Table 1. Differences between oropharyngeal cancer HPV + and HPV -.

	HPV-positives	HPV-negatives
Age	Younger individuals (30-50)	Older individuals (50-70)
Risk factor	Oral sex, French kiss, high number of sexual partners, history of STI	Long history of tobacco and/or alcohol consumption
Incidence	Increasing	Decreasing
Localization	Tongue base, amygdalae	Oral mucosa
Field cancerization	No	Yes
Histology	Poorly differentiated - basaloid	Clearly differentiated
Stage at diagnosis	T3-4; N2-3	Variable
Biomarkers	Over-expressed P16; Inactivation of P16 and pRb	Loss of P16; P53 and pRb mutation; cyclin-D1, EGFR and survivine over-expression
Chromosomal mutations	Less frequent	Frequent
Prognosis	Very good, increased sensitivity to radiotherapy and chemotherapy	Poor
Distant metastasis	Rare	Frequent
Second primaries	Rare	Frequent
Five year survival rate	60%-90%	20%-70%

BMC Public Health

BioMed Central
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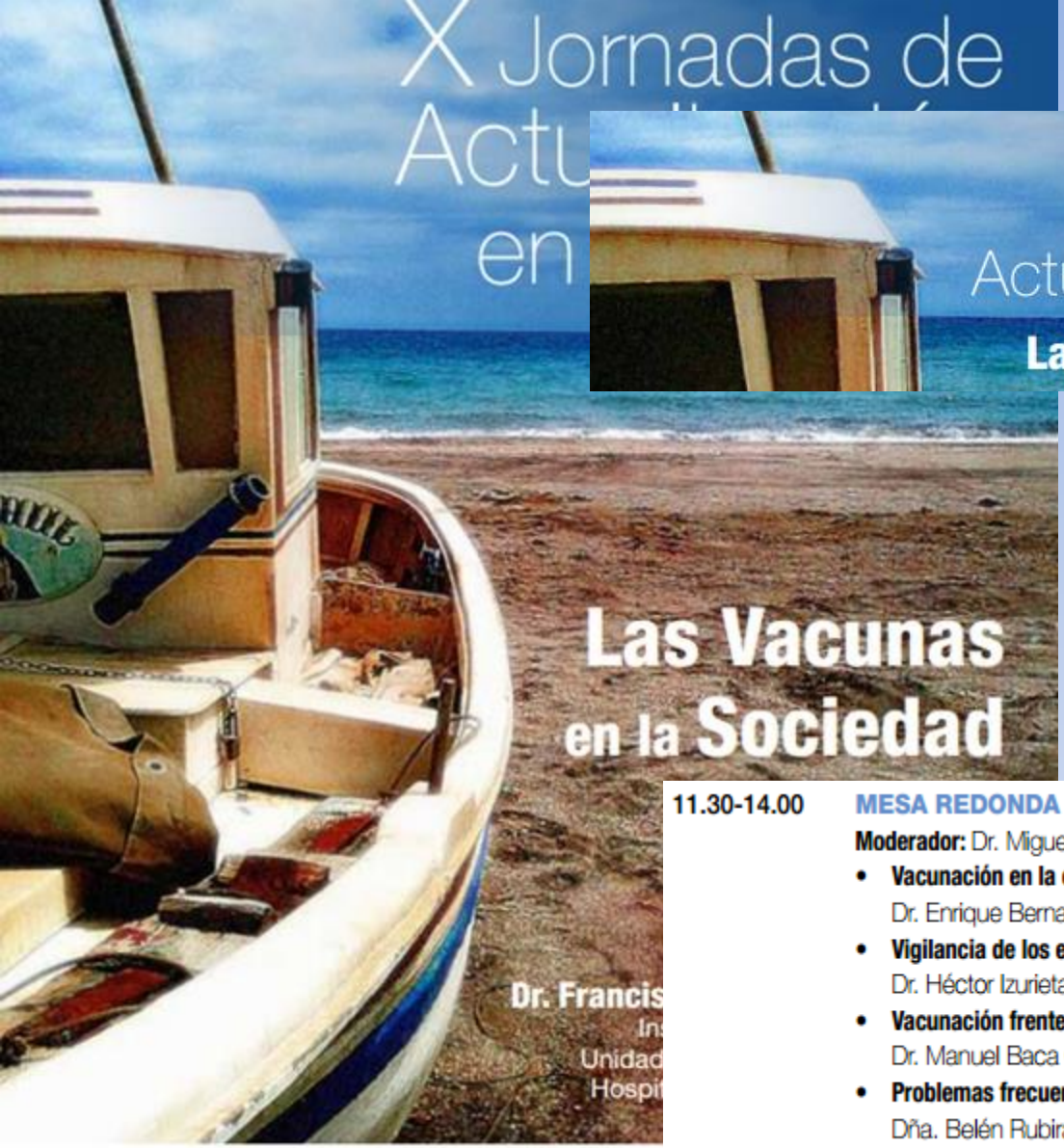
Towards the eradication of HPV infection through universal specific vaccination

