Pandemia e vaccinazioni nei pazienti fragili

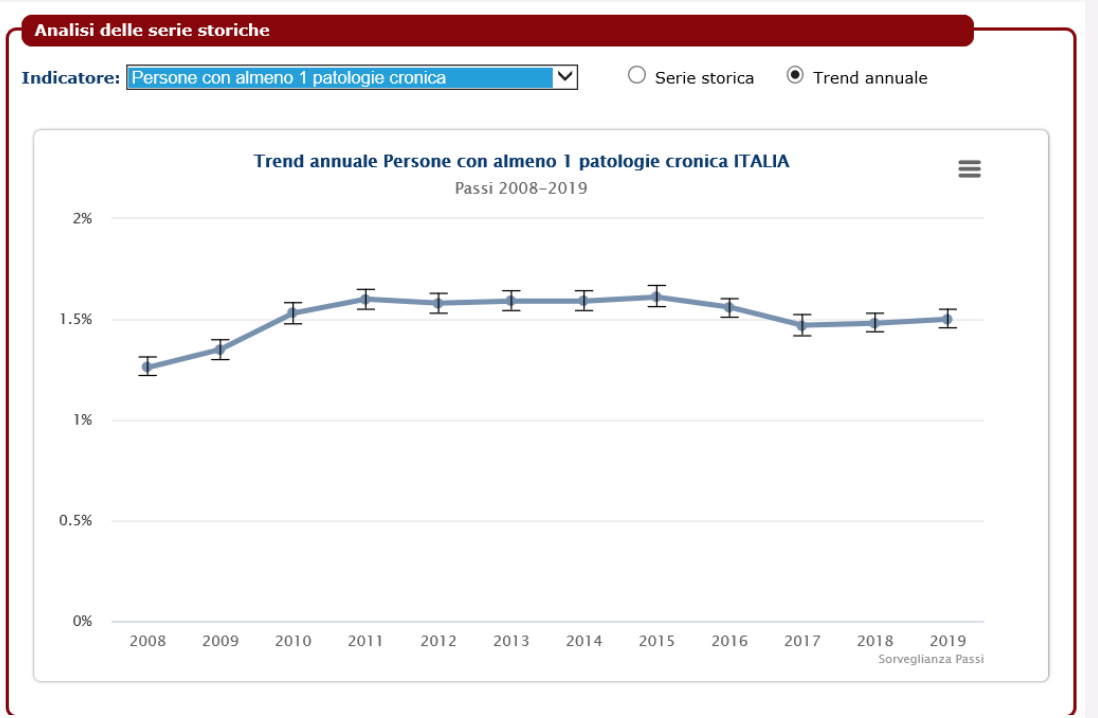
Massimo Galli

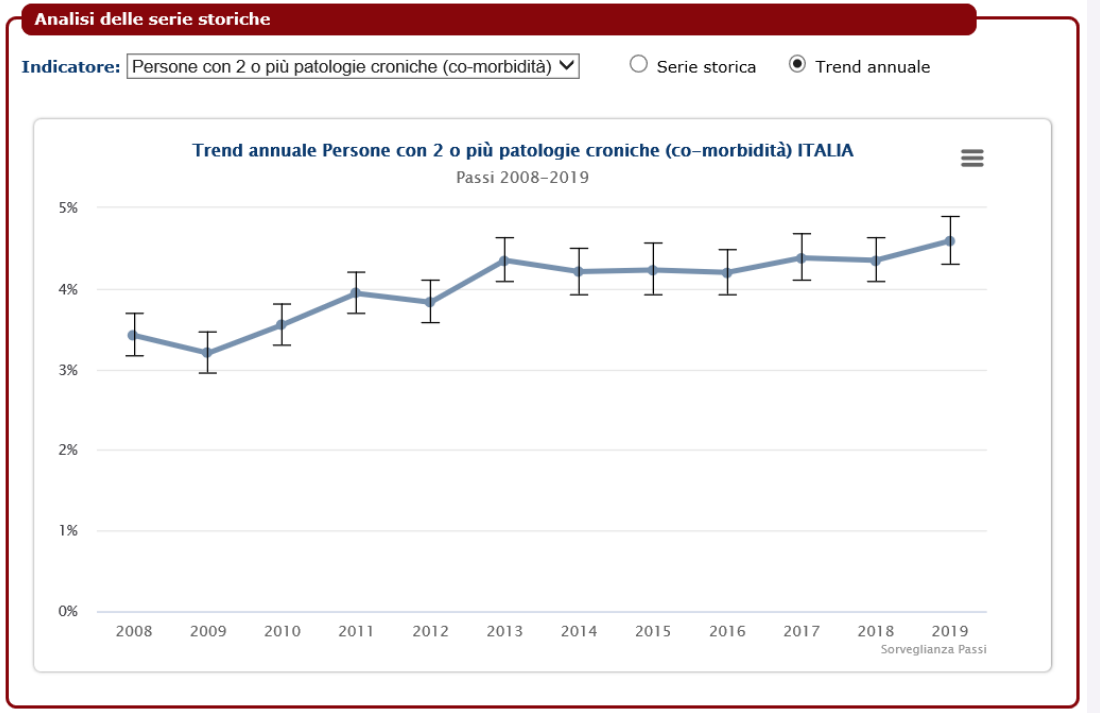
La cronicità in Italia

		Persone in buona salute	Persone con almeno 1 patologia cronica	Persone con almeno 2 patologie croniche
periodo	Classi di età			
2019	0-14 years	95,9	8,9	1,7
	15-17 years	91,6	16	3,2
	18-19 years	89,7	16,5	3,3
	20-24 years	89	20,4	4,3
	25-34 years	87,3	21,2	4,8
	35-44 years	78,6	24,1	7,5
	45-54 years	68,8	38,7	14
	55-59 years	60,3	54,1	25
	60-64 years	54,9	63	33,8
	65-74 years	43,7	74,7	48
	75 years and over	27,5	85,4	64,4

Fonte: Dati ISTAT 2019

Fonte: https://www.epicentro.iss.it/passi/dati/croniche





Perché vaccinare contro l'influenza gli anziani e i portatori di comorbosità

- Riduzione della letalità del 65% nei pazienti con ictus, del 55% nei diabetici, del 45% nei pazienti con malattie CV[1]
- Riduzione del 60% le riacutizzazioni di BPCO[2]
- Riduzione delle ospedalizzazioni>76,8%[3]

[1] *Wang CS, et al. Vaccine 2007; 25:1196-1203*
[2] *Varkey JB, Varkey AB, Varkey B. Curr Opin Pulm Med 2009: 90-9*
[3] *Talbot HK, et al. Clin Infect Dis 2013;56:1774-77*

Le possibili conseguenze a breve e lungo termine dell'influenza

8x

Aumento del rischio di **ictus**

*Aumento **del 73%** rischio di **Parkinson** >10 anni dopo*

Neurologiche

15%

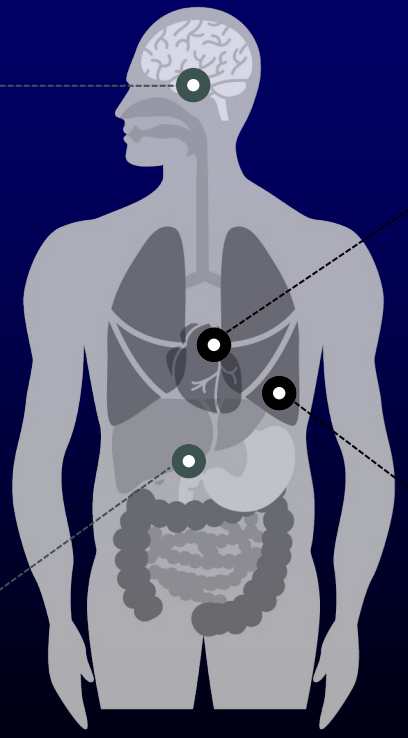
Va incontro a **perdita dell'autonomia**

