



Erişkinde Pnömonokok Hastalık

Yükü

Dr.H.Selçuk Özger

Gazi Üniversitesi Tıp Fakültesi Enfeksiyon Hastalıkları ve Klinik

Mikrobiyoloji Anabilim Dalı

hselcukozger@gazi.edu.tr

Eriřkinde Pnömokok Hastalık **Yükü**



Herkesin hastalık ve sakatlık olmadan yaşadığı ideal bir durum ile mevcut sağlık durumu arasındaki boşluk



Saęlık, Ekonomik, Sosyal

Epidemiyolojik

(İnsidans, prevelans, hastane yatış oranı, fatalite oranı...)

Ekonomik

(Direk ve indirek maliyetler...)

Sosyal-toplumsal

Quality of life year-QALY

Disability Adjusted Life Years-DALY

Search: (**Streptococcus pneumoniae Infections OR Pneumococcal Diseases OR Pneumococcal Infection OR Pneumococcal pneumonia OR Pneumococcal meningitis OR Pneumococcal bacteremia OR Pneumococcal septicemia AND (Turkey)AND (y_5[Filter]))**) Filters: in the last 5 years



83 Makale



HUMAN VACCINES & IMMUNOTHERAPEUTICS
2020, VOL. 16, NO. 8, 1923–1936
<https://doi.org/10.1080/21645515.2019.1708668>



Taylor & Francis
Taylor & Francis Group

RESEARCH PAPER

OPEN ACCESS

Check for updates

Indirect costs of adult pneumococcal disease and the productivity-based rate of return to the 13-valent pneumococcal conjugate vaccine for adults in Turkey

J. P. Sevilla ^a, Andrew Stawasz ^{a*}, Daria Burnes^a, Anubhav Agarwal^{a#}, Basak Hacibedel^b, Kerem Helvacioğlu^b, Reiko Sato^c, and David E. Bloom^a

Olasılık teorisi: **Markov modeli yapısı**

Popülasyon

- Büyükölük
- Yaşam beklentisi
- Risk/alt grupları
- Aşı uygulaması
- Aşı kapsayıcılığı

İnfeksiyon

- İnsidans
- Hastane yatış oranı
- Fatalite oranı
- Sekel oranı

Etkinlik

- Aşı etkililiği
- Serotip dağılımı- deęişimi
- Çocukluk aşılmasının etkisi

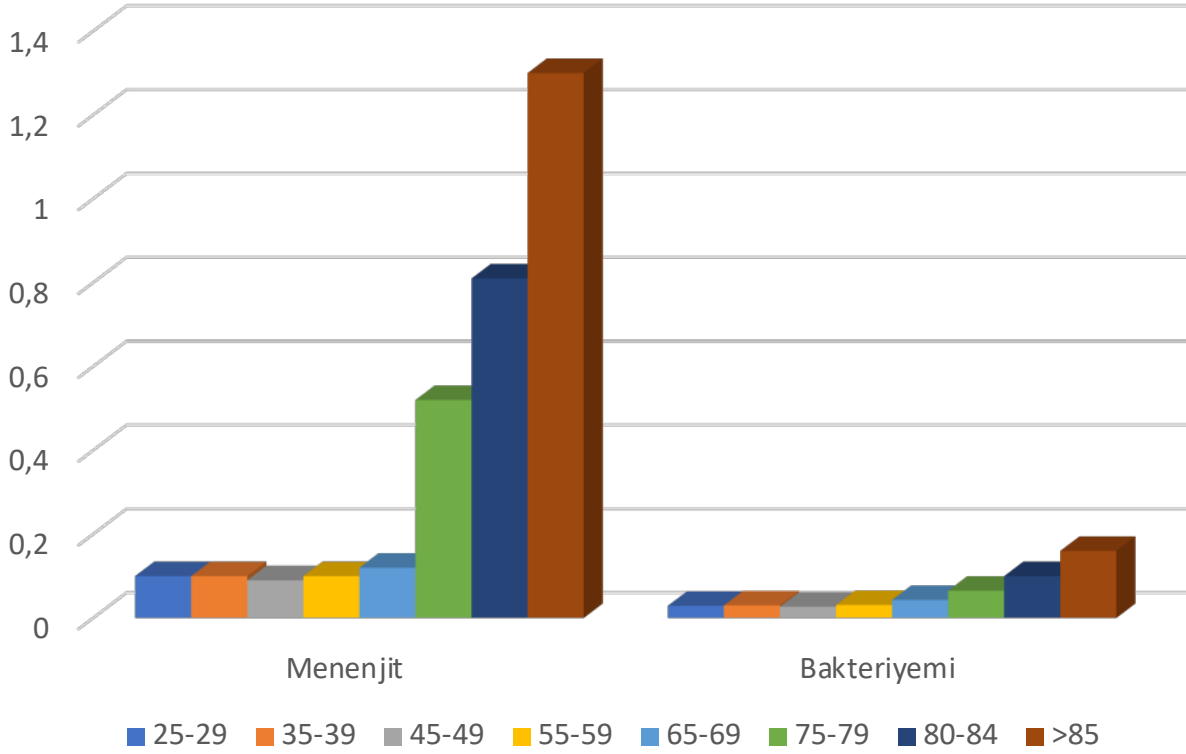
Ekonomik

- Aşı ve uygulama
- Tedavi maliyeti
- Verimlilik
- İş gücü kaybı

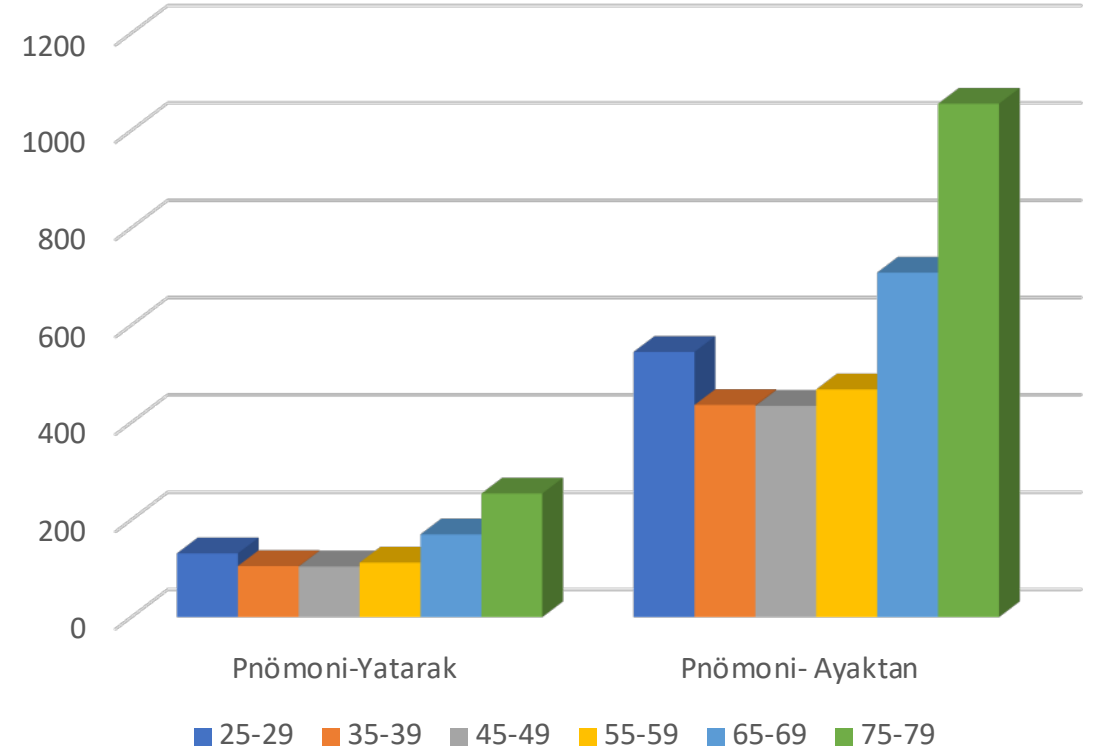
Kısıtlılık: Türkiye'de verilerin sınırlı olması birçok varsayım kullanılmasını yol açmıştır.

Parameter	18–19	20–24	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85	Source	
Epidemiological parameters, elderly population																	
Vaccine-type incidence per 100,000 of																	
Inpatient CAP	209.72	144.25	131.20	118.17	105.15	100.65	104.64	108.70	112.75	133.47	170.64	216.29	254.08	313.78	390.76	*	
Outpatient CAP	871.31	599.32	545.10	490.94	436.88	418.18	434.74	451.60	468.44	554.53	708.96	898.63	1,055.60	1,303.64	1,623.47	*	
Bacteremia	0.14	0.10	0.10	0.09	0.10	0.09	0.09	0.09	0.10	0.12	0.35	0.43	0.52	0.81	1.30	*	
Meningitis	0.044	0.032	0.029	0.029	0.030	0.029	0.027	0.028	0.031	0.036	0.043	0.053	0.065	0.10	0.16	*	
Case fatality rate																	
Inpatient CAP	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	⁴³
Outpatient CAP	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	⁴³
Bacteremia	0.05	0.05	0.17	0.17	0.17	0.17	0.28	0.28	0.28	0.28	0.29	0.29	0.29	0.29	0.29	0.29	*
Meningitis	0.02	0.02	0.07	0.07	0.07	0.07	0.11	0.11	0.11	0.11	0.29	0.29	0.29	0.29	0.29	0.29	*
Probability of meningitis causing																	
Persistent vegetative state	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	⁴⁴
Severe disability	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	⁴⁴
Moderate disability	0.14	0.14	0.14	0.14	0.14	0.14	0.14	0.14	0.14	0.14	0.14	0.14	0.14	0.14	0.14	0.14	⁴⁴
Temporary disability	0.78	0.78	0.73	0.73	0.73	0.73	0.69	0.69	0.69	0.69	0.51	0.51	0.51	0.51	0.51	0.51	*

