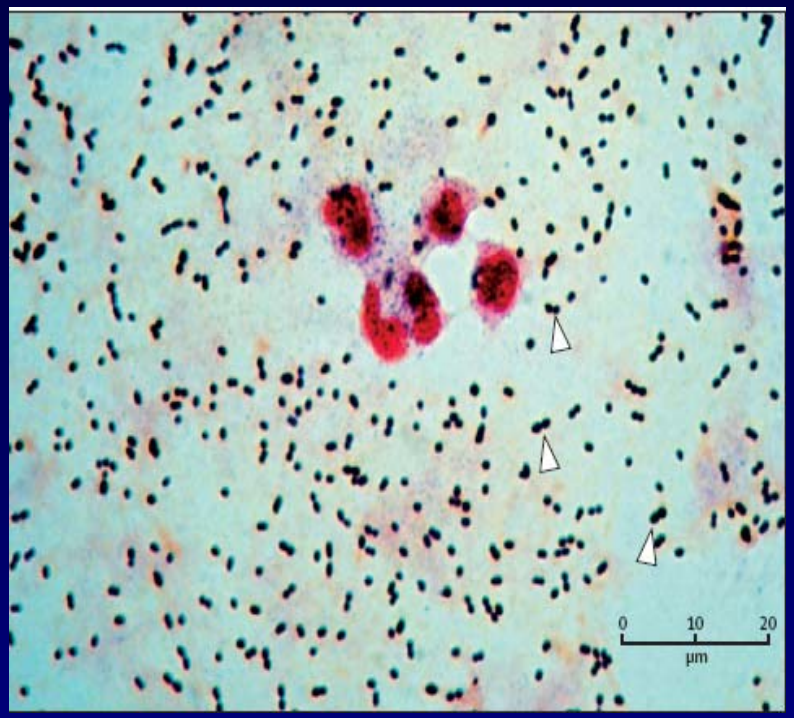


Pneumococcal Vaccine : It's Essential for Adults

Terapong Tantawichien, M.D.
Division of Infectious Diseases
Department of Medicine,
Chulalongkorn University
And Queen Saovabha Memorial Institute,
Thailand

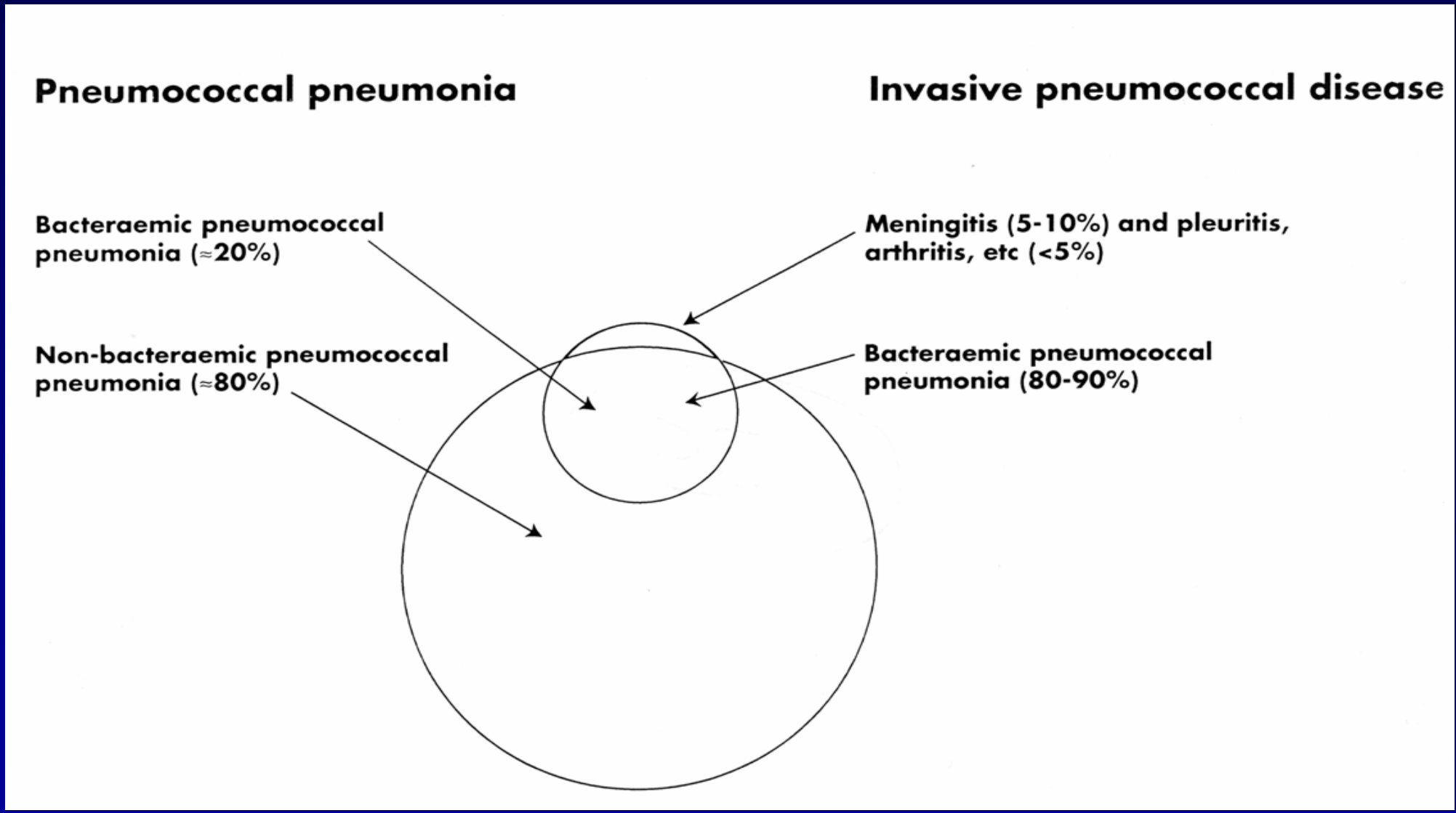
Overview :

- Pneumococcal Disease Burden
- Pneumococcal Vaccine : Effectiveness of Polysaccharide Pneumococcal Vaccine
- Recommendation of Polysaccharide Pneumococcal Vaccine
- Pneumococcal Vaccination in Pandemic Influenza

What is the most important risk factor of pneumococcal diseases ?

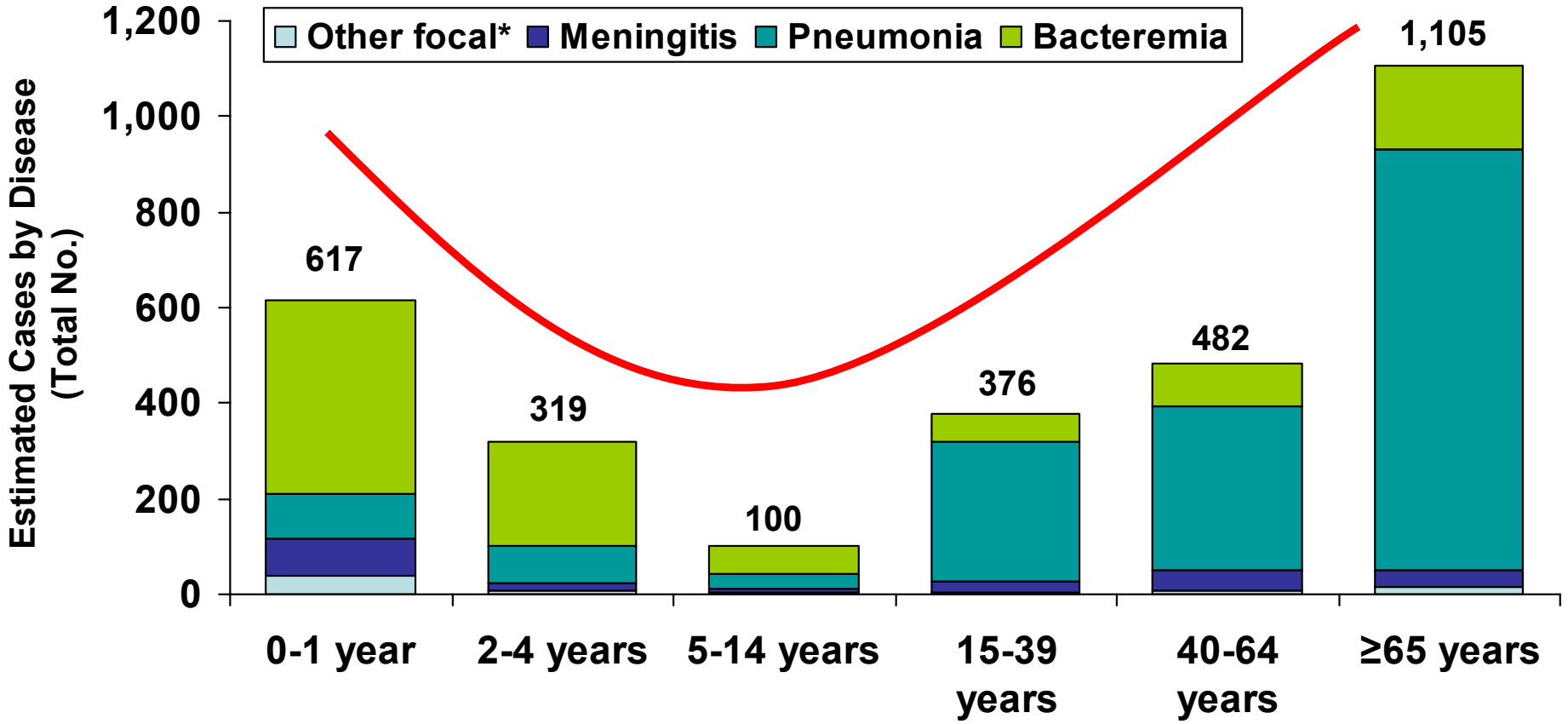
A Elderly
B Asplenia
C Immunosuppressive therapy
D HIV infection
E Smoker

The Overlap Between Pneumococcal Pneumonia and Invasive Pneumococcal Disease



Fedson DS. *Drugs Aging* 1999

Incidence of IPD by Type/Age (Australia)



IPD by age is a "U-shaped curve," with more bacteremia in the young and more pneumonia in the elderly

Active Surveillance of Manifestations of IPD by Age, Metropolitan NSW, 1997-2001

*Other focal diseases included cellulitis, arthritis, and epiglottitis

McIntyre P, et al. *NSW Public Health Bull.* 2003;14:85-89.

Table 1 Epidemiological data for invasive pneumococcal disease in the base-case analyses

	Belgium[a]	Denmark[b]	England and Wales[b]	France[a]	Germany[b]	Italy[b]	The Netherlands[b]
Incidence (per 100,000)							
65–74 years	28.3	50.0	23.0	20.5	–	–	42.0
75–84 years	41.2	72.9	37.0	28.6	–	–	66.0
≥85 years	65.4	99.3	95.0	67.7	–	–	92.1
≥65 years	35.6	63.9	36.0	29.3	50.0[c]	50.0[c]	55.1
Mortality (%)							
65–74 years	12.8[d]	12.8	16.0	18.9	–	–	15.7[d]
75–84 years	19.9[d]	31.4	20.0	20.6	–	–	16.9[d]
≥85 years	26.3[d]	40.0	17.0	42.4	–	–	17.8[d]
≥65 years	19.3[d]	22.8	18.0	25.8	20.0[c]	20.0[c]	16.6[d]

Evers SM; Eur J Clin Microbiol Infect Dis (2007) 26:531–540

[a] Reported earlier [12]

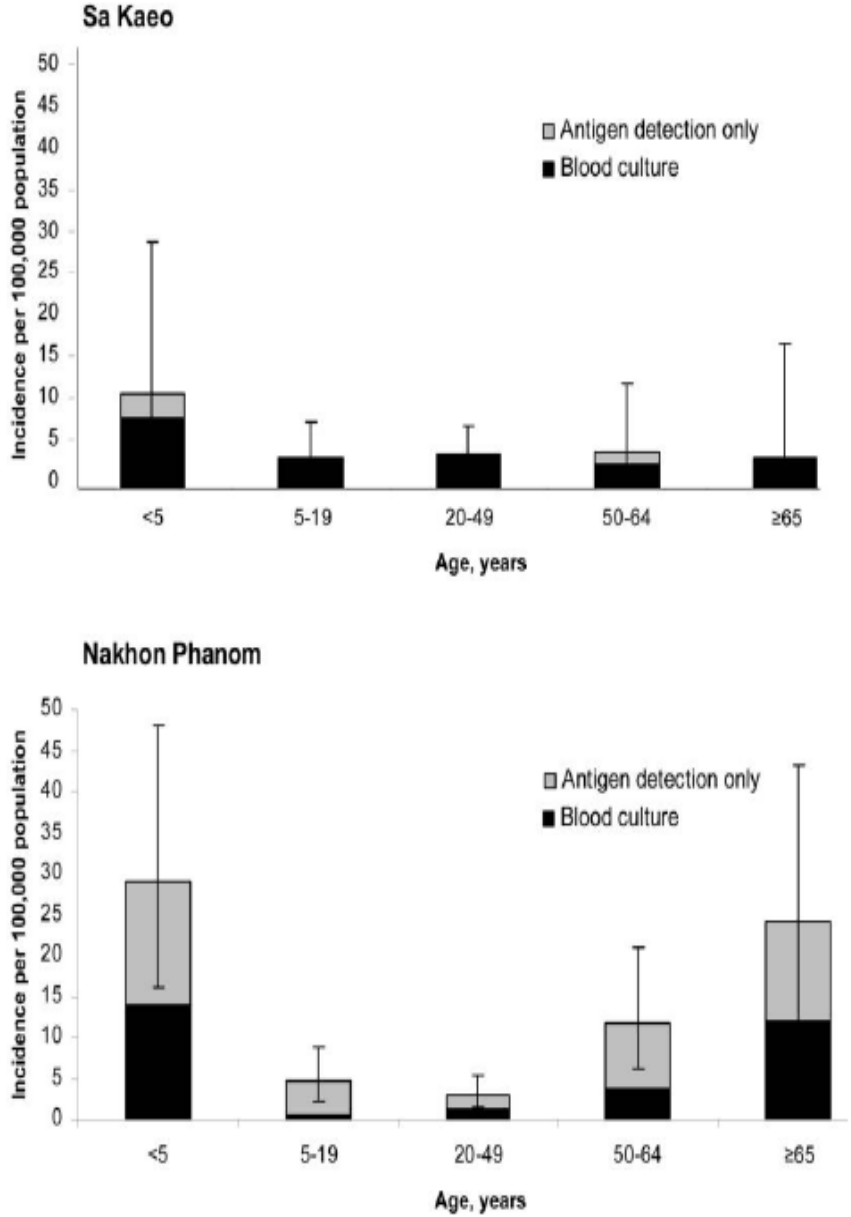


Figure 1. Annualized incidence of pneumococcal bacteremia cases requiring hospitalization in the Sa Kaeo and Nakhon Phanom provinces, Thailand, November 2005–June 2007. "Antigen detection only" refers to patients who had positive blood culture media that failed to grow a pathogen on subculture but that tested positive by an immunochromatographic test of pneumococcal antigen (NOW *Streptococcus pneumoniae* Antigen Test; Binax) [11].

