



PNÖMOKOK ENFEKSİYONLARINDA SON DURUM

Doç.Dr. Ener Çağrı DİNLEYİCİ

20 Ocak 2014

Eskişehir

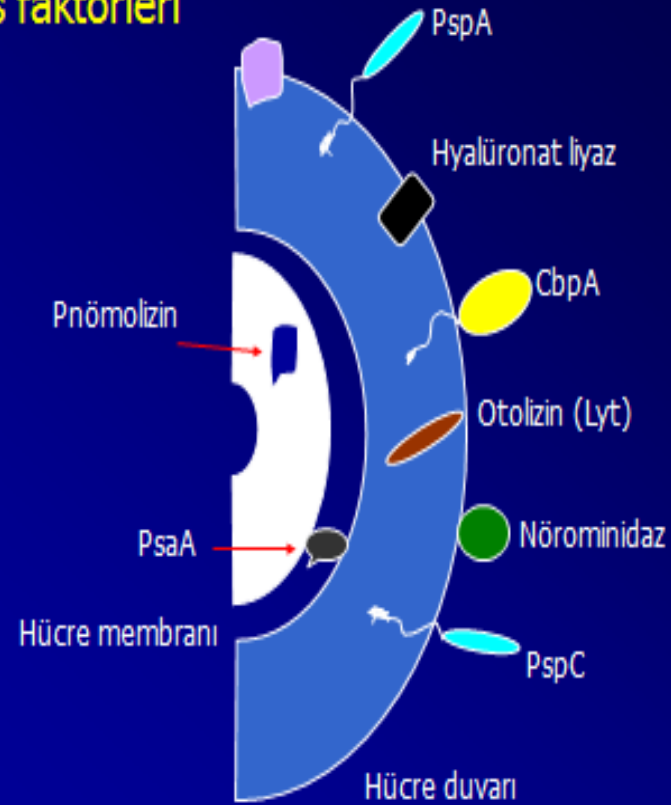


Amaç:

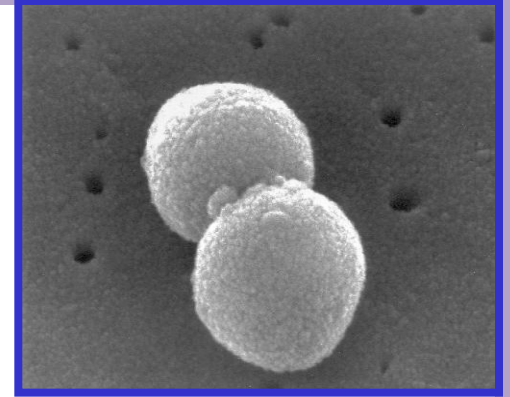
**Hastalıkları
oluşmadan
Önlemek!!!!**

- Streptococcus pneumoniae
- Gram pozitif diplokok
- Polisakarid kapsül
 - Serotiplerin belirlenmesi
 - Virülans faktörleri
- 90'dan fazla tanınmış serotip
 - 6C ve 6D

Virülans faktörleri



- Streptococcus pneumoniae
- Gram pozitif diplokok
- Polisakarid kapsül
 - Serotiplerin belirlenmesi
 - Virülans faktörü
- 90'dan fazla tanımlanmış serotip mevcut
 - 6C ve 6D



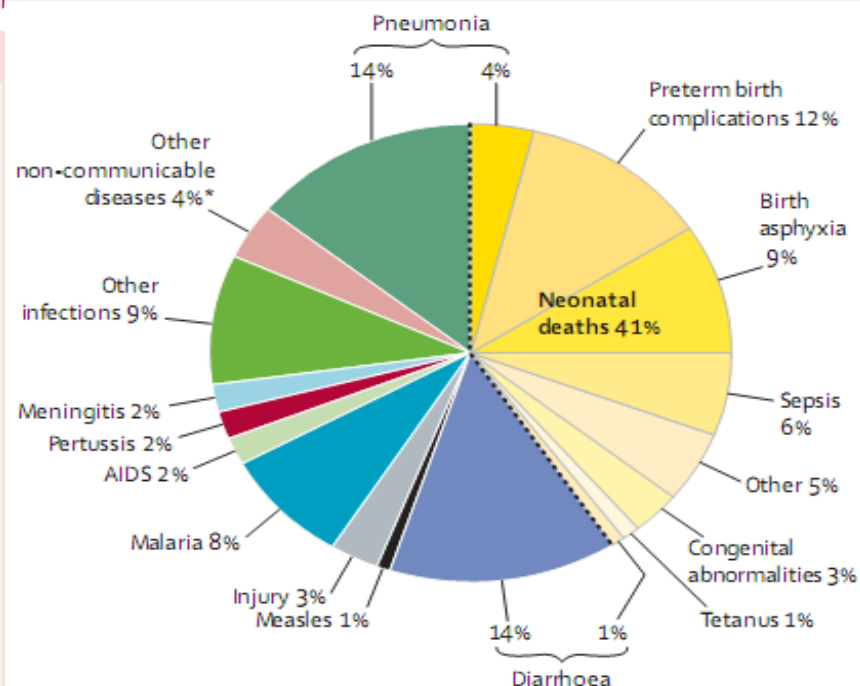
Global, regional, and national causes of child mortality in 2008: a systematic analysis

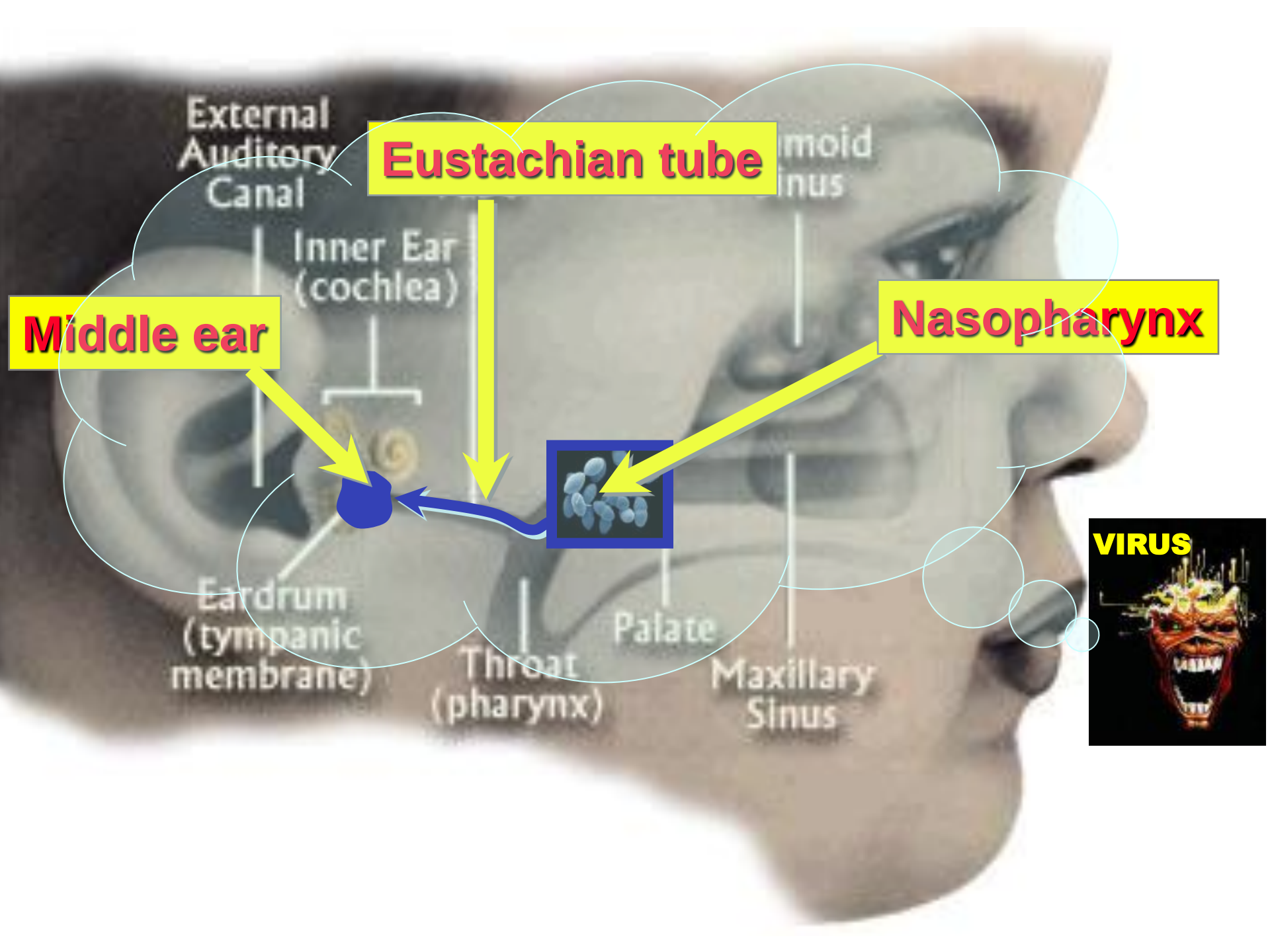


Robert E Black, Simon Cousens, Hope L Johnson, Joy E Lawn, Igor Rudan, Diego G Bassani, Prabhat Jha, Harry Campbell, Christa Fischer Walker, Richard Cibulskis, Thomas Eisele, Li Liu, Colin Mathers, for the Child Health Epidemiology Reference Group of WHO and UNICEF*

Children aged 1-59 months

Diarrhoea‡	1.257 (0.774-1.886)
Pneumonia*	1.189 (0.789-1.415)
Other infections	0.753 (0.479-2.830)
Malaria	0.732 (0.601-0.851)
Other non-communicable diseases	0.228 (0.143-0.606)
Injury	0.279 (0.174-0.738)
AIDS§	0.201 (0.186-0.215)
Pertussis¶	0.195 (—)
Meningitis	0.164 (0.110-0.728)
Measles	0.118 (0.075-0.180)
Congenital abnormalities†	0.104 (0.078-0.160)





Eustachian tube

Middle ear

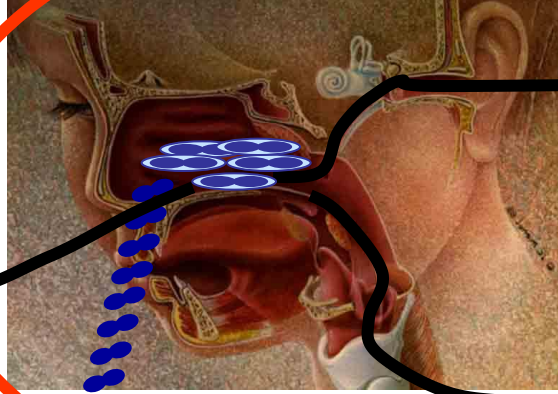
Nasopharynx

VIRUS

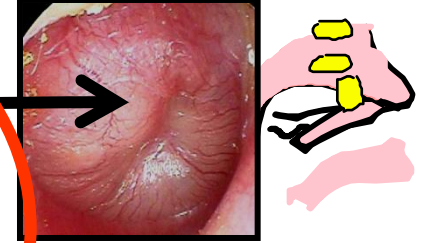


Invaziv Enfeksiyon

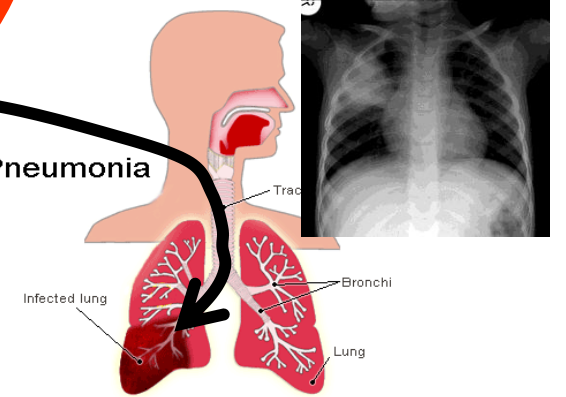
- Sepsis
- Menenjit



Diğer kişilere dağılım



Pneumonia



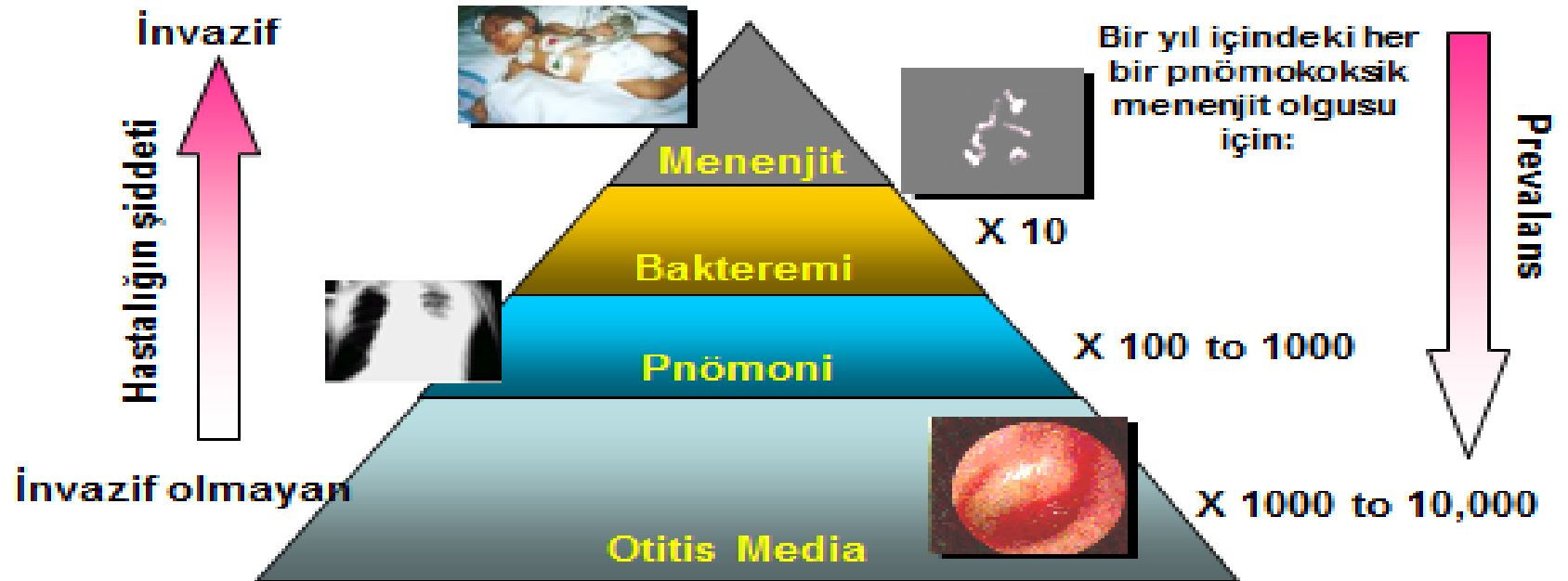
Antibiyotik direnci



Mukozaal Enfeksiyon

- Otit
- Sinüzit
- Konjonktivit
- Pnömoni

- **Pnömoni**
- **Menenjit**
- **Sinüzit**
- **Akut otitis media**
- **Primer odağı saptanamayan bakteremi**
- **Endokardit**
- **Septik artrit**
- **Osteomyelit**
- **Selülit**
- **Perikrdit**
- **Purpura fulminans**
- **Piyomiyozit**
- **Epidural apse**
- **Beyin apsesi**
- **Peritonit**
- **Mastoidit**
- **Hemolitik üremik sendrom**



PNÖMONİ



PNÖMOKOK PNÖMONİSİ MORTALİTE

8%-10%

Non Bakteremik pnömoni (sağlıklı kişide
%1)

Bakteremik pnömoni: 15%-20%
Yüksek riskli gruplarda 50%

Table 6. Most common etiologies of community-acquired pneumonia.