IPD / 100 000 Popülasyon



TKP pnömoni/ 100 000 popülasyon



J. P. Sevilla et al. Human Vaccines & Immunotherapeutics 2020
(Kaynaktan alınan veriler grafikleştirilmiştir)

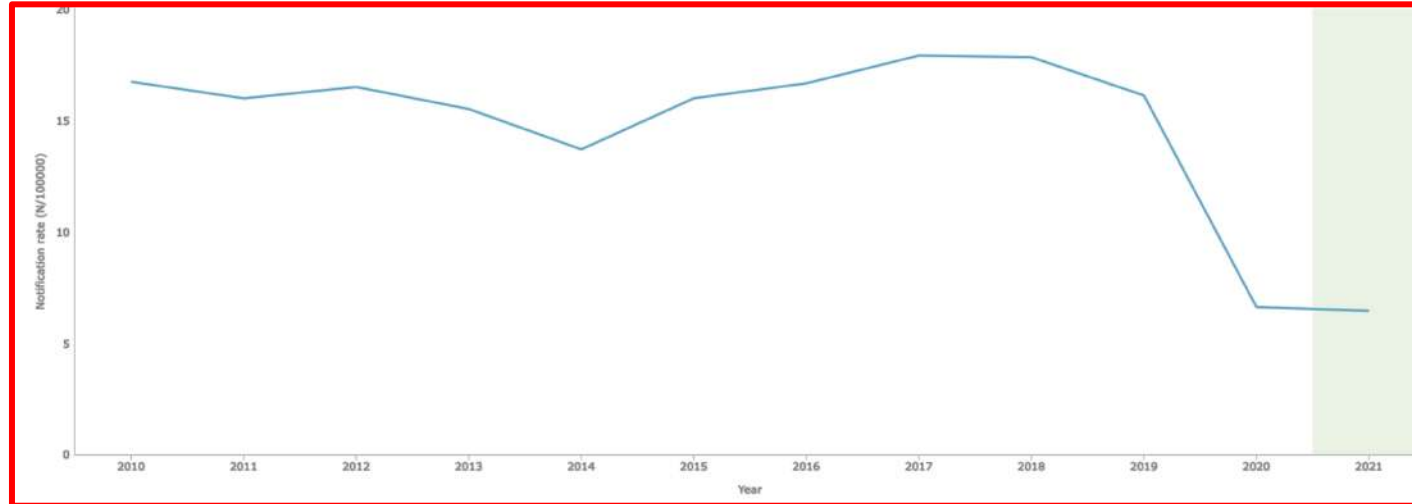
Türkiye'de IPD insidansı, 2017

Bakteriyemi: 0.14-1.30/ 100 000 popülasyon

Menenjit: 0.043-0.16/ 100 000 popülasyon

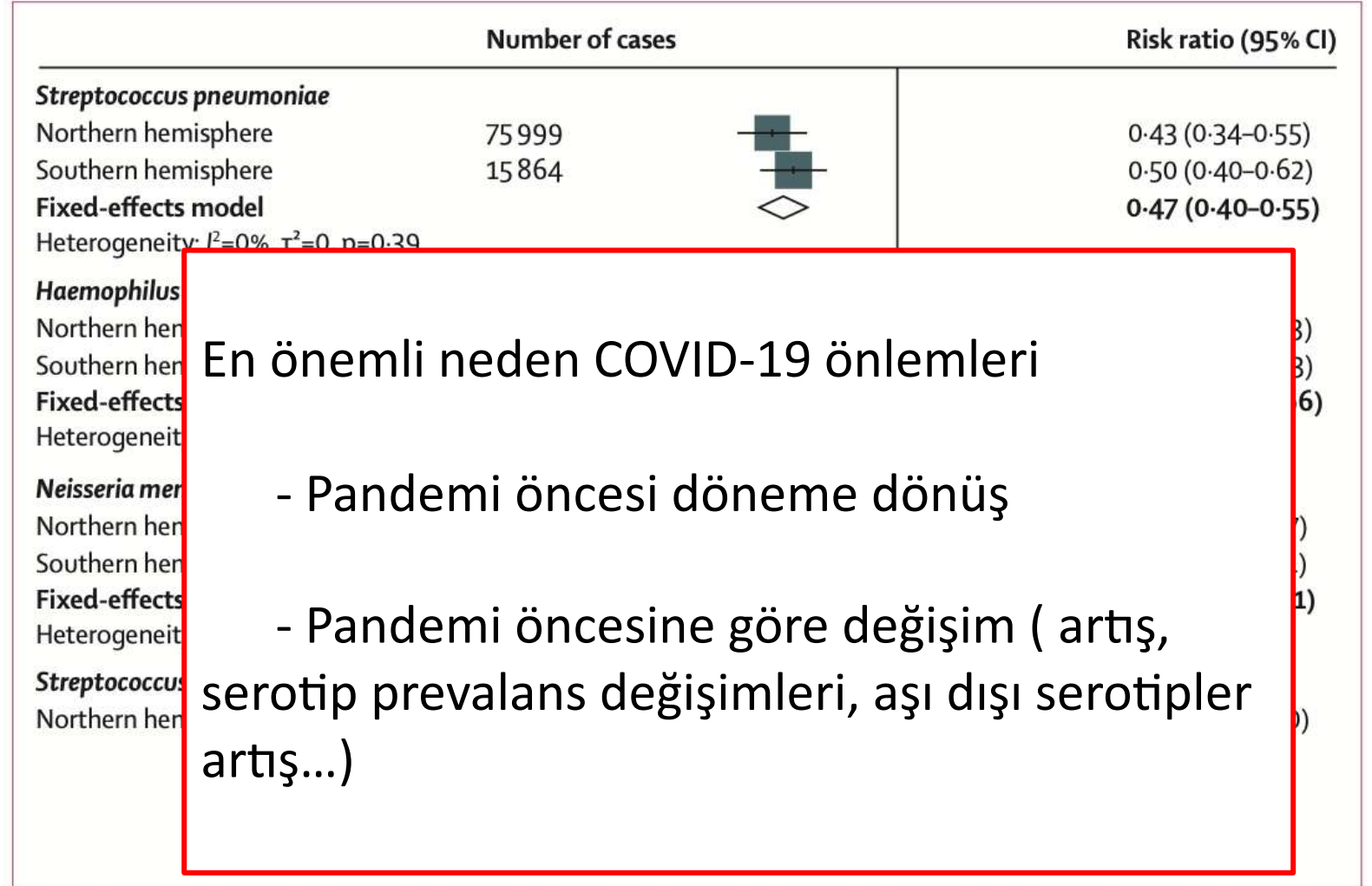


Türkiye'ye yakın, GSMH benzer, sosyo-demografik index benzer ve verisi olan 6 ülke (Çek cumhuriyeti, Slovenya, Slovakya, Polonya, Macaristan) verisi



COVID-19'un IPD epidemiyolojisine etkisi

2018-2019 ile
2020-2021 arasında
invaziv bakteriyel
hastalık deęiřimi



Almanya'da yaş gruplarına göre 2020-2021 IPD insidans değişimi

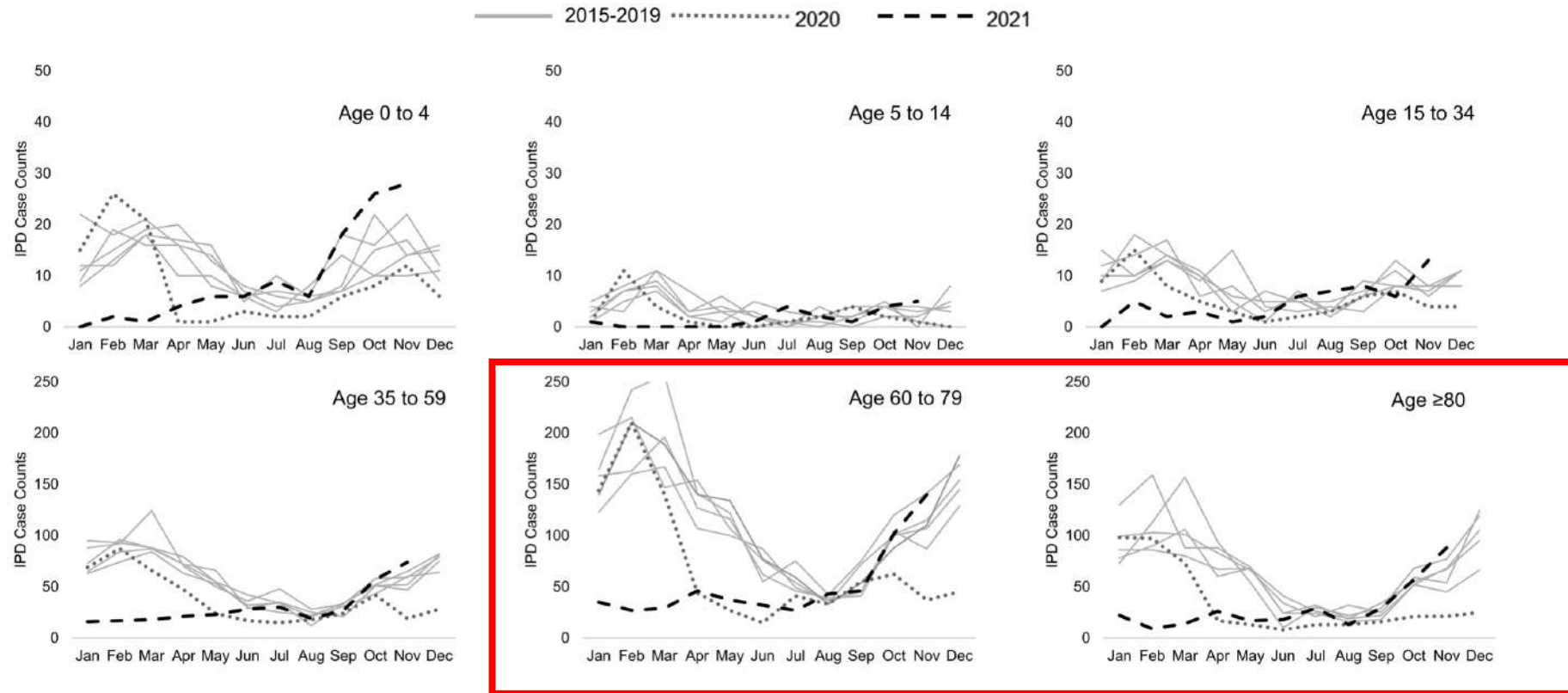
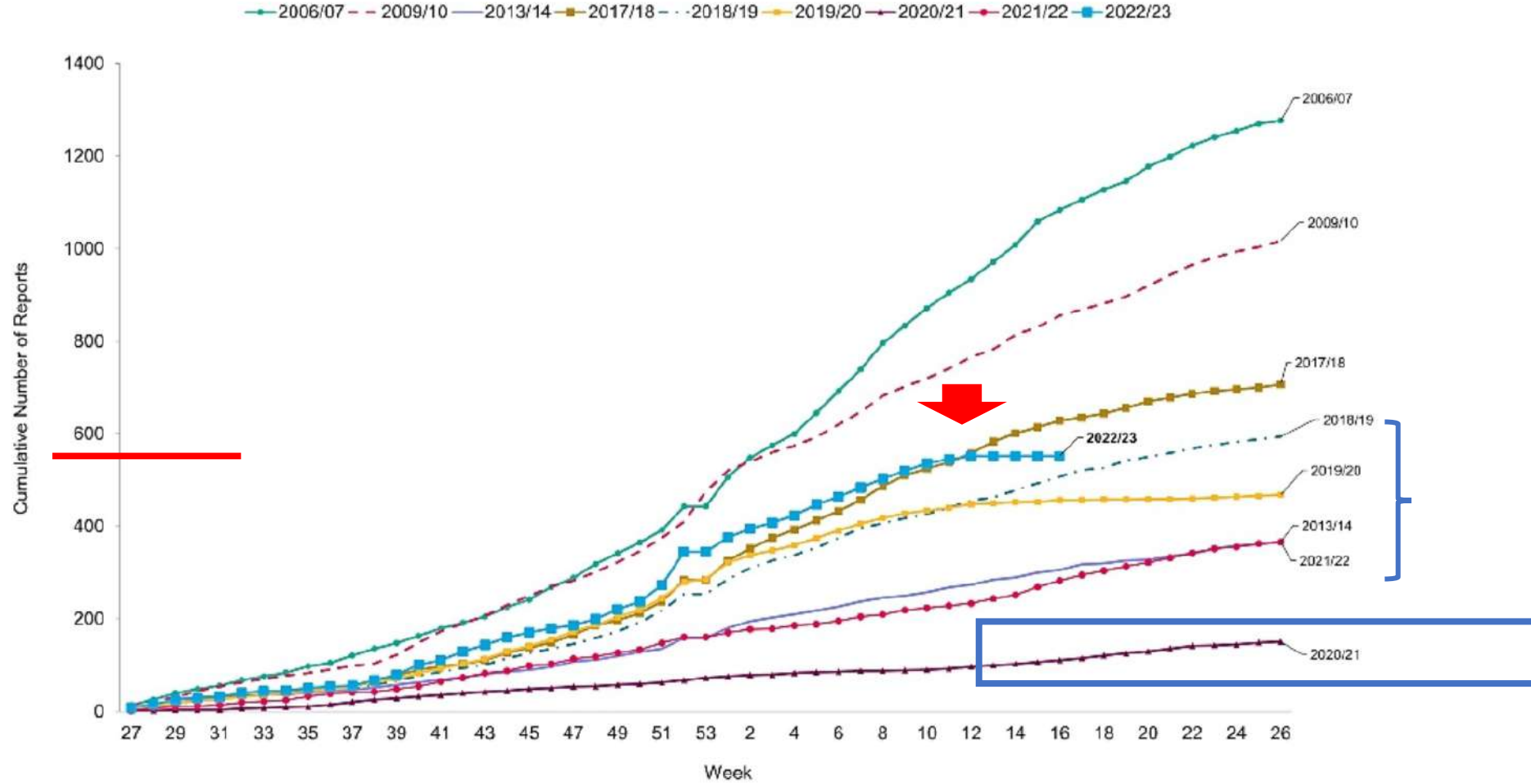
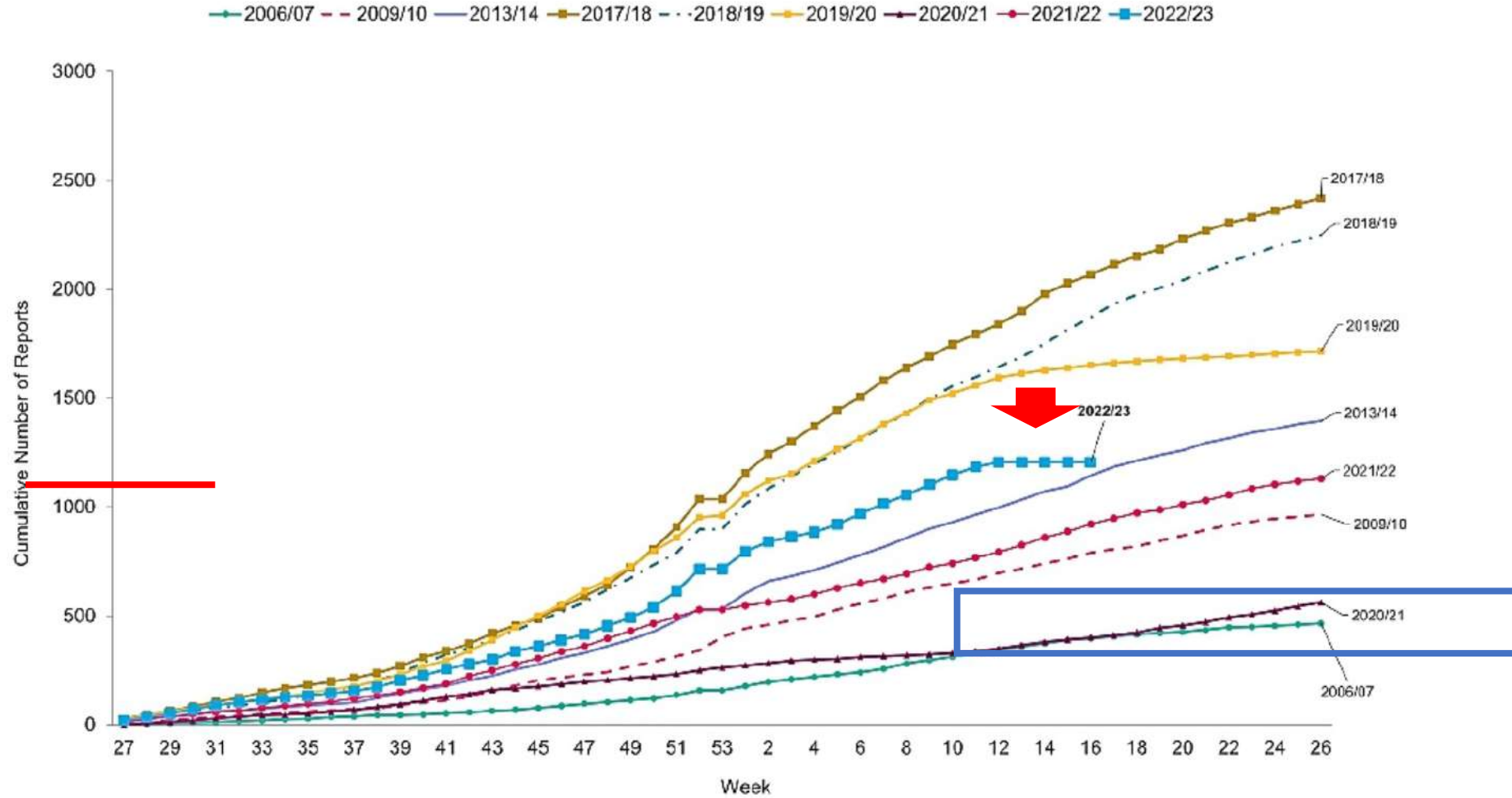


