Vaccino anti pneumococco sequenziale

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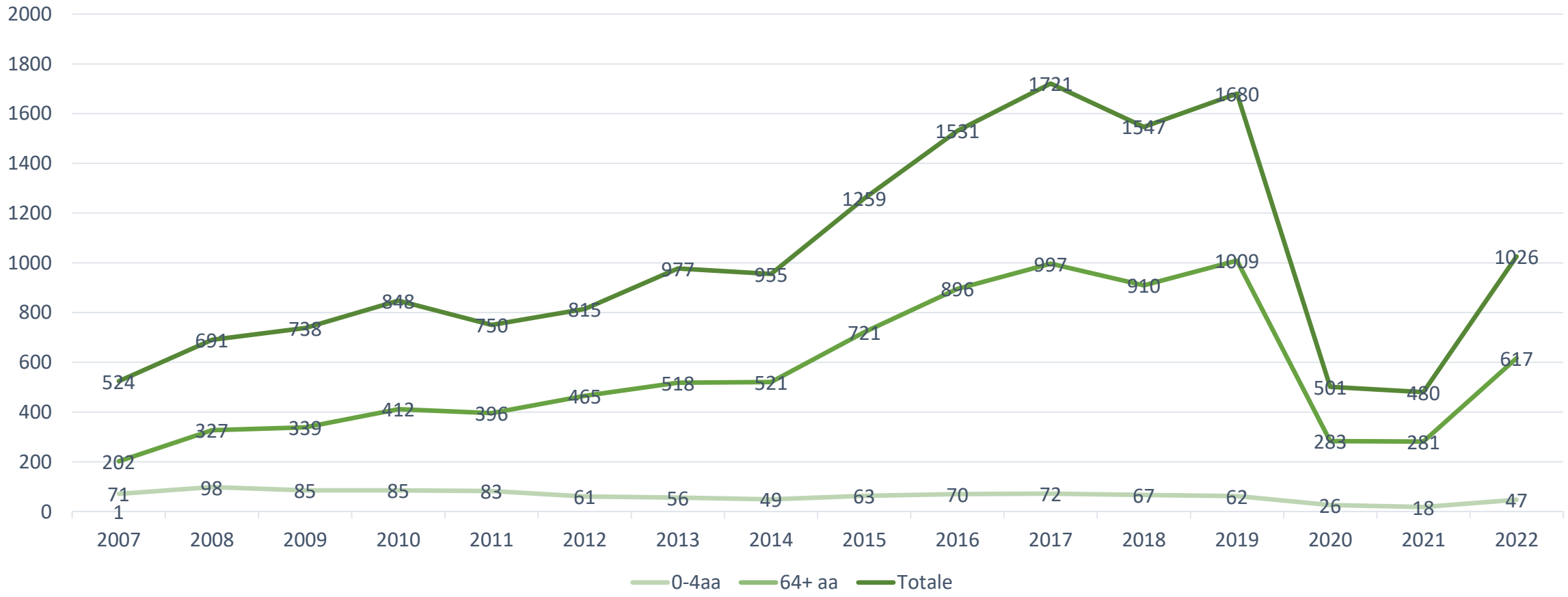
Le dimensioni del problema Pneumococco (Cedrone F et al. Vaccines 2023, 11, 1324)

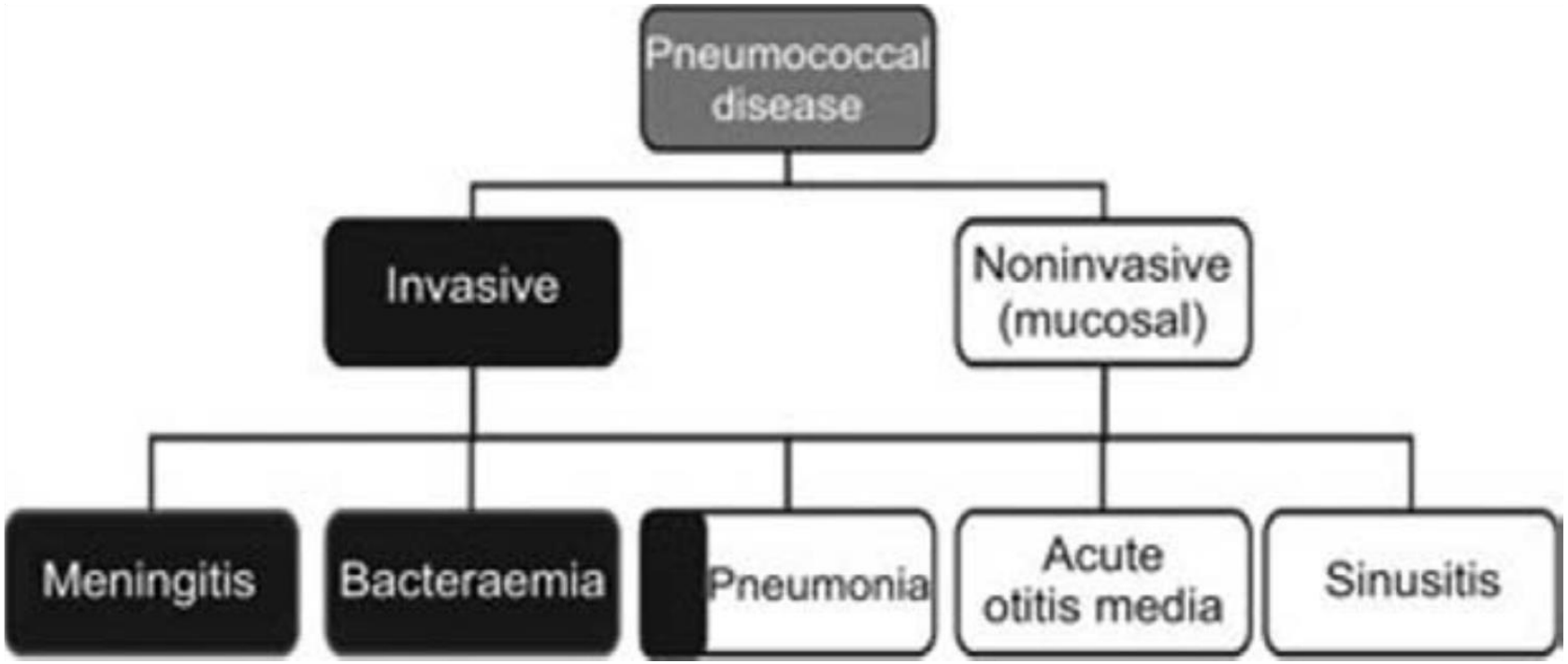
Table 3. (**a**) Admission rate per 100,000 Pescara province people for all S.P.-related admissions and for S.P.-related diseases: pneumonia, meningitis, and bacteremia. (**b**) In-hospital mortality rate per 100,000 Pescara province people for all S.P.-related admissions and for S.P.-related diseases: pneumonia, meningitis, and bacteremia.

(a)	*Streptococcus pneumoniae* Admission Rate							
	All	IC 95%	Pneumonia	IC 95%	Meningitis	IC 95%	Bacteremia	IC 95%
2015	343.3	323.2–363.4	290.3	271.8–308.8	1.2	0–2.5	1.5	0.4–2.5
2016	388.4	366.9–409.8	323.6	304.0–343.1	0.6	0–1.5	1.9	0.4–3.4
2017	469.5	446–493.1	389.3	367.9–410.8	3.1	1.2–5.1	1.9	0.4–3.4
2018	443.9	421–466.8	350.5	330.2–370.8	0.9	0–2.0	0.3	0–0.8
2019	501.1	476.6–525.6	392.4	370.7–414.0	0.9	0–2.0	7.6	4.5–10.6
2020	446.1	423.1–469.1	344.8	324.6–365.1	1.0	0–2.1	4.1	1.9–6.3
2021	381.7	360.5–402.9	253.1	235.9–270.4	0.3	0–1.0	5.0	2.6–7.5
2022	361.4	340.7–382	241.9	225.0–258.7	2.2	0.6–3.8	5.3	2.8–7.9
(b)	***Streptococcus pneumoniae* In-Hospital Death Rate**							
	All	IC 95%	Pneumonia	IC 95%	Meningitis	IC 95%	Bacteremia	IC 95%
2015	61.3	52.8–69.9	45.9	38.5–53.2	0	-	0	-
2016	61.6	53.0–70.1	54.5	46.4–62.6	0	-	0	-
2017	77.2	67.6–86.8	73.1	63.7–82.4	0	-	0	-
2018	71.1	61.9–80.4	67.8	58.8–76.9	0.6	0–1.4	0.3	0–0.8
2019	76.6	65.7–84.7	76.4	66.9–86.0	0	-	0.6	0–1.4
2020	150.9	137.6–164.2	79.2	69.5–88.9	0	-	0.3	0–0.9
2021	127.5	115.4–139.7	63.7	55.1–72.2	0	-	0.6	0–1.5
2022	111.9	100.4–123.3	57.9	49.7–66.2	0	-	0.6	0–1.5

Andamento delle infezioni pneumococciche invasive in Italia (fonte: ISS)



Espressioni del danno da Pneumococco



Il danno indiretto, cardiovascolare, ha qui un meccanismo specifico (Anderson R et al. Int. J. Mol. Sci. 2023, 24, 11038)

Table 2. Summary of pneumolysin-mediated mechanisms of immunosuppression and cardiotoxicity in the pathogenesis of severe myocardial dysfunction.