Risk Factors for IPD

Age[1]	Underlying Medical Conditions[2,3]	Demographic Features[3,4]
• Children ≤2 years of age • Adults ≥65 years of age	• Congenital or acquired immunodeficiency • Sickle cell disease, asplenia, HIV • Pulmonary disease • Chronic heart disease • Chronic renal insufficiency, nephrotic syndrome • Diabetes • Cerebrospinal fistula • Existing or cochlear implants	• Day care attendance • Ethnicity

- **Age is the most important risk factor for pneumococcal disease[1]**

1. CDC. *Morb Mortal Wkly Rep*. 1997;46(RR-8):1-24.
2. Pickering LK. *Red Book.* 26th ed; 2003.
3. CDC. *Morb Mortal Wkly Rep*. 2000;49(RR-9):1-35.
4. Levine OS, et al. *Pediatrics.* 1999;103:1-5.

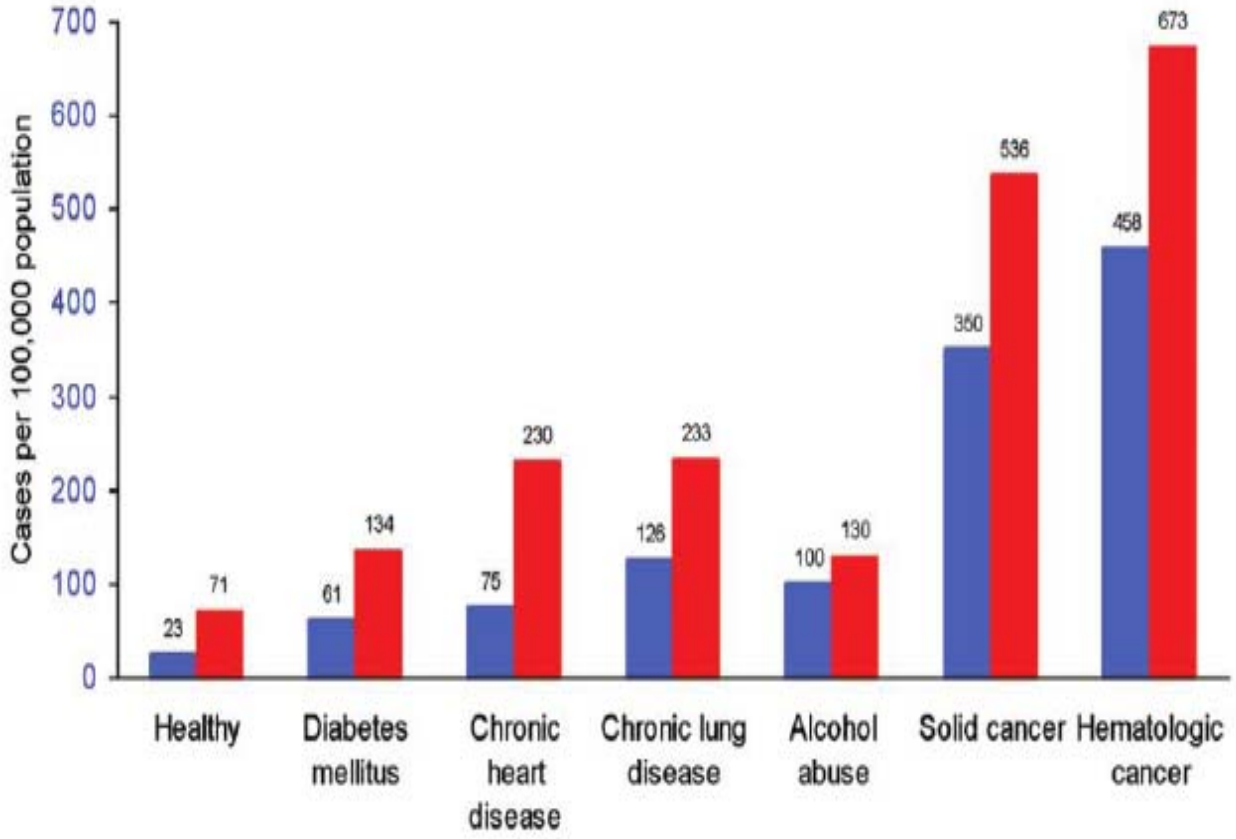


Figure 2. Risk of invasive pneumococcal disease in elderly adults, by age group and chronic illness category. *Blue bars*, aged 65–79 years; *red bars*, aged ≥80 years. Figure adapted from Kyaw et al. [22].

Jackson LA: Clin Infect Dis 2008

Overview :

- Pneumococcal Disease Burden
- Pneumococcal Vaccine : Effectiveness of Polysaccharide Pneumococcal Vaccine
- Recommendation of Polysaccharide Pneumococcal Vaccine
- Pneumococcal Vaccination in Pandemic Influenza

Do you recommend 23-valent polysaccharide pneumococcal vaccine for your elderly patients who had diabetes and chronic renal failure ?

A Yes
B Sometime
C No

23-Valent Polysaccharide Pneumococcal Vaccine (PPV) vs. Pneumococcal Conjugate vaccine (7,10,13-Valent)

Property	Polysaccharide	Conjugate
B cell dependent immune response	YES	YES
T cell dependent immune response	NO	YES
Immune memory	NO	YES
Booster effect	NO	YES
Long term protection	NO	YES
Reduction of carriage	NO	YES
Herd immunity	NO	YES
Immunogenicity children <2 years	NO	YES

Adapted from Granoff DM. Vaccines. 2004

Serotypes included in pneumococcal vaccines.

Vaccine	Serotypes
PPV_{23}	1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, 33F
PCV_7	4, 6B, 9V, 14, 18C, 19F, 23F
PCV_9	1, 4, 5, 6B, 9V, 14, 18C, 19F, 23F
PCV_{11}	1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F
PCV_{13}	1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F

23-valent Polysaccharide Pneumococcal Vaccine

Children & adults

- 0.5 ml intramuscular or subcutaneous
- Revaccination as indicated
- Not recommended for children <2 years of age
- Slide effects & adverse reactions
  - Mild local reactions (~50%)
  - Systemic reactions (rare)

* Simultaneous administration of other vaccines

Pneumococcal Conjugated Vaccine (7,10,13-valent)

Pneumococcal Conjugated Vaccine for children and adults ?

Review of pneumococcal conjugate vaccine in adults: implications on clinical development

Betsy Abraham-Van Parijs : Vaccine 2004

Adult : No clear evidence of the superiority of the conjugate vaccine over the currently licensed polysaccharide vaccine.

Initial and Subsequent Response to Pneumococcal Polysaccharide and Protein-Conjugate Vaccines Administered Sequentially to Adults Who Have Recovered from Pneumococcal Pneumonia

J Infect Dis 2008

Daniel M. Musher,[1,2,3] Adriana M. Rueda,[1,2] Moon H. Nahm,[5] Edward A. Graviss,[2,4] and Maria C. Rodriguez-Barradas,[1,2]

[1]Medical Service, Infectious Diseases Section, Michael E. DeBakey Veterans Affairs Medical Center, and the Departments of [2]Medicine, [3]Molecular Virology and Microbiology, and [4]Pathology, Baylor College of Medicine, Houston, Texas; [5]Department of Pathology, University of Alabama at Birmingham

Immunogenicity and Reactogenicity of Pneumococcal Polysaccharide and Conjugate Vaccines in Alaska Native Adults 55–70 Years of Age

Clin Infect Dis 2009

Karen M. Miernyk,[1] Jay C. Butler,[2] Lisa R. Bulkow,[2] Rosalyn J. Singleton,[1,2] Thomas W. Hennessy,[2] Catherine M. Dentinger,[2] Helen V. Peters,[1] Barbara Knutsen,[3] Jack Hickel,[3] and Alan J. Parkinson[2]

[1]Alaska Native Tribal Health Consortium, [2]Arctic Investigations Program, Division of Emerging Infections and Surveillance Systems, National Center for Preparedness, Detection, and Control of Infectious Diseases, Coordinating Center for Infectious Diseases, Centers for Disease Control and Prevention, and [3]Southcentral Foundation, Anchorage, Alaska

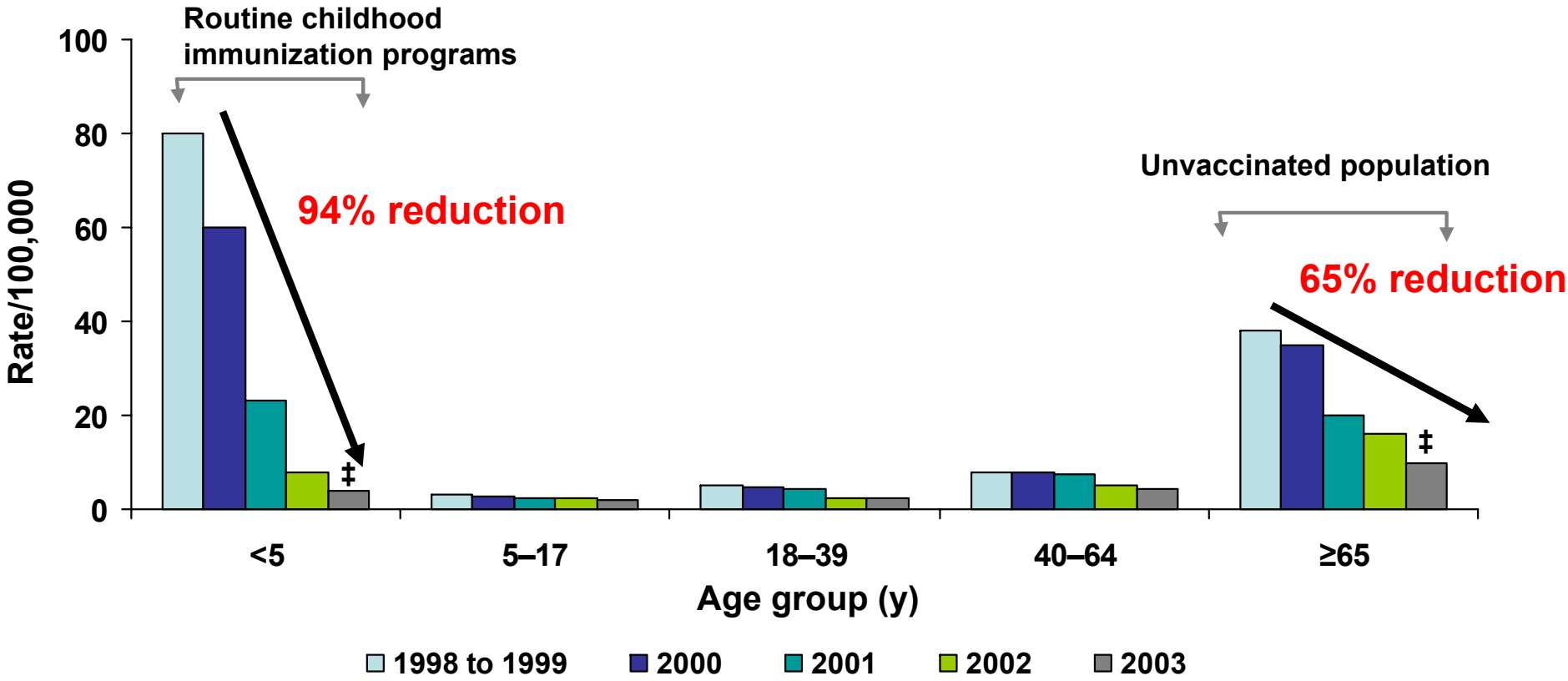
Table 1. Varying Effects of Conjugate Pneumococcal Vaccine.

