SOCIETÀ ITALIANA DI GERONTOLOGIA E GERIATRIA
68° CONGRESSO NAZIONALE SIGG
Ritorno al futuro
FIRENZE, 13-16 DICEMBRE 2023
PALAZZO DEI CONGRESSI

La prevenzione vaccinale nelle infezioni da virus sinciziale respiratorio

Claudio Pedone

Università Campus Bio-Medico di Roma

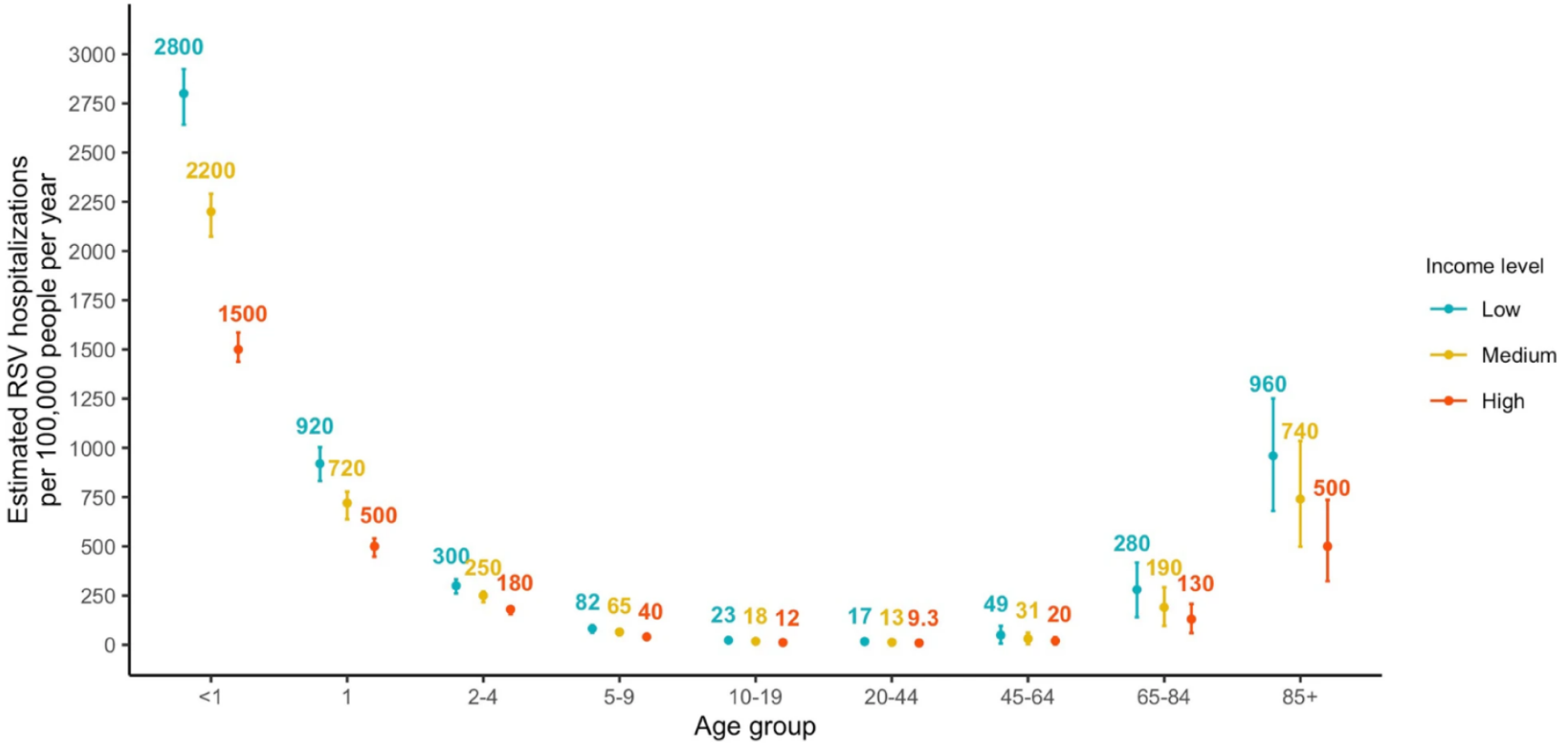
LXVIII Congresso Nazionale SIGG
Firenze, 13-16/12/2023

Impatto di RSV nella popolazione anziana

- La maggior parte delle infezioni da RSV non ha un impatto clinico rilevante;
- La maggior parte dei pazienti anziani, tuttavia, ha uno dei fattori di rischio per infezione da RSV clinicamente rilevante:
  - Patologie polmonari e cardiovascolari;
  - Altre comorbilità rilevanti: diabete mellito; patologie neurologiche, epatiche o renali;
  - Compromissione immunologica;
  - Istituzionalizzazione.
- I dati sull'effettiva incidenza di infezione grave da RSV sono molto variabili.

Incidenza di ospedalizzazioni da RSV

Dati amministrativi



Zheng Z, et al. Pneumonia (Nathan): 2022;14(1):6.

Incidenza di ospedalizzazioni da RSV

Dati clinici

		RSV			HMPV			Influenza Virus		
Age Group	Population	No. of Cases	Weight	Rate/10 000 (95% CI)	No. of Cases	Weight	Rate/10 000 (95% CI)	No. of Cases	Weight	Rate/10 000 (95% CI)
50–64 years	308 329	12	254	8.2 (3.3–12.3)	4	57	1.8 (.3–4.0)	23	356	11.5 (6.8–16.2)
≥65 years	200 711	19	510	25.4 (13.1–38.0)	19	443	22.1 (12.1–33.7)	10	247	12.3 (5.3–21.4)
Overall	509 040	31	764	15.0 (8.6–19.8)	23	500	9.8 (5.8–14.4)	33	603	11.8 (7.6–16.2)

Abbreviations: CI, confidence interval; HMPV, human metapneumovirus; RSV, respiratory syncytial virus.

Widmer K et al. J Infect Dis 2012; 206:56.

Ospedalizzazioni attribuibili al RSV in ospiti di RSA

Table 2. Influenza and Respiratory Syncytial Virus (RSV)-Attributable Cardiopulmonary Hospitalizations (Events) by Risk Group, Tennessee Medicaid Nursing Home Residents from 1995 to 1999

Risk Group	Rates, Events, and Person-Years by Season			Total Rates, Events, and Person-Years	Estimated Annual Events Attributable to Winter Viruses per 1,000 Person-Years* (95% Confidence Interval)		Percentage of Total Events Attributable to Winter Viruses†		
	Influenza	RSV	Non-winter viral		Influenza	RSV	Influenza	RSV	Both
No high risk					6.6 (4.1–9.2)	6.0 (1.9–10.0)	7.6	6.9	14.5
Hospitalizations per 1,000 person-years	113	87	74	88					
Number of hospitalizations	827	707	1,121	2,655					
Person-years	7,310	8,075	15,112	30,497					
High risk					28.1 (23.4–32.9)	11.4 (3.5–19.3)	4.8	2.5	7.3
Hospitalizations per 1,000 person-years	707	571	545	588					
Number of hospitalizations	8,106	7,943	14,177	30,226					
Person-years	11,459	13,901	26,029	51,389					

Ellis SE et al. J Am Geriatr Soc 2003; 51:761.