Mechanism	References
• Ply-mediated suppression of the protective activities of infiltrating and resident sentinel cardiac macrophages via induction of necroptosis following adherence of the pathogen to the vascular endothelium of myocardial capillaries	[68–70]
• Following invasion of the myocardium the pneumococcus becomes established in intra-cardiac microlesions in which it transitions to a biofilm-forming, high Ply-producing phenotype	[71,73,74]
• Cardiotoxicity results from interaction of the pneumococcal adhesins PspA, CbpA, and Psrp with cardiomyocytes, resulting in exposure of these cells to Ply, leading to cell death and myocardial dysfunction	[75,76]

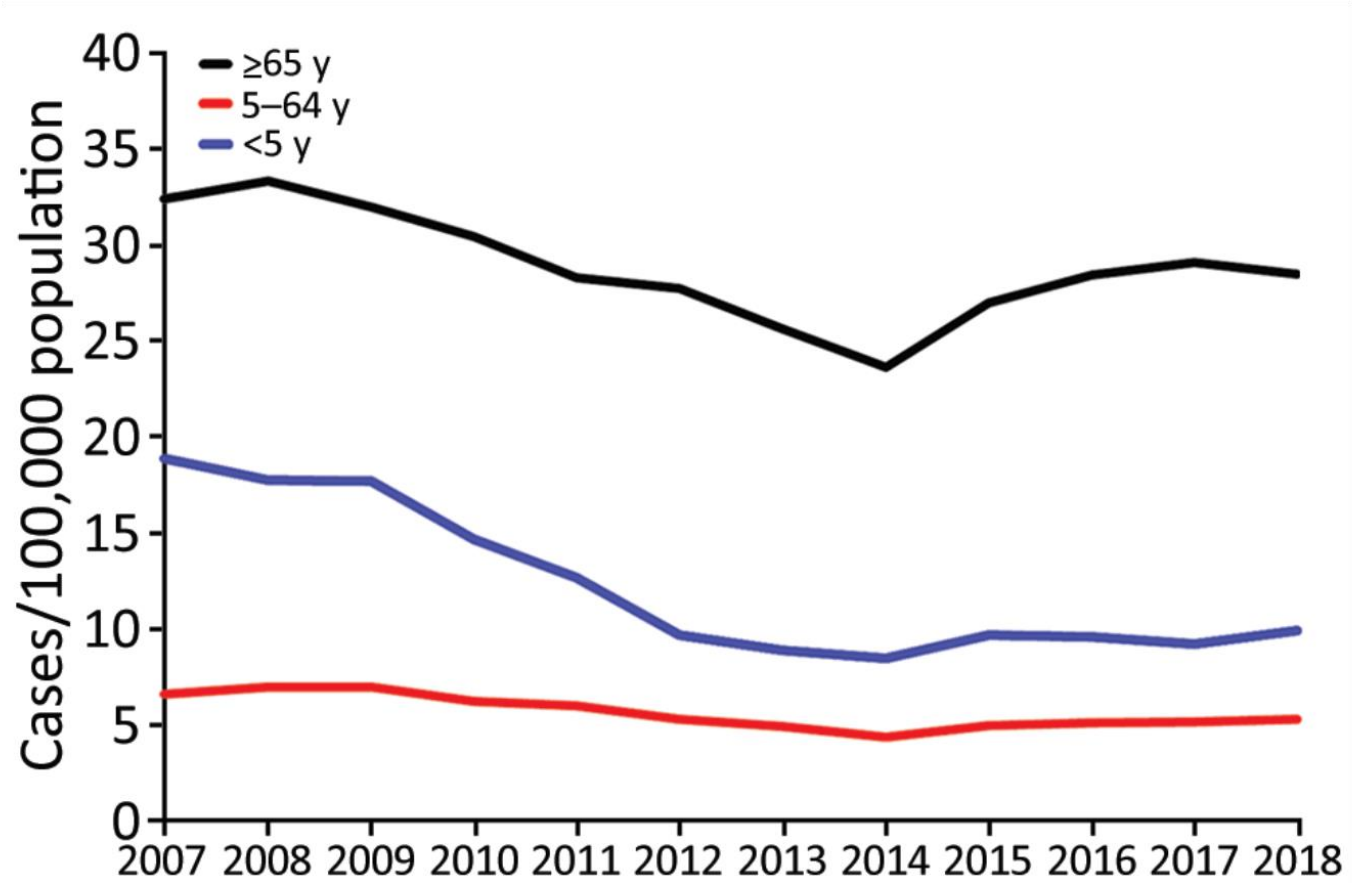
Abbreviations: Ply (pneumolysin); PspA (pneumococcal surface protein A); CbpA (choline-binding protein A); Psrp (pneumococcal serine-rich repeat protein).

La soluzione del problema Pneumococco

Joint OECD/Eurostat lists of preventable and treatable causes of mortality

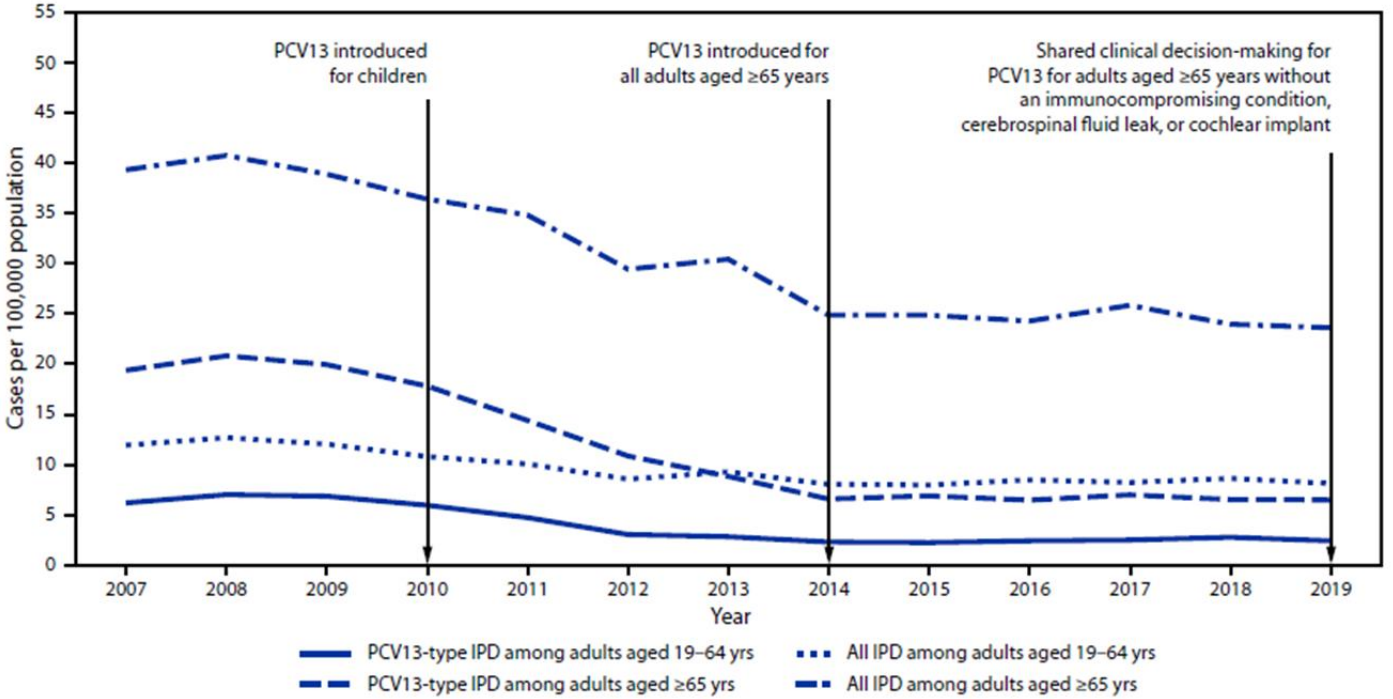
Group	Causes of death	Preventable mortality	ICD 10 Code	Age threshold	Rationale for inclusion	
Infectious diseases	Sepsis due to streptococcus pneumonia and sepsis due to hemophilus	x	A40.3, , A41.3	0-74	Most of these infections can be prevented through vaccination.	
	Pneumonia due to Streptococcus pneumonia or Haemophilus influenza	x	13 -J14	0-74	Most of these infections can be prevented through vaccination.	

…almeno entro certi limiti, in Europa (Hanquet G et al. Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 28, No. 1, January 2022)



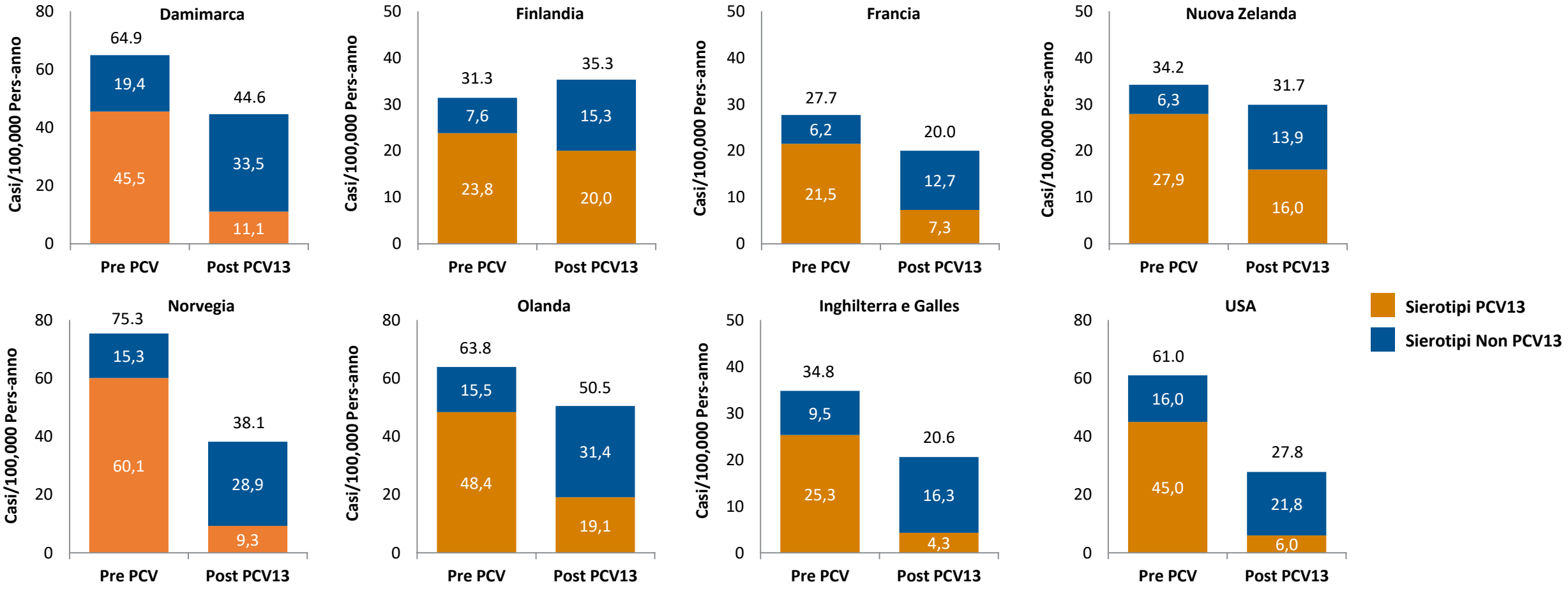
…ma negli USA va meglio (Kobayashi M et al. MMWR Morb Mortal Wkly Rep 2022;71:[)

FIGURE. Incidence of all invasive pneumococcal disease and 13-valent pneumococcal conjugate vaccine-type* invasive pneumococcal disease among adults aged ≥19 years, by invasive pneumococcal disease type and age group — United States, 2007–2019†



Abbreviations: IPD = invasive pneumococcal disease; PCV13 = 13-valent pneumococcal conjugate vaccine.
* Includes serotype 6C, which shows cross-protection from 6A antigen in PCV13 and was grouped with PCV13 serotypes for IPD incidence.
† Active Bacterial Core surveillance, 2021.

L' introduzione del vaccini PCV in età pediatrica ha prodotto un aumento percentuale dei casi di IPD da sierotipo non vaccinale negli adulti >64 anni.



