HPV Aşıları:

Dr. Alpay AZAP
Ankara Üniversitesi Tıp Fakültesi

Lancet Glob Health 2020;8: e180–90

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

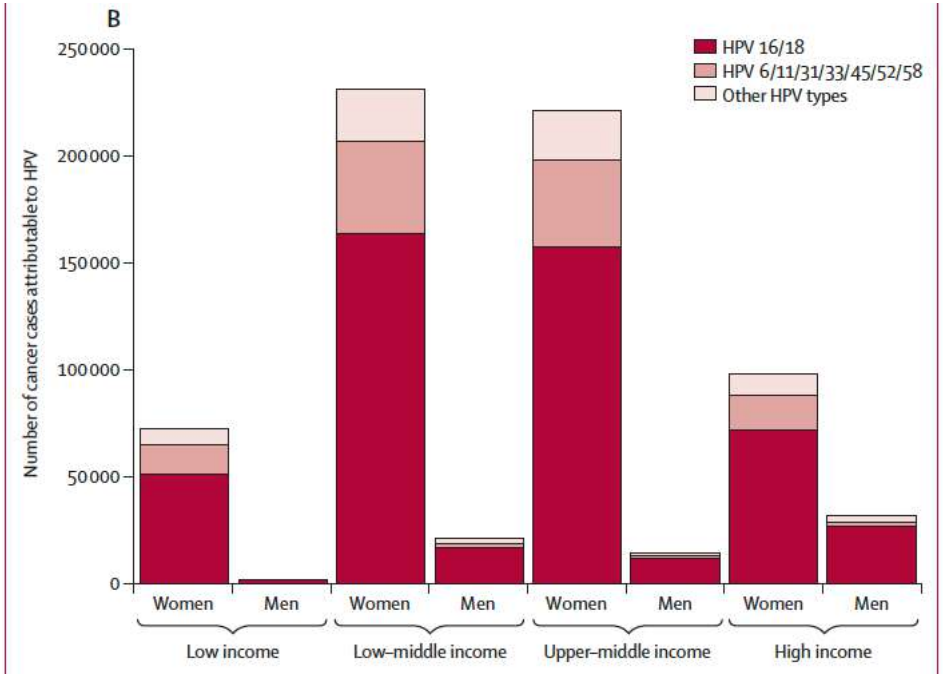
Catherine de Martel, Damien Georges, Freddie Bray, Jacques Ferlay, Gary M Clifford

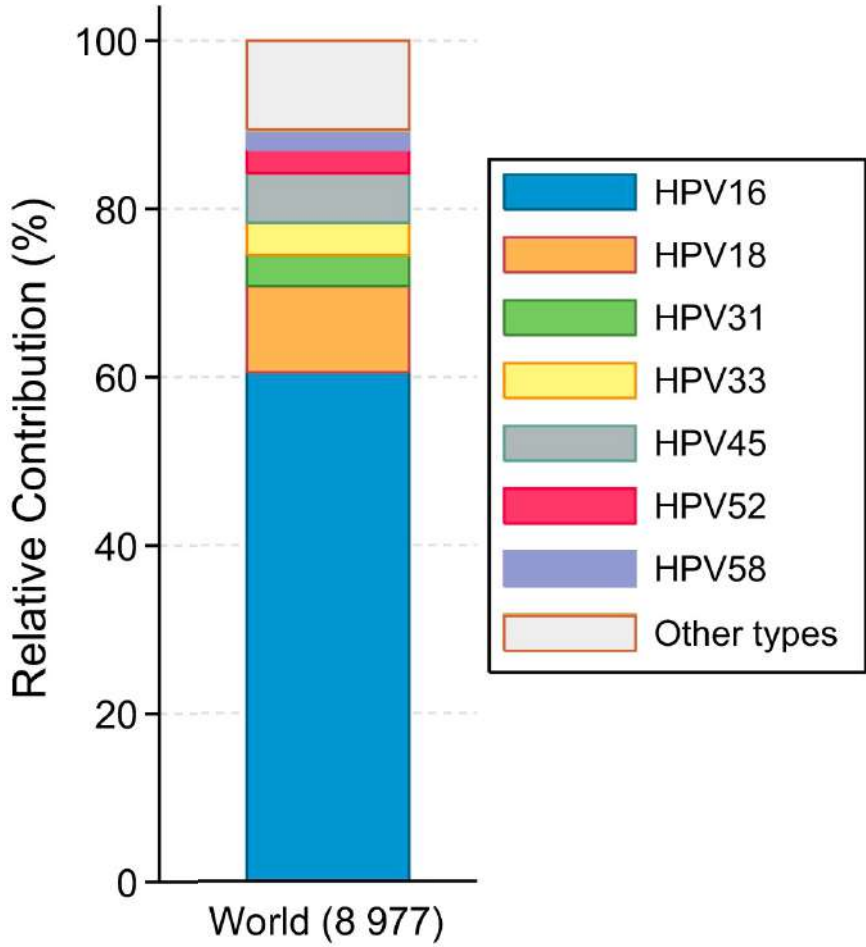
2018'de infeksiyon kaynaklı kanser: 2.2 milyon

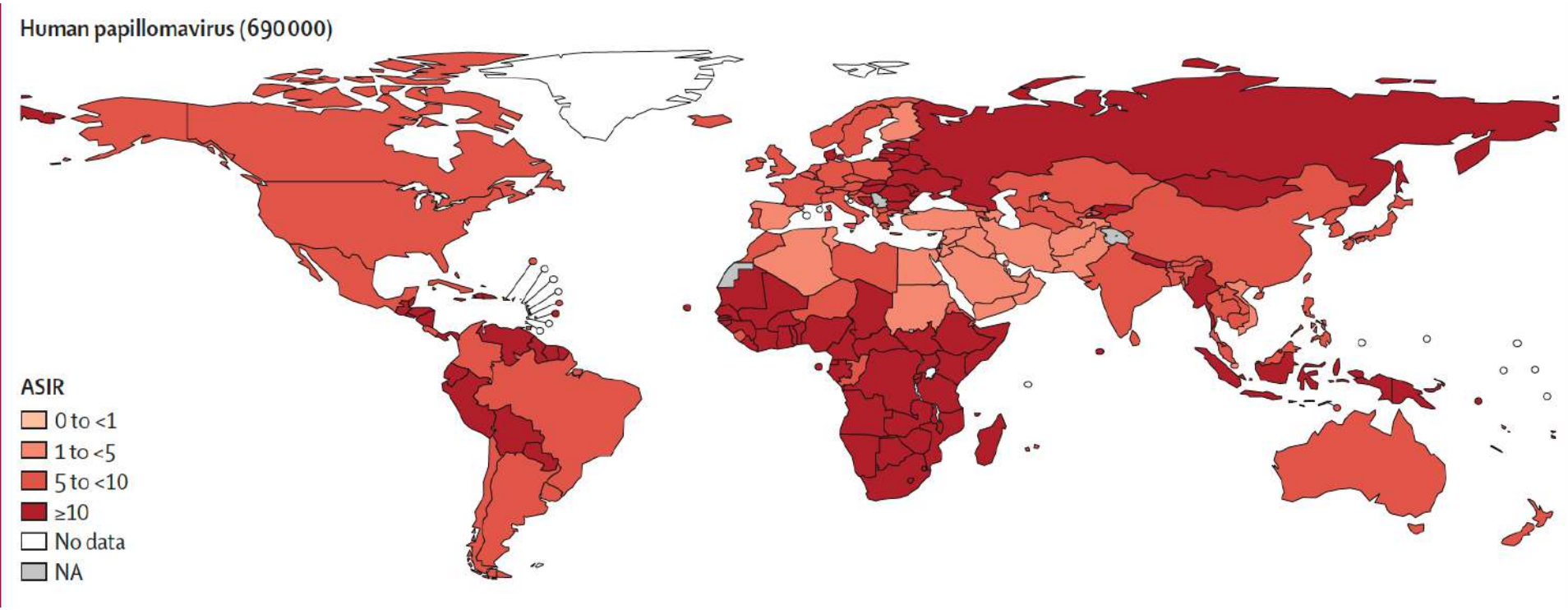
Yaşa göre standardize insidans hızı (ASIR):

100 000 kişi-yıl başına 25

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







HPV'ye bağlı kanser insidansı gelir düzeyi ile doğrudan ilişkili:

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)	Erkek	Kadın
Rahim ağzı kanseri	-	5.93
Anal Kanser	0.26	0.29
Vulva Kanseri	-	0.67
Vajinal Kanser	-	0.26
Penil Kanser	0.06	-
Farinks	0.41	0.12

Rahim Ağzı Kanseri Yükü	İnsidans	Ölüm
Yıllık yeni vaka/ölüm	**2532**	**1245**
Kaba Oran	5.9	3.1
ASIR	**4.8**	**2.5**
Kümülatif Risk (0-74 yaş)	0.5	0.3

http://www.hpvcentre.net/statistics/reports/TUR.pdf

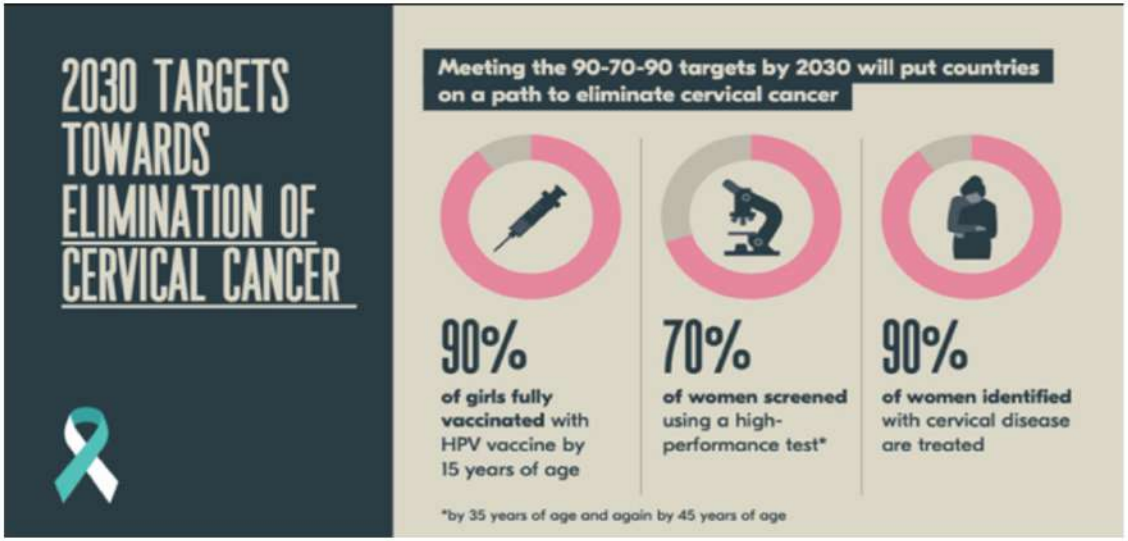
KLİMİK TÜRK KLİNİK MİKROBİYOLOJİ VE İNFEKSİYON HASTALIKLARI DERNEĞİ

Bilimle Sağlıkla 35 Yıl

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

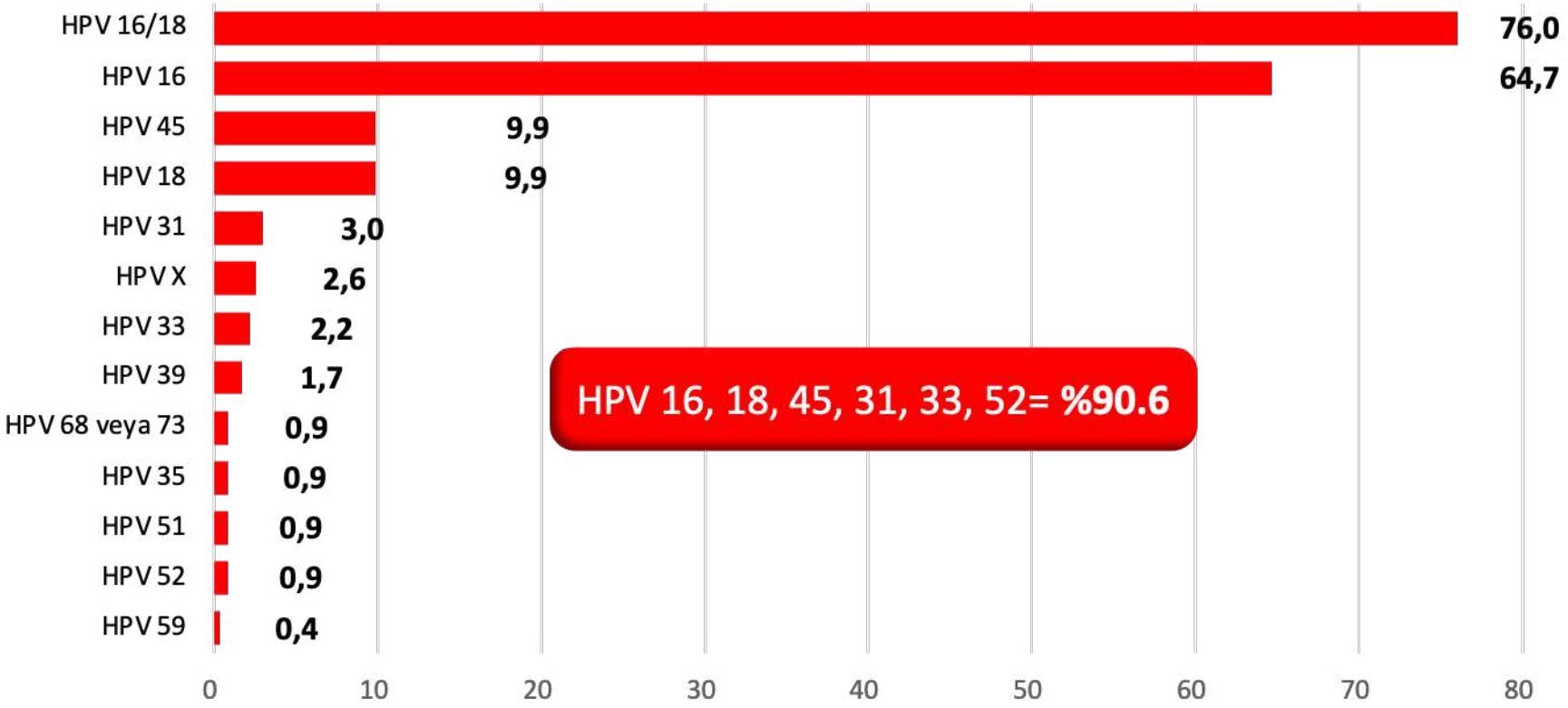
«Dünya Sağlık Asamblesi 2030 hedeflerini kabul etti» Ağustos 2020

