

HPV Aşıları:
Gerçek Yaşam Verileri

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Global burden of cancer attributable to infections in 2018: a worldwide incidence analysis

Catherine de Martel, Damien Georges, Freddie Bray, Jacques Ferlay, Gary M Clifford

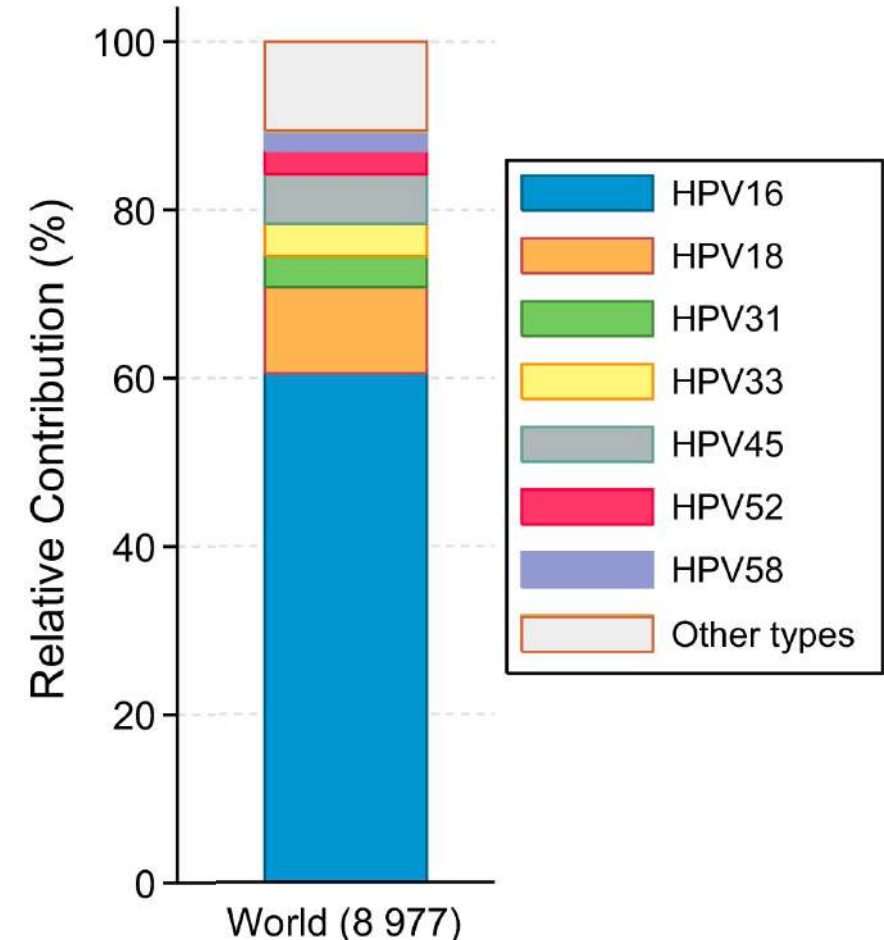
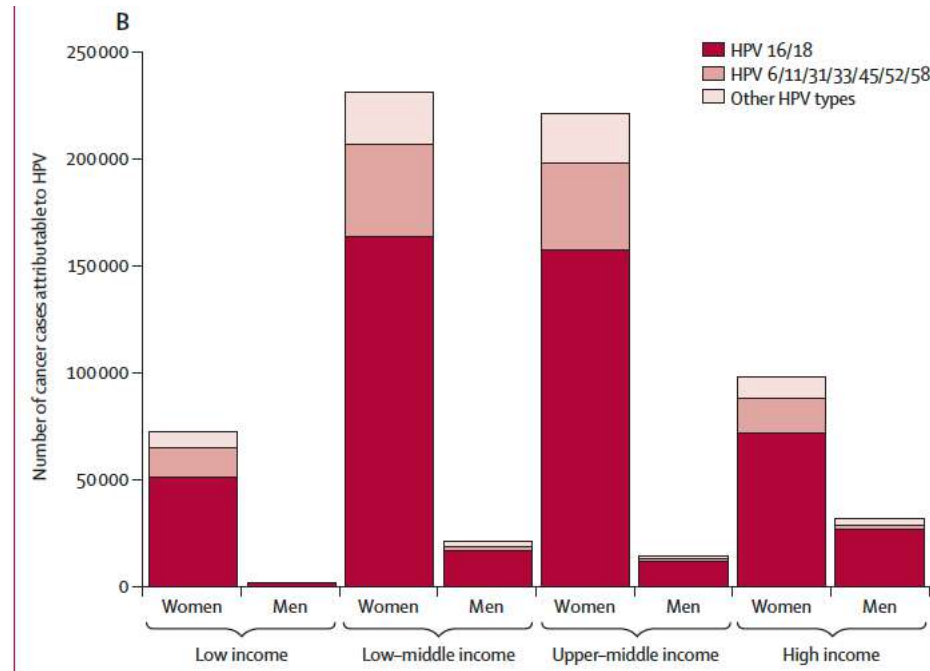


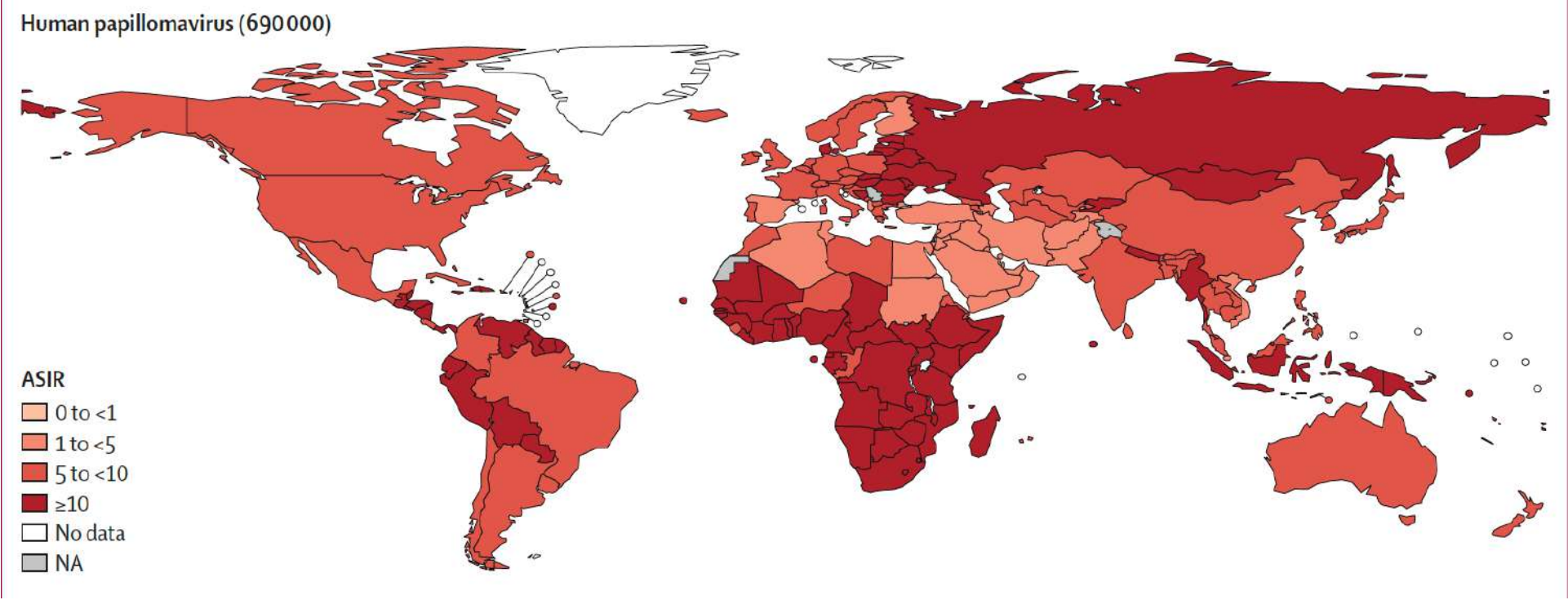
2018'de infeksiyon kaynaklı kanser: 2.2 milyon

Yaşa göre standardize insidans hızı (ASIR):

100 000 kişi-yıl başına 25

#1 *H. pylori* (ASIR:8.7) #2 HPV (ASIR:8.0)





HPV'ye baęlı kanser insidansı gelir düzeyi ile doğrudan ilişkilidir:

Düşük gelir düzeyine sahip ülkelerde ASIR: 16.1

Yüksek gelir düzeyine sahip ülkelerde ASIR: 6.9

Türkiye’de HPV ile İlişkili Kanserlerin Yükü (2021)

HPV ile ilişkili Kanserlerin Kaba İnsidans Oranı (100 000’de)			Rahim Ağzı Kanseri Yükü		
	Erkek	Kadın		İnsidans	Ölüm
Rahim ağzı kanseri	-	5.93	Yıllık yeni vaka/ölüm	2532	1245
Anal Kanser	0.26	0.29	Kaba Oran	5.9	3.1
Vulva Kanseri	-	0.67	ASIR	4.8	2.5
Vajinal Kanser	-	0.26	Kümülatif Risk (0-74 yaş)	0.5	0.3
Penil Kanser	0.06	-			
Farinks	0.41	0.12			



DERNEK

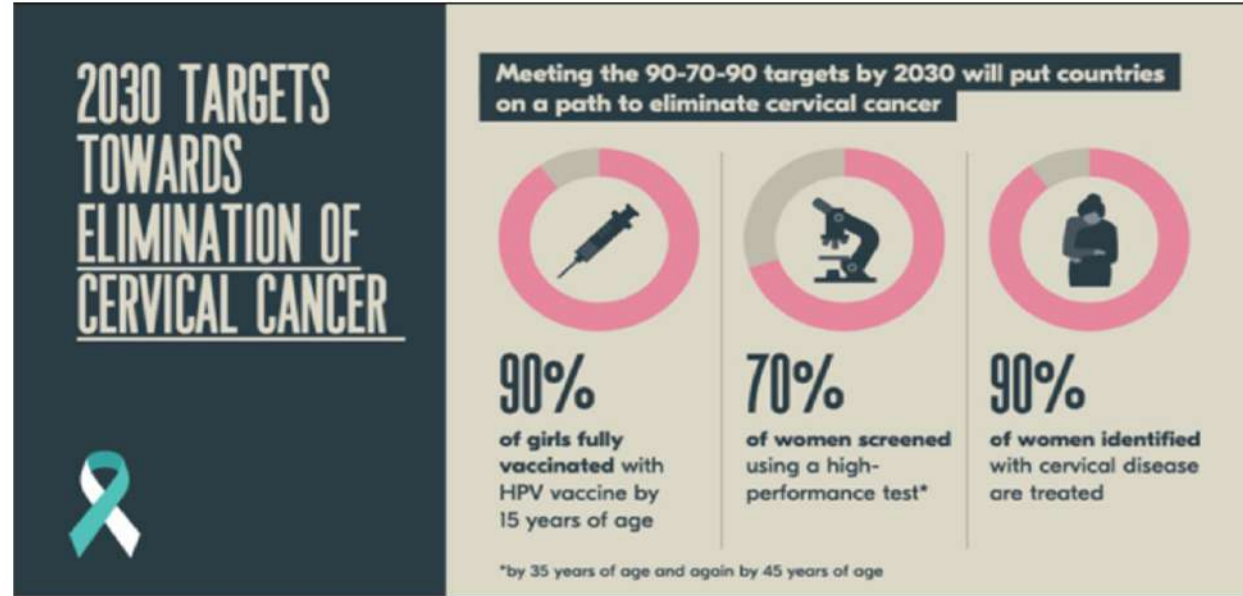
YETERLİK
KURULU

ÇALIŞMA
GRUPLARI

TOPLANTILAR

DUYURULAR »

