

HPV assoziierte Erkrankungen

FOKUS: Urologie

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HPV und Krebs

TABLE 2. Average annual number and percentage of cancer cases attributable to human papillomavirus and to HPV 16 and HPV 18, by anatomic site and sex — United States, 2006–2010.

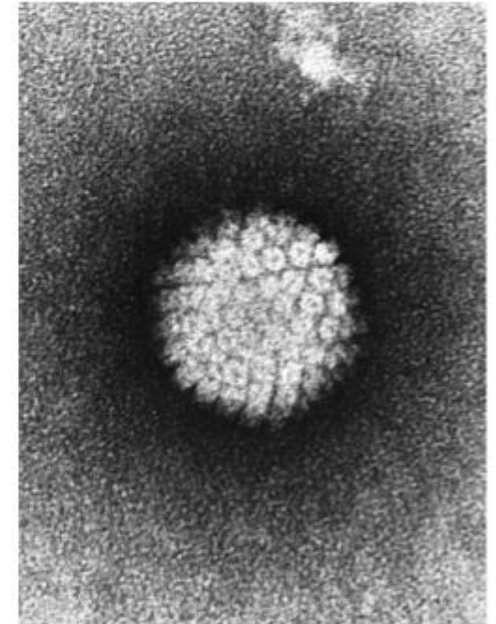
Anatomic site	Average no. of cancers per year in sites where HPV is often found (HPV-associated cancers)*				Cancers attributable to any HPV				Cancers attributable to HPV 16/18			
	Male	Female	Both sexes	%	Average no.†			%	Average no.†			
					Male	Female	Both sexes		Male	Female	Both sexes	
Cervix	0	11,422	11,422	91 [§]	0	10,400	10,400	67	0	7,000	7,000	
Anus	1,549	2,821	4,370	91	1,400	2,600	4,000	80	1,100	2,100	3,200	
Oropharynx	9,974	2,443	12,417	72	7,200	1,800	9,000	63	4,500	1,100	5,600	
Penis	1,048	0	1,048	63	700	0	700	48	300	0	300	
Vagina	0	735	735	75	0	600	600	55	0	300	300	
Vulva	0	3,168	3,168	69	0	2,200	2,200	49	0	1,100	1,100	
Total	12,571	20,589	33,160		9,300	17,600	26,900		5,900	11,600	17,500	

HPV Verbreitung

- eine der weltweit häufigsten sexuell übertragbaren Erkrankungen
- 2/3 aller Menschen stecken sich mit HPV an
- Frauen = Männer

Infektionsweg

- sexueller Kontakt
- Hautkontakt mit infizierter Stelle reicht aus
- Schmierinfektion
- Mikroverletzungen



HPV klinisches Bild

- HPV: infiziert Epithelzellen von Haut und Schleimhaut
- Virus Freisetzung und Verbreitung durch Abschilferung alter Hautzellen

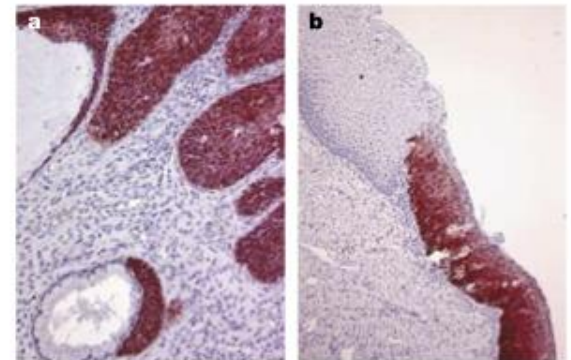
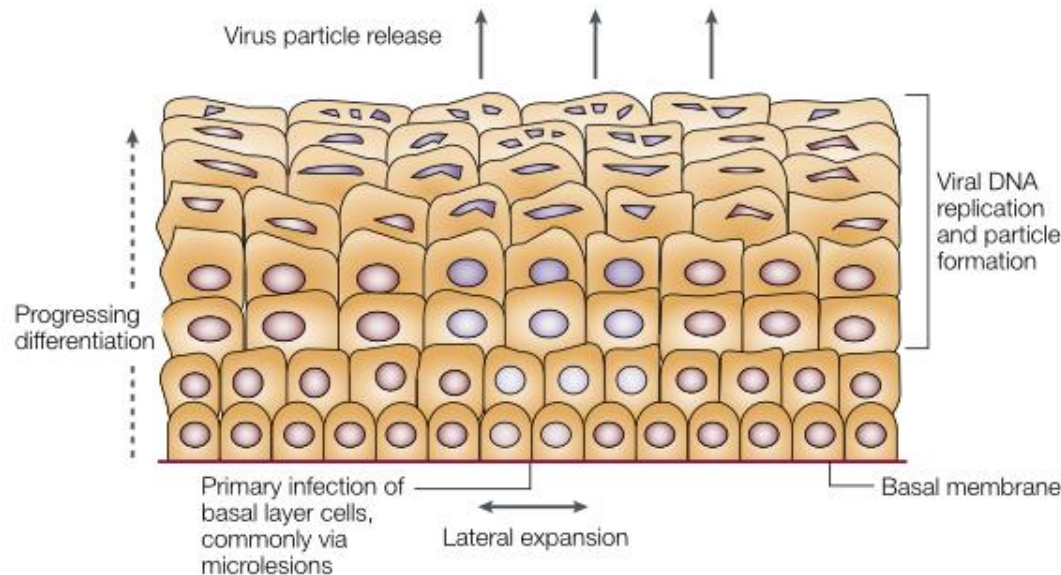


