Aging and Immunity III

11-13 January 2016
Campus GSK
Auditorium Building 35
Via Fiorentina 1
53100 Siena, Italy

Pneumoccocal vaccination in the elderly

Paolo Bonanni

Department of Health Sciences

University of Florence, Italy

Streptococcus pneumoniae is a leading cause of CAP, meningitis and bacteremia[1]

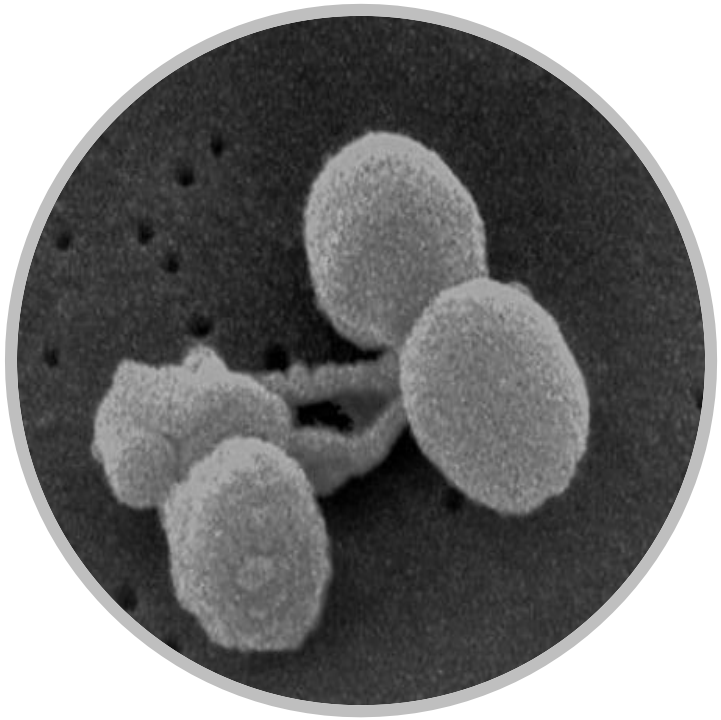


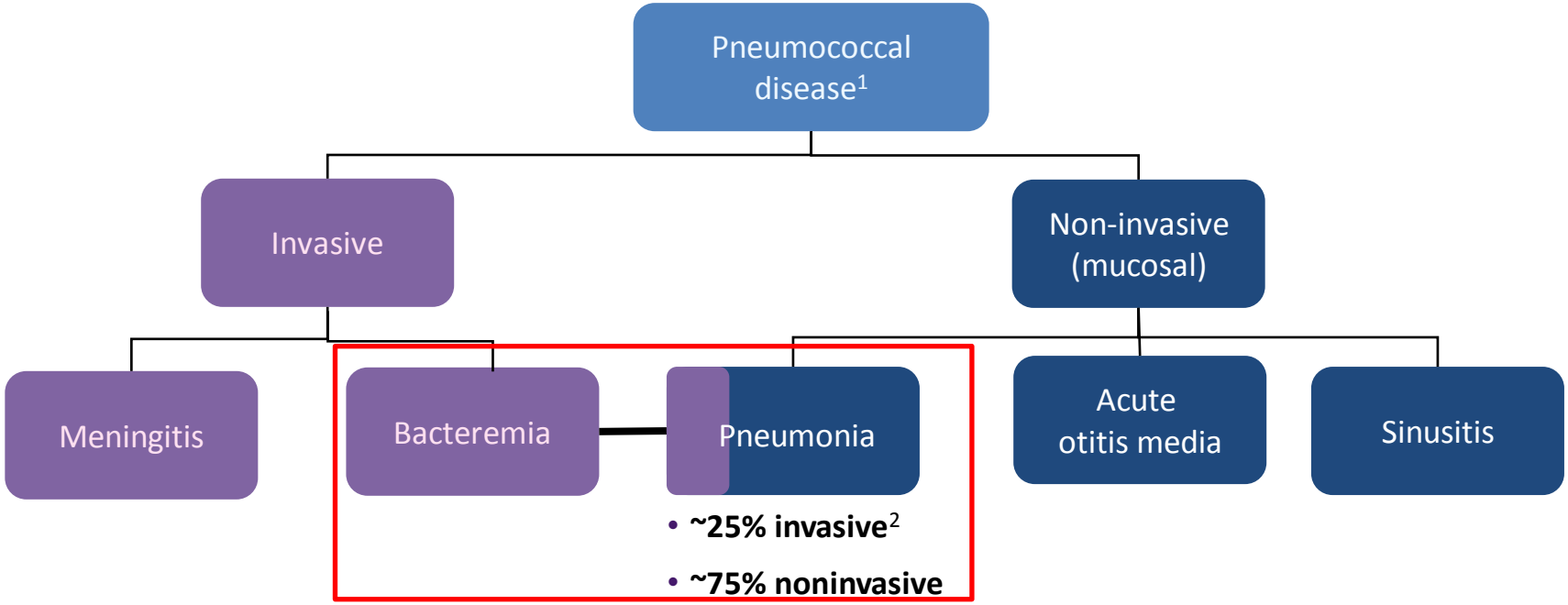
Image obtained from the website of the Centers for Disease Control and Prevention/Janice Carr. http://phil.cdc.gov/phil/details.asp. Image #9996.

- A human pathogen commonly carried in the nasopharynx[1]
- Organism has a polysaccharide capsule[1,2]
  - Defines the serotype
  - Functions as virulence factor
  - Is a vaccine target
- At least 90 serotypes of *S. pneumoniae* have been identified[1,2]
  - Serotypes are not equally pathogenic
- Antibiotic resistance in *S. pneumoniae* is a global concern[1,2]
  - Serotypes found to be antibiotic resistant include 6A, 6B, 9V, 14, 15A, 19A, 19F and 23F[3,4]

CAP, community-acquired pneumonia.

1. Centers for Disease Control and Prevention. Pneumococcal disease. In: Atkinson W, et al, eds. Epidemiology and Prevention of Vaccine-Preventable Diseases. 12th ed., second printing. Washington, DC: Public Health Foundation; 2012:233–48. http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/pneumo.pdf. Accessed March 2015. 2. World Health Organization. Available from: http://www.who.int/immunization/diseases/pneumococcal/en/Accessed March 2015. 3. Linares J, et al. Clin Microbiol Infect 2010;16:402–10. 4. Kim SH, et al. Antimicrob Agents Chemother 2012;56:1418–26.

Pneumococcal disease can be broadly grouped into categories of invasive and non-invasive (mucosal) disease

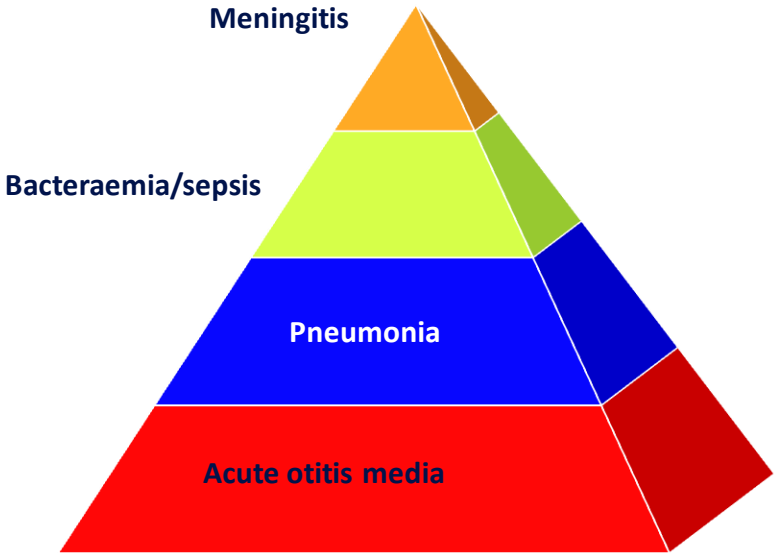


- Non-invasive forms may become invasive (e.g. pneumonia when accompanied by bacteremia)[1]
- Disease severity and invasiveness differ based on serotype[3]

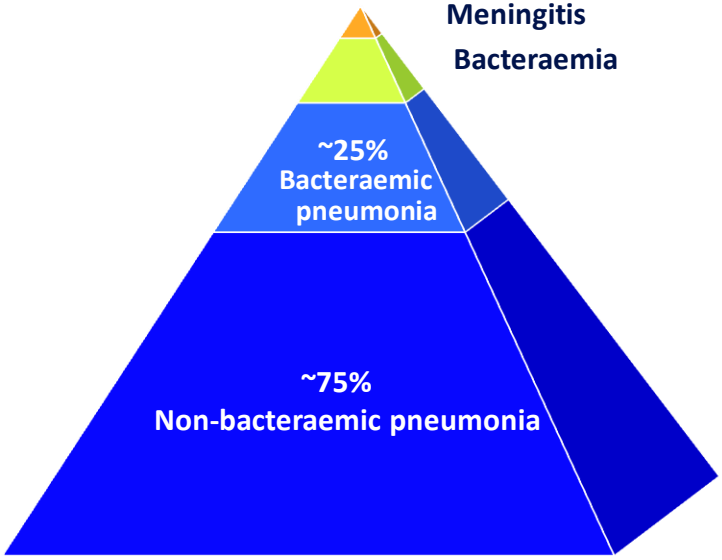
1. World Health Organization (WHO). Wkly Epidemiol Rec 2012;87:129–44. 2. Said MA, et al. PLoS One 2013;8:e60273.
3. Jansen AG, et al. Clin Infect Dis 2009;49:e23–29.

S.pneumoniae: disease

Children



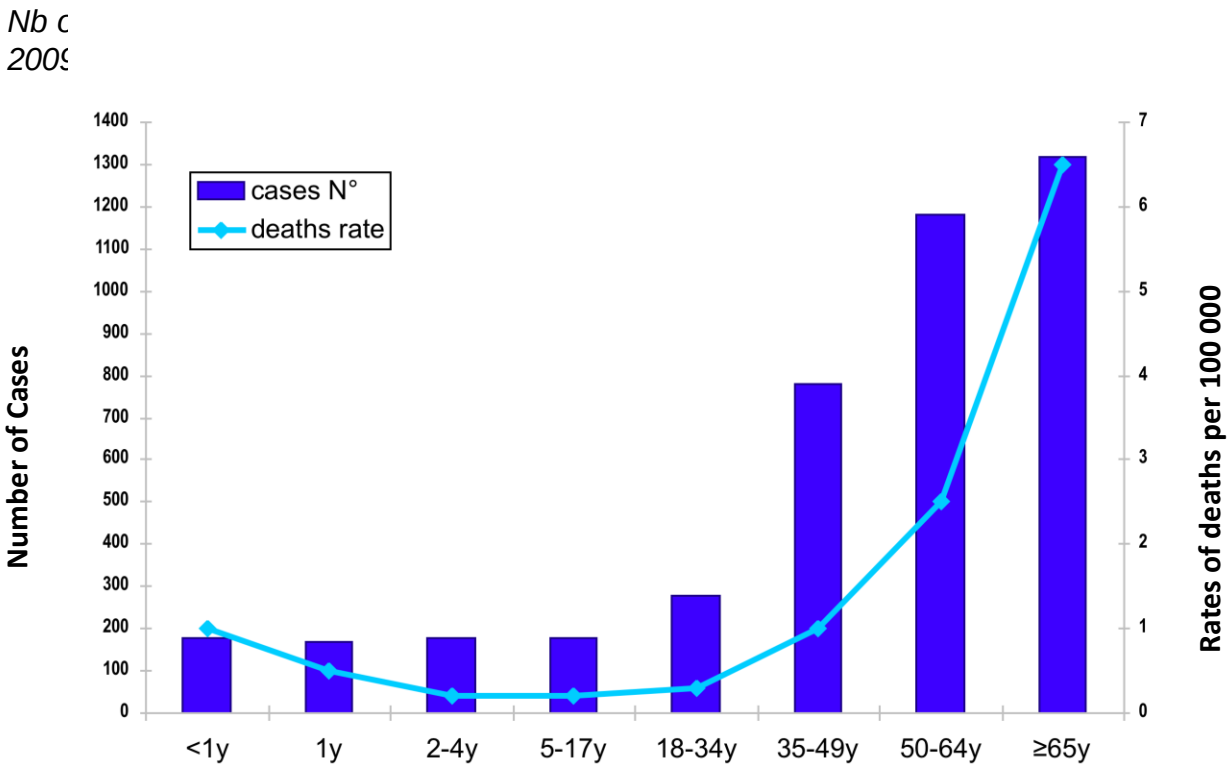
Adults



CDC. Pneumococcal disease. www.cdc.gov/vaccines/pubs/pinkbook/index.html
Huang SS, et al. Vaccine 2011;29:3398-412. Said MA, et al. PLoS ONE 2013;8:e60273

US, 2009 : high incidence of IPD in subjects aged >50 years

Incidence < 5yrs: 21.1/100 000, ≥ 65+: 38.7 /100 000[1]

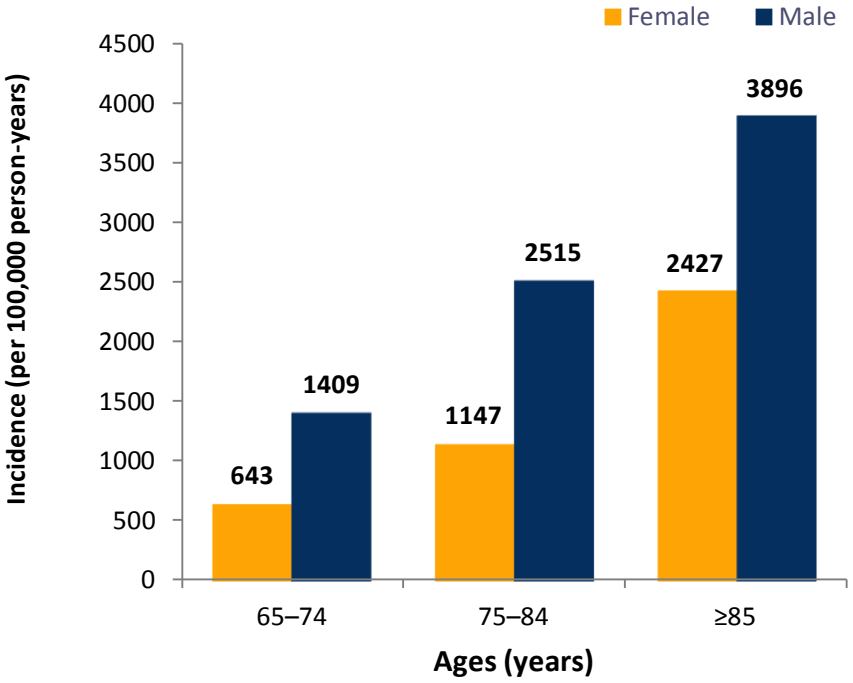


1.CDC, Active Bacterial Core Surveillance (ABCs) Report Emerging Infections Program Network *Streptococcus pneumoniae*, 2009 http://www.cdc.gov/abcs/reports-findings/survreports/spneu09.pdf accessed on 5-04-2011

