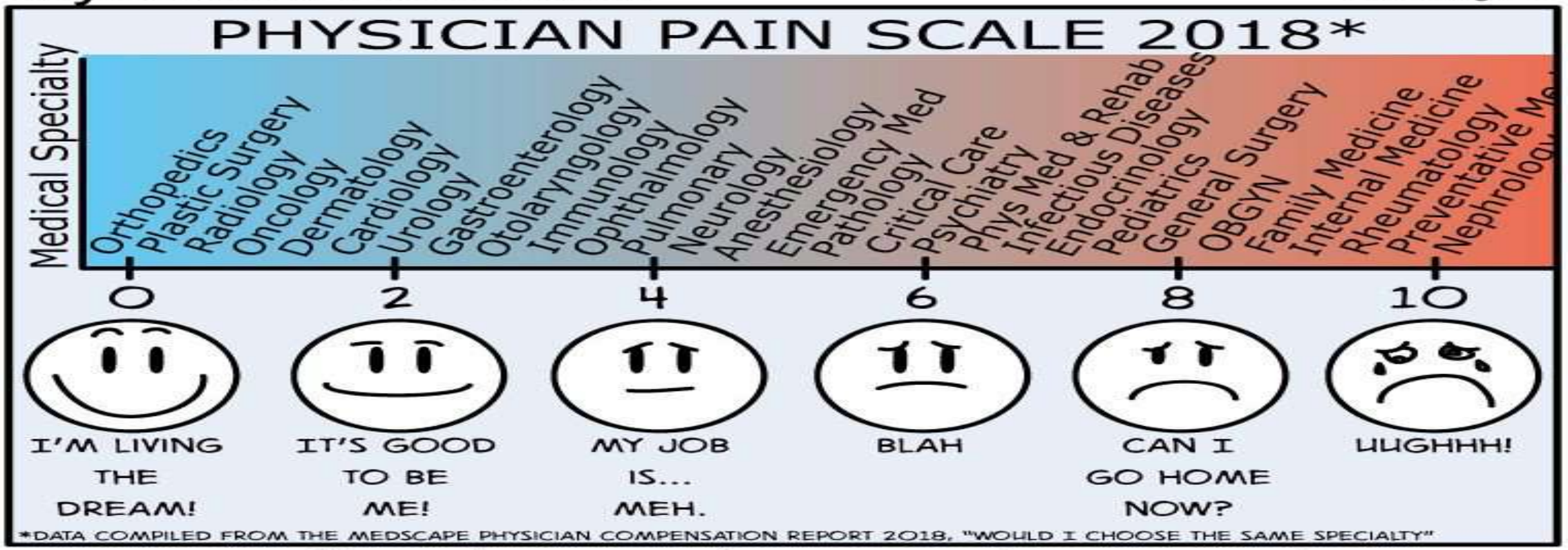
MENİNGOKOK ENFEKSİYONLARI EPİDEMİYOLOJİ ve MENİNGOKOK AŞILARI

Prof.Dr. Ener Çağrı Dinleyici
Eskişehir Osmangazi Üniversitesi Tıp Fakültesi
Çocuk Sağlığı ve Hastalıkları Anabilim Dalı
8 KASIM 2019

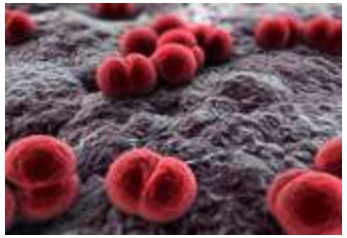
ener çağrı dinleyici

MyDoctorGear.com

J.Chang MD



How do you rate your pain on a scale from Orthopedics to Nephrology?



İNVAZİV MENİNGO

KLİNİK T

Feldman and Anderson *Pneumonia* (2019) 11:3
https://doi.org/10.1186/s41479-019-0062-0

Pneu

REVIEW

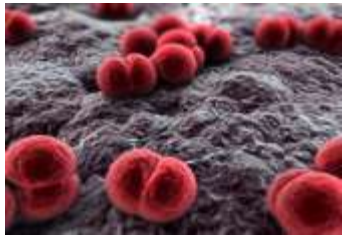
Meningococcal pneumonia: a review

Charles Feldman[1*] and Ronald Anderson[2]

Background: Although *Neisseria meningitidis* is one of the maj
is the most common non-neurological organ disease caused b

Table 1 Possible risk factors for invasive meningococcal disease and/or meningococcal pneumonia

- Age (older individuals)
- Smoking
- Close contact with persons with meningococcal infection
- People living in close quarters (e.g. military recruits, university students, Hajj)
- Chronic respiratory conditions (asthma, COPD)
- Coronary artery disease (or CABG)
- Diabetes mellitus
- Cirrhosis
- HIV infection
- Systemic lupus erythematosus
- Sickle cell anaemia (or asplenia)
- Deficiencies in mannose-binding lectin and other genetic abnormalities
- Preceding viral infection (especially influenza)
- Preceding bacterial infection (including *S. pneumoniae* and *H. influenzae*)
- Meningococcal serogroups Y, W-135, B
- Immunoglobulin and complement deficiencies
- Haematological malignancies (lymphoma, myeloma)



İNVAZİV MENİNGOKOKAL HASTALIK

YAŞLI BAKIM EVİ?

ener çağrı dinleyici

OUTBREAKS

Suspected cluster of *Neisseria meningitidis* W invasive disease in an elderly care home: do new laboratory methods aid public health action? United Kingdom, 2015

IMD case/ carriage	Month of specimen collection[a], 2015	Staff/resident	Age group (years)	Serogroup	Phenotype		Molecular type
					PorA	PorB	Sequence type (clonal complex)
Case 1	0	Resident	80–90	W	2a	(P1.5/P1.2/NT)	ST-11 (cc11)
Case 2	7	Resident	90+	W	2a	(NT/NT/NT)	ST-11 (cc11)
Carriage	10	Resident	80–90	W	2a	(P1.5 / P1.2 / NT)	ST-11 (cc11)
Carriage	10	Staff	20–30	W	2a	(P1.5 / P1.2 / NT)	ST-11 (cc11)
Carriage	10	Staff	20–30	C	NT	(P1.5 / P1.2 / NT)	ST-1157 (cc1157)
Carriage	10	Staff	30–40	C	NT	(P1.5 / P1.2 / NT)	ST-1157 (cc1157)

İNVAZİV MENİNGOKOKAL HASTALIK 2019

ener çağrı dinleyici

The Global Meningococcal Initiative meeting on prevention of meningococcal disease worldwide: epidemiology, surveillance, hypervirulent strains, antibiotic resistance and high-risk populations

Reinaldo Acevedo, Xilian Bai, Ray Borrow, Dominique A. Caugant, Josefina Carlos, Mehmet Ceyhan, Hannah Christensen, Yanet Climent, Philippe De Wals, Ener Cagri Dinleyici, Gabriela Echaniz-Aviles, Ahmed Hakawi, Hajime Kamiya, Andromachi Karachaliou, Jay Lucidarme, Susan Meiring, Konstantin Mironov, Marco A.P. Sáfadi, Zhujun Shao, Vinny Smith, Robert Steffen, Bianca Stenmark, Muhamed-Kheir Taha, Caroline Trotter, Julio A. Vázquez & Bingqing Zhu

Accepted author version posted online: 10 Dec 2018.

İNVAZİV MENİNGOKOKAL HASTALIK 2019

Prevention and control of meningococcal disease: updates from the Global Meningococcal Initiative in Eastern Europe

Xilian Bai , Ray Borrow , Suzana Bukovski , Dominique A. Caugant , Davor Culic , Snezana Delic , Ener Cagri Dinleyici , Medeia Eloshvili , Tímea Erdősi , Jelena Galajeva , Pavla Křížová , Jay Lucidarme , Konstantin Mironov , Zuridin Nurmatov , Marina Pana , Erkin Rahimov , Larisa Savrasova , Anna Skoczyńska , Vinny Smith , Muhamed-Kheir Taha , Leonid Titov , Julio Vázquez , Lyazzat Yeraliyeva

PII: S0163-4453(19)30332-9
DOI: https://doi.org/10.1016/j.jinf.2019.10.018
Reference: YJINF 4366

To appear in: *Journal of Infection*

Accepted date: 26 October 2019

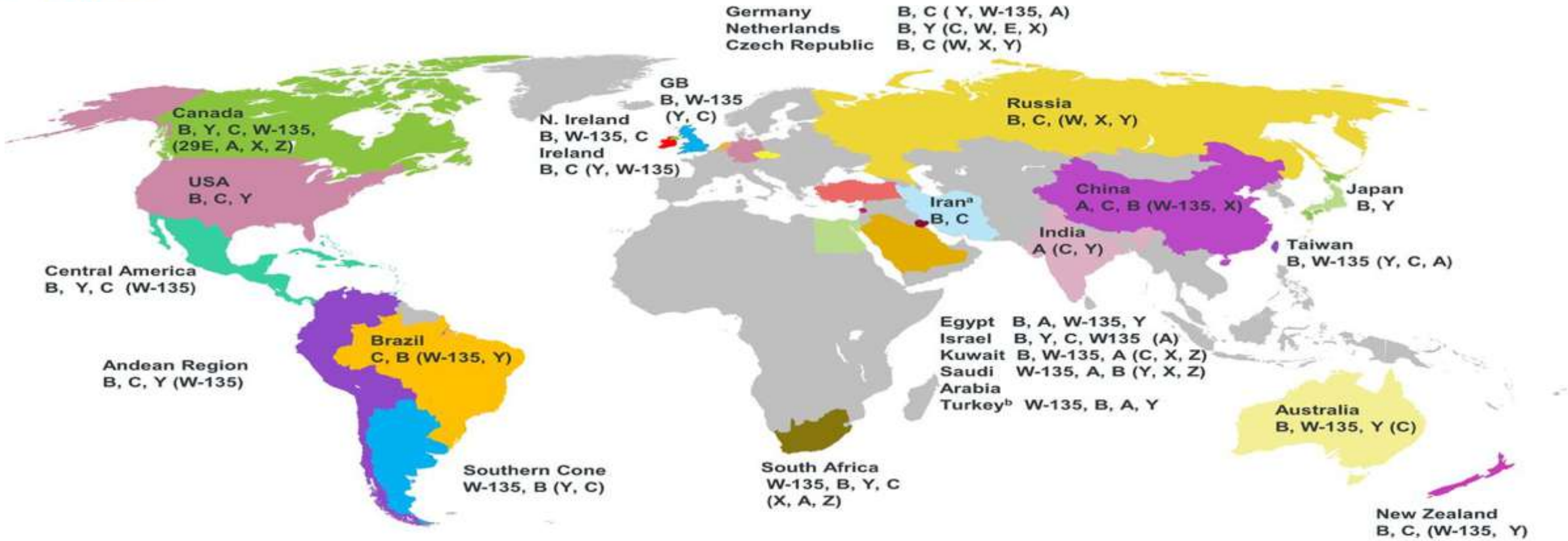
İNVAZİV MENİNGOKOKAL HASTALIK EPİDEMİYOLOJİ

- 100.000 kişide
- Global insidans 0.01 (Meksika)- 3.6 (Fas)
- 0.70 Avrupa, 0.12 ABD, 0.30 Kanada
- 0.02 Menenjit kuşağı (MenAfriVac sonrası, Nijer/Nijerya C salgını öncesi)
- 0.05 Çin, 0.45-1.0 Rusya, 1.6 Yeni Zelanda, 0.23 Güney Afrika
- 0.01-0.03 Tayvan, 0.01-0.08 Güney Kore, 0.028 Japonya
- <0.01 Bolivya, Küba, Meksika, Paraguay, Peru
- 2.0 Brezilya

Dinleyici EC et al. EMGM 2019, Avecedo et al. Expert Rev Vaccines 2019

İNVAZİV MENİNGOKOKAL HASTALIK
SEROGRUP DAĞILIMI

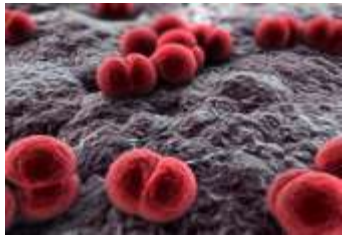
ener çağrı dinleyici



*listed in order of prevalence
[a]not listed in order of prevalence
[b]as observed in children

Meningococcal disease: has the battle been won?

Millar BC, *et al. J R Army Med Corps* 2016;**0**:1–7. doi:10.1136/jramc-2016-000695