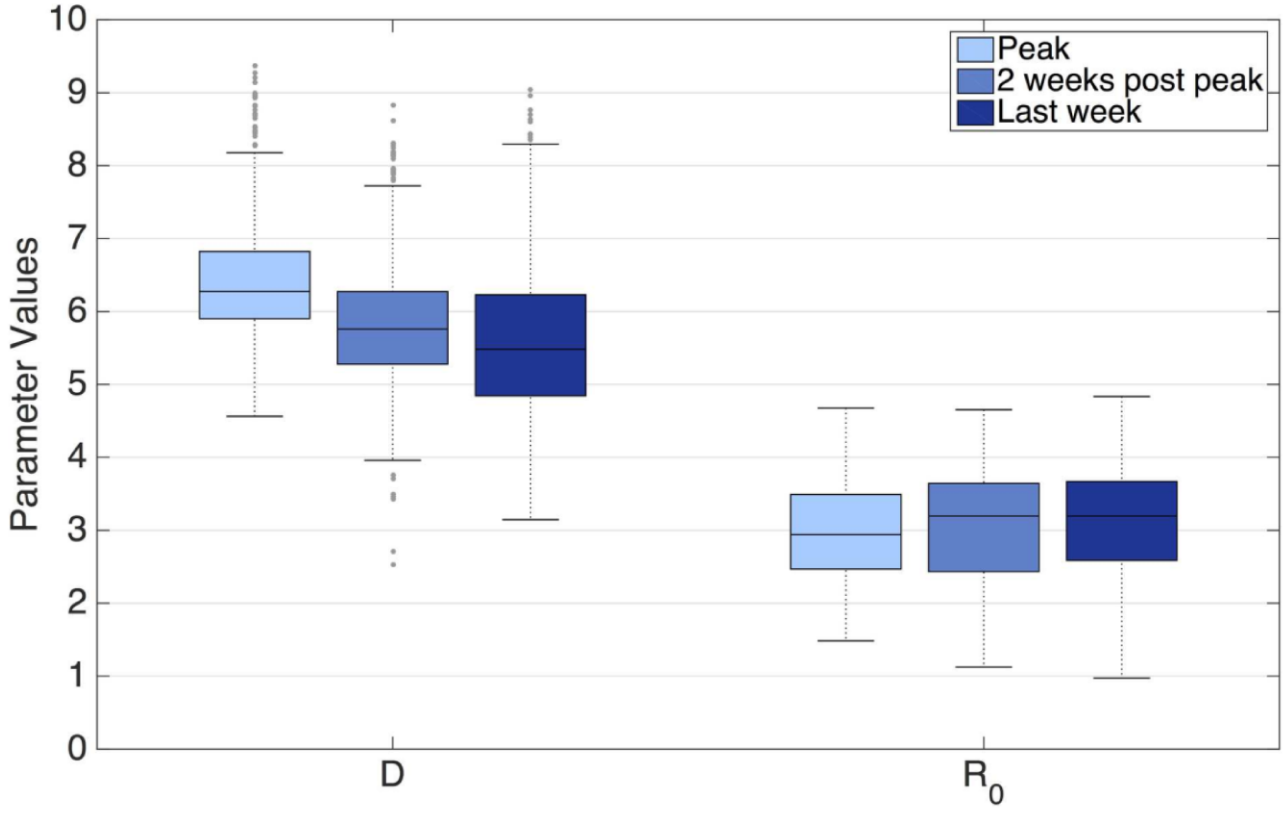
Mortalità attribuibile al RSV in ospiti di RSA

Table 4. Influenza and Respiratory Syncytial Virus (RSV)-Attributable Deaths (Events) by Risk Group, Tennessee Medicaid Nursing Home Residents from 1995 to 1999

Risk group	Rates, Events, and Person-Years by Season			Total Rates, Events, and Person-Years	Estimated Annual Events Attributable to Winter Viruses per 1,000 Person-Years* (95% Confidence Interval)		Percentage of Total Events Attributable to Winter Viruses†		
	Influenza	RSV	Non-winter viral		Influenza	RSV	Influenza	RSV	Both
No high risk									
Deaths per 1,000 person-years	201	175	143	165	6.2 (2.7–9.8)	16.3 (10.7–22.0)	3.8	9.9	13.7
Deaths	1,467	1,411	2,153	5,031					
Person-years	7,310	8,075	15,112	30,497					
High risk									
Deaths per 1,000 person-years	400	335	298	331	14.5 (11.0–18.1)	17.3 (11.5–23.3)	3.4	5.2	8.6
Deaths	4,582	4,661	7,767	17,010					
Person-years	11,459	13,901	26,029	51,389					

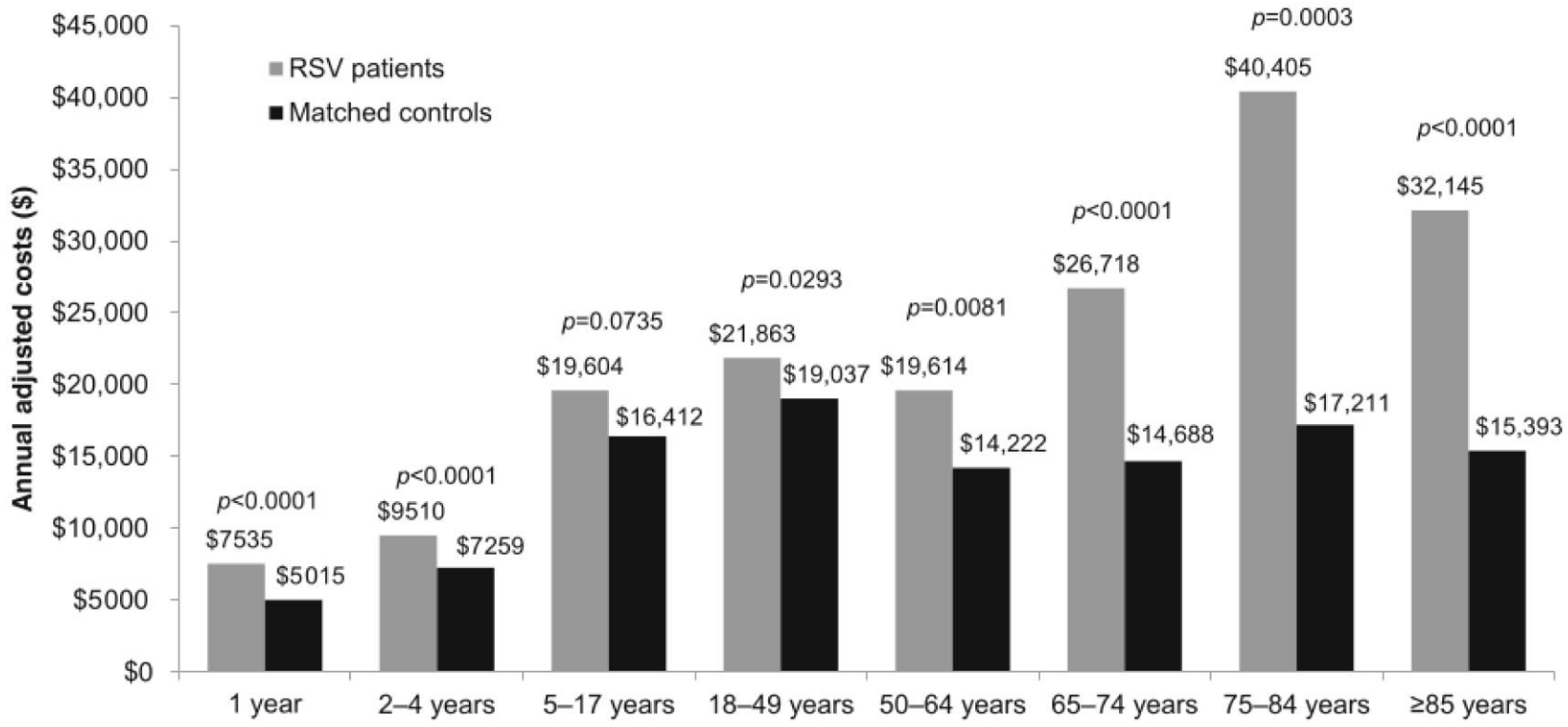
Ellis SE et al. J Am Geriatr Soc 2003; 51:761.