Incidence of CAP in adults increases with age

Spain, 2002–2005[1]

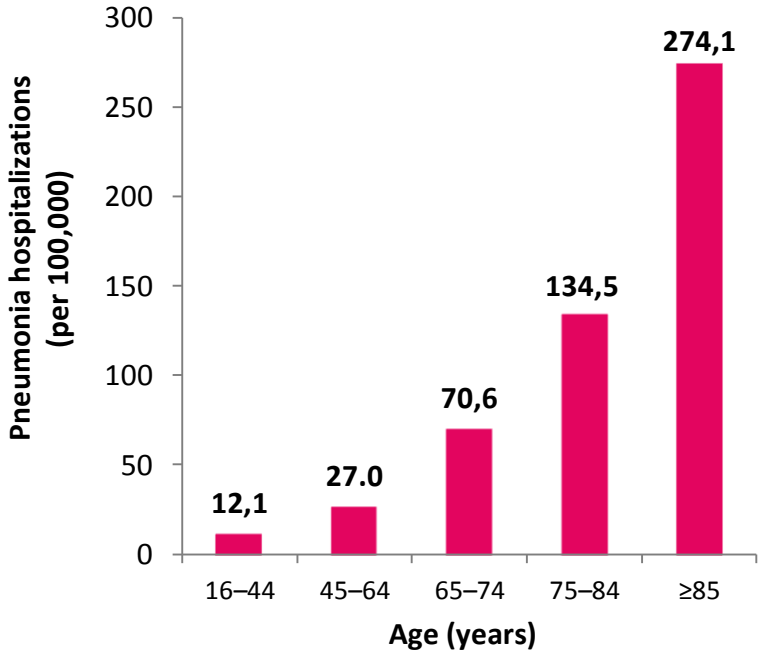
Incidence rates of all cause CAP



Prospective cohort study of Spanish community-dwelling elderly individuals aged 65 years or older (n=11,240). All-cause CAP (hospitalized and outpatient) was a primary study endpoint. All cases were radiographically proved and validated by checking clinical records.[1]

United Kingdom, 2008–2010[2]

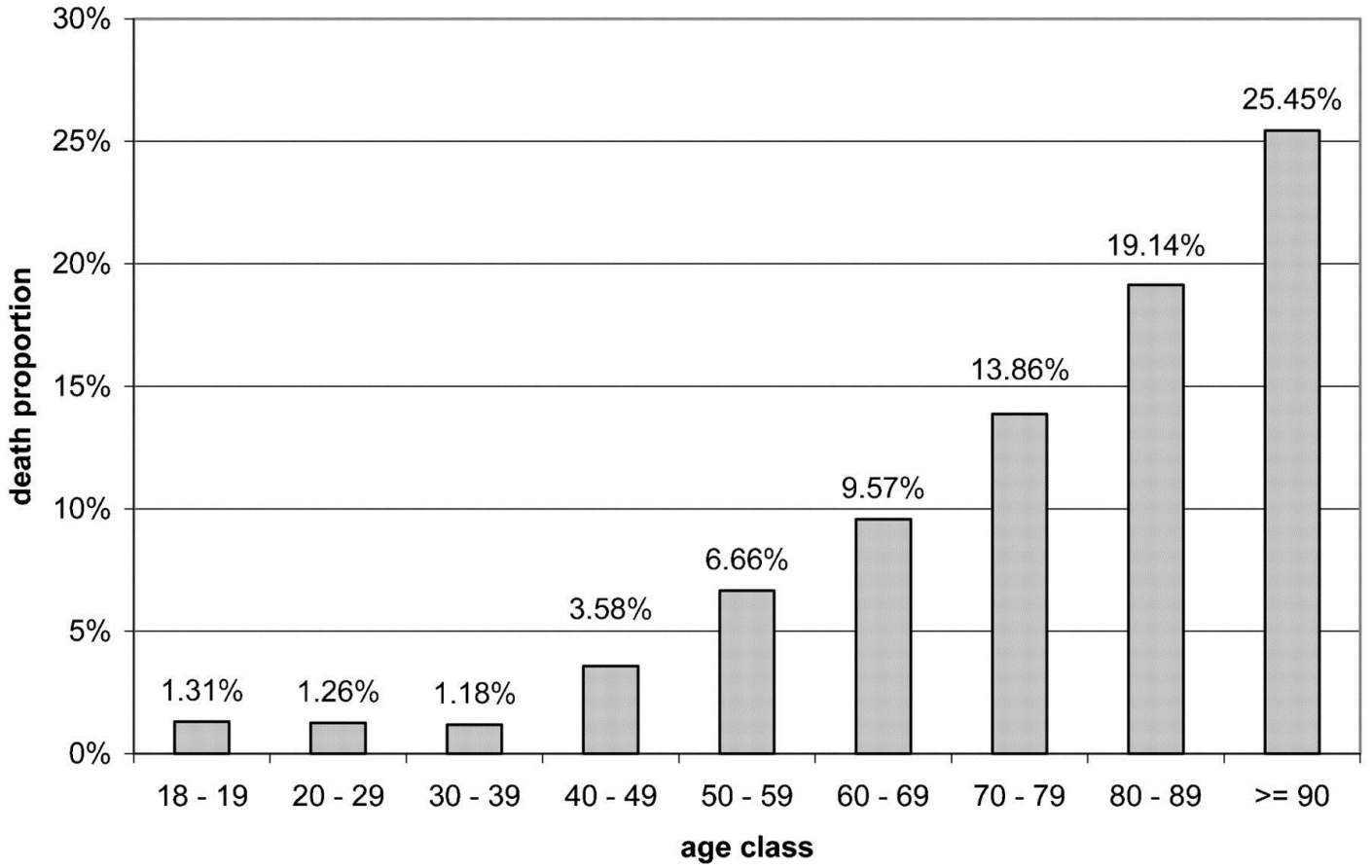
Annual incidence of pneumococcal CAP hospitalizations



A 2-year, prospective, observational cohort study conducted in a large UK teaching hospital trust. The study included 920 patients with CAP; 366 had pneumococcal CAP.[2]

1. Ochoa-Gondar O, et al. BMC Public Health. 2008;8:222
2. Bewick T, et al. Thorax. 2012;67:540–5.

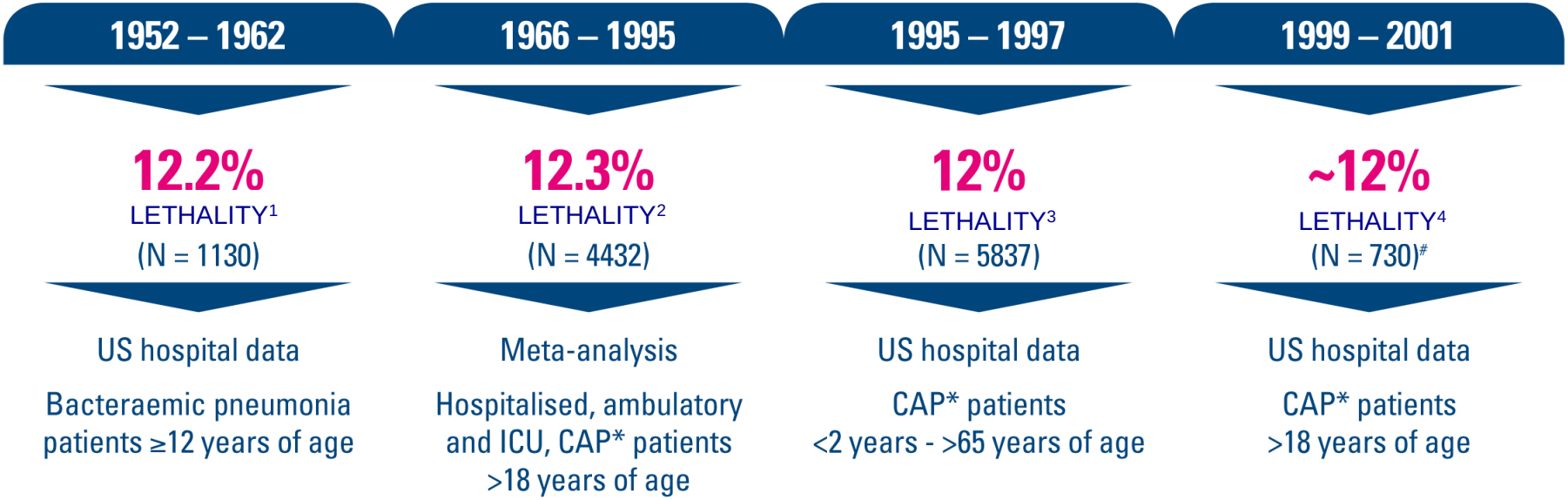
In patients >40 years, case-fatality rates for CAP increase with age, Germany



Ewig S *et al. Thorax* 2009;64:1062–1069

Case-fatality rates for hospitalised patients with IPD and CAP have remained constant over time[1-4]

Mixed patient populations in different settings and countries

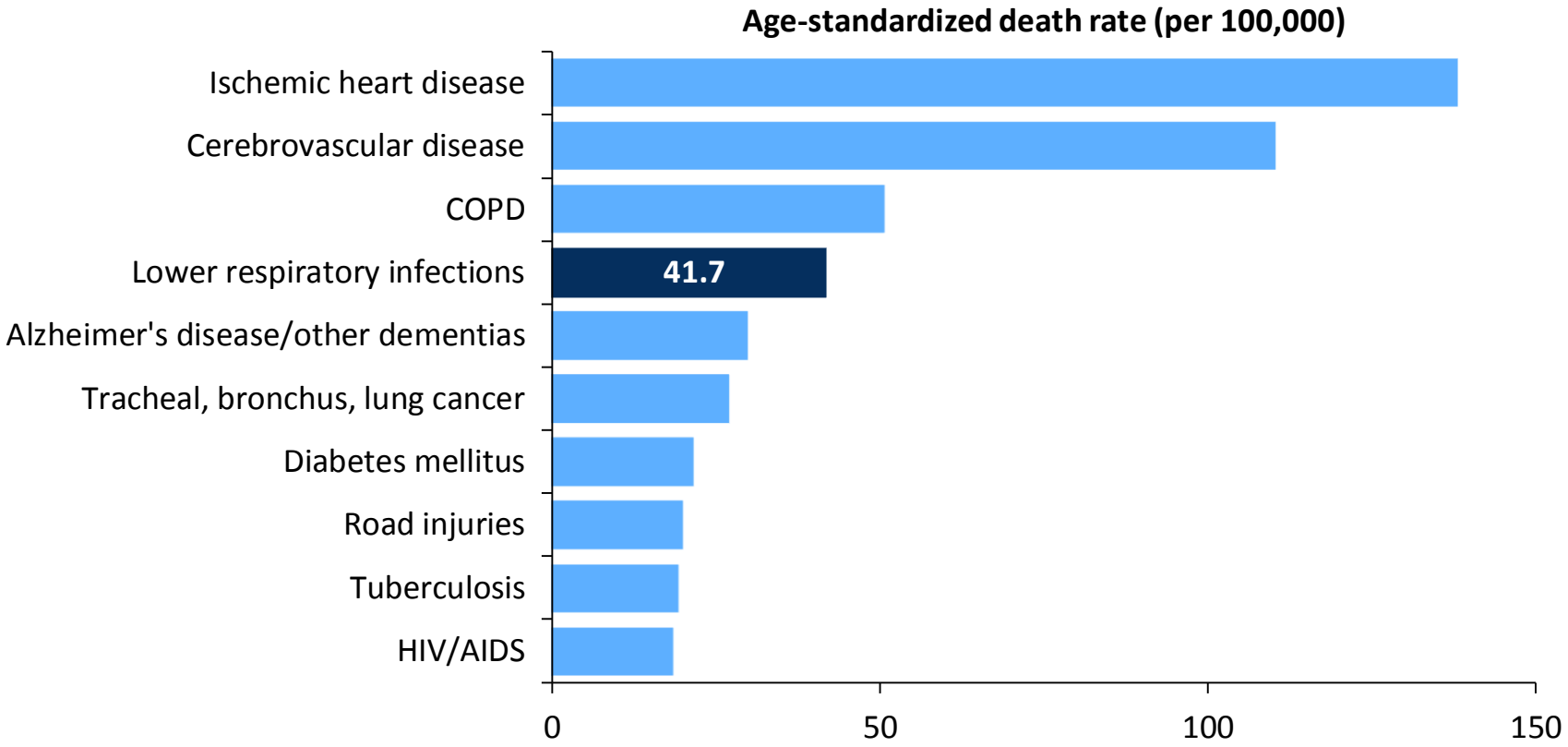


*CAP=Community acquired pneumonia
average of 30-day and 90-day mortality in ICU vs ward patients, with average of 2 rates ~ 12%

1. Austrian R *et al.* Ann Intern Med. 1964;60:759-776;
2. Fine MJ *et al.* JAMA. 1996;274:134-141;
3. Feikin DR *et al.* Am J Pub Health. 2000;90:223-229
4. Restrepo MI *et al.* Chest. 2008;133:610-617.

