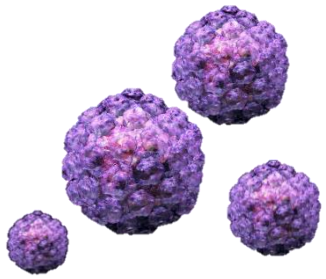
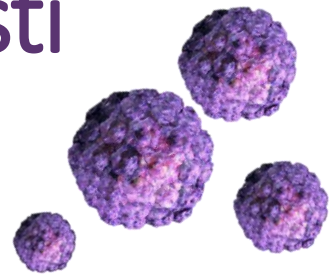


Cepljenje proti HPV - novosti



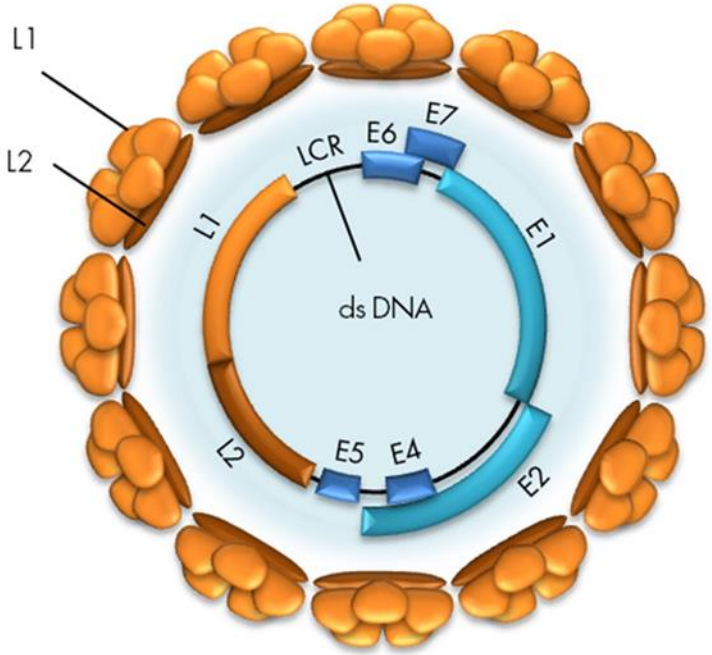
ASIST. DR. ANJA ŠTERBENC, DR. MED.

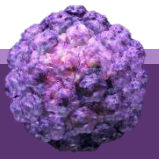
INŠTITUT ZA MIKROBIOLOGIJO IN IMUNOLOGIJO

MEDICINSKA FAKULTETA, UNIVERZA V LJUBLJANI

Človeški papilomavirusi (HPV)

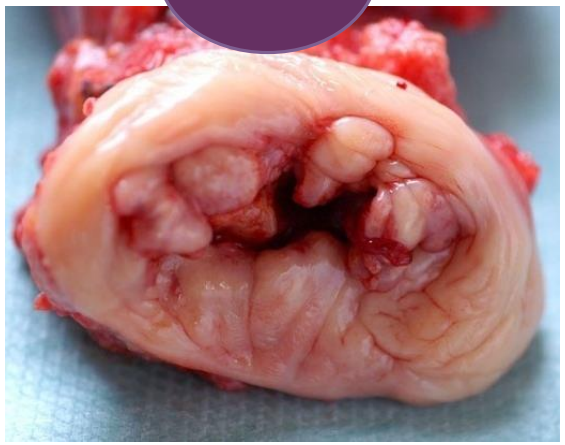
- Najpogostejša spolno prenosljiva okužba
- Družina *Papillomaviridae* (PV)
- Krožna, ds DNA (7.500-8.000 bp)
- 220+ genotipov HPV, 14 visokorizičnih

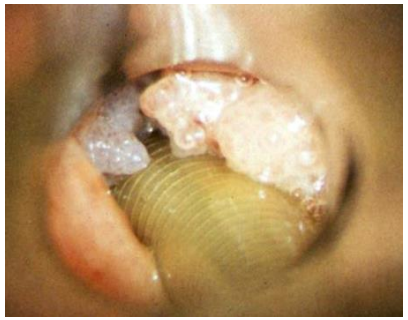




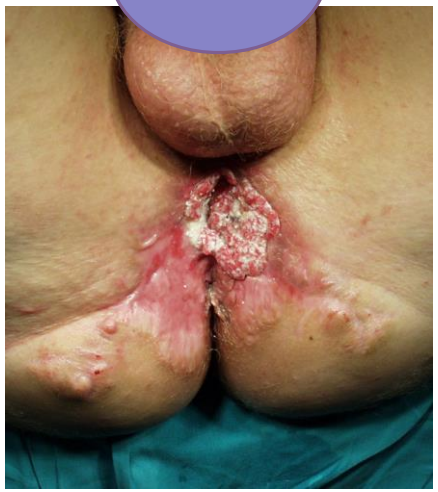
S HPV povezujemo

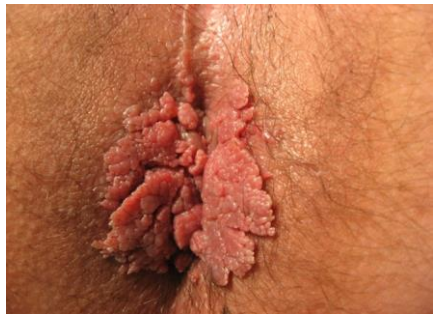
>99%



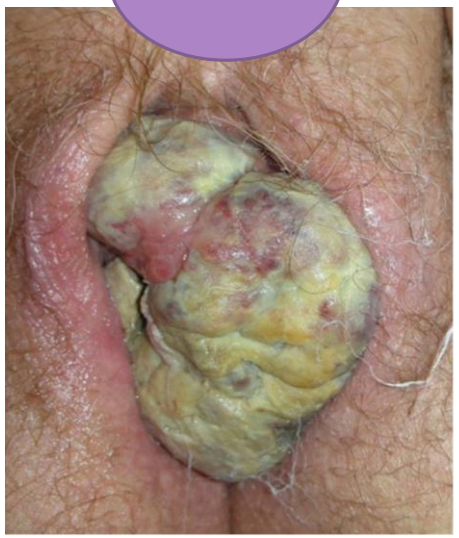


>90%

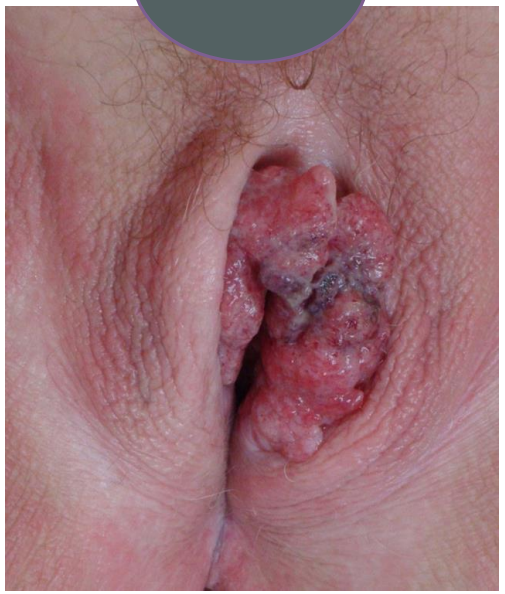




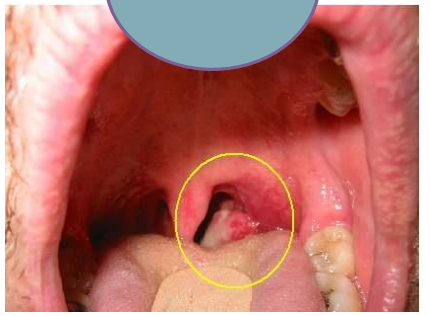
≈75%



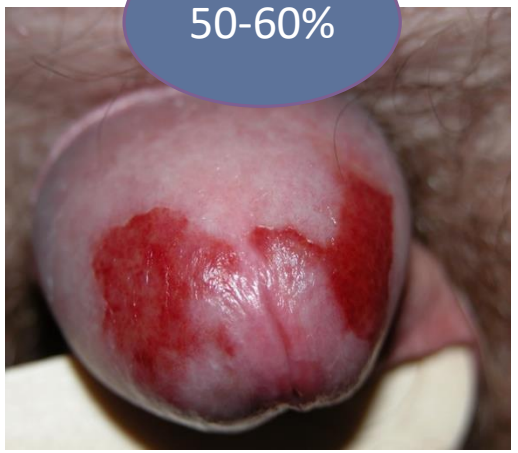
≈70%

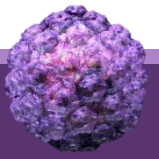


≈70%



50-60%





World Health Organization

Cervical Cancer Elimination Initiative

Our 2030 Goals

90%

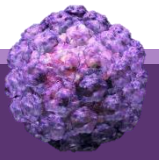
of girls are **fully vaccinated** against cervical cancer at the age of 15

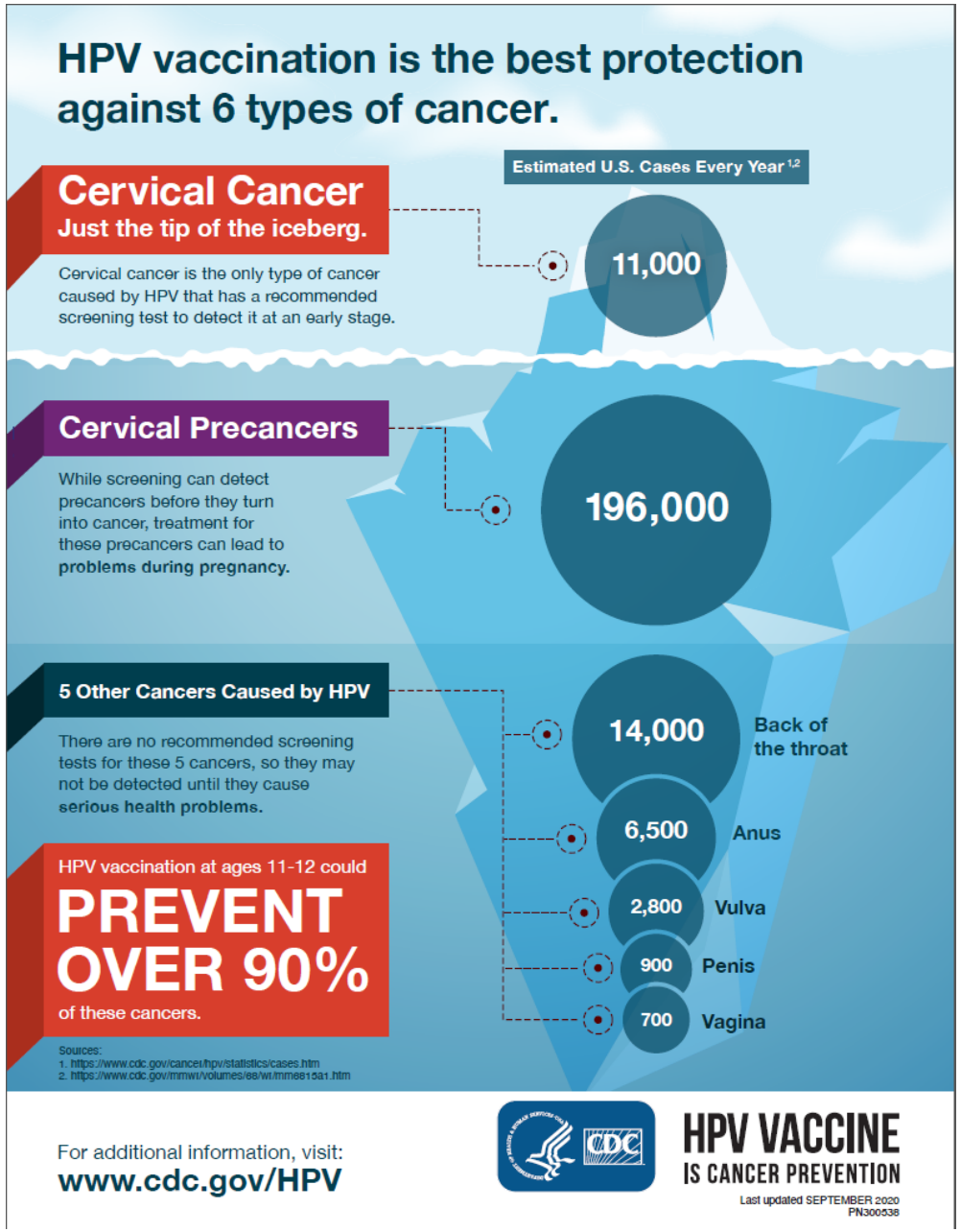
70%

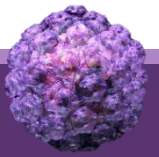
of women are **screened for cervical cancer** at the age of 35 and 45

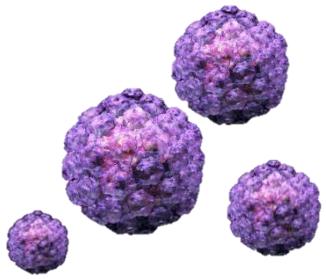
90%

of women with positive cervical screening **receive treatment**

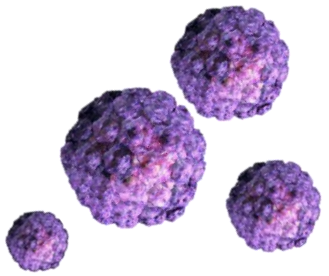


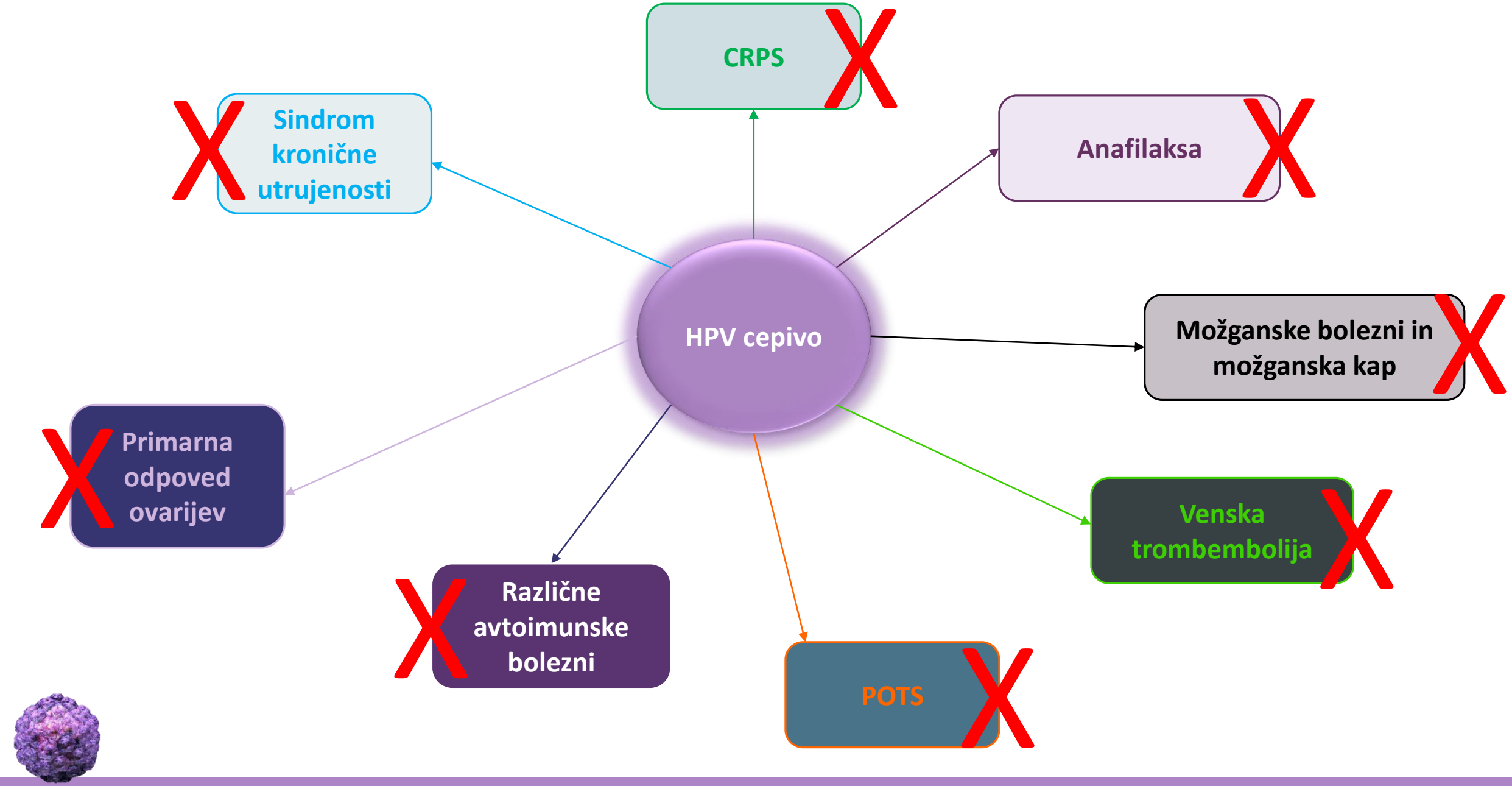

HPV vaccination is the best protection against 6 types of cancer.
Estimated U.S. Cases Every Year 1,2
Cervical Cancer
Just the tip of the iceberg.
Cervical cancer is the only type of cancer caused by HPV that has a recommended screening test to detect it at an early stage.
11,000
Cervical Precancers
While screening can detect precancers before they turn into cancer, treatment for these precancers can lead to problems during pregnancy.
196,000
5 Other Cancers Caused by HPV
There are no recommended screening tests for these 5 cancers, so they may not be detected until they cause serious health problems.
14,000 Back of the throat
6,500 Anus
2,800 Vulva
900 Penis
700 Vagina
HPV vaccination at ages 11-12 could
PREVENT OVER 90%
of these cancers.
Sources:
1. https://www.cdc.gov/cancer/hpv/statistics/cases.htm
2. https://www.cdc.gov/mmwr/volumes/68/wr/mm6815a1.htm
For additional information, visit:
www.cdc.gov/HPV
HPV VACCINE
IS CANCER PREVENTION
Last updated SEPTEMBER 2020
PN300538

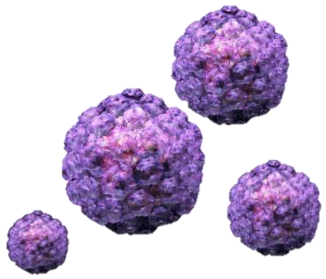




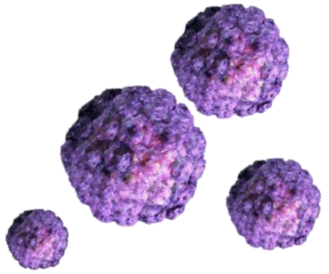
Varnost cepiv proti HPV




CRPS
Sindrom kronične utrujenosti
Anafilaksa
HPV cepivo
Možganske bolezni in možganska kap
Primarna odpoved ovarijev
Venska trombembolija
Različne avtoimunske bolezni
POTS



Dolgotrajna učinkovitost?



Sustainability of neutralising antibodies induced by bivalent or quadrivalent HPV vaccines and correlation with efficacy: a combined follow-up analysis of data from two randomised, double-blind, multicentre, phase 3 trials

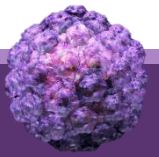
Filipe Colaço Mariz, Penelope Gray, Noemi Bender, Tiina Eriksson, Hanna Kann, Dan Apter, Jorma Paavonen, Emma Pajunen, Kristina M Prager, Peter Sehr, Heljä-Marja Surcel, Tim Waterboer, Martin Müller, Michael Pawlita, Matti Lehtinen

Background Quadrivalent and bivalent vaccines against oncogenic human papillomavirus (HPV) are used worldwide with different reported overall efficacies against HPV infections. Although protective concentrations of vaccine-induced antibodies are still not formally defined, we evaluated the sustainability of neutralising antibodies in vaccine trial participants 2–12 years after vaccination and the correlation with reported vaccine efficacy.

