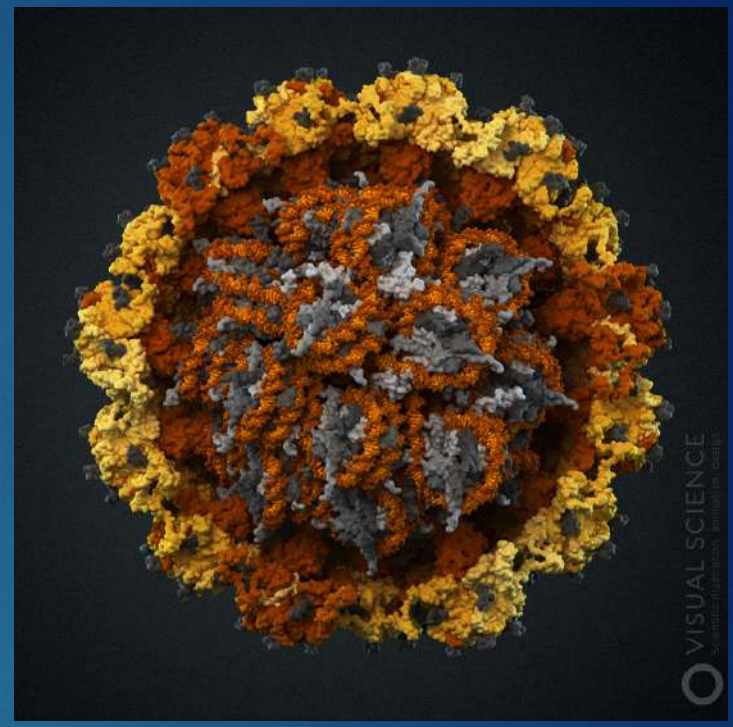
KLİMİK TÜRK KLİNİK MİKROBİYOLOJİ VE İNFEKSİYON HASTALIKLARI DERNEĞİ

Bilimle Sağlıkla 33 .Yıl

HPV

Simpozyum: Aşılarda Yeni Ne Var?



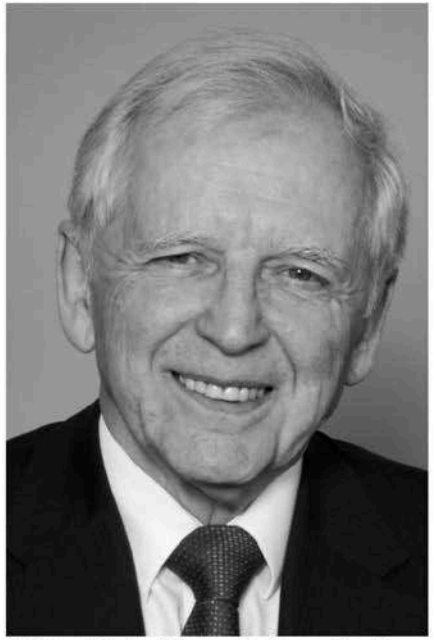
Doç Dr Uluhan Sili
Marmara Üniversitesi Tıp Fakültesi
Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji AD

MARMARA ÜNİVERSİTESİ 1883 Tıp Fakültesi

25 ŞUBAT 2020

Harald zur Hausen

Facts



© The Nobel Foundation. Photo: U. Montan

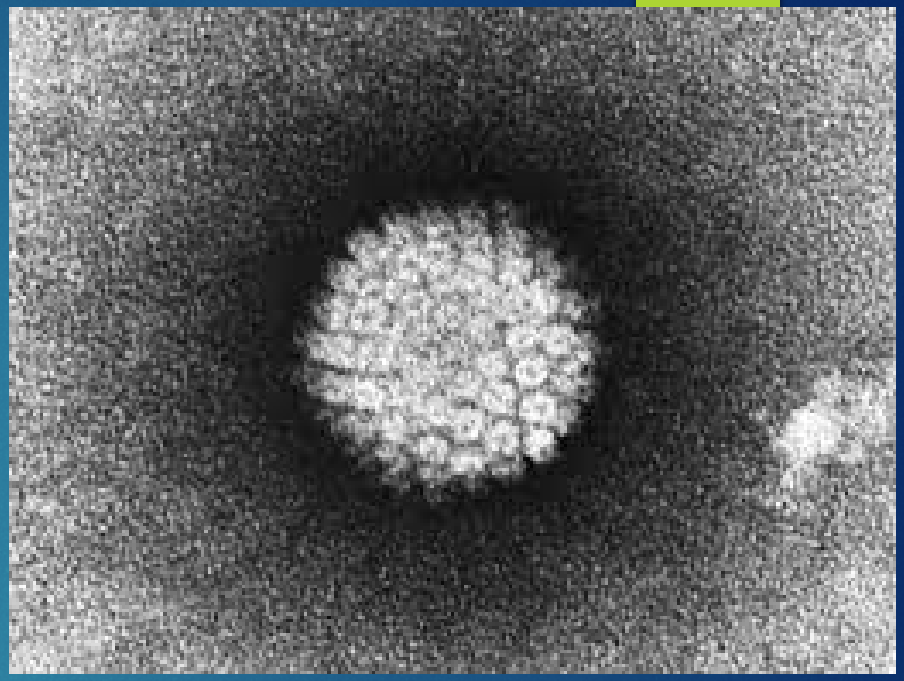
Harald zur Hausen
The Nobel Prize in Physiology or Medicine 2008

Born: 11 March 1936, Gelsenkirchen, Germany

Affiliation at the time of the award: German Cancer Research Center, Heidelberg, Germany

Prize motivation: "for his discovery of human papilloma viruses causing cervical cancer."

Prize share: 1/2



Work

The growth, division, and death of living cells are regulated by their genes. If these functions are out of balance, tumors can form. One reason for this may be the incorporation of virus genes into the genes of host cells. Harald zur Hausen demonstrated in 1983 that cervical cancer in humans is caused by certain types of papilloma viruses (wart viruses), the genes from which are incorporated into the host cells' DNA. This discovery made it possible to develop a vaccine against cervical cancer, which had been the second most common tumor disease in women.

Cervical cancer

WHO Director-General calls for all countries to take action to help end the suffering caused by cervical cancer

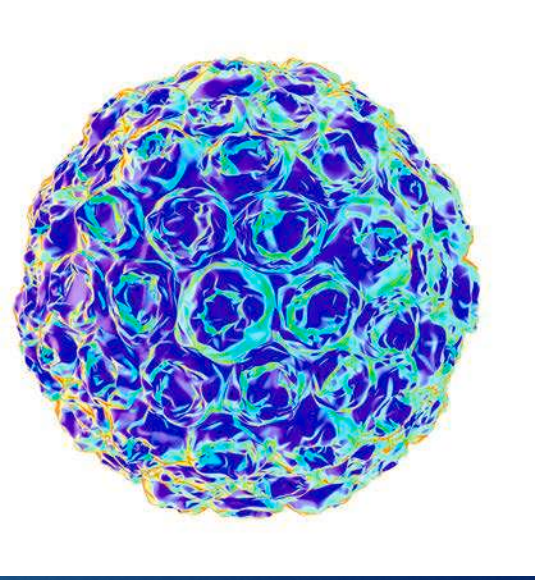
Jonathan Torgovnik

Woman being screened for cervical cancer in a rural clinic, Kenya

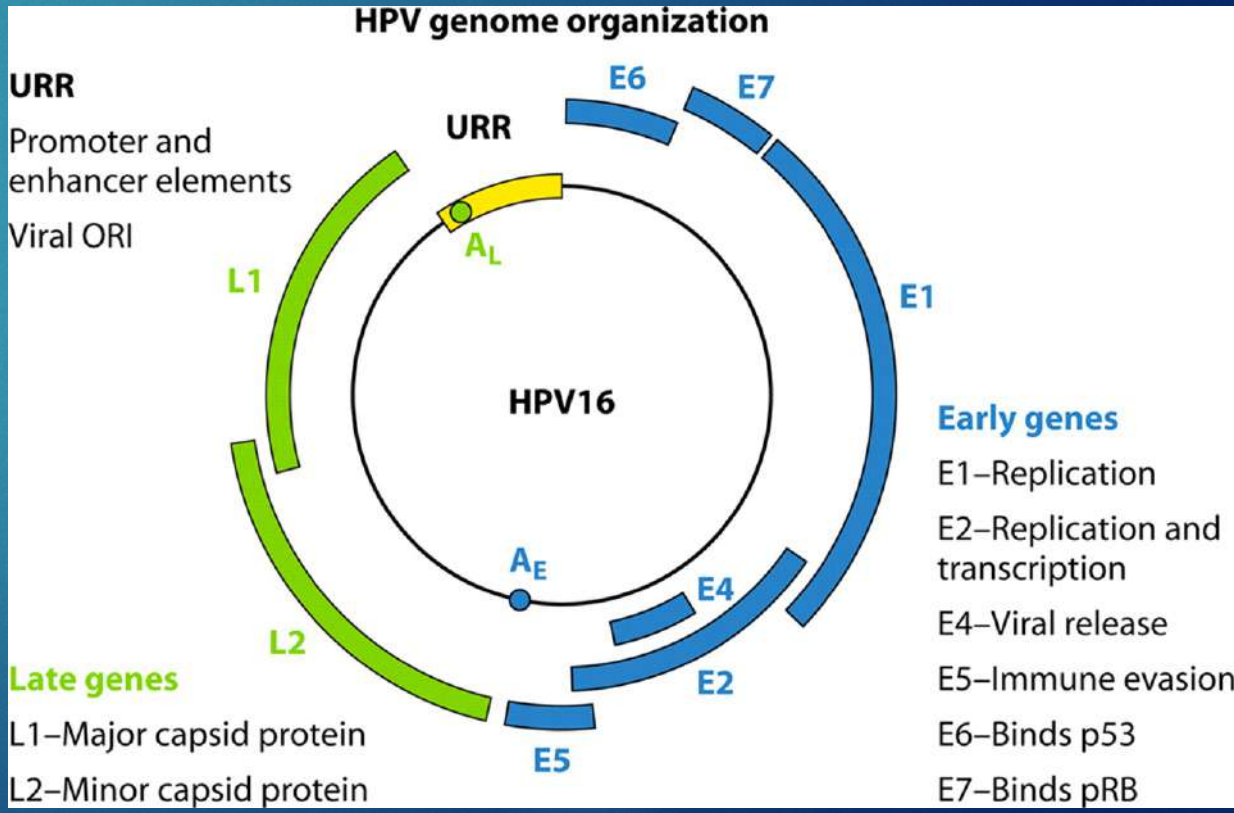
19 May 2018: Cervical cancer is one of the most preventable and treatable forms of cancer as long as it is prevented with HPV vaccination, detected early, and managed effectively. Prevention and early treatment are highly cost-effective. Worldwide however, cervical cancer remains one of the gravest threats to women's lives, and globally, one woman dies of cervical cancer every two minutes.

- Read the call to action
- Unitaid launches call for proposals to help eliminate cervical cancer
- Quiz on cervical cancer

İnsan Papilloma Virüsü
Human Papilloma Virus (HPV)



- zarfsız, çift zincirli DNA virüsü
- türe (insan) kısıtlı
- >200 tip
- 8 kb genom, 8 gen
  - L1 → virüs-like particle (VLP) → AŞI



Lancet. 2019 Jan 12;393(10167):169-182. doi: 10.10

Cervical cancer.

Cohen PA[1], Jhingran A[2], Oaknin A[3], Denny L[4].

