three events occurred after administrative censoring: one death in the influenza group, one death in the placebo group, and one case of pneumonia in the placebo group.

Table 2: **Events by treatment group**

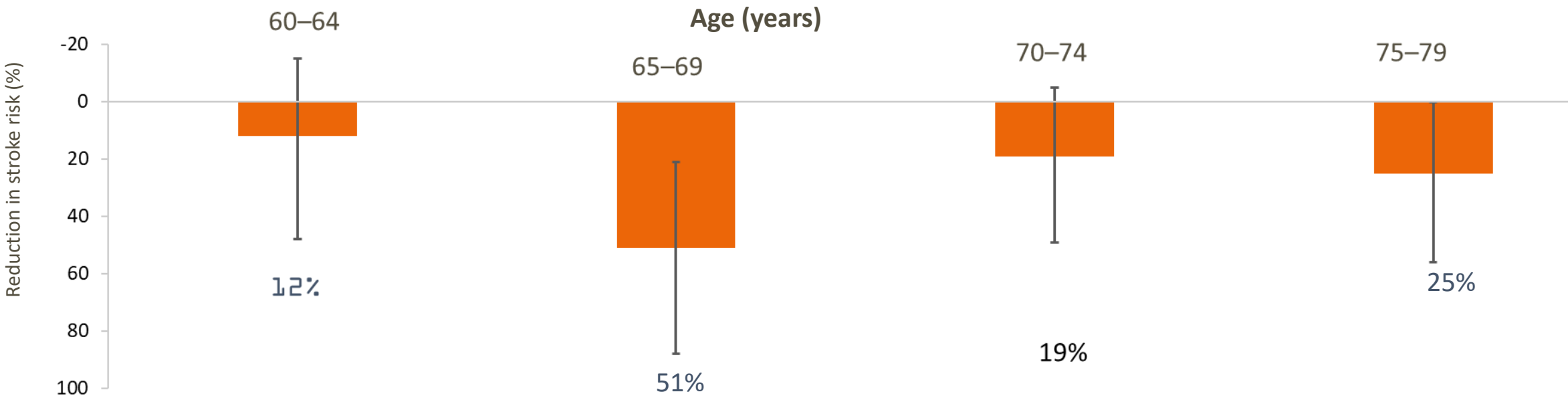
…except for the period of influenza peak (Loeb M et al. *Lancet Glob Health* 2022; 10: e1835–44)

	Number of events during peak influenza circulation period (%)				Number of events outside of peak influenza circulation period (%)			
	Influenza vaccine (n=2560)	Placebo (n=2569)	Hazard ratio (95% CI)	p value	Influenza vaccine (n=2560)	Placebo (n=2569)	Hazard ratio	p value
Primary outcomes								
First co-primary outcome: cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke	193 (7·5%)	237 (9·3%)	0·82 (0·68–0·99)	0·038	187 (7·3%)	173 (6·8%)	1·08 (0·88–1·33)	0·045
Second co-primary outcome: cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, or hospitalisation for heart failure	270 (10·5%)	307 (12·0%)	0·88 (0·74–1·03)	0·045	254 (9·9%)	263 (10·3%)	0·96 (0·81–1·14)	0·66
Secondary outcomes								
Death—all causes	212 (8·3%)	269 (10·5%)	0·79 (0·66–0·95)	0·0099	215 (8·4%)	204 (8·0%)	1·05 (0·87–1·28)	0·59
Death—cardiovascular	170 (6·6%)	221 (8·6%)	0·77 (0·63–0·94)	0·0099	164 (6·4%)	153 (6·0%)	1·07 (0·86–1·34)	0·54
Non-fatal myocardial infarction	9 (0·4%)	13 (0·5%)	0·69 (0·29–1·61)	0·39	12 (0·5%)	10 (0·4%)	1·20 (0·52–2·77)	0·67
Non-fatal stroke	23 (0·9%)	24 (0·9%)	0·98 (0·55–1·74)	0·95	24 (1·0%)	19 (0·8%)	1·26 (0·69–2·31)	0·44
Hospitalisation—all causes	195 (7·6%)	230 (9·0%)	0·84 (0·69–1·01)	0·067	193 (7·5%)	225 (8·8%)	0·85 (0·70–1·03)	0·091
Hospitalisation—for heart failure	128 (5·0%)	124 (4·8%)	1·03 (0·80–1·31)	0·84	117 (4·6%)	153 (6·0%)	0·76 (0·60–0·97)	0·027
Pneumonia	28 (1·1%)	54 (2·1%)	0·51 (0·32–0·81)	0·0034	33 (1·3%)	50 (2·0%)	0·65 (0·42–1·01)	0·054

Data are n (%) or hazard ratio (95% CI). Data exclude events during 2-week period following vaccination and events occurring after administrative censoring.

***Table 3*: Events by treatment group during and outside of peak influenza circulation periods**

Stroke risk in US subjects after vaccination against herpes zoster vs unvaccinated subjects; results from a nationwide survey (N = 172,770)



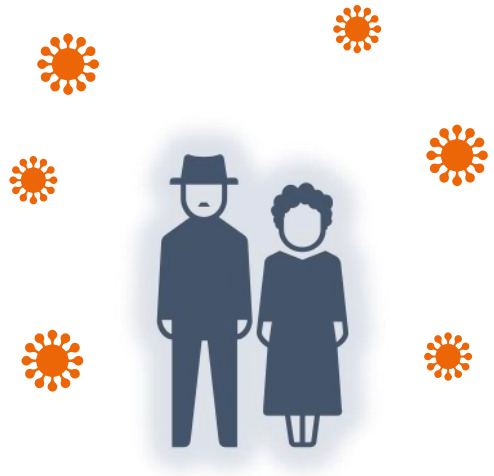
Vaccination against herpes zoster significantly reduced the risk of stroke **by 51%** in older adults aged 65–69 years

OR, odds ratio

Klaric JS et al. Mil Med. 2019;184:126–132

While vaccination against influenza does not prevent COVID-19 infection, there are many important benefits

Flu vaccination can reduce the risk of **flu-associated hospitalisation** for all ages



Getting vaccinated can help to **protect more vulnerable people** around you

Getting a flu vaccine helps **save healthcare resources** for the care of patients with COVID-19

Centers for Disease Control and Prevention (CDC), 2020. What are the benefits of flu vaccination?