Figure 6 | **Cytological smears.** **a** | A cervical adenocarcinoma and **b** | a cervical neoplasia stained for the expression of INK4A. The intensive red staining pattern of the human-papillomavirus-infected tissue sharply demarcates it from non-infected cells. Photographs kindly provided by Magnus von Knebel Doeberitz, Heidelberg.

HPV - Transfer

Übertragung auch ohne Sexualkontakt

- Körperkontakt/Geburt
- Spontangeburt: 50 %
- Sectio: 27%

Circumcision:

Neugeborene: 4%

ältere kinder: bis zu 83%

HPV - eine grosse Familie....

Mehr als 200 Subtypen, davon 40 relevant für Anogenitaltrakt

- high risk - low risk

low risk: 6, 11, 40, 42, 43,
44, 54, 61, 70, 72, 8

high risk: 16, 18, 31, 33, 35,
39, 45, 51, 52, 56, 58, 59, 66

HPV - Progression

- Infektion zumeist durch Immunsystem eliminiert
- **high risk:**

höhere Rate an Persistenz

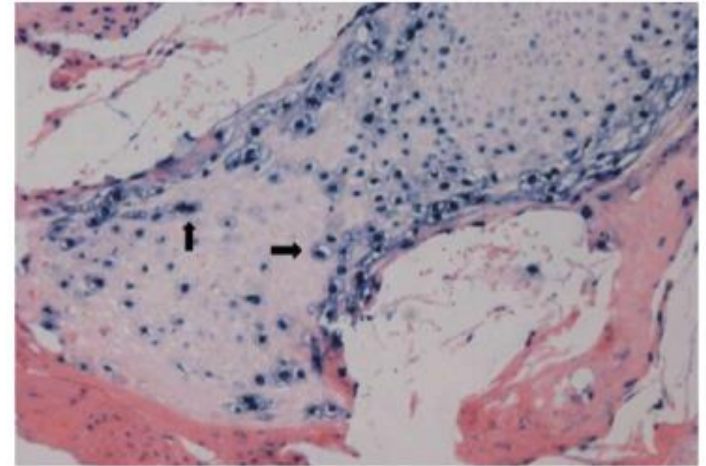
höhere Progressionsrate



kanzerogen

HPV - Condyloma accuminata

- gutartig
- infektiöse Epitheliome
- low-risk HPV- Typen 6 und 11
- Inkubationszeit: 3-24 Wochen



HPV Virus Nachweis
in Condyloma accuminata

Lokalisation bei Männern:

- **Circumcidiert:**
perineal, Penisstamm, perianale Haut
- **nicht Circumcidiert:**
Sulcus coronarius, Glans, Frenulum

HPV - Condyloma accuminata

Therapie:

- Cremes, Salben, Lösungen mit Podophyllotoxin 0,5%, Imiquimod 5%, Sinecatechin 10%
- Trichloressigsäure 80-90%
- Kryotherapie



Operativ:

- Excision, Laserabtragung, Kontrolle nach 3 Monaten
- keine konservative Therapieoption für high risk HPV

HPV - Urethra

Selten: distale Urethra (Männer: 25%, Frauen: 8%)