Contagiosità del RSV



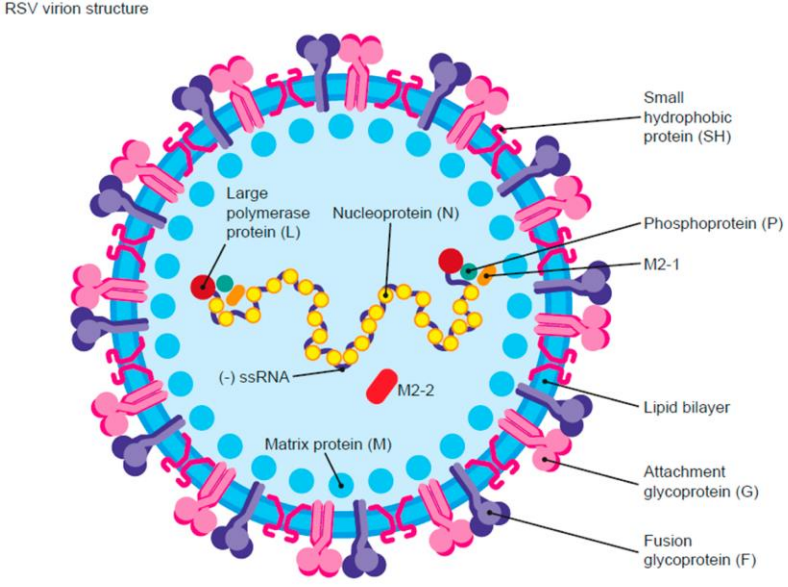
Reis J & Shaman J. PLoS Comput Biol 2016; 12:e1005133.

Costi collegati al RSV



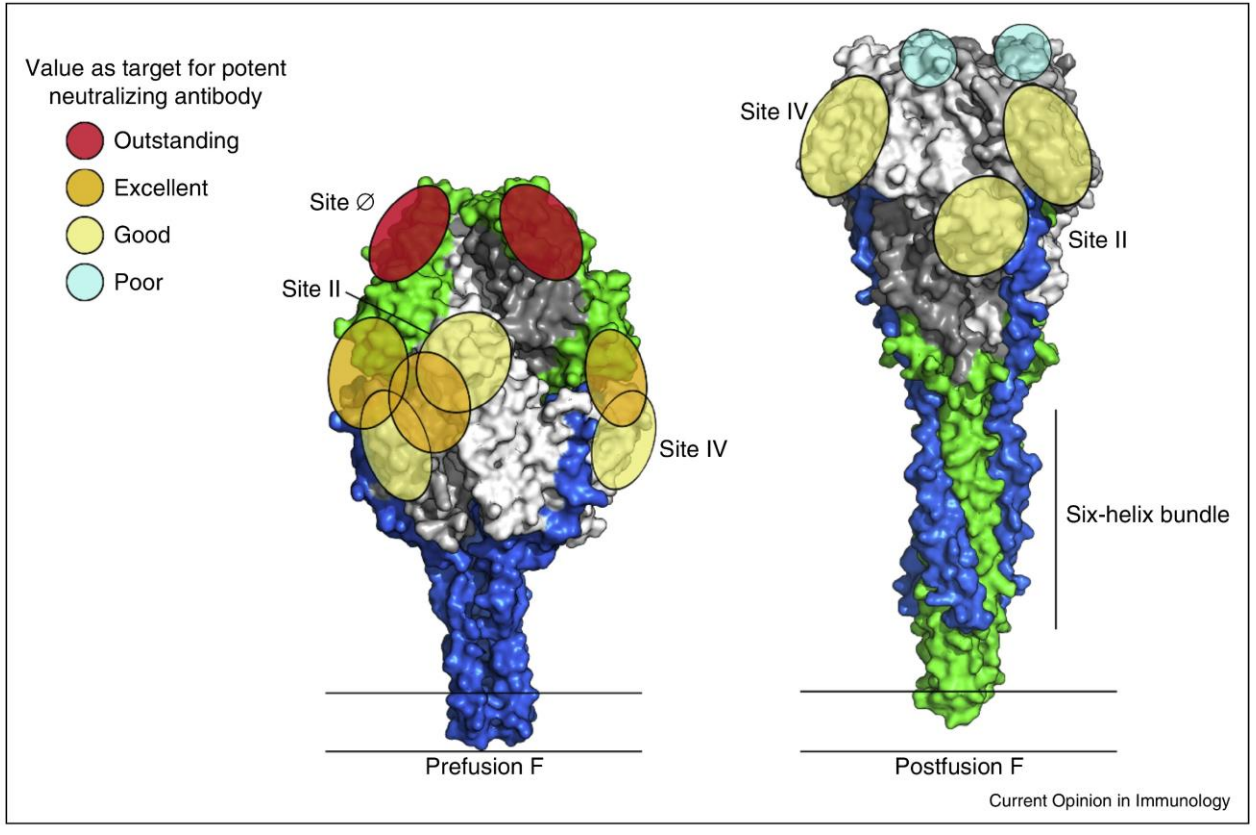
Amand C et al. BMC Health Serv Res 2018; 18:294.

Il virus respiratorio sinciziale



Jenkins VA et al. Vaccines 2023; 11:382.

Target del vaccino



Graham BS et al. Curr Opin Immunol 2015; 35:30.

Come valutare l'efficacia del vaccino?

- La clinica dell'RSV è indistinguibile da quella delle altre *influenza-like infections* e nell'anziano si può manifestare come peggioramento di una condizione pre-esistente;
- Non esistono strumenti validati per stratificare la gravità dell'infezione;
- Non sono facilmente identificabili outcome clinicamente significativi e riproducibili per valutare l'impatto del vaccino sulla gravità della patologia.

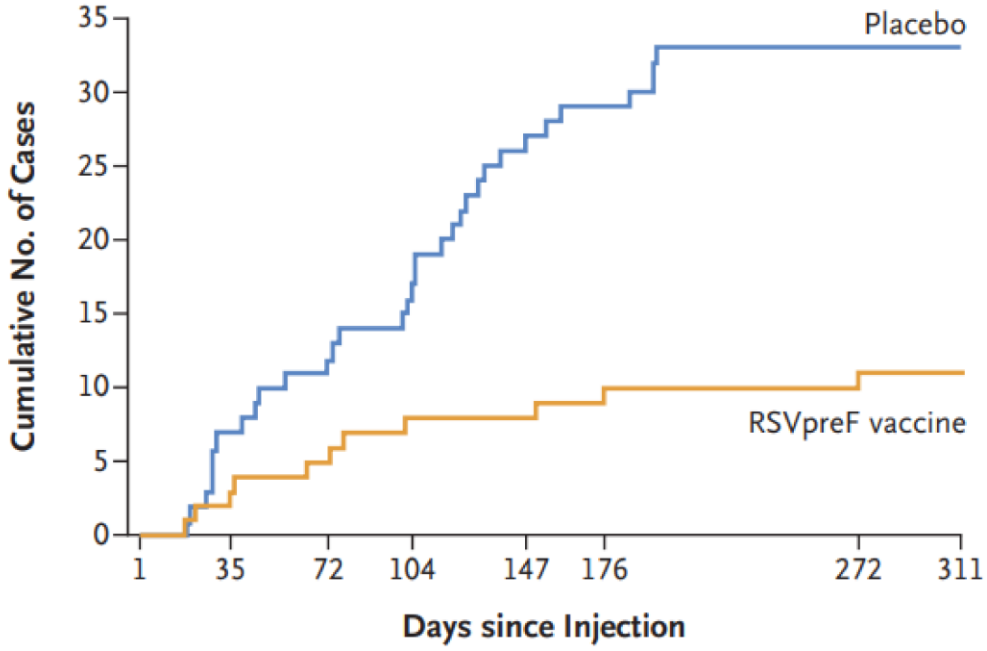
Roberts JN et al. Vaccine 2016; 34:4843.