İNVAZİV MENİNGOKOK ENFEKSİYONU
SEROGRUP EPİDEMİYOLOJİSİ

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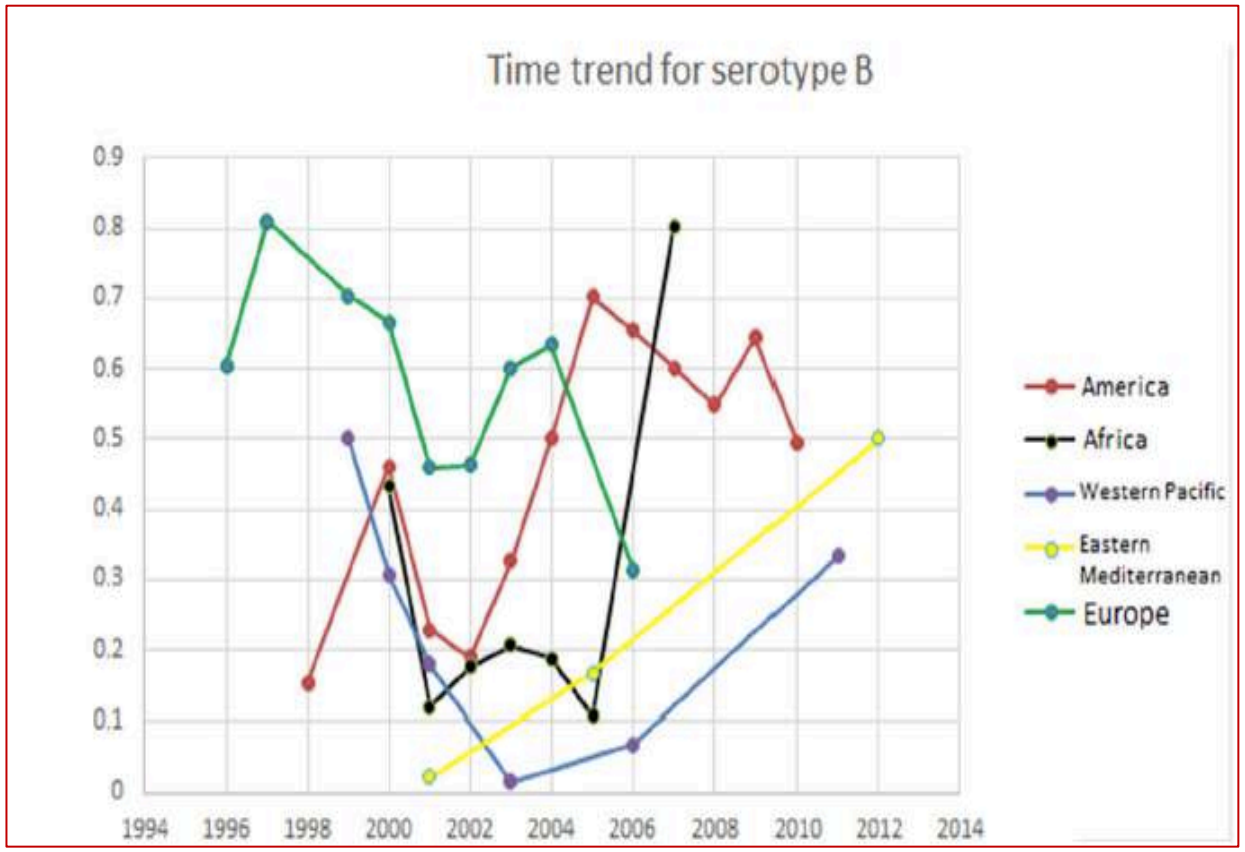
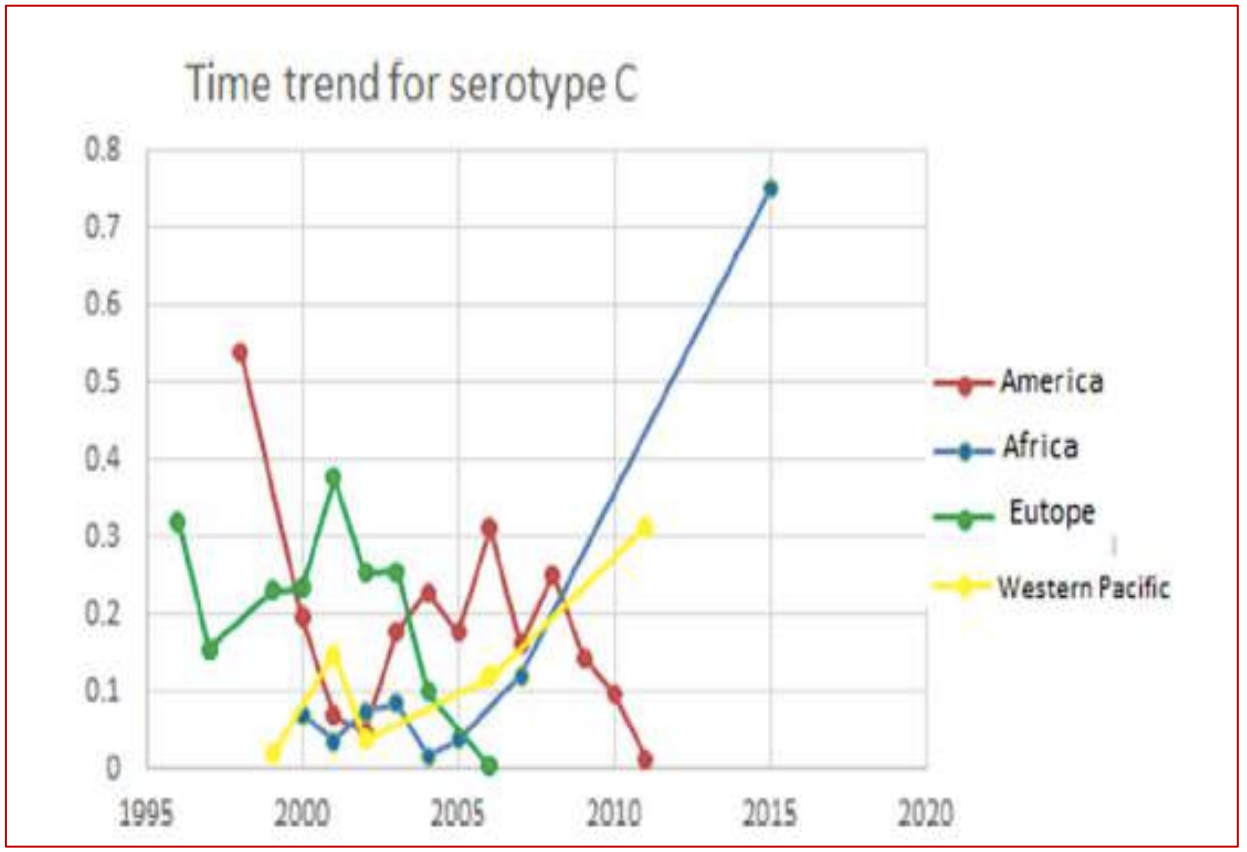
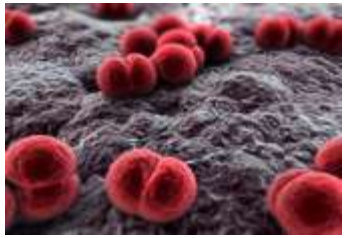




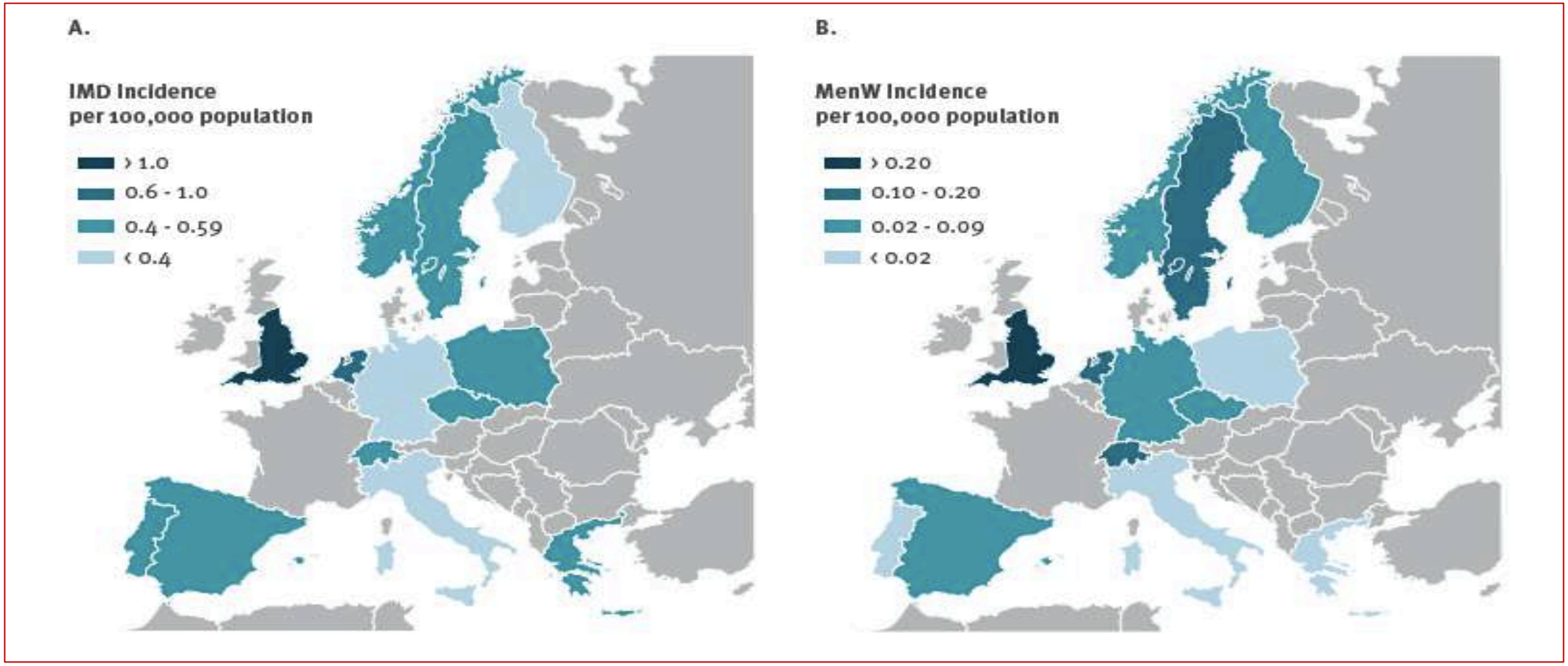
Purmohamad et al. Microbial Pathogens 2019



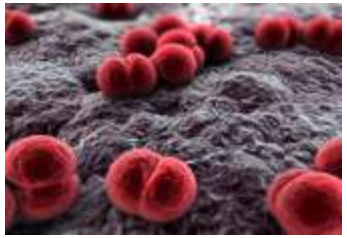
İNVAZİV MENİNGOKOK ENFEKSİYONU

SEROGRUP W

ener çağrı dinleyici



Krone et al. Euro Surveilance 2019



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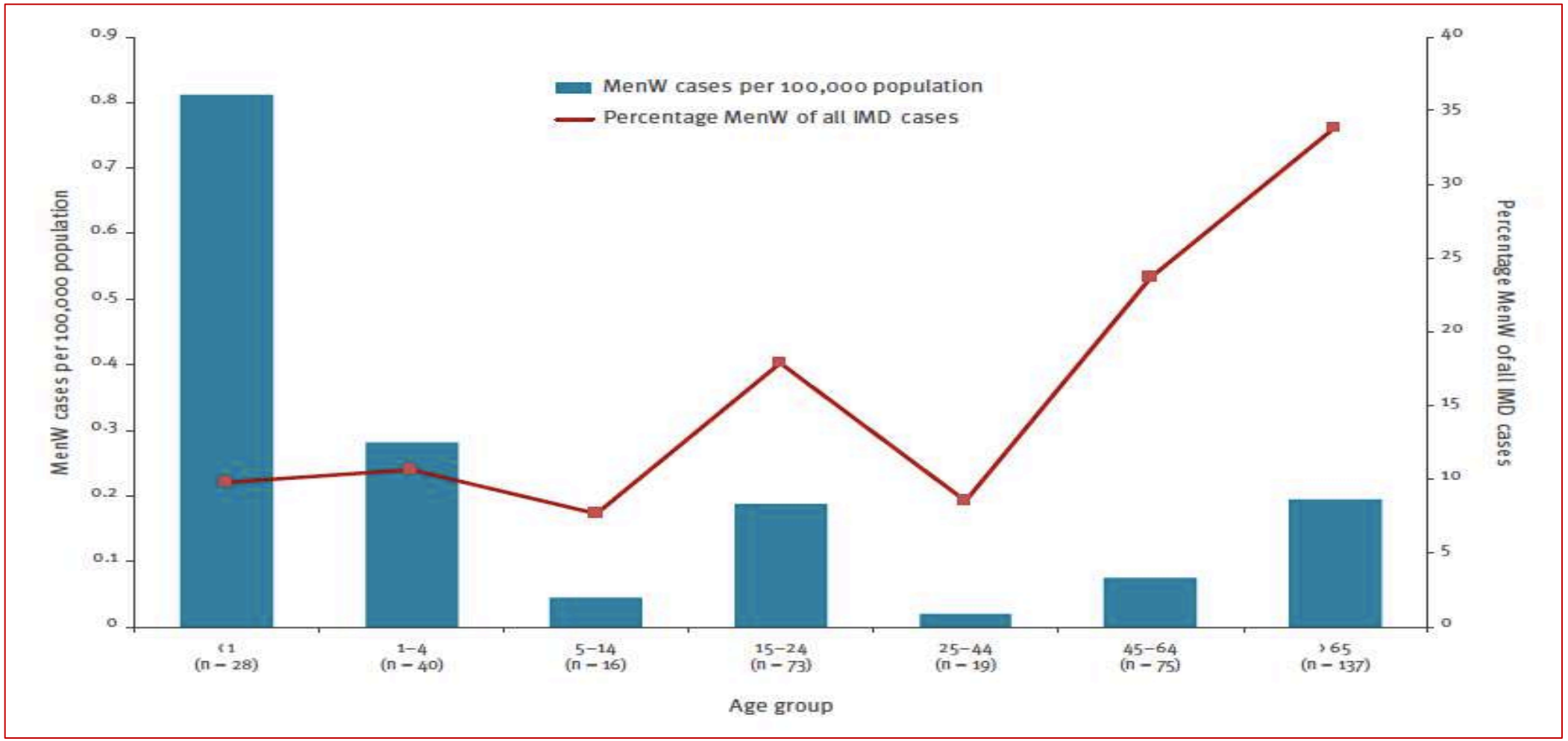
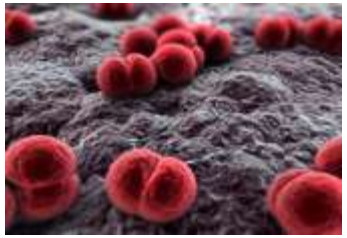
SEROGRUP W



Krone et al. Euro Surveilance 2019

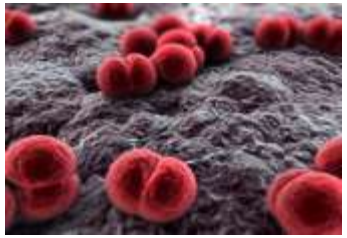


İNVAZİV MENİNGOKOK ENFEKSİYONU
SEROGRUP W

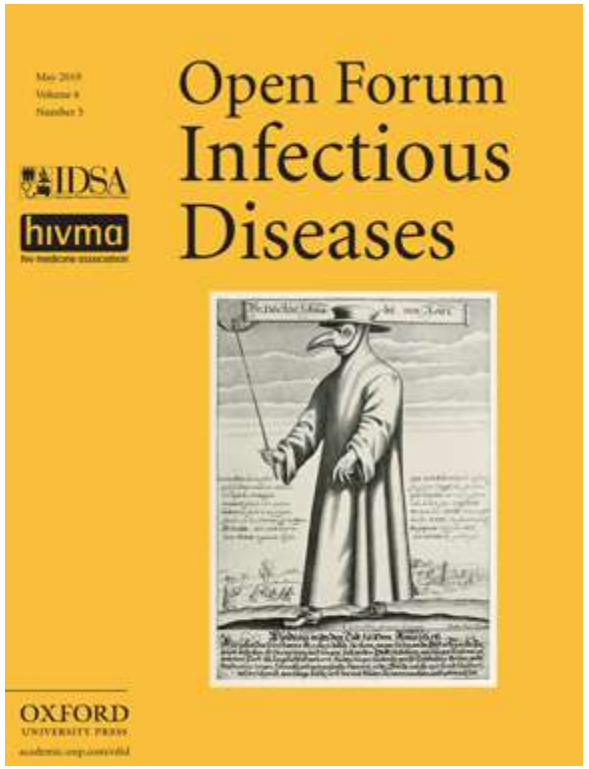
ener çağrı dinleyici

Figure 2. Age distribution of MenW cases in the UK following immunization of adolescents aged 14–18 years with conjugate MenACWY vaccine, which commenced in 2015.[41]

Bai et al. J Infection 2019.