35. Izurieta et al, Public health impact of pneumococcal conjugate vaccine infant immunization programs: assessment of invasive pneumococcal disease burden and serotype distribution *Expert Rev Vaccines*, 2018.

I sierotipi dello Pneumococco sono 96 e quelli coperti dai vaccini…

TABLE I. Serotypes covered by main polysaccharide and conjugate pneumococcal vaccines

Vaccine	Included serotypes
PPV23	1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, 33F
PCV7	4, 6B, 9V, 14, 18C, 19F, 23F
PCV10	1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 23F
PCV13	1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F

Anche nella popolazione BPCO, ad alto rischio, l'efficacia del vaccino anti pneumococco è eterogenea. (Ontario Health Technology Assessment Series; Vol. 12: No. 3, pp. 1–64, March 2012)

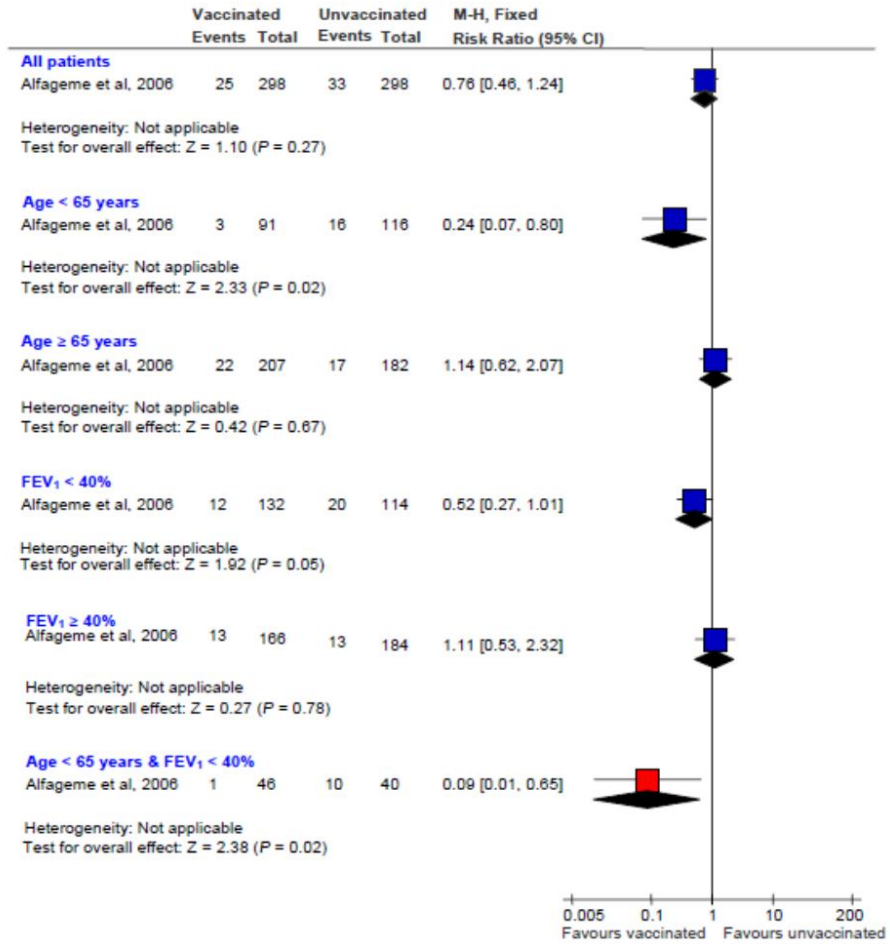


Figure 4: First Episode of Community-Acquired Pneumonia of Unknown Etiology and Pneumococcal Pneumonia in Vaccinated and Unvaccinated Patients*

*Abbreviations: CI, confidence interval; FEV_1, Forced expiratory volume in one second; M-H, Mantel-Haenszel.

Efficacia del vaccino-23 anti PN in soggetti>65 anni immunizzati verso l'influenza (Kawakami K et al. Vaccine 2010, 28: 7063)

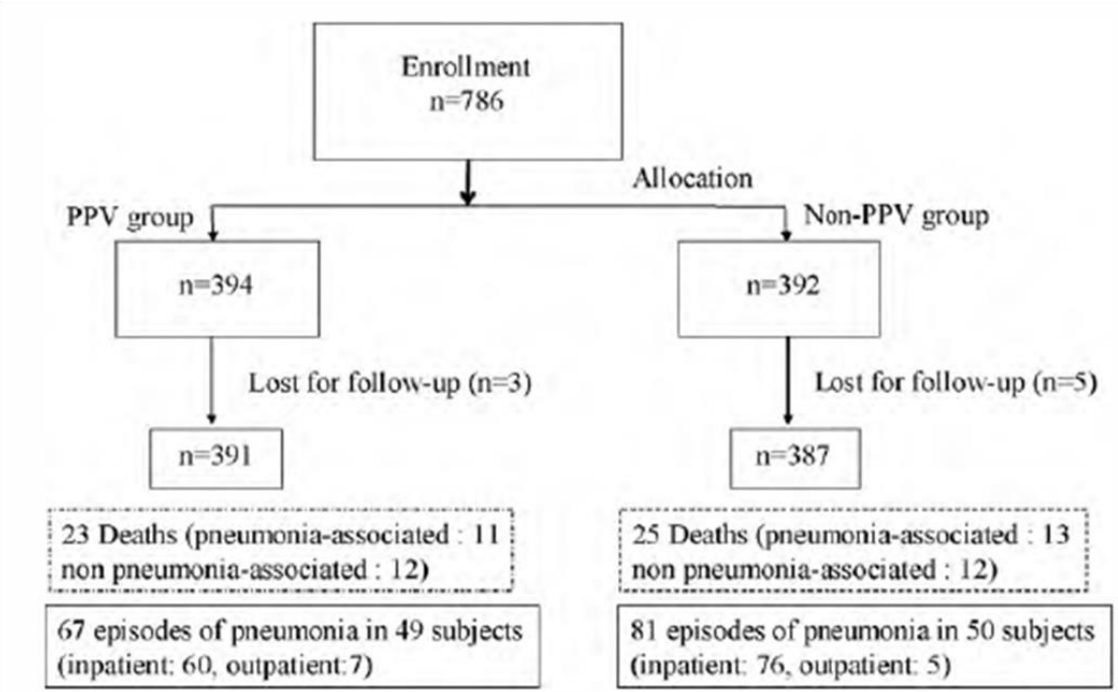
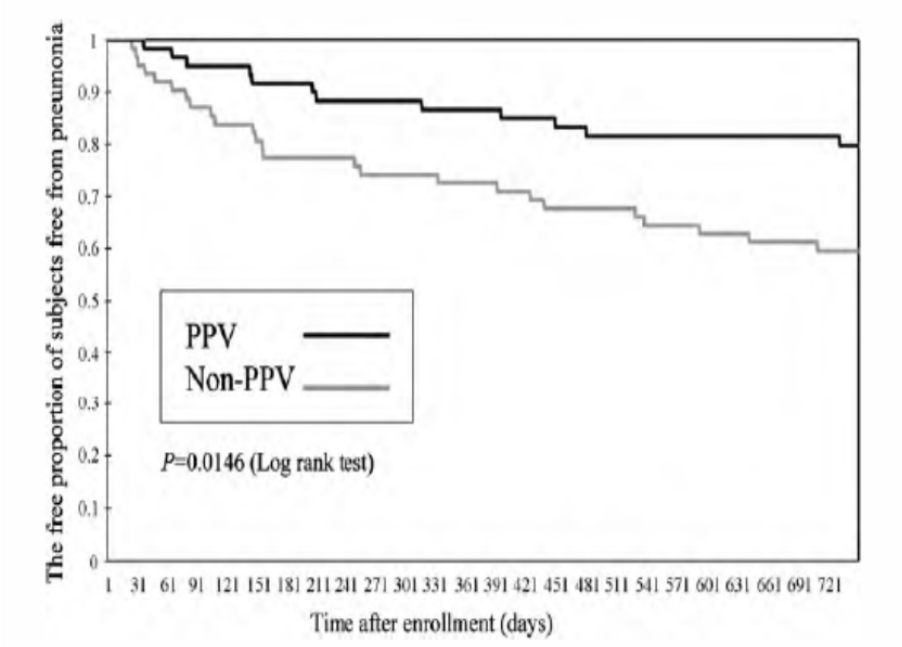


Fig. 1. Flow diagram of study subjects.

Efficacia del vaccino-23 anti PN in soggetti>65 anni immunizzati verso l'influenza e con difficoltà nella deambulazione (Kawakami K et al. Vaccine 2010, 28: 7063)



In uno studio test negativo, anziani (65-74), ma non grandi anziani beneficiano della sequenziale PCV13>PPSV23 e non di PCV13 né di PPSV23 (Heo JY et al. The Journal of Infectious Diseases® 2022;225:836–45)

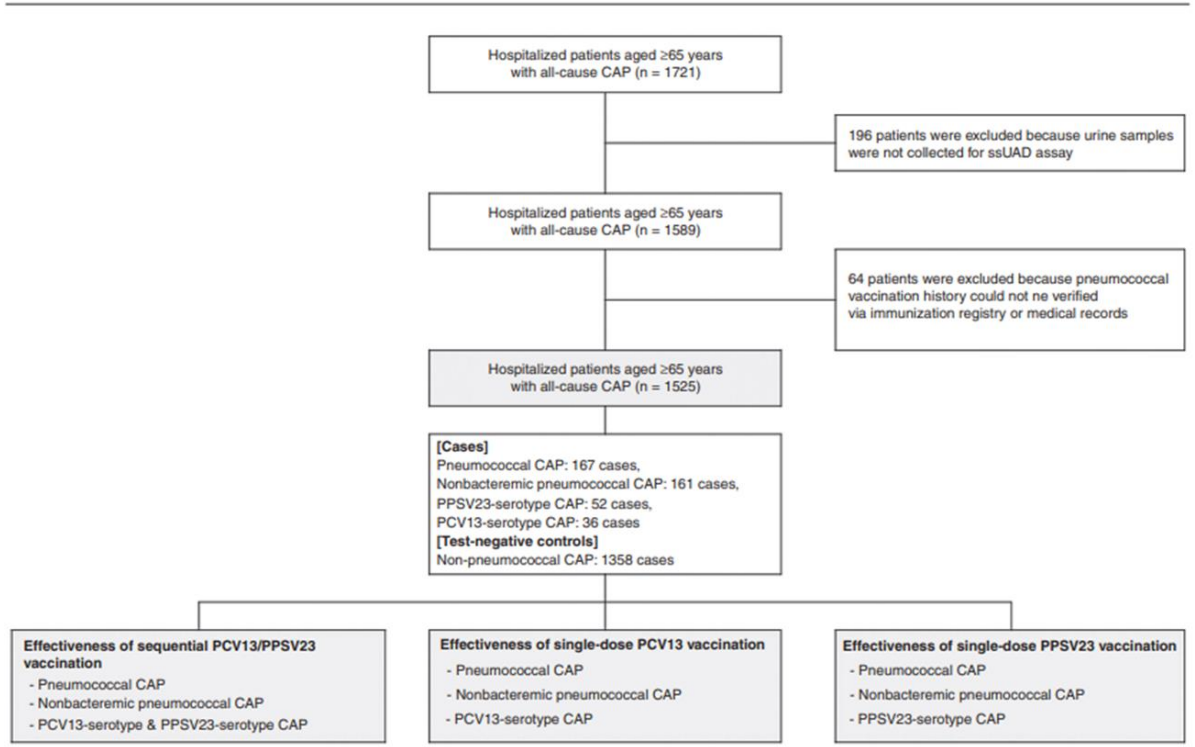


Figure 1. Study flowchart. Abbreviations: CAP, community-acquired pneumonia; PCV13, 13-valent pneumococcal conjugate vaccine; PPSV23, 23-valent pneumococcal polysaccharide vaccine; ssUAD, serotype-specific urinary antigen detection.

