Unità di Pediatria ad Alta Intensità di Cura
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34 Congresso Nazionale di
ANTIBIOTICOTERAPIA
in età pediatrica

La prevenzione della patologia pneumococcica nei soggetti a rischio

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LA PREVENZIONE DELLA PATOLOGIA PNEUMOCOCCICA NEI SOGGETTI A RISCHIO

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Il rischio di IPD aumenta in presenza di patologie concomitanti

Patologie di Base (Fattori di rischio) [1-6]

- **Immunocompromissione**
  - Diabete Mellito
  - Immunodeficienza congenita o acquisita (compreso HIV)
  - Neoplasie ematologiche o generalizzate
  - Trapianto ematopoietico
  - Terapia immunosoppressiva (compresi corticosteroidi sistemici)
- **Organo-correlate**
  - Asplenia anatomica o funzionale
  - Malattie croniche di cuore, polmoni, fegato e reni
  - Perdita di liquido cerebrospinale
  - Trapianto d'organo
- **Legati allo stile di vita**
  - Alcolismo
  - Fumo
- **Altro**
  - Impianto cocleare

1. Butler JC *et al.* Epidemiology of pneumococcal infections in the elderly. Drugs Aging. 1999;15 Suppl 1:11-9. 2. Centers for Disease Control and Prevention. MMWR. Prevention of Pneumococcal Disease. ACIP Recommendations 1997;46:RR–8. 3. World Health Organization. 23-valent pneumococcal polysaccharide vaccine. WHO position paper. Wkly Epidemiol Rec. 2008;83:373-384. 4. Centers for Disease Control and Prevention. MMWR Recommendations and Reports. Preventing Pneumococcal Disease Among Infants and Young Children. 2000;49 (RR-9):1–35. 5. Centers for Disease Control and Prevention. MMWR. Recommended Adult Immunization Schedule 2009;57:Q1–Q4. http://www.cdc.gov/mmwr/preview/mmwrhtml/ mm5753a6.htm. Accessed May 26 2011. 6. Centers for Disease Control and Prevention. Epidemiology and Prevention of Vaccine Preventable Diseases. The Pink Book. 11th Edition. May 2009.

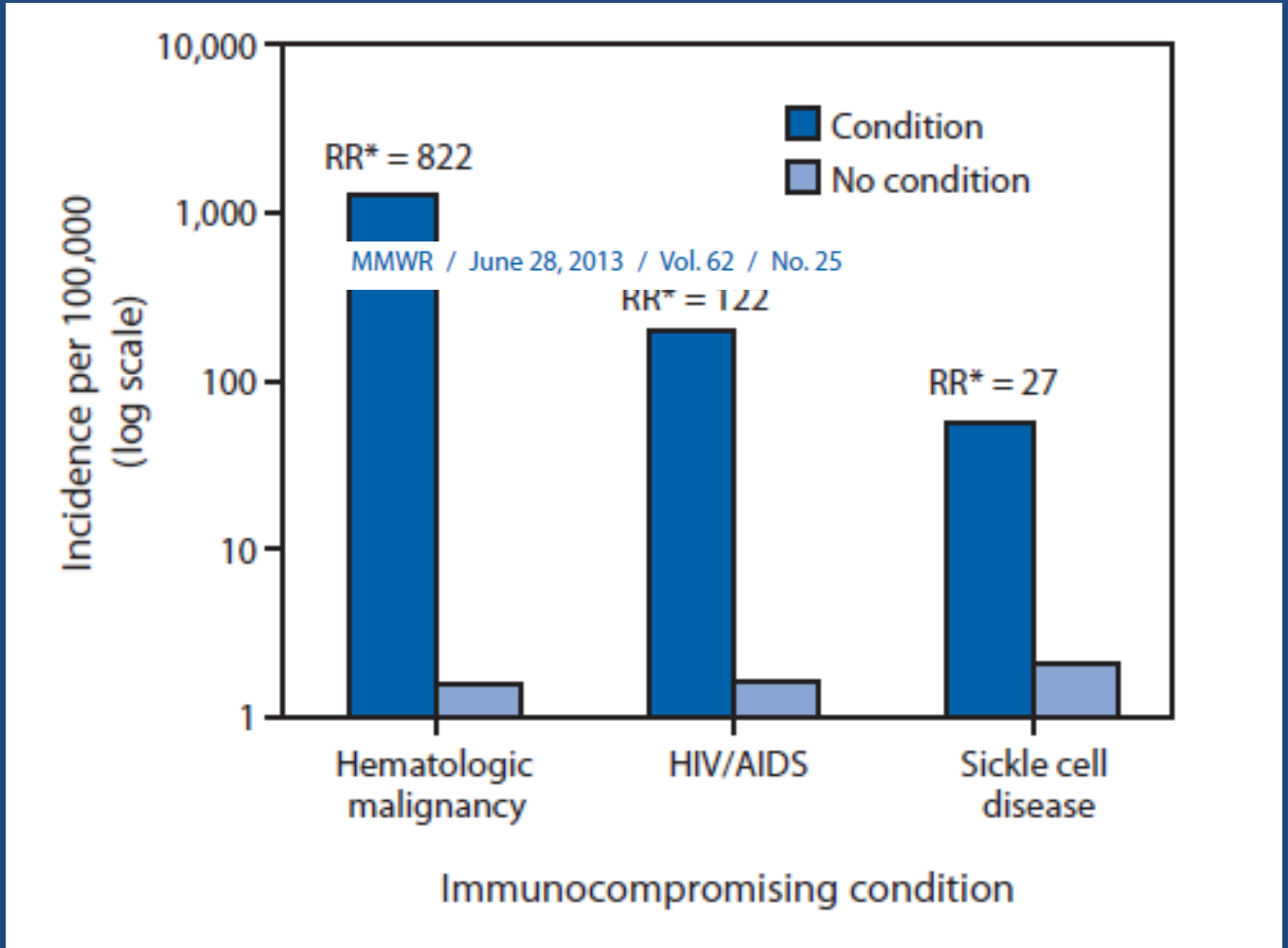
The observed number of cases, the odds ratio comparing the risk groups and the non-risk groups, and the estimated annual incidence of IPD per 100,000 in 2008-2009 in England

(From van Hoek AJ et al., J Infect 2012)

Age group	2–15 years		
	n	Odds ratio	Incidence
No risk group	1246	1	3.9
One or more risk factors	261	11.7 (10.2–13.3)	46 (40–52)
Asplenia/splenic dysfunction	11	4.7 (2.6–8.5)	19 (10–34)
Chronic respiratory disease	19	12.7 (8.1–20.0)	50 (32–79)
Chronic heart disease	48	4.1 (3.1–5.5)	16 (12–22)
Chronic kidney disease	33	11.7 (8.3–16.6)	46 (33–65)
Chronic liver disease	9	29.6 (15.3–57.2)	117 (60–226)
Diabetes	9	3.8 (2.0–7.3)	15 (8–29)
Immunosuppression	174	41.0 (35.0–48.0)	162 (138–189)
HIV infection	6	100.8 (44.7–227.2)	398 (176–896)

Annual average incidence of PCV13 type IPD in children aged 6-18 years, with and without selected underlying immunocompromising conditions – USA 2007-2009

(From CDC. MMWR, June 28, 2013)



Population at risk of IPD according to risk factors and age groups in Latin America

(From Falleiros-Arlant LH et al., Int J Infect Dis 2015)

Prevalence (%)	Age group (years)						Total population under risk (0-19)	Total population under risk (5-19)	Ref.
	0 – 4	5 – 9	10 – 14	15 – 19	0 – 19	5-19			
Total population	52,247,302	53,313,660	55,130,977	54,505,497	215,197,435	162,950,134	23,427,783 – 85,541,780	17,340,529 – 64,586,955	CELADE 2013[17]
Asthma[a]	10 – 31.2	10 – 31.2	8.5 – 30.5	8.5 – 30.5	10 – 31.2/8.5 – 30.5	10 – 31.2/8.5 – 30.5	19,875,196 – 66,374,145	14,650,466 – 50,072,986	Chong Neto 2012[18]
Renal diseases (dialysis)[b]	0.05	0.05	0.05	0.05	0.05	0.05	107,599	81,475	Sesso 2012[19]
Diabetes type 2[c]	1.2 – 8.0	1.2 – 8.0	1.2 – 8.0	1.2 – 8.0	1.2 – 8.0	1.2 – 8.0	2,582,369 – 17,215,795	1,955,402 – 13,036,011	Aschner 2002[20]
Sickle cell disease	0.00085 – 0.257	0.00085 – 0.257	0.00085 – 0.257	0.00085 – 0.257	0.00085 – 0.257	0.00085 – 0.257	1,829 – 553,057	1,385 – 418,782	Lervolino 2011[21]
HIV[e]	0.4 – 0.6	0.4 – 0.6	0.4 – 0.6	0.4 – 0.6	0.4 – 0.6	0.4 – 0.6	860,790 – 1,291,185	651,801 – 977,701	WHO 2012[22]

[a] Prevalence refers to 6-7 years and 13-14 years age groups in South America (lower limit, Bogota; upper limit, São Paulo West).

[b] Prevalence calculated from the information provided by the Brazilian census of chronic dialysis.