Lower respiratory infections, including pneumonia, are a leading cause of death worldwide[1]

Ten of the leading causes of death in the world, 2013



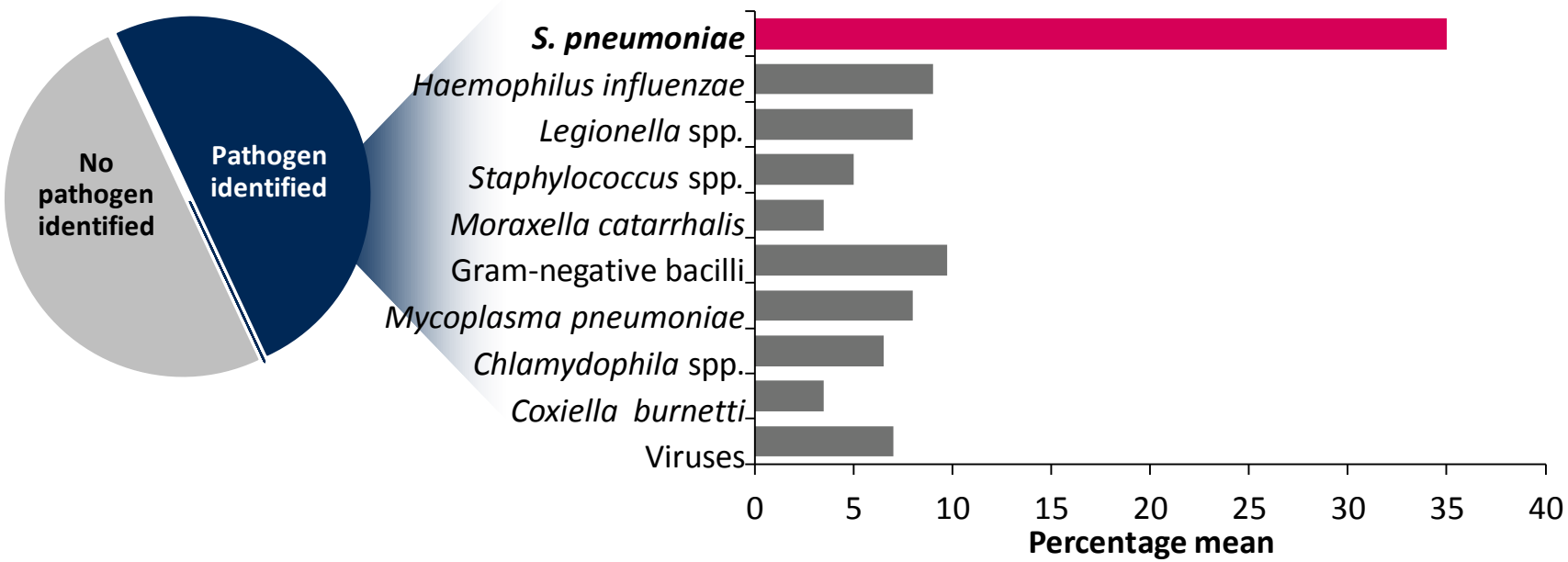
Pneumococcal pneumonia was the leading known cause of lower respiratory infection mortality, causing approximately 22% of lower respiratory infection deaths in 2013

AIDS, acquired immunodeficiency syndrome; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus.

1. Naghavi M, et al. Lancet. 2015;385:117–71. Figure adapted from Naghavi et al.

Streptococcus pneumoniae is the most frequently isolated pathogen in CAP: Europe

Frequency of causative organisms of CAP in Europe, 1990–2009[1*]



S. pneumoniae: most frequently isolated pathogen in CAP patients within the hospital, ICU and outpatient settings[1,2]

*Data are presented as percentage means of frequency of isolation of the respective pathogens from the studies included. Studies were identified by a literature review of all primary articles reporting studies of the clinical and economic burden of CAP in adults in Europe from January 1990 to April 2009.

CAP, community-acquired pneumonia; ICU, intensive care unit.

Figure reproduced from Welte T, et al. Thorax 2012;67:71–79 with permission from BMJ Publishing Group Ltd.

1. Welte T, et al. Thorax 2012;67:71–79. 2. Lode HM. Respir Med 2007;101:1864–73.

The risk of IPD and pneumococcal pneumonia is influenced by host and environmental factors

Age[1]	Host factors		Environmental factors[3,4]	Behavioral factors[2,3]
	At-risk[2,3,5-7]	High risk[2,3,5-7]		
• ≤ 2 years • ≥ 65 years	• Chronic heart disease • Chronic lung disease* • Diabetes • Functional or anatomic asplenia • Chronic liver disease • Chronic renal disease	• HIV infection • Nephrotic syndrome • Cancer (solid and hematologic) • Transplantation • Autoimmune diseases • Immunosuppressive therapy and corticosteroids • Immunodeficiency • Cerebrospinal fluid leaks	• Preceding viral respiratory infection (e.g. influenza) • Residence in an institution (e.g. nursing home)	• Smoking • Alcohol abuse

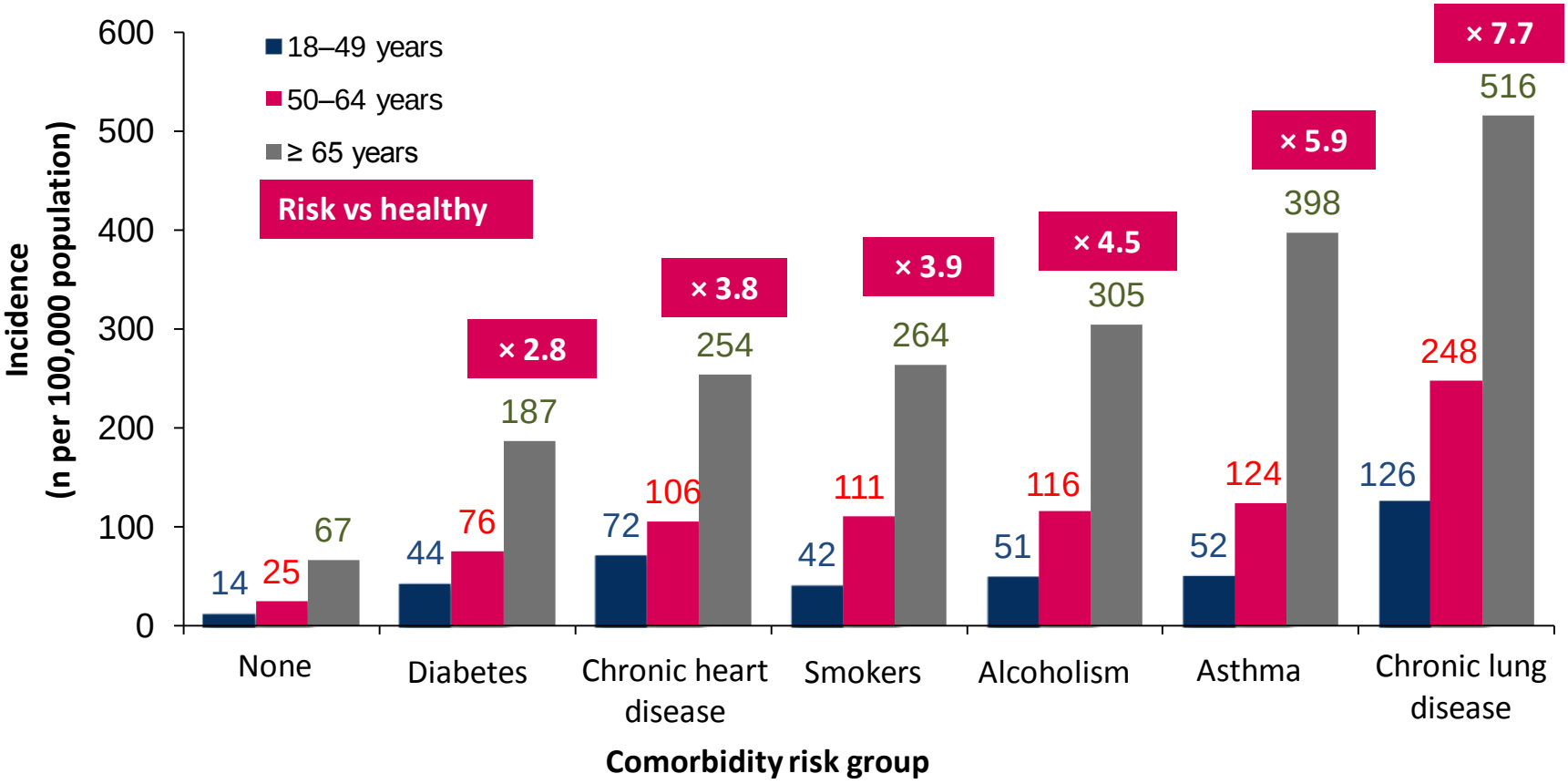
*Including chronic obstructive pulmonary disease, emphysema and asthma.

HIV, human immunodeficiency virus; IPD, invasive pneumococcal disease.

1. Centers for Disease Control and Prevention. Available from: http://www.cdc.gov/abcs/reports-findings/survreports/spneu12.pdf. Accessed March 2015.
2. Centers for Disease Control and Prevention. MMWR Morb Mortal Wkly Rep 2010;59:1102–6. 3. Musher DM. In: Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 7th edn, 2010:2623–42. 4. Centers for Disease Control and Prevention. Available from: http://www.cdc.gov/h1n1flu/vaccination/provider/provider_pneumococcal.htm. Accessed March 2015. 5. van Hoek AJ, et al. J Infect 2012;65:17–24.
6. Klemets P, et al. BMC Infect Dis 2008;8:96. 7. Castiglia P, Advances in Therapy 2014. DOI 10.1007/s12325-014-0157-1

Common medical conditions increase pneumococcal pneumonia risk in adults[1]

Data from a retrospective cohort study from three large, longitudinal, US healthcare databases of medical and outpatient pharmacy claims from 2007 to 2010*



*Persons aged 18–49 years, 50–64 years, and ≥ 65 years contributed a total of 49.3 million, 30.6 million,and 11.7 million person-years of observation, respectively.

Figure adapted from: 1. Shea KM, et al. Open Forum Infect Dis. Published online May 8, 2014. doi:10.1093/ofid/ofu024.

Vaccination is an important part of promoting a healthy lifestyle among patients

Factors associated with increased risk of CAP and how to reduce them

Smoking[1–3]
Cessation

High alcohol consumption[1,2]
Reduce consumption

Nutrition: Being underweight[1,2] **and weight gain during adulthood**[3]
Dietary advice to ensure good nutritional status

Contact with children[2]
Avoid contact with children with lower respiratory tract infections

Factors associated with decreased risk of CAP

Dental hygiene[1,2]
Visit to the dentist in the past month

Physical activity[3]
Increase

Vaccination against influenza and *Streptococcus pneumoniae*[1,2]
Ensure compliance with guidelines

Promoting healthy habits among your patients may help to reduce the burden of CAP[2]

CAP, community-acquired pneumonia.

1. Almirall J, et al. Eur Respir J 2008;31:1274–84. 2. Torres A, et al. Thorax 2013;68:1057–65.
3. Baik I, et al. Arch Intern Med 2000;160:3082–88.

Summary of evidence and controversy on PPV23 efficacy

- **PPV23 is effective in preventing invasive infections in healthy adults and, to a lesser extent, in the elderly**
- **No definitive conclusion possible for high risk subjects (very heterogeneous)**
- **Inconsistent data on efficacy against CAP (heterogeneous studies, insufficient statistical weight), evidence of effectiveness from some observational studies**
- **Most studies conclude there is no impact on mortality**

WHO position paper on PPV23

World Health Organization

Organisation mondiale de la Santé

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

17 OCTOBER 2008, 83rd YEAR / 17 OCTOBRE 2008, 83e ANNÉE
No. 42, 2008, 83, 373–384
http://www.who.int/wer

23-valent pneumococcal polysaccharide vaccine
WHO position paper

Vaccin antipneumococcique polyosidique 23-valent
Note de synthèse de l'OMS

"Despite multiple studies conducted during > 30 years, the efficacy and effectiveness of PPV in children and adults remain poorly defined and the subject of controversy."

"There is a need for more efficacious conjugate vaccine covering the majority of pneumococcal serotypes that cause serious diseases in older children and adults worldwide and that are responsible for resistance to commonly used antimicrobial drugs"

"WHO supports the ongoing efforts to develop such products"

WHO position paper on 23-valent pneumococcal polysaccharide vaccine, 2008

Coverage of invasive pneumococcal disease serotypes by PPV23 versus PCV13

Country (Region)	Lead Author, Journal, Year	Age Group (y)	Interval Analyzed	Proportion of Isolates Corresponding to Types in:		
				PPV23	PCV13	Δ
UK	Miller, *Lancet Infect Dis*, 2011	65+ 5-64	2008-2010	81% 91%	58% 63%	23% 28%
France	Grall, *Eur J Clin Microbiol Inf Dis*, 2011	≥16	2009	89%	70%	19%
Germany	Imöhl, *Int J Med Microbiol*, 2010	>16	2008	85%	71%	14%
Spain (Tarragona)	Vila-Córcoles, *Vaccine*, 2011	65+	2008	69%	63%	6%
Portugal	Horacio, *Vaccine*, 2011	18+	2006-2008	84%	68%	16%

