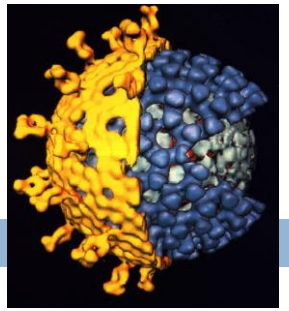
Rotavirus Aşısı

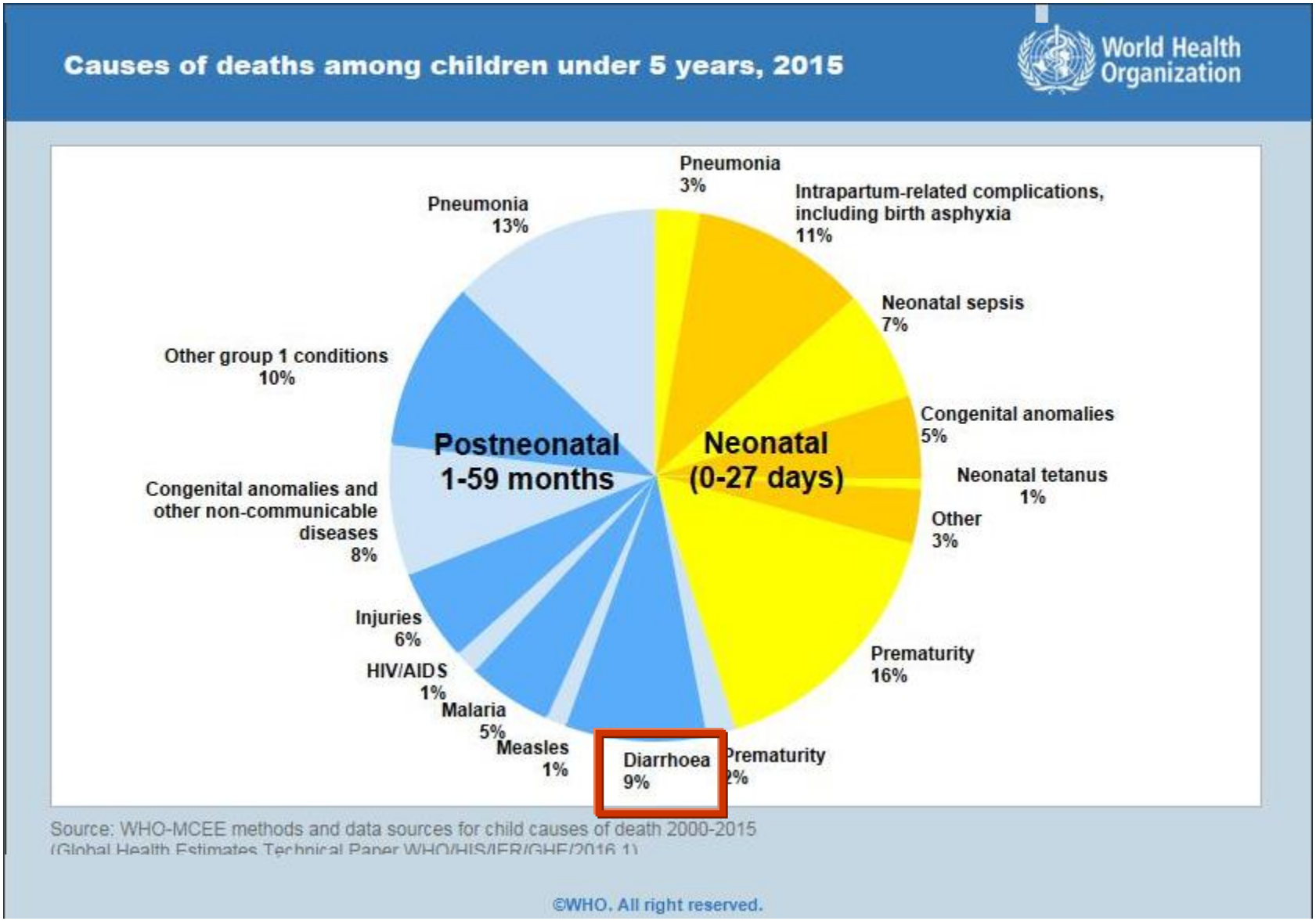
Prof. Dr. Zafer Kurugöl

60. Türkiye Milli Pediatri Kongresi
9 - 13 Kasım 2016, Antalya

Rotavirus



- **Rotaviruslar, dünya genelinde, gelişmiş ve gelişmekte olan ülkelerde, 5 yaş altı çocuklarda görülen ağır gastroenteritin önde gelen nedenidir**
- **Önemli hastalık yüküne sahiptir.**



6.3 milyon 5 yaş altı çocuk ölümünün %51.8'i (3.257 milyon) enfeksiyon hastalıklarından, %44'ü (2.761 million) neonatal ölümler

Global, regional, and national causes of child mortality in 2000–13, with projections to inform post-2015 priorities: an updated systematic analysis

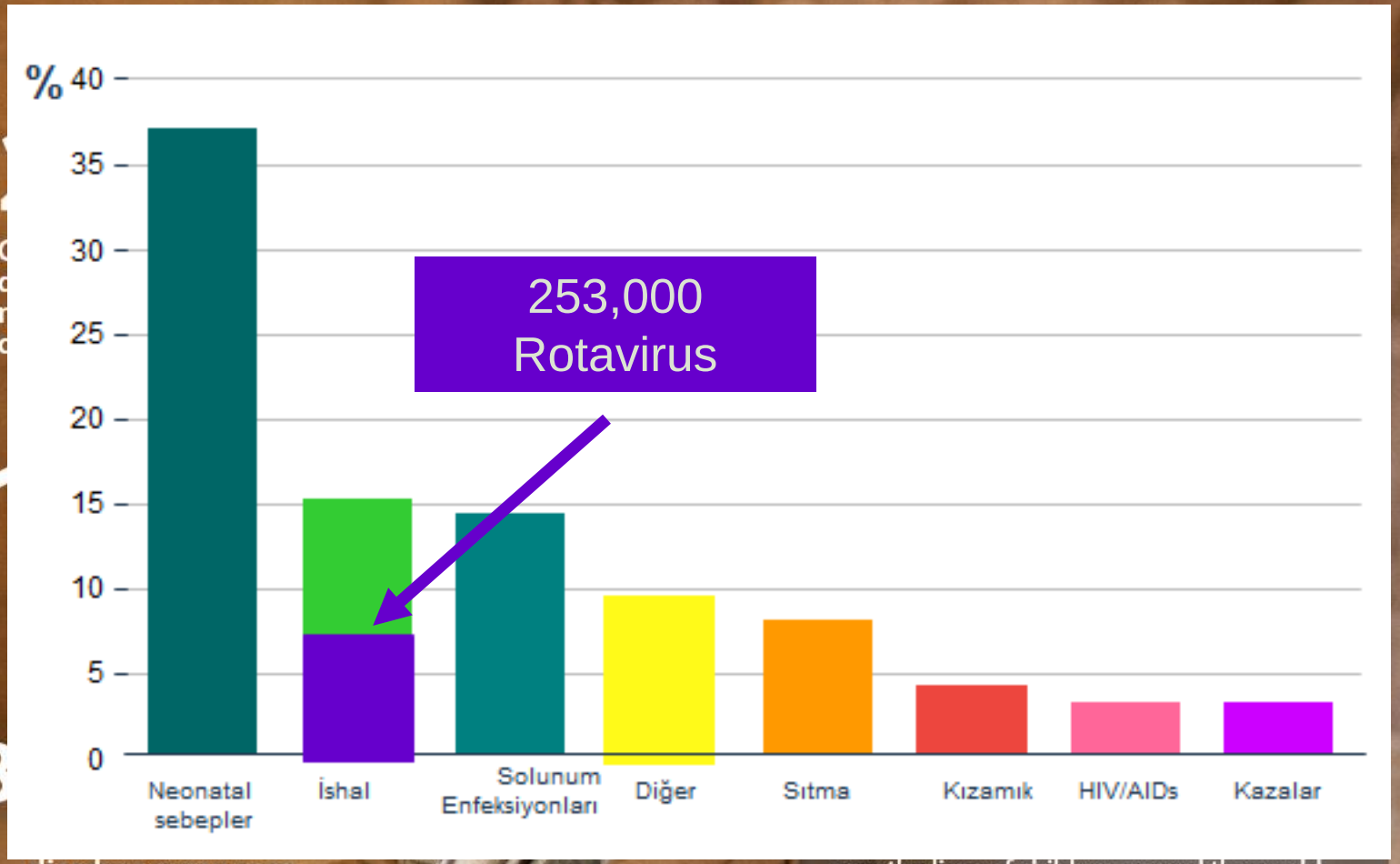
Li Liu, Shefali Oza, Daniel Hogan, Jamie Perin, Igor Rudan, Joy E Lawn, Simon Cousens, Colin Mathers, Robert E Black

6.3 milyon çocuk ölümü < 5 yaş		
51.8% (3.257 milyon) ölüm enfeksiyon hastalıklarından		
Pnömoni	%14.9 (13-16.8)	0.935 milyon (0.817–1.057 milyon)
İshal	**%9.2 (7.1-11.9)**	**0.578 milyon (0.448–0.750 milyon)**
Malarya	%7.3 (5.6-8.7)	0.456 milyon (0.351–0.546 milyon)

Lancet 2015; 385: 430–40

Diarrhea: Common Illness, Global Killer

Diarrhea kills 2,195 children every day—more than AIDS, malaria, and measles combined.



diarrhea every year

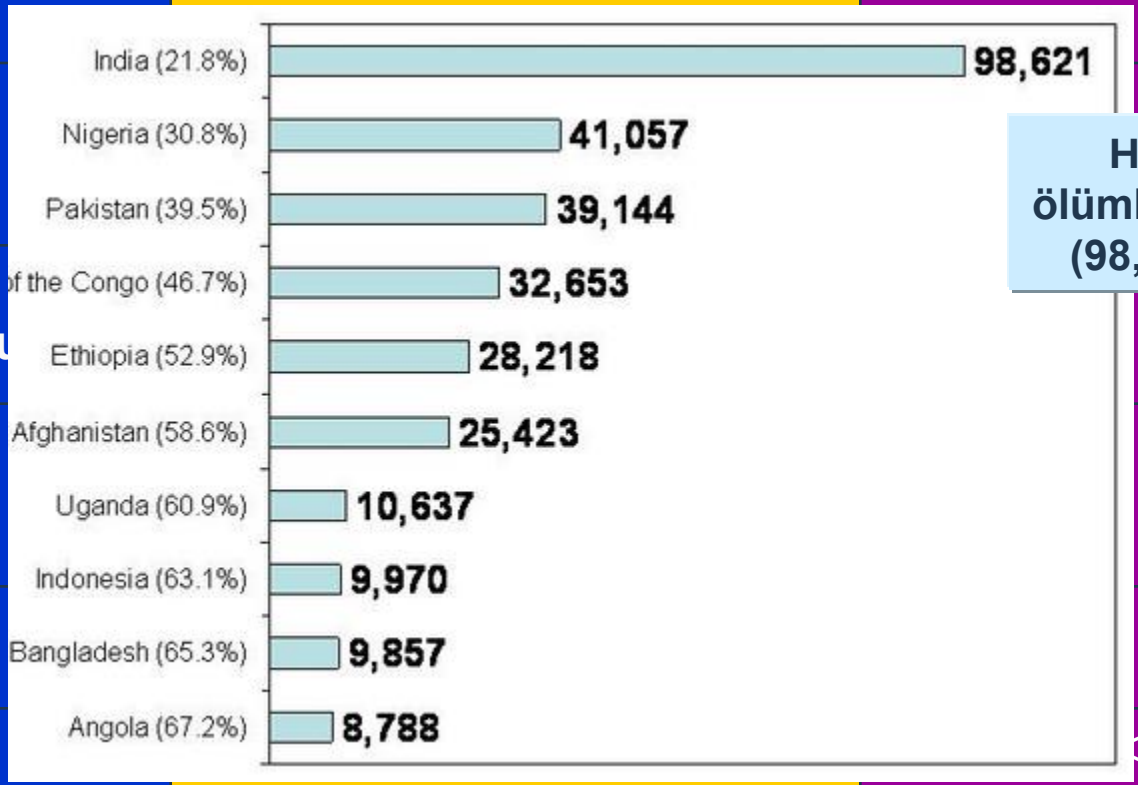
save the lives of children around the world.

WHO-**Global Rotavirus** Surveillance Network.
Lancet Infect Dis. 2012;12:136-41.

World Health Organization

Dünyada rotavirus hastalık yükü

	Gelişmekte Olan Ülkeler	Gelişmiş Ülkeler
İnsidans		
İshal epizodu		
Poliklinik başvu		
Hastane yatışı		
Maliyet		
Mortalite		<1000 ölüm/yıl



Hindistan ölümlerin % 22'si (98,621 ölüm)

WHO. Lancet Infect Dis. 2012;12:136-41.

Dünyada rotavirus hastalık yükü

	Gelişmekte Olan Ülkeler	Gelişmiş Ülkeler
İnsidans	Evrensel	Evrensel
İshal episodu		
Poliklinik başvurusu		
Hastane yatışı		
Maliyet		
Mortalite	Yüksek: 453 000 ölüm/yıl	Düşük: <1000 ölüm/yıl

WHO. Lancet Infect Dis. 2012;12:136-41.

Dünyada rotavirus hastalık yükü

	Gelişmekte Olan Ülkeler	Gelişmiş Ülkeler
İnsidans	Evrensel	Evrensel
İshal episodu		**111 milyon**
Poliklinik başvurusu		**25 milyon poliklinik**
Hastane yatışı		**2 milyon yatış**
Maliyet		**Yüksek (1 milyar ABD $)**
Mortalite	Yüksek: 453 000 ölüm/yıl	Düşük: <1000 ölüm/yıl

WHO. Lancet Infect Dis. 2012;12:136-41.

GÜNCEL ROTAVİRUS AŞILARI

Aşı	Doz	Özellikleri
RV1 (Rotarix)	2 doz	Monovalent canlı attenüe insan RV aşısı, G1P1A[8] RIX4414 suşu
RV5 (RotaTeq)	3 doz	Pentavalent Bovine /Human reassortant RV aşısı, İnsan G1,G2,G3,G4 ; P1A[8] Sığır RV → P7[5] ; G6

Offit et al, Sem Pediatr Infect Dis 2002; 13: 190-195

KLİNİK ETKİNLİK ÇALIŞMALARI

	RV1 (Avrupa)	RV5 (REST)
Ciddi RV enf.	%96	%98
Hastane yatışları	%96	%96
Acil başvurusu	%94	%93
Doktor başvurusu	%84	%86

AAP. Pediatrics 2009; 123: 1412-20.