With the risk of COVID-19 co-circulation, minimising the impact of other infectious diseases through vaccination is crucial

Continued COVID-19 circulation may coincide with influenza season, significantly **increasing pressure on healthcare systems**[1,2]

Health bodies have emphasised the **importance of timely, maximal vaccination**, and have expanded outreach efforts[1,2]

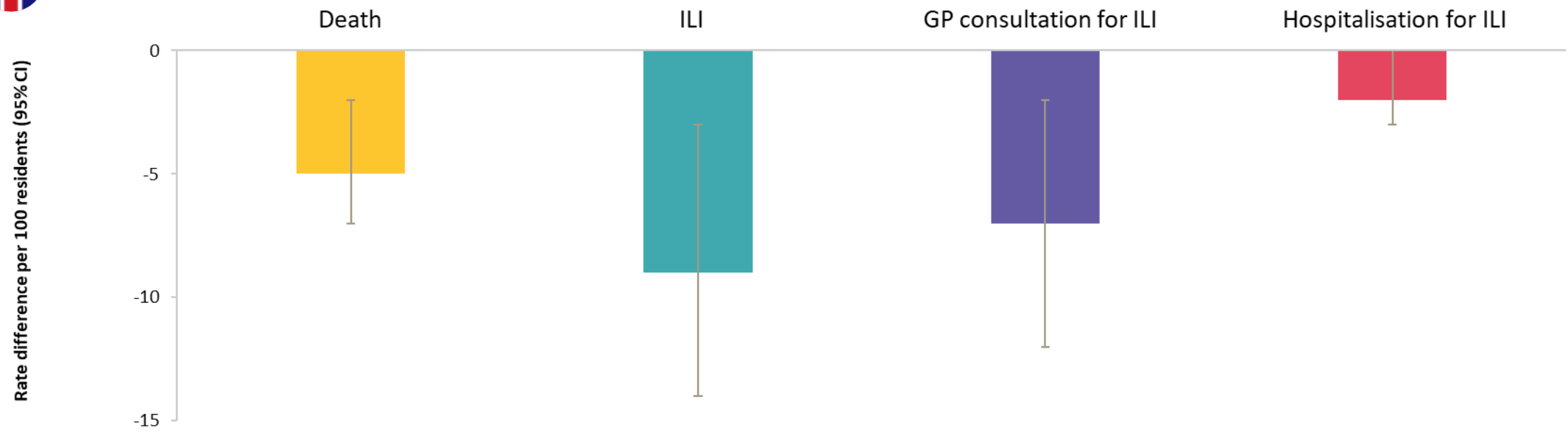
Alongside vaccination, correct **hand hygiene and PPE** are essential for patients and HCWs for reducing the risk of viral transmission[3]

HCW, healthcare worker; PPE, personal protective equipment

1. Public Health England (PHE), 2020. The national flu immunisation programme 2020/21. https://www.england.nhs.uk/wp-content/uploads/2020/05/national-flu-immunisation-programme-2020-2021.pdf; 2. Centers for Disease Control and Prevention (CDC), 2020. Frequently asked influenza (flu) questions: 2020-2021 Season. https://www.cdc.gov/flu/season/faq-flu-season-2020-2021.htm; 3. Public Health England (PHE), 2020. COVID-19: Guidance for the remobilisation of services within health and care settings https://nhsproviders.org/media/690124/guidance-for-remobilisation-of-services.pdf (URLs accessed June 2022)

Routine vaccination of HCWs and at-risk groups forms an essential part of infectious disease risk reduction

Difference in rates of all-cause death, influenza-like illness and health service use in residents at care homes with staff vaccinated against influenza vs with unvaccinated staff (N = 2604)



HCW vaccination **significantly reduced the risk** to vulnerable care residents

CI, confidence interval; GP, general practitioner; HCW, healthcare worker; ILI, influenza-like illness

Hayward AC *et al. BMJ* 2006;333:1241

I vaccini potenziati: analisi di costo/efficacia

Significato e ruolo dei vaccini potenziati: analisi di costo/efficacia

(Choi MJ et al. *Vaccines* **2022**, *10*, 445)

Table 2. Vaccine efficacy and coverage rates.

		Target Groups			
		At-Risk		50–64 Years	≥65 Years
		19–49 Years	50–64 Years		
Vaccine efficacy	TIV	59%	59%	59%	58%
	QIV	64.2% (59–70.3%)	64.2% (59–70.3%)	64.2% (59–70.3%)	63.2% (58–69.3%)
	ATIV				66.4% (62.2–74.8%)
	HD-QIV				72.0% (68.1–76.7%)
Vaccination coverage rates		35.8%	35.8%	41.4%	84.3%

TIV, trivalent influenza vaccine; QIV, quadrivalent influenza vaccine; ATIV, adjuvanted trivalent influenza vaccine; HD-QIV, high-dose quadrivalent influenza vaccine.

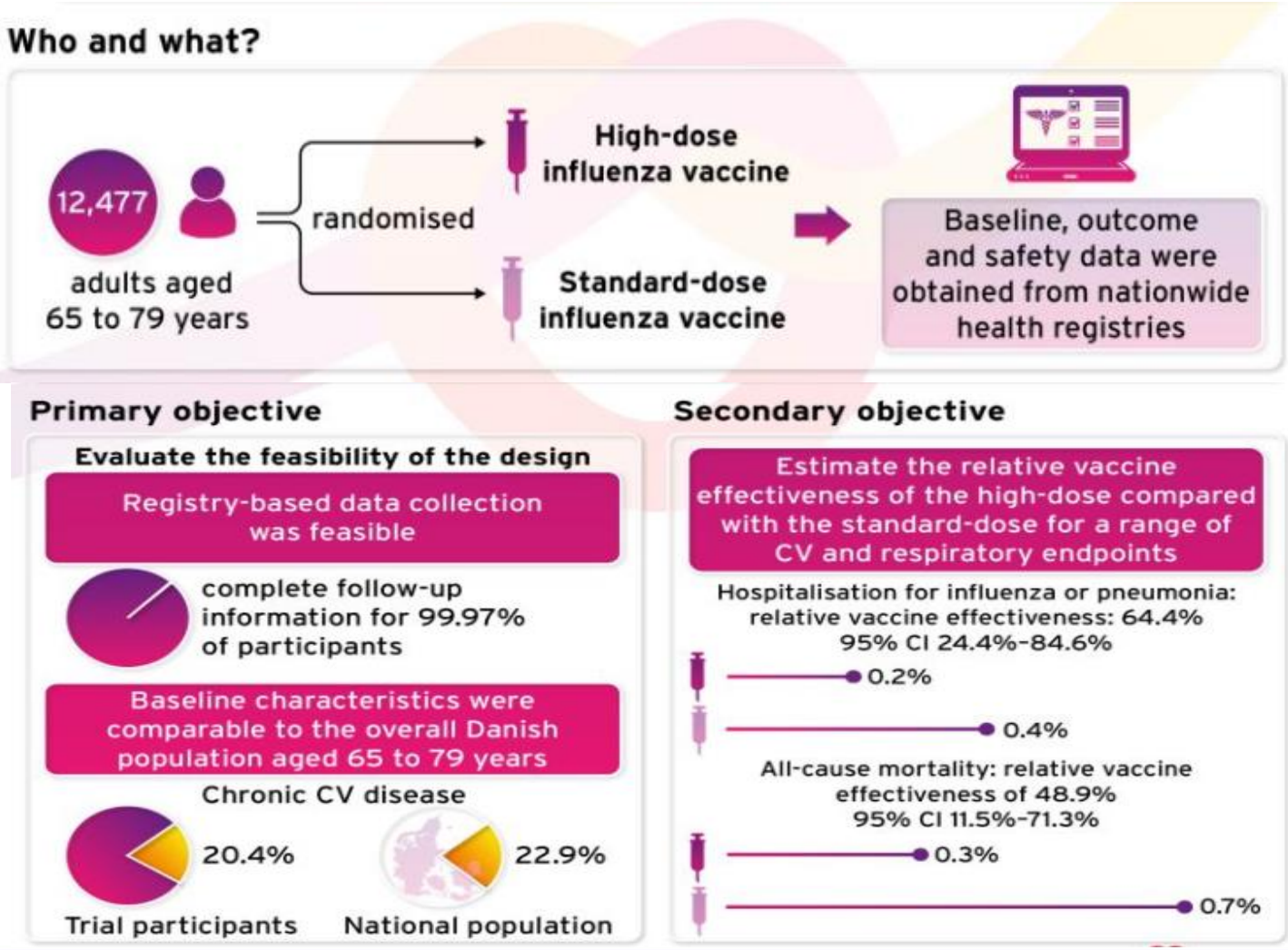
High dose influenza vaccine is effective in the elderly (Van Aalst R et al. Vaccine 2020; 38: 372–379)