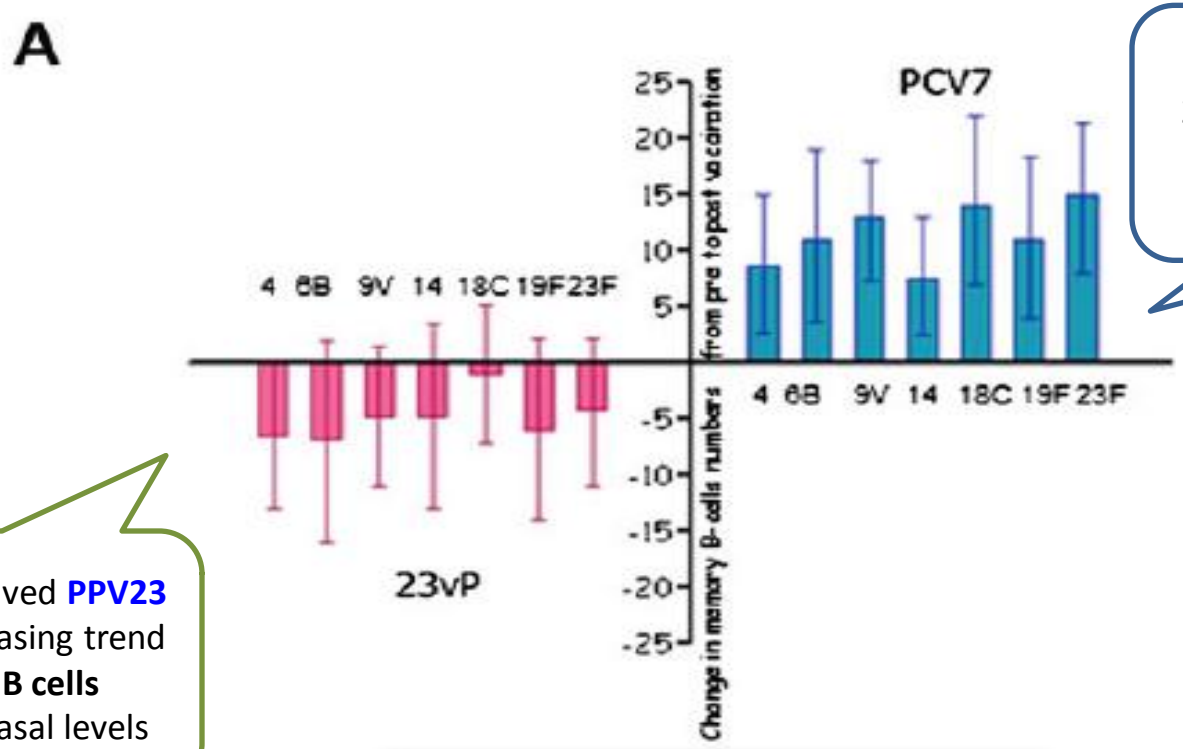
Effect of a dose of PCV or PPV on memory B cells one month after vaccination

Clutterbuck E at al, J Infect Dis, 2012

PPV

PCV

Before any vaccinaion, 86% of subjects had some basal level of antibody-secreting MBC to at leaast 1 of 7 serotypes, although being *naive*



28 days after vaccination in those receiving **PCV7**

Those who received **PPV23** showed a decreasing trend of **memory B cells** compared to basal levels

Memory B cells

CAP caused by PCV13 serotypes in adults

	Pfizer-sponsored study (6115A-4007)	CDC (EPIC)	CAPiTA (Community-Acquired Pneumonia Immunization Trial in Adults)
Inclusion criteria	Adults presenting to hospitals with radiographically confirmed CAP	CAP etiology among hospitalized adults	Adults presenting to sentinel centers with suspected pneumonia
	≥ 50 years	≥ 18 years	≥ 65 years
Number of subjects	710	2044	84,496
Study dates	Feb 2010–Sep 2011	Jan 2010–June 2012	Sep 2008–Aug 2013
Location	13 sites, geographical spread across ASM regions	Hospitals in Atlanta, Chicago and Nashville	59 sentinel centers throughout the Netherlands
PCV13 positive (%)	**11.0%**	**9.0%**	**13.0%**

Sherwin RL, et al. J Infect Dis 2013;208:1813–20; Grijalva CG, et al. ISPPD-9, 2014; Hyderabad, India; Bonten MJM, et al. N Engl J Med 2015;372:1114–25

Key criteria for regulatory approval of PCV13 for prevention of pneumococcal pneumonia

Immunogenicity studies

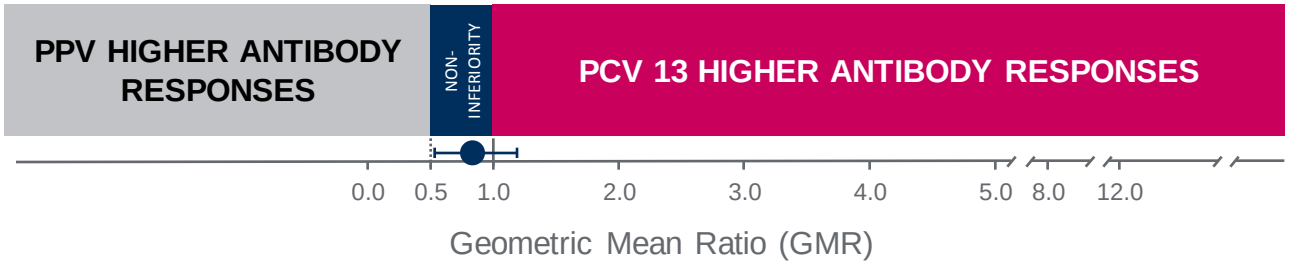
Unmet need for pneumococcal pneumonia

Confirmatory efficacy study

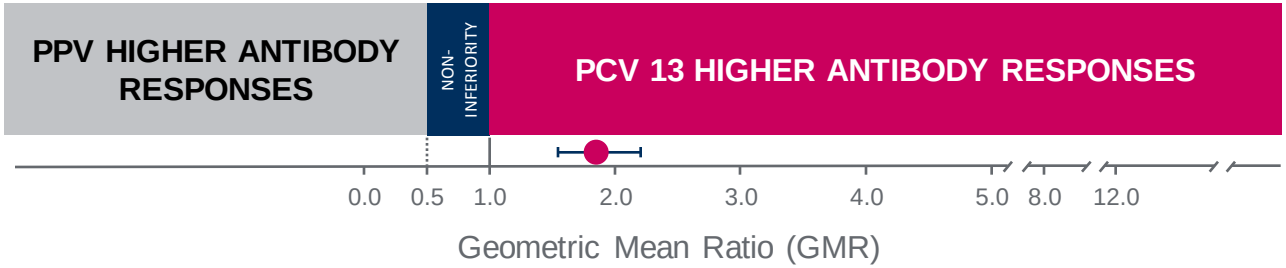
Pneumococcal Conjugate Vaccine (PCV13) in adults > 50 years: immunogenicity studies

Pivotal non-inferiority comparisons of immune responses

- Definitions for the 12 serotypes in common
  - Noninferiority (primary endpoint)
    - Lower limit of the 95% CI for the GMT ratio is **> 0.5**,



  - Statistically significantly higher (secondary endpoint)
    - Lower limit of the 95% CI for the GMT ratio is **> 1**

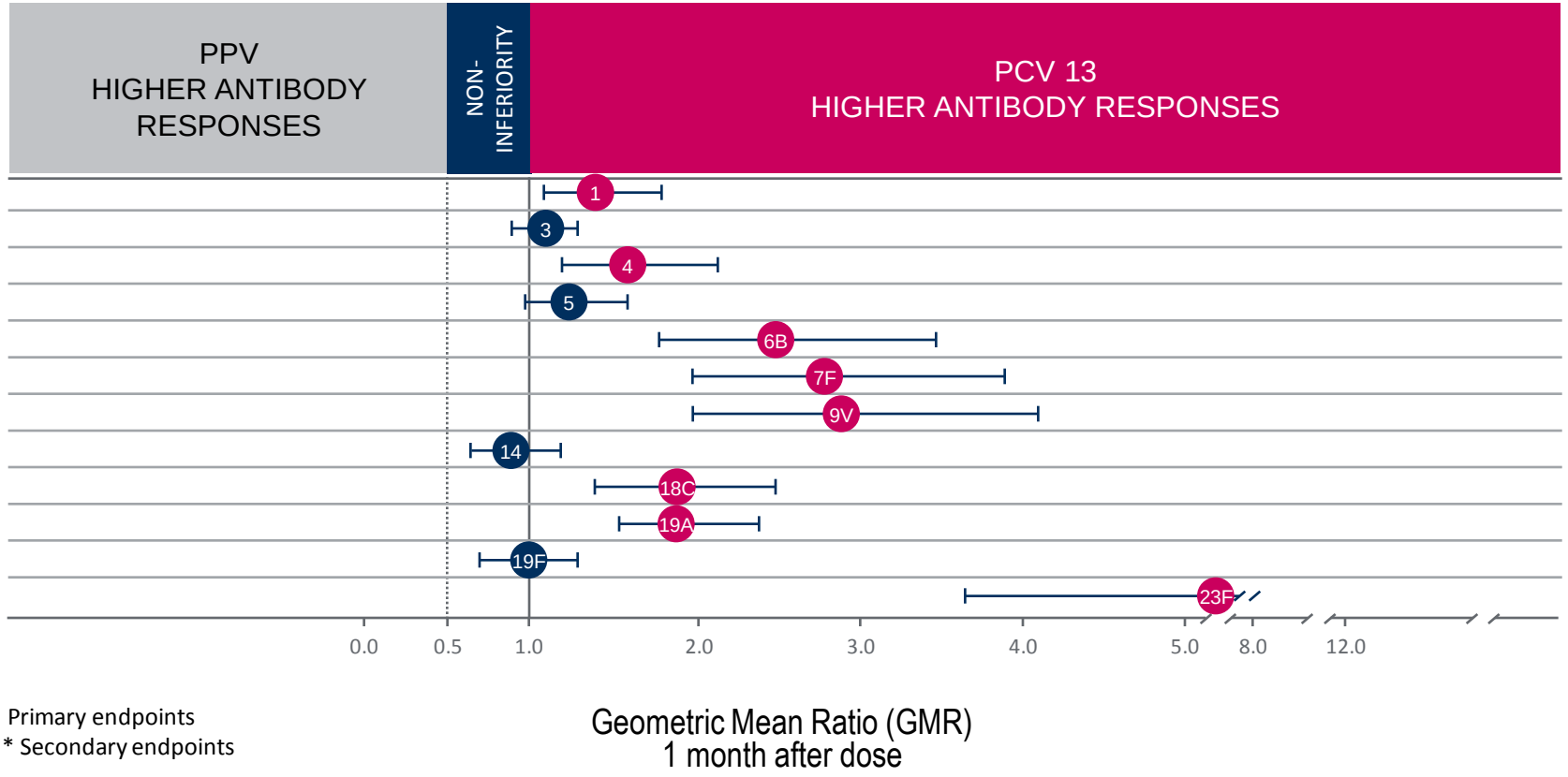


CI: confidence interval
GMT: geometric mean titre

PCV13 impact on functional antibody responses in adults aged 60-64 years not previously vaccinated with PPV23

Trial 004: OPA responses elicited by PCV13 for the 12 serotypes in common:

- Non-inferior to PPV23 for all of the serotypes in common*
- Statistically significantly superior to PPV23 for 10 of the serotypes in common** and for serotype 6A*



* Primary endpoints
** Secondary endpoints

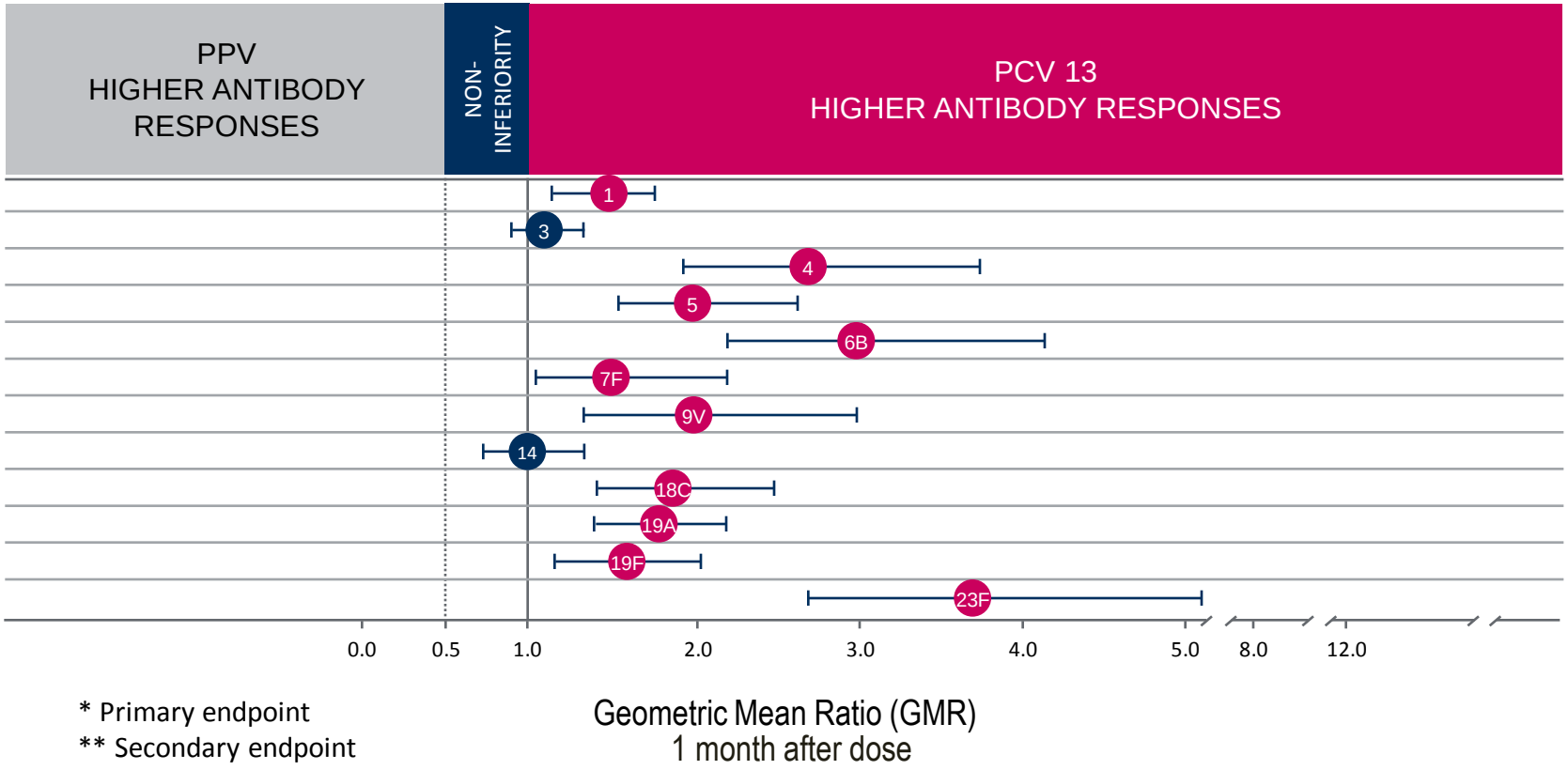
†Serotype 6A is not included in PPV. GMT, geometric mean titer; OPA, opsonophagocytic assay; PPV, pneumococcal polysaccharide vaccine.