HPV - Peniskarzinom

- Vorläufer: undifferenzierte intraepitheliale Neoplasie
- HPV **16,18**
- Nachweis in bis > 50%

HPV 16: 60.2%

HPV 18: 13.3%

HPV 6/11: 8.13%



HPV - Peniskarzinom

- 0.5% aller Krebserkrankungen beim Mann
Zentralisierung der Behandlung!
- Ätiologie: 2 Wege
 - HPV Infektion
 - lokale Risikofaktoren:
Phimose,
chronische Entzündung,
Lichen Sclerosus
- HPV Seropositivität:
höheres Risiko für Peniskarzinom



HPV - Impfung

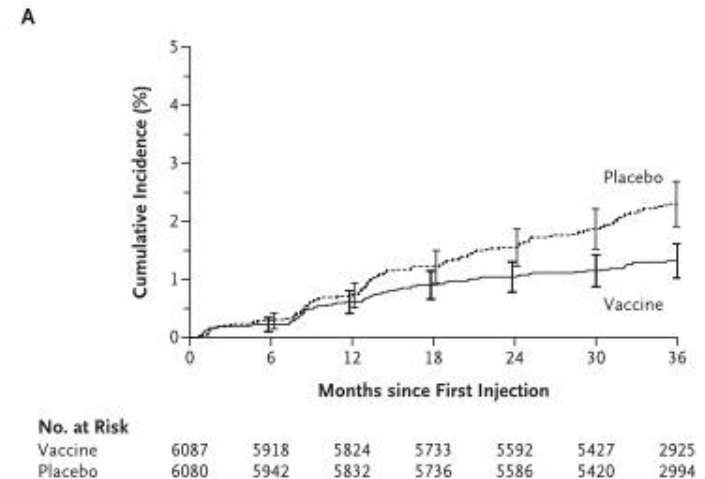
- empfohlen für **Buben und Mädchen ab 9. Lj.**
- Impfprogramm:
 - 71 Länder: Mädchen
 - 11 Länder: Buben
- **Herdenimmunität:** ab 80% Durchimpfung bei Mädchen
- 2 Dosen im Abstand von 6 Monaten
- nach 15 Lj: 3 Dosen erforderlich
- vor sexueller Aktivität, da nach Exposition keine Immunität
- erster GV nach 14. Lj: 94% Mädchen, 97% Buben

HPV - Impfung

Mehrere Impfstoffe:

- 2fach: 16/18
- 4fach: 6/11/16/18
- 9fach: 6/11/16/18/31/33/45/52/58

- enthält **keine Virus DNA** und **kein vitales Material**
- Virus-like-particles:
leere Hüllen aus synthetisch hergestelltem Strukturprotein
- Impfschutz **bis zu 10 Jahre** je nach Impfstoff



HPV - Impfung

In der Schule

Kostenfrei

Mädchen und Buben in der 4. Schulstufe
ab dem vollendeten 9. Lj

Ausserhalb der Schule

Kostenfrei

Mädchen und Buben

ab dem vollendeten 9. Lj bis zum vollendeten 12. Lj

HPV - Impfung

Mädchen und Buben

ab dem vollendeten 12. Lj bis zum vollendeten 15. Lj:

„Nachholimpfungen“ (Catch-up-HPV-Impfungen)

(vergünstigter Selbstkostenpreis)

Frauen ab dem 45. J und für Männer ab dem 26. Lj:

keine Studiendaten der Wirksamkeit

Verhinderung von Infektionen wahrscheinlich

Männer und Frauen mit Resistenzminderung:

(Chemotherapie, HIV-Infektion, vor Organtransplantation)

HPV - Impfung: Wirksamkeit Frauen

Table 3. Efficacy against Persistent Infection with HPV Type 6, 11, 16, or 18 and against Detection of HPV DNA in the Intention-to-Treat Population.*