Table 4
Relative vaccine effectiveness (rVE) with 95% confidence intervals of high dose (HD-IIV3) versus adjuvanted influenza vaccine (aIIV3) for respiratory seasons 2016–17, 2017–18 and the two seasons combined (summary rVE), adjusted for baseline characteristics.

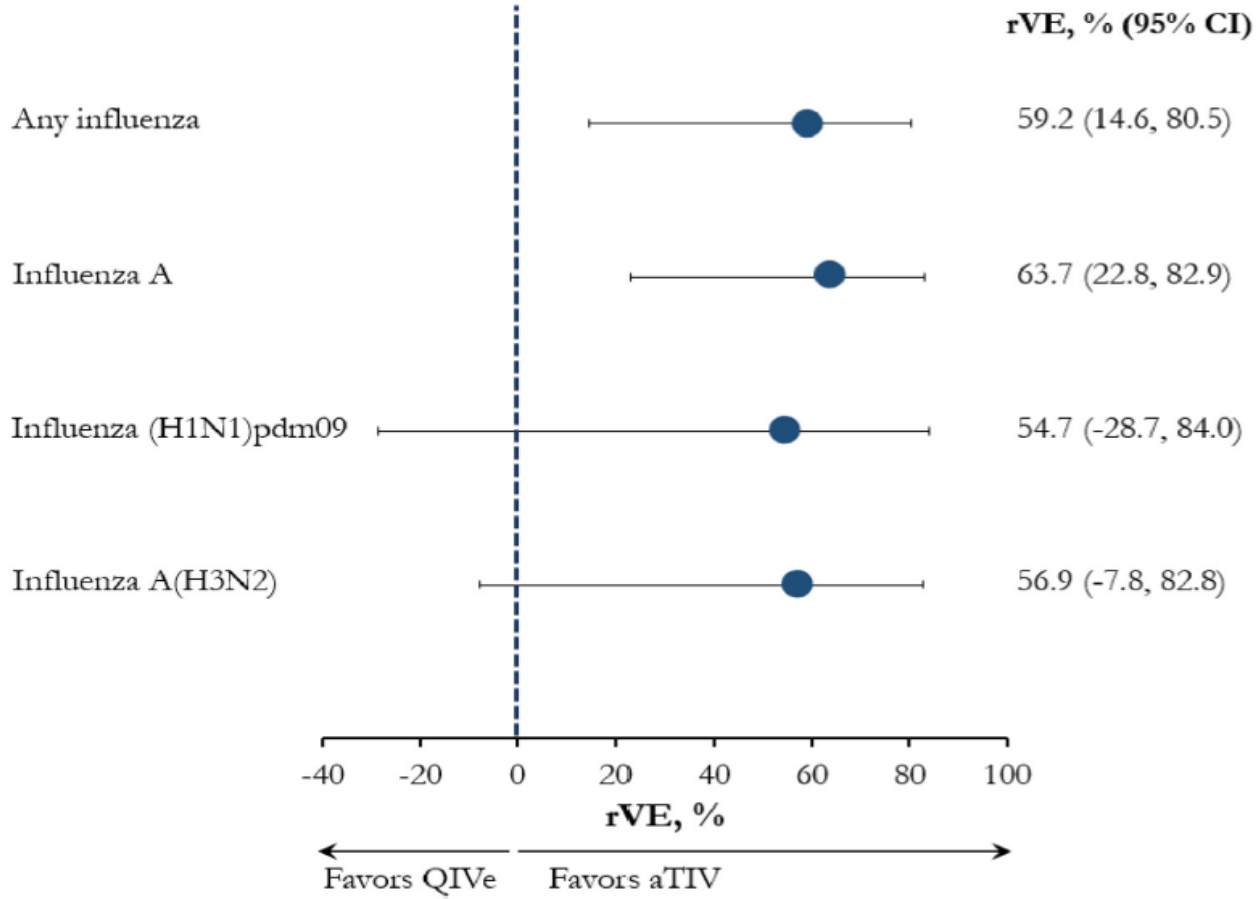
Hospitalizations	2016–17 season	2017–18 season	Summary rVE
Respiratory disease	13% (−6.3%, 32%)	12% (2.1%, 21%)	12% (3.3%, 20%)
Cardio-respiratory disease	13% (2.3%, 23%)	6% (0.6%, 11%)	7.0% (2.3%, 12%)
Urinary Tract Infection	−20% (−59%, 19%)	2.5% (−12%, 17%)	−0.7% (−14%, 13%)

Confidence intervals were calculated using a robust variance estimator. We applied the Previous Event Rate Ratio (PERR) to address unmeasured confounders by including an interaction term of Period (observation versus baseline period) and treatment (HD-IIV3 versus aIIV3). The PERR was adjusted for observed confounding factors by including all the baseline characteristics of Table 1 as covariates, except for Age Groups and the Deyo-Charlson Score, to prevent collinearity with Age and individual comorbid conditions. Hospitalizations were classified using the principal discharge diagnosis.