Vaccini in commercio

- Sono attualmente disponibili diversi vaccini per il RSV;
- Tutti i vaccini sono diretti contro la proteine di prefusione F, ciò che cambia è la tecnologia:
  - Vaccino ricombinante non adiuvato;
  - Vaccino ricombinante adiuvato;
  - Vaccino con vettore adenovirale.

Efficacia del vaccino RSVPreF

A **RSV-Associated Lower Respiratory Tract Illness with ≥2 Signs or Symptoms**



Cumulative No. of Cases								
Placebo	0	7	12	17	27	29	33	33
RSVpreF vaccine	0	3	5	8	8	10	11	11

Vaccine Efficacy (96.66% CI)

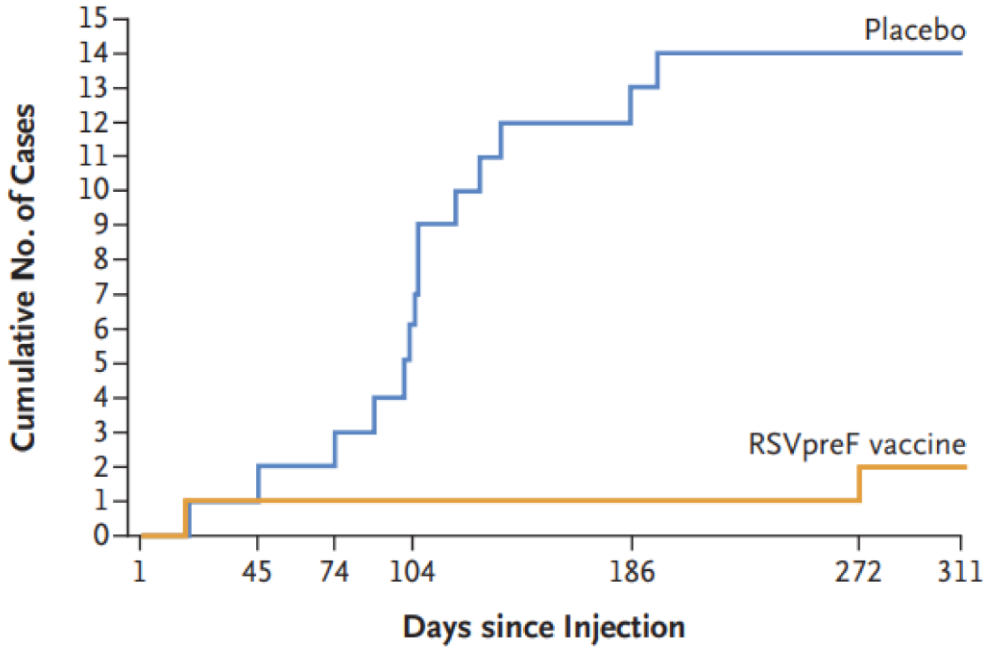
percent

66.7 (28.8–85.8)

Walsh EE et al. N Engl J Med 2023; 388:1465.

Efficacia del vaccino RSVPreF

B **RSV-Associated Lower Respiratory Tract Illness with ≥3 Signs or Symptoms**



Cumulative No. of Cases							
Placebo	0	2	3	7	13	14	14
RSVpreF vaccine	0	1	1	1	1	2	2

Vaccine Efficacy (96.66% CI)

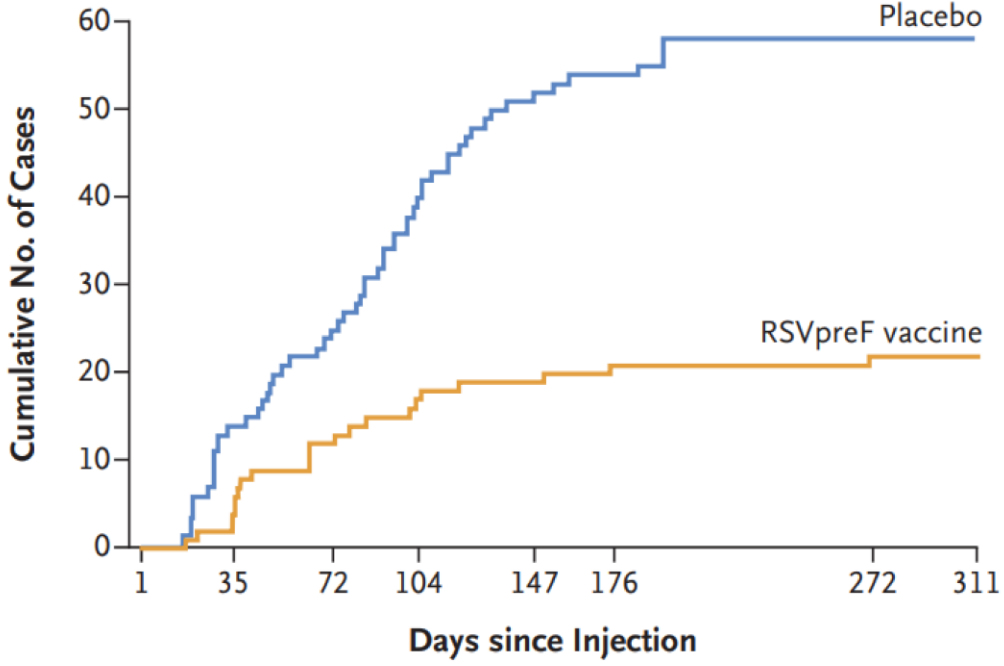
percent

85.7 (32.0–98.7)

Walsh EE et al. N Engl J Med 2023; 388:1465.

Efficacia del vaccino RSVPreF

C **RSV-Associated Acute Respiratory Illness**



Cumulative No. of Cases								
Placebo	0	14	25	40	52	54	58	58
RSVpreF vaccine	0	4	12	17	19	21	22	22