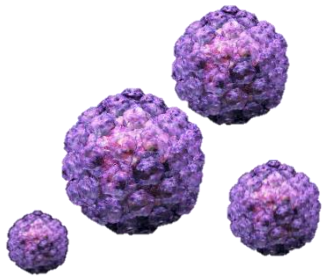
Methods We did a follow-up analysis of data from the Finnish cohorts of two international, randomised, double-blind, phase 3 trials of HPV vaccines, PATRICIA (bivalent, HPV16 and 18) and FUTURE II (quadrivalent, HPV6, 11, 16, and 18). In 2002 and 2004–05, respectively, Finnish girls aged 16–17 years participated in one of these two trials and consented to health registry follow-up with the Finnish Cancer Registry. The cohorts were also linked with the Finnish Maternity Cohort (FMC) that collects first-trimester serum samples from nearly all pregnant Finnish women, resulting in 2046 post-vaccination serum samples obtained during up to 12 years of follow-up. We obtained serum samples from the FMC-based follow-up of the FUTURE II trial (from the quadrivalent vaccine recipients) and the PATRICIA trial (from corresponding bivalent vaccine recipients who were aligned by follow-up time, and matched by the number of pregnancies). We assessed neutralising antibody concentrations (type-specific seroprevalence) to HPV6, 16, and 18, and cross-neutralising antibody responses to non-vaccine HPV types 31, 33, 45, 52, and 58 from 2 to 12 years after vaccination.

Findings Up to Dec 31, 2016, we obtained and analysed 577 serum samples from the quadrivalent vaccine recipients and 568 from the bivalent vaccine recipients. In 681 first-pregnancy serum samples, neutralising antibodies to HPV6, 16, and 18 were generally found up to 12 years after vaccination. However, 51 (15%) of 339 quadrivalent vaccine recipients had no detectable HPV18 neutralising antibodies 2–12 years after vaccination, whereas all 342 corresponding bivalent vaccine recipients had HPV18 neutralising antibodies.. In seropositive quadrivalent vaccine recipients, HPV16 geometric mean titres (GMT) halved by years 5–7 (GMT 3679, 95% CI 2377 to 4708) compared with years 2–4 (6642, 2371 to 13 717). Between 5 and 12 years after vaccination, GMT of neutralising antibodies to HPV16 and 18 were 5·7 times and 12·4 times higher, respectively, in seropositive bivalent vaccine recipients than in the quadrivalent vaccine recipients. Cross-neutralising antibodies to HPV31, 33, 45, 52, and 58 were more prevalent in the bivalent vaccine recipients but, when measurable, sustainable up to 12 years after vaccination with similar GMTs in both vaccine cohorts. Seroprevalence for HPV16, 31, 33, 52, and 58 significantly correlated with vaccine efficacy against persistent HPV infections in the bivalent vaccine recipients only (r_s=0·90, 95% CI 0·09 to 0·99, p=0·037, compared with r_s=0·62, 95% CI –0·58 to 0·97, p=0·27 for the quadrivalent vaccine recipients). Correlation of protection with prevalence of neutralising or cross-neutralising HPV antibodies was not significant in the quadrivalent vaccine recipients.

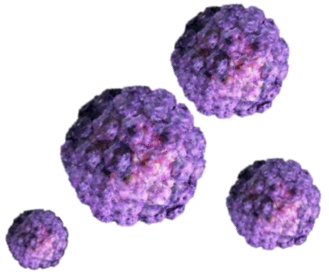
Interpretation The observed significant differences in the immunogenicity of the two vaccines are in line with the differences in their cross-protective efficacy. Protective HPV vaccine-induced antibody titres can be detected up to 12 years after vaccination.



Lancet Infect Dis. 2021:S1473-3099(20)30873-2.



Navzkrižna reaktivnost?



Systematic literature review of cross-protective effect of HPV vaccines based on data from randomized clinical trials and real-world evidence

Darron R. Brown [a], Elmar A. Joura [b], Glorian P. Yen [c], Smita Kothari [c,*], Alain Luxembourg [d], Alfred Saah [e], Anuj Walia [f], Gonzalo Perez [g], Hanane Khoury [h], Danielle Badgley [h], Margaret Stanley [i]

Vaccine 39 (2021) 2224–2236

PubMed and Embase databases were searched to identify **randomized controlled trials (RCT) and observational studies** published between 2008 and 2019 reporting on efficacy and effectiveness of HPV vaccines in women against **non-vaccine types** 31, 33, 45, 52, 58, and 6 and 11 (non-bivalent types).

Key outcomes of interest: vaccine efficacy against 6- and 12-month persistent infection or genital lesions, and type-specific genital HPV prevalence or incidence.

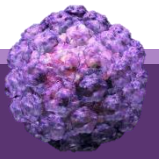
The **cross-protective effect** of the 2vHPV and 4vHPV vaccines **is not consistently demonstrated**.

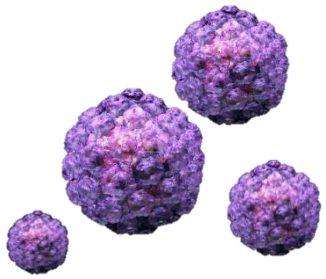
Cross-protective effects toward only **some non-vaccine HPV types—HPV 31 and 45 for the 2vHPV** and **HPV 31 for the 4vHPV vaccine,** few reported significant cross-protective effect for HPV types 33 and 52.

None of the reported cross-protective effects of the 2vHPV and 4vHPV vaccines compares to the observed efficacy of the **9vHPV vaccine** (**95% efficacious** to prevent the endpoints of the 5 HPV types 31, 33, 45, 52, and 58).

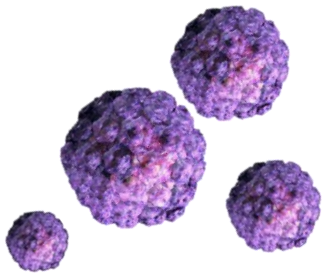
Cross-protection **wanes over time**, efficacy does not appear to exist in **< 3 doses** of the bivalent vaccine.

For all HPV types, **cross-protective effect has a lower magnitude versus direct protection** provided by the vaccines.





Alternativne sheme



Three-Year Follow-up of 2-Dose Versus 3-Dose HPV Vaccine

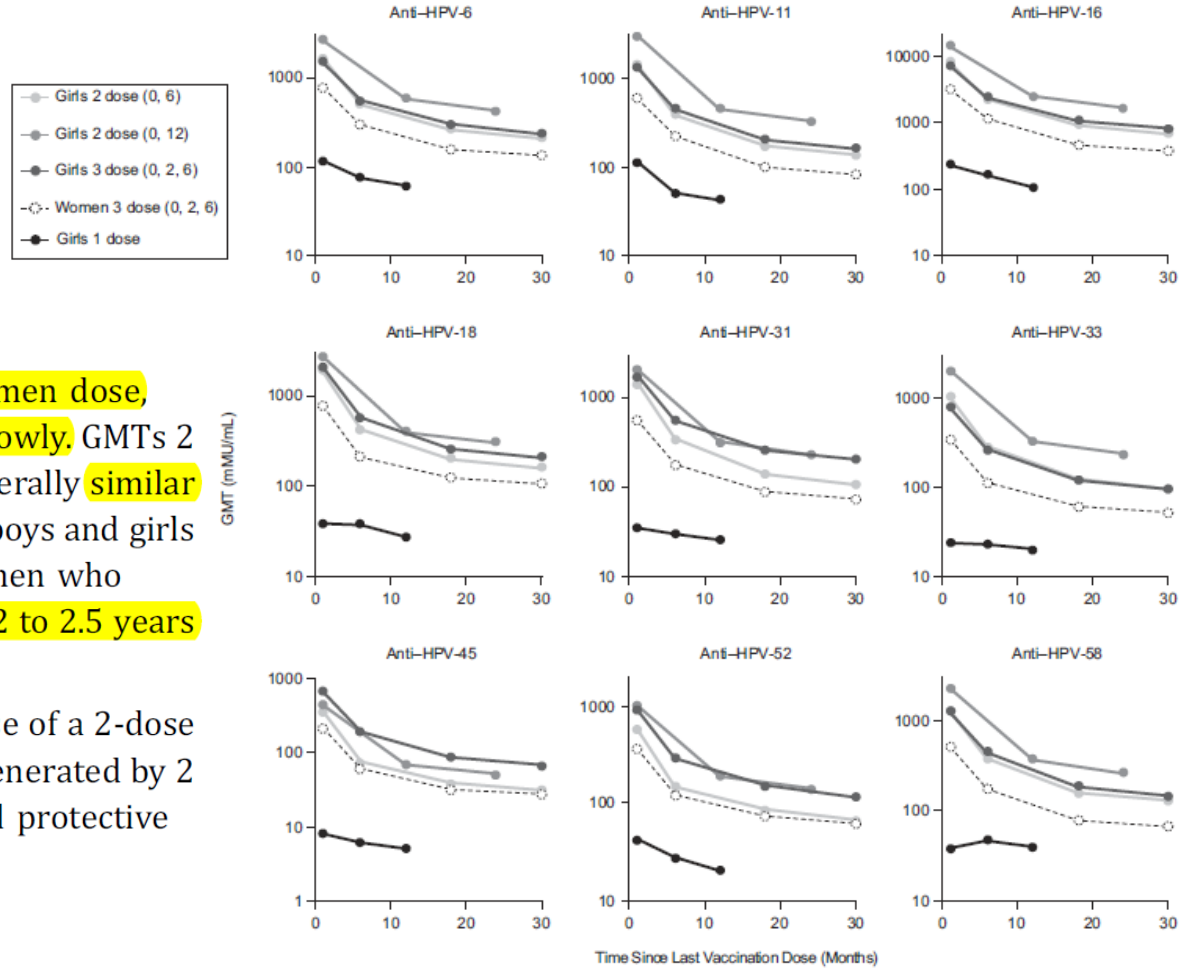
Pediatrics. 2021;147(1):e20194035.

Jacob Bornstein, MD, MPA,[a] Surita Roux, MBChB, MPH,[b] Lone Kjeld Petersen, MD, DMSc,[c] Li-Min Huang, MD,[d] Simon R. Dobson, MD, FRCPC,[e] Punnee Pitisuttithum, MD,[f] Javier Diez-Domingo, MD, PhD,[g] Andrea Schilling, MD,[h] Hany Ariffin, MD, PhD,[i] Richard Tytus, MD,[j] Richard Rupp, MD,[k] Shelly Senders, MD,[l] Eli Engel, MD, PhD,[m] Daron Ferris, MD,[n] Yae-Jean Kim, MD, PhD,[o] Young Tae Kim, MD, PhD,[p] Zafer Kurugol, MD,[q] Oliver Bautista, PhD,[r] Katrina M. Nolan, PhD,[r] Sandhya Sankaranarayanan, PhD,[r] Alfred Saah, MD, MPH,[r] Alain Luxembourg, MD, PhD[r]

RESULTS: Anti-HPV GMTs were highest 1 month after the last 9vHPV vaccine regimen dose, decreased sharply during the subsequent 12 months, and then decreased more slowly. GMTs 2 to 2.5 years after the last regimen dose in girls and boys given 2 doses were generally similar to or greater than GMTs in young women given 3 doses. Across HPV types, most boys and girls who received 2 doses (cLIA: 81%–100%; IgG-LIA: 91%–100%) and young women who received 3 doses (cLIA: 78%–98%; IgG-LIA: 91%–100%) remained seropositive 2 to 2.5 years after the last regimen dose.

CONCLUSIONS: Antibody responses persisted through 2 to 2.5 years after the last dose of a 2-dose 9vHPV vaccine regimen in girls and boys. In girls and boys, antibody responses generated by 2 doses administered 6 to 12 months apart may be sufficient to induce high-level protective efficacy through at least 2 years after the second dose.

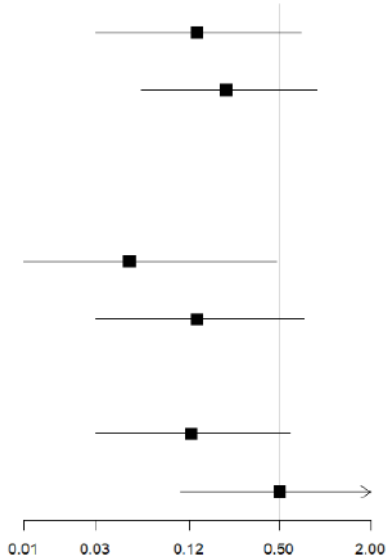
Anti-HPV GMTs (based on cLIA) after the last 9vHPV vaccine dose, by vaccination regimen



Single dose versus standard regimen

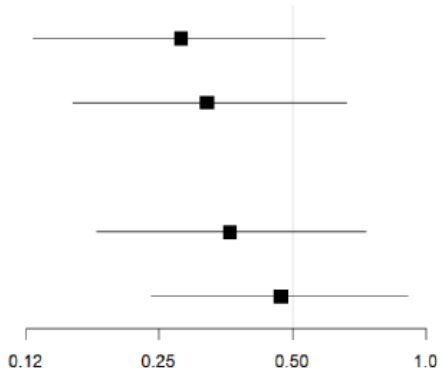
A. 9 to 14 year olds

	HPV type	N (standard)	N (single)	GMT ratio (95% CI)
Bivalent				
36 month				
	16	1579	36	0.14 (0.03, 0.69)
	18	1589	36	0.22 (0.06, 0.87)
Quadrivalent				
36 month				
	16	1071	11	0.05 (0.01, 0.47)
	18	1087	11	0.14 (0.03, 0.72)
72 month				
	16	101	11	0.13 (0.03, 0.58)
	18	101	11	0.50 (0.11, 2.40)



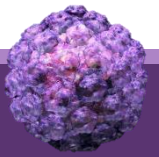
B. 15 to 26 year olds

	HPV type	N (standard)	N (single)	GMT ratio (95% CI)
Bivalent				
36 month				
	16	3334	104	0.28 (0.13, 0.59)
	18	3366	104	0.32 (0.16, 0.66)
72 month				
	16	442	104	0.36 (0.18, 0.73)
	18	442	104	0.47 (0.24, 0.91)



Non-inferiority was not demonstrated for 2vHPV or 4vHPV vaccines at any time point; however, data were limited!!!

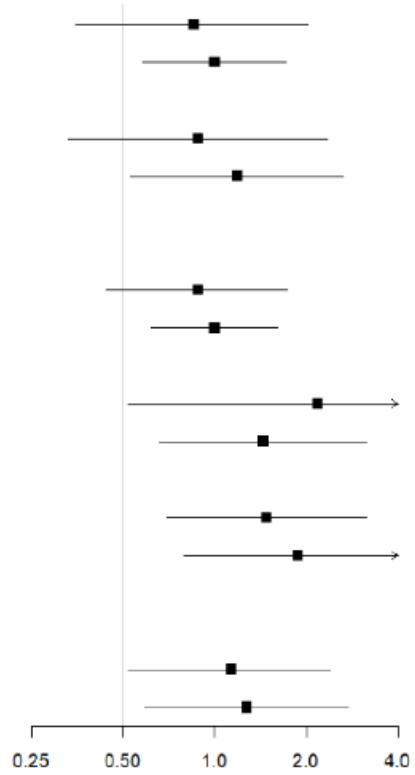
No established threshold of HPV titer that indicates protection!



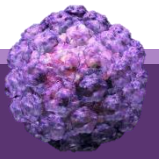
Extended interval (at least 12 m) versus standard regimen

9 to 14 years

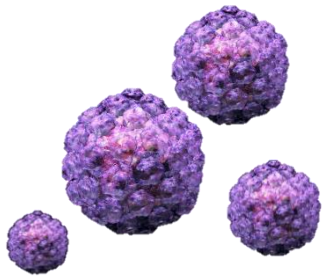
	HPV type	N (standard)	N (extended)	GMT ratio (95% CI)
Bivalent				
1 month				
	16	2560	355	0.85 (0.35, 2.03)
	18	2568	369	1.00 (0.58, 1.73)
36 month				
	16	1579	339	0.88 (0.33, 2.35)
	18	1589	355	1.19 (0.53, 2.65)
Quadrivalent				
1 month				
	16	1747	155	0.88 (0.44, 1.74)
	18	1763	155	1.00 (0.62, 1.61)
36 month				
	16	1071	212	2.17 (0.52, 8.94)
	18	1087	213	1.45 (0.66, 3.17)
72 month				
	16	101	124	1.48 (0.70, 3.17)
	18	101	124	1.87 (0.79, 4.42)
Nonavalent				
1 month				
	16	409	31	1.13 (0.52, 2.41)
	18	409	31	1.28 (0.70, 2.35)



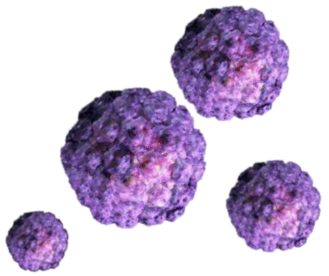
Non-inferiority demonstrated for all three vaccines at multiple time points for both HPV 16 and HPV 18 titers, with the exception of HPV 16 titers of the bivalent vaccine at one month post-last dose and 36 months post-first dose, and HPV 16 titers for the quadrivalent vaccine one month post-last dose.



Secor AM, et al. Vaccines (Basel). 2020;8(4):618.



HPV cepljenje odraslih?



Prevalence, incidence, and natural history of HPV infection in adult women ages 24 to 45 participating in a vaccine trial

Papillomavirus Research 10 (2020) 100202

Daron G. Ferris[a,*], Darron R. Brown[b], Anna R. Giuliano[c], Evan Myers[d], Elmar A. Joura[e], Suzanne M. Garland[f], Susanne K. Kjaer[g], Gonzalo Perez[h,1], Alfred Saah[h], Alain Luxembourg[h], Christine Velicer[h]

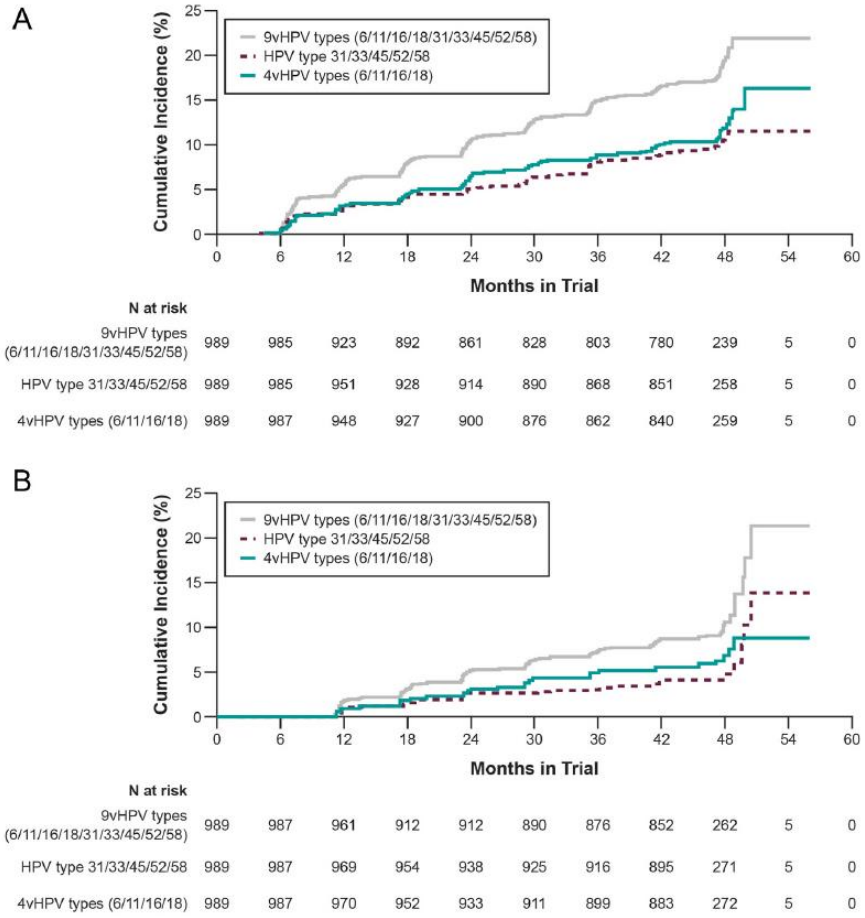
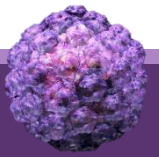


Fig. 1. 48-month cumulative incidence Kaplan–Meier curves among women aged 24 to 45 years for (A) incident infection and (B) incident-persistent infection. "4vHPV": quadrivalent human papillomavirus; "9vHPV": 9-valent human papillomavirus.