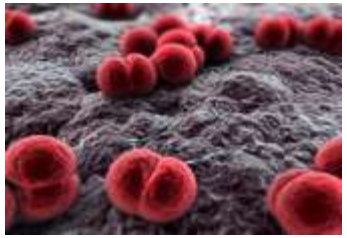
İNVAZİV MENİNGOKOK ENFEKSİYONU
NON-GROUPABLE



Invasive Meningococcal Disease due to Nongroupable *Neisseria meningitidis*—Active Bacterial Core Surveillance Sites, 2011–2016

Lucy A. McNamara,[1] Caelin C. Potts,[1] Amy Blain,[1] Nadav Topaz,[1] Mirasol Apostol,[2] Nisha B. Alden,[3] Susan Petit,[4] Monica M. Farley,[5] Lee H. Harrison,[6] Lori Triden,[7] Alison Muse,[8] Tasha Poissant,[9] Xin Wang,[1] and Jessica R. MacNeil[10]

McNamara et al. Open Forum Infectious Diseases 2019



İNVAZİV MENİNGOKOK ENFEKSİYONU

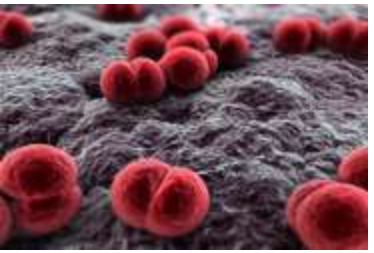
NON-GROUPABLE

ener çağrı dinleyici

Demographics	Nongroupable	All Other ABCs	*P* Value[a]
Median age (IQR), y	21 (17–25)	34 (11–60)	<.01
Sex, No. (%)			
Female	7 (32)	210 (52)	.08
Male	15 (68)	196 (48)	
Race (n = 21 vs 362), No. (%)			
Asian			
Black			
White			
Ethnicity (n = 1			
Hispanic			
Non-Hispanic			
Clinical			
Presentation, No. (%)			
Meningitis[c]	14 (63)	Not done[b]	
Bacteremia[d]	19 (86)		
Septic shock	8 (36)		
Other[e]	3 (14)		
Outcome (n = 22 vs 401), No. (%)			
Died	3 (14)	61 (15)	1
Survived	19 (86)	340 (85)	
With sequelae	2 (11)[f]	Not done[b]	
ICU (n = 19 vs 318)	12 (63)[f]	184 (58)	.81

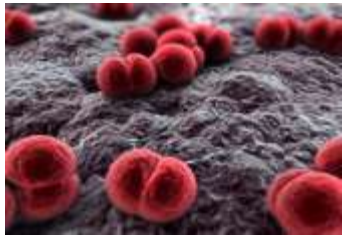
Molecular			
Genogroup,[g] No. (%)			
B	6 (27)	147 (36)	<.0001
C	3 (14)	111 (27)	
E	7 (32)	2 (0.5)	
			(13)
			(23)
			)
			t done
Eculizumab (induced complement deficiency)	3 (14)	1 (0.3)	<.001
Innate complement deficiency[i]	4 (18)	Not done[b]	
None	4 (18)		
Phase variable off	2 (9)		
IS*1301* insertion	3 (14)		
Internal stops/truncated genes	5 (23)		
Missing genes	8 (36)		
Clonal complex (n = 22 vs 390), No. (%)			
Hyperinvasive[h]	6 (27)	203 (52)	.03
Other CC	16 (73)	187 (48)	

McNamara et al. Open Forum Infectious Diseases 2019



İNVAZİV MENİNGOKOK ENFEKSİYONU

KLİNİK SEYİR



İNVAZİV MENİNGOKOKAL HASTALIK

KLİNİK TABLO

- ARTRİT
- PNÖMONİ
- Otitis media, Epiglotit
- Perikardit
- Konjuktivit
- Endoftalmit
- Uretrit
- Postenfeksiyöz inflamatuvar sendrom
- Kronik meningokoksemi

% 24.9

MENENJİT

%37.1

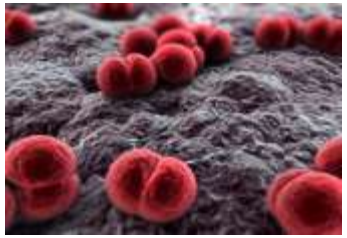
MENİNGOKOKSEMİ

% 38

MENENJİT

+

MENİNGOKOKSEMİ



İNVAZİV MENİNGOKOKAL HASTALIK

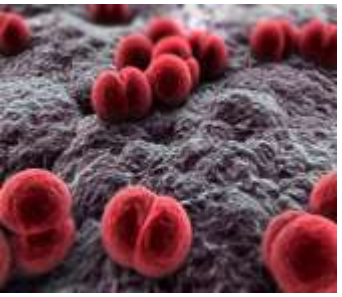
TANI

ener çağrı dinleyici

PLOS ONE

Conclusions

In conclusion our study demonstrated that qPCR is significantly (at least 3 times) more sensitive than culture in the laboratory confirmation of IMD. The study also demonstrated that culture negativity is not associated with lower bacterial loads and with less severe cases. On the other side, in patients with sepsis, qPCR can predict fatal outcome since higher bacterial load, evaluated by qPCR, appears strictly associated with most severe cases and fatal outcome. The study also showed that molecular techniques such as qPCR can provide a valuable addition to the proportion of diagnosed and serotyped cases of IMD.



İNVAZİV MENİNGOKOKAL HASTALIK

KLASİK RİSK FAKTÖRLERİ

ener çağrı dinleyici

ASPLENİ

SPLENEKTOMİ

ÜSYE ÖYKÜSÜ

İnfluenza, mycoplasma

SİGARA İÇİLMESİ

- **Kompleman Eksikliği**
- **HIV /AIDS**
- **Humoral immün yetmezlik**
- **Genetik polimorfizmler**

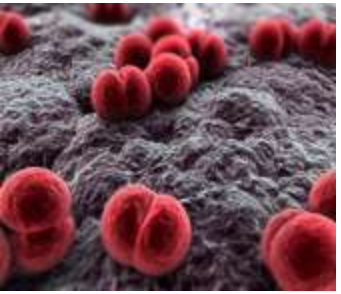
ECULIZUMAB

HAC-ÜMRE

SEYAHAT

ASKERİ BİRLİKLER

LABORATUAR ÇALIŞANLARI

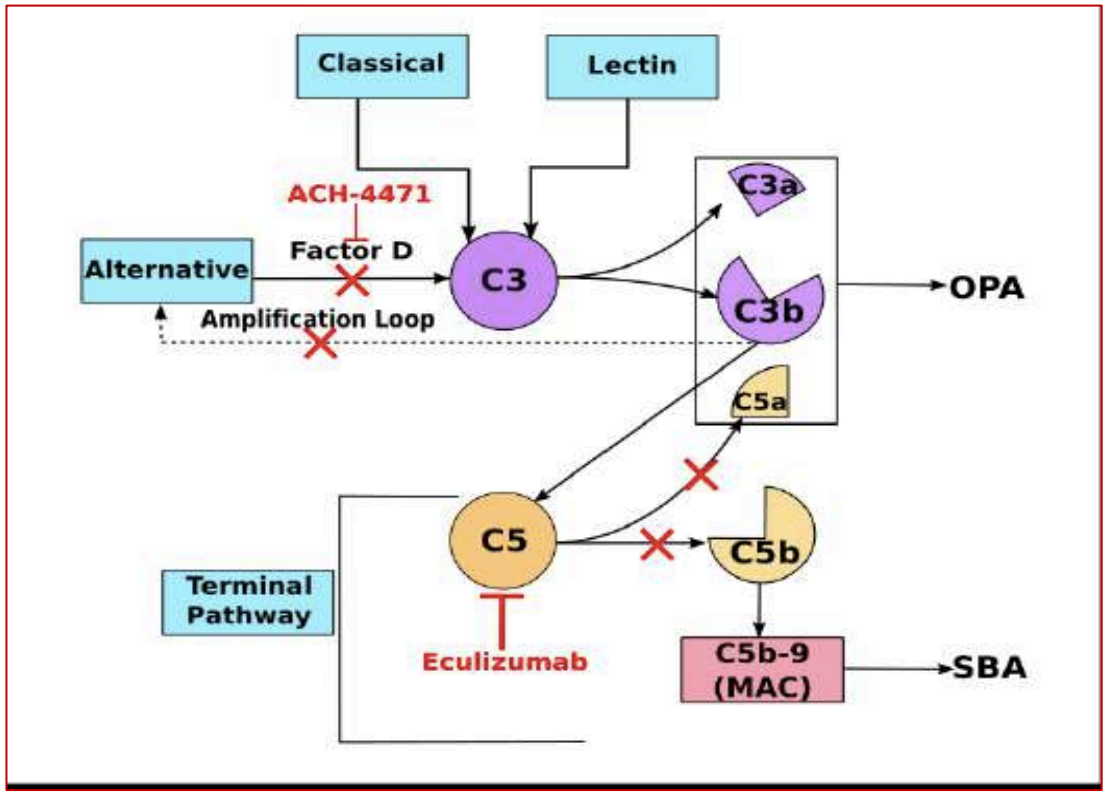


İNVAZİV MENİNGOKOKAL HASTALIK

ECULIZUMAB

ener çağrı dinleyici

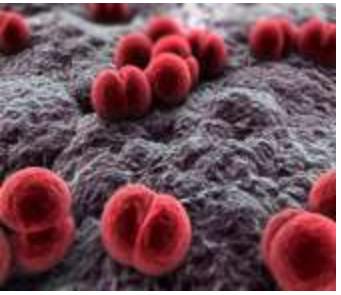
Eculizumab is licensed for the treatment of paroxysmal nocturnal hemoglobinuria, atypical hemolytic uremic syndrome, and generalized myasthenia gravis. By blocking C5, eculizumab inhibits meningococcal serum bactericidal activity (SBA), leaving patients at an approximately 2000-fold higher risk of meningococcal disease than the general population.[1] This increased risk includes invasive disease caused by unencapsulated (non-groupable, NG) strains,[1,2] which rarely cause invasive disease in normal hosts.[3]



Differential effects of therapeutic complement inhibitors on serum bactericidal activity against non-groupable meningococcal isolates recovered from patients treated with eculizumab

Dan M. Granoff,[1] Howard Kim,[1] Nadav Topaz,[2] Jessica MacNeil,[2] Xin Wang[2] and Lucy A. McNamara[2]

haematologica 2019; 104:e344



İNVAZİV MENİNGOKOKAL HASTALIK

İNGİLTERE

ener çağrı dinleyici

Vaccine xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Epidemiology, clinical presentation, risk factors, intensive care admission and outcomes of invasive meningococcal disease in England, 2010–2015

Sydel R. Parikh[a,*], Helen Campbell[a], Stephen J. Gray[b], Kazim Beebeejaun[a], Sonia Ribeiro[a], Ray Borrow[c], Mary E. Ramsay[a], Shamez N. Ladhani[a,c]

% 99.5

DAHA ÖNCEDEN SAĞLIKLI

% 0.5

18/3411 HASTA

6 ASPLENİ

11 KOMPLEMAN EKSİKLİĞİ

İNVAZİV MENİNGOKOKAL HASTALIK

YENİ RİSK FAKTÖRLERİ 2019

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BÜYÜK KİTLESEL AKTİVİTELER
KAMPLAR
SPOR OYUNLARI ?
OLİMPİYATLAR
FESTİVALLER

Lessons from the Field

Meningococcal disease outbreak related to the World Scout Jamboree in Japan, 2015

Mizue Kanai,[a,b] Hajime Kamiya,[c] Alison Smith-Palmer,[d] Hideyuki Takahashi,[e] Yushi Hachisu,[a] Munehisa Fukusumi,[c,f] Takehito Saitoh,[c] Makoto Ohnishi,[e] Tomimasa Sunagawa,[c] Tamano Matsui[c] and Kazunori Oishi[c]

Correspondence to Hajime Kamiya (email: hakamiya@niid.go.jp)

İNVAZİV MENİNGOKOKAL HASTALIK

YENİ RİSK FAKTÖRLERİ 2019

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23rd WORLD SCOUT JAMBOREE SCOUT MONDIAL JAPAN 2015 和

Table 1. Linelist of confirmed cases of meningococcal outbreak associated with World Scout Jamboree (n = 6)

Case No.	Unit	Onset date	Symptoms	Serogroup	Outcome
1	North of Scotland Scout	8 Aug	Conjunctivitis, Fever, Headache, Nausea	W (ST11)	Remission
2	North of Scotland Scout	11 Aug	Cough, Headache, Neck stiffness	W (ST11)	Remission
3	North of Scotland Scout	12 Aug	Sour throat, Fever, Headache, Photophobia	W (ST11)	Remission
4	Parent of a North of Scotland scout	16 Aug	Vomit, Myalgia, Headache, Photophobia	W (ST11)	Remission
5	Sweden Scout	14 Aug	Signs of meningitis and septicemia	W (ST11)	Remission
6	Sweden Scout	12 Aug	No info	W (ST11)	Remission

www.wpro.who.int/wpsar WPSAR Vol 8, No 2, 2017 | doi: 10.5365/wpsar.2016.7.3.007

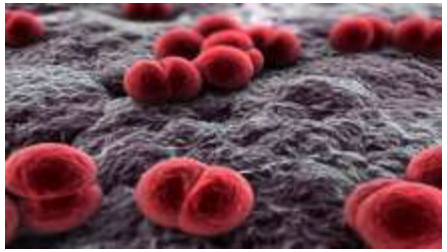
Norwegian Russefeiring-2017

Funeral related- LIber1a

Meningococcal septicaemia associated with attending a funeral – Liberia

Disease outbreak news
6 July 2017

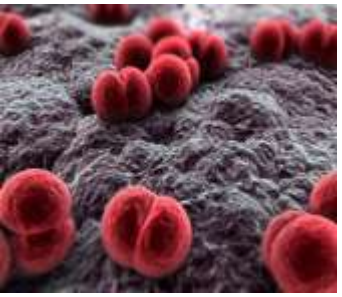
Hajj-Umrah visits to Saudi Arabia



GÖÇMEN SAĞLIĞI
ENFEKSİYON HASTALIKLARI

- Göçmenler ile enfeksiyon hastalıklarının yayılımı ile direk ilişki yok.
- Solunum yolu enfeksiyonları ve influenza için direk risk yok
- Aşı ile engellenebilir hastalıklar (domestik enfeksiyon)
  - Toplu yaşam alanları, kalabalık, düşük hijyen
  - Aşılama oranlarının düşük olması
  - Uzun ve tehlikeli seyahatler
- Tüberküloz
- HIV
  - Göçmenler, 2016 yılında yeni HIV olgularının %40'I
- ANTİBİYOTİK DİRENCİ

Dinleyici EC, Borrow R. Refugee and migrant health-Meningoococcal Infections (in preparation)



İNVAZİV MENİNGOKOKAL HASTALIK

KOMPLİKASYONLAR

ener çağrı dinleyici

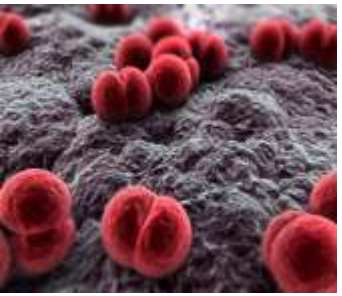
THE CLINICAL FEATURES AND LONG-TERM SEQUELAE OF INVASIVE MENINGOCOCCAL DISEASE IN CHILDREN

Chen Stein-Zamir, MD, MPH,† Hanna Shoob, MPH,*
Irina Sokolov, MD,* Amin Kunbar, MD,*
Nitza Abramson, MD, MPH,*
and Deena Zimmerman, MD, MPH**

IMH vakalarının %10-20'si ölümle sonuçlanır.