Perdita di autonomia

75%

Aumentati episodi di iper/ipo-**glicemia**

Complicanze diabete



Cardiovascolari

10x

Aumento del rischio di IMA

Basse vie respiratorie

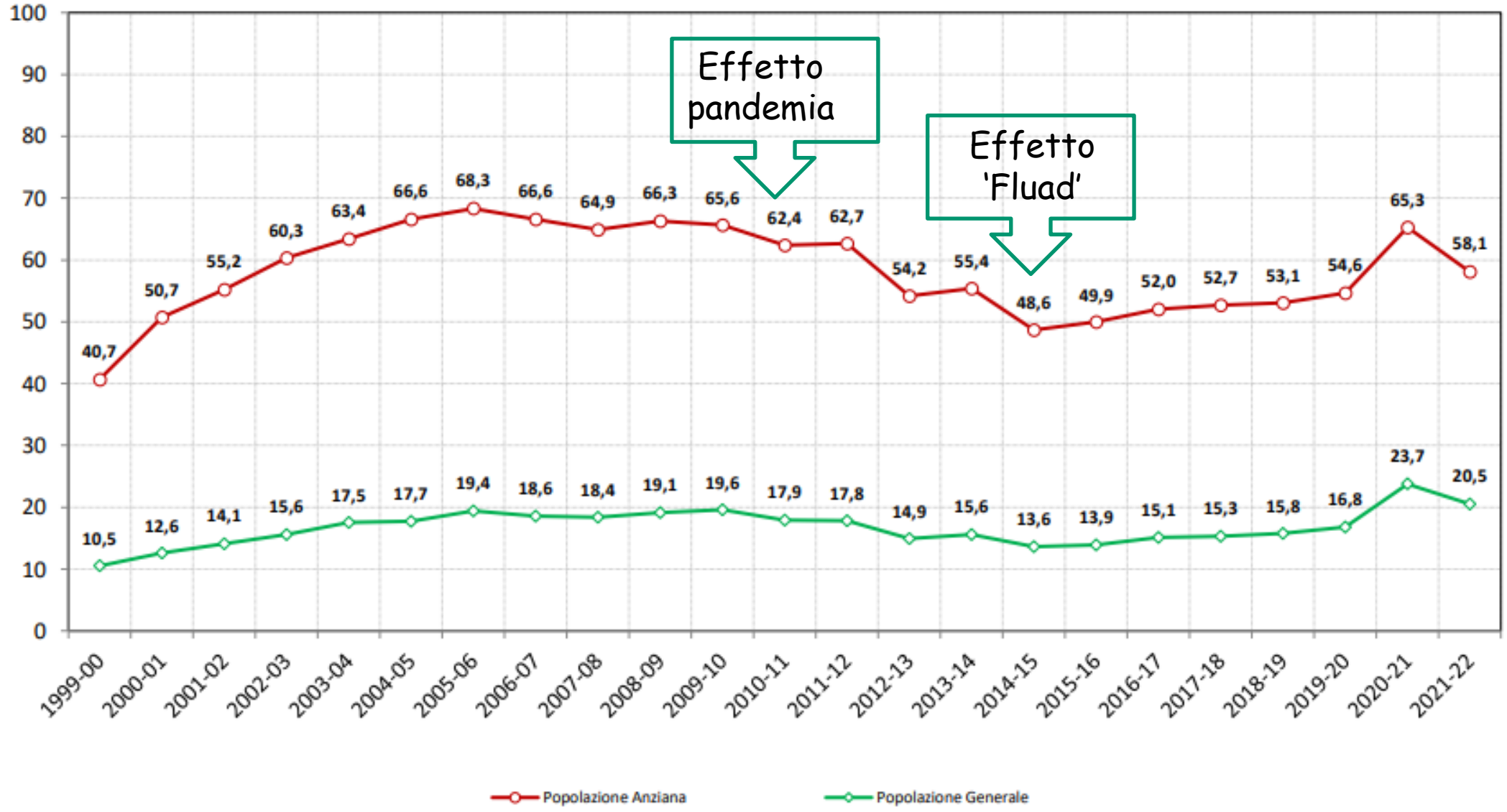
8x

Aumento del rischio di **polmonite**

Warren-Gash, Eur respir J, 2018; Barker, Arch.Intern.Med 1998;
Samson, J Diabetes Sci Technol. 2021; Kubale, Clin Inf Dis. 2020; Cocoros, JAMA Neurology, 2021

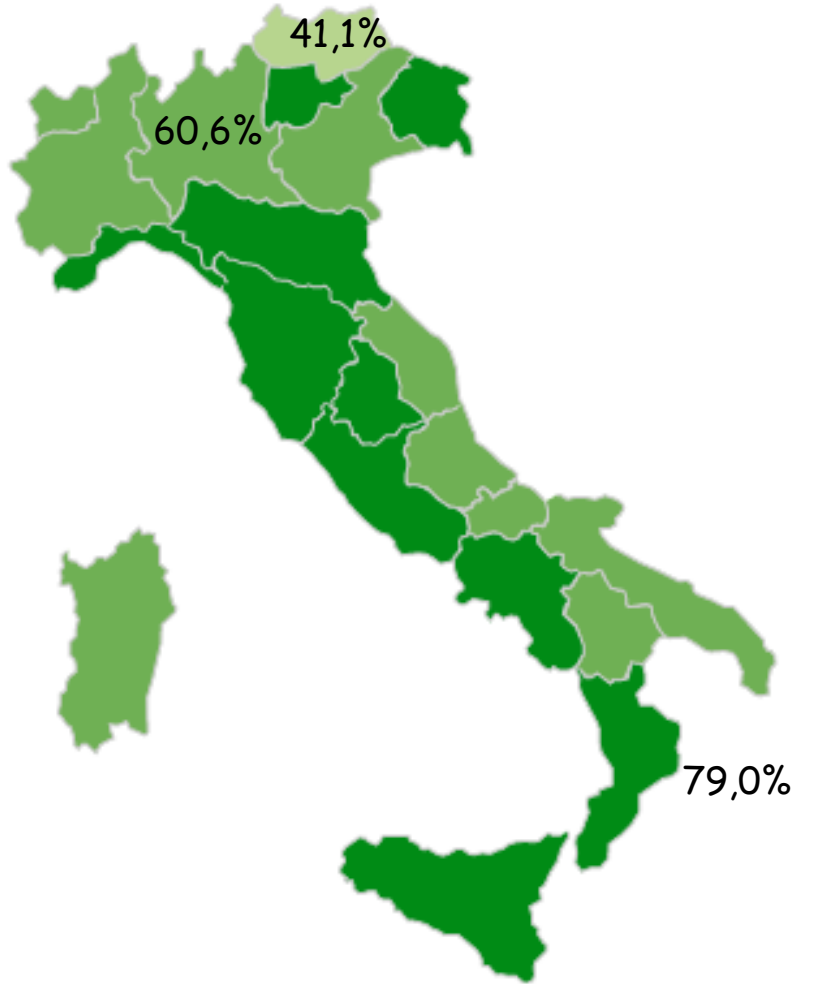
8000 decessi per influenza e le sue complicanze ogni anno in Italia

Vaccinazione antinfluenzale nella popolazione italiana
Stagioni: 1999/00 - 2021/22



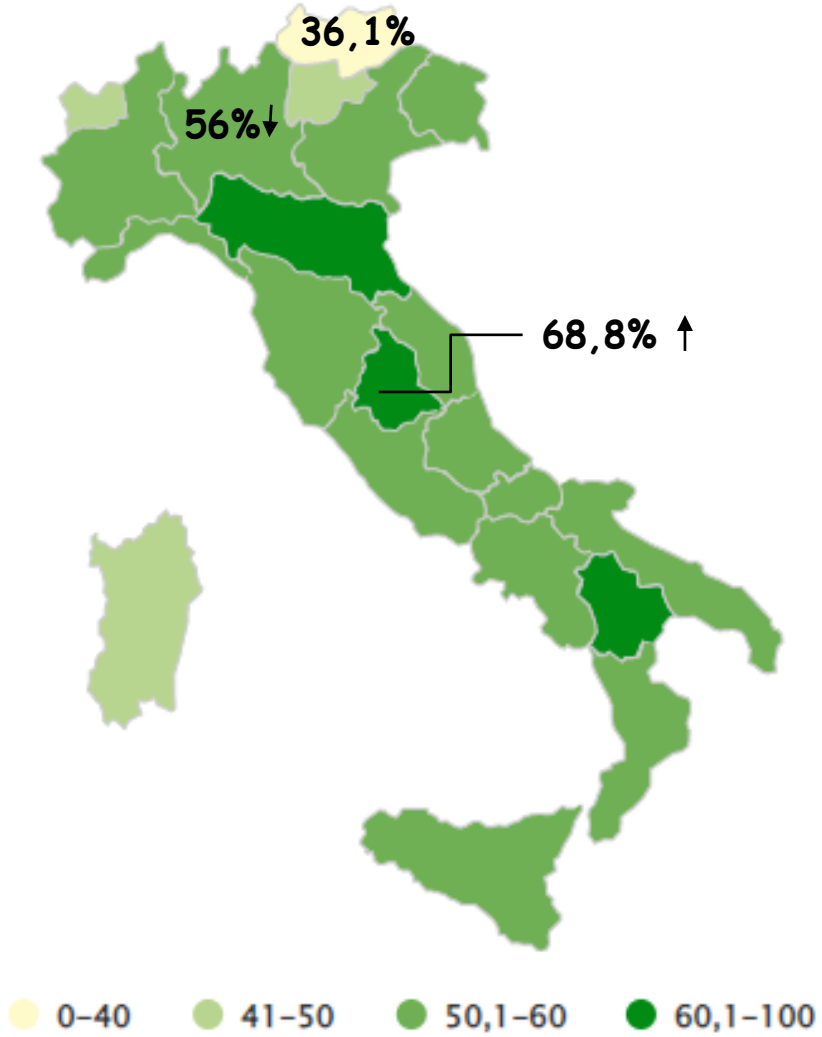
Copertura vaccino Antinfluenzale negli anziani (età >= 65 anni)

dato nazionale 65,3 (per 100 abitanti - 2020-2021)