High dose influenza vaccine is effective in the elderly (The DANFLU-1 trial)



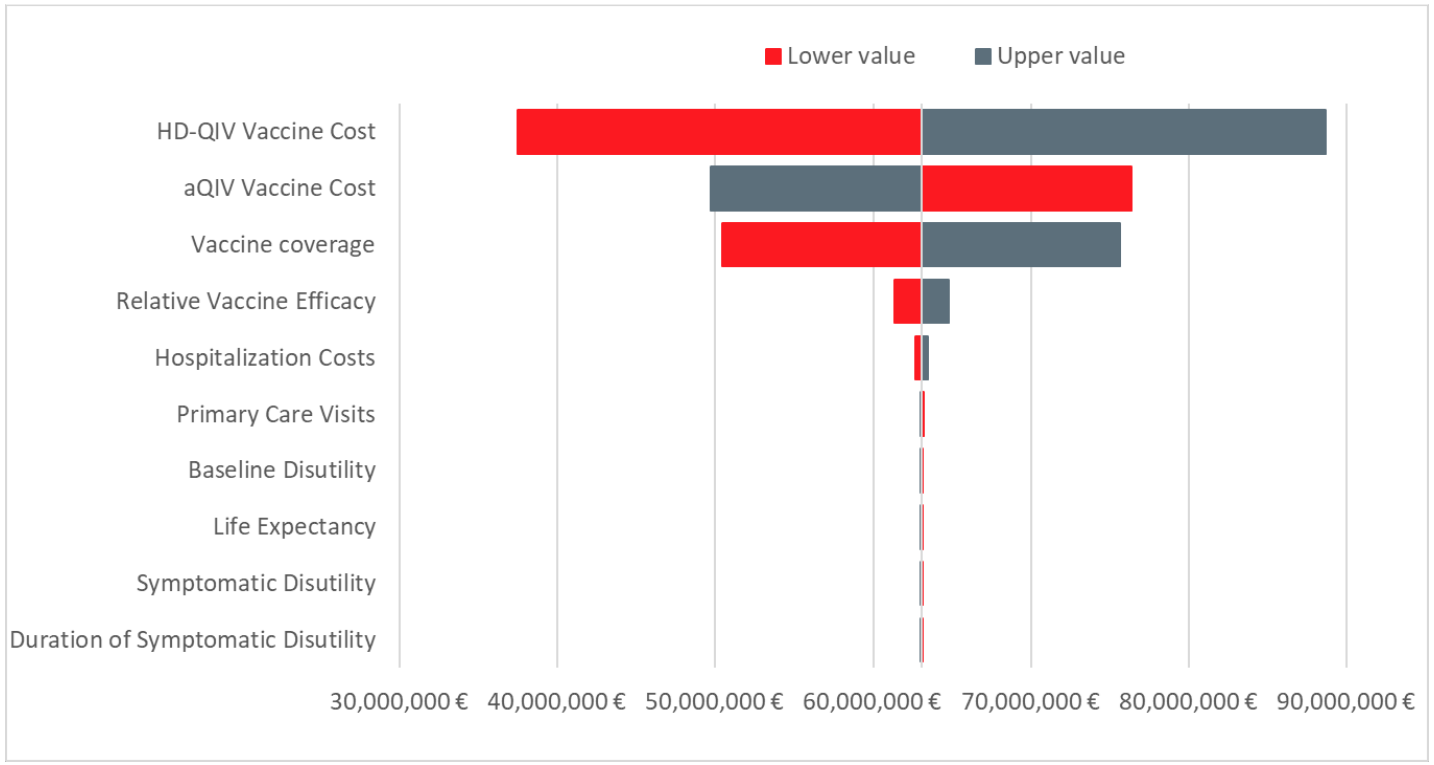
Relative effectiveness of the adjuvanted vs non-adjuvanted seasonal influenza vaccines against severe laboratory-confirmed influenza among hospitalized Italian older adults
(Domnich A et al. Int J Infect Dis 2022; 125: 164–169)



Regarding the type of SIV, about two-thirds (65.8%; 337/512) of subjects were vaccinated with aTIV. As shown by SMDs (Supplementary Table S1), aTIV and QIVe subgroups were severely unbalanced for several variables, suggesting an important confounding by indication. For instance, aTIV users were, on average older…

an SMD of 0.34 (95% CI: 0.16, 0.53

Costo e copertura sono determinanti maggiori del rapporto costo/efficacia (Ruiz-Aragòn J et al. *Vaccines* 2022, *10*, 176)



Una nota di cautela

Given unknown but theoretical concerns of increased reactogenicity when administering two adjuvanted vaccines, selection of a nonadjuvanted influenza vaccine may be considered when influenza vaccine and another vaccine containing a novel adjuvant are administered at the same time.1 Examples of vaccines containing a novel adjuvant include Shingrix and Heplisav-B. Vaccination should not be delayed if a specific product is not available and another opportunity to vaccinate the patient before the end of October is uncertain.

*An adjuvant is a substance that enhances the body's immune response to a vaccine

Washington State Department of Health. Office of Immunization and Child Profile VACCINE ADVISORY COMMITTEE High-Dose and Adjuvanted Flu Vaccine for Persons 65 Years and Older DOH 348-518 March 2020