Hayatta kalan hastaların %20-33'ünde uzun dönemli sekeller görülür.

The Pediatric Infectious Disease Journal • Volume 33, Number 7, July 2014



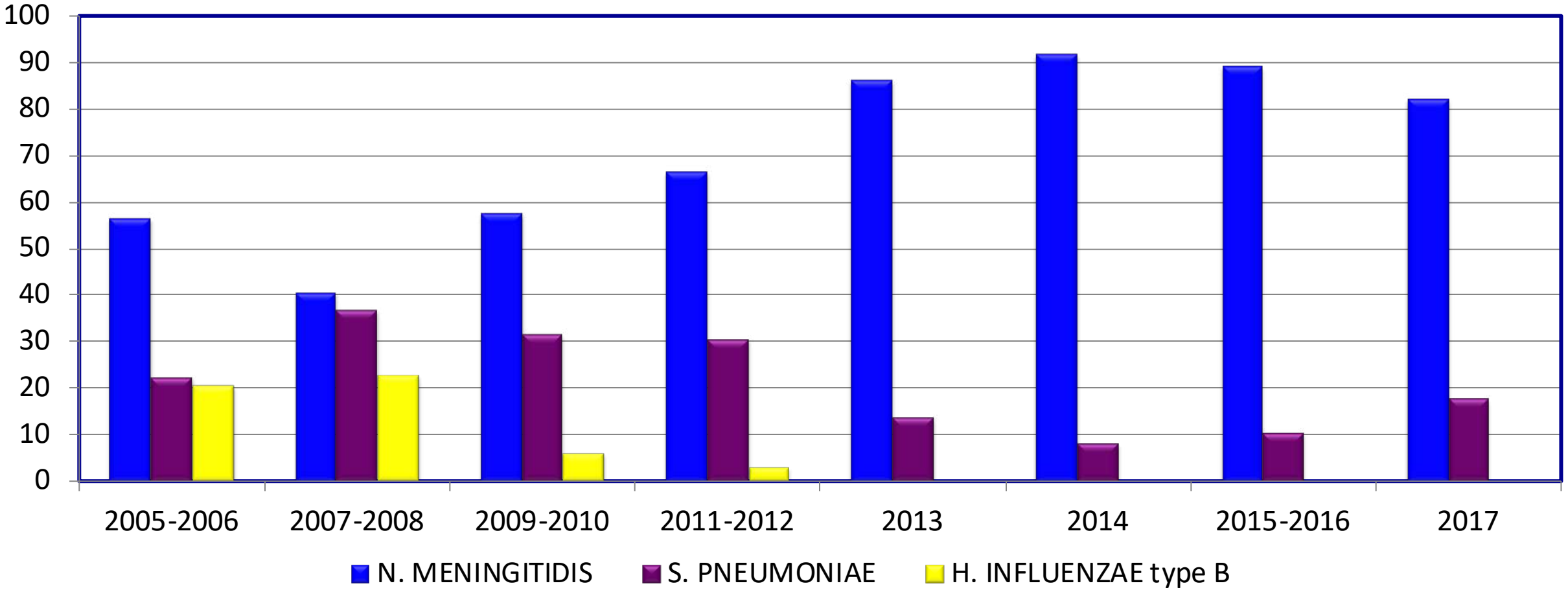
İNVAZİV MENİNGOKOKAL HASTALIK
KOMPLİKASYONLAR

ener çağrı dinleyici

- UZUN DÖNEM TÜM SEKELLER %33
- İŞİTME KAYBI % 7 (ağır %3.5)
  KOKLEAR İMPLANT %1
- ÖĞRENME GÜÇLÜKLERİ %22.6
- DAVRANIŞ PROBLEMLERİ %14.8
- KRONİK BAŞ AĞRISI %14
- KONUŞMA BOZUKLUKLARI %12
- MOTOR İŞLEVLERDE BOZULMA %10.4
- AĞIR NÖROMOTO GERİLİK %3.5
- AMPUTASYON %1.7
- KONVÜLZİYON %1.7

The Pediatric Infectious Disease Journal • Volume 33, Number 7, July 2014

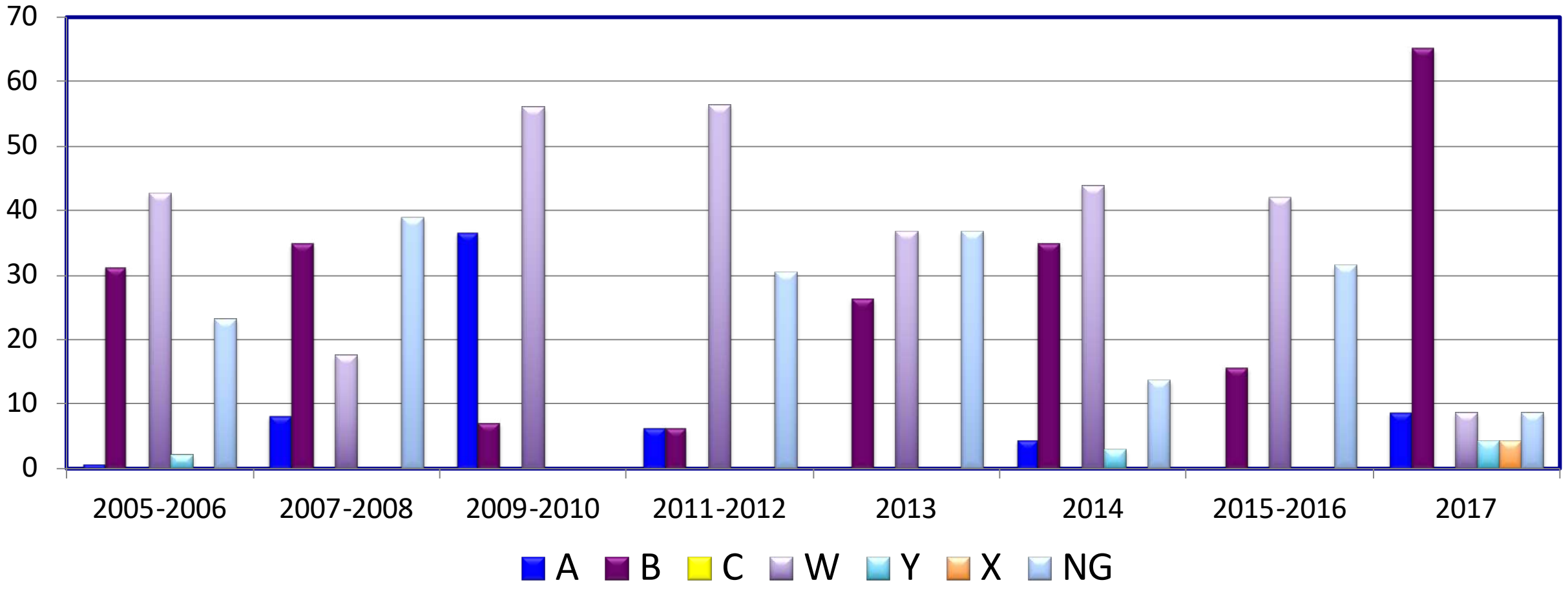
MENİNGOKOK EPİDEMİYOLOJİSİ
TÜRKİYE



AKUT BAKTERİYEL MENENJİT

Ceyhan et al. Human Vaccine Immunotherapeutics 2014, 2016

MENİNGOKOK EPİDEMİYOLOJİSİ
TÜRKİYE



AKUT BAKTERİYEL MENENJİT

Ceyhan et al. Human Vaccine Immunotherapeutics 2014, 2016

MENİNGOKOK EPİDEMİYOLOJİSİ
ŞANLIURFA 2018-2019

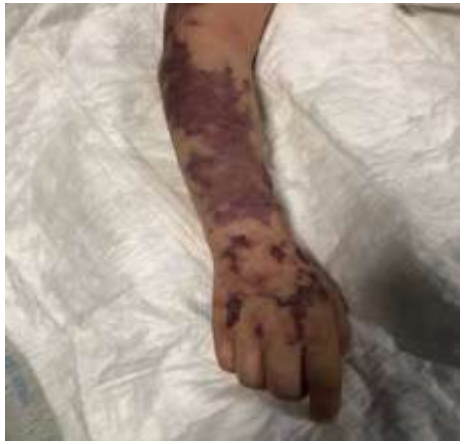
- Ocak 2018-Haziran 2019, Şanlıurfa Eğitim ve Araştırma Hastanesi Çocuk Yoğun Bakım'da 12 invaziv meningokok
- 5-168 ay (dört olgu <1 yaş); 6 kız-6 erkek
- Meningokok aşısı olan olgu yok.
- Semptomların başlamasından 12-72 saat içerisinde yoğun bakım
- Dokuz meningokoksemi + menenjit, 3 meningokokoksemi
- 7 olguda septik şok + DİK, 3 olguda katekolamin refrakter septik şok
- Ateş ve döküntü %100.
- PRISM Skoru 5 ile 37 arasındaydı
- 2 olguda CVVH, bir olguda plazmaferez
- Mortalite %16.6
- **100.000'de 0.84, 1 yaş altında 100.000 6.4**

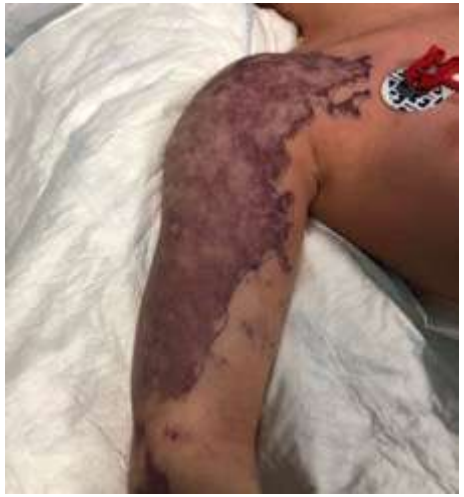
Kiral E, Yetimakman F. ÇAYD KONGRESİ 2019

MENİNGOKOK EPİDEMİYOLOJİSİ TÜRKİYE (model)

- Türkiye'de invaziv meningokok enfeksiyonu sıklığı 100.000'de 1 olduğunda (en yüksek tahmin)
  - 820 olgu yıl (0-99 yaş aralığında)
  - **420 olgu meningokoksemi** (Eskişehir 0.24%)
  - 420 olgu meningokok menenjiti
  - **82 IMD (kesin/şüpheli IMD ilişkili ölüm)**

    18-99 yaş arası olgular ve ölüm nedenleri





Dinleyici EC, 2020, in preparation

MENİNGOKOK EPİDEMİYOLOJİSİ
NAZOFARİNGEAL TAŞIYICILIK

ener çağrı dinleyici

HUMAN VACCINES & IMMUNOTHERAPEUTICS
2017, VOL. 13, NO. 5, 1182–1189
http://dx.doi.org/10.1080/21645515.2016.1268304

Taylor & Francis
Taylor & Francis Group

RESEARCH PAPER

The prevalence, serogroup distribution and risk factors of meningococcal carriage in adolescents and young adults in Turkey

Rahmi Tuna Tekin[a], Ener Cagri Dinleyici[a], Mehmet Ceyhan[b], Adem Karbuz[c], Nuran Salman[d], Murat Sutçu[d], Zafer Kurugol[e], Yasemin Balliel[f], Melda Celik[g], Mustafa Hacimustafaoglu[h], Necdet Kuyucu[i], Meda Kondolot[j], Gülnar Sensoy[k], Ozge Metin[l], Soner Sertan Kara[m], Meltem Dinleyici[a], Omer Kılıç[a], Cihangul Bayhan[b], Venhar Gurbuz[b], Emre Aycan[b], Aygun Memedova[e], Arzu Karli[k], Gulçin Bozlu[i], and Solmaz Celebi[h]

MENİNGOKOK EPİDEMİYOLOJİSİ
NAZOFARİNGEAL TAŞIYICILIK

ener çağrı dinleyici

%65 SEROGRUP W

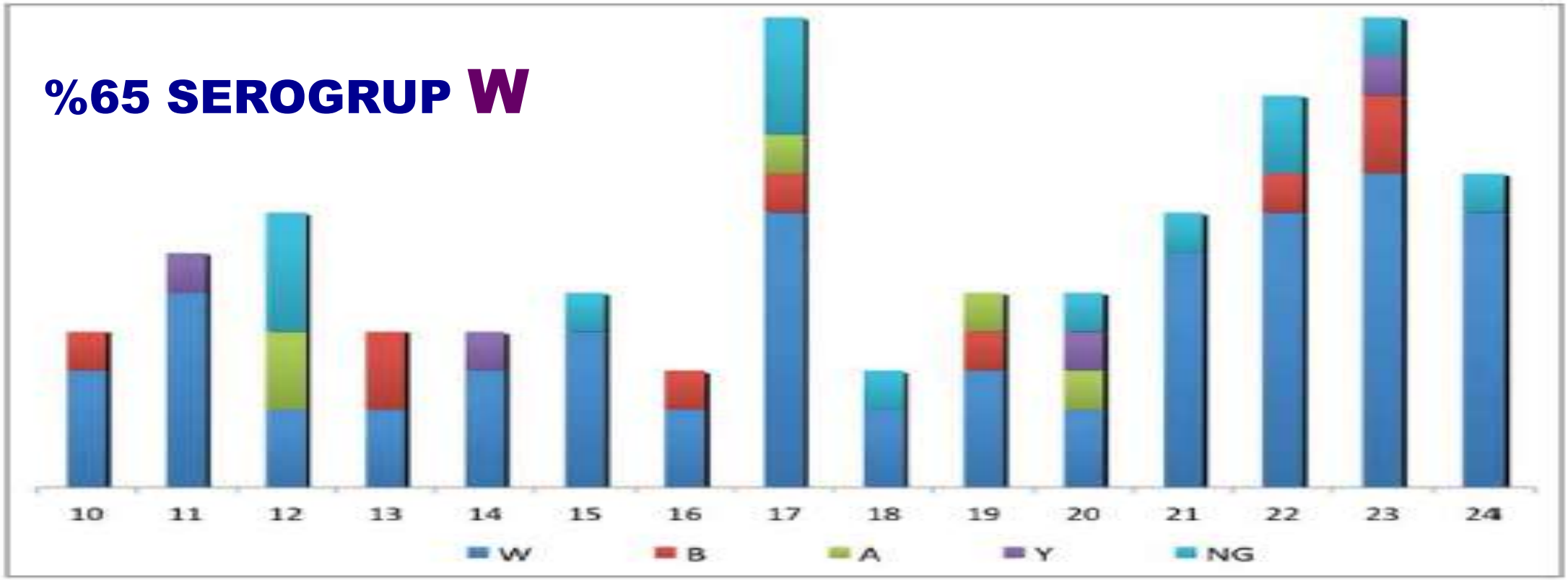


Figure 2. *Neisseria meningitidis* serogroup distribution according to age.