2019'da HPV aşı kapsayıcılığı %15

Bruni L. Preventive medicine 2021;144:106399

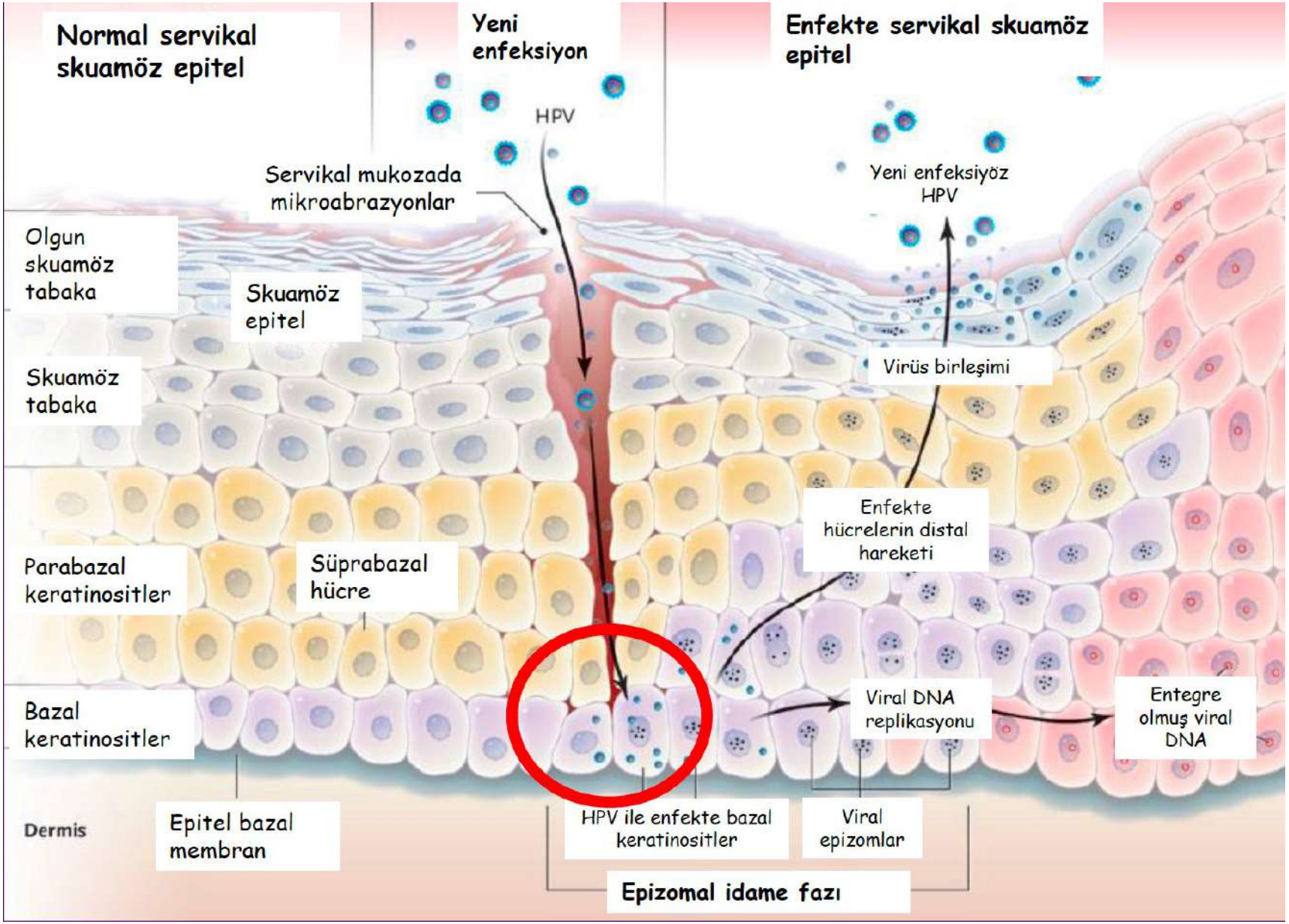
HPV Tipleri ve Taşıdığı Riskler

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

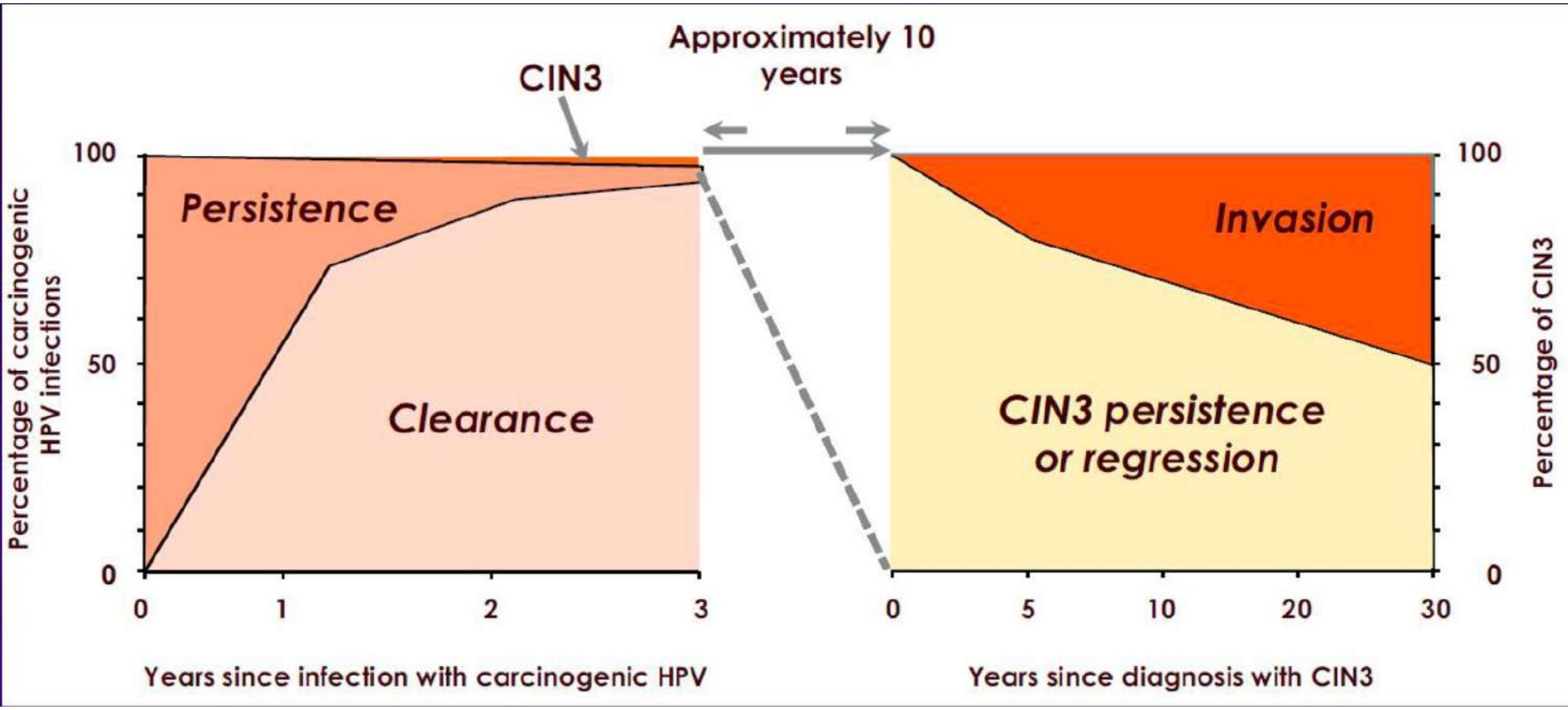


Muñoz N, et al. N Engl J Med.2003;348:518-27. Usubutun A, Int J Gynecol Pathol, 2009;28:541–548.

HPV Patogenezi



N Engl J Med 2009;361:271-8.



Vaccine 30S (2012) F24–F33

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:

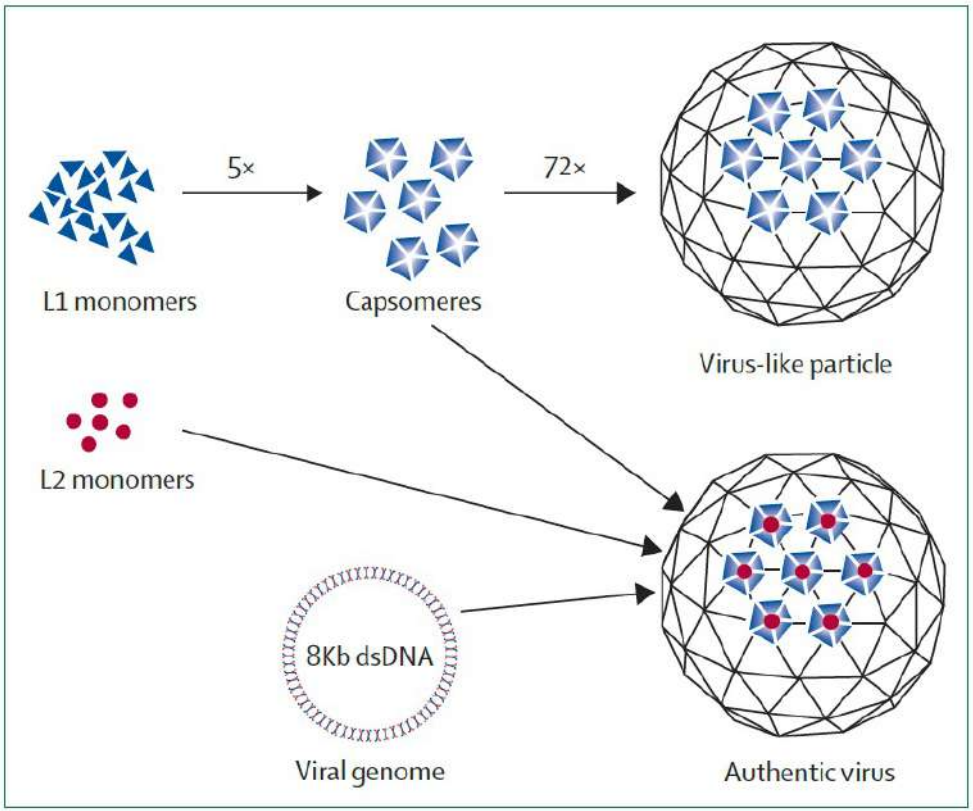
- Viremi Ø,
- Lenf nodlarına erişim az / Ø,
- IFN yanıtı baskılı

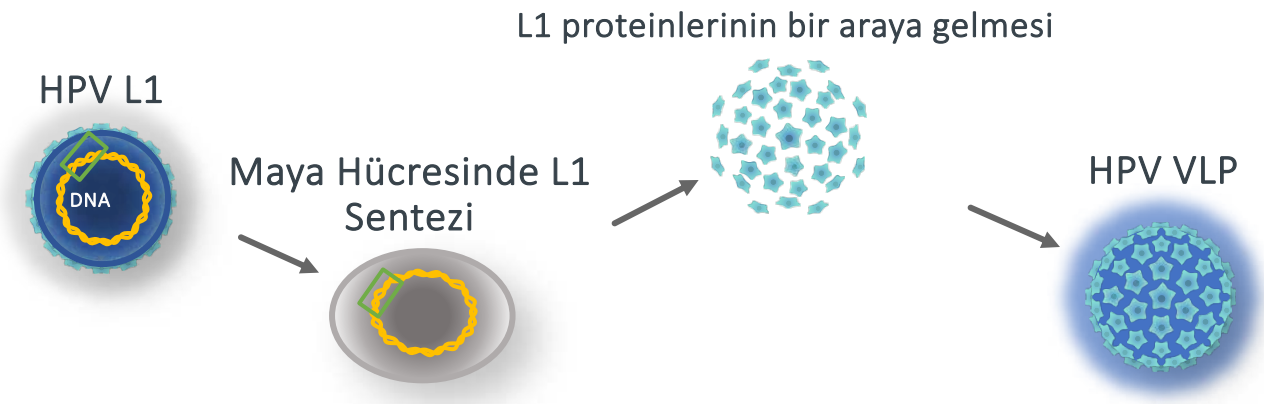
HPV aşıları bağışık yanıtı güçlü uyarıyor:

- İM uygulama → VLP'lerin kan ve lenf nodlarına erişimi
- VLP'ler virüsten daha fazla epitop içeriyor
- VLP'ler T-hücre yanıtını da tetikliyor

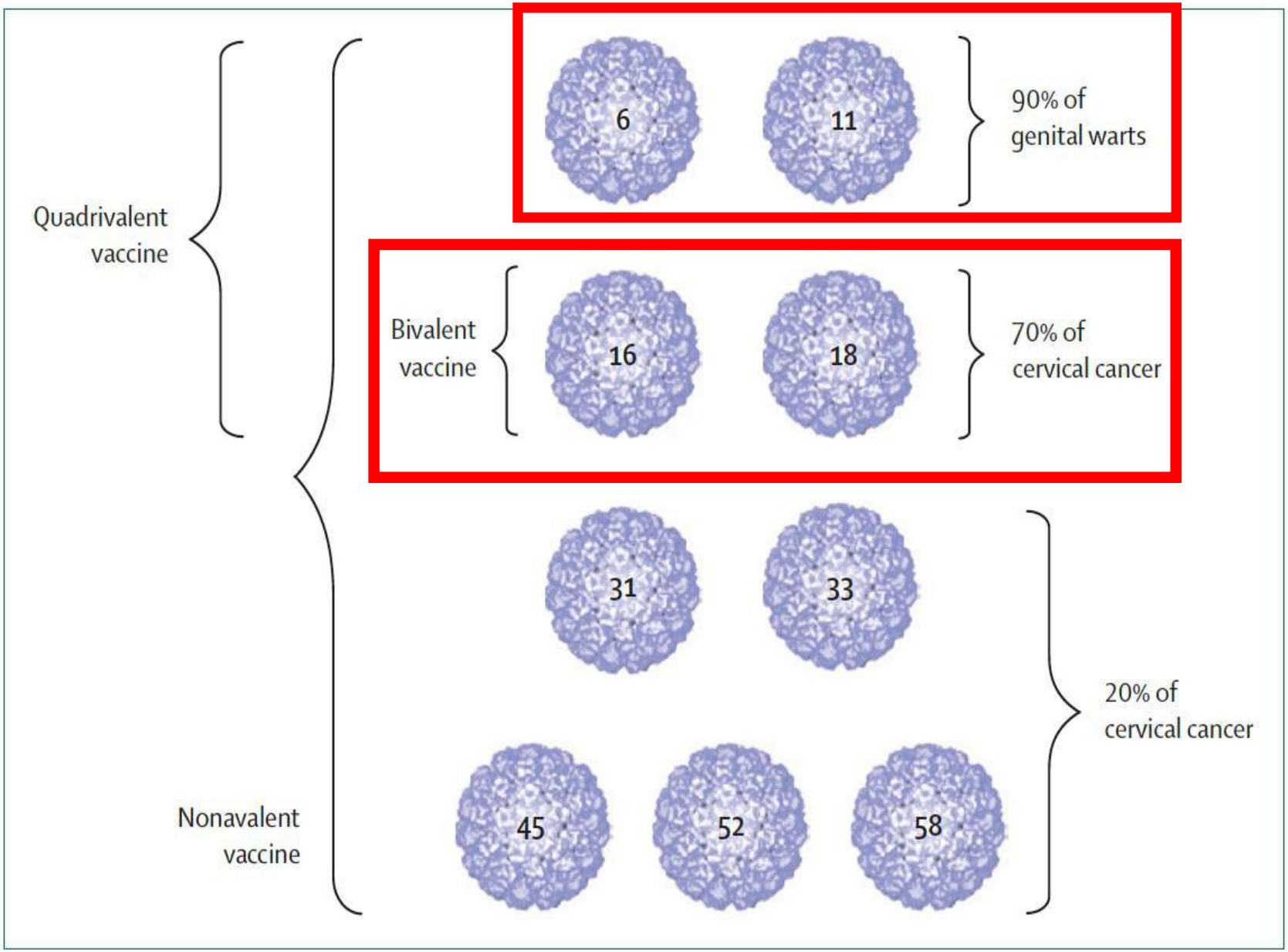
Cell Mol Life Sci. 2019;76(1):67-87.