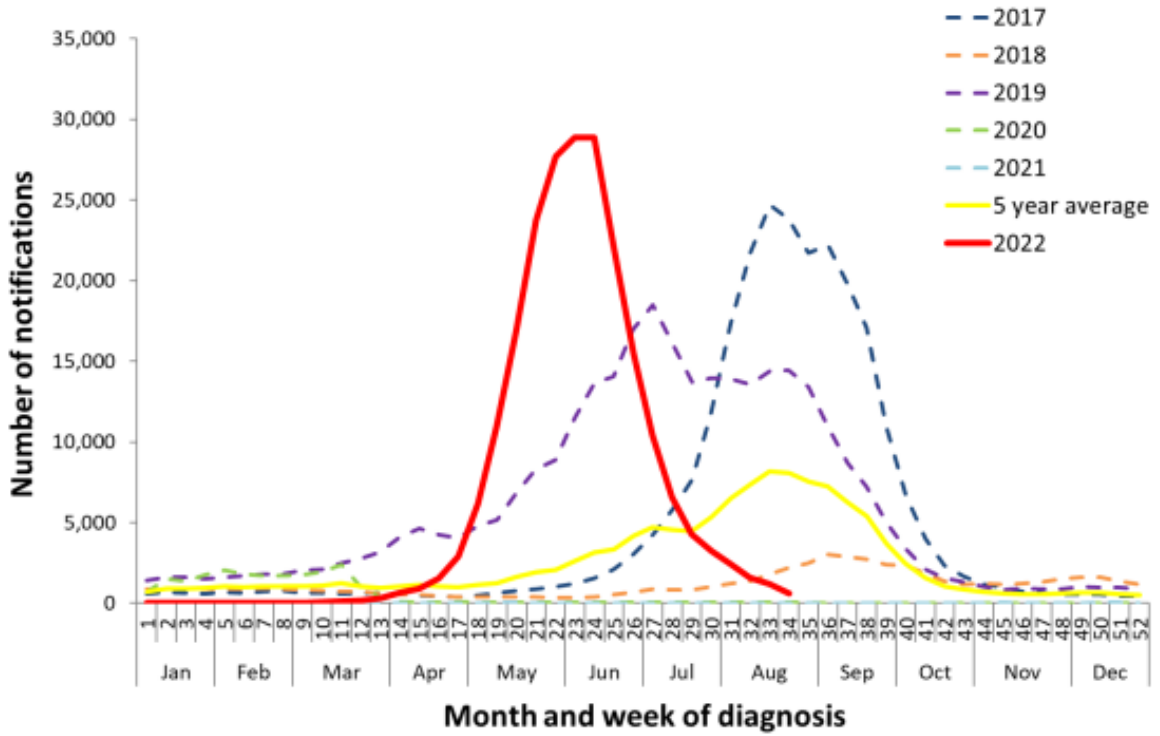
Copertura vaccino Antinfluenzale negli anziani (età >= 65 anni)

dato nazionale 58,1 (per 100 abitanti - 2021-2022)



Cosa ci aspettiamo dalla prossima stagione influenzale? Notizie dall'Australia

Aumento del numero di casi Australia – Agosto 2022



Source: NNDSS

*NNDSS notification data provided for the current and most recent weeks may be incomplete. All data are preliminary and subject to change as updates are received, with most recent weeks considered particularly subject to revisions. Please refer to Data considerations for interpretation of the 5 year average.

- **Importante aumento di ILI già da marzo**, con superamento della media degli ultimi 5 anni già da aprile e picco della curva epidemica anticipato rispetto alle precedenti stagioni
- Registrati 204911 casi confermati in laboratorio, prevalentemente di influenza A (82.7%)
- **Livelli di copertura vaccinale** ben al di sotto dell'obiettivo
- Scarsa circolazione del virus influenzale nelle ultime due stagioni: riduzione di immunità della popolazione con rischio di insorgenza di focolai rilevanti

AUSTRALIAN INFLUENZA SURVEILLANCE REPORT No. 11, 2022 Reporting fortnight: 15-28 aug 2022
Circolare Ministeriale Prevenzione e controllo dell'influenza:raccomandazioni per la stagione 2022-2023

Vaccini influenzali stagione 2022-23

- A/Victoria/2570/2019 (H1N1)pdm09-like
- **A/Darwin/6/2021 (H3N2)-like**
- B/Washington/02/2019-like (ligniaggio B/Victoria)
- [B/Phuket/3073/2013-like (ligniaggio B/Yamagata)]

Circolare ministeriale 2022/2023: vaccini disponibili per la popolazione anziana

Prevenzione e controllo dell'influenza: raccomandazioni per la stagione 2022-2023

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

The NEW ENGLAND JOURNAL of MEDICINE
2014;371:635-45

ORIGINAL ARTICLE

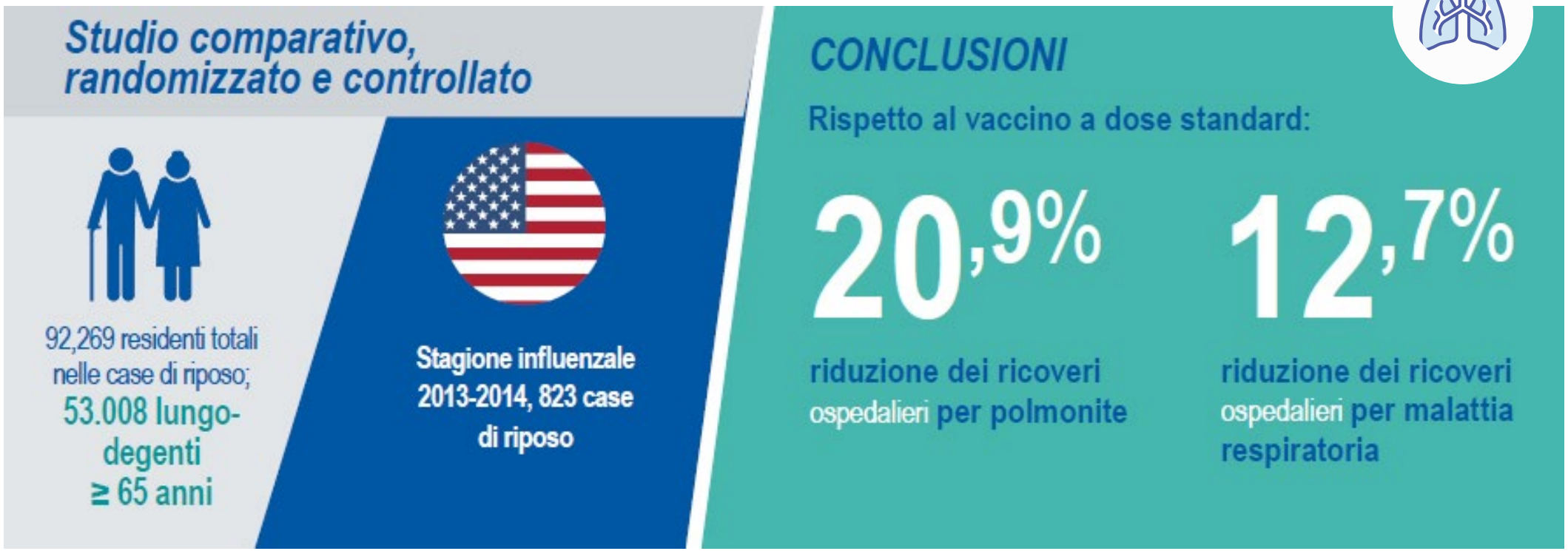
Efficacy of High-Dose versus Standard-Dose

- A total of 31,989 participants were enrolled from 126 research centers in the US and Canada (15,991 were randomly assigned to receive IIV3-HD, and 15,998 to receive IIV3-SD).
- In the intention-to-treat analysis, 228 participants in the IIV3-HD group (1.4%) and 301 participants in the IIV3-SD group (1.9%) had laboratory-confirmed influenza (relative efficacy, 24.2%; 95% CI, 9.7 to 36.5).
- At least one serious adverse event during the safety surveillance period was reported by 1323 (8.3%) of the participants in the IIV3-HD group, as compared with 1442 (9.0%) of the participants in the IIV3-SD group (relative risk, 0.92; 95% CI, 0.85 to 0.99).
- After vaccination,the percentage of participants with HAI titers ≥1:40 were significantly higher in the IIV3-HD group

Comparative effectiveness of high-dose versus standard-dose influenza vaccination on numbers of US nursing home residents admitted to hospital: a cluster-randomised trial

Stefan Gravenstein, H Edward Davidson, Monica Taljaard, Jessica Ogarek, Pedro Gozalo, Lisa Han, Vincent Mor

OBIETTIVO: Stimare riduzione delle ospedalizzazioni per cause respiratorie e polmonite nei soggetti vaccinati con vaccino ad alto dosaggio in confronto a vaccinati con dose standard



Reference: Gravenstein S, et al. Lancet Respir Med. 2017;5(9):738-746.