Figure 1. Invasive pneumococcal disease (IPD) case count by age group, from January 2015 to November 2021. Gray lines represent cases counts in the years before 2020 (2015–2019); orange line, 2020; and green line, 2021.

65 yaş ve üzeri: PCV 13'ün kapsadığı serotipler ile gelişen IPD



65 yaş ve üzeri : PCV 13'ün kapsamadığı serotipler ile gelişen IPD



Türkiye'de TKP insidansı(65-69 yaş grubu)

Hastanede takip edilen:

170.6-390.7/ 100 000 popülasyon

Ayaktan takip edilen:

708.9- 1623.4/100 000 popülasyon



Türkiye'ye özgü 2017 Küresel Hastalık Yüğü (GBD) tahminlerinde ASYE insidansı, pnömokokal pnömoniye bağı ASYE'nin oranı

Lokal verilerin kullanımı

Burden of Lower Respiratory Tract Infections Preventable by Adult Immunization With 15- and 20-Valent Pneumococcal Conjugate Vaccines in the United States

Joseph A. Lewnard,^{1,2,3} Vennis Hong,⁴ Katia J. Bruxvoort,⁵ Lindsay R. Grant,⁶ Luis Jódar,⁶ Alejandro Cané,⁶ Adriano Arguedas,⁶ Magdalena E. Pomichowski,⁸ Bradford D. Gessner,⁶ and Sara Y. Tartof^{4,7}

Clinical and economic burden of pneumococcal disease among individuals aged 16 years and older in Germany

Original Paper

Cite this article: Deb A *et al* (2022). Clinical and economic burden of pneumococcal disease among individuals aged 16 years and older in Germany. *Epidemiology and Infection* 150, e204, 1–11. <https://doi.org/10.1017/S0950268822001182>

Arijita Deb¹, Bélène Podmore^{2,3}, Rosemarie Barnett^{2,4}, Dominik Beier⁵, Wolfgang Galetzka⁵, Nawab Qizilbash^{2,3}, Dennis Haeckl⁶, Sarah Mihm⁷, Kelly D. Johnson¹ and Thomas Weiss¹

¹Merck & Co., Inc., Rahway, NJ, USA; ²OXON Epidemiology, London, UK; ³London School of Hygiene & Tropical Medicine, London, UK; ⁴University of Bath, Bath, UK; ⁵InGef – Institute for Applied Health Research Berlin GmbH, Berlin, Germany; ⁶WIG2 GmbH, Leipzig, Germany and ⁷MSD Sharp & Dohme GmbH, Munich, Germany



ABD

Tüm hastalar: 1430 (1330-1530)/100 000 popülasyon

Hastanede takip edilen: 330 (320-350) /100 000 popülasyon



Almanya

Tüm hastalar: 512-4286 /100 000 popülasyon
(Farklı yaş ve risk)

The Role of Pneumococcal Pneumonia among Community-Acquired Pneumonia in Adult Turkish Population: TurkCAP Study

Esin Şenol¹, Aykut Çilli², Hakan Günen³, Alper Şener⁴, Rıdvan Dumlu⁴, Ayşe Ödemiş²



Pnömonokokal pnömoni: % 12.7



% 85 Üriner antijen test ile tanı, test duyarlılığı % 63 (45-81)

Pnömonokokal pnömoni: % 22.8

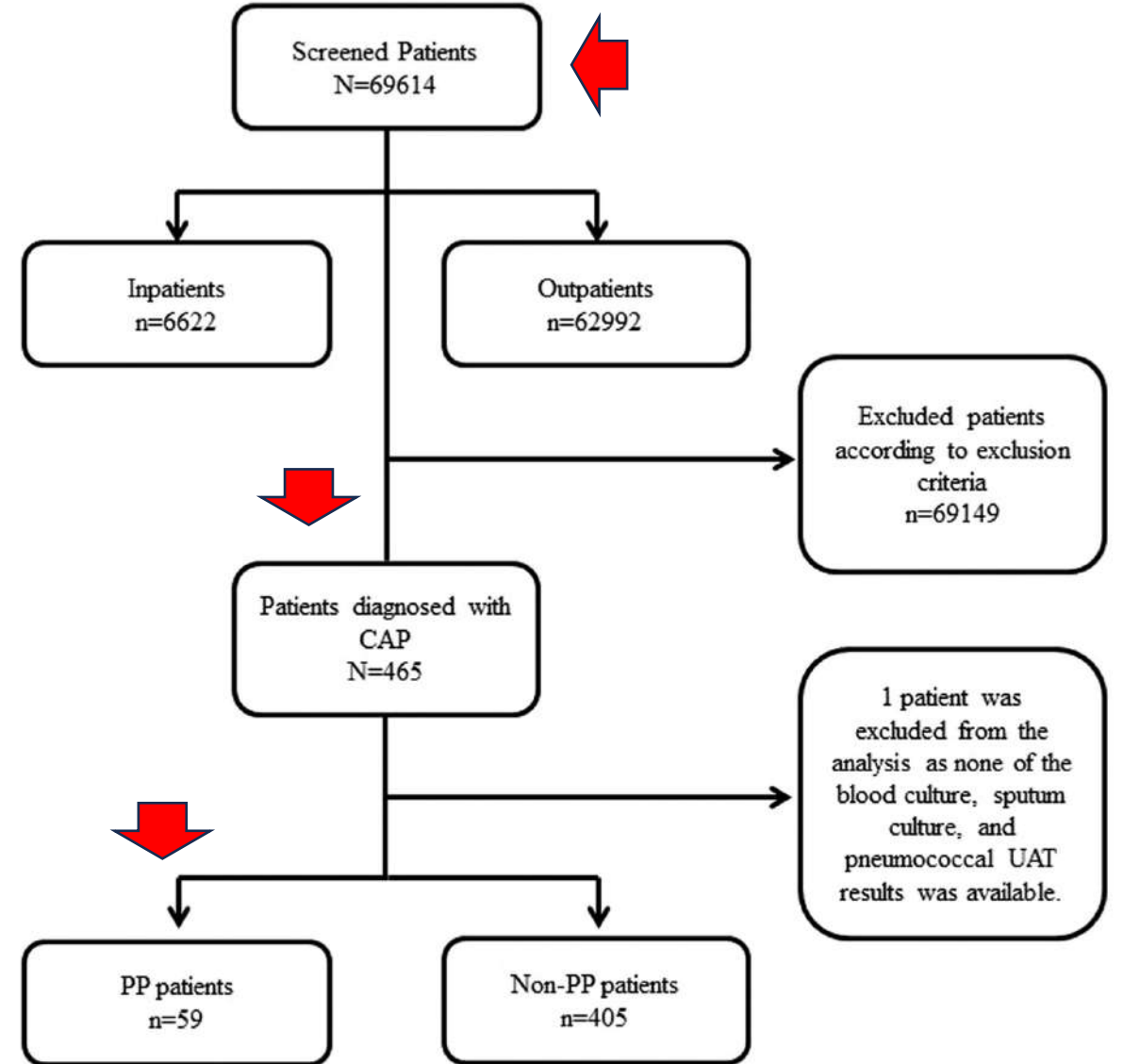


Table 2. Summary values for prevalence of pneumococcal disease in Southern European countries*.