Major reduction in invasive disease caused by vaccine serotypes in vaccinated children (expected direct effect)*
Reduction in other diseases (e.g., otitis media) attributable to pneumococcus (expected direct effect, attenuated by dilution of pneumococcal with nonpneumococcal disease)*
Reduced rate of colonization by vaccine serotypes in vaccinated children (unanticipated direct effect)†
Reduced rate of infection and colonization by antibiotic-resistant strains (unanticipated direct and indirect or herd effect)‡§
Reduction in disease caused by vaccine serotypes in nonvaccinated persons of all ages (indirect or herd effect)‡
Increased prevalence of colonization and disease by nonvaccine strains (bacterial replacement) (unanticipated direct and indirect effect)¶

Pneumococcal Vaccine — Direct and Indirect ("Herd") Effects Daniel M. Musher, M.D.N Engl J Med 2006

Effectiveness of PCV7
Indirect Effect—IPD (U.S.)

Rate of Vaccine-type (VT) IPD Before and After Introduction of PVC-7, by Age Group and Year†



†Active Bacterial Core surveillance, United States, 1998 to 2003
‡$p<0.05$, 2003 vs 1998-1999

PCV-7 vaccination was associated with a reduction in IPD in vaccinated and unvaccinated populations

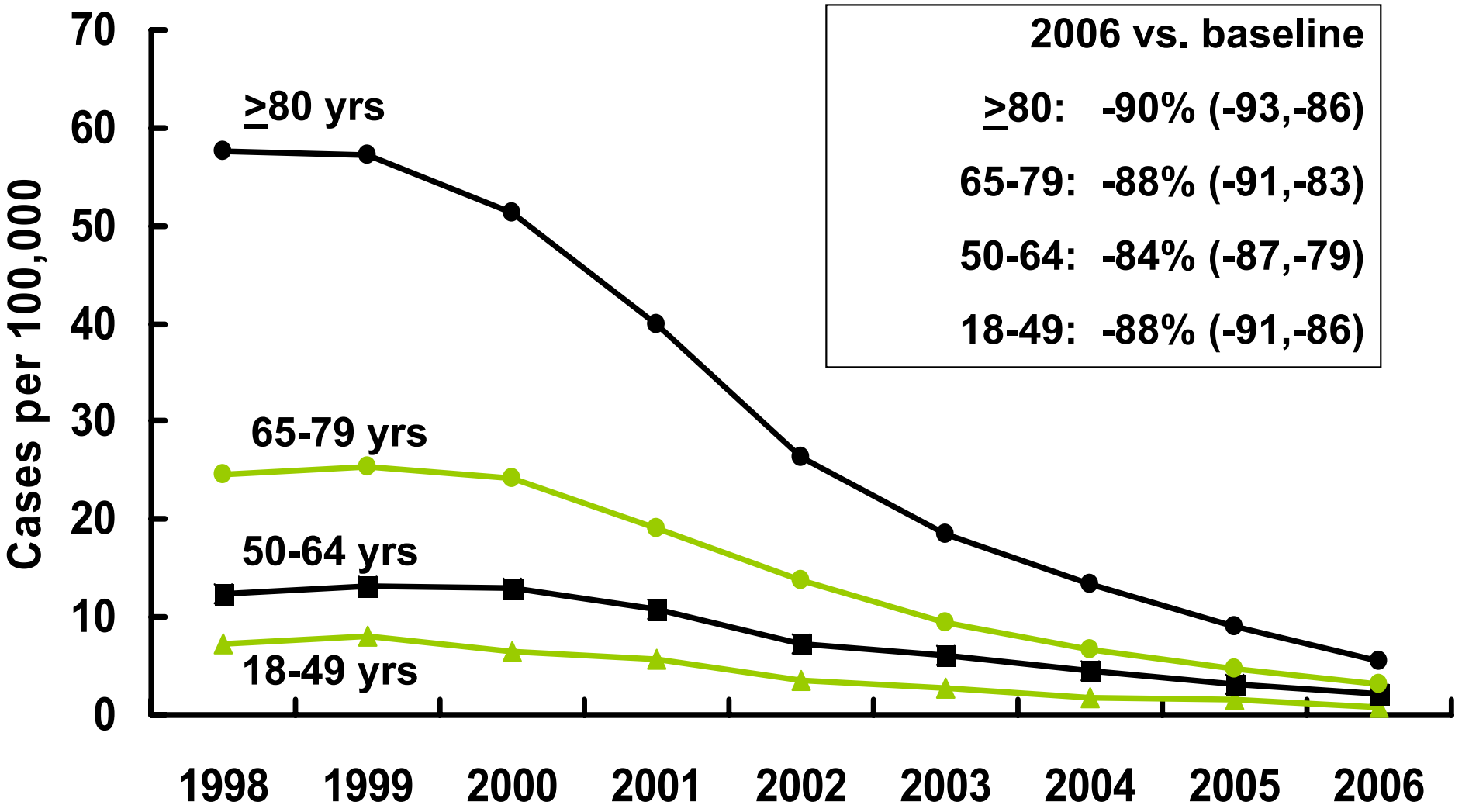
Adapted from CDC. *Morb Mortal Wkly Rep*. 2005;54:893-897.

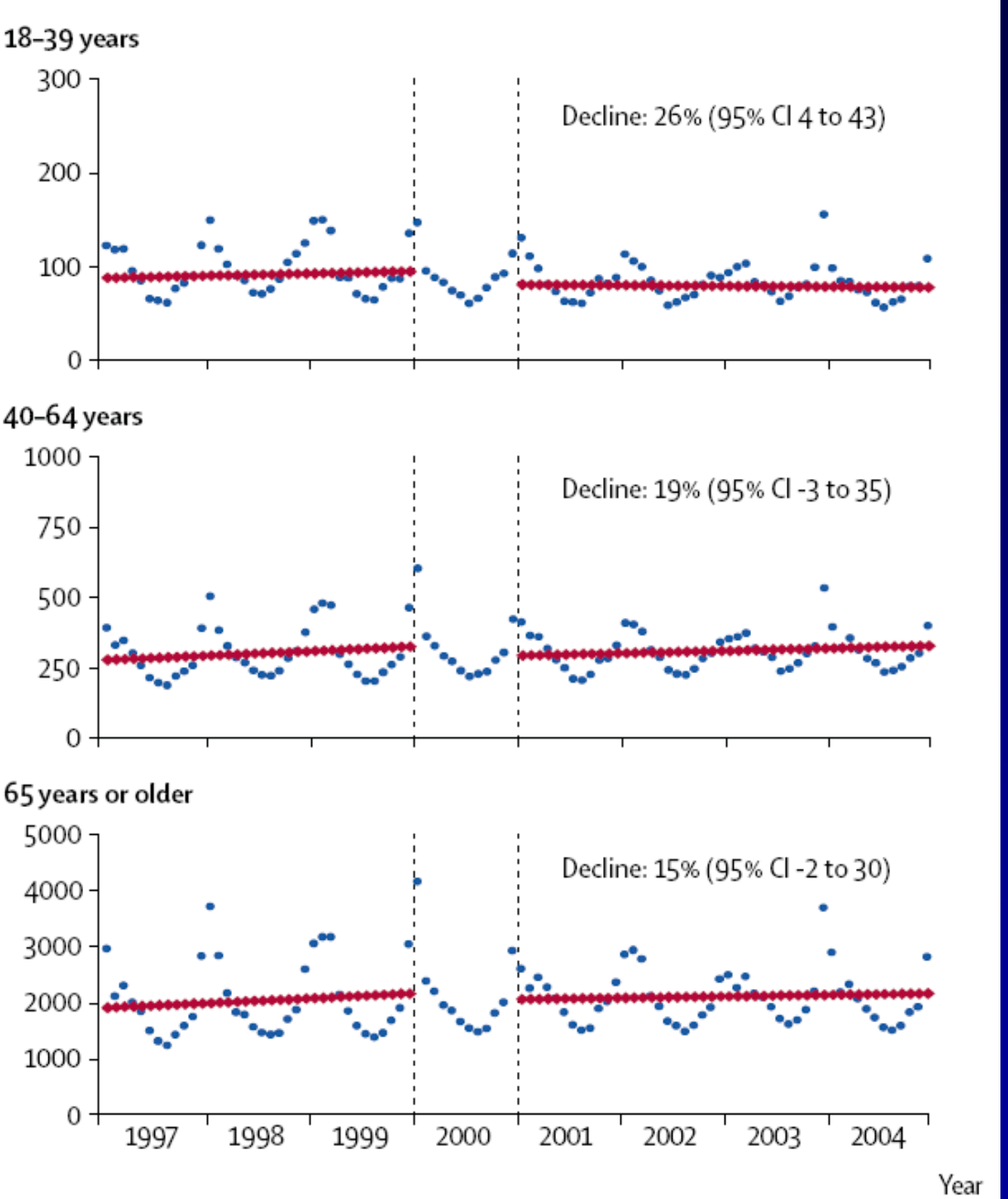
Declining invasive pneumococcal disease in the U.S. elderly. A. Marshall McBean: Vaccine 2005

Pneumococcal polysaccharide vaccine (PPV_{23}) has been recommended for the elderly, since 1989. PPV_{23} vaccination rates in the elderly increased by 25.2% during the baseline period but by <5% during the period PCV_7 has been available.

Thus, during the period that PCV_7 vaccine has been used in children, **rates of IPD in the elderly have declined appreciably more compared to the immediately prior period when PPV_{23} was the only vaccine available.**

Rates of PCV7-type Invasive Pneumococcal Disease among Adults, U.S., 1998/99-2006

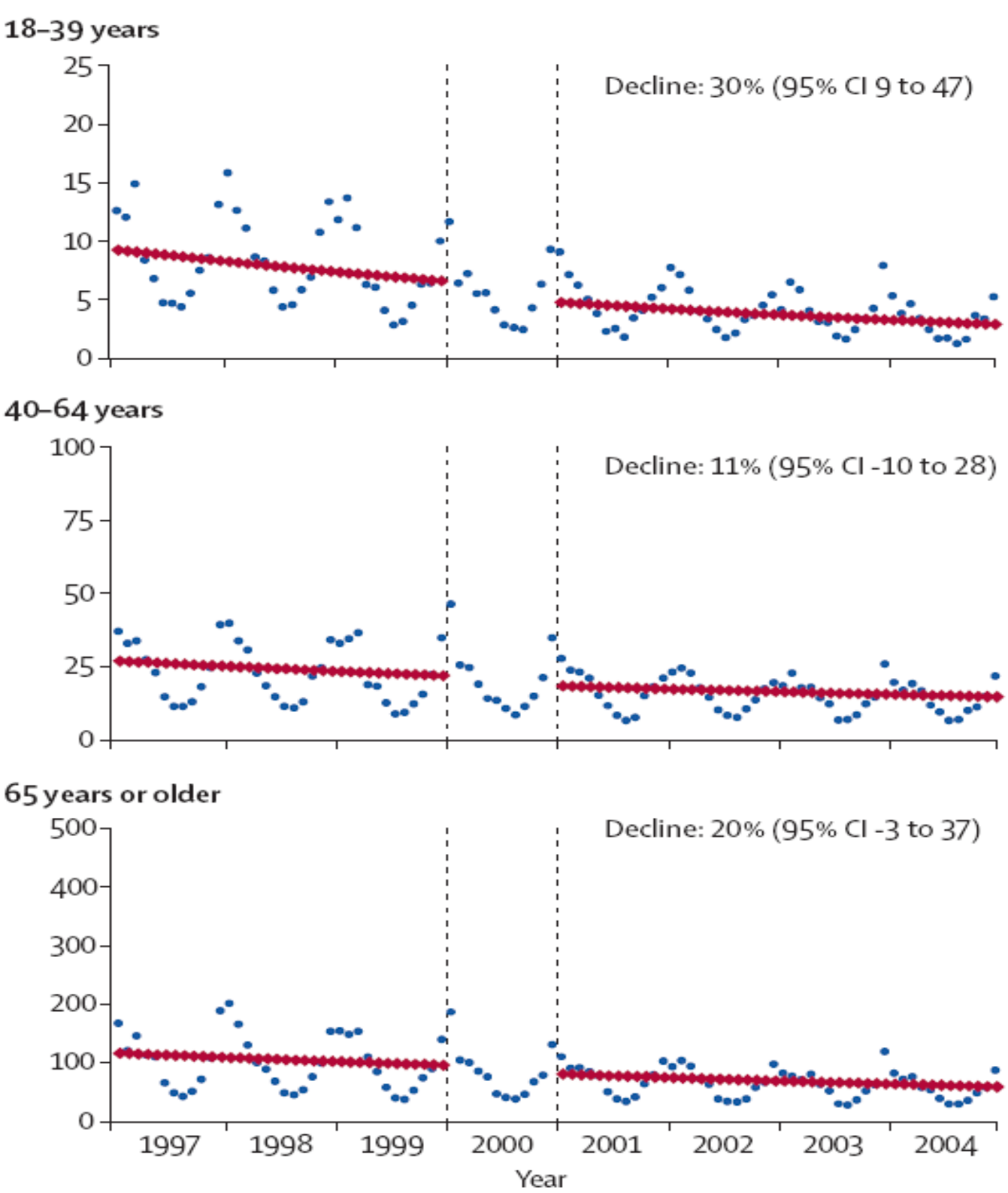




All-cause Pneumonia ; USA

Decline in pneumonia admissions after routine childhood immunisation with pneumococcal conjugate vaccine in the USA: a time-series analysis