BMC Public Health 2013, **13**:642 doi:10.1186/1471-2458-13-642



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11.30-14.00 **MESA REDONDA 4: Vacunación en situaciones especiales**

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- **Vacunación en la embarazada: prevenir antes de nacer**
  Dr. Enrique Bernaola Iturbe. *Hospital Virgen del Camino, Pamplona.*
- **Vigilancia de los efectos adversos de las vacunas**
  Dr. Héctor Izurieta. *Brighton Collaboration. EE.UU.*
- **Vacunación frente a VPH: ¿también en el hombre?**
  Dr. Manuel Baca Cots. *Hospital Quirón, Málaga.*
- **Problemas frecuentes en la administración diaria de vacunas**
  Dña. Belén Rubira Golbano. *Centro de Salud Berja. Distrito Poniente, Almería.*

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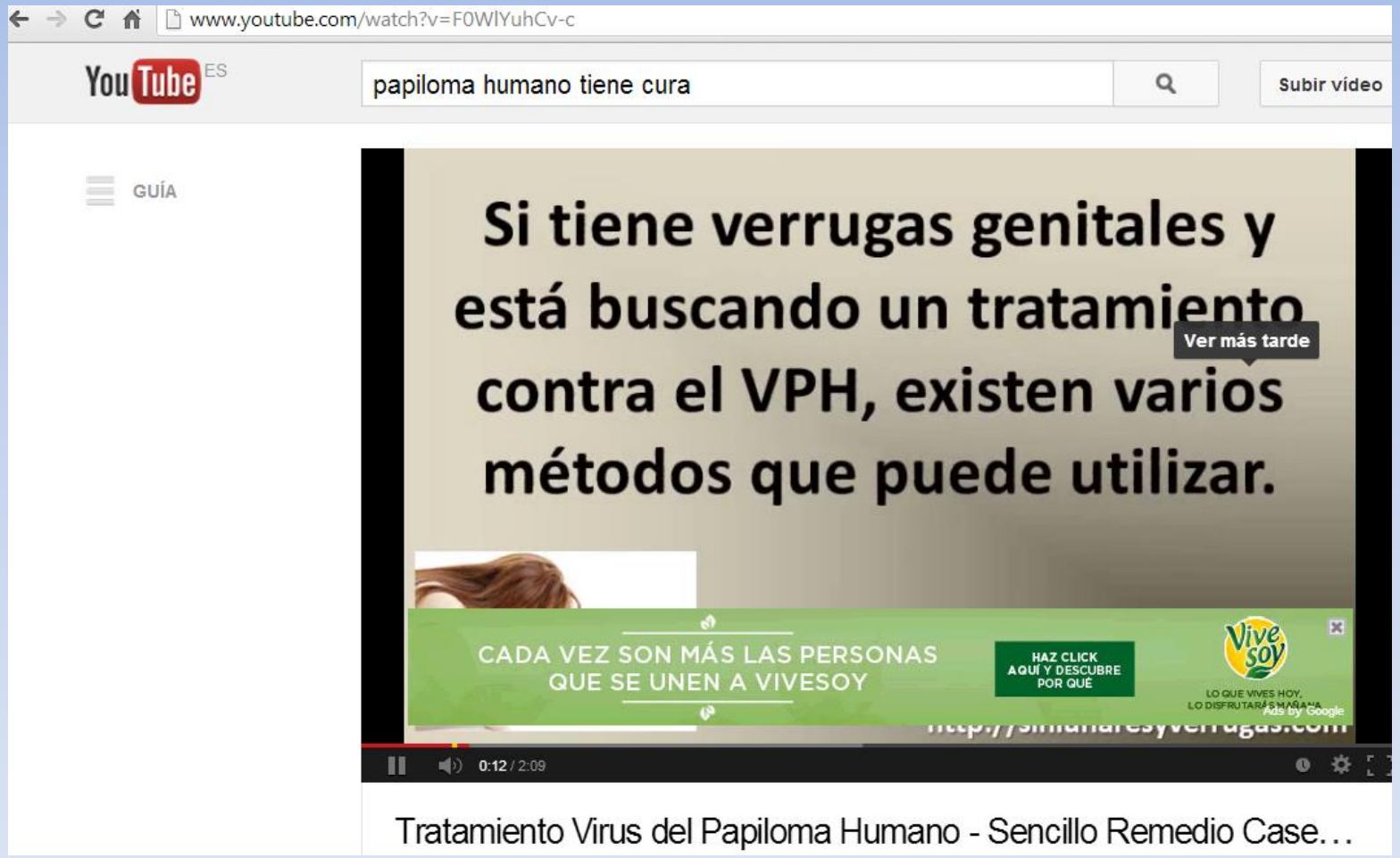
www.youtube.com/watch?v=F0WlYuhCv-c
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Si tiene verrugas genitales y está buscando un tratamiento contra el VPH, existen varios métodos que puede utilizar.
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HAZ CLICK AQUÍ Y DESCUBRE POR QUÉ
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Tratamiento Virus del Papiloma Humano - Sencillo Remedio Case…