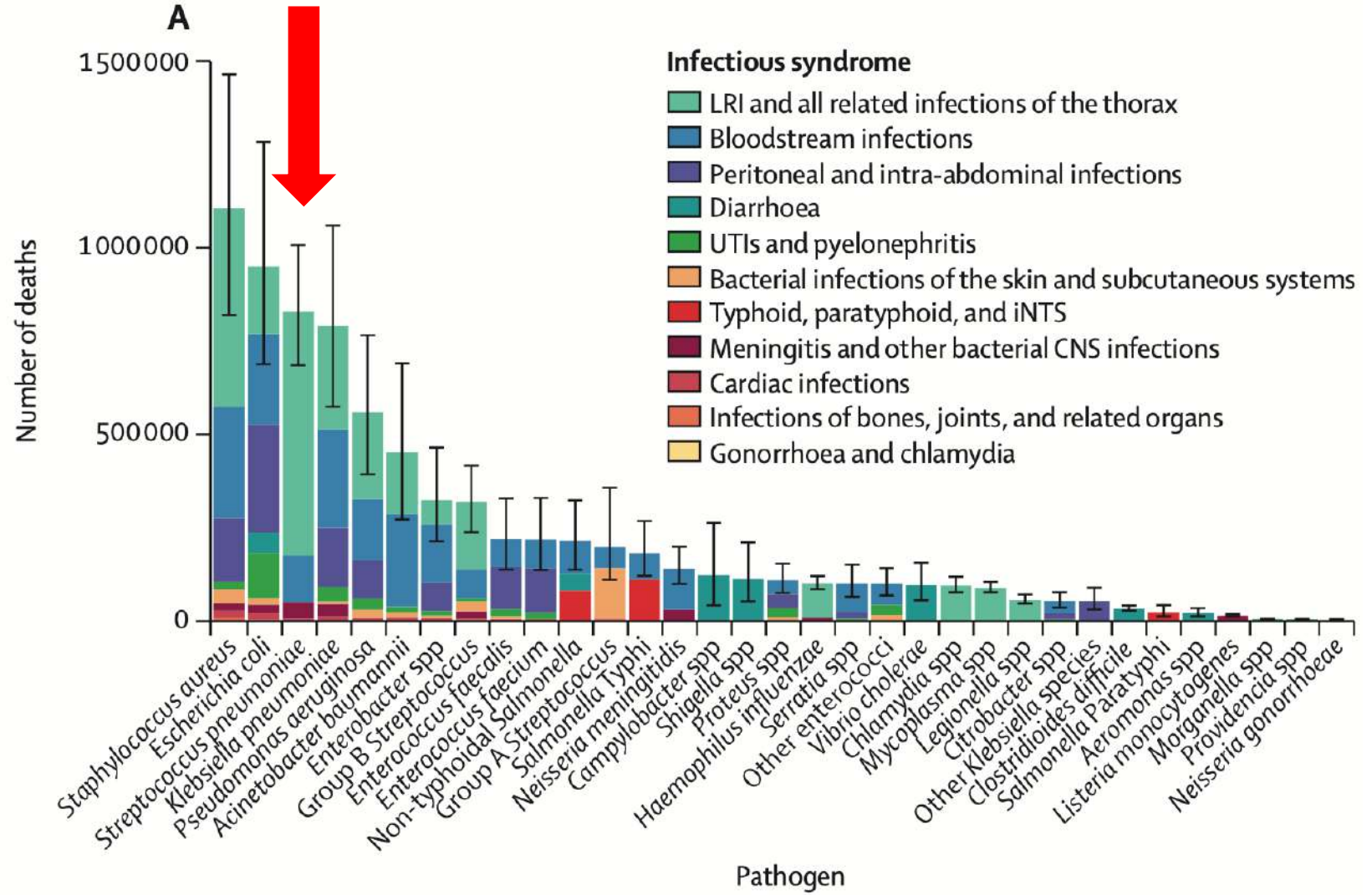
Pneumococcal disease type	Country	Number of records	Prevalence	95%CI
Bacteremia	Overall	31	6%	4%-8%
	<i>Spain</i>	29	6%	4%-8%
	<i>Italy</i>	2	5%	0%-24%
	<i>Portugal</i>	0	-	-
	<i>Greece</i>	0	-	-
Pneumonia	Overall	182	16%	15%-18%
	<i>Spain</i>	140	19%	17%-20%
	<i>Italy</i>	26	8%	7%-9%
	<i>Portugal</i>	12	11%	5%-18%
	<i>Greece</i>	4	5%	2%-10%
Noninvasive pneumonia	Overall	31	64%	56%-71%
	<i>Spain</i>	28	64%	55%-71%
	<i>Italy</i>	2	77%	53%-95%
	<i>Portugal</i>	1	40%	21%-60%
	<i>Greece</i>	0	-	-
Meningitis	Overall	18	25%	17%-35%
	<i>Spain</i>	11	21%	9%-35%
	<i>Italy</i>	6	33%	23%-42%
	<i>Portugal</i>	1	35%	29%-42%
	<i>Greece</i>	0	-	-

2019 yılında 13.7 milyon
(95% 10.9–17.1) **infeksiyon**
ilişkili ölüm

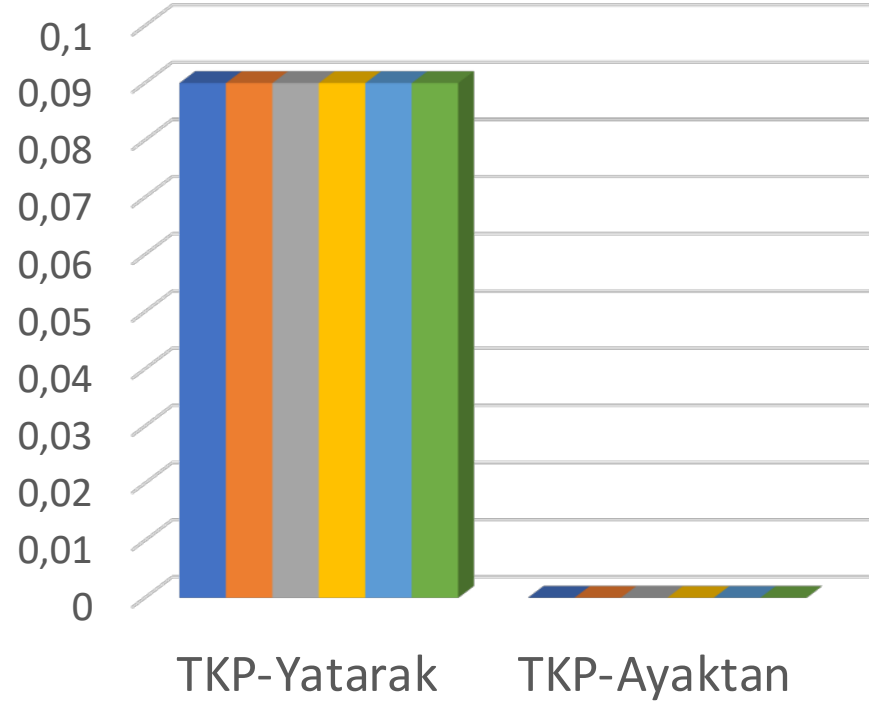
7.7milyon (5.7–10.2) ölüm

33 bakteri ile ilişkili

Alt solunum yolu infeksiyonları



Fatalite Hızı



■ 25-29 ■ 35-39 ■ 45-49
■ 55-59 ■ 65-69 ■ 75-79

Fatalite Hızı



Benzer ülke verileri

Bakteriyemi/Menenjit %10- 29

Menenjit

Bakteriyemi

■ 25-29 ■ 35-39 ■ 45-49 ■ 55-59
■ 65-69 ■ 75-79 ■ 80-84 ■ >85

2011-2013 yılları ,retrospektif, çok merkezli çalışma (Türk toraks derneği veri tabanı)

Örneklem büyüklüğü; 735

Sonlanımlar: Kısa ve uzun dönem mortalite

Mikrobiyolojik değerlendirme yok

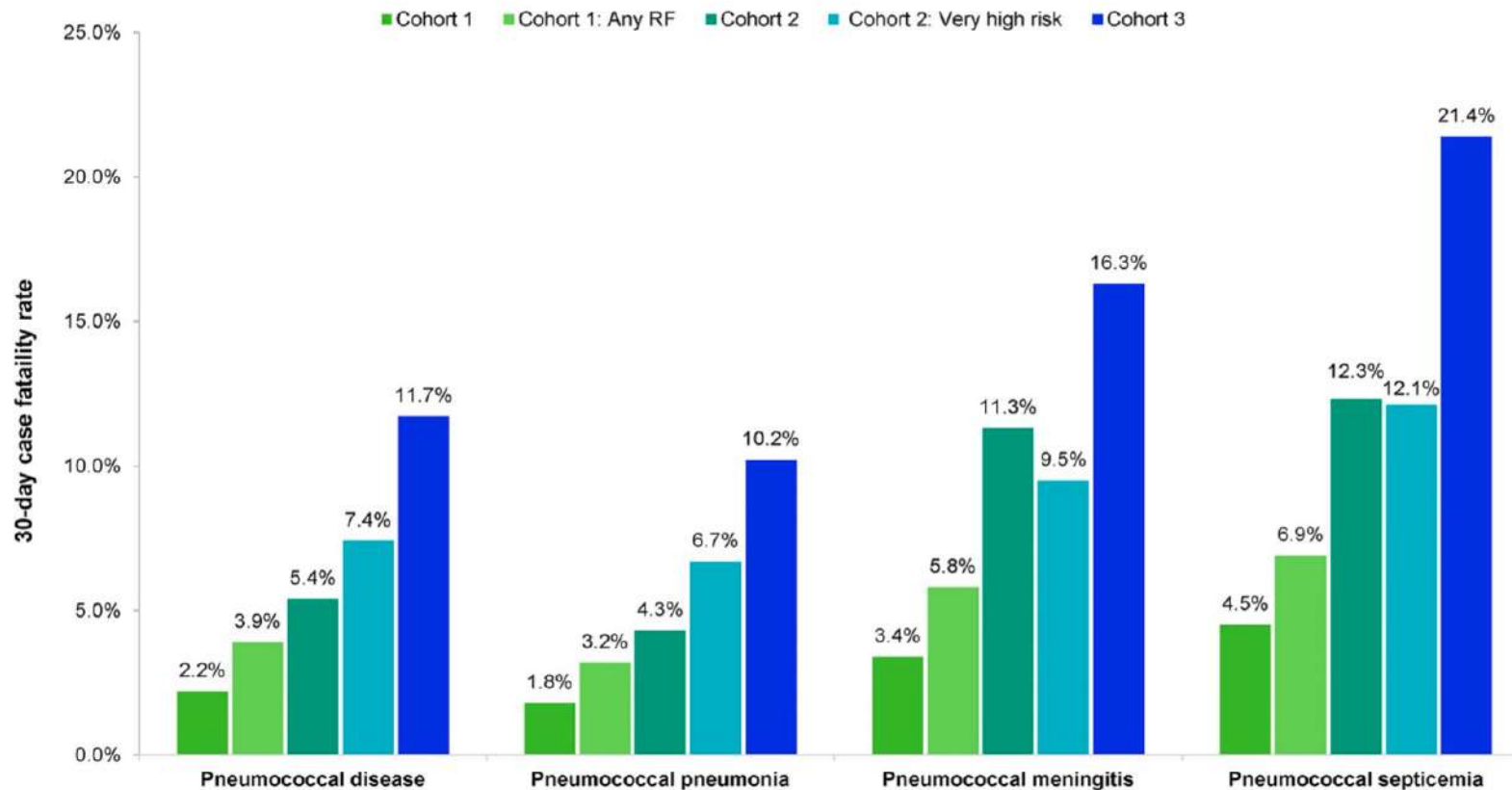


Table 2 All-cause mortality of all patients (N = 785).

	N	%
30-Day	72	9.2
90-Day	132	16.8
1-Year	235	29.9
2-Year	296	37.7
3-Year	336	42.8
4-Year	453	57.7
5-Year	587	74.8

Pnömonokal hastalık ve yaşa göre fatalite hızı

İşveç, erişkin popülasyon, 2015-2019 Pnömoni, menenjit, septisemi (n=10391 epizod)