1. Jackson LA, et al. Vaccine 2013;31:3577–84.

PCV13 impact on functional antibody response in adults ≥70 years of age previously vaccinated with PPV

Trial 3005, OPA responses elicited by Prevenar 13 for the 12 serotypes in common:

- Non-inferior to PPV for all of the serotypes in common*
- Statistically significantly superior to PPV for 10 of the serotypes in common** and for serotype 6A*



†Serotype 6A is not included in PPV. GMR, geometric mean ratio; GMT, geometric mean titer; OPA, opsonophagocytic assay; PPV23, 23-valent pneumococcal polysaccharide vaccine.

1. Jackson LA, et al. Vaccine. 2013;31:3585-3593.

Main immunogenicity results with PCV13

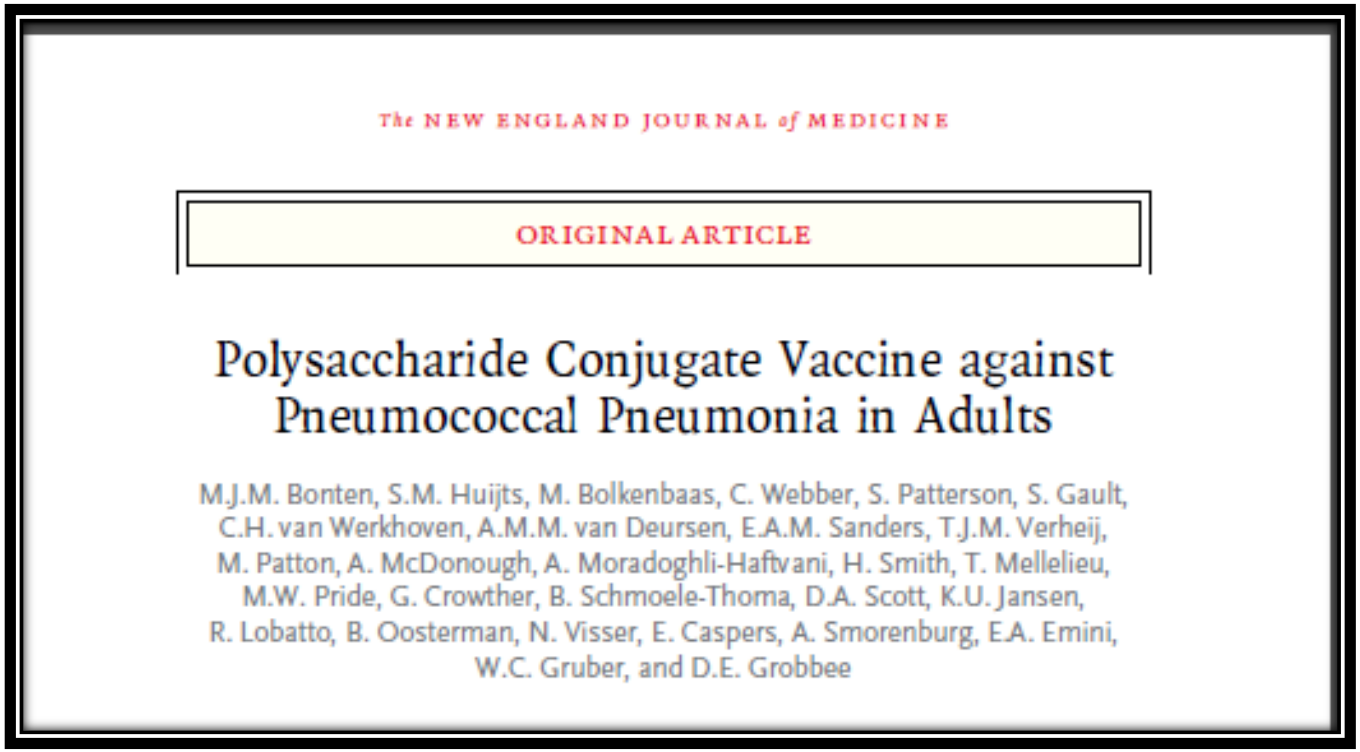
Registered in Europe for the prevention of invasive pneumococcal diseases based on immunogenicity data.

It elicits higher levels of functional antibodies both in naive subjects and in individuals already vaccinated with PPV23

If a sequential vaccination is recommended, PCV13 should be always administered as first vaccine

The incremental serotype coverage of PPV23 vs PCV13 ranges from 6 to 28% in different countries (average around 15%) in invasive diseases

CAPiTA trial (Community-Acquired Pneumonia Immunization Trial in Adults) published in March 2015 in the New England Journal of Medicine[1]



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Polysaccharide Conjugate Vaccine against Pneumococcal Pneumonia in Adults

M.J.M. Bonten, S.M. Huijts, M. Bolkenbaas, C. Webber, S. Patterson, S. Gault, C.H. van Werkhoven, A.M.M. van Deursen, E.A.M. Sanders, T.J.M. Verheij, M. Patton, A. McDonough, A. Moradoghli-Haftvani, H. Smith, T. Mellelieu, M.W. Pride, G. Crowther, B. Schmoele-Thoma, D.A. Scott, K.U. Jansen, R. Lobatto, B. Oosterman, N. Visser, E. Caspers, A. Smorenburg, E.A. Emini, W.C. Gruber, and D.E. Grobbee

1. Bonten MJ, et al. N Engl J Med 2015;372:1114–25.

CAPiTA (Community-Acquired Pneumonia Immunization Trial in Adults) study objectives[1]

Demonstrate the efficacy of PCV13 in the prevention of a first episode of:

- 1° VT pneumococcal CAP
  - Invasive or non-invasive
- 2° VT non-bacteremic/non-invasive pneumococcal CAP
- 2° VT invasive pneumococcal disease
  - With or without pneumonia

Analyses populations are per protocol and modified intention-to-treat.

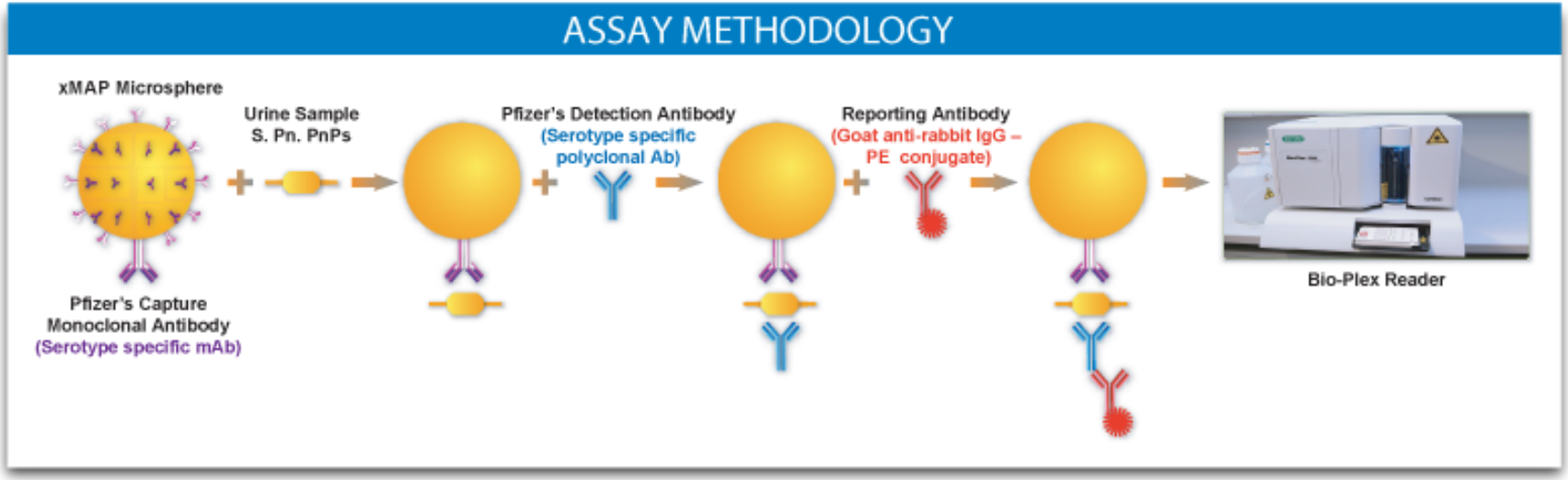
CAP, community-acquired pneumonia; VT, vaccine type.

1. Hak E, et al. Neth J Med 2008;66:378–83.

PCV13 is a pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed). Please refer to the Summary of Product Characteristics and official recommendations.

The serotype-specific urinary antigen detection (SSUAD) assay

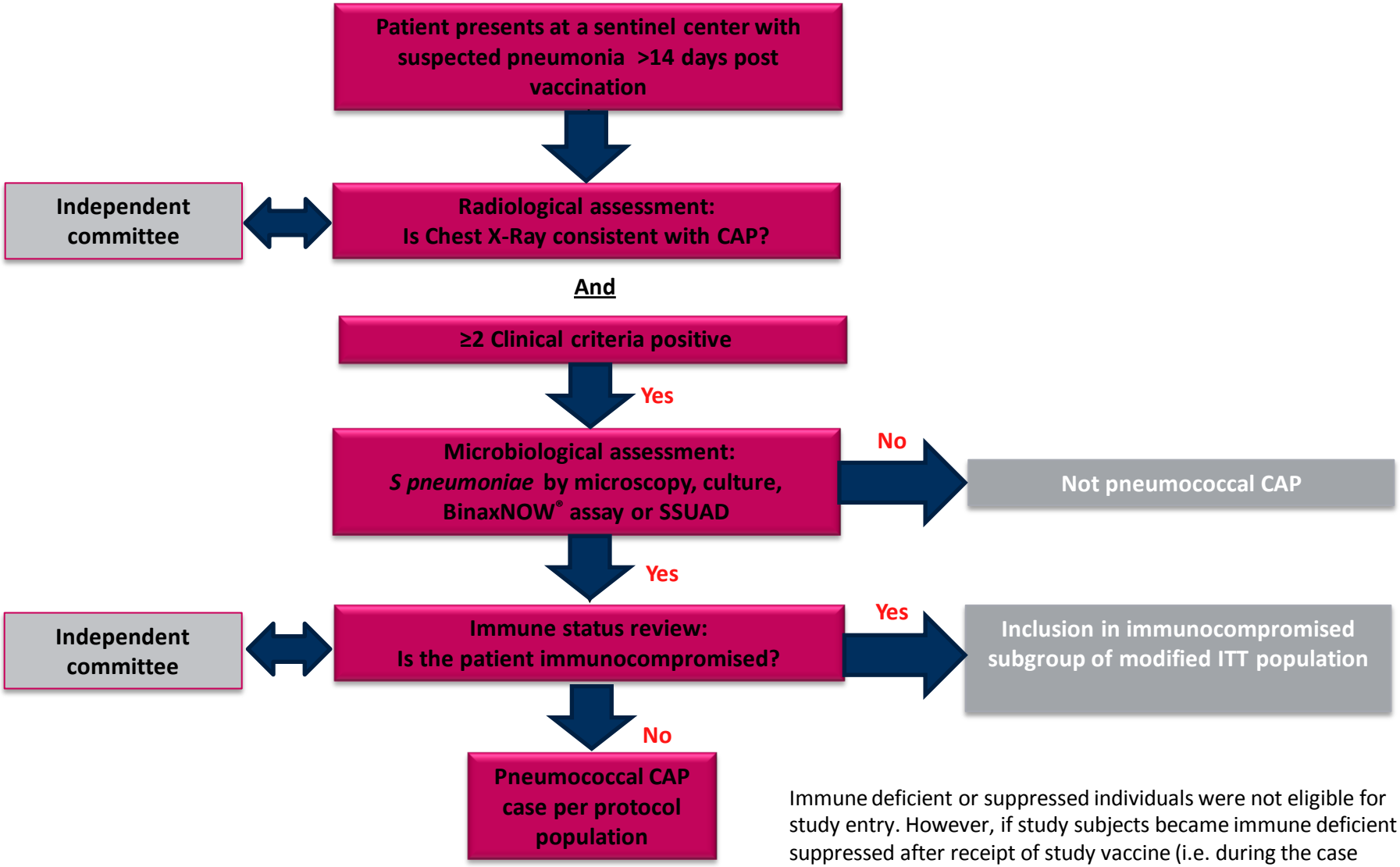
- Developed specifically for the Community-Acquired Pneumonia Immunization Trial in Adults (CAPiTA) study[1]
- A multiplex antigen-binding assay for detection of PCV13-type capsular polysaccharide[1]
- Enables accurate testing of urine for the **presence of a PCV13 serotype:** 97% sensitivity and 100% specificity[2]



1. Bonten MJM, et al. N Engl J Med 2015;372:1114–25 (supplementary appendix).
2. Pride MW et al. Clin. Vaccine Immunol. 2012;19(8):1131-1141.

PCV13 is a pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed). Please refer to the Summary of Product Characteristics and official recommendations.

Community-acquired pneumonia (CAP) case capture[1]



Immune deficient or suppressed individuals were not eligible for study entry. However, if study subjects became immune deficient or suppressed after receipt of study vaccine (i.e. during the case accrual period) and experienced an episode of CAP or IPD these events were included in the modified ITT analyses.

IPD, invasive pneumococcal disease; ITT, intent to treat.