Variable	Quadrivalent HPV Vaccine (N=1817)				Placebo (N=1815)				Observed Efficacy % (95% CI)
	No. of Subjects	Cases no.	Person-Yr at Risk	Rate no./100 person-yr at risk	No. of Subjects	Cases no.	Person-Yr at Risk	Rate no./100 person-yr at risk	
Persistent infection†									
HPV type									
Type 6, 11, 16, or 18	1817	148	4094.3	3.61	1815	273	3942.6	6.92	47.8 (36.0 to 57.6)
Type 6	1817	63	4213.8	1.50	1815	112	4139.4	2.71	44.7 (24.1 to 60.1)
Type 11	1817	16	4284.6	0.37	1815	39	4238.7	0.92	59.4 (25.7 to 78.8)
Type 16	1817	71	4199.5	1.69	1815	131	4112.7	3.19	46.9 (28.6 to 60.8)
Type 18	1817	25	4267.0	0.59	1815	56	4210.1	1.33	56.0 (28.2 to 73.7)
Sexual orientation									
Heterosexual males	1542	96	3723.7	2.58	1541	187	3596.8	5.20	50.4 (36.2 to 61.6)
Males who had sex with male partners	275	52	370.6	14.03	274	86	345.8	24.87	43.6 (19.5 to 60.8)
DNA detection									
HPV type									
Type 6, 11, 16, or 18	1817	384	3851.1	9.97	1815	511	3736.5	13.68	27.1 (16.6 to 36.3)
Type 6	1817	158	4123.4	3.83	1815	239	4047.5	5.90	35.1 (20.3 to 47.3)
Type 11	1817	50	4254.0	1.18	1815	87	4202.6	2.07	43.2 (18.7 to 60.7)
Type 16	1817	189	4070.9	4.64	1815	259	4014.2	6.45	28.0 (12.9 to 40.7)
Type 18	1817	89	4205.4	2.12	1815	133	4151.5	3.20	33.9 (13.0 to 50.1)
Sexual orientation									
Heterosexual males	1542	268	3516.2	7.62	1541	379	3416.8	11.09	31.3 (19.4 to 41.5)
Males who had sex with male partners	275	116	334.9	34.64	274	132	319.7	41.29	16.1 (-8.5 to 35.2)

HPV - Impfung: Wirksamkeit

Frauen

Centers for Disease Control and Prevention

MMWR

Morbidity and Mortality Weekly Report

TABLE 4. Per-protocol efficacy for prevention of human papillomavirus vaccine-type disease outcomes among females in trials of the bivalent and quadrivalent human papillomavirus vaccines, end-of-study analyses

Vaccine/Endpoint related type	Vaccine		Control		Vaccine efficacy	
	No.	Cases	No.	Cases	%	(95% CI)
Quadrivalent vaccine*						
<i>CIN2/3 or AIS[†]</i>						
HPV 6, 11, 16, 18	7,864	2	7,865	110	98.2	(93.3–99.8)
HPV 16	6,647	2	6,455	81	97.6	(91.1–99.7)
HPV 18	7,382	0	7,316	29	100.0	(86.6–100.0)
<i>VIN/VaiN2/3[†]</i>						
HPV 6, 11, 16, 18	7,900	0	7,902	23	100.0	(82.6–100.0)
HPV 16	6,654	0	6,467	17	100.0	(76.5–100.0)
HPV 18	7,414	0	7,343	2	100.0	(<0–100.0)
<i>Genital warts[‡]</i>						
HPV 6 and/or 11	6,718	2	6,647	186	98.9	(96.1–99.9)
Bivalent vaccine[¶]						
<i>CIN2/3 or AIS</i>						
HPV 16 and/or 18	7,338	5	7,305	97	94.9	(87.7–98.4)
HPV 16	6,296	2	6,160	81	97.6	(91.0–99.7)
HPV 18	6,789	3	6,739	23	87.1	(57.2–97.5)

HPV - Impfung: Wirksamkeit

Männer

TABLE 5. Per-protocol efficacy of quadrivalent human papillomavirus vaccine for prevention of HPV 6-, 11-, 16-, and 18-related disease among males aged 16–26 years*

Endpoint	Vaccine		Control		Vaccine efficacy	
	No.	Cases	No.	Cases	%	(95% CI)
Genital warts [†]	1,397	3	1,408	28	89.4	(65.5–97.9)
PIN [†]	1,397	0	1,408	3	100.0	(-141.2–100.0)
AIN 1/2/3 [§]	194	5	208	24	77.5	(39.6–93.3)
AIN2/3 [§]	194	3	208	13	74.9	(8.8–95.4)