Kohort 3 : > 75 yaş

Kohort 2: 65-74 yaş

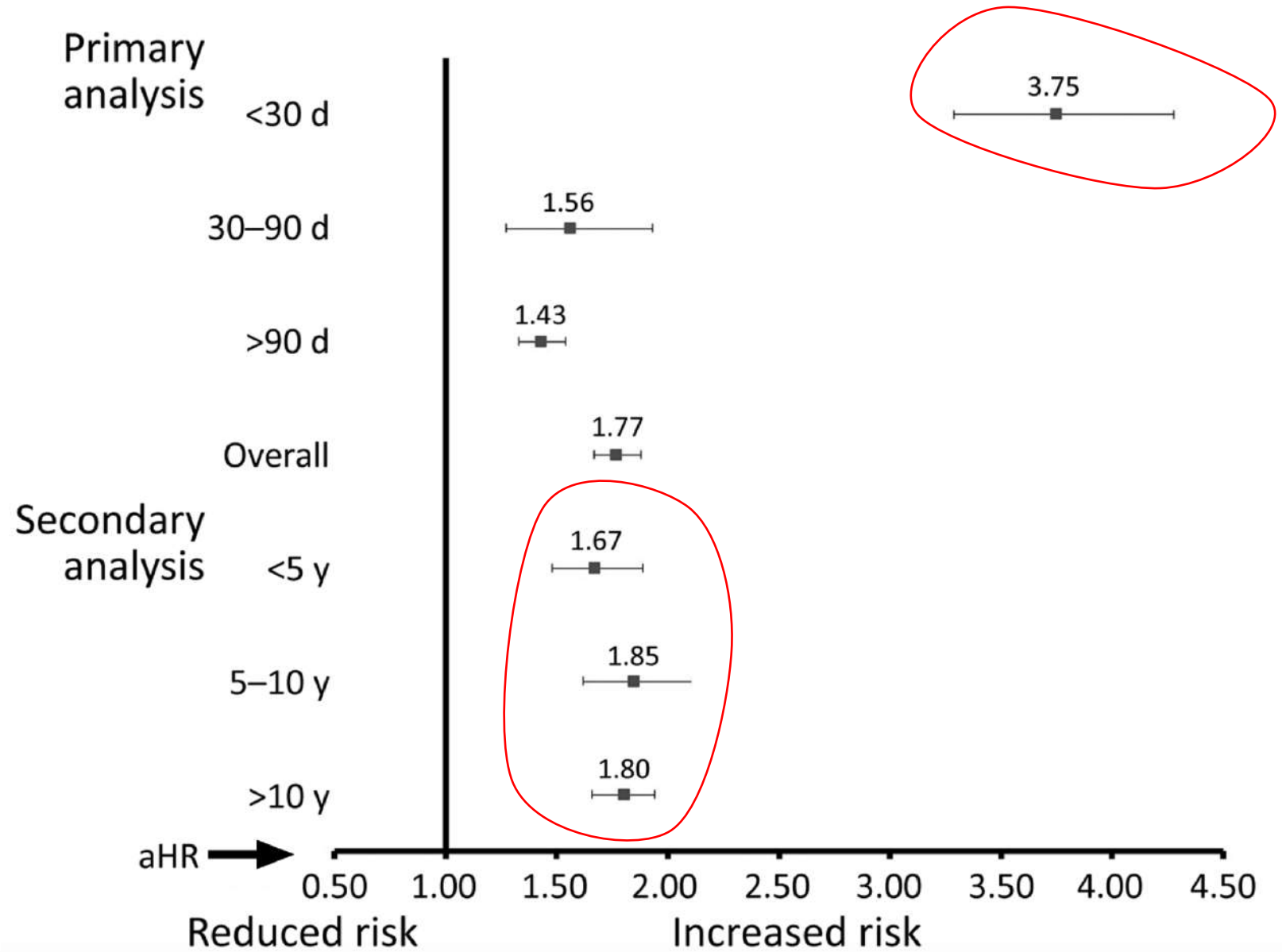
Kohort 1: 18-64 yaş

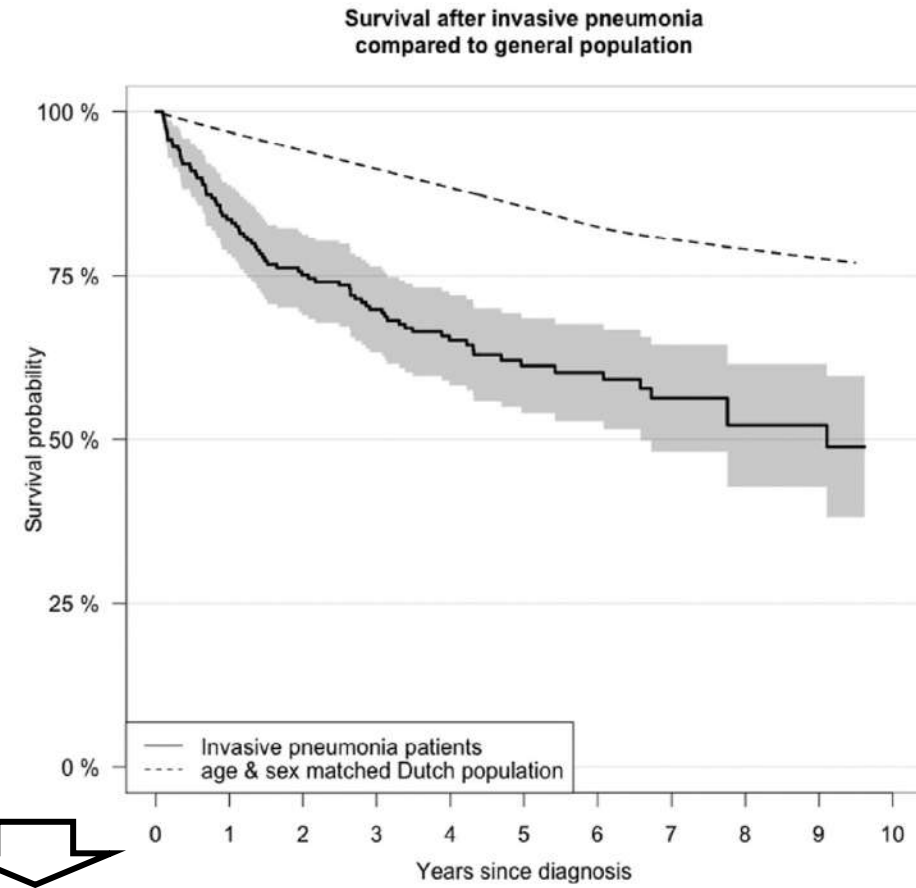
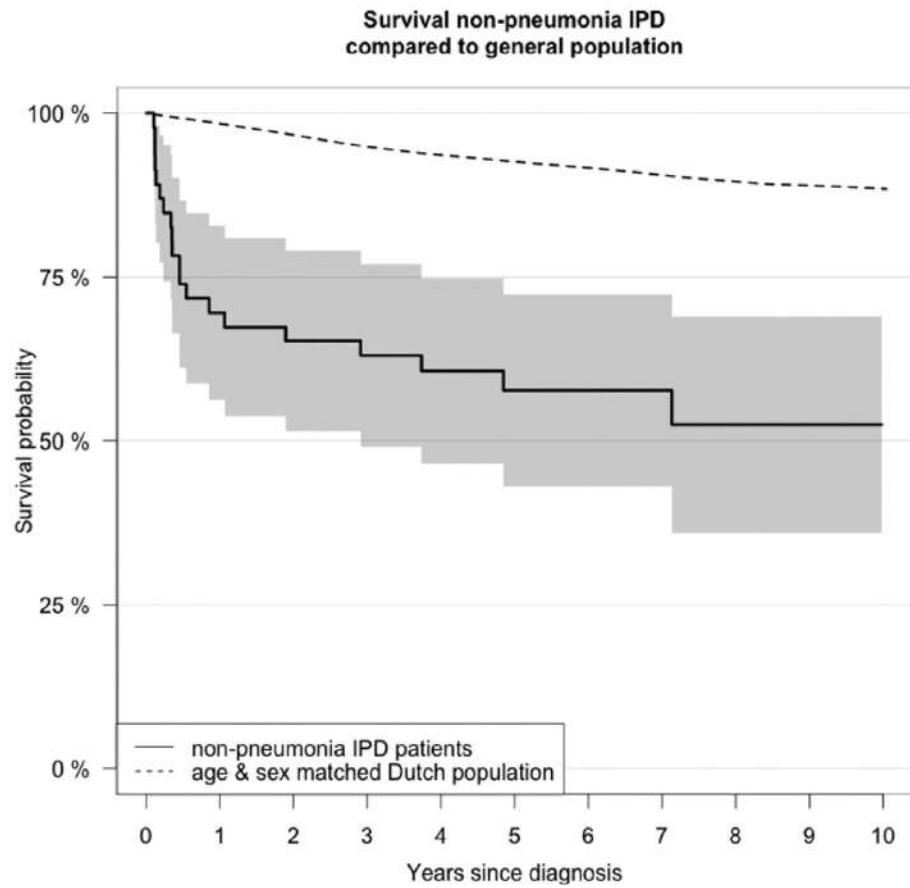
Natalie Zarab et al., PLOS ONE, 2023

Fig 2. Average (all-cause) 30-day case fatality rate in 2015–2019, by clinical presentation and age cohort.

IPD sonrası erken ve geç dönem mortalite risk

Mortalite risk faktörleri açısından eşleştirme çabası





Nedensellik ilişkisi ?

Pnömonokokal hastalıklarda hastane yatış yükü

Ortalama yatış sayısı:1.13-1.31

Ortalama yatış günü: 6.46-8.78 gün

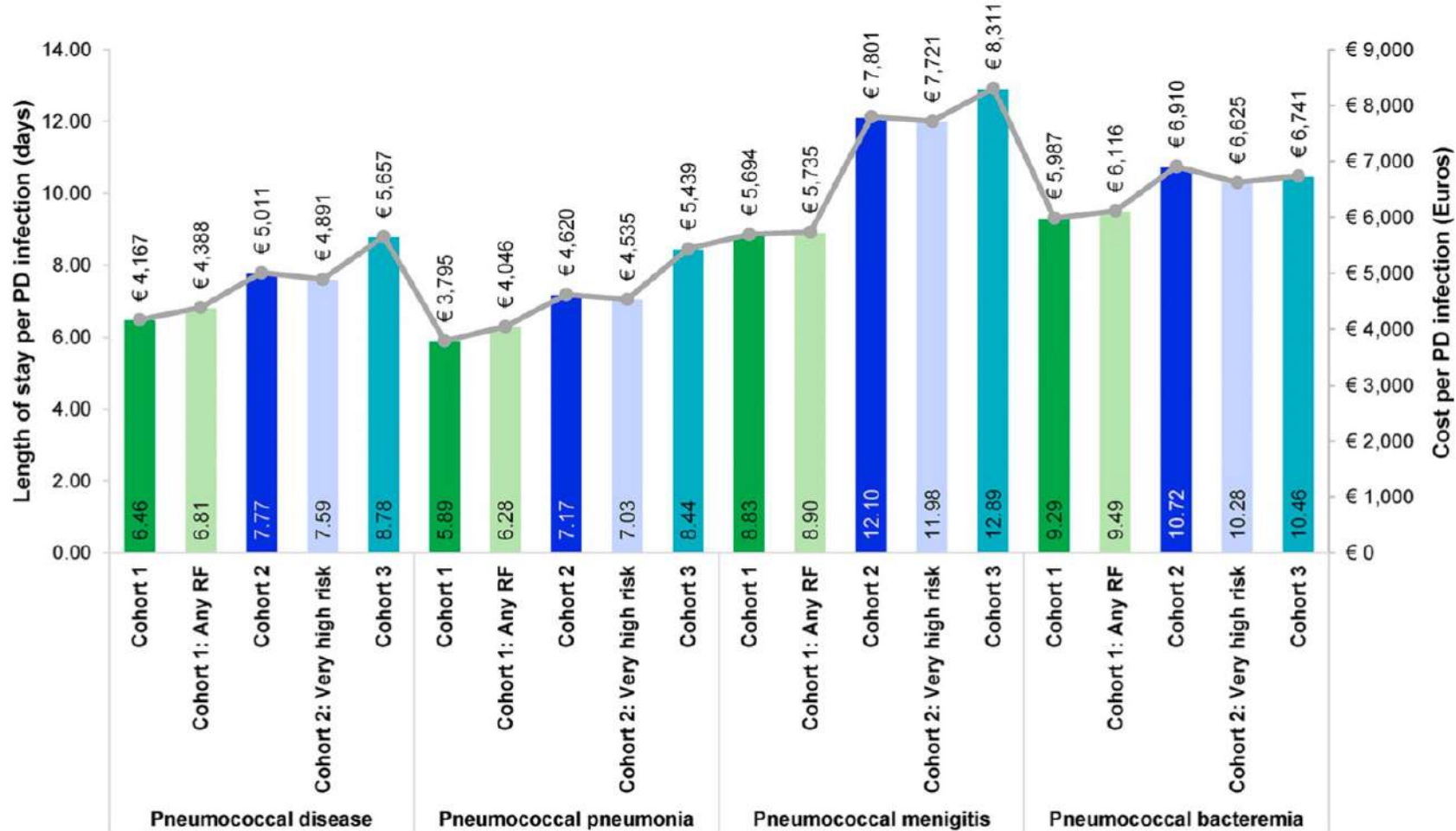
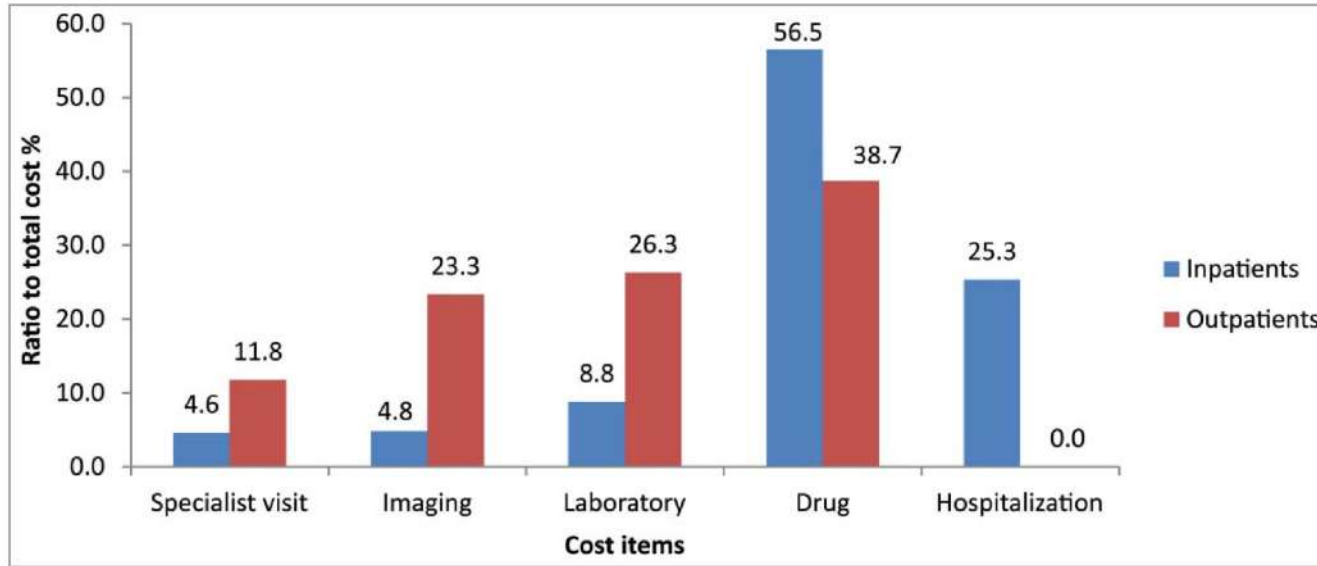


Fig 3. Average 30-day all-cause HCRU and costs per PD infection.