Carlos G Grijalva,Lancet 2007



Pneumococcal Pneumonia: USA

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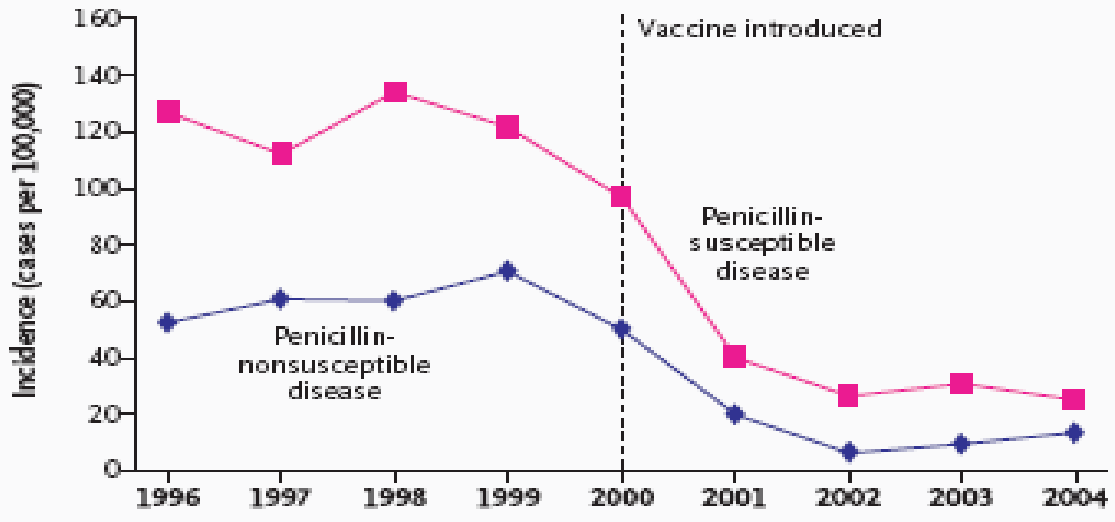


Figure 1. Annual Incidence of Invasive Disease Caused by Penicillin-Susceptible and Penicillin-Nonsusceptible Pneumococci among Children under Two Years of Age, 1996 to 2004.

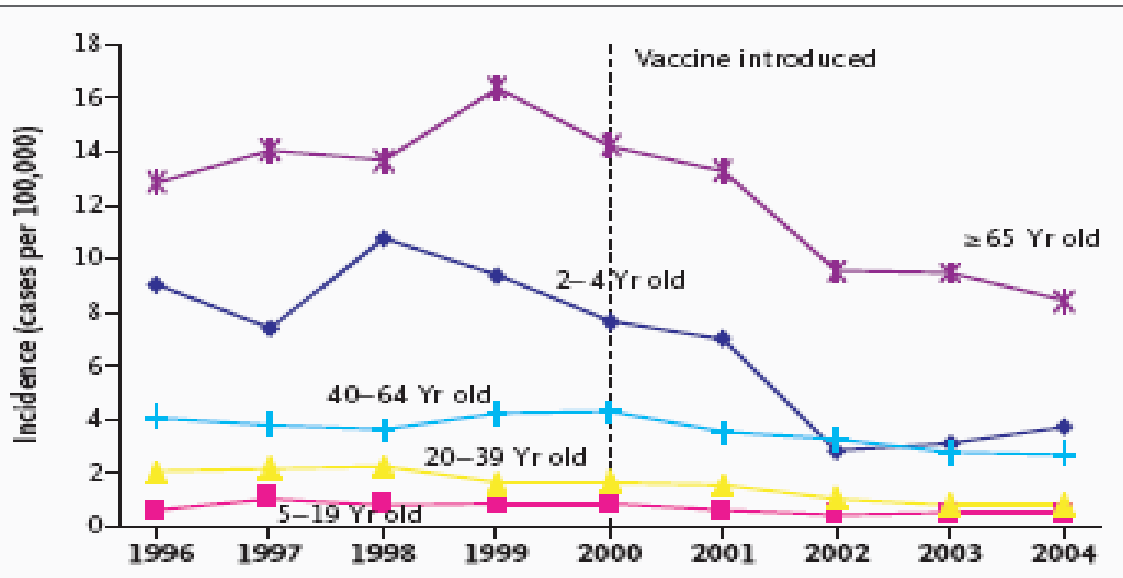


Figure 2. Annual Incidence of Invasive Disease Caused by Penicillin-Nonsusceptible Pneumococci in Persons Two Years of Age or Older, 1996 to 2004.

Kyaw MH ,
N Engl J Med 2006

Effectiveness of the 23-valent polysaccharide pneumococcal vaccine

- 58 – 81% effective for bacteremic pneumococcal diseases
- 50 –70% effective for invasive pneumococcal infection in elderly immunocompetent people
- Younger people with chronic medical illness

  Effective - confirmed in asplenia, COPD , CHF , coronary vascular diseases, DM

  Effective - not confirmed in malignancy ,CRF, alcoholism, cirrhosis, HIV infection

Elderly with chronic lung disease

27% reduction of hospitalization

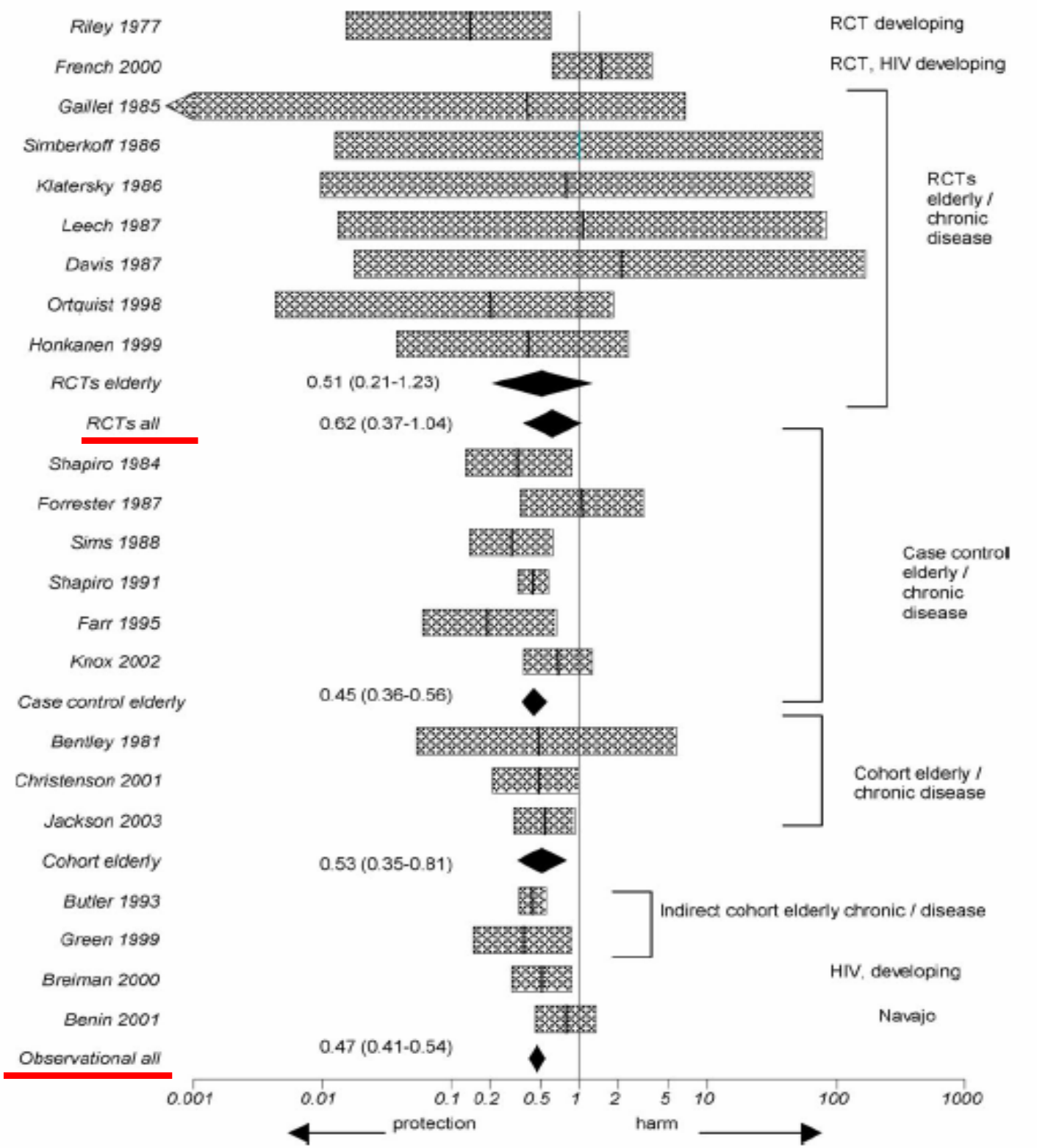
37% reduction in the risk of death

The effectiveness of pneumococcal polysaccharide vaccines in adults: a systematic review of observational studies and comparison with results from randomised controlled trials.

Stephen Conaty; Vaccine 2004

13 observational studies the estimate of vaccine efficacy against invasive pneumococcal disease was 53% (46-59%) compared with 38% (-4 - 63%) from 9 RCTs.

Estimates of protection against all-cause pneumonia were based on fewer, heterogeneous studies that were not consistent with the findings from RCTs for this outcome.


Riley 1977
French 2000
Gaillet 1985
Simberkoff 1986
Klatersky 1986
Leech 1987
Davis 1987
Ortquist 1998
Honkanen 1999
RCTs elderly
0.51 (0.21-1.23)
RCTs all
0.62 (0.37-1.04)
Shapiro 1984
Forrester 1987
Sims 1988
Shapiro 1991
Farr 1995
Knox 2002
Case control elderly
0.45 (0.36-0.56)
Bentley 1981
Christenson 2001
Jackson 2003
Cohort elderly
0.53 (0.35-0.81)
Butler 1993
Green 1999
Breiman 2000
Benin 2001
Observational all
0.47 (0.41-0.54)
0.001
0.01
0.1
0.2
0.5
1
2
5
10
100
1000
protection
harm
RCT developing
RCT, HIV developing
RCTs elderly / chronic disease
Case control elderly / chronic disease
Cohort elderly / chronic disease
Indirect cohort elderly chronic / disease
HIV, developing
Navajo

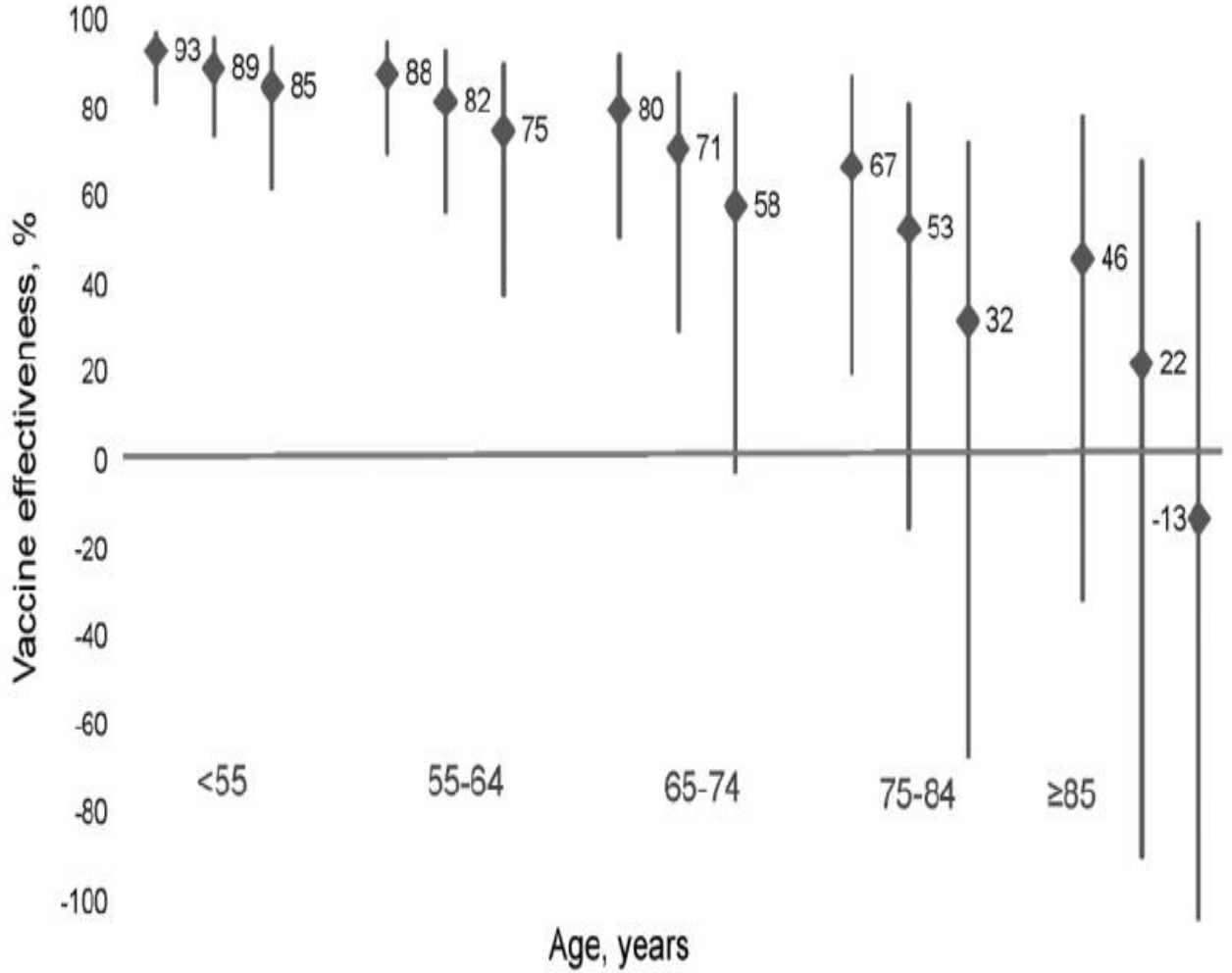


Figure 3. Pneumococcal vaccine effectiveness against invasive pneumococcal disease by age of recipient and time since vaccination. The point estimate of vaccine effectiveness and 95% CI are indicated. Within each age group, 3 data points represent the vaccine effectiveness at <3 years, 3–5 years, and >5 years since vaccination, from left to right. Data adapted from Shapiro et al. [5].