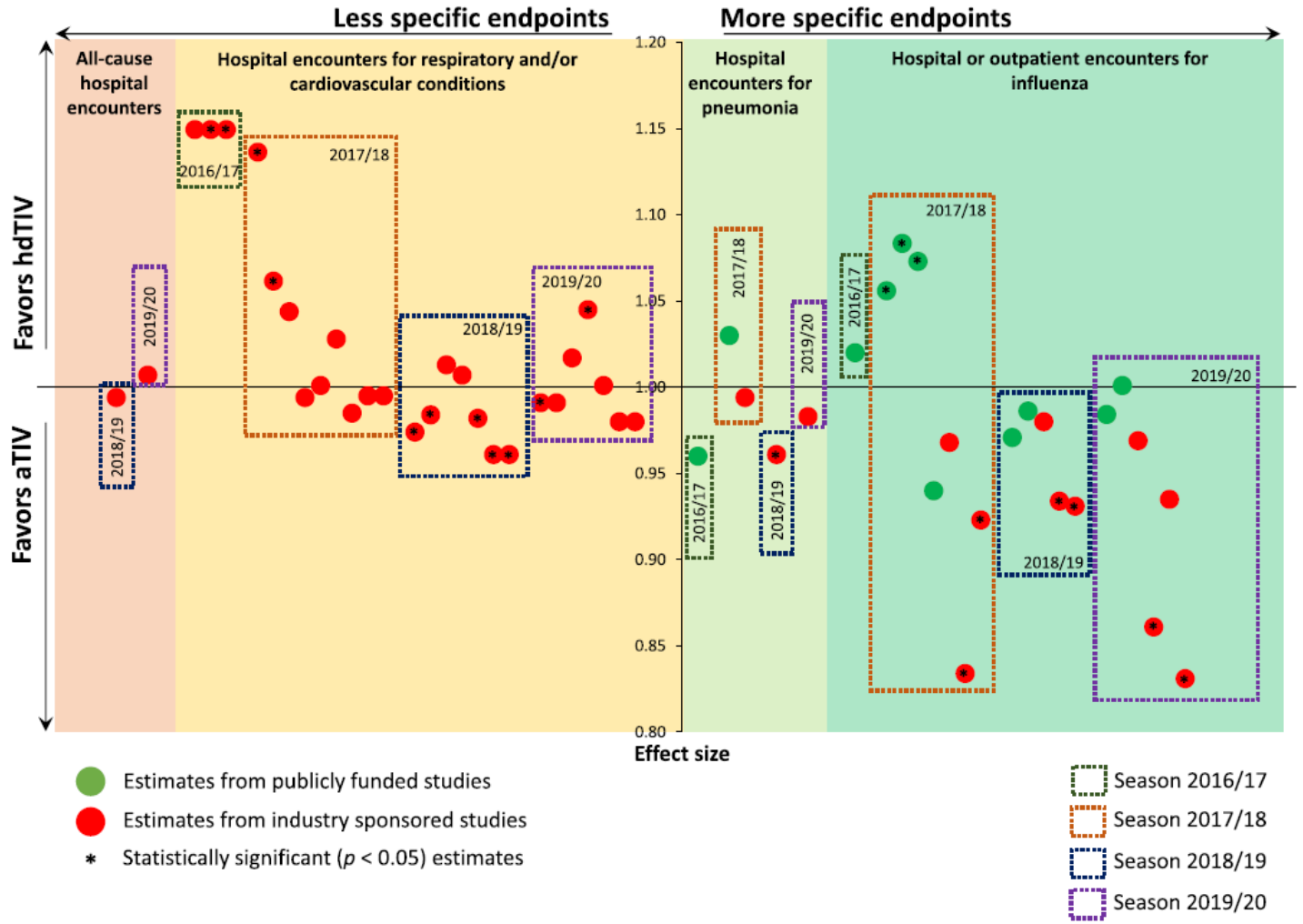


Figure 1. Bubble plot of the reported effect sizes, by influenza-related end point, season and sponsor.

Non dimentichiamo le misure di prevenzione generiche (Circolare ministeriale 2022/23)

- Lavare regolarmente le mani e asciugarle correttamente. Le mani devono essere lavate accuratamente con acqua e sapone, per almeno 40-60 secondi ogni volta, specialmente dopo aver tossito o starnutito e asciugate. I disinfettanti per le mani a base alcolica riducono la quantità di virus influenzale dalle mani contaminate e possono rappresentare una valida alternativa in assenza di acqua.
- Osservare una buona igiene respiratoria: coprire bocca e naso quando si starnutisce o tossisce, con fazzoletti monouso da smaltire correttamente e lavarsi le mani.
- Isolarsi volontariamente a casa se si presentano sintomi attribuibili a malattie respiratorie febbrili specie in fase iniziale.
- Evitare il contatto stretto con persone ammalate, ad es. mantenendo un distanziamento fisico di almeno un metro da chi presenta sintomi dell'influenza ed evitare posti affollati. Quando non è possibile mantenere il distanziamento fisico, ridurre il tempo di contatto stretto con persone malate.
- Evitare di toccarsi occhi, naso o bocca. I virus possono diffondersi quando una persona tocca qualsiasi superficie contaminata da virus e poi si tocca occhi, naso o bocca.

Le mascherine chirurgiche indossate da persone con sintomatologia influenzale possono ridurre le infezioni tra i contatti stretti.

Popolazioni particolari

Frailty does not weaken the Antibody response to influenza vaccine…

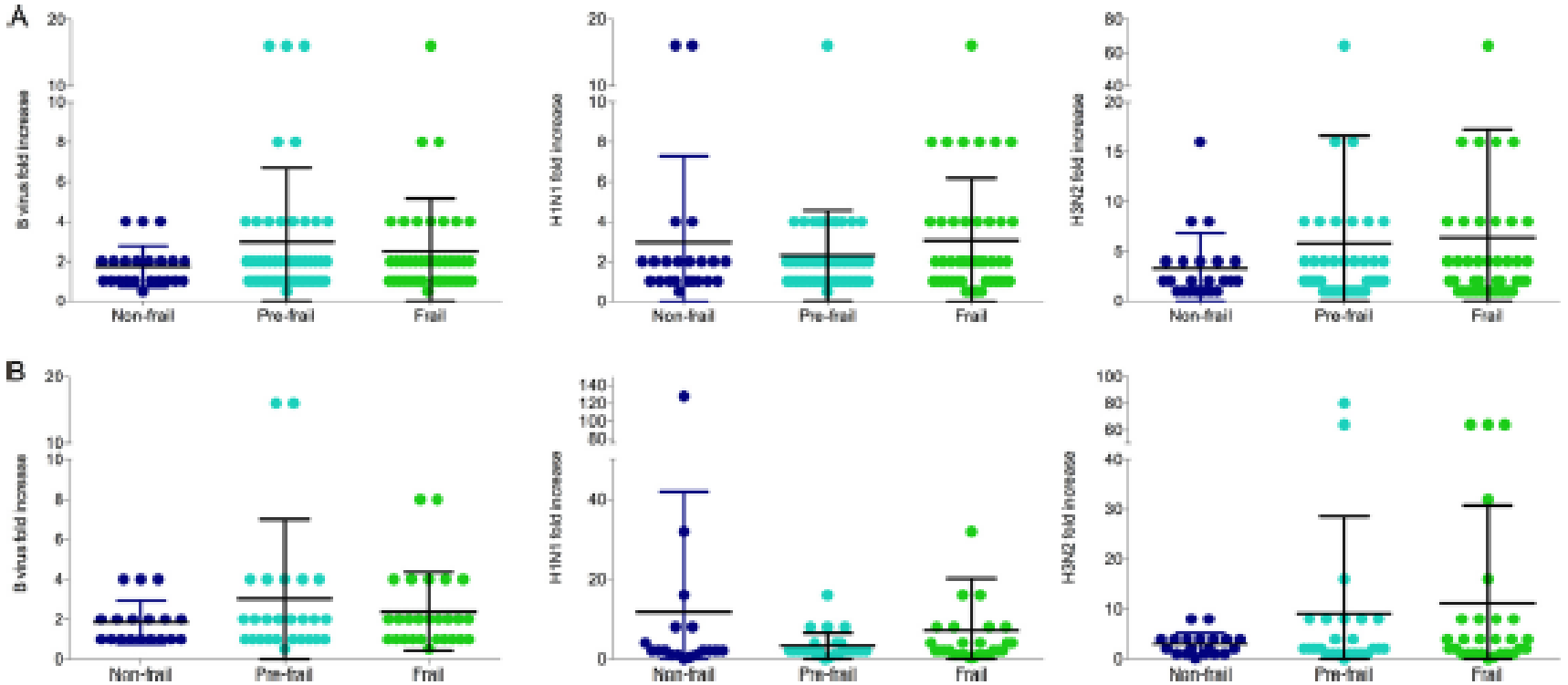


FIG 1 Comparison of hemagglutination inhibition (HI) (A) and microneutralization (MN) (B) postvaccination/prevaccination geometric mean titer (GMT) ratios within frailty groups. No statistically significant differences, as measured by one-way ANOVA, were found between frailty groups. Horizontal black lines represent the mean, and the vertical lines represent 1 standard deviation (SD).