Patient type	Etiology
Outpatient	<i>Streptococcus pneumoniae</i> <i>Mycoplasma pneumoniae</i> <i>Haemophilus influenzae</i> <i>Chlamydophila pneumoniae</i> Respiratory viruses ^a
Inpatient (non-ICU)	<i>S. pneumoniae</i> <i>M. pneumoniae</i> <i>C. pneumoniae</i> <i>H. influenzae</i> <i>Legionella</i> species Aspiration Respiratory viruses ^a
Inpatient (ICU)	<i>S. pneumoniae</i> <i>Staphylococcus aureus</i> <i>Legionella</i> species Gram-negative bacilli <i>H. influenzae</i>

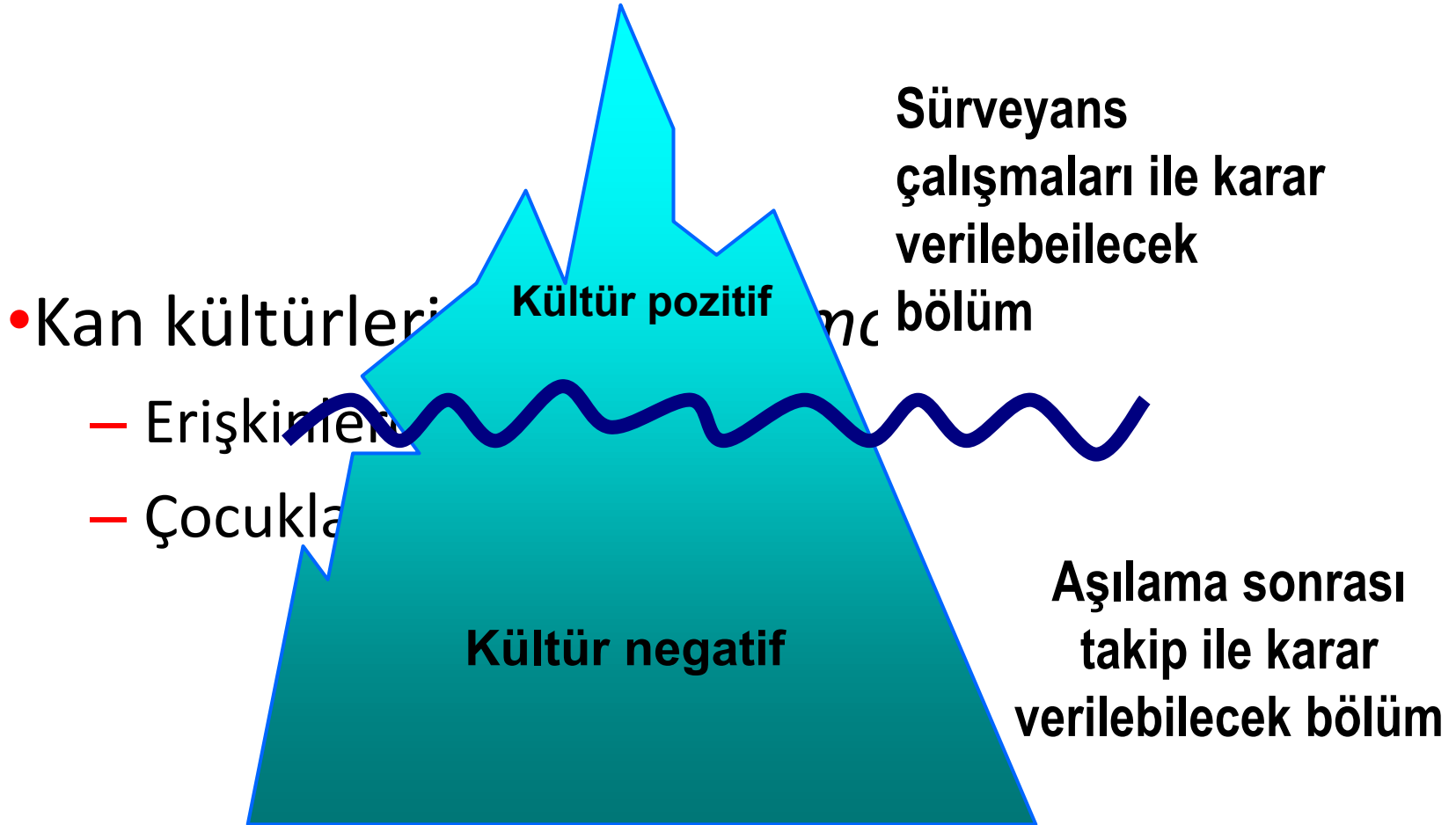
Table 6. Most common etiologies of community-acquired pneumonia.

Condition	Commonly encountered pathogen(s)
Alcoholism	<i>Streptococcus pneumoniae</i> , oral anaerobes, <i>Klebsiella pneumoniae</i> , <i>Acinetobacter</i> species, <i>Mycobacterium tuberculosis</i>
COPD and/or smoking	<i>Haemophilus influenzae</i> , <i>Pseudomonas aeruginosa</i> , <i>Legionella</i> species, <i>S. pneumoniae</i> , <i>Moraxella carathalis</i> , <i>Chlamydophila pneumoniae</i>
Inpatient (ICU)	Aspiration Respiratory viruses ^a <i>S. pneumoniae</i> <i>Staphylococcus aureus</i> <i>Legionella</i> species Gram-negative bacilli <i>H. influenzae</i>

Erişkinde Menenjit Etkenleri

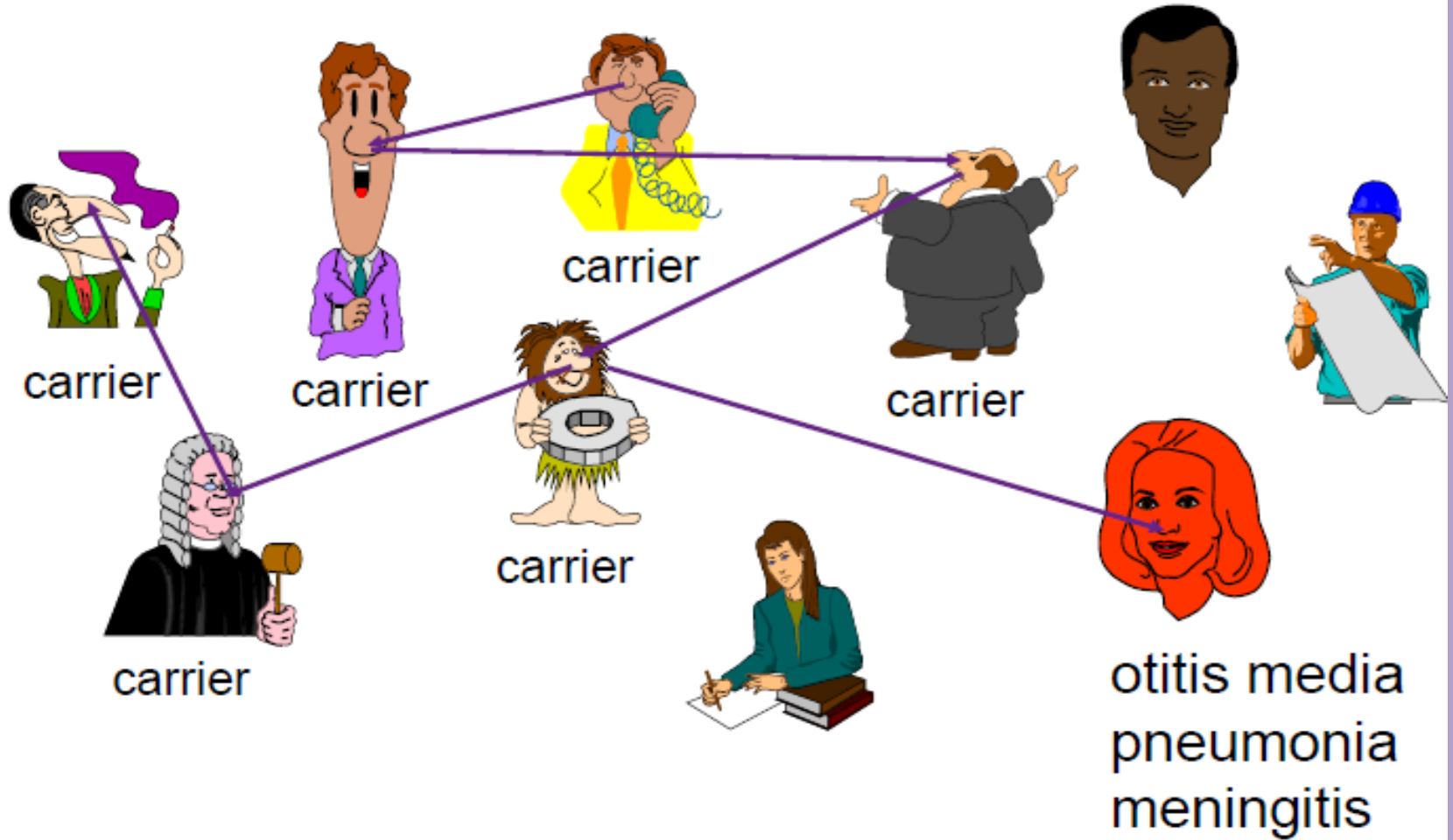
- *S. pneumoniae* % 60
- *N. meningitidis* % 20
- *H. influenzae* % 10
- *L. monocytogenes* % 6
- Grup B streptokok % 4

HASTALIK SIKLIĞININ BELİRLENMESİ

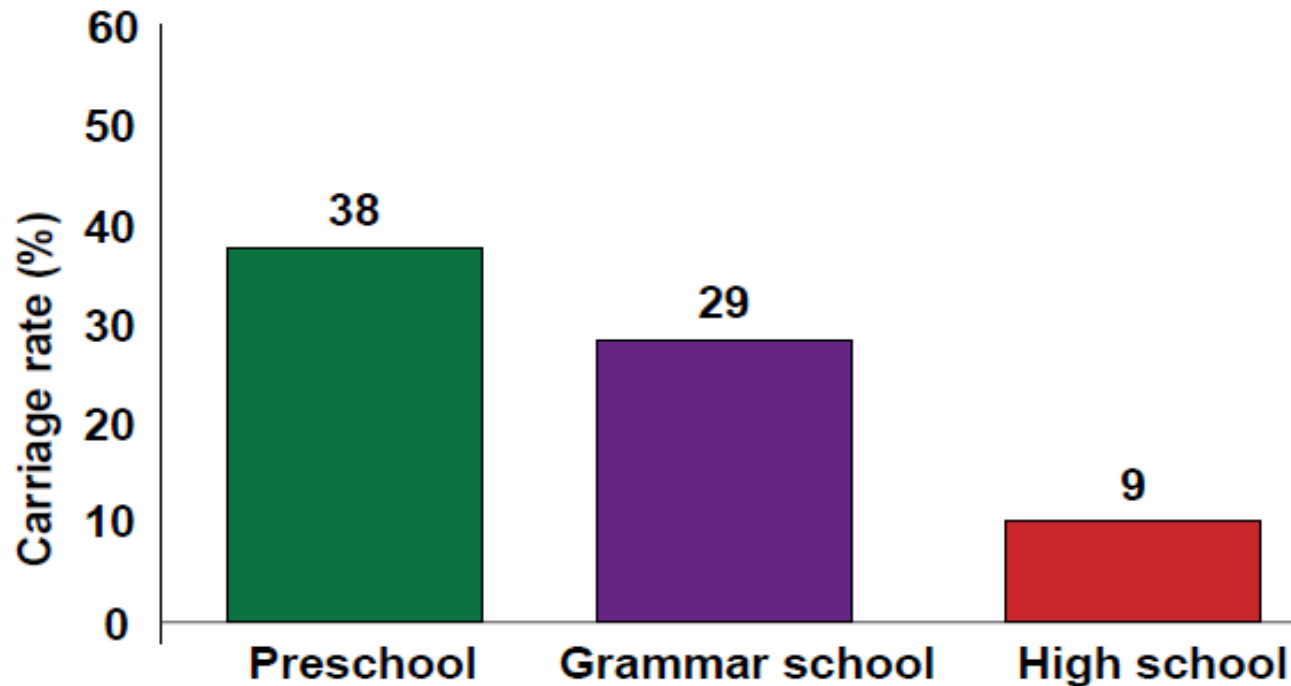


- 6 ay- 5 yaş arası çocukların %91'i zaman içinde en az bir kez pnömokokları taşır.
- Pnömokok izolasyon oranı ilk 2 yaşta doruğa ulaşır ve sonra yavaşça azalır.
- Sıklıkla uzun bir zaman (45 gün- 6 ay) aynı serotip taşınır.
- Taşıyıcılık aynı serotip ile tekrar kolonizasyonu engelleyecek bağışıklık sağlamaz.
- Kolonizasyon kış ortalarında en yüksektir
- Yeni serotip yerleşen çocukların %15'inde bir ay içinde hastalık gelişir.