RAHİM AĞZI (SERVİKS) KANSERİ FARKINDALIK AYI: HPV AŞISI RUTİN ÇOCUKLUK ÇAĞI AŞILAMA TAKVİMİNE DAHİL EDİLMELİ

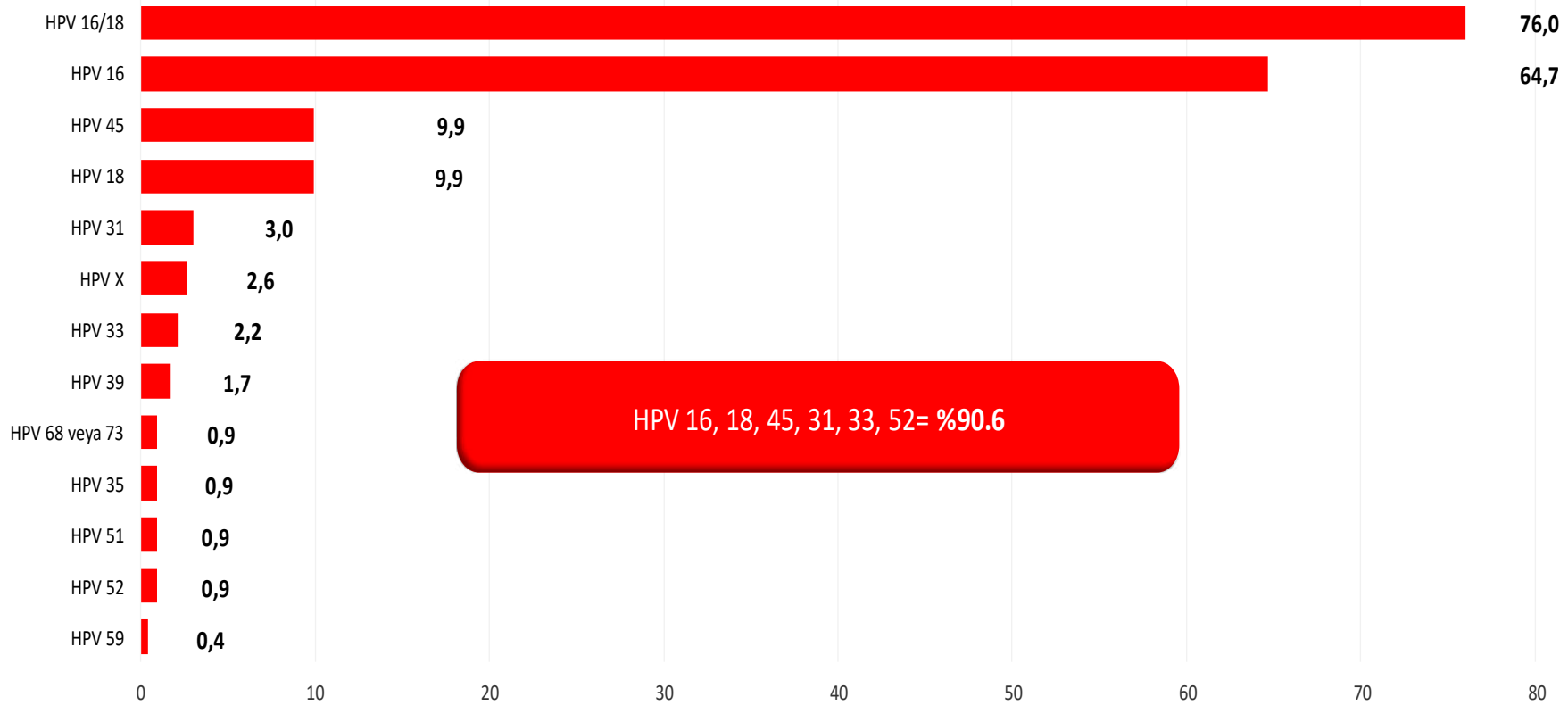


«İlk elimine edilecek kanser türü Serviks Kanseri olabilir» DSÖ, Mayıs 2018

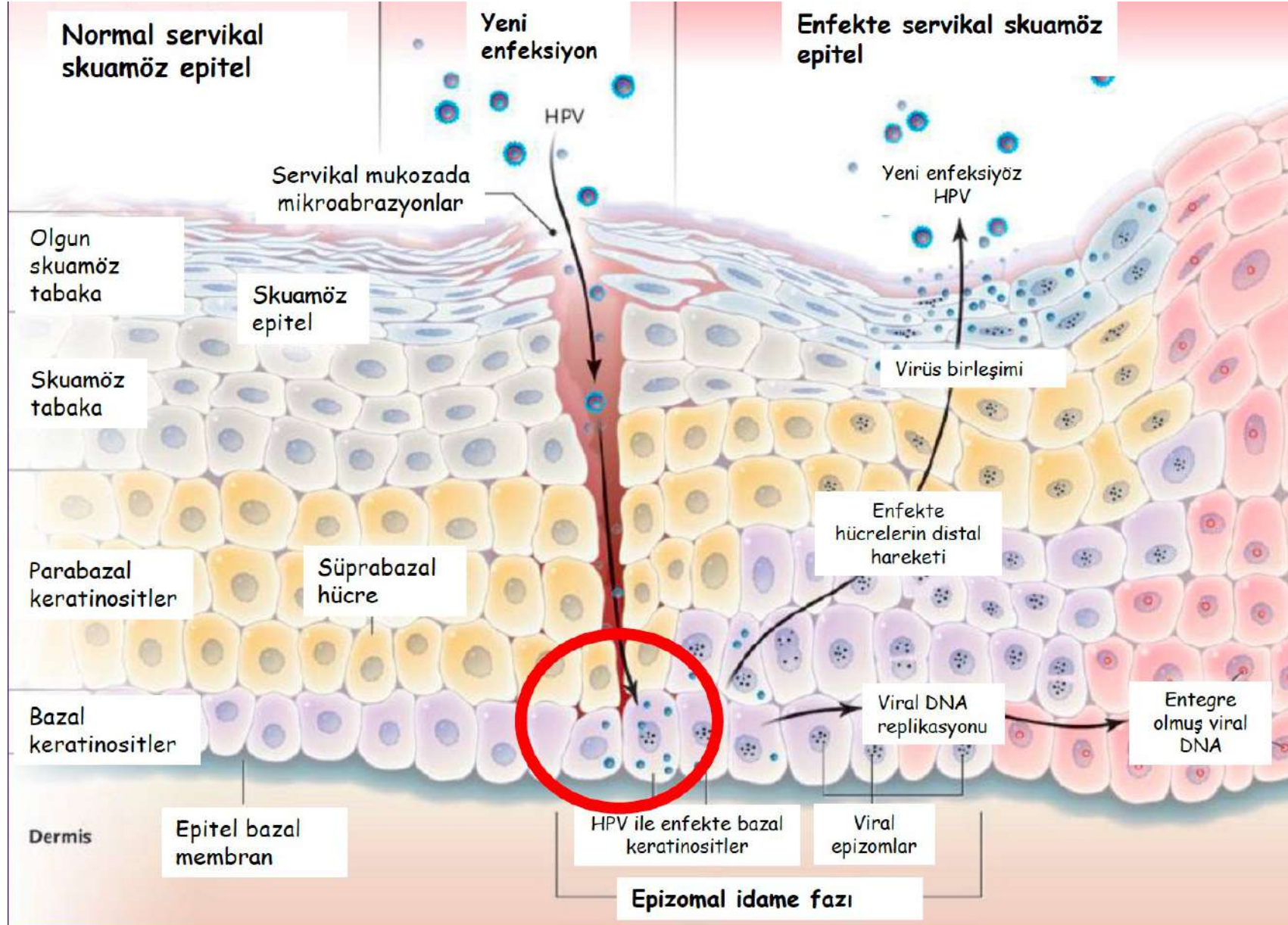
«Dünya Sağlık Asamblesi 2030 hedeflerini kabul etti» Ağustos 2020

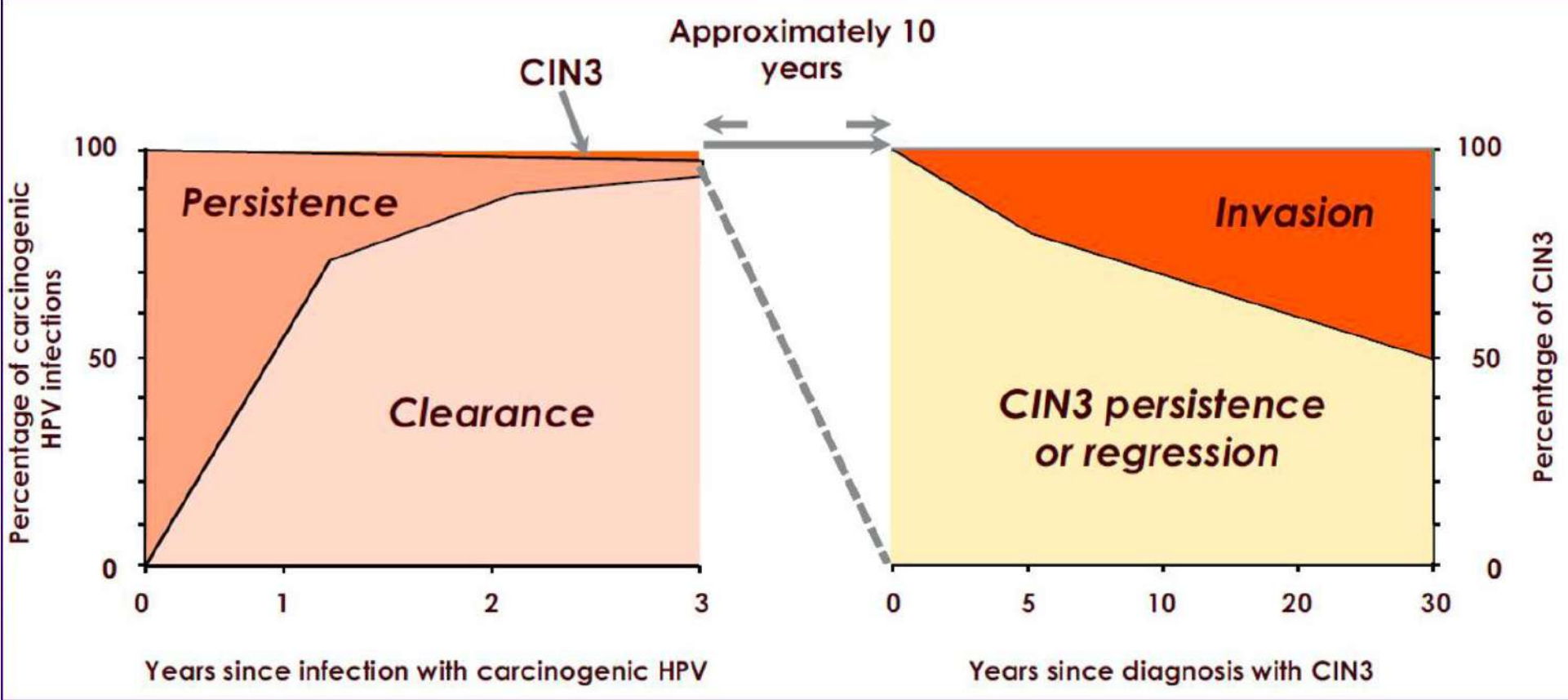
HPV Tipleri ve Taşıdığı Riskler

Yüksek Risk	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, 82
Orta Risk	26, 53, 66
Düşük Risk	6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81, CP6108



HPV Patogenezi





İnfeksiyon tamamen epitel ile sınırlı → Antijen sunumu YOK !

Keratinositleri parçalamıyor → hücre ölümü YOK → İnflamasyon YOK

HPV infeksiyon döngüsünde bakteremi YOK → Antikor yanıtı SINIRLI

İmmün yanıt
sınırlı



Kadınlar:

%54-69'unda serokonversiyon
Düşük düzeyde antikor
Reenfeksiyondan kısmi koruma

Erkekler:

%7-10'unda serokonversiyon
Düşük düzeyde antikor
Reenfeksiyondan koruma YOK

Aşıyla serokonversiyon: ~%100

?

Neden HPV aşıları doğal infeksiyondan daha iyi?

Doğal infeksiyonda virüs bağışıklık sisteminden kaçabiliyor:

Viremi \emptyset ,

Lenf nodlarına erişim az / \emptyset ,

IFN yanıtı baskılı

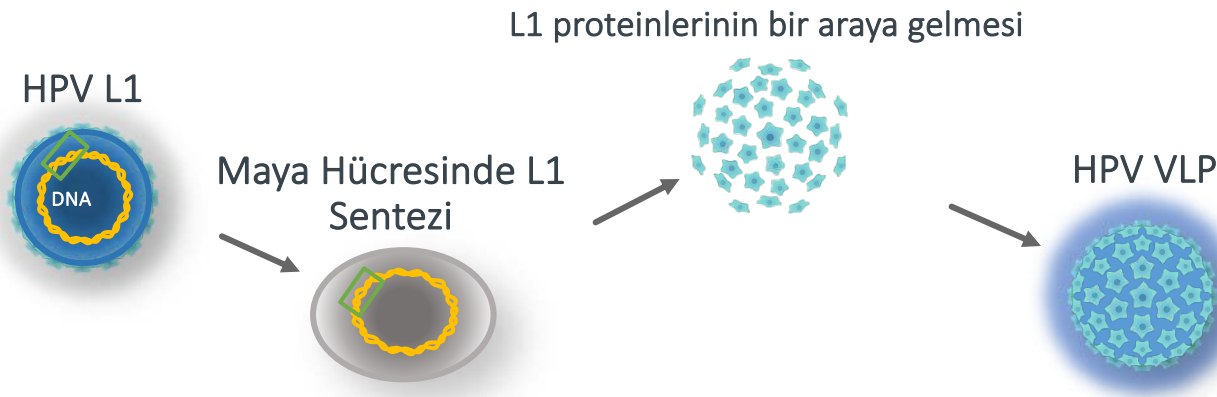
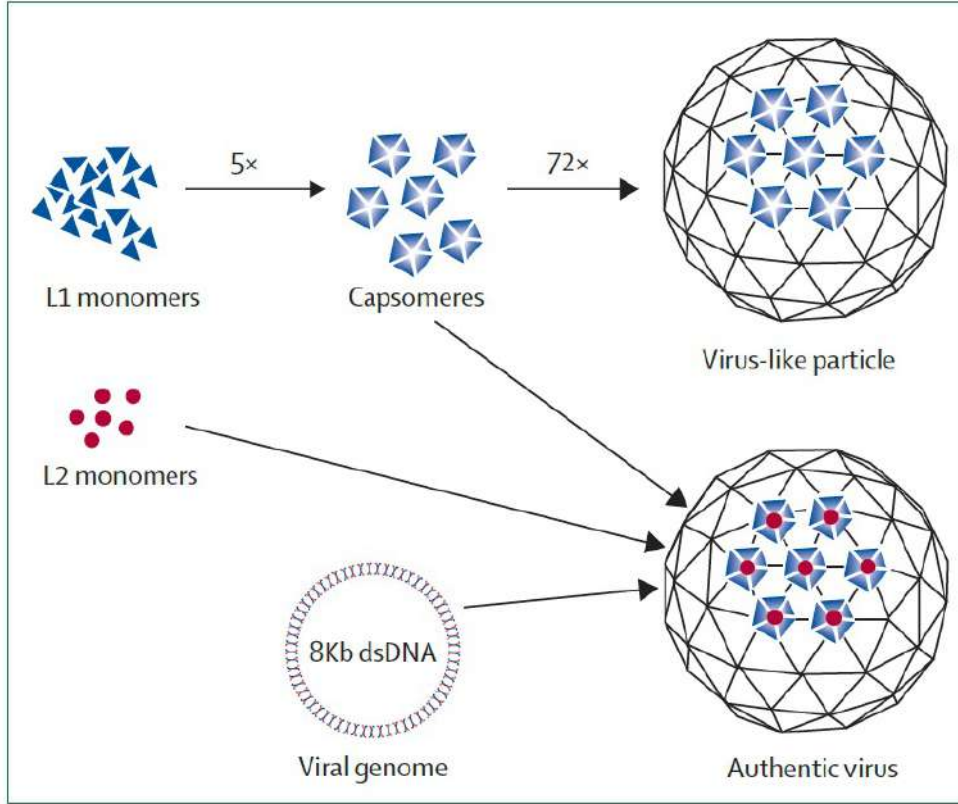
HPV aşıları bağışık yanıtı güçlü uyarıyor:

İM uygulama \rightarrow VLP'lerin kan ve lenf nodlarına erişimi

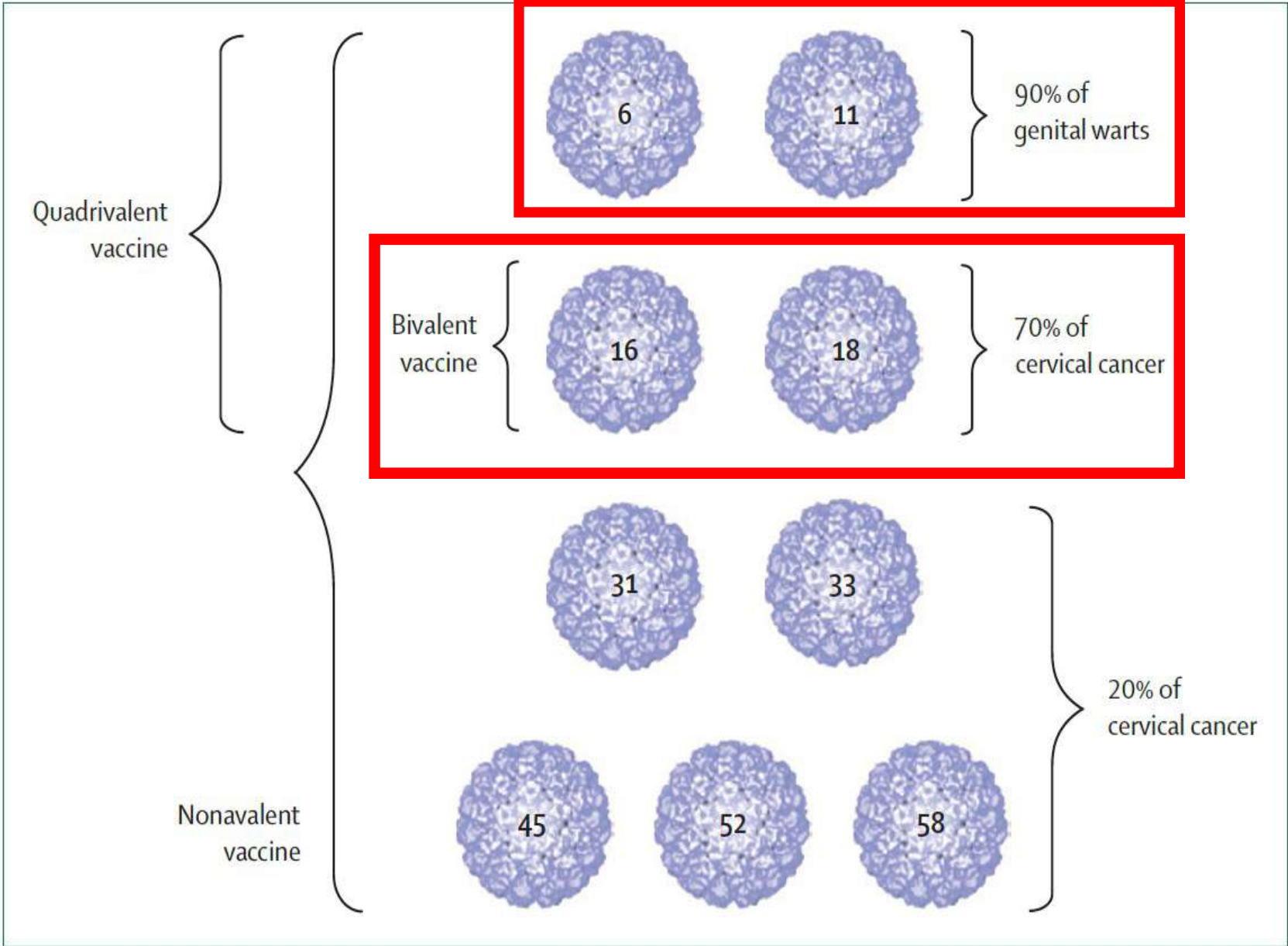
VLP'ler virüsten daha fazla epitop içeriyor