MENINGO-CARR STUDY

Tekin, Dinleyici, Ceyhan et al. Human Vaccine Immunotherapeutics 2017

15th EMGM Congress
The European Meningococcal and Haemophilus Disease Society
27-30 May 2019
PT Meeting Centre | Lisbon | Portugal

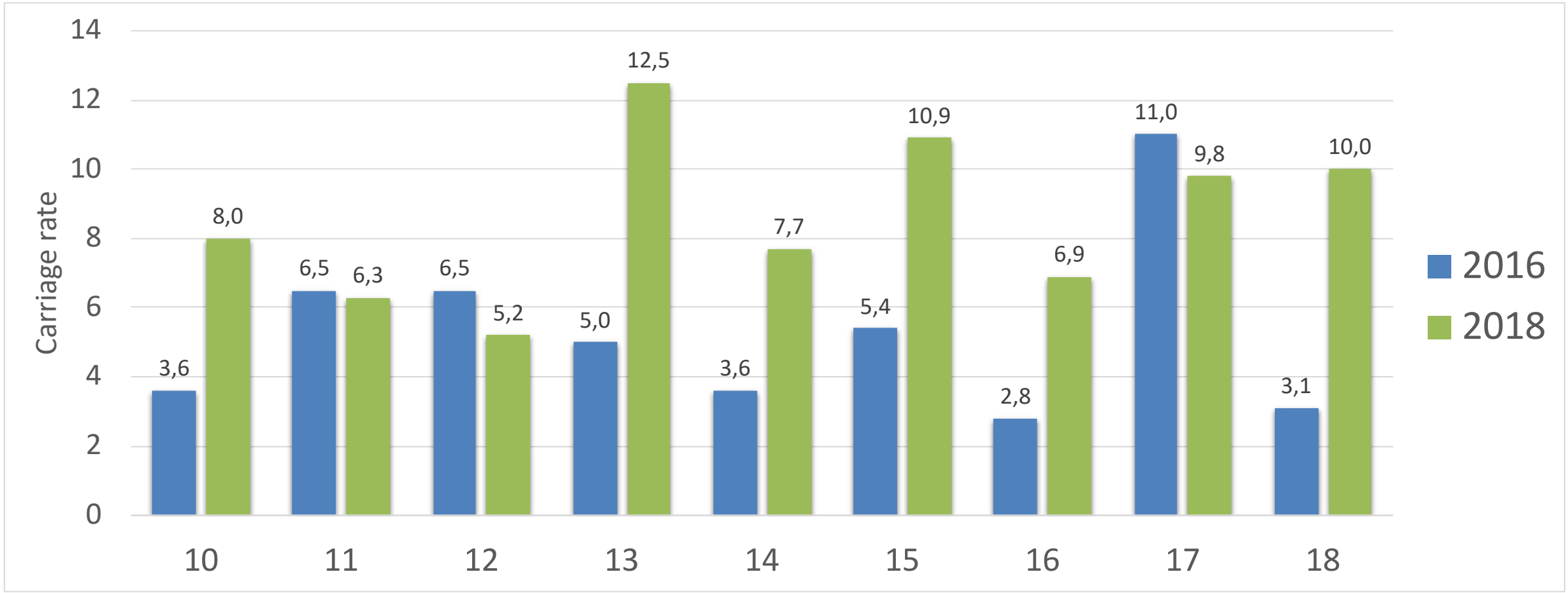
PREVALENCE, SEROGROUP DISTRIBUTION AND RISK FACTORS FOR MENINGOCOCCAL CARRIAGE AMONG CHILDREN AND ADOLESCENTS IN TURKEY-2018: UNEXPECTED-HIGH SEROGROUP X CARRIAGE

Mahmut Can Kizil, Omer Kilic, Mehmet Ceyhan, Merve Iseri Nepesov, Adem Karbuz, Zafer Kurugol, Mustafa Hacimustafaoglu, Meltem Dinleyici, Kursat Bora Carman, Cihangul Bayhan, Yasemin Balliel, Murat Sutcu, Necdet Kuyucu, Meda Kondolot, Soner Sertan Kara, Sevliya Ocal Demir, Ummuhan Cay, Zeynep Gokce Gayretli Aydin, Solmaz Celebi, **Ener Cagri Dinleyici**

29 May 2019, Lisbon, Portugal

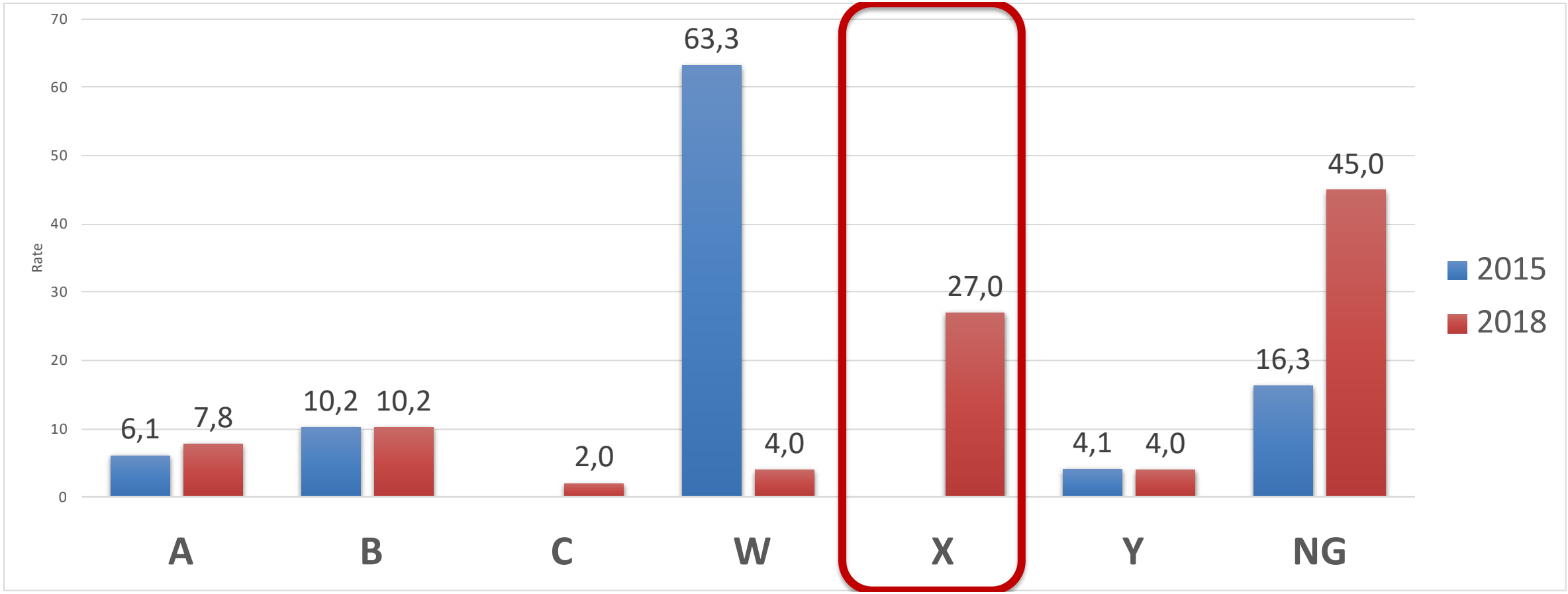
15th EMGM Congress

NAZOFARİNGEAL TAŞIYICILIK
2016 vs. 2018



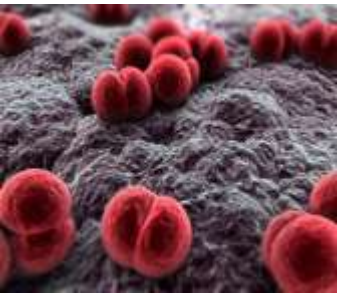
MENINGO-CARR STUDY 1-2

NAZOFARİNGEAL TAŞIYICILIK 2016 vs. 2018



MENINGO-CARR-2 STUDY

Tekin RT et al. Human Vaccine Immunother 2017; Kizil MC et al. EMGM 2019



MENENJİT-SEPSİS KORUNMA

H influenzae[1]
(1 pathogenic type)
INVASIVE DISEASE

S pneumoniae[2]
(25 pathogenic serotypes)
INVASIVE DISEASE

N meningiditis[3]
(5 pathogenic serogroups)
FULMINANT INVASIVE DISEASE

A C W Y B X

HİB AŞILARI

KONJUGE PNÖMOKOK AŞILARI

KUADRİVALAN

KONJUGE MENİNGOKOK AŞILARI

MENİNGOKOK **B** AŞILARI

MENİNGOKOK AŞILARI

ener çağrı dinleyici

Timeline

- 1975: Polysacharide Vaccine MenAC licensed in UK
- 1981: Polysacharide Vaccine MenAC licensed in US
- 1999: MenC conjugate vaccines licensed in EU
- 2005: MenACWY-D conjugate vaccine licensed in the US
- 2009: MenA conjugate vaccine licensed in Africa
- 2010: MenACWY-CRM conjugate vaccine licensed in the US and EU
- 2012: MenACWY-TT conjugate vaccine licensed in EU
- 2013: 4CMenB protein vaccine licensed in the EU
- 2014: Bivalent RLp2086 protein vaccine licensed in US

MENİNGOKOK AŞILARI

AŞI	TAŞIYICI PROTEİN	SEROGRUP	DİĞER ANTİJENLER	
Nimenrix™	TT	A, C, W-135, Y	–	Pfizer
Menveo™	CRM_{197}	A, C, W-135, Y	–	GSK
Menactra™	DT	A, C, W-135, Y	–	Sanofi Pasteur
Neisvac-C™	TT	C	–	Baxter
Meningitec™	CRM_{197}	C	–	Nuron
Menjugate™	CRM_{197}	C	–	
Menitorix™	TT	C	*Haemophilus* type b	GSK
Menhibrix™	TT	C,Y	*Haemophilus* type b	GSK
MenAfriVac™	TT	A	–	Meningitis Vaccine Project
Mencevax™	–	A, C, W-135, Y	–	
Bexsero™	–	B	–	GSK
Trumenba	–	B	–	Pfizer

MEN ACWY-TT
NİMENRİX

- Serogrup A,C,W,Y içeren dört bileşenli konjuge meningokok aşısı
- Taşıyıcı protein: Tetanoz toksoidi (TT)
- Adjuvan ve thimerosal içermez
- İntramuskuler olarak uygulanır.

NİMENRİX, Türkiye'de 13.12.2017 tarihinde, 6. haftadan itibaren sağlıklı bebekler için, *N. meningitidis* A,C,W,Y serogruplarının neden olduğu İnvaziv Meningokok Hastalığına karşı aktif immünizasyon endikasyonu için ruhsat almıştır. 72 ülke , 52 ülke infant

6 -12 haftalık bebekler

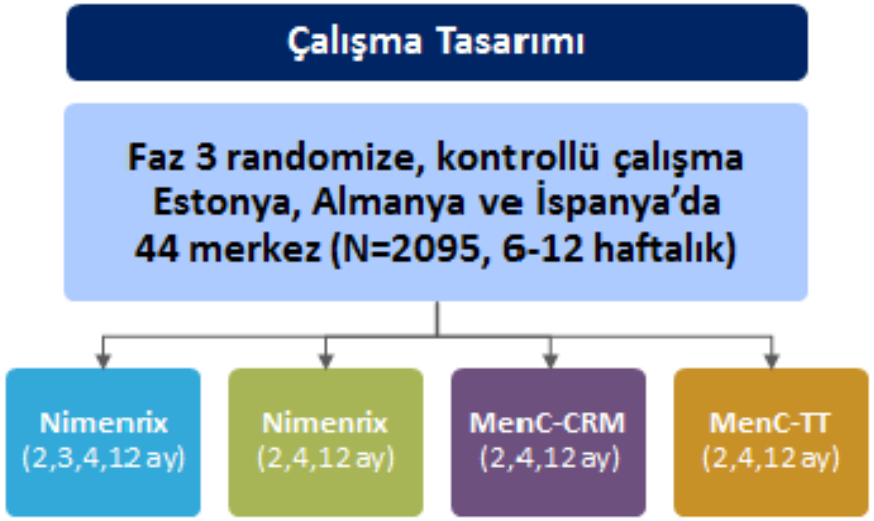
Doz 1	Doz 2	Rapel Doz
0 ay	2 ay	12. ay

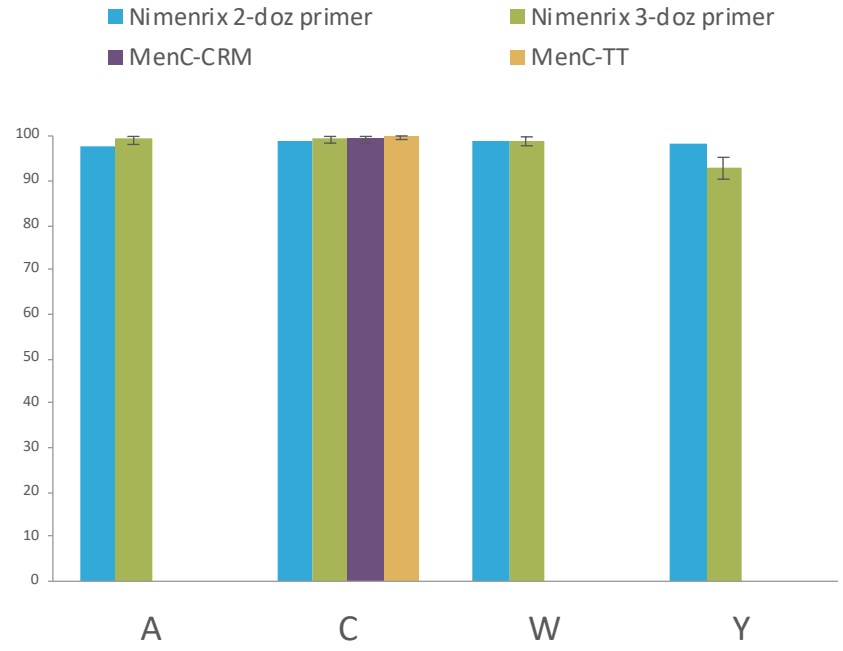
≥12 ay çocuklar, adolesanlar ve erişkinler