HPV - Impfung: Nebenwirkung

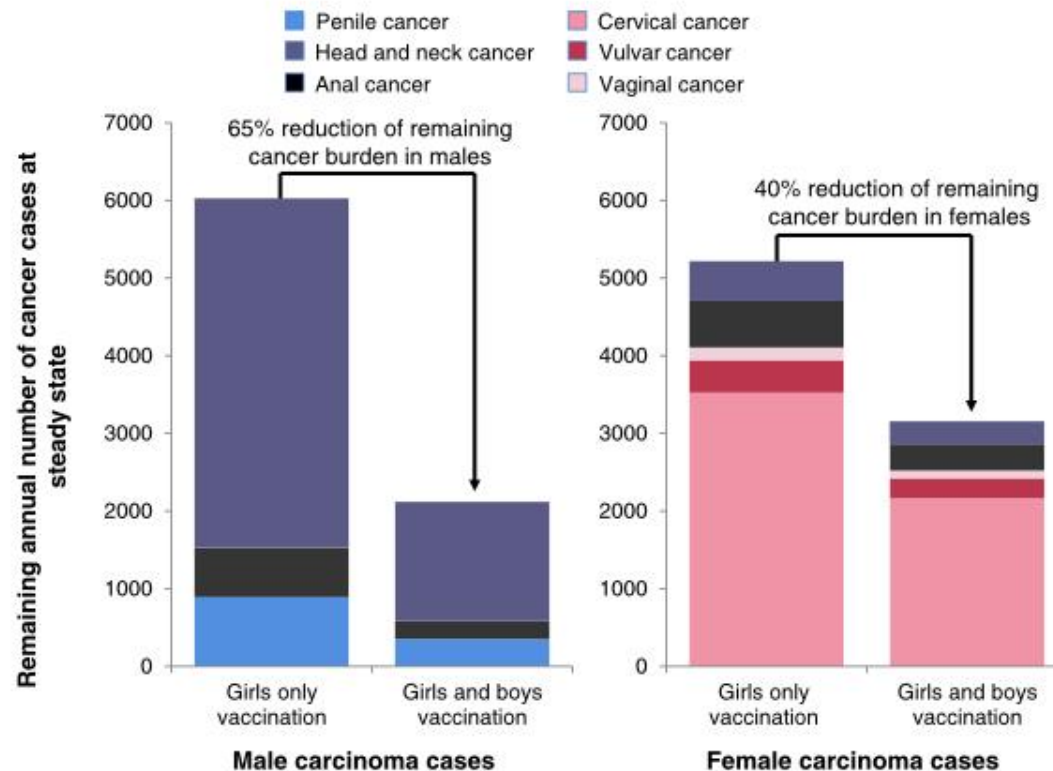
Table 4. Summary of Adverse Events.*

Adverse Event	Quadrivalent HPV Vaccine	Placebo	Difference in Risk (95% CI) <i>percentage points</i>	P Value†
	<i>no. (%)</i>			
No. of subjects	2020	2029		
No. of subjects with follow-up data	1945	1950		
Subjects with events during entire study period				
No event	599 (30.8)	698 (35.8)		
One or more events	1346 (69.2)	1252 (64.2)	5.0 (2.0 to 8.0)	<0.001
Injection site	1169 (60.1)	1047 (53.7)	6.4 (3.3 to 9.5)	<0.001
Systemic	616 (31.7)	622 (31.9)	-0.2 (-3.2 to 2.7)	0.88
Vaccine-related events‡	1242 (63.9)	1134 (58.2)	5.7 (2.6 to 8.8)	<0.001
Injection site	1169 (60.1)	1046 (53.6)	6.5 (3.3 to 9.6)	<0.001
Systemic	274 (14.1)	284 (14.6)	-0.5 (-2.7 to 1.7)	0.67
Serious events§	8 (0.4)	11 (0.6)	-0.2 (-0.7 to 0.3)	0.49
Serious vaccine-related events‡§	0	0	0.0 (-0.2 to 0.2)	1.00
Death	3 (0.2)	10 (0.5)	-0.4 (-0.8 to 0.01)	0.052

HPV - Impfung

Estimating the clinical benefits of vaccinating boys and girls against HPV-related diseases in Europe

Rémi Marty^{1*}, Stéphane Roze¹, Xavier Bresse², Nathalie LARGERON² and Jayne Smith-Palmer³



HPV - Langzeiteffekt



Centers for Disease Control and Prevention
 CDC 24/7: Saving Lives. Protecting People™

National, Regional, State, and Selected Local Area Vaccination Coverage Among Adolescents Aged 13–17 Years — United States, 2016