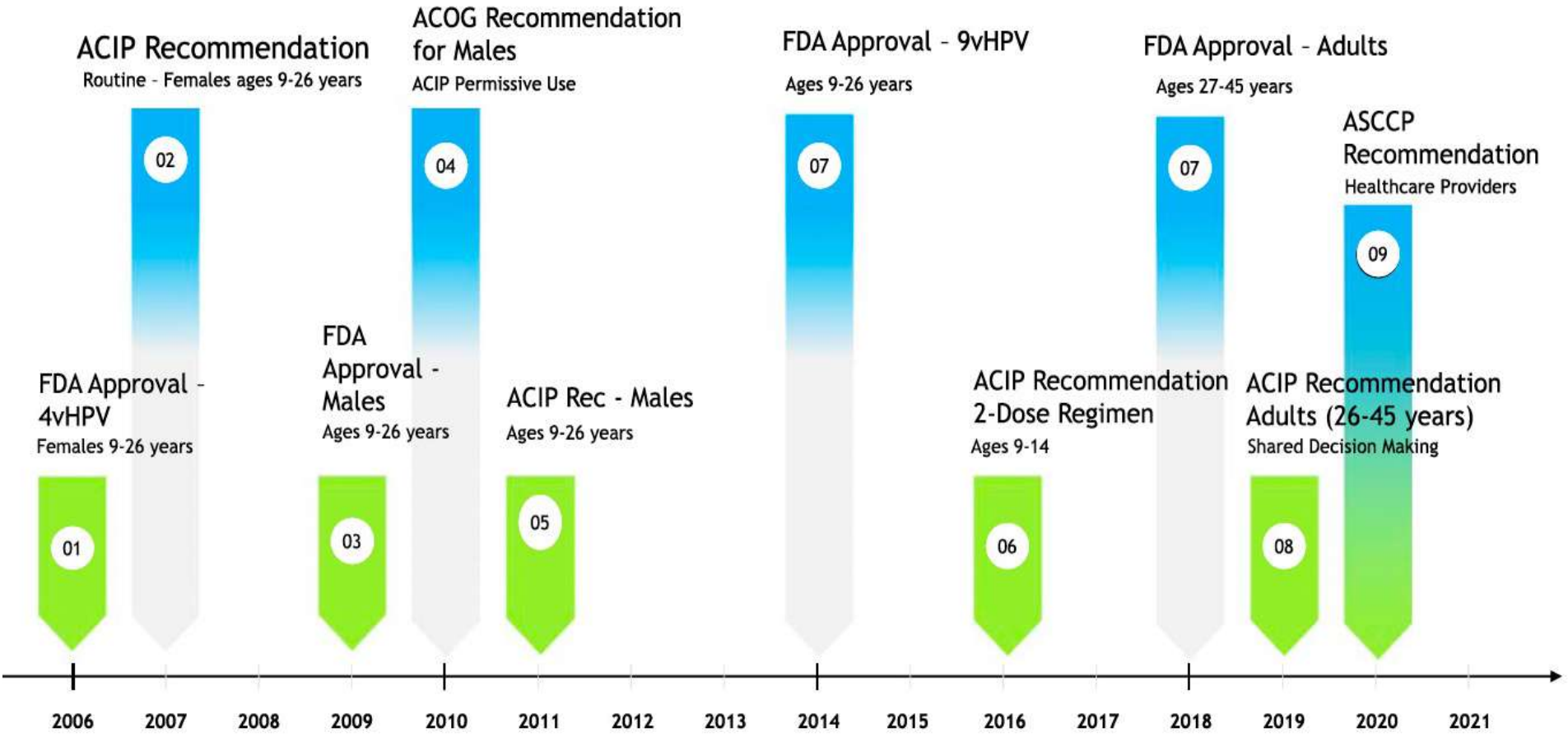
HPV Aşı Teknolojisi – Rekombinant DNA





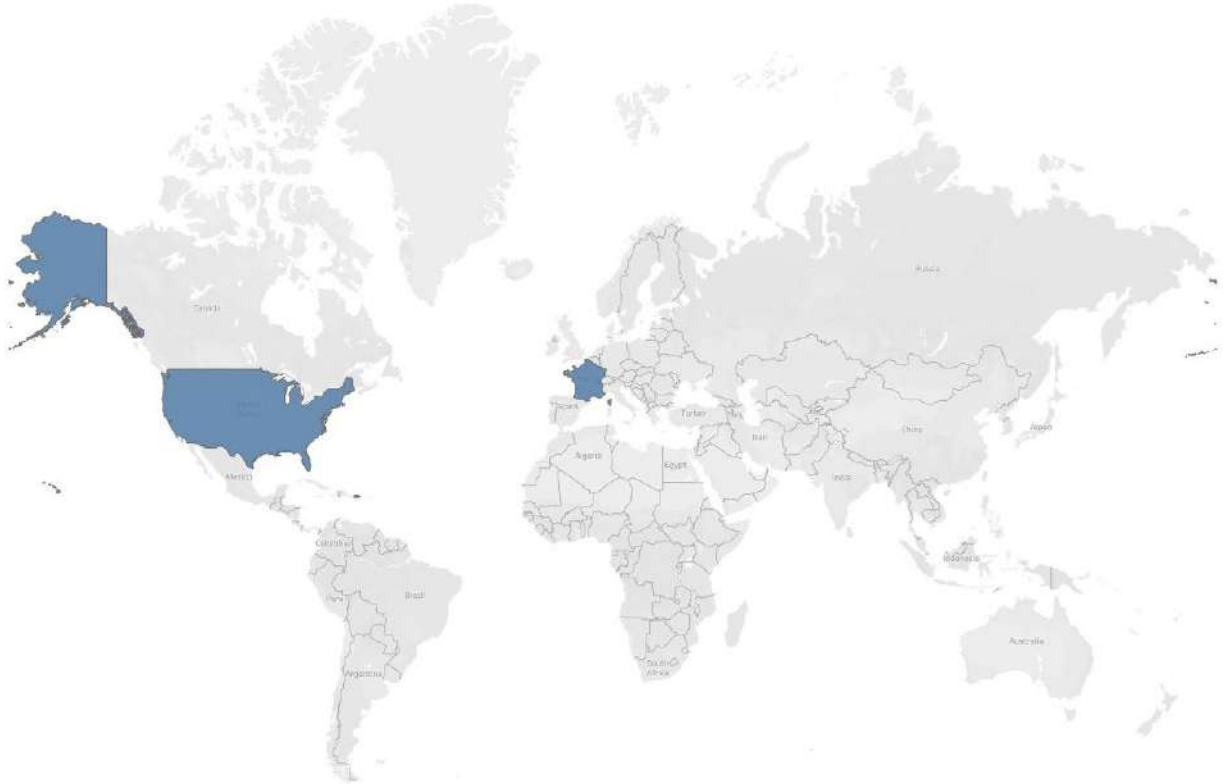
Gardasil®


Quadrivalent vaccine
Bivalent vaccine
Nonavalent vaccine
6
11
90% of genital warts
16
18
70% of cervical cancer
31
33
45
52
58
20% of cervical cancer


ACIP Recommendation
Routine - Females ages 9-26 years
02
ACOG Recommendation for Males
ACIP Permissive Use
04
FDA Approval - 9vHPV
Ages 9-26 years
07
FDA Approval - Adults
Ages 27-45 years
07
ASCCP Recommendation
Healthcare Providers
09
FDA Approval - 4vHPV
Females 9-26 years
01
FDA Approval - Males
Ages 9-26 years
03
ACIP Rec - Males
Ages 9-26 years
05
ACIP Recommendation 2-Dose Regimen
Ages 9-14
06
ACIP Recommendation Adults (26-45 years)
Shared Decision Making
08
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
2021

Global HPV Vaccine Introduction

Year:
2006



Introduction status
- Demonstration
- National
- Subnational
- Demo complete*

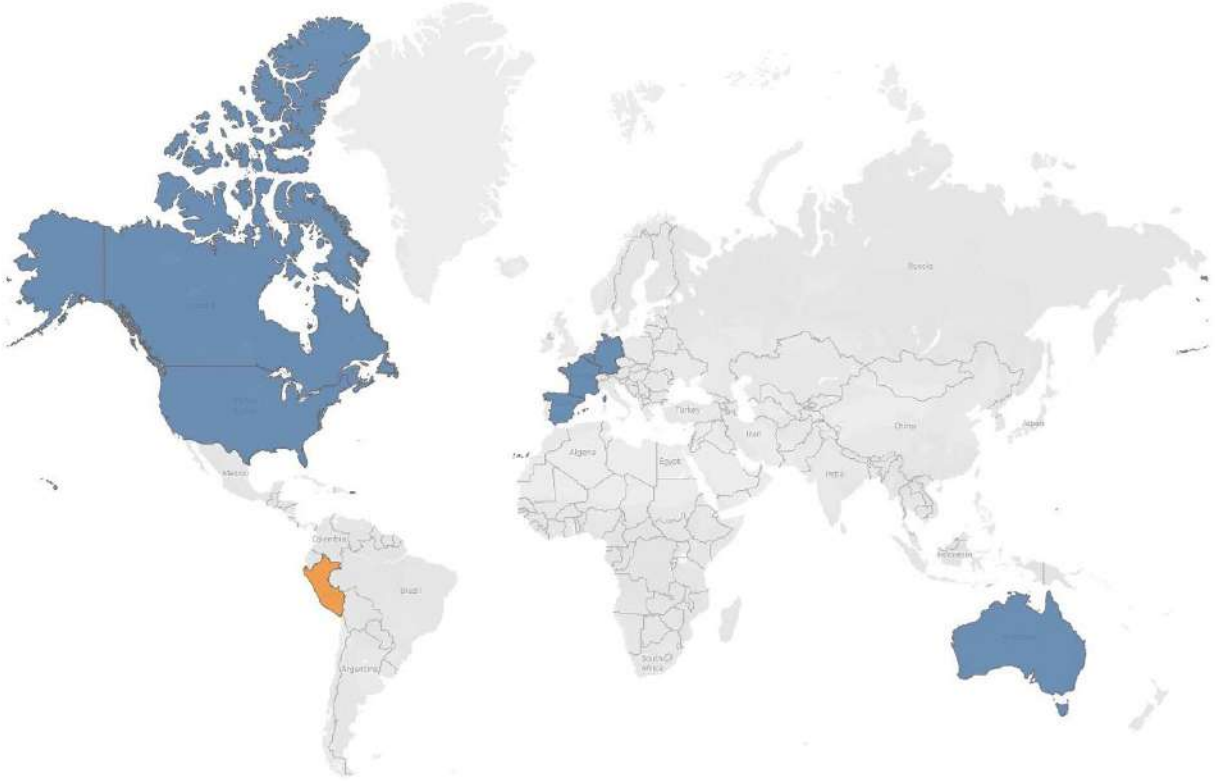
* *Decision pending on national introduction*

As of 17 Mar 2022

PATH

Global HPV Vaccine Introduction

Year:
2007



Introduction status
- Demonstration
- National
- Subnational
- Demo complete*

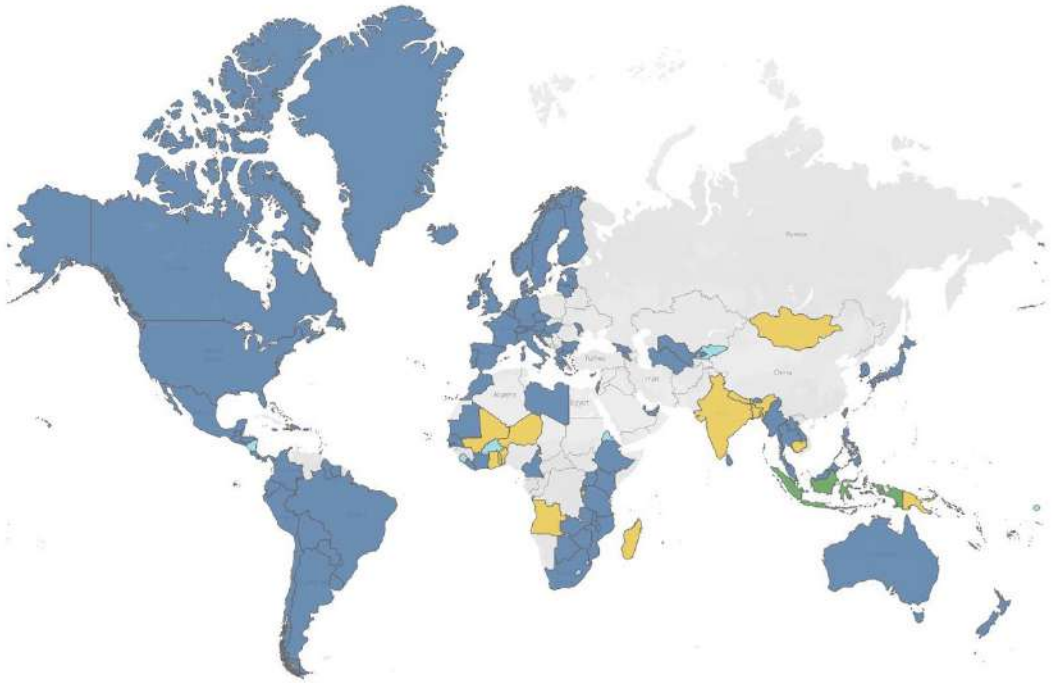
* *Decision pending on national introduction*

As of 17 Mar 2022

PATH

Global HPV Vaccine Introduction

Year:
2022



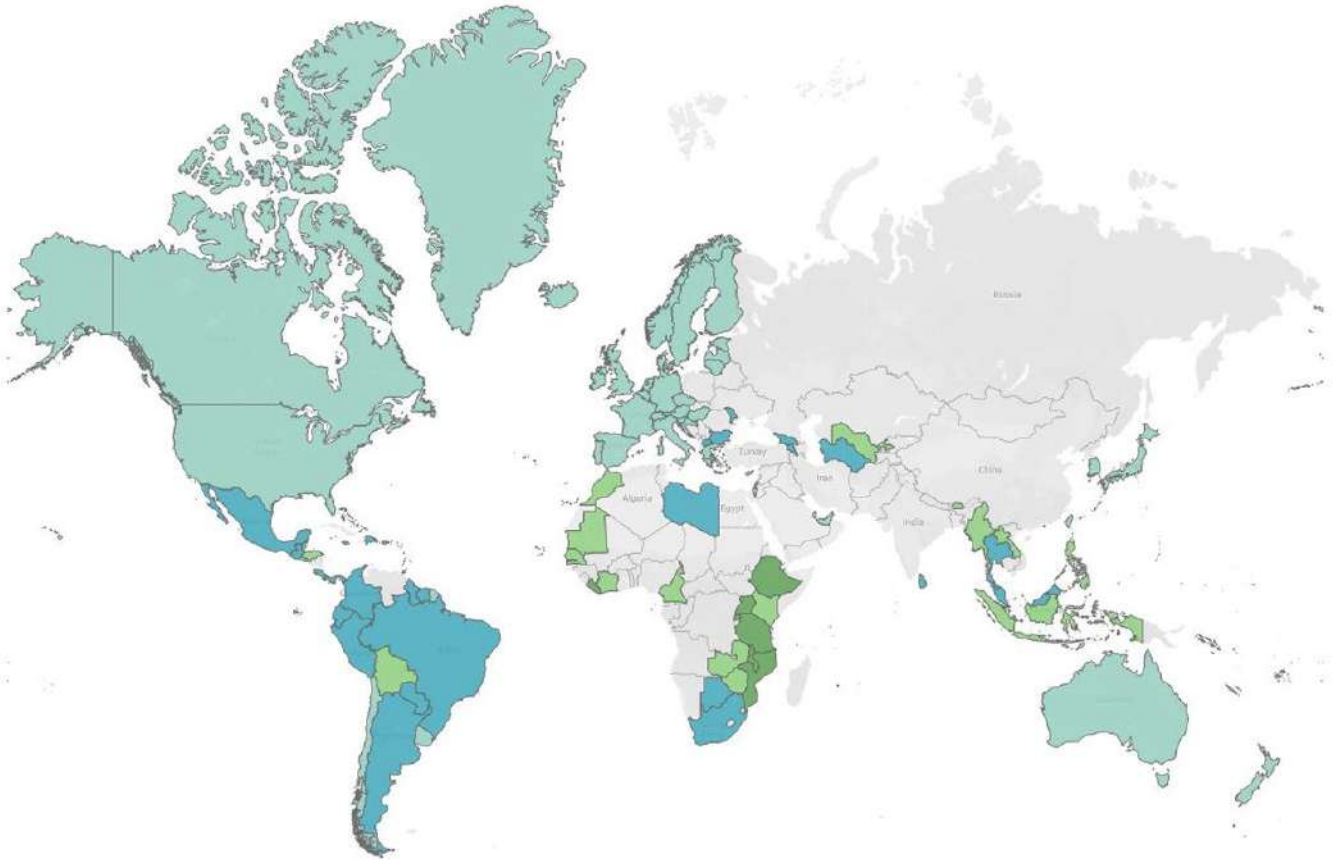
Introduction status
- National
- Subnational
- Demo complete*
- Projected - national

* *Decision pending on national introduction*

As of 17 Mar 2022

PATH

Global HPV Vaccine Introductions by World Bank Category



World Bank Category (2021)

LIC	**8 of 29** have introduced
LMIC	**22 of 51** have introduced
UMIC	**39 of 61** have introduced
HIC	**75 of 84** have introduced
Not classified	

As of 17 Mar 2022

PATH

Countries and territories with HPV vaccine on national routine immunization schedule

WHO Member States (n=122 active; n=3 stopped)

Andorra (2014)	Czech Republic (2012)	Jamaica (2017)	Netherlands (2010)	St. Lucia (2019)
Antigua & Barbuda (2018)	Denmark (2008)	Japan (2011)	New Zealand (2008)	St. Vincent and the Grenadines (2017)
Argentina (2011)	Dominica (2019)	Kazakhstan (subnational 2013-2015; stopped 2015)	Niue (2019)	Suriname (2013)
Armenia * (2018)	Dominican Republic (2017)	Kenya * (2019)	Norway (2009)	Sweden (2012)
Australia (2007)	Ecuador (2014)	Lao PDR * (2020)	Palau (2008)	Switzerland (2008)
Austria (2008)	El Salvador (2020)	Lesotho * (2012, stopped 2015)	Panama † (2008)	Tanzania * (2018)
Bahamas (2015)	Estonia (2018)	Latvia (2010)	Paraguay (2013)	Thailand * (2017)
Barbados (2014)	Ethiopia * (2018)	Liberia * (2019)	Peru * (2011, stopped 2012; 2014)	Trinidad & Tobago (2012, stopped 2013; 2015)
Belgium (2007)	Federated States of Micronesia (2009)	Libya (2014)	Philippines † (2015)	Turkmenistan (2016)
Belize (2016)	Fiji † (2008-09, stopped 2010; 2013)	Lithuania (2016)	Portugal (2008)	Tuvalu (2021)
Bhutan * (2010)	Finland (2013)	Luxembourg (2008)	Qatar (2020)	Uganda *† (2015)
Bolivia * (2017)	France (2006)	Macedonia FYR (2009)	Romania (2009-10, stopped 2011)	United Arab Emirates † (subnational 2008-2012; 2013)
Botswana * (2015)	The Gambia (2019) *†	Malawi * (2019)	Rwanda (2011)	United Kingdom (2008)
Brazil * (2014)	Georgia (2019)	Malaysia (2010)	Samoa (2021)	United States (2006)
Brunei (2012)	Germany (2007)	Maldives (2019)	San Marino (2008)	Uruguay (2013)
Bulgaria (2012)	Greece (2008)	Malta (2012)	Sao Tome And Principe * (2021)	Uzbekistan * (2019)
Cameroon (2020)	Grenada (2019)	Marshall Islands § (2009)	Senegal * (2018)	Zambia * (2019)
Canada (2007)	Guatemala (2018)	Mauritania (2021)	Seychelles (2014)	Zimbabwe * (2018)
Cape Verde (2021)	Guyana *† (Subnational 2012-13; 2017)	Mauritius (2016)	Singapore (2010)	
Chile (2014)	Honduras (2016)	Mexico † (subnational 2008-2011; 2012)	Slovenia (2009)	
Colombia † (2012)	Hungary (2014)	Moldova * (2020)	Solomon Islands * (2019)	
Cook Islands (2011)	Iceland (2011)	Monaco (2011)	South Africa * (2014)	
Costa Rica (2019)	Indonesia (2019)	Morocco (2021)	South Korea (2016)	
Côte d'Ivoire * (2019)	Ireland (2010)	Mozambique * (2021)	Spain (2007)	
Croatia (2016)	Israel (2013)	Myanmar (2020)	Sri Lanka (2017)	
Cyprus (2016)	Italy (2008)	Nauru (2021)	St. Kitts and Nevis (2019)	

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

As of 17 Mar 2022

Non-members (n=27)