VLP'ler T-hücre yanıtını da tetikliyor

HPV Aşı Teknolojisi – Rekombinant DNA

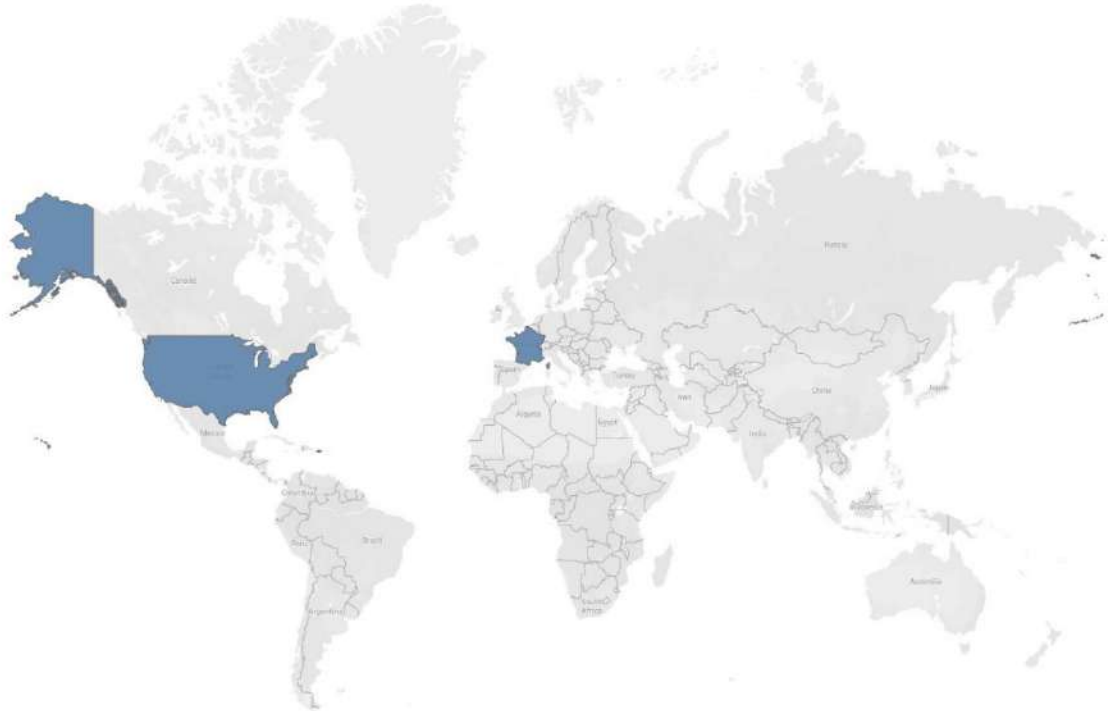


Gardasil®



Global HPV Vaccine Introduction

Year:
2006



Introduction status

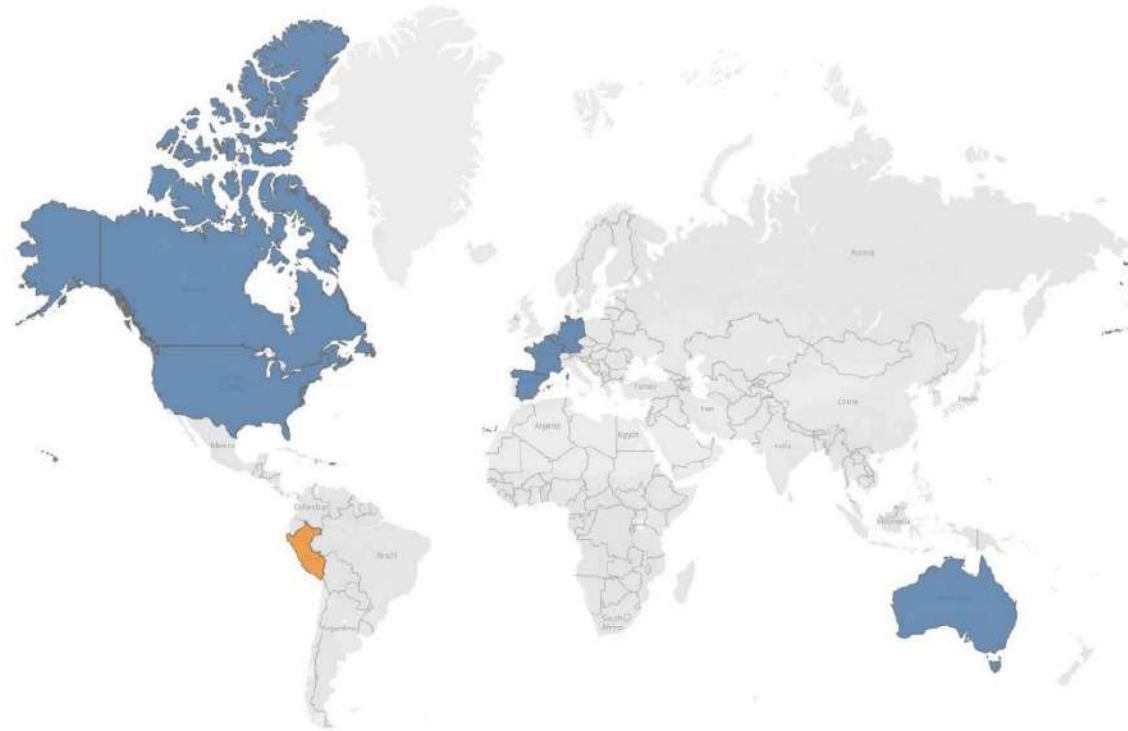
- Demonstration
- National
- Subnational
- Demo complete*

** Decision pending on national introduction*

As of 17 Aug 2021

Global HPV Vaccine Introduction

Year:
2007



Introduction status

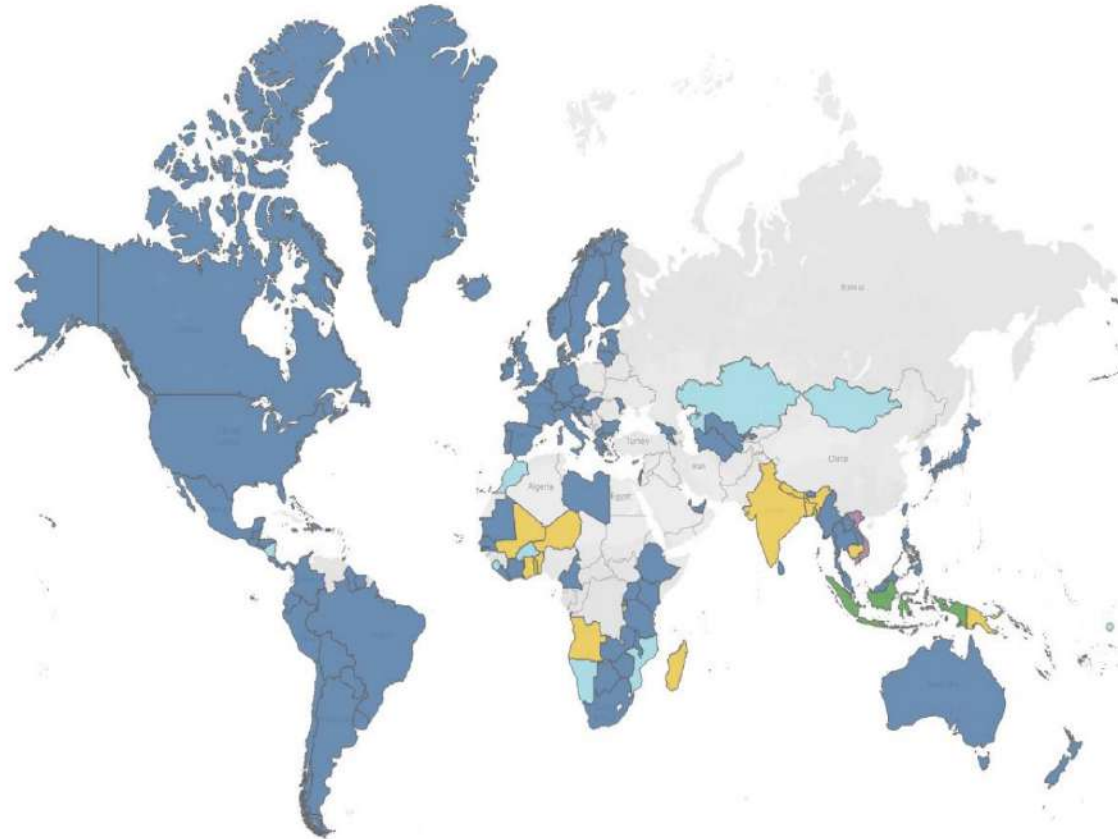
- Demonstration
- National
- Subnational
- Demo complete*

* Decision pending on national introduction

As of 17 Aug 2021

Global HPV Vaccine Introduction

Year:
2021



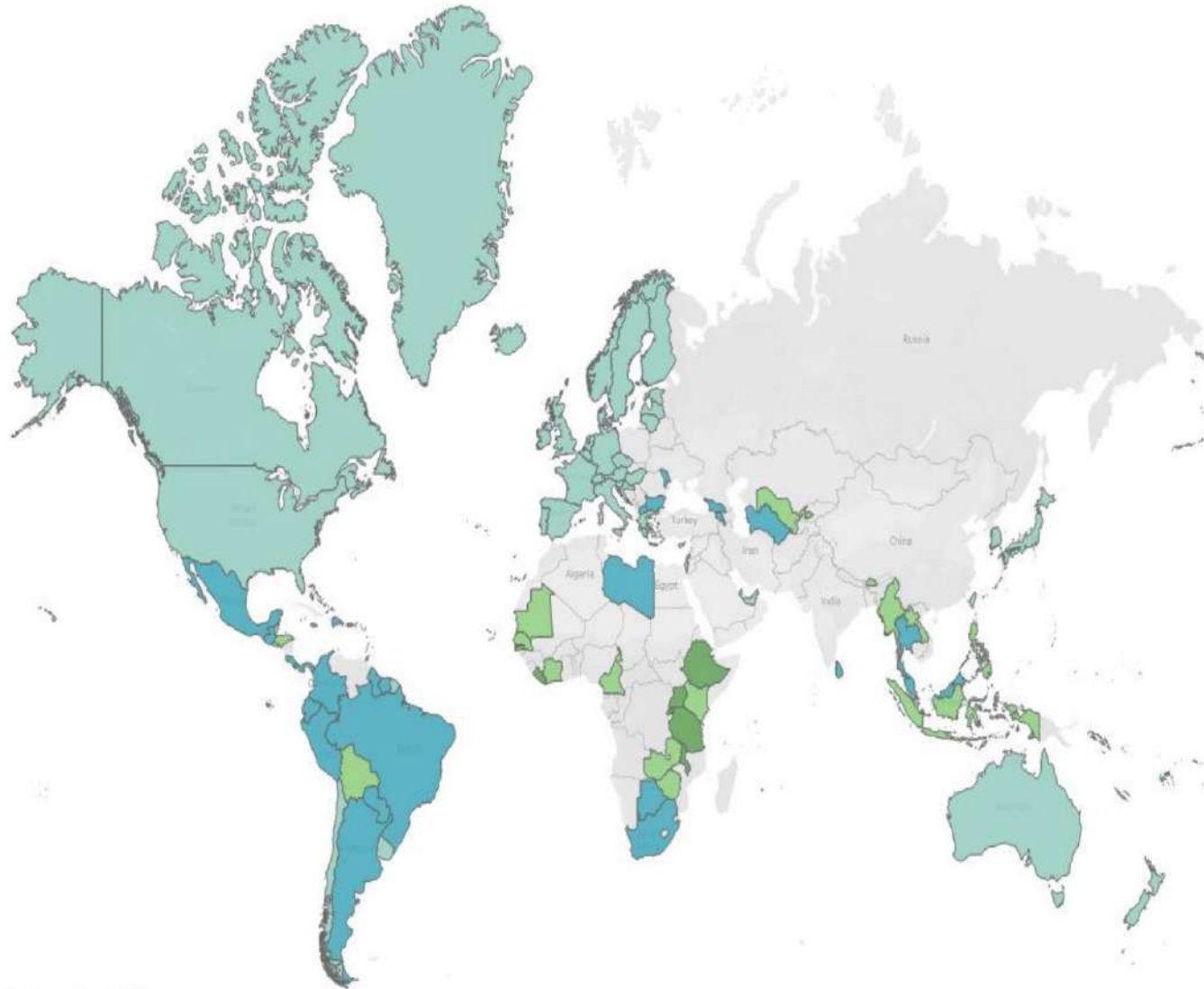
Introduction status

- National
- Subnational
- Demo complete*
- Projected - national
- Projected - subnational

** Decision pending on national introduction*

As of 17 Aug 2021

Global HPV Vaccine Introductions by World Bank Category



World Bank Category (2021)

■ LIC	7 of 29 have introduced
■ LMIC	21 of 51 have introduced
■ UMIC	37 of 61 have introduced
■ HIC	74 of 84 have introduced
■ Not classified	

As of 17 Aug 2021

Countries and territories with HPV vaccine on national routine immunization schedule

WHO Member States (n=114 active; n=3 stopped)					Non-members (n=27)
Andorra (2014)	Cyprus (2016)	Israel (2013)	Netherlands (2010)	St. Lucia (2019)	American Samoa (2009)
Antigua & Barbuda (2018)	Czech Republic (2012)	Italy (2008)	New Zealand (2008)	St. Vincent and the Grenadines (2017)	Anguilla (2016)
Argentina (2011)	Denmark (2008)	Jamaica (2017)	Niue (2019)	Suriname (2013)	Aruba (2014)
Armenia * (2018)	Dominica (2019)	Japan (2011)	Norway (2009)	Sweden (2012)	Bermuda (2007)
Australia (2007)	Dominican Republic (2017)	Kazakhstan (subnational 2013-2015; stopped 2015)	Palau (2008)	Switzerland (2008)	Bonaire (2015)
Austria (2008)	Ecuador (2014)	Kenya * (2019)	Panama † (2008)	Tanzania * (2018)	British Virgin Islands (2019)
Bahamas (2015)	El Salvador (2020)	Lao PDR * (2020)	Paraguay (2013)	Thailand * (2017)	Cayman Islands (2012)
Barbados (2014)	Estonia (2018)	Lesotho * (2012, stopped 2015)	Peru * (2011, stopped 2012; 2014)	Trinidad & Tobago (2012, stopped 2013; 2015)	French Guiana (2007)
Belgium (2007)	Ethiopia * (2018)	Latvia (2010)	Philippines † (2015)	Turkmenistan (2016)	Guernsey (2019)
Belize (2016)	Federated States of Micronesia (2009)	Liberia * (2019)	Portugal (2008)	Uganda *† (2015)	Gibraltar (2008)
Bhutan * (2010)	Fiji † (2008-09, stopped 2010; 2013)	Libya (2014)	Qatar (2020)	United Arab Emirates † (subnational 2008-2012; 2013)	Greenland (2008)
Bolivia * (2017)	Finland (2013)	Lithuania (2016)	Romania (2009-10, stopped 2011)	United Kingdom (2008)	Guam (2007)
Botswana * (2015)	France (2006)	Luxembourg (2008)	Rwanda (2011)	United States (2006)	Isle of Man (2008)
Brazil * (2014)	The Gambia (2019) *†	Macedonia FYR (2009)	Samoa (2021)	Uruguay (2013)	Jersey (2008)
Brunei (2012)	Georgia (2019)	Malawi * (2019)	San Marino (2008)	Uzbekistan * (2019)	Liechtenstein (2013)
Bulgaria (2012)	Germany (2007)	Malaysia (2010)	Senegal * (2018)	Zambia * (2019)	Macau (2013)
Cameroon (2020)	Greece (2008)	Maldives (2019)	Seychelles (2014)	Zimbabwe * (2018)	Montserrat (2017)
Canada (2007)	Grenada (2019)	Malta (2012)	Singapore (2010)		New Caledonia (2011)
Cape Verde (2021)	Guatemala (2018)	Marshall Islands § (2009)	Slovenia (2009)		Northern Mariana Islands (2008)
Chile (2014)	Guyana *† (Subnational 2012-13; 2017)	Mauritania (2021)	Solomon Islands * (2019)		Puerto Rico (2008)
Colombia † (2012)	Honduras (2016)	Mauritius (2016)	South Africa * (2014)		Saba (2013)
Cook Islands (2011)	Hungary (2014)	Mexico † (subnational 2008-2011; 2012)	South Korea (2016)		St. Eustatius (2014)
Costa Rica (2019)	Iceland (2011)	Moldova * (2020)	Spain (2007)		St. Maarten (2013)
Côte d'Ivoire * (2019)	Indonesia (2019)	Monaco (2011)	Sri Lanka (2017)		Taiwan (2018)
Croatia (2016)	Ireland (2010)	Myanmar (2020)	St. Kitts and Nevis (2019)		Turks and Caicos (2019)
					U.S. Virgin Islands (2012)
					Wallis and Futuna (2013)

* National/territorial introduction has followed pilot.
 † National/territorial introduction in phases, either based on geography, target population, or both.