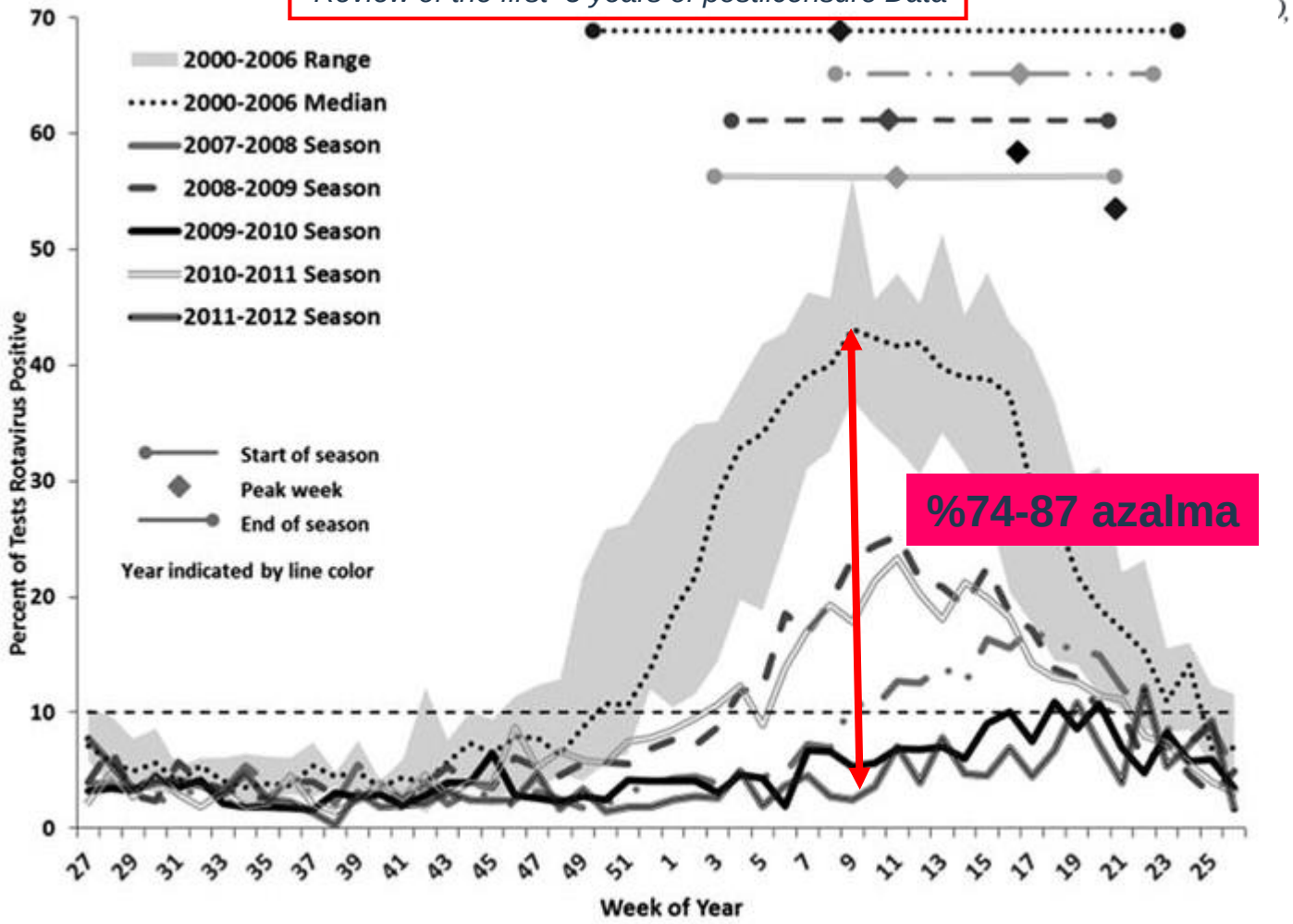
Rotavirus Aşısı Etkinlik (3 yıllık izlem, RV5)

Herhangi bir Rotavirus Serotipine Karşı	Vaka Sayısı	Aşı Grubu	Plasebo	Azalma Oranı (95% CI)
Hastahane Yatış	57,054	15	248	**%94** (90,97)
Acil Başvurusu	57,054	18	298	**%94** (90,96)
Hastahane + Acil	57,054	33	546	**%94** (91,96)

Vesikari T, et al. Eur J Pediatr 2010;169(11):1379-86.

Trends in National Rotavirus Activity Before and After Introduction of Rotavirus Vaccine into the National Immunization Program in the United States, 2000 to 2012

Review of the first 5 years of postlicensure Data



THE JOURNAL OF PEDIATRICS • www.jpeds.com

ORIGINAL ARTICLES

Sustained Effectiveness of Monovalent and Pentavalent Rotavirus Vaccines in Children

Lilly Cheng Immergluck, MD, MS[1,2,3], Trisha Chan Parker, MPH[1,2], Shabnam Jain, MD, MPH[3,4], Elham Laghaie, MS[1,2], Philip Spandorfer, MD[5], Robert C. Jerris, PhD[3,6], Michael D. Bowen, PhD[7], Umesh D. Parashar, MBBS, MPH[7], and Margaret M. Cortese, MD[7]

Objective Using case-control methodology, we measured the vaccine effectiveness (VE) of the 2-dose monovalent rotavirus vaccine (RV1) and 3-dose pentavalent rotavirus vaccine (RV5) series given in infancy against rotavirus disease resulting in hospital emergency department or inpatient care.

Study design Children were eligible for enrollment if they presented to any 1 of 3 hospitals in Atlanta, Georgia with diarrhea ≤10 days duration during January-June 2013 and were born after RV1 introduction. Stool samples were tested for rotavirus by enzyme immunoassay and immunization records were obtained from providers and the state electronic immunization information system. Case-subjects (children testing rotavirus antigen-positive) were

ABD'de 2007-2013 yılları arasında uygulanan RV aşısının RVGE hastane yatışlarını önlemeye direkt etkisi yıllara göre %87-92 arasındadır. İndirekt etkisi de göz önüne alınırsa, total etkinliği %90-100'e ulaşmaktadır.

Conclusions Under routine use, the RV1 and RV5 series were both effective against moderate-to-severe rotavirus disease during a G12P[8] season, and both vaccines demonstrated sustained protection beyond the first 2 years of life. *(J Pediatr 2016;■:■-■).*

RESEARCH ARTICLE Open Access

Burden of community-acquired and nosocomial rotavirus gastroenteritis in the pediatric populati g review

Isla Ogilvie[1], Hanar iaquinto[3]

Abstract

Background: Ro
dehydrating diar
the Western Euro

Methods: A com
WHO, others). Da
–including hospit

Results: 76 studi
caused by rotavir
of RVGE ranged f
among infected
acquired AGE an
medical costs an

cause of severe
astroenteritis (RVGE) in

her sources (CDC;
in Western Europe

enteritis (AGE) cases
winter. Incidence rates
d from 7% to 81%
9% of all hospital-
3.6 million in direct
ping data was available

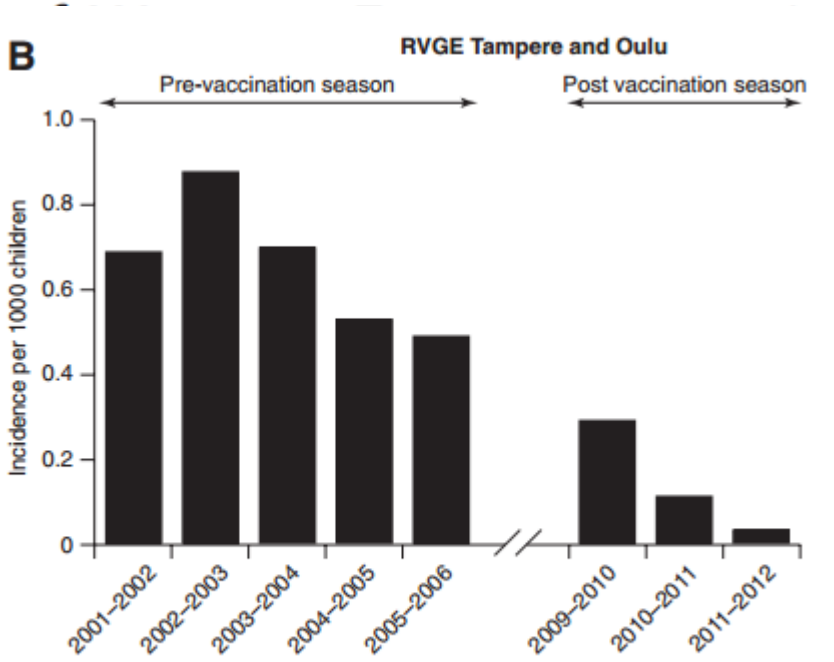


FIGURE 4. Incidence of all-cause AGE and of RVGE per 1000 children by year in Finland (Tampere and Oulu

Both vaccines were able to decrease the number of cases of rotavirus acute gastroenteritis and of severe rotavirus diseases. Vaccination was also associated with a dramatic reduction in hospitalizations and outpatient visits for all-cause acute gastroenteritis. Indirect protection after infant mass vaccination has been strongly suggested.

Keywords: Rotavirus, Burden of illness, Gastroenteritis, Pediatric population

Rutin RV aşılamasının beklenmedik etkisi herd immünite

Bölge	Rotavirüse bağlı hastane başvuruları	
	Aşılamaya uygun yaş grubu	Aşılamaya uygun olmayan yaş grubu
Nationwide, USA[1]	79-81%	69-78%
Nationwide, USA[2]	74-85%	41-80%
Nationwide, USA[3]	87-96%	92%
Queensland, Australia[4]	50-70%	30-70%
Nationwide, Belgium[5]	65-80%	20-64%
Nationwide, Austria[6]	76-79%	35%
São Paulo, Brazil[7]	56-69%	24%
Nationwide, El Salvador[8]	79-86%	41-81%
New South Wales, Australia[9]	51-88%	48-73%
Australian Capital Territory, Australia[9]	59-89%	74-100%

%20-92 azalma

MAJOR ARTICLE

April 15, 2016 62 (8)

Indirect Protection of Adults From Rotavirus by Pediatric Rotavirus Vaccination

Evan J. Anderson,[1,2,3,4,a] Deanna B. Shippee,[1,3] Melissa H. Weinrobe,[1,2,3,4] Melissa D. Davila,[2,4] Ben Z. Katz,[1,3] Susheel Reddy,[2,4] Mary Gene Karen P. Cuyugan,[1,3] Samuel Y. Lee,[1,3] Yael M. Simons,[1,3] Ram Yogev,[1,3] and Gary A. Noskin[2,4]

Departments of [1]Pediatrics and [2]Medicine, Northwestern University Feinberg School of Medicine, Divisions of Infectious Diseases, [3]Children's Memorial Hospital, and [4]Northwestern Memorial Hospital, Chicago, Illinois

Background. Pediatric vaccination has resulted in declines in disease in unvaccinated individuals through decreasing pathogen circulation in the community. About 2 years after implementation of pediatric rotavirus vaccination in the United States, dramatic declines in rotavirus disease were observed in both vaccinated and unvaccinated children. Whether this protection extends to adults is unknown.

Methods. The prevalence of rotavirus, as determined by Rotaclone enzyme immunoassay, in adults who had stools submitted for bacterial stool culture (BSC) between February to May to Northwestern Memorial Hospital, Chicago, was compared between the prepediatric impact era (2006–2007) and the pediatric impact era (2008–2010). Isolates were genotyped and clinical characteristics of those with rotavirus were compared.

Results. Of the 5788 BSC sent, 4725 met inclusion criteria and 3530 of these (74.7%) were saved for rotavirus testing. The prevalence of rotavirus among adults who had stool sent for BSC declined from 4.35% in 2006–2007 to 2.24% in 2008–2010 (a relative decline of 48.4%; $P = .0007$). The decline in the prevalence of rotavirus was of similar significant magnitude in both outpatients and inpatients. Marked year-to-year variability was observed in circulating rotavirus genotypes, with strain G2P[4] accounting for 24%; G1P[8], 22%; G3P[8], 11%; and G12P[6], 10% overall. About 30% of adults from whom rotavirus was isolated were immunocompromised and this remained constant.

Conclusions. Pediatric rotavirus vaccination correlated with a relative decline of almost 50% in rotavirus identified from adult BSC during the peak rotavirus season, suggesting that pediatric rotavirus vaccination protects adults from rotavirus.

Value of Post-Licensure Data on Benefits and Risks of Vaccination to Inform Vaccine Policy

The Example of Rotavirus Vaccines

Umesh D. Parashar, Margaret M. Cortese, Daniel C. Payne, Benjamin Lopman, Catherine Yen, Jacqueline E. Tate

In 1999, the first rhesus-human reassortant rotavirus vaccine licensed in the U.S. was withdrawn within a year of its introduction after it was linked with intussusception at a rate of ~1 excess case per 10,000 vaccinated infants. While clinical trials of 60,000–70,000 infants of each of the two current live oral rotavirus vaccines, RotaTeq (RV5) and Rotarix (RV1), did not find an association

Orta ve yüksek gelir grubundaki ülkelerde (Avrupa, Amerika, Avusturalya gibi) yapılan çalışmalarda, RV aşılarının RV ishaline, özellikle ciddi RV ishaline karşı etkin ve güvenli bir koruma sağladığı gösterilmiştir.

Cochrane Database Syst Rev, 2010 May 12;(5):CD00852 .

Rotavirus

- Rotaviruslar dünya genelinde önemli hastalık yüküne sahiptir,
- Rotavirus aşıları, RV ishaline karşı etkin ve güvenli bir koruma sağlar.
- Birçok önemli kurum (DSÖ, ESPID, ESPGHAN), rotavirus aşılarının tüm dünya ülkelerinin ulusal aşı şemalarına dahil edilmesini önermektedir.

Journal of Pediatric Gastroenterology and Nutrition
46:619–621 © 2008 by European Society for Pediatric Gastroenterology, Hepatology, and Nutrition and
North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition

European Society for Paediatric Gastroenterology, Hepatology, and Nutrition/European Society for Paediatric Infectious Diseases Evidence-Based Guidelines for the Management of Acute Gastroenteritis in Children in Europe: Executive Summary

The European Society for Pediatric Infectious Disease and the European Society for Pediatric Gastroenterology, Hepatology and Nutrition have said they support rotavirus vaccination of infants in Europe.

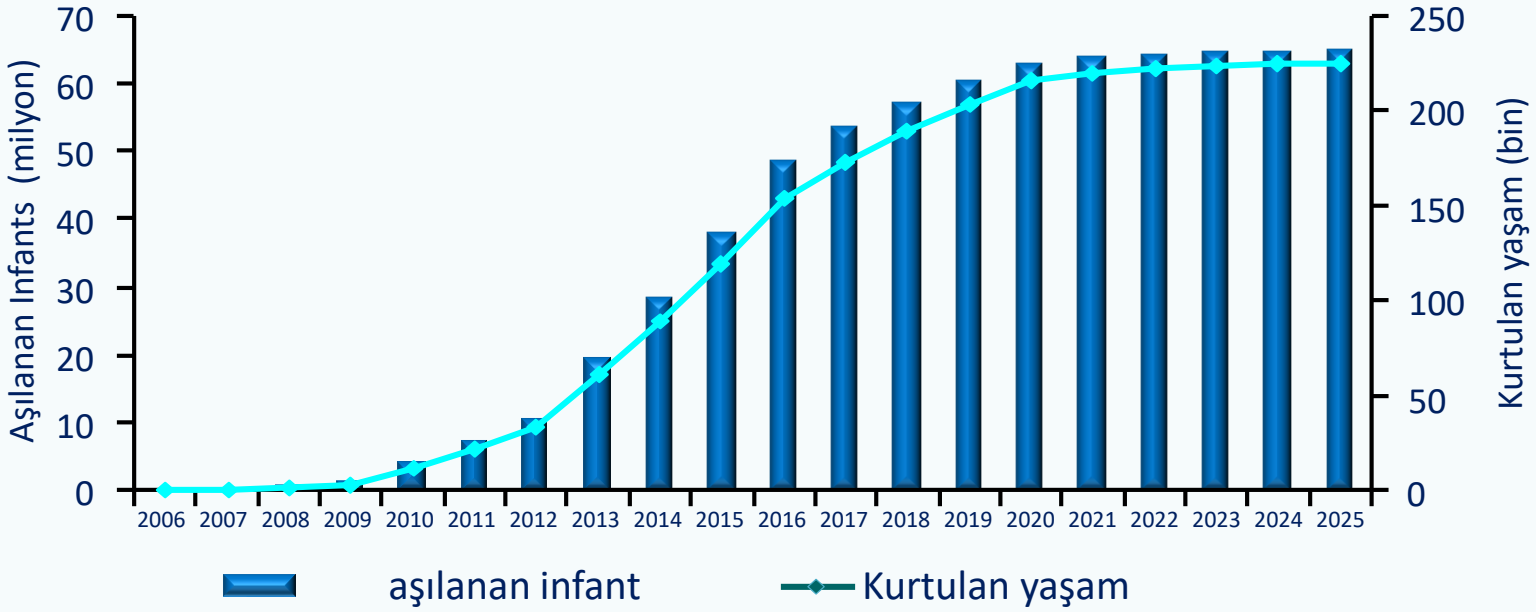
Represented by the ESPID-ESPGHAN Rotavirus Expert Group, they announced during the 25th ESPID Congress in Porto, Portugal, on May 1, the development of evidence-based guidelines to advise physicians on the effective and safe use of rotavirus vaccines in Europe, providing a "framework" for such vaccination programs at a national level.