American Samoa (2009)
Anguilla (2016)
Aruba (2014)
Bermuda (2007)
Bonaire (2015)
British Virgin Islands (2019)
Cayman Islands (2012)
French Guiana (2007)
Guernsey (2019)
Gibraltar (2008)
Greenland (2008)
Guam (2007)
Isle of Man (2008)
Jersey (2008)
Liechtenstein (2013)
Macau (2013)
Monserrat (2017)
New Caledonia (2011)
Northern Mariana Islands (2008)
Puerto Rico (2008)
Saba (2013)
St. Eustatius (2014)
St. Maarten (2013)
Taiwan (2018)
Turks and Caicos (2019)
U.S. Virgin Islands (2012)
Wallis and Futuna (2013)

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

WHO Member States (n=39)	
Antigua and Barbuda (2018)	Israel (2015)
Argentina (2017)	Italy (2018*)
Australia (2013)	Luxembourg (2019)
Austria (2014)	Netherlands (2009)
Bahamas (2015)	New Zealand (2017)
Barbados (2017)	Niue (2019)
Belgium (2019)	Norway (2018)
Bhutan (2020)	Panama (2016)
Brazil (2017)	Portugal
Canada (2017*)	St. Kitts and Nevis (2019)
Chile (2019)	St. Lucia (2019)
Croatia (2016)	Sweden (2019)
Czech Republic (2016)	Switzerland (2016)
Denmark (2019)	Turkmenistan (2016)
Dominica (2019)	Trinidad and Tobago (2015)
France (2020)	United Kingdom (2019)
Germany (2019)	United States (2011)
Guyana (2019)	Uruguay (2019)
Hungary	
Ireland (2019)	
Israel (2015)	

Non-members (n=13)
American Samoa † (2014)
Bermuda (2016)
Gibraltar †
Guam † (2011)
Greenland †
Guernsey †
Isle of Man †
Jersey †
Liechtenstein (2016)
Northern Mariana Islands † (2011)
Niue (2019)
Puerto Rico †
U.S. Virgin Islands †

** province or region specific*
† territory

As of 17 Mar 2022

PATH

Countries or territories projected to add HPV vaccine to routine immunization schedule

2022	
Burkina Faso *	Samoa
Curacao	**Sierra Leone** *
Eritrea *	Tokelau
eSwatini	Tonga
Kyrgyzstan	Tuvalu
Lesotho *	Vanuatu *
Nicaragua	

2023	
Afghanistan	Mongolia *
Bangladesh *	Nepal *
Benin *	Niger *
Burundi *	Nigeria
Cambodia *	Papua New Guinea *
Djibouti	Republic of Congo
Ghana *	**Timor-Leste**
Mali *	**Togo** *

BOLD *signifies the country was already approved for introduction by Gavi*

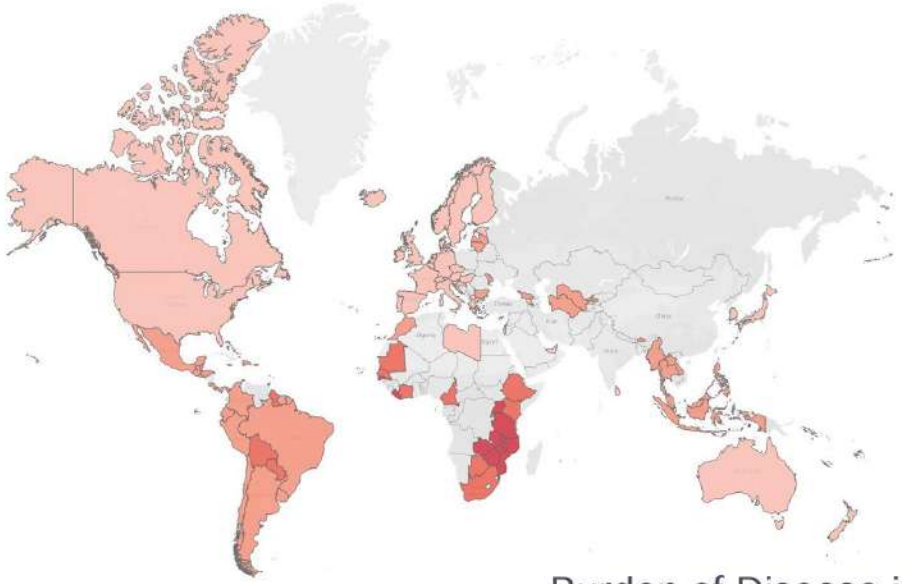
** National/territorial introduction will follow pilot.*

29 additional countries and territories are projected to have HPV vaccine on national schedule by the end of 2023.

As of 17 Mar 2022

PATH

Burden of Disease in Countries **with** National HPV Vaccination



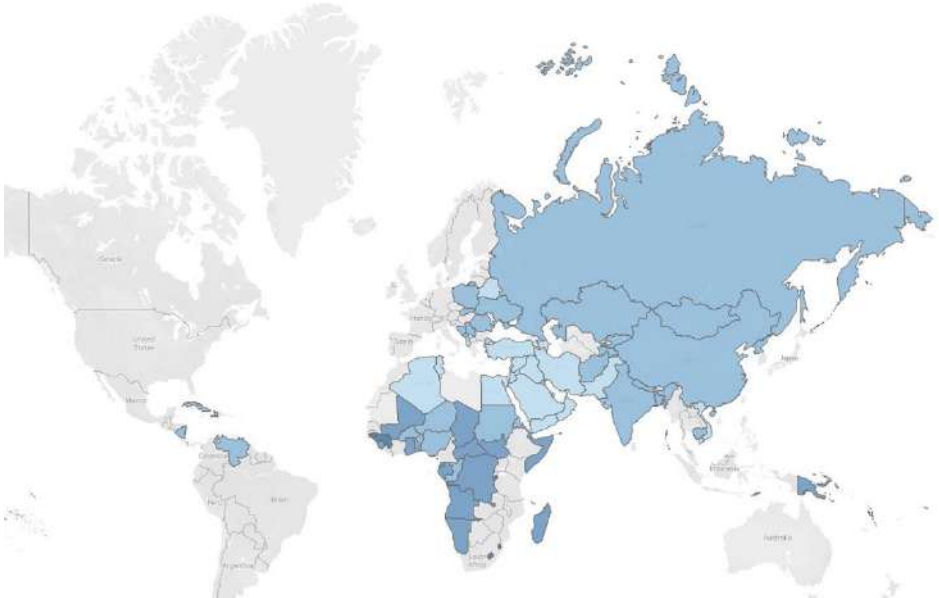
Mortality rate (ASR)*

- <5
- 5 - 14.9
- 15 - 29.9
- ≥30

*rates per 100,000 women per year; estimated 2020 cervical cancer mortality rates from IARC Globocan data

As of 17 Mar 2022

Burden of Disease in Countries **without** National HPV Vaccination



Mortality rate (ASR)*

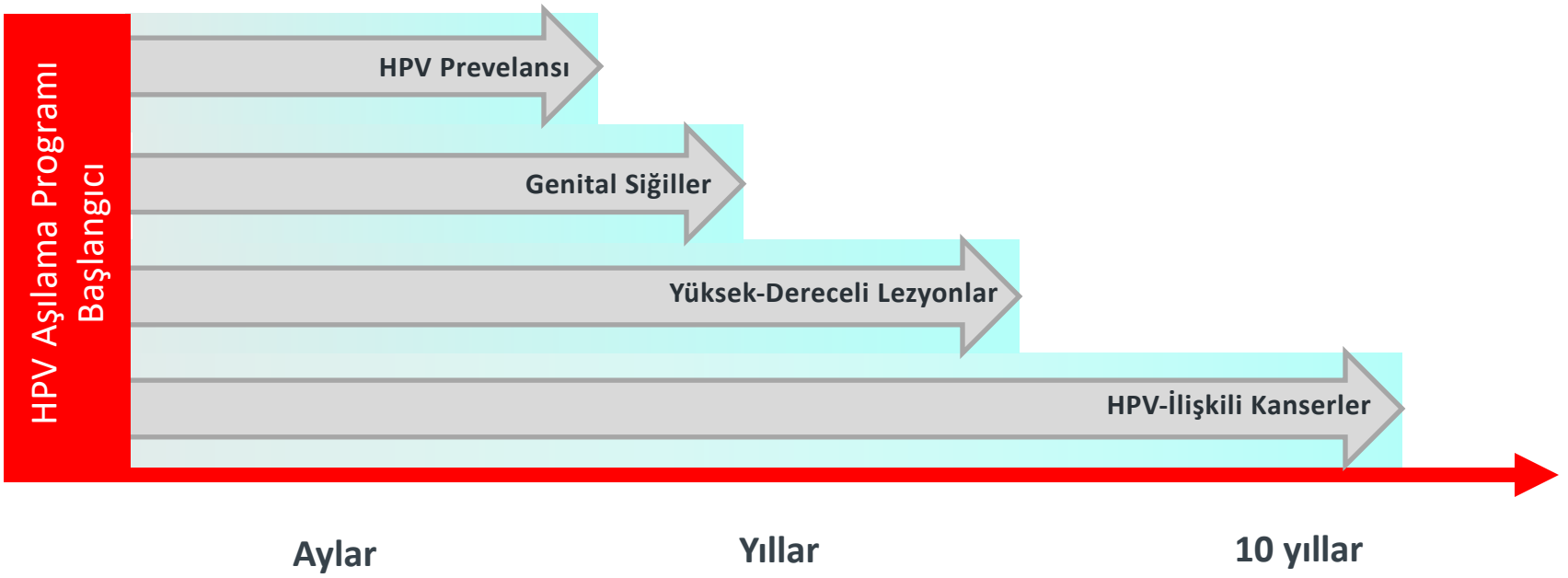
- <5
- 5 - 14.9
- 15 - 29.9
- ≥30

*rates per 100,000 women per year; estimated 2020 cervical cancer mortality rates from IARC Globocan data

As of 17 Mar 2022

HPV Aşılamasının Gerçek Dünyadaki Etkisinin Değerlendirilmesi

Aşılama Programının Başlangıcından Etkinin Ölçülmesine Tahmini Süre

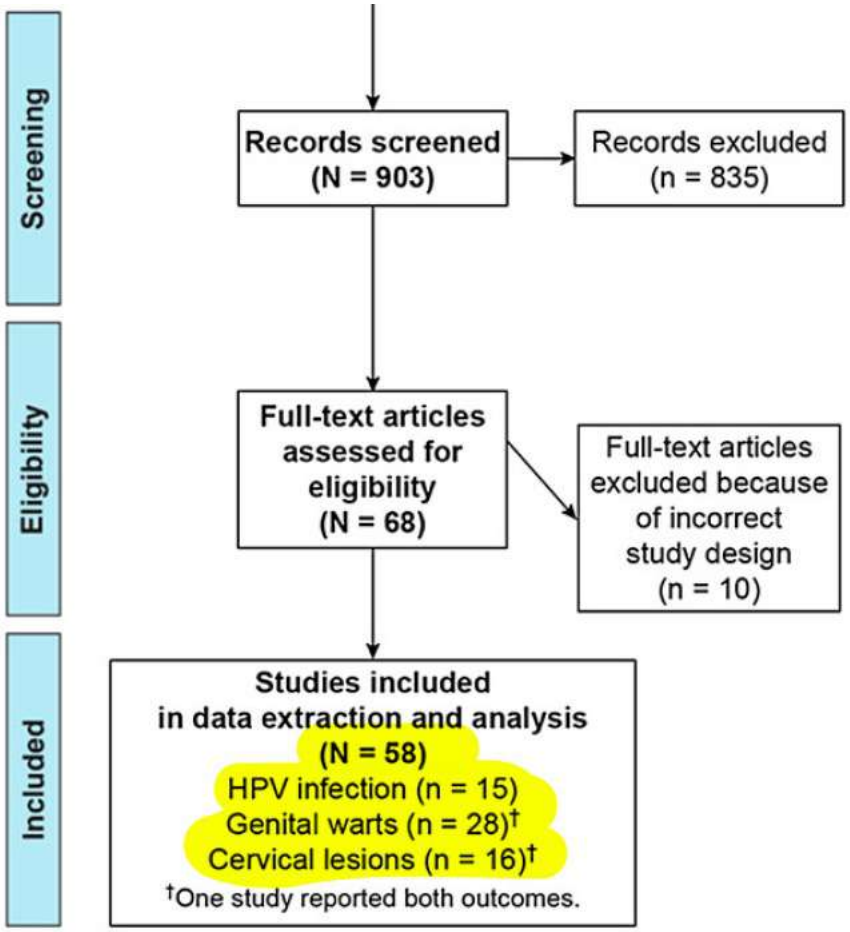


Clinical Infectious Diseases
REVIEW ARTICLE

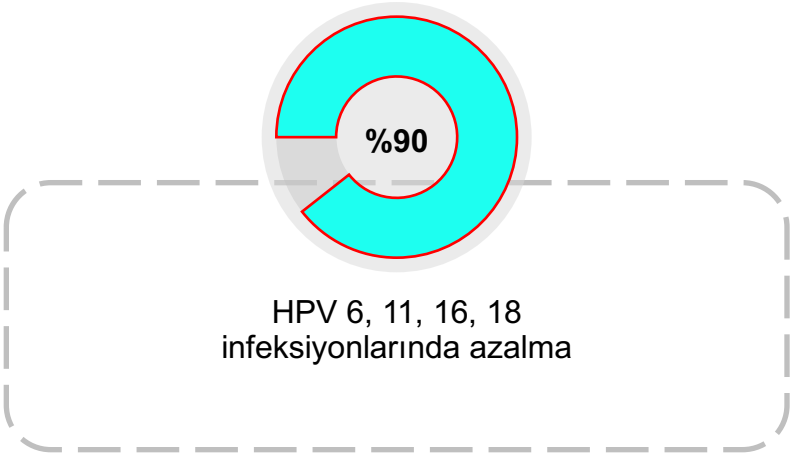
Impact and Effectiveness of the Quadrivalent Human Papillomavirus Vaccine: A Systematic Review of 10 Years of Real-world Experience

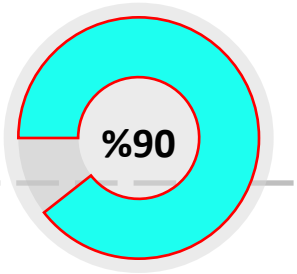
Suzanne M. Garland,[1] Susanne K. Kjaer,[2] Nubia Muñoz,[3] Stan L. Block,[4] Darron R. Brown,[5] Mark J. DiNubile,[6] Brianna R. Lindsay,[6] Barbara J. Kuter,[6] Gonzalo Perez,[6,7] Geraldine Dominiak-Felden,[8] Alfred J. Saah,[6] Rosybel Drury,[8] Rituparna Das,[6] and Christine Velicer[6]

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

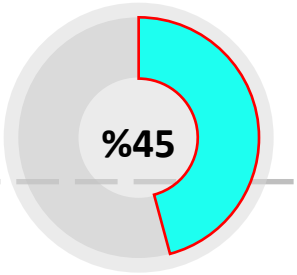


2007-2016 arası gözlemsel çalışmalar

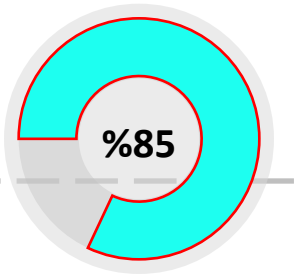




Kadın ve erkeklerde genital siğil oranında azalma



Düşük grade servikal sitolojik anomalilerde azalma



Histolojik olarak dokümante edilmiş yüksek grade servikal sitolojik anomalilerde azalma

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

EClinicalMedicine 23 (2020) 100401

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

		Young women 16–23 years of age (N=2750)		
IgG-LIA	Time since Dose 1	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)