İstanbul 2 merkez, retrospektif çalışma, Yatarak (n=211) ve ayaktan (n=208) TKP olgularında maliyet karşılaştırılması

Aşı endikasyonu olan (<65 yaş üstü: %28.9-48.6, komorbidite: % 71.6-80.8), Aşısız hasta grubu (her grupta bir hasta aşıllı)



Yatan hasta € 556.09 ± 1,004.77

Ayaktan hasta € 51.16 ± 40.92

Yaş, komorbidite, Hastane yatış (YB yatış, yatış süresi)

Pnömonokokal pnömoni - Hastane yatış yükü

	PP	Non-PP	
CURB-65	2 (1-3)	1 (1-2)	0.002
Ayaktan takip	14 (23.7%)	118 (29.1%)	0.390
Yatarak takip	45 (76.3)	287 (70.9%)	
Klinik takip	34 (75.6%)	255 (89.8%)	0.007
YB takibi	11 (24.4 %)	29 (10.2%)	

Türkiye Çok merkezli, prospektif - kohort çalışma, Aşı sonrası 12 ay takip

Aşı sonrası **yoğun bakım dışı hospitalizasyon** (Pnömoni, COPD, Astım, malignite) ve **maliyet (Aşılı (n=400) ve Aşısız (n=400) yatan hasta (2018-2020 PCV-13)**

Her iki grup karşılaştırması komorbidite, COPD ve Kalp hastalığı aşılı grupta daha sık ($p<0.001$)



Table 2. Vaccination Status vs. Length of Stay and Cost

Variables	Total (n = 800)		Unvaccinated (n = 400)		Vaccinated (n = 400)		P
	Mean	SD	Mean	SD	Mean	SD	
Cost	3781.8454	5673.1697	4231.6153	6805.4092	3332.0756	4210.8405	0.025
Length of stay	10.76	12.67	12.41	15.71	9.11	8.34	<0.001

Pnömonok aşılması ile hastane yatış gününde 41.7 % ve maliyet 27.8% bir azalma

Impact of the 13-Valent Pneumococcal Conjugate Vaccine Among Adults: A Systematic Review and Meta-analysis

Nirma Khatri Vadlamudi, Anna Chen, and Fawziah Marra

Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, Canada

Meta-analiz, n=2 033 961

Çocukluk dönemi PVC13 uygulanması IPD, non-invaziv PD, hastane yatış ve meortalite üzerine etkisi

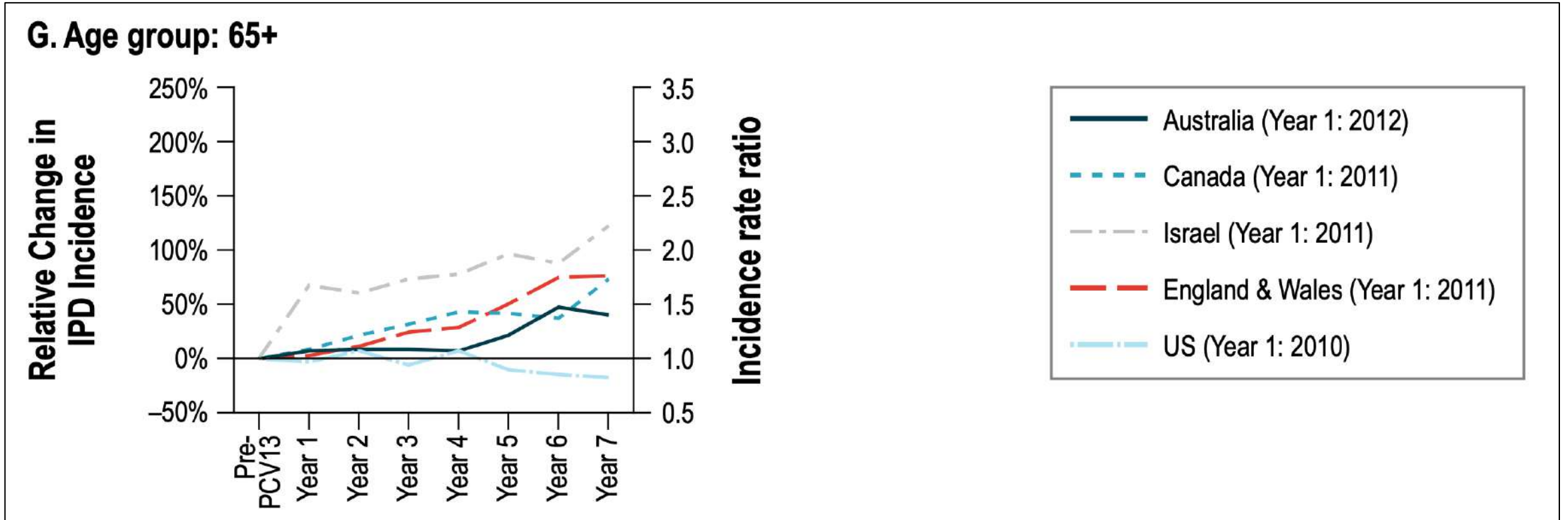
<65 yaş, ≥65 yaş

	<65 yaş, IRR	≥65 yaş, IRR
IPD	0.78 (0.72–0.85)	0.86 (0.81–0.91)
IPD, PCV7 serotipleri	0.49 (0.39-0.63)	0.39 (0.29-0.51)
IPD, PCV13 serotipleri	0.59 (0.49-0.69)	0.61 (0.52-0.71)
IPD, Aşı dışı serotipler	1.04 (0.95-1.14)	1.20 (1.21-1.29)
Mortalite	0.68 (0.56-0.83)	0.71 (0.54-0.93)

Australya, US, İngiltere, İsrail, Kanada

Çocukluk çağı aşılama programına 2010-2018 yılları arasında PCV13

Farklı yaş gruplarında IPD insidans değişimleri



Aşı serotip dağılımları

Vaccine	Pneumococcal Serotype																											
	1	3	4	5	6A	6B	7F	9V	14	18C	19A	19F	23F	22F	33F	8	10A	11A	12F	15B	2	9N	17F	20	15C	6C		
PCV13	●	●	●	●	●	●	●	●	●	●	●	●	●														●	
PCV15	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●													●
PCV20	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●							●
PPV23	●	●	●	●		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●			

Moore et al. *Lancet Infect Dis* 2017

Oligbu et al. *Clin Infect Dis* 2017

Hausdorff & Hanage. *Hum Vacc Immunother* 2016

Andrews N et al. *Vaccine*. 2019;37(32):4491-4498.

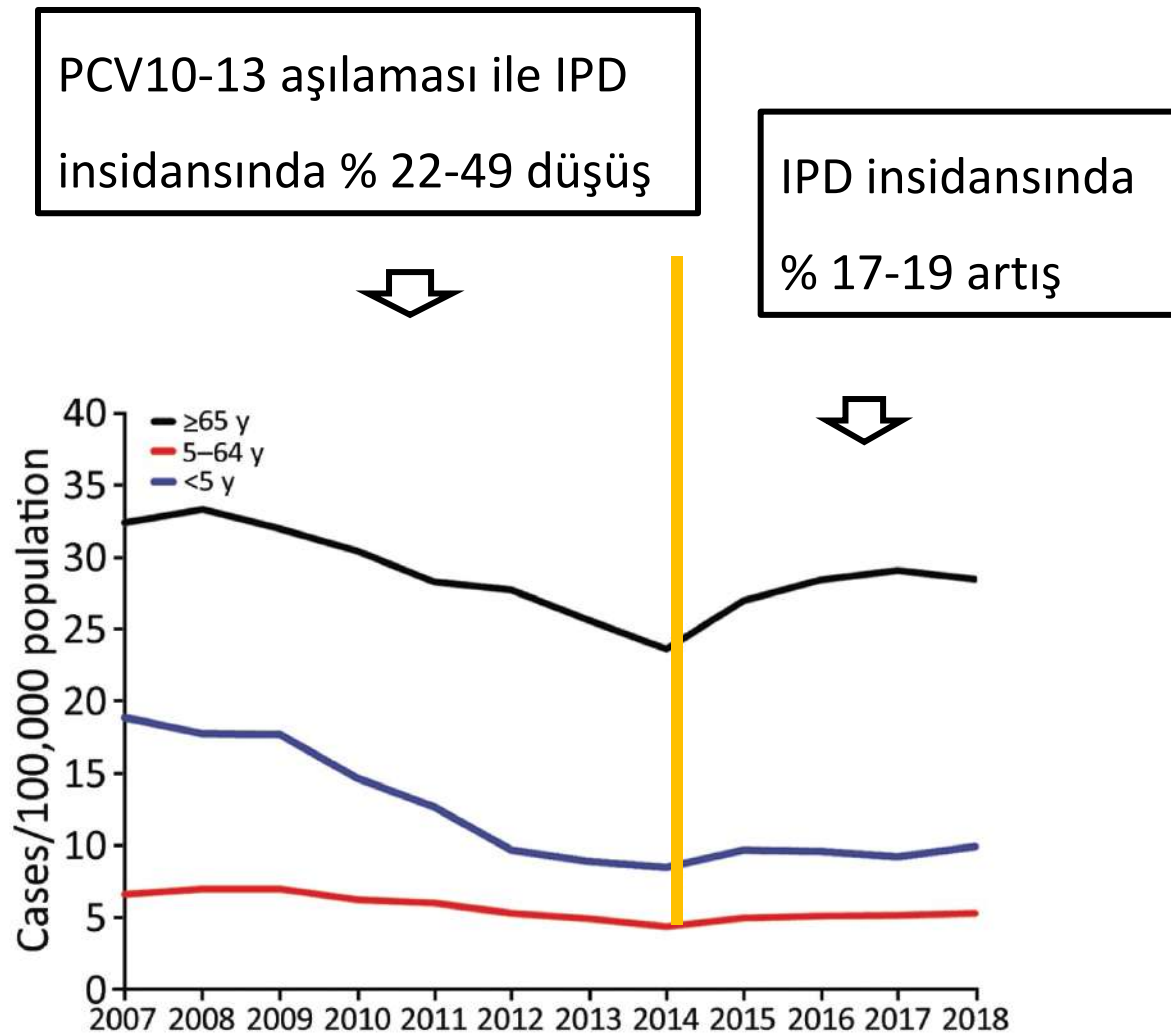
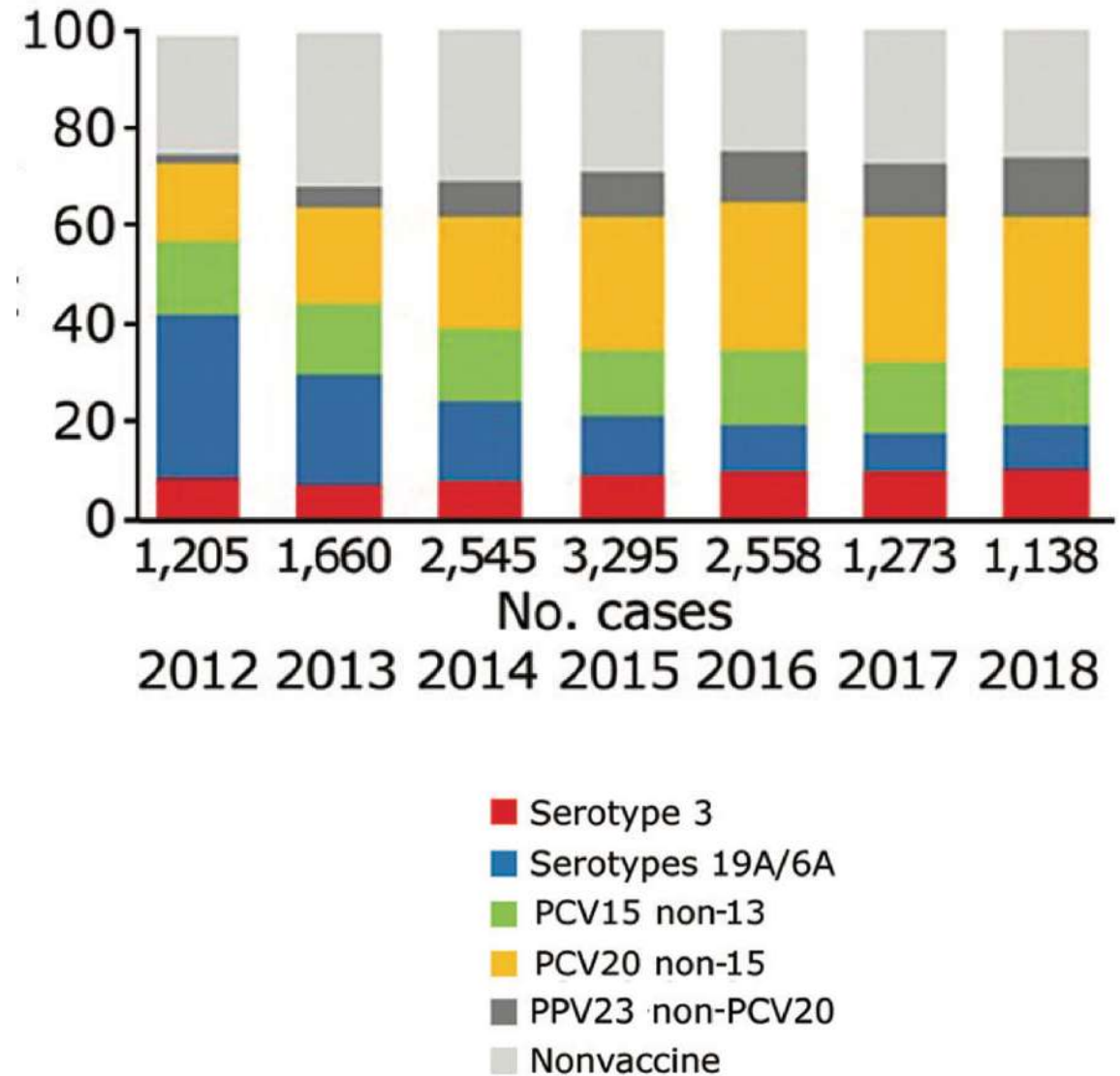