WHO recommendations

- Rotavirus vaccine for infants should be included in all national immunization programmes.
- In countries where diarrhoeal deaths account for ≥10% of mortality among children aged <5 years, the introduction of the vaccine is strongly recommended.
- WHO recommends that the first dose of either RotaTeq® or Rotarix™ be administered at age 6–15 weeks.
- The maximum age for administering the last dose of either vaccine should be 32 weeks.
- It is recommended that 2 doses of Rotarix™ be administered with the first and second doses of DTP rather than with the second and third doses. This ensures maximum immunization coverage and reduces the potential for late administration beyond the approved age window.

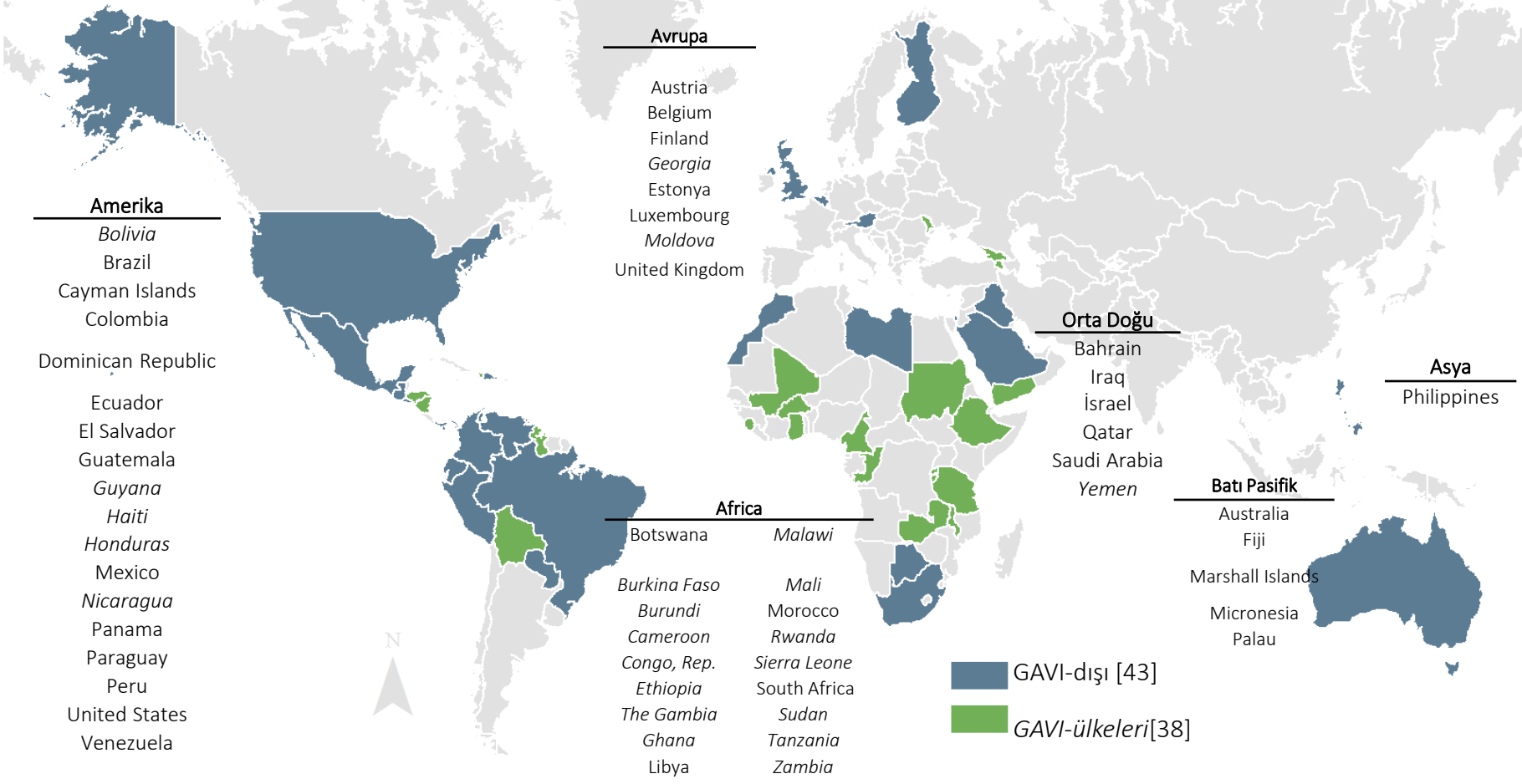
Global RV aşılamasının potensiyel etkileri (projeksiyon)

- 2007 ile 2025 arasında 716 milyon infant aşılanması:
  - 2.4 milyon yaşam kurtulacak
  - 93 milyon hastane yatışı ve acil başvurusu önlenecek
  - yaklaşık 500 milyon ABD $ direkt medikal kazanç sağlıyacak



Accelerating the Introduction of Rotavirus Vaccines into GAVI-Eligible Countries: Investment Case for GAVI Secretariat Submitted by PATH's Rotavirus Vaccine Program in Collaboration with WHO and the US CDC.

Rutin aşı takviminde RV aşısı uygulayan ülkeler



81 ülkenin rutin aşı takviminde 38'i Gavi-destekli ülke

*Mayıs 2016 itibariyle ulusal aşı şemasında rotavirus aşılaması

Kaynak: WHO vaccine-preventable diseases: monitoring system

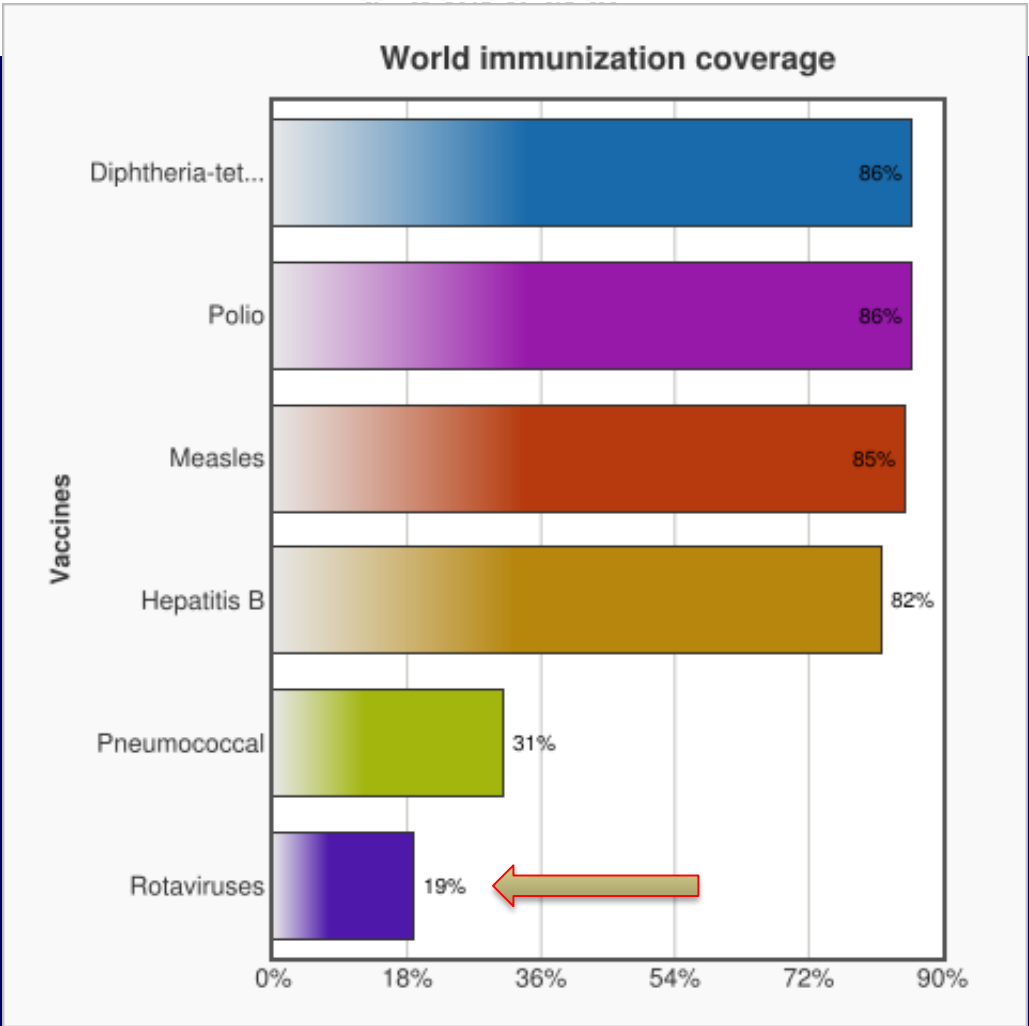
2015, 90, 617-632 No. 46

World Health Organization

Organisation mondiale de la Santé

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

13 NOVEMBER 2015, 90th YEAR / 13 NOVEMBRE 2015, 90e ANNÉE



WHO, Global immunization coverage 2015

Rutin RV aşılaması

- **Rotaviruslar dünya genelinde önemli hastalık yüküne sahip olmasına,**
- **Etkin ve güvenli RV aşıları olmasına,**
- **DSÖ, ESPID, ESPGHAN tarafından rutin aşı önerilerine rağmen,**

RV aşıları henüz birçok ülkenin ulusal aşı şemasına dahil edilmemiştir.

Rotavirus aşıları
Potansiyel Engeller - Bariyerler

Rotavirus aşıları
Potansiyel Engeller - Bariyerler

- Hastalık yükü ile ilgili düşük farkındalık,
- Aşı etkisinin gelişmekte olan ülkelerde düşük olduğu inancı,
- Potansiyel invajinasyon riski kaygısı,
- Yaş kısıtlaması,
- Maliyet/etkinlilik,
- Aşının tedarik edilmesindeki mali zorluklar

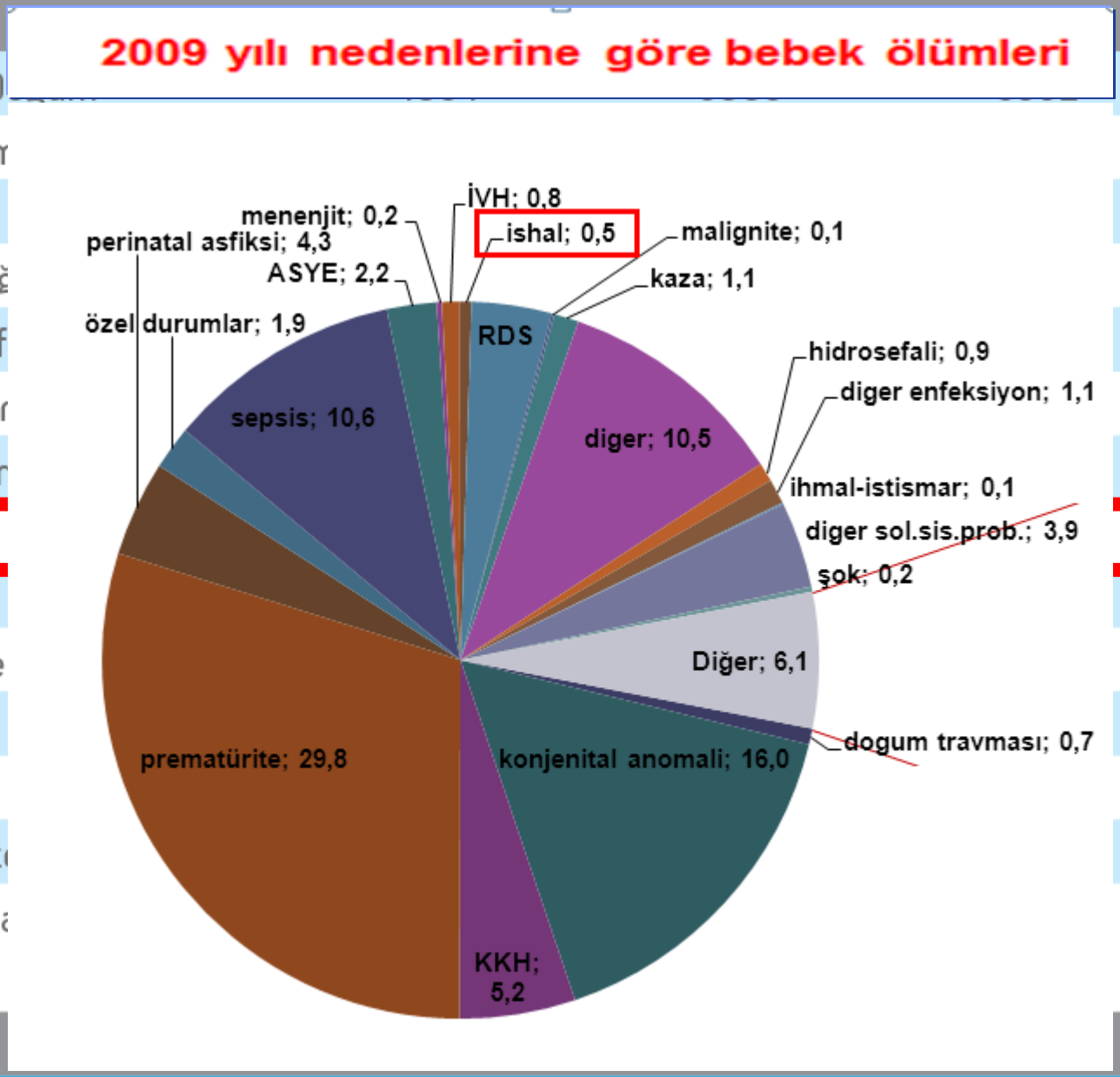
Rotavirus aşıları
Engeller - Bariyerler

- **Hastalık yükü ile ilgili düşük farkındalık,**
  - **Yeterli epidemiyolojik veri olmayışı,**
  - **Sürveyans sisteminin,**
  - **Maliyet-etkinlik verisinin olmayışı**

Türkiye’de rotavirus epidemiyolojisi

Tablo 8.5 Bildirilen Bebek Ölüm Nedenleri, Türkiye, Sağlık Bakanlığı

	%'si
Prematüre D	%31
Doğum Anom	%17
Sepsis	%10
Kalp Hastalığ	%8
Perinatal Asf	%6
Akut Solunur	%3
Doğum Travr	%1
İshal	%1
Kaza	%1
Intravasküle	<%1
Menenjit	<%1
Malignansi	<%1
Yenidoğan t	<%1
Özel Durumla	%6
Diğer	%15
Toplam	%100.0



Kaynak: Sağlık Bakanlığı, Bebek Ölümleri – 2009

Beş yaş altı çocuklarda ölüm nedenleri (2008)