As of 17 Aug 2021

Countries or territories with gender-neutral HPV vaccination schedules (year of recommendation)

<i>American Samoa</i> (2014)	Ireland (2019)
Antigua and Barbuda (2018)	Isle of Man (?)
Argentina (2017)	Israel (2015)
Australia (2013)	Italy (2018*)
Austria (2014)	Jersey (?)
Bahamas (2015)	Liechtenstein (2016)
Barbados (2017)	Luxembourg (2019)
<i>Bermuda</i> (2016)	New Zealand (2017)
Belgium (2019)	Niue (2019)
Brazil (2017)	<i>Northern Mariana Islands</i> (2011)
Canada (2017*)	Norway (2018)
Chile (2019)	Panama (2016)
Croatia (2016)	Puerto Rico (?)
Czech Republic (2016)	St. Kitts and Nevis (2019)
Denmark (2019)	St. Lucia (2019)
Dominica (2019)	Switzerland (2016)
Dominican Republic (?)	Turkmenistan (2016)
Germany (2019)	Trinidad and Tobago (2015)
<i>Guam</i> (2011)	United Kingdom (2019)
Guernsey (?)	United States (2011)
Guyana (2019)	Uruguay (2019)

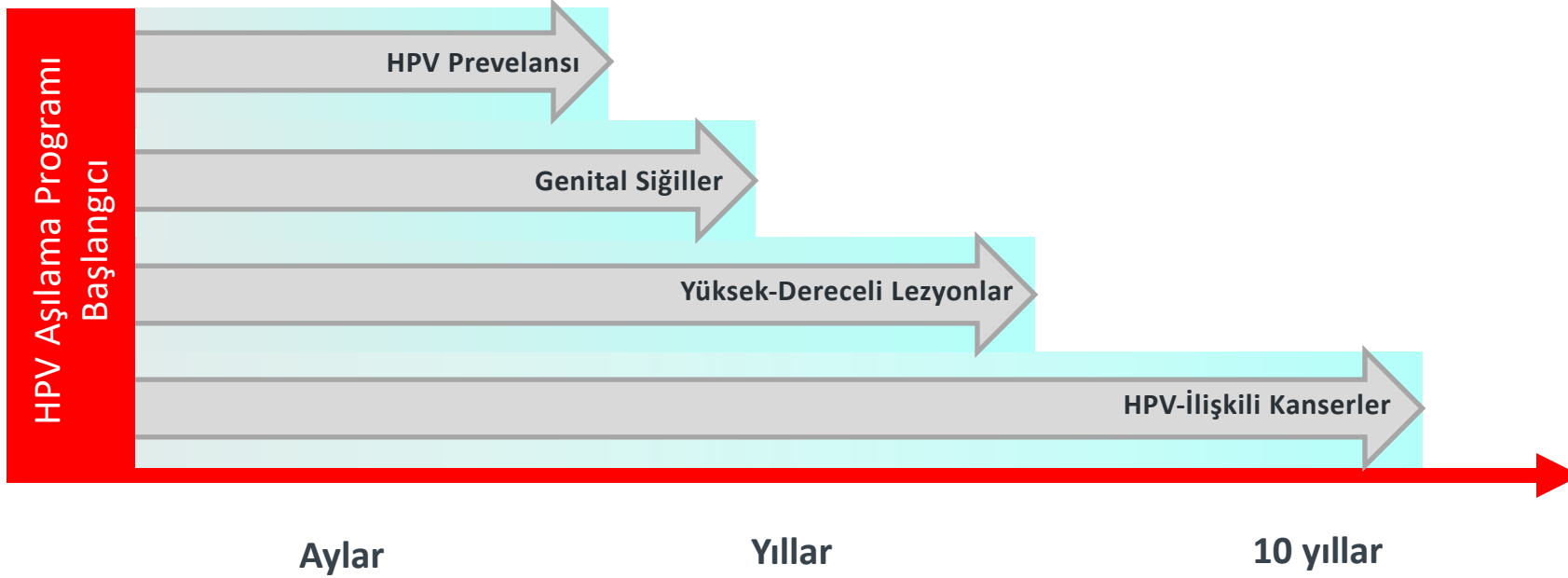
42 countries and 4 territories have **gender-neutral HPV vaccination schedules**

As of 17 Aug 2021

** province or region specific*

HPV Aşılmasının Gerçek Dünyadaki Etkisinin Değerlendirilmesi

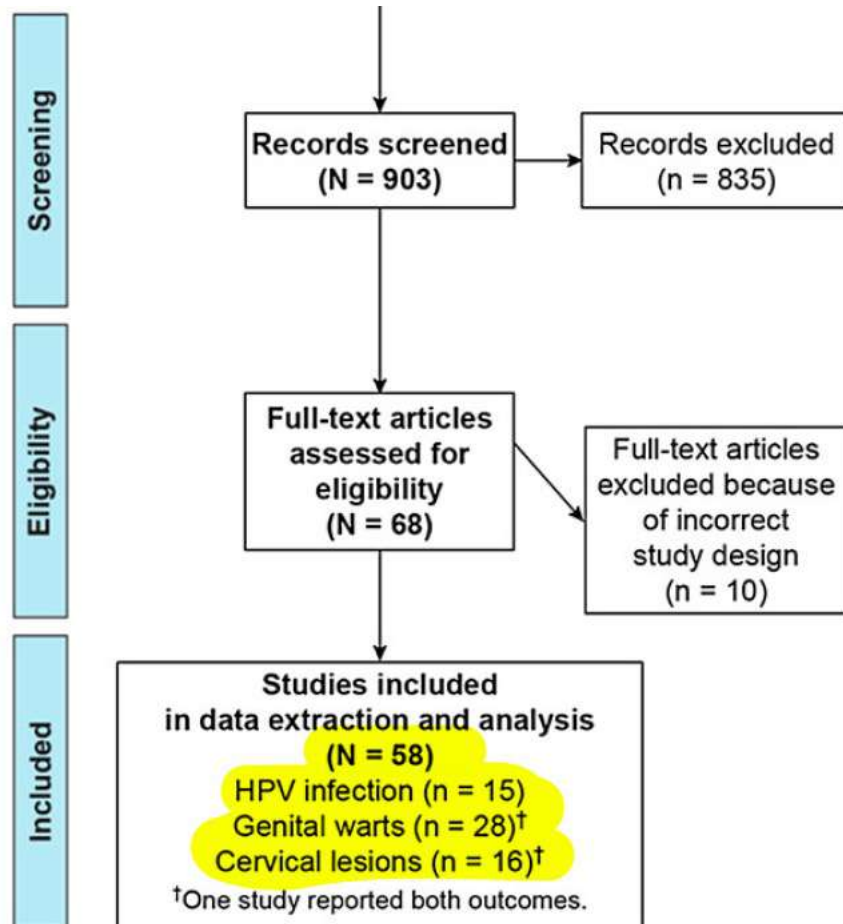
Aşılama Programının Başlangıcından Etkinin Ölçülmesine Tahmini Süre



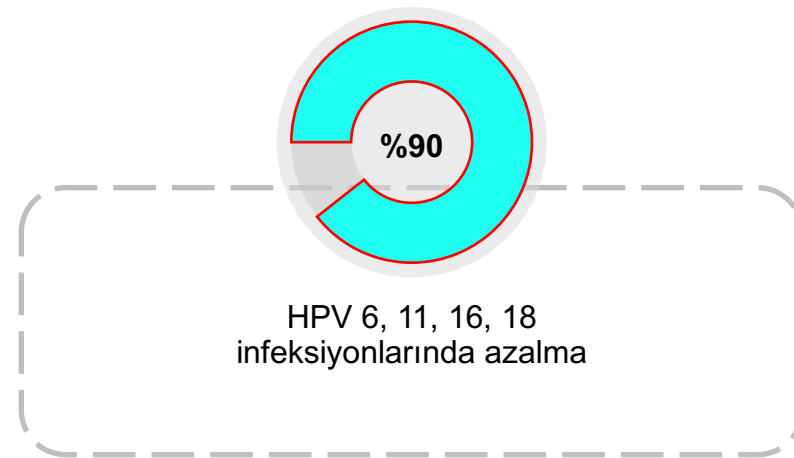
Impact and Effectiveness of the Quadrivalent Human Papillomavirus Vaccine: A Systematic Review of 10 Years of Real-world Experience

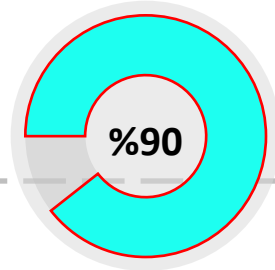
Suzanne M. Garland,¹ Susanne K. Kjaer,² Nubia Muñoz,³ Stan L. Block,⁴ Darron R. Brown,⁵ Mark J. DiNubile,⁶ Brianna R. Lindsay,⁶ Barbara J. Kuter,⁶ Gonzalo Perez,^{6,7} Geraldine Dominiak-Felden,⁸ Alfred J. Saah,⁶ Rosybel Drury,⁸ Rituparna Das,⁶ and Christine Velicer⁶

Clinical Infectious Diseases 2016;63(4):519–27

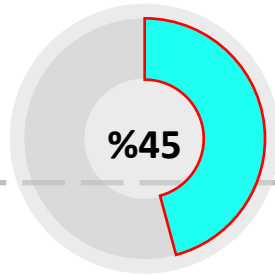


2007-2016 arası gözlemsel çalışmalar

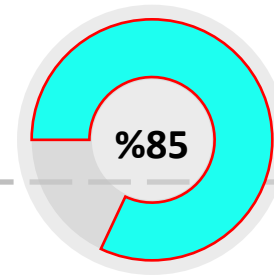




Kadın ve erkeklerde genital siğil oranında azalma



Düşük grade servikal sitolojik anomalilerde azalma



Histolojik olarak dokümante edilmiş yüksek grade servikal sitolojik anomalilerde azalma



Contents lists available at ScienceDirect

EClinicalMedicine

journal homepage: <https://www.journals.elsevier.com/eclinicalmedicine>

Research Paper

Final analysis of a 14-year long-term follow-up study of the effectiveness and immunogenicity of the quadrivalent human papillomavirus vaccine in women from four nordic countries

Susanne K. Kjaer^{a,*}, Mari Nygård^b, Karin Sundström^c, Joakim Dillner^c, Laufey Tryggvadottir^d,

İsveç, Norveç, Danimarka, İzlanda

FUTURE-II çalışmasına (4 yıl) katılan 16-23 yaş kadınların çalışma sonrası 10 yıllık takipleri

0, 1 ve 6. aylarda 3 doz 4vHPV aşısı yapılan 2121 kadın gönüllü (24 099 kişi-yıl takip)

5 (9) ve 10. (14) yıllarda immünojenite için serum alınmış,

Servikal Smear taramasını isteyen (%96,9) yaptırmış

Analysis of qHPV vaccine effectiveness against HPV16/18-related CIN2 or worse by time since qHPV vaccination, HPV type, and lesion type

	Young women 16–23 years of age (N=2650)			
	Cases/n	Person-years' follow-up [†]	Rate per 100 person-years (95% CI)	Vaccine effectiveness, % (95% CI)
PPE population[†]				
HPV16/18-related CIN2 or worse	0/2121	24099.0	0.0 (0.0–<0.1)	100 (94.7–100.0)
By time since qHPV vaccine Dose 1				
≤4 years	0/2121	7246.8	0.0 (0.0–0.1)	
>4 to 6 years	0/2121	4220.4	0.0 (0.0–0.1)	
>6 to 8 years	0/2089	4121.8	0.0 (0.0–0.1)	
>8 to 10 years	0/2022	3901.0	0.0 (0.0–0.1)	
>10 to 12 years	0/1855	3197.6	0.0 (0.0–0.1)	
>12 to 14 years	0/1211	1393.4	0.0 (0.0–0.3)	
>14 to 16 years	0/122	18.0	0.0 (0.0–20.5)	
By HPV type				
HPV16-related	0/1814	20583.9	0.0 (0.0–<0.1)	
HPV18-related	0/2018	22940.6	0.0 (0.0–<0.1)	
By lesion type				
CIN2	0/2121	24099.0	0.0 (0.0–<0.1)	
CIN3	0/2121	24099.0	0.0 (0.0–<0.1)	
AIS	0/2121	24099.0	0.0 (0.0–<0.1)	
Cervical cancer	0/2121	24099.0	0.0 (0.0–<0.1)	

14 yıl sonunda katılımcıların >%90 aşı tiplerine karşı yüksek düzey antikor varlığı

IgG-LIA	Time since Dose 1	Young women 16–23 years of age (N=2750)		
		n	IgG-LIA GMT (95% CI), mMu/mL	IgG-LIA Seropositivity [†] (95% CI) [‡] , %
Anti-HPV6	Month 108	1235	95.2 (90.5, 100.1)	97.6 (96.6, 98.4)
	Month 168	1054	81.2 (76.1, 86.5)	98.1 (97.1, 98.8)
Anti-HPV11	Month 108	1235	67.4 (64.3, 70.8)	96.3 (95.1, 97.3)
	Month 168	1055	53.5 (50.2, 57.0)	98.0 (97.0, 98.8)
Anti-HPV16	Month 108	1181	346.1 (327.3, 365.9)	100 (99.7, 100)
	Month 168	1000	290.2 (271.0, 310.8)	100 (99.6, 100)
Anti-HPV18	Month 108	1333	46.1 (43.3, 49.2)	91.4 (89.7, 92.8)
	Month 168	1036	36.5 (33.7, 39.5)	93.8 (92.2, 95.2)

Sonuç: 4vHPV aşısı

>CIN2 lezyonlara karşı 14 yıl sonunda %100 koruyucu

>90'dan fazla antikor pozitifliği (Rapel doza gerek yok)

Prophylactic vaccination against human papillomaviruses to prevent cervical cancer and its precursors (Review)

Arbyn M, Xu L, Simoens C, Martin-Hirsch PPL

Review question

Does HPV vaccination prevent the development of cervical precancer or cancer and what are the harms?

Main results

We included 26 studies involving 73,428 adolescent girls and women. All trials evaluated vaccine safety over a period 0.5 to 7 years and ten trials, with follow-up 3.5 to 8 years, addressed protection against precancer. Cervical cancer outcomes are not available. Most participants enrolled were younger than 26 years of age. Three trials recruited women between 25 to 45 years. The studies compared HPV vaccine with a dummy vaccine.

We assessed protection against precancer in individuals who were free of hrHPV, free of HPV16/18 or those with or without HPV infection at the time of vaccination. We separately assessed precancer associated with HPV16/18 and any precancer.