FIGURE 2. Estimated vaccination coverage* of ≥ 1 dose of human papillomavirus vaccine† among female adolescents aged 13–17 years^{§,¶} — National Immunization Survey – Teen, United States, 2016

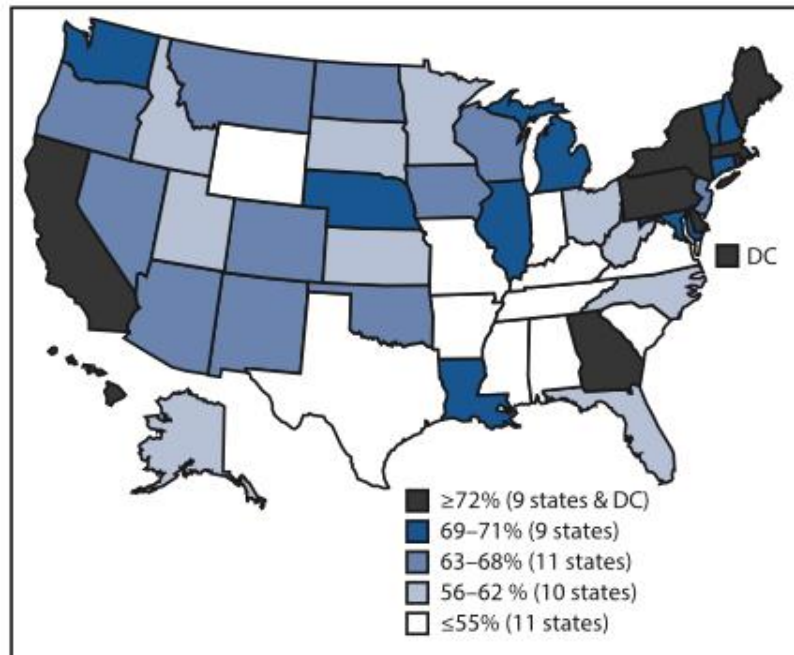
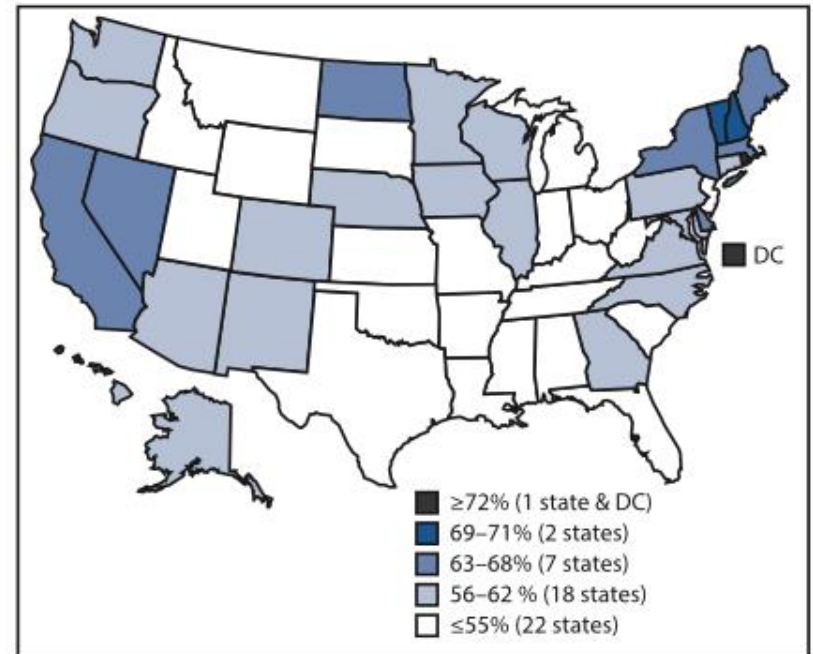