Ölüm İstatistikleri, 2008 — Death Statistics, 2008

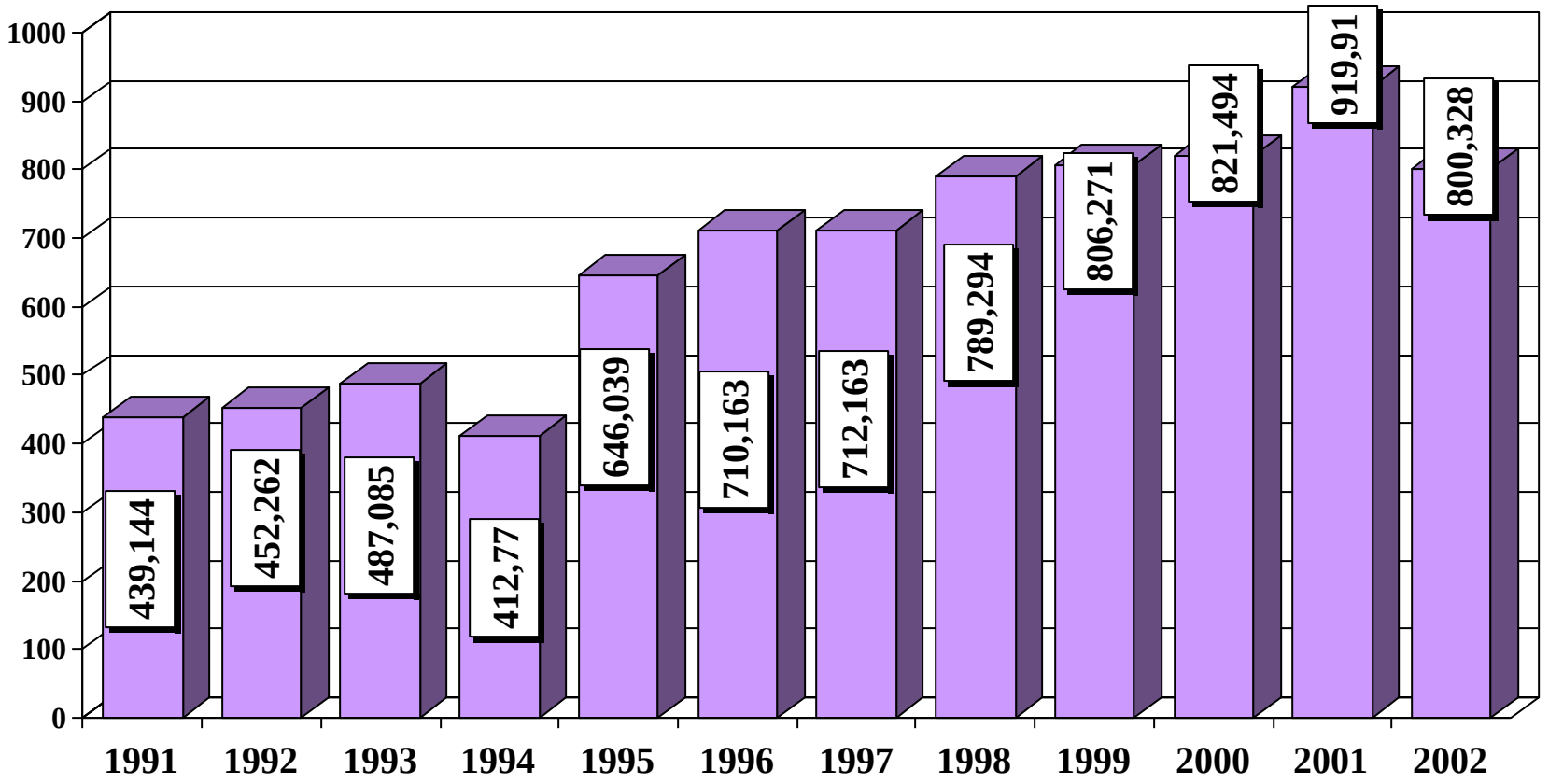
2.6 Seçilmiş 50 neden, cinsiyet ve yaş grubuna göre ölümler, 2008
[İl ve ilçe merkezleri]
A. Toplam B. Erkek C. Kadın

Ölüm nedeni (UHS-8)		Toplam Total	Yaş grubu 0	1-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39
Toplam	A	215 562	11 030	2 017	920	798	1 399	1 710	2 001	2 294	3 078
	B	119 391	6 266	1 103	538	457	870	1 142	1 325	1 479	1 938
	C	96 171	4 764	914	382	341	529	568	676	815	1 140
1. Kolera	A	-	-	-	-	-	-	-	-	-	-
	B	-	-	-	-	-	-	-	-	-	-
	C	-	-	-	-	-	-	-	-	-	-
2. Tifo	A	-	-	-	-	-	-	-	-	-	-
	B	-	-	-	-	-	-	-	-	-	-
	C	-	-	-	-	-	-	-	-	-	-
3. Basilli dizanteri ve amoebiasis	A	5	2	1	-	-	-	-	-	-	-
	B	2	1	1	-	-	-	-	-	-	-
	C	3	1	-	-	-	-	-	-	-	-
4. Enterit ve diyareli diğer hastalıklar	A	138	35	8	4	3	3	4	2	-	2
	B	75	21	2	1	3	2	3	2	-	1
	C	63	14	6	3	-	1	1	-	-	1

İshal nedeniyle ölen <5 yaş çocuk sayısı: 50-75

RV ishali nedeniyle ölen çocuk sayısı: 20-25

YILLARA GÖRE BİLDİRİLEN İSHAL OLGULARI TÜRKİYE



FORM 18

Türkiye'de AGE prevalansı

TÜRKİYE NÜFUS SAĞLIĞI ARAŞTIRMASI	1993 Ağustos-Ekim 8619 hane halkı
Son 2 hafta içinde ishal <5 yaş	%25

Türkiye'de AGE prevalansı

TÜRKİYE NÜFUS SAĞLIĞI ARAŞTIRMASI	1993 Ağustos-Ekim 8619 hane halkı	2013 Ağustos-Ekim 8159 hane halkı
Son 2 hafta içinde ishal <5 yaş	%25	%23

Ülkemizde her çocuk (özellikle <5 yaş) yaklaşık yılda en az bir AGE atağı geçirmektedir

SAĞLIK ARAŞTIRMASI

TÜİK

Çocukların son 6 ay içinde geçirdiği hastalıkların cinsiyet ve yerleşim yerine göre dağılımı, 2012
Percentage of children who were exposed to diseases in the past 6 months by sex and residence, 2012
[0-6 yaş grubundaki çocuklar - Children in 0-6 age group]

(%)

Hastalık/Kaza türü Diseases/Accidents	Türkiye-Turkey Toplam Total	 Erkek Male	 Kadın Female	Kent-Urban Toplam Total	 Erkek Male	 Kadın Female	Kır-Rural Toplam Total	 Erkek Male	 Kadın Female
İshal									
Diarrhea	27,9	29,7	26,1	27,5	28,8	26,3	28,8	31,8	25,5
Skin diseases	3,4	4,0	2,8	3,7	4,4	3,0	2,8	3,0	2,5
Diğer									
Other	2,8	3,1	2,4	3,2	3,4	2,9	2,0	2,5	1,4

Sayı: 13490
25 Nisan 2013
10:00

Türkiye Sağlık Araştırması, 2012

0-6 yaş grubundaki çocuklarda, %27,9 ile ishal en sık görülen hastalık olmuştur.

Araştırmanın alan uygulamasının yapıldığı Mayıs-Haziran 2012 öncesindeki 6 ay içinde, 0-6 yaş grubundaki çocuklarda ishalden sonra sırasıyla; %27,6 ile üst solunum yolu enfeksiyonu, %11,7 ile bulaşıcı hastalıklar, %9,2 ile kansızlık ve %8,7 ile ağız ve diş sağlığı sorunları en çok görülen hastalık türleri olmuştur.

Bu ishallerin ne kadarı RV ishali ?

Türkiye'de rotavirus çalışmaları-I

İsim	Yapıldığı yer	Süre	Yaş grupları	Hasta sayısı	Olgu sayısı	Sıklık	Yöntem	Yıl
Ceyhan	Ankara	12 ay	0-2	333	61	16,30%	RNAelektroforez	1984
Çelebi	Erzurum		0-2	200	48	% 24.0	ELISA	1992
Şıklar	Ankara	10 ay, Nisan-ocak	0-2	88	20	% 22.4	ELISA	2000
Gökay	Istanbul		0-2	125	58	% 46.4	EIISA	1995
Yıldırmak	Ankara	12 ay	0-2	106	31	% 29.0	ELISA	1992
Akbulut	Istanbul		0-3	120	38	% 31.6	ELISA	1994
Ulukanlıgil	Ş.Urfa	12 ay	0-5	218	17	% 7.8	LA	2001
Hilmioğlu	İzmir	6 ay yaz-sanbahar	0-5	57	13	% 23.0	ELISA	1994
Öztürk			0-5	187	39	% 21.2	ELISA /LA	1995
Çoşkun	İzmir		0-5	39	7	% 20.5	ELISA	1993
Kanra	Ankara	12 ay	0-5	187	40	21,50%	ELISA	1992
Karslıgil	Gaziantep	18 ay (2 kış)	0-6	46	9	% 19.6	Stat-Pak	1999
Aşcı	Elazığ		0-6	200	59	% 30.0	ELISA	1996
Gültekin	Sıvas		0-6	111	14	% 13.0	LA	1993
Akdoğan	Kayseri	12 ay	0-6	217	71	% 32.0	ELISA / LA	1999
Başustaoğlu	Ankara	yaz-kış	0-14	368	62	% 16.8	ELISA	1995
Kükner	Ankara	12 ay	0-14	110	28	% 25.0	ELISA	1993
Bora	Istanbul		0-14	56	28	% 50.0	LA	1992
Baysallar	Ankara		0-14	80	17	% 21.2	ELISA	1995
Ergüven			0-14	519	110	% 21.2	ELISA	1994
Türkoğlu	Istanbul	6 yıl	0-14	826	210	% 25.4	ELISA / LA	1993
Göçmen	Istanbul		0-14	160	21	% 13.1	ELISA	1995
Özsan	Ankara	kış-ilkbahar	0-14	86	18	% 22.0	Jel Elektroforez	1997

Türkiye'de rotavirus çalışmaları-II

İsim	Yapıldığı yer	Süre	Yaş grupları	Hasta sayısı	Sıklık	Yöntem	Yıl
Kurugöl	İzmir	1 yıl	0-5	920	%39.8	ELISA	2003
Çataloluk	Gaziantep	18 ay	0-5	508	%32.1	ELISA	2004
Karadağ	Ankara	3 yıl	0-5	1099	%36.8	Immunokr.	2005
Şimşek	Ankara	2 yıl	0-5	127	%29.1	ELISA	2005
Kurugöl	İzmir	18 ay	0-5	219	%48.9	ELISA-HK	2006
Biçer	İstanbul	1 yıl	0-5	1767	%23.9	ELISA	2008
İnci	Konya	1 yıl	0-5	1258	%21.0	ELISA	2008
Bayraktar	İstanbul	1 yıl	0-5	1358	%25.0	ELISA	2009
Ceyhan	Türkiye	1 yıl	0-5	338	%53.1	ELISA	2009

Türkiye'de rotavirus çalışmaları-III

İsim	Yapıldığı yer	Süre	Yaş grupları	Hasta sayısı	Sıklık	Yöntem	Yıl
Balcı	Denizli	1 yıl	0-5	930	%26.5	ELISA	2009
Özdemir	Mersin	1 yıl	0-5	363	%32.2	ELISA	2010
Meral	Ankara	1 yıl	0-5	251	%21.1	ELISA	2011
Köroğlu	Malatya	2005 salgını	0-91	9907	%52.7	ELISA,PCR	2011
Hacımusta	Bursa	1 yıl	0-15	5988	%25.0	ELISA	2011
Biçer	İstanbul	1 yıl	0-5	1543	%25.0	ELISA	2011
Tapısız	Ankara	1yıl	0-5	494	%28.1	ELISA	2011
Çelik		6 yıl	0-5	4702	%17.3		2015
Durmaz	Türkiye	2 yıl	0-5	1644	%38.7	ELISA	2015

Ortalama: %30.1

Multicenter Prospective Study on the Burden of Rotavirus Gastroenteritis in Turkey, 2005–2006: A Hospital-Based Study

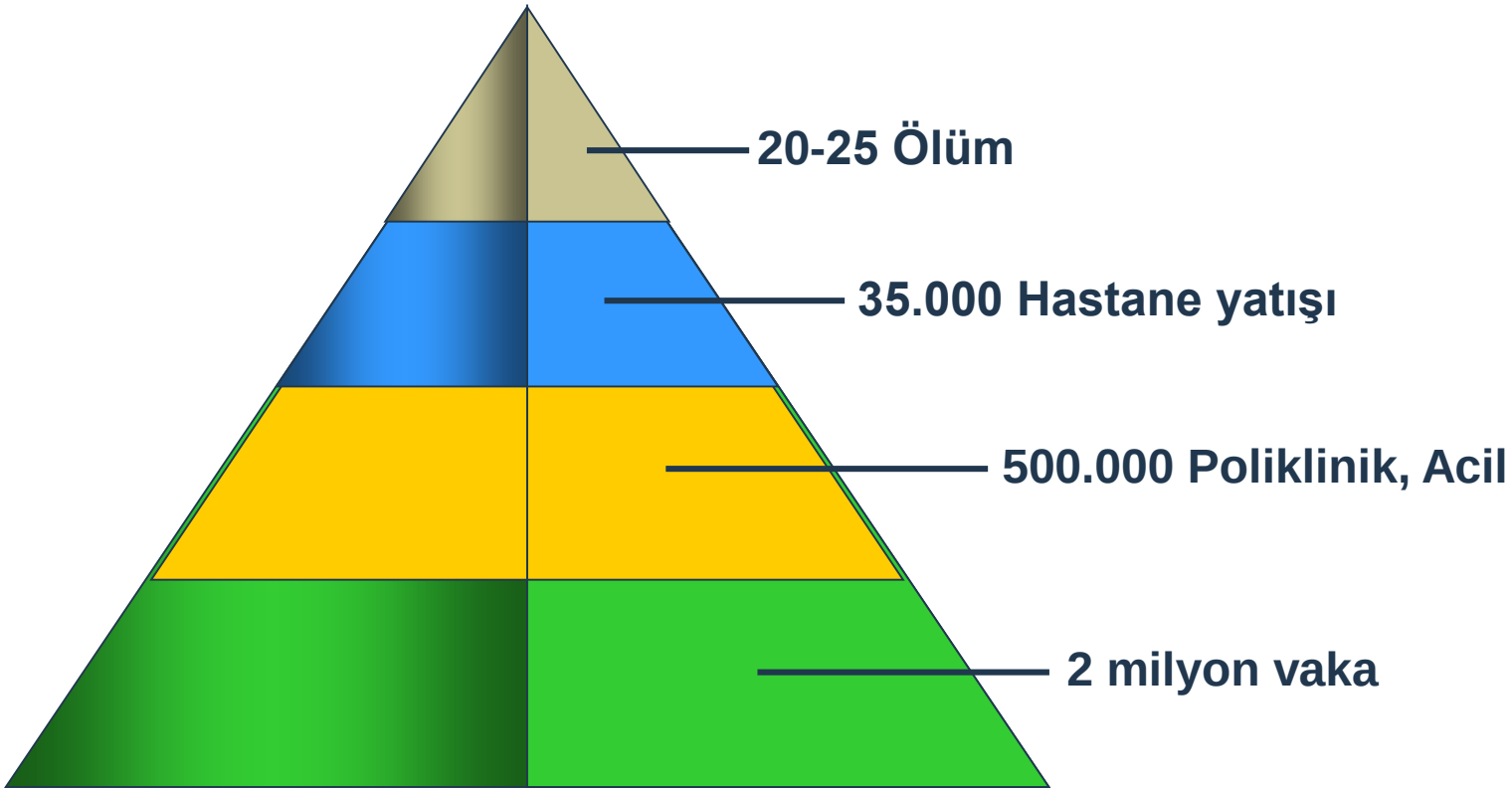
Center	ELISA (%)		Total
	-	+	
Çapa (Istanbul)	32 (34.9)	54 (65.1)	94
Çukurova (Adana)	57 (67.6)	34 (32.4)	94
Ege (Izmir)	16 (22.6)	33 (67.4)	49
HUTF (Ankara)	34 (32.6)	58 (57.4)	99
Total	159 (47.0)	179 (53.1)	338

Polikinik/acil sevise başvuran ishal vakalarının 1/3'ünden, hastaneye yatırılanların yarısından rotavirus sorumludur.