In uno studio test negativo, anziani (65-74), ma non grandi anziani beneficiano della sequenziale PCV13>PPSV23 e non di PCV13 né di PPSV23 (Heo JY et al. The Journal of Infectious Diseases® 2022;225:836–45)

- Results. Of 1525 cases with CAP hospitalization, 167 (11.0%) were identified as pneumococcal CAP. In the elderly aged ≥65 years, the adjusted VE of pneumococcal vaccines against pneumococcal CAP was statistically insignificant: 40.0% (95% confidence interval [CI], –10.8% to 67.5%) for PCV13 and 11.0% (95% CI, –26.4% to 37.3%) for PPSV23. However, in the younger subgroup (aged 65–74 years), sequential PCV13/PPSV23 vaccination showed the highest adjusted VE of 80.3% (95% CI, 15.9%–95.4%), followed by single-dose PCV13 (adjusted VE, 66.4% [95% CI, .8%–88.6%]) and PPSV23 (adjusted VE, 18.5% [95% CI, –38.6% to 52.0%]).
- Conclusions. Sequential PCV13/PPSV23 vaccination is most effective for preventing pneumococcal CAP among the elderly aged 65–74 years

Indicazioni prevalenti e loro basi 1

Vaccino	Tipo	Indicazione	Età
Influenza	Vari tipi, inattivati	Popolazione generale Categorie a rischio	>65 Nessuna soglia
Pneumococco	PPSV23*	Popolazione generale Categorie a rischio§	>65 Nessuna soglia
HVZ	ZVL: vivo RZV: liofilizzato, ricombinante	Pazienti immunocompetenti Anche pazienti immunocompromessi	>50 (In Italia: >65) Nessuna soglia
Tetano		Popolazione generale	Adulta
Pertosse		Popolazione generale	Adulta

- * PCV13: il vaccino coniugato non è più considerato propedeutico al polisaccaridico PPS23
- §: anche portatori di impianto cocleare

Indicazioni e loro basi 2

Vaccino	Tipo	Efficacia	Copertura attesa
Influenza	Vari tipi, inattivati (Tetravalente ad alta carica o adiuvato nell'anziano)	Riduce mortalità e ricoveri sia nell'anziano che nel paziente a rischio	75% 95% in categorie a maggiore rischio
Pneumococco	PPSV23*	Particolarmente efficace nei soggetti a maggiore rischio	75%
HVZ	ZVL: vivo RZV: liofilizzato, ricombinante	Previene sia la malattia, primaria o recidiva, che la nevralgia postherpetica RZV pare più efficace del pur efficace ZVL RZV può essere somministrato in chi abbia già ricevuto ZVL	50%

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

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

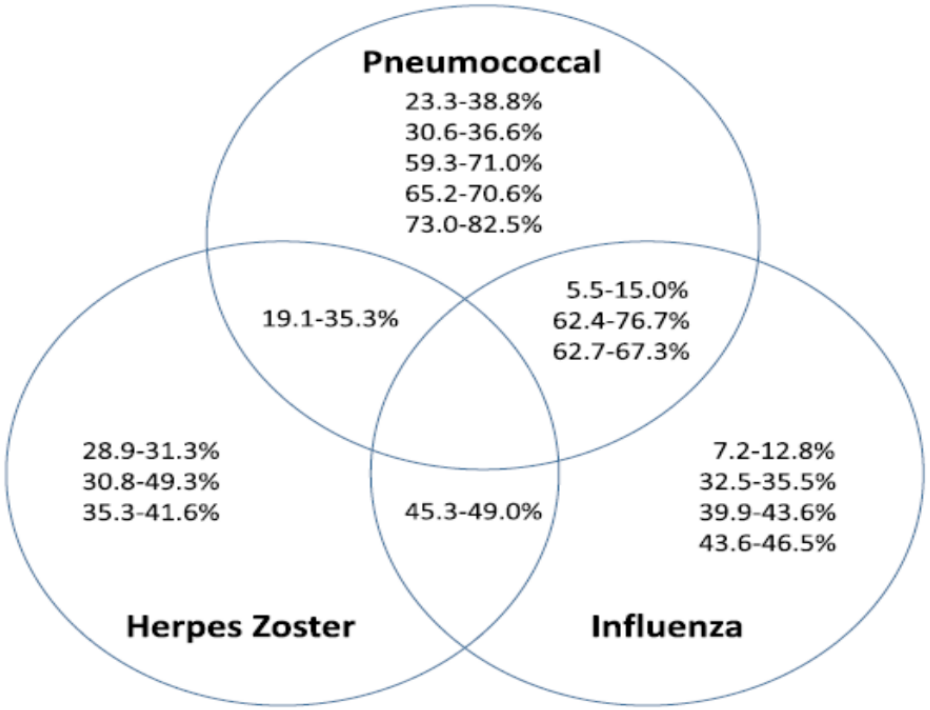


Fig. 1. Range (minimum and maximum) of correct response rates achieved on each question by qualified specialists and residents, according to the vaccine mentioned in the question. (Note: the single question about measles is not included).

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

Eterogeneità nelle indicazioni (Antonelli Incalzi R et al , ACER 2020)

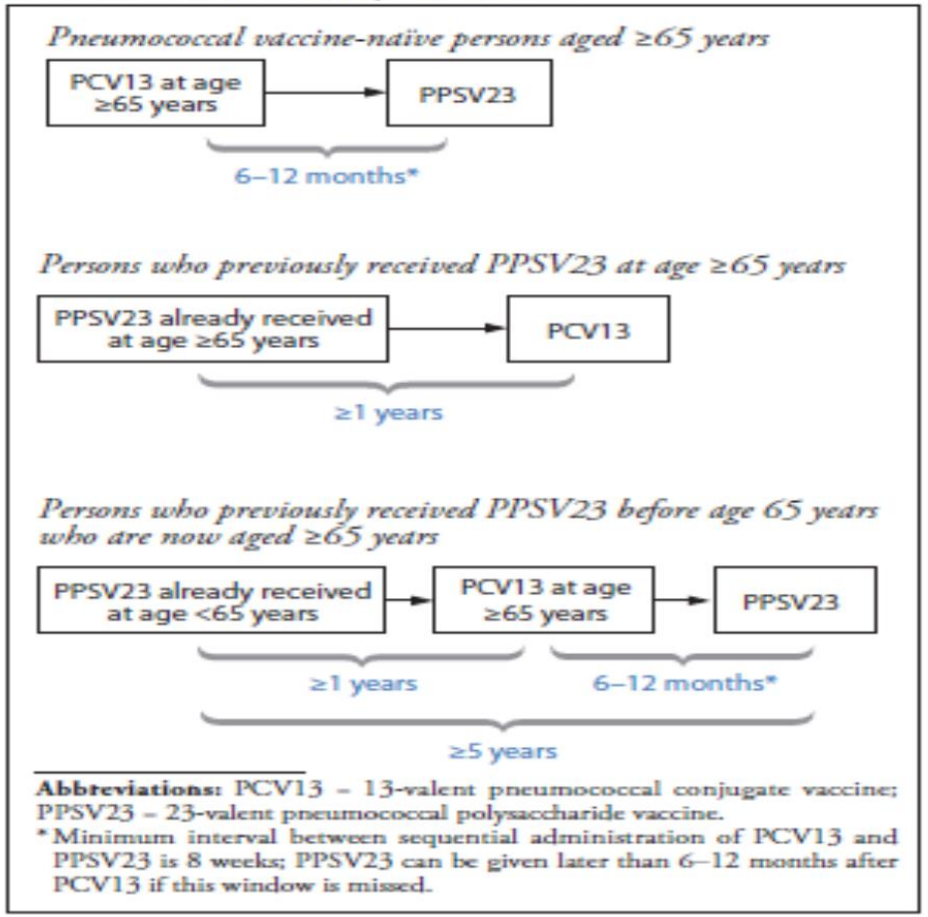
Country	Influenza Age	Pneumococcal Age, type of vaccine	Herpes zoster Age, type of vaccine
Australia	≥65	≥65; PPV	70–79; ZVL°
Austria	All adults	≥50; PCV+PPV*	≥50; RZV°
Belgium	≥65	≥65; PCV+PPV*	≥65; catch up 79
Bulgaria	≥65	–	–
Canada	All adults(a)	≥65; PPV(b)	≥50; RZV(c)
Croatia	≥65	–	–
Cyprus	≥65	≥65; PPV	–
Czech Republic	All adults	≥65; PCV+PPV*	≥50; ZVL
Denmark	≥65	≥65; PCV or PPV	–
Estonia	≥65	–	–
Finland	≥65	≥65; PCV or PPV	–
France	≥65	–	65–74; catch-up 75–79; ZVL
Germany	≥60	≥60; PPV	≥60; RZV
Greece	≥60	≥65; PCV	≥60; ZVL
Hungary	≥60	≥50; PPV	–
Island	≥60	≥60; PPV	–
Ireland	≥65	≥65; PPV	–
Italy	≥65	≥65; PCV+PPV*	≥65; ZVL

ZVL = Zoster vaccine live attenuated; RZV = recombinant zoster vaccine

The United States Advisory Committee on Immunization Practices (ACIP) recommends one dose pf PPSV23 for adults 65 years of age

Le indicazioni al vaccino anti Pneumococcico del 2014 (Tomczyk S et al. MMWR / September 19, 2014 / Vol. 63 / No. 37)