PNÖMOKOK TAŞIYICILIK

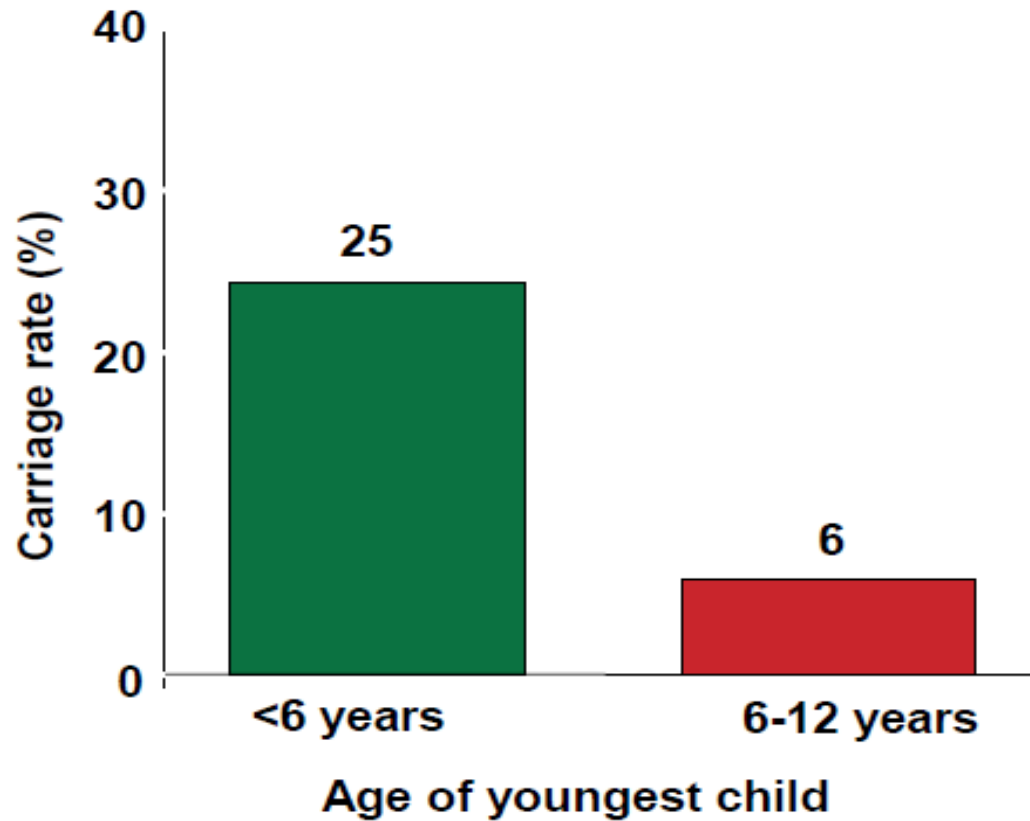


PNÖMOKOK TAŞIYICILIK



Hendley JO et al. *J Infect Dis* 1975;132:55

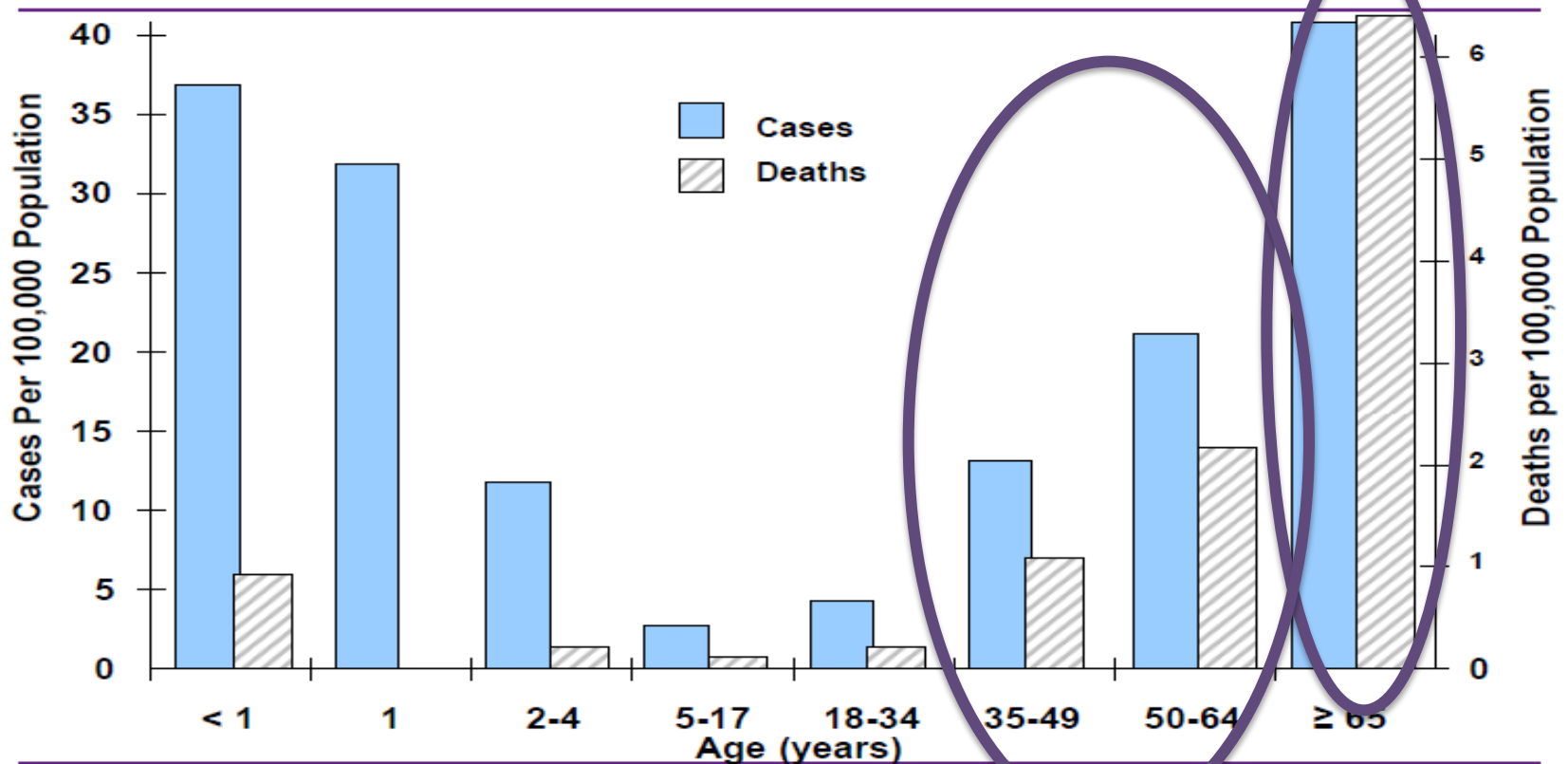
PNÖMOKOK TAŞIYICILIK



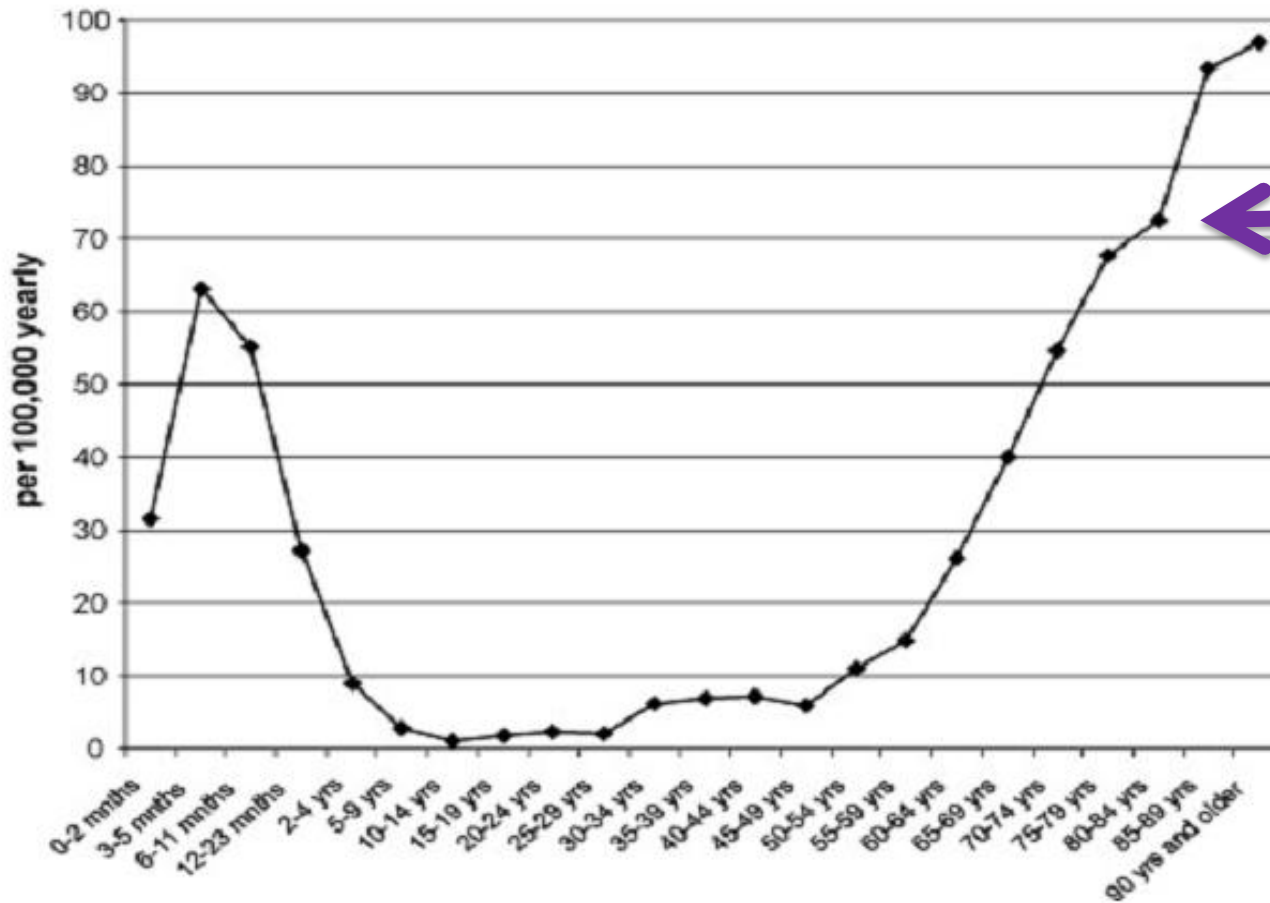
Hendley JO et al. *J Infect Dis* 1975;132:55