Protective Effects of the 23-Valent Pneumococcal Polysaccharide Vaccine in the Elderly Population: The EVAN-65 Study

Angel Vila-Co´ rcole, Clin Infect Dis 2006

Results. Pneumococcal vaccination was associated with significant reductions in the risk of hospitalization for pneumonia (hazard ratio 0.74) and in the overall pneumonia rate(HR, 0.79).

The incidence of invasive pneumococcal disease was low (64 cases per 100,000 person-years), and a considerable protective effect against invasive pneumococcal disease did not attain statistical significance .

However, the vaccine showed a significant effectiveness of 45% to prevent pneumococcal pneumonia (HR, 0.55).

Finally, vaccination was associated with a significant 59% reduction in the risk of death due to pneumonia among vaccinated subjects (HR, 0.41)

Table 2. Vaccine effectiveness (VE) against all-cause pneumonia reported by clinical trials in older adults.

Reference	Vaccine valency	Study population	VE[a] (95% CI)	No. of cases of pneumonia/ no. of vaccinated persons	No. of cases of pneumonia/ no. of nonvaccinated persons
Austrian [24][b]					
Study 1	12	Inpatients at the Dorothea Dix psychiatric hospital in Raleigh, North Carolina	−22 (−49 to 0)	154/607	144/693
Study 2	12	Members of the Kaiser Permanente Health Plan in San Francisco ≥45 years of age	2 (−16 to 7)	268/6782	274/6818
Gaillat et al. [25][c]	14	Residents of 48 long-term care institutions in France	79 (53 to 91)	7/937	27/749
Simberkoff et al. [26]	14	US veterans, immunocompetent, and either aged ≥55 years or with renal, hepatic, cardiac, or pulmonary disease; alcoholism; or diabetes mellitus	−39 (−110 to 8)	56/1145	41/1150
Koivula et al. [27]	14	Residents of age of a small town in Finland ≥60 years	−17 (−66 to 17)	69/1364	64/1473
Örtqvist et al. [28]	23	Immunocompetent persons 50–85 years of age who had been previously discharged after a hospitalization for community-acquired pneumonia in Sweden	−20 (−72 to 11)	63/339	57/352
Honkanen et al. [29]	23	Persons ≥65 years of age in Northern Finland	−20 (−50 to 10)	145/13980	116/12945
Alfageme et al. [30]	23	Immunocompetent patients with COPD 61–73 years of age in Seville, Spain	3 (−52 to 38)	33/298	34/298

Jackson LA: Clin Infect Dis 2008

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In your opinion, what is the most appropriate indication of pneumococcal vaccination for population in developing countries ?

A Healthy elderly person
B Elderly person with co-morbidity (DM,CHF…)
C Immunosuppressive person (HIV-infected person…..)
D Person with asplenia
E Children < 2 years (with PCV)

Guideline of Polysaccharide Pneumococcal Vaccination

Vaccination	Revaccination (c)
I.) Immunocompetent persons (>2 years)	
- Age > 65 years (A)	Once after 5 years (if first vaccination was given before age 65 year)
- Age 2 - < 65 years	
- Asplenia (77%)(A)	Consider revaccination after 5 years
- Medical illness: diabetic mellitus(84%), chronic cardiovascular eg. congestive heart failure (69%), coronary vascular dis (73%), cardiomyopathies or pulmonary diseases eg COPD (65%)((A)	Not recommended
- Chronic liver disease or alcoholism, CSF leakage (B)	Not recommended
-Age 19-64 years - Smoker	
- Asthma	

Guideline of Pneumococcal Vaccination

Vaccination	Revaccination (c)
II.) Immunocompromised persons (>2 years)	
- HIV infection or congenital immunodeficiency (C)	Once after 5 years
- Malignancy; multiple myeloma, chronic lymphocytic leukemia, lymphoma, leukemia, generalized maligancy (C)	Once after 5 years
- Immunosuppressive therapy or corticosteroid therapy (C)	Once after 5 years
- Chronic renal failure (C)	Once after 5 years
- Organ or hematopoietic cell transplantation (C)	Once after 5 years

*If previous vaccination status is unknown, vaccine should be given; ( ) reflects the strength of evidence supporting the recommendations for vaccination (A = strong evidence support, B = moderate evidence support, C = effectiveness of vaccination is not proven but benefit and safety of the vaccine justify vaccination)

National Recommendations for Pneumococcal Vaccination in 19 European Countries, 2003

Condition recommending	Countries
≥ 65 years (or 60 yrs)	17
Splenic dysfunction	all 19
Cardiovascular / pulmonary	17 / 18
Diabetes mellitus	13
Alcoholism / liver disease	9 / 15
Immunocompromise / HIV	17 / 16
Nursing home residents	8
Revaccination in 3-6 years	4

Pebody RG et al. *Eurosurveillance* 2005; 10: 174-8.

Polysaccharide Pneumococcal Vaccine Effectiveness Against IPD in Adults: By Age and Time Since Vaccination

Age (Years)	Time Since Vaccination		
	< 3 Yrs	3 – 5 Yrs	> 5 Yrs
	Vaccine Effective,% (95%CI)		
< 55	93 (82-97)	89 (74-96)	85 (62-94)
55 – 64	88 (70-95)	82 (57-93)	75 (38-90)
65 – 74	80 (51-92)	71 (30-88)	58 (-2-83)
75 – 84	67 (20-87)	53 (-15-81)	32 (- 67-72)
> 85	46 (-31-78)	22 (-90-68)	-13 (-174-56)

Plotkin S ; Vaccines ;5th edition

Guideline of Polysaccharide Pneumococcal Vaccination

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Review

Cost-effectiveness of pneumococcal polysaccharide vaccination in adults: A systematic review of conclusions and assumptions

Isla Ogilvie[a], Antoine El Khoury[b,c], Yadong Cui[b], Erik Dasbach[b], John D. Grabenstein[b], Mireille Goetghebeur[a,*]

[a] BioMedCom Consultants inc., 1405 TransCanada Highway, Suite 310, Montreal, Quebec, Canada H9P 2V9
[b] Merck & Co., PA 19486, USA
[c] University of Arkansas for Medical Sciences, Little Rock, AR, USA

Vaccine 2009

In general, all 11 studies found that vaccination with PPV-23 is a cost-effective, and in some cases a cost-saving strategy for the prevention of invasive pneumococcal disease (IPD).

The systematic assessment indicated that the results of the cost-effectiveness studies of PPV-23 are influenced by the values applied to vaccine efficacy, IPD incidence and case-fatality.

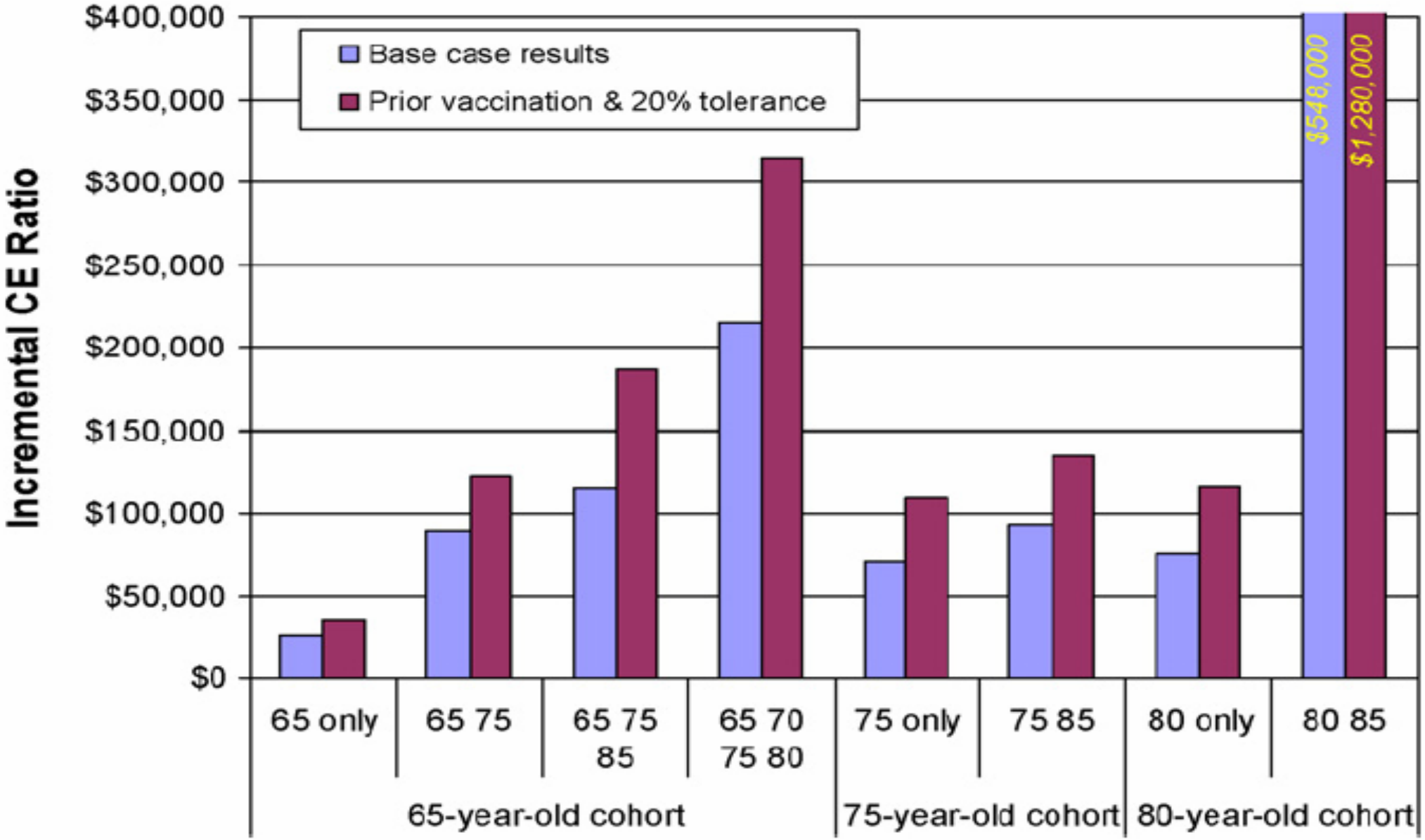
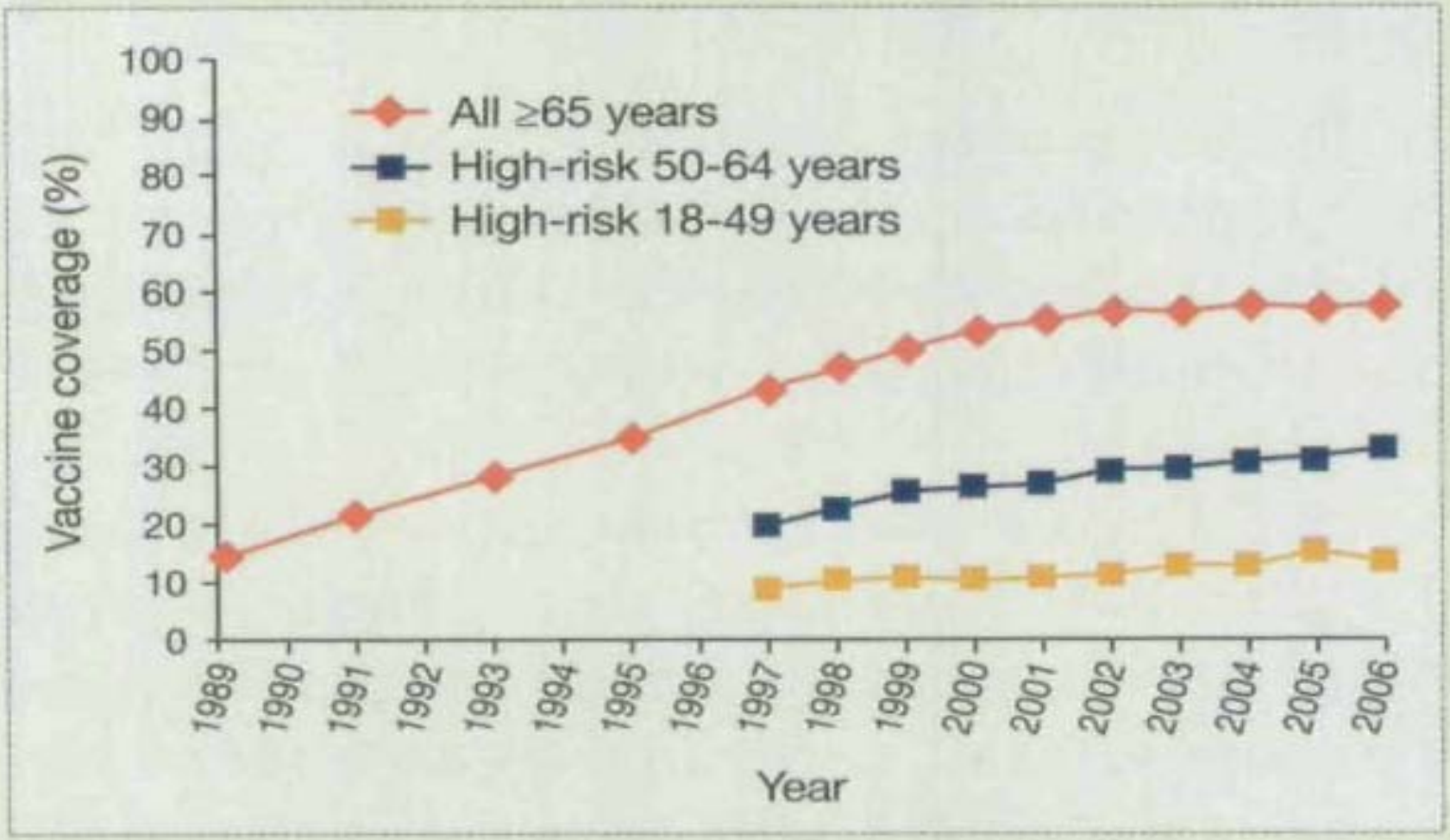


Fig. 3. Sensitivity analysis results, when the combined effects of prior pneumococcal polysaccharide vaccination (PPV) and a 20% decrease in PPV effectiveness due to prior vaccination are assumed. Light bars depict base case results, dark bars show results when these assumptions are in place.