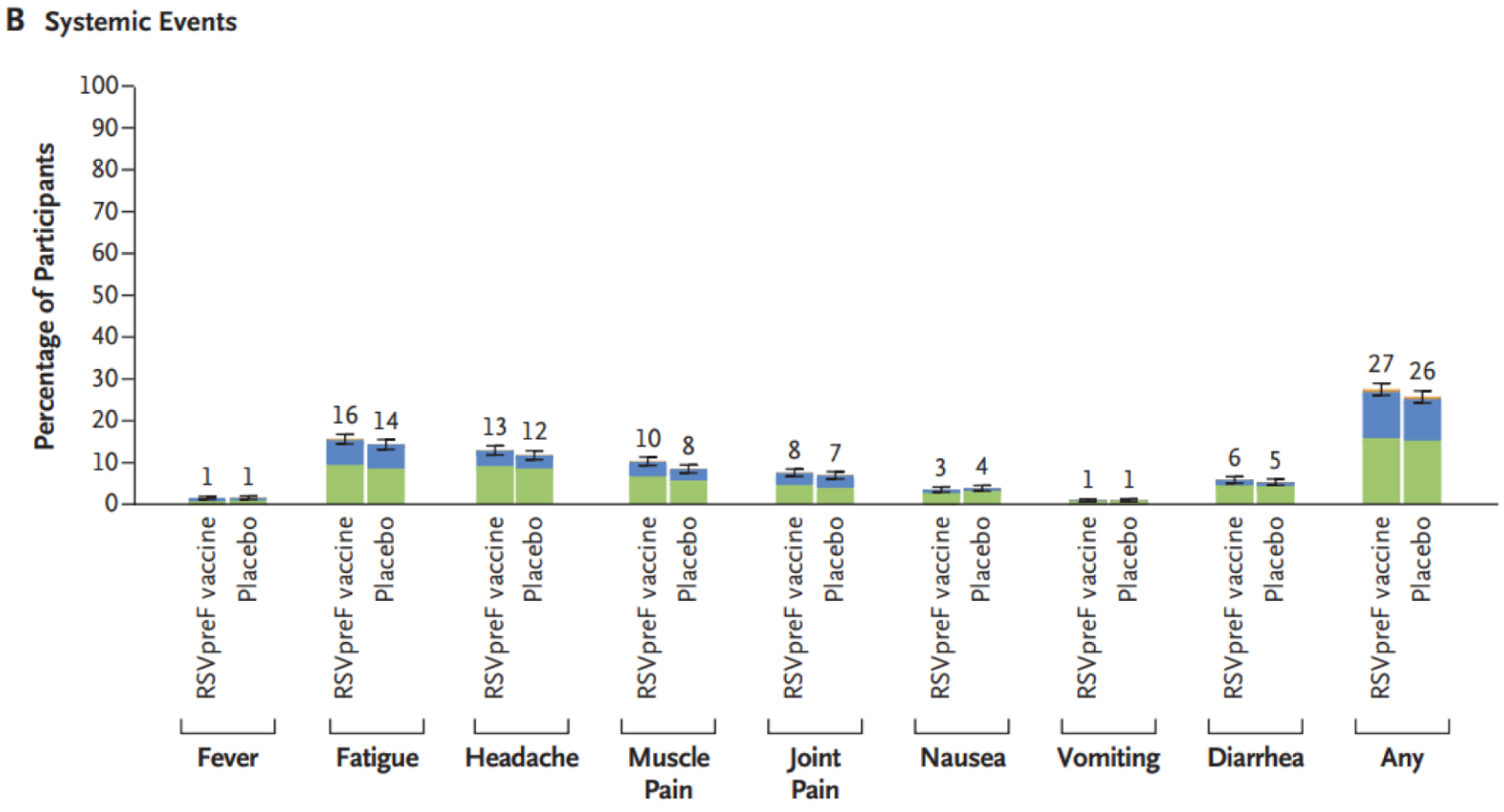
Vaccine Efficacy (95% CI)

percent

62.1 (37.1–77.9)

Walsh EE et al. N Engl J Med 2023; 388:1465.

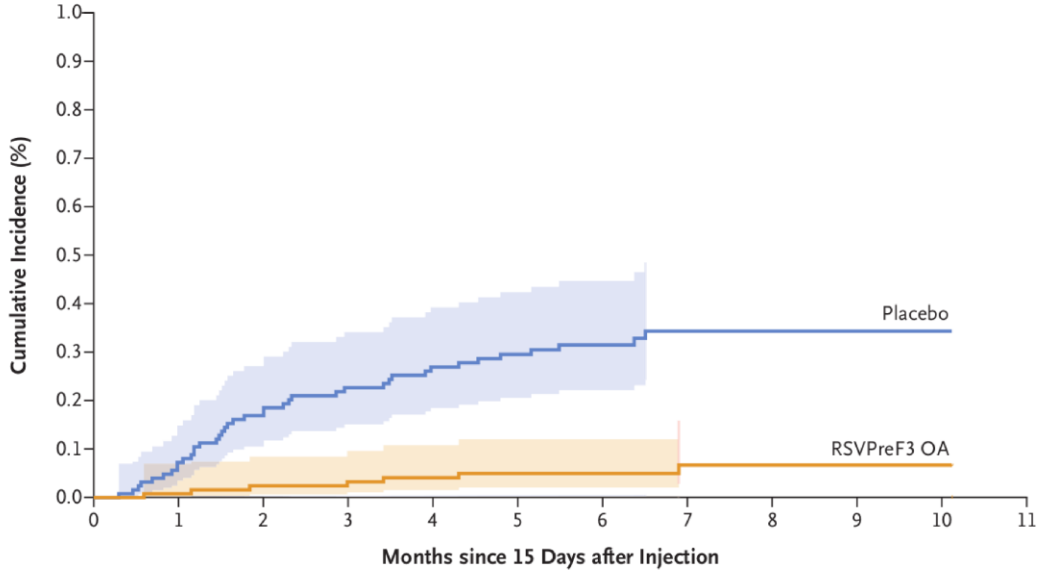
Sicurezza del vaccino RSVPreF



Walsh EE et al. N Engl J Med 2023; 388:1465.

Efficacia del vaccino RSVPreF3 OA

A **RSV-Related Lower Respiratory Tract Disease**

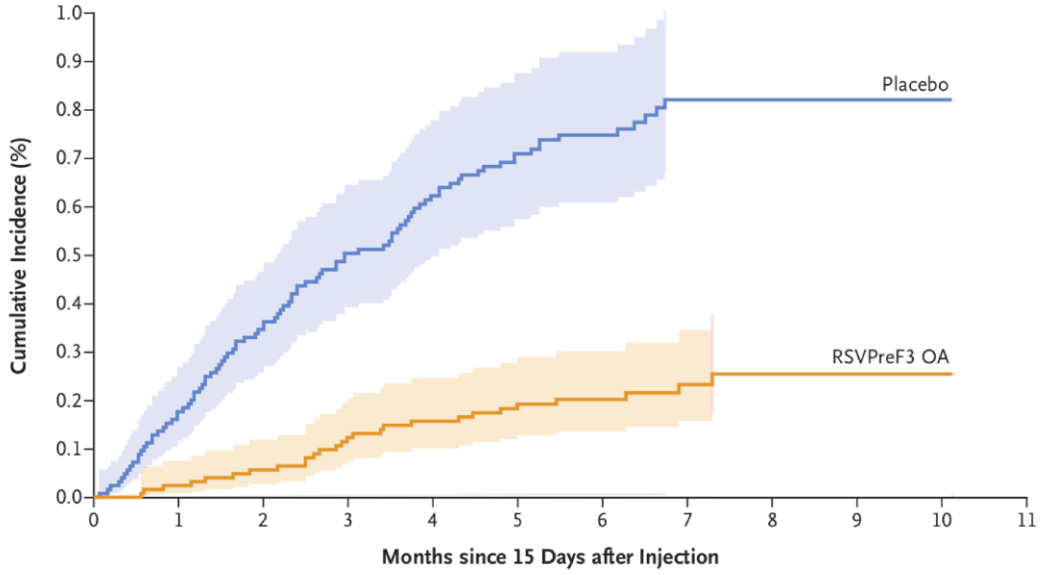


No. at Risk												
Placebo	12,494	12,403	12,290	11,887	11,640	11,022	8291	5464	2709	559	2	0
RSVPreF3 OA	12,466	12,392	12,286	11,892	11,655	11,046	8320	5495	2727	571	2	0
Cumulative No. of Cases												
Placebo	0	9	21	28	33	36	38	40	40	40	40	40
RSVPreF3 OA	0	1	3	4	5	6	6	7	7	7	7	7

Papi A et al. N Engl J Med 2023; 388:595.