Rotavirus Komplikasyonları - Türkiye

	Makale sayısı	Olgu sayısı	Komplikasyon araştırılan RVGE olgu sayısı	Olgu sayısına göre yüzde
Komplikasyon	**9**	**328**	**2784**	**%11.8**
Bakteriyemi	3	17	1018	1,7
Kandidemi	2	3	665	0,5
Konvülziyon	2	16	757	2,1
Aseptik menenjit	1	2	353	0,6
Ensefalit	2	12	757	1,6
Hepatit	3	173	1047	16.5
Nötropeni	2	59	950	6,2
Miyokardit	1	1	353	0,3
Bronkopnömoni	1	4	597	0,7
DİK	1	1	289	0,3
Paralitik ileus	1	2	37	5.4
Kreatinin artışı	1	37	272	13,6
Ölüm	1	1	353	0,3

Rotavirus hastalık yükü-Türkiye



Tahmini RV hastalık yükü (Türkiye)

Kurugöl Z. Aşı Kitabı 2012

Rotavirus aşıları
Engeller - Bariyerler

- Hastalık yükü ile ilgili düşük farkındalık,
- **Aşı etkisinin gelişmekte olan ülkelerde, gelişmiş ülkelere göre, daha düşük olduğu inancı**

RV aşılarının etkinlikleri (ülke gelir grubuna göre)

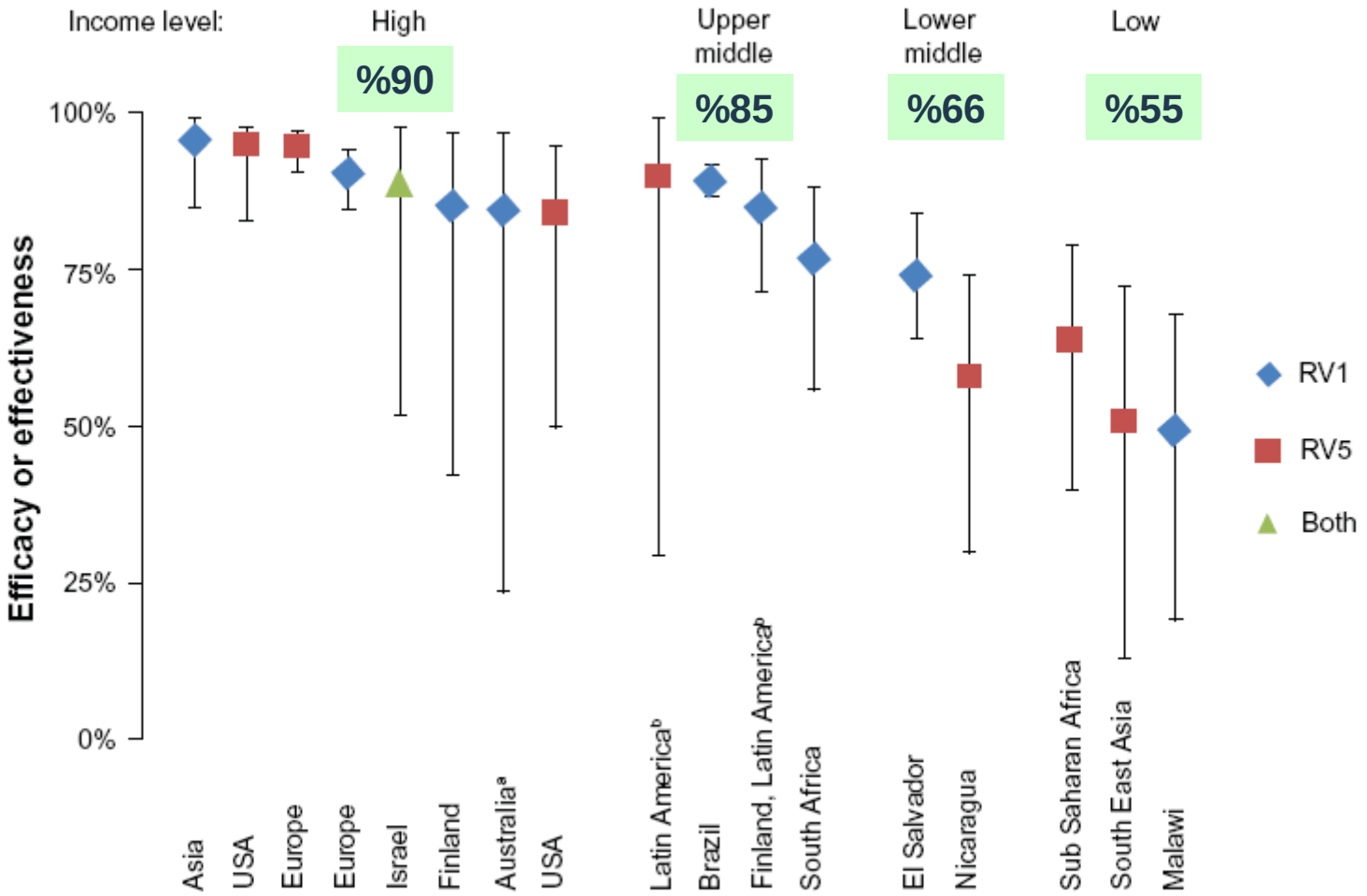
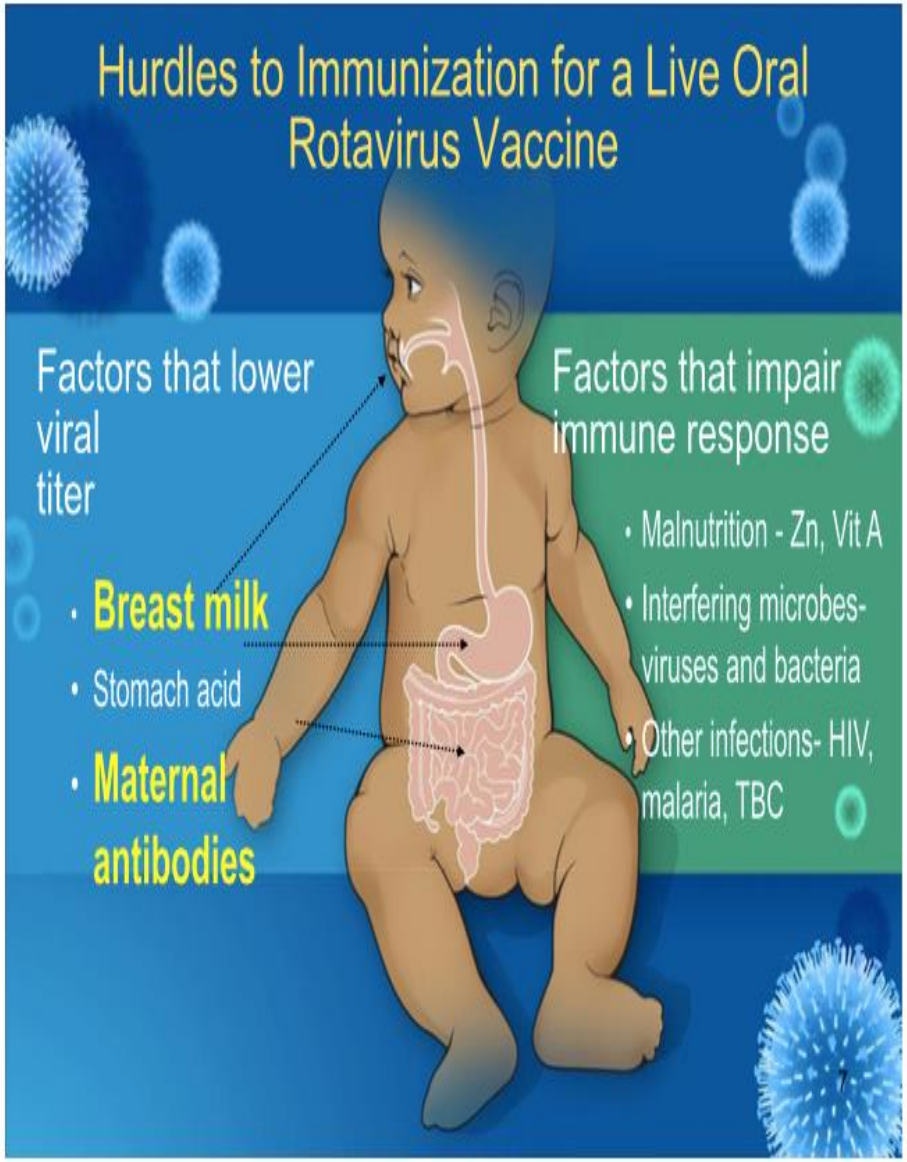


Figure 1 Comparison of vaccine efficacy and effectiveness estimations from clinical trials of RV1 and RV5 against any serotype severe rotavirus gastroenteritis, stratified by country income status.

Aşı immünojenitesini – etkinliğini etkileyen faktörler

- Anne sütü?
- İlk doğal enfeksiyonun erken yaşta olması?
- Enterik koenfeksiyonlar ve barsak mikrobiatası?
- Malnütrisyon?
- Rotavirus enfeksiyonuna genetik yatkınlık?
- OPV aşısı?
- Suşların çeşitliliği / mikst enfeksiyon ve hayvan kaynaklı suşların sıklığı?



Roger I Glass. Journal of Infection. 2014 68, S9eS18

2013, 88, 49–64 No. 5

World Health Organization

Organisation mondiale de la Santé

Weekly epidemiological record

Rotavirus vaccines

WHO position paper – January 2013

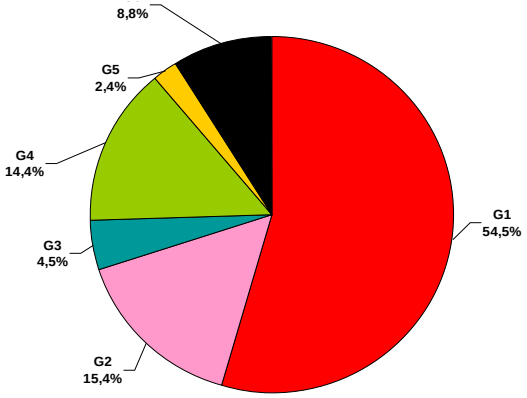
Simultaneous administration of RV1 or RV5 with other vaccines of the infant immunization programme, including combined diphtheria, tetanus toxoid and acel-

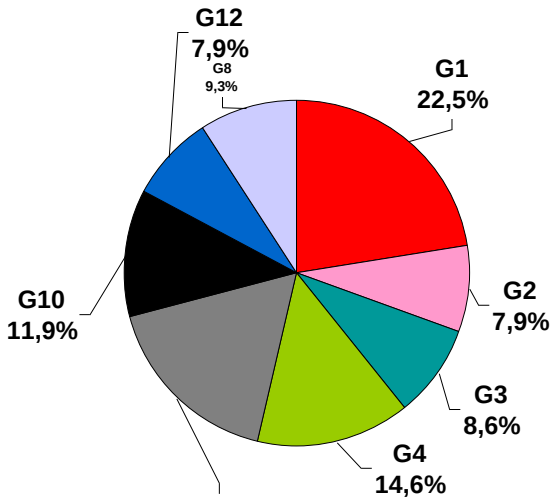
Gelişmekte olan ülkelerde RV ve OPV'nin birlikte uygulanması tercih edilen bir yoldur (DSÖ).

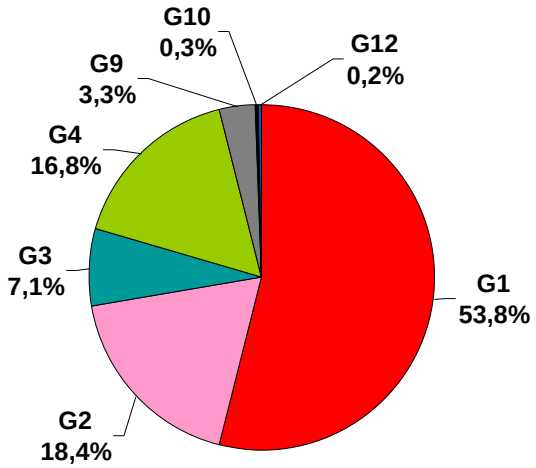
Ref:http://www.who.int/immunization_standards/vaccine_ quality/pq_system/en/index.html

respective vaccines.[39, 40] Although OPV may have an inhibitory effect on the immune response to the first dose of both rotavirus vaccines, this interference does not persist after administration of subsequent doses of rotavirus vaccines.[41]

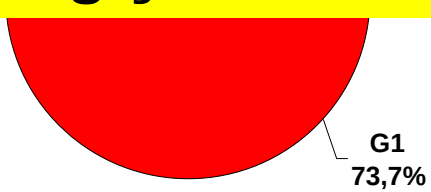
Rotavirus Serotip Dağılımı



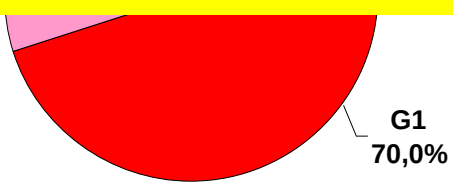




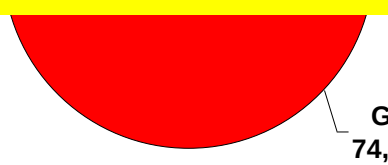
- **Dolaşan suşların çeşitliliği - Aşı etkinliği?**
- **Aşının rutin kullanımı - Dolaşan suşların prevelansında değişiklik? Anlamı ?**



Kuzey Amerika, N=2892



Avrupa, N=17475



Avustralya/Okyanusya, N=6995

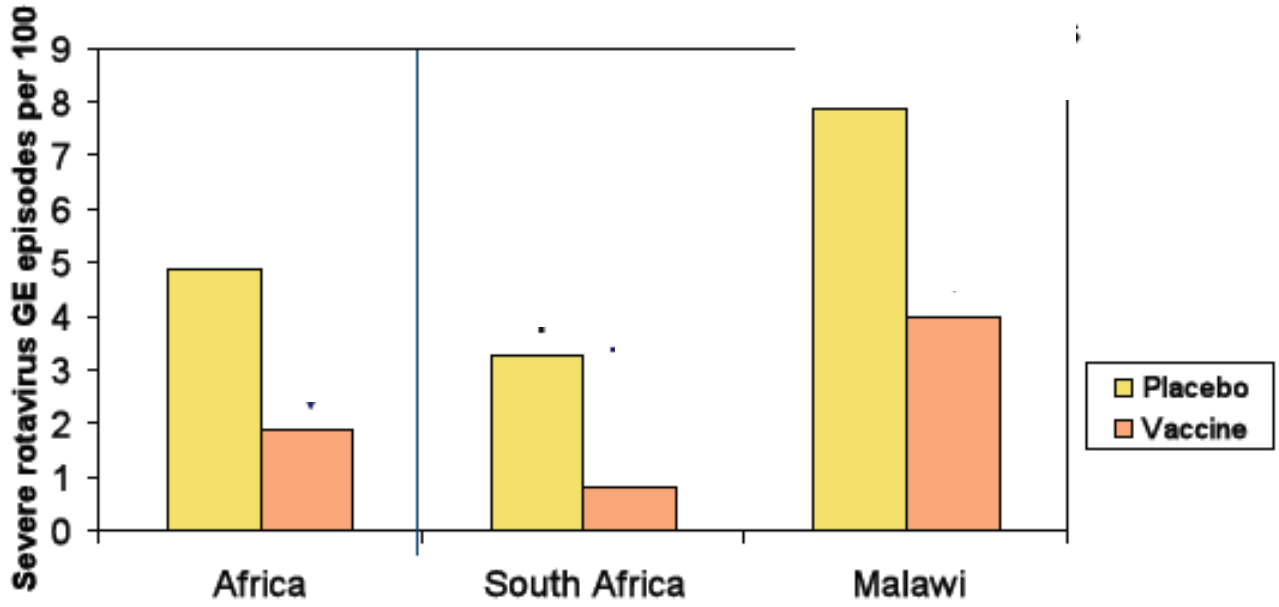
Afrika → G1
%22-24

Afrika → G1-4, G8, G9, G5, G12
G3P1A[8], G2P1B [4], G4P1A [8]