FIGURE 3

Self-reported pneumococcal vaccination in high-risk adult population groups



1989-2006 National Health Interview Survey. Singleton JA. Vaccination Coverage Among Adults. Presented at: National Vaccine Advisory Committee Session on Adult Immunization; Oct 22, 2007; Washington, DC.

Schaffner W; J Fam Med 2008

Reasons for the Low Usage of Pneumococcal Vaccination in USA

- Lack of understanding of importance of pneumococcal diseases
- Inconclusive results from clinical trials : prevention of pneumococcal pneumonia
- Uncertainly about benefits of vaccination
- Lack of reimbursement for the cost of vaccine
- Problems of adult vaccination
- Evaluation of response of vaccine ?
- Problem of revaccination

Pneumococcal Polysaccharide Vaccination

- The incidence of invasive pneumococcal disease in elderly adults is at least 50 cases / 100,000
- Prospective vaccine trials in older adults have been inconclusive, but retrospective studies show vaccination reduces invasive pneumococcal disease by 50-70%
- Vaccination of older adults is very cost-effective in 11 developed countries
- Pneumococcal vaccine is recommended for elderly persons and those with cardiovascular and pulmonary diseases, diabetes mellitus, renal disease, cancer and other immunosuppresssive diseases, including splenctomy. Recently, asthma and smoking were added.
- Vaccine use has increased in some countries (and in a few rapidly developing countries), but many countries are still reluctant to use the vaccine and coverage needs to improve in all

Overview :

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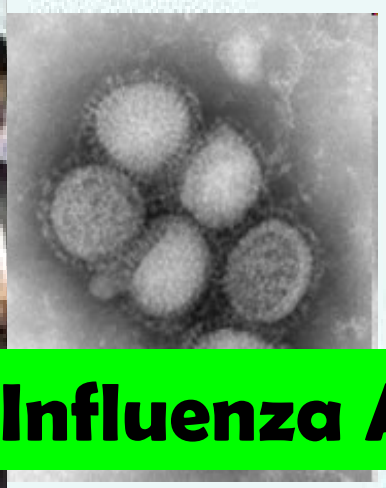
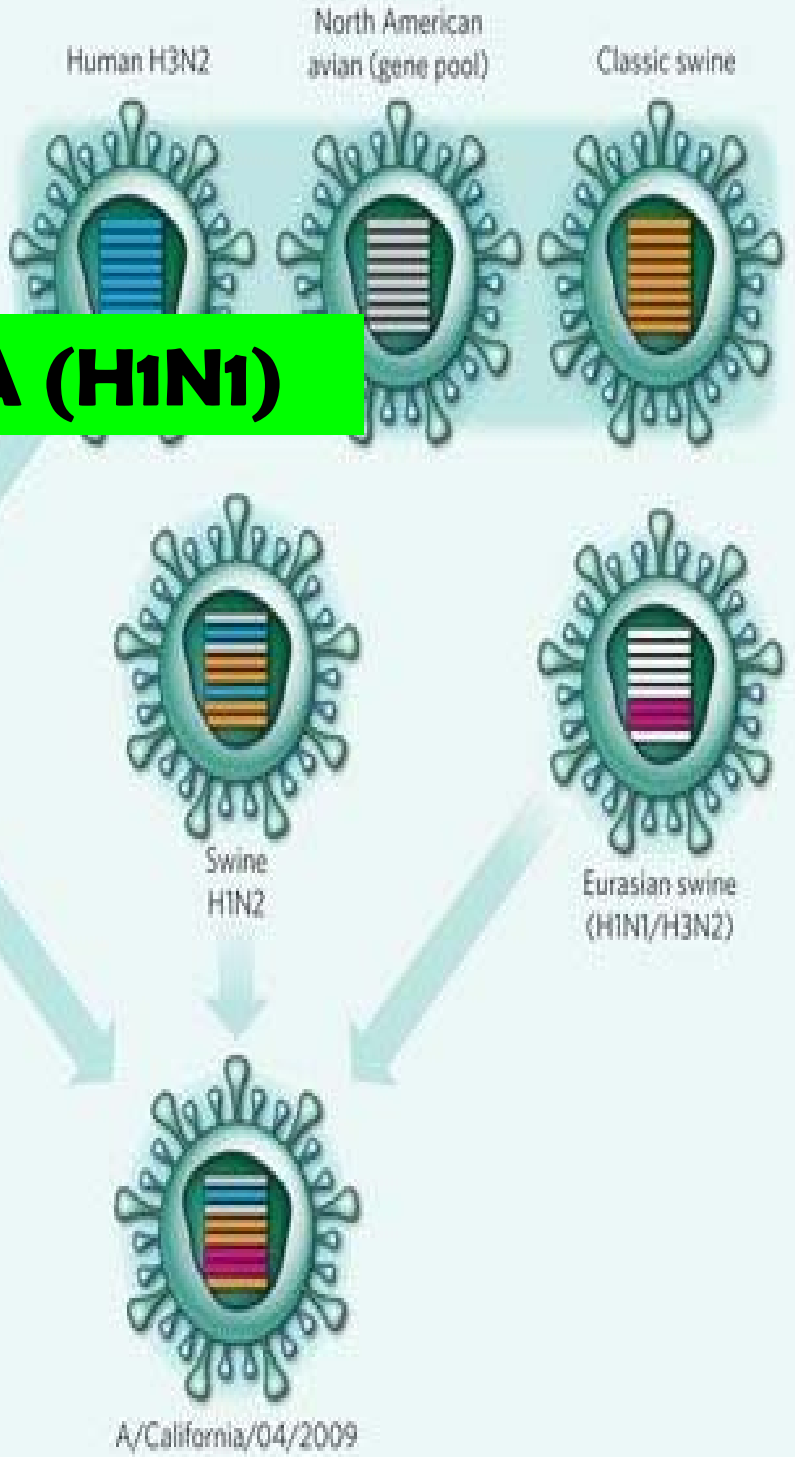


Novel Influenza A (H1N1)

A stadium worker watches a football match from which the public have been excluded in Mexico City

Claudio Cruz/AP/Press Association Images



Immunization and Influenza
Is There a Role for Bacterial Vaccination?

- **Secondary bacterial infection is an important cause of morbidity and death in influenza epidemics**
- ***S. pneumoniae* causes a substantial portion of influenza-associated pneumonia during these epidemics**
- **Should pneumococcal vaccine be part of an influenza pandemic or interpandemic planning strategy?**

U.S. Department of Health and Human Services. Use of pneumococcal vaccines for influenza pandemic preparedness. http://www.pandemicflu.gov/vaccine/pneumococcal.html. Accessed June 5, 2008.

Evidence that Bacterial Pneumonia Caused Most of the Deaths in the 1918-1919 Pandemic

- **Pathological**
  - autopsies showed common URTI organisms
  - pathologic findings and case fatality rates typical of pneumonia in non-pandemic periods
  - mixed infections more fatal
  - lung tissue showed repair of 'viral' pneumonia underway

- **Epidemiological**
  - most cases were mild, uncomplicated, with full recovery
  - mortality at all ages associated with bacterial pneumonia rates, not influenza attack rates or pneumonia case-fatality rates,
  - children 5-15 years had the highests attack rates but lowest mortality rates (inconsistent with viral influenza alone)
  - average time from onset to death (~10 days) more consistent with bacterial pneumonia

Morens DM et al. *J Infect Dis* 2008

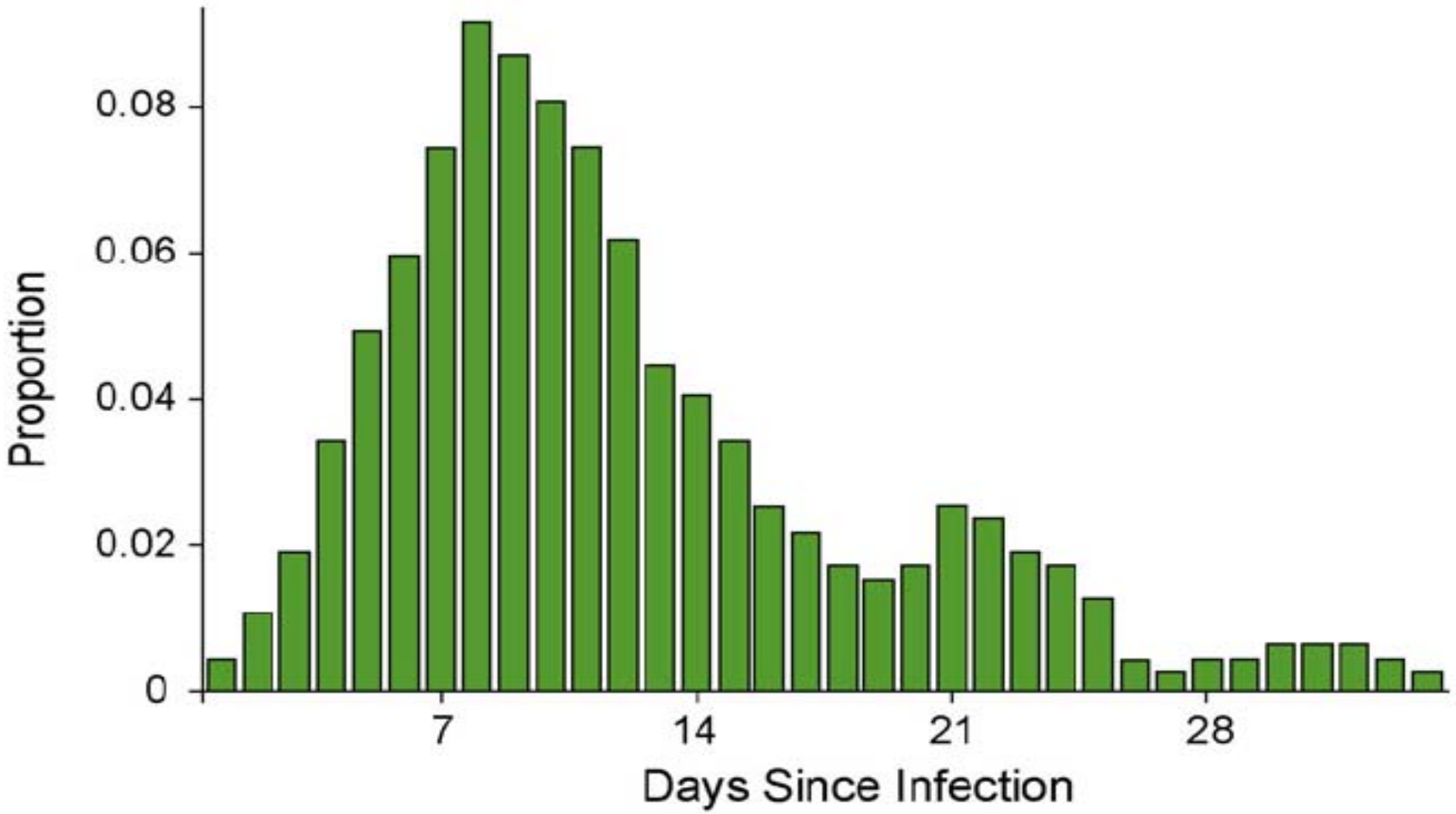


Fig. 1. Timeline post-infection of influenza deaths—1918 epidemic. Adapted by permission from Macmillan Publishers Ltd., copyright 2004 [41].