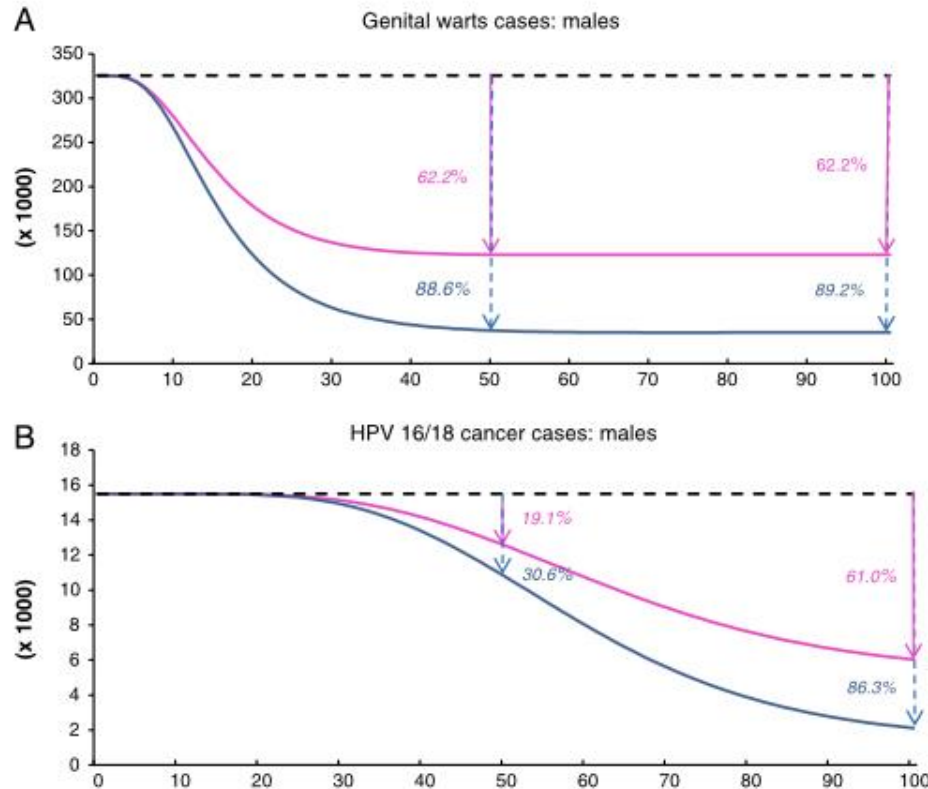
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HPV - Langzeiteffekt

Estimating the clinical benefits of vaccinating boys and girls against HPV-related diseases in Europe

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HPV - Rolle der Circumcision

- HPV: Nachweis auch bei noch nicht sexuell aktiven Buben

Table 3. Male Circumcision and the Prevalence of Human Papillomavirus (HPV) Infection.*

HPV Genotype	HPV-Positive		Risk Ratio (95% CI)
	Intervention Group	Control Group	
	<i>no./total no. (%)</i>		
All genotypes			
At baseline	190/307 (61.9)	189/302 (62.6)	0.99 (0.81–1.21)
At 24 mo	83/233 (35.6)	147/287 (51.2)	0.70 (0.53–0.91)
Low-risk genotypes			
At baseline	146/307 (47.6)	145/302 (48.0)	0.99 (0.79–1.25)
At 24 mo	61/233 (26.2)	113/287 (39.4)	0.66 (0.49–0.91)
High-risk genotypes			
At baseline	117/307 (38.1)	112/302 (37.1)	1.03 (0.79–1.33)
At 24 mo	42/233 (18.0)	80/287 (27.9)	0.65 (0.45–0.94)

HPV - Rolle der Circumcision

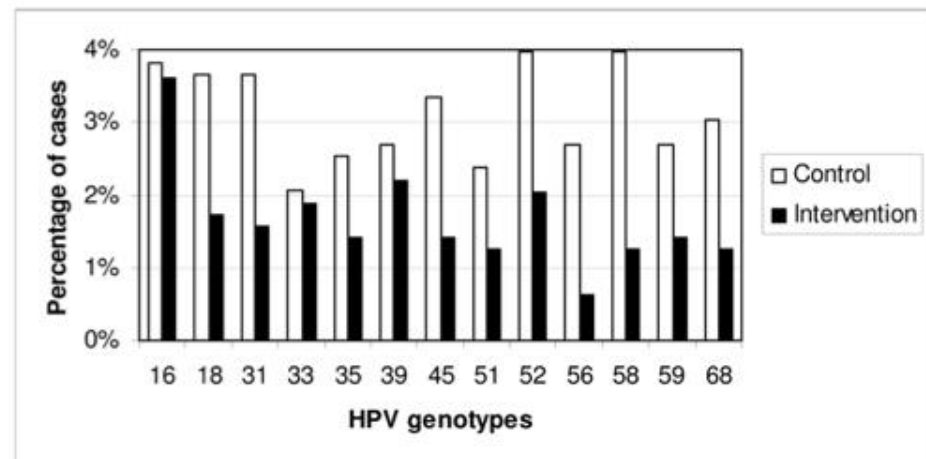
- HPV: Prävalenz bei circumcidierten Buben niedriger