Figure 1. Overall incidence rates of invasive pneumococcal disease (pooled) per year, by age group in 13 SpIDnet (*Streptococcus pneumoniae* Invasive Disease network) sites, Europe.



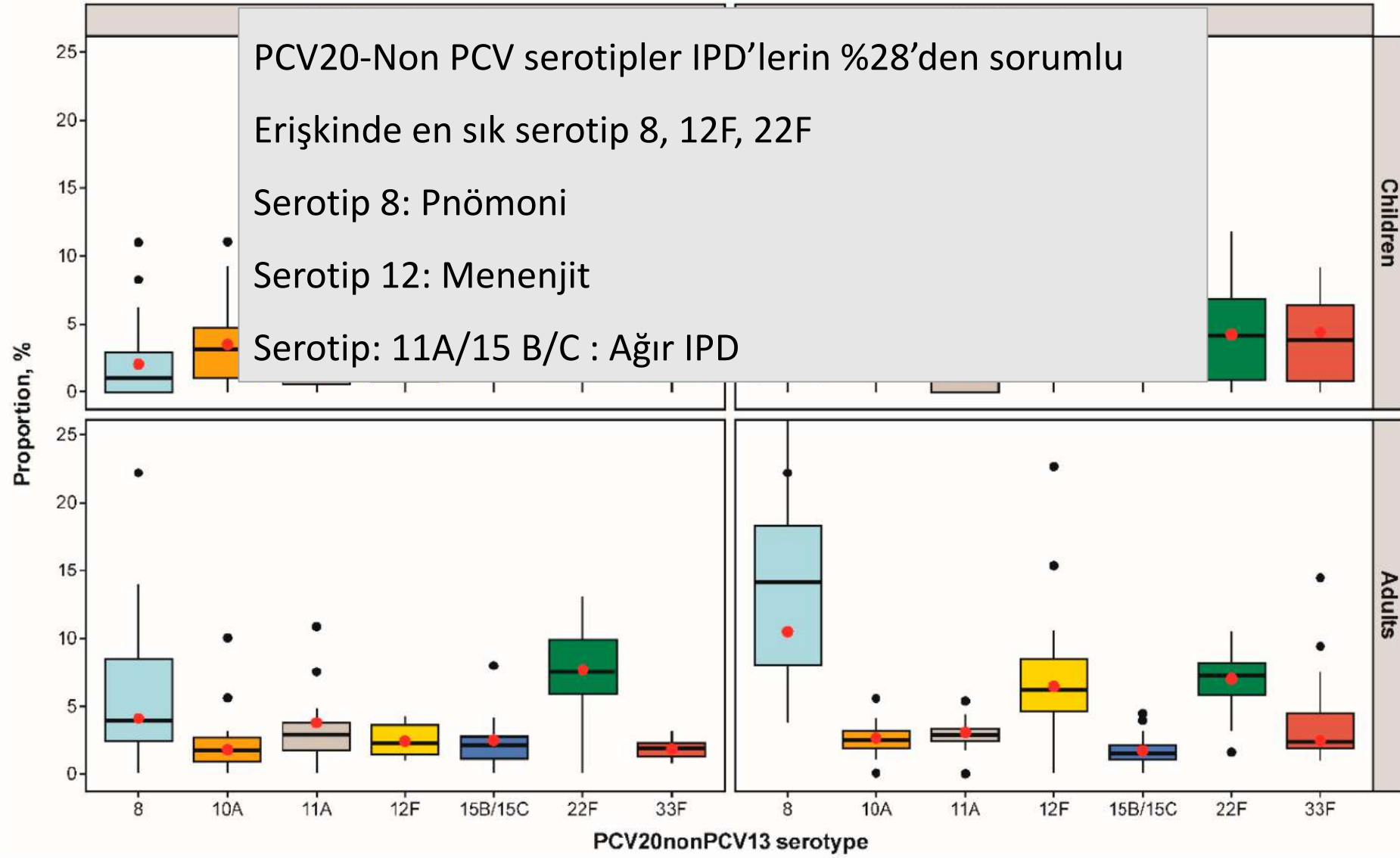
Systematic Literature Review of the Epidemiological Characteristics of Pneumococcal Disease Caused by the Additional Serotypes Covered by the 20-Valent Pneumococcal Conjugate Vaccine

Estelle Méroc ¹, Mark A. Fletcher ², Germaine Hanquet ¹, Mary P. E. Slack ³, Marc Baay ¹, Kyla Hayford ⁴, Bradford D. Gessner ⁴ and Lindsay R. Grant ^{4,*}

Meta analiz-127 çalışmanın meta-analizi
 2010-2020



Age Group	Sampling Site and Clinical Presentation	Proportion All PCV20nonPCV13 ¹		Proportion All PCV20nonPCV15 ¹	
		n, Studies (Isolates)	Mean (Min–Max)	n, Studies (Isolates)	Mean (Min–Max)
Adults	Sterile site: IPD overall	20 (44,349)		23 (49,699)	19.7 (8.0–37.3)
	IPD, presentation specified:	16 (42,323)	27.5 (8.9–55.4)	18 (47,505)	
	Pneumococcal bacteremia	1 (101)	26.7	1 (101)	22.7
	Pneumococcal meningitis	1 (98)	27.5	2 (375)	25.7 (20.4–31.0)
	Bacteremic pneumococcal pneumonia	3 (1071)	23.1 (19.9–28.1)	4 (5976)	17.1 (14.6–23.3)
	Other IPD ²	1 (51)	25.5	1 (51)	23.5
	IPD, presentation unspecified ³	13 (41,002)	28.6 (8.9–55.4)	13 (41,002)	19.6 (8.0–37.3)
	Non-sterile site: Non-IPD overall	2 (312)	15.8 (9.5–22.0)	2 (312)	10.8 (5.7–15.8)
	Non-IPD, presentation specified	2 (312)	15.8 (9.5–22.0)	2 (312)	10.8 (5.7–15.8)
	Undifferentiated site	3 (1714)	14.6 (8.7–23.9)	4 (1882)	8.0 (4.8–17.5)
	All pneumococcal pneumonia	3 (1714)	14.6 (8.7–23.9)	4 (1882)	8.0 (4.8–17.5)



Fatalite oranları: +: ≤ 2 %, ++: 3-5 %, +++ 6-8 %, ++++: > 8%



Population	Epidemiological Characteristic (Cause of)	Serotype						
		8	10A	11A	12F	15B/C	22F	33F
Children	IPD ^{1,2}	++	++	+	++	+++	++	++
	Pneumococcal meningitis ^{2,3}	+++	++	+	++	++++	+++	++
	Bacteremic pneumococcal pneumonia ^{2,3}	++	++	+	++	++	+	++
	Non-IPD ^{2,3}	+	+++	+	+	++++	nr	+
	Pneumococcal AOM ^{2,3}	+	+++	+++	+	++++	++	+
Adults	IPD ¹	++++	+	+	+++	+	+++	+
	Pneumococcal meningitis ³	+++	++	++	++++	+	++	+
	Bacteremic pneumococcal pneumonia ³	++++	+	+	+++	+	++	+
	Non-IPD ³	+	+	+	+	+	+	+
Children	Death due to IPD ⁴	+	++++	++	++	++++	+++	++
Adults	Death due to IPD ⁵	++	+++	++++	++	++++	++	+++
All Ages	Penicillin non-susceptible IPD or Non-IPD ⁶	+	+	+	+	++	+	+
	Macrolide non-susceptible IPD or Non-IPD ⁶	++	+++	+++	nr	++++	+++	++++

**Türkiye’de < 5 yaş altı çocuklarda (PVC
13 ile aşılı) (N=580 Sağlıklı)**

Pnömonokok taşıyıcılık: 17.8 %

72.8 % aşı dışı seroptipler

En sık saptanan serotipler;

Serotip 15B (9.7%)

Serotip 23F (8.7%),

Serotip 23A (8.7%)

Serotip 11A (6.7%)

Serotip 19F (4.8%)

Serotip 15F (4.8%)