- Frailty does not weaken the Antibody response to influenza vaccine (Van Epps P et al. March 2017 Volume 24 Issue 3 e00498-16 Clinical and Vaccine Immunology)

…, while previous immunization strengthens it (Van Epps P et al. March 2017 Volume 24 Issue 3 e00498-16 Clinical and Vaccine Immunology)

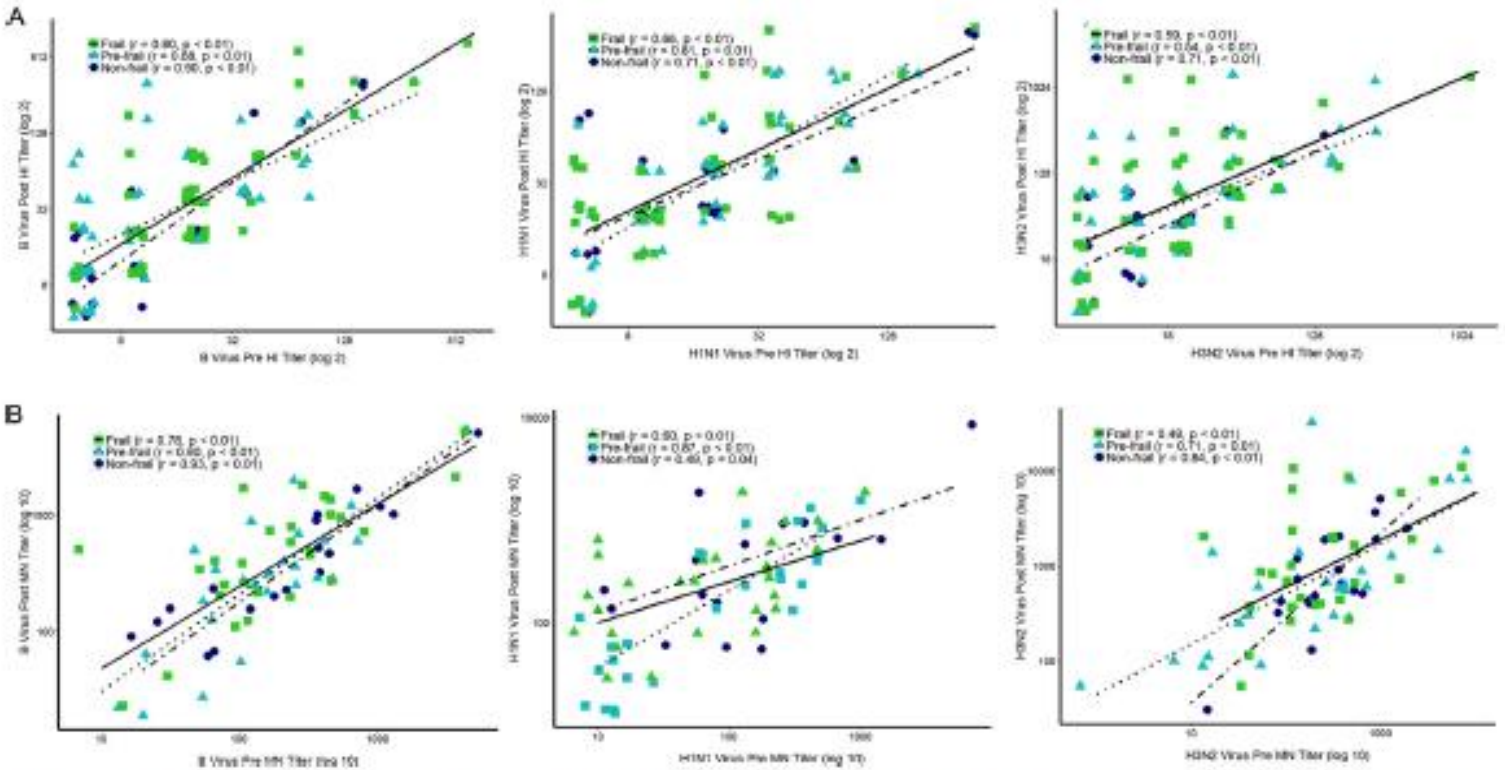


FIG 2 Correlation of preexisting immunity with postvaccination responses, as measured by hemagglutination inhibition (HI) (A) and microneutralization (MN) (B) assays. Antibody levels were plotted within frailty groups, and correlations were calculated to determine the effect of preexisting immunity on postvaccination antibody titers. The Spearman correlation coefficient and *P* value are presented for each frailty group.

L'analogia con la risposta del «grande vecchio» al vaccino Covid-19: lo studio GeroVax (Fedele G et al. JAMDA 2022)

Table 1
Geometric Means (GMs) and SEs of SARS-CoV-2 TrimericS IgG Serum Concentration at Baseline Assessment (Prior to Vaccination, T0), 2 and 6 Months After First Dose (T1 and T2), and 2 Months After Third Dose (T3) in Nursing Home Residents

	SARS-CoV-2 TrimericS IgG Serum Concentration, BAU/mL											
	T0: Prior to Vaccination			T1: 2 mo After First Dose			T2: 6 mo After First Dose			T3: 2 mo After Third Dose		
	GM	SE	*P* Value	GM	SE	*P* Value	GM	SE	*P* Value	GM	SE	*P* Value
Whole sample (n=144)	4.9	0.1	<.001	833.7	89.8	Ref.	92.0	8.7	<.001	3597.9	339.5	<.001
Sex												
Women (n=104)	5.0	0.1	<.001	812.0	103.3	Ref.	98.3	11.9	<.001	3690.6	663.9	<.001
Men (n=40)	4.8	0.1	<.001	892.7	183.0	Ref.	95.3	18.5	<.001	3562.9	397.5	<.001
Age group												
<80 y (n=35)	4.8	0.14	<.001	1176.1	255.0	Ref.	124.8	23.9	<.001	4832.0	919.1	<.001
≥80 y (n=109)	5.0	0.08	<.001	746.4	91.7	Ref.	83.4	9.0	<.001	3272.8	352.7	<.001

Ref., reference.
All participants received 2 doses of BNT162b2 vaccine 3 weeks apart and a third dose of an mRNA vaccine (mRNA-1273 or BNT162b2) between 6 and 9 months from the first vaccine dose. GMs were compared across the 4 time points (T1 is the reference).

Paura di deficit cognitivo indotto? Il contrario in una popolazione esente da MCI o demenza al baseline (Bukhbinder AS et al. Journal of Alzheimer's Disease xx (2022) x–x)