Brundage JF; Lancet Infect Dis 2006

Bacterial Pneumonia as the Primary Cause of Death in the 1918-1919 Pandemic

Specimen	No. of reports	No. of specimens	*S. pneumo*	Other bacteria	No Growth
Lung tissue	96	5266	23.5	72.3	4.2
Pleural fluid	35	1245	21.1	59.3	19.6
Blood	42	1867	27.0	43.3	29.7

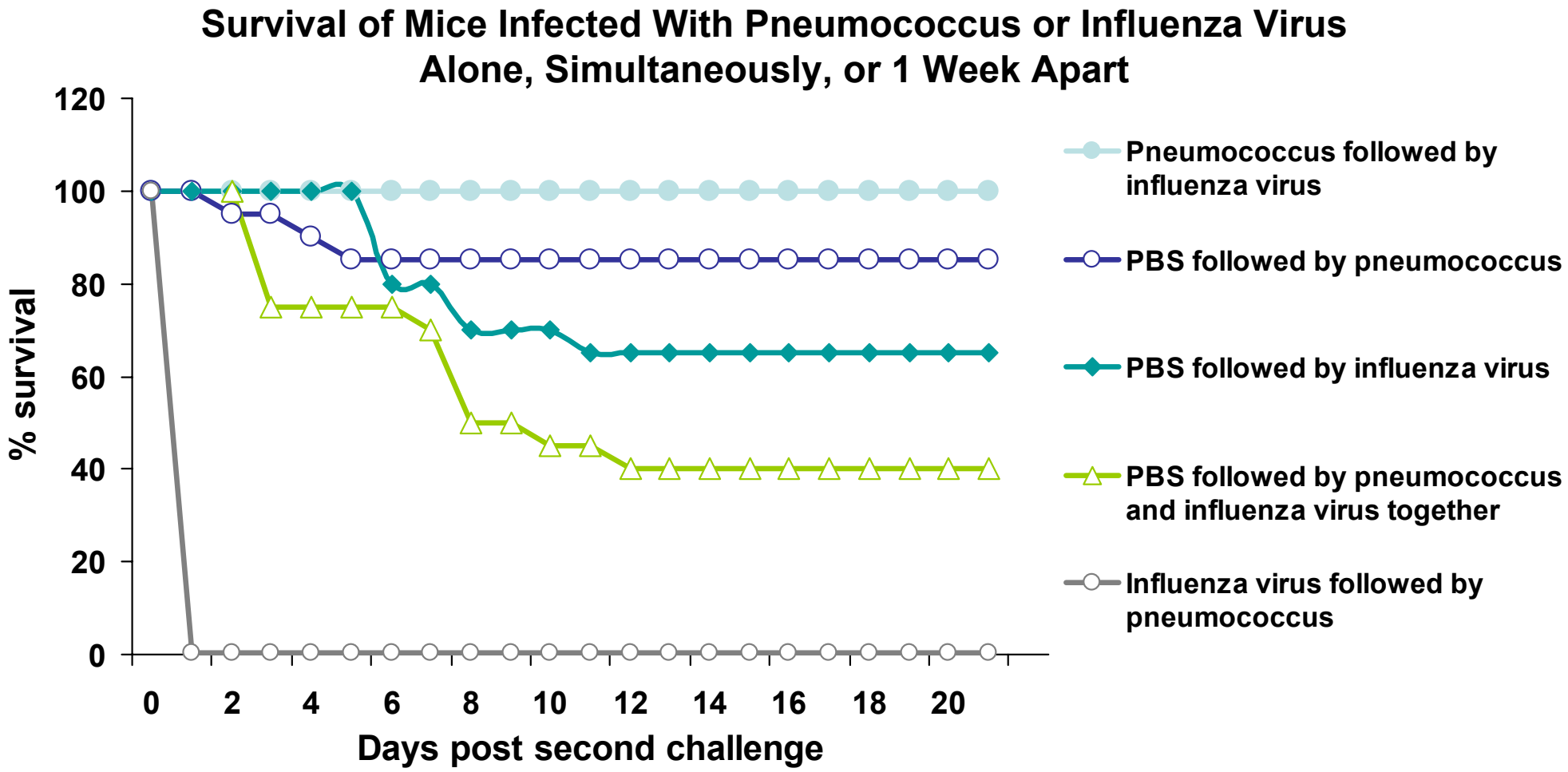
Morens DM et al. *J Infect Dis* 2008

Table 2. Bacterial culture results in autopsy series involving culture of blood and pleural fluid or empyema fluid from victims of the 1918–1919 influenza epidemic.

Type of autopsy series	No. of results	No. (%) of cultures from which organism was recovered, by organism							
		Streptococcus pneumoniae	*Streptococcus hemolyticus*	*Staphylococcus aureus*	*Diplococcus intracellulare meningitidis*	Mixed pneumopathogens	*Bacillus influenzae*	Other bacteria	No growth
Blood culture (n = 42)									
All military and civilian	1887	509 (27.0)	377 (20.0)	68 (3.6)	5 (0.3)	28 (1.5)	61 (3.2)	278 (14.7)	**561 (29.7)**
Pleural fluid or empyema fluid culture (n = 35)									
All military and civilian	1245	263 (21.1)	**539 (43.3)**	59 (4.7)	0 (0.0)	74 (5.9)	21 (1.7)	45 (3.6)	244 (19.6)

Morens DM;J Infect Dis 2008

Influenza and *S. pneumoniae* Synergistic Effect on Mortality (Animal Data)

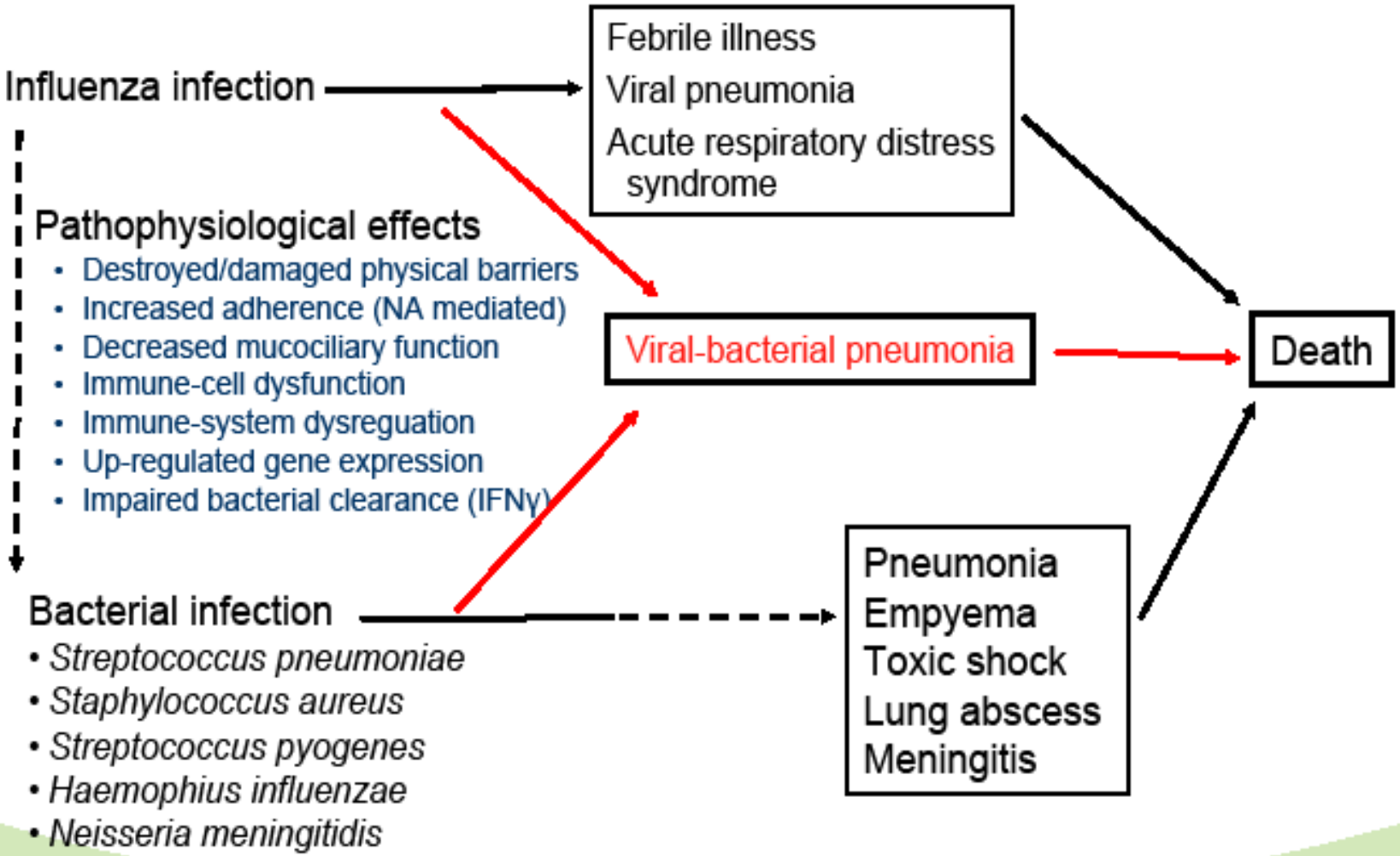


Mortality was 100% in mice challenged with *S. pneumoniae* after influenza

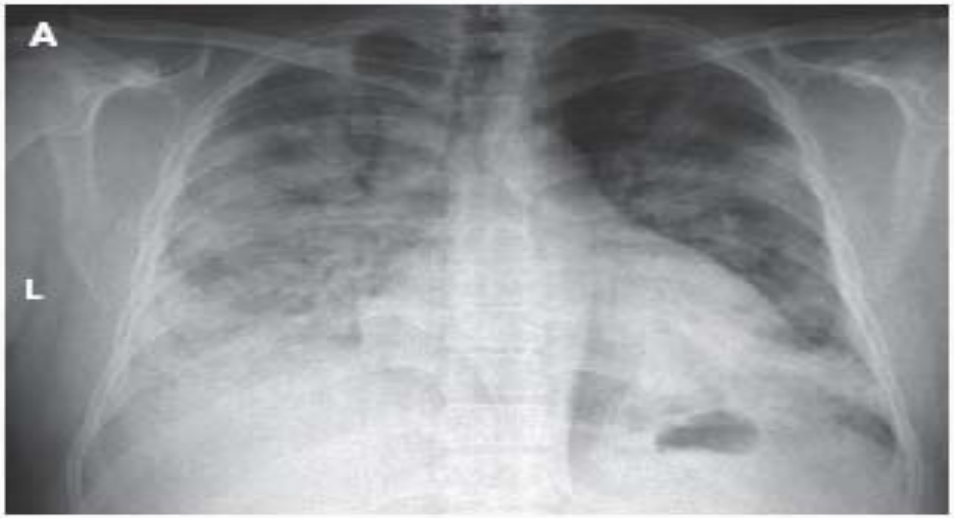
PBS=phosphate buffered saline

Adapted from McCullers JA, Rehg JE. *J Infect Dis*. 2002;186:341-350.
Slide courtesy of Dr. Keith Klugman.

Pathophysiological Interactions Between Influenza and Bacterial Respiratory Pathogens and Clinical Expression



Brundage JF, et al. *Lancet Infect Dis*. 2006;6:303-312.



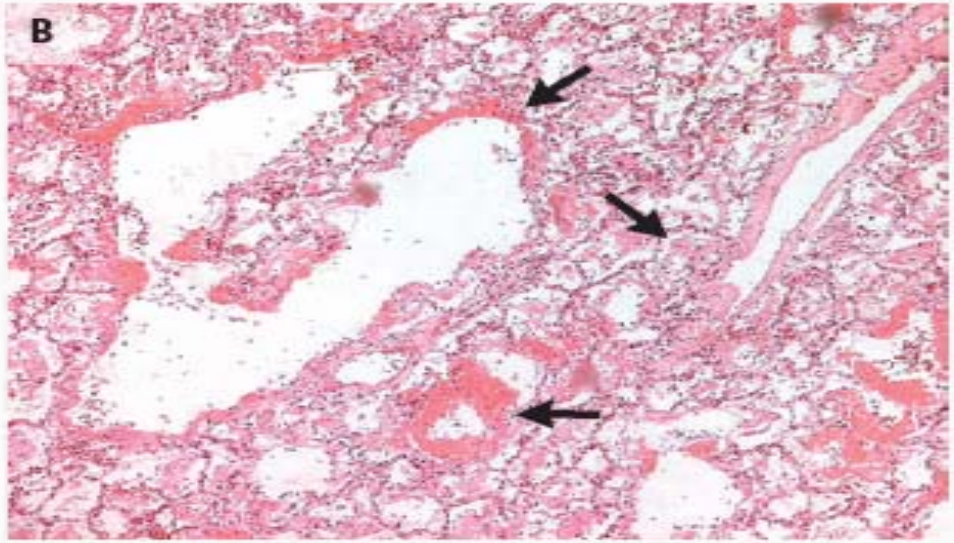
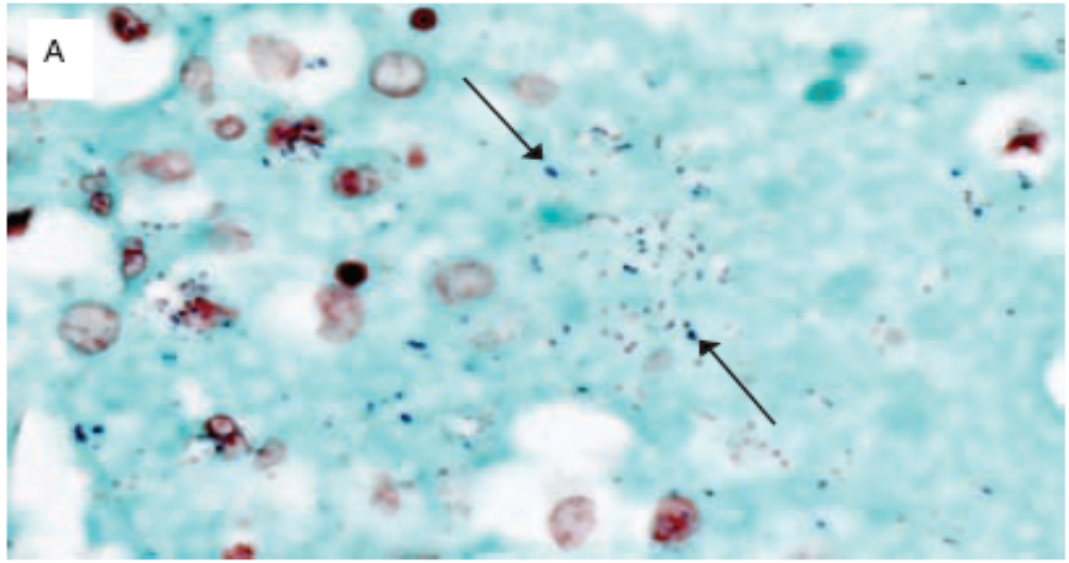


Figure 3. Initial Radiograph of the Lung and Lung-Tissue Sample from Patient 3.