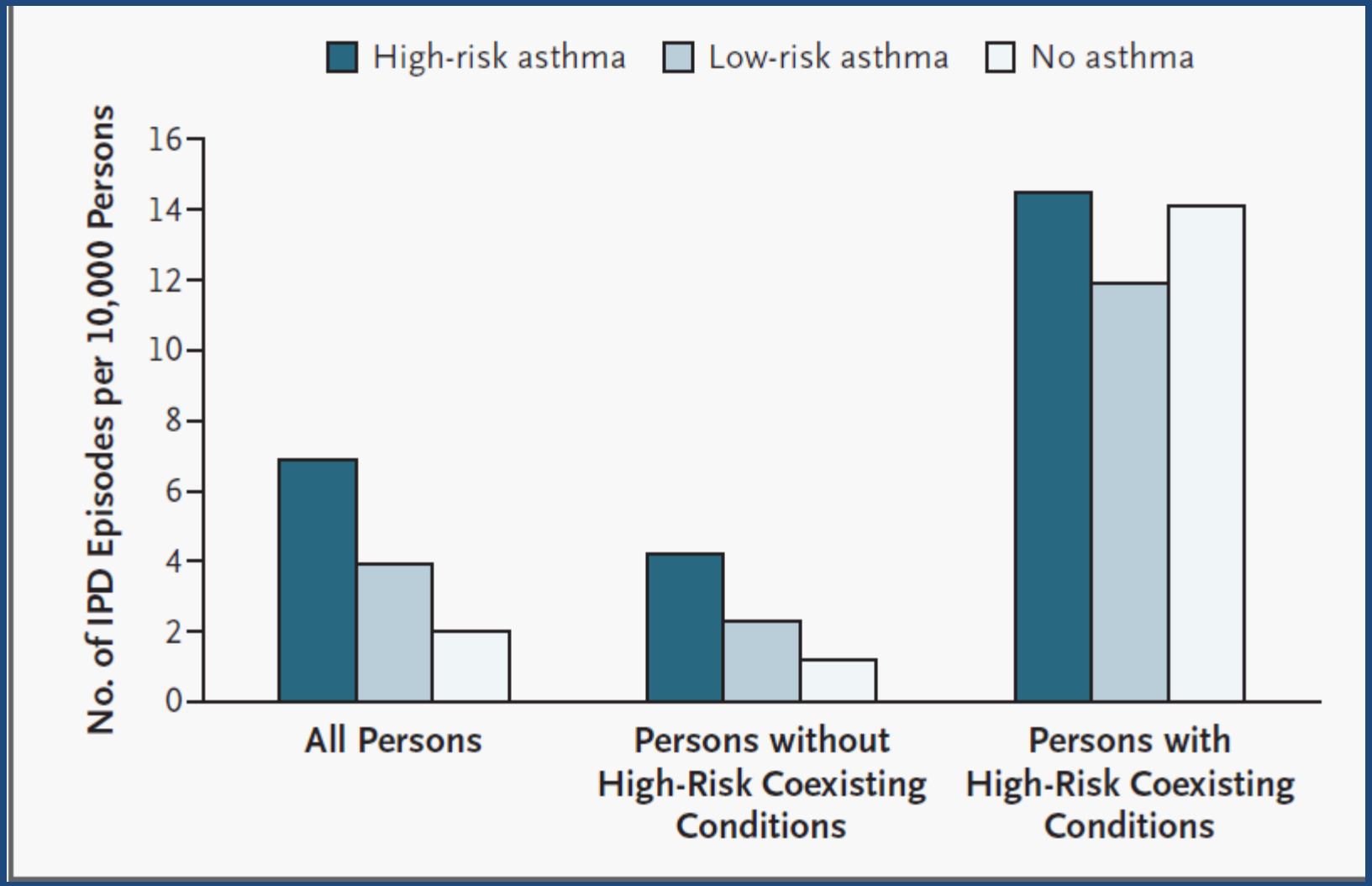
[c] The prevalence of type 2 diabetes in children and adolescents up to 15 years old in Latin America was considered.

[d] The prevalence of sickle cell disease at birth in Brazil was considered.

[e] Prevalence for the entire Latin America population, 15-49 years old.

Incidence of IPD in patients with asthma

(From Talbot MR et al., NEJM 2005)



Ragioni addotte per spiegare la maggiore incidenza di patologia pneumococcica negli asmatici

A) Modificazioni anatomico-funzionali dell'albero respiratorio indotte dalla flogosi cronica

B) Riduzione delle difese indotta dalla terapia steroidea

C) Immunocompromissione primitiva degli asmatici o, genericamente, dei soggetti atopici

Colonization at the first month of life in relation to asthma diagnosis, lung function and allergy

(From Bisgaard H et al., NEJM 2007)

Outcome	Colonized	Not Colonized	Odds Ratio (95% CI)	Percent Estimated Difference (95% CI)*
Asthma at 5 yr (no.)				
Yes	17	20	4.57 (2.18 to 9.57)	
No	35	188		
Specific IgE at 4 yr (no.)				
>0.35 kU/liter	15	49	1.28 (0.65 to 2.54)	
≤0.35 kU/liter	36	151		
Mean postbronchodilator specific airway resistance at 5 yr (kPa·sec·liter^{-1})†	0.94	1.00		−7 (−13 to 1)
Reversibility of specific airway resistance after β_2-agonist inhalation at 5 yr (%)‡	−23	−18		5 (0 to 10)
Blood eosinophil count at 4 yr (×10^{-9}/liter)§	0.42	0.29		31 (6 to 62)
Total IgE at 4 yr (kU/liter)¶	90	60		47 (1 to 115)

* Relative differences are given, except for reversibility of specific airway resistance after β_2-agonist inhalation, for which absolute differences are given. Estimated relative differences were calculated as the ratio of geometric means for the colonized and not colonized groups.
† Of 213 infants, 39 were colonized and 174 were not colonized.
‡ Of 213 infants, 39 were colonized and 174 were not colonized.
§ Of 239 infants, 47 were colonized and 192 were not colonized.
¶ Of 248 infants, 49 were colonized and 199 were not colonized.

Association between daily use (*) of corticosteroids and risk of colonization with *S. pneumoniae* among children with asthma

(From Zhang L et al., Respirology 2013)

Type of analysis	Prevalence of colonization by *S. pneumoniae*, *n*/*N* (%)		*P*-value	PR for colonization (95% CI, *P*-value)	
	Exposed group	Non-exposed group		Crude	Adjusted
All patients ($n = 192$)	26/96 (27.1%)	8/96 (8.3%)	0.001[†]	3.25 (1.47–7.18, $P = 0.004$)	3.75 (1.72–8.18, $P = 0.001$)[§]
Sensitivity analyses					
Excluding patients younger than 2 years ($n = 154$)	22/77 (28.6%)	7/77 (9.1%)	0.002[†]	3.14 (1.34–7.36, $P = 0.008$)	3.43 (1.50–7.81, $P = 0.003$)[¶]
Excluding patients with intermittent asthma ($n = 143$)	26/96 (27.1%)	3/47 (6.4%)	0.004[‡]	4.24 (1.28–14.02, $P = 0.018$)	6.23 (1.50–25.92, $P = 0.012$)[¶]

[†] Chi-square test.

[‡] Fisher's exact test.

[§] Model 1—PR adjusted for gender, race, household size, number of siblings, attending day-care facilities/school, maternal smoking, concomitant use of intranasal steroids, vaccination against *S. pneumoniae*, antibiotic use in the last 3 months and hospitalization in the last 6 months.

[¶] Model 2—model 1 plus adjustment for age.

CI, confidence interval; PR, prevalence ratio.

(*) A mean dose of 400 g of beclomethasone or equivalent for at least 30 days (mean duration 8.6 months)

Subjects Variables	All subjects Unadjusted OR for SPD (95% CI), *P* value	 Adjusted OR for SPD (95% CI), *P* value
Atopic conditions		
No	Referent	Referent
Yes	1.98 (1.11-3.55), $P = .02$	2.13 (1.04- 4.35), $P = .04$
Ethnicity		
Caucasian	Referent	Referent
Non-Caucasian	2.50 (0.99-6.33), $P = .05$	3.88 (1.34-11.27), $P = .01$
Tobacco smoke exposure at index date		
Active	Referent	Referent
Passive	1.76 (0.60-5.13), $P = .30$	1.80 (0.52-6.19), $P = .35$
Nonsmokers	0.31 (0.18-0.52), $P < .001$	0.28 (0.15-0.51), $P < .001$
High-risk conditions (before index date)		
No	Referent	Referent
Yes	7.31 (3.96-13.47), $P < .001$	8.27 (4.19-16.31), $P < .001$
Educational status*		
<High school education	Referent	Referent
High school graduate	0.69 (0.38-1.25), $P = .22$	0.85 (0.42-1.75), $P = .66$
Some college education	0.33 (0.14-0.76), $P = .01$	0.31 (0.12-0.78), $P = .01$
College graduate	0.70 (0.35-1.41), $P = .32$	0.85 (0.37-1.96), $P = .70$

*For children, parents' educational status was used.[32,33]

The association between atopic conditions other than asthma (*) and serious pneumococcal disease

(From Jung JA et al., J Allergy Clin Immunol 2010)

(*) atopic dermatitis, allergic rhinitis hay fever

PNEUMOCOCCAL CARRIAGE IN ASTHMATIC CHILDREN

(Esposito S et al., BMC Infect Dis 2015 in press)

	Carriers (n=192) n (%)	Non-carriers (n=231) n (%)	Crude OR (95% CI)	OR (95% CI)[a]
Age				
<10	93 (48.4)	83 (35.9)	1 (reference)	1 (reference)
10-14	90 (46.9)	117 (50.6)	0.69 (0.46-1.03)	0.69 (0.46-1.04)
≥15	9 (4.7)	31 (13.4)	0.26 (0.12-0.58)	0.25 (0.11-0.56)
Gender				
Male	136 (70.8)	164 (71.0)	1 (reference)	1 (reference)
Female	56 (29.2)	67 (29.0)	1.01 (0.66-1.54)	0.94 (0.61-1.45)
Siblings[b]				
No	46 (24.2)	54 (23.5)	1 (reference)	1 (reference)
Yes	144 (75.8)	176 (76.5)	0.96 (0.61-1.51)	0.96 (0.61-1.53)
Parental smoking habit				
Both non-smokers	119 (62.0)	157 (68.0)	1 (reference)	1 (reference)
At least one smoker	73 (38.0)	74 (32.0)	1.30 (0.87-1.95)	1.36 (0.90-2.07)
Asthma type				
Intermittent	40 (20.8)	34 (14.7)	1 (reference)	1 (reference)
Mild, persistent	64 (33.3)	80 (34.6)	0.68 (0.39-1.19)	0.66 (0.37-1.17)
Moderate, persistent	79 (41.1)	103 (44.6)	0.65 (0.38-1.12)	0.67 (0.38-1.18)
Severe, persistent	9 (4.7)	14 (6.1)	0.55 (0.21-1.42)	0.59 (0.22-1.57)
Systemic corticesteroid therapy (previous 3 mos)[b]				
No	158 (84.0)	194 (85.8)	1 (reference)	1 (reference)
Yes	30 (16.0)	32 (14.2)	1.15 (0.67-1.98)	1.03 (0.59-1.81)
Antibiotic therapy (previous 3 months)[b]				
No	171 (90.5)	184 (81.8)	1 (reference)	1 (reference)
Yes	18 (9.5)	41 (18.2)	0.47 (0.26-0.85)	0.41 (0.22-0.76)
Respiratory relapses (previous 3 months)[b]				
No	144 (76.2)	159 (70.3)	1 (reference)	1 (reference)
Yes	45 (23.8)	67 (29.7)	0.74 (0.48-1.15)	0.70 (0.45-1.10)
Asthma under control[b]				
No	33 (17.5)	54 (23.9)	1 (reference)	1 (reference)
Yes	156 (82.5)	172 (76.1)	1.48 (0.91-2.41)	1.41 (0.86-2.31)