Efficacia del vaccino RSVPreF3 OA

B RSV-Related Acute Respiratory Infection

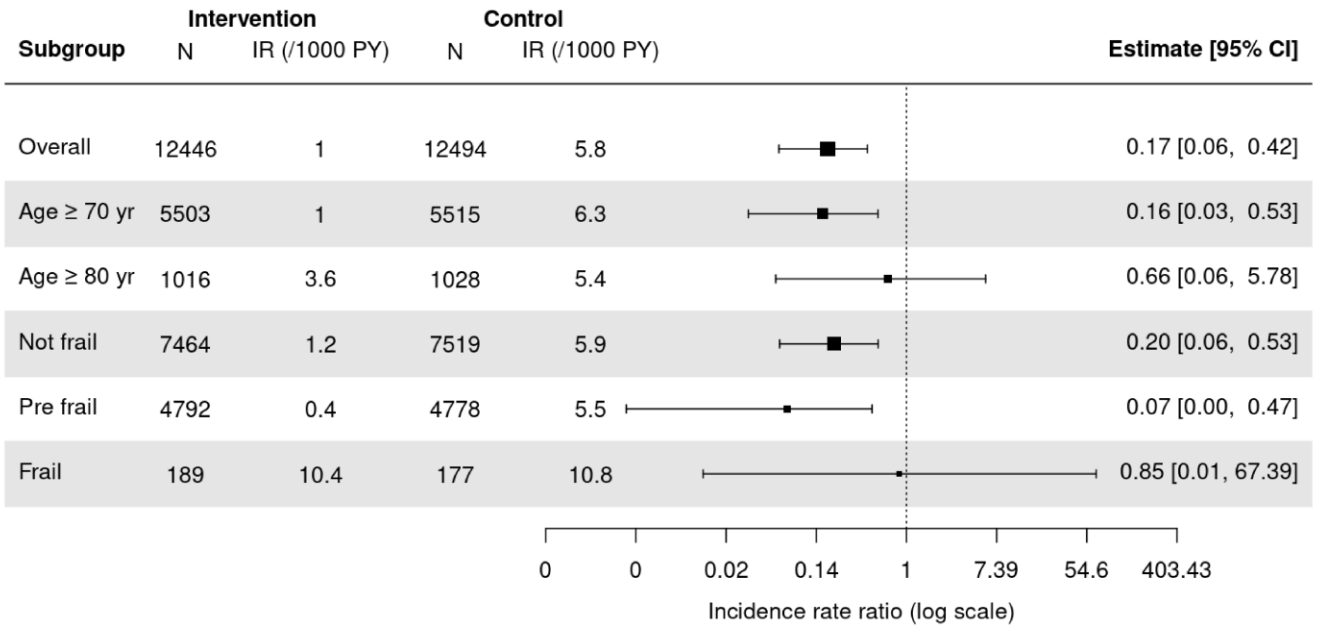


No. at Risk												
Placebo	12,494	12,390	12,268	11,853	11,597	10,973	8255	5441	2697	554	2	0
RSVPreF3 OA	12,466	12,390	12,282	11,881	11,641	11,029	8305	5481	2717	570	2	0

Cumulative No. of Cases												
Placebo	0	22	43	62	76	86	90	95	95	95	95	95
RSVPreF3 OA	0	3	7	15	19	23	24	26	27	27	27	27

Papi A et al. N Engl J Med 2023; 388:595.

RSVPreF3 OA - Subgroup analysis



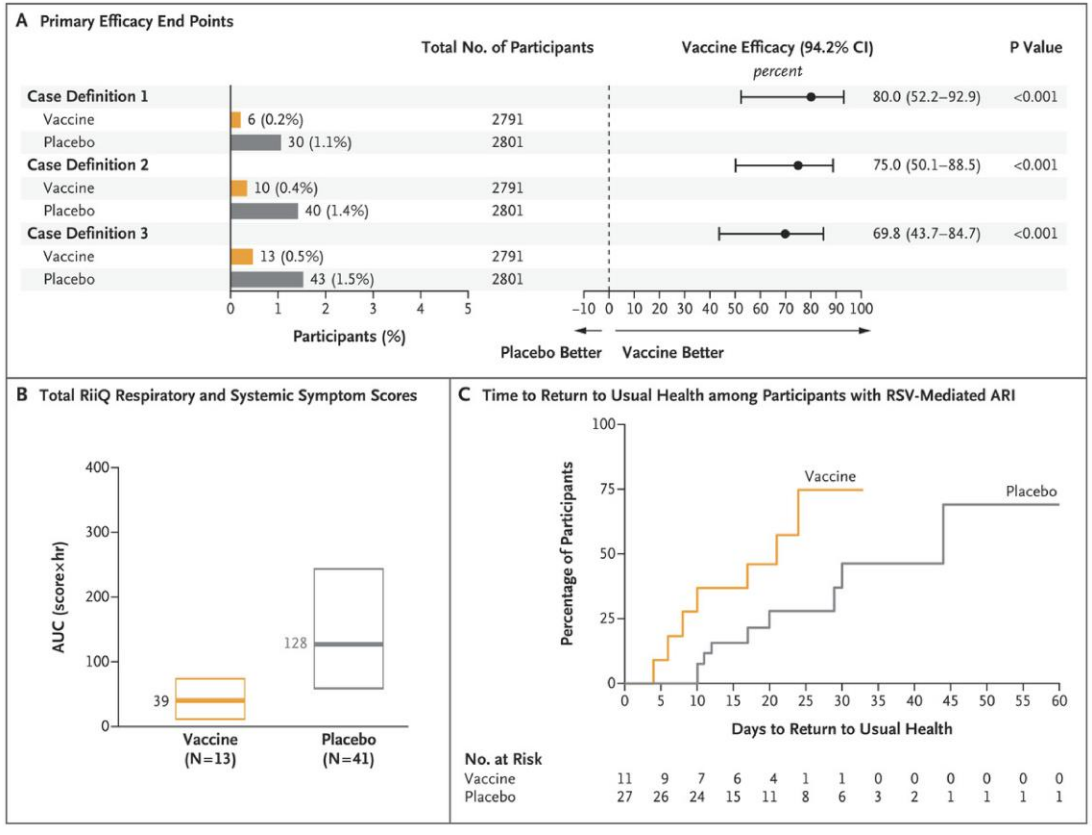
Elaborazione da Papi A et al., N Engl J Med 2023; 388:595.