The NEW ENGLAND JOURNAL of MEDICINE

Effect of Human Rotavirus Vaccine on Severe Diarrhea in African Infants

Shabir A Madhi, Nigel A Cunliffe, Duncan Steele, Desirée Witte, et al. The New England Journal of Medicine. Boston: Jan 28, 2010. Vol. 362, Iss. 4; pg. 289

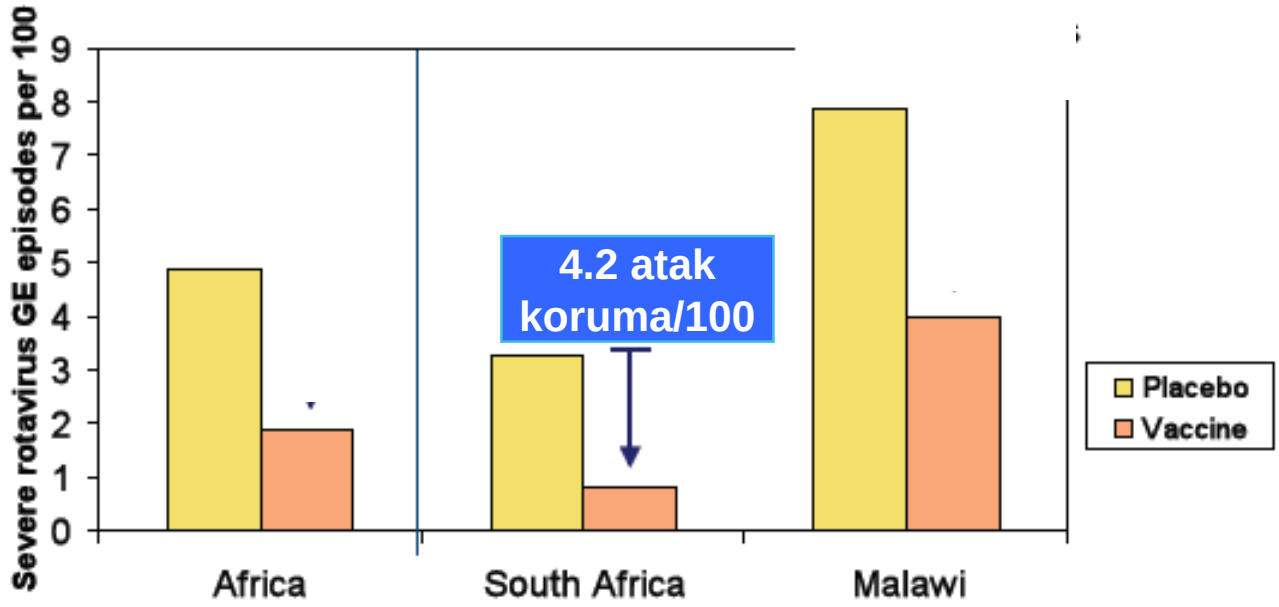


	Africa	South Africa	Malawi
Efficacy	61.2% (44.0 – 73.2)	76.9% (56.0 – 88.5)	49.5% (19.2 – 68.3)

The NEW ENGLAND JOURNAL of MEDICINE

Effect of Human Rotavirus Vaccine on Severe Diarrhea in African Infants

Shabir A Madhi, Nigel A Cunliffe, Duncan Steele, Desirée Witte, et al. The New England Journal of Medicine. Boston: Jan 28, 2010. Vol. 362, Iss. 4; pg. 289



	Africa	South Africa	Malawi
Efficacy	61.2% (44.0 – 73.2)	76.9% (56.0 – 88.5)	49.5% (19.2 – 68.3)

The NEW ENGLAND JOURNAL of MEDICINE

Effect of Human Rotavirus Vaccine on Severe Diarrhea in African Infants

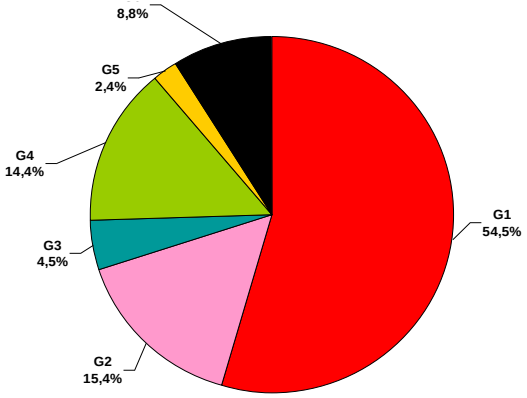
Shabir A Madhi, Nigel A Cunliffe, Duncan Steele, Desirée Witte, et al. The New England Journal of Medicine. Boston: Jan 28, 2010. Vol. 362, Iss. 4; pg. 289

Düşük gelirli ülkelerde rotavirus aşılarının etkinliği orta ve yüksek gelirli ülkelere göre daha düşük olmasına rağmen, halk sağlığı üzerine olan etkileri daha anlamlıdır.

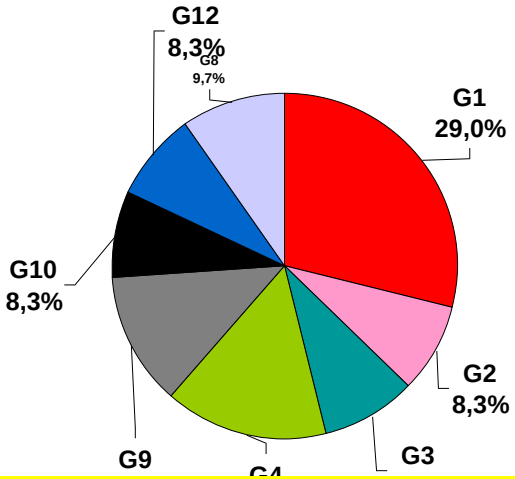
Cochrane Database Syst Rev, 2012 Feb 15;2:CD008521.

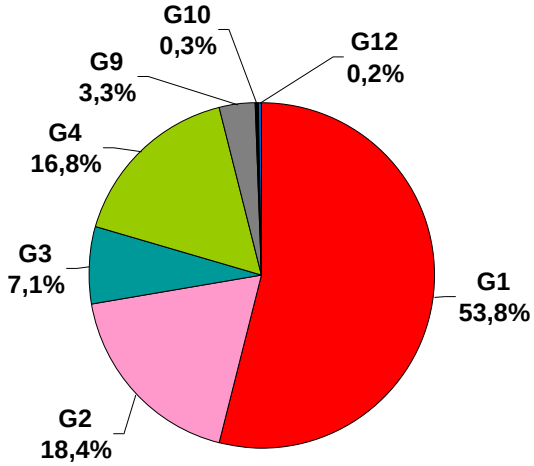
Efficacy	61.2% (44.0 – 73.2)	76.9% (56.0 – 88.5)	49.5% (19.2 – 68.3)

Rotavirus Serotip Dağılımı



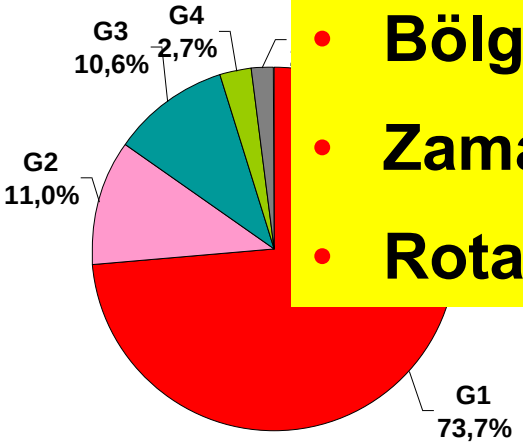
Güney Amer



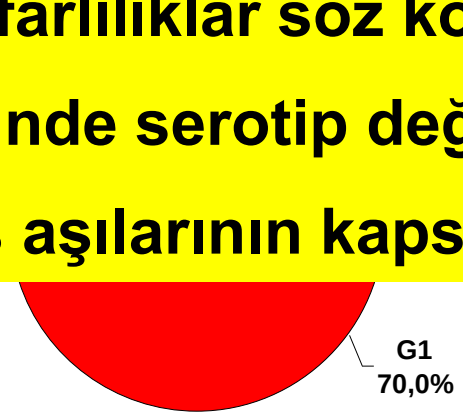


N=13126

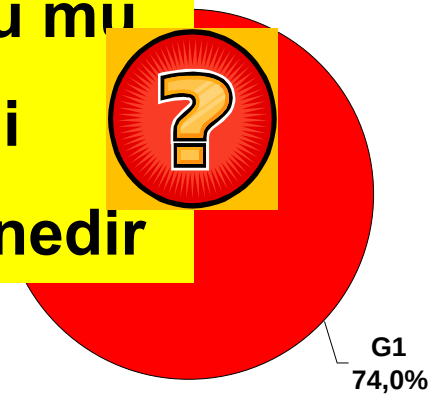
- **Türkiye'de serotip dağılımı nasıl**
- **Bölgesel farlılıklar söz konusu mu**
- **Zaman içinde serotip değişimi**
- **Rotavirus aşılarının kapsamı nedir**



Kuzey Amerika, N=2892



Avrupa, N=17475

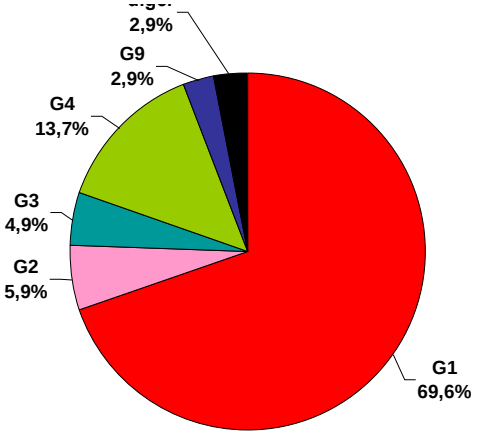


Avustralya/Okyanusya, N=6995

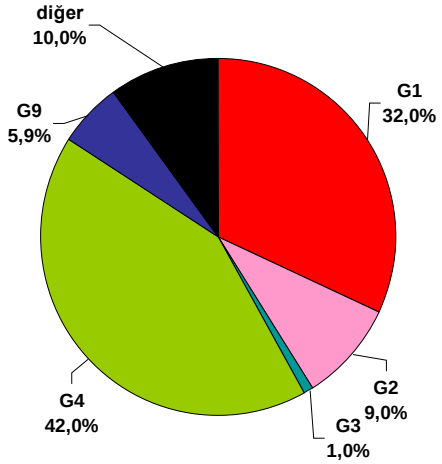
Afrika → G1
%23-34

Afrika → G1-4, G8, G9, G5, G12
G3P1A[8], G2P1B [4], G4P1A [8]

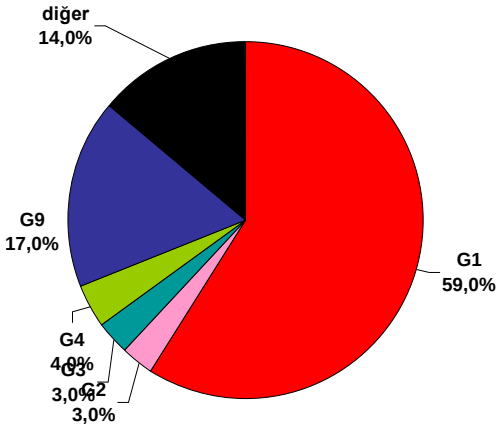
Rotavirus Serotip Dağılımı-Türkiye



İzmir, N= 920
2003



Gaziantep, N=119
2005



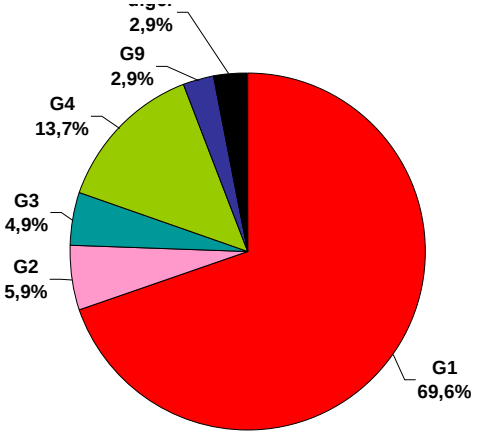
Ankara, N=332
2008

Kurugöl Z, et al. Turk J Ped 2003; 45: 290-294.

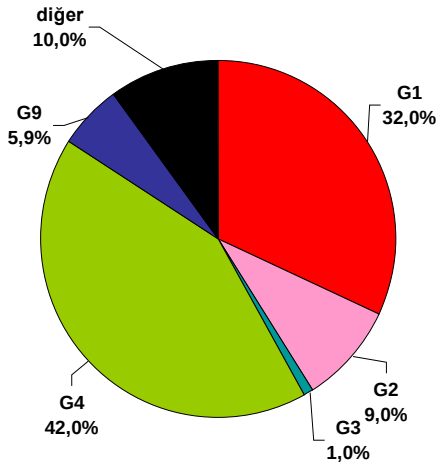
Çataloluk O, et al. Epidemiol Infect 2005;133:673-8.

Bozdayı G, et al. J Med Virol 2008; 80: 733-40.

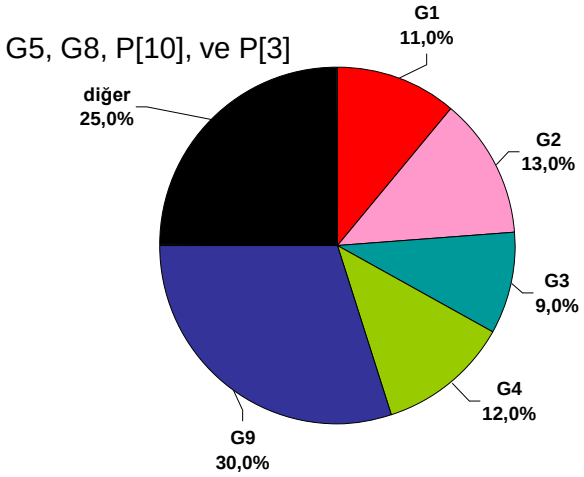
Rotavirus Serotip Dağılımı-Türkiye



İzmir, N= 920
2003



Gaziantep, N=119
2005



Ankara, N=100
2011

Kurugöl Z, et al. Turk J Ped 2003; 45: 290-294.