Vicious Circle Hypothesis

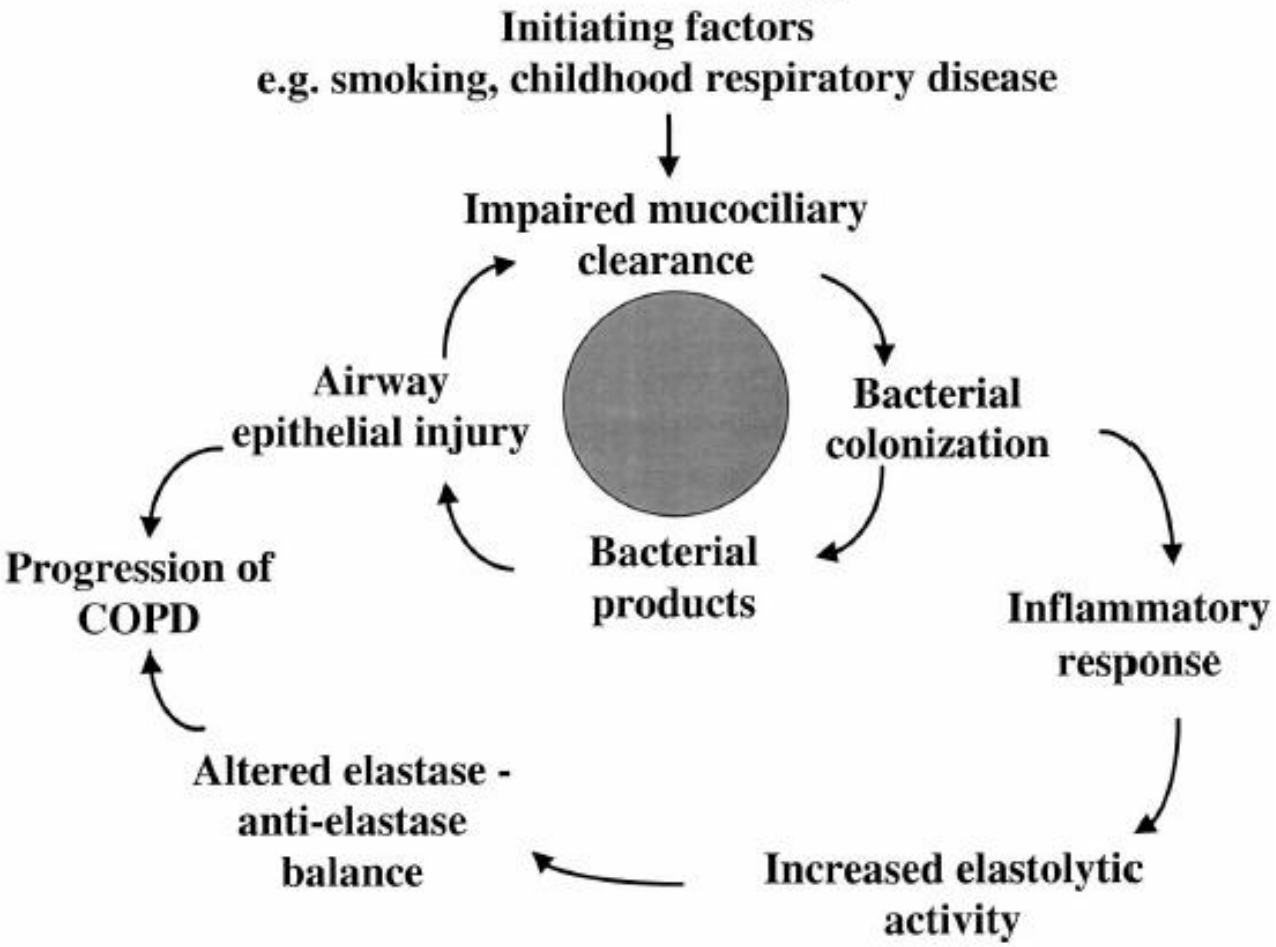


FIGURE 1. Schematic diagram of the vicious circle hypothesis of the role of bacterial colonization in the progression of COPD.

	Carriers (n = 42)	Non-carriers (n = 170)	OR (95% CI)[a]
Age			
<10	18 (42.9)	45 (26.5)	1 (reference)
10–14	18 (42.9)	84 (49.4)	0.42 (0.18–0.95)
≥15	6 (14.3)	41 (24.1)	0.16 (0.04–0.60)
Sex			
Male	22 (52.4)	80 (47.1)	1 (reference)
Female	20 (47.6)	90 (52.9)	0.93 (0.43–1.98)
Siblings[b]			
No	11 (29.0)	46 (27.9)	1 (reference)
Yes	27 (71.0)	119 (72.1)	1.27 (0.54–2.98)
Parental smoking habit[b]			
Both non-smokers	25 (65.8)	108 (63.9)	1 (reference)
At least one smoker	13 (34.2)	61 (36.1)	0.92 (0.42–2.04)
Hospitalization (last 3 months)[b]			
No	15 (35.7)	48 (28.4)	1 (reference)
Yes	27 (64.3)	121 (71.6)	0.79 (0.36–1.77)
Systemic antibiotic therapy (last 3 months)[b]			
No	38 (90.5)	104 (61.9)	1 (reference)
Yes	4 (9.5)	64 (38.1)	0.23 (0.07–0.69)
Antibiotic inhalation therapy (last 3 months)[b]			
No	37 (88.1)	109 (64.9)	1 (reference)
Yes	5 (11.9)	59 (35.1)	0.26 (0.08–0.77)
Steroid therapy (last 3 months)[b]			
No	37 (88.1)	145 (85.8)	1 (reference)
Yes	5 (11.9)	24 (14.2)	0.96 (0.30–3.09)
The main bacteria at the last expectoration control[b]			
None	4 (9.8)	12 (7.1)	1 (reference)
Staphylococcus aureus	26 (63.4)	96 (56.8)	1.22 (0.24–6.17)
Haemophilus influenzae/ parainfluenzae	7 (17.1)	20 (11.8)	2.10 (0.35–12.6)
Pseudomonas aeruginosa	0 (0.0)	27 (16.0)	NE
Others	4 (9.8)	14 (8.3)	1.20 (0.17–8.50)
Vitamin D level[b]			
<30 ng/mL	18 (81.8)	42 (64.6)	1 (reference)
≥30 ng/mL	4 (18.2)	23 (35.4)	0.35 (0.08–1.49)

PNEUMOCOCCAL CARRIAGE IN CHILDREN AND ADOLESCENTS WITH CYSTIC FIBROSIS

(Esposito S et al., J Cyst Fibros 2015)

Diabete mellito
Perché un fattore di rischio per PD?

Nei soggetti affetti da diabete mellito, le infezioni batteriche e virali sono fonte di un considerevole incremento della morbosità e della mortalità [1]

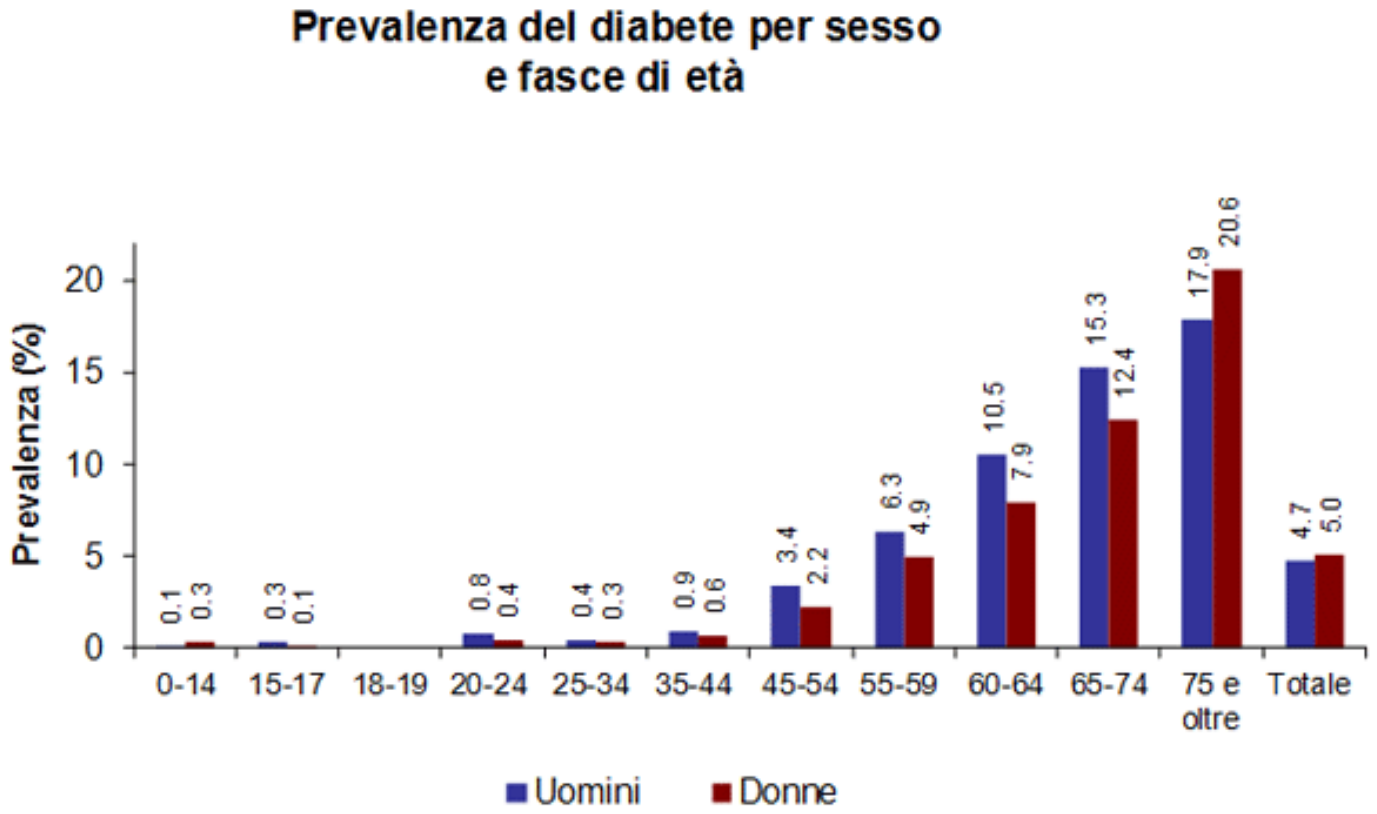
Questo rischio è stato attribuito alle alterazioni genetiche e metaboliche che si verificano in questi pazienti, in primo luogo allo scarso controllo glicemico e all'acidosi [1]

Sono state evidenziate alterazioni della risposta immunitaria cellulo-mediata (e di quella umorale correlata) come:

- riduzione del rapporto linfociti CD4+/CD8+
- alterazioni nella funzionalità dei linfociti NK
- ridotta blastogenesi linfociti
- riduzione dell'attività fagocitica dei monociti
- difetti nella produzione di IL-2 [1]

1. Smith SA, Poland GA. Diabetes Care 2000;23: 95–108

Diabete mellito e prevalenza in Italia



La prevalenza del diabete aumenta con l'età fino a raggiungere il 19,5% nelle persone con età uguale o superiore ai 75 anni [1]