1 doz

MEN ACWY-TT
NİMENRİX
İMMUNOJENİSİTE

6-12 HAFTALIK BEBEKLERDE MENACWY-TT AŞISI





6-12 Haftalık İnfantlarda, Nimenrix (MenACWY-TT) 2- ya da 3- doz Primer Serisini Takiben Benzer Güçlü İmmün Yanıt

MEN ACWY-TT
NİMENRİX
İMMUNOJENİSİTE

ener çağrı dinleyici

12 AY BEBEKLERDE
TEK DOZ MENACWY-TT İMMUNOJENİK VE GÜVENİLİR

Vaccine 34 (2016) 3363–3370

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Safety and immunogenicity of a CRM or TT conjugated meningococcal vaccine in healthy toddlers

Gianni Bona[a], Paolo Castiglia[b], Giorgio Zoppi[c], Maurizio de Martino[d], Annaelisa Tasciotti[e], Diego D'Agostino[f], Linda Han[g], Igor Smolenov[f,*]

2-10 YAŞ ARASI ÇOCUKLARDA TEK DOZ MENACWY-TT İMMUNOJENİK VE GÜVENİLİR

Eur J Pediatr (2013) 172:601–612
DOI 10.1007/s00431-012-1924-0

ORIGINAL ARTICLE

Immunogenicity and safety of the quadrivalent meningococcal serogroups A, C, W-135 and Y tetanus toxoid conjugate vaccine (MenACWY-TT) in 2–10-year-old children: results of an open, randomised, controlled study

Markus Knuf · Olivier Romain · Klaus Kindler · Uta Walther · Phu-My Tran · Heidemarie Pankow-Culot · Thomas Fischbach · Dorothee Kieninger-Baum · Véronique Bianco · Yaela Baine · Jacqueline Miller

MEN ACWY-TT
NİMENRİX
İMMUNOJENİSİTE

ener çağrı dinleyici

10-25 YAŞ ARASI ADÖLESAN VE GENÇ ERİŞKİNLERDE TEKDOZ MENACWY-TT İMMUNOJENİK VE GÜVENİLİR

ORIGINAL STUDIES

Immunogenicity and Safety of an Investigational Quadrivalent Meningococcal ACWY Tetanus Toxoid Conjugate Vaccine in Healthy Adolescents and Young Adults 10 to 25 Years of Age

Roger Baxter, MD, Yaela Baine, PhD,† Kathleen Ensor, BA, RN,* Veronique Bianco, MS,‡ Leonard R. Friedland, MD,† and Jacqueline M. Miller, MD†*

11-55 YAŞ ARASI ERİŞKİNLERDE TEK DOZ MENACWY-TT İMMUNOJENİK VE GÜVENİLİR

Borja-Tabora *et al. BMC Infectious Diseases* 2013, **13**:116
http://www.biomedcentral.com/1471-2334/13/116

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Immune response, antibody persistence, and safety of a single dose of the quadrivalent meningococcal serogroups A, C, W-135, and Y tetanus toxoid conjugate vaccine in adolescents and adults: results of an open, randomised, controlled study

Charissa Borja-Tabora[1], Cecilia Montalban[2], Ziad A Memish[3*], Marie Van der Wielen[4], Veronique Bianco[4], Dominique Boutriau[4] and Jacqueline Miller[5]

MEN ACWY-TT
NİMENRİX
İMMUNOJENİSİTE

ener çağrı dinleyici

56-103 YAŞ DENEYİMLİ ERİŞKİNLERDE
TEK DOZ MENACWY-TT İMMUNOJENİK VE GÜVENİLİR

Drugs Aging (2013) 30:309–319
DOI 10.1007/s40266-013-0065-0

ORIGINAL RESEARCH ARTICLE

Immunogenicity and Safety of a Quadrivalent Meningococcal Serogroups A, C, W-135 and Y Tetanus Toxoid Conjugate Vaccine (MenACWY-TT) Administered to Adults Aged 56 Years and Older: Results of an Open-Label, Randomized, Controlled Trial

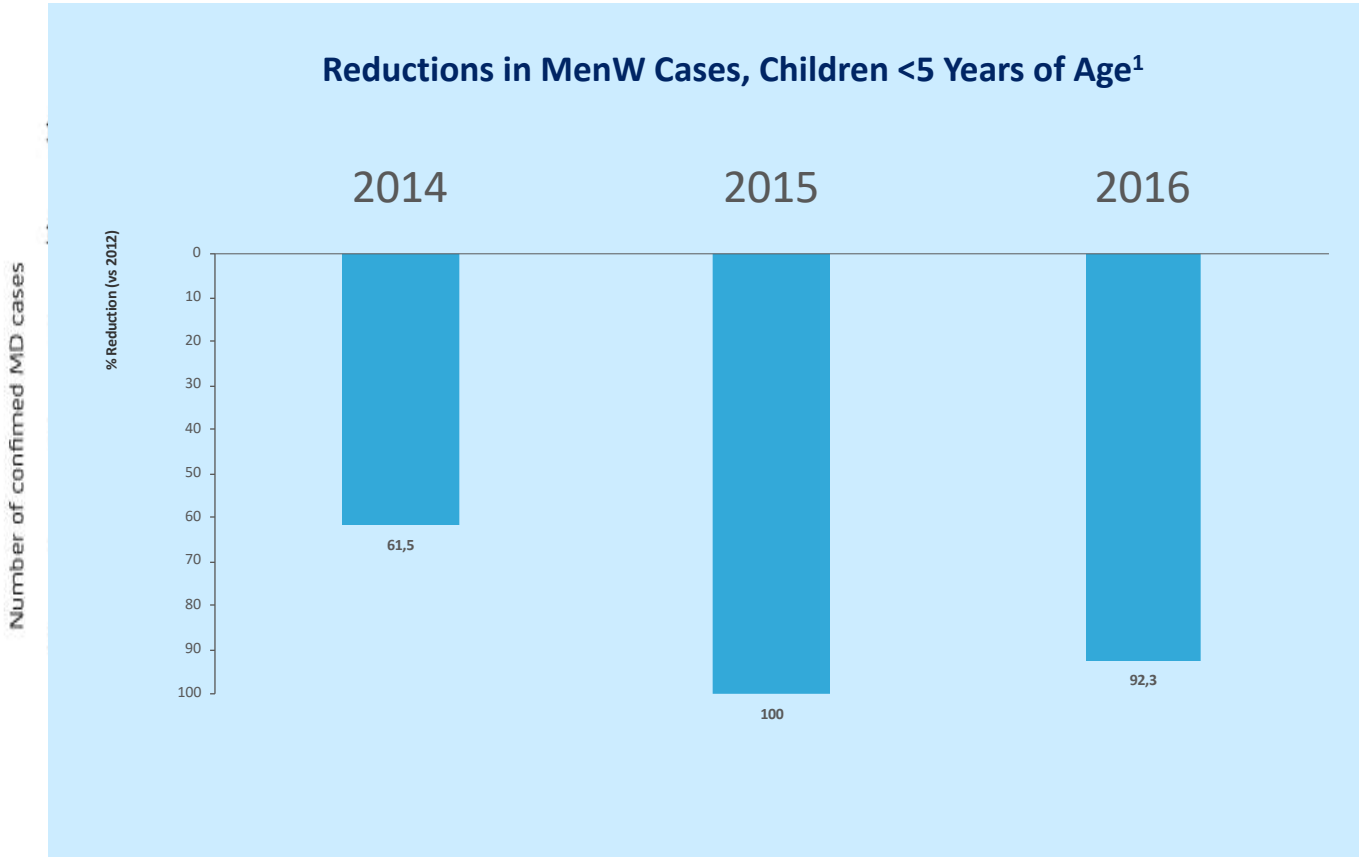
Ghassan Dbaibo · Nabil El-Ayoubi · Soha Ghanem · Farah Hajar · Veronique Bianco · Jacqueline M. Miller · Narcisa Mesaros

MEN ACWY-TT

NİMENRİX

RUTİN TAKVİM

- ŞİLİ: 12. AYDA TEK DOZ
- AVUSTRALTA: 12. AYDA TEK DOZ
- HOLLANDA: 14. AYDA TEK DOZ
- YUNANİSTAN: ERGEN
- İTALYA: ERGEN
- İNGİLTERE: ERGEN
- HOLLANDA: ERGEN



MEN ACWY-D

MENACTRA

- İNFANT DÖNEMİNDE AŞILAMA (9 AY-2 YAŞ)
- ÇOCUKLUK ÇAĞINDA AŞILAMA
- ADÖLESAN VE GENÇ ERİŞKİNLERDE AŞILAMA
- ERİŞKİNLERDE AŞILAMA

MEN ACWY-D

MENACTRA

- 0.5 ml tek doz olan aşı
  - Her serogruptan 4 g içermekte (A, C, Y, W135) ve kapsül polisakaritler
  - 4.8 g difteri toksoidine konjuge edilmiştir.
  - Adjuvan ya da prezervatif içermemektedir.
  - İntramuskuler uygulanmaktadır.

- Dünyada **67** ülkede ruhsatlı
- **12 YILDIR** KULLANIMDA
- **90** milyon dozdan fazla aşı kullanılmış durumda.

- 2005 yılında FDA tarafından onay almıştır.
- 2005yılında ACIP tarafından
  - 2-55 yaş arası grupta meningokok enfeksiyonu için risk grubu oluşturanlarda kullanımı ve 11-12 yaş grubundaki tüm adölesanlara uygulanmaya başlamıştır.
- Ülkemizde 9 ay -55 yaş arasında ruhsatlı

MEN ACWY-D

MENACTRA

- Adölesanlarda yapılan çalışmalarda MenACWY-D sonrasında antikor titrelerinin yüksek olduğu ve rapel doz MenACWY-D yapılan olgularda antikor yanıtının serogrup A dışındaki serogruplara ilk kez aşı uygulanan kişilere göre daha yüksek olduğu gösterilmiştir.
- MenACWY-D ile diğer **Td VE Tdap** aşılarının birlikte uygulanmasında etkinlik ve güvenirlik açısından sorun bulunmamaktadır.
- MenACWY-D ile diğer adölesan dönemde uygulanan aşılar ile ilgili (**Hepatit A ve B, HPV gibi**) henüz veri bulunmamaktadır.

MEN ACWY-D

MENACTRA

Vaccine 34 (2016) 5273–5278

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Safety and immunogenicity of a booster dose of meningococcal (groups A, C, W, and Y) polysaccharide diphtheria toxoid conjugate vaccine

Corwin A. Robertson [a,*], David P. Greenberg [a,b], James Hedrick [c], Michael Pichichero [d], Michael D. Decker [a,e], Martha Saunders [f]

Conclusions: Booster vaccination with MenACWY-D was safe and induced robust bactericidal antibody responses, consistent with immune memory, among adolescents and adults 4–6 years after primary vaccination.

MEN ACWY-D

MENACTRA

GÜVENLİK

ener çağrı dinleyici

MenACYW-DT : Post-Licensure Safety Experience

- The Kaiser Permanente study - 2005-2006 among >30,000 members
  - **Conclusion:** "We did not identify any serious, clinically meaningful safety concerns"
- The Harvard study involved 12.5 million adolescents who received 1.4 million doses from 2005-2008
  - **Conclusion:** MenACYW-DT vaccine "was not associated with increased GBS risk"
- The Vaccine Safety Datalink study - additional 0.9 million doses among adolescents and confirmed and extended the preceding results, providing further assurance regarding the safety of MenACYW-DT vaccine.

[1]Zhang. ID Week 2012, Abstract #378, San Diego, October 18, 2012; [2]Valentgas. *Pharmacoepidemiol Drug Saf.* 2012;21(12)
[3]Yih. *Pharmacoepidemiol Drug Saf.* 2012;21(12);

MEN ACWY-CRM 197

- İNFANT DÖNEMİNDE AŞILAMA (2 AY-2 YAŞ)
- ÇOCUKLUK ÇAĞINDA AŞILAMA
- ADÖLESAN VE GENÇ ERİŞKİNLERDE AŞILAMA
- ERİŞKİNLERDE VE YAŞLILARDA AŞILAMA

MEN ACWY-CRM197

İNFANT

DİĞER ÇOCUKLUK ÇAĞI AŞILARI İLE UYGULANABİLME

2-12 AY

- DTaP
- IPV
- Hib
- HBV
- PCV7
- PCV13

- **12-24 AY**
- MMR + suçiçeği
- MMRV
- Hepatit A
- PCV7
- PCV13

Klein NP, et al. *Pediatr Infect Dis J*. 2012;31:64-71;
Tregnaghi M, et al. ESPID Annual Meeting; June 7-11, 2011; The Hague;
Klein NP, et al. *Vaccine*. 2012;30:3929-3936.

MEN ACWY-CRM197

ADÖLESAN

11-17 YAŞ ARASINDA MEN ACWY-CRM ile MPSV4 KARŞILAŞTIRMASINDA, MEN ACWY-CRM İYİ TOLERE EDİLMİŞ, LOKAL VE SİSTEMİK YAN ETKİLER KABUL EDİLEBİLİR DÜZEYDEDİR.

11-17 YAŞ ARASINDA MEN ACWY-CRM ile MEN ACWY-D KARŞILAŞTIRMASINDA, MEN ACWY-CRM İYİ TOLERE EDİLMİŞ, LOKAL VE SİSTEMİK YAN ETKİLER KABUL MEN ACWY-D İLE BENZERDİR

Jackson LA, et al. *Pediatr Infect Dis J*. 2009;28:86-91.