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

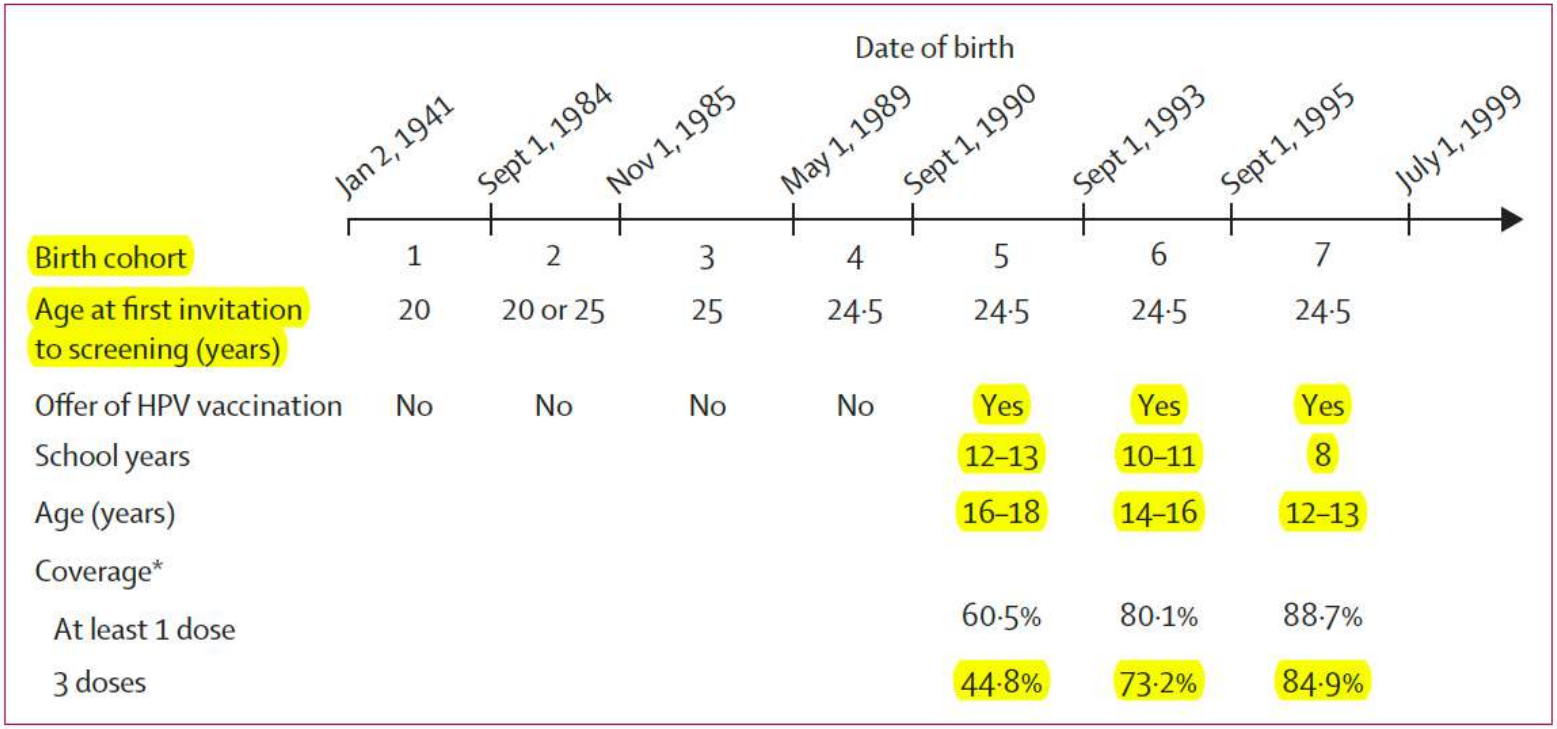
Lancet 2021; 398: 2084–92
Published Online
November 3, 2021
https://doi.org/10.1016/
S0140-6736(21)02178-4

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

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



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 (10 522)	446·9 (42 443)
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 (20 298)	476·4 (25 020)
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 (11 452)	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 bağlı 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 aşılaması sayesinde, 2019 yılına kadar beklenenden;

448 (339-556) daha az servikal kanser

17235 (15919-18552) daha az CIN3 gelişti

The NEW ENGLAND JOURNAL of MEDICINE

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

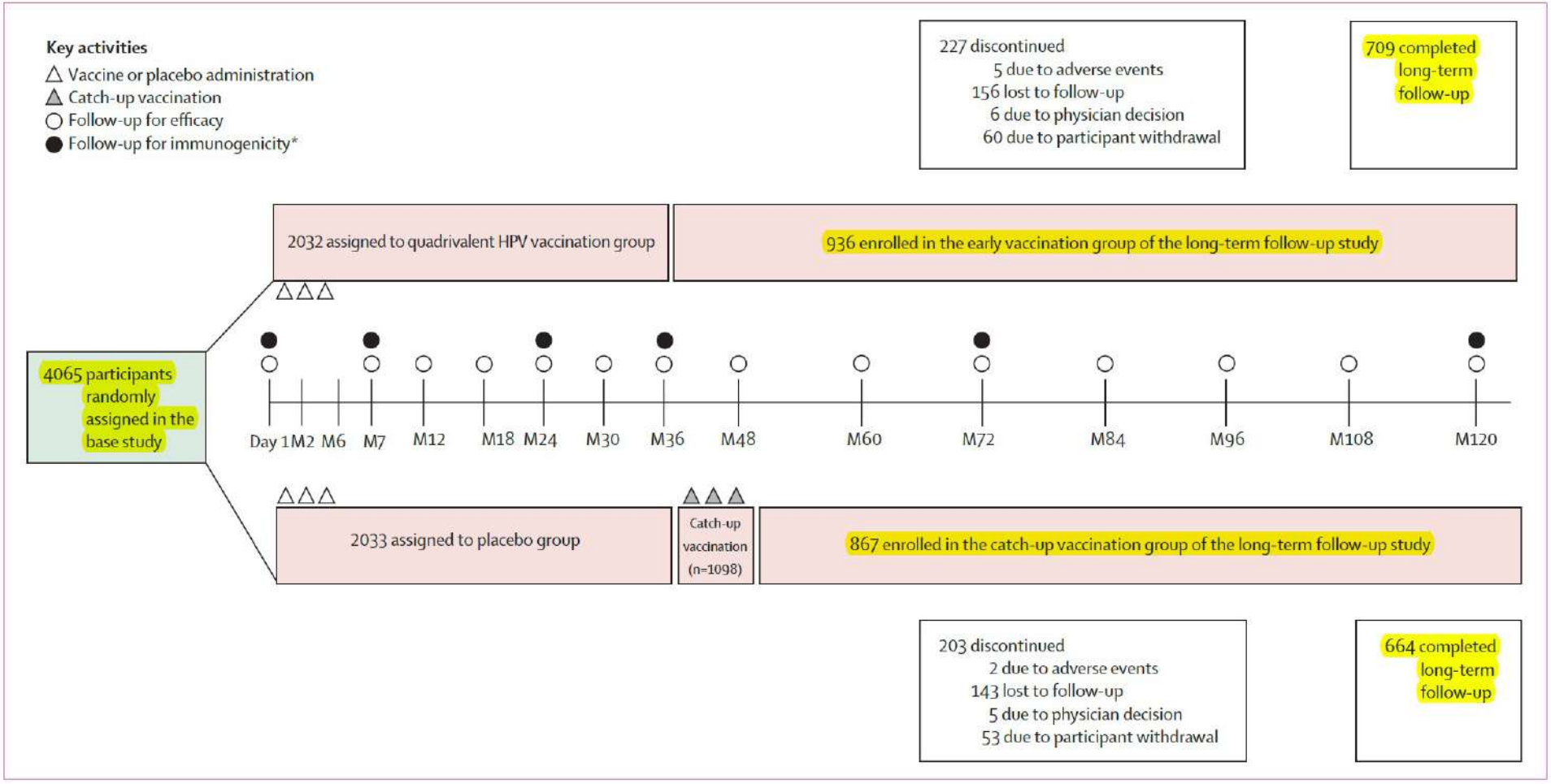
Aşılanma Durumu	# Servikal Kanser	İnsidans Hızı (100,000 kişi yıl)	Düzeltilmiş insidans hızı oranı (95% CI)
Aşısız (n=1,145,112)	538	5.27	1.00
HPV Aşılı (n=527,871)	19	0.73	0.37 (0.21, 0.57)
<17 y aşılanmış	2	0.10	0.12 (0.00, 0.34)
17-30 y aşılanmış	17	3.02	0.47 (0.27, 0.75)

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

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

Lancet Infect Dis 2021

Published Online
November 12, 2021
https://doi.org/10.1016/S1473-3099(21)00327-3



	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)

HUMAN VACCINES & IMMUNOTHERAPEUTICS
2021, VOL. 17, NO. 4, 943–949
https://doi.org/10.1080/21645515.2020.1839292

Taylor & Francis
Taylor & Francis Group

SHORT REPORT

Long-term effectiveness of the nine-valent human papillomavirus vaccine in Scandinavian women: interim analysis after 8 years of follow-up

Susanne K. Kjaer[a,b], Mari Nygård[c], Karin Sundström[d], Christian Munk[a], Sophie Berger[c], Mensur Dzabic[e],

Table 1. Analysis of 9vHPV vaccine effectiveness against HPV16/18/31/33/45/52/58-related CIN2, CIN3, AIS, and cervical cancer by time since 9vHPV vaccination, HPV type, and lesion type (PPE population).[a]

	Young women 16–26 years of age (N = 2029)			
	Cases/n	Person-years' follow-up	Rate per 100,000 person-years (95% CI)	Vaccine effectiveness,[b] % (95% CI)
From the start of the LTFU study				
HPV16/18/31/33/45/52/58-related CIN2 or worse[c]	0/1448	4084.2	0.0 (0.0–90.3)	100 (79.4–100)
By time since start of the LTFU study				
>0 to 2 years[d]	0/1448	2682.5	0.0 (0.0–137.5)	
>2 to 4 years[d]	0/1094	1351.0	0.0 (0.0–273.1)	
>4 to 6 years[d]	0/194	50.8	0.0 (0.0–7266.3)	
From the start of the base study				
HPV16/18/31/33/45/52/58-related CIN2 or worse[e]	1/1783	10,303.1	9.7 (0.2–54.1)	
By time since 9vHPV vaccine Dose 1				
≤4 years[f]	1/1783	5938.6	16.8 (0.4–93.8)	
>4 to 6 years[d]	0/1586	2767.0	0.0 (0.0–133.3)	
>6 to 8 years[d]	0/1147	1488.0	0.0 (0.0–247.9)	
>8 to 10 years[d]	0/271	109.5	0.0 (0.0–3370.0)	
By HPV type				
HPV16-related	0/1391	8128.6	0.0 (0.0–45.4)	
HPV18-related	1/1564	9059.2	11.0 (0.3–61.5)	
HPV31-related	0/1541	8981.7	0.0 (0.0–41.1)	
HPV33-related	0/1604	9338.6	0.0 (0.0–39.5)	
HPV45-related	0/1685	9752.9	0.0 (0.0–37.8)	
HPV52-related	0/1583	9156.9	0.0 (0.0–40.3)	
HPV58-related	0/1627	9464.0	0.0 (0.0–39.0)	
By lesion type				
CIN2 or CIN3	1/1783	10,302.9	9.7 (0.2–54.1)	
CIN2	1/1783	10,291.6	9.7 (0.2–54.1)	
CIN3	0/1783	10,301.2	0.0 (0.0–35.8)	
AIS	0/1783	10,303.5	0.0 (0.0–35.8)	
Cervical cancer	0/1783	10,303.5	0.0 (0.0–35.8)	

Papillomavirus Research 10 (2020) 100203

Contents lists available at ScienceDirect

Papillomavirus Research

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

Long-term immunogenicity, effectiveness, and safety of nine-valent human papillomavirus vaccine in girls and boys 9 to 15 years of age: Interim analysis after 8 years of follow-up

Sven-Eric Olsson [a], Jaime Alberto Restrepo [b], Julio Cesar Reina [c], Punnee Pitisuttithum [d],

Table 2
Incidence of HPV6/11/16/18/31/33/45/52/58-related persistent infection and disease in vaccinated participants (PPE population).

	Females (N = 971)			Males (N = 301)		
	Cases/ n	Person-years follow-up[a]	Rate per 10,000 person-years (95% CI)	Cases/ n	Person-years follow-up[a]	Rate per 10,000 person-years (95% CI)
HPV6/11/16/18/31/33/45/52/58-related disease[c]	1/856[e]	2865.0	3.5 (0.1–19.4)	0/251	808.8	0.0 (0.0–45.6)
CIN1[f]	1/856	2865.0	3.5 (0.1–19.4)	–	–	–
CIN2 or CIN3[f]	0/856	2865.9	0.0 (0.0–12.9)	–	–	–
AIS[f]	0/856	2865.9	0.0 (0.0–12.9)	–	–	–
Cervical cancer[f]	0/856	2865.9	0.0 (0.0–12.9)	–	–	–
Condyloma	0/856	2865.9	0.0 (0.0–12.9)	0/251	808.8	0.0 (0.0–45.6)
VIN1 or worse[f]	0/856	2865.9	0.0 (0.0–12.9)	–	–	–
VaIN1 or worse[f]	0/856	2865.9	0.0 (0.0–12.9)	–	–	–
PIN1 or worse[g]	–	–	–	0/251	808.8	0.0 (0.0–45.6)

TABLE 2. Current Advisory Committee on Immunization Practices Recommendations

Ages (y)	Recommendation	Dosing	Schedule
Females and males			
11-12 (9-14 permissible)	Recommended	2-dose regimen	0, 6-12 mo
15-26	Recommended: catch-up	3-dose regimen	0, 1-2, 6 mo
27-45	Shared decision making: catch-up	3-dose regimen	0, 1-2, 6 mo
Special populations			
Pregnancy	Not recommended		
Breastfeeding or lactating	Recommended	Based on age	
Immunocompromise aged 9-26	Recommended	3-dose regimen	0, 1-2, 6 mo

Gebe olduğu bilinmeden yapıldıysa abortus endikasyonu YOK!!!

>2000 aşılanmış gebede gebelik komplikasyonu veya fetal risk gösterilmemiş

Conageski C. Clin Obs Gyn 2023;66(3):433-47

1 ve 2. doz arasında 12 ay olması daha yüksek antikor düzeyi sağlıyor!

WHO 2019 HPV raporu

WHO updates recommendations on HPV vaccination schedule

20 December 2022 | Departmental news |Reading time: 1 min (333 words)

WHO now recommends:

- **A one or two-dose schedule** for girls aged **9-14 years**
- **A one or two-dose schedule** for girls and women aged **15-20 years**
- Two doses with a 6-month interval for women **older than 21 years**

The position paper underscores the importance of vaccinating as a priority immunocompromised people, or those living with HIV. Immunocompromised individuals should receive at a minimum two doses and where possible three doses.

The primary target of vaccination is girls aged 9-14, prior to the start of sexual activity. The vaccination of secondary targets such as boys and older females is recommended where feasible and affordable.

Tek Doz Yapsak Olur mu?

Tek doz HPV aşısının <20y grupta 2 veya 3 doz kadar et
çalışmaların sayısında artış var.

Table 2
Summarised HPV16/18 infection results up to four and seven years following vaccination from studies reporting efficacy data for participants who re

Reference	Follow up duration	Infection endpoint[a]	3 dose HPV arm		2 dose HPV arm[b]		1 dose HPV arm		RR or PR (95%CI), *p value*[d]		
			# events / participants	% (95%CI)[d]	# events / participants	% (95%CI)[d]	# events / participants	% (95%CI)[e]	1 dose/ 3 doses[c]	1 dose/ 2 doses[c]	1 dose/ control
CERVARIX®											
One-time incident and cumulative incident infections											
Kreimer 2015[25]	Mean: 4.0y SD: 0.7y	One-time incident	529/11,110	4.8 (4.4–5.2)	22/611	3.6 (2.3–5.4)	8/292	2.7 (1.2–5.3)	0.6 (0.3–1.1) ***0.12***	0.8 (0.3–1.7) ***0.56***	0.2 (0.1–0.3) ***< 0.01***
Safaeian 2018[26]	Median: 6.9y IQR: 6.5–7.3y	One-time incident	9/2,042	0.4 (0.2–0.8)	0/78	0.0 (0.0–4.6)	0/134	0.0 (0.0–2.7)	0.8 (0.0–13.6) ***1.0***	0.6 (0.0–29.2) ***UTC***[i]	–
		Cumulative incident	88/2,036	4.3 (3.5–5.3)	3/78	3.8 (0.8–10.8)	2/133	1.5 (0.2–5.3)	0.3 (0.1–1.4) ***0.17***	0.4 (0.1–2.3) ***0.36***	–
One-time prevalent infections											
Safaeian 2018[26]	Median: 6.9y IQR: 6.5–7.3y	One-time prevalent	20/2,043	1.0 (0.6–1.5)	1/79	1.3 (0.0–6.9)	0/134	0.0 (0.0–2.7)	0.4 (0.0–6.1) ***0.63***	0.2 (0.0–4.8) ***0.37***	0.1 (0.0–0.9) ***<0.01***
Persistent infections[h]											
Kreimer 2011[24]	Median: 4.2y[g]	6 m persistent	37/2957	1.3 (0.9–1.7)	5/422	1.2 (0.4–2.7)	0/196	0.0 (0.0–1.9)	0.2 (0.0–3.2) ***0.17***	0.2 (0.0–3.5) ***0.18***	0.0 (0.0–0.5) ***<0.01***
		12 m persistent	25/2957	0.9 (0.6–1.2)	3/422	0.7 (0.1–2.1)	0/196	0 0.0 (0.0–1.9)	0.3 (0.0–4.8) ***0.40***	0.3 (0.0–5.9) ***0.56***	0.0 (0.0–0.8) ***<0.01***
Kreimer 2015[25]	Mean: 4.0y SD: 0.7y	6 m persistent	114/11,104	1.0 (0.8–1.2)	4/611	0.7 (0.2–1.7)	1/292	0.3 (0.0–1.9)	0.3 (0.0–2.4) ***0.37***	0.5 (0.1–4.7) ***1.00***	0.0 (0.0–0.3) ***<0.01***
		12 persistent	84/11,104	0.8 (0.6–0.9)	3/611	0.5 (0.1–1.4)	1/292	0.3 (0.0–1.9)	0.5 (0.1–3.2) ***0.72***	0.7 (0.1–6.7) ***1.00***	0.1 (0.0–0.4) ***<0.01***
GARDASIL®											
One-time incident and cumulative incident infections											
Sankaranarayanan 2016 [27]	Median: 4.7y IQR: 4.2–5.1y	Cumulative first incident	2/536	0.4 (0.0–1.3)	4/526	0.8 (0.2–1.9)	10/870	1.1 (0.6–2.1)	3.1 (0.7–14.0) ***0.17***	1.5 (0.5–4.8) ***0.059***	–
Sankaranarayanan 2018 [28]	Up to 7y[f]	Cumulative incident	11/1,180	0.9 (0.5–1.7)	11/1,179	0.9 (0.5–1.7)	30/1,823	1.6 (1.1–2.3)	1.8 (0.9–3.5) ***0.1***	1.8 (0.9–3.5) ***0.1***	0.3 (0.2–0.4) ***<0.01***
Persistent infections[h]											
Sankaranarayanan 2018 [28]	Up to 7y[f]	12 m persistent	1/604	0.2 (0.0–0.9)	0/608	0.0 (0.0–0.6)	0/959	0.0 (0.0–0.4)	0.2 (0.0–5.1) ***0.39***	0.6 (0.0–31.9) ***UTC***	0.0 (0.0–0.7) ***<0.01***