The Journal of Infectious Diseases 2019;219:1525–35

REVIEW ARTICLE

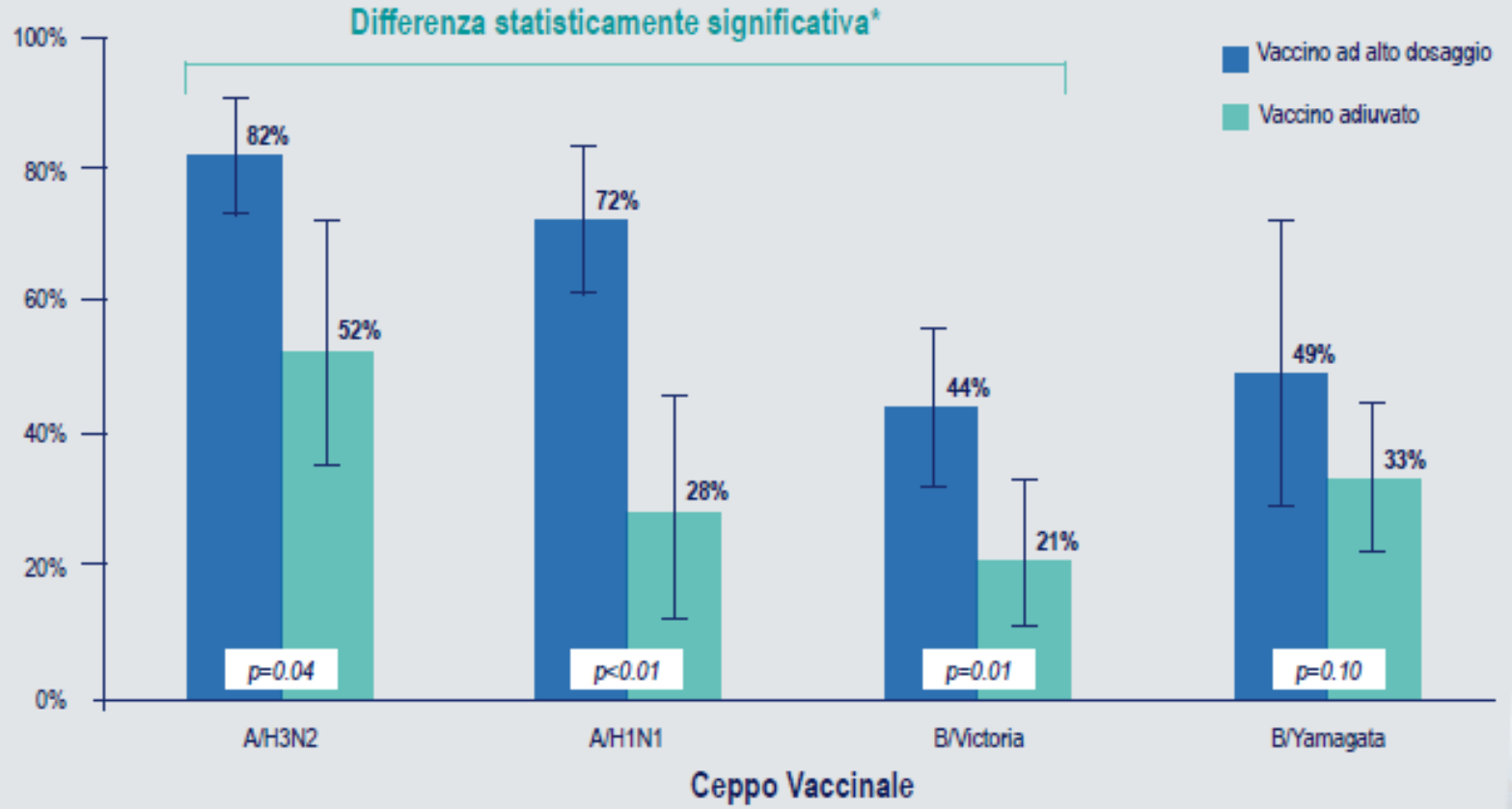
IDSA Infectious Diseases Society of America
hivma hiv medicine association
OXFORD

Incremento dei titoli anticorpali post-vaccinazione rispetto al vaccino a dose standard†

review sistematica di

39 RCT

condotti su adulti di età ≥60 anni



†media geometrica dei titoli anticorpali 30 giorni dopo la vaccinazione a confront con la baseline (prima della vaccinazione).

Incidenza di malattia invasiva da pneumococco in Italia per età e anno

- È importante offrire attivamente la vaccinazione con vaccino pneumococcico coniugato seguita da una dose di vaccino polisaccaridico (PCV+PPSV).
- Bisogna porre attenzione a non invertire l'ordine di somministrazione dei due vaccini, perché ciò comporterebbe una più bassa risposta immune
- La vaccinazione pneumococcica può essere offerta simultaneamente alla vaccinazione antiinfluenzale, ma può pure essere somministrata indipendentemente e in qualsiasi stagione dell'anno e, secondo le attuali indicazioni, una sola volta nella vita.

Piano Nazionale Vaccinale: Obiettivi di copertura dal 2017 al 2020

		Obiettivo di Copertura Vaccinale			
Fascia d'età	Vaccinazioni	2017	2018	2019	2020
I anno di vita	Meningococco B	≥ 60%	≥ 75%	≥ 95%	≥ 95%
	Rotavirus	-	≥ 60%	≥ 75%	≥ 95%
II anno di vita	Varicella (1° dose)	≥ 60%	≥ 75%	≥ 95%	≥ 95%
5-6 anni di età	Varicella (2° dose)	-	-	-	-
Adolescenti	HPV nei maschi 11enni	-	≥ 60%	≥ 75%	≥ 95%
	IPV	-	≥ 60%	≥ 75%	≥ 90%
	Meningococco tetravalente ACWY135	≥ 60%	≥ 75%	≥ 95%	≥ 95%
Anziani	Pneumococco (PCV13+PPV23)	40%	55%	75%	75%
	Zoster	-	20%	35%	50%

Shingles vaccines

	Zostavax (SPS)	(GSK clinical trial III)
Vaccine type	Live, attenuated VZV Oka strain	Nonlive, recombinant subunit glycoprotein E + adjuvant AS01
Recommendations	⩾60 years immunocompetent adults	⩾50 years immunocompetent adults
Administration	1 subcutaneous injection	2 intramuscular injections (2 months apart)
Vaccine efficacy for HZ incidence (95% CI)	**Overall:** 51.3%* (44.2–57.6) **50–59 years:** 69.8% (54.1–80.6) **60–69 years:** 63.9% (55.5–70.9) ⩾**70 years:** 37.6% (25.0–48.1)	**Overall:** 97.2%* (93.7–99.0) **50–59 years:** 96.6% (89.6–99.3) **60–69 years:** 97.4% (90.1–99.7) ⩾**70 years:** 97.9% (87.9–100.0)
Immunity duration	Age-dependent	Age-independent
FDA approval	Yes	Not yet