- nicht circumcidiert:

Mikroverletzungen am Frenulum und Kontakt der SH des inneren Präputialblattes

mit Vaginalsekret

- Präventionsvorteil

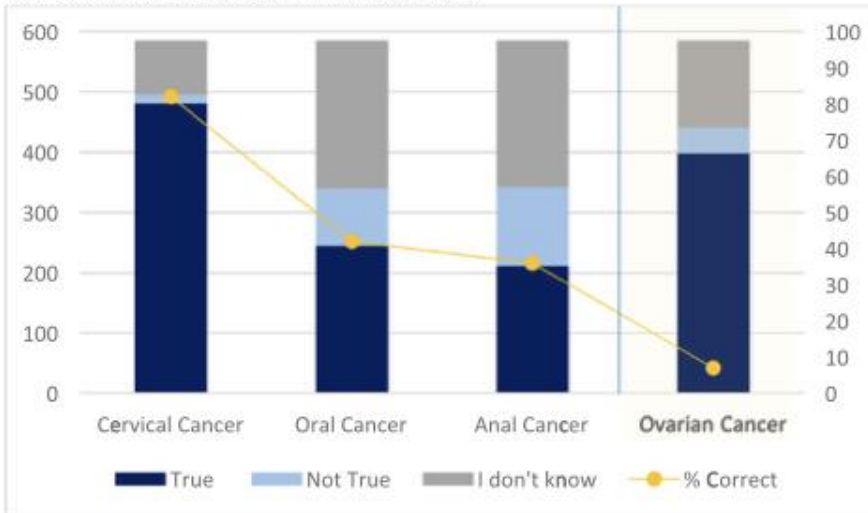


HPV - Breiteninformation

Influencers and preference predictors of HPV vaccine uptake among US male and female young adult college students

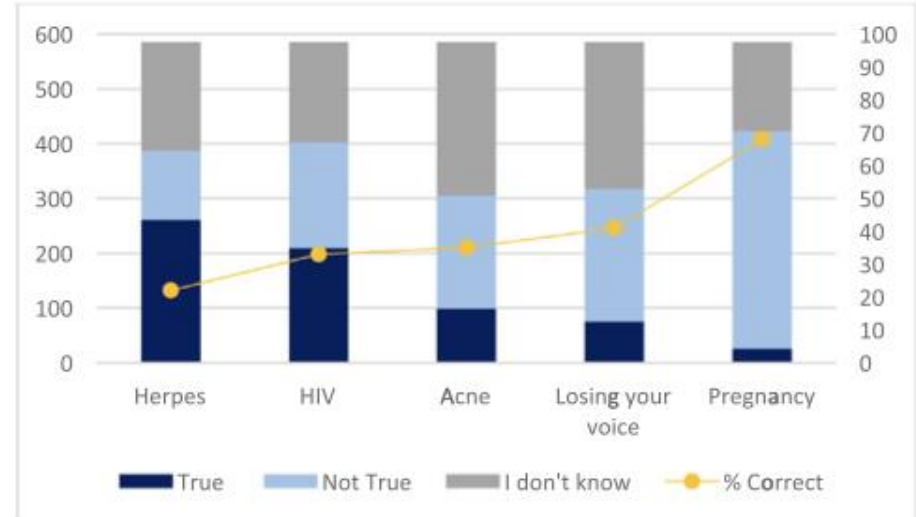
A. Scott LaJoie^a, Jelani C. Kerr^a, Richard D. Clover^{a,1}, Diane M. Harper^{b,*}

Perceived HPV associations with cancers



*Ovarian cancer is not associated with HPV

Perceived HPV associations with non-HPV associated diseases



Was wir gelernt haben... HPV

- eine der **häufigsten sexuell übertragbaren Erkrankungen**
- Übertragung auch ohne Sexualkontakt
- **Cond. accuminata: low-risk HPV- Typen 6 und 11**
- **Peniskarzinom: HPV 16,18**

- **Impfung:**
empfohlen für **Buben und Mädchen ab 9. Lj.**
HPV: Prävalenz bei circumzidierten Buben niedriger