1. Bonten MJM, et al. N Engl J Med 2015;372:1114–25 (supplementary appendix).

Primary and secondary end points, per protocol population[1]

Efficacy endpoint	Vaccine group		VE (%)	95.2% CI	p-value
	PCV13 (n=42,240)	Placebo (n=42,256)			
1°: First episode of confirmed VT pneumococcal CAP	49	90	45.56	(21.82,62.49)	0.0006
2°: First episode of confirmed NB/NI VT pneumococcal CAP	33	60	45.00	(14.21, 65.31)	0.0067
2°: First episode of VT-IPD	7	28	75.00	(41.43, 90.78)*	0.0005

* 95% CI

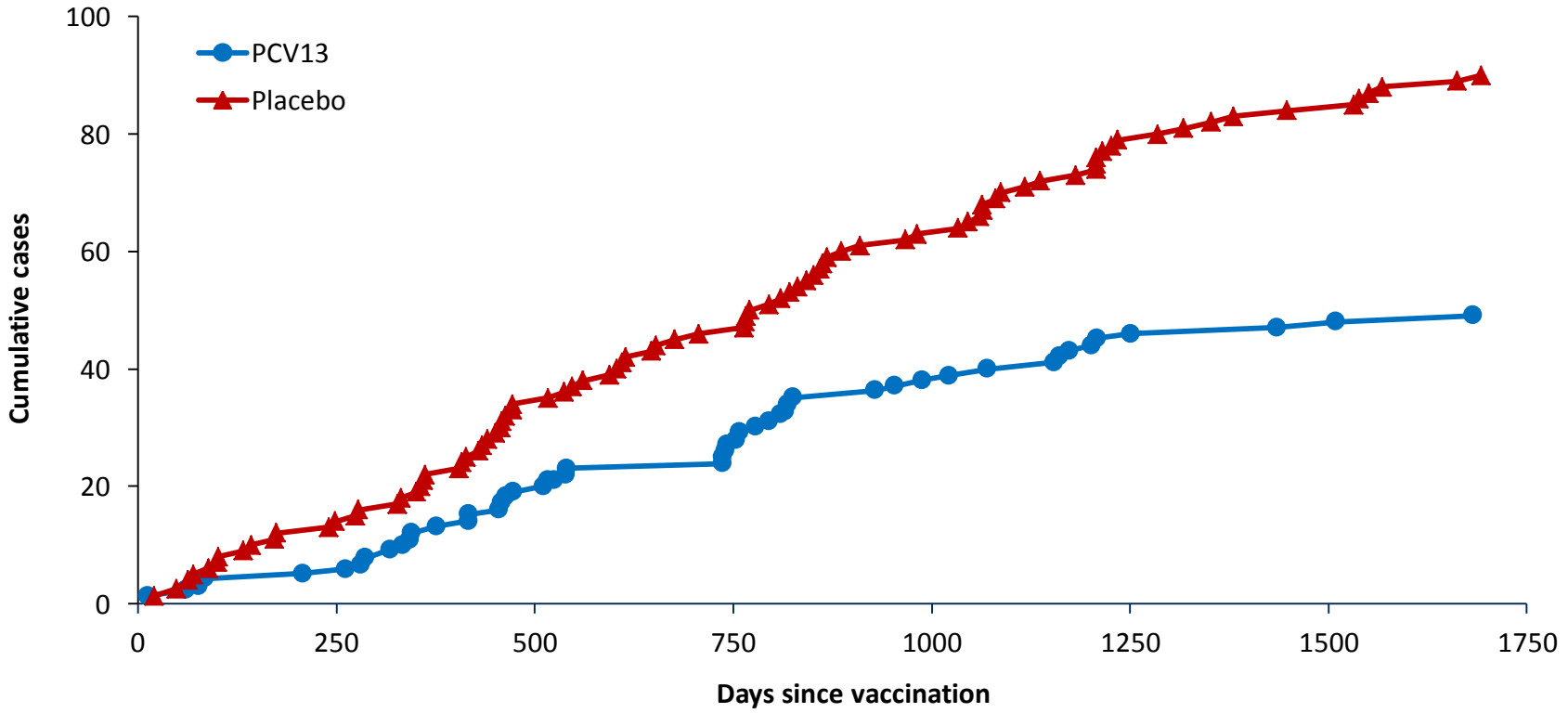
CAP, community-acquired pneumonia; CI, confidence interval; IPD, invasive pneumococcal disease; NB/NI, nonbacteremic/noninvasive; VE, vaccine efficacy; VT, vaccine-type.

1. Bonten MJM, et al. N Engl J Med 2015;372:1114–25.

PCV13 is a pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed). Please refer to the Summary of Product Characteristics and official recommendations.

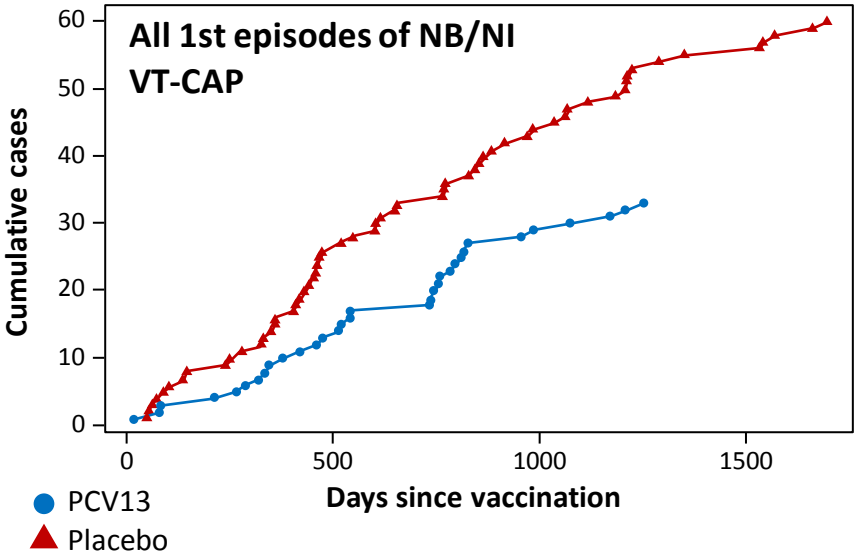
Duration of protective efficacy extended throughout the 4-year study[1]

Mean duration of follow-up = 3.97 years (all 1st episodes VT-CAP)†

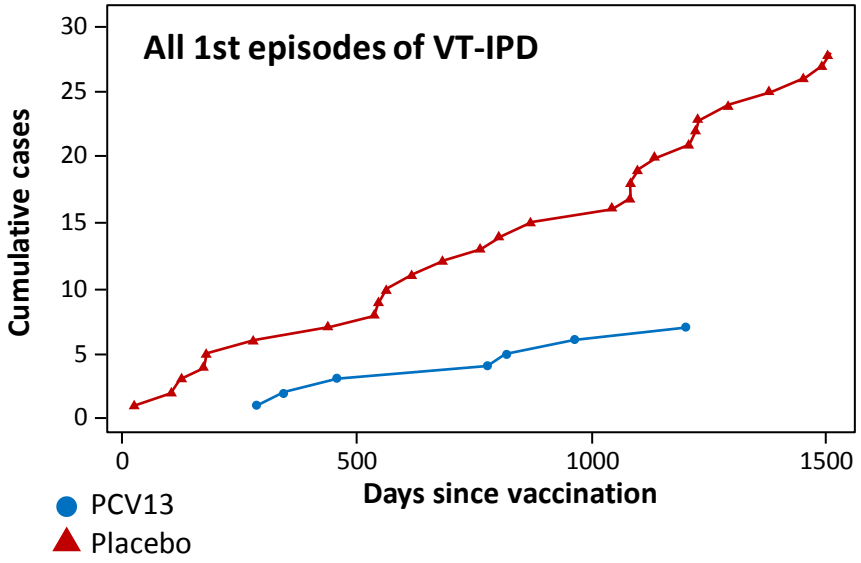


†Post-hoc analysis.
VT-CAP, vaccine-type community-acquired pneumonia.
Figure adapted from: 1. Bonten MJM, et al. N Engl J Med 2015;372:1114–25.

Duration of protective efficacy extended throughout the 4-year study[1]



Mean duration of follow-up = 3.97 years



CAP, community-acquired pneumonia; IPD, invasive pneumococcal disease; NB, non-bacteremic; NI; non-invasive; VT, vaccine type.

Figures adapted from: 1. Bonten MJM, et al. N Engl J Med 2015;372:1114–25.

PCV13 is a pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed). Please refer to the Summary of Product Characteristics and official recommendations.

Vaccine efficacy of first episode of confirmed VT-CAP, per protocol population, by age[1]*

	Vaccine group**		VE (%)	95.2% CI	p-value
	PCV13 (N=42,240)	Placebo (N=42,256)			
Overall	49	90	45.56	21.82, 62.49	<0.001
Number of <75	29,006	29,064			
Age <75 Years (n)	28	59	52.54	24.09, 70.99	0.001
Number of ≥75 and <85	11,727	11,753			
Age ≥75 and <85 Years (n)	15	28	46.43	-4.33, 73.57	0.07
Number of ≥85	1,504	1,438			
Age ≥85 Years (n)	6	3	-100.0	-1156.63, 57.78	0.51

* Post hoc analyses, study not powered to statistically analyze sub-groups

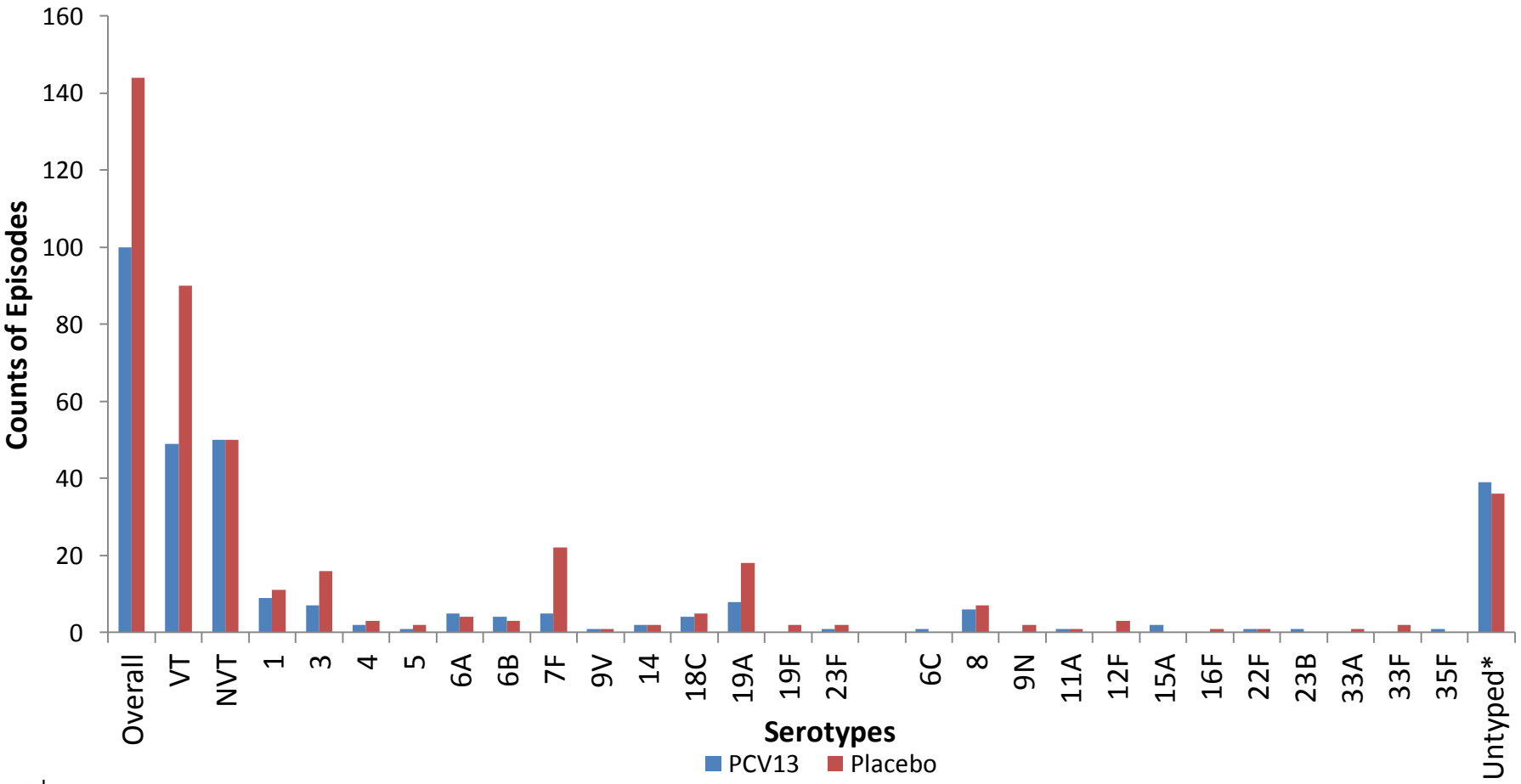
** Four subjects (3 in the PCV13 group and 1 in the placebo group) were excluded because they had no safety data.

CAP, community-acquired pneumonia; CI, confidence interval; NB, non-bacteremic; NI, non-invasive; VE, vaccine efficacy; VT, vaccine type; IPD, invasive pneumococcal disease.

1. Bonten MJM, et al. N Engl J Med 2015;372:1114–25 (supplementary appendix).

PCV13 is a pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed). Please refer to the Summary of Product Characteristics and official recommendations.

First episodes of confirmed pneumococcal CAP by individual serotypes: Per-protocol population[1,2]



*Untyped:
- Episodes with missing or untyped serotype from culture and negative UAD results (for all VT serotypes) are assumed to be NVT (37 PCV13; 32 placebo).
- Episodes with missing culture, or culture with missing serotype, also lacking sufficient UAD information allowing VT or NVT categorization (2 PCV13; 4 placebo).

CAP, community-acquired pneumonia; NVT, nonvaccine-type; UAD, urinary antigen detection; VT, vaccine-type.

1. Bonten MJM, et al. N Engl J Med 2015;372:1114–25 (supplementary appendix). 2. Webber C, Exploratory Efficacy Endpoints in the Community-Acquired Pneumonia Immunization Trial in Adults (CAPiTA), ECCMID 2015, Copenhagen, Denmark, 26 April 2015

PCV13 is a pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed). Please refer to the Summary of Product Characteristics and official recommendations.

What is the impact of PCV13 data?