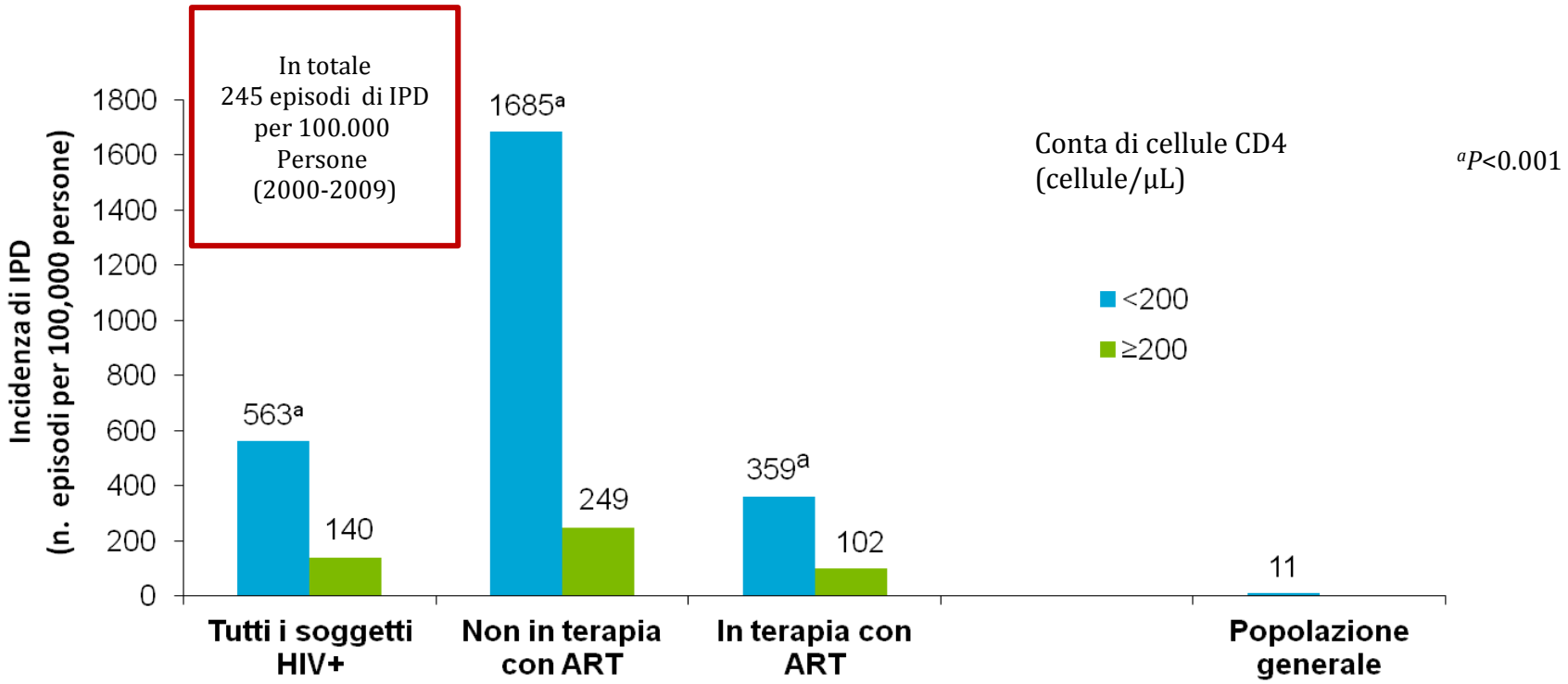
1. http://www.epicentro.iss.it/igea/PrimoPiano/prevalenza.asp

PNEUMOCOCCAL CARRIAGE IN CHILDREN AND ADOLESCENTS WITH DIABETES

(Esposito S et al., Hum Vaccin Immunother 2015 in press)

	Carriers (n=148)	Non-carriers (n=151)	OR (95% CI) Univariate	OR (95% CI)[a] Multivariate
Age (years)				
<10	38 (25.7)	24 (15.9)	1 (reference)	1 (reference)
10-14	83 (56.1)	72 (47.7)	0.73 (0.40-1.33)	0.66 (0.35-1.23)
≥15	27 (18.2)	55 (36.4)	0.31 (0.16-0.62)	0.28 (0.14-0.57)
Sex				
Male	87 (58.8)	66 (43.7)	1 (reference)	1 (reference)
Female	61 (41.2)	85 (56.3)	0.54 (0.34-0.86)	0.56 (0.35-0.91)
Ethnicity				
Caucasian	141 (95.3)	135 (89.4)	1 (reference)	1 (reference)
Non-Caucasian	7 (4.7)	16 (10.6)	0.42 (0.17-1.05)	0.34 (0.13-0.89)
Siblings[b]				
No	35 (23.6)	32 (21.5)	1 (reference)	1 (reference)
Yes	113 (76.3)	117 (78.5)	0.88 (0.51-1.52)	0.97 (0.55-1.72)
Parental smoking habit				
Both non-smokers	94 (63.5)	113 (74.8)	1 (reference)	1 (reference)
At least one smoker	54 (36.5)	38 (25.2)	1.71 (1.04-2.81)	1.76 (1.04-2.97)
Antibiotic therapy (last 3 months)[b]				
No	141 (96.6)	131 (87.3)	1 (reference)	1 (reference)
Yes	5 (3.4)	19 (12.7)	0.24 (0.09-0.67)	0.21 (0.07-0.62)
Other therapies (last 3 months)[b]				
No	131 (89.1)	133 (88.7)	1 (reference)	1 (reference)
Yes	16 (10.9)	17 (11.3)	0.96 (0.46-1.97)	0.94 (0.44-2.00)
Concurrent endocrinological disease[b]				
No	136 (92.5)	136 (91.3)	1 (reference)	1 (reference)
Yes	11 (7.5)	13 (8.7)	0.85 (0.37-1.96)	0.91 (0.38-2.19)

Pazienti HIV+



- L'incidenza annuale media di IPD tra gli adulti HIV+ era 245 di episodi per 100.000, >20 volte rispetto alla popolazione adulta generale.
- L'incidenza di IPD era significativamente più alta con una conta CD4 <200 cellule/µL, in particolare se non ricevevano terapia ART.
- Anche con una conta di cellule CD4 >200 cellule/µL e con terapia ART, il tasso rimaneva ben al di sopra rispetto a quello della popolazione generale.

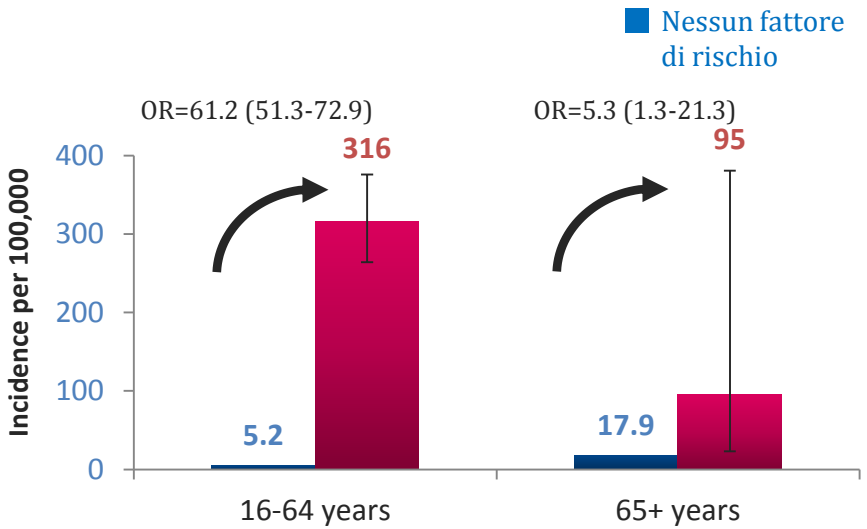
Yin Z et al. *Invasive pneumococcal disease among HIV-positiveindividuals, 2000–2009 AIDS.* 2012;26(1):87–94.

L'infezione da HIV aumenta il rischio e la mortalità per IPD nei pz HIV[1]

In 22.298 pazienti di tutte le età, Inghilterra, 2008-2009 [1]

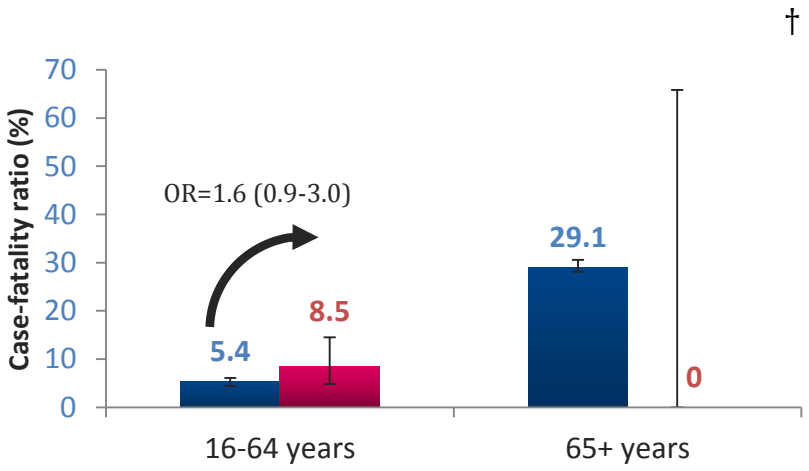
IPD incidence [1]

Stima di incidenza annuale di per 100,000 nel 2008-2009 e odds ratio (OR) in gruppi a rischio e gruppi non a rischio[1]



Case-fatality ratio di IPD [1**]

Case-fatality ratio per età e fattore di rischio, e odds ratio (OR) in gruppi a rischio con IPD e gruppi non a rischio [1]



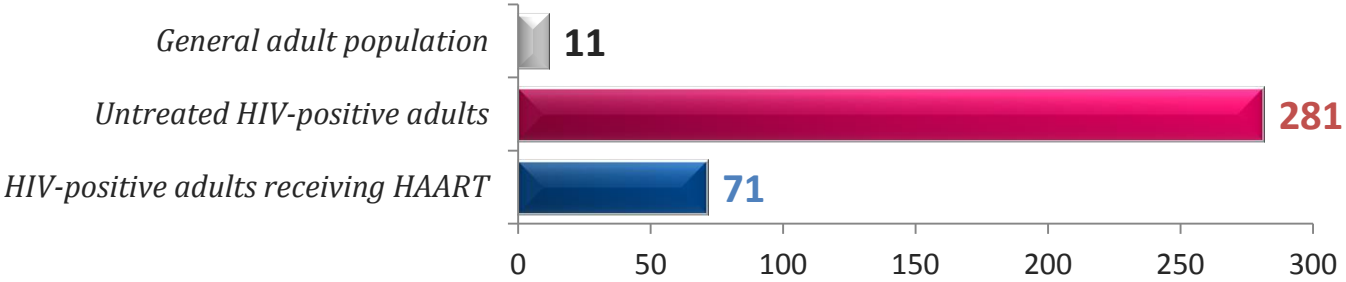
1. van Hoek AJ *et al.* J Infect. 2012 Jul;65(1):17-24. 2.

† Il case-fatality ratio è 0% in adulti 65+ per il basso numero di soggetti HIV+ in questa popolazione.
‡ A population of 130 patients aged 16-64 years and 2 patients aged 65+ years with HIV infection, England, 2008-2009.