The radiograph (Panel A) shows bilateral alveolar opacities in the base of both lungs that progressed and became confluent. The specimen (Panel B, hematoxylin and eosin) shows necrosis of bronchiolar walls (top arrow), a neutrophilic infiltrate (middle arrow), and diffuse alveolar damage with prominent hyaline membranes (bottom arrow). Bacterial cultures were negative on admission, and no evidence of bacterial infection of the lungs was found. The patient ultimately died.

FIGURE. Histochemical and immunohistochemical diagnosis of *Streptococcus pneumoniae* infection in a patient with confirmed 2009 pandemic influenza A (H1N1). (A) Detection of Gram-positive cocci (arrows) with use of Lillie- Twort Gram stain of lung tissue (original magnification ×63). (B) Immunohistochemical staining of multiple *S. pneumoniae* (arrows) with use of immunoalkaline phosphatase with naphthol-fast red and hematoxylin counterstain (original magnification ×63).



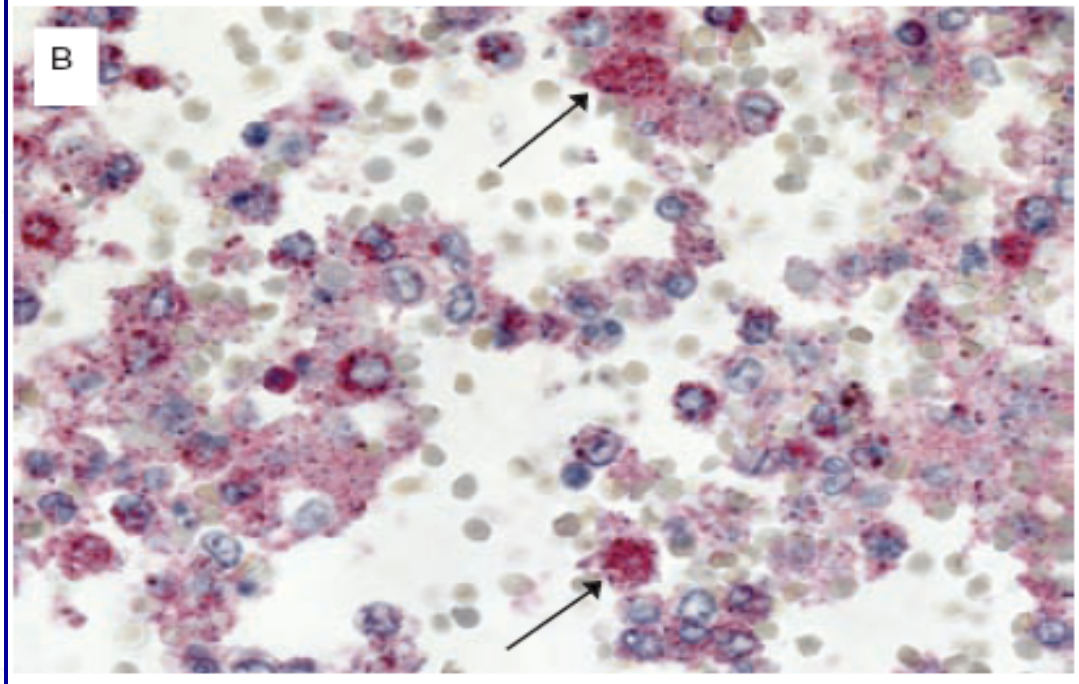
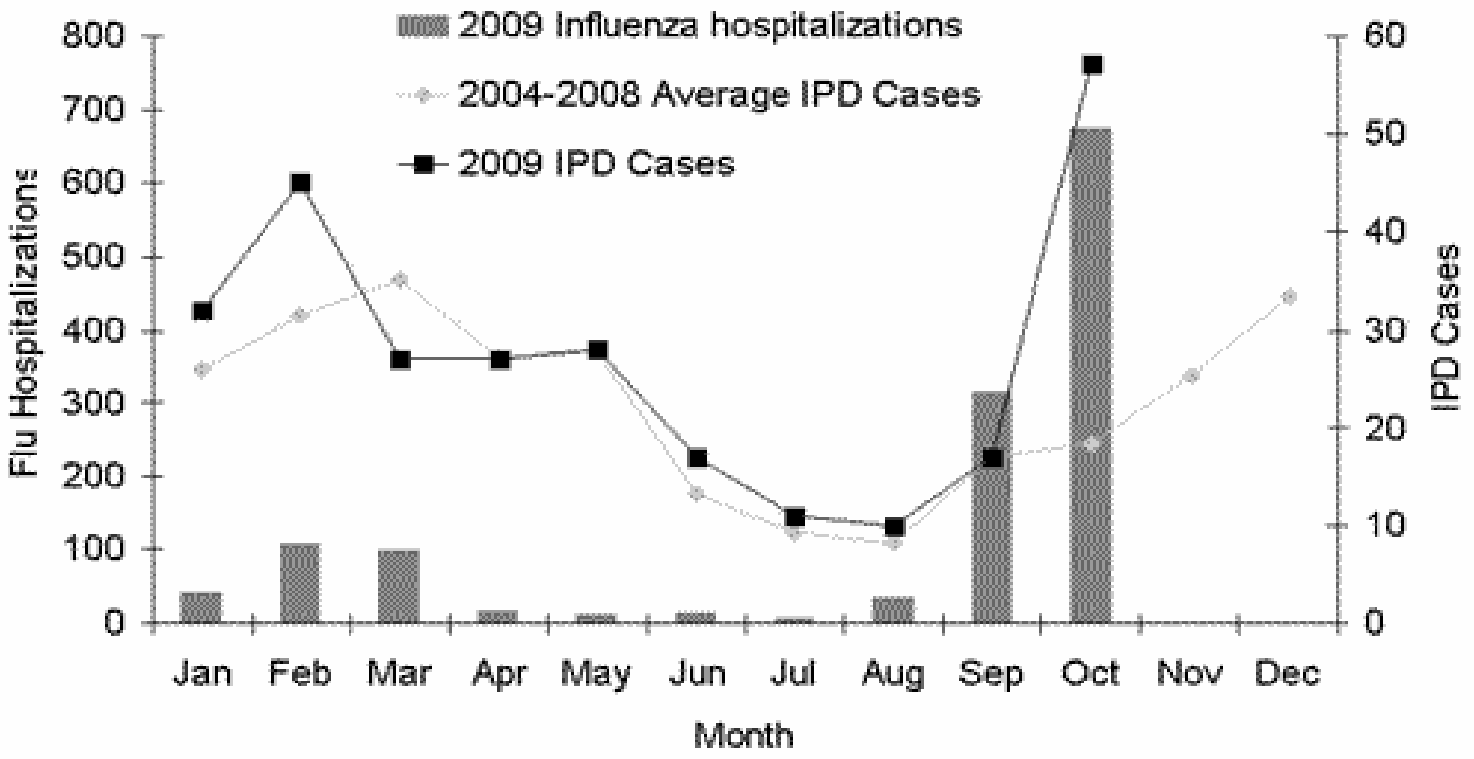


TABLE. Characteristics of patients with fatal 2009 pandemic influenza A (H1N1) and histopathologic evidence of bacterial lung infection — United States, May–August 2009

			Receipt of health care		Receipt of antimicrobials			
Age	Sex	Illness duration	Sought medical care	Hospitalized	Antibiotics	Antivirals	Relevant medical history	Bacteria detected
2 mos	M	1 day	Yes	No	No	No	None reported	*Streptococcus pneumoniae* (serotype 15B/15C)
9 yrs	F	6 days	Yes	No	No	No	None reported	Group A *Streptococcus* (*S. pyogenes*)
9 yrs	F	15 days	Yes	Yes	Yes	Yes	None reported	*Staphylococcus aureus* (methicillin-resistant *S. aureus* [MRSA])
11 yrs	F	6 days	No	No	No	No	Obesity	Group A *Streptococcus* (*S. pyogenes*) and *S. pneumoniae* (serotype 19A)
13 yrs	M	~5 days	Yes	Yes	Unknown	Yes	None reported	*S. aureus*
15 yrs	M	2 days	No	No	No	No	Down syndrome	*S. aureus*
15 yrs	M	9 days	Yes	Yes	Yes	No	None reported	*S. aureus* (MRSA) and *Haemophilus influenzae*
27 yrs	M	5 days	Yes	Yes	Yes	Yes	Human immunodeficiency virus (HIV) infection	*S. aureus* (MRSA) and group A *Streptococcus* (*S. pyogenes*)
28 yrs	M	Unknown	Unknown	Unknown	Unknown	Unknown	Asthma, obesity	*S. pneumoniae*
30 yrs	M	3 days	No	No	Unknown	Unknown	Drug use	Group A *Streptococcus* (*S. pyogenes*) and *Streptococcus mitis*
30 yrs	M	Unknown	Yes	Yes	Yes	Yes	Hypertension, diabetes mellitus, obesity	*S. pneumoniae*
34 yrs	M	~3 days	Yes	No	Unknown	Unknown	Hypertension, obesity	*S. pneumoniae* (serotype 10F/10C/33C)
36 yrs	F	5 days	No	No	Yes	No	None reported	*S. mitis*
43 yrs	F	3 days	Yes	No	Yes	Yes	Asthma, chronic obstructive pulmonary disease, hypothyroidism	*S. aureus* (MRSA)
44 yrs	M	5 days	Unknown	Unknown	Unknown	Unknown	Unknown	*S. pneumoniae* (serotype 6A/B)
46 yrs	F	~4 days	Yes	Yes	Yes	Yes	Stroke	*S. pneumoniae* (serotype 15A/15F)
47 yrs	F	7 days	Yes	No	Unknown	Unknown	Obesity, smoking	Group A *Streptococcus* (*S. pyogenes*)
47 yrs	F	11 days	No	No	Yes	Yes	Obesity	*S. pneumoniae* (serotype 6A/B)
47 yrs	M	25 days	Yes	Yes	Yes	Yes	Asthma, hypertension, previous splenectomy	*S. aureus* (MRSA)
48 yrs	F	7 days	No	No	No	No	Non–insulin-dependent diabetes mellitus, thyroid adenoma	*S. pneumoniae*
55 yrs	F	7 days	Yes	Yes	Yes	Yes	Down syndrome, hepatitis B	*S. pneumoniae* (serotype 11A/11D)
56 yrs	F	7 days	Yes	No	Unknown	Unknown	Obesity, hypertensive cardiovascular disease	Group A *Streptococcus* (*S. pyogenes*, type M18)

Influenza Hospitalizations & Invasive Pneumococcal Cases, All Ages, ABCs Site, Provisional 2009 (year-to-date) vs. 5 -Year Average (2004-2008)



Bacterial Pneumonia and Pandemic Influenza Planning

Ravindra K. Gupta,* Robert George,† and Jonathan S. Nguyen-Van-Tam‡

Emerg Infect Dis 2008

Bacterial pneumonia and Pandemic Flu
Bacterial pneumonia and Seasonal Flu
Pathogens : *Strep. pneumoniae*, MSSA,CA-MRSA
***H. influenza*, Strep gr A,**
Other pathogens, Mixed infection

- **Stockpiling and Strategic Use of Antibiotics**
- **Real-Time Surveillance for Antibiotic Resistance**
- **Treatment and Prophylaxis Strategies**
- **Pneumococcal Vaccination**

Recommendation for use of PPSV23 during influenza A(H1N1) outbreak (US-CDC;June 2009)

All people who have existing indications for 23-PPV should continue to be vaccinated according to current ACIP recommendations during the outbreak of novel influenza A(H1N1).

PCV7 is recommended for all children aged less than 5 years; national coverage among 19-35 month olds with 3 or more PCV7 doses is currently > 90% (National Immunization Survey, July 2007-June 2008).

Summary Thoughts

National recommendations for PPV in most developed countries include all elderly people and those with at-risk conditions

Safety and immunogenicity of PPV well-established, but antibody levels decline within a few years

Disappointing prospective trials of vaccine efficacy, but general acceptance of retrospective studies of vaccination effectiveness

- Pneumococcal pneumonia vs invasive pneumococcal disease; preventing IPD is enough

Failure to vaccinate is largely due to the failure of physicians and nurses to offer the vaccine

Pneumococcal vaccination with PPV and PCV can be considered as part of pandemic preparedness, but supplies of both vaccines will be very limited and pneumococcal infections will probably account for only a minority of bacterial complications


Thank you