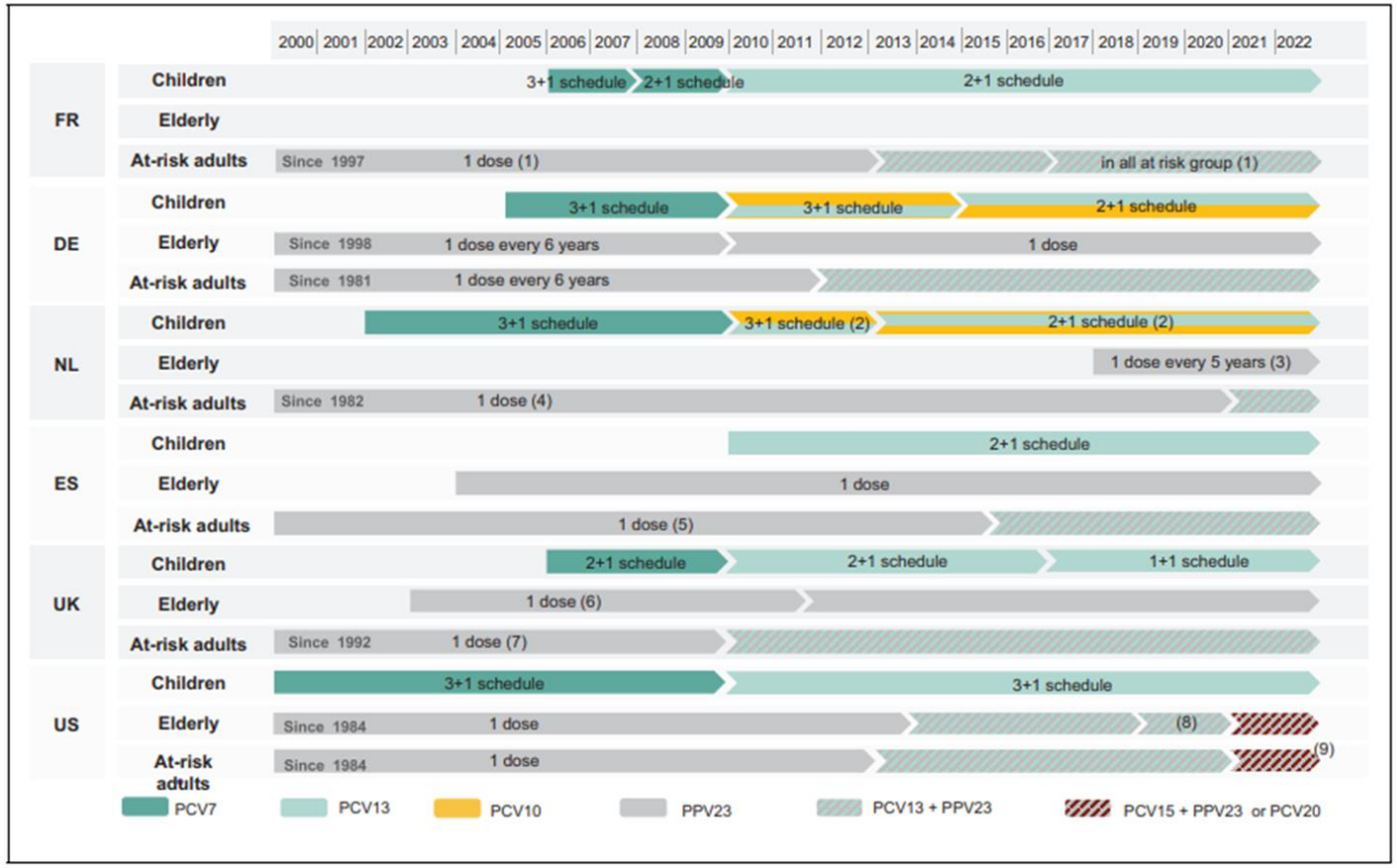
BOX. Sequential administration and recommended intervals for PCV13 and PPSV23 for adults aged ≥65 years — Advisory Committee on Immunization Practices, United States



Abbreviations: PCV13 = 13-valent pneumococcal conjugate vaccine; PPSV23 = 23-valent pneumococcal polysaccharide vaccine.

*Minimum interval between sequential administration of PCV13 and PPSV23 is 8 weeks; PPSV23 can be given later than 6–12 months after PCV13 if this window is missed.

Come evolve l'indicazione al vaccino? (Noharet-Koenig et al. MDM Policy & Practice 2023, Vol. 8(1) 1–18)



In sintesi, le raccomandazioni del CDC prima e dopo il 2021 (CDC, Recommendations and Reports / Vol. 72 / No. 3 September 8, 2023)

Before 2021, ACIP recommended 23-valent pneumococcal polysaccharide vaccine (PPSV23) alone (up to 2 doses), or both a single dose of 13-valent pneumococcal conjugate vaccine (PCV13) in combination with 1–3 doses of PPSV23 in series (PCV13 followed by PPSV23), for use in U.S. adults depending on age and underlying risk for pneumococcal disease. In 2021, two new pneumococcal conjugate vaccines (PCVs), a 15-valent and a 20-valent PCV (PCV15 and PCV20), were licensed for use in U.S. adults aged ≥18 years by the Food and Drug Administration.

ACIP recommendations specify the use of either PCV20 alone or PCV15 in series with PPSV23 for all adults aged ≥65 years and for adults aged 19–64 years with certain underlying medical conditions or other risk factors who have not received a PCV or whose vaccination history is unknown. In addition, ACIP recommends use of either a single dose of PCV20 or ≥1 dose of PPSV23 for adults who have started their pneumococcal vaccine series with PCV13 but have not received all recommended PPSV23 doses. Shared clinical decision-making is recommended regarding use of a supplemental PCV20 dose for adults aged ≥65 years who have completed their recommended vaccine series with both PCV13 and PPSV23.

Pneumococcal Vaccine Timing for Adults

Make sure your patients are up to date with pneumococcal vaccination.

CDC recommends pneumococcal vaccination for

- Adults 65 years old and older
- Adults 19 through 64 years old with certain underlying medical conditions or other risk factors:
  - Alcoholism
  - Cerebrospinal fluid leak
  - Chronic heart/liver/lung disease
  - Chronic renal failure*
  - Cigarette smoking
  - Cochlear implant
  - Congenital or acquired asplenia*
  - Congenital or acquired immunodeficiencies*
  - Diabetes
  - Generalized malignancy*
  - HIV infection*
  - Hodgkin disease*
  - Iatrogenic immunosuppression*
  - Leukemia*
  - Lymphoma*
  - Multiple myeloma*
  - Nephrotic syndrome*
  - Sickle cell disease or other hemoglobinopathies*
  - Solid organ transplants*

* Considered an immunocompromising condition

Pneumococcal vaccines

PCV13: 13-valent pneumococcal conjugate vaccine (Prevnar13®)
PCV15: 15-valent pneumococcal conjugate vaccine (Vaxneuvance™)
PCV20: 20-valent pneumococcal conjugate vaccine (Prevnar20®)
PPSV23: 23-valent pneumococcal polysaccharide vaccine (Pneumovax®)

For those who have never received a pneumococcal vaccine or those with unknown vaccination history

Administer one dose of PCV15 or PCV20.

If **PCV20** is used, their pneumococcal vaccinations are complete.

PCV20

If **PCV15** is used, follow with one dose of PPSV23.

- The recommended interval is at least 1 year.
- The minimum interval is 8 weeks and can be considered in adults with an immunocompromising condition*, cochlear implant, or cerebrospinal fluid leak.
- Their pneumococcal vaccinations are complete.

PCV15 → At least 1 year apart (8 weeks can be considered) → PPSV23

For those who previously received PPSV23 but who have not received any pneumococcal conjugate vaccine (e.g., PCV13, PCV15, PCV20)

You may administer one dose of PCV15 or PCV20.

Regardless of which vaccine is used (PCV15 or PCV20):

- The minimum interval is at least 1 year.
- Their pneumococcal vaccinations are complete.

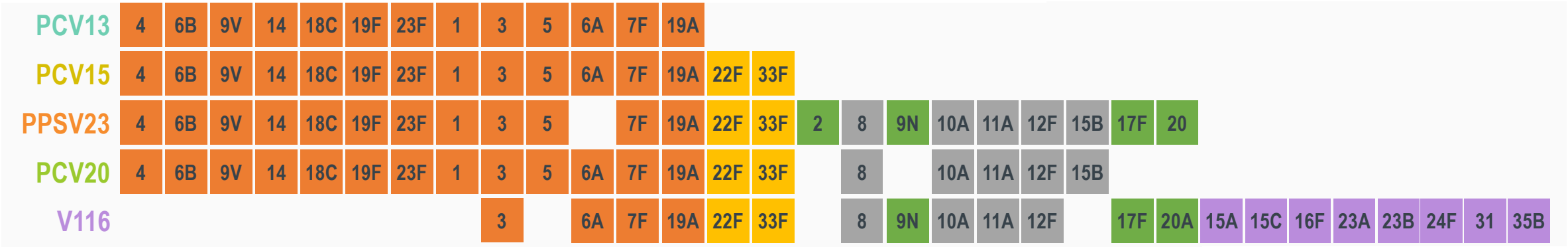
PPSV23 → At least 1 year apart → PCV15 or PCV20

NCIRDig410 | 04/01/22

www.cdc.gov/pneumococcal/vaccination.html

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Lo spettro di efficacia: vaccini a confronto



V116 includes 8 serotypes not found in currently licensed pneumococcal vaccines[c] (15A, 15C[a,b], 16F, 23A, 23B, 24F, 31, and 35B) that accounted for approximately 30% of IPD in US adults ≥65 years in 2019[1,2]

	US[1] ≥65	Canada[2] ≥65	UK[3] ≥65	Germany[4] ≥60	France[5] ≥65	Japan[6] ≥65	Australia[7] ≥65	China[8,a] ≥50
PCV13	22.7%	25.3%	22.6%	30.4%	30.8%	29.1%	31.9%	79.5%
PCV15 (V114)	38.1%	37.7%	34.4%	39.4%	41.2%	36.0%	44.6%	79.5%
PCV20	51.3%	54.6%	66.8%	64.0%	65.7%	66.1%	54.5%	83.9%
PPSV23	58.0%	61.7%	76.2%	71.7%	72.9%	66.4%	62.1%	82.7%
V116	**82.4%**	**82.7%**	**93.8%**	**83.9%**	**81.3%**	**82.0%**	**73.5%**	**27.2%**

Perché molte nazioni europee, a differenza degli USA, hanno abbandonato la sequenziale per gli anziani? (Noharet-Koenig et al. MDM Policy & Practice 2023, Vol. 8(1) 1–18)

- Elderly: in the European countries, strategies involving PCV13 appeared to be not cost-effective compared with the use of PPV23 alone, primarily due to the importance of the herd effect from childhood NIPs, its higher cost, and its lower serotype coverage. Conversely, when PCV13 was registered in the United States for adults, PCV13 in series with PPV23 had an acceptable ICER even if additional benefits of PCV13 use among adults was predicted to decline over time with continued use of PCV13 among children.82 This difference may be explained by various methodological approaches and assumptions (e.g., vaccine efficacy, the indirect effects of childhood vaccination assumptions), which greatly affected cost-effectiveness estimates.89