HPV vaccine effects on cervical lesions in adolescent girls and women who are hrHPV DNA negative at baseline

Patient or population: adolescent girls and women aged 15 to 26 years who are hrHPV negative before vaccination

Setting: Europe, Asia Pacific countries, South & North America

Intervention: HPV vaccines (at least one dose of bivalent or quadrivalent vaccines)

Comparison: Placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo	Risk with HPV vaccination ¹			
Cervical cancer - not measured	-	-	-	-	-
CIN2+ associated with HPV16/18. Follow-up: 3 to 5 years	164 per 10,000	2 per 10,000 (0 to 8)	RR 0.01 (0.00 to 0.05)	23,676 (3 RCTs)	⊕⊕⊕⊕ HIGH
CIN3+ associated with HPV16/18 Follow-up: 3 to 5 years	70 per 10,000	0 per 10,000 (0 to 7)	RR 0.01 (0.00 to 0.10)	20,214 (2 RCTs)	⊕⊕⊕⊕ HIGH
AIS associated with HPV16/18 Follow-up: 3 to 5 years	9 per 10,000	0 per 10,000 (0 to 7)	RR 0.10 (0.01 to 0.82)	20,214 (2 RCTs)	⊕⊕⊕⊖ MODERATE ²
Any CIN2+ irrespective of HPV type, bivalent or quadrivalent vaccine Follow-up: 2 to 6 years	287 per 10,000	106 per 10,000 (72 to 158)	RR 0.37 (0.25 to 0.55)	25,180 (5 RCTs)	⊕⊕⊕⊕ HIGH
Any CIN2+ irrespective of HPV type Follow-up (bivalent): 3.5 to 6 years Follow-up (quadrivalent): 3.5 years	Bivalent vaccine 285 per 10,000	94 per 10,000	RR 0.33 (0.25 to 0.43)	15,884 (4 RCTs)	⊕⊕⊕⊕ HIGH

HPV vaccine effects on cervical lesions in adolescent girls and women unselected for HPV DNA status at baseline

Patient or population: adolescent girls and women aged 15 to 45 years regardless of HPV DNA status at baseline

Setting: Europe, Asia Pacific countries, South & North America and Africa

Intervention: HPV vaccines (at least one dose of bivalent or quadrivalent vaccines)

Comparison: Placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	N° of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with HPV vaccination ¹				
Cervical cancer - not measured	-	-	-	-	-	
CIN2+ associated with HPV16/18	15 to 26 years		RR 0.46	34,852	⊕⊕⊕⊕	
Follow-up (age 15 to 26 years): 3.5 to 8.5 years	341 per 10,000	157 per 10,000 (126 to 194)	(0.37 to 0.57)	(3 RCTs)	HIGH	
Follow-up (age 24 to 45 years): 3.5 years						
Any CIN2+ irrespective of HPV type	15 to 26 years		RR 0.70	35,779	⊕⊕⊕⊕	
Follow-up (age 15 to 26 years): 3.5 to 8.5 years	559 per 10,000	391 per 10,000 (324 to 475)	(0.58 to 0.85)	(4 RCTs)	HIGH	
Follow-up (age 24 to 45 years): 3.5 to 6 years						
	24 to 45 years		RR 1.04	9287	⊕⊕⊕○	
	343 per 10,000	356 per 10,000 (284 to 445)	(0.83 to 1.30)	(2 RCTs)	MODERATE²	
Any CIN3+ irrespective of HPV type (age 15 to 26 years)	266 per 10,000	178 per 10,000 (231 to 247)	RR 0.67	35,489	⊕⊕⊕○	
Follow-up: 3.5 to 4 years			(0.49 to 0.93)	(3 RCTs)	MODERATE	

The effects of the national HPV vaccination programme in England, UK, on cervical cancer and grade 3 cervical intraepithelial neoplasia incidence: a register-based observational study

Lancet 2021; 398: 2084-92

Published Online

November 3, 2021

[https://doi.org/10.1016/](https://doi.org/10.1016/S0140-6736(21)02178-4)

S0140-6736(21)02178-4

Milena Falcaro, Alejandra Castañon, Busani Ndlela, Marta Checchi, Kate Soldan, Jamie Lopez-Bernal, Lucy Elliss-Brookes, Peter Sasieni

İngiltere 1988'de 20-60 yaş kadınları taramaya başlamış

2004'te alt sınır 25 yaş, 2012'de 24.5 yaş olarak değiştirilmiş, 2vHPV aşısı:2008, 4vHPV aşısı:2012

Aşılama durumu ve taramaya başlama yaşına göre 7 kohort belirlenerek aşı etkisi araştırılmış

	Date of birth							
	Jan 2, 1941	Sept 1, 1984	Nov 1, 1985	May 1, 1989	Sept 1, 1990	Sept 1, 1993	Sept 1, 1995	July 1, 1999
Birth cohort	1	2	3	4	5	6	7	
Age at first invitation to screening (years)	20	20 or 25	25	24.5	24.5	24.5	24.5	
Offer of HPV vaccination	No	No	No	No	Yes	Yes	Yes	
School years					12-13	10-11	8	
Age (years)					16-18	14-16	12-13	
Coverage*								
At least 1 dose					60.5%	80.1%	88.7%	
3 doses					44.8%	73.2%	84.9%	

2006- 2019 döneminde, 20-64 yaş kadınlarda CIN3 (27 946) ve Servikal kanser (318 058)
13.7 milyon takip yılı

	Cervical cancer			CIN3		
	20.0 to <24.5 years	24.5 to <26.0 years	26.0 to <30.0 years	20.0 to <24.5 years	24.5 to <26.0 years	26.0 to <30.0 years
Unvaccinated cohorts						
Cohort 1: invited from age 20.0 years and no vaccine	4.2 (70)	11.7 (246)	16.1 (1532)	233.8 (3893)	498.3 (10522)	446.9 (42443)
Cohort 2: invited from age 20.0 years or 25.0 years and no vaccine	2.5 (38)	27.0 (176)	20.4 (352)	100.6 (1504)	847.3 (5520)	489.0 (8443)
Cohort 3: invited from age 25.0 years and no vaccine	2.0 (109)	28.2 (557)	18.8 (987)	52.9 (2868)	1027.6 (20298)	476.4 (25020)
Cohort 4: invited from age 24.5 years and no vaccine	1.8 (37)	27.8 (211)	18.0 (315)	29.9 (629)	1141.7 (8680)	452.9 (7948)
Vaccinated cohorts						
Cohort 5: invited from age 24.5 years and offered vaccine in school years 12-13	1.0 (47)	20.0 (340)	11.5 (174)	15.9 (755)	673.2 (11452)	312.8 (4752)
Cohort 6: invited from age 24.5 years and offered vaccine in school years 10-11	0.7 (21)	14.5 (49)	..	6.3 (188)	434.9 (1466)	..
Cohort 7: not invited before age 24.5 years and offered vaccine in school year 8	0.3 (7)	2.0 (49)

Data are incidence (number of cases) CIN=cervical intraepithelial neoplasia.

Table 2: Crude incidence rates per 100 000 women-years by cohort and age group (for simplicity, restricted to age <30.0 years) for cervical cancer and CIN3

Servikal Kanser ve CIN3 sıklığında 2vHPV aşı uygulamasına bađlı azalma

Aşı uygulama yaşı/ Sonuç	12-13 y	14-16y	16-18y
Servikal Kanser	%87 (72-94)	%62 (52-71)	%34 (25-41)
CIN3	%97 (96-98)	%75 (72-77)	%39 (36-41)

İngiltere'de 2vHPV aşılması sayesinde, 2019 yılına kadar beklenenden;

448 (339-556) daha az servikal kanser

17235 (15919-18552) daha az CIN3 gelişti

ORIGINAL ARTICLE

HPV Vaccination and the Risk of Invasive Cervical Cancer

Jiayao Lei, Ph.D., Alexander Ploner, Ph.D., K. Miriam Elfström, Ph.D.,

N Engl J Med 2020;383:1340-8.

İsveç, 2006-2017 yılları arasında 10-30 yaş arası 1 672 983 kadın takip edilmiş

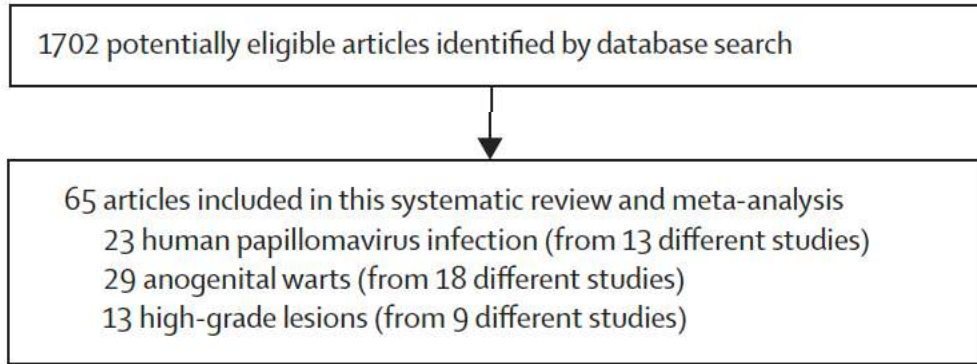
Yaş, doğduğu şehir, yaşadığı şehir, hane geliri, eğitim ve annede hastalık öyküsü

Aşılama Durumu	# Servikal Kanser	İnsidans Hızı (100,000 kişi yıl)	Düzeltilmiş insidans hızı oranı (95% CI)
Aşısız (n=1,145,112)	538	5.27	1.00
HPV Aşılı (n=527,871)	19	0.73	0.37 (0.21, 0.57)
<17 y aşılanmış	2	0.10	0.12 (0.00, 0.34)
17-30 y aşılanmış	17	3.02	0.47 (0.27, 0.75)

Population-level impact and herd effects following the introduction of human papillomavirus vaccination programmes: updated systematic review and meta-analysis

Mélanie Drolet, Élodie Bénard, Norma Pérez, Marc Brisson, on behalf of the HPV Vaccination Impact Study Group