- Women aged 24 to 45 years (an age group rarely targeted for HPV immunization) are at risk for acquiring new HPV infections, including infections with HPV types targeted by the 9vHPV vaccine.
- Most infections in this low-risk group of women are single-type HPV infections -> a sizable proportion of adult women remain susceptible to infections with other HPV types to which they may not have yet been exposed.

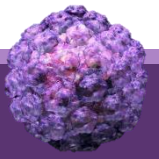


Immunogenicity and safety of a nine-valent human papillomavirus vaccine in women 27–45 years of age compared to women 16–26 years of age: An open-label phase 3 study

Seropositivity rates at month 7 for HPV types 6/11/16/18/31/33/45/52/58 in women aged 16–26 years and women aged 27–45 years (PPI population).

Assay (cLIA)	Women aged 16–26 years (N = 570)			Women aged 27–45 years (N = 640)		
		Seropositivity			Seropositivity	
	n	m (%)	95% CI	n	m (%)	95% CI
Anti-HPV 6	421	420 (99.8)	98.7–100.0	448	448 (100.0)	99.2–100.0
Anti-HPV 11	421	421 (100.0)	99.1–100.0	448	447 (99.8)	98.8–100.0
Anti-HPV 16	436	436 (100.0)	99.2–100.0	448	448 (100.0)	99.2–100.0 [a]
Anti-HPV 18	421	421 (100.0)	99.1–100.0	471	469 (99.6)	98.5–99.9 [a]
Anti-HPV 31	447	447 (100.0)	99.2–100.0	488	487 (99.8)	98.9–100.0 [a]
Anti-HPV 33	457	457 (100.0)	99.2–100.0	493	492 (99.8)	98.9–100.0 [a]
Anti-HPV 45	470	468 (99.6)	98.5–99.9	515	511 (99.2)	98.0–99.8 [a]
Anti-HPV 52	456	456 (100.0)	99.2–100.0	496	496 (100.0)	99.3–100.0 [a]
Anti-HPV 58	451	451 (100.0)	99.2–100.0	478	477 (99.8)	98.8–100.0 [a]

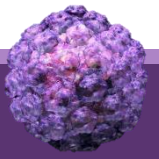
- Antibody responses in women 27–45 y.o. were non-inferior to those observed in women 16–26 y.o.
- The 9vHPV vaccine was generally well tolerated, and the safety profile was similar between women 16–26 y.o. and women 27–45 y.o.
- This supports bridging of efficacy findings from young women 16– 26 y.o. to women 27–45 y.o.



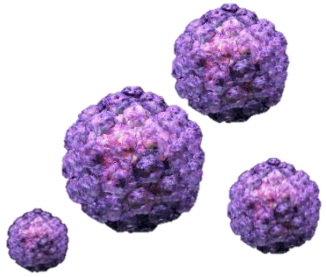
Effectiveness of the Quadrivalent HPV Vaccine in Preventing Anal ≥ HSILs in a Spanish Population of HIV+ MSM Aged > 26 Years

Carmen Hidalgo-Tenorio [1,*], Juan Pasquau [1], Mohamed Omar-Mohamed [2], Antonio Sampedro [3], Miguel A. López-Ruz [1], Javier López Hidalgo [4] and Jessica Ramírez-Taboada [1]

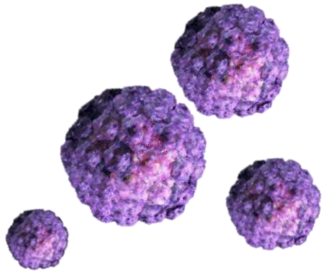
- Randomized, double-blind, placebo-controlled trial of the 4vHPV vaccine, enrollment between May 2012-May 2014 + a 48-month follow-up.
- Participants: 66 (51.2%) in vaccine arm and 63 (48.4%) in placebo arm.
- **The vaccine and placebo groups did not differ in ≥ HSILs** (14.1 vs. 13.1%, respectively, p = 0.98) or **EAGL** (11.1 vs. 6.8%, p = 0.4) rates during follow-up; however, a protective effect against HPV 6 was observed during the first year of follow-up in the vaccine versus placebo group (7.5% vs. 23.4%; p = 0.047).
- A **long-lasting immune response** was observed in almost all the vaccinated men.
- It does not appear recommendable to administer the qHPV vaccine to HIV+ MSM over the age of 26 years.



Viruses. 2021;13(2):144.



HPV cepljenje po odstranitvi predrakavih sprememb na maternični vratu?



Adjuvant HPV Vaccination to Prevent Recurrent Cervical Dysplasia after Surgical Treatment: A Meta-Analysis

Violante Di Donato [1], Giuseppe Caruso [1,*], Marco Petrillo [2,3], Evangelos Kontopantelis [4], Innocenza Palaia [1], Giorgia Perniola [1], Francesco Plotti [5], Roberto Angioli [5], Ludovico Muzii [1], Pierluigi Benedetti Panici [1] and Giorgio Bogani [6]

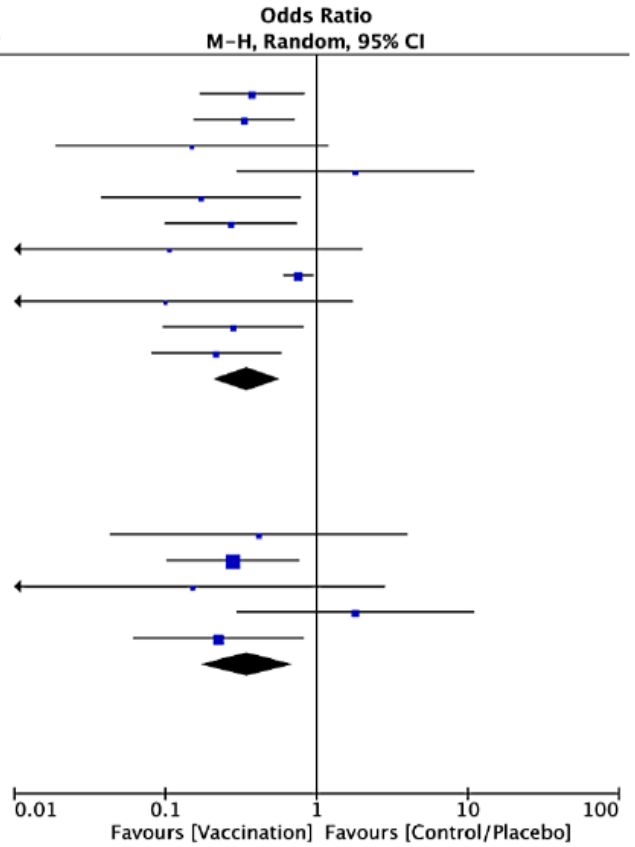
Vaccines **2021**;9:410.

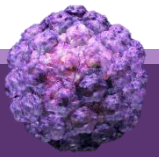
- 11 studies included.
- Prophylactic HPV vaccines as adjuvants to surgery ↓ the risk of relapse of CIN2+ (OR 0.35; 95% CI 0.21–0.56; p < 0.0001).
- Restricting the analysis to HPV16 and 18 = the benefit still equally evident.

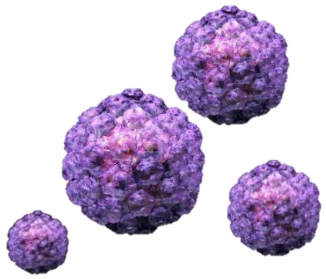
- No consensus on timing.
- 2vHPV vs 4vHPV vs 9vHPV?

Figure 3. Forest plot of comparison: CIN 2+ recurrence regardless of HPV types and CIN2+ recurrence correlated with HPV 16/18.

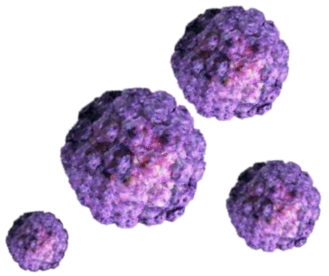
Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
1.1.1 CIN2+ recurrence							
Joura 2012	8	474	26	592	13.1%	0.37 [0.17, 0.83]	2012
Kang 2013	9	360	27	377	13.5%	0.33 [0.15, 0.72]	2013
Garland 2016	1	190	9	264	4.4%	0.15 [0.02, 1.19]	2016
Hildesheim 2016	3	142	2	169	5.4%	1.80 [0.30, 10.94]	2016
Ghelardi 2018	2	172	11	172	6.8%	0.17 [0.04, 0.79]	2018
Ortega 2018	5	103	22	139	10.9%	0.27 [0.10, 0.74]	2018
Pieralli 2018	0	89	4	89	2.4%	0.11 [0.01, 2.00]	2018
Sand 2019	82	2074	777	15054	19.5%	0.76 [0.60, 0.95]	2019
Bogani 2020	0	100	9	200	2.6%	0.10 [0.01, 1.74]	2020
Del Pino 2020	5	153	12	112	10.3%	0.28 [0.10, 0.82]	2020
Petrillo 2020	6	182	14	103	11.1%	0.22 [0.08, 0.58]	2020
Subtotal (95% CI)		**4039**		**17271**	**100.0%**	**0.35 [0.21, 0.56]**	
Total events	121		913				
Heterogeneity: $Tau^2 = 0.30$; $Chi^2 = 24.35$, df = 10 (P = 0.007); $I^2 = 59\%$							
Test for overall effect: Z = 4.25 (P < 0.0001)							
1.1.2 CIN2+ recurrence (HPV 16–18)							
Joura 2012	1	474	3	592	9.3%	0.42 [0.04, 4.00]	2012
Kang 2013	5	197	18	211	43.4%	0.28 [0.10, 0.77]	2013
Garland 2016	0	190	4	264	5.6%	0.15 [0.01, 2.84]	2016
Hildesheim 2016	3	142	2	169	14.5%	1.80 [0.30, 10.94]	2016
Ortega 2018	3	51	15	69	27.2%	0.23 [0.06, 0.82]	2018
Subtotal (95% CI)		**1054**		**1305**	**100.0%**	**0.35 [0.17, 0.69]**	
Total events	12		42				
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 4.15$, df = 4 (P = 0.39); $I^2 = 4\%$							
Test for overall effect: Z = 2.98 (P = 0.003)							







Anogenitalne bradavice



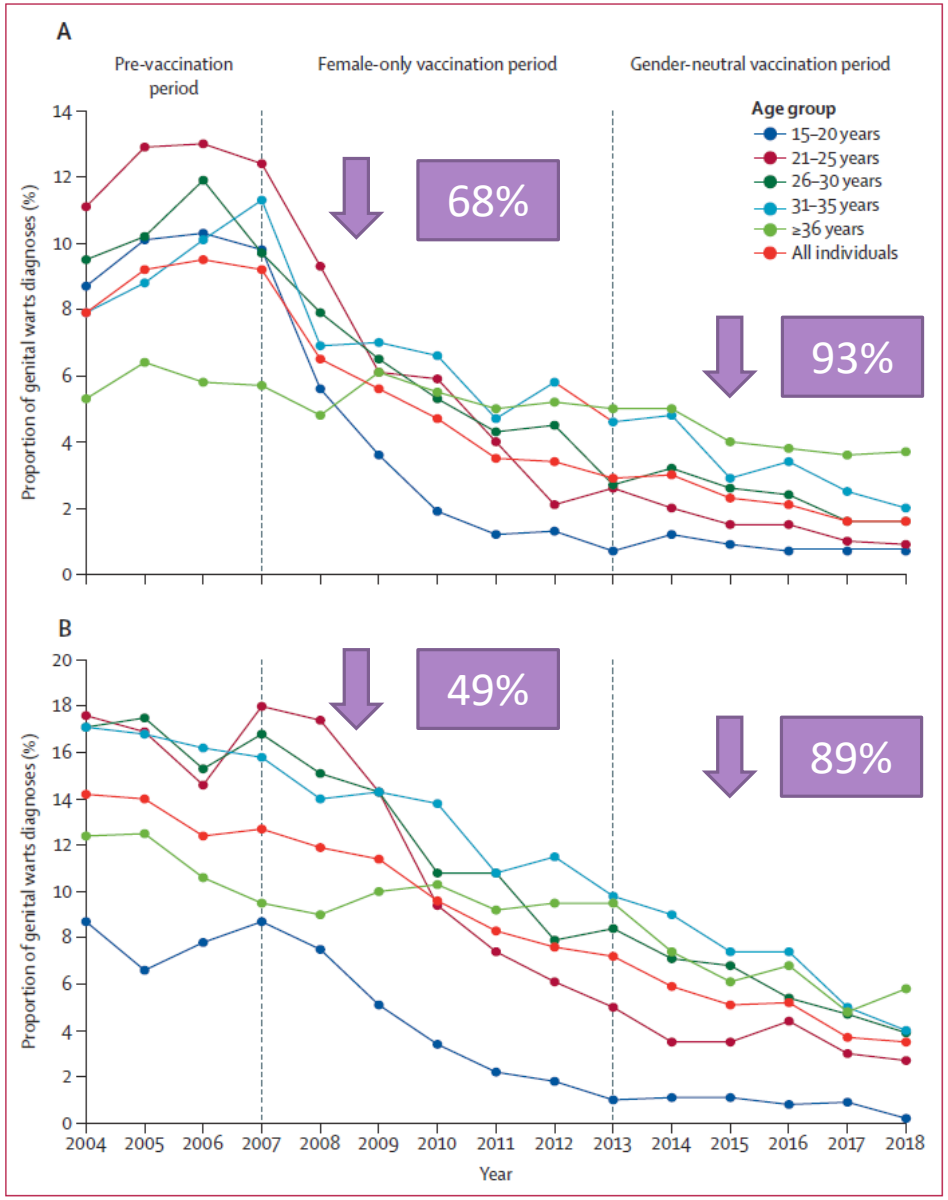
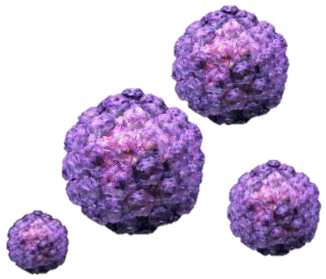


Figure 2: Proportions of genital wart diagnoses in Australian-born female (A) and heterosexual male (B) individuals between 2004 and 2018

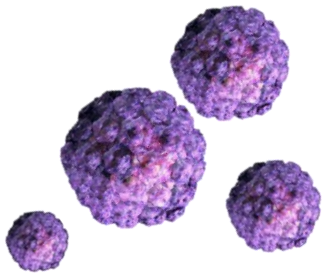
- a **significant and ongoing reduction** in genital warts in both Australian-born female individuals and heterosexual male individuals **11 years after** introduction of the national HPV vaccination
- **substantial ↓** in genital warts were observed among heterosexual males and females **aged 15-20** during the **gender-neutral HPV** vaccination programme
- percentage of genital wart diagnoses in individuals aged 15–20 years has remained at **less than 1%** in the last 3 years of the study period, suggesting **near-elimination of genital warts in young Australian-born women and heterosexual men**

Only 16 diagnoses in 2018

Chow EPF, et al. Lancet Infect Dis 2021;S1473-3099(21)00071-2.

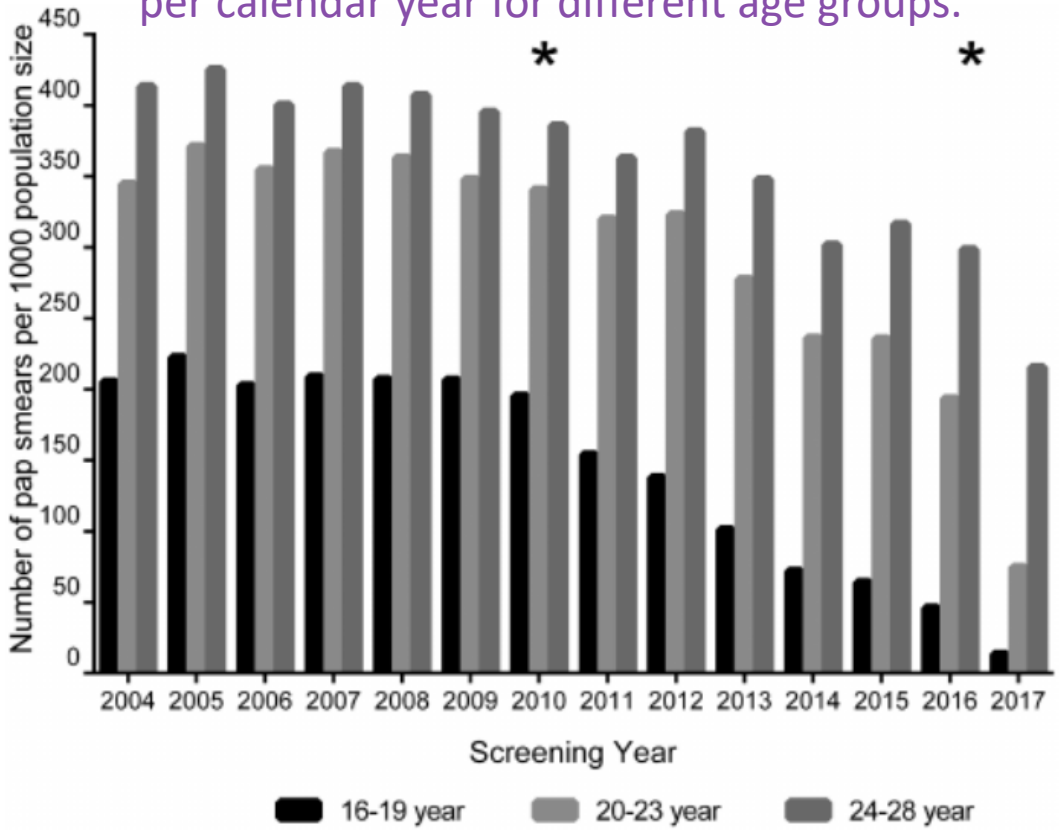


Predrakave spremembe

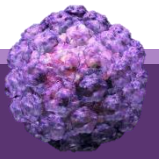


Declining rates of cervical intraepithelial neoplasia in British Columbia, Canada: An ecological analysis on the effects of the school-based human papillomavirus vaccination program

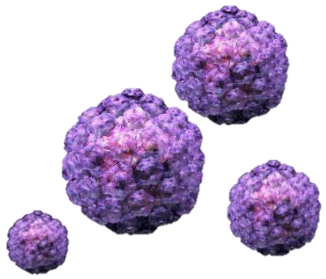
Screening rates (number of smears/population size) per calendar year for different age groups.



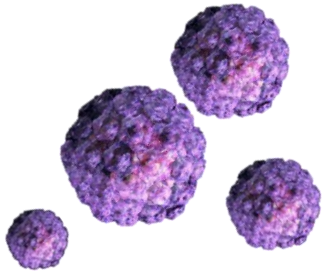
The overall reduction postvaccination for CIN2 and 3 in women 16-23 years was respectively 62% (95% CI 54-68%) and 65% (95% CI 58-71%).



Donken R, et al. Int J Cancer. 2021;149(1):191-199.



Posredni učinki HPV cepljenja



Preterm birth rate after bivalent HPV vaccination: Registry-based follow-up of a randomized clinical trial

Preventive Medicine 146 (2021) 106473

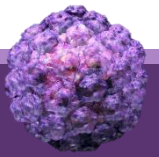
Ilkka Kalliala [a,b], Tiina Eriksson [c], Karoliina Aro [a], Mari Hokkanen [c], Matti Lehtinen [d,e], Mika Gissler [f,g], Pekka Nieminen [a,*]

Table 1
Duration and number of pregnancies among HPV-vaccinated and hepatitis B vaccinated and non-vaccinated reference cohort.