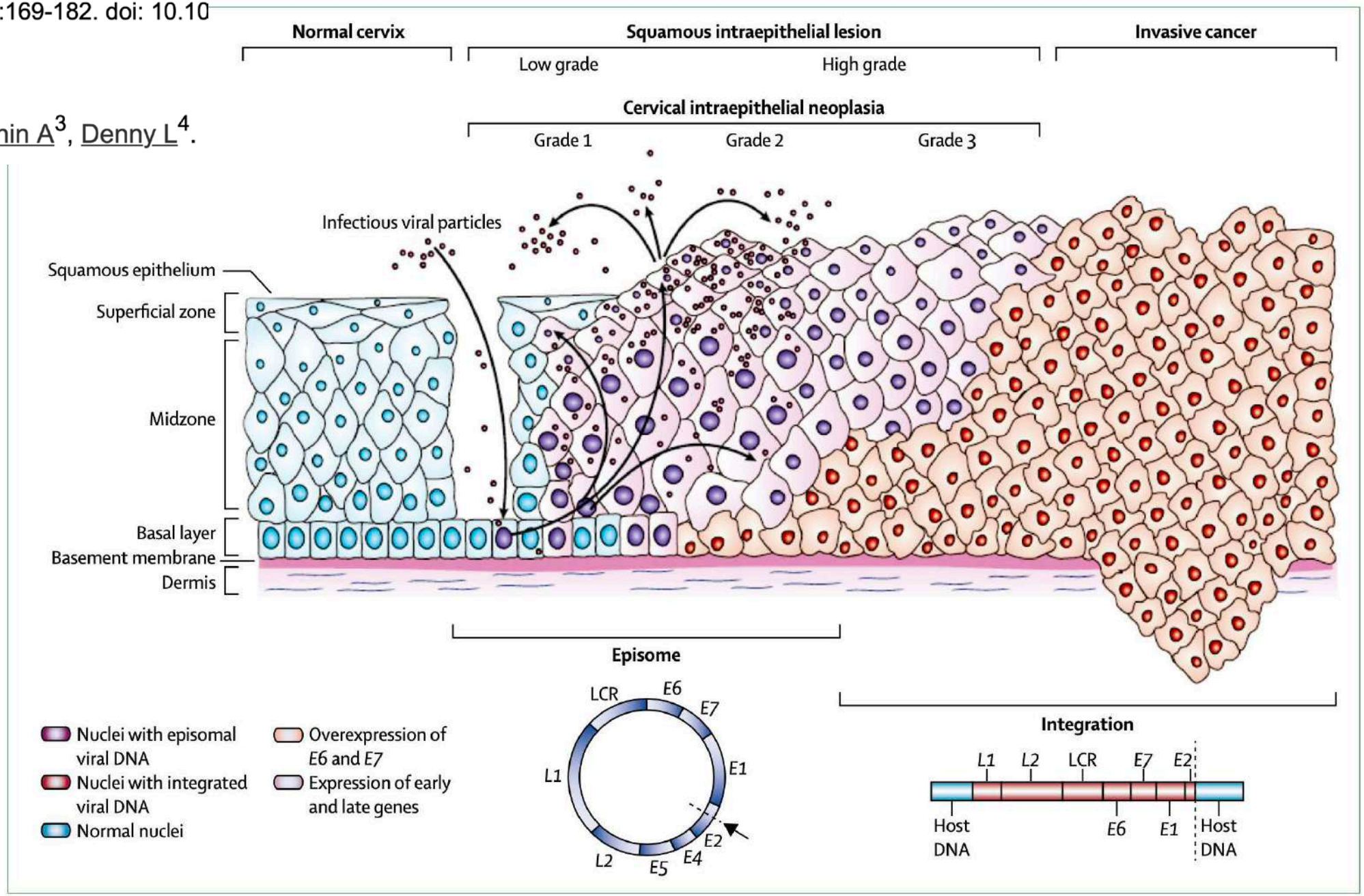
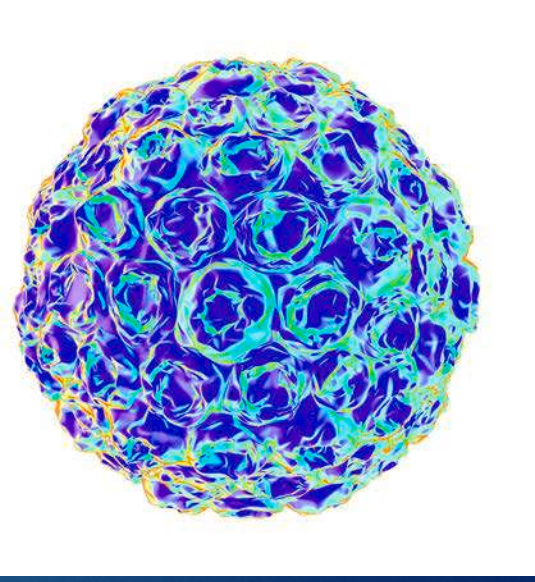


Figure 1: **Pathogenesis of cervical cancer**
Reproduced from Crosbie and colleagues,[20] by permission of Elsevier.

İnsan Papilloma Virüsü
Human Papilloma Virus (HPV)



Doğal seyir

- Çoğu HPV enfeksiyonu -karsinojenik genotipler dahil- genelde 12 ay içerisinde geriler
- >12 ay devam edenler kanser öncesi lezyona veya kansere dönüşebilir
- Kanser öncesi lezyona dönüş için medyan süre 10 yıl
- Latentlik

Disease associations with selected human papillomavirus types

Disease	HPV type frequently associated
Cutaneous warts	
Common and plantar warts	1, 2, and 4
Flat wart	3, 10
Butcher's wart	7, 2
Bowen's disease	
Genital	16
Extragenital	2, 3, 4, 16
Epidermodysplasia verruciformis	2, 3, 5, 8, 9, 10, 12, 14, 15, 17
Condylomata acuminata	6, 11
Squamous intraepithelial lesions*	
Low grade	16, 31, 6, 11
High grade	16, 31, 52, 18
Oropharyngeal cancer	16
Anal cancer	16
Respiratory papillomatosis	6, 11

UpToDate®

* These include squamous intraepithelial lesions and cancers of the cervix, vagina, vulva, anus, and penis. Other high-risk types associated with squamous intraepithelial lesions include 33, 45, and 58.

Kadınlarda HPV ile ilişkili hastalıklar

- Serviks kanseri
  - kadınlarda en sık görülen 4. kanser
  - senede 530 000 invazif servikal karsinom ve 260 000 ölüm
  - neredeyse tüm serviks kanserleri HPV infeksiyonu ile ilişkili
    - %50 HPV 16, %20 HPV 18, %19 31, 33, 45, 52, 58
  - yüksek risk: HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73 ve 82
- Vulvar ve vajinal kanser

UpToDate®

- Erkeklerde HPV ile ilişkili hastalıklar
  - penil kanser ve öncü lezyonları

- Erkek ve kadınlarda HPV ile ilişkili hastalıklar
  - anogenital siğiller
    - %90'ı HPV 6 ve 11 ile ilişkili
  - genital bölge dışı siğiller
  - anal kanser
    - %90'ı HPV 16 ve 18 ile ilişkili
  - orofarenks kanseri
  - tekrarlayıcı solunum sistemi papillomatozu

Anogenital infeksiyonun epidemiyolojisi

- Küresel ölçekte anogenital HPV en sık gözlenen cinsel yolla bulaşan hastalık
- Diğer CYBH'lar gibi cinsel aktif hale geldikten sonraki ilk 10 yılda tepe yapar
  - genelde 15 – 25 yaş arası
- Cinsel aktif kadın ve erkeklerin >%80'inin ömürleri boyunca en az 1 kez HPV'ye maruz kaldıkları tahmin edilmektedir

An Update on HPV Prophylactic Vaccines

John Schiller, Center for Cancer Research, NCI

ID week 2019

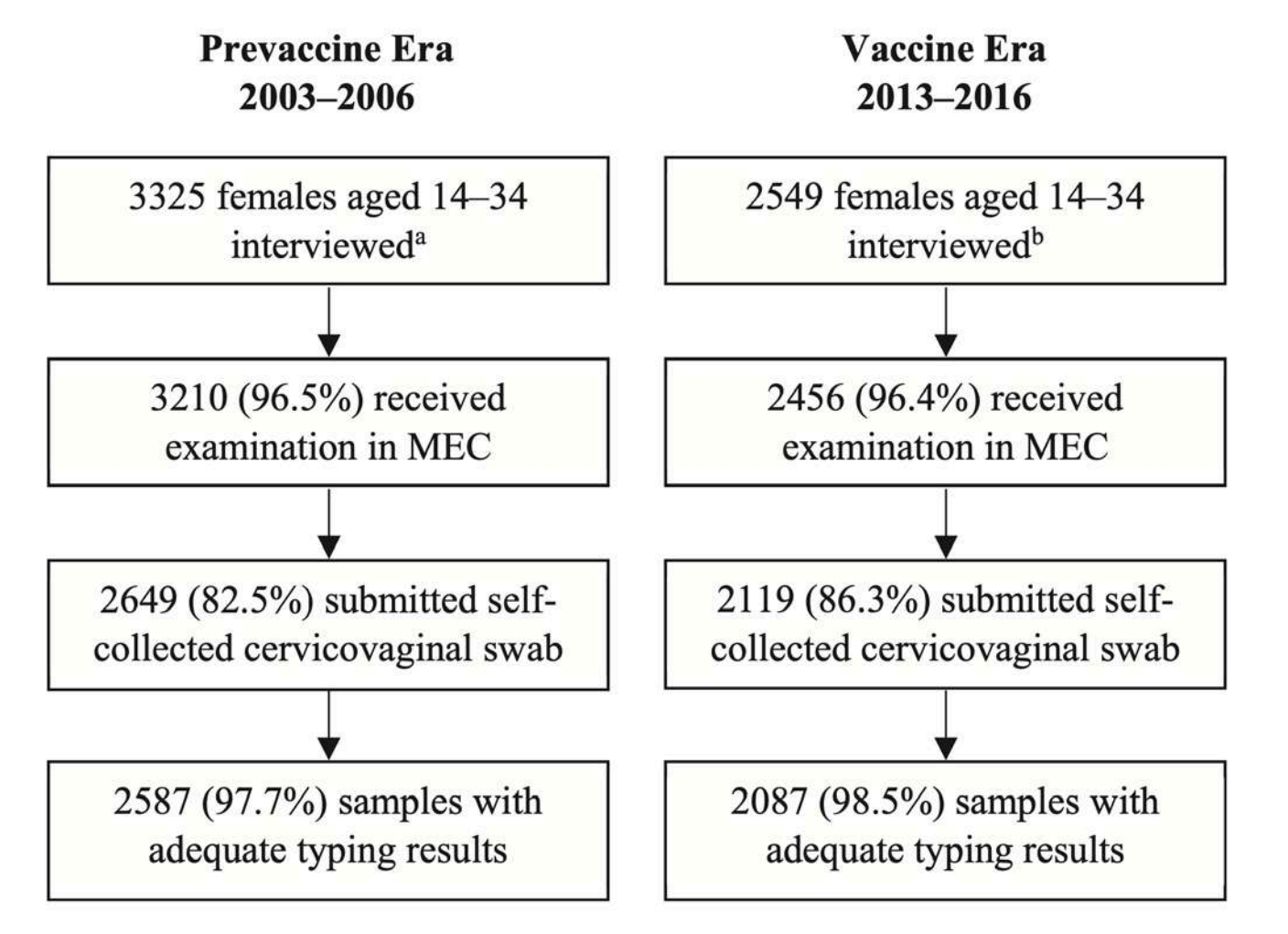
3 Distinct HPV L1 VLP Vaccines Have Been Commercialized

Name	Producer	VLP types	Adjuvant	Production	Licensed
Cervarix	GSK	16,18	AS04*	Insect cells	2007
Gardasil	Merck	16,18,6,11	Alum	Yeast	2006
Gardasil-9	Merck	16,18,31,33,45, 52,58,6,11	Alum	Yeast	2014

J Adolesc Health. 2019 Dec;65(6):715-722. doi: 10.1016/j.jadohealth.2019.07.003. Epub 2019 Sep 9.

Declines in Vaccine-Type Human Papillomavirus Prevalence in Females Across Racial/Ethnic Groups: Data From a National Survey.

McClung NM[1], Lewis RM[2], Gargano JW[3], Querec T[4], Unger ER[4], Markowitz LE[3].