Lancet 2019; 394: 497–509

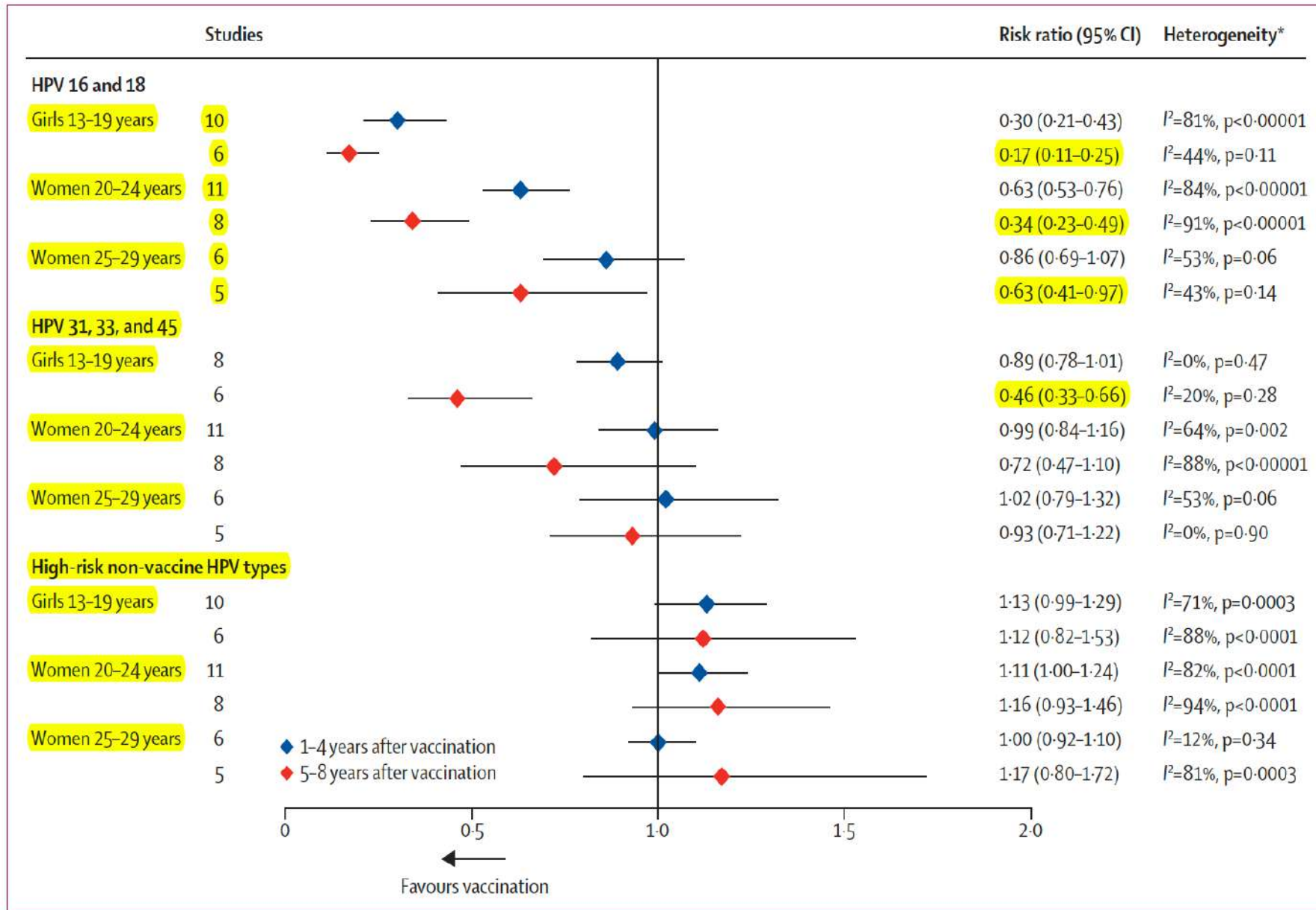


14 yüksek gelirli ülkeden

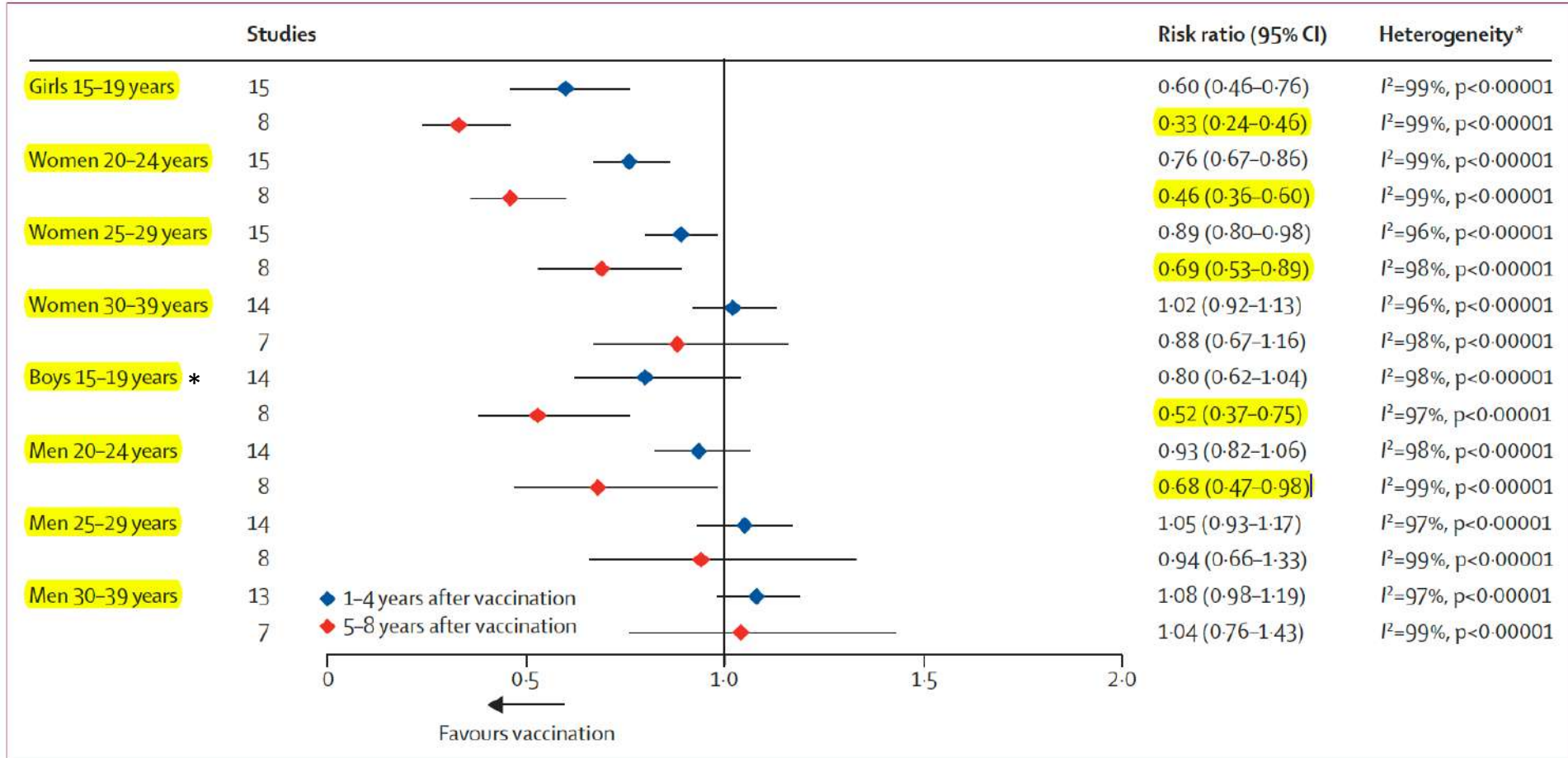
60 milyon kişinin

~9 yıllık takip verileri

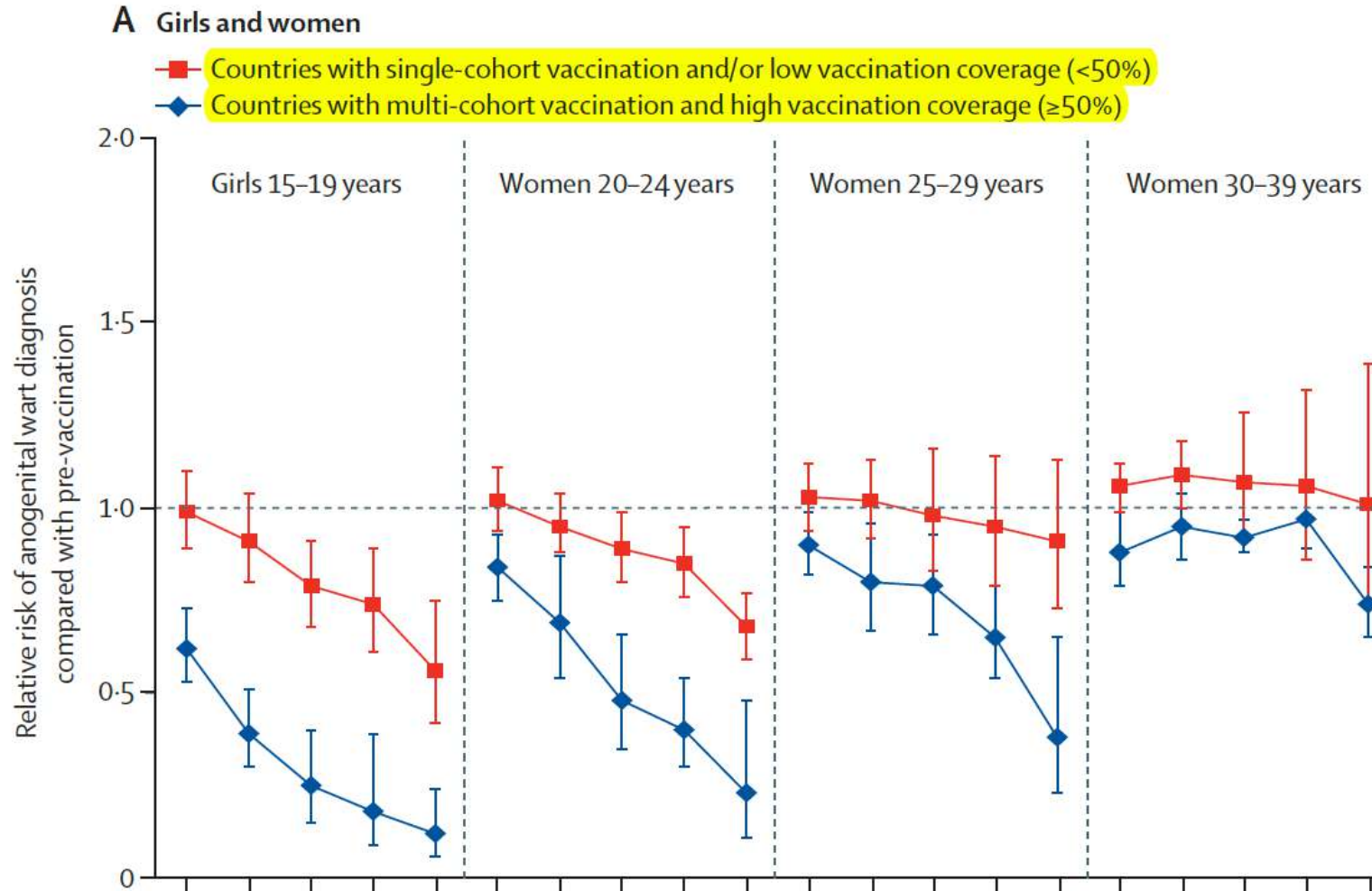
HPV infeksiyonu



Anogenital siğil sıklığı (4vHPV uygulaması öncesi sonrası)

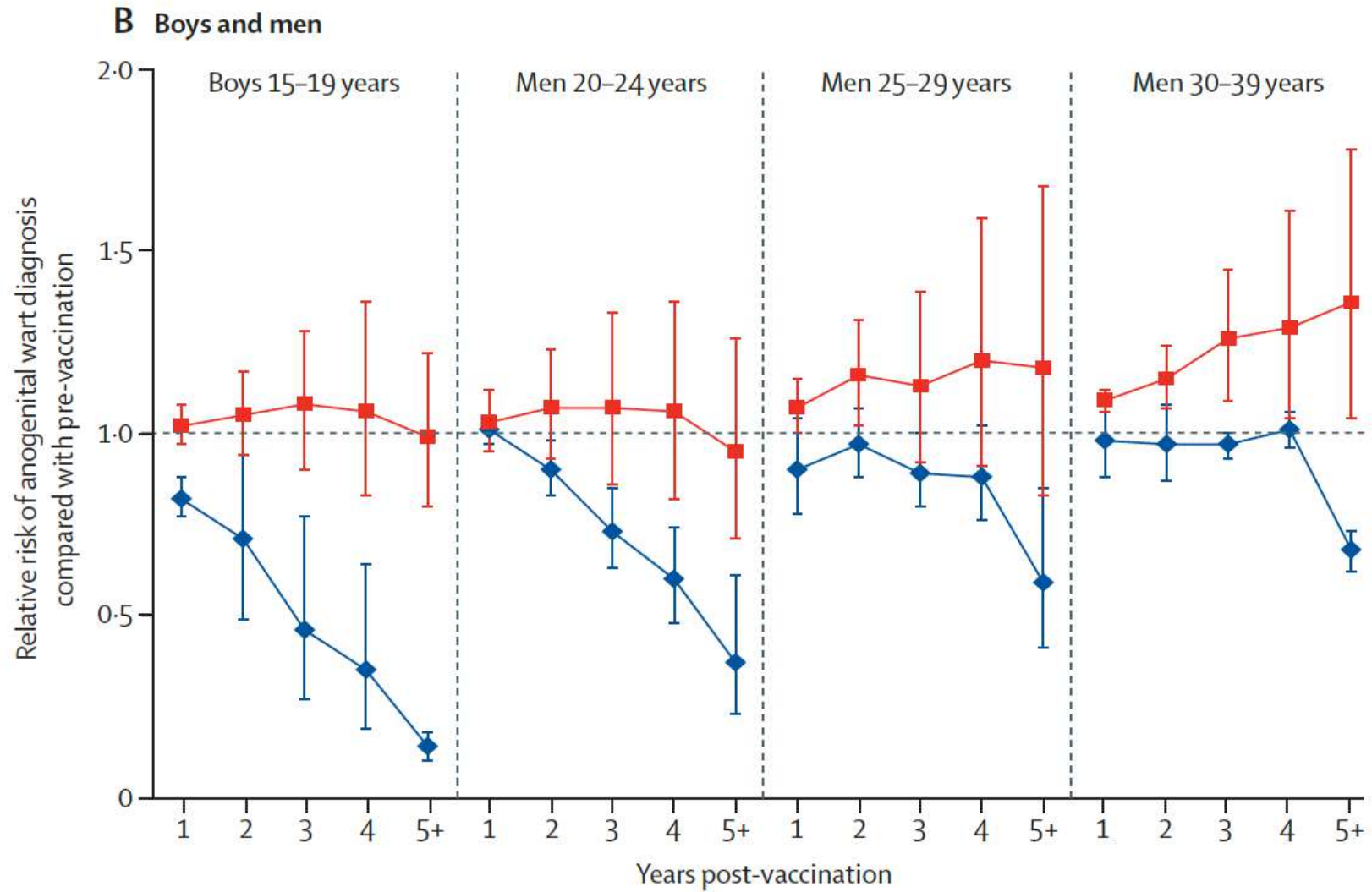


*: erkekler aşısız



Mavi ülkeler: Avustralya, Danimarka, Yeni Zelanda ve Kanada (Quebec)

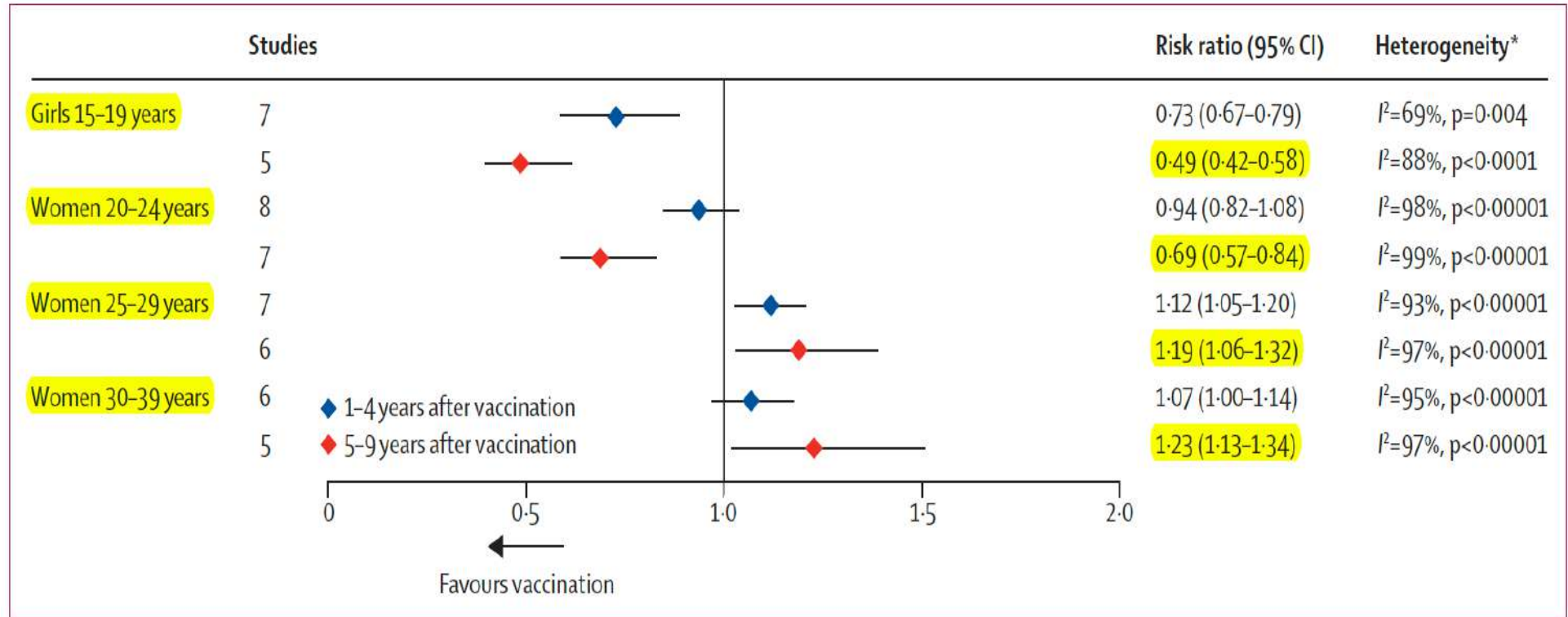
Kırmızı Ülkeler: Kanada (Manitoba, Ontario), İtalya, Almanya, Belçika, İsveç ve ABD



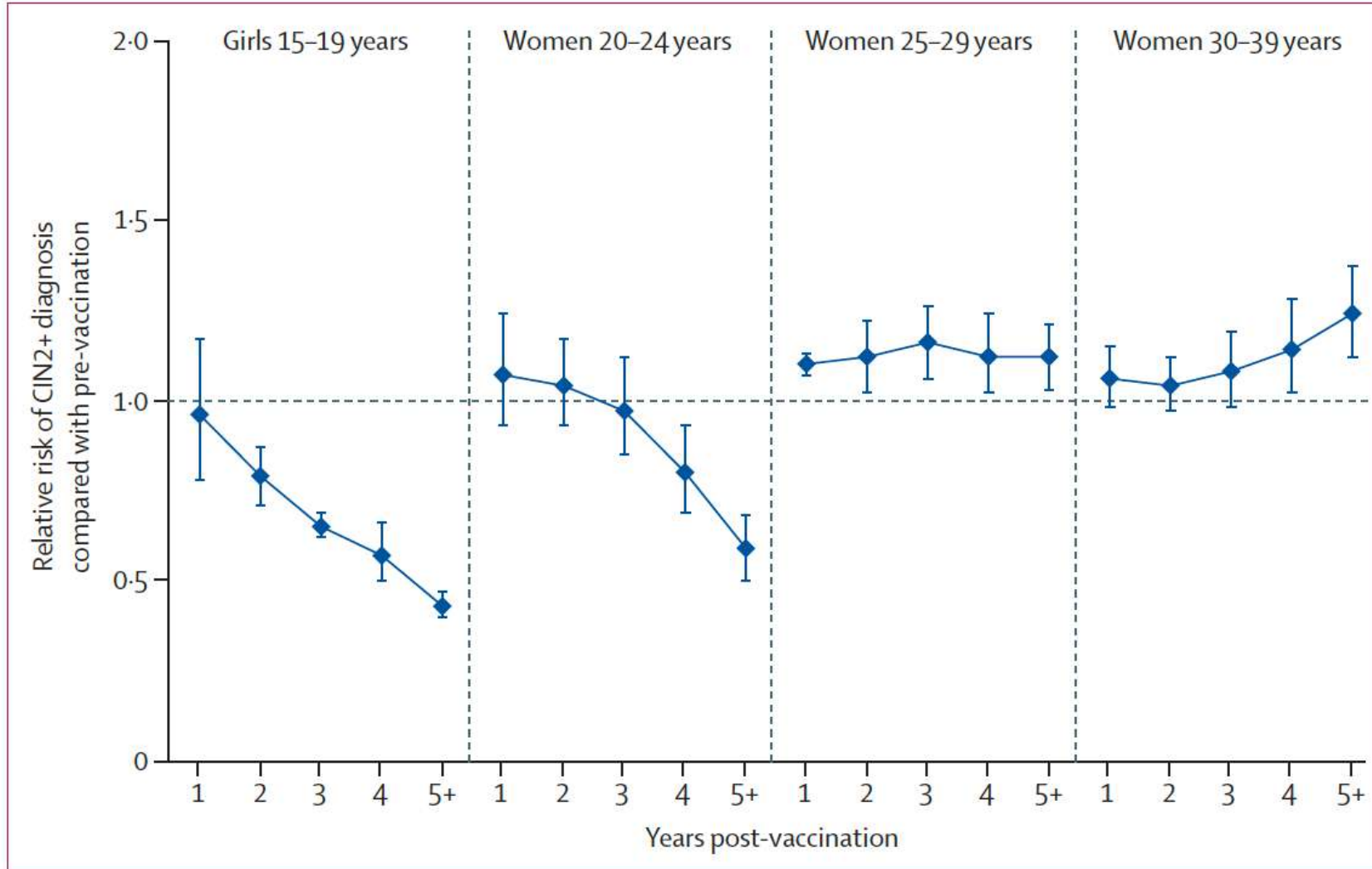
Mavi ülkeler Avustralya, Danimarka, Yeni Zelanda ve Kanada (Quebec)

Kırmızı Ülkeler: Kanada (Manitoba, Ontario), İtalya, Almanya, Belçika, İsveç ve ABD

CIN2+ sıklığında değişim



Çoklu kohort ve geniş (≥ 50) aşı kapsamı olan ülkelerde* CIN2+ sıklığında değişim (7 yıl)