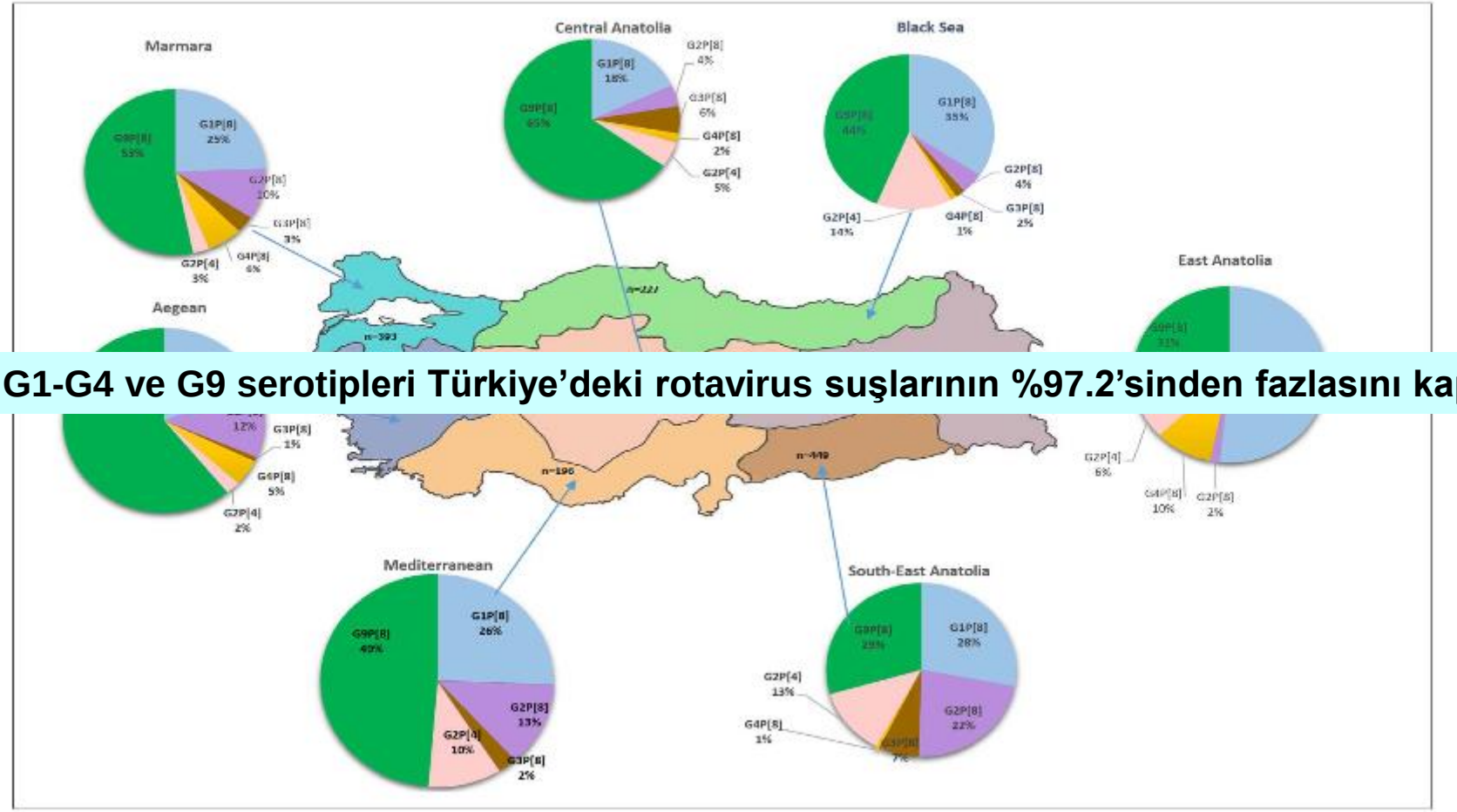
Çataloluk O, et al. Epidemiol Infect 2005;133:673-8.

Tapısız A, et al. Curr Microbiol 2011; 63:517–22.

Rotavirus Serotip Dağılımı-Türkiye

PLOS ONE

Report of Rotavirus Surveillance in Turkey

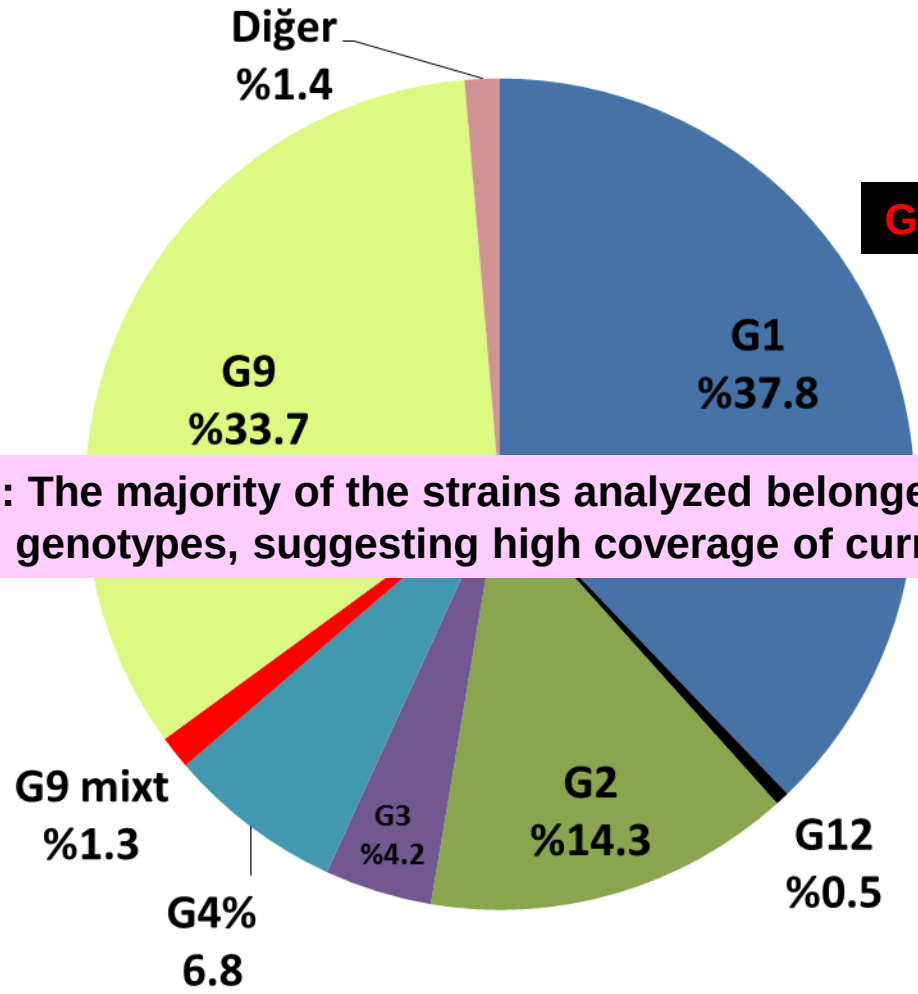


G1-G4 ve G9 serotipleri Türkiye'deki rotavirus suşlarının %97.2'sinden fazlasını kapsar.

Figure 4. Distribution of common G and P genotype combinations among seven geographic regions of Turkey. The "n" indicates the total number of antigen-positive samples collected in each region.

Durmaz R, Turkish Rotavirus Surveillance Network. PLoS One 2014 Dec 1;9(12):e113674.

Tiplendirilebilen G Tipleri (n=2941)
Türkiye Metaanaliz



G1+G2+G3+G4+G9 = %96.8

Conclusion: The majority of the strains analyzed belonged to the G1–G4 and G9 genotypes, suggesting high coverage of current rotavirus vaccines.

Sayın Anıl Tapısız'ın izniyle

Rotavirus aşıları
Potansiyel Engeller - Bariyerler

- Hastalık yükü ile ilgili düşük farkındalık,
- Gelişmekte olan ülkelerde aşı etkisinin düşük olduğu inancı,
- **Potansiyel invajinasyon riski kaygısı,**

Vaccine 30S (2012) A179–A184

Contents lists available at SciVerse ScienceDirect

Vaccine

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

Research priorities regarding rotavirus vaccine and intussusception: A meeting summary☆

Jacqueline E. Tate[a,*], A. Duncan Steele[b], Julie E. Bines[c,d,e], Patrick L.F. Zuber[f], Umesh D. Parashar[a]

[a] Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, GA, USA
[b] Rotavirus Vaccine Program, PATH, Seattle, WA, USA
[c] Department of Paediatrics, University of Melbourne, Melbourne, Australia
[d] Royal Children's Hospital, Melbourne, Australia
[e] Murdoch Children's Research Institute, Melbourne, Australia
[f] Department of Immunization, Vaccines and Biologicals, World Health Organization, Geneva, Switzerland

ABSTRACT

Currently available rotavirus vaccines have been associated with a small increased risk of intussusception (~1–2 cases per 100,000 vaccinated infants) in some populations. In response to this newly emerging data on intussusception related to current rotavirus vaccines, a group of technical experts convened by the Program for Applied Technology in Health met to review the data, establish what gaps in knowledge exist, and identify what future research is needed. This manuscript outlines the evidence that is currently available and the research agenda that was generated during this meeting. It also highlights the need for countries that are using or considering introducing the rotavirus vaccine to evaluate both the benefits and risks of vaccination.

The Pediatric Infectious Disease Journal
Issue: Volume 34(7), July 2015, p 763–768

Risk of Intussusception After Rotavirus Vaccination

Meta-analysis of Postlicensure Studies

Dominique Rosillon, PhD, Hubert Buyse, MD,* Leonard R. Friedland, MD,† Su-Peing Ng, MBBS,* F. Raúl Velázquez, MD, MSc,‡ and Thomas Breuer, MD**

Yarar- risk analizleri

Table 6

Risk of intussusception and benefits of rotavirus vaccination in Mexico, Brazil, Australia

Country	Diarrhea hospitalizations (deaths) prevented by vaccination	Intussusception cases (deaths) potentially caused by vaccination	Referenc
Mexico	11 600 (663)	41 (2)	94
Brazil	69 600 (640)	55 (3)	94
Australia	7000 (0)	6 (0)	102
US	53 444 (14)	45–213 (0.1–0.5)	103

[a]Data are for one fully vaccinated birth cohort followed to age 5 y.

HUMAN VACCINES & IMMUNOTHERAPEUTICS
2016, VOL. 0, NO. 0, 1–10
http://dx.doi.org/10.1080/21645515.2016.1197452

Taylor & Francis
Taylor & Francis Group

REVIEW

OPEN ACCESS

Rotavirus vaccination and intussusception – Science, surveillance, and safety: A review of evidence and recommendations for future research priorities in low and middle income countries

Catherine Yen[a], Kelly Healy[b], Jacqueline E. Tate[a], Umesh D. Parashar[a], Julie Bines[c], Kathleen Neuzil[d], Mathuram Santosham[b], and A. Duncan Steele[e]

[a]Division of Viral Diseases, Centers for Disease Control and Prevention, Atlanta, GA, USA; [b]Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD, USA; [c]Murdoch Childrens Research Institute, The University of Melbourne, Victoria, Australia; [d]University of Maryland School of Medicine, Baltimore, MD, USA; [e]Enteric and Diarrhoeal Diseases, Global Health, Bill and Melinda Gates Foundation, Seattle, WA, USA

Yarar- risk analizleri,
RV aşılarının sağladığı yararların (hastane yatışları ve ölümlerde azalma), invajinasyon riskindeki küçük artışa (1-2/100.000) ağır bastığını göstermektedir.

Aşı programlarında RV1 ve RV5'in rutin kullanımını desteklemeye ve tüm dünyada rutin RV aşılamasını teşvike devam edilmesi önerilir.

Rotavirus aşıları
Engeller - Bariyerler

- Hastalık yükü ile ilgili düşük farkındalık,
- Gelişmekte olan ülkelerde aşı etkisinin düşük olduğu inancı,
- Potansiyel invajinasyon riski,
- **Yaş kısıtlaması**

Rotavirus Aşıları Öneriler

	RV5 (RotaTeq)	RV1 (Rotarix)
İlk doz için min. yaş	6 hafta	6 hafta
İlk doz için max. yaş	12 hafta 0 gün 14 hafta 6 gün	LA: 12 hafta Avrupa: 14 hafta 6 gün 14 hafta 6 gün

- **Yaş kısıtlaması, aşılama oranlarını gelişmiş ülkelerde %5-10; gelişmekte olan ülkelerde %30-40 azaltıyor.**
- **Aşılamanın başlanmasında gecikmeler, hastalık yükü yüksek olan birçok ülkede ilk 15 haftada aşılanamayan çocuklarda, RV-ilişki ölümlerin engellenmesi için önemli bir fırsatın kaçırılmasına neden olmaktadır.**

CDC. 2006 önerisi, 2008 önerisi

Rotavirus aşıları
Engeller - Bariyerler

- Hastalık yükü ile ilgili düşük farkındalık,
- Gelişmekte olan ülkelerde aşı etkisinin gelişmiş ülkelerden düşük olduğu inancı,
- Potansiyel invajinasy
- Yaş kısıtlaması,
- **Maliyet/etkinlik,**
- **Aşının tedarik edilmesindeki mali zorluklar**

RV aşılaması maliyet-etkin midir?

中国婴幼儿普遍接种轮状病毒疫苗的成本效果分析

孙树柳　高玉琦　尹娟　庄贵华

中华流行病学杂志, 2016,37(02): 238-242. DOI: 10.3760/cma.j.issn.0254-6450.2016.02.018

摘要

目的 对中国现阶段是否应将婴幼儿接种轮状病毒疫苗纳入免疫规划进行经济学评价，并探讨其成本效果。

方法 通过构建决策树Markov模型，模拟2012年中国出生的新生儿分别在不接种轮状病毒疫苗及接种Rotarix疫苗或Rotateq疫苗3种方案下的成本和健康结局，基于各方案间的增量成本效果比（ICER）与中国2012年人均国内生产总值（GDP）的比较确定最优方案。

结果 与不接种方案相比，Rotarix疫苗和Rotateq疫苗接种方案可分别减少发生238万和253万例轮状病毒腹泻，避免12.6万和13.3万个伤残调整寿命年的损失，ICER分别为3 760元和7 578元，均小于我国2012年人均GDP（38 420元）；Rotateq疫苗相对于Rotarix疫苗，ICER为81 068元，介于1与3倍人均GDP之间。

结论 在中国婴幼儿中开展轮状病毒疫苗普遍接种具有高的成本效果，应考虑将其纳入计划免疫；考虑到疫苗免疫费用、大规模组织实施的难度等因素，在现阶段更适宜推广接种Rotarix疫苗。

引用本文: 孙树柳, 高玉琦, 尹娟, 等. 中国婴幼儿普遍接种轮状病毒疫苗的成本效果分析 [J]. 中华流行病学杂志,2016,37(2): 238-242. DOI: 10.3760/cma.j.issn.0254-6450.2016.02.018

正文　作者信息　English Abstract　评论　相关资源

基金　关键词　主题词　阅读 33 引用 0　视频 0 论文 0 大综述 0

Surveillance

A cost-effectiveness analysis on universal infant rotavirus vaccination strategy in China

Sun Shuliu,Gao Yuqi,Yin Juan,Zhuang Guihua

Corresponding author: Zhuang Guihua, Email:zhuanggh@mail.xjtu.edu.cn

DOI: 10.3760/cma.j.issn.0254-6450.2016.02.018

Published 2016-02-10 | Received 2015-6-29

Cite as Chin J Epidemiol, 2016,37(02): 238-242.

Abstract

Objective To evaluate the cost-effectiveness of current universal infant rotavirus vaccination strategy, in China.

Methods Through constructing decision tree-Markov model, we simulated rotavirus diarrhea associated cost and health outcome on those newborns in 2012 regarding different vaccination programs as: group with no vaccination, Rotavirus vaccination group and Rotateq vaccination group, respectively. We determined the optimal program, based on the comparison between incremental cost-effectiveness ratio (ICER) and China' s 2012 per capital gross domestic product (GDP).

Results Compared with non-vaccination group, the Rotavirus vaccination and Rotateq vaccination groups had to pay 3 760 Yuan and 7 578 Yuan (both less than 2012 GDP per capital) to avert one disability adjusted life years (DALY) loss, respectively. Results from sensitivity analysis indicated that both results were robust. Compared with Rotavirus vaccination program, the Rotateq vaccination program had to pay extra 81 068 Yuan (between 1 and 3 times GDP per capital) to avert one DALY loss. Data from the sensitivity analysis indicated that the result was not robust.

Conclusion From the perspective of health economics, both two-dose Rotarix vaccine and three-dose' s Rotateq vaccine programs were highly cost-effective, when compared to the non-vaccination program. It was appropriate to integrate rotavirus vaccine into the routine immunization program. Considering the large amount of extra cost that had to spend on Rotateq vaccination program, results from the sensitivity analysis showed that it was not robust. Rotateq vaccine required one more dose than the Rotarix vaccine, to be effective. However, it appeared more difficult to practice, suggesting that it was better to choose the Rotarix vaccine, at current stage.

Çocuk Enfeksiyon Dergisi
Journal of Pediatric Infection

Cost effectiveness of both (monovalent and pentavalent) Rotavirus vaccines

Objective: Rotavirus (RV) infections constitute a substantial burden in Turkey, particularly in children under 5 years of age. RV vaccines are employed to infants by only paying and no reimbursement is available. The first aim of this study is to evaluate the cost effectiveness of implementing a national basis monovalent or pentavalent RV vaccination program in target populations.

Methods:A decision tree model was employed using demographic and epidemiological input obtained from a study sources conducted before in our region and international literature. Monovalent or pentavalent vaccination was assumed to protect with 83.7% or 90% of severe RV acute gastroenteritis (RVAGE) in children respectively. Costs input were obtained from a provincial study conducted in 2007. Univariate sensitivity analyses and Monte-Carlo simulations were performed.