4vHPV (16/18+6/11)

kadınlar ♀ >2006

erkekler ♂ >2011

11 – 12 yaş arası aşıla yakalama aşısı

- kadınlarda ≤26 yaş
- erkeklerde ≤21 yaş
- erkek + özel grup ≤26 yaş

Çalışma kadınlarda (14 – 34 yaş) yapılmış

4vHPV tipinin prevalansı araştırılmış

Data from the National Health and Nutrition Examination Survey (NHANES)

Table 1

Lifetime sex partners, poverty status, and vaccination history among females

Age group, characteristics	Overall	
	n = 4,674	
	2003–2006	2013–2016
	% (95% CI)	% (95% CI)
14–19 y	n = 1,363	n = 783
Lifetime sex partners		
0	46.1 (43.0–49.3)	56.2 (51.9–60.5)[a]
1–2	28.2 (25.0–31.7)	25.2 (22.2–28.4)
≥3	25.6 (22.5–29.0)	18.6 (15.3–22.4)
Poverty level		
Living below	23.0 (18.7–27.9)	21.6 (17.0–27.0)
HPV vaccination		
≥1 dose	-	53.9 (48.1–59.6)
3 doses	-	34.8 (29.4–40.6)
20–24 y	n = 432	n = 413
Lifetime sex partners		
0	8.6 (5.2–14.0)	5.4 (3.4–8.4)
1–2	30.7 (26.4–35.4)	27.5 (23.1–32.4)
≥3	60.7 (53.7–67.2)	67.1 (62.2–71.7)
Poverty level		
Living below	25.7 (19.8–32.7)	29.3 (24.0–35.2)
HPV vaccination		
≥1 dose	-	51.5 (44.0–59.0)
3 doses	-	30.9 (24.5–38.1)

Age group, characteristics	Overall	
	n = 4,674	
	2003–2006	2013–2016
	% (95% CI)	% (95% CI)
25–29 y	n = 403	n = 447
Lifetime sex partners		
0	5.0 (2.9–8.3)	4.4 (2.6–7.4)
1–2	21.8 (15.9–29.1)	26.7 (21.2–32.9)
≥3	73.2 (66.4–79.0)	69.0 (63.1–74.3)
Poverty level		
Living below	16.3 (12.5–21.0)	20.8 (16.6–25.7)
HPV vaccination		
≥1 dose	-	33.3 (28.2–38.9)
3 doses	-	24.8 (19.9–30.6)
30–34 y	n = 389	n = 444
Lifetime sex partners		
0	1.6 (.6–4.6)[c]	2.7 (1.2–6.2)[b]
1–2	24.8 (20.5–29.6)	23.5 (18.7–29.1)
≥3	73.6 (68.2–78.4)	73.8 (68.4–78.6)
Poverty level		
Living below	16.0 (12.7–20.1)	21.3 (16.9–26.4)
HPV vaccination		
≥1 dose	-	14.3 (10.7–18.7)
3 doses	-	9.5 (6.5–13.7)

Table 2
HPV prevalence among females aged 14–34 years, by age group—NHANES 2003–2006 and 2013–2016

Age group/HPV types	Prevaccine era 2003–2006 % (95% CI)	Vaccine era 2013–2016 % (95% CI)	PR (95% CI)	aPR[a] (95% CI)
14–19 y				
Any HPV	32.9 (29.5–36.5)	21.6 (18.5–25.0)	.66 (.55–.79)[b]	.85 (.72–1.01)
Non-4vHPV	31.2 (27.9–34.8)	21.0 (18.0–24.4)	.67 (.56–.81)[b]	.89 (.74–1.07)
HPV 31/33/45/52/58	8.4 (6.6–10.6)	3.9 (2.5–5.9)	.46 (.29–.74)[b]	.69 (.39–1.20)
4vHPV	11.5 (9.1–14.4)	1.8 (1.1–2.9)	.15 (.09–.26)[b]	.14 (.08–.24)[b]
20–24 y				
Any HPV	53.7 (45.9–61.4)	54.6 (48.0–61.0)	1.01 (.84–1.22)	1.01 (.87–1.18)
Non-4vHPV	50.7 (43.4–58.0)	54.4 (47.9–60.8)	1.07 (.89–1.29)	1.08 (.92–1.26)
HPV 31/33/45/52/58	16.5 (11.3–23.4)	13.3 (9.5–18.2)	.80 (.50–1.30)	.92 (.56–1.50)
4vHPV	18.5 (14.9–22.8)	5.3 (2.9–9.4)	.29 (.16–.53)[b]	.29 (.15–.56)[b]
25–29 y				
Any HPV	46.8 (42.9–50.8)	43.5 (38.8–48.3)	.93 (.81–1.07)	.92 (.80–1.06)
Non-4vHPV	43.8 (38.9–48.9)	41.8 (36.8–46.9)	.95 (.81–1.12)	.95 (.80–1.12)
HPV 31/33/45/52/58	10.8 (7.3–15.7)	11.5 (8.2–15.9)	1.06 (.65–1.75)	.92 (.53–1.58)
4vHPV	11.8 (8.8–15.6)	8.0 (5.6–11.4)	.68 (.43–1.07)	.61 (.36–1.04)
30–34 y				
Any HPV	47.9 (42.3–53.5)	35.4 (30.4–40.7)	.74 (.62–.89)[b]	.72 (.60–.86)[b]
Non-4vHPV	44.5 (39.1–50.1)	34.2 (29.1–39.7)	.77 (.63–.93)[b]	.76 (.63–.91)[b]
HPV 31/33/45/52/58	9.8 (7.1–13.5)	6.2 (3.7–10.3)	.63 (.35–1.15)	.58 (.29–1.17)
4vHPV	9.5 (6.7–13.2)	6.5 (4.4–9.7)	.69 (.41–1.15)	.73 (.41–1.32)

%86 ↓

%71 ↓

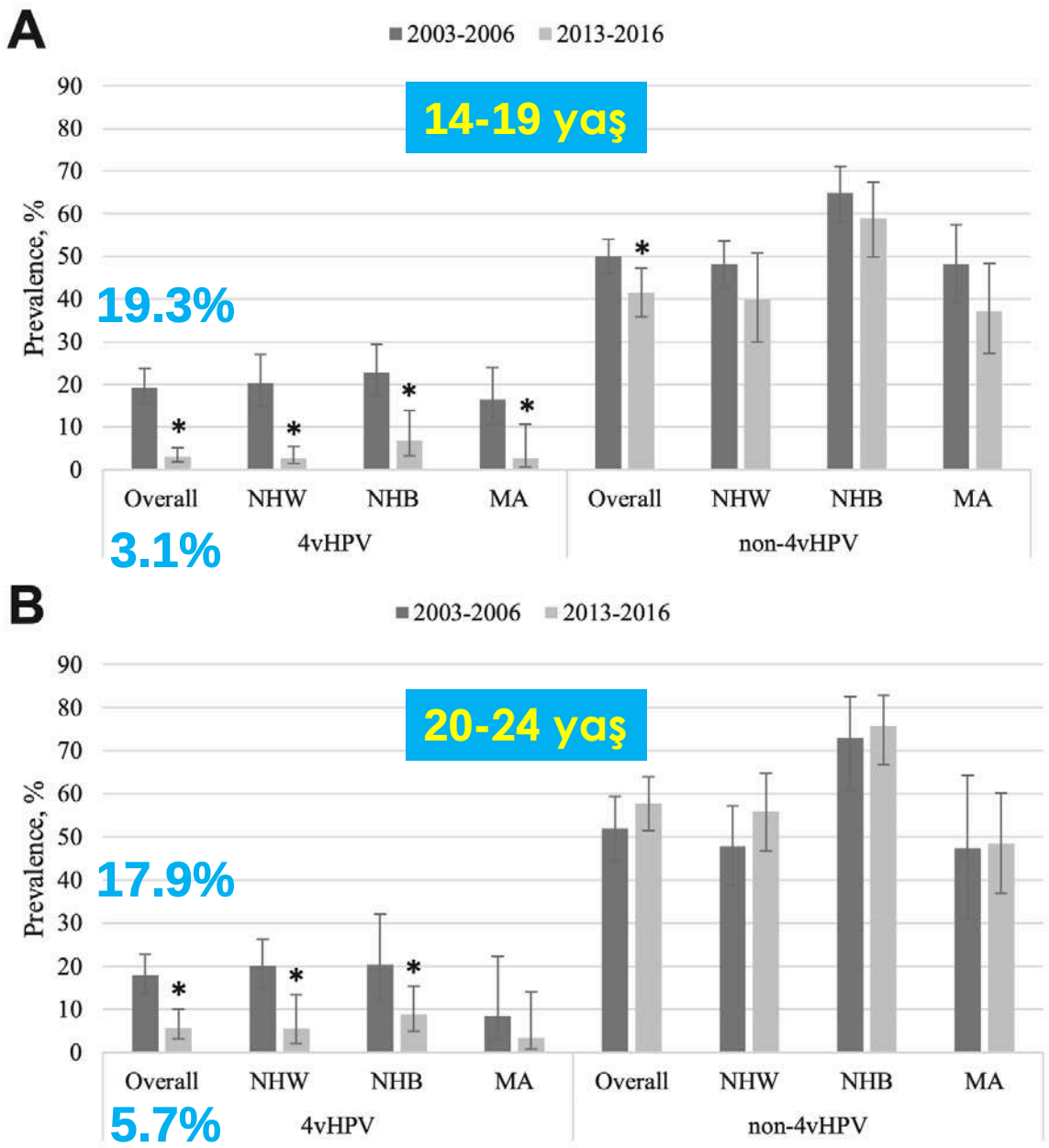


Figure 2. 4vHPV-type and non-4vHPV-type prevalences among sexually experienced[a] females aged (A) 14–19 years and (B) 20–24 years overall and by race/ethnicity, NHANES 2003–2006 and 2013–2016. NHW: non-Hispanic white, NHB:

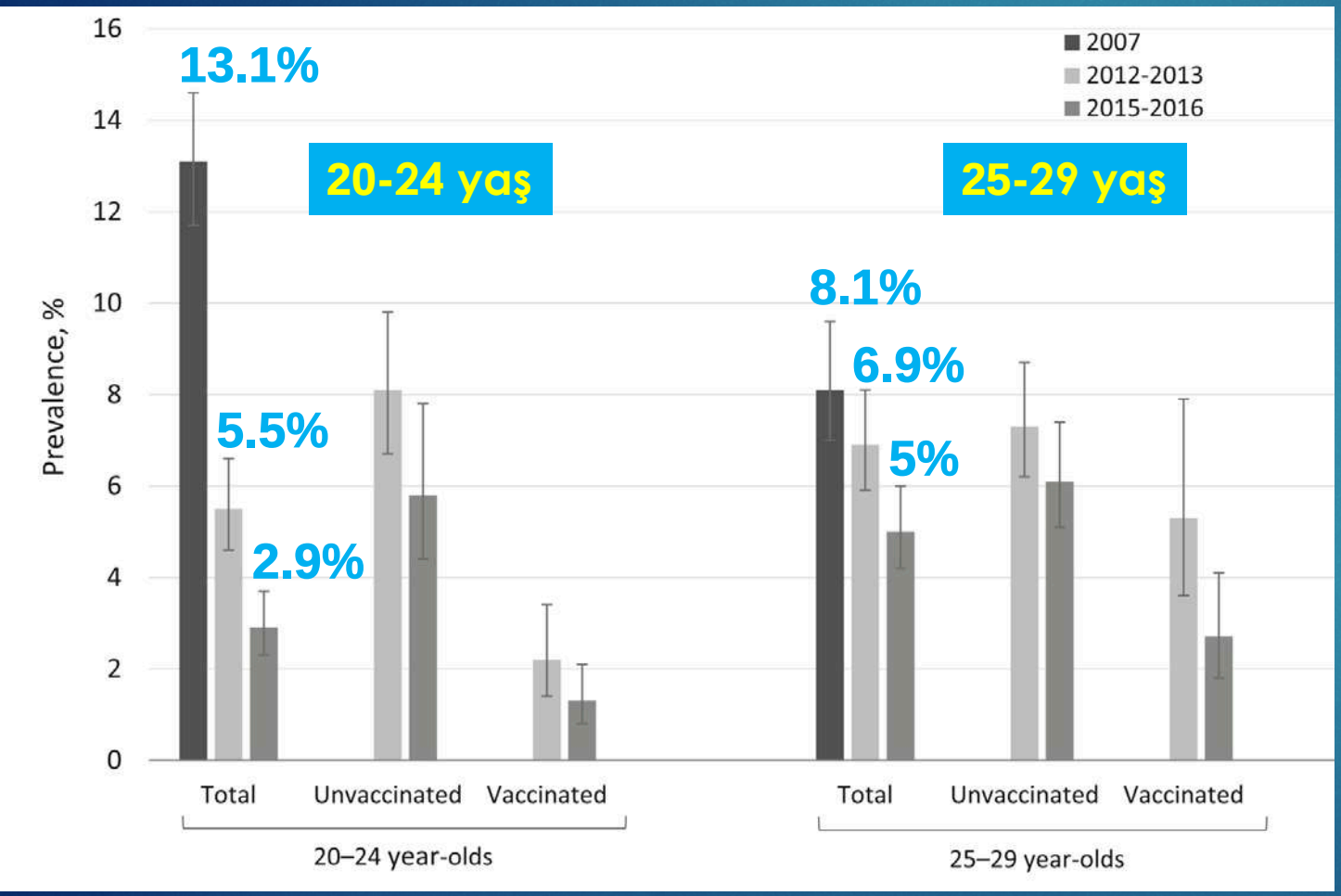
Cinsel ilişki (oral, anal veya vajinal) deneyimli kadınların analizi

- 14 – 19 yaş (19.3% → 3.1%, 86% ↓)
- 20 – 24 yaş (17.9% → 5.7%, 68% ↓)

Vaccine. 2019 Jun 27;37(29):3918-3924. doi: 10.1016/j.vaccine.2019.04.099. Epub 2019 May 31.