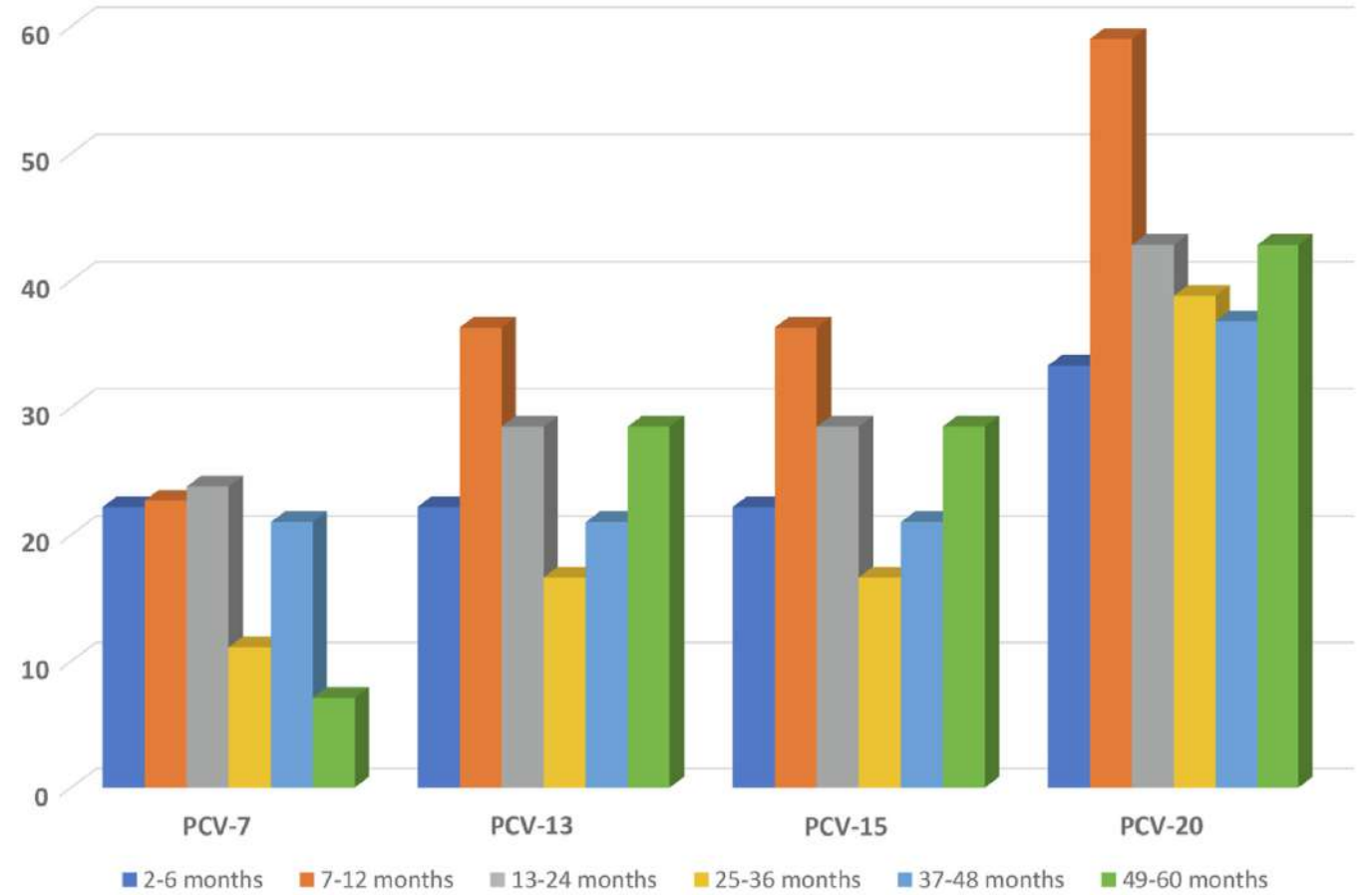
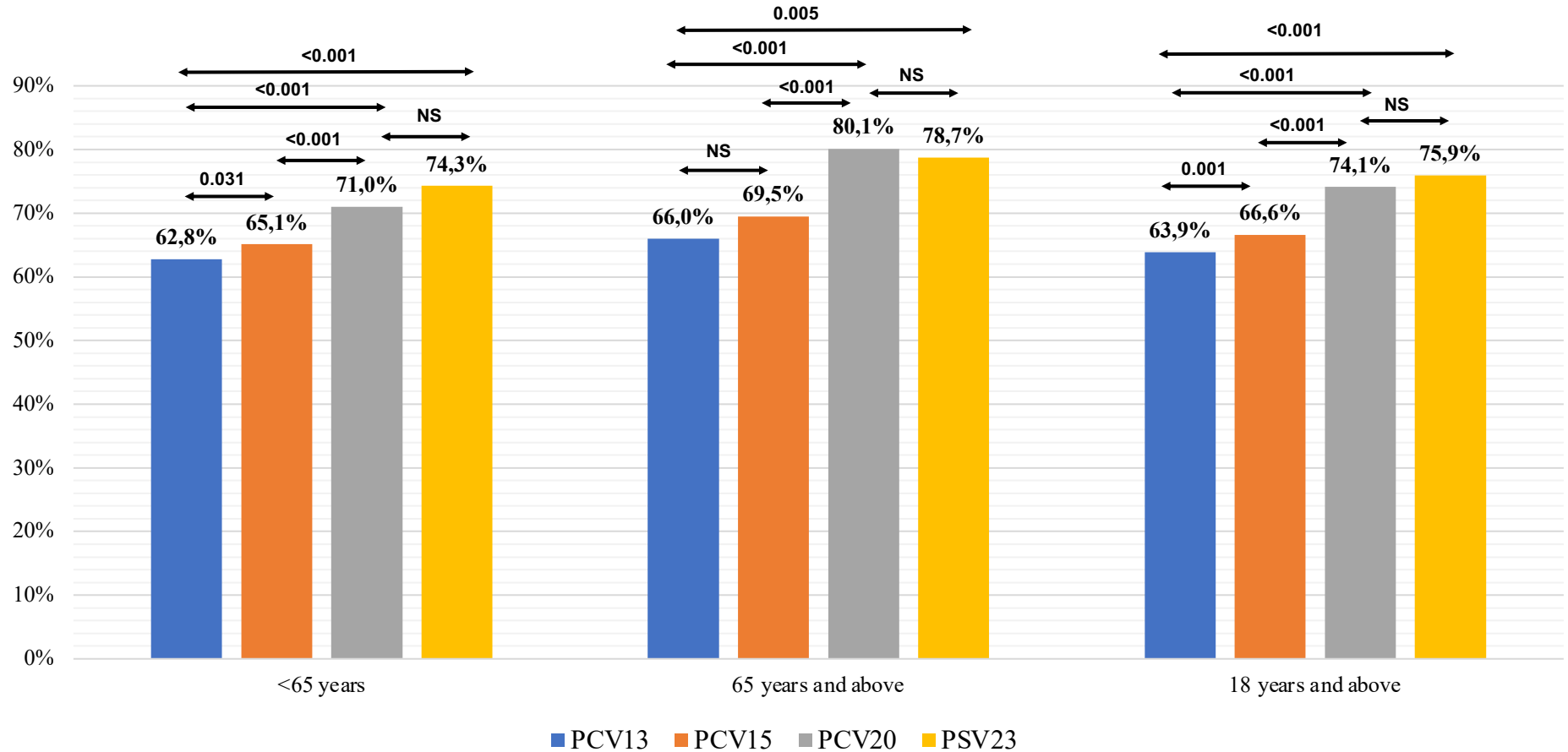


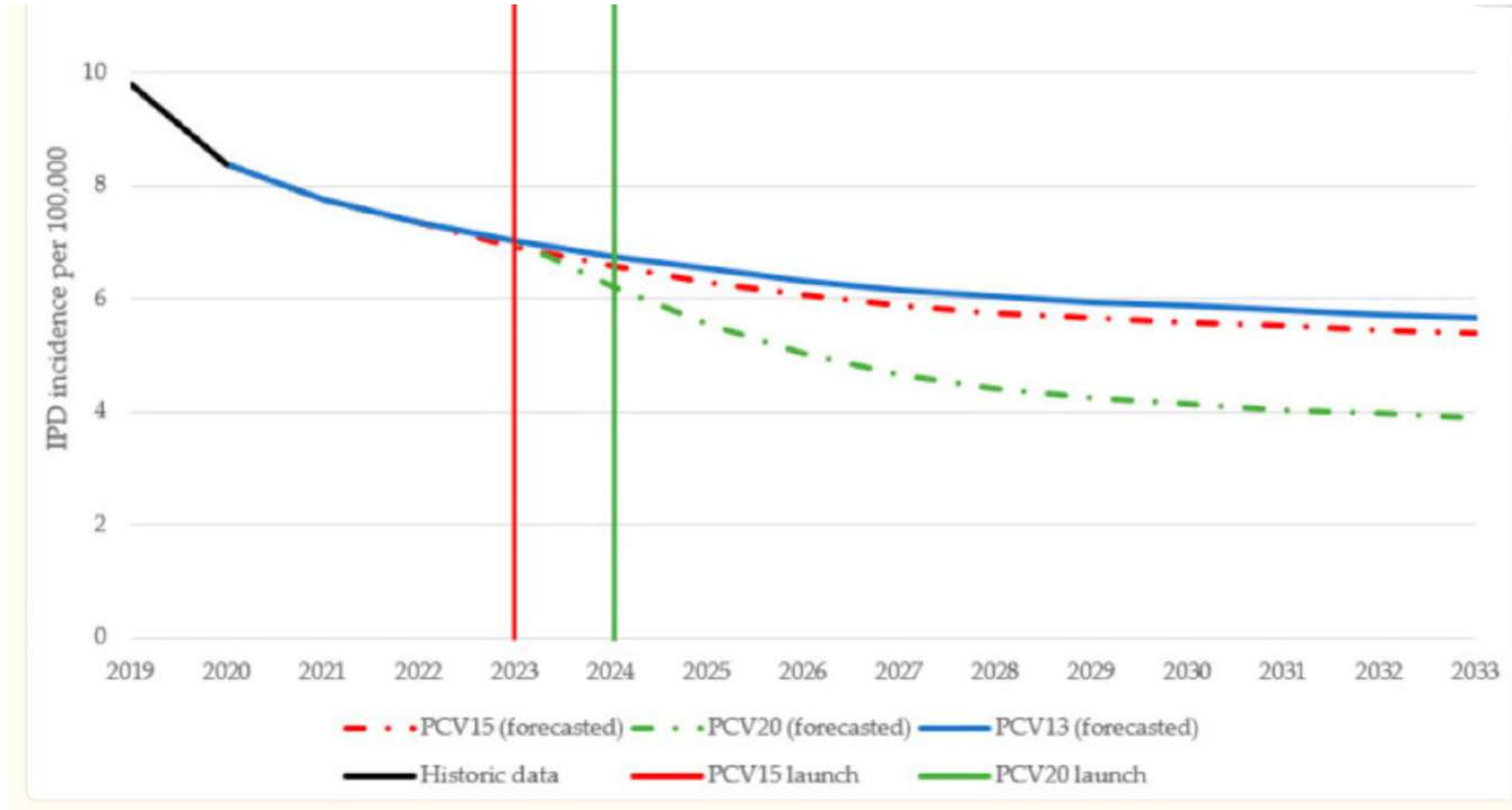
Fig. 1. Pneumococcal vaccine serotype coverage percentages according to age groups of the participants.

Pasif srveyans alıřması, 2015-2018 yılları, Eriřkin hastalar

Pnmoni, bakteriyemi, menenjit, plrit ve peritonitli hasta (≥ 18 yař rneklerinden izole edilen *S. pneumoniae* ($n=410$))



Yunanistan, Farklı pnökokok aşı stratejileri <2 yaş altı IPD insidansına olası etkisi





Cost-utility analysis of the use of the 20-valent anti-pneumococcal vaccine (PCV20) in adults older than 60 years in Spain

David Cantarero^a, Daniel Ocaña^b, María Ángeles Onieva-García^c, Juan Rodríguez-García^d, Paulina Gálvez^e, Cristina Méndez^e, Carlos Crespo^{f,g,*}, Alejandra López-Ibáñez de Aldecoa^h

Table 6

Base case analysis results (Cohort).

Strategy	Cost(€M)	QALYs (in thousands)	Δcost(€M)	ΔQALYs (in thousands)	ICER (€)
PCV20	4,775	63,951.6	−85.7	+5.9	Dominant (-14,605)
PCV15 + PPSV23	4,861	63,945.7	–	–	–

ICER: incremental cost-effectiveness ratio; LY: life years; QALY: quality-adjusted life years; PCV15: Pneumococcal conjugate vaccine 15-valent; PCV20: pneumococcal conjugate vaccine 20-valent; PPSV23: Pneumococcal polysaccharide vaccine 23-valent.

PCV20 aşılması ile 2.161 IPD vakasını, 19.470 Non-bakteriyemik PP vakasını ve 3.396 ölümü önlecek

Article

Cost-Effectiveness of Vaccination with the 20-Valent Pneumococcal Conjugate Vaccine in the Italian Adult Population

Barbara Polistena ¹, Giancarlo Icardi ², Andrea Orsi ², Federico Spandonaro ^{3,*}, Roberto Di Virgilio ⁴ and Daniela d'Angela ¹

Vaccine	PCV13	PCV15	PCV20	PCV20 vs. PCV13	PCV20 vs. PCV15
Disease cases					
Bacteraemia (excluding meningitis)	4982	4751	3811	−1171	−940
Meningitis	965	921	738	−227	−183
Hospitalised NBP cases	771,594	770,098	761,748	−9845	−8350
Non-hospitalised NBP cases	1,651,431	1,648,231	1,630,373	−21,058	−17,858
Outcomes					
Deaths (from IPD and NBP)	99,715	99,516	98,506	−1208	−1009
Life years (LY) (×1000)	75,044.2	75,042.2	75,050.7	+6.6	+5.5
QALY (×1.000)	52,687.2	52,688.0	52,692.0	+4.7	+4.0
Costs					
Vaccination costs (× EUR 1000)	EUR 448,495	EUR 448,495	EUR 489,063	EUR +40,568	EUR +40,568
Other health costs (× EUR 1000)	EUR 2,523,553	EUR 2,515,726	EUR 2,475,521	EUR −48,032	EUR −40,205
Total health costs (× EUR 1000)	EUR 2,972,047	EUR 2,964,220	EUR 2,964,584	EUR −7464	EUR −0.364