Whitworth HS Vaccine 2020;38:1302–1314

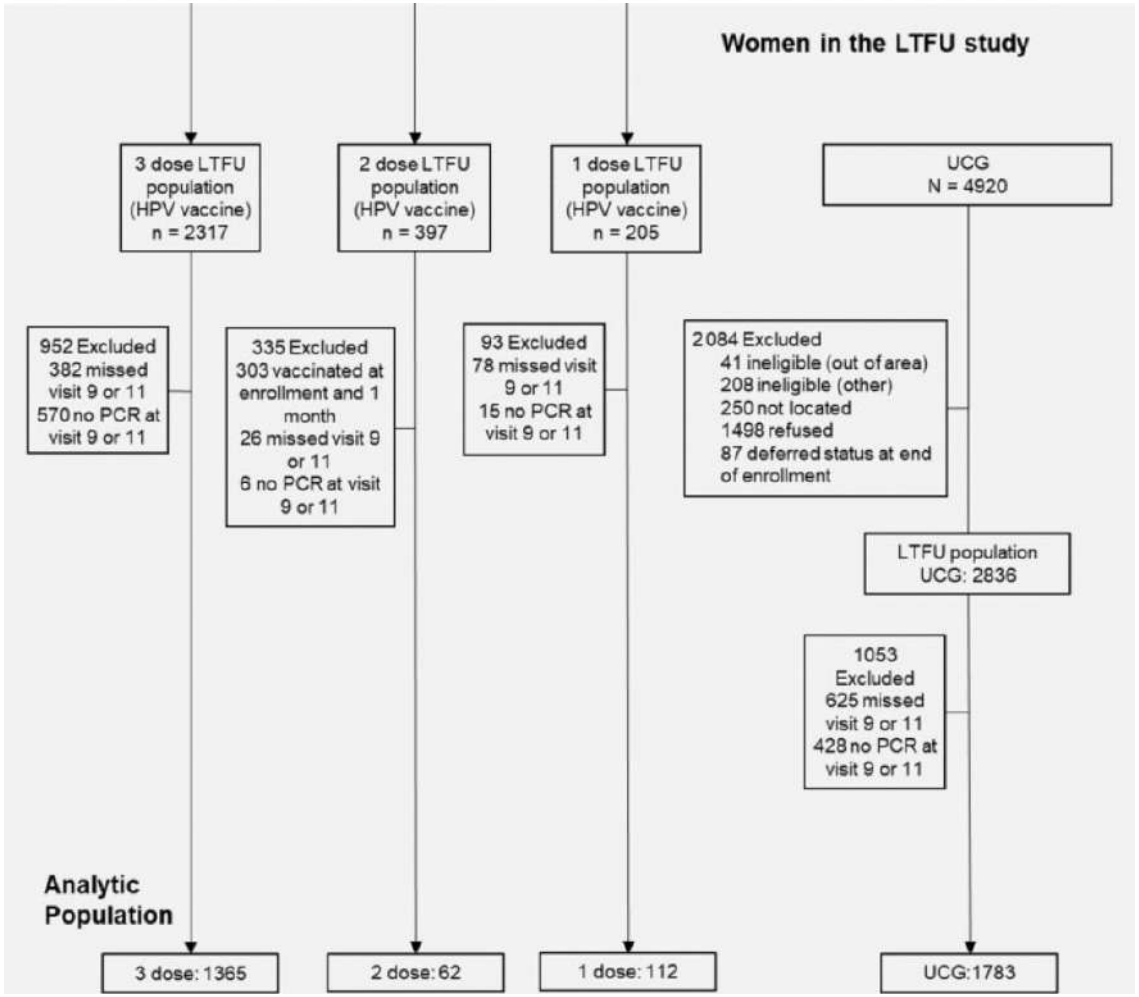
JNCI J Natl Cancer Inst (2020) 112(10): djaa011

doi: 10.1093/jnci/djaa011
First published online February 10, 2020
Article

Kreimer AR J Natl Cancer Inst 2020;112: 1038-46

Evaluation of Durability of a Single Dose of the Bivalent HPV Vaccine: The CVT Trial

Aimée R. Kreimer, PhD,[1,*,‡] Joshua N. Sampson, PhD,[1,‡] Carolina Porras, MSc,[2] John T. Schiller, PhD,[1]

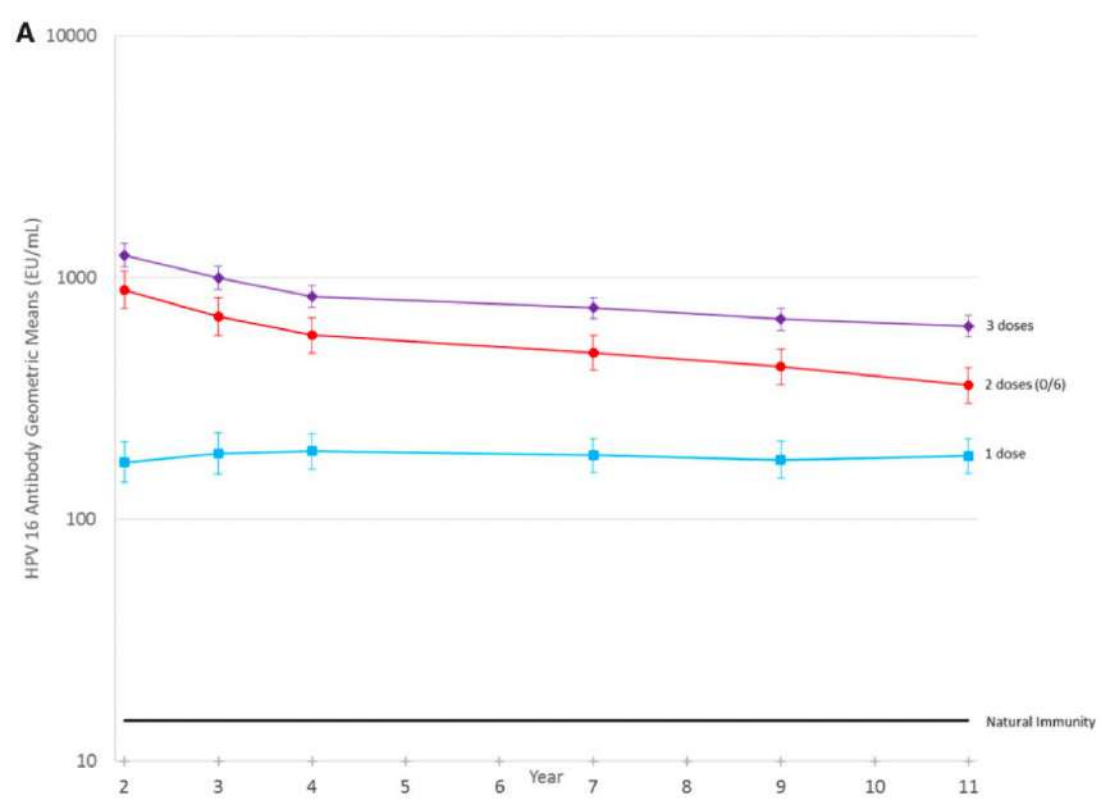


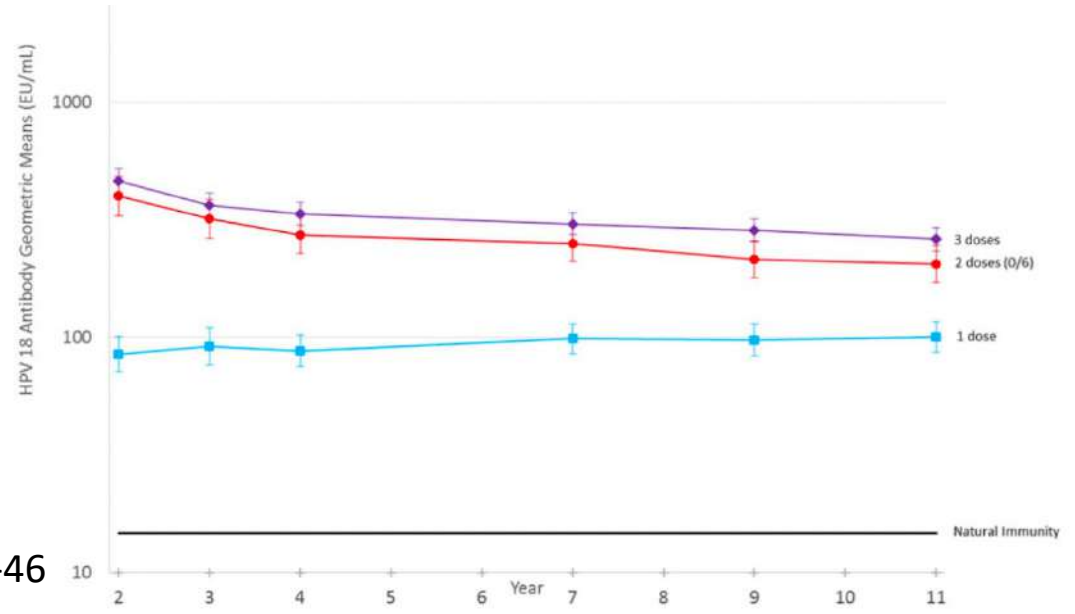
Persistan HPV16/18 Aşı etkililiği:

Tek doz: %82.1 (40.2-97)

İki doz: %83.8 (19.5-99.2)

Üç doz: %80.2 (70.7-78.0)





Kreimer AR J Natl Cancer Inst 2020;112: 1038-46

KEN SHE çalışması:

Barnabas RV, NEJM Evid 2022 Jun;1(5):EVIDoa2100056.

Kenya, 2018-2021, 15-20y arası 2275 kadın, RKÇ, çift kör.

Sonuç: 18 ay sonunda persistan HPV 16/18 infeksiyonu

9vHPV aşısı (1 olgu), 2vHPV aşısı (1 olgu), Meningokok aşısı (36 olgu)

Tek doz aşı etkililiği: %97,5

Gruplar kör bir şekilde çaprazlanarak 36. ay sonuçlarına da bakılacak

		HPV 16/18 mITT			HPV 16/18/31/33/45/52/58 mITT	
		Nonavalent HPV	Bivalent HPV	Meningococcal	Nonavalent HPV	Meningococcal
Characteristic	**Category**					
	Total	496	489	473	325	290

Arm	Enrolled (n)	HPV 16/18/31/33/45/52/58 naïve^ (mITT) (n)	Incident persistent HPV 16/18/31/33/45/52/58 (n)	Woman-years of Follow-up**	Incidence of persistent HPV 16/18/31/33/45/52/58 per 100 Woman-years	Lower Bound	Upper Bound	Comparison	Vaccine Efficacy	95% CI	P-value (Log-rank)
Nonavalent HPV	758	325	4	389.18	1.03	0.28	2.63	Nonavalent v. Meningococcal	88.9%	(68.5%, 96.1%)	<.0001
Meningococcal	757	290	29	307.81	9.42	6.31	13.53				

Hindistan Çalışması

Vaccine efficacy against persistent human papillomavirus (HPV) 16/18 infection at 10 years after one, two, and three doses of quadrivalent HPV vaccine in girls in India: a multicentre, prospective, cohort study

Basu P. Lancet Oncol 2021; 22: 1518–29

2009-2010'da 10-18 yaş bekar kadınlar 2 doz ve 3 doz 4vHPV aşısı için randomize edilmiş

Hindistan hükümeti hasta alımı ve aşılamayı yasaklamış → prospektif kohorta dönüşmüş

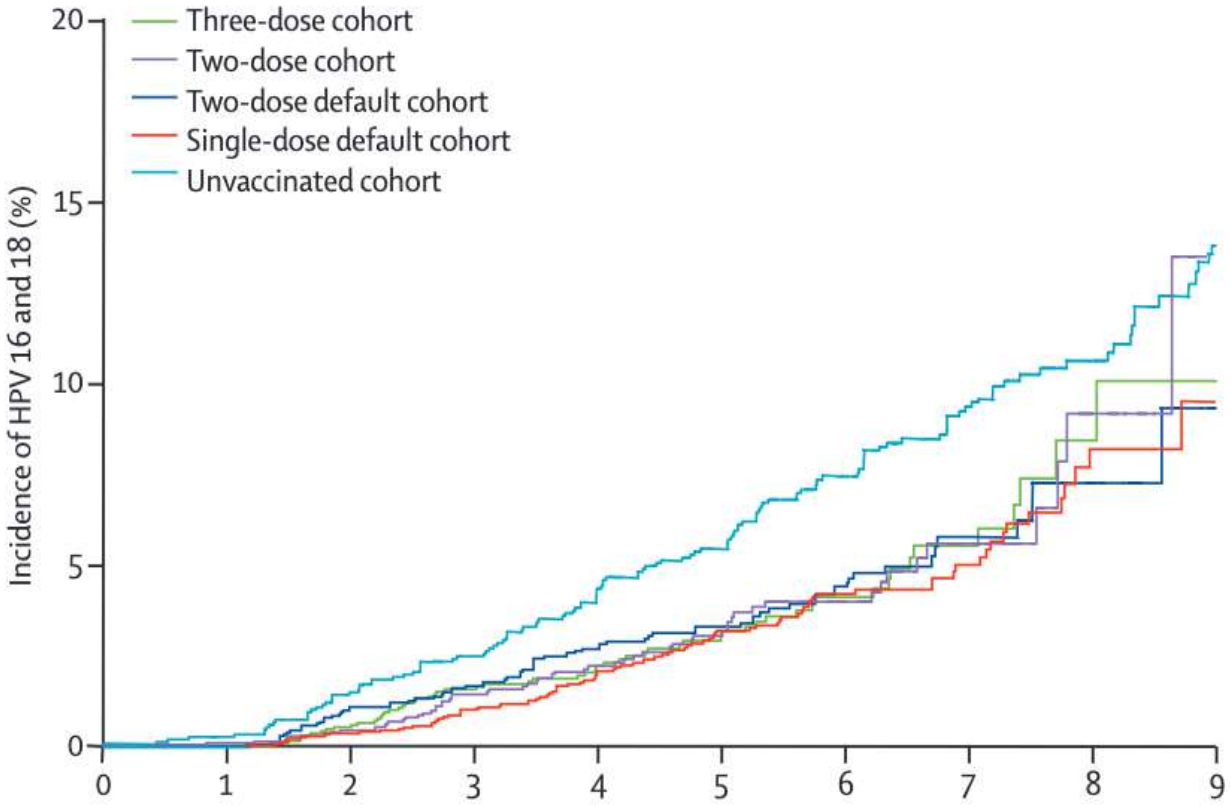
1460 3 doz, 1452 2 doz, 2135 1 doz aşılanmış kadın değerlendirilmiş.

Yaş eşleştirilmiş kadın kontrol grupları (#1541 ve #3631) ile 9-10 yılın sonunda karşılaştırma:

Persistan HPV16/18 infeksiyonu (1^0), anlık HPV 16/18 infeksiyonu, servikal neoplazi (2^0)

	Unvaccinated cohort	Single-dose default cohort	Two-dose cohort	Three-dose cohort
Incident HPV				
Women assessed	1479	2858	2166	2019
Incident HPV 16 and 18 infections				
Observed events	138	92	59	59
Crude attack rates	9·33%	3·22%	2·72%	2·92%
Adjusted vaccine efficacy* (95% CI)	..	63·5% (51·2 to 73·1)	67·7% (55·2 to 77·2)	66·4% (53·6 to 76·3)
Difference in vaccine efficacy† (95% CI)	..	..	4·2% (–7·1 to 16·0)	3·0% (–9·1 to 14·8)

Persistan HPV 16/18 infeksiyonu:



Aşı etkililiği:

Tek doz: %95.4 (85-99.9)

İki doz: %93.1 (77.3-99.88)

Üç doz: %93.33 (77.5-99.7)

Alternative single-dose schedule. As an off-label option, a single-dose schedule can be used in girls and boys aged 9–20 years.

Current evidence suggests that a single dose has comparable efficacy and duration of protection as a 2-dose schedule and may offer programme advantages, be more efficient and affordable, and contribute to improved coverage.[138] From a public health perspective, the use of a single dose schedule can offer substantial benefits that outweigh the potential risk of a lower level of protection if efficacy wanes over time, although there is no current evidence of this.

Hatırlatma dozu gerekli mi?

Çoklu doz uygulama sonrası antikor düzeyleri;

- ✓ 2vHPV aşısında min. 12 yıl
- ✓ 4vHPV aşısında min. 12 yıl
- ✓ 9vHPV aşısında min. 8 yıl yüksek ve stabil gidiyor.