Declines in HPV vaccine type prevalence in women screened for cervical cancer in the United States: Evidence of direct and herd effects of vaccination.

Markowitz LE[1], Naleway AL[2], Lewis RM[3], Crane B[2], Querec TD[4], Weinmann S[2], Steinau M[4], Unger ER[4].



Tüm grup
20 – 24 yaş
13.1% → 5.5% (58% ↓) → 2.9% (78% ↓)
25 – 29 yaş
8.1% → 6.9% (15% ↓) → 5% (38% ↓)

Prevalansta azalma (2007 ile 2015-2016 karşılaştırması)
aşılanmışlarda **%90** ↓
aşılanmamışlarda **%55** ↓

Hemen hemen tüm kadınlar "yakalama aşısı" yaptırmış

Fig. 1. Vaccine-type HPV prevalence (HPV 6/11/16/18) among women aged 20–24 years and 25–29 years, 2007, 2012–2013 and 2015–2016, overall and by vaccination status. Vaccinated, receipt of at least one HPV vaccine dose 30 or more days before specimen collection. Error bars represent 95% confidence intervals.

Lancet. 2019 Aug 10;394(10197):497-509. doi: 10.1016/S0140-6736(19)30298-3. Epub 2019 Jun 26.

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

Drolet M[1], Bénard É[2], Pérez N[1], Brisson M[3]; HPV Vaccination Impact Study Group.

- HPV aşısı başlatılı >10 yıl oldu
- kız çocukları ve genç kadınları aşılamanın toplumsal düzeyde etkisi?
  - HPV infeksiyonu
  - anogenital siğil
  - servikal intraepitel neoplazi 2+ (CIN2+)
- gerçek hayat verisi
- 14 yüksek gelir ülkesinden 65 yayın
- 60 milyon bireyin veri analizi, aşı sonrası 8 yıllık takip

HPV İnfeksiyonu Prevalansı

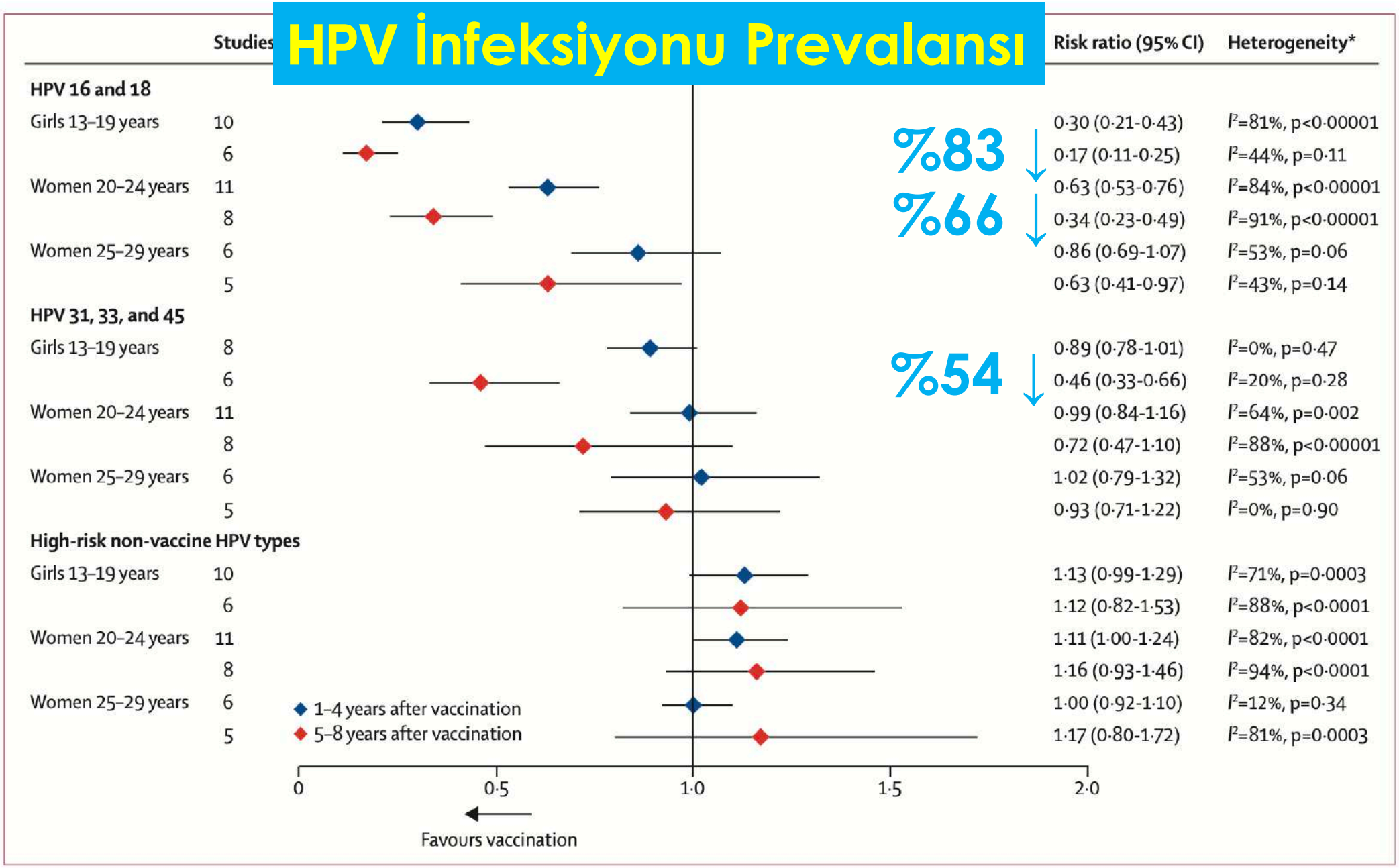


Figure 2: **Changes in the prevalence of HPV infections between pre-vaccination and post-vaccination periods**
HPV=human papillomavirus. *p values are associated with the χ^2 statistic.

Anogenital Siğil Tanısı

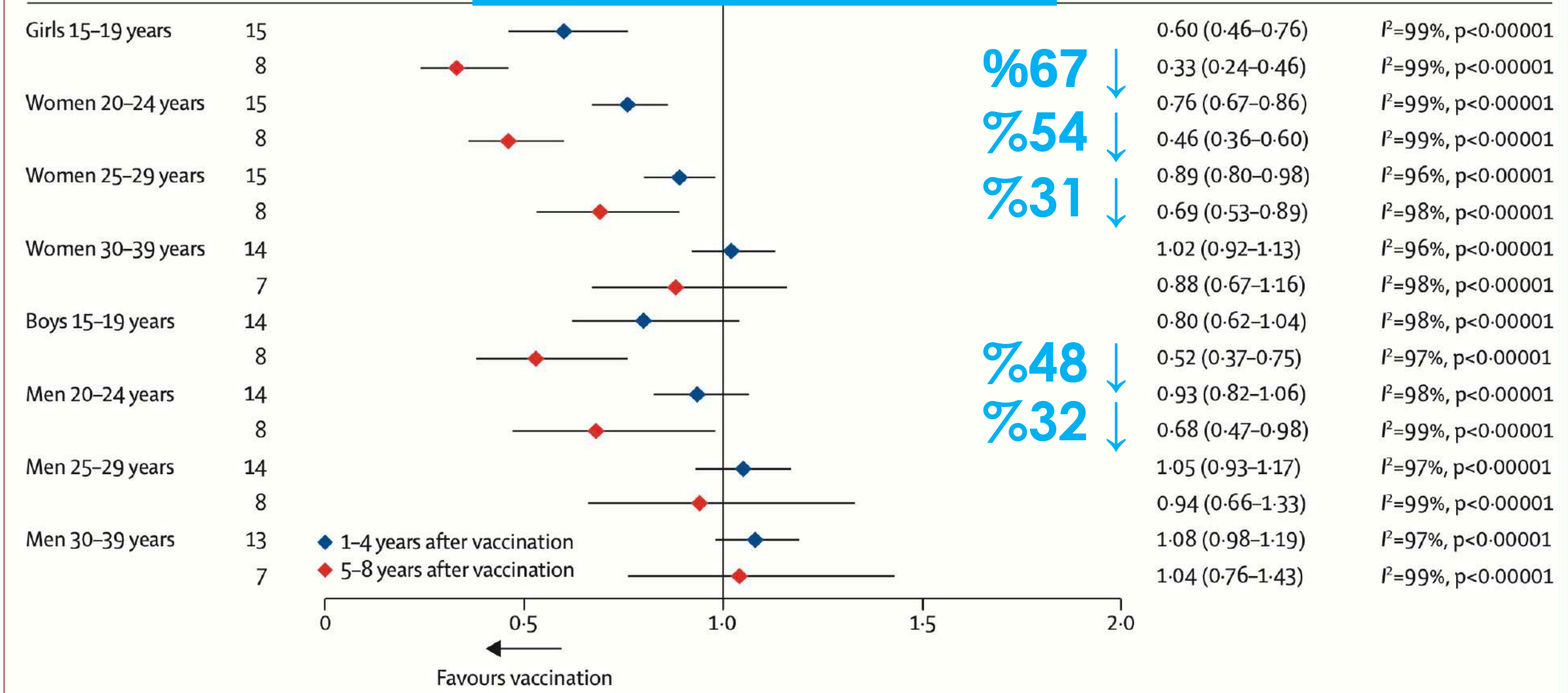


Figure 3: **Changes in anogenital wart diagnoses between pre-vaccination and post-vaccination periods in countries using the quadrivalent vaccine**

*p values are associated with the χ^2 statistic.