PNÖMOKOK ENFEKSİYONLARI- YAŞ

Invasive pneumococcal disease incidence and mortality, U.S. ABCs sites, 2008



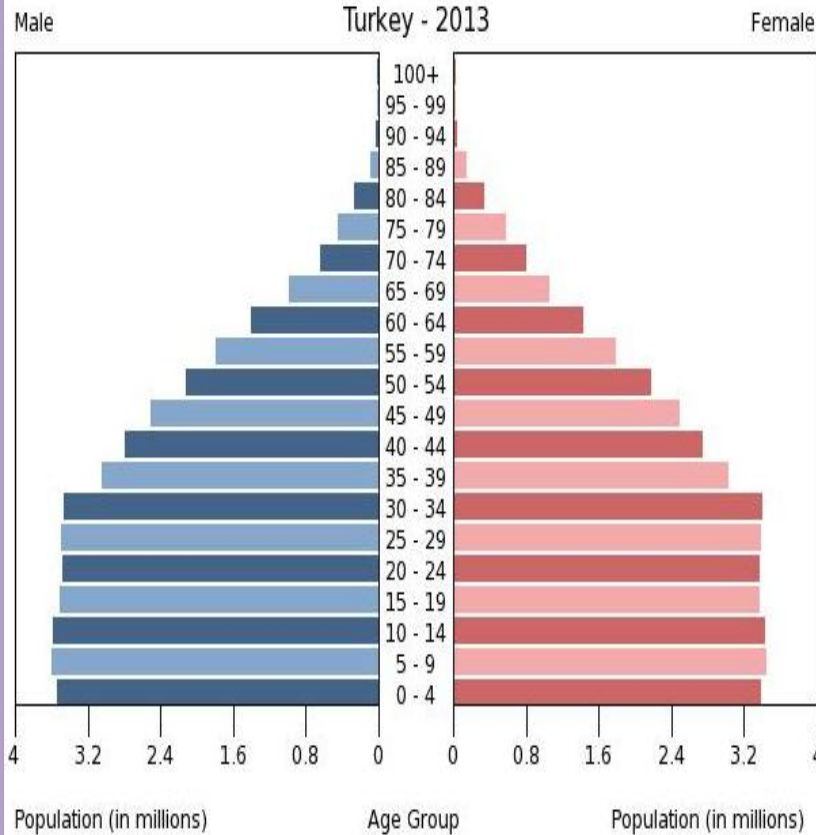
PNÖMOKOK ENFEKSİYONLARI- YAŞ



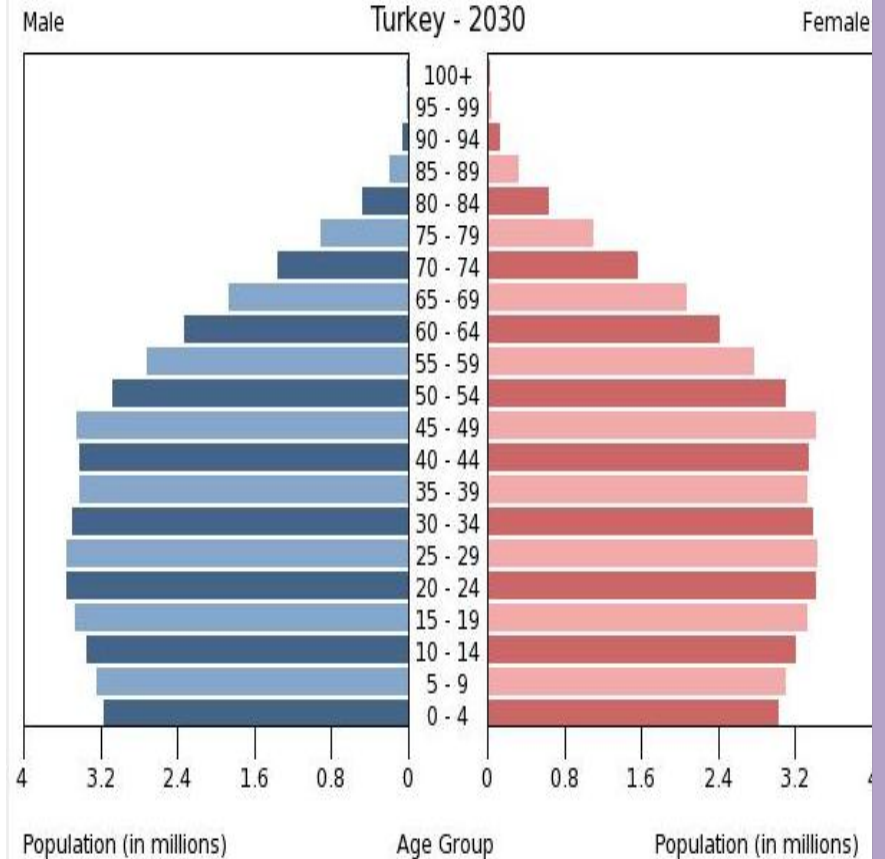
Jansen A et al 2009. Invasive pneumococcal disease in the Netherlands. Vaccine 27 (17)

PNÖMOKOK ENFEKSİYONLARI- YAŞ

2013



2030



Risk factors for pneumococcal disease

- Age <2 years, ≥65 years
- Exposure to cigarette smoke, multiple children in household
- Comorbidities
 - Alcohol abuse
 - Congestive heart failure
 - Chronic lung disease
 - Cigarette smoking
 - Asthma
 - Influenza
 - Diabetes mellitus
 - Neurological disorders
- Certain ethnic groups
 - American Indians, Alaska Natives, African Americans (U.S.)
- Immune deficiencies
 - B cell defects
 - Deficiencies of early components of classical pathway of complement
 - Asplenia
 - Sickle cell disease
 - Hematological or solid malignancies
 - Organ transplant recipients
 - HIV infection
 - Immunosuppressive drugs

Risk factors for death from community-acquired invasive pneumococcal pneumonia, United States

Disease	Relative Risk (95% CI)
Cirrhosis	5.8 (3.7, 9.2)
Congestive heart failure	4.7 (3.3, 6.7)
Diabetes	2.9 (2.0, 4.3)
Chronic lung disease	2.8 (1.9, 4.0)
Asplenia	3.2 (1.1, 9.3)
AIDS	2.3 (1.5, 3.6)
Solid organ malignancy	3.7 (2.5, 5.4)
Hematologic malignancy	2.2 (1.2, 4.3)

MAJOR ARTICLE

Prevention of Acute Myocardial Infarction and Stroke among Elderly Persons by Dual Pneumococcal and Influenza Vaccination: A Prospective Cohort Study

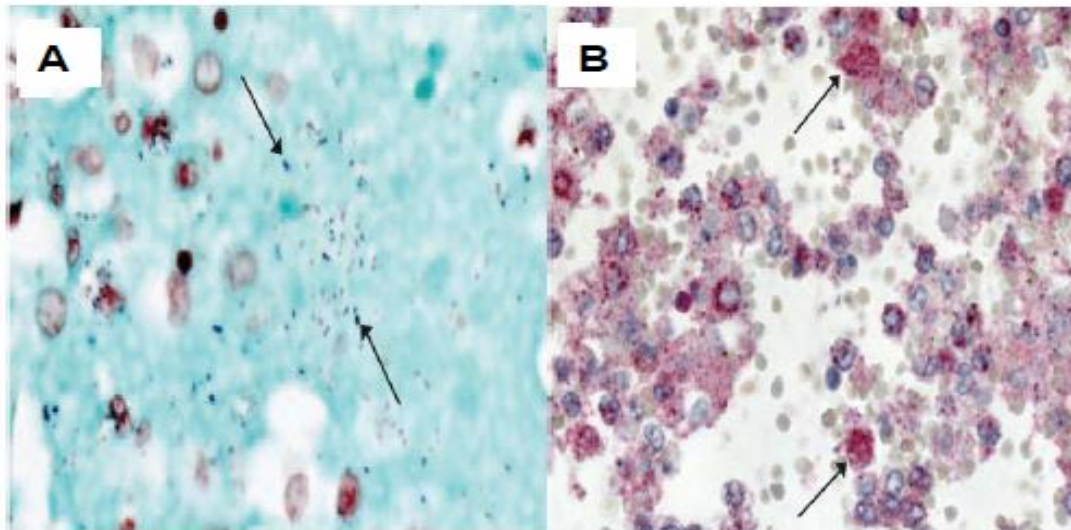
Ivan F. N. Hung,^{1,2} Angela Y. M. Leung,³ Daniel W. S. Chu,⁵ Doris Leung,³ Terence Cheung,⁷ Chi-Kuen Chan,² Cindy L. K. Lam,² Shao-Haei Liu,⁶ Chung-Ming Chu,⁸ Pak-Leung Ho,¹ Sophia Chan,³ Tai-Hing Lam,⁴ Raymond Liang,² and Kwok-Yung Yuen¹

¹Infectious Disease Division, Queen Mary Hospital, State Key Laboratory of Emerging Infectious Diseases, Carol Yu Centre for Infection, The University of Hong Kong, Departments of ²Medicine and ³Nursing Studies and ⁴School of Public Health, The University of Hong Kong, ⁵Family Medicine and Primary Healthcare and ⁶Department of Infection, Emergency, and Contingency, Hospital Authority, ⁷Centre for Health Protection, Department of Health, and ⁸Department of Medicine, United Christian Hospital, Hong Kong SAR, China

İNVAZİV HASTALIK İÇİN RİSK FAKTÖRLERİ



Bacterial infections in lung tissue of 22 (29%) of 77 fatal U.S. cases of H1N1 pandemic influenza



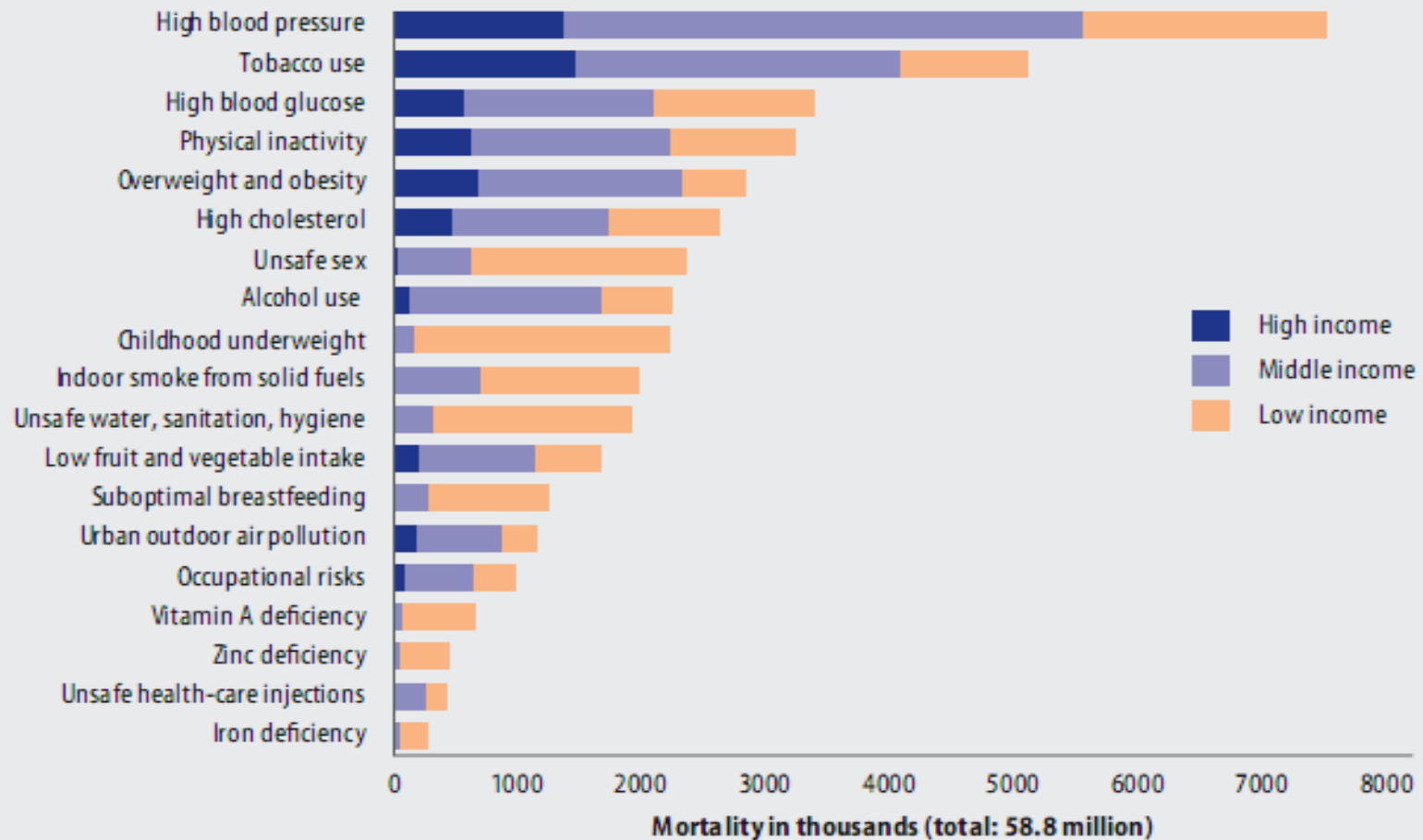
<u>Bacteria</u>	<u># cases</u>
<i>S. pneumoniae</i>	10
<i>S. aureus</i>	7
<i>S. pyogenes</i>	6
<i>S. mitis</i>	2
<i>H. influenzae</i>	1
Multiple pathogens	4

Histochemical and immunohistochemical diagnosis of *S. pneumoniae* infection

A: Lillie-Twort Gram stain of lung tissue

B: Immunohistochemical staining of multiple *S. pneumoniae* organisms

Figure 6: Deaths attributed to 19 leading risk factors, by country income level, 2004.



RİSK FAKTÖRLERİ



Risk Factors for Invasive Pneumococcal Disease in Children in the Era of Conjugate Vaccine Use

Tamar Pilishvili, Elizabeth R. Zell, Monica M. Farley, William Schaffner, Ruth Lynfield, Ann-Christine Nyquist, Marietta Vazquez, Nancy M. Bennett, Arthur Reingold, Ann Thomas, Delois Jackson, Anne Schuchat and Cynthia G. Whitney

Pediatrics 2010;126:e9-e17; originally published online Jun 14, 2010;

DOI: 10.1542/peds.2009-2150

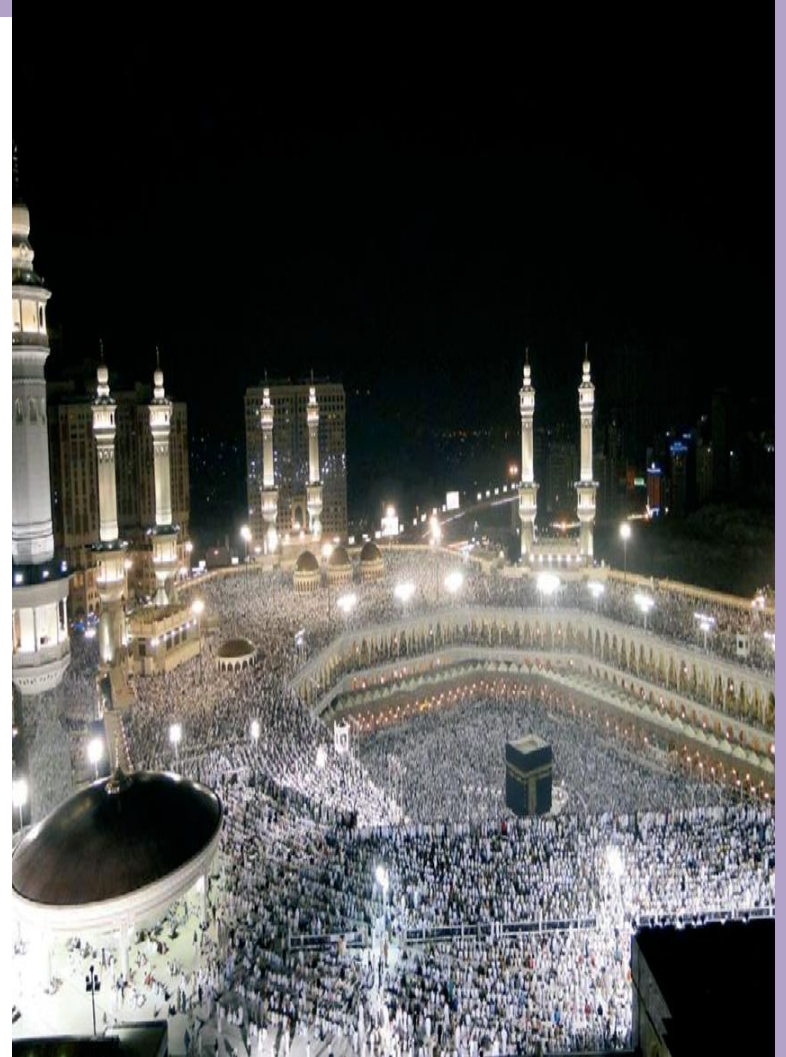
PEDIATRICS®

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İNVAZİV HASTALIK İÇİN RİSK FAKTÖRLERİ