Results: The vaccination program was cost effective and cost saving compared to no vaccination with 85% coverage. Monovalent and pentavalent RV vaccination led to a mean of 2,316 (95% CI; 2,240-2,392) and 2,972 (95% CI; 2,677-3,267) life-years gained (LYG) with 83.7% and 90% efficacy level respectively. Monovalent and pentavalent RV vaccinations avoided 551,820 (95% CI: 539,032; 564,609) and 683,529 (95% CI 638,906 - 728,158) individuals with clinical acute gastroenteritis (AGE) cases required hospital visits respectively. In the simulation for monovalent and pentavalent vaccines, the cost of RVAGE was 116.1 million TL (€59.2 million) in the non-vaccinated cohort and 35 and 22.5 million TL (€17.8 and 11.5 million) in the vaccinated cohort respectively. The cost of the vaccination program was estimated to be approximately 65.6 and 83.4 million TL (€33.5 and 42.5 million) and the incremental cost was approximately -15,4 million TL (-€7,9 million) and -15.3 million TL(-€. 9.6 million) respectively.

Conclusion: This analysis suggests that both (monovalent or pentavalent) RV vaccinations of children are very cost effective and also cost saving. Therefore, RV vaccination is associated with a positive return on investment from a public payers' perspective and supports the continued recommendation of RV vaccines as well as their full funding in Turkey.

Hacımustafa M, et al. Çocuk Enf Derg 2013; 7: 13-20.

Vaccine 31 (2013) 979–986

Contents lists available at SciVerse ScienceDirect

Vaccine

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

Estimating and comparing the clinical and economic impact of paediatric rotavirus vaccination in Turkey using a simple versus an advanced model

Mustafa Bakir[a], Baudouin Standaert[b,*], Ozden Turel[c,1], Zeynep Ece Bilge[d], Maarten Postma[e]

[a] Division of Paediatric Infectious Diseases, Department of Paediatrics, Marmara University School of Medicine, Pendik, Istanbul 34899, Turkey
[b] GlaxoSmithKline Vaccines, Parc de la Noire Epine, Avenue Fleming 20, B-1300 Wavre, Belgium
[c] Division of Paediatric Infectious Disease, Kanuni Sultan Suleyman Training and Research Hospital, Istanbul, Turkey
[d] GlaxoSmithKline Turkey, Buyukdere Cd. 173-B, 1 Levent, Istanbul, Turkey
[e] Unit of Pharmacoepidemiology & Pharmacoeconomics (PE2), Department of Pharmacy, University of Groningen, Groningen, The Netherlands

ARTICLE INFO

Article history:
Received 10 July 2012
Received in revised form
20 November 2012
Accepted 25 November 2012
Available online 6 December 2012

Keywords:
Rotavirus
Vaccination

ABSTRACT

Background: The burden of rotavirus disease is high in Turkey, reflecting the large birth cohort (>1.2 million) and the risk of disease. Modelling can help to assess the potential economic impact of vaccination. We compared the output of an advanced model with a simple model requiring fewer data inputs. If the results are similar, this could be helpful for countries that have few data available.
Methods: The advanced model was a previously published static Markov cohort model comparing costs and quality-adjusted life-year (QALY) outcomes of vaccination versus no vaccination. In contrast, the simple model used only a decision tree. Both models included data on demography, epidemiology, vaccine efficacy, resource use, unit costs, and utility scores from national databases and published papers. Only the perspective of the health care payer was considered in the analysis. The simple model had 23 variables.

Rutin RV aşılaması,
RV hastalık yükünü anlamlı derecede azaltarak sağlık bütçesinde 1.699.001 $ tasarruf sağlayan cost-effective bir uygulamadır.

Rotavirus aşıları
Engellerin Kaldırılması

- **Yaş sınırlamasının önemli olmadığı, özellikle düşük gelir düzeyli, hastalık yükünün yüksek olduğu ülkeler için daha uygun fiyatlı aşılarının geliştirilmesi…**

ADAY ROTAVİRUS AŞILARI

Lanzhou monovalent G10P[12] aşısı (Çin)	**Çin'de ruhsatlı**
RotaVac, monovalan neonatal G9P[10], 116-E RV aşısı (Bharat Biotech, Hindistan)	**Hindistan'da ruhsatlı**
Rotavin-IM G1P[8] (Vietnam)	**Vietnam'da ruhsatlı**

OPEN

Emerging Microbes and Infections (2015) 4, e64; doi:10.1038/emi.2015.64
www.nature.com/emi

ORIGINAL ARTICLE

Effectiveness of the live attenuated rotavirus vaccine produced by a domestic manufacturer in China studied using a population-based case–control design

Shan-Shan Zhen[1,*], Yue Li[1,*], Song-Mei Wang[2,*], Xin-Jiang Zhang[3,*], Zhi-Yong Hao[3,*], Ying Chen[1], Dan Wang[1], Yan-Hong Zhang[3], Zhi-Yong Zhang[3], Jing-Chen Ma[4], Peng Zhou[1], Zhen Zhang[1], Zhi-Wei Jiang[5], Yu-Liang Zhao[4] and Xuan-Yi Wang[1]

A universal rotavirus (RV) immunization program is a potentially cost-effective measure for preventing RV infection in China. However, the efficacy of the only licensed RV vaccine (Lanzhou lamb rotavirus vaccine, LLR), which is made by a domestic manufacturer, has not been proven by a properly designed clinical trial. In October 2011 to March 2012, to measure the potential protection provided by LLR, a case–control study nested in a population-based active diarrhea surveillance study of children <5 years of age was conducted in rural Zhengding county. During the study period, 308 episodes of diarrhea were identified as being caused by RV infection, resulting in an incidence rate of 48.0/1000 people/year. The predominant RV serotype was G3 (61.5%), followed by G1 (15.2%), and G9 (6.5%). Overall, a protection of 35.0% (95% confidence interval (CI), 13.0%–52.0%) was identified, and higher protection was found among moderate RV gastroenteritis cases caused by the serotype G3 (52.0%; 95% CI: 2.0%–76.1%). A concurrently conducted case–control study comparing non-RV viral diarrheal cases with non-diarrheal controls in the same population found that the RV vaccine offered no protection against non-RV diarrhea. Even under a less ideal immunization schedule, the oral LLR conferred a certain level of protection against RV gastroenteritis. However, further studies are needed to understand the full characteristics of the LLR, including its efficacy when administered following the optimal regimen, the potential risk of inducing intussusception, and the direct and indirect protective effects of LLR.
Emerging Microbes and Infections (2015) **4**, e64; doi:10.1038/emi.2015.64; published online 28 October 2015

ADAY ROTAVİRUS AŞILARI

Lanzhou monovalent G10P[12] aşısı (Çin)	Çin'de ruhsatlı
RotaVac, monovalan neonatal G9P[10], 116-E RV aşısı (Bharat Biotech, Hindistan)	Hindistan'da ruhsatlı
Rotavin-IM G1P[8] (Vietnam)	Vietnam'da ruhsatlı

THE LANCET

Efficacy of a monovalent human-bovine (116E) rotavirus vaccine in Indian infants: a randomised, double-blind, placebo-controlled trial

4532 infants were assigned to receive the 116E vaccine and 2267 to receive placebo, of whom 4354 (96%) and 2187 (96%) infants, respectively, were included in the primary per-protocol efficacy analysis. 71 events of severe rotavirus gastroenteritis were reported in 4752 person-years in infants in the vaccine group compared with 76 events in 2360 person-years in those in the placebo group; vaccine efficacy against severe rotavirus gastroenteritis was 53·6% (95% CI 35·0–66·9; p=0·0013) and 56·4% (36·6–70·1; p<0·0001) in the first year of life. The number of infants needed to be immunised to prevent one severe rotavirus gastroenteritis episode was 55 (95% CI 37–97). The incidence of severe rotavirus gastroenteritis per 100 person-years was 1·5 in the vaccine group and 3·2 in the placebo group, with an incidence rate ratio of 0·46 (95% CI 0·33–0·65). Prevalence of immediate, solicited, and serious adverse events was similar in both groups. One case of urticaria in the vaccine group and one each of acute gastroenteritis and suspected sepsis in the placebo group were regarded as related to the study product. We recorded six cases of intussusception in the vaccine group and two in the placebo group, all of which happened after the third dose. 25 (<1%) infants in the vaccine group and 17 (<1%) in the placebo group died; no death was regarded as related to the study product.

Interpretation

Monovalent human-bovine (116E) rotavirus vaccine is effective and well tolerated in Indian infants.

Bhandari N, et al. *The Lancet*. 2014;383(9935):2136-2143.

World Health Organization

Safety profile of a novel live attenuated rotavirus vaccine

Extract from report of GACVS meeting of 11-12 June 2014, published in the WHO Weekly Epidemiological Record on 18 July 2014

As the available safety data support further use of the vaccine, a post-licensure study of at least 45 000 vaccinated infants is planned. However, based on the experience with similar vaccines, it will be important that additional data be continuously collected in order to assess the risk of intussusception as well as to identify any other rare adverse events that may occur. Based on the experience with other rotavirus vaccines, the infrastructure of sentinel sites that exists in India should be utilized for continued intussusception surveillance in order to fully characterize the safety profile of this new rotavirus vaccine.

Viral Immunology

Comparison of Antigenic Dominants of VP7 in G9 and G1 Rotavirus Strains Circulating in La Rioja, Argentina, with the Vaccine Strains

ABSTRACT

A massive vaccination in Argentina was implemented recently. The antigenic dominants of VP7 in G9 and G1 rotavirus strains, circulating in La Rioja, Argentina with strain vaccines were compared. From 2000 to 2010 in several attention centers of La Rioja, at northwestern Argentina, 418 stool samples from children younger than 5 years old were collected. Ninety were positive by immunochromatography and 51 were genotyped by reverse transcriptase–polymerase chain reaction followed by nested-multiplex polymerase chain reaction (PCR) with type-specific primers. Six G9 strains and four G1 strains were sequenced by MACROGEN Korea. The phylogenetic analysis was conducted in MEGA 6.0. The 940 bp were aligned using CLUSTALW and the tree was inferred using the UPGMA method. The antigenic dominants of VP7, 7-1a, 7-1b, and 7-2 were studied using BioEdit, 7.2.5. In the comparison between G9-lineage III d rotavirus (RV) strains circulating in La Rioja with ROTAVAC vaccine strain, three differences were detected corresponding to 100, 211, and 145 positions. In the comparison between G1-Lineage 1 strains and G1 Rotarix and G1 RotaTeq, three differences were observed in 94, 123, and 217 positions. All these positions were important for the escape to neutralization for study with monoclonal antibody. In conclusion, the differences between the G1 strains in La Rioja, Argentina and the G1 components of the RotaTeq and Rotarix vaccine strains are few, but important for the escape immunologic, and need to be monitored for appropriate evaluation of long-term impact of vaccine used in Argentina. Nevertheless, the VP7 antigenic regions of G9 RV strains circulating in La Rioja and ROTAVAC vaccine strains are different to other zones of Argentina and could play an important role in the failure of vaccine response in these regions and Argentina.

Cuffia VI, et al. *Viral Immunol. 2016 Jul-Aug;29(6):367-71.*

ADAY ROTAVİRUS AŞILARI

Lanzhou monovalent G10P[12] aşısı (Çin)	**Çin'de ruhsatlı**
RotaVac, monovalan neonatal G9P[10], 116-E RV aşısı (Bharat Biotech, Hindistan)	**Hindistan'da ruhsatlı**
Rotavin-IM G1P[8] (Vietnam)	**Vietnam'da ruhsatlı**

Contents lists available at ScienceDirect

Vaccine

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

A dose-escalation safety and immunogenicity study of a new live attenuated human rotavirus vaccine (Rotavin-M1) in Vietnamese children☆,☆☆

Dang Duc Anh[a,*], Nguyen Van Trang[a], Vu Dinh Thiem[a], Nguyen Thi Hien Anh[a], Nguyen Duc Mao[b], Yuhuan Wang[c], Baoming Jiang[c,**], Nguyen Dang Hien[d,1], Le Thi Luan[d,1], the Rotavin-M1 Vaccine Trial Group[2]

[a] The National Institute of Hygiene and Epidemiology, Hanoi, Viet Nam
[b] Preventive Medicine Center, Phu Tho Province, Viet Nam
[c] Centers for Disease Control and Prevention, CDC, Atlanta, GA, USA
[d] Center for Research and Production of Vaccines and Biologicals, Hanoi, Viet Nam

ARTICLE INFO

Article history:
Received 13 May 2011
Received in revised form 14 July 2011
Accepted 25 July 2011

Keywords:
Rotavirus vaccine
Rotavin-M1
Vietnam
Safety
Immunogenicity
Vaccine dose
Rotarix™

ABSTRACT

We tested a candidate live, oral, rotavirus vaccine (Rotavin-M1™) derived from an attenuated G1P [8] strain (KH0118-2003) isolated from a child in Vietnam. The vaccine was tested first for safety in 29 healthy adults. When deemed safe, it was further tested for safety and immunogenicity in 160 infants (4 groups) aged 6–12 weeks in a dose and schedule ranging study. The vaccine was administered in low titer ($10^{6.0}$ FFU/dose) on a 2-dose schedule given 2 months apart (Group 2L) and on a 3-dose schedule given 1 month apart (Group 3L) and in high titer ($10^{6.3}$ FFU/dose) in 2 doses 2 months apart (Group 2H) and in 3 doses 1 month apart (Group 3H). For comparison, 40 children (group Rotarix™) were given 2 doses of the lyophilized Rotarix™ vaccine ($10^{6.5}$ $CCID_{50}$/dose) 1 month apart. All infants were followed for 30 days after each dose for clinical adverse events including diarrhea, vomiting, fever, abdominal pain, irritability and intussusception. Immunogenicity was assessed by IgA seroconversion and viral shedding was monitored for 7 days after administration of each dose. Two doses of Rotavin-M1 ($10^{6.3}$ FFU/dose) were well tolerated in adults. Among infants (average 8 weeks of age at enrollment), administration of Rotavin-M1 was safe and did not lead to an increased rate of fever, diarrhea, vomiting or irritability compared to Rotarix™, indicating that the candidate vaccine virus had been fully attenuated by serial passages. No elevation of levels of serum transaminase, blood urea, or blood cell counts were observed. The highest rotavirus IgA seroconversion rate (73%, 95%CI (58–88%)) was achieved in group 2H (2 doses – $10^{6.3}$ FFU/dose, 2 months apart). The 2 dose schedules performed slightly better than the 3 dose schedules and the higher titer doses performed slightly better than the lower titer doses. These rates of seroconversion were similar to that of the Rotarix™ group (58%, 95%CI (42–73%)). However more infants who received Rotarix™ (65%) shed virus in their stool after the first dose than those who received Rotavin-M1 (44–48%) ($p < 0.05$) and the percent shedding decreased after subsequent doses of either vaccine. Rotavin-M1 vaccine is safe and immunogenic in Vietnamese infants. A trial in progress will assess the safety, immunogenicity and efficacy of Rotavin-M1 (2 doses at $10^{6.3}$ FFU/dose) in a larger number of infants. The trial registration numbers are NCT01375907 and NCT01377571.

ADAY ROTAVİRUS AŞILARI

	Faz I	Faz II
RV3-BB G3P[6] aşısı (Murdoch Children's Research Institute, Avustralya)	**Faz I ve II imunojenite çalışmaları tamamlandı**	**Faz IIb imunojenite/güvenirlik çalışmaları devam ediyor.**
BRV Pentavalan RV aşısı (Serum Institute of India)		**Faz II çalışmaları devam ediyor.**
Tetravalan G1- 4 aşıları • ChengDu Institute of Biological (Çin) • Instituto Butantan (Brezilya) • Shanto Biotech, (Hindistan)	X	 X X

Korunmak tüm çocukların hakkı