Anogenital Siğil Tanısı

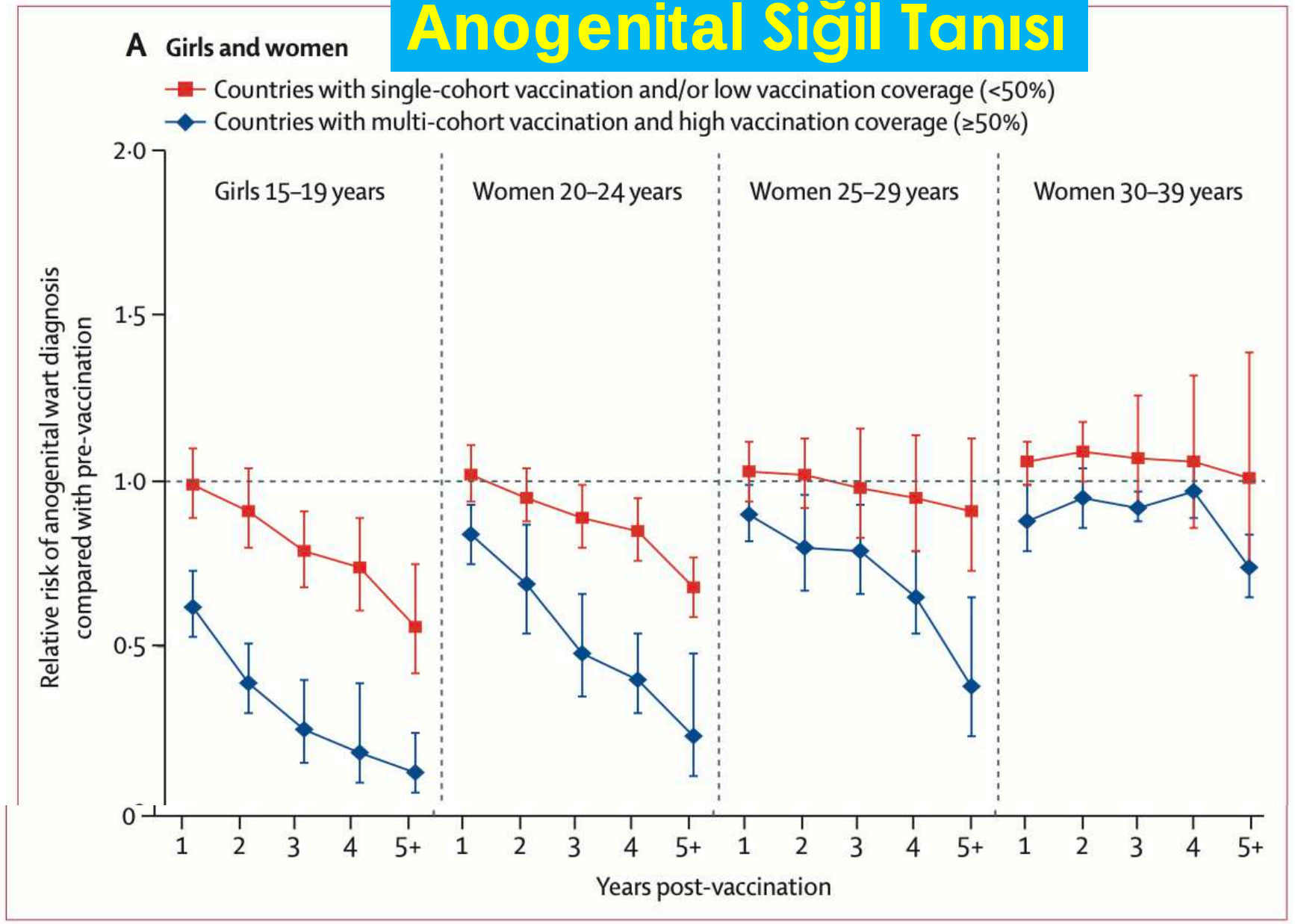


Figure 4: **Changes in anogenital wart diagnoses during the 8 years after the introduction of girls-only human papillomavirus vaccination in countries using the quadrivalent vaccine**

Servikal İntraepitel Neoplazi Tanısı

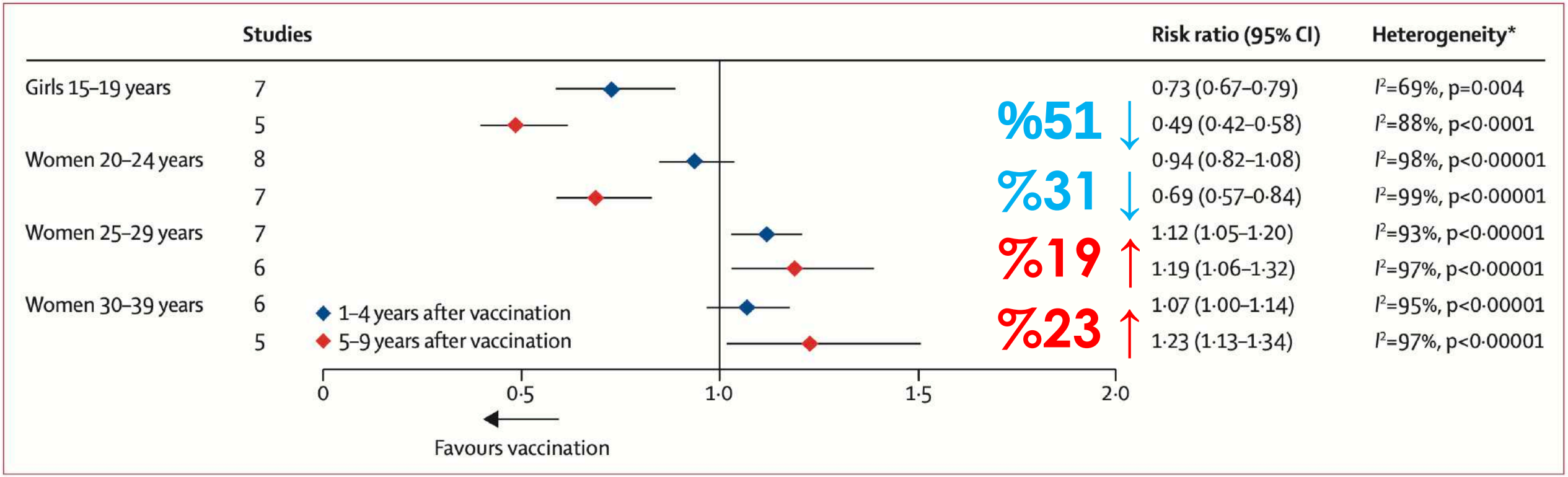


Figure 5: **Changes in CIN2+ among screened girls and women between the pre-vaccination and post-vaccination periods**
CIN2+=cervical intraepithelial neoplasia grade 2+. *p values are associated with the χ^2 statistic.

Servikal İntraepitel Neoplazi Tanısı

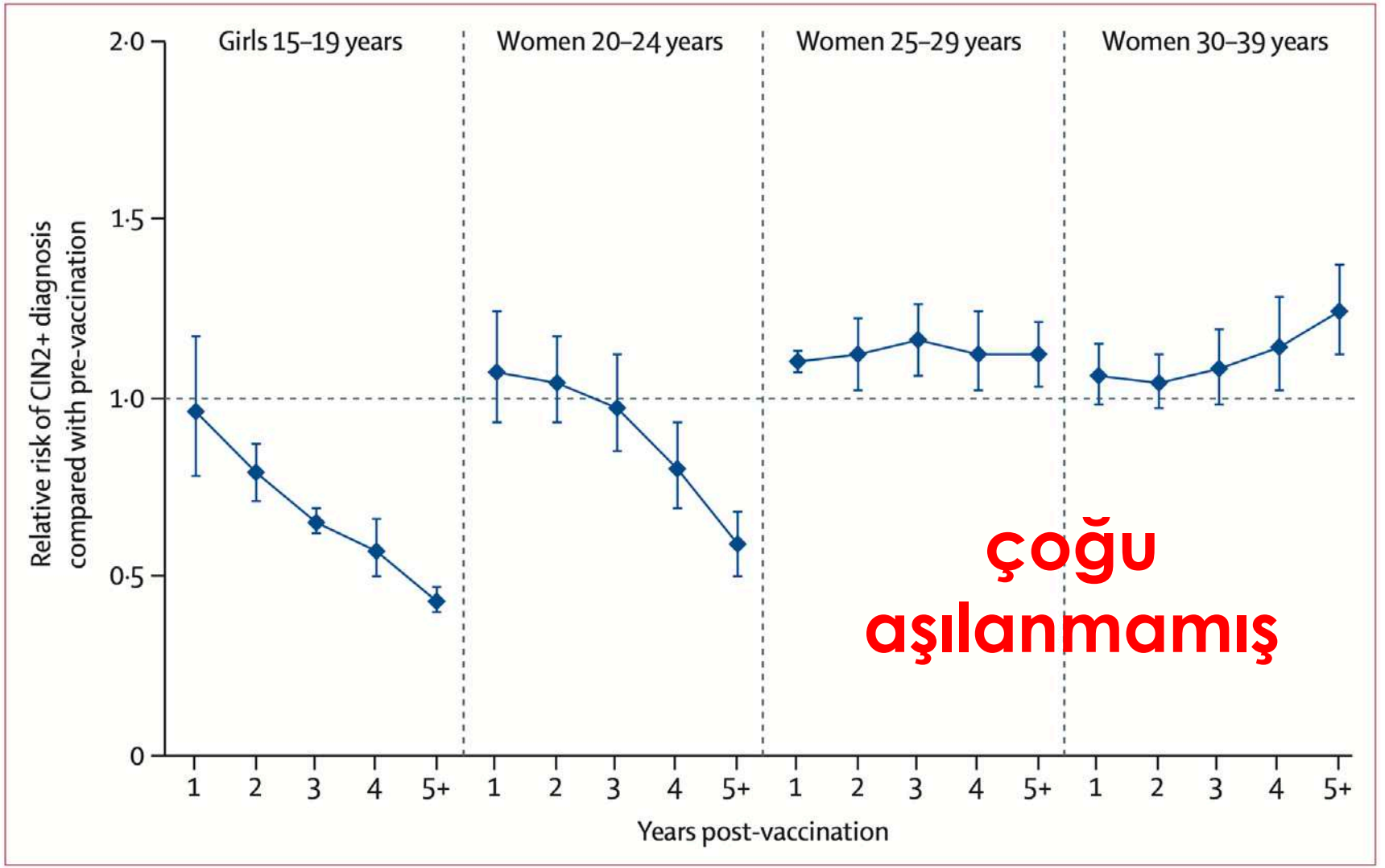


Figure 6: **Changes in CIN2+ among screened girls and women during the first 7 years after the introduction of girls-only human papillomavirus vaccination, in countries with multi-cohort vaccination and high vaccination coverage**

Lancet. 2019 Aug 10;394(10197):497-509. doi: 10.1016/S0140-6736(19)30298-3. Epub 2019 Jun 26.

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

Drolet M[1], Bénard É[2], Pérez N[1], Brisson M[3]; HPV Vaccination Impact Study Group.

- HPV aşısı ile HPV 16/18 infeksiyonu, anogenital siğil ve CIN2+ prevalansı genç kız ve kadınlarda anlamlı azaltıyor
  - çapraz koruma (HPV 31, 33 ve 45) görülüyor
  - sadece kız çocukları aşılansa da "sürü bağışıklığı" etkisi ile genç ve erişkin erkeklerde anagenital siğil prevalansı düşüyor
- "multi cohort" ve yüksek (≥%50) aşılanma oranları ile bu etkileri daha hızlı görmek mümkün
- Aşılama CIN2+ (servikal kansere en yakın sonlanım noktası) prevalansını anlamlı azaltıyor

Morbidity and Mortality Weekly Report

Human Papillomavirus Vaccination for Adults: Updated Recommendations of the Advisory Committee on Immunization Practices

Elissa Meites, MD[1]; Peter G. Szilagyi, MD[2]; Harrell W. Chesson, PhD[3]; Elizabeth R. Unger, PhD, MD[4]; José R. Romero, MD[5]; Lauri E. Markowitz, MD[1]

MMWR / August 16, 2019 / Vol. 68 / No. 32

- HPV aşısı rutin olarak 11 ya da 12 yaşında yapılmalı
  - >9, ≤14 yaş ise 0. ve 6. – 12. ay olmak üzere 2 doz
- Yakalama aşısı
  - >14 yaş veya immünkompromize (HIV+) ise 0., 1. – 2. ay, 6. ay olmak üzere 3 doz
  - >2006; kadınlar için ≤26 yaş
  - >2011; erkekler için ≤21 yaş veya MSM/ immünkompromize ise ≤26 yaş
- Haziran 2019
  - Yakalama aşısı: herkes için ≤26 yaş
  - >26, ≤45 yaş için "shared clinical decision making (kararı beraber alın)"
- WHO: >9, ≤14 yaş kız çocukları hedef grup olarak görmekte

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MMWR / August 16, 2019 / Vol. 68 / No. 32