Sicurezza del vaccino RSVPreF3 OA

Event	RSVPreF3 OA Group		Placebo Group	
	Participants	Incidence (95% CI)	Participants	Incidence (95% CI)
	no.	%	*no.*	%
Solicited safety population	879		878	
Solicited reactions				
Any solicited reaction	632	71.9 (68.8–74.9)	245	27.9 (25.0–31.0)
Any grade 3 solicited reaction	36	4.1 (2.9–5.6)	8	0.9 (0.4–1.8)
Solicited injection-site reactions				
Pain	535	60.9 (57.5–64.1)	81†	9.3 (7.4–11.4)
Erythema	66	7.5 (5.9–9.5)	7†	0.8 (0.3–1.6)
Swelling	48	5.5 (4.1–7.2)	5†	0.6 (0.2–1.3)
Solicited systemic reactions				
Fever‡	18	2.0 (1.2–3.2)	3	0.3 (0.1–1.0)
Headache	239	27.2 (24.3–30.3)	111	12.6 (10.5–15.0)
Fatigue	295	33.6 (30.4–36.8)	141	16.1 (13.7–18.7)
Myalgia	254	28.9 (25.9–32.0)	72	8.2 (6.5–10.2)
Arthralgia	159	18.1 (15.6–20.8)	56	6.4 (4.9–8.2)
Unsolicited adverse events				
Any unsolicited adverse event	131	14.9 (12.6–17.4)	128	14.6 (12.3–17.1)
Grade 3 unsolicited adverse event	12	1.4 (0.7–2.4)	12	1.4 (0.7–2.4)

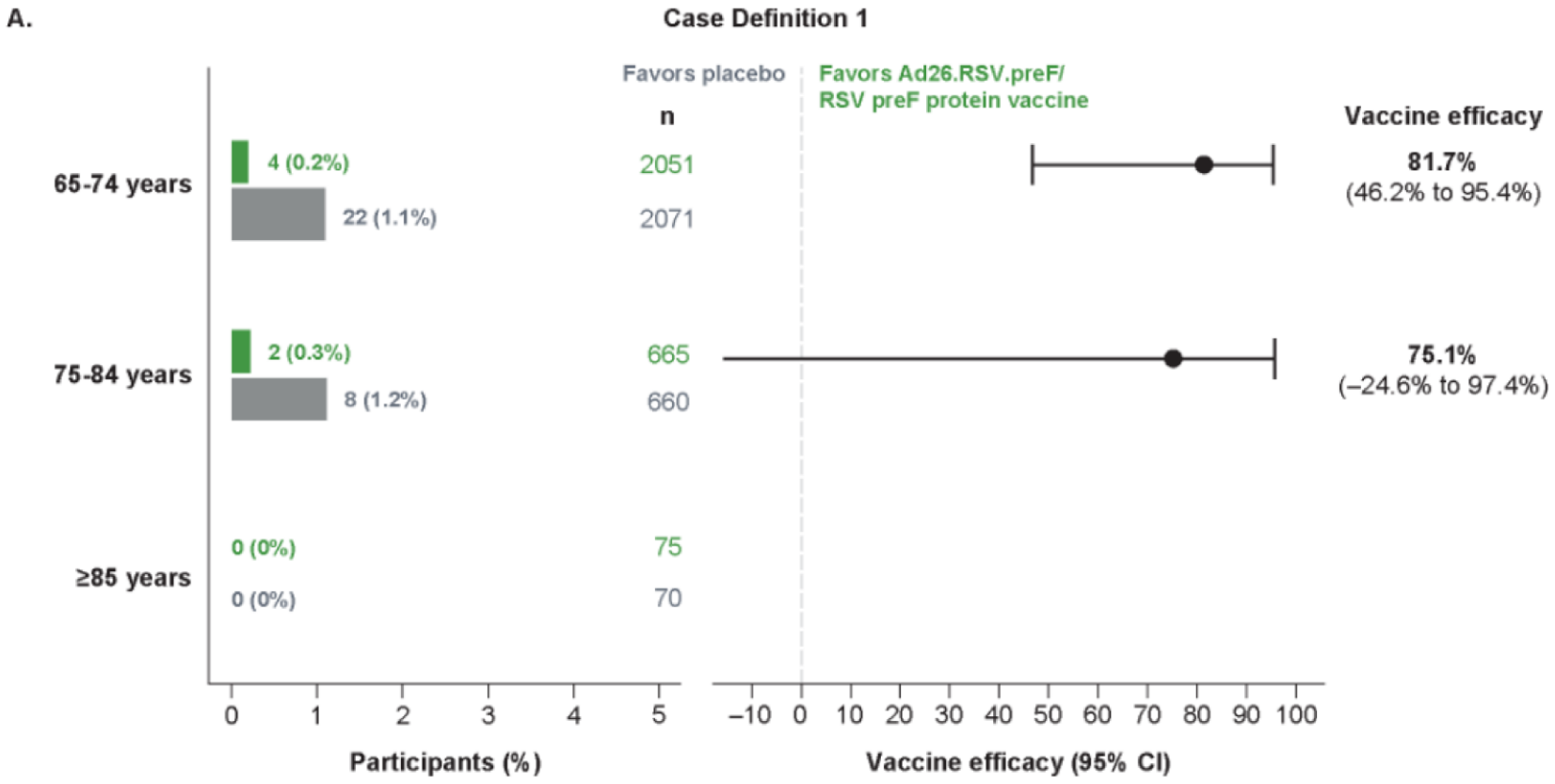
Papi A et al., N Engl J Med 2023; 388:595.

Efficacia del vaccino Ad26.RSV.preF



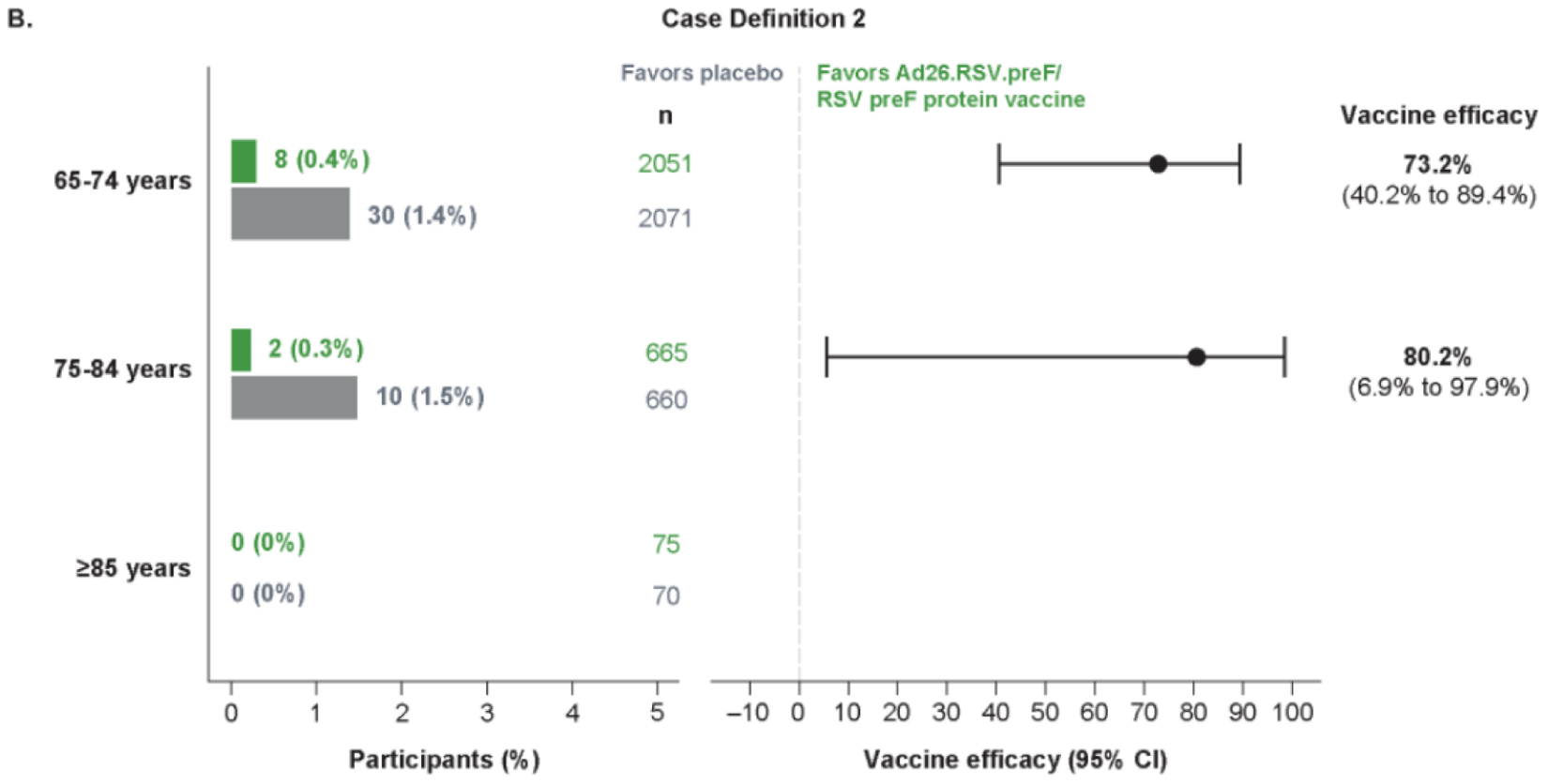
Falsey AR et al. N Engl J Med 2023; 388:609.