Vaccination status	HPV[a]					HBV[b,c]					Unvaccinated					HBV[b,c] or unvaccinated				
Order of pregnancy	1st	2nd	3rd	4th	Total	1st	2nd	3rd	4th	Total	1st	2nd	3rd	4th	Total	1st	2nd	3rd	4th	Total
Duration of pregnancy (weeks)																				
Early preterm 22 + 0 to 31 + 6	0	0	0	0	0	0	0	0	0	0	20	1	1	0	22	20	1	1	0	22
Preterm 32 + 0 to 36 + 6	13	3	0	0	16	10	3	0	0	13	68	9	1	0	78	78	12	1	0	91
Term ≥ 37 + 0	396	68	1	0	465	170	41	2	1	214	1658	361	36	2	2057	1825	405	38	3	2271
Total	409	71	1	0	481	180	44	2	1	227	1746	371	38	2	2157	1923	418	40	3	2384

[a] CervarixVR (AS04-HPV-16/18) -vaccine.
[b] EngerixTM B (hepatitis B-virus, HBV) -vaccine.
[c] Women cross-vaccinated with HPV-vaccine at the age of 18.5 ($n = 2256$) excluded.

- Interestingly, early preterm birth rate was 0/409 (0%) in HPV-vaccinated women and 20/1923 (1.0%) in non-HPV-vaccinated women (p = 0.04).
- Small study & overall PTB rates non-statistically significantly lower but early PTB (<32 pregnancy weeks) rates significantly less common among HPV-vaccinated women.

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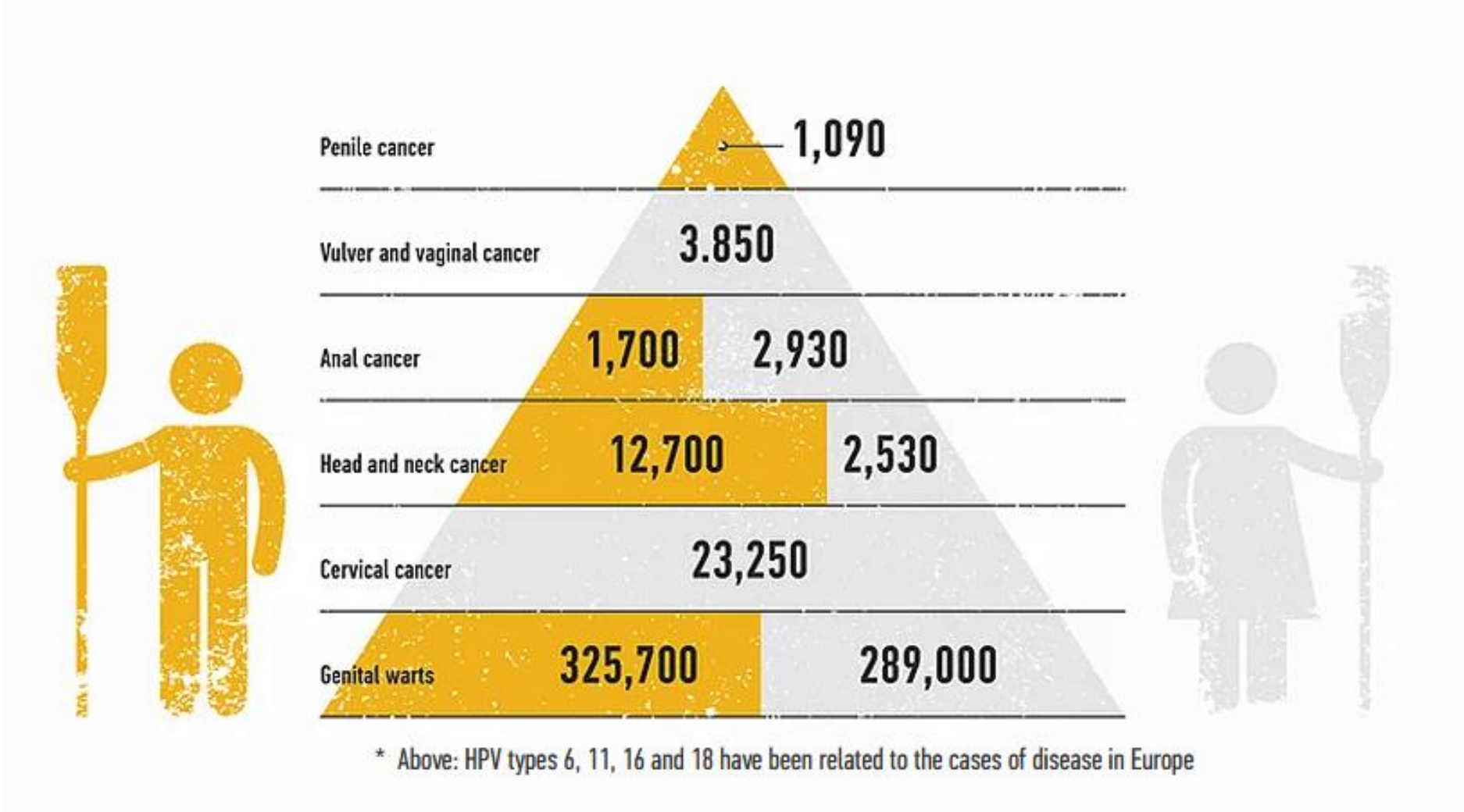


* Above: HPV types 6, 11, 16 and 18 have been related to the cases of disease in Europe

Zakaj sploh cepiti?

NARAVNA OKUŽBA

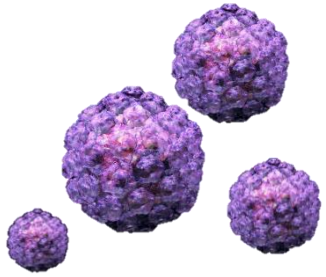
- **Ženske** :
  - Serokonverzija pri 54-69% okuženih
  - Nizki titri protiteles
  - Delna zaščita pred ponovnimi okužbami

- **Moški**:
  - Serokonverzija pri 7-10% okuženih
  - Nizki titri protiteles
  - Ni zaščite pred ponovnimi okužbami

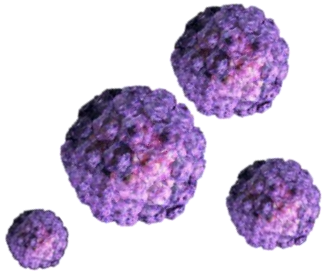
CEPLJENJE

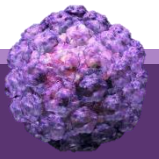
- **Skoraj 100% serokonverzija pri obeh spolih!!**
- **VLP so zelo imunogeni:**
  - **Izražajo več nevtralizirajočih epitopov kot HPV**
  - **Pomembni za protitelesni in celični imunski odziv**

Zakaj cepiti oba spola?



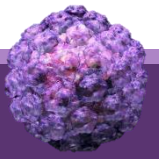
HPV okužbe in predrakave spremembe v analnem področju





Sexual positioning practices and anal human papillomavirus infection among young men who have sex with men and transgender women — Chicago, Illinois, 2016–2018

- Among 666 young MSM and transgender women aged 18-26 years in Chicago (IL), **400 (60.1%) had any anal HPV**, and **146 (21.9%) had a 4vHPV type**.
- Risk for a detectable 4vHPV type and any HPV type in anal specimen:
  - older individuals
  - those engaging in any condomless anal sex
  - HIV-infected
- Compared to participants reporting exclusively insertive anal sex, odds of any HPV were significantly higher among participants **engaging exclusively in receptive anal sex** (aOR=5.90, 95% CI: 2.52-13.78) as well as those engaging in both (aOR=3.32; 95% CI: 1.71-6.44).
- **Vaccinated participants**, compared with unvaccinated participants, had **lower odds of 4vHPV-type regardless of sexual positioning practices** (aOR=0.56; 95% CI: 0.34-0.92).

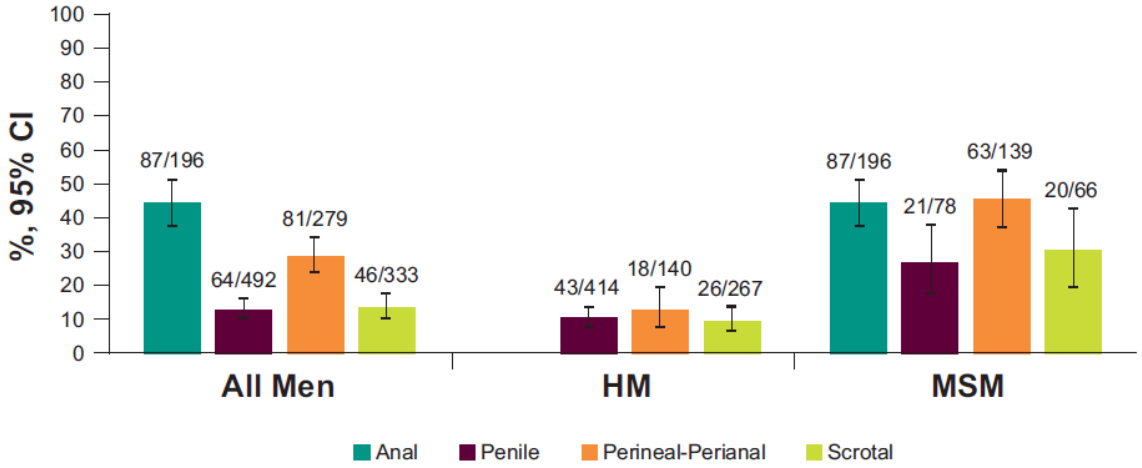


Morgan E, et al. Sex Transm Dis. 2021. doi: 10.1097/OLQ.0000000000001433.

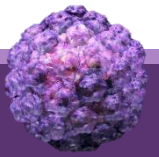
Anogenital Human Papillomavirus (HPV) Infection, Seroprevalence, and Risk Factors for HPV Seropositivity Among Sexually Active Men Enrolled in a Global HPV Vaccine Trial

Joseph E. Tota,[1] Anna R. Giuliano,[2] Stephen E. Goldstone,[3] Brady Dubin,[1] Alfred Saah,[1] Alain Luxembourg,[1] Christine Velicer,[1] and Joel M. Palefsky[4]

Seroprevalence (for any 9vHPV vaccine type) among participants who were DNA positive to concordant 9vHPV vaccine types, stratified by anatomic site and sexual orientation.



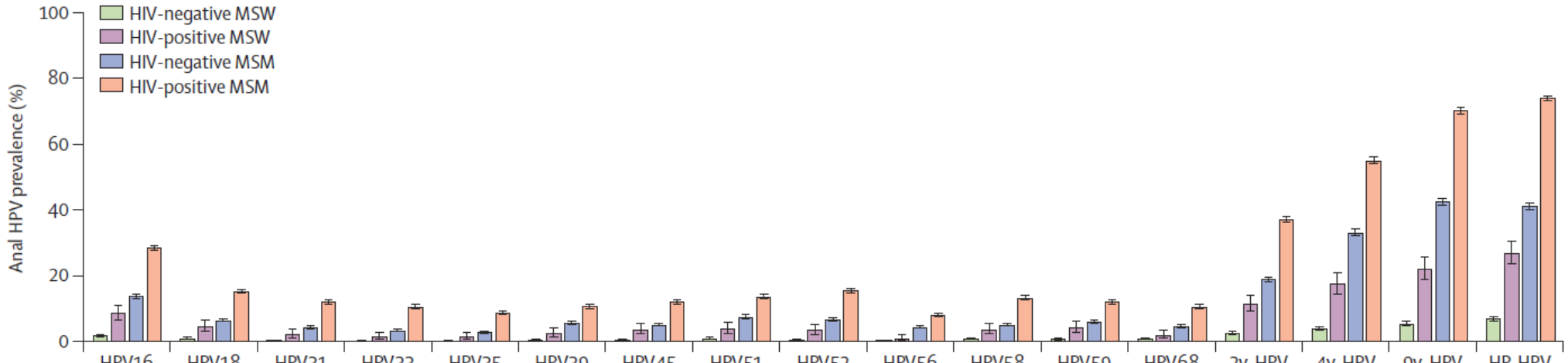
- Overall, 455/3463 (13.1%) heterosexual and 228/602 (37.9%) MSM were HPV DNA positive for any 9vHPV vaccine type at baseline.
- Risk of seropositivity among MSM increased with:
  - the number of receptive anal sex partners
  - younger age at sexual debut
  - infrequent lifetime condom use
- a substantial proportion of young sexually active men with <6 lifetime sexual partners have either not been exposed to HPV types targeted by the 9vHPV vaccine, or if exposed, have not seroconverted after infection→ **vaccination!**



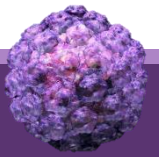
Clin Infect Dis. 2021;ciab603.

Epidemiology of anal human papillomavirus infection and high-grade squamous intraepithelial lesions in 29 900 men according to HIV status, sexuality, and age: a collaborative pooled analysis of 64 studies

Prevalence of type-specific and grouped type HPV infection in four male risk groups

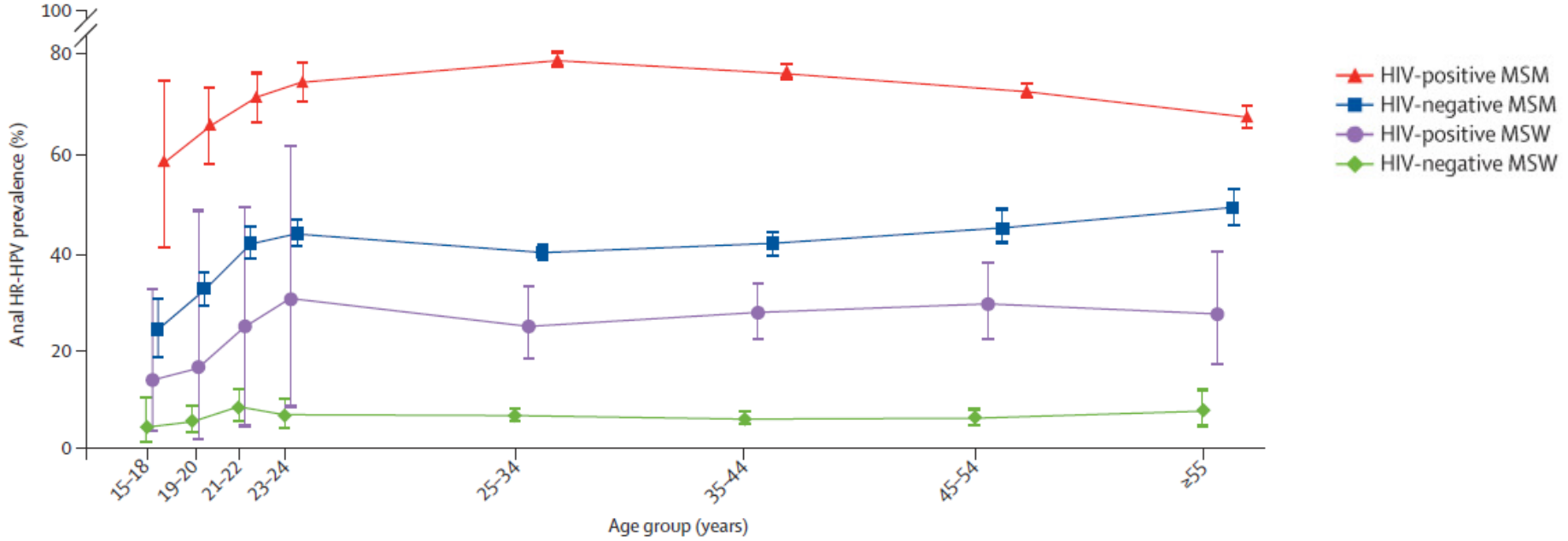


	HPV16	HPV18	HPV31	HPV33	HPV35	HPV39	HPV45	HPV51	HPV52	HPV56	HPV58	HPV59	HPV68	2v-HPV	4v-HPV	9v-HPV	HR-HPV
HIV-negative MSW (n/N, %)	91/5190 (1·8%)	45/5190 (0·9%)	12/4984 (0·2%)	5/4984 (0·1%)	4/5161 (0·1%)	22/5161 (0·4%)	26/5161 (0·5%)	45/5161 (0·9%)	26/5161 (0·5%)	14/5161 (0·3%)	38/5161 (0·7%)	32/5161 (0·6%)	39/5161 (0·8%)	134/5190 (2·6%)	204/5158 (4·0%)	269/4981 (5·4%)	345/5003 (6·9%)
HIV-positive MSW (n/N, %)	59/682 (8·7%)	32/682 (4·7%)	12/572 (2·1%)	8/572 (1·4%)	8/583 (1·4%)	15/583 (2·6%)	22/614 (3·6%)	22/583 (3·8%)	20/583 (3·4%)	5/583 (0·9%)	21/583 (3·6%)	24/583 (4·1%)	11/583 (1·9%)	78/682 (11·4%)	102/582 (17·5%)	127/571 (22·2%)	179/666 (26·9%)
HIV-negative MSM (n/N, %)	1455/10 617 (13·7%)	684/10 617 (6·4%)	361/8673 (4·2%)	285/8673 (3·3%)	232/8710 (2·7%)	481/8710 (5·5%)	463/9112 (5·1%)	650/8710 (7·5%)	574/8710 (6·6%)	377/8710 (4·3%)	438/8710 (5·0%)	508/8710 (5·8%)	373/7997 (4·7%)	1795/9497 (18·9%)	2809/8447 (33·3%)	3415/8008 (42·6%)	3798/9215 (41·2%)
HIV-positive MSM (n/N, %)	3819/13 411 (28·5%)	2007/13 213 (15·2%)	1115/9341 (11·9%)	982/9341 (10·5%)	773/8917 (8·7%)	945/8917 (10·6%)	1260/10 448 (12·1%)	1211/8917 (13·6%)	1460/9387 (15·6%)	708/8917 (7·9%)	1239/9388 (13·2%)	1065/8917 (11·9%)	898/8586 (10·5%)	4730/12 645 (37·4%)	4962/8990 (55·2%)	5982/8490 (70·5%)	8765/11 803 (74·3%)



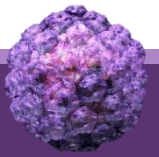
Wei F, et al. Lancet HIV. 2021:S2352-3018(21)00108-9.

HR-HPV infection in four male risk groups



Age group, years	15–18	19–20	21–22	23–24	25–34	35–44	45–54	≥55
HIV-positive MSM	21/36	100/152	209/293	346/465	2345/2982	2503/3281	2111/2915	1130/1679
(n/N, %)	(58·3%)	(65·8%)	(71·3%)	(74·4%)	(78·6%)	(76·3%)	(72·4%)	(67·3%)
aPR (95% CI)	0·77 (0·59–1·02)	0·85 (0·76–0·96)*	0·94 (0·88–1·00)	0·96 (0·90–1·01)	1 (ref)	0·96 (0·94–0·99)*	0·91 (0·88–0·94)*	0·83 (0·80–0·87)*
HIV-negative MSM	54/221	216/665	373/892	501/1142	1236/3095	673/1611	392/867	353/722
(n/N, %)	(24·4%)	(32·5%)	(41·8%)	(43·9%)	(39·9%)	(41·8%)	(45·2%)	(48·9%)
aPR (95% CI)	0·74 (0·58–0·94)*	0·90 (0·80–1·02)	0·99 (0·90–1·08)	0·99 (0·92–1·08)	1 (ref)	1·04 (0·96–1·11)	0·99 (0·90–1·09)	0·99 (0·89–1·11)
HIV-positive MSW	4/28	2/12	5/20	4/13	36/143	67/240	43/145	18/65
(n/N, %)	(14·3%)	(16·7%)	(25·0%)	(30·8%)	(25·2%)	(27·9%)	(29·7%)	(27·7%)
aPR (95% CI)	1·83 (0·44–7·67)	1·15 (0·31–4·20)	0·87 (0·43–1·78)	1·41 (0·63–3·16)	1 (ref)	0·94 (0·67–1·31)	0·68 (0·44–1·03)	0·57 (0·35–0·95)*
HIV-negative MSW	5/103	18/303	28/317	24/333	108/1513	82/1269	62/942	18/223
(n/N, %)	(4·9%)	(5·9%)	(8·8%)	(7·2%)	(7·1%)	(6·5%)	(6·6%)	(8·1%)
aPR (95% CI)	0·57 (0·23–1·44)	0·91 (0·57–1·43)	1·11 (0·90–1·37)	0·79 (0·52–1·21)	1 (ref)	0·96 (0·74–1·25)	1·07 (0·86–1·32)	0·86 (0·53–1·39)

High anal HPV prevalence among young HIV-positive and HIV-negative MSM highlights the benefits of gender-neutral HPV vaccination before sexual activity over catch-up vaccination.