- ABD: yılda HPV ile ilişkili 33700 kanser tanısı konuyor
  - 12900 orofarengeal kanser
  - 10800 serviks kanseri
  - 6000 anal kanser
  - vajen, vulvar ve penil kanser
  - HPV aşısı ile bu kanserlerin çoğundan korunulacağı düşünülmekte

- 2017'de ≥1 doz aşı olan 13 – 17 yaş arası gençlerin oranı %65.5
  - Healthy People 2020'nin %80 hedefinin altında (2010'da ilan edilmiş)

Morbidity and Mortality Weekly Report

Human Papillomavirus Vaccination for Adults: Updated Recommendations of the Advisory Committee on Immunization Practices

Elissa Meites, MD[1]; Peter G. Szilagyi, MD[2]; Harrell W. Chesson, PhD[3]; Elizabeth R. Unger, PhD, MD[4]; José R. Romero, MD[5]; Lauri E. Markowitz, MD[1]

MMWR / August 16, 2019 / Vol. 68 / No. 32

>26, ≤45 yaş için "beraber karar alırken" düşünülmesi gerekenler:

- >26 yaşındaki çoğu erişkin ile aşıyı konuşmaya gerek yok
- Bazı erişkinler yeni HPV infeksiyonu için risk altındalar
  - herhangi bir yaşta yeni cinsel eş bir risk
- Uzun dönemli, karşılıklı monogam ilişki içinde olanların yeni HPV infeksiyonu alma olasılıkları düşük
- Öncesinde test yaparak infeksiyon durumunu anlamak uygun değil
- Aşı etkinliği öncesinde birden çok cinsel eşi olanlarda ve immünkompromize bireylerde düşük olabilir
- HPV aşıları profilaktik

CNN health Food Fitness Wellness Parenting Vital Signs Edition

Just 1 dose of the HPV vaccine may protect against infection, new study suggests

By Jacqueline Howard, CNN

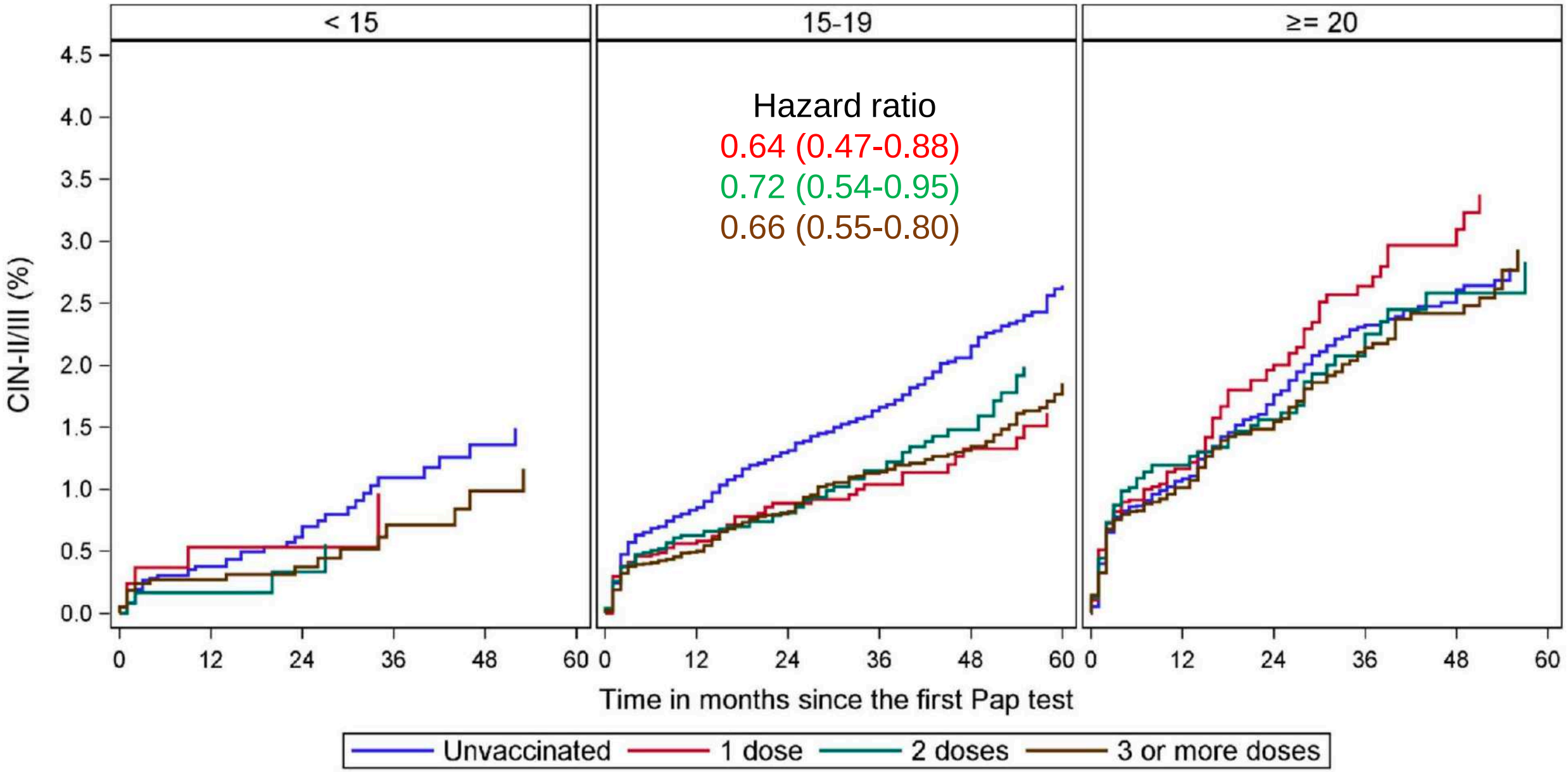
Updated 1846 GMT (0246 HKT) December 27, 2019

Cancer. 2020 Feb 10. doi: 10.1002/cncr.32700. [Epub ahead of print]

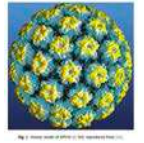
Comparison of the long-term impact and clinical outcomes of fewer doses and standard doses of human papillomavirus vaccine in the United States: A database study.

Rodriguez AM[1,2], Zeybek B[3], Vaughn M[1], Westra J[4], Kaul S[4], Montealegre JR[5], Lin YL[4], Kuo YF[4].

- Olunan HPV aşısı sayısı ile preinvazif servikal hastalık arasındaki ilişkiyi incelemek
- "Retrospective matched cohort"
- 9 – 26 yaş arası ≥1 4vHPV aşı dozu; 1/2006 – 6/2015 arası
- *Papanicolaou* yayma testi ile histolojik teyit
- 133,802 kadın (66541 aşı olan ve olmayan)

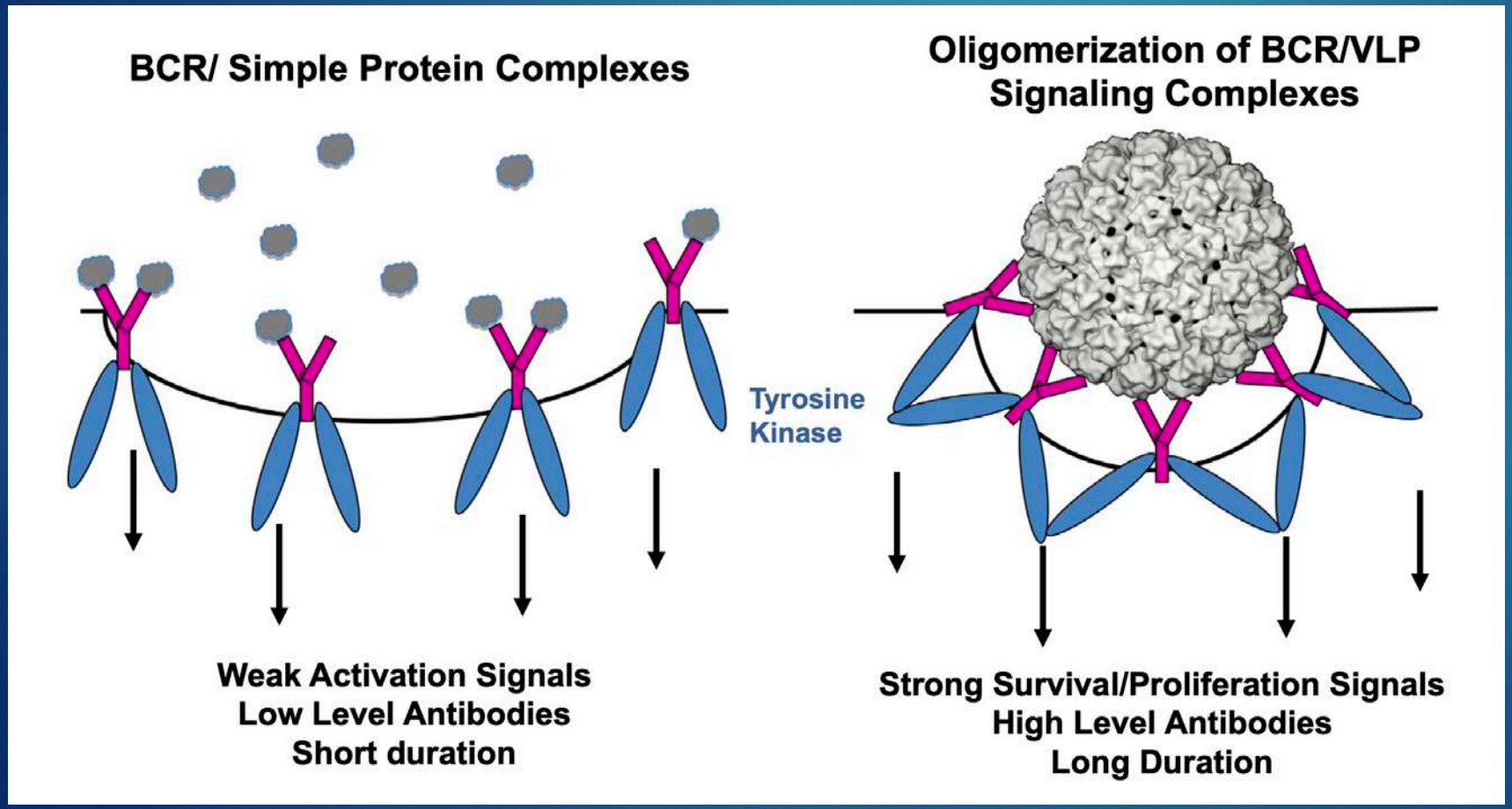

< 15
15-19
≥= 20
Hazard ratio
0.64 (0.47-0.88)
0.72 (0.54-0.95)
0.66 (0.55-0.80)
CIN-II/III (%)
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
0
12
24
36
48
60
Time in months since the first Pap test
Unvaccinated
1 dose
2 doses
3 or more doses

Vaccine. 2018 Aug 6;36(32 Pt A):4768-4773. doi: 10.1016/j.vaccine.2017.12.079. Epub 2018 Jan 8.



Explanations for the high potency of HPV prophylactic vaccines.

Schiller J[1], Lowy D[2].