*: Avustralya, Kanada (BC), Danimarka, İskoçya, ABD

effects of vaccination in countries which implement these measures. After 5–8 years of girls-only vaccination in countries with multi-cohort vaccination and high routine vaccination coverage, reductions in anogenital wart diagnoses were 44 percentage points greater among girls aged 15–19 years than among girls the same age in countries with single-cohort vaccination or low routine vaccination coverage, and reductions in CIN2+ were more than 100 percentage points greater. Reductions in anogenital wart diagnoses among boys aged 15–19 years were 85 percentage points greater than among boys the same age in countries with single-cohort vaccination or low routine vaccination coverage. The greater impact of multi-cohort vaccination was similar when restricting the analyses to countries with high routine vaccination coverage. Our results are also in line with a 2017

Tek kohort düşük kapsama oranı vs Çoklu kohort yüksek kapsama oranı

15-19 yaş kadınlar:

Anogenital siğil sıklığında 44 puanlık, CIN2+ lezyonlarda 100 puanlık azalma

15-19 yaş erkekler:

Anogenital siğil sıklığında 85 puanlık azalma

impact, WHO revised its position in 2016 to recommend HPV vaccination of multiple age cohorts of girls (9–14 years old) when the vaccine is introduced in a country, rather than vaccination of a single cohort.⁵ However, the optimal number of age cohorts to vaccinate remains an open question and might be country-specific. Increasing the number of cohorts will increase the population-level impact, but will have diminishing returns on investment for each additional older cohort included. Number needed

DSÖ HPV aşısının uygulamaya alınacağı ülkelerde çoklu yaş kohortlarının (9-14y) aşılmasını öneriyor (2016)

Efficacy, immunogenicity, and safety of a quadrivalent HPV vaccine in men: results of an open-label, long-term extension of a randomised, placebo-controlled, phase 3 trial

Lancet Infect Dis 2021

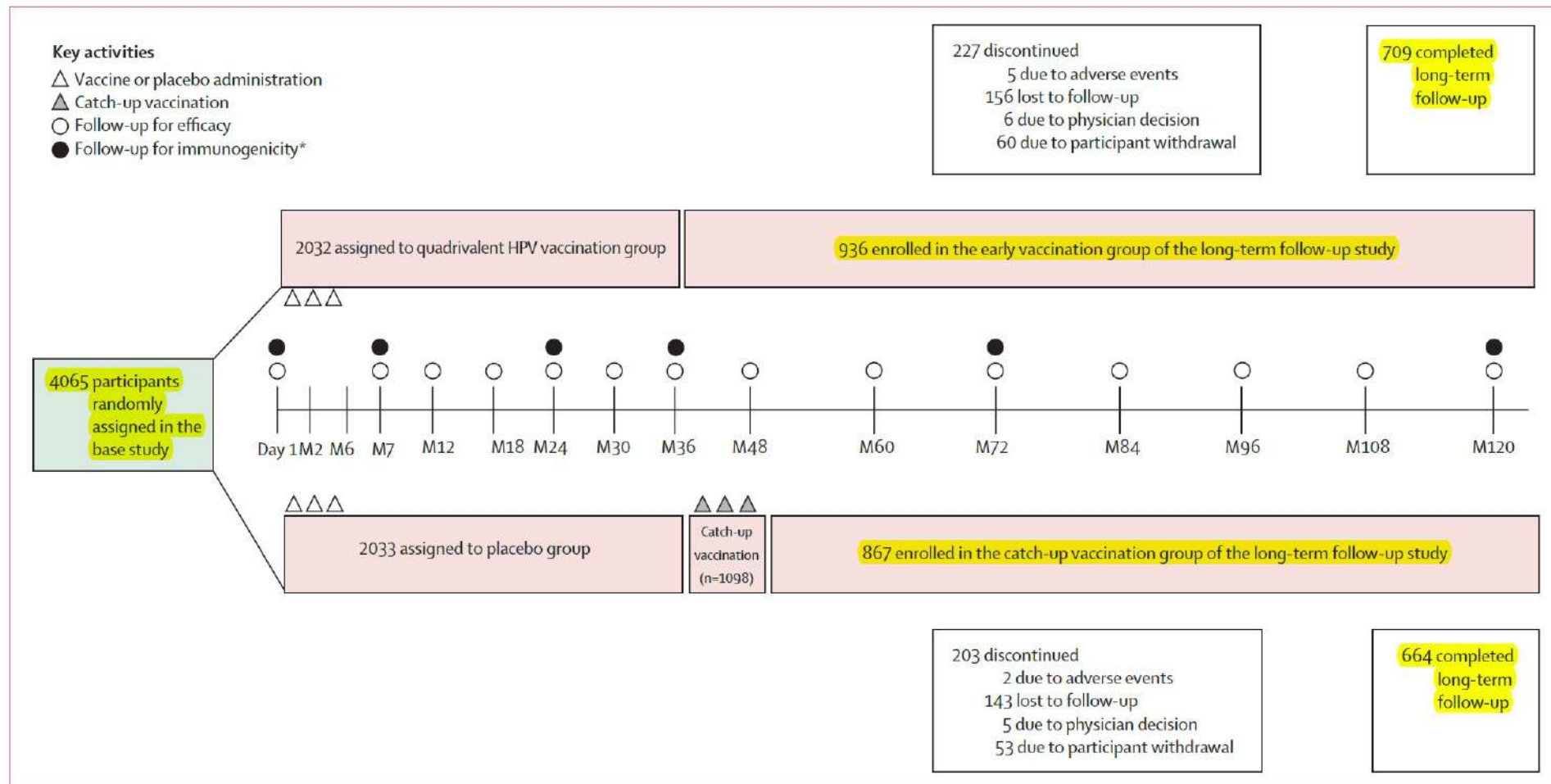
Published Online

November 12, 2021

[https://doi.org/10.1016/](https://doi.org/10.1016/S1473-3099(21)00327-3)

S1473-3099(21)00327-3

Stephen E Goldstone, Anna R Giuliano, Joel M Palefsky, Eduardo Lazcano-Ponce, Mary E Penny, Robinson E Cabello, Edson D Moreira Jr,

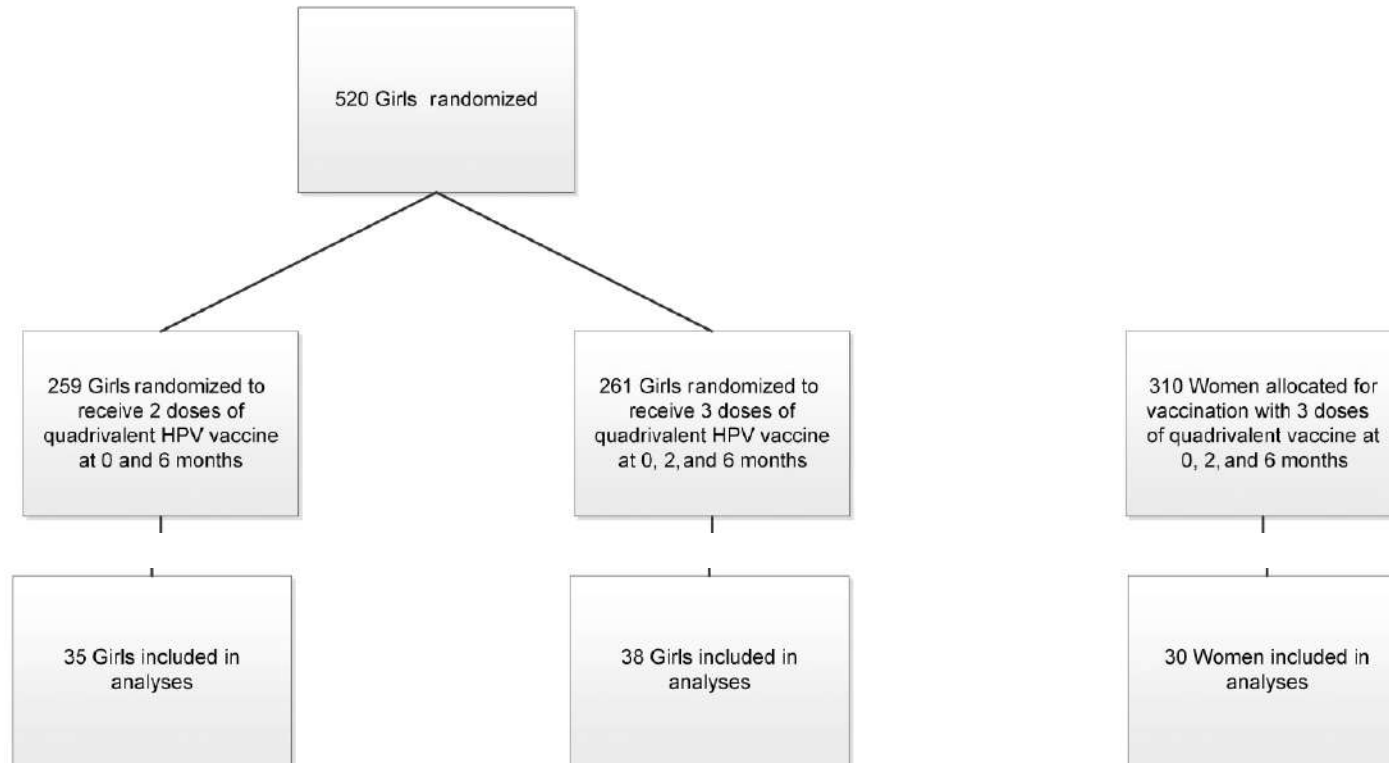


	Early vaccination group (n=936)			Catch-up vaccination group (n=867)			Early vaccination vs catch-up vaccination risk reduction estimate (95% CI)*
	Participants	Person-years follow-up	Incidence per 10 000 person-years (95% CI)	Participants	Person-years follow-up	Incidence per 10 000 person-years (95% CI)	
External genital warts related to HPV6 or 11							
Per-protocol population							
Base study	2/640	1518.9	13.2 (1.6–47.6)	20/623	1456.5	137.3 (83.9–212.1)	90.4% (62.3 to 98.4)
Long-term follow-up study	0/639	4225.4	0.0 (0.0–8.7)
mITT population							
Base study	6/763	2203.9	27.2 (10.0–59.3)	31/725	2072.2	149.6 (101.6–212.3)	81.8% (55.9 to 92.6)
Long-term follow-up study	0/763	5054.1	0.0 (0.0–7.3)	0/567	2737.2	0.0 (0.0–13.5)	..
External genital lesions† related to HPV6, 11, 16, or 18							
Per-protocol population							
Base study	2/731	1728.4	11.6 (1.4–41.8)	23/704	1638.1	140.4 (89.0–210.7)	91.8% (69.4 to 98.6)
Long-term follow-up study	0/730	4798.4	0.0 (0.0–7.7)
mITT population							
Base study	8/848	2444.5	32.7 (14.1–64.5)	35/791	2256.4	155.1 (108.0–215.7)	78.9% (53.9 to 91.2)
Long-term follow-up study	0/848	5603.0	0.0 (0.0–6.6)	0/740	3608.5	0.0 (0.0–10.2)	..
AIN and anal cancer related to HPV6, 11, 16, or 18 (MSM only)							
Per-protocol population							
Base study	4/88	176.6	226.5 (61.7–580.0)	20/109	220.7	906.2 (553.5–1399.5)	75.0% (27.7 to 92.2)
Long-term follow-up study	1/84‡	487.0	20.5 (0.5–114.4)
mITT population							
Base study	5/105	265.7	188.2 (61.1–439.2)	27/119	304.7	886.0 (583.9–1289.1)	78.8% (46.3 to 92.2)
Long-term follow-up study	1/101‡	579.7	17.2 (0.4–96.1)	5/96	493.7	101.3 (32.9–236.3)	83.0% (–26.8 to 99.3)

Immunogenicity of 2 and 3 Doses of the Quadrivalent Human Papillomavirus Vaccine up to 120 Months Postvaccination: Follow-up of a Randomized Clinical Trial

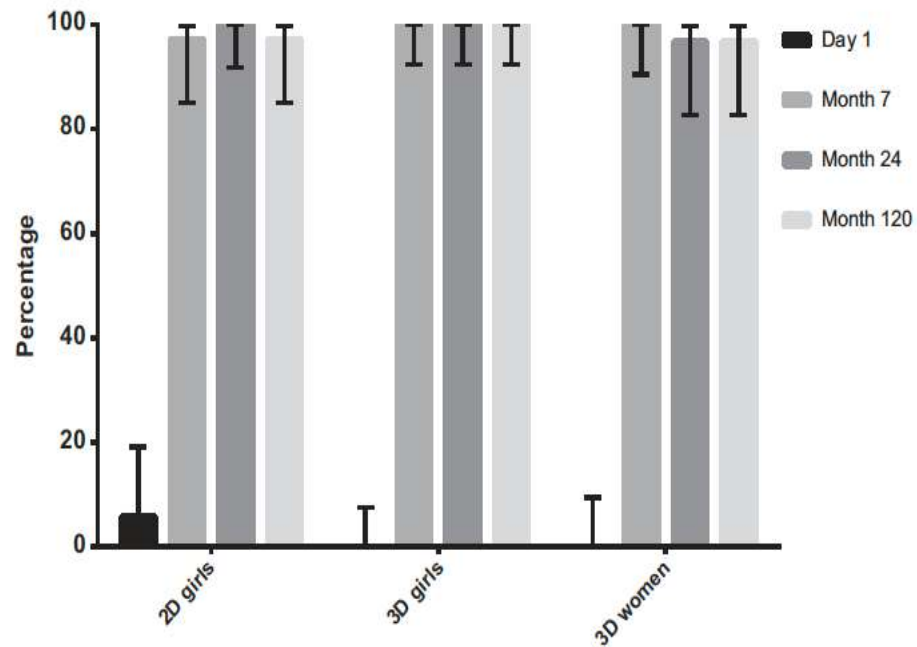
Robine Donken,^{1,2,3} Simon R.M. Dobson,¹ Kim D. Marty,¹ Darrel Cook,⁴ Chantal Sauvageau,^{5,6} Vladimir Gilca,⁵ Marc Dionne,⁶ Shelly McNeil,⁷