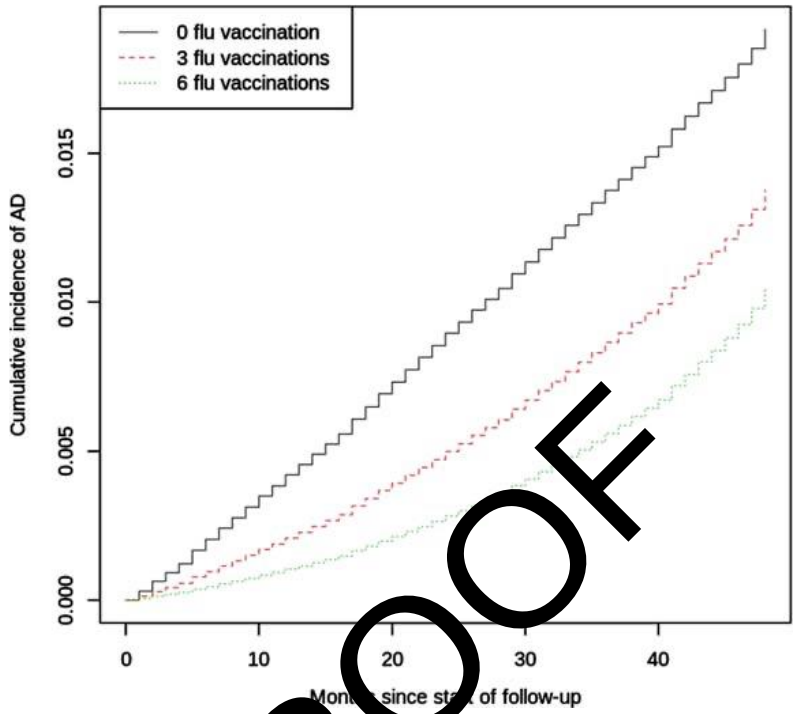


Fig. 3. Estimated CIF Curves of Incident AD by Number of Influenza Vaccinations. Quantitative results from the regression model are presented in Supplementary Table 3.

Il caso dei malati neoplastici trattati con inibitori dell'immune checkpoint (Tsiakos K et al. J Immunother 2022;45:291–298)

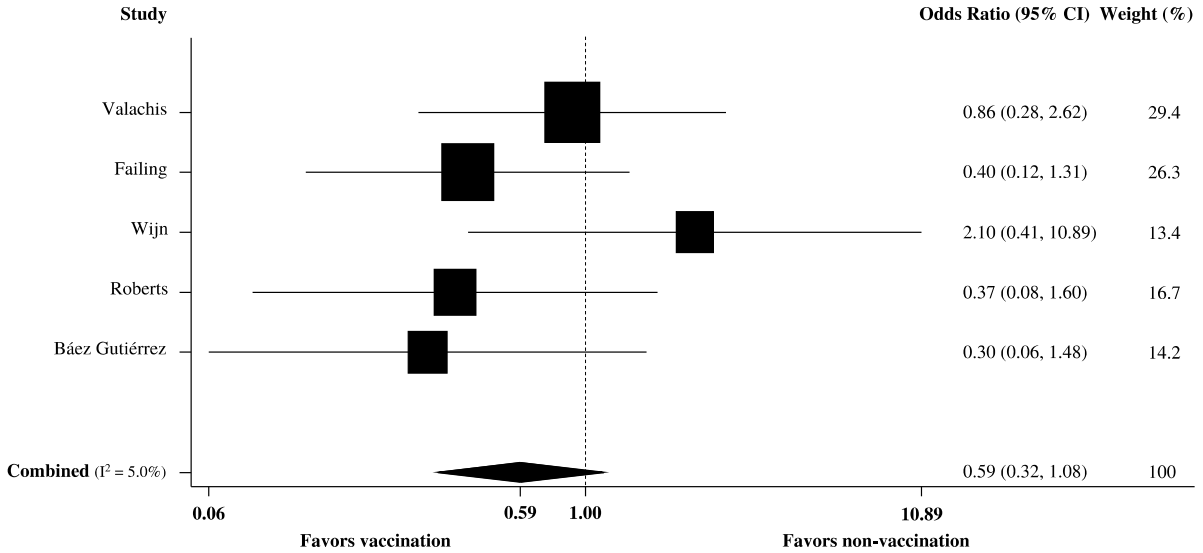


FIGURE 3. Forest plot of odds ratio for serious immune-related adverse events in influenza vaccinated versus nonvaccinated cancer patients receiving immune checkpoint inhibitors. CI indicates confidence interval.

I malati con artrite reumatoide (Meroni PL et al. Clin Exp Rheumatol 2018; 36: 317-328)

Table III. 2015 recommendations regarding the use of vaccines in patients with rheumatoid arthritis of the American College of Rheumatology (ACR) (7).

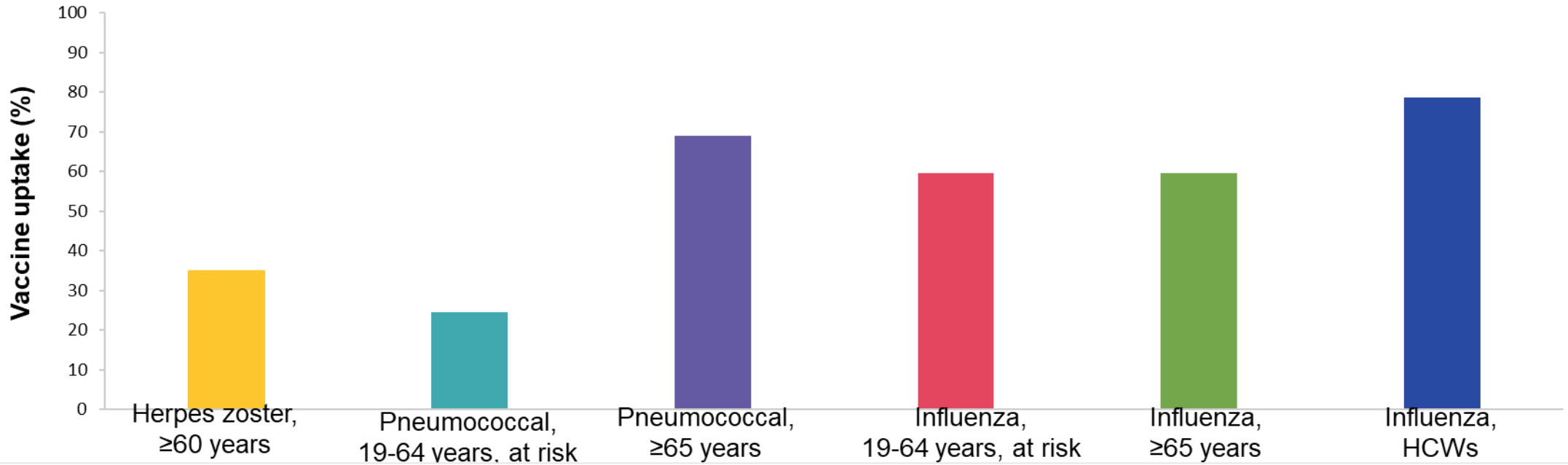
	Killed vaccines			Recombinant vaccine	Live attenuated vaccine
	Pneumococcal [1]	Influenza [2]	Hepatitis B [3]	Human papilloma	Herpes zoster
Before initiating therapy					
DMARD monotherapy	Recommended	Recommended	Recommended	Recommended	Recommended
Combination DMARD	Recommended	Recommended	Recommended	Recommended	Recommended
TNFi biologics	Recommended	Recommended	Recommended	Recommended	Recommended [4]
Non-TNF biologics	Recommended	Recommended	Recommended	Recommended	Recommended [4]
While already taking therapy					
DMARD monotherapy	Recommended	Recommended	Recommended	Recommended	Recommended
Combination DMARD	Recommended	Recommended	Recommended	Recommended	Recommended
TNFi biologics	Recommended	Recommended	Recommended	Recommended	Not recommended
Non-TNF biologics	Recommended	Recommended	Recommended	Recommended	Not recommended

[1]one-time pneumococcal revaccination after 5 years is recommended; [2] RA patients should use the intramuscular influenza vaccine, as the live intranasal vaccine is contraindicated. [3] If hepatitis B risk factors are present (*e.g.* intravenous drug abuse, multiple sex partners in the previous 6 months, health care personnel); [4] conditionally recommended giving the herpes zoster vaccine before the patient receives biologic therapy or tofacitinib for their RA in both early or established RA patients ages ≥50 years. After giving the herpes zoster vaccine, there should be a 2-week waiting period before starting biologics.