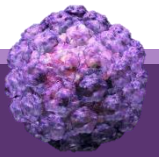
Wei F, et al. Lancet HIV. 2021:S2352-3018(21)00108-9.

Prevalence of anal HSIL

	Anal HSIL+ in all MSM (n=12 577)		HPV16-positive anal HSIL+* in all MSM (n=12 577)		Anal HSIL+ in HPV16-positive MSM (n=3409)	
	n/N (%)	aPR (95% CI)	n/N (%)	aPR (95% CI)	n/N (%)	aPR (95% CI)
Age group, years						
15–24	72/794 (9·1%)	0·98 (0·78–1·22)	23/794 (2·9%)	0·76 (0·50–1·17)	23/183 (12·6%)	0·89 (0·62–1·29)
25–34	452/2847 (15·9%)	1 (ref)	200/2847 (7·0%)	1 (ref)	200/847 (23·6%)	1 (ref)
35–44	725/3307 (21·9%)	1·00 (0·91–1·10)	334/3307 (10·1%)	0·99 (0·84–1·17)	334/965 (34·6%)	1·13 (0·99–1·28)
45–54	778/3278 (23·7%)	0·95 (0·86–1·05)	343/3278 (10·5%)	0·90 (0·76–1·07)	343/903 (38·0%)	1·09 (0·95–1·24)
≥55	480/2351 (20·4%)	0·89 (0·79–0·99)†	221/2351 (9·4%)	0·91 (0·75–1·10)	221/511 (43·2%)	1·19 (1·03–1·36)†
Age, per 10 years	..	0·96 (0·94–0·99)†	..	0·97 (0·92–1·02)	..	1·05 (1·01–1·09)†
HIV status						
Negative	314/2785 (11·3%)	1 (ref)	138/2785 (5·0%)	1 (ref)	138/514 (26·8%)	1 (ref)
Positive	2193/9792 (22·4%)	1·54 (1·36–1·73)†	983/9792 (10·0%)	1·66 (1·36–2·03)†	983/2895 (34·0%)	1·19 (1·04–1·37)†

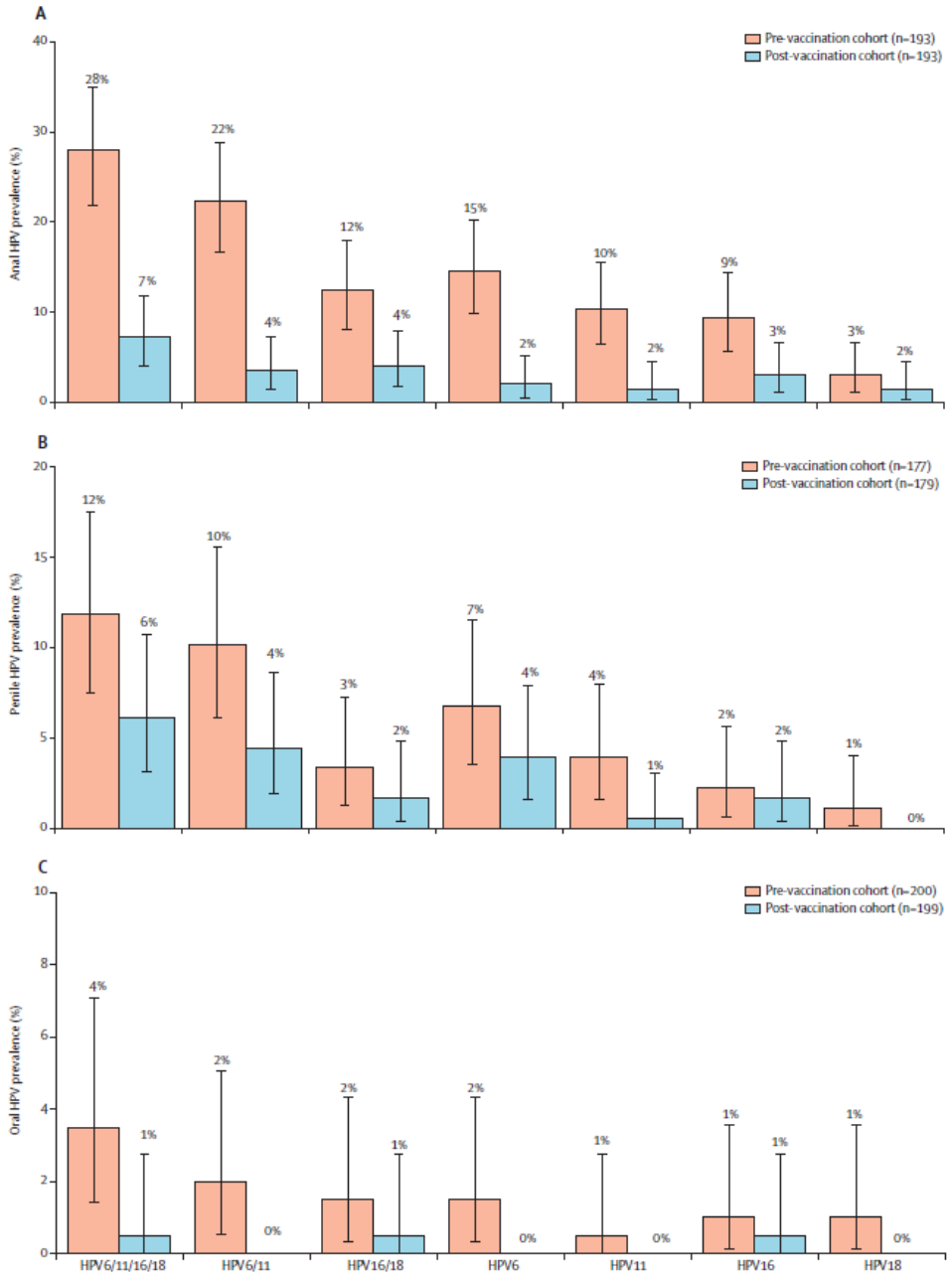
PRs were adjusted for study, age group, and HIV status, as appropriate. aPR=adjusted prevalence ratio. HPV=human papillomavirus. HSIL+=high-grade squamous intraepithelial lesions or worse. MSM=men who have sex with men. *Only includes participants with HSIL+ plus HPV16-positive swabs. †Significant aPRs relative to the reference group.

Anoscopy?

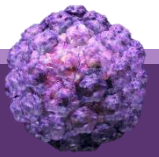


Prevalence of human papillomavirus in young men who have sex with men after the implementation of gender-neutral HPV vaccination: a repeated cross-sectional study

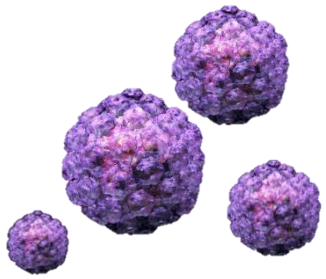
Eric P F Chow, Sepehr N Tabrizi, Christopher K Fairley, Rebecca Wigan, Dorothy A Machalek, Suzanne M Garland, Alyssa M Cornall, Steph Atchison, Jane S Hocking, Catriona S Bradshaw, Prisha Balgovind, Gerald L Murray, Marcus Y Chen



- Among MSM aged 16–20 years who were recruited 4 years after the implementation of a gender-neutral 4vHPV vaccination programme, we found ↓ in prevalence of HPV types 6, 11, 16, or 18 in the anus (76%), penis (52%), and oral cavity (90%) compared with a pre-vaccination cohort.
- These data suggest that overall HPV carriage in young MSM was lower after the inclusion of adolescents in the national school-based HPV vaccination programme.
- 70% reduction in the prevalence of anal HPV16—the genotype most commonly linked with anal cancer.



Lancet Infect Dis. 2021:S1473-3099(20)30687-3.



Rak ustnega dela žrela

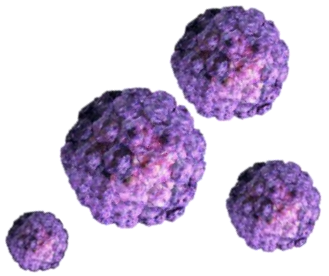
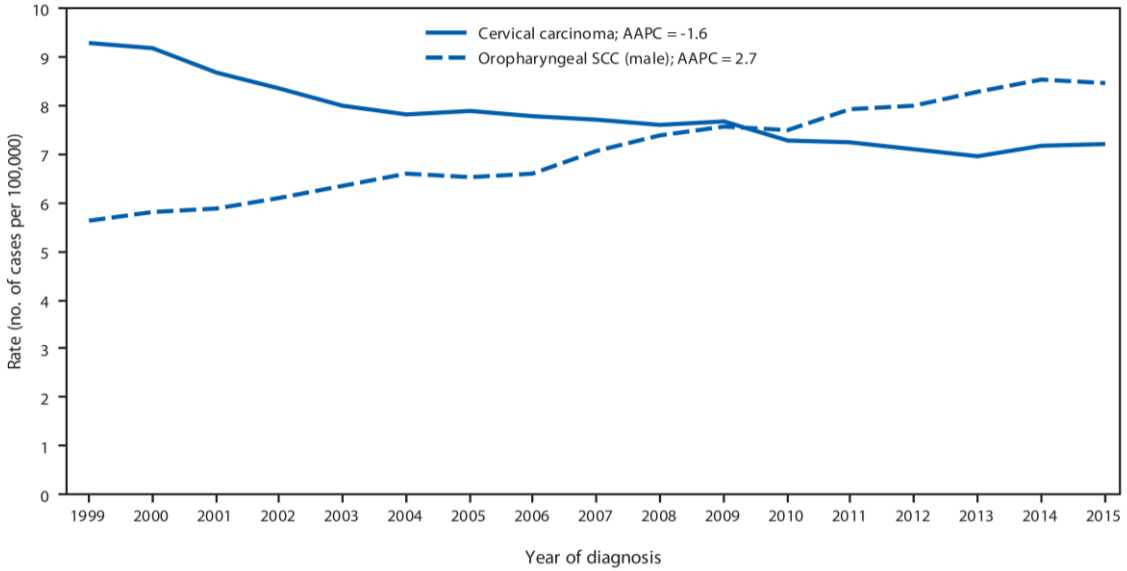


FIGURE 1. Trends* in age-adjusted incidence of cervical carcinoma among females and oropharyngeal SCC among men,† — United States,§ 1999–2015



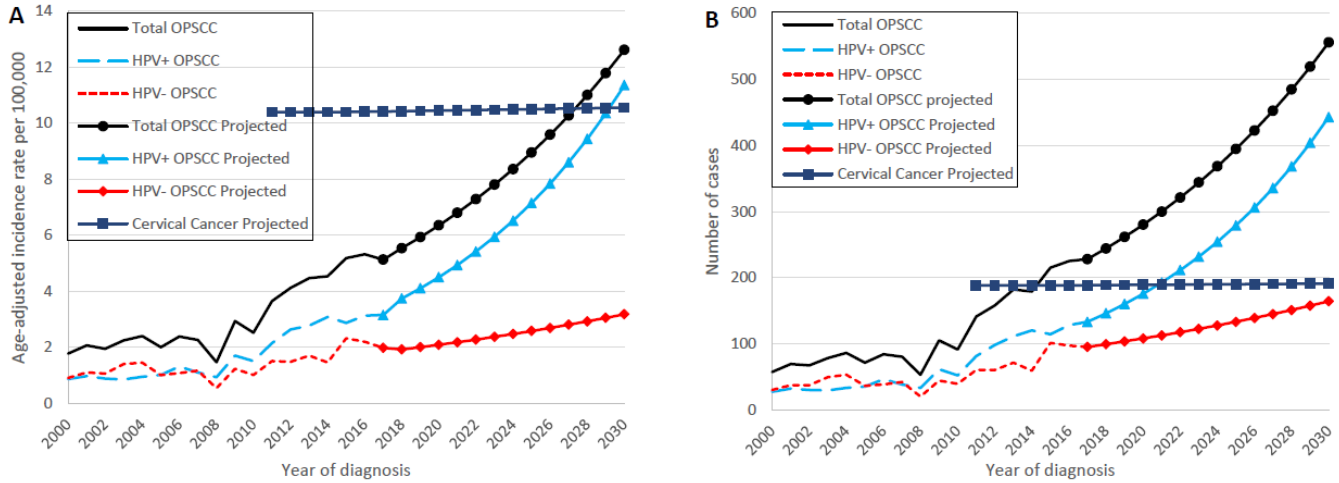


Fig. 1. Age-adjusted incidence rate per 100,000 (A) and absolute number of cases of OPSCC (B) in Eastern Denmark from 2000 to 2017, stratified by HPV status. Projected numbers for 2018–2030, calculated using the average-annual percentage change, are also shown. *OPSCC = oropharyngeal squamous cell carcinoma, HPV = human papillomavirus.*

Van Dyne EA, et al. MMWR Morb Mortal Wkly Rep 2018;918–24.

Zamani M, et al. Eur J Cancer 2020;134:52–59.

GARDASIL 9

STN: 125508
Proper Name: Human Papillomavirus 9-valent Vaccine, Recombinant
Tradename: GARDASIL 9
Manufacturer: Merck Sharp & Dohme Corp.
Indications:

- Indicated in girls and women 9 through 45 years of age for the prevention of the following diseases:
  - Cervical, vulvar, vaginal, anal, oropharyngeal and other head and neck cancers caused by Human Papillomavirus (HPV) types 16, 18, 31, 33, 45, 52, and 58.
  - Genital warts (condyloma acuminata) caused by HPV types 6 and 11.
- And the following precancerous or dysplastic lesions caused by HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58:
  - Cervical intraepithelial neoplasia (CIN) grade 2/3 and cervical adenocarcinoma *in situ* (AIS).
  - Cervical intraepithelial neoplasia (CIN) grade 1.
  - Vulvar intraepithelial neoplasia (VIN) grade 2 and grade 3.
  - Vaginal intraepithelial neoplasia (VaIN) grade 2 and grade 3.
  - Anal intraepithelial neoplasia (AIN) grades 1, 2, and 3.
- Indicated in boys and men 9 through 45 years of age for the prevention of the following diseases:
  - Anal, oropharyngeal and other head and neck cancers caused by HPV types 16, 18, 31, 33, 45, 52, and 58.
  - Genital warts (condyloma acuminata) caused by HPV types 6 and 11.
- And the following precancerous or dysplastic lesions caused by HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58:
  - Anal intraepithelial neoplasia (AIN) grades 1, 2, and 3.

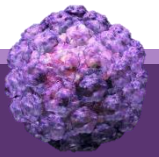
Content current as of:
08/21/2020

Regulated Product(s)
Biologics

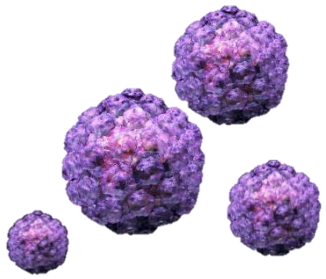
Table 4 Knowledge of reported risk factor for oropharyngeal cancer in the general Dutch population ($N = 1044$)

Risk factor	Yes		No		Not sure	
	N	%	*N*	%	*N*	%
Excessive alcohol consumption	626	60.0	139	13.3	279	26.7
Smoking	1016	97.3	10	1.0	18	1.7
Chewing of tobacco	778	74.5	48	4.6	218	20.9
Chewing of betel leaf. catchu and areca nuts	317	30.4	87	8.3	640	61.3
Marijuana use	547	52.4	109	10.4	388	37.2
Poor oral hygiene	398	38.1	274	26.2	372	25.6
Herpes simplex virus infection	277	26.5	139	13.3	628	60.2
Human papilloma virus infection	281	26.9	112	10.7	651	62.4
Family history of cancer	646	61.9	136	13.0	262	25.1
Low fruit and vegetable consumption	253	24.2	338	32.4	453	43.4
Sun exposure	167	16.0	454	43.5	423	40.5

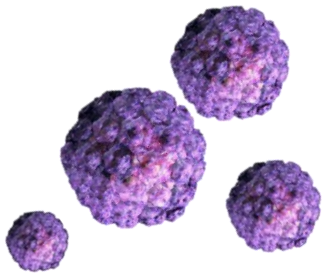
- 1044 ♀ ♂ 18+
- 30.6% of the population had heard of HPV
- lower knowledge
  - males
  - people older than 65 years
  - low education level
  - current smokers
- 49.7% of the population knew of the existence of an HPV vaccine



Verhees F, et al. Eur J Public Health. 2021:ckab081. doi: 10.1093/eurpub/ckab081.



Rak penisa



Effectiveness Of Human Papillomavirus (HPV) Vaccination Against Penile Hpv Infection In Men Who Have Sex With Men And Transgender Women

Rachel L Winer ✉, John Lin, Troy D Querec, Elizabeth R Unger, Joshua E Stern, Jessica M Rudd, Matthew R Golden, Fred Swanson, Lauri E Markowitz, Elissa Meites ✉

The Journal of Infectious Diseases, jiab390, https://doi.org/10.1093/infdis/jiab390

Published: 28 July 2021 **Article history** ▾

Abstract

Background

In the United States, HPV vaccination has been recommended since 2011 for males aged 11–12 years, with catch-up vaccination recommended through age 26 years for previously unvaccinated men who have sex with men (MSM).

Methods

During 2016-2018, a cross-sectional study enrolled MSM and transgender women aged 18–26 years in Seattle, Washington. Participants submitted self-collected penile swab specimens for HPV genotyping. HPV vaccination history was self-reported. We compared HPV prevalence among vaccinated participants versus participants with no/unknown vaccination history using log-binomial regression to estimate adjusted prevalence ratios (aPR) and confidence intervals (CI).

Results

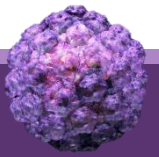
Among 687 participants, 348 (50.7%) self-reported ever receiving ≥1 HPV vaccine dose; median age at first HPV vaccination was 21 years and median age at first sex was 17 years. Overall, prevalence of penile quadrivalent HPV vaccine (4vHPV)-type HPV was similar in vaccinated participants (12.1%) and participants with no/unknown vaccination (15.6%) (aPR=0.69, 95%CI:0.47-1.01). However, prevalence was significantly lower in participants vaccinated at age ≤18 years than in participants with no/unknown vaccination (aPR=0.15, 95%CI:0.04-0.62), corresponding to a vaccine effectiveness of 85% against 4vHPV-type HPV.

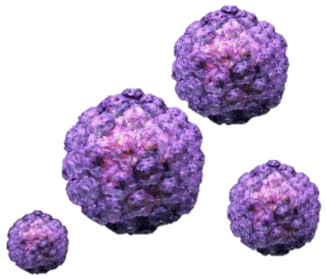
Conclusions

Results suggest HPV vaccination is effective in preventing penile HPV infections in young MSM when administered at age ≤18 years.

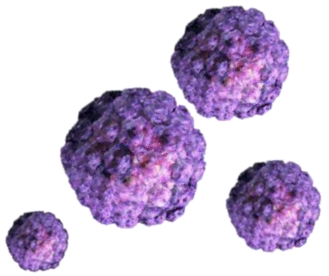
There is **no** **FDA indication for the prevention of penile cancers**; the one HPV vaccine efficacy trial that included penile outcomes was not powered for efficacy against penile intraepithelial neoplasias.

Vaccine Impact in Men (VIM) study: penile HPV prevalence (48.5% for any type); **no 4vHPV-type HPV** was detected in participants who reported that their **age at first HPV vaccine dose was < than their age at first sex**.