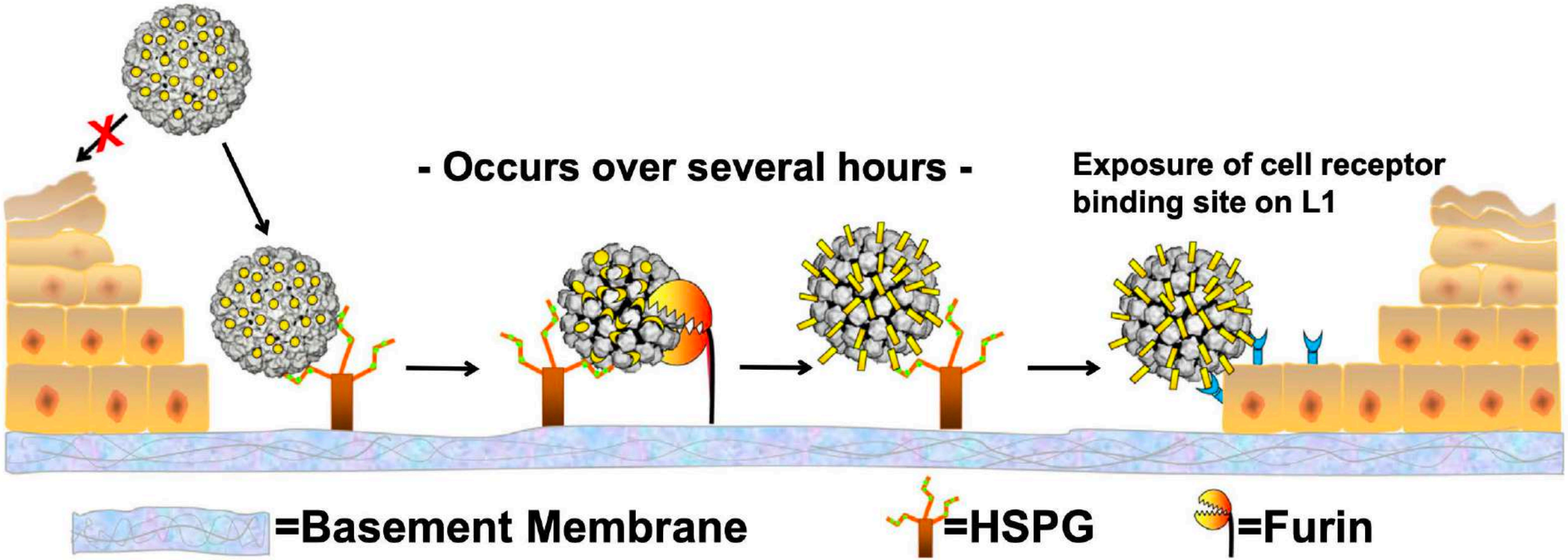


- yüksek ve kalıcı nötralizan antikor oluşumu
- virüsün hedef dokuda nötralizasyona yatkın oluşu
- ”sterilizing immunity”
- tek dozla bile yeterli immün yanıt oluşabiliyor
- devamlı spesifik antikor üreten uzun ömürlü plazma hücresi
- serokonversiyon oranı %100
- ergenlik öncesi yaşlarda immün yanıt daha güçlü

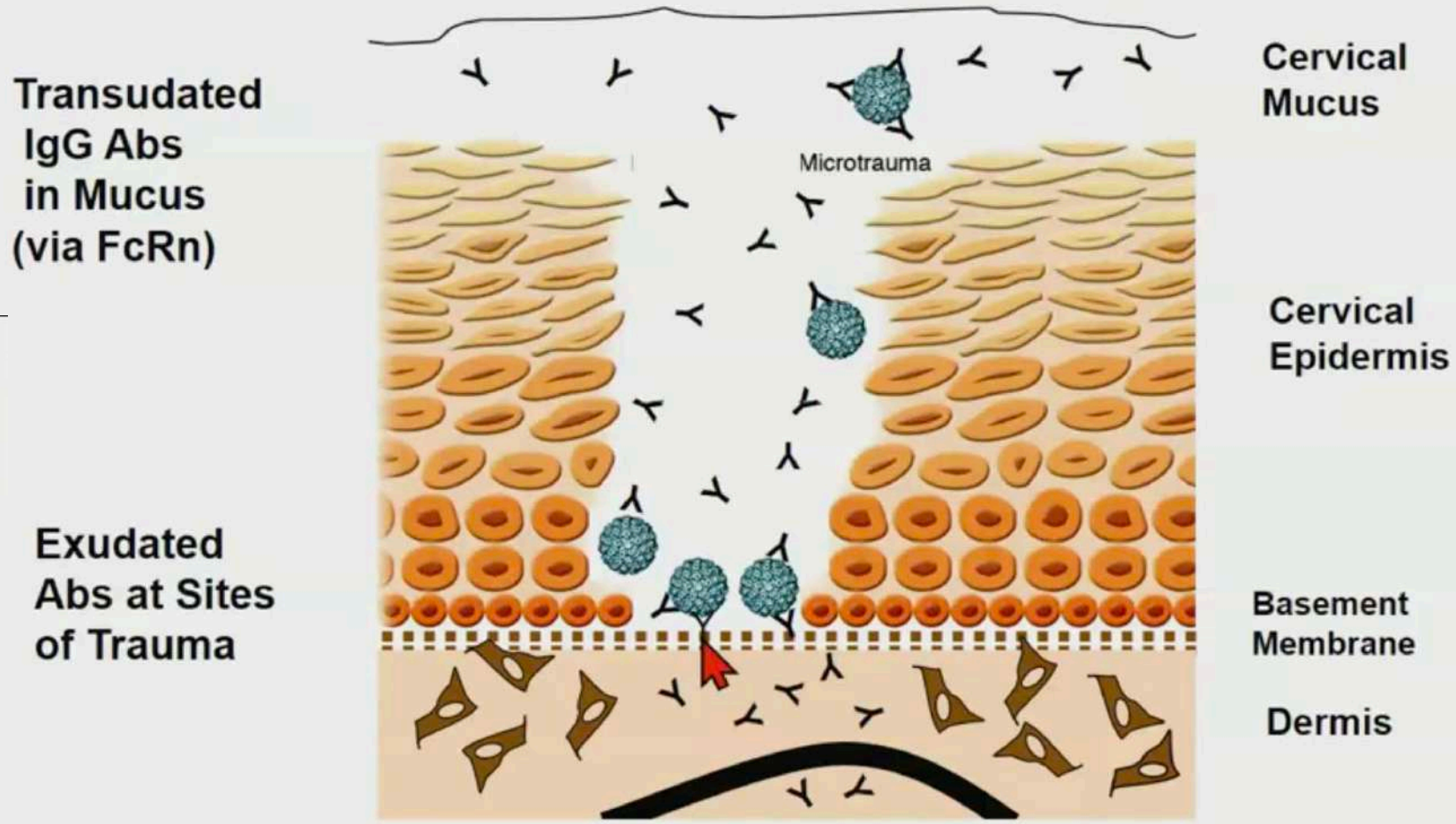
Vaccine. 2018 Aug 6;36(32 Pt A):4768-4773. doi: 10.1016/j.vaccine.2017.12.079. Epub 2018 Jan 8.

Explanations for the high potency of HPV prophylactic vaccines.

Schiller J[1], Lowy D[2].



How Could IM Injection of a VLP Vaccine Induce a Protective Ab Response at the Cervix?



- VLP-specific IgG in women's cervical mucus after IM vaccination: but 10-100X less than in serum - *Nardelli et al. JNCI, 2003*
- Cervicovaginal HPV infection in a mouse model requires epithelial trauma: *Roberts et al., Nat Med, 2007*

An Update on HPV Prophylactic Vaccines

John Schiller, Center for Cancer Research, NCI

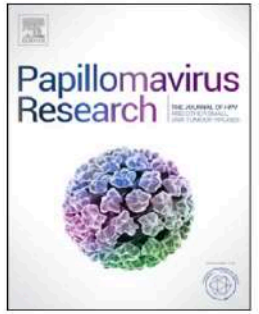
ID week 2019

Papillomavirus Research 8 (2019) 100174

Contents lists available at ScienceDirect

Papillomavirus Research

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



HPV vaccination in HIV infection

Charles JN. Lacey

University of York, UK

A B S T R A C T

Persons with HIV are at increased risk of HPV infection, HPV disease, and HPV-related cancers compared to HIV negative persons. In persons with HIV, immune responses to vaccination are often sub-optimal, and while these improve with ART, they often remain lower and decline more rapidly than in HIV-negative individuals. Although the evidence base to support the ***immunogenicity*** of HPV vaccines in HIV + ve persons is reasonable, the evidence base to support the ***efficacy*** of HPV vaccines in HIV + ve individuals is inconsistent. There is one study in HIV + ve men who have sex with men (MSM) which showed ***no effect***, and two other studies, one in HIV + ve women and one in HIV + ve adolescents that showed ***reduced effectiveness***. All these effectiveness studies used Gardasil 4 (G4). Two studies in HIV + ve persons have shown superior immunogenicity of Cervarix (which uses a TLR4 agonist adjuvant) compared to G4. Studies of Hepatitis B vaccines in HIV + ve persons have shown that either (i) increased number of doses (ii) increased vaccine dose, or (iii) TLR agonist adjuvanted vaccines, all produce increased immunogenicity compared to standard vaccine regimes. Therefore, questions remain as to optimal HPV vaccine regimes in HIV and further clinical trials with different HPV vaccine regimes are needed.

Human Papillomavirus Disease (Last updated November 29, 2018; last reviewed June 26, 2019)

NOTE: Update in Progress

Recommendations for Preventing Human Papillomavirus Infections

Preventing First Episode of HPV Infection

Indications for HPV Vaccination:

- HIV-infected; aged 13 to 26 years **(AIII)**

Note: Please refer to Pediatric OI Guidelines for vaccination of boys and girls younger than age 13 years.

Vaccination Schedules

HPV recombinant vaccine 9 valent (Types 6, 11, 16, 18, 31, 33, 45, 52, 58) 0.5 mL IM at 0, 1 to 2, and 6 months **(AIII)**

- For patients who have completed a vaccination series with the recombinant bivalent or quadrivalent vaccine, many experts would give additional full series of vaccination with recombinant 9-valent vaccine, but there are no data to define who might benefit or how cost effective this approach might be **(CIII)**

EACS European AIDS Clinical Society

EACS Guidelines 10.0

Infection	Vaccination rationale in PLWH	Comment
Human Papilloma Virus (HPV)	Shared risk with HIV of contracting infection. Higher rate of cervical and anal cancer	Vaccinate all PLWH with 3 doses between ages 9 and 40 (health insurance coverage differs by country according to age, sex, sexual orientation). Use 9-valent vaccine if available. Persons treated for high grade cervical dysplasia could benefit from a full course vaccination for secondary prevention

GARDASIL IM ENJEKSİYON İÇİN SÜSPANSİYON İÇEREN KULLA

1x0.5ml enjektör/kutu

Firma	Form	NFC	ATC Kodu
MERCK SHARP & DOHME	hazır enjektör-i.m.	FND	J07BM01

Beyaz Reçete

Barkod	8699636950104
Fiyat	**584.78**
Fiyat Tarihi	19.02.2020
İndirimler	
Kamu Fiyatı	
Kamu Ödenen	
Depocu Fiyatı	467.25+KDV
İmalatçı Fiyatı	450.64+KDV
KDV	%8
Eşdeğer Grup	
J/O-Orijin	ORİJİNAL-İthal
Ruhsat Tarihi	15.01.2007
Raf Ömrü	36 Ay
Özel Durumlar	• Dondurulmamalıdır.
Etiketler	

GARDASIL 9 IM ENJEKSİYONLUK SÜSPANSİYON

1x0.5ml enjektör/kutu

Firma	Form	NFC	ATC Kodu
MERCK SHARP & DOHME	hazır enjektör-i.m.	FND	J07BM03

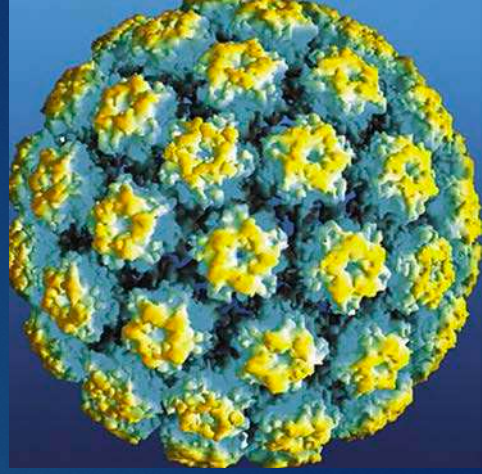
Henüz Kullanıma Sunulmadı

Beyaz Reçete

Barkod	8699636951262
Fiyat	
Fiyat Tarihi	
İndirimler	
Kamu Fiyatı	
Kamu Ödenen	
Depocu Fiyatı	
İmalatçı Fiyatı	
KDV	
Eşdeğer Grup	
Orijin	İthal
Ruhsat Tarihi	21.11.2019
Raf Ömrü	36 Ay
Özel Durumlar	• Dondurulmamalıdır.
Etiketler	