L'infezione da HIV aumenta il rischio e la mortalità per IPD negli adulti[1-3]

- La polmonite batterica, in particolare quella pneumococcica e le sue complicanze invasive, rimane una importante causa di morbosità e mortalità in pazienti con infezione da HIV [4]

Incidenza di IPD in adulti con infezione da HIV da 15 o più anni [1]

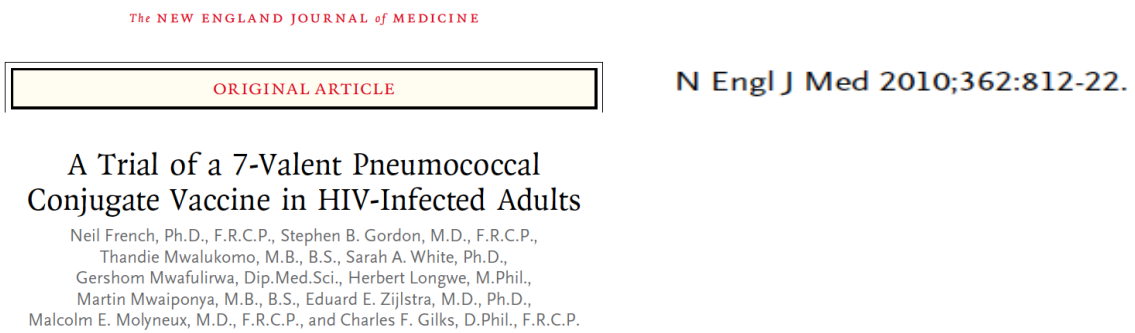


Incidenza annuale media per 100,000 in England e Galles (2000/2009, post-HAART era)

L'incidenza di IPD è più bassa in pazienti trattati con terapia antiretrovirale (Highly-Active Antiretroviral Therapy - HAART) rispetto ai pazienti non trattati, ma rimane più alta rispetto alla popolazione generale [1,4-7]

1. Yin Z *et al.* AIDS 2012;26:87-94. 2. Jordano *et al.* Clin Infect Dis 2004:1623-8. 3. Van Hoek AJ *et al.* J Infection 2012;65(1):17–24. 4. Feikin DR *et al.* Lancet Infect Dis. 2004;4(7):445-55. 5. Burgos J *et al.* J AIDS 2012;59:31-38. 6. Grau I *et al.* Arch Intern Med 2005;165:1533-1540. 7. Heffernan RT *et al.* J Infect Dis. 2005;191(12):2038-45

A trial of PCV7 in HIV-infected adults [1]



Study design and population [1]**:** double-blind, randomized (1:1), placebo-controlled clinical efficacy trial among predominantly (88%) HIV-infected adolescents and adults (n= 496) who recovered from documented IPD

Period: February 2003 – May 2007

Schedule: two doses of PCV7, given 4 weeks apart

Primary outcome: a further episode of pneumococcal infection by VT serotypes or serotype 6A

1. French N *et al.* N Engl J Med. 2010;362:812-822.

A trial of PCV7 in HIV-infected adults [1]

Study results

PCV7† efficacy results	
Vaccine serotype IPD or serotype 6A	74% (30%, 90%)*
All-cause pneumonia	25% (-19%, 53%)*

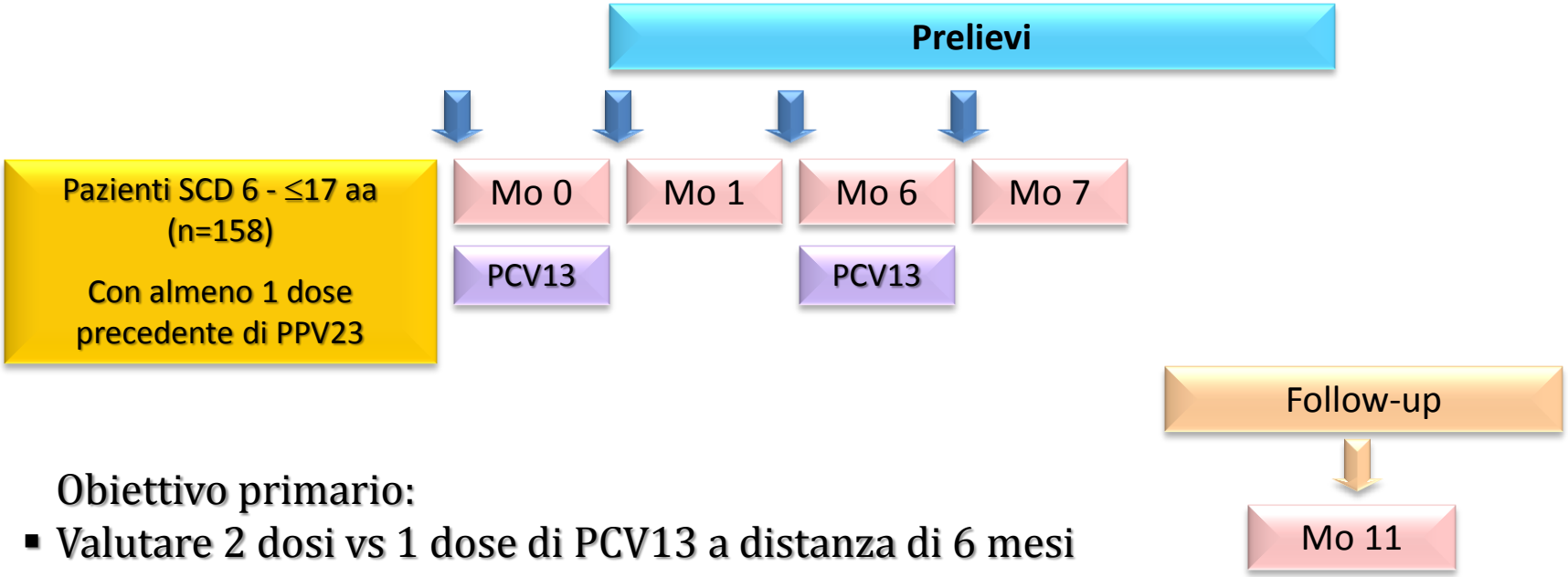
"PCV7 protects HIV-infected adults from recurrent IPD of vaccine serotype or serotype 6A" [1]

The number of serious adverse events within 14 days after vaccination was significantly lower in the vaccine group than in the placebo group (3 vs. 17, P = 0.002), and the number of minor adverse events was significantly higher in the vaccine group (41 vs. 13, P = 0.003).[1]

† PCV7(Two doses given 4 weeks apart.): n = 248 (HIV+, n = 220); placebo: n = 248, (HIV+ n = 219)
* 95% CI

1. French N *et al.* N Engl J Med. 2010;362:812-822.

Studio 6096A1-3014 SCD
(Sickle Cells Disease, anemia a cellule falciformi)
Popolazione pre-vaccinata con PPV23 (Età 6 - ≤ 17y)



Obiettivo primario:

- Valutare 2 dosi vs 1 dose di PCV13 a distanza di 6 mesi

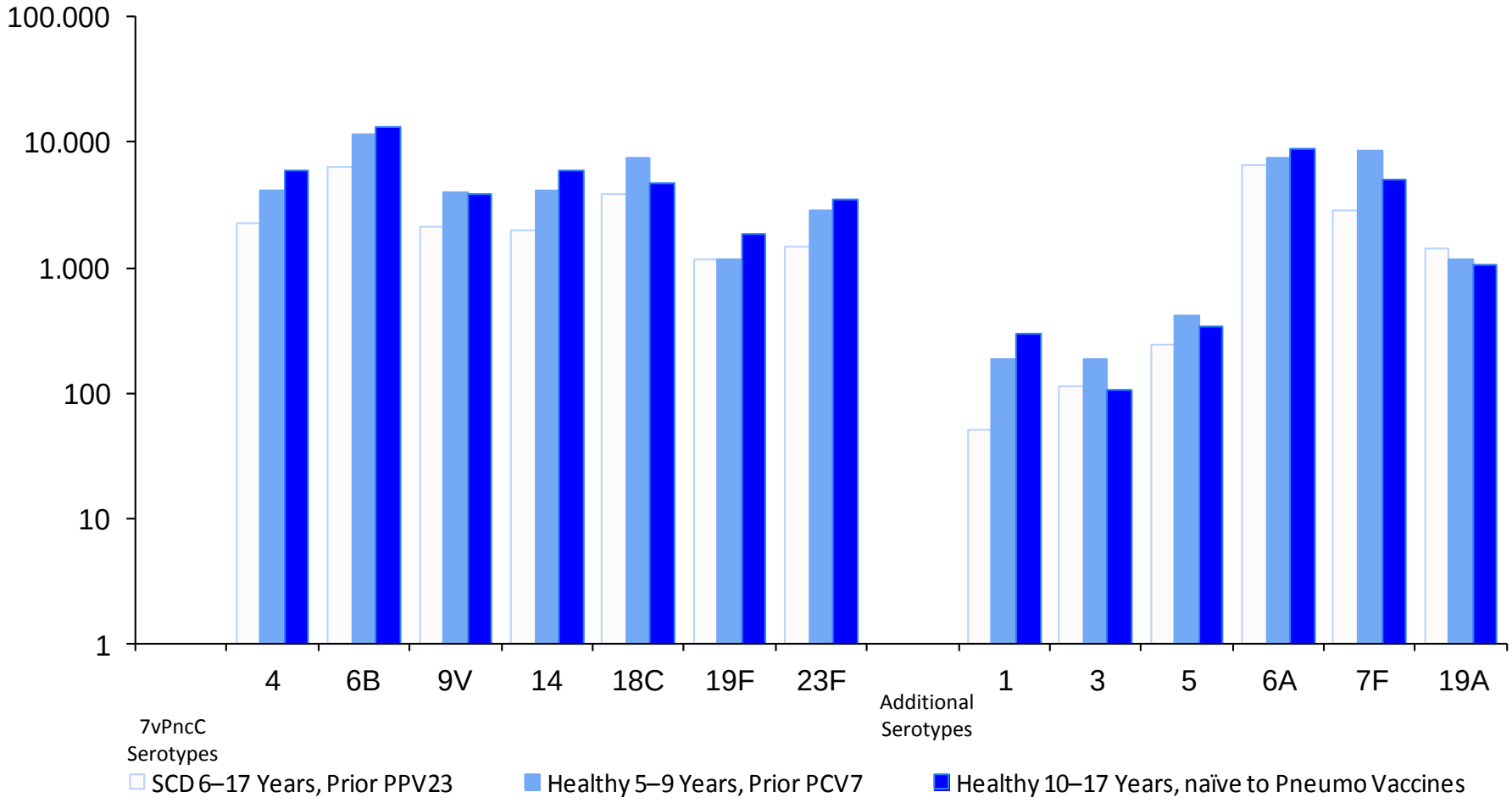
Note:

- Lo studio prevedeva un prelievo aggiuntivo 1 anno dopo l'ultima vaccinazione

Sedi di studio: US, Francia, Italia, UK, Egitto, Arabia Saudita, Libano

De Montalembert M et al
Poster Congresso ASH, Novembre 2013

OPA GMTs dopo 1 Dose di PCV13: Pazienti SCD vs. Volontari Sani



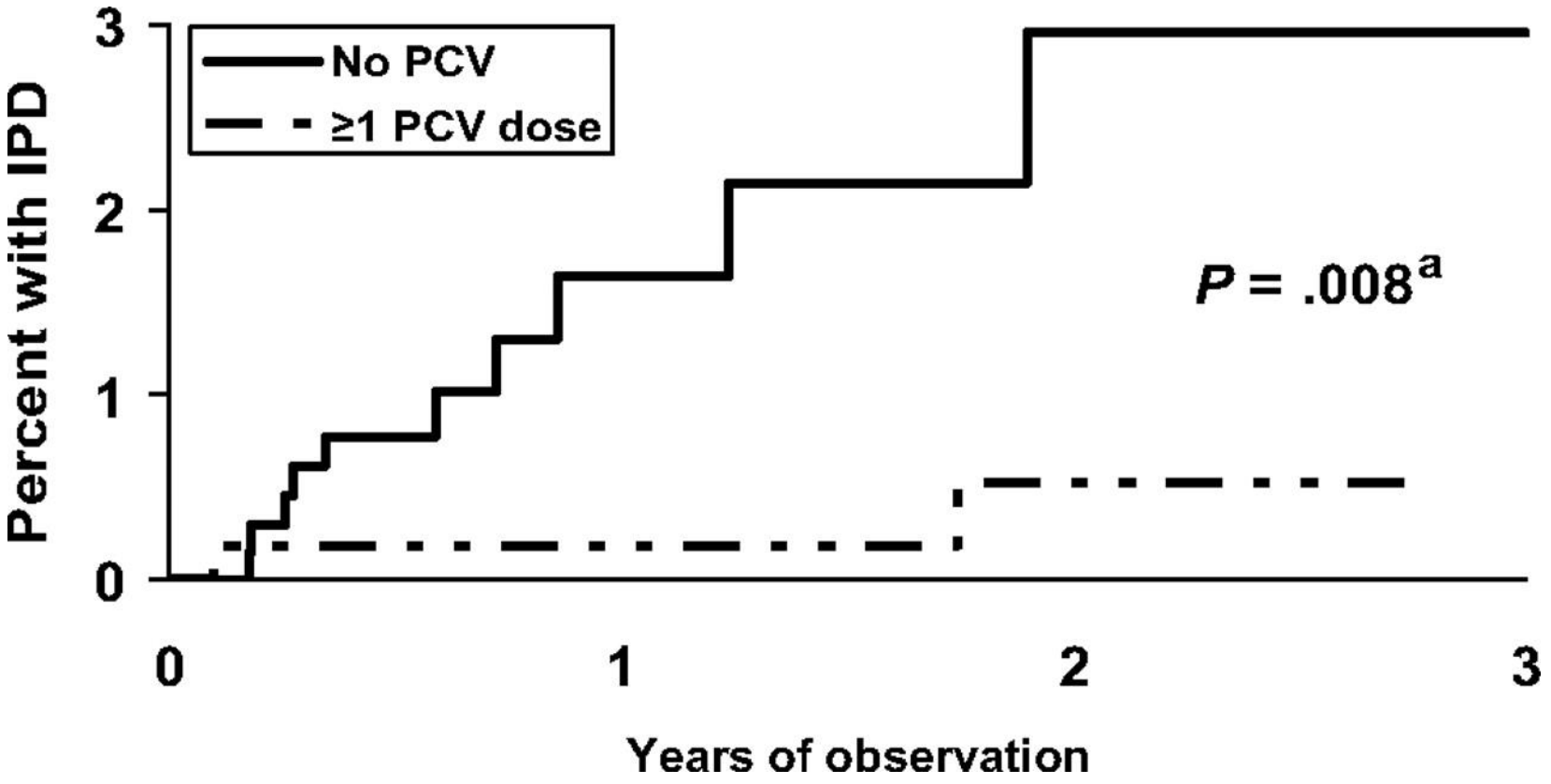
De Montalembert M et al
Poster Congresso ASH, Novembre 2013

Conclusioni (Sickle Cells Disease)

- PCV13 si è dimostrato sicuro ed immunogenico nei pazienti SCD precedentemente vaccinati con PPV23
- Una 2° dose di PCV13 ha indotto solo un modesto aumento degli anticorpi funzionali in confronto ad una dose singola
- Il profilo AE/SAE osservato in questo studio ha riflesso la condizione clinica di base della anemia a cellule falciformi (SCD)

De Montalembert M et al
Poster Congresso ASH, Novembre 2013

Kaplan-Meier curve of IPD in children with SCD according to PCV vaccination status from January 1, 2000, through January 1, 2003 for PCV serotypes (4, 6B, 9V, 14, 18C, 19F, and23F) and untyped isolates only



Thomas V. Adamkiewicz et al.

PEDIATRICS®

Variazione in Scheda Tecnica PCV13 (19 ott. 2013)

Popolazioni speciali

Gli individui affetti da condizioni concomitanti che li predispongono a malattia pneumococcica (quali quelli affetti da anemia a cellule falciformi o infezione da HIV), compresi quelli precedentemente vaccinati con una o più dosi di vaccino pneumococcico polisaccaridico 23-valente, possono ricevere almeno una dose di Prevenar 13 (vedere paragrafo 5.1).

Linee Guida HIV: Update

Linee Guida Italiane sull'utilizzo dei farmaci antiretrovirali
e sulla gestione diagnostico-clinica delle persone con infezione da HIV-1

Novembre 2013

Su mandato del *Ministro della Salute*

ISTITUTO SUPERIORE DI SANITÀ
CENTRO NAZIONALE AIDS

In collaborazione con

Ministero della Salute

Commissione Nazionale per la lotta contro l'AIDS
Consulta delle Associazioni per la lotta contro l'AIDS

e

SIMIT
Società Italiana di Malattie Infettive e Tropicali

Linee Guida HIV: Update

Tabella 2 - Vaccinazioni raccomandate nel bambino HIV+.

Pneumococco	• Tutti. • I bambini con infezione da HIV hanno un rischio elevato di malattia pneumococcica invasiva se comparati a bambini non infetti.	• Utilizzare PCV 13 (+ 1 dose di PPV 23 almeno dopo almeno 6 mesi se età > 2 anni). • Tempi, n. dosi e modalità di somministrazione come da indicazioni nazionali. • Considerare 1 dose di PPV 23 dopo 5-10 anni.	[29-32, 56]
RACCOMANDAZIONE (FORZA/EVIDENZA)	*La vaccinazione antipneumococcica è ben tollerata ed efficace anche nei bambini HIV positivi* **[AII]**.		

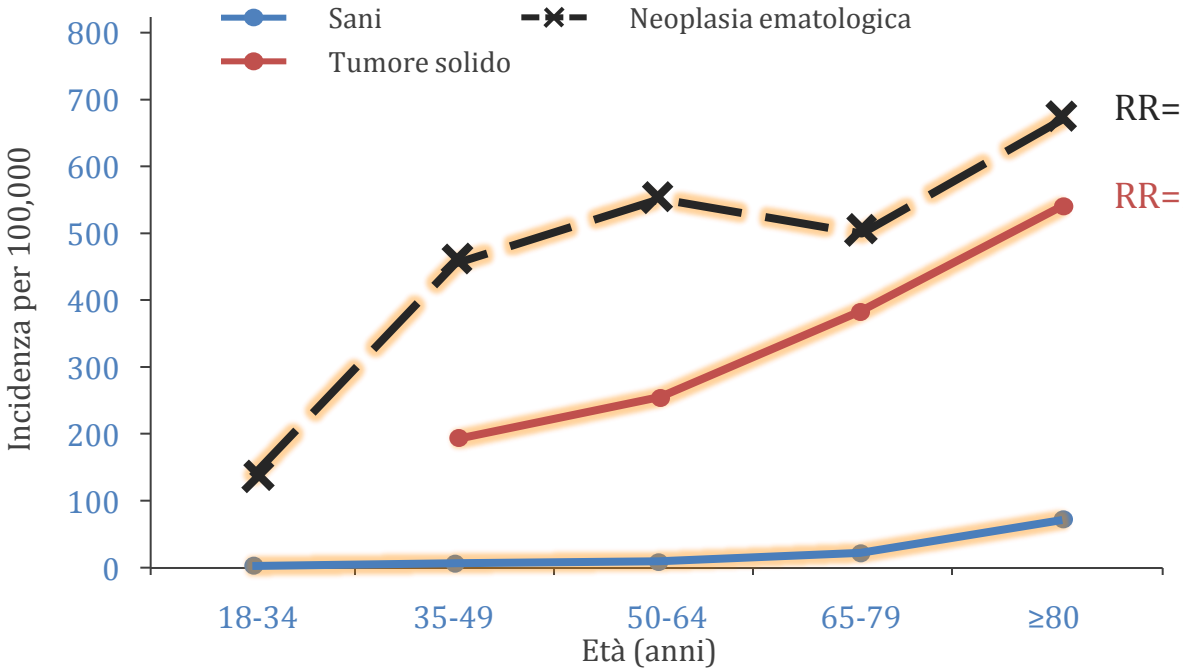
Linee Guida HIV: Update

Tabella 1 - Principali vaccinazioni raccomandate nell'adulto HIV+.

VACCINO	• INDICAZIONE • RAZIONALE	POSOLOGIA: A = PRIMO CICLO; B = RICHIAMI/RIVACCINAZIONI	COMMENTI	RIFERIMENTI BIBLIOGRAFICI
Pneumococco	• Tutti. • Più alta frequenza e severità della malattia invasiva.	A: almeno 1 dose di PCV 13 + 1 dose di PPV 23 dopo almeno 6 mesi); (se già vaccinato in precedenza con PPV 23, considerare PCV 13 a distanza di 1 anno). B: considerare dose di PPV 23 dopo 5-10 anni.		[6, 7-19, 61, 68, 72]
RACCOMANDAZIONE (FORZA/EVIDENZA)	*La vaccinazione antipneumococcica è raccomandata in tutti i soggetti HIV positivi con >200 T CD4+ cellule/µL se in trattamento e con > 500 T CD4+ cellule/µL se naïve* **[AI]**. *Al di sotto del livello di 200 T CD4+ cellule/µL è comunque verosimile un effetto protettivo* **[BII]**. *Anche se non è ben chiaro il rapporto tra livello anticorpale e protezione da eventi clinici significativi, una rivaccinazione può essere considerata trascorsi 5-10 anni nei soggetti il cui livello anticorpale tenda a diminuire nel tempo* **[BII]**. *Quest'ultima indicazione si riferisce al solo vaccino polisaccaridico (PPV 23) non essendo noto, al momento, se PCV 13 necessita di richiami in quanto gli studi sono ancora in corso.*			

I pazienti neoplastici sono a rischio più alto di IPD[1]

Incidenza età-specifica di IPD in adulti sani (età ≥18 anni)
vs. adulti con tumori solidi e neoplasie ematologiche e rischi relativi (RR)
per adulti sani e adulti con specifiche condizioni croniche, USA, 1999-2000 [1]



RR=38.3 (15.9–92.2) [1]

RR=22.9 (11.9–44.3) [1]

Pazienti con neoplasie emotologiche hanno un'incidenza più alta di IPD rispetto ai pazienti con tumori solidi (503 *vs.* 300 casi per 100,000) [1]

1.Kyaw MH *et al.* J Infect Dis. 2005;192:377-386.