Low birth weight (<2500 g)	10	7	.010	1.6 (1.2–2.2)
Chronic medical conditions (any)	11.3	4.2	<.001	3.3 (2.4–4.5)
Chronic lung condition	1.3	0.6	.020	3.5 (1.5–8.0)
Heart disease	4.4	1.5	<.001	3.5 (2.1–5.7)
Diabetes	0.0	0.1	—	Not measured
Kidney disease (no dialysis)	0.8	0.2	.040	3.6 (1.1–11.4)
Immunocompromising condition (any)	11.3	2.7	<.001	4.9 (3.4–6.9)
Asplenia	0.4	0.1	.090	3.9 (0.6–23.5)
Immune system disorder or HIV/AIDS	2.8	0.2	<.001	14.5 (5.7–36.8)
Bone marrow or organ transplant	0.8	0.0	—	Not measured
Nephrotic syndrome or renal failure	0.9	0.1	.003	14.7 (2.9–76)
Cancer	2.80	0.04	<.001	78.0 (10.2–593)
Cerebrospinal fluid leak	0.0	0.0	—	—
Sickle cell disease	1.0	0.2	.002	5.6 (1.6–19.4)
Systemic steroid use	9.2	4.5	<.001	2.2 (1.6–3.0)
Asthma	27	18	<.001	1.8 (1.5–2.2)
Congenital/developmental disorders	6	1	<.001	4.9 (3.0–8.0)
Antibiotics prescribed within 30 d before case IPD onset	29	19	<.001	1.8 (1.4–2.1)

- Hac ve Ümre ziyaretleri
pnömokok enfeksiyonları için
risk faktörümüdür?
 - Kalabalık
 - Farklı toplumlardan insanlar biraraya geliyor
 - Yaş
 - Kronik hastalık varlığı



Obesity, diabetes and pneumonia: the menacing interface of non-communicable and infectious diseases

Susan P. Fisher-Hoch, Christine E. Mathews and Joseph B. McCormick

Division of Epidemiology, Human Genetics and Environmental Sciences, University of Texas School of Public Health, Brownsville, TX, USA

RESULTS In 2008, globally 10% of men and 14% of women were obese and an estimated 371 million had diabetes; half undiagnosed and many obese. Numbers are rising rapidly in low- and middle-income countries where the majority reside, but reliable data are lacking. The most frequent pneumonias in obesity and diabetes are tuberculosis, influenza and pneumococcal, staphylococcal and opportunistic pathogens. Diabetes impacts tuberculosis control and increases drug resistance and mortality. Mortality and morbidity from pneumococcal pneumonia and influenza are increased in obesity and diabetes. In addition to mechanical and physiological effects, there are considerable immunological abnormalities characterised by chronic, low-grade inflammation. Simultaneous up-regulation and dysregulation of both innate and adaptive immune responses impair control and killing of invading organisms. Prevention in those at risk is poorly practised, although screening for tuberculosis in diabetes is beginning in high-burden settings.

BMC Infectious Diseases



Research article

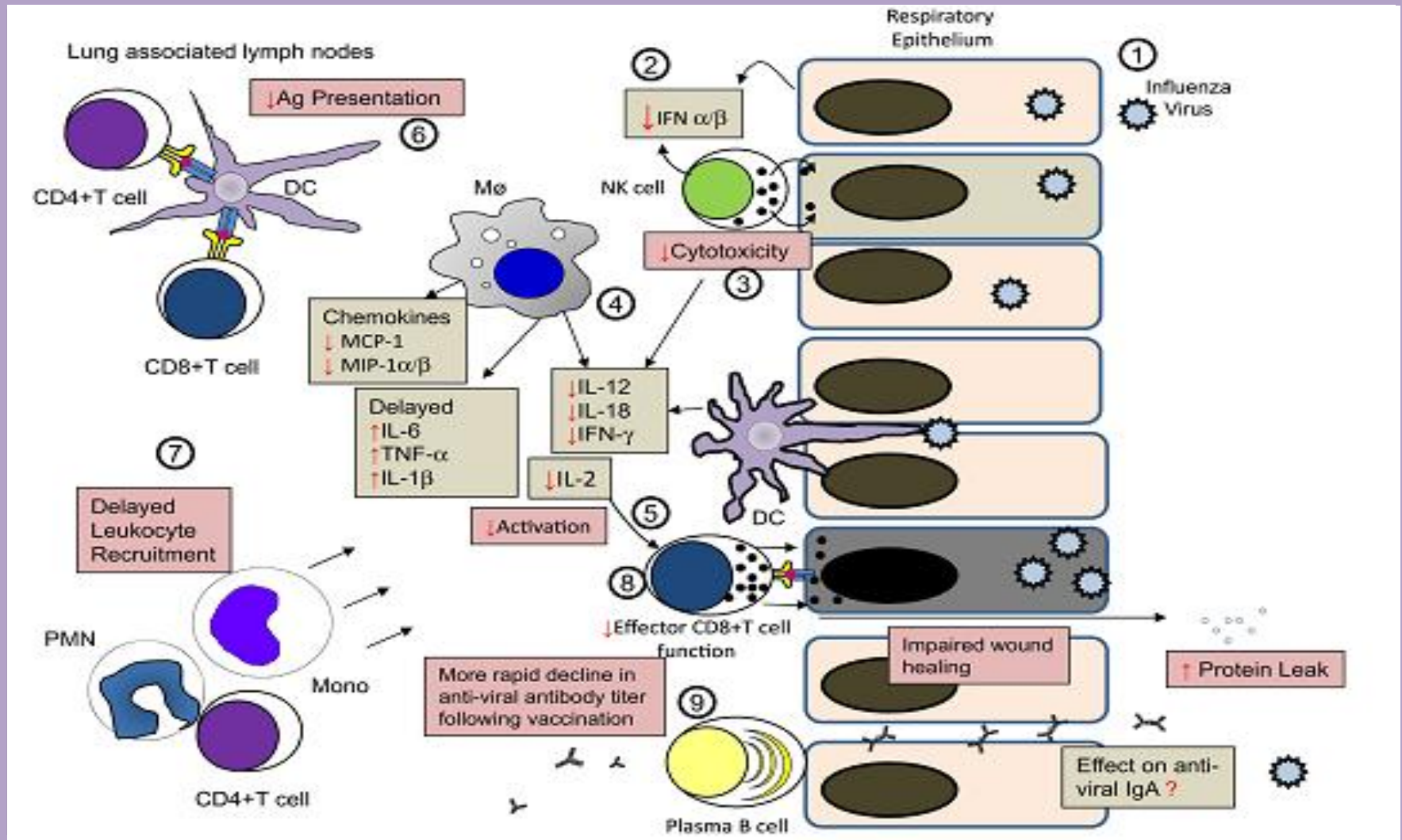
Open Access

Obesity and smoking are factors associated with poor prognosis in patients with bacteraemia

Reetta Huttunen^{*1,2}, Janne Laine¹, Jukka Lumio¹, Risto Vuento³ and Jaana Syrjänen^{1,2}

Obesity and smoking, in addition to mechanical and physiological factors, have an effect on immunological abnormalities characterised by chronic, low-grade inflammation. Simultaneous up-regulation and dysregulation of both innate and adaptive immune responses impair control and killing of invading organisms. Prevention in those at risk is poorly practised, although screening for tuberculosis in diabetes is beginning in high-burden settings.

İNVAZİV HASTALIK İÇİN RİSK FAKTÖRLERİ



- Serotip dağılımı dünyada farklılıklar göstermektedir.
- Tüm serotiplerin patojen olma potansiyelleri farklı
- Hastalık etkeni olan izolatlar genelde 30 serotip (94 serotip içerisinde)
- Serotipler yaşa bağlı olarak değişim göstermektedir.
 - Yaşa bağlı değişen kronik hastalıkları
- Serotipler zamana bağlı olarak değişim göstermektedir.
- Aşılama stratejileri
- Antibiyotik kullanım politikaları
- Sosyoekonomik koşullar
- Kan kültür alım alışkanlıkları

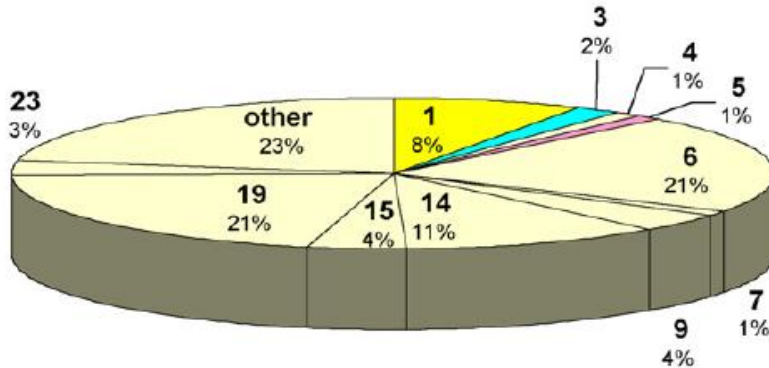
PNÖMOKOKAL TOPLUM KAYNAKLI PNÖMONİLERDE SEROTİP SIKLIĞI

(Esposito S et al. Vaccine 2003)

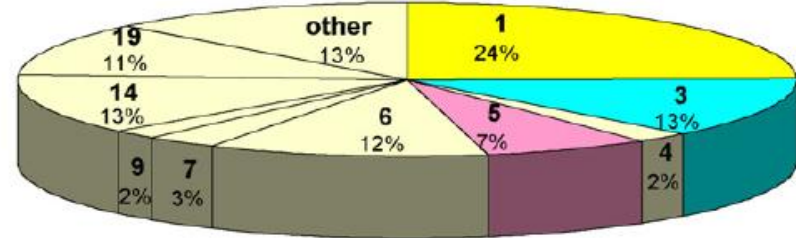
Serotip	N (%)
1	16 (31.4)
14	11 (21.6)
9V	6 (11.8)
4	4 (7.8)
6B	4 (7.8)
19F	4 (7.8)
18C	3 (5.9)
23F	2 (3.9)
5	1 (2.0)

PNÖMOKOKAL TOPLUM KAYNAKLI PNÖMONİLERDE SEROTİP SIKLIĞI

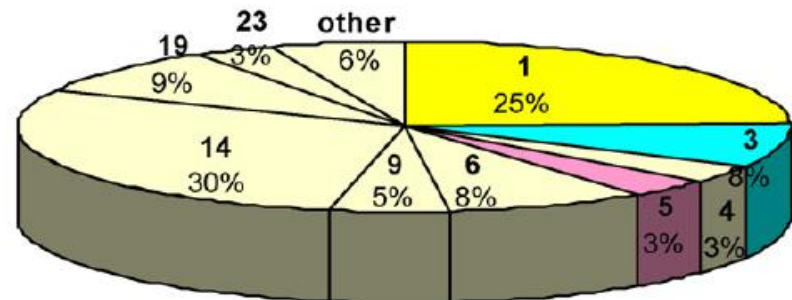
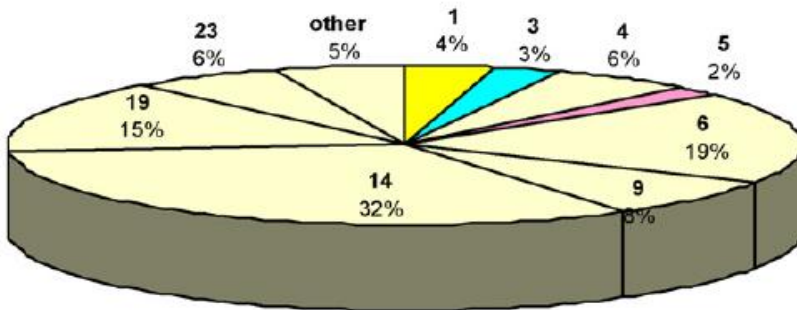
Uncomplicated Pneumonia



Complicated Pneumonia



Russia



US

Clinical and Vaccine Immunology

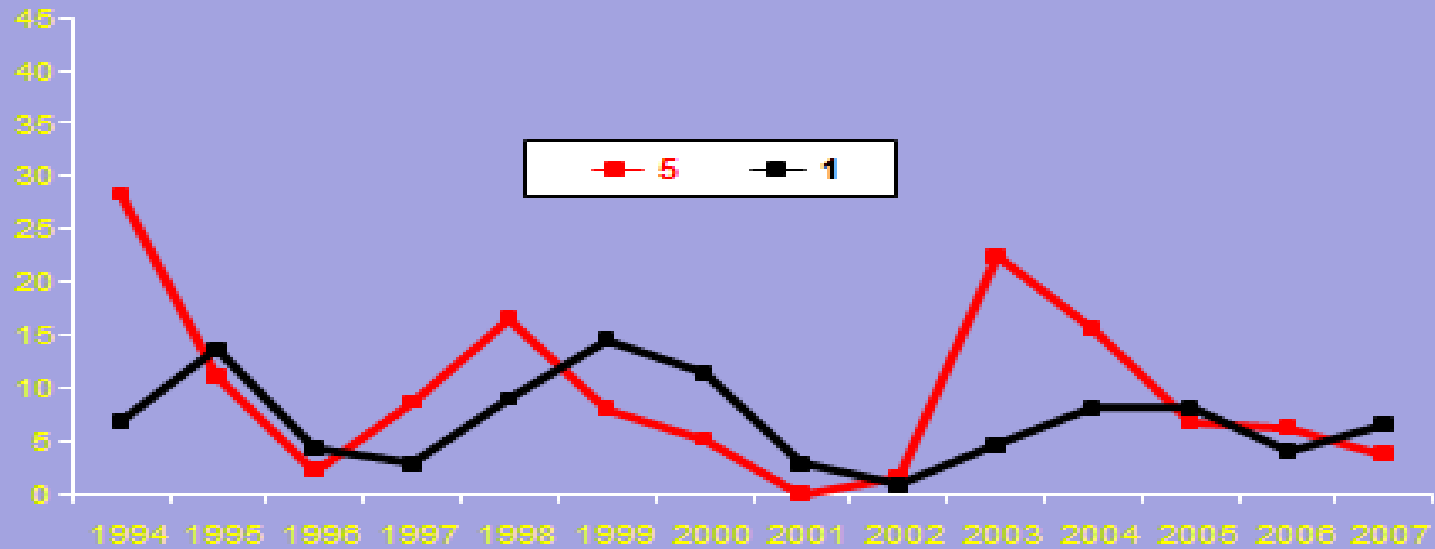
Distribution of *Streptococcus pneumoniae* Serotypes That Cause Parapneumonic Empyema in Turkey