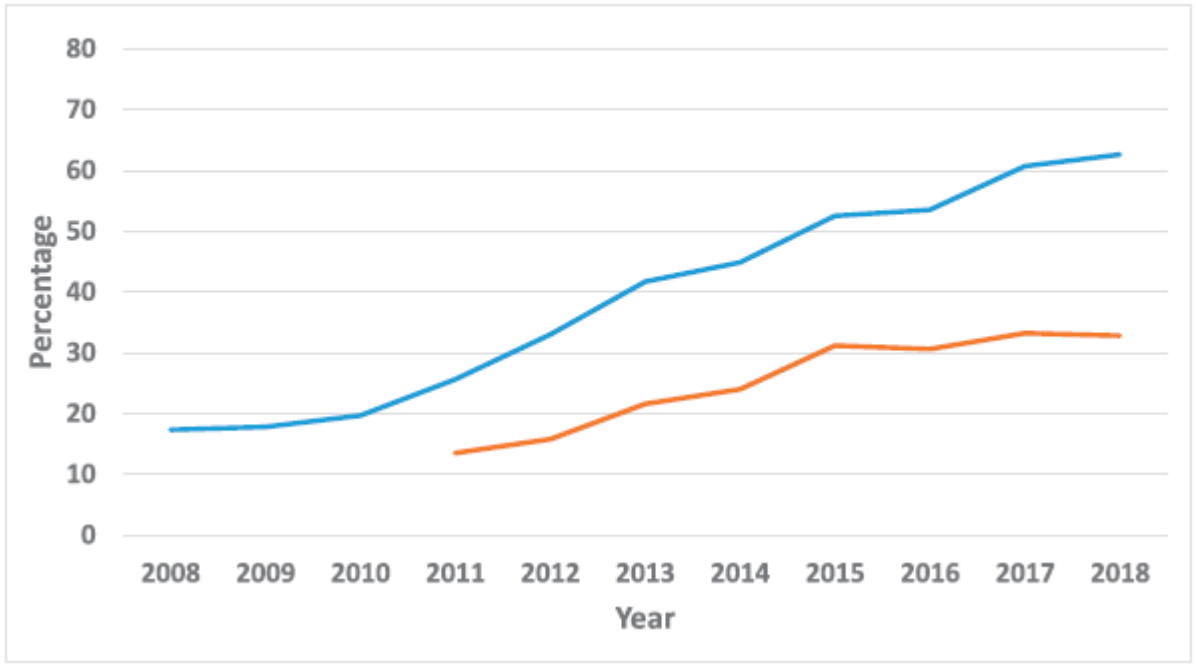
HPV cepljenje v Evropi in po svetu



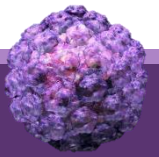
Trends in HPV Vaccination Initiation and Completion Within Ages 9–12 Years: 2008–2018

Onyema Greg Chido-Amajuoyi, MBBS, MPH,[a,*] Rajesh Talluri, PhD,[b,*] Chizoba Wonodi, MBBS, DrPH,[c] Sanjay Shete, PhD[a,d,e]

Trends in routine HPV vaccination within ages 9 to 12 years, USA

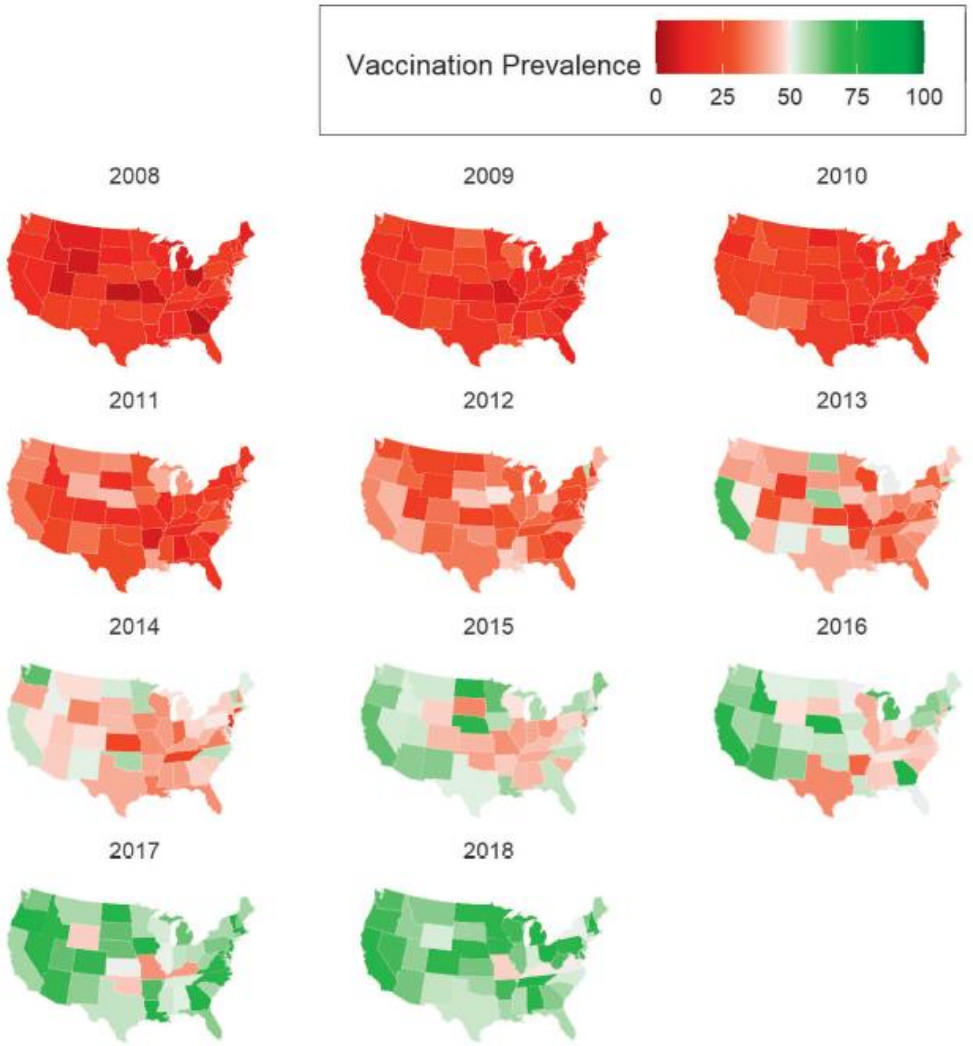


Uptake of HPV vaccination rose steadily over the years, completion of the vaccination series by age 13 years was low, with a large proportion of adolescents getting their full series as catch-up shots.

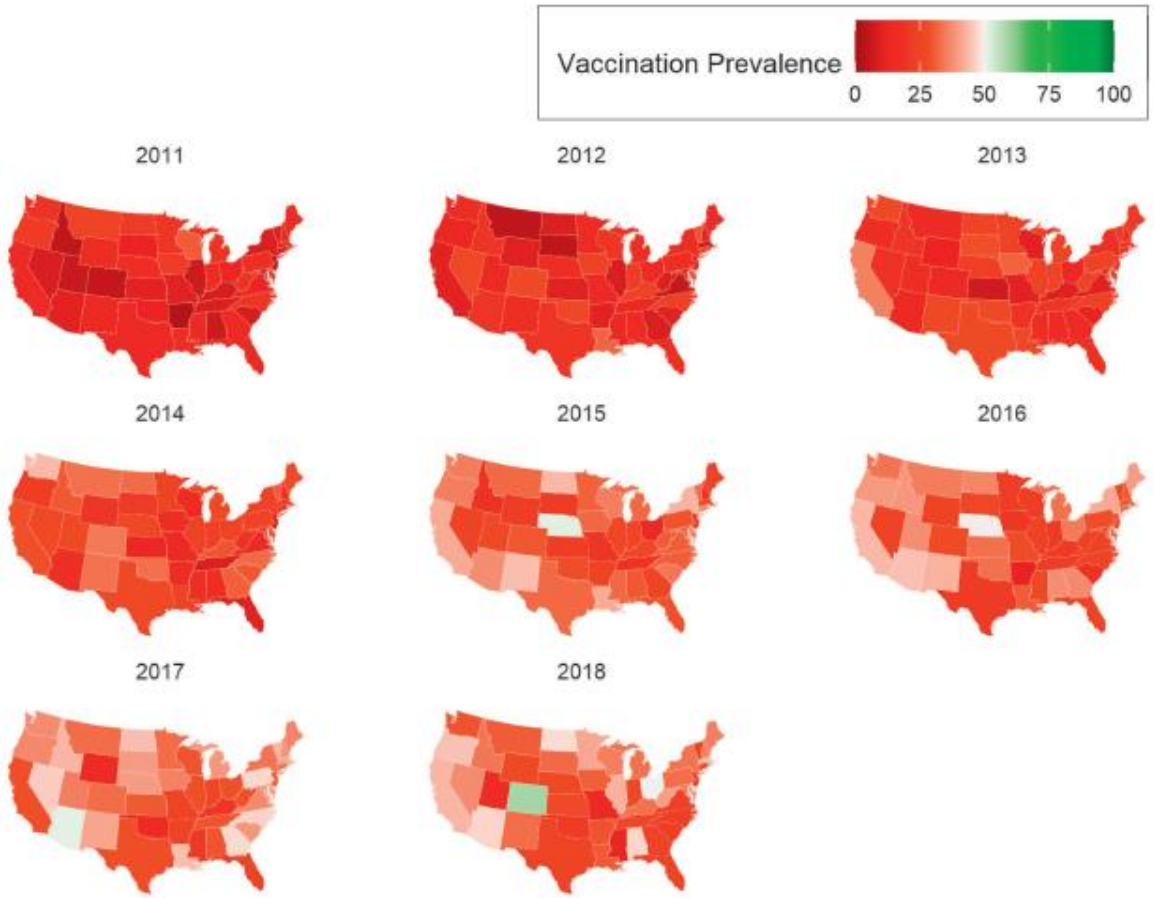


Pediatrics. 2021;147:e2020012765.

National maps depicting trends in HPV vaccination initiation within ages 9 to 12 years, by state



National maps depicting trends in HPV-UTD within ages 9 to 12 years, by state

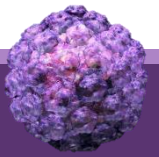


Chido-Amajuoyi OG, et al. Pediatrics. 2021;147:e2020012765.

Trends in routine HPV vaccination within ages 9 to 12 years by sociodemographic factors, NIS-Teen, 2008–2018.

Initiation

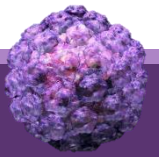
Up-to-date



Chido-Amajuoyi OG, et al. Pediatrics. 2021;147:e2020012765.

The status of human papillomavirus vaccination recommendation, funding, and coverage in WHO Europe countries (2018–2019)

Background: There is a need to better understand HPV vaccination (HPVv) implementation in WHO Europe Region (WHO/ER), including recommendations, funding, and vaccination coverage rates (VCR).
Methods: A targeted literature review (up to 31 January 2020) was conducted using national health ministry websites, WHO database, and published studies from WHO/ER countries (n = 53). HPVv recommendations and funding data (target age, gender, schedule, setting, target and monitored VCR) for primary and catch-up cohorts were collected.
Results: National recommendations for HPVv exist in 46/53 (87%) countries, of which 38 (83%), 2 (4%), and 6 (13%) countries provided full, partial, or no funding, respectively, for the primary cohort. Fully or partially funded HPVv was provided for girls only in 25/53 (47%) countries and for both boys and girls in 15/53 (28%) countries. HPVv catch-up was fully or partially funded in 14/53 (26%) countries. Among 40 countries with a national immunization program (NIP), monitored VCRs ranged from 4.3% to 99% (n = 30). Of the 10 countries reporting VCR targets, only Portugal exceeded its target.
Conclusion: Of the 53 WHO/ER countries, 40 have funded HPVv NIPs, among which 30 report VCRs. Additional efforts are required to ensure HPVv NIPs are fully funded and high VCRs maintained.



Bonanni P, et al. Expert Rev Vaccines. 2020;19:1073-1083.

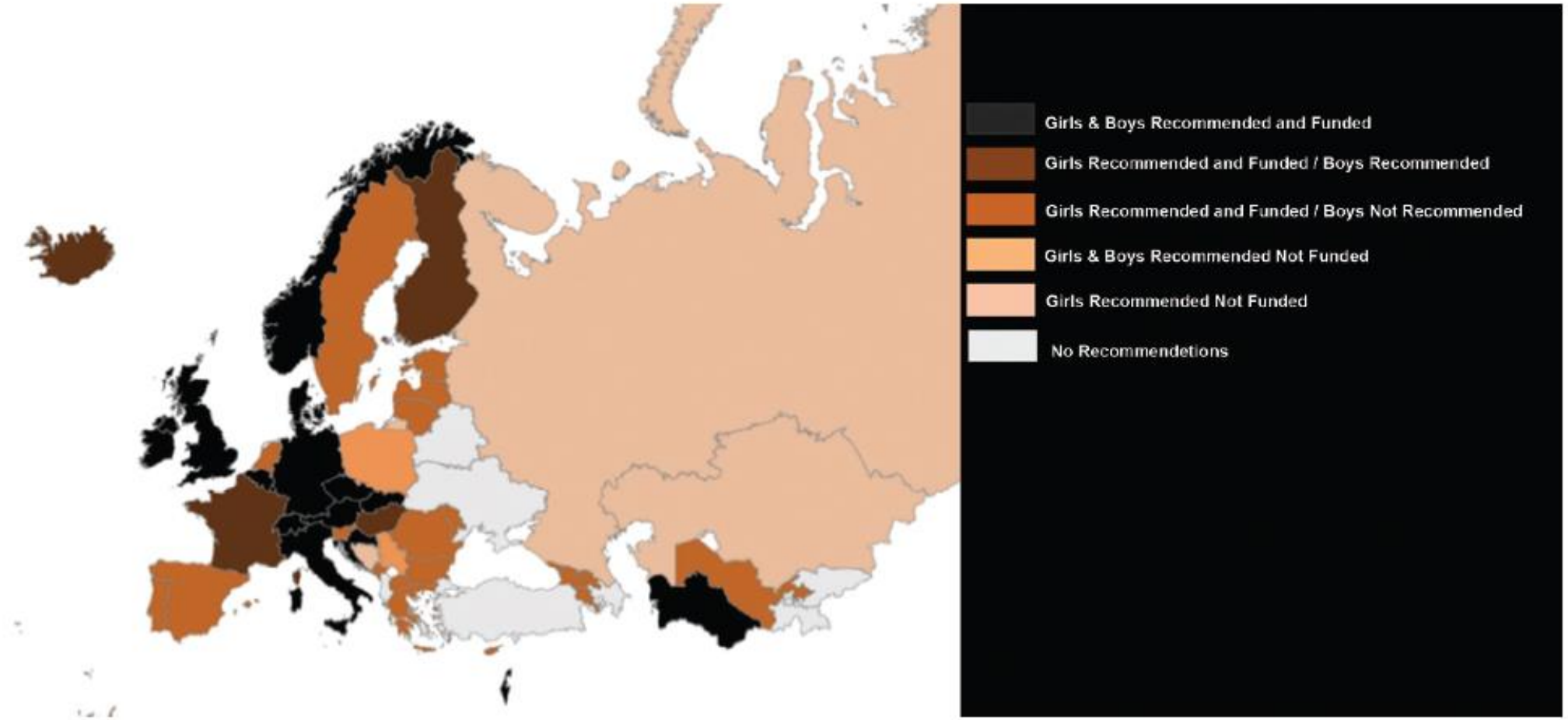
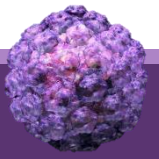


Figure 1. Recommendations and funding status across the WHO/ER for the primary cohort in girls and boys.

Table 5. List of WHO/ER countries with target VCR (n = 10).

Country	Target VCR (%, definition where available)	Monitored VCR	VCR range	Primary cohort gender	Target year	HPVv dose received	Primary cohort age
Portugal	85%, for 10–14 y/o girls	90%-94%*	○○○○	F	2018	≥2	2004–2006 birth cohort
Sweden	>90%	84%*	○○○○	F	2019	≥2	2006 birth cohort
UK	90%, for 13–14 y/o girls to receive 2 doses	84%*	○○○○	F	2018–2019	2	13–14 y/o (Grade 9)
Ireland	≥80, for girls to receive to receive 2 doses	72%*	○○○○	F	2016	2	12–13 y/o
Switzerland	80%, for girls and boys to receive 2 doses	60%*	○○○	F	2018	2	16 y/o
		17%	○	M	2018	NA	16 y/o
Luxembourg	80%, for the recommended population to receive 2 doses	56%*	○○○	F	2016	2	1991–2003 birth cohort
Italy	≥95%, for 11–12 y/o girls	50%*	○○	F	2017	2	2005 birth cohort
France	60%, for girls to receive complete regimen	24%*	○	F	2019	2	16 y/o
Bulgaria	75%	4%*	○	NA	2018	2	12–13 y/o
Greece	90%	NA	NA	NA	NA	NA	NA

Abbreviations: WHO/ER, WHO Europe; VCR, vaccination coverage rate; F, Female; M, Male; HPVv, Human papillomavirus vaccination; y/o, years old.
NA, not available.
Legend: ○○○○ – High VCR (>70%); ○○○ – Moderate VCR (51–70%); ○○ – Low VCR (31–50%); ○– Very low VCR (≤30%).
* VCR from national-level data source; in the case, dose-related VCR is specified, the VCR for the target population who received 2 doses is presented.



Global estimates of expected and preventable cervical cancers among girls born between 2005 and 2014: a birth cohort analysis

Lancet Public Health 2021; 6: e510–21

Maxime Bonjour, Hadrien Charvat, Eduardo L Franco, Marion Piñeros, Gary M Clifford, Freddie Bray, Iacopo Baussano

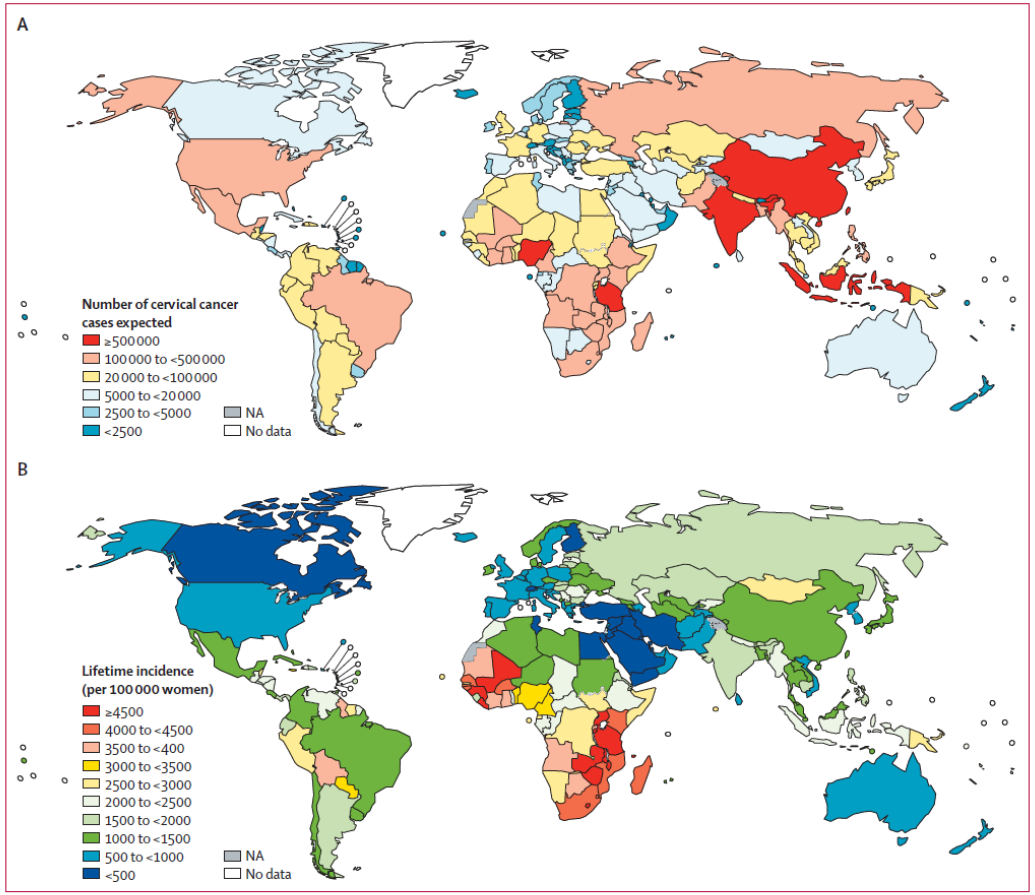
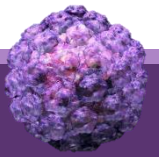


Figure 1: Number of cervical cancer cases (A) and lifetime incidence (B) expected among women born between 2005 and 2014, by country
NA=not applicable.