Jackson LA, et al. *Clin Infect Dis*. 2009;49:e1-e10.

MEN ACWY-CRM197

ERİŞKİN

19-55 YAŞ ARASINDA MEN ACWY-CRM ile MEN ACWY-D KARŞILAŞTIRMASINDA, MEN ACWY-CRM İYİ TOLERE EDİLMİŞ, LOKAL VE SİSTEMİK YAN ETKİLER KABUL MEN ACWY-D İLE BENZERDİR

56-65 YAŞ ARASINDA MEN ACWY-CRM ile MPSV4 KARŞILAŞTIRMASINDA, MEN ACWY-CRM İYİ TOLERE EDİLMİŞ, LOKAL VE SİSTEMİK YAN ETKİLER KABUL EDİLEBİLİR DÜZEYDEDİR.

*.

Stamboulian D, et al. *Int J Infect Dis.* 2010;14:e868-e875;

Reisinger KS, et al. *Clin Vaccine Immunol*. 2009;16:1810-1815.

MEN ACWY-CRM197
İSTENMEYEN ETKİ

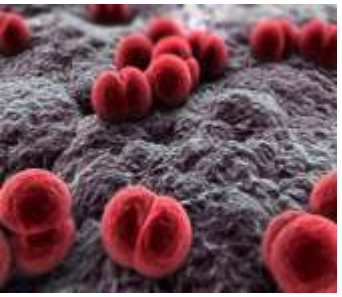
Safety of Quadrivalent Meningococcal Conjugate Vaccine in 11- to 21-Year-Olds
Hung-Fu Tseng, Lina S. Sy, Bradley K. Ackerson, Rulin C. Hechter, Sara Y. Tartof, Mendel Haag, Jeffrey M. Slezak, Yi Luo, Christine A. Fischetti, Harp S. Takhar, Yan Miao, Marianne Cunnington, Zendi Solano and Steven J. Jacobsen
Pediatrics 2017;139;
DOI: 10.1542/peds.2016-2084 originally published online December 26, 2016;

- **48.899 MENVEO**
- 11-21 yaş arasındaki genç 1 yıl süre ile takip edilmiş
  - 21 farklı klinik durum izlenmiş (nörolojik, romatolojik, hematolojik, endokrin, renal, infeksiyon hastalıkları).
- **Hiçbir yan etki bildirimi olmamış.**
- Sadece geçici yüz felci (Bell's Palsy) ile istatistik ilişki? Diğer aşılar ile birlikte uygulanması durumunda saptanmış, tek başına uygulamada rastlanmamış.

MEN ACWY-CRM197

RUTİN TAKVİM?

- ARJANTİN
- 3 ve 5. aylarda iki doz aşılama
- 15.ayda pekiştirme dozu
- 11 yaş adölesanlarda aşılama



MENİNGOKOK B AŞILARI

ener çağrı dinleyici

Table 1. Outer membrane vesicle vaccines licensed for clinical use.

OMV type	Trade name	Countries employing	Number of doses administered
Finlay 4:P1.19, 15	VA-MENGOC-BC®	Cuba, Chile and Brazil	2
NIPH 15:P1.7, 16	MenBVac®	Norway and France	3
NIPH/Novartis 4:P1.7–2,4	MeNZB®	New Zealand	3

OMV: Outer membrane vesicle.

Table 2. Examples of subcapsular proteins under investigation for use in meningococcal serogroup B vaccines.

Protein(s)	Type of vaccine	Latest research stage initiated
Single PorA	wtOMV	Licensed for use against specific clonal groups
Multiple PorA	Recombinant OMV	Early clinical trials
OpcA	OMV	Early clinical trials
Bivalent PorA with fHbp and NadA	Multicomponent	Early clinical trials
Bivalent fHbp	Multicomponent	Advanced clinical trials
fHbp with NadA and NHBA (rMenB)	Multicomponent	Early clinical trials
rMenB with Norway strain OMV	Multicomponent	Early clinical trials
4CMenB (rMenB with New Zealand strain OMV)	Multicomponent	Application for licensure

MenB: Neisseria meningitidis serogroup B; OMV: Outer membrane vesicle; wtOMV: Wild-type OMV.

MENİNGOKOK B AŞISI
TRUMENBA

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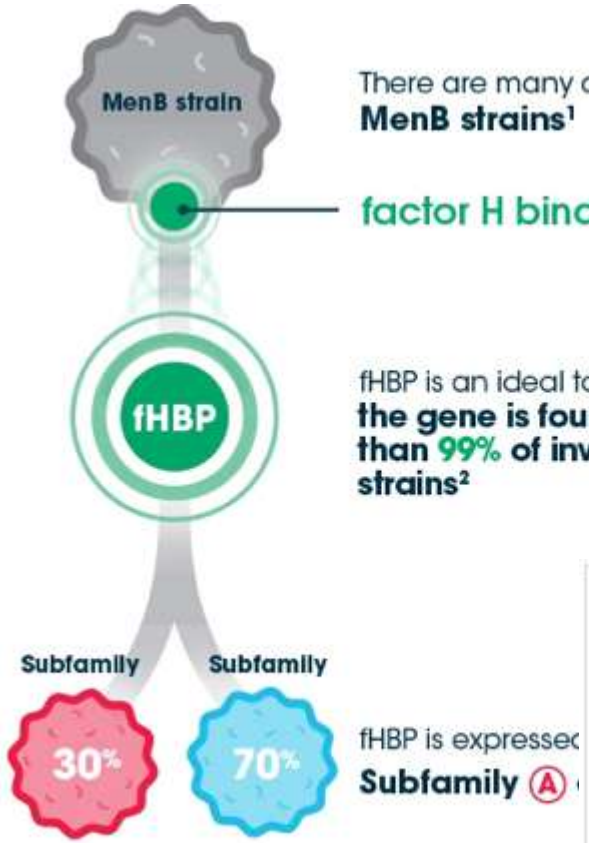


2-Dose Schedule[1*]

Dose 1	Dose 2
0	6
Administer dose at month 0	Administer dose 6 months after the first dose

- If the second dose is administered earlier than 6 months after the first dose, a third dose should be administered at least 4 months after the second dose[1]

dvisory Committee on Immunization Practices

Enroll in the REMEMBER TRUMENBA Program

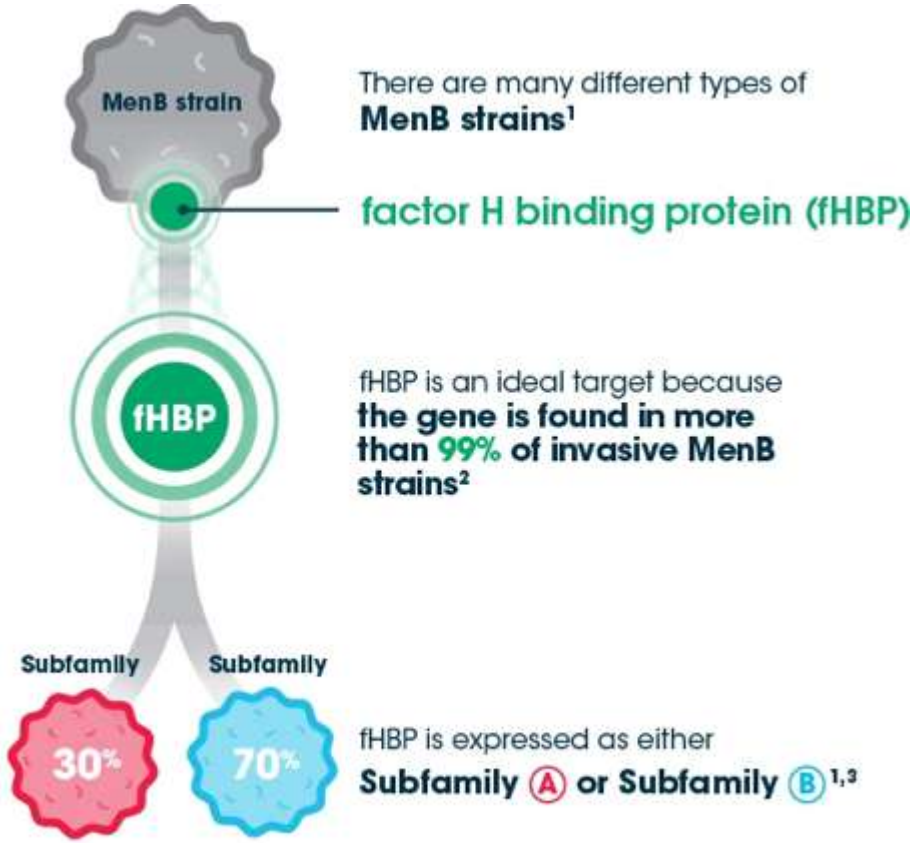
2-dose series – text "TRUMENBA2" to the number 37500

TRUMENBA + HPV4[1]

TRUMENBA + MCV4[1] + Tdap[1]

MENİNGOKOK B AŞISI
TRUMENBA

ener çağrı dinleyici



3-Dose Schedule[1*]

Dose 1	Dose 2	Dose 3
0	1-2	6
Administer dose at month 0	Administer dose 1-2 months after the first dose	Administer dose 6 months after the first dose

ACIP recommends the 3-dose schedule for persons aged ≥10 years, who are in a MenB outbreak situation or at increased risk for meningococcal disease, as a category A recommendation.[§] These persons include those with persistent complement component deficiencies,[‖] those with anatomic or functional asplenia, or microbiologists routinely exposed to isolates of *Neisseria meningitidis*.

Enroll in the REMEMBER TRUMENBA Program

3-dose series – text **"TRUMENBA3"** to the number **37500**

*The choice of dosing schedule may depend on the risk of exposure and the patient's susceptibility to meningococcal serogroup B disease.[1]

†Category B recommendations are made for individual clinical decision-making.

‡Data collected in March 2017 from a survey of 593 young adults (aged 16-21 years) and/or patients/caregivers across the United States.

§Category A recommendations are made for all persons in an age- or risk factor-based group.

‖Including inherited or chronic deficiencies in C3, C5-9, properdin, factor D, factor H, or who are taking eculizumab (Soliris®; Alexion Pharmaceuticals, Inc.).

MENİNGOKOK B AŞISI
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Brief Report

Rapid response to a college outbreak of meningococcal serogroup B disease: Nation's first widespread use of bivalent rLP2086 vaccine

Theresa M. Fiorito , MD, Suzanne Bornschein , MD, Alysia Mihalakos , MPH, Catherine M. Kelleher , RN, Nicole Alexande Scott , MD, MPH, Koren V. Kanadanian , MS, ...show all

Pages 1-3 | Received 20 Jul 2016, Accepted 10 Jan 2017, Accepted author version posted online: 25 Jan 2017, Published online: 25 Jan 2017

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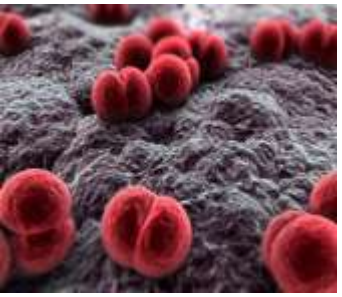
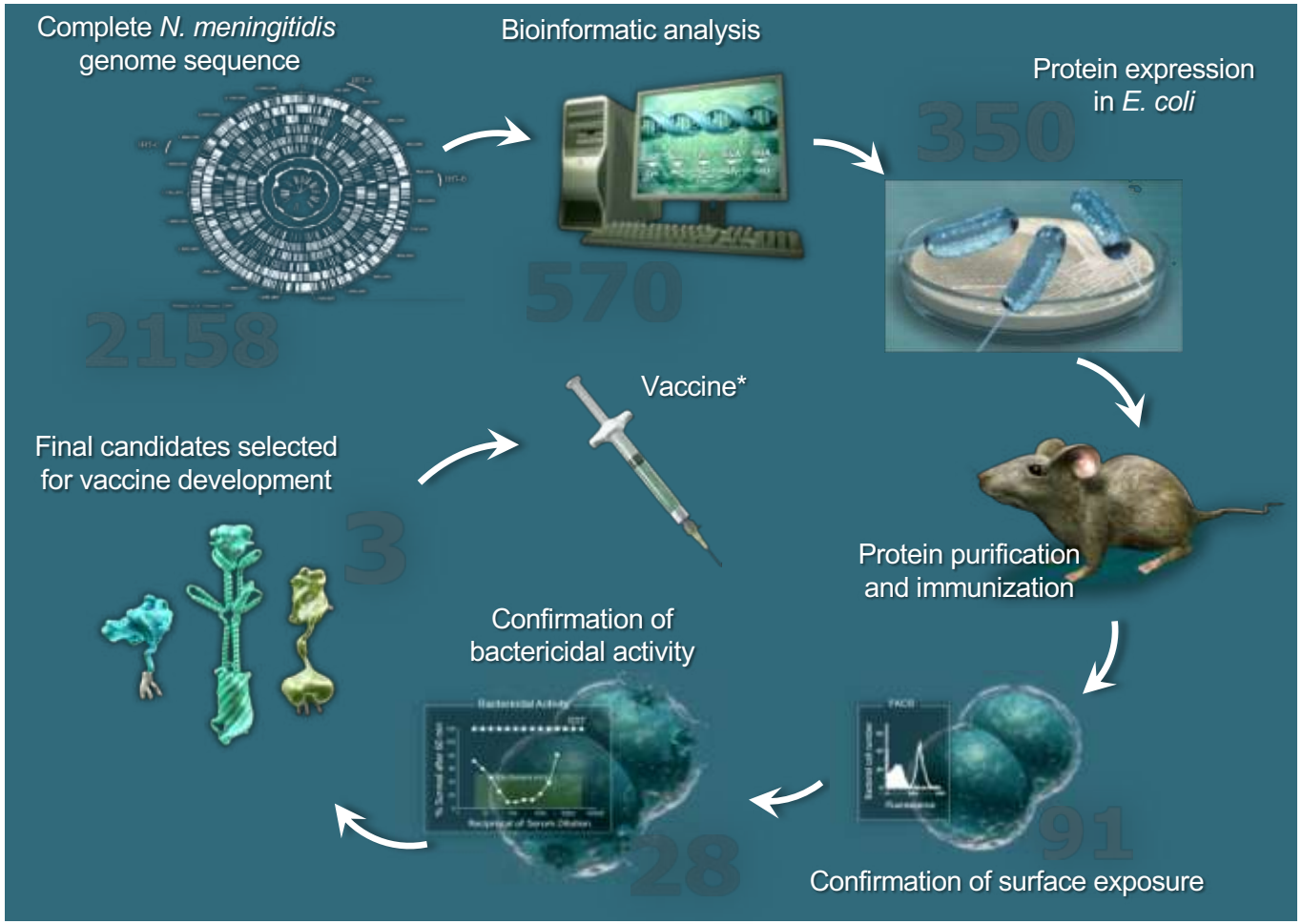


MENİNGOKOK B AŞISI (BEXSERO)

REVERSE VACCINOLOGY



Tettelin H, et al. *Science*. 2000;287:1809-1815; Rappuoli R. *Vaccine*. 2001;19:2688-2691; Pizza M, et al. *Science*. 2000;287:1816-1820.