Clin Infect Dis 2020;71(4):1022–9

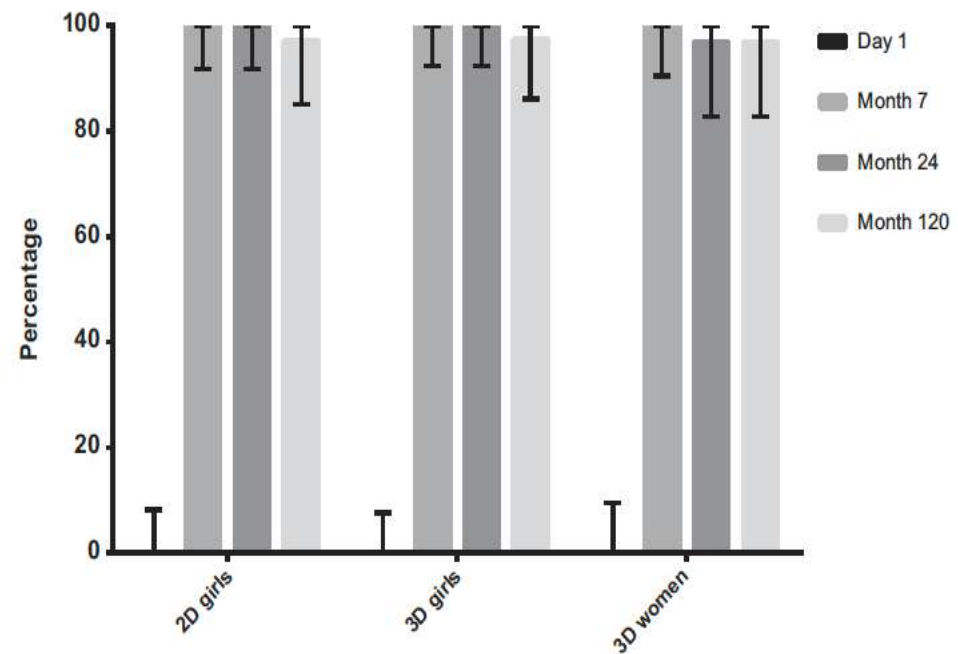


Girls: 9-13, Women: 16-26 y

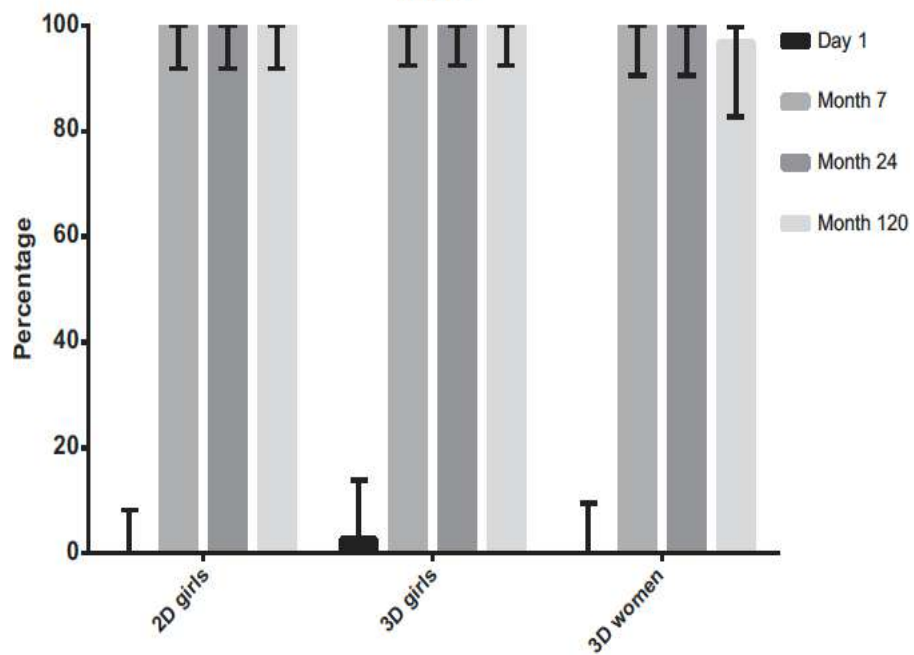
HPV6



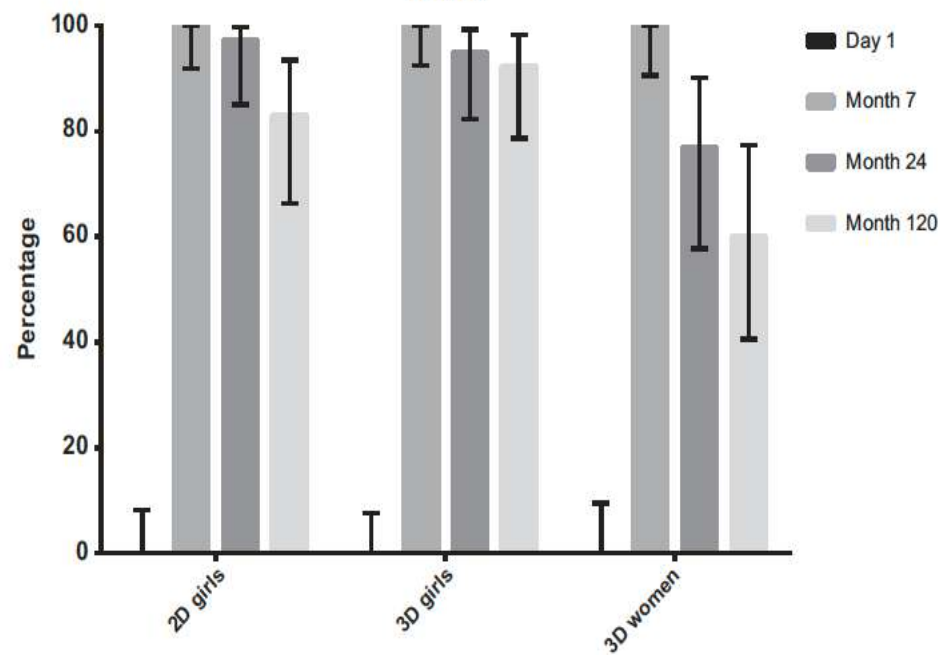
HPV11



HPV16



HPV18



Immunogenicity of 2 Doses of HPV Vaccine in Younger Adolescents vs 3 Doses in Young Women

A Randomized Clinical Trial

Simon R. M. Dobson, MD

JAMA. 2013;309(17):1793-1802

Antibodies	Girls, 9-13 y				Women, 16-26 y		GMT Ratio (95% CI), mMU/mL		
	2 Doses		3 Doses		3 Doses		Girls (2 Doses)/ Women (3 Doses)	Girls (2 Doses)/ Girls (3 Doses)	Girls (3 Doses)/ Women (3 Doses)
No. of Patients	GMT (95% CI), mMU/mL	No. of Patients	GMT (95% CI), mMU/mL	No. of Patients	GMT (95% CI), mMU/mL				
Month 7									
HPV-16	254	7344 (6310-8547)	256	7736 (6651-8999)	300	3545 (3083-4076)	2.07 (1.62-2.65) ^b	0.95 (0.73-1.23)	2.18 (1.71-2.79)
HPV-18	254	1169 (1021-1338)	256	1730 (1512-1980)	300	664 (586-752)	1.76 (1.41-2.19) ^b	0.68 (0.54-0.85)	2.61 (2.09-3.25)
HPV-6	253	2117 (1787-2508)	254	1876 (1585-2221)	300	943 (807-1101)	2.25 (1.71-2.96)	1.13 (0.85-1.50)	1.99 (1.51-2.62)
HPV-11	254	2339 (2088-2619)	256	2117 (1891-2370)	300	1268 (1143-1408)	1.84 (1.53-2.22)	1.10 (0.91-1.34)	1.67 (1.39-2.01)
Month 18									
HPV-16	100	1579 (1322-1885)	100	1806 (1512-2156)	104	840 (706-999)	1.88 (1.40-2.53)	0.87 (0.65-1.18)	2.15 (1.60-2.89)
HPV-18	100	137 (107-176)	100	238 (186-305)	104	77 (61-98)	1.78 (1.17-2.69)	0.58 (0.38-0.88)	3.08 (2.03-4.66)
HPV-6	100	346 (291-411)	100	351 (295-417)	104	203 (171-241)	1.70 (1.27-2.28)	0.99 (0.74-1.32)	1.73 (1.29-2.31)
HPV-11	100	451 (381-532)	100	429 (363-507)	104	286 (242-336)	1.58 (1.19-2.09)	1.05 (0.79-1.39)	1.50 (1.14-1.99)
Month 24									
HPV-16	201	1407 (1234-1606)	188	1726 (1506-1978)	230	844 (746-954)	1.67 (1.34-2.07)	0.82 (0.65-1.02)	2.05 (1.64-2.55)
HPV-18	201	131 (108-158)	188	264 (218-321)	230	96 (81-114)	1.36 (1.00-1.85)	0.49 (0.36-0.68)	2.75 (2.01-3.77)
HPV-6	201	278 (244-315)	188	357 (313-407)	230	217 (193-244)	1.28 (1.04-1.58)	0.78 (0.62-0.97)	1.65 (1.33-2.04)
HPV-11	201	370 (326-420)	188	423 (371-482)	230	272 (242-306)	1.36 (1.11-1.67)	0.87 (0.70-1.09)	1.56 (1.26-1.92)
Month 36									
HPV-16	86	1151 (919-1441)	85	1407 (1122-1764)	111	719 (590-876)	1.60 (1.12-2.29)	0.82 (0.56-1.20)	1.96 (1.37-2.80)
HPV-18	86	104 (76-141)	85	237 (174-322)	111	74 (57-97)	1.40 (0.86-2.29)	0.44 (0.26-0.74)	3.19 (1.95-5.21)
HPV-6	86	243 (199-296)	85	376 (308-460)	111	189 (159-225)	1.28 (0.94-1.76)	0.65 (0.46-0.90)	1.99 (1.45-2.74)
HPV-11	86	298 (245-363)	85	404 (332-493)	111	215 (181-255)	1.39 (1.01-1.90)	0.74 (0.53-1.03)	1.88 (1.37-2.58)

HPV Aşılarının Güvenliliği

Dünya Sağlık Örgütü (DSÖ):

“Mevcut güvenlilik profili, önceki 7 GACVS toplantısında tartışıldığı gibi son derece olumlu olmaya devam ediyor ve lisans öncesi güvenlik profiliyle tutarlı.”

ABD Hastalık Kontrol ve Önleme Merkezleri (CDC):

“Pek çok aşı güvenliği izleme sisteminden ve 160'tan fazla çalışmadan elde edilen veriler, HPV aşılarının olumlu bir güvenlik profiline sahip olduğunu göstermiştir. Bilimsel kanıtlar aşıların güvenliliğini ezici bir çoğunlukla desteklemektedir.”

1. Global Advisory Committee on Vaccine Safety, 4–5 December 2019. *Weekly Epidemiological Record*. 2020;95(4):25-36.
2. CDC. Vaccine Safety- Human Papillomavirus (HPV) Vaccine. <https://www.cdc.gov/vaccinesafety/vaccines/hpv-vaccine.html>



Safety of HPV vaccines

Extract from report of GACVS meeting of 7-8 June 2017, published in the WHO Weekly Epidemiological Record of 14 July 2017

Since licensure in 2006, over 270 million doses of HPV vaccines have been distributed. GACVS first reviewed the safety data in 2007,¹² and subsequently in 2008,¹³ 2009,¹⁴ 2013,¹⁵ 2014,¹⁶ and 2015.¹⁷ Early on, the Committee was presented signals related to anaphylaxis and syncope. The risk of anaphylaxis has been characterized as approximately 1.7 cases per million doses, and syncope was established as a common anxiety or stress-related reaction to the injection. No other adverse reactions have been identified and GACVS considers HPV vaccines to be extremely safe.

GACVS = Global Advisory Committee on Vaccine Safety.

http://www.who.int/vaccine_safety/committee/topics/hpv/June_2017/en/.

4vHPV Aşısı - Yan Etkiler

- Aşı canlı veya ölü herhangi bir virüs içermez: Virüse ait herhangi bir infeksiyon veya benzeri istenmeyen etki mümkün değildir
- Aşı yerinde enjeksiyona bağlı;
- Kızarıklık
- Minimal ağrı
- Şişlik
- Hafif sıcaklık artışı
- Bulantı, baş dönmesi, göz kararması

DSÖ - HPV Aşılması Önerileri

- <15 yaş; **2 doz** (0 ve 6. aylar) 6
- ≥15 yaş ; **3 doz** (0, 2 ve 6. aylar)

Bağışıklığı baskılanmış ve/veya HIV ile enfekte olduğu bilinen kişiler için yaştan bağımsız olarak **3 dozluk bir program gereklidir.**

4vHPV Aşısı / Gardasil® - Pozoloji

Aşı öncesi pap-smear veya HPV-DNA çalışılması gerekli değildir

9-13 yaş arası bireyler

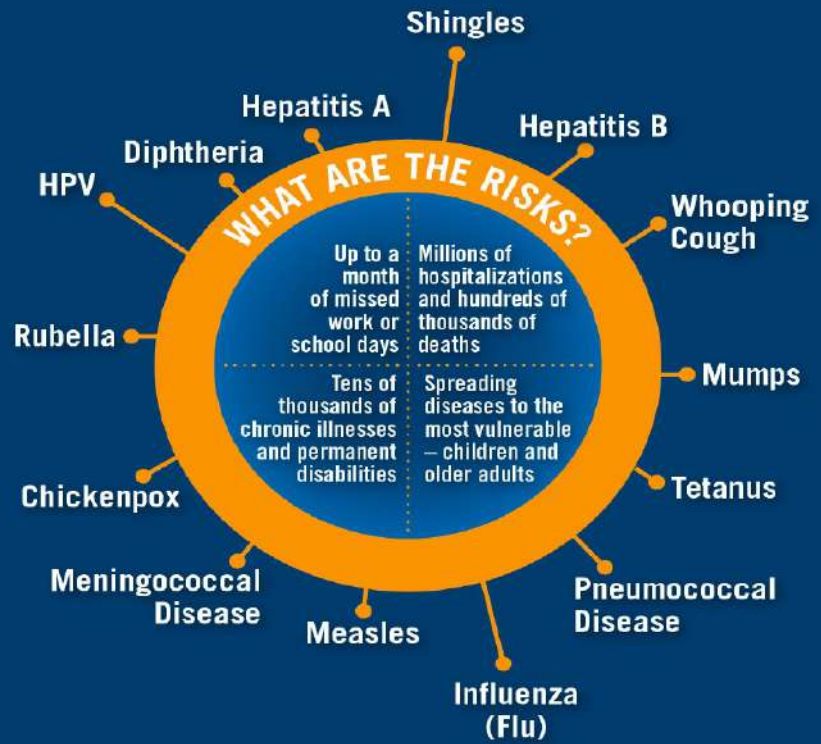
- GARDASIL iki doz aşılama şeması şeklinde uygulanabilir **(0. ve 6. ayda)**
- Eğer ikinci doz ilk dozdan sonra, 6. aydan daha erken uygulanırsa, 3. doz her zaman uygulanmalıdır
- Alternatif olarak, GARDASIL üç doz olarak uygulanabilir **(0., 2., 6. ayda 0.5 ml)**

14 yaş ve üzeri bireyler

- GARDASIL üç doz aşılama şeması şeklinde uygulanmalıdır **(0., 2., 6. ayda 0.5 ml)**
- İkinci doz birinci dozdan en az 1 ay sonra, üçüncü doz ise ikinci dozdan en az 3 ay sonra uygulanmalıdır.

Tüm dozlar 1 yıl içinde uygulanmalıdır.

VACCINES AREN'T JUST FOR CHILDREN
ADULTS CAN BE PROTECTED
 FROM 14 DEADLY DISEASES



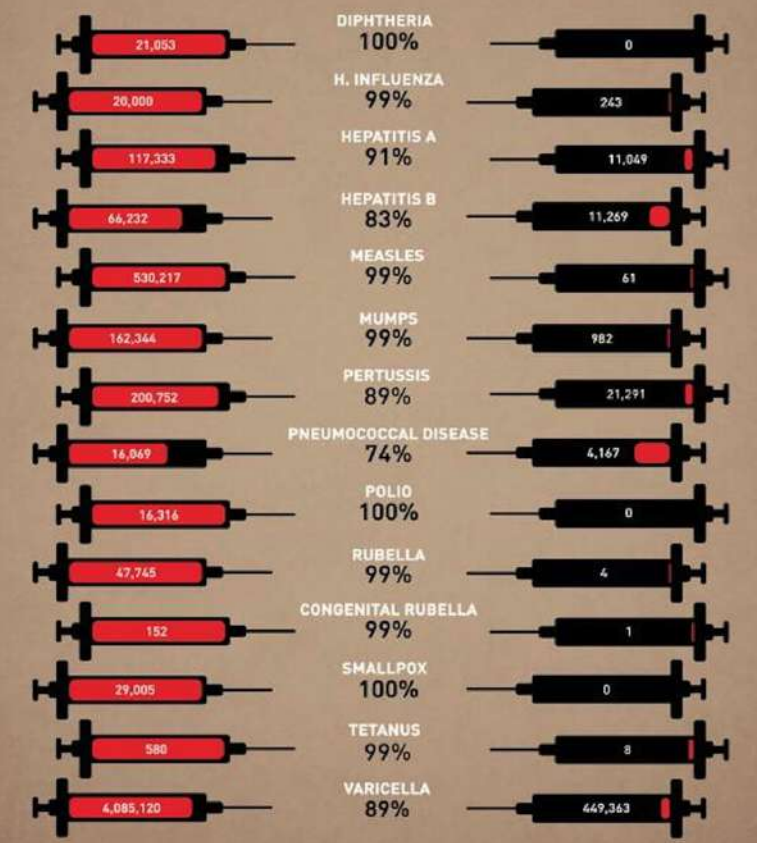
Talk to your healthcare provider about which vaccines are right for you

For more information, visit adultvaccination.org



PRE-VACCINE ERA ESTIMATED ANNUAL MORBIDITY IN THE U.S. % MOST RECENT REPORTS OF CASES IN THE U.S.

----- DECREASE -----



INFORMATION COURTESY OF THE CDC (JANUARY 2011)

Teşekkürler...