CAPiTA (Community-Acquired Pneumonia Immunization Trial in Adults) efficacy results in context: 46% in older adults[1]*

Elderly adults with influenza[2]

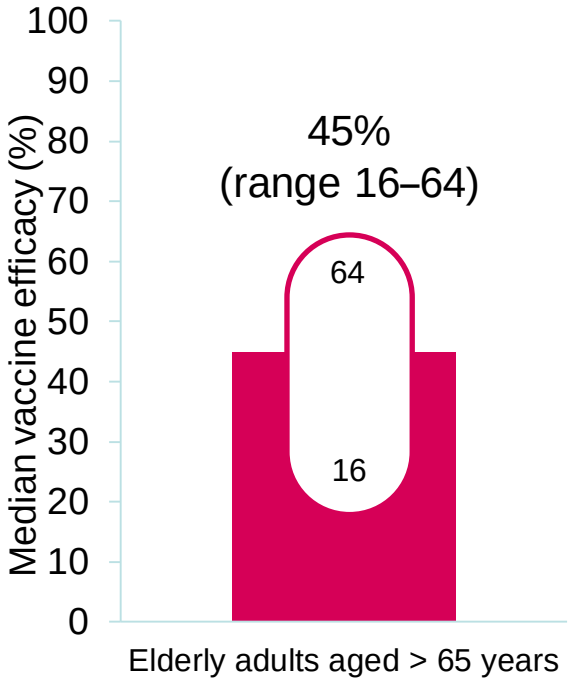


Figure adapted from data in Jefferson et al.[2]

Elderly adults with CAP[1]

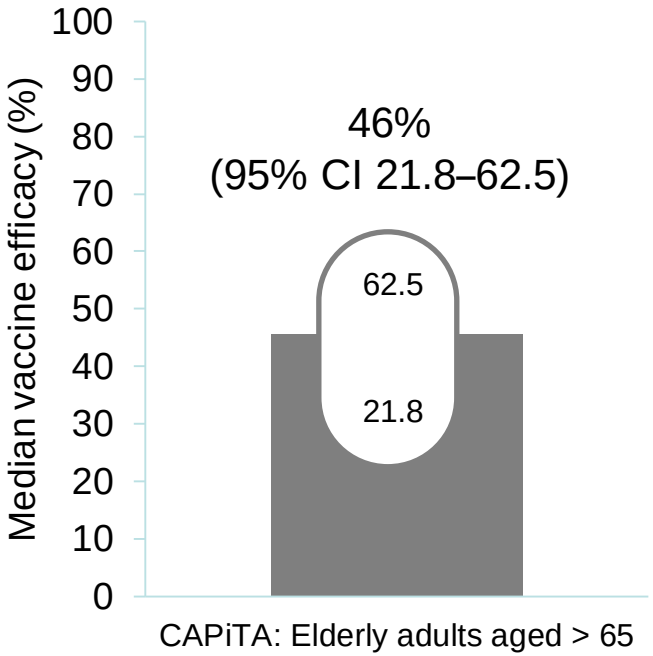


Figure adapted from data in Bonten et al.[1]

*Data shown are taken from meta-analysis of published influenza vaccine trials. Please refer to source references for more details. Figures developed using data from Bonten et al[1] and Jefferson et al.[2]

CAP, community acquired pneumonia.

1. Bonten MJM, et al. N Engl J Med 2015;372:1114–25. 2. Jefferson T, et al. Cochrane Database Syst Rev 2010(2):CD004876.

Estimated preventable vaccine-serotype CAP: EU adults

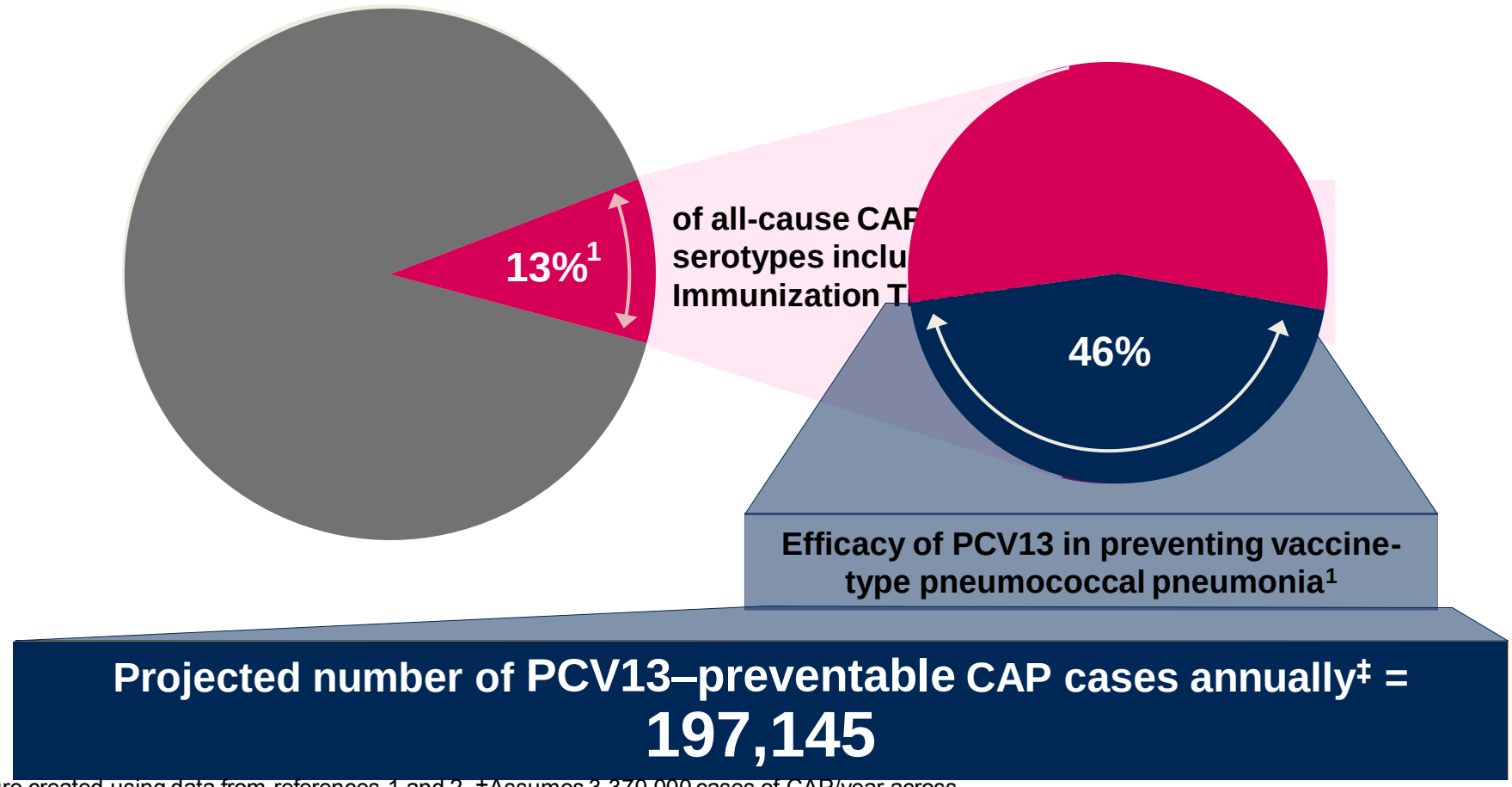


Figure created using data from references 1 and 2. †Assumes 3,370,000 cases of CAP/year across all age groups in the EU[2] ‡Assumes 100% vaccine coverage. CAP, community-acquired pneumonia; CAPiTA, Community-Acquired Pneumonia Immunization Trial in Adults.

1 Bonten MJM, et al. N Engl J Med 2015;372:1114–25. 2. European Respiratory Society (ERS). European Lung White Book – Chapter 18. Avaliable at: http://www.erswhitebook.org/chapters/acute-lower-respiratory-infections/pneumonia/ Accessed September 2015.

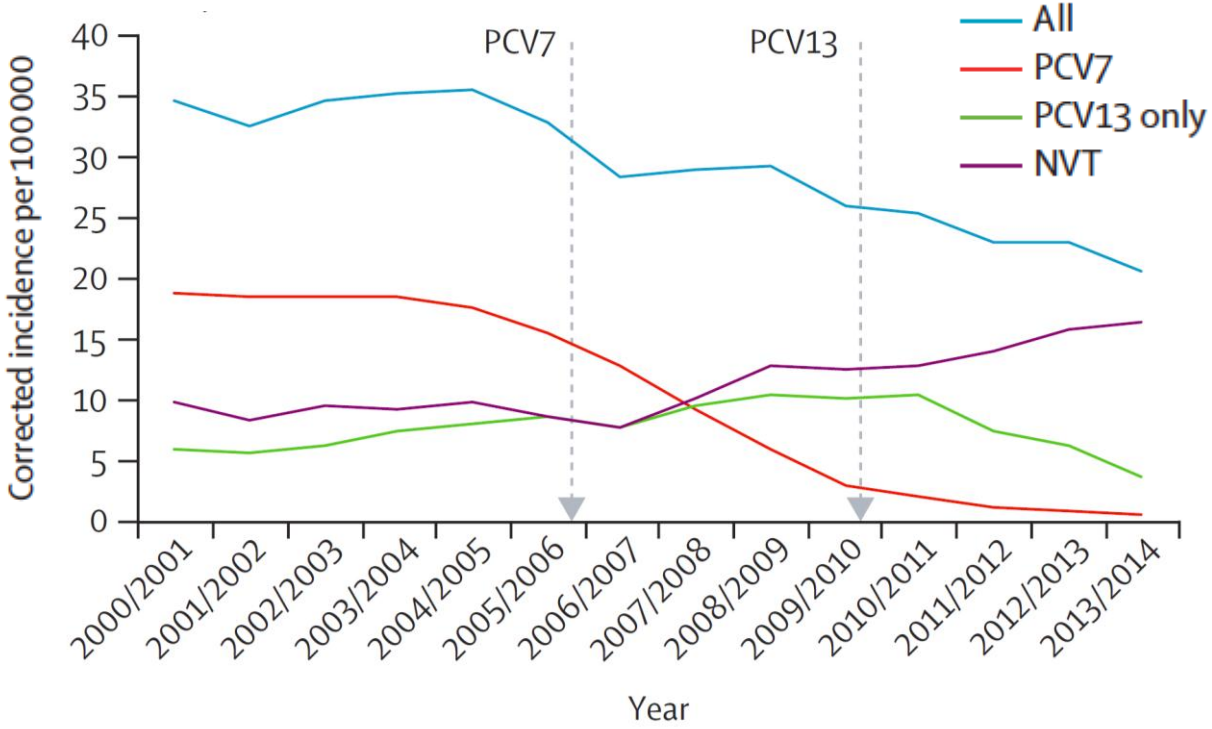
Possible sequential strategy PCV13 / PPV23

- **Target: subjects aged > 64 years (one or more cohorts by age)**
- **Vaccination with PCV13 (priming) + PPV23 , 1 year apart (to be discussed)**
- **Opportunistic vaccination?: co-administration with influenza vaccine**
- **Possible extension of vaccination offer in all seasons (single injection)**

PCV7 and 13: Impact on IPD in adults

PCV7: 2006
PCV13: 2010

England and Wales, Adults ≥65 years

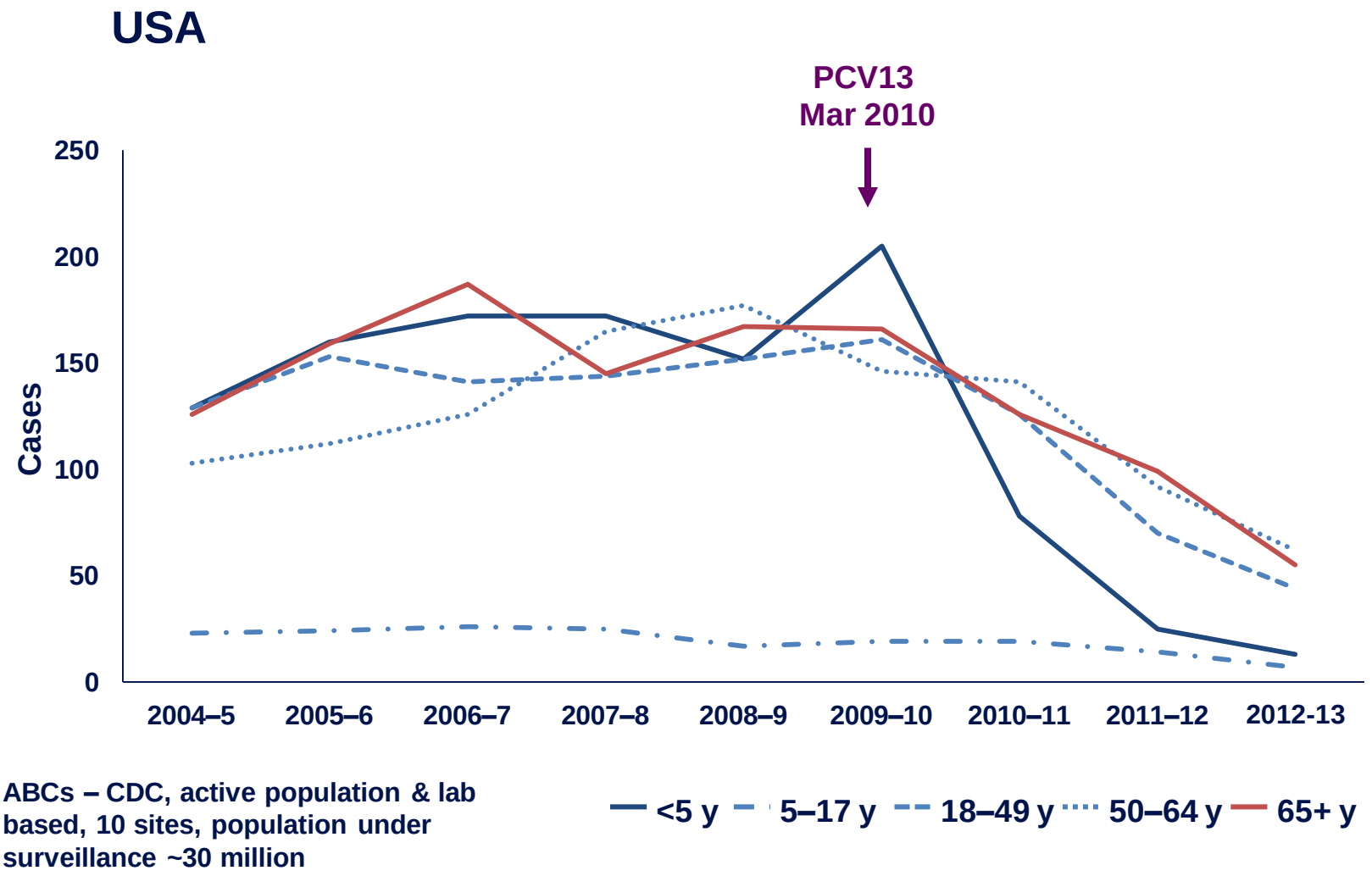


National dataset of electronically reported and serotyped IPD cases

Waight PA, et al. Lancet Infect Dis 2015;15:629

PCV13 is a pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed). Please refer to the Summary of Product Characteristics and official recommendations.