Tek dozda oluşan antikor düzeyi 2 ve 3'lü dozdan anlamlı olarak daha düşük, doğal bağışıklıktan çok yüksek ve aynı süreyle stabil

There is no evidence to suggest that a booster dose several years after the primary HPV vaccination is needed. However, data continue to be evaluated.[101]

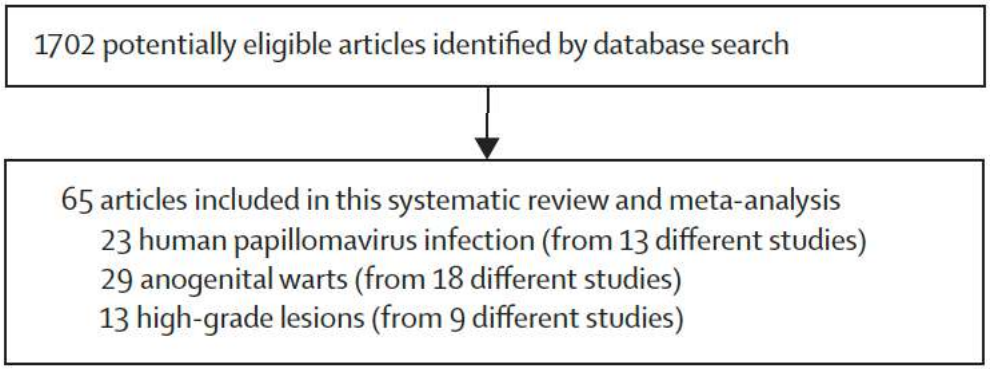
WHO, WEEKLY EPIDEMIOLOGICAL RECORD, NO 50, 16 DECEMBER 2022

Toplum Bağışıklığı

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

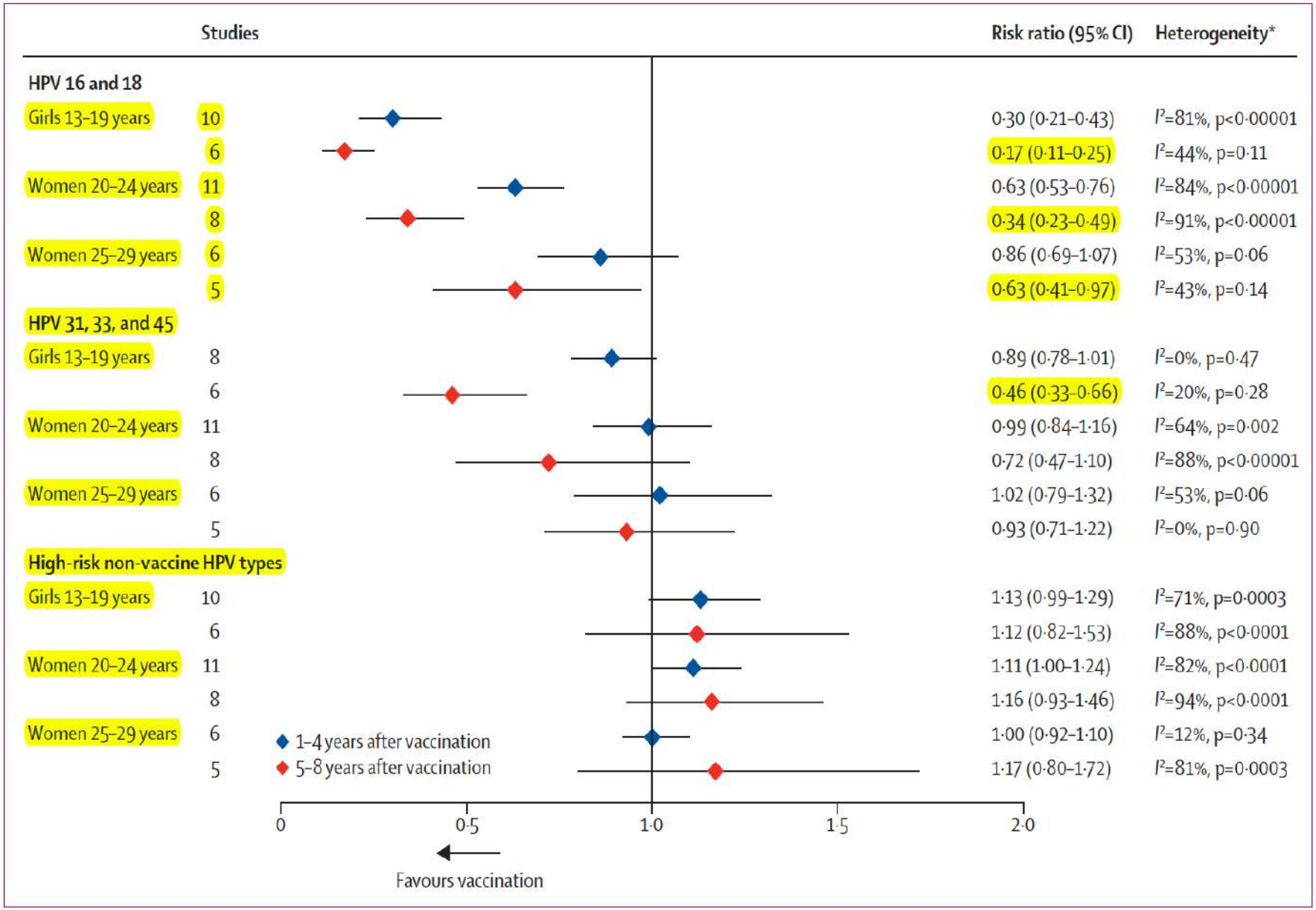


14 yüksek gelirli ülkeden

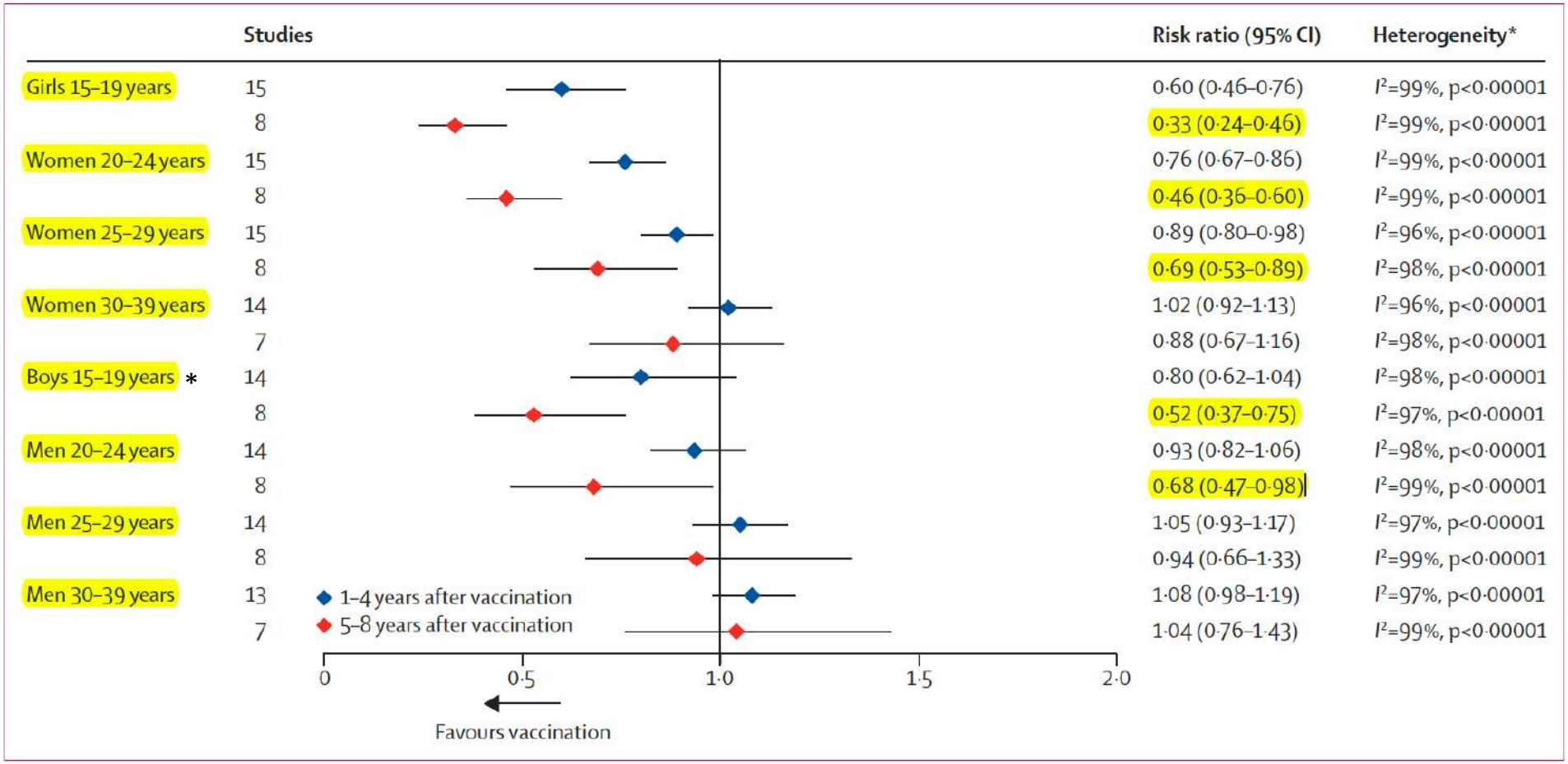
60 milyon kişinin

~9 yıllık takip verileri

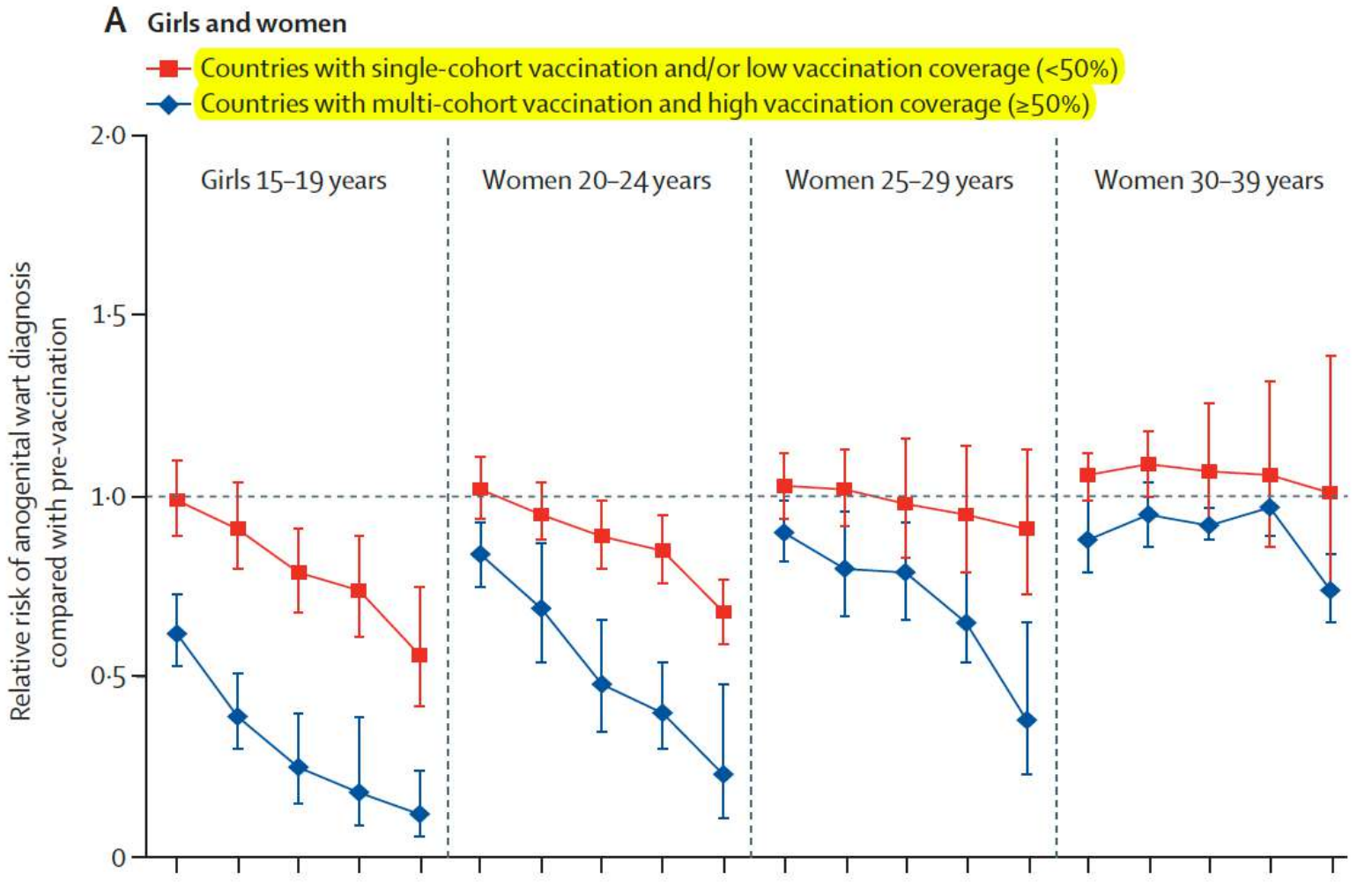
HPV infeksiyonu



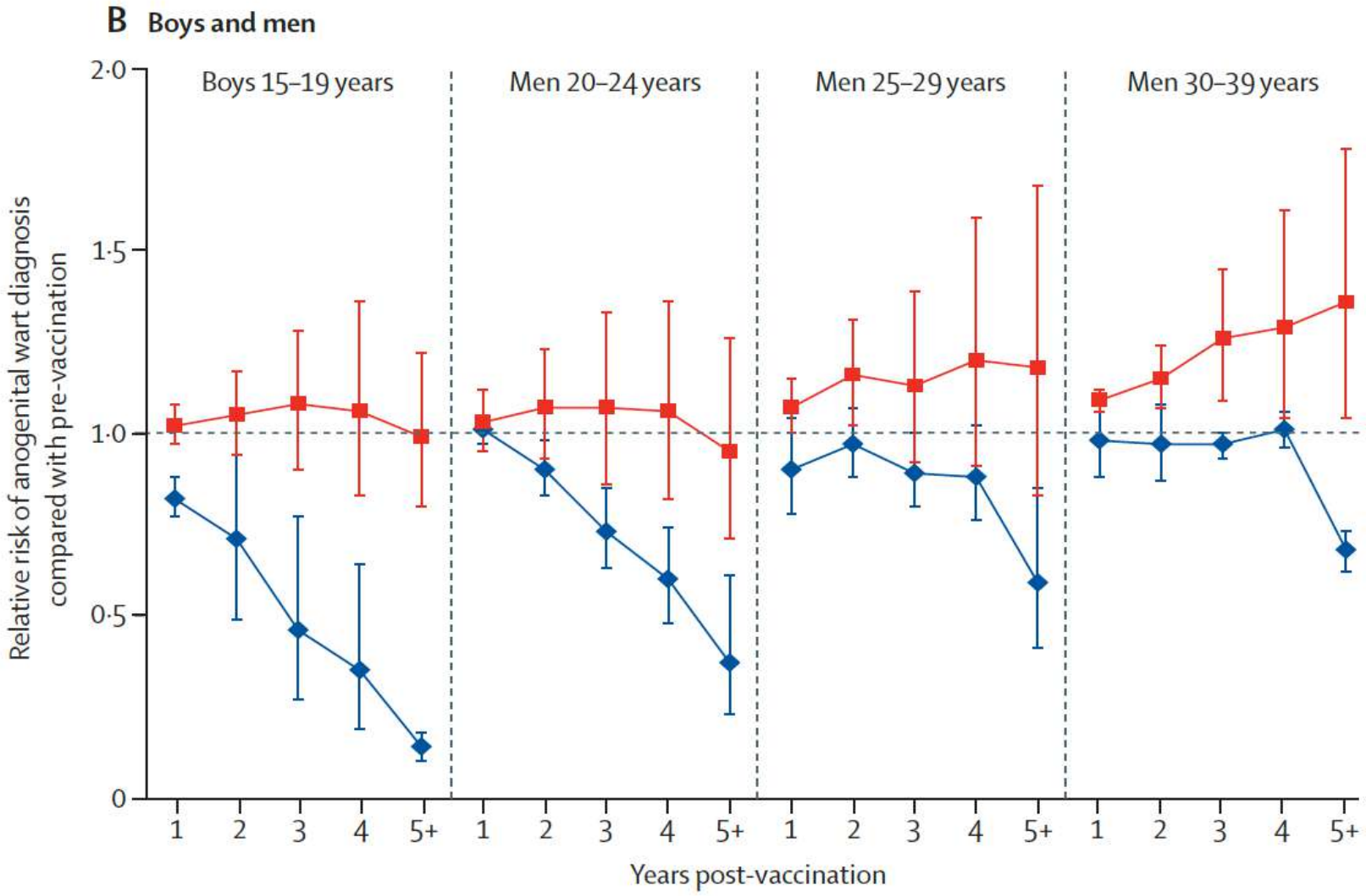
Anogenital siğil sıklığı (4vHPV uygulaması öncesi sonrası)



*: 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

Toplum Bağışıklığı

Toplumda HPV insidansını aşı öncesi vs sonrası karşılaştıran çalışmalarda aşılanmayan kadınlarda da HPV insidansının azaldığı gösterilmiş.