Perché il tumore è associato a infezione pneumococcica invasiva?

PAZIENTI CON TUMORE POSSONO ESSERE IMMUNOCOMPROMESSI PER [1,2]

LA MALATTIA
(es. leucemia, limfoma, morbo di Hodgkin, mieloma multiplo, o neoplasia sistemica) [1,2]

LA TERAPIA
(es. chemioterapia, corticosteroidi ad alte dosi, radiazioni, o trapianti) [1,2]

I pazienti neoplastici che fanno chemioterapia tendono a svilupare infezioni che possono ritardare l'inizio del trattamento e portare a ulteriori complicanze .
Sono quindi necessarie misure preventive. [3]

1. Centers for Disease Control and Prevention (CDC). ACIP. MMWR Morb Mortal Wkly Rep. 2010;59(34):1102-6. 2. Centers for Disease Control and Prevention (CDC). MMWR Recomm Rep. 1997;46(RR-8):1-24. 3. Nordøy T *et al.* Med Oncol. 2002;19(2):71-8.

	All children (n=277)	Carriers (n=52)	Non-carriers (n=225)	p-value
Age at enrolment				
<10	124 (44.8)	35 (67.3)	89 (39.6)	
10-14	102 (36.8)	12 (23.1)	90 (40.0)	
≥15	51 (18.4)	5 (9.6)	46 (20.4)	<0.01
Sex				
Male	183 (66.1)	34 (65.4)	149 (66.2)	
Female	94 (33.9)	18 (34.6)	76 (33.8)	0.91
Ethnicity				
Caucasian	257 (92.8)	50 (96.1)	207 (92.0)	
Non-Caucasian	20 (7.2)	2 (3.9)	18 (8.0)	0.39
Diagnosis				
Leukemia/lymphoma	235 (84.8)	47 (90.4)	188 (83.6)	
Other cancers	42 (15.2)	5 (9.6)	37 (16.4)	0.22
Phase				
Maintenance/In therapy	159 (57.4)	24 (46.1)	135 (60.0)	
Therapy stopped within the last 6 months	118 (42.6)	28 (53.9)	90 (40.0)	0.07
Co-trimoxazole prophylaxis				
No	57 (20.6)	18 (34.6)	39 (17.3)	
Yes	220 (79.4)	34 (65.4)	186 (82.7)	**<0.01**
No. of siblings				
0	61 (22.0)	16 (30.8)	45 (20.0)	
1	133 (48.0)	22 (42.3)	111 (49.3)	
2	56 (20.2)	9 (17.3)	47 (20.9)	
≥3	27 (9.8)	5 (9.6)	22 (9.8)	0.28
Parental smoking habit				
Both non-smokers	168 (60.6)	31 (59.6)	137 (60.9)	
At least one smoker	109 (39.4)	21 (40.4)	88 (39.1)	0.87
Gestational age (weeks)[a]				
<37	18 (6.5)	4 (7.8)	14 (6.2)	
≥37	258 (93.5)	47 (92.2)	211 (93.8)	0.75
Birth weight (g)[a]				
<2,500	10 (3.6)	1 (2.0)	9 (4.0)	
≥2,500	265 (96.4)	50 (98.0)	215 (96.0)	0.69
Exclusive breastfeeding				
No	61 (22.0)	12 (23.1)	49 (21.8)	
Yes	216 (78.0)	40 (76.9)	176 (78.2)	0.84
Infections (last 3 months)				
No	222 (80.1)	46 (88.5)	176 (78.2)	
Yes	55 (19.9)	6 (11.5)	49 (21.8)	0.10

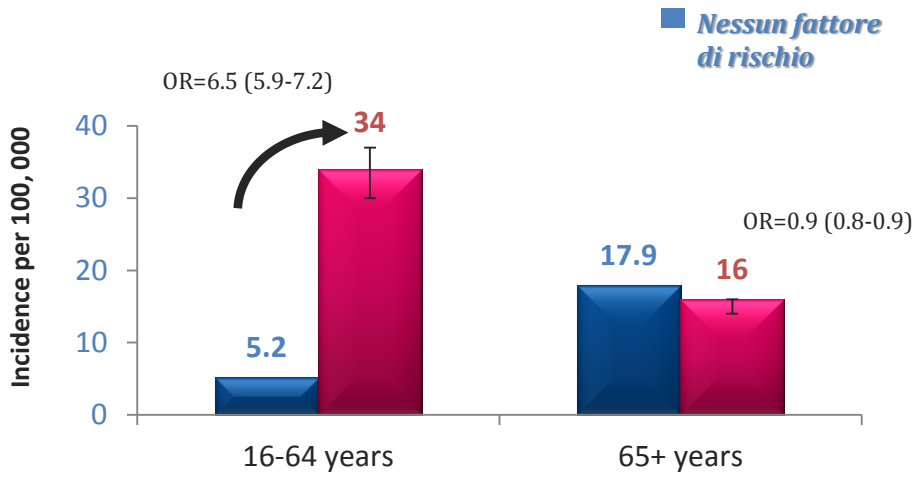
PNEUMOCOCCAL CARRIAGE IN CHILDREN AND ADOLESCENTS WITH CANCER
(Esposito S et al., Hum Vaccin Immunother 2015)

La malattia renale cronica aumenta il rischio e la mortalità per IPD negli adulti

In 22.298 pazienti di tutte le età, Inghilterra, 2008-2009 [1]

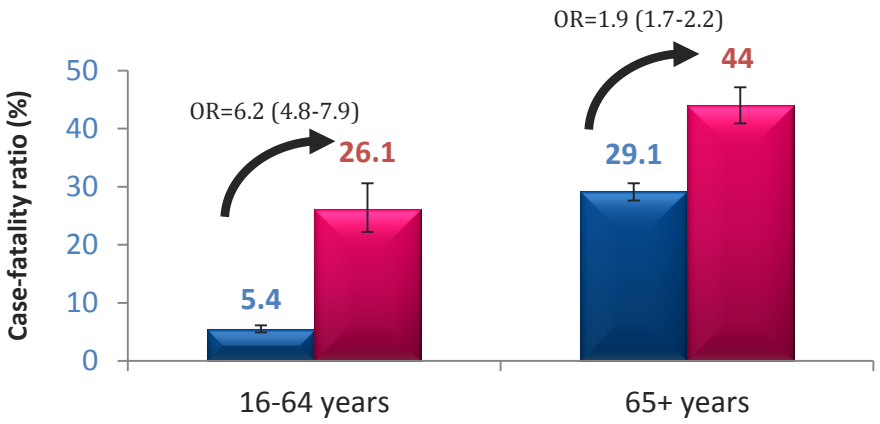
Incidenza di IPD[1]

Stima di incidenza annuale di IPD per 100,000 nel 2008-2009 e odds ratio (OR) gruppo a rischio vs gruppo non a rischio[1]



Case-fatality ratio per IPD[1]

Case-fatality ratio per età e gruppo di rischio, e odds ratio (OR) gruppo a rischio con IPD vs gruppo non a rischio[1]



1. van Hoek AJ et al. J Infect. 2012;65(1):17-24.

Perché la malattia renale cronica è associata con infezione pneumococcica invasiva?[1-3]

MALATTIA RENALE CRONICA

DIFETTO BARRIERA MUCOCUTANEA

DEFICIT SISTEMA IMMUNE

CONTAMINAZIONE DEGLI ACCESSI VASCOLARI E DEI CATETERI PER DIALISI PERITONEALE

1. Mahmoodi M *et al.* Eur Cytokine Netw. 2009;20(2):69-74. 2. de Montalembert M *et al*. Poster abstract 3212. ASH 2012. 3. Glesby MJ *et al*. Poster abstract 880. CROI 2013.

Epatopatie croniche
Perché un fattore di rischio per IPD?

- Le infezioni batteriche rappresentano pericolose, e spesso fatali, complicazioni in pazienti con malattie epatiche
- A più *alto rischio* sono i pazienti con:
  - cirrosi da abuso alcolico
  - patologia epatica scompensata cronica
  - epatopatia acuta che evolve rapidamente verso insufficienza epatica fulminante
  - necrosi epatica subacuta [1]

Tra le infezioni più comuni :

Batteriemie [1]

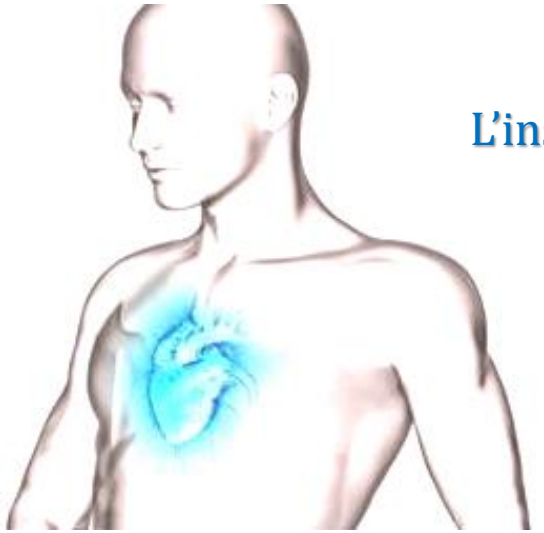
Polmoniti [1]

Endocarditi infettive e meningiti [1]

principalmente indotte dallo pneumococco [1]

1. Wyke RJ. Baillieres Clin Gastroenterol 1989;3(1):187-210

Patologie cardiache
Perché un fattore di rischio per PD?