Ad26.RSV.preF - subgroup analysis



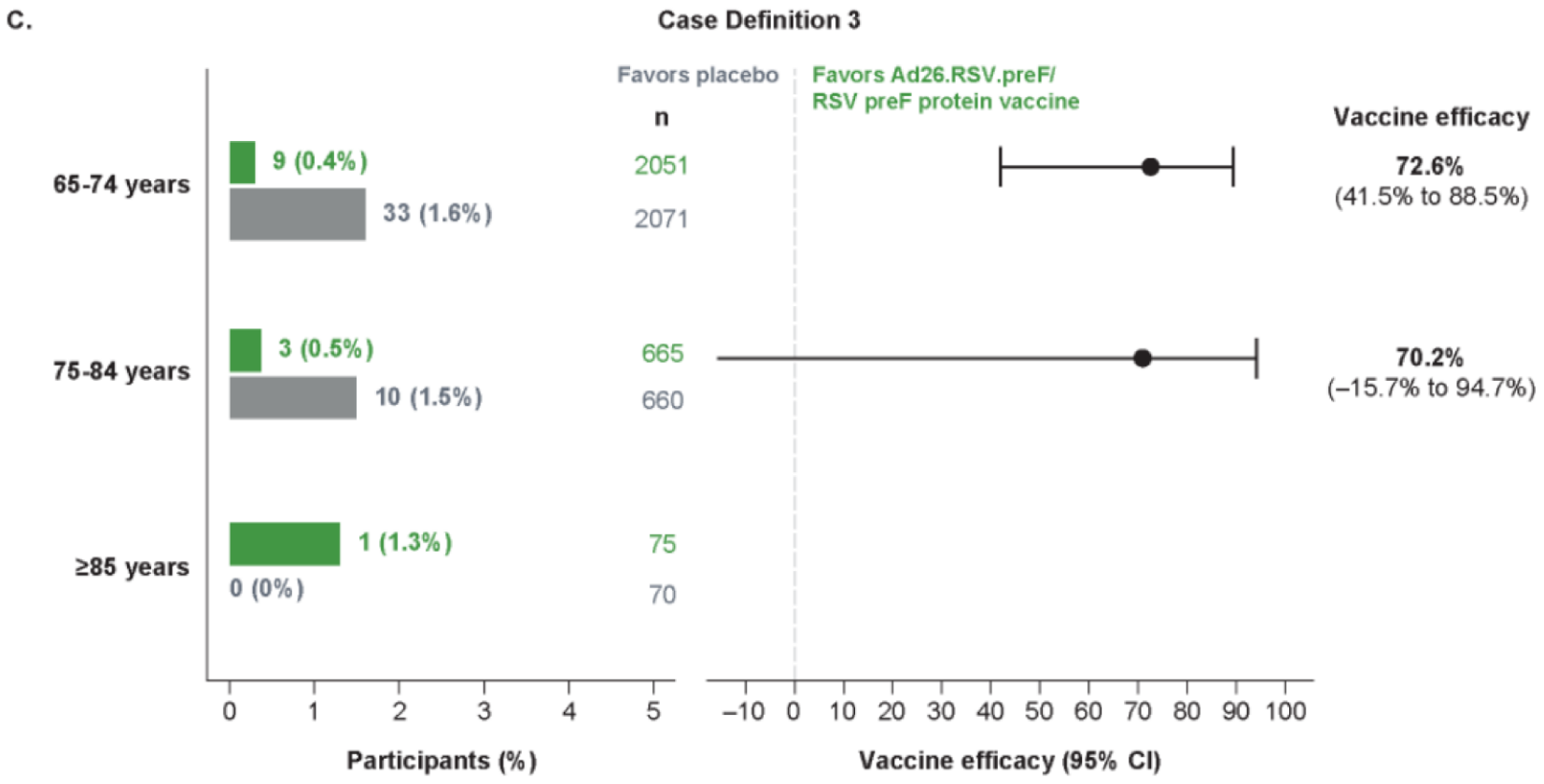
Falsey AR et al. N Engl J Med 2023; 388:609.

Ad26.RSV.preF - subgroup analysis



Falsey AR et al. N Engl J Med 2023; 388:609.

Ad26.RSV.preF - subgroup analysis



Falsey AR et al. N Engl J Med 2023; 388:609.

Sicurezza del vaccino Ad26.RSV.preF

Adverse Event	Vaccine	Placebo
	no. of participants with event/total no. (%)	
Solicited adverse events (safety subpopulation, within 7 days after injection)		
Any event	179/348 (51.4)	70/347 (20.2)
Event of grade ≥3	11/348 (3.2)	2/347 (0.6)
Local event†	132/348 (37.9)	29/347 (8.4)
Local event of grade ≥3†	6/348 (1.7)	1/347 (0.3)
Systemic event‡	144/348 (41.4)	57/347 (16.4)
Systemic event of grade ≥3‡	7/348 (2.0)	1/347 (0.3)
Unsolicited adverse events (safety subpopulation, within 28 days after injection)		
Any event	58/348 (16.7)	50/347 (14.4)
Event of grade ≥3	6/348 (1.7)	5/347 (1.4)
Event thought to be related to vaccine or placebo	18/348 (5.2)	8/347 (2.3)
Serious adverse events and adverse events leading to discontinuation of participation in trial (primary safety population)		
Serious adverse event	132/2891 (4.6)	136/2891 (4.7)
Serious adverse event thought to be related to vaccine or placebo	0	0
Adverse event with fatal outcome	8/2891 (0.3)	12/2891 (0.4)
Adverse event with fatal outcome thought to be related to vaccine or placebo	0	0
Adverse event leading to permanent discontinuation of participation in trial	10/2891 (0.3)	15/2891 (0.5)

Falsey AR et al. N Engl J Med 2023; 388:609.

Conclusioni

- La vaccinazione RSV è efficace nel prevenire le infezioni delle basse vie respiratorie nei soggetti con età ≥ 60 anni;
- Non ci sono dati conclusivi sull'efficacia del vaccino nella popolazione più anziana (eta ≥ 75 anni);
- Non ci sono segnali che indichino problemi di sicurezza del vaccino;
- In considerazione dell'efficacia e dei potenziali rischi legati all'infezione da RSV, il vaccino andrebbe raccomandato ai soggetti almeno fino ai 75 anni di età, soprattutto in presenza di fattori di rischio per grave infezione respiratoria.