I limiti delle coperture vaccinali

Despite the importance of vaccination, coverage in adults remains below recommended levels

Vaccine uptake in older adults, adults aged <65 years with high-risk conditions and HCWs, 2017*[1,2]



Vaccine uptake remains **below target**, both for HCWs and vulnerable individuals

'High-risk' defined as medical conditions such as asthma, heart disease and diabetes. HCW, healthcare worker; CDC, Centers for Disease Control and Prevention

1. Centers for Disease Control and Prevention (CDC), 2018. Vaccination coverage among adults in the United States, National Health Interview Survey, 2017. https://www.cdc.gov/vaccines/imz-managers/coverage/adultvaxview/pubs-resources/NHIS-2017.html; 2. Black CL *et al. MMWR Morb Mortal Wkly Rep* 2017;66:1009–1015; 3. HealthyPeople.gov. Immunization and infectious diseases. https://www.healthypeople.gov/2020/topics-objectives/topic/immunization-and-infectious-diseases/objectives (URLs accessed June 2022)

The obstacles to vaccines

Obstacles	Note	Suggested intervention
Heterogeneity between countries	Poor attitude to co-operation	Organisms like WHO should promote international coordination
Available professional resources are frequently underpowered	Differences in the role of general practitioners and in the quality of ambulatory and home care services	To value the role of the general practitioner and selected other health professionals, as available and as needed
Poor information about vaccines	The information strategy differs among countries	Suggested multimodal strategy: «convenient» approach, ie, tailored to the target population
No universal informative system on vaccinated people is available	This prevents a careful assessment of the health effects of vaccines	Immunization registers should be the rule
The education of health professionals is frequently defective in vaccinology	This limits the role of health professionals as vaccine promoters	Vaccines should be a key didactic topic either in the degree course or in many post-doctoral courses
Disinformation and mystification of the reality	Multiple causes	Communication campaigns involving influencers

Antonelli Incalzi R et al. Vaccines 2021; 9 (11): 1232.

The obstacles to vaccines: the view of the diabetic patient

Table 2 – Reasons for being or not being vaccinated.

Variables	Age		*p*
	<65 (*n* = 373)	⩾65 (*n* = 206)	
Reasons for not being vaccinated [*n* (%)]			
I do not need	366 (98.1)	189 (91.7)	**<0.001**
Disease gives	0	2 (1.0)	0.126
Forgot	1 (0.3)	0	0.995
Side effects	0	5 (2.4)	**0.006**
I did not think would protect	4 (1.1)	6 (2.9)	0.178
The doctor did not mention vaccines	275 (73.7)	148 (71.8)	0.626
I did not have the opportunity to reach	0	3 (1.5)	0.076
I do not trust	1 (0.3)	5 (2.4)	**0.023**

The categorical variables are showed as *n* (%).
Bold values were considered statistically significant.

- (Altay M et al. diabetes research and clinical practice (2016; 120: 117–123)

I limiti delle conoscenze tra specialisti e specializzandi in Geriatria: quadro sinottico

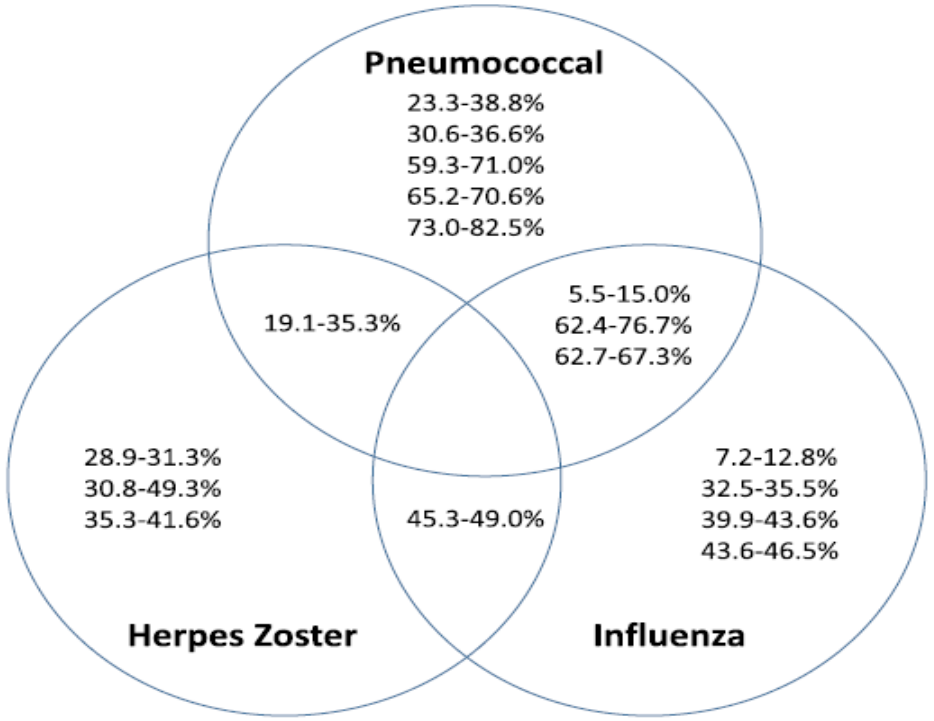


Fig. 1. Range (minimum and maximum) of correct response rates achieved on each question by qualified specialists and residents, according to the vaccine mentioned in the question. (Note: the single question about measles is not included).

Ecarnot F et a. Vaccine 38 (2020) 1535–1540

Intenzione di proporre la vaccinazione agli anziani da parte degli specialisti e specializzandi in Geriatria

Vaccino	Intenzione	Target
Antiinfluenzale	76,5	75% (95% categorie ad alto rischio)
Antipneumococcico	46,3	75%
AntiHVZ	24,8	50%

Ecarnot F et a. Vaccine 38 (2020) 1535–1540

Aging Clinical and Experimental Research
https://doi.org/10.1007/s40520-020-01622-z

CONSENSUS DOCUMENT

Vaccines in older age: moving from current practice to optimal coverage—a multidisciplinary consensus conference

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To be updated upon vaccines

Recommended Vaccines by Age | CDC

https://www.cdc.gov › vpd › vacc.

CDC Resources: Immunization schedules

https://www.immunize.org › cdc