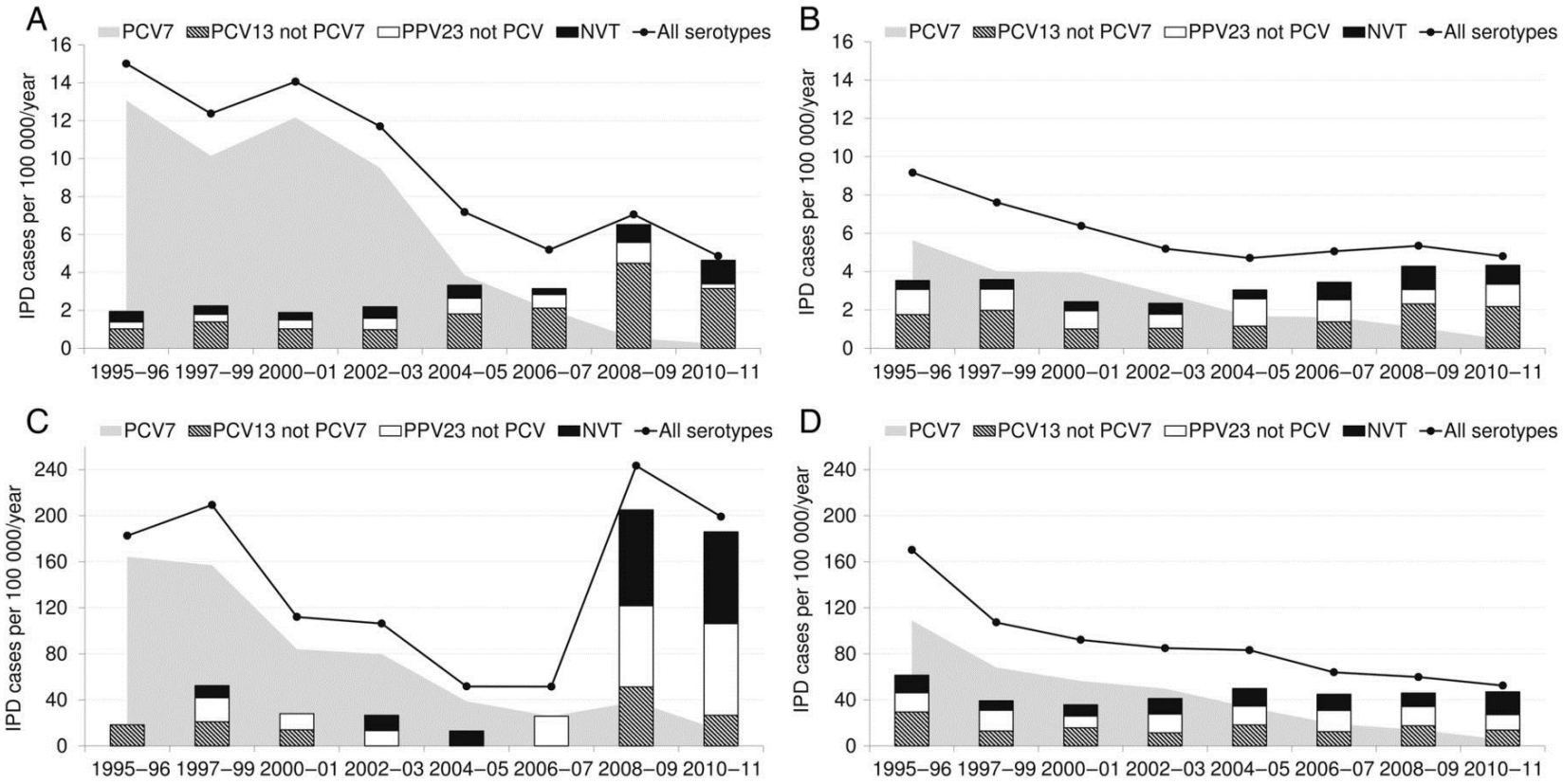
L'insufficienza cardiaca cronica (CHF) è associata a diverse alterazioni della funzionalità immunitaria [1]

Numerosi studi hanno evidenziato:

- Compromissione della reattività linfocitaria
- Aumento dei livelli di TNF circolante, di IL-2 e IL-6
- Alterazioni nel numero e nella funzione dei linfociti NK, T helper/inducer e linfociti suppressor [1]

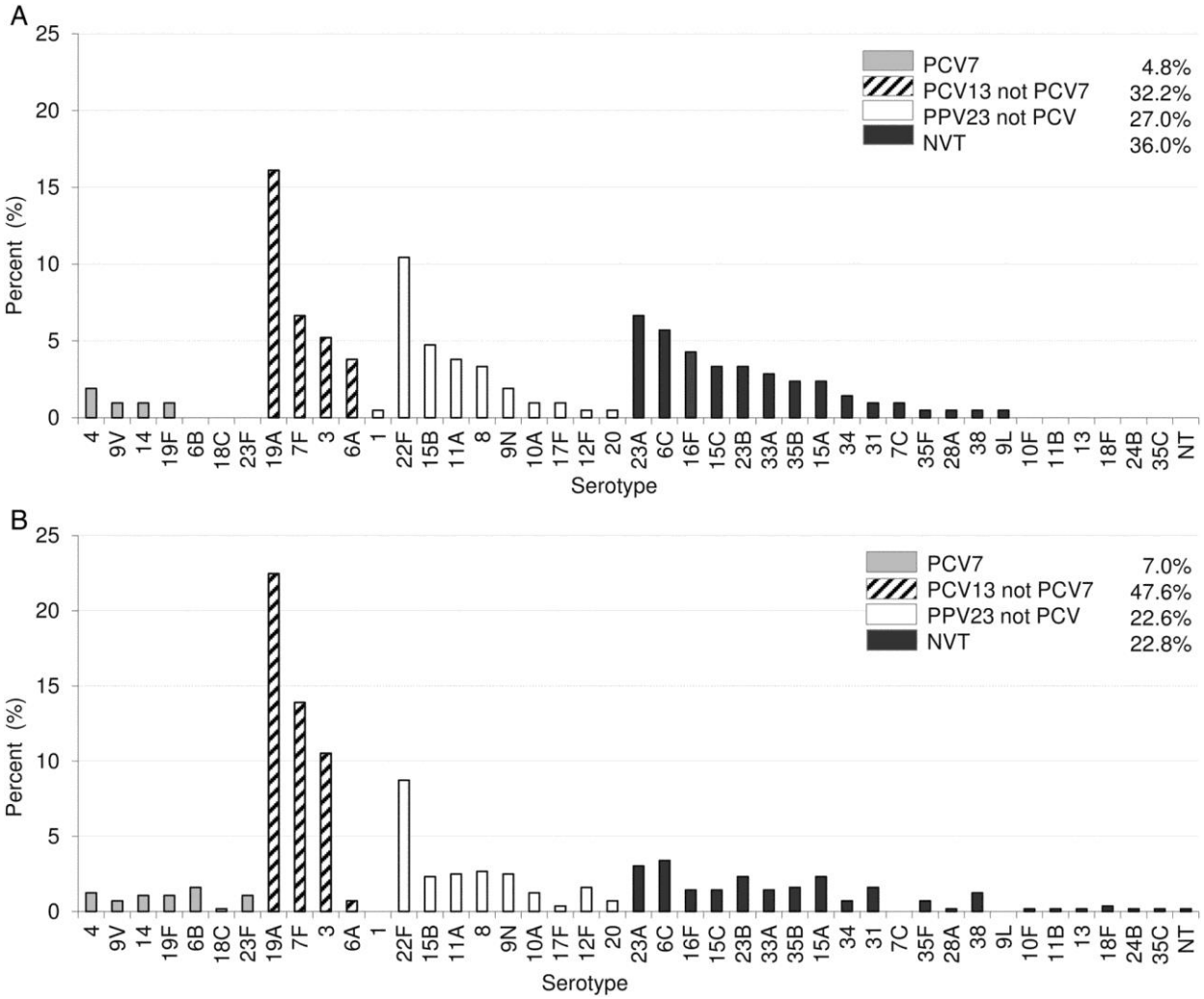
1. Doing A, et al. J Card Fail 2001;7(4):318-21

Annual incidence of invasive pneumococcal disease (IPD) among healthy (A and B) or immunocompromised (C and D) children and adults and by vaccine-covered serotype groups, Toronto Invasive Bacterial Diseases Network, 1996/1997–2010/2011



Altynay Shigayeva et al. Clin Infect Dis 2015

Distribution of pneumococcal serotypes in cases of IPD in immunocompromised (A) and immunocompetent (B) patients, Toronto Invasive Bacterial Diseases Network, 2011/2012



Altynay Shigayeva et al. Clin Infect Dis 2015

Conditions for PCV13 and/or PPSV23 administration in children aged 6-18 years (I)

(From CDC. MMWR, June 28, 2013)

		PCV13	PPSV23	
Risk group	Underlying medical condition	Recommended	Recommended	Revaccination 5 yrs after first dose
Immunocompetent persons	Chronic heart disease¶		✓	
	Chronic lung disease**		✓	
	Diabetes mellitus		✓	
	Cerebrospinal fluid leaks	✓	✓	
	Cochlear implants	✓	✓	
	Alcoholism		✓	
	Chronic liver disease		✓	
	Cigarette smoking		✓	
Persons with functional or anatomic asplenia	Sickle cell disease/other hemaglobinopathies	✓	✓	✓
	Congenital or acquired asplenia	✓	✓	✓

¶ Including congestive heart failure and cardiomyopathies.
** Including chronic obstructive pulmonary disease, emphysema, and asthma.

Conditions for PCV13 and/or PPSV23 administration in children aged 6-18 years (II)

(From CDC. MMWR, June 28, 2013)

		PCV13	PPSV23	
Risk group	Underlying medical condition	Recommended	Recommended	Revaccination 5 yrs after first dose
Immunocompromised persons	Congenital or acquired immunodeficiencies††	✓	✓	✓
	Human immunodeficiency virus infection	✓	✓	✓
	Chronic renal failure	✓	✓	✓
	Nephrotic syndrome	✓	✓	✓
	Leukemia	✓	✓	✓
	Lymphoma	✓	✓	✓
	Hodgkin disease	✓	✓	✓
	Generalized malignancy	✓	✓	✓
	Iatrogenic immunosuppression§§	✓	✓	✓
	Solid organ transplant	✓	✓	✓
	Multiple myeloma	✓	✓	✓

†† Includes B-(humoral) or T-lymphocyte deficiency, complement deficiencies (particularly C1, C2, C3, and C4 deficiencies), and phagocytic disorders (excluding chronic granulomatous disease).

§§ Diseases requiring treatment with immunosuppressive drugs, including long-term systemic corticosteroids and radiation therapy.

Vaccinazione pneumococcica in Italia, per gruppi di rischio:
Piano Nazionale Prevenzione Vaccinale 2012-2014

La vaccinazione antipneumococcica è consigliata ai soggetti di qualsiasi età a rischio di contrarre la malattia per la presenza di patologie o condizioni predisponenti:

- cardiopatie croniche
- malattie polmonari croniche
- cirrosi epatica, epatopatie croniche evolutive
- da alcoolismo
- diabete mellito, in particolare se in difficile compenso
- fistole liquorali
- anemia falciforme e talassemia,
- immunodeficienze congenite o acquisite,
- asplenia anatomica o funzionale,
- leucemie, linfomi, mieloma multiplo
- neoplasie diffuse
- trapianto d'organo o di midollo
- immunosoppressione iatrogena clinicamente significativa
- insufficienza renale cronica, sindrome nefrosica
- HIV positivi,
- portatori di impianto cocleare.

Ministero della Salute, disponibile su http://www.governo.it/Notizie/Ministeri/dettaglio.asp?d=67507

Possible limitations of PPSV23 vaccine

- Reduced antibody response in comparison to PCVs
- Poor immune memory
- No effect on carriage
- Risks of adverse events when booster doses are given
- Efficacy against IPD but not against pneumonia

CONCLUSIONS

- Patients with specific chronic diseases including asthma showed an incresed risk of IPD
- Further studies are needed to clarify the frequency of pneumococcal colonization and IPD in patients with different chronic diseases
- Vaccination with PCV13 should be recommended in children with various chronic diseases
- PPSV23 is recommended in addition to PCV13 in these patients, but it is not clear whether booster doses are recommended
- Further data are needed in order to clarify whether there are differences in the risk of IPD and in immune response to PCV13 in relation to chronic underlying disease

SEE YOU IN MILAN!