Branković et al. International Journal for Equity in Health 2013, 12:14
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INTERNATIONAL JOURNAL FOR EQUITY IN HEALTH

RESEARCH Open Access

Applying a gender lens on *human papillomavirus* infection: cervical cancer screening, HPV DNA testing, and HPV vaccination

Ivan Branković[1*], Petra Verdonk[2] and Ineke Klinge[3]

Table 1 Numbers of included papers per each year with reference numbers in square brackets

Publication year	Cervical cancer screening	HPV DNA testing	HPV vaccination
2005	**2** [18,19]	**3** [20-22]	**0**
2006	**3** [23-25]	**4** [26-29]	**2** [30,31]
2007	**2** [32,33]	**1** [34]	**7** [5,7,35-39]
2008	**5** [40-44]	**0**	**1** [45]
2009	**12** [46-57]	**0**	**9** [46,58-65]
2010	**6** [66-71]	**0**	**3** [72-74]
2011	**2** [75,76]	**0**	**4** [77-80]
2012	**1** [81]	**1** [82]	**4** [83-86]
total	**33**	**8**	**30**

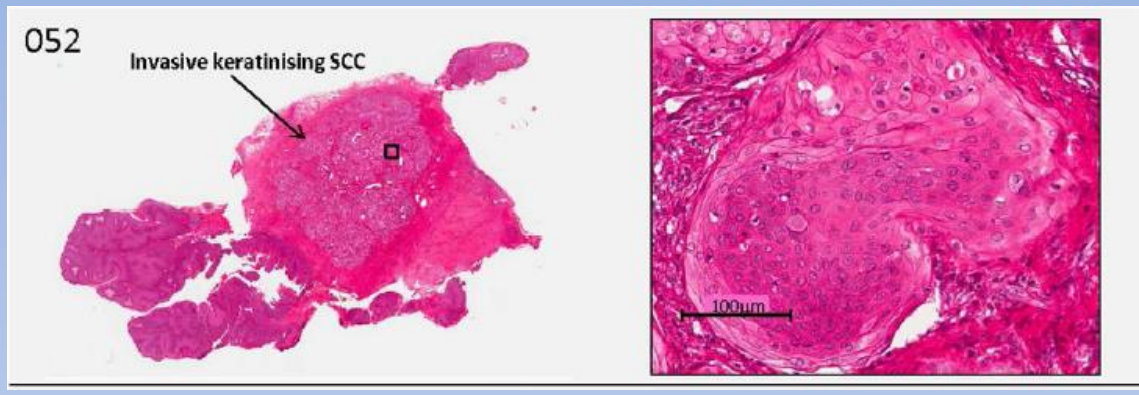

Table 1. Histological grade and HPV genotype of eight anal or perianal biopsy sections

nd = not detected; SCC = Squamous Cell Carcinoma; HSIL = High-grade Squamous Intra-epithelial Lesion.

Sample ID	Biopsy site	Whole section HPV genotype	Histopathological diagnosis	Lesion HPV genotype	Patient HIV Status
052	Intra-anal	6	SCC	6	unknown
093	Intra-anal	6	SCC	6	negative
068	Intra-anal	11	HSIL	11	positive
100	Intra-anal	11	HSIL	11	unknown
060	Perianal	6	SCC	6	unknown
074	Perianal	6	SCC	6	unknown
107	Perianal	11	SCC	nd	positive