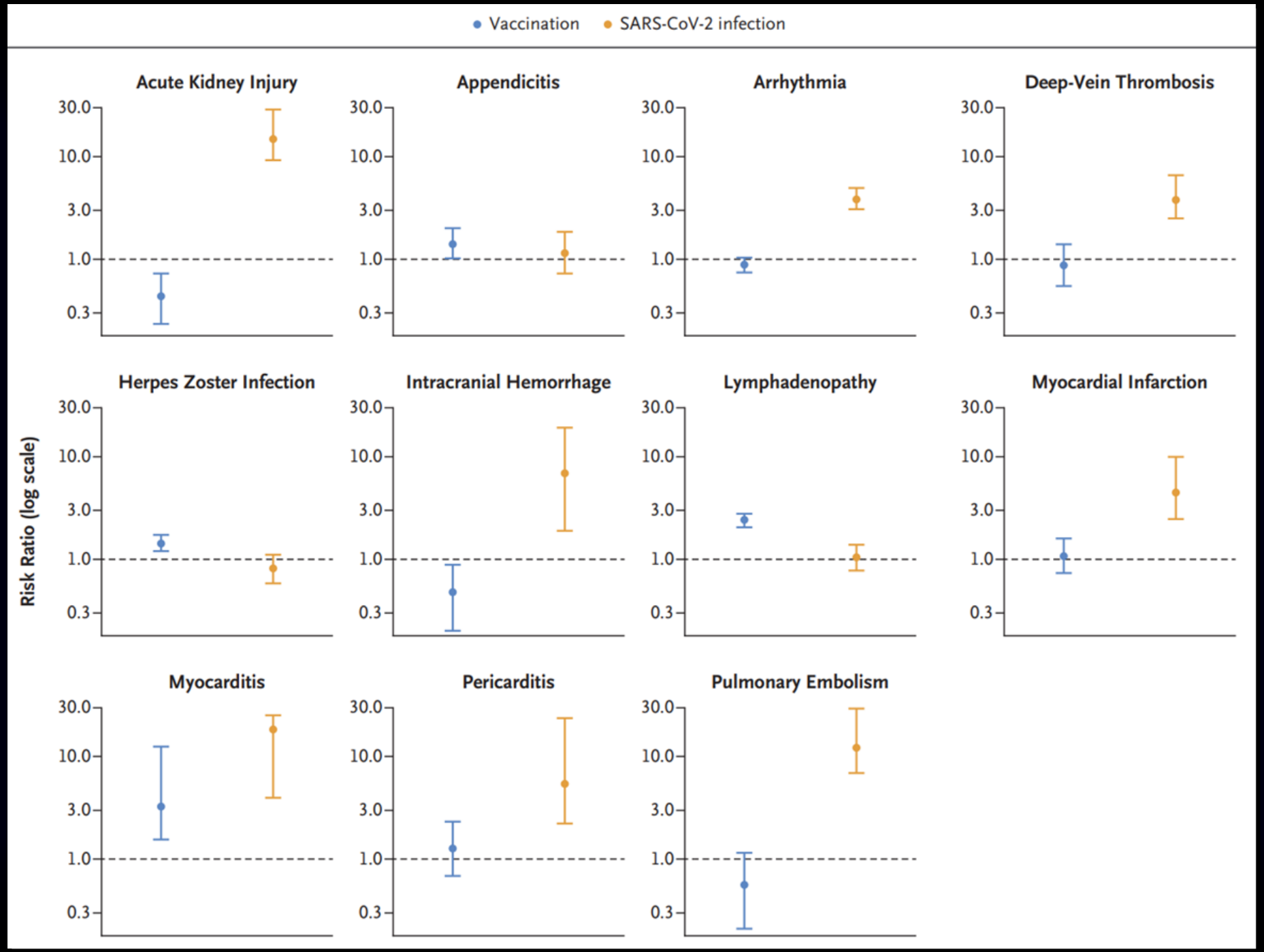
*Percentage reduction in vaccine, compared with placebo.
CI, confidence interval; FDA, US Food and Drug Administration; GSK, GlaxoSmithKline; HZ, herpes zoster; HZ/Su, HZ-adjuvanted subunit vaccines ZOSTER-006 and ZOSTER-022; SPS, Shingles Prevention Study; VZV, varicella-zoster virus.

Lili Wang, Ther Adv Vaccines 2016

Effectiveness of the recombinant zoster vaccine among Kaiser Permanente Hawaii enrollees aged 50 and older: A retrospective cohort study

- A total of 78 356 adults were included in this study, with 11 864 (15.1%) adults receiving two valid doses of the RZV.
- The incidence rate of HZ was 325.6 (95% CI: 217.7 to 464.4) cases per 100 000 person-years in vaccinated persons compared to 1063.3 cases per 100 000 person-years (95% CI: 1006.0 to 1122.8) in the unvaccinated group.
- The incidence rate of HZ ophthalmicus was 11.9 (95% CI: 0.7 to 52.3) cases per 100 000 person-years in the vaccinated group compared to 72.1 (95% CI: 58.0 to 88.3) in the unvaccinated group.
- RZV was **83.5%** (95% CI: 74.9% to 89.2%) effective against HZ and **93.3%** (95% CI: 48.7% to 99.1%) effective against HZO.

Sun et al. Vaccine 2021;39: 3974-3982


Vaccination
SARS-CoV-2 infection
Acute Kidney Injury
Appendicitis
Arrhythmia
Deep-Vein Thrombosis
Herpes Zoster Infection
Intracranial Hemorrhage
Lymphadenopathy
Myocardial Infarction
Myocarditis
Pericarditis
Pulmonary Embolism
Risk Ratio (log scale)
30.0
10.0
3.0
1.0
0.3

Pandemia: situazione a oggi

Cases | Deaths by Country/Region/Sovereignty

Germany
28-Day: 1.873.585 | 2.415
Totals: 34.517.327 | 151.260

US
28-Day: 1.307.161 | 11.558
Totals: 96.911.257 | 1.064.798

France
28-Day: 1.271.553 | 1.093
Totals: 36.319.858 | 156.777

Taiwan*
28-Day: 1.201.002 | 1.263
Totals: 7.050.750 | 11.686

Japan
28-Day: 1.184.727 | 2.417
Totals: 21.684.899 | 45.799

Russia
28-Day: 989.975 | 2.836
Totals: 20.960.802 | 380.757

Italy
28-Day: 875.778 | 1.321
Totals: 22.990.201 | 177.785

Korea, South
28-Day: 759.937 | 1.058
Totals: 25.076.239 | 28.783

Austria
28-Day: 303.522 | 234
Totals: 5.306.372 | 20.895

Engineering (CSSE) at Johns Hopkins University (JHU)