- Globally, in the absence of vaccination, 11.6 million cervical cancer cases are expected in all women born between 2005 and 2014, eligible for HPV vaccination.
- Approximately 75% of the burden will be concentrated in 25 countries mostly located in Africa and Asia, where the future number of cases is expected to increase manyfold, reaching 5·6 million (5·4–6·0) cases in Africa and 4·5 million (4·4–4·6) cases in Asia.
- In these birth cohorts, HPV vaccination (with a vaccine targeted against HPV types 16 and 18, and assuming partial cross-protection against HPV types 31, 33, and 45) could prevent 8·7 million cases.



Optimal human papillomavirus vaccination strategies to prevent cervical cancer in low-income and middle-income countries in the context of limited resources: a mathematical modelling analysis

Lancet Infect Dis. 2021:S1473-3099(20)30860-4.

Mélanie Drolet, Jean-François Laprise*, Dave Martin, Mark Jit, Élodie Bénard, Guillaume Gingras, Marie-Claude Boily, Michel Alary, Iacopo Baussano, Raymond Hutubessy, Marc Brisson*

Research in context

Evidence before this study

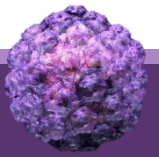
Approximately 500 000 new cases of cervical cancer are diagnosed in low-income and middle-income countries (LMICs) each year. Human papillomavirus (HPV) vaccines are highly effective: the Papillomavirus Rapid Interface for Modelling and Economics (PRIME) model predicted that HPV vaccination of girls aged 12 years with two doses of the vaccine was cost-effective in 156 (87%) of 179 countries. However, less than 40% of LMICs have introduced HPV vaccination programmes. Key barriers to introduction include financial and human resource constraints, and, since 2019, a worldwide shortage of HPV vaccine supply that might last until 2024. These barriers might have been intensified by the COVID-19 pandemic. In parallel, the WHO director-general has issued a global call to eliminate cervical cancer as a public health problem, which will result in sustained efforts to achieve high vaccination coverage across LMICs.

Added value of this study

In this modelling analysis we identified two novel HPV vaccination strategies that should minimise the number of doses needed to prevent one case of cervical cancer and the cost per DALY averted: two-dose routine vaccination of girls aged 14 years with or without a later switch to routine vaccination of girls aged 9 years, and routine vaccination of girls aged 9 years with an extended interval of 5 years between doses and a catch-up programme for girls aged 14 years. These strategies would maximise prevention of cervical cancer with the fewest doses in the short term and at the lowest cost, which would allow a maximum of LMICs to introduce HPV vaccination and could reduce the effect of HPV vaccine supply shortage on efforts to eliminate cervical cancer.

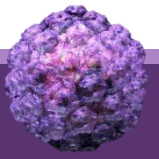
Implication of all the available evidence

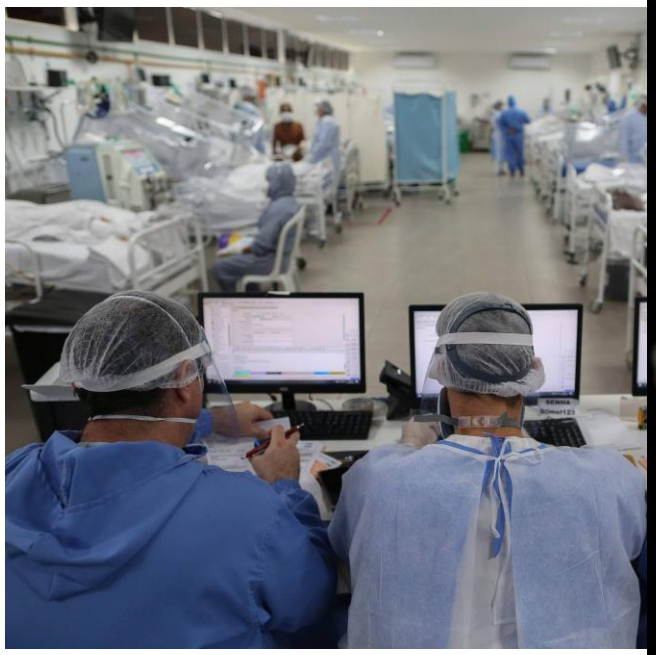
Our modelling results have directly informed WHO Strategic Advisory Group of Experts on Immunization's recommendation in October, 2019, to continue vaccination with a two-dose schedule; temporarily postpone vaccination of multiple-age cohorts, older age groups (≥15 years), and gender-neutral vaccination; and consider implementing strategies such as those identified in our study.

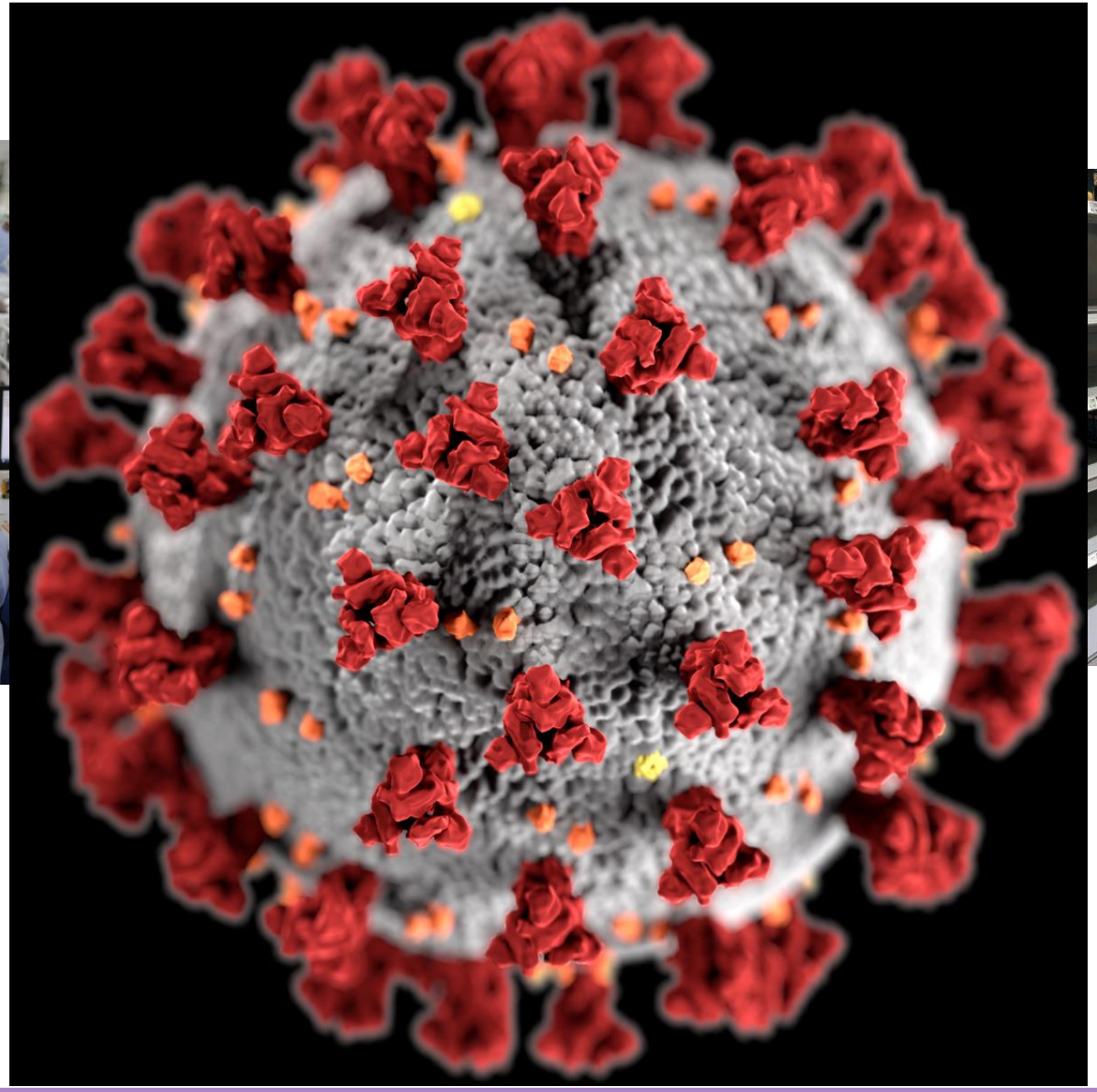


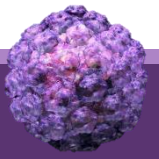
Butan

- **1st LMIC country** that introduced a nationwide HPV vaccination program for adolescent girls in 2010 + one-time catch-up campaign where 44 849 girls aged 12–18 years were vaccinated during the 1st year of the program.
- In 2019, the crude HPV vaccination coverage was **90.5% among the primary target population**.
- 4vHPVvaccine, switched to the two-dose regimen in 2016.
- In September 2020, Bhutan became the **first country in the Southeast Asia region to initiate vaccination for boys**. → During the initial launch of the program, 8114 boys including monks aged 11–14 years were vaccinated and it is now included in the routine vaccination schedule beginning of 2021.
- In 2019, the Ministry of Health allocated a budget of 186 million US$ for a **flagship program that aims to reduce the burden of stomach and breast cancer and to eliminate cervical cancer**.









Impact of reduced human papillomavirus vaccination coverage rates due to COVID-19 in the United States: A model based analysis

Vincent Daniels [a], Kunal Saxena [a], Craig Roberts [a], Smita Kothari [a], Shelby Corman [b,*], Lixia Yao [a], Linda Niccolai [c]

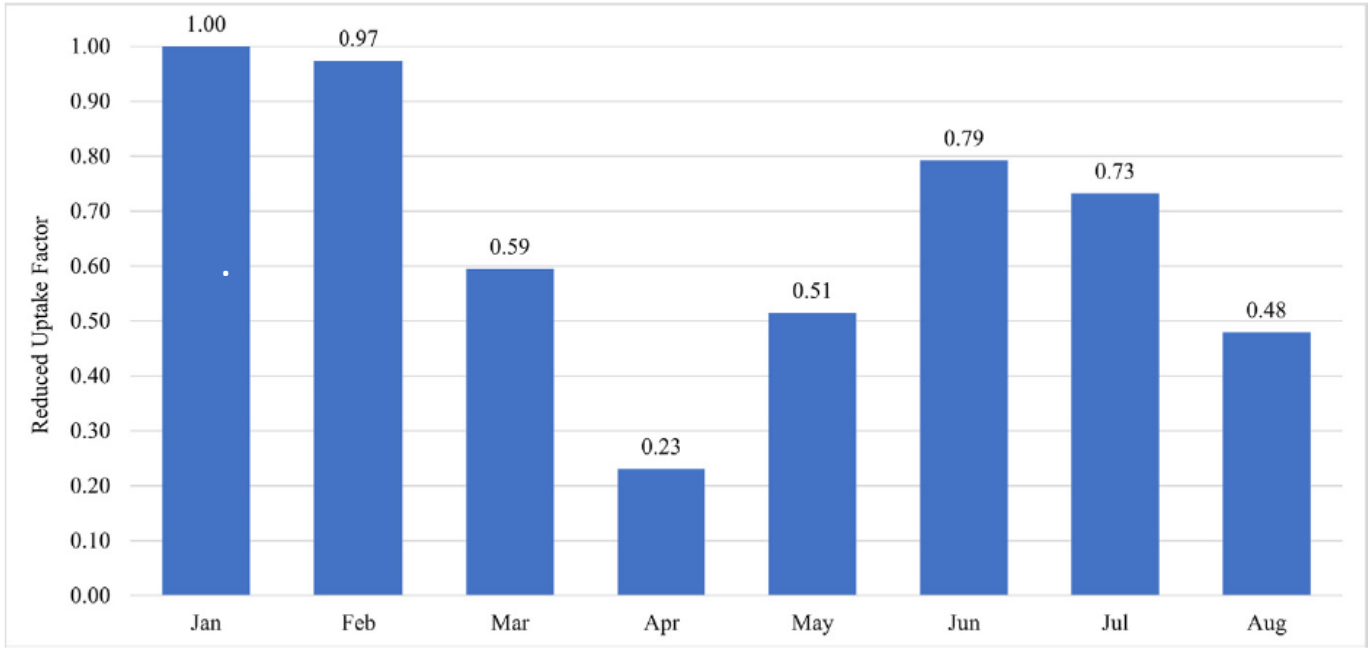
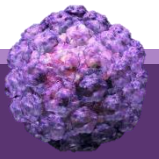


Fig. 1. Normalized HPV vaccine coverage factor by month in 2020 in comparison to 2018/2019. In all scenarios, we assume the August factor remains constant through June 2021.



Vaccine. 2021;39(20):2731-2735.

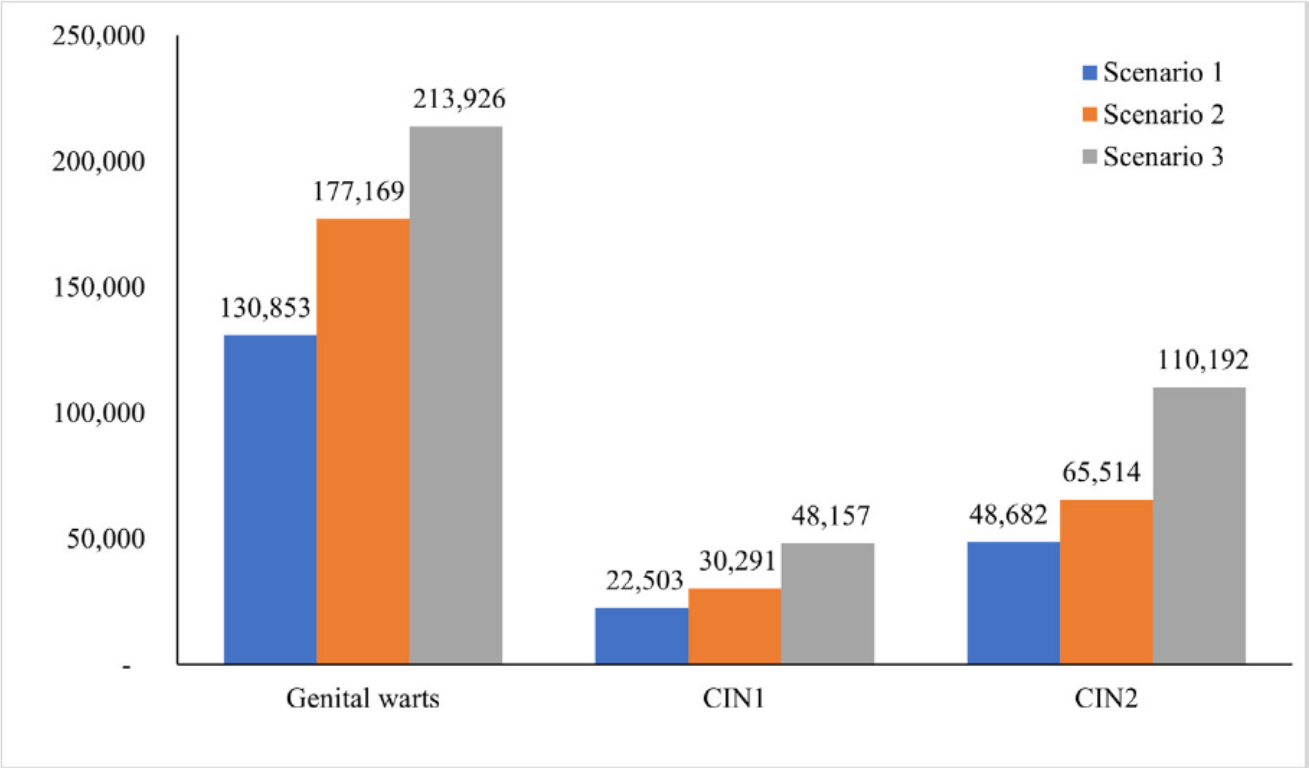
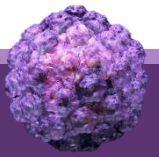
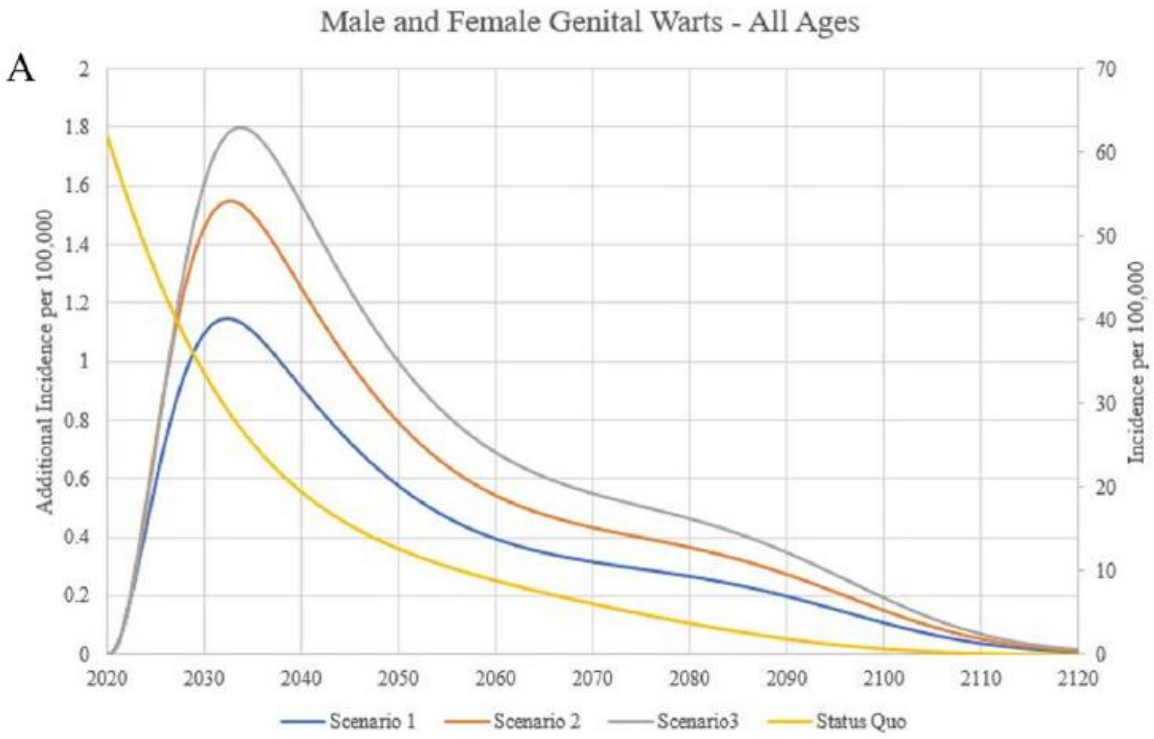
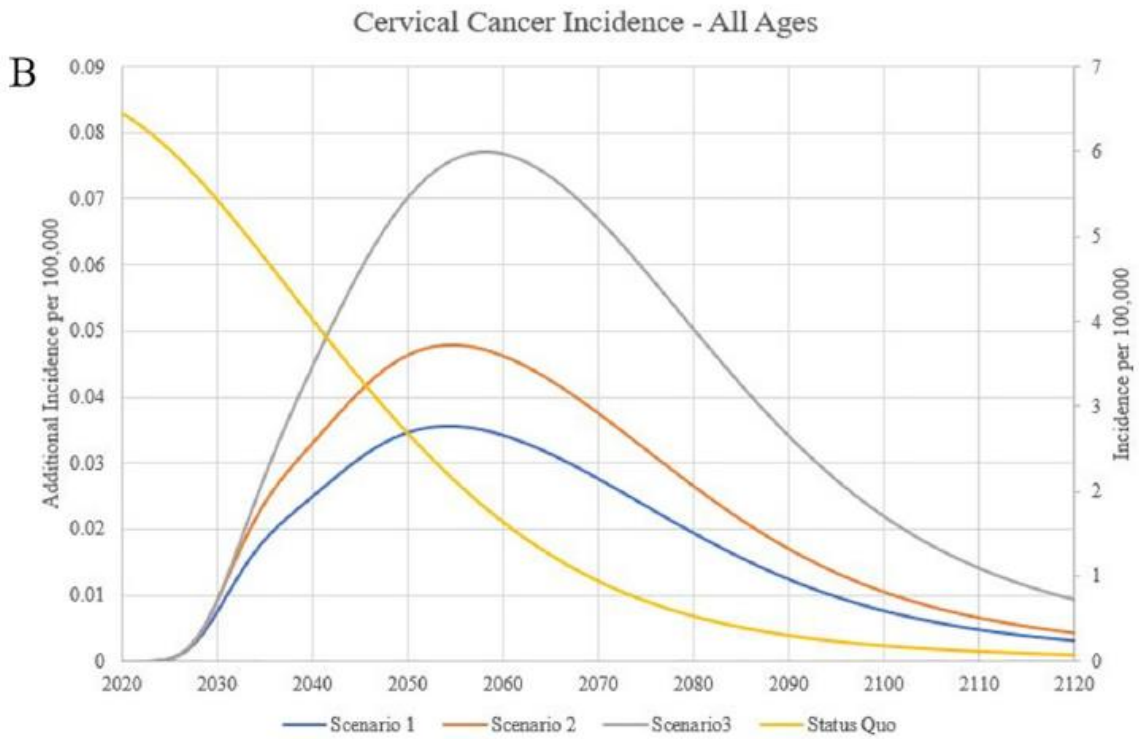


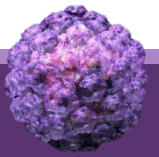
Fig. 2. Additional cases of genital warts and cervical intraepithelial neoplasia (CIN) over 100 years compared to status quo. Scenario 1, Reduced coverage during the COVID-19 pandemic with rapid recovery to baseline coverage by January 2022; Scenario 2, Reduced coverage during the COVID-19 pandemic with slow recovery to baseline coverage by the end of December 2022; Scenario 3, Reduced coverage during the COVID-19 pandemic with partial recovery to 85% of previous years' coverage by the end of December 2021 and full recovery by 2028.