ÖZET

HPV aşısı



- 2vHPV, 4vHPV ve 9vHPV
- Kadın ya da erkek aşılananı yüksek riskli HPV tiplerinin neden olduğu kanserlerden koruyor
  - serviks kanseri, anüs kanseri, orofarengeal kanser, vulvar/ vajinal kanser ve penil kanser + anogenital siğillerden koruyor
- >9, ≤14 yaş: 0. ve 6.-12. ay toplam 2 doz
  >14, ≤26 yaş: 0., 1. – 2. ve 6.-12. ay toplam 3 doz (immünkompromizelerde de)
  >26, ≤45 yaş: etkinliği?
- Hamilerde yapılmamalı; hamile kalırsa seriyi durdur
- Aşı güvenli ve iyi tolere ediliyor; aşı sonrası senkopa dikkat edilmeli!
- Aşı var olan lezyonları tedavi etmez
- Aşı serviks kanseri tarama programını değiştirmez

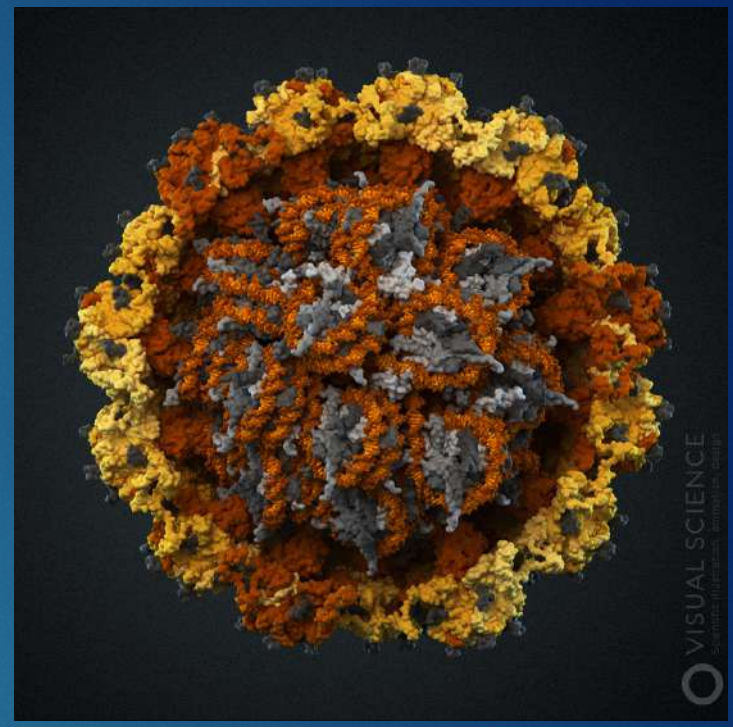
KLİMİK TÜRK KLİNİK MİKROBİYOLOJİ VE İNFEKSİYON HASTALIKLARI DERNEĞİ

Bilimle Sağlıkla 33 .Yıl

HPV

Simpozyum: Aşılarda Yeni Ne Var?

İlginiz için teşekkürler!



Doç Dr Uluhan Sili
Marmara Üniversitesi Tıp Fakültesi
Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji AD
uluhan@hotmail.com

MARMARA ÜNİVERSİTESİ 1883 Tıp Fakültesi

25 ŞUBAT 2020

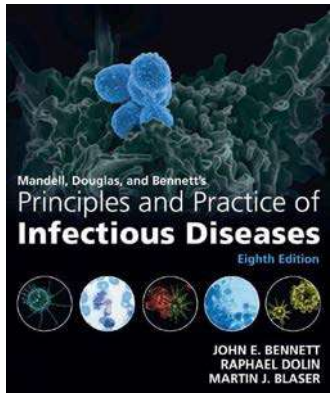
Vaccine. 2019 Jun 27;37(29):3918-3924. doi: 10.1016/j.vaccine.2019.04.099. Epub 2019 May 31.

Declines in HPV vaccine type prevalence in women screened for cervical cancer in the United States: Evidence of direct and herd effects of vaccination.

Markowitz LE[1], Naleway AL[2], Lewis RM[3], Crane B[2], Querec TD[4], Weinmann S[2], Steinau M[4], Unger ER[4].

Table 1
Characteristics of study population, 2012–2013 and 2015–2016, by age group.

	20–24 years			25–29 years		
Characteristic	2012–2013 N = 2057 n (%)	2015–2016 N = 2059 n (%)	p-value	2012–2013 N = 2114 n (%)	2015–2016 N = 2420 n (%)	p-value
Median age, years (IQR)	22 (21–23)	22 (21–24)		27 (26–28)	27 (26–28)	
Race/ethnicity						
NH white	1424 (69.2)	1473 (71.5)	<0.01	1494 (70.7)	1715 (70.9)	<0.01
NH Asian	70 (3.4)	94 (4.6)		114 (5.4)	166 (6.9)	
NH black	78 (3.8)	91 (4.4)		64 (3.0)	91 (3.8)	
Hispanic	177 (8.6)	256 (12.4)		173 (8.2)	261 (10.8)	
Other	62 (3.0)	78 (3.8)		60 (2.8)	76 (3.1)	
Unknown	246 (12.0)	67 (3.3)		209 (9.9)	111 (4.6)	
Family poverty						
≥20% below	484 (24.0)	521 (25.4)	0.28	533 (25.8)	654 (27.1)	0.34
<20% below	1536 (76.0)	1528 (74.6)		1534 (74.2)	1764 (73.0)	
HPV vaccination history[a]						
≥1 dose	898 (43.7)	1323 (64.3)	<0.01	433 (20.5)	775 (32.0)	<0.01
3 doses	612 (29.8)	1060 (51.5)	<0.01	251 (11.9)	498 (20.6)	<0.01
Median age at first dose, years (IQR)	17 (16–18)	15 (14–17)	<0.01	23 (21–24)	20 (18–23)	<0.01


Mandell, Douglas, and Bennett's
Principles and Practice of
Infectious Diseases
Eighth Edition
JOHN E. BENNETT
RAPHAEL DOLIN
MARTIN J. BLASER

Hyperkeratosis
Parakeratosis
Koilocyte
Acanthosis
Papillomatosis
Infection
S. corneum
S. granulosum
S. spinosum
S. basale
Basal lamina
Epidermis
3rd Plexus
Dermis
2nd Plexus
Artery
Vein
1st Plexus
Lymphatic vessel
A
HPV virion
HPV DNA
Dead keratinocyte releasing viral particles
Dead keratinocyte
S. corneum
Keratin
S. granulosum
Keratohyaline granule
Koilocyte
Vacuole
Nucleus
Inclusion body
S. spinosum
Tonofibrils
S. basale
Basal lamina
B

Aşı Etkinliği
efficacy/ effectiveness

- 24– 45 yaş kadınlar
- birleşik sonlanım noktası
  - inatçı infeksiyon
    genital bölge dışı lezyonlar
    HPV tipleri 6, 11, 16 ve 18 ile ilişkili CIN 1+
- Aşı etkinliği (Castellsagué X et al. 2011)
  - per-protocol 88.7% (95% CI = 78.1–94.8)
  - intention-to-treat 47.2% (95% CI = 33.5–58.2)

Morbidity and Mortality Weekly Report

Human Papillomavirus Vaccination for Adults: Updated Recommendations of the Advisory Committee on Immunization Practices

Elissa Meites, MD[1]; Peter G. Szilagyi, MD[2]; Harrell W. Chesson, PhD[3]; Elizabeth R. Unger, PhD, MD[4]; José R. Romero, MD[5]; Lauri E. Markowitz, MD[1]

MMWR / August 16, 2019 / Vol. 68 / No. 32

- 3 profilaktik HPV aşısı
- bivalent (2vHPV, Cervarix, GlaxoSmithKline) 16, 18
- quadrivalent (4vHPV, Gardasil, Merck) 6, 11, 16, 18
- 9-valent (9vHPV, Gardasil 9, Merck) 6, 11, 16, 18, 31, 33, 45, 52, 58
  - 2016 sonundan beri ABD'de sadece 9-valanlı aşı yapılıyor
  - 10-2018: >9, ≤45 yaşa kadar kullanımı FDA onaylı

Expert Rev Vaccines. 2018 Dec;17(12):1085-1091. doi: 10.1080/14760584.2018.1548282. Epub 2018 Nov 29.

Efficacy and safety of prophylactic HPV vaccines. A Cochrane review of randomized trials.

Arbyn M[1], Xu L[1].

	Outcome	A hr HPV DNA- ≥ 1 dose	B HPV16/18 DNA- 3 doses	C Regardless of HPV ≥ 1 dose
	Age group 15-26			
	High-grade intraepithelial neoplasia associated with HPV16/18			
1	CIN2+	0.01 (0.00 to 0.05)[b2q1] [Fig1] ⊕⊕⊕⊕	0.07 (0.03 to 0.15)[b4q2] [Fig2a] ⊕⊕⊕⊕	0.46 (0.37 to 0.57)[b1q2] [F3a] ⊕⊕⊕⊕
2	CIN3+	0.01 (0.00 to 0.10)[b1q1] ⊕⊕⊕⊕	0.07 (0.02 to 0.29)[b1q2] ⊕⊕⊕⊕	0.55 (0.45 to 0.67)[b1q1] ⊕⊕⊕⊕
3	AIS+	0.10 (0.01 to 0.82)[b1q1] ⊕⊕⊕	0.12 (0.02 to 0.70)[b1q2] ⊕⊕⊕	0.36 (0.17 to 0.78)[b1q1] ⊕⊕⊕
	Any high-grade intraepithelial neoplasia irrespective of HPV types			
4	CIN2+	0.33 (0.25 to 0.43)[b4] ⊕⊕⊕⊕ 0.57 (0.44 to 0.76)[q1] ⊕⊕⊕	0.40 (0.25 to 0.64)[b2q1] ⊕⊕⊕⊕	0.70 (0.58 to 0.85)[b2q1] [F4a] ⊕⊕⊕⊕
5	CIN3+	0.08 (0.03 to 0.23)[b2] ⊕⊕⊕⊕ 0.54 (0.36 to 0.82)[q1] ⊕⊕⊕	-	0.55 (0.43 to 0.71)[b2] [Fig4] ⊕⊕⊕⊕ 0.81 (0.69 to 0.96)[q1] [Fig4] ⊕⊕⊕
6	AIS+	0.10 (0.01 to 0.76)[b1q1] ⊕⊕⊕	-	0.32 (0.15 to 0.67)[b1q1] ⊕⊕⊕⊕
	Persistent HPV16/18 infection			
7	6M persisting	0.07 (0.05 to 0.90)[b1] ⊕⊕⊕	0.06 (0.05 to 0.08)[b4] ⊕⊕⊕⊕	0.44 (0.38 to 0.51)[b2] ⊕⊕⊕
	Age group 24-45			
	High-grade intraepithelial neoplasia associated with HPV16/18			
8	CIN2+	-	0.16 (0.04 to 0.74)[b1q1] [Fig2b] ⊕⊕⊕	0.74 (0.52 to 1.05)[b1q1] [Fig3b] ⊕⊕⊕
9	CIN3+	-	-	-
10	AIS+	-	-	-
	Any high-grade intraepithelial neoplasia irrespective of HPV types			
11	CIN2+	-	-	1.04 (0.83 to 1.30)[b1q1] [F4b] ⊕⊕
12	CIN3+	-	-	-
13	AIS+	-	-	-
	Persistent HPV16/18 infection			
14	6M persisting	-	0.11 (0.06 to 0.20)[b1q1] ⊕⊕⊕⊕	0.57 (0.47 to 0.69)[b1q1] ⊕⊕⊕⊕

Level of protection (RR)
Excellent: RR ≤0.10, 1 excluded from CI
Good: RR>0.10 & ≤ 0.20, 1 excluded from CI
Moderate: RR>0.20 & ≤ 0.80, 1 excluded from CI
Weak: RR>0.80 & <1, 1 excluded from CI
No protection: 1 included in CI
Adverse protection: RR>1 and 1 excluded from CI

Quality of evidence*
High ⊕⊕⊕⊕
Moderate ⊕⊕⊕
Low ⊕⊕
Very low ⊕