ICER: incremental cost-effectiveness ratio guida le scelte

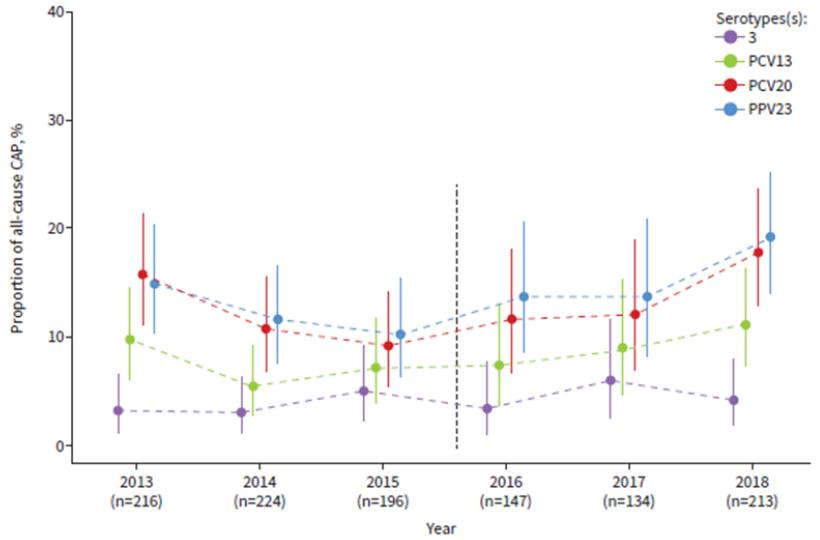
- Cost-effectiveness evaluations were in favor of using higher-valent PCVs instead of PCV7 in the Netherlands,32 the United Kingdom,26,58,59 and the United States30 (no incremental cost-effectiveness ration [ICER] reported in the Netherlands and the United Kingdom—strategy being either dominant or with an ICER less than $35,000/quality-adjusted life-year [QALY] according to scenarios in the United States).

In ciascuna nazione la scelta della pratica vaccinale tiene conto almeno di:

- Carico di malattia: polmonite, sepsi, meningite, otite
- Costo ammissibile per QALY guadagnato
- *Verosimile immunità di gregge*
- Immunogenicità del vaccino
- Efficacia clinica
- (Sicurezza)
- Prevenzione antibiotico resistenza
- Percezione del «serotype replacement»
- Costo del vaccino
- Possibili alternative di sanità pubblica

A supporto dei dubbi sull'immunità di gregge… (Bahrs C et al. Eur Respir J 2022; 59: 2102432)

- In conclusion, PCV20 had a substantially higher coverage of all-cause CAP in adults compared to PCV13 (11.7% versus 7.3% for age group 18–59 years with ⩾1 comorbidity and 12.6% versus 7.7% for age group ⩾60 years). Our data show: 1) no decline of PCV13 serotypes in all-cause CAP between 2013–2019 mainly due to a persistently high proportion of serotype 3, suggesting no meaningful effect of childhood PCV13 vaccination on PCV13 coverage in pneumonia in adults during this time period; and 2) that the gap in the coverage between PCV20 and PPV23 was small and did not increase over the entire observation time.



N.B. Sequenziale è anche PCV15>PPSV23 e PCV20>PPSV23 (Noharet-Koenig et al. MDM Policy & Practice 2023, Vol. 8(1) 1–18)

- Recently, the United States introduced PCV15 and PCV20 in the elderly vaccination program, driven by expected public health benefits, positive economic evaluations (the CDC model found cost savings in all scenarios for both strategies in adults aged 65 y), and comparable safety and immunogenicity profiles between PCV20, PCV15, and PCV13. No preferential recommendation was issued for PCV20 due to the lack of a head to-head trial with PCV15 and the uncertainty of the impact of PCV20 alone.1

Anzi, negli USA PCV15 e PCV20 tendono a imporsi su PCV13 (CDC, Recommendations and Reports / Vol. 72 / No. 3 September 8, 2023)

TABLE 7. Recommendations for use of PCV15 or PCV20 in pneumococcal conjugate vaccine–naïve adults aged ≥19 years — Advisory Committee on Immunization Practices, United States, 2023

Medical indication group	Specific underlying medical condition	Age group, yrs	
		19–64	≥65
None	None	None	1 dose of PCV20 alone, or 1 dose of PCV15 followed by a dose of PPSV23 ≥1 year later*
Underlying medical conditions or other risk factors	Alcoholism Chronic heart disease† Chronic liver disease Chronic lung disease§ Chronic renal failure¶ Cigarette smoking Cochlear implant Congenital or acquired asplenia¶ Congenital or acquired immunodeficiencies¶,** CSF leak Diabetes mellitus Generalized malignancy¶ HIV infection Hodgkin disease¶ Iatrogenic immunosuppression¶,†† Leukemia¶ Lymphoma¶ Multiple myeloma¶ Nephrotic syndrome¶ Sickle cell disease or other hemoglobinopathies¶ Solid organ transplant¶	1 dose of PCV20 alone or 1 dose of PCV15 followed by a dose of PPSV23 ≥1 year later*	1 dose of PCV20 alone or 1 dose of PCV15 followed by a dose of PPSV23 ≥1 year later*

Abbreviations: CSF = cerebrospinal fluid; PCV15 = 15-valent pneumococcal conjugate vaccine; PCV20 = 20-valent pneumococcal conjugate vaccine; PPSV23 = 23-valent pneumococcal polysaccharide vaccine.

…sebbene PCV15 e PCV20 siano in uso solo dal 2021

TABLE 1. Licensed and available pneumococcal vaccines — United States, 2023

Vaccine product	Manufacturer	Trade name	Indications and age groups approved per package insert	No. of ACIP-recommended doses for adults	Year licensed or approved for adults
Polysaccharide					
PPSV23	Merck	Pneumovax23	PPSV23-type pneumococcal disease • Aged ≥50 years and aged ≥2 years who are at increased risk for pneumococcal disease	1–3 doses, depending on age and indications	1983
Conjugate					
PCV13	Pfizer	Prevnar13	PCV13-type IPD and PCV7-type otitis media • Aged 6 weeks through 5 years • PCV13-type IPD • Aged 6–17 years • PCV13-type IPD and pneumonia • Aged ≥18 years	1 dose	2011
PCV15	Merck	Vaxneuvance	PCV15-type IPD • Aged ≥6 weeks	1 dose	2021
PCV20	Pfizer	Prevnar20	PCV20-type IPD and PCV-type otitis • Aged 6 weeks through 5 years • PCV20-type IPD • Aged 6–17 years • PCV20-type IPD and pneumonia • Aged ≥18 years	1 dose	2021

Abbreviations: ACIP = Advisory Committee on Immunization Practices; IPD = invasive pneumococcal disease; PCV7 = 7-valent pneumococcal conjugate vaccine; PCV13 = 13-valent pneumococcal conjugate vaccine; PCV15 = 15-valent pneumococcal conjugate vaccine; PCV20 = 20-valent pneumococcal conjugate vaccine; PPSV23 = 23-valent pneumococcal polysaccharide vaccine.

Le raccomandazioni italiane: piano vaccinale 2017-2019 (Antonelli Incalzi R et al. Vaccines 2021, 9, 1232)

Vaccination / Risk factor	Herpes Zoster	Tdap [a]	MenACWY +MenB	Influenza [b]	PCV+PPSV	*Haemophilus influenzae* type b	MMRV or MMR+V [c]	Hepatitis A	Hepatitis B
Age	≥65 years	≥19 years		≥65 years	≥65 years				
Diabetes	≥50 years		For type I diabetes						
Respiratory diseases	≥50 years								
Cardiovascular diseases	≥50 years								
Immunosuppressive therapy candidate	≥50 years						For varicella only		
Immunodepression (congenital or acquired)							MMR only [d]		
Nephropathy/renal insufficiency									Hemodialysis patients
Asplenia									
Chronic liver disease									
Healthcare worker									
Pregnancy		In the third trimester of pregnancy		At any time during pregnancy					

Recommended

Le raccomandazioni italiane: calendario vaccinale 2022

Fascia di età	Vaccinazione	Obiettivo a medio-termine di copertura vaccinale	Obiettivo a lungo-termine di copertura vaccinale
A 12 mesi	Ciclo completo di rotavirus	≥70%	≥90%
A 24 mesi	3° dose di difterite, tetano, pertosse, poliomielite, epatite B, Hib	≥95%	≥95%
	1° dose di meningococco B	≥95%	≥95%
	1° dose di meningococco ACWY	≥80%	≥90%
	1° dose di varicella	≥95%	≥95%
	1° dose di morbillo parotite rosolia	≥95%	≥95%
	Ciclo completo di pneumococco coniugato (PCV)	≥90%	≥95%
A 36 mesi	2° dose di morbillo parotite rosolia e varicella	≥95%	≥95%
A 6 anni	4° dose difterite, tetano, pertosse, poliomielite	≥95%	≥95%
A 14 anni	Meningococco tetravalente ACWY	≥95%	≥95%
	Ciclo completo di HPV	≥80%	≥95%
	5° dose di Difterite, Tetano, Pertosse, Poliomielite	≥90%	≥90%
	2° dose di Morbillo Parotite Rosolia (recuperi)	≥95%	≥95%
	2° dose di Varicella (recuperi)	≥95%	≥95%
Anziani	Pneumococco (PCV+PPV23)	≥75%	≥75%
	Influenza	≥65%	≥75%
	Herpes Zoster	≥40%	≥50%

Perché PCV13 > PPSV23? Perché dopo un anno?

- Studies have previously evaluated the immunogenicity of sequential administration of 7-valent conjugate vaccine (PCV7) or PCV13 followed by PPSV23 in elder individuals [3–8]. The rationale of this sequential administration of the two vaccines is that the memory B-cells generated by the prior PCV13 vaccination can induce booster responses to 12 shared serotypes after PPSV23 vaccination, although the main B-cell subset in humans involved in the immune response to PCVs is not fully understood.