Rosenblum HG, MMWR Morb Mortal Wkly Rep. 2021;70:415–420.
Tabrizi SN. Lancet Infect Dis. 2014; 14:958–966.

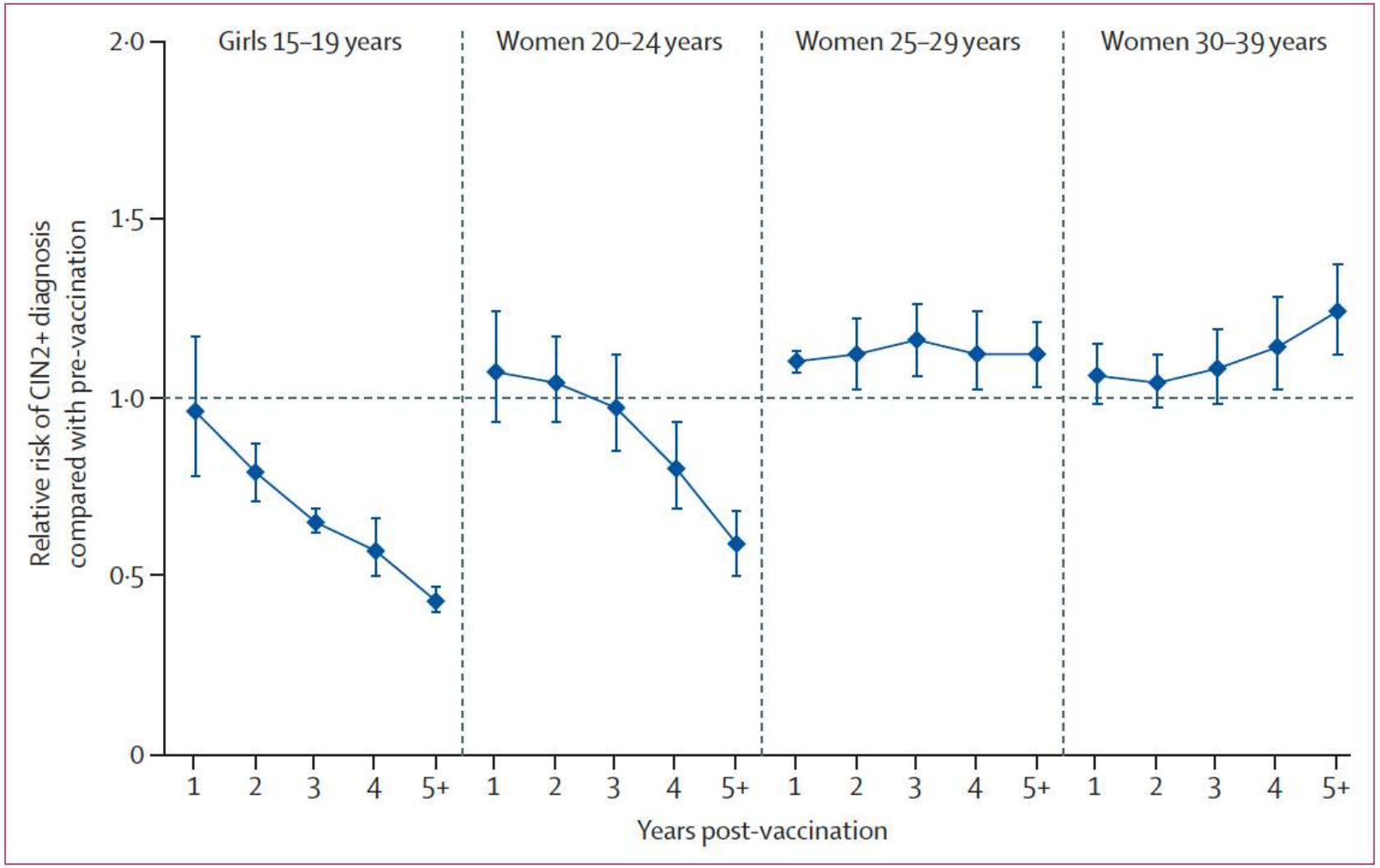
Sadece kadınların aşılandığı toplumlarda erkeklerde de HPV insidansı azalmış

Bollerup S. Sex Transm Dis. 2016;43:238e42.
Ali H. BMJ 2013;346:f2032.

WHO SAGE Önerisi (Ekim 2016):

Implementation considerations	Reaching high vaccination coverage in girls also results in herd protection for boys, which illustrates the importance of prioritizing high HPV vaccination coverage in adolescent girls. When the coverage in girls is ≥80%, gender-neutral vaccination including adolescent boys is less cost-effective than when targeting only girls and women aged 9–18 years. At lower levels of coverage, vaccination targeting only girls and women aged 9–18 years is still likely to be more cost-effective than gender-neutral vaccination.

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



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

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

Lancet 2019; 394: 497–509

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) aşılanmasını öneriyor (2016)

Lancet 2019; 394: 497–509

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

World Health Organization

Health Topics | Countries | Newsroom | Emergencies | Data | About WHO

Home / Groups / The Global Advisory Committee on Vaccine Safety / Topics / Human papillomavirus vaccines / Safety

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.

Where HPV vaccination programmes have been implemented effectively, the benefits are already very apparent. Several countries that have introduced HPV vaccines to their immunization programme have reported a 50% decrease in the incidence rate of uterine cervix precancerous lesions among younger women. In contrast, the mortality rate from cervical cancer in Japan, where HPV vaccination is not proactively recommended, increased by 3.4% from 1995 to 2005 and is expected to increase by 5.9% from 2005 to 2015. This acceleration in disease burden is particularly evident among women aged 15–44 years.[28] Ten years after introduction, global HPV vaccine uptake remains slow, and the countries that

GACVS = Global Advisory Committee on Vaccine Safety.
http://www.who.int/vaccine_safety/committee/topics/hpv/June_2017/en/.

Global Health & Medicine - Advance Publication

LETTER

DOI: 10.35772/ghm.2023.01010

Underlying background of the current trend of increasing HPV vaccination coverage in Japan

Mira Namba[1,§], Yudai Kaneda[2,§,*], Chiharu Kawasaki[3], Rajeev Shrestha[4], Tetsuya Tanimoto[5]

Glob Health Med 2023 Aug 31;5(4):255-256. doi:10.35772/ghm.2023.01010

Abstract: Cervical cancer is prevalent among women, with a reported 604,127 cases in 2020 worldwide. The incidence of cervical cancer has been mitigated in most high-income countries by promoting the human papilloma virus (HPV) vaccine. However, in Japan, cervical cancer is still a leading cause of mortality and the most prevalent cancer among women aged between 15 and 39. This can be attributed to the 7-year suspension of HPV vaccination recommendations by the Japanese government. A decline in vaccination coverage followed this suspension, caused by a small number of reported adverse events, resulting in a steep decline in vaccination coverage from over 70% to less than 1%. However, there have been indications of a change in trend in Japan. In 2020, a group of volunteer doctors initiated awareness-raising activities through social networking services and other platforms, and the target population that received at least one dose of the vaccine in 2020 increased to 15.9%. Additionally, in July 2020, the Japanese government approved the updated 9-valent HPV vaccine and resumed recommendations in November 2021. As a result, 30.1% of those eligible for routine HPV vaccination received at least one dose of the vaccine from April to September, 2022. However, the HPV vaccine coverage in Japan is still far from the 90% recommended by the World Health Organization, and continued communication and education on the vaccine's benefits are necessary to achieve optimal coverage.

Başka Aşılarla Birlikte Uygulama

Yan etki: Daha fazla değil

Etkililik: dTaP ile birlikte uygulamada benzer
Hepatit B aşısıyla 9 valan aşı bilikte uygulandığında Anti HBs titresi
İkinci dozdan sonra fark yok! Klinik Önemi YOK!

Results	6 mo after 1st dose of HAV/HBV vaccine*		1 mo after 2nd dose of HAV/HBV vaccine	
	Group Co-adm n = 207 (95%CI)	Group Sep n = 199 (95%CI)	Group Co-adm n = 207 (95%CI)	Group Sep n = 199 (95%CI)
Anti-HAV +	100% (98.3–100)	100% (98.2–100)	100% (98.2–100)	100% (98.2–100)
Anti-HAV ≥ 20IU/L	67.1% (60.3–73.4)	72.9% (66.1–78.8)	100% (98.2–100)	99.5% (97.2–99.9)
Anti-HAV GMTs	30.5 IU/L (27.1–34.3)	38.2 IU/L (33.4–43.6)	2962 IU/L (2598–3379)	2129 IU/L (1808–2507)
Anti-HBs +	56.5% (49.5–63.4)	72.9% (66.1–78.9)	98.1% (95.1–99.5)	99.0% (96.4–99.9)
Anti-HBs ≥ 10IU/L	43.5% (36.6–50.5)	59.3% (52.1–66.2)	97.6% (94.5–99.2)	97.5% (94.2–99.2)
Anti-HBs GMTs	7.3 IU/L (5.8–9.2)	12.5 IU/L (9.8–15.8)	1701 IU/L (1339–2159)	2005 IU/L (1585–2536)

Gilca V. Hum Vaccin Immunother 2014;10(8):2438-45. doi: 10.4161/hv.29617

HPV Aşısı - Yan Etkiler

- Aşı canlı veya ölü herhangi bir virüs içermez: Virüse ait herhangi bir infeksiyon veya benzeri istenmeyen etki mümkün değildir
- En sık görülen yan etkiler:

1-Aşı yerinde enjeksiyona bağlı;

Kızarıklık, ağrı, şişlik, hafif sıcaklık artışı

%39-87 (şiddetli ağrı %6)

2- Bulantı, baş dönmesi, baş ağrısı, göz kararması, sersemlik, kas-eklem ağrısı

Farklı ülkelerde yapılmış >160 çalışma sonucunda:

Aşıyla tromboemboli, GBS, inme, senkop, erken ovaryan yetmezlik,

kronik yorgunluk sendromu veya otoimmün hastalık ilişkisi gösterilememiştir.

Arbyn M, Expert Rev Vaccines. 2018;17: 1085–1091
Gee J. Vaccine. 2017;35:5756–5758
Gidengil C. Vaccine. 2021;39:3696–3716
Arana J. Vaccine. 2018;36:1781–1788

9vHPV Aşısı / Gardasil® - **Pozoloji**

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

9-14 yaş arası bireyler

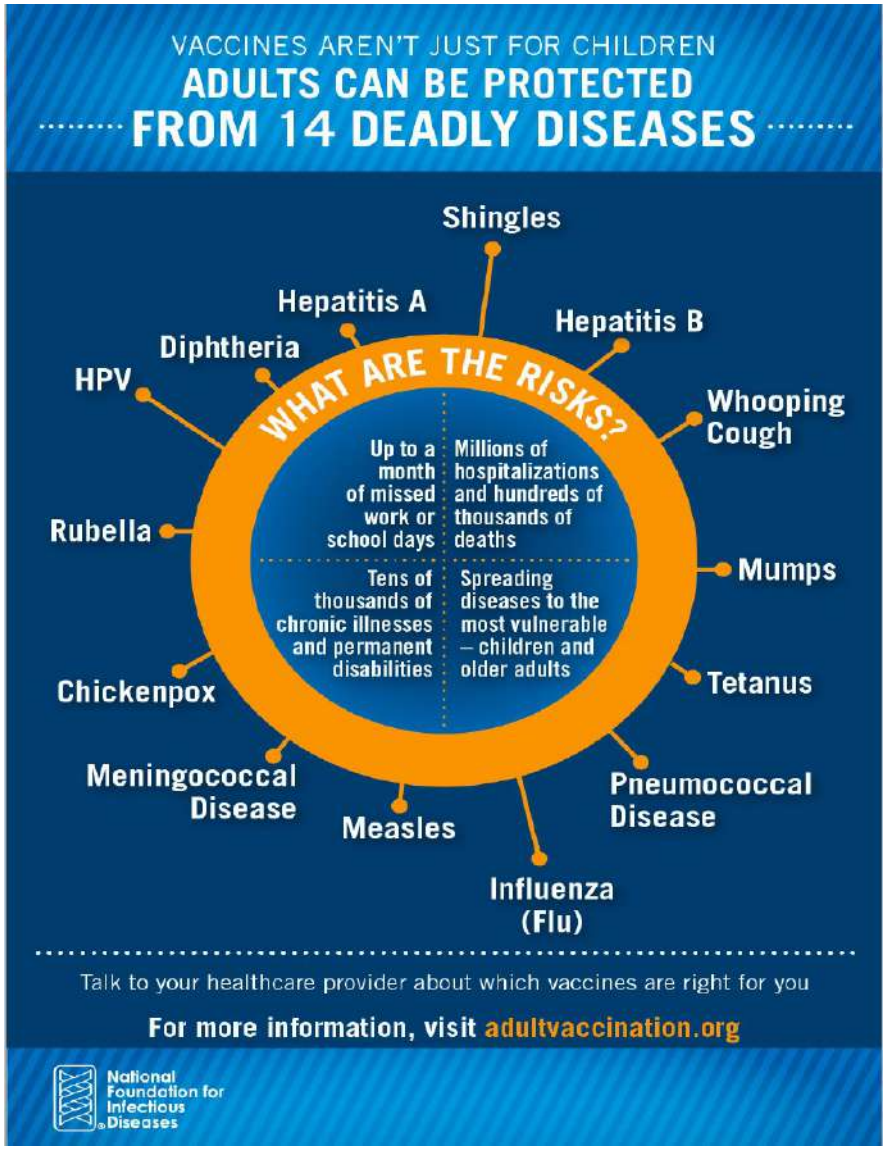
- GARDASIL iki doz aşılama şeması şeklinde uygulanabilir **(0. ve 6. ayda)**
- Eğer ikinci doz ilk dozdan sonra, 6. aydan daha erken uygulanırsa, 3. doz her zaman uygulanmalıdır
- Alternatif olarak, GARDASIL üç doz olarak uygulanabilir **(0., 2., 6. ayda 0.5 ml)**

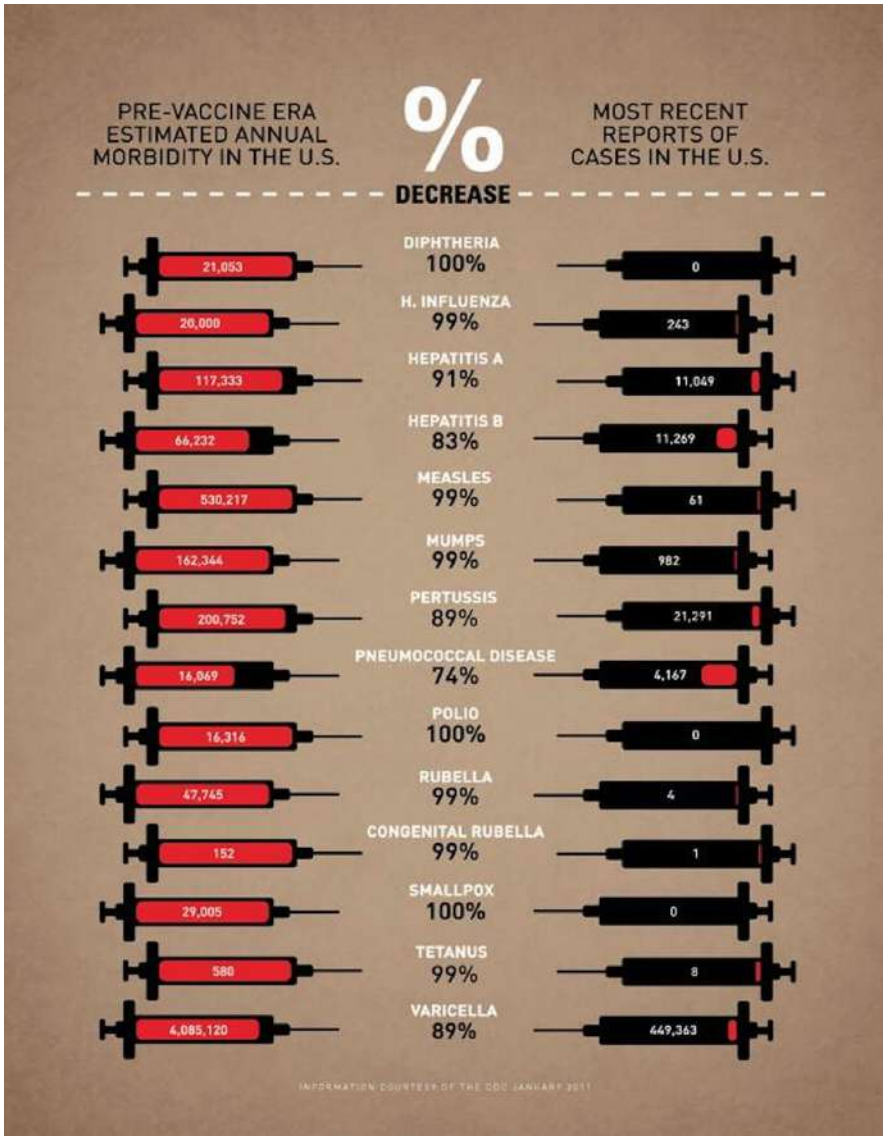
15 yaş ve üzeri bireyler

- 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.

Ref: Gardasil Kısa Ürün Bilgisi





Teşekkürler…