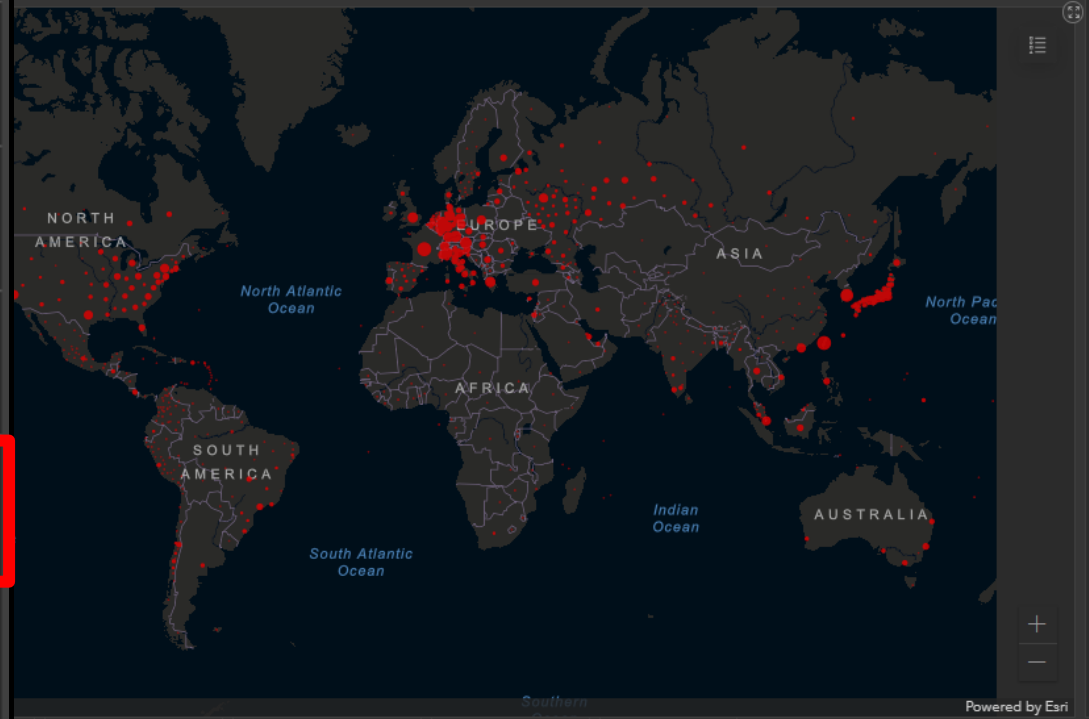
040

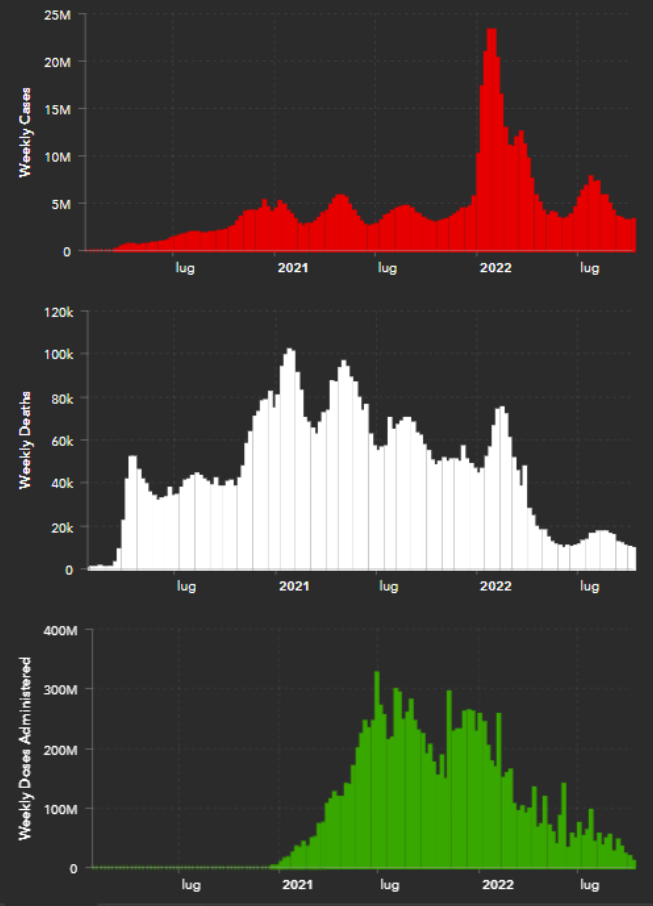
Total Deaths
6.564.921

Total Vaccine Doses Administered
9.089.833.851

28-Day Deaths
40.680

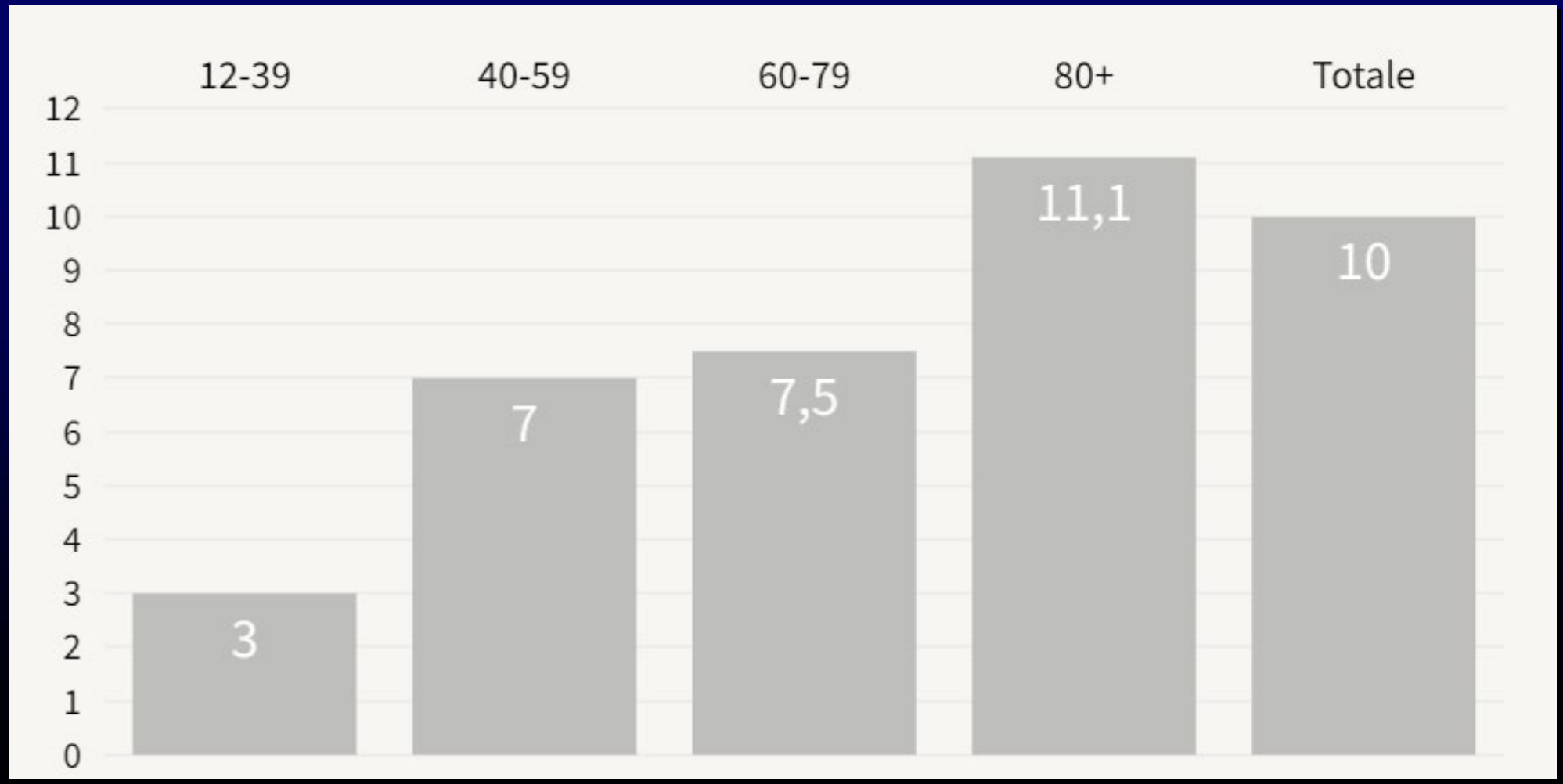
28-Day Vaccine Doses Administered
46.898.842





Case-Fatality Ratio | Global Vaccinations | US Vaccinations | Terms of Use | Weekly | 28-Day

Rischio di decesso nei non vaccinati rispetto ai vaccinati con tre dosi



Fonte: Report Iss pubblicato il 16 aprile 2022

The NEW ENGLAND JOURNAL of MEDICINE

This article was published on April 13,2022, at NEJM.org. DOI: 10.1056/NEJMoa2201688

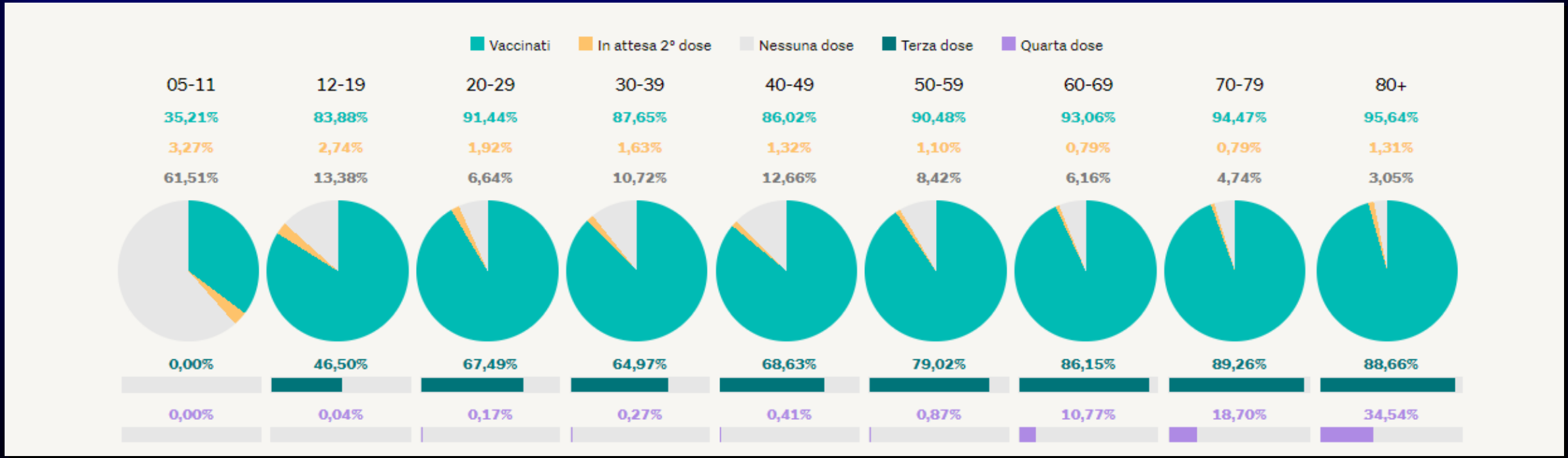
ORIGINAL ARTICLE

Fourth Dose of BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting

Ori Magen, M.D., Jacob G. Waxman, M.D., Maya Makov-Assif, M.D., Roni Vered, M.D., Dror Dicker, M.D., Miguel A. Hernán, M.D., Marc Lipsitch, D.Phil., Ben Y. Reis, Ph.D., Ran D. Balicer, M.D., and Noa Dagan, M.D.

182,122 matched pairs of persons 60 years of age or older
Relative vaccine effectiveness in days 7 to 30 after the fourth dose was estimated to be 45% (95% CI, 44 to 47) against infection, 55% (95% CI, 53 to 58) against symptomatic Covid-19, 68% (95%CI, 59 to 74) against hospitalization, 62% (95% CI, 50 to 74) against severe Covid-19, and 74% (95% CI, 50 to 90) against Covid-19–related death.