PCV13: Impact on ST 19A IPD in adults



ABCs – CDC, active population & lab based, 10 sites, population under surveillance ~30 million

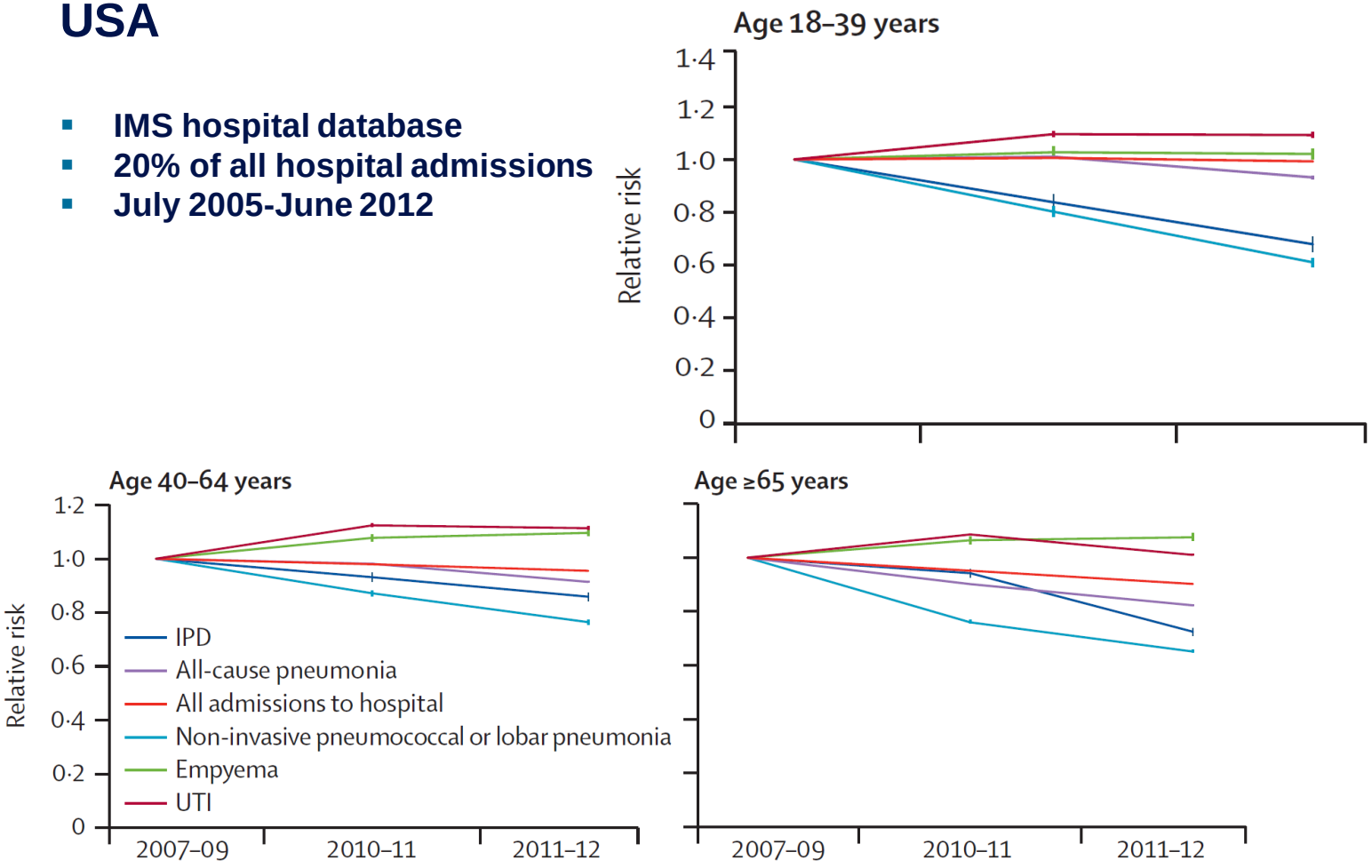
ST, serotype; IPD, invasive pneumococcal disease
Moore MR et al. Lancet Infect Dis 2015;15:301-309

PCV13 is a pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed). Please refer to the Summary of Product Characteristics and official recommendations.

PCV13: Impact on pneumonia in adults

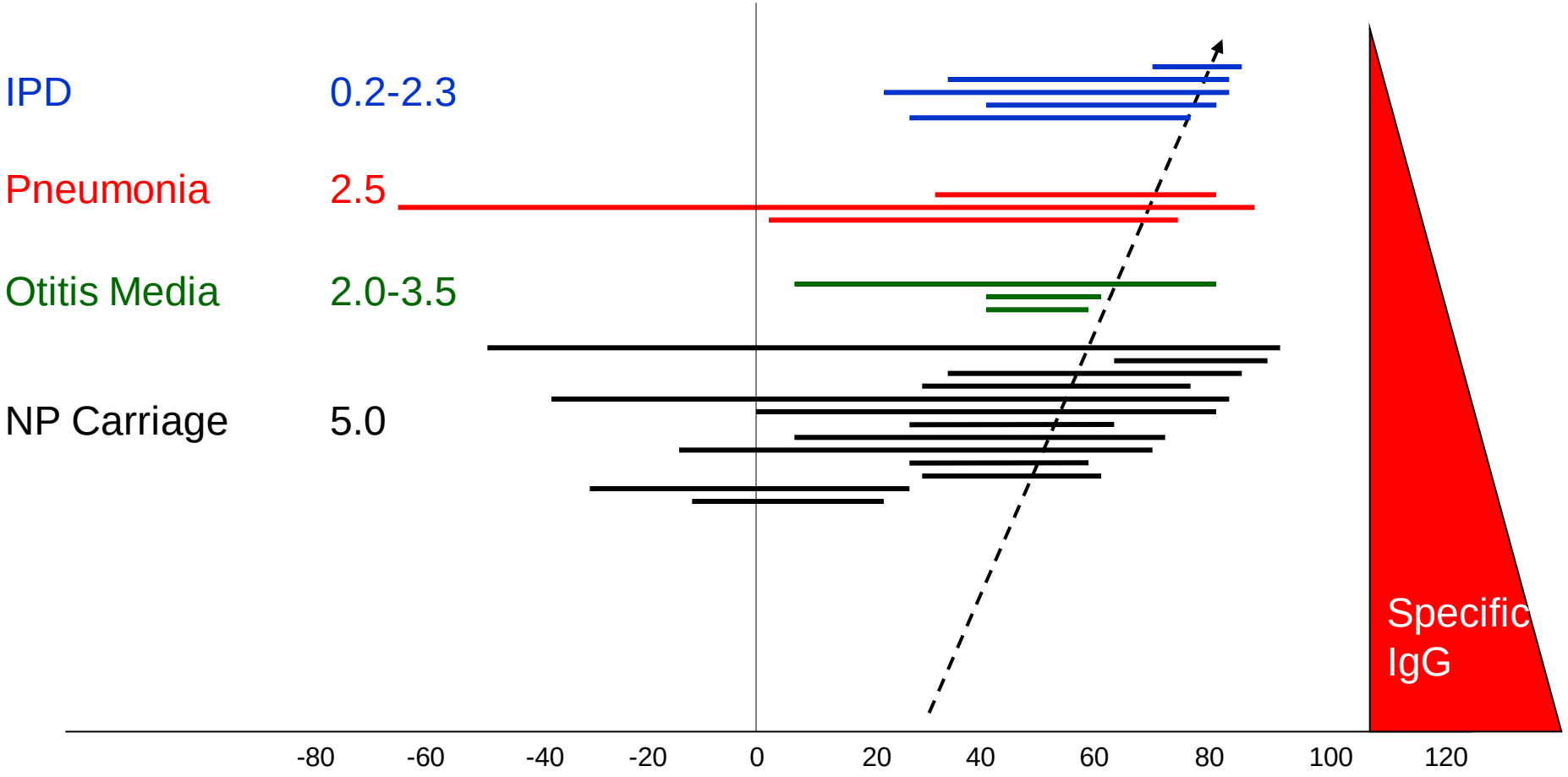
USA

- IMS hospital database
- 20% of all hospital admissions
- July 2005-June 2012



Simonsen L et al. Lancet Respir Med. 2014;2:387-94

Pneumococcal Conjugate vaccine efficacy against various endpoints (µg/ml)



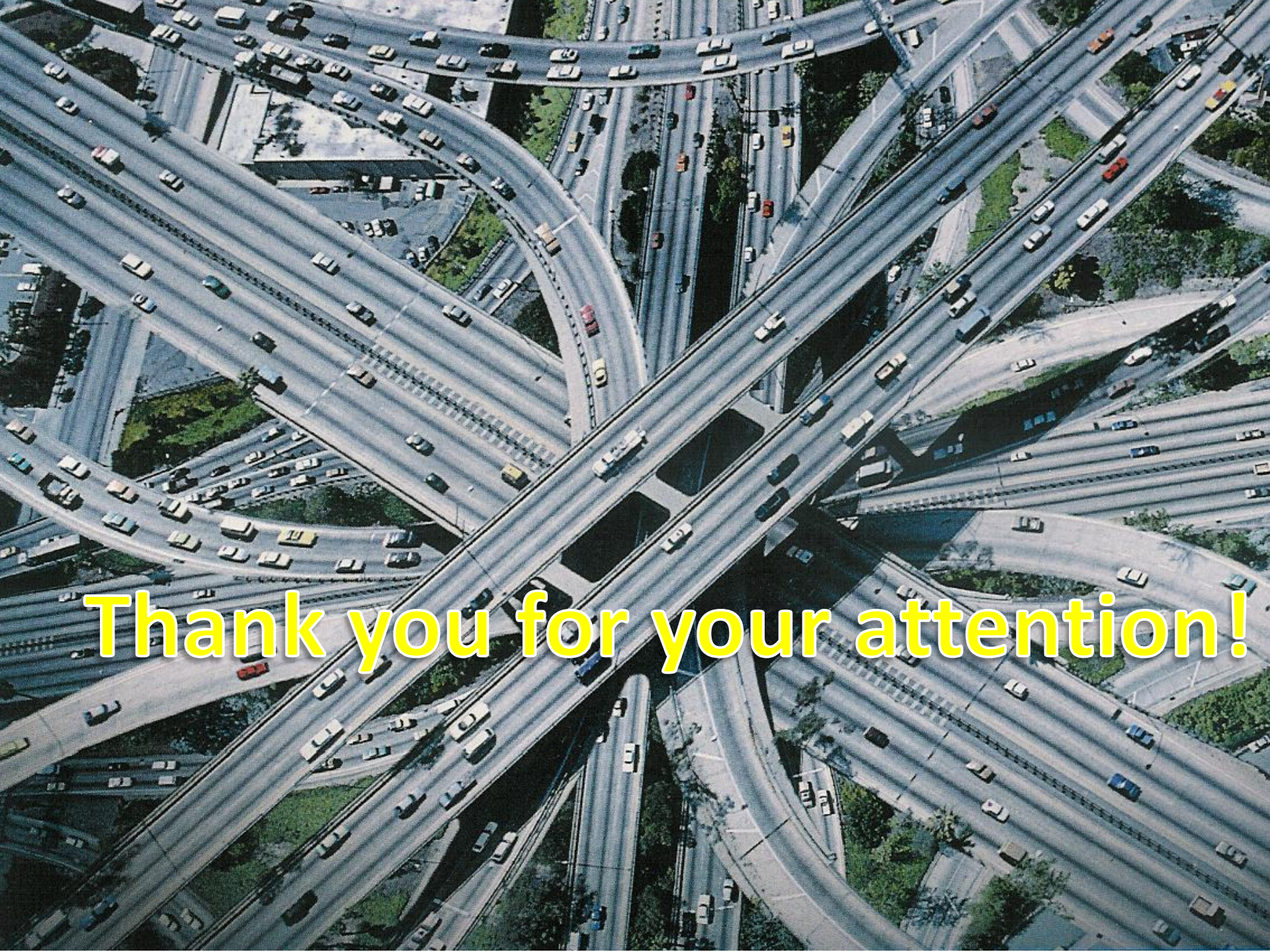
Source: D. Goldblatt, 2008

European adult national recommendations for PCV13

* Recommended At Risk >5 years but not approved by Health Authority.
** National Age based funded but not recommended.
Last update 2015-09-09. References are available on request.

Conclusions

- Conjugate vaccines may induce a stronger immune response and memory compared with polysaccharide vaccines
- They had a dramatic impact on IPD and pneumonia in children
- Their efficacy in adults has now been demonstrated, being 45% against first episode VT pneumococcal CAP (Invasive or non-invasive), and 75% against VT IPD
- The best vaccination scheme and schedule needs to be investigated in the near future. However, if also the polysacccharide vaccine needs to be used in a sequential scheme, PCV must be the first to be given
- VT pneumococcal CAP are around 13% of all CAP. Given the results of the CAPiTA Study, a universal vaccination of ≥65-year olds in Europe would have the potential of preventing almost 200,000 cases of CAP every year
- Countries are now considering which vaccination strategy best fits their epidemiological situation and need to evaluate the impact of infant vaccination programs on disease in the elderly


Thank you for your attention!