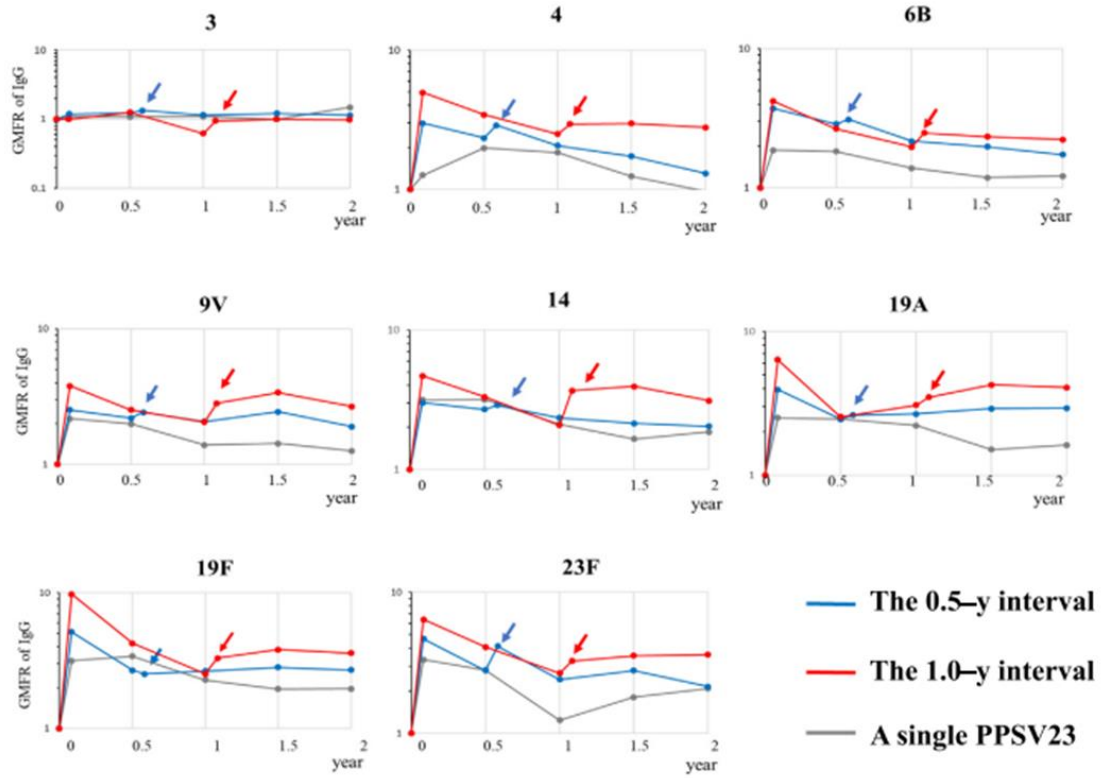


Fig. 2. Comparison of GMFRs of IgG between the 0.5-y and 1.0-y interval groups. Blue line: sequential administration of PCV13 followed by PPSV23 with an interval of 0.5 years; red line: serial administration of PCV13 followed by PPSV23 with an interval of 1 year; gray line: administration of PPSV23 alone. Arrows indicate the time points of 1 month after serial administration of PPSV23. PPSV23, 23-valent pneumococcal polysaccharide vaccine; PCV-13, 13-valent pneumococcal conjugate vaccine; GMFR, geometric mean fold rise; 0.5-y, 0.5-year interval; 1.0-y, 1-year interval. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

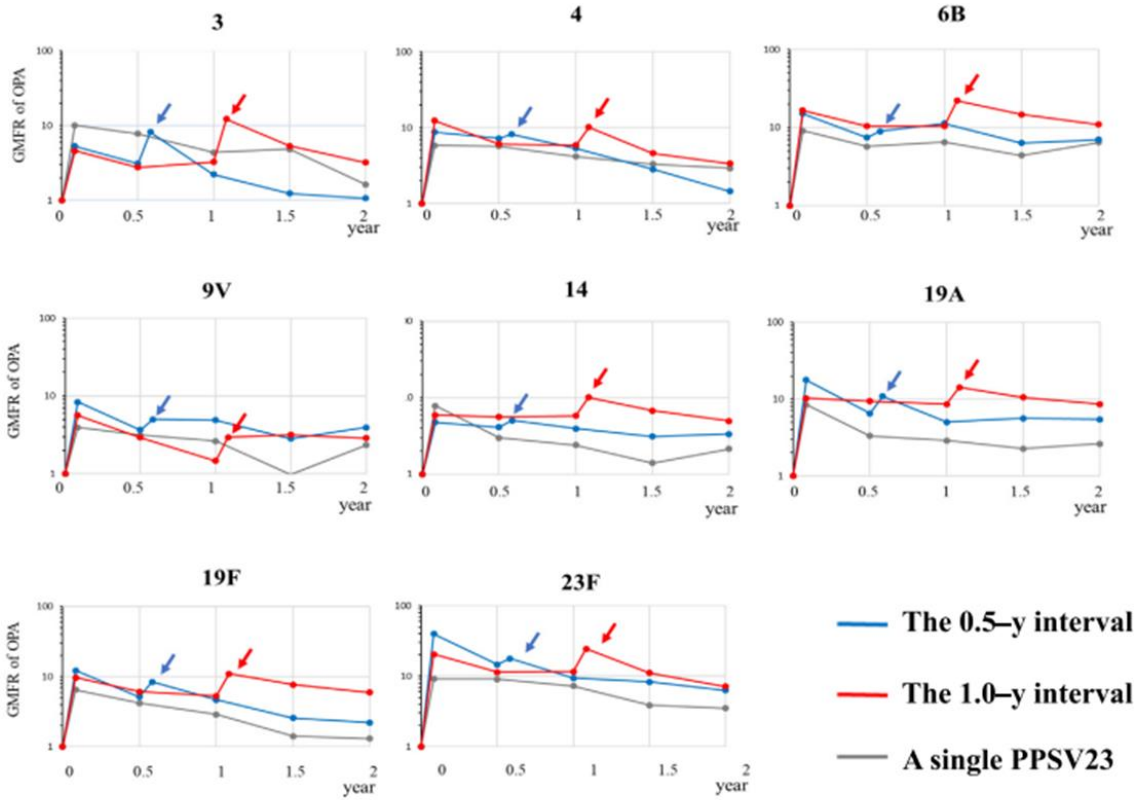


Fig. 3. Comparison of GMFRs of OPA between the 0.5-y and 1.0-y intervals. Blue line: sequential administration of PCV13 followed by PPSV23 with an interval of 0.5 years; red line: serial administration of PCV13 followed by PPSV23 with an interval of 1 year; gray line: administration of PPSV23 alone. Arrows indicate the time points of 1 month after serial administration of PPSV23. PPSV23, 23-valent pneumococcal polysaccharide vaccine; PCV13, 13-valent pneumococcal conjugate vaccine; GMFR, geometric mean fold rise; 0.5-y, 0.5-year interval; 1.0-y, 1-year interval; OPA, opsonophagocytic activity. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

PCV vs PPSV

	PCV	PPSV
Risposta umorale (L B e sintesi Ab)	+	+
Risposta cellulare	+	-
L T stimolo su L B	+	-
L B della memoria	+	+/-
Tipi	PVV13, PCV15, PCV20, (PCV24)	PPSV23

Perché un anno dopo? In sintesi…(Azuma M et al. Vaccine 41 (2023) 1042–1049)

- The present study showed that booster doses of PPSV23 at 1.0-y interval could provide an immunological advantage over those administered at 0.5-y interval. This finding suggests that a shorter interval between PCV13 and PPSV23 led to a low antibody response elicited by PPSV23 vaccination for eight common serotypes. When PPSV23 is administered shortly after PCV13, the anti-polysaccharide antibodies induced by PCV13 may bind to PPSV23 polysaccharide antigens, and the immune complexes formed subsequently may reduce antigen presentation to B-cells and reduce antibody production [16]. We found no difference in the frequencies of adverse events between sequential administration at intervals of 0.5-y and 1.0-y.

Perché non prevedere richiami periodici? (CDC, Recommendations and Reports / Vol. 72 / No. 3 September 8, 2023)

In a more recent systematic review of immunogenicity studies, immune responses were lower with repeat PPSV23 than with the initial vaccination for certain serotypes when the interval between PPSV23 doses was <5 years. …No hyporesponsiveness has been observed in studies which used an interval>5 years….. However, no clinical trials are investigating multiple doses PPSV23 regimens.

A sostegno della scelta del CDC

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www.aginganddisease.org
Volume 10, Number 2; 404-418, April 2019
http://dx.doi.org/10.14336/AD.2018.0512

Review

Efficacy and Safety of the Pneumococcal Conjugate-13 Valent Vaccine in Adults

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ABSTRACT: Invasive pneumococcal disease and pneumococcal pneumonia cause substantial morbidity and mortality in the elderly. This review focuses on the immunogenicity, safety, efficacy and effectiveness data on the use of the 13-valent conjugate pneumococcal vaccine (PCV13) in adults. A MEDLINE literature search was performed from January 1946 to December 2017. Additional references were identified from a review of literature citations. All English-language randomized trials, observational studies and meta-analyses assessing the immunogenicity, efficacy, effectiveness and safety of PCV13 in adults were evaluated. Six randomized controlled studies evaluated immunogenicity and safety of PCV13 in adults and showed that the conjugated vaccine elicited a greater immune response to the majority of the 13 serotypes compared to the 23-valent polysaccharide pneumococcal vaccine (PPV23). Administering PCV13 prior to PPV23 elicits greater immune responses and multiple doses of PCV13 demonstrated modest advantage. PCV13 titers declined after a year but remained above baseline. A randomized clinical trial (CAPiTA) showed that PCV13 was effective in preventing community-acquired pneumonia (CAP) and vaccine-type invasive pneumococcal disease, but not any cause pneumonia. Safety data shows PCV13 elicits minor local reactions, such as pain at the injection site. Major side effects that were commonly reported included muscle fatigue and headache. Both local and systemic adverse events were comparable to PPV23. While PCV13 has a well-established immunogenicity and safety profile in adults, there is sparse data on sequential or multiple dosing, efficacy and effectiveness in adults. As there are few countries who have adopted PCV13 for routine adult immunization, there is a need to evaluate the effectiveness of PCV13 in a real-world setting.

Un modello analitico sviluppato a Hong Kong sostiene la sequenziale PCV13>PPSV23 per costo/efficacia (Shami JJP et al. HUMAN VACCINES & IMMUNOTHERAPEUTICS 2020, VOL. 16, NO. 8, 1937–1944)

Results, summary, and comparison with other studies

In this study, sequential administration of PCV13 followed by PPSV23 has proven to be cost-saving compared to a single dose of PPSV23. The analysis incorporated local demographic, clinical, and economic factors to produce results relevant to Hong Kong. The findings were representative for adults aged 20–64 years with high-risk conditions and older adults aged ≥65 years. The ICER was sensitive to PCV13 vaccine effectiveness in the prevention of inpatient pneumonia, the incidence rate of inpatient pneumonia and inpatient medical costs but the baseline conclusion was robust to variations in all the tested parameters. Nevertheless, cost-effectiveness was maintained even with the variations in ICER.