Situazione vaccini



Vaccinazioni anti SARS-CoV-2 in Abruzzo al 18 febbraio 2022

	Unvaccinated	1 Dose [A]	2 Doses [B]	3 Doses [C]	Total Sample
	(*n* = 313,068)	(*n* = 29,401)	(*n* = 684,860)	(*n* = 252,365)	(*n* = 1,279,694)
Gender					
Females	23.9	2.3	52.8	21.0	50.9 (651,752)
Males	25.1	2.3	54.2	18.4	49.1 (627,942)
Mean age in years (SD)	35.3 (26.6)	41.6 (21.6)	47.6 (19.7)	64.3 (16.9)	47.8 (23.3)
Age category in years					
0–29	45.6	3.3	48.4	2.7	25.3 (323,613)
30–59	19.2	2.4	61.8	16.7	42.0 (537,148)
60 or more	15.0	1.4	46.8	36.8	32.7 (418,933)
Risk factors and comorbidities [D]					
No hypertension	25.8	2.4	55.3	16.4	87.4 (1,117,986)
Hypertension	14.9	1.4	41.1	42.6	12.6 (161,708)
No diabetes	24.9	2.3	54.4	18.4	94.7 (1,212,278)
Diabetes	16.8	1.4	38.4	43.3	5.3 (67,416)
No CVD	24.8	2.3	54.7	18.2	93.6 (1,198,232)
CVD	19.7	1.5	36.7	42.0	6.4 (81,462)
No COPD	24.5	2.3	53.8	19.4	97.5 (1,247,276)
COPD	25.1	2.0	42.2	30.7	2.5 (32,418)
No kidney disease	24.4	2.3	53.9	19.5	98.5 (1,260,117)
Kidney disease	30.3	1.6	31.7	36.4	1.5 (19,577)
No cancer	24.7	2.3	54.3	18.7	95.4 (1,220,868)
Cancer	20.6	1.2	36.7	41.5	4.6 (58,826)
Type of vaccine [E]					
BNT162b2	–	64.6	65.4	59.7	63.9 (617,751)
mRNA-1273	–	29.7	14.2	7.6	13.0 (125,551)
ChAdOx1 nCoV-19	–	5.7	16.1	0.1	11.5 (111,658)
JNJ-78436735	–	–	1.7	0.0	1.2 (11,510)
Mixed [F]	–	–	2.6	32.6	10.4 (100,156)
Mean follow-up in days (SD) [G]	367 (58)	130 (87)	188 (51)	71 (18)	244 (99)
SARS-CoV-2-positive swab before the second dose [H]	0.3 (877)	–	0.4 (2758)	0.1 (236)	0.3 (3871)
SARS-CoV-2-positive swab before the third dose [H]	4.7 (14,835)	–	–	0.7 (1745)	1.3 (16,580)

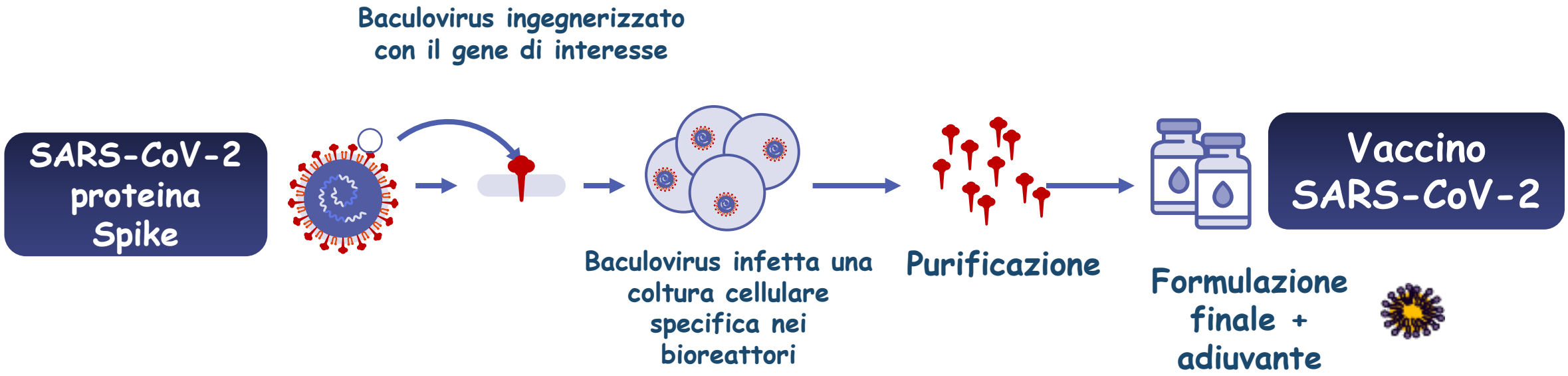
Acuti Martellucci et al Vaccines 2022, 10, 662.2022

Persistence of protection against SARS-CoV-2 clinical outcomes up to 9 months since vaccine completion: a retrospective observational analysis in Lombardy, Italy

Giovanni Corrao, Matteo Franchi, Danilo Cereda, Francesco Bortolan, Alberto Zoli, Olivia Leoni, Catia Rosanna Borriello, Giulia Petra Della Valle, Marcello Tirani, Giovanni Pavesi, Antonio Barone, Michele Ercolanoni, Jose Jara, Massimo Galli, Guido Bertolaso, Giuseppe Mancia

- **The increasing infection rate was greater for individuals aged 60 years or older who received adenovirus-vectored vaccines (from 4·0 to 23·5 cases every 10 000 person-months).**
- **The increasing severe illness rates were similar for individuals receiving mRNA-based vaccines (from 1·1 to 1·5 every 10000 person-months) and adenovirus-vectored vaccines (from 0·5 to 0·9 every 10000 person-months)**

Piattaforma tecnologica a DNA ricombinante



Cox MM, Anderson KD. Influenza Other Respir Viruses. 2007;1:35-40.

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Immunogenicity and Safety of Beta-Adjuvanted Recombinant Booster Vaccine

R346X, N460X, F486X

R346X, L452X, F486X

K444X, L452X, F486X

K444X, **L452X, N460X**

R346X, **L452X, N460X**

R346X, **L452X, N460X**, F486X

K444X, **L452X, N460X**, F486X

R346X, K444X, **L452X, N460X**, F486X

+R346

BQ.1.1 "Cerberus"

*changed to F486V in BF.12

Grazie per l'attenzione

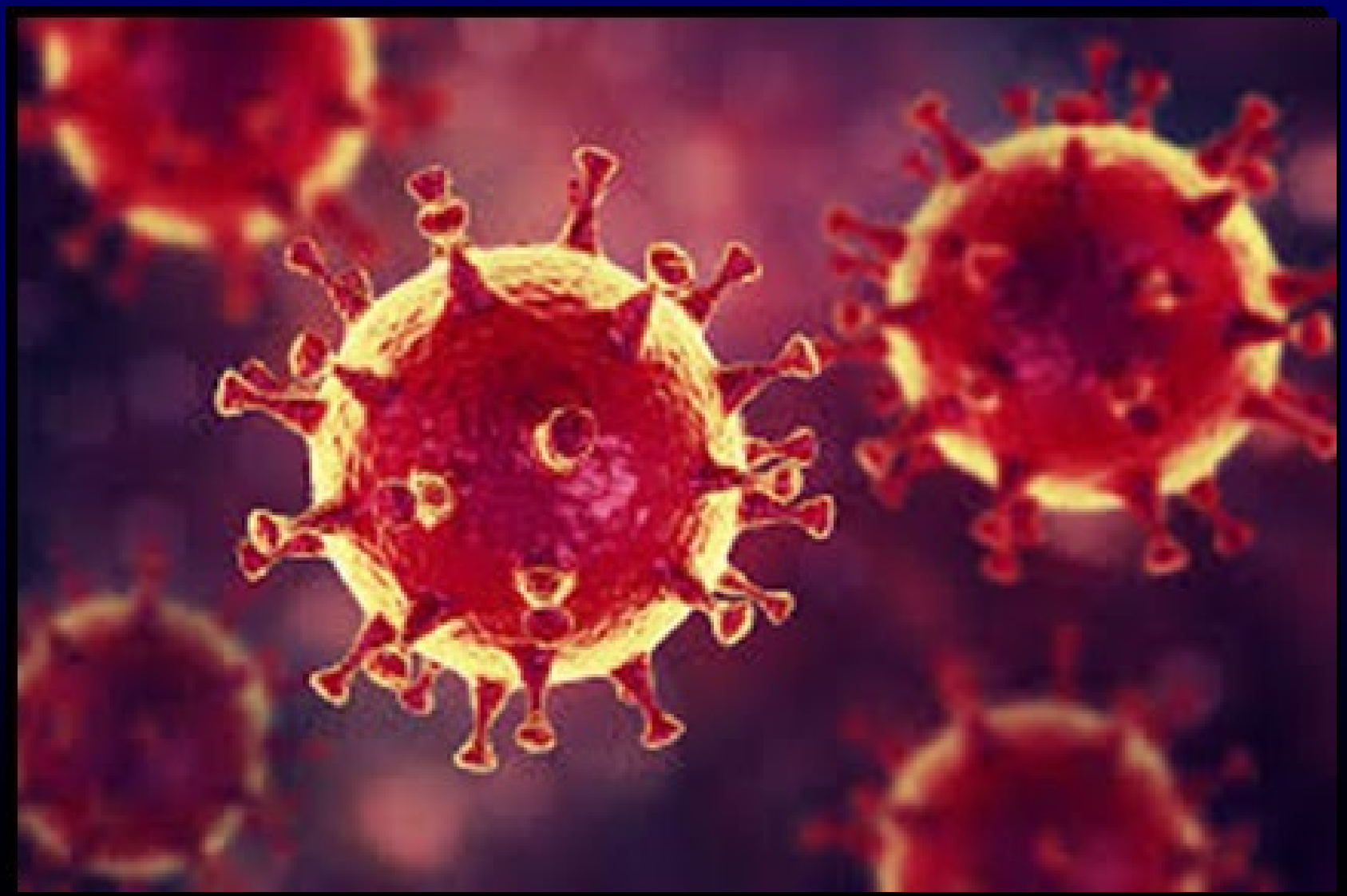
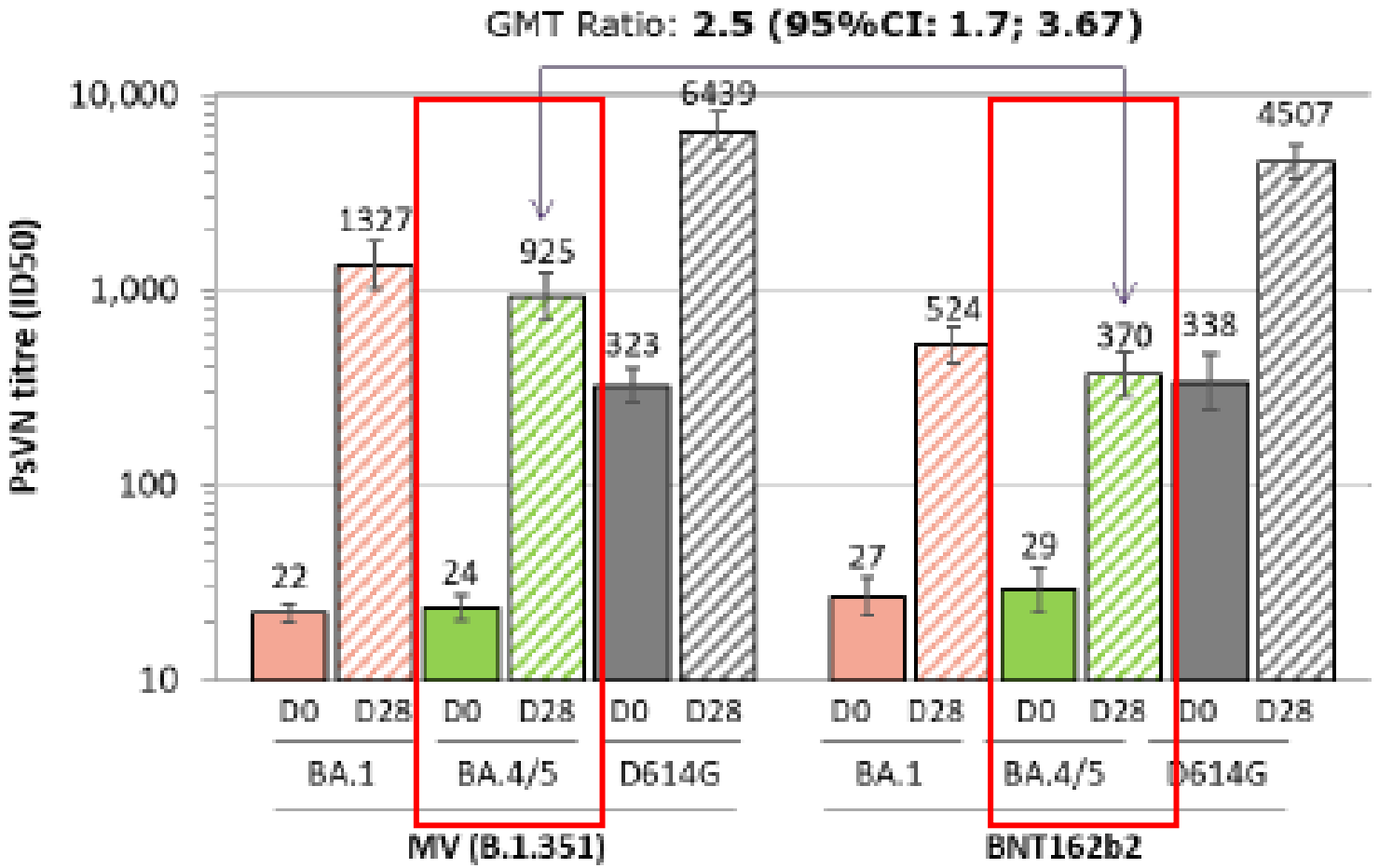


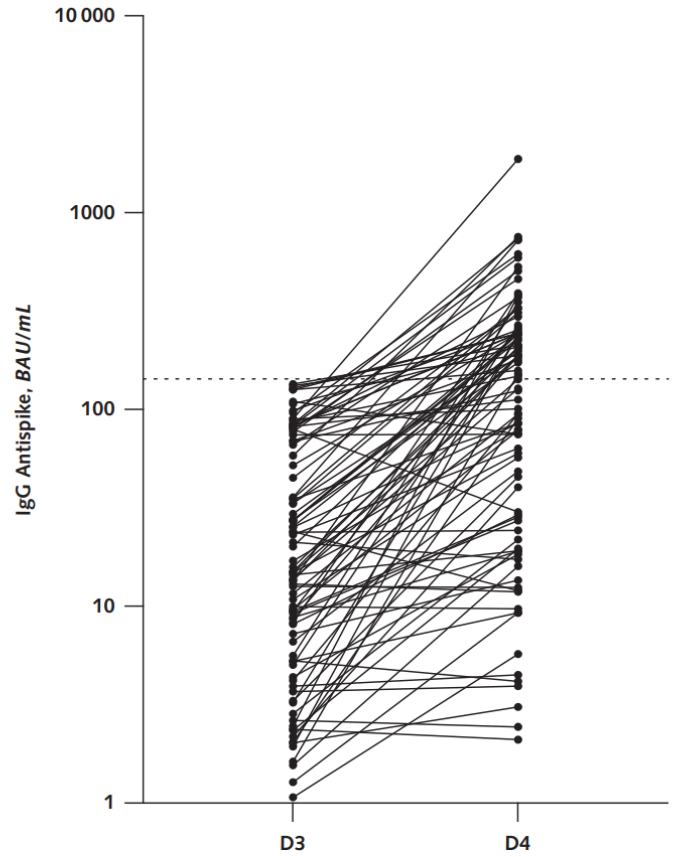
Figure 2: VAT00013 - Neutralizing antibody titers for CoV2 preS dTM-AS03 (B.1.351) vs Pfizer/BioNTech vaccines against D614G, Omicron BA.1, and Omicron BA.4/BA.5 at D28 - PPAS_MONOGRAM



- **La formulazione del vaccino proteico adiuvato mirato alla variante B.1.351 (Beta) ha fornito una migliore risposta di neutralizzazione crociata anche contro Omicron BA.4/BA.5 rispetto al BNT162b2 basato su mRNA (2,5 volte)**

Antibody Response to a Fourth Messenger RNA COVID-19 Vaccine Dose in Kidney Transplant Recipients: A Case Series

Figure. Antispike IgG titers measured 2-6 wk after the third and fourth vaccine doses in 92 kidney transplant recipients.



Titers are expressed in BAU after calibration to the World Health Organization standard. The dotted line indicates the threshold of 143 BAU/mL. BAU = binding antibody units; D3 = third dose; D4 = fourth dose.

Entire Cohort (*n* = 92)	IgG >143 BAU/mL After 4 Doses (*n* = 46)	IgG <143 BAU/mL After 4 Doses (*n* = 46)
55.9 (47.1-64.2)	57.5 (49.9-64.6)	53 (45.6-61.9)
64 (69.5)	35 (76)	29 (63)
26.3 (22.8-30.2)	26.6 (22.2-29.1)	25.3 (22.8-30.6)
28 (30.4)	13 (28.3)	15 (32.6)
30 (32.6)	16 (34.8)	14 (30.4)
76 (82.6)	37 (80.3)	38 (82.6)
20 (21.7)	9 (19.6)	11 (23.6)
5.5 (2.3-11.4)	7.2 (3-11.7)	4.5 (1.6-11.1)
79 (85.8)	37 (80.4)	42 (91.4)
77 (83.6)	37 (80.4)	40 (86.9)
70 (76)	32 (69.6)	38 (82.6)
17 (18.5)	11 (23.9)	6 (13)
5 (5.4)	3 (6.5)	2 (4.3)
74 (80.4)	36 (78.3)	38 (82.6)
16 (17.4)	9 (19.6)	7 (15.2)
59 (64.1)	23 (50)	36 (78.3)
132 (113.3-162.7)	136.2 (121.9-164.5)	131.5 (100.7-159.3)
1.49 (1.28-1.84)	1.54 (1.38-1.86)	1.49 (1.14-1.80)
58	30	28
34	16	18
68 (61-74.7)	68 (63-76)	63 (56.7-73.2)
16.4 (5.9-62.3)	35.6 (14.7-83.3)	9.5 (3.6-21.7)

= interquartile range; MMF = mycophenolate mofetil; MPA = mycophenolic acid; ycin.

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