Mehmet Ceyhan, Yasemin Ozsurekci, Nezahat Gürler, Sengul Ozkan, Gulnar Sensoy, Nursen Belet, Mustafa Hacimustafaoglu, Solmaz Celebi, Melike Keser, Ener Cagri Dinleyici, Emre Alhan, Ali Baki, Ahmet Faik Oner, Hakan Uzun, Zafer Kurugol, Ahmet Emre Aycan, Venhar Gurbuz, Eda Karadag Oncel, Melda Celik and Aslinur Ozkaya Parlakay

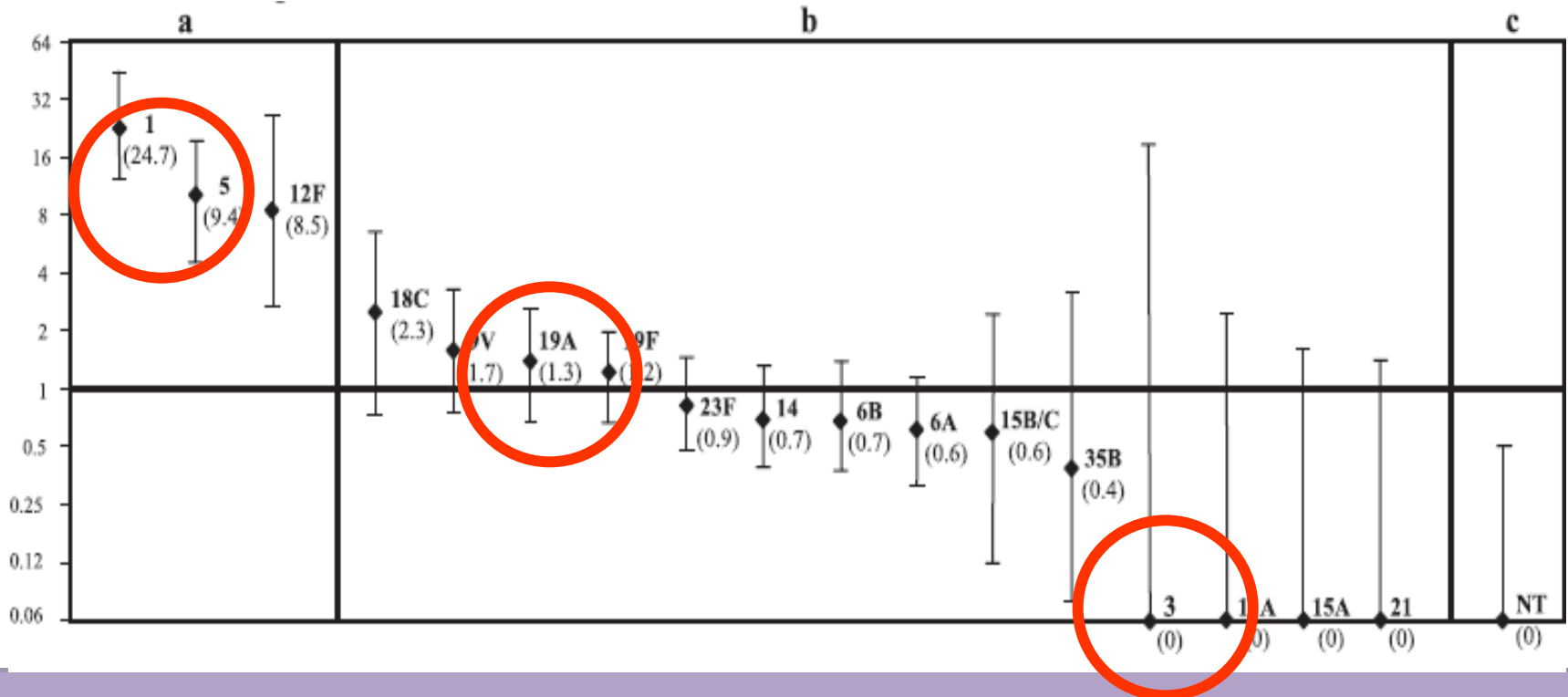
Clin. Vaccine Immunol. 2013, 20(7):972. DOI:
10.1128/CVI.00765-12.

Published Ahead of Print 1 May 2013.

SEROTİPLER ARASINDAKİ FARKLILIKLAR



Serotiplerin invaziv hastalık oluşturma kapasiteleri arasında belirgin farklılıklar mevcut



Association of Serotype with Risk of Death Due to Pneumococcal Pneumonia: A Meta-Analysis

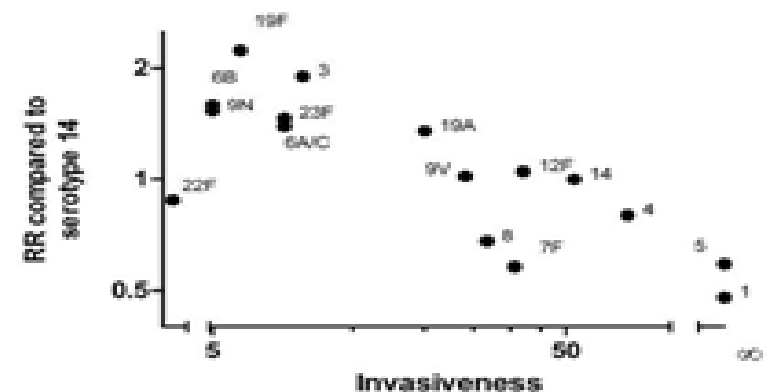
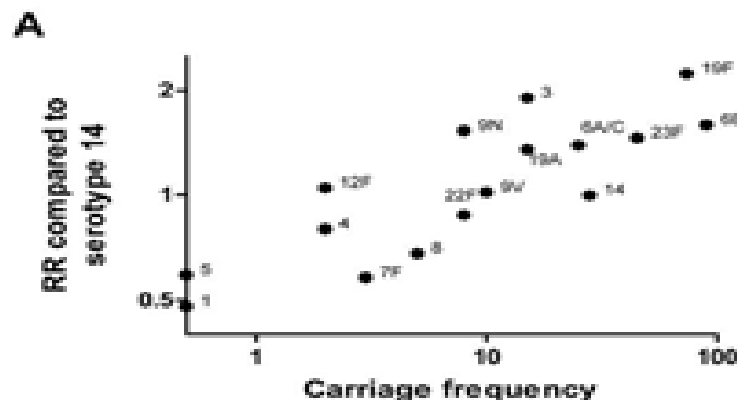
Daniel M. Weinberger,¹ Zitta B. Harboe,^{6,7} Elisabeth A. M. Sanders,⁸ Moses Ndiritu,¹⁰ Keith P. Klugman,^{3,12} Simon Rückinger,⁹ Ron Dagan,¹³ Richard Adegbola,¹¹ Felicity Cutts,¹¹ Hope L. Johnson,⁴ Katherine L. O'Brien,⁵ J. Anthony Scott,¹⁰ and Marc Lipsitch²

Clinical Infectious Diseases 2010; 51(5):692–699

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1058-4838/2010/5106-0008\$15.00

DOI: 10.1093/cid/cir228



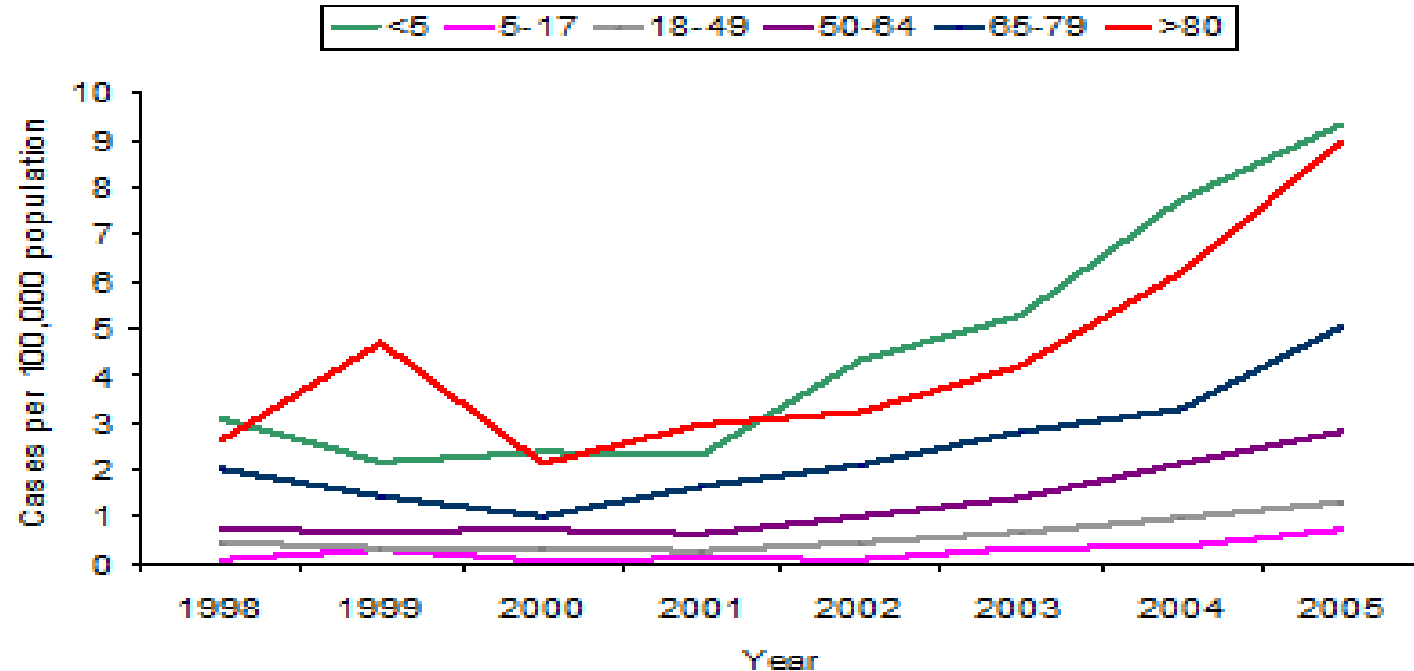
Serotype 7F invaziv Hastalık riski ve fatalite hızı en yüksek

Table 1: Serotype specific case fatality rates and standardized mortality ratios (95% Confidence Interval) for 494 children with IPD in Germany between 1997 and 2003

Serotype	Observed cases of IPD	Expected deaths	Observed deaths	case fatality rate %	SMR ^a (95% CI)
7F	27	1.3	4	14.8	3.1 (1.2-8.2)
23F ^b	35	1.7	3	8.6	1.8 (0.6-5.5)
3	12	0.6	1	8.3	1.7 (0.2-11.8)
6A	14	0.7	1	7.1	1.4 (0.2-10.1)
9V ^b	17	0.8	1	5.9	1.3 (0.2-8.9)
14 ^b	146	7.1	9	6.2	1.3 (0.7-2.4)
4 ^b	19	0.9	1	5.3	1.1 (0.3-4.2)
6B ^b	38	1.9	2	5.3	1.1 (0.2-7.9)
Other	72	3.5	3	4.2	0.9 (0.3-2.7)
19F ^b	30	1.5	1	3.3	0.7 (0.1-4.7)
1	24	1.2	0	0	-
18C ^b	36	1.8	0	0	-
19A	17	0.8	0	0	-

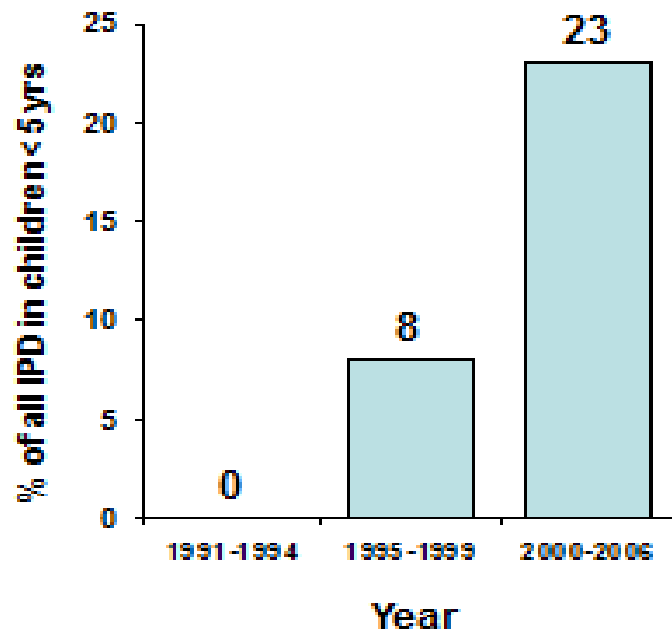
SEROTİPLER ARASINDAKİ FARKLILIKLAR

1998-2005 yılları arasında **19A** insidansı





Güney Kore



- Tüm 19A, çoğul antibiyotik dirençli
- ST 320

Serotype 19A'ya bağlı IPD'de aşı
Güney Kore'de kullanılmadan önce
Artış göstermekte.

EARSS 2006

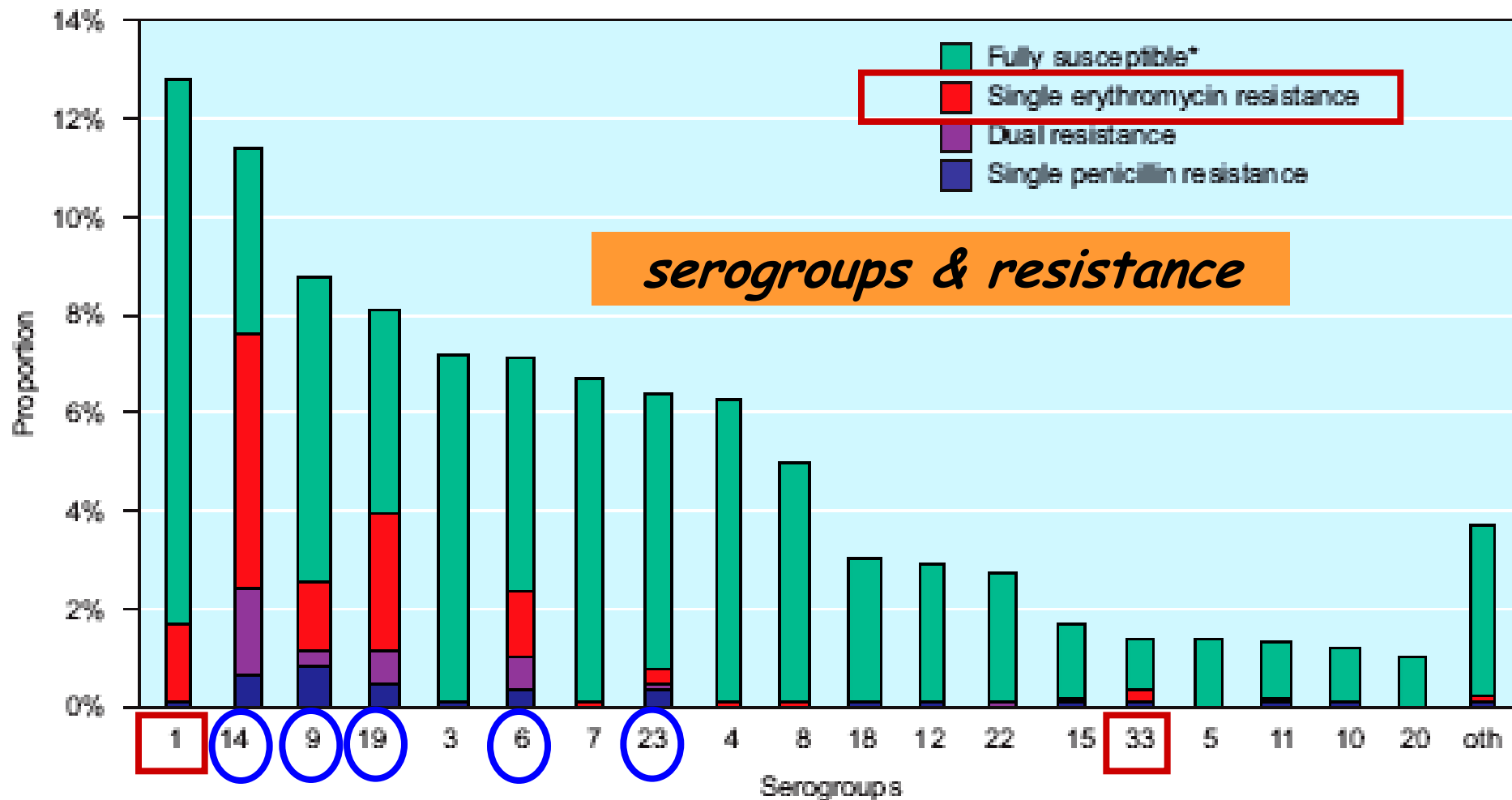


Figure 5.7. The distribution of serogroups and the resistance profile (single erythromycin, single penicillin or dual resistance) per serogroup of *S. pneumoniae* isolates in the EARSS database, in 2006. Only countries that reported serogroup information for more than 30 isolates (Austria, Belgium, Czech Republic, Denmark, Ireland, Iceland, Slovenia and the United Kingdom) were included in this figure. * Susceptible to at least penicillin and erythromycin.

- Penisilin NSP= 40%
- Penisilin rezistan SP= 5-10%
- Erythromycin rezistan 15-20%
- TMP-SMX > 50%
- Tetrasiklin <10%
- Amoksisilin klavulanik asit <5%
- İzolatların büyük bölümü rifampisin, kinolonlar, linezolid, quinupristin-dalfopristin duyarlı

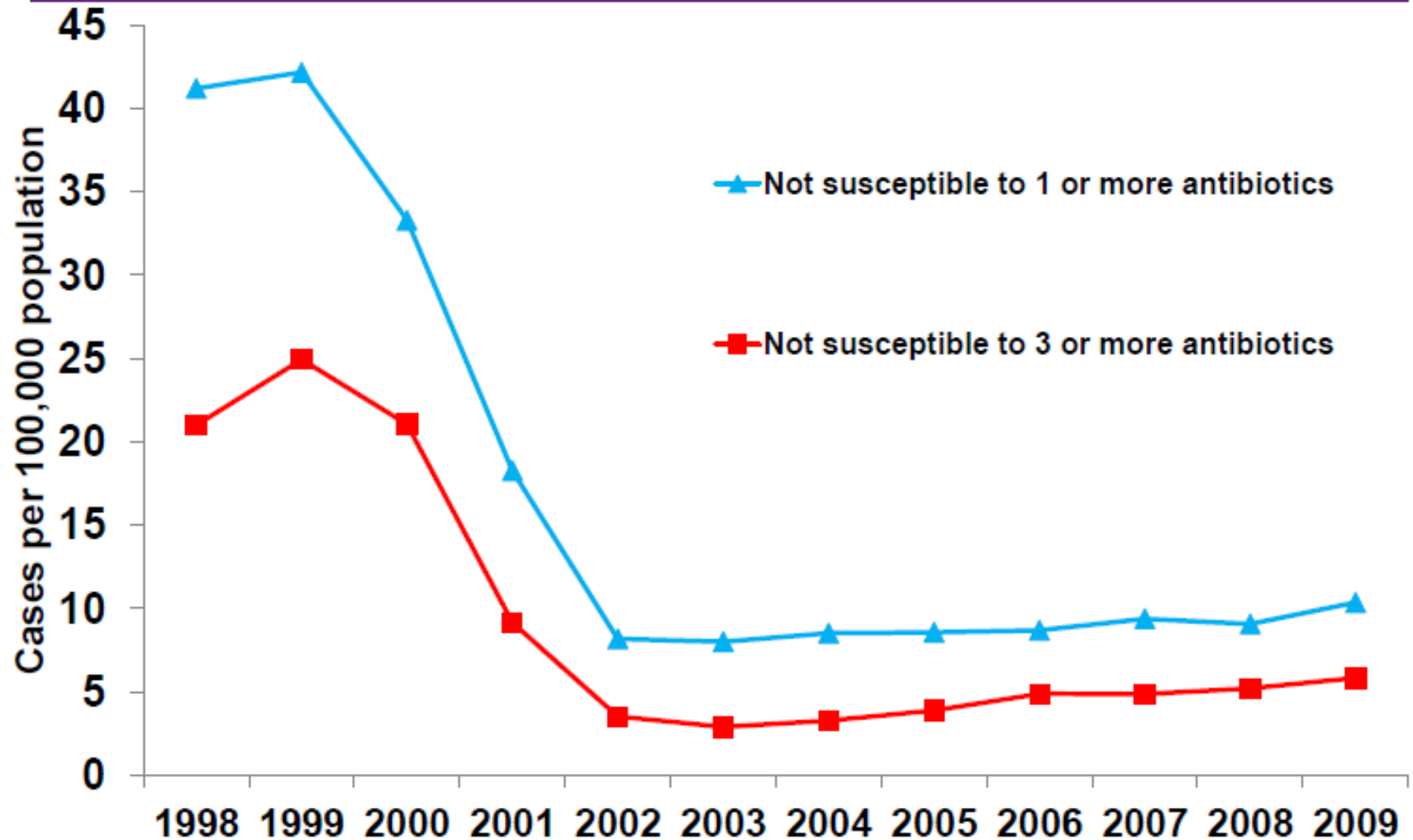
- Eşlik eden hastalık
 - Kardiyovasküler sistem
 - Alkolizm
 - Diabet
 - KOAH
- Yaş
 - < 2 yaş, > 65 yaş
- Son 3 ayda betalaktam antibiyotik kullanımı
- İmmünsüpresyon veya immünsüpresif tedavi
- Kreş çocuğu ile temas

Pneumococcal conjugated vaccines: impact of PCV-7 and new achievements in the postvaccine era

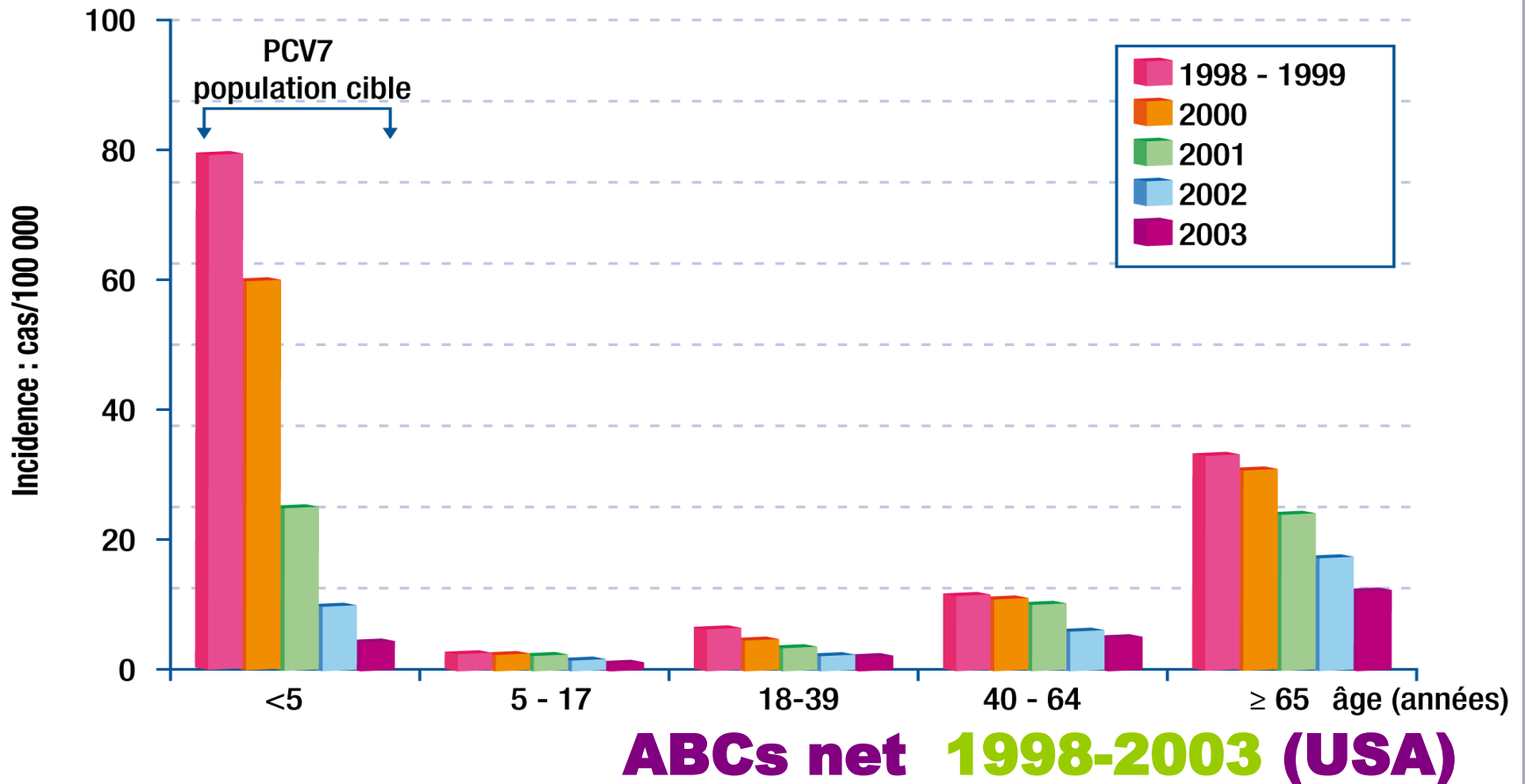
Expert Rev. Vaccines 7(9), 1367–1394 (2008)

- İnvaziv pnömokok enfeksiyonlarında ↓↓
- Menenjitlerde azalma ↓ ↓
- Pnömonilerde azalma ↓
- Otit sayısı ve hastaneye başvuru ↓
- Otit nedeni ile antibiyotik kullanımı ↓
- Herd immunity

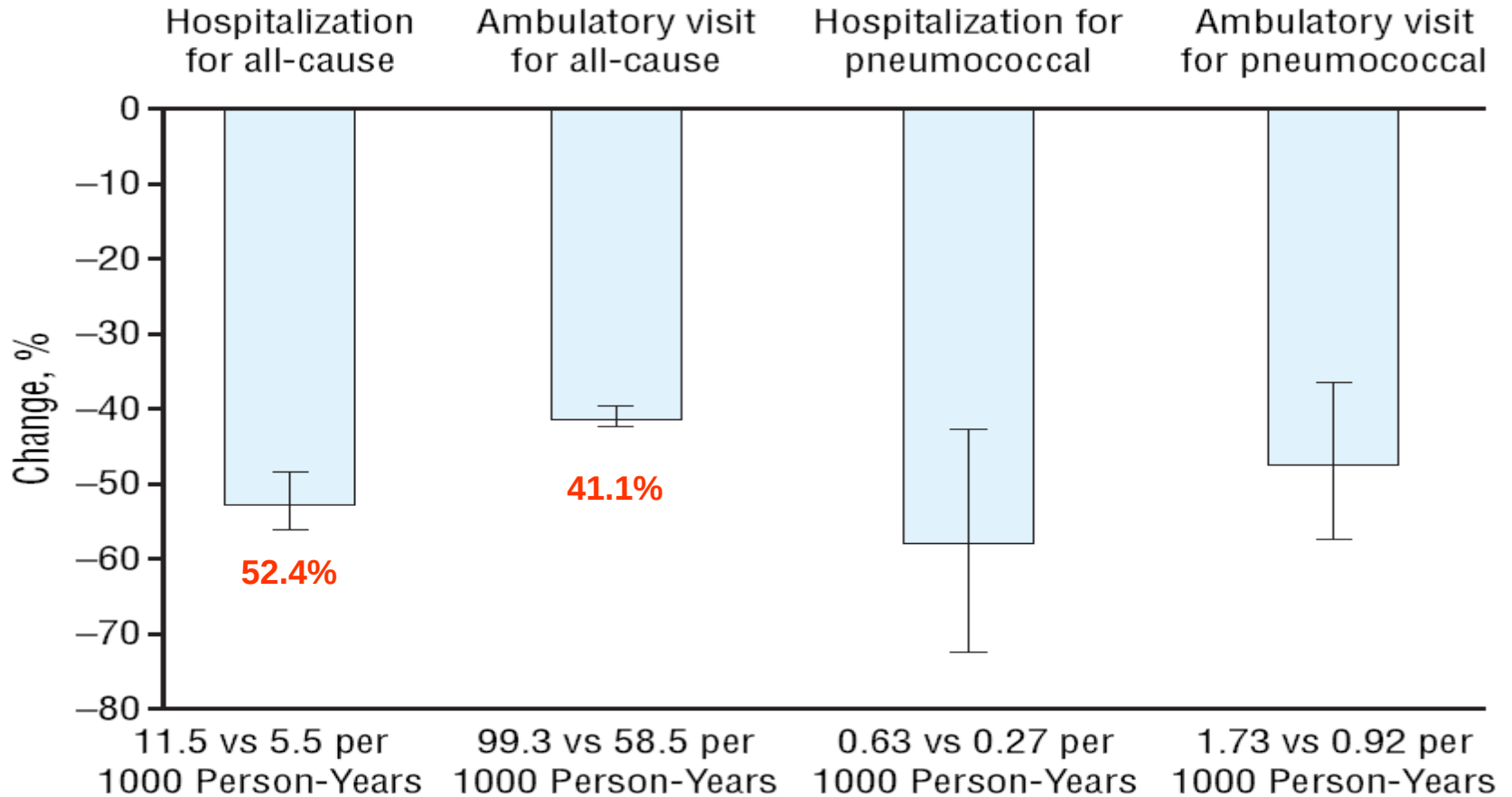
ÇOCUKLARDA KONJUGE PNÖMOKOK AŞILARI KULLANIMI SONRASI??



ÇOCUKLARDA KONJUGE PNÖMOKOK AŞILARI KULLANIMI SONRASI??



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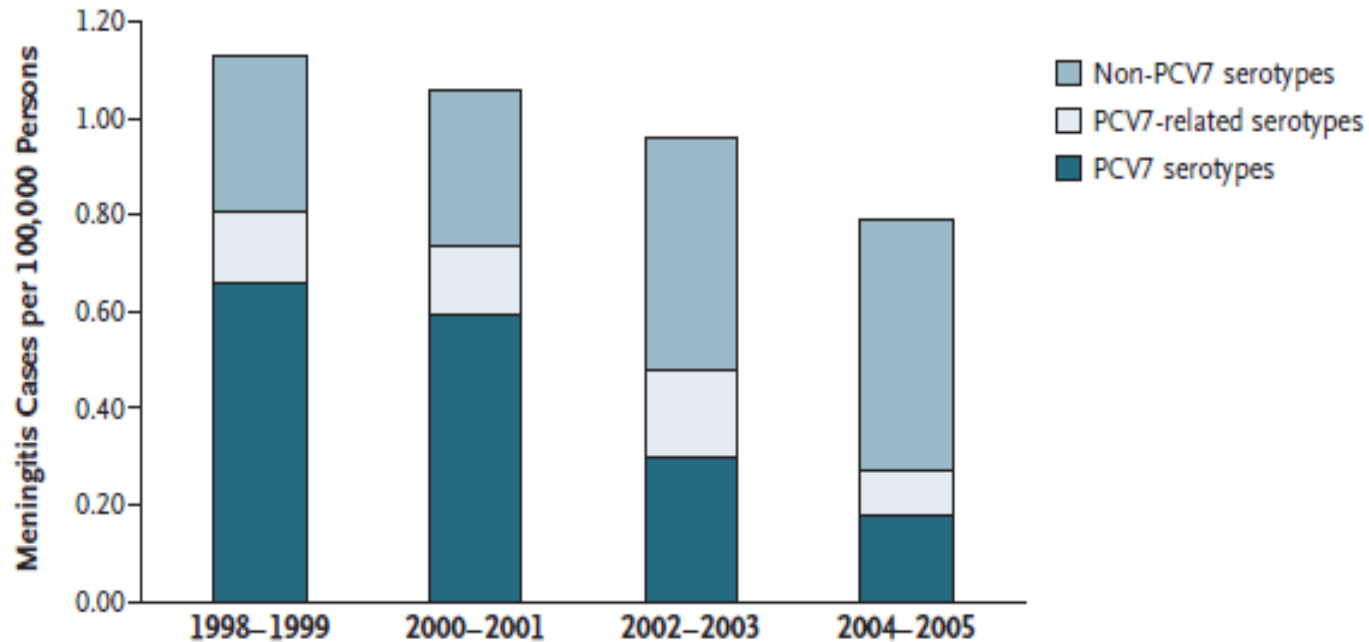
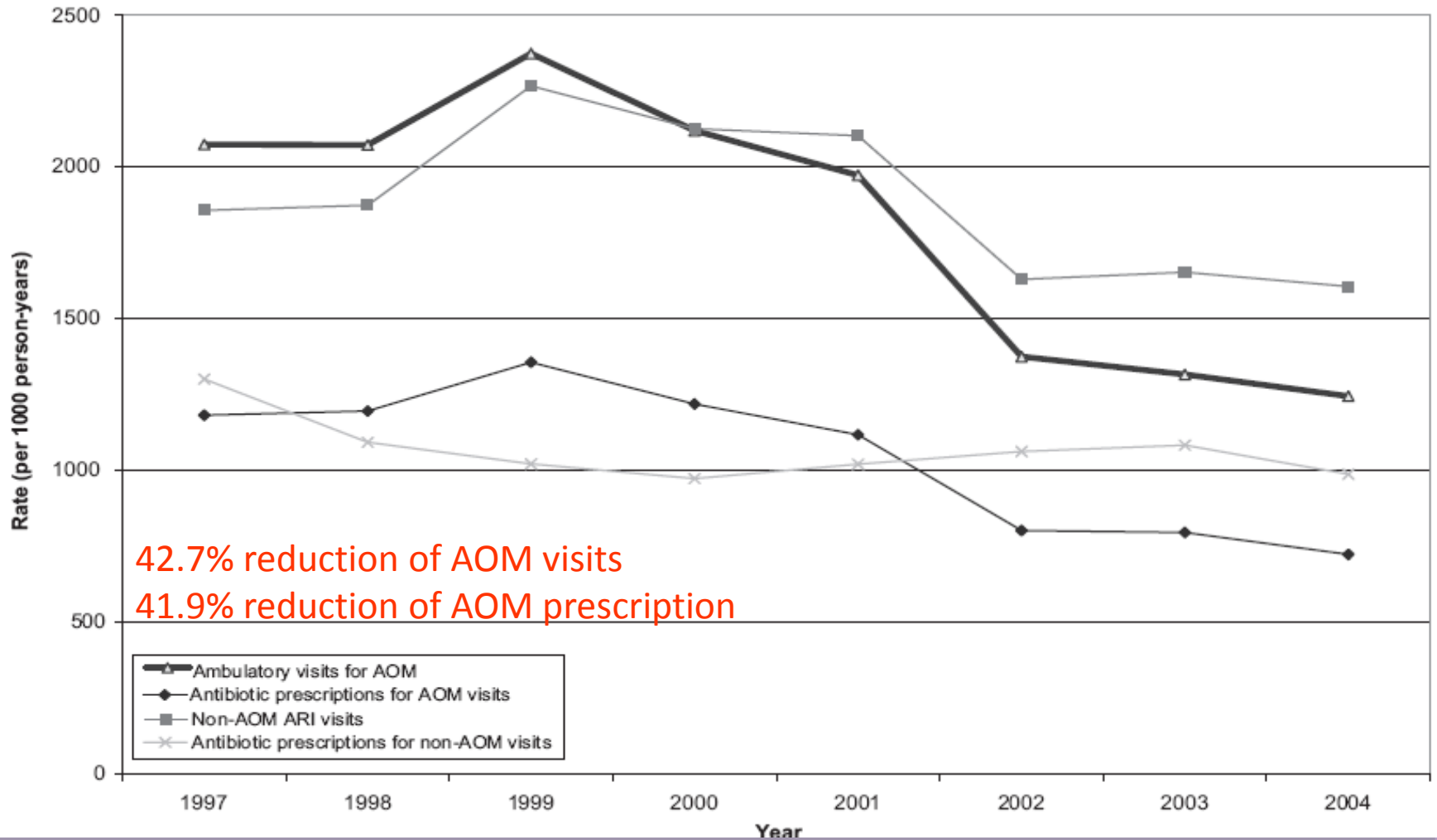


Figure 1. Mean Annual Incidence of Pneumococcal Meningitis, According to Serotype Group and Time Period.

Serotypes of the heptavalent pneumococcal conjugate vaccine (PCV7) were 4, 6B, 9V, 14, 18C, 19F, and 23F. PCV7-related serotypes were 6A, 9A, 9L, 9N, 18A, 18B, 18F, 19B, 19C, 23A, and 23B. Non-PCV7 serotypes were 3, 7F, 10A, 11A, 12F, 15A, 15B/C, 16F, 19A, 22F, 33F, 35B, 35F, and 38.

ÇOCUKLARDA KONJUGE PNÖMOKOK AŞILARI KULLANIMI SONRASI??



The dynamic and changing epidemiology of meningococcal disease at the country-based level: the experience in Turkey

Expert Rev. Vaccines 11(5), 00–00 (2012)



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“Changes in the epidemiology of invasive meningococcal disease over time in Turkey has shown that continued surveillance of meningococcal disease is essential.”

Invasive meningococcal disease (IMD) is an important condition, affecting more than 500,000 people worldwide, resulting in approximately 50,000 deaths and 10–20% severe long-term complications [1,2]. The reported incidence of IMD varies by region, ranging from less than 0.5 cases per 100,000 in North America and less than one case per 100,000 in Europe to 10–1000 cases per 100,000 people during epidemic years in Africa [2]. There

basis of the Turkish Statistical Institute (TurkStat) data, 1982–1985 cases per year were reported as IMD. According to the TurkStat data since 2009, IMD are responsible for 10% of all causes of mortality for children younger than 5 years of age [10]. On the basis of the Ministry of Health (MoH) records, the case numbers are lower than those of the TurkStat reports. Between 1989 and 1999, the incidence of IMD varied between 1 and 35

Current status of pneumococcal vaccines: lessons to be learned and new insights

Expert Rev. Vaccines 9(9), 1017–1022 (2010)

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- Konjuge pnömokok aşıları
 - 7 valan KPA (Prevenar)
 - 10 Valan KPA (Synflorix)
 - 13 Valan KPA (Pevnar 13)
 - 15 Valan KPA (Merck) (Faz 1)
- Polisakarit pnömokok aşısı
 - 23 valan polisakarit aşı (Pneumo 23)
- Protein bazlı pnömokok aşıları
 - Serotip bağımsız korunma
 - StkP, PcsB ve PsaA, IC31® adjuvanı ile (Faz çalışmalarında)

Risk faktörü	OR (% 95 CI)	P
Yaş > 65 yıl	2.9 (1.6-5.2)	0.0004
Ciddi hastalık *	21.1 (12.5-35.6)	0.0001
İmmünsüpresyon	3.1 (1.8-5.3)	0.0001
Penisilin duyarlılığı	1.4 (0.8-2.4)	0.19



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Mortality indicators in pneumococcal meningitis: therapeutic implications[☆]

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Table 1

Descriptive characteristics of patients with pneumococcal meningitis (n = 306)

Variable	n (%)
Male gender	213 (69.61)
Leukopenia or leukocytosis	269 (87.91)
Head trauma	98 (32.03)
Diabetes mellitus	40 (13.07)
Cerebrovascular event	14 (4.58)
Chronic obstructive lung disease	13 (4.25)
Splenectomy operation	11 (3.59)
Malignancy	8 (2.61)
HIV infection	3 (0.98)
Pregnancy	2 (0.65)
Collagen tissue disorder	1 (0.33)

Aysun Yalçı^{ab}, Yasemin Akkoyunlu^{abc}, Emisal Aydın^{ab}, Hüseyin Diktas^{abcd}, Sukran Köse^{abc},
Asim Ulcay^a, Derya Seyman^c, Umit Savasci^{oo}, Hakan Leblebicioglu^m, Haluk Vahaboglu^{bb}

Table 4

Independent risk factors for death in pneumococcal meningitis (multivariate logistic regression analysis)

	Adjusted OR	95% CI
Male gender	0.480	0.221–1.041
Empirical vancomycin use	2.159	0.949–4.912
Meningitis due to penicillin-susceptible pneumococcus	0.441	0.195–0.996
Age >50 years	3.908	1.820–8.390
Critical case ^a	7.089	3.230–15.557
Constant	0.0711	0.024–0.206

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Fight Pneumonia. Save a Child. **November 12th.**





*Excellence is a road, not a destination
Cont'd, 2014. Ener Cagri Dinleyici*