Catch-up vaccination?

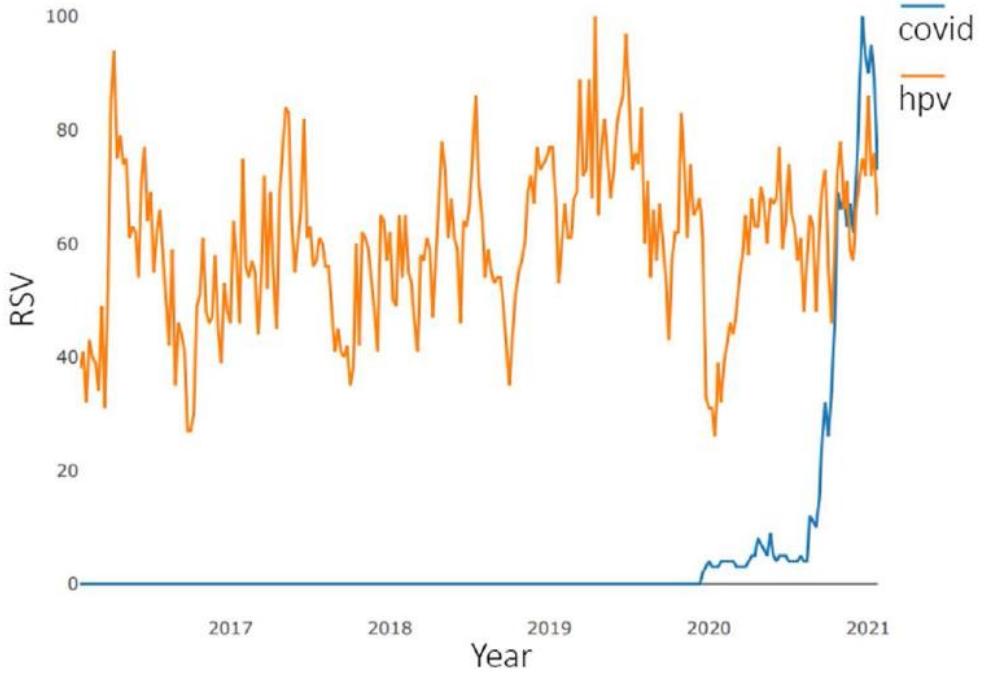


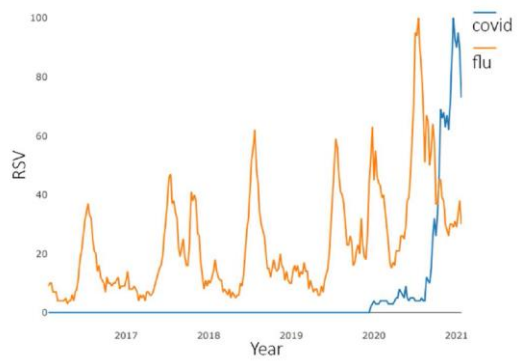
Daniels V, et al. Vaccine. 2021;39(20):2731-2735.

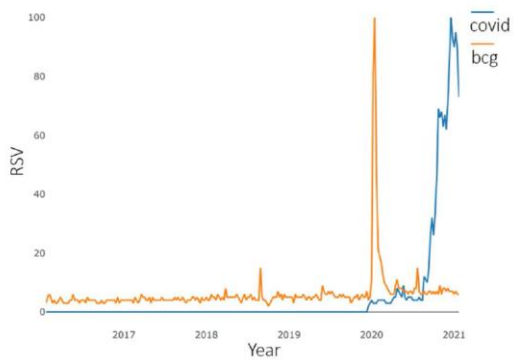
The Global Interest in Vaccines and Its Prediction and Perspectives in the Era of COVID-19. Real-Time Surveillance Using Google Trends

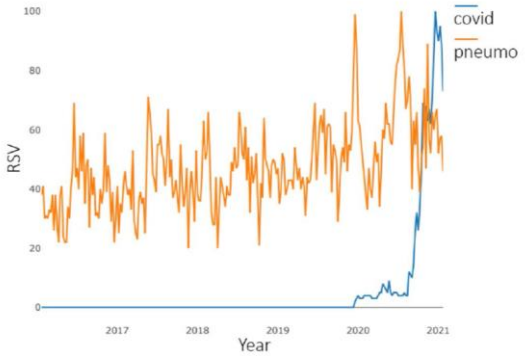
Int J Environ Res Public Health 2021;18:7841.

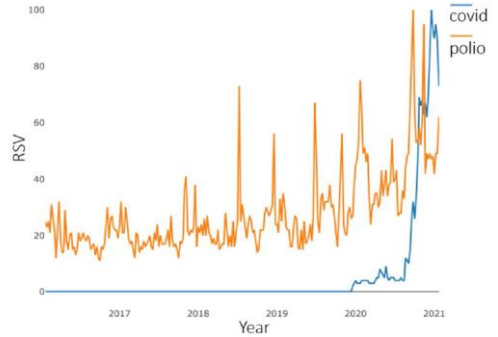
Magdalena Sycinska-Dziarnowska [1,*], Iwona Paradowska-Stankiewicz [2] and Krzysztof Woźniak [1]



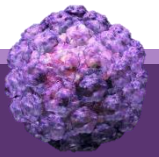


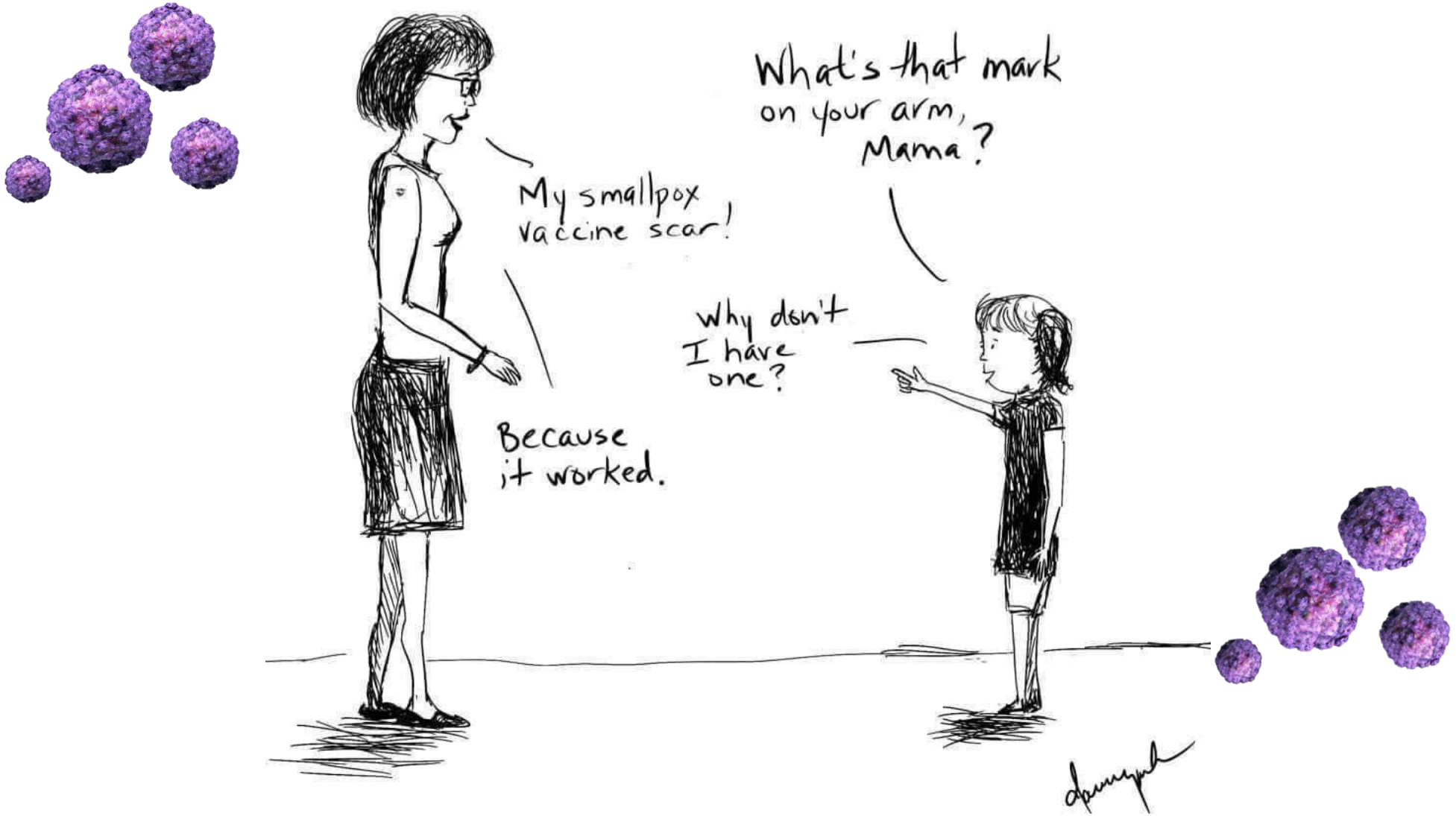






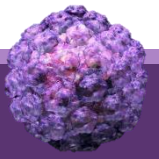
no ↓ in the interest in the HPV vaccine, which can be perceived as a positive finding due to the fact that interest in this vaccine represents concern regarding non-respiratory diseases




What's that mark on your arm, Mama?
My smallpox vaccine scar!
Why don't I have one?
Because it worked.

Characteristics of Antivaccine Messages on Social Media: Systematic Review

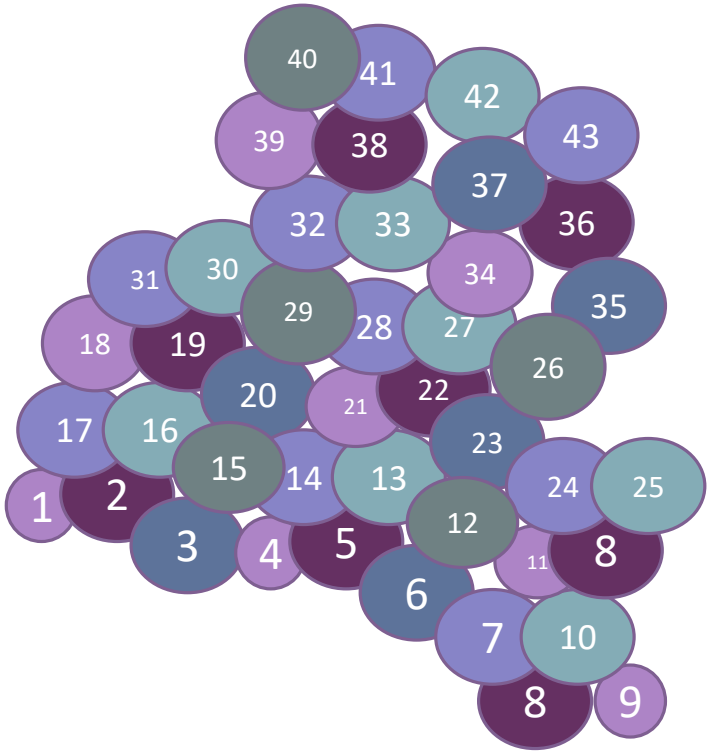
- Proponents of the antivaccine movement use a limited number of arguments in their messages.
- **Antivaccine messages are more liked and shared** than provaccine content (YouTube & Instagram; exeption: HPV vaccine on Twitter).
- Antivaccine users share **more user-friendly content** than provaccine users (emotions!).
- Antivaccine users **describe vaccines as harmful for health** (side effects > cancer protection; „toxic“, „syringe“) and **ineffective**.
- **Antivaccine users share conspiracy theories** or claims that are not scientifically proven („evil government“) - conspiracism is not a product of ignorance; it can be explained by the human willingness to believe in the unseen.
- HPV vaccine was the second most common topic, after the topic of vaccines in general:
  - In many countries, this vaccine is not mandatory -> it can be more effectively discouraged.
  - The minimum age for receiving the first dose is 9 years; thus, often both parents' consent and the preteen or teenager's acceptance are required.
  - Conservative religious groups suggest that protection against sexually transmitted diseases encourages licentious teen sex.



Cepljenje obeh spolov

Po svetu leta 2013

Po svetu junij 2021



EU: 11 držav v EU s spolno nevtralnim cepljenjem proti HPV


JUMBO
VISMA
LCL
31
JUMBO
VISMA
Vision

Cepljenje proti HPV za fante

29. 9. 2014

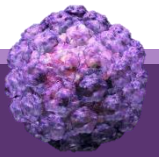
Dognanje, da je vzrok za nastanek raka na maternicnem vratu okužba z enim od onkogenih tipov humanih virusov papiloma, je omogocilo razvoj cepiva, s katerim naj bi preprecili vsaj 70 odstotkov tega raka pri cepljenih ženskah. Cepljenje proti HPV je pri deklicah sestavni del Nacionalnega programa cepljenja in tako široko dostopno vsem deklicam v Sloveniji. Za hitrejše izkoreninjenje tega raka je potrebna dovolj visoka precepljenost deklet oziroma cepljenje obeh spolov, saj okužba s humanimi papiloma virusi spada med spolno prenosljive bolezni.

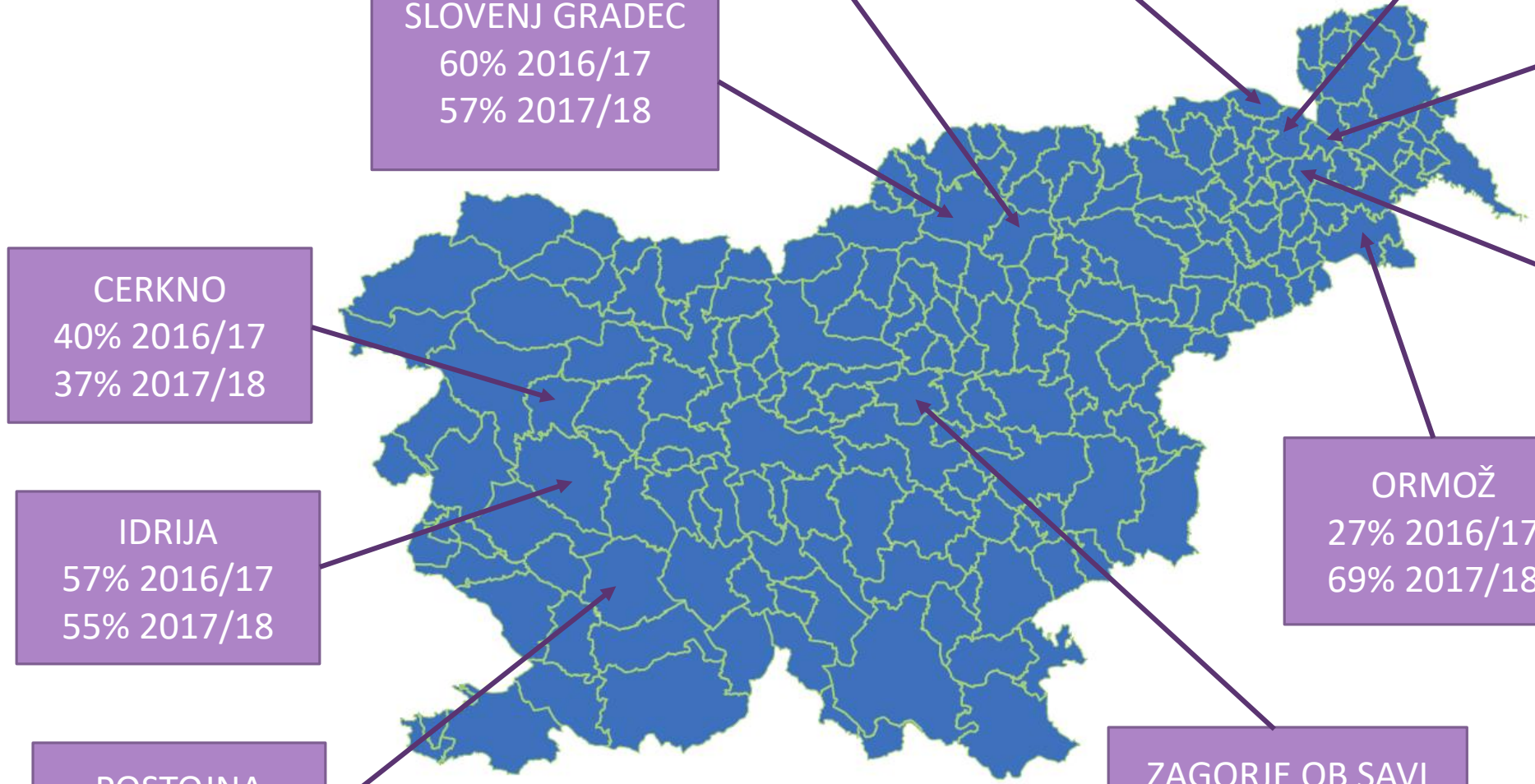
Zdravstveni dom Idrija bo kot prvi v Sloveniji zacel s cepljenjem decków proti humanemu papiloma virusu. Doslej smo v skladu z Nacionalnim programom cepljenja cepili deklice v 6. razredu osnovnih šol. Ker so nova dognanja pokazala, da se zaščita proti virusu neprimerno izboljša, če sta enakopravno cepljena oba spola, smo se v ZD Idrija ob pokroviteljski podpori občin Idrija in Cerkno odlocili, da zacnemo tudi s cepljenjem fantov.

Stroške cepiva bosta pokrili obe občini, medtem, ko stroške cepljenja krije Zdravstveni dom Idrija.

Vse fante iz občin Idrija in Cerkno, v starosti 12 let in njihove starše vljudno vabimo, da se odlocijo za cepljenje in se našemu vabilu odzovejo v cim vecjem številu. Vec informacij dobite v šolskem dispanzerju ZD Idrija, in sicer od ponedeljka – cetrtka.

Ob tej priložnosti izrekamo iskreno zahvalo obema županoma – idrijskemu g. Bojanu Severju in cerkljanskemu g. Miranu Cigliču, ki sta prisluhnila naši prošnji in akcijo tudi finančno podprla.





MISLINJA
55% 2016/17
47% 2017/18

APAČE
40% 2016/17

GORNJA RADGONA
36% 2017/18

SLOVENJ GRADEC
60% 2016/17
57% 2017/18

RADENCI
68% 2016/17
40% 2017/18

SV. JURIJ OB ŠČAVNICI
40% 2016/17
37% 2017/18

CERKNO
40% 2016/17
37% 2017/18

ORMOŽ
27% 2016/17
69% 2017/18

IDRIJA
57% 2016/17
55% 2017/18

ZAGORJE OB SAVI
25% 2017/18

POSTOJNA
29% 2017/18

Zdravstveni dom
za študente
Univerze v Ljubljani

09. 07. 2021

Končno tudi fantje v programu cepljenja proti HPV

PREGLEJ VSE


JUMBO VISMA
HEMA
JUMBO VISMA

GIVE LOVE NOT HPV