ICER: incremental cost-effective ratio, defined as incremental cost per QALY gained

La risposta sierologica dei trapiantati di rene a supporto della sequenziale PCV13>PPSV23 (Mulling N et al, Infection 2023)

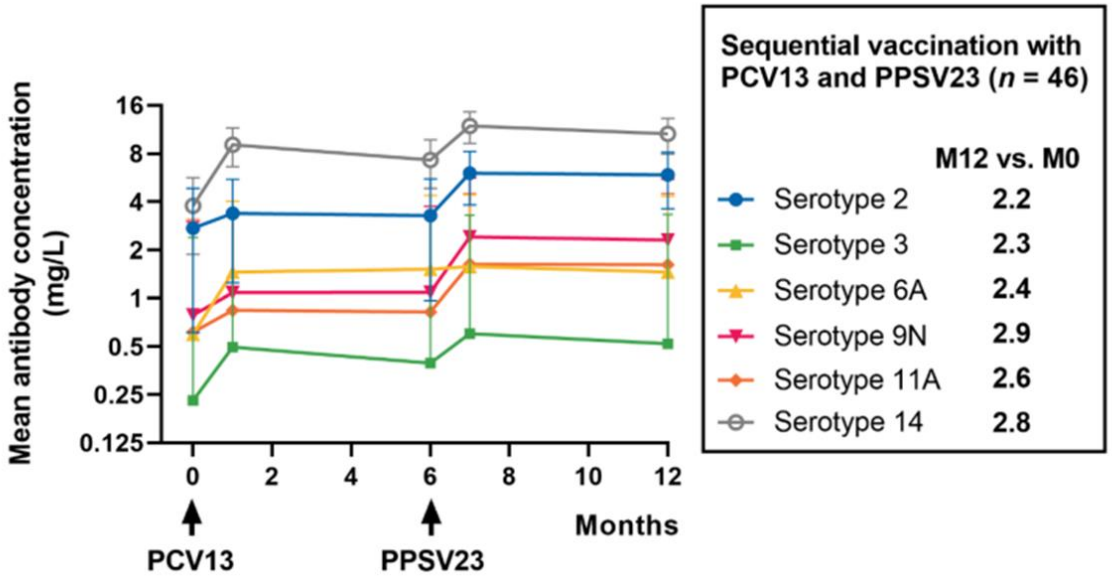
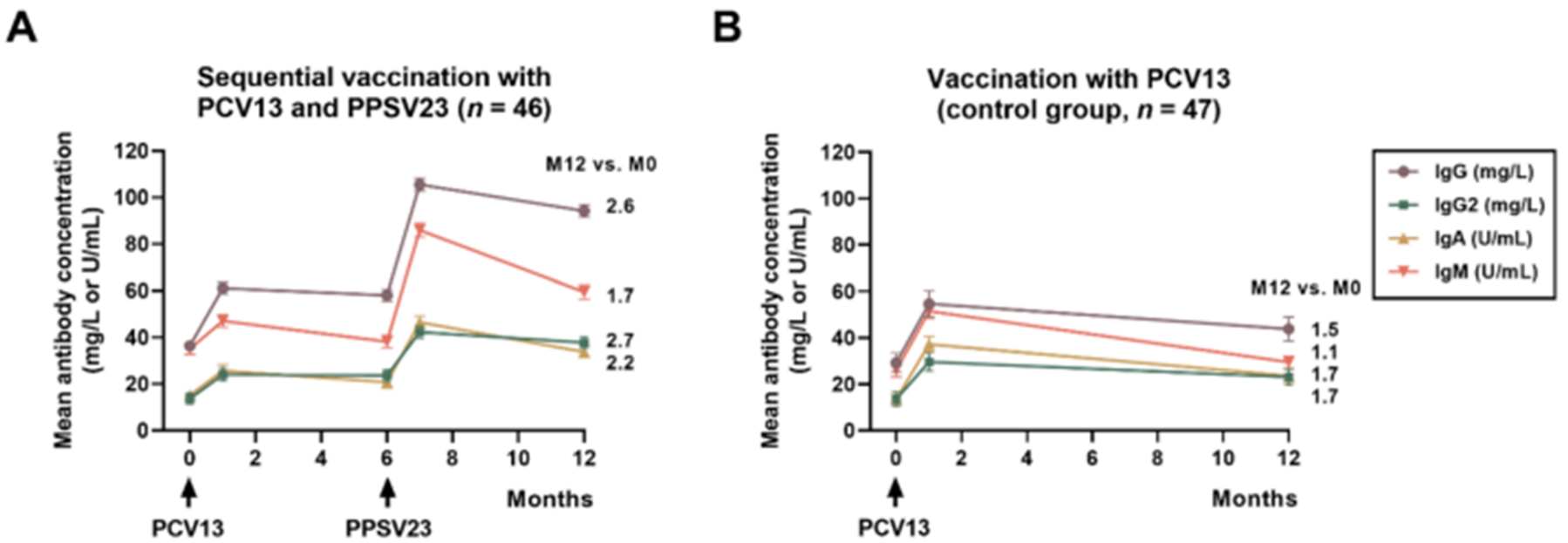


Fig. 3 Concentrations of serotype-specific pneumococcal antibodies in time course of 12 months after first vaccination. Antibodies were determined prior to first vaccination with PCV13 (M0), 1 month after (M1), prior to second vaccination with PPSV23 (M6), at month 7 (M7) and month 12 (M12) thereafter for 46 kidney transplant recipients. Pneumococcal antibodies are given as geometric mean concentration and geometric standard deviation factor. The time of vaccination is indicated by an arrow

La risposta sierologica dei trapiantati di rene a supporto della sequenziale PCV13>PPSV23 (Mulling N et al, Infection 2023)



Invece, un'analisi comparativa in 9 popolazioni (dati osservazionali) depone a favore di PCV13 (Dunne EM et al. Archivos de Bronconeumología 59 (2023) 157–164)

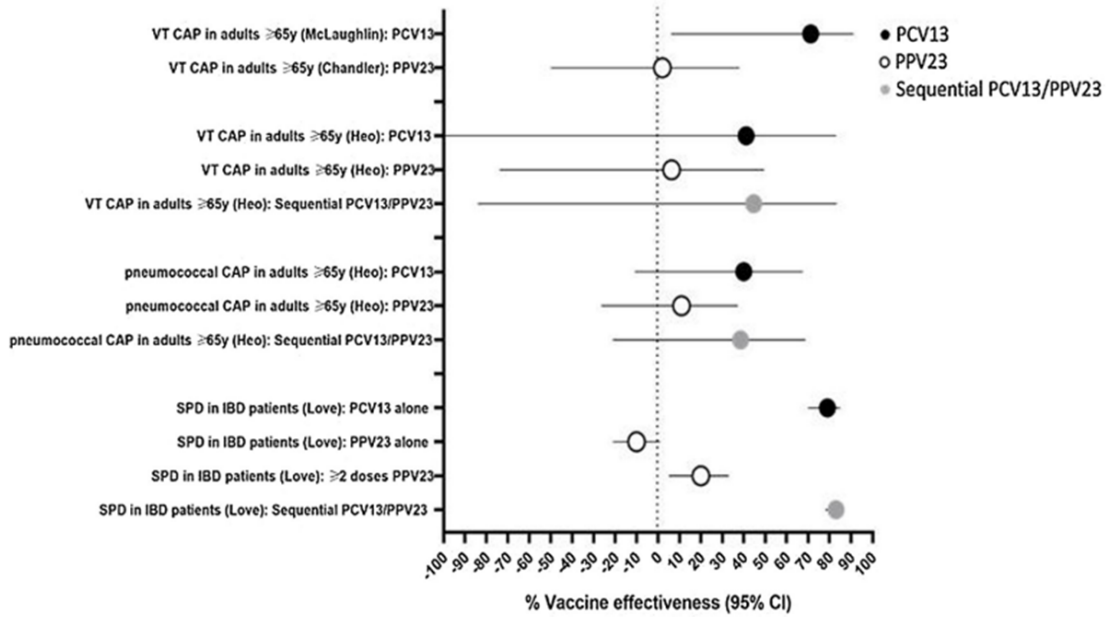


Fig. 2. Vaccine effectiveness against pneumococcal disease outcomes. Results are from studies on pneumococcal community-acquired pneumonia (CAP) in hospitalized adults aged ≥65 years and severe pneumococcal disease (SPD) in inflammatory bowel disease (IBD) patients aged ≥18 years, described in Table 1. For vaccine-type CAP (VT CAP), PCV13 VE assessed PCV13-type CAP, PPV23 VE assessed PPV23-type CAP, and sequential PCV13/PPV23 VE assessed CAP caused by either PCV13 or PPV23 serotypes.

La valutazione di costo/efficacia è funzione della soglia di spesa ammessa per QALY guadagnato (Restivo V et al. Vaccines 2023, 11, 1253)

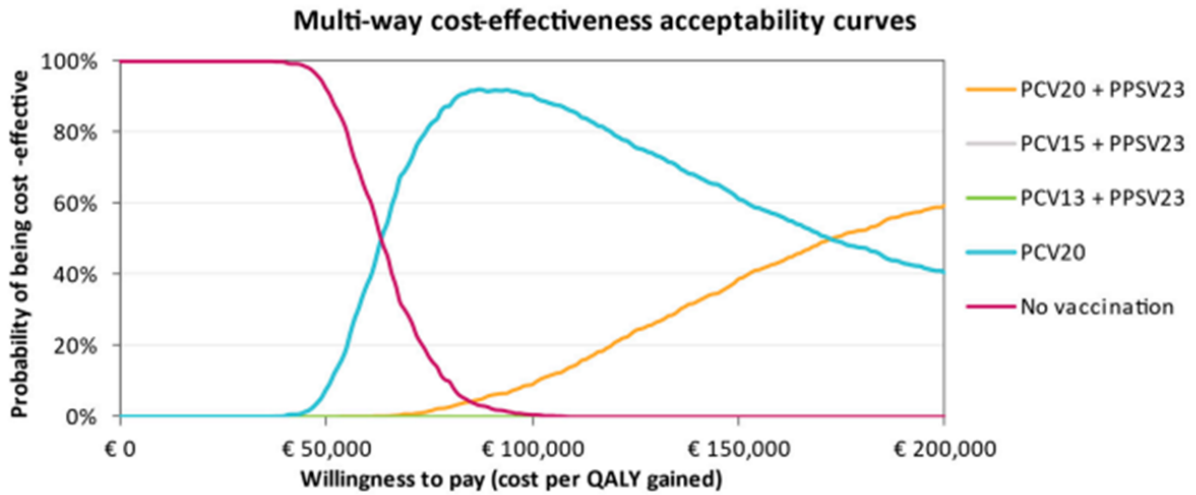


Figure 5. Cost-effectiveness acceptability curve of all vaccination strategies for the low-risk group. Where comparators are seemingly not visible in the CEACs, their probability of being cost-effective is 0%.

Conclusioni

- La sequenziale PCV13>PPSV23 o PCV15>PPSV23 ha ancora solide basi.
- Verosimilmente, è d'elezione in categorie con particolare profilo di rischio, specie immunologico.
- In prospettiva, merita rigoroso confronto con la singola dose PCV20.
- La scelta deve tenere conto del livello di immunità di gregge conseguito grazie a PCV13 nei bambini.
- Gli effetti indiretti nella prevenzione della antibioticoresistenza andrebbero misurati e considerati.
- La disponibilità dei nuovi vaccini implica una continua analisi critica delle raccomandazioni.