MENİNGOKOK B AŞILARI

4CMENB- BEXSERO

fHbp: factor H binding protein

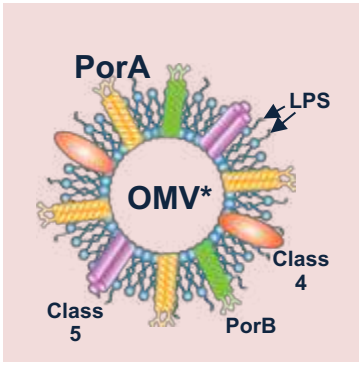
- Binds factor H, which enables bacterial survival in the blood[1,2]

NadA: neisserial adhesin A

- Promotes adherence to and invasion of human epithelial cells[3-5]
- May be important for colonisation[4]

NHBA: neisseria heparin-binding antigen

- Binds heparin, which may promote bacterial survival in the blood[7]
- Present in virtually all strains[6,7]



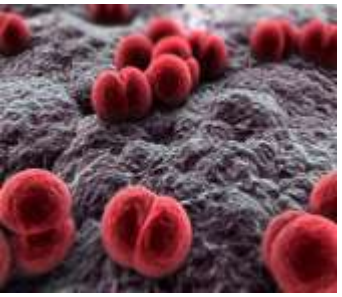
NZ PorA P1.4: porin A

- Major outer membrane vesicle protein—induces strain-specific bactericidal response[8]

MENİNGOKOK B AŞILARI

4CMENB- BEXSERO

- DİĞER ÇOCUKLUK ÇAĞI AŞILARI İLE UYGULANABİLİR.
- LOKAL ENJEKSİYON YAN ETKİLERİ YÖNÜNDEN DİĞER AŞILAR İLE BENZER.
- DİĞER ÇOCUKLUK ÇAĞI AŞILARI İLE BİRLİKTE UYGULANDIĞINDAN LOKAL YAN ETKİ SIKLIĞI ARTMIŞ
- ATEŞ?



MENİNGOKOK B AŞILARI
BEXSERO
KANADA

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Clinical Infectious Diseases

MAJOR ARTICLE

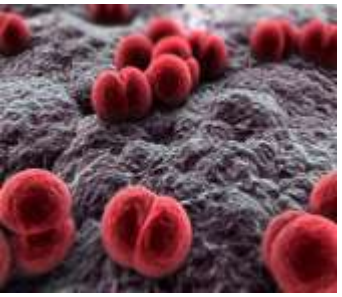
IDSA Infectious Diseases Society of America

hivma hiv medicine association

OXFORD

Impact of an Immunization Campaign to Control an Increased Incidence of Serogroup B Meningococcal Disease in One Region of Quebec, Canada

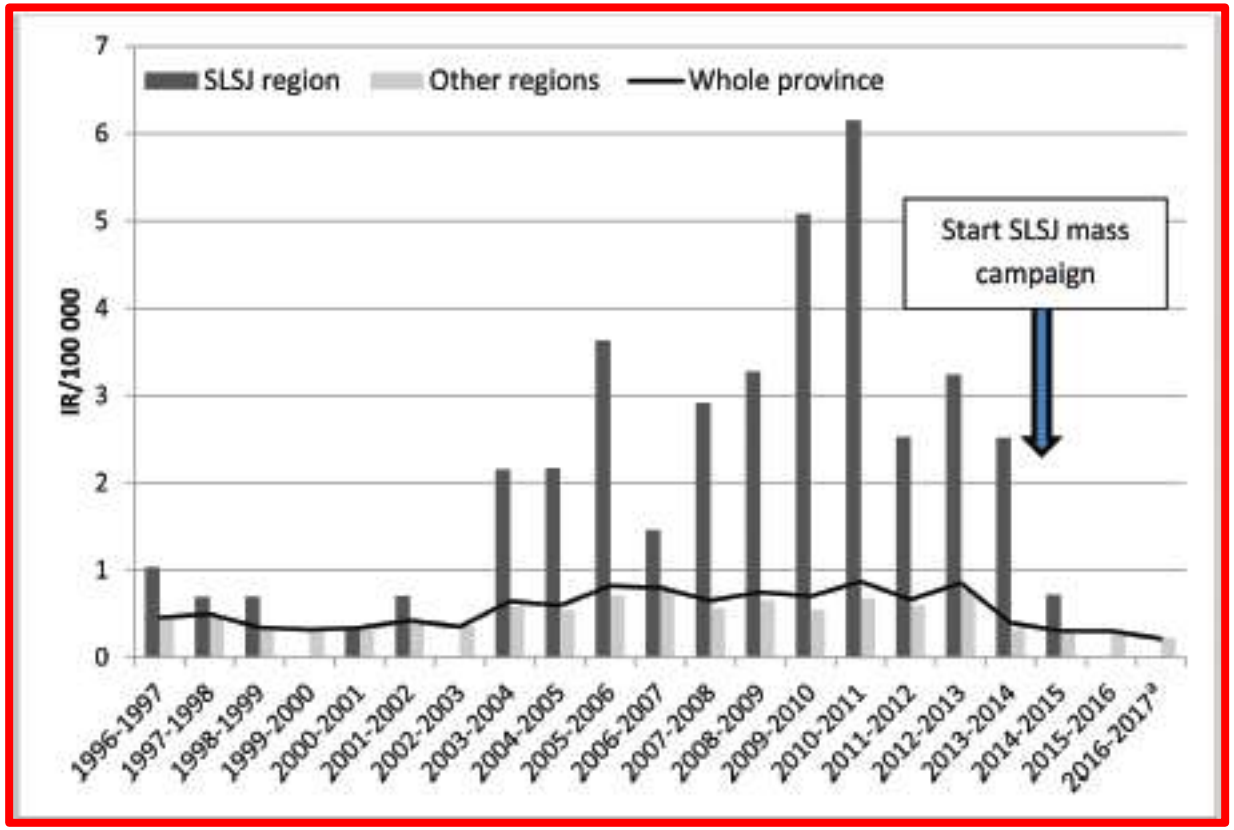
Philippe De Wals,[1,2,3] Geneviève Deceuninck,[3] Brigitte Lefebvre,[4] Raymond Tsang,[5] Dennis Law,[5] Gaston De Serres,[2] Vladimir Gilca,[2] Rodica Gilca,[2] and Nicole Boulianne[2]

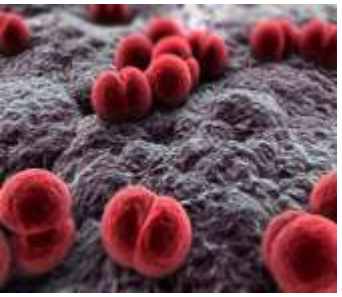


MENİNGOKOK B AŞILARI
BEXSERO
KANADA

Table 1. Uptake of 4-Component Protein-Based Meningococcal Vaccine in the Saguenay-Lac-Saint-Jean Region of Quebec, Canada, According to Age and Number of Doses

	Target	No. of Doses					
Age Group[a]	No.	0	1	2	3	4	≥1
Newborns[b]	2168	7%	2%	2%	7%	82%	93%
Residents[c]	57205	18%	6%	73%	2%	1%	82%
2–5 mo	831	6%	2%	4%	23%	65%	94%
6–11 mo	1277	8%	2%	22%	67%	...	92%
1–4 y	11024	14%	6%	80%	...	...	86%
5–11 y	18919	7%	3%	91%	...	...	93%
12–16 y	12997	8%	6%	86%	...	...	92%
17–20 y	12157	53%	14%	34%	...	...	47%
All ages	59373	18%	6%	70%	2%	4%	82%





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KÜBA

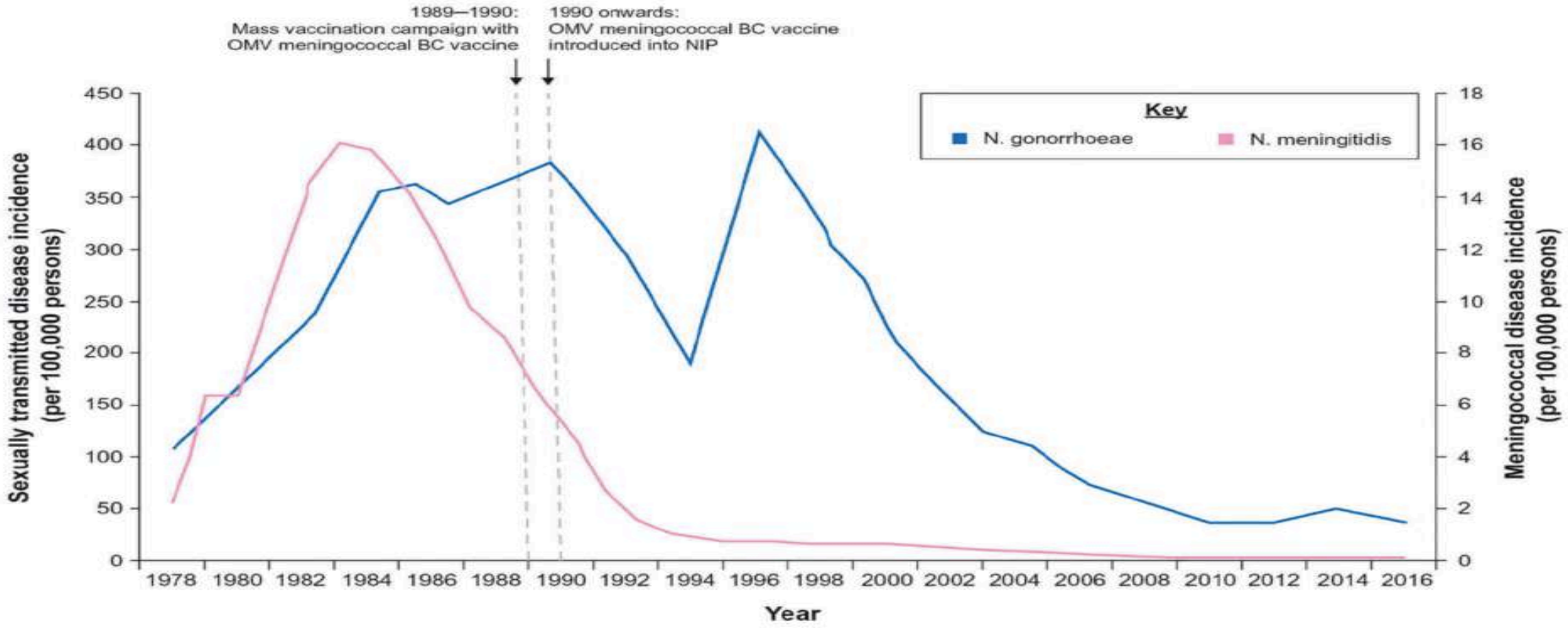

Figure 3. Incidence of *N. gonorrhoeae* vs. *N. meningitidis* in Cuba (1978–2016) [130].

MENİNGOKOK AŞILARI

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Results: Approximately 72.9% (n = 247) of the respondents followed a patient with meningitis in the last year. A 49.5% of participants preferred to perform computerized cranial tomography (CCT) for suspected meningitis cases before lumbar puncture (LP) at 75–100% frequency (27.5% PAS; 72% APS, $p < .01$). In addition 27.1% of the respondents reported using a routine steroid as an adjunctive treatment (19% PAS; 35% APS, $p < .01$). For meningococcal meningitis, 72.5% of the participants preferred to use third-generation cephalosporins (63.1% PAS; 82.1% APS, $p < .05$). For pneumococcal meningitis, approximately 50% of the participants preferred to use a third-generation cephalosporin plus glycopeptide (41.5% PAS; 58.9% APS, $p < .05$). While 32.7% of the sample preferred to administer a 7-day course of antibiotics for meningococcal meningitis, 40.9% preferred a course of 14 days or more. For pneumococcal meningitis, 88.4% of the sample preferred a 10–14 day course of antibiotics. In addition, 67% of the PAS group and 50% ($p < .001$) of the APS group thought that a conjugated meningococcal vaccine should be a part of the National Immunization Program. The top five groups recommended for routine immunization included all children, asplenia/splenectomy patients, immunodeficient patients, those who planned to travel to endemic areas, including Hajj, and military personnel.

Conclusion: In this large convenient sample of physicians in Turkey, we showed that there are heterogenous approaches to the diagnosis and treatment of bacterial meningitis, also differences between pediatricians and non-pediatricians regarding their beliefs and attitudes, which may be due to differences in the epidemiology and clinical presentation between children and adults. We observed appropriate but unnecessary extended courses of antibiotics for meningitis. Most of the participants thought that children are a vulnerable risk group that should potentially be immunized and that meningococcal vaccines should be included in the National Immunization Program. Our results imply that more awareness is needed regarding diagnosis, treatment, and further recommendations for meningitis at the country level in Turkey.

HUMAN VACC
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RESEARCH

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Table 4. Ten risk groups who are recommended for routine meningococcal vaccines.

	PAS Group (n = 171)	APS Group (n = 168)	Total (n = 339)
1	All children 16.3%	Asplenia/splenectomy patients 16.8%	All children 14.4%
2	Children < 2 years of age 5.8%	Immunodeficient patients 13.0%	Asplenia/splenectomy patients 9.7%
3	Children < 1 year of age 5.8%	All children 8.9%	Immunodeficient patients 9.7%
4	Adolescents 5.8%	Travel to endemic areas, Hajj/Umrah 8.3%	Travel to endemic areas, Hajj/Umrah 6.7%
5	Asplenia/splenectomy patients 5.2%	Dormitory 6.5%	Military service 3.8%
6	Children < 5 years of age 5.2%	Military service 5.9%	Children < 5 years of age 3.5%
7	Travel to endemic areas, Hajj/Umrah 4.6%	Nursing home* 4.7%	Children < 2 years of age 3.5%
8	Immunodeficient patients 4.0%	> 65 years of age 4.1%	Children < 1 year of age 3.2%
9	All age groups 4.0%	Healthcare professionals 2.9%	Dormitory 3.2%
10	Healthcare professionals 2.9%	HIV 2.3%	Adolescents 2.9%

AŞILAR

Excellence is a road, not a destination

Cont'd, 2020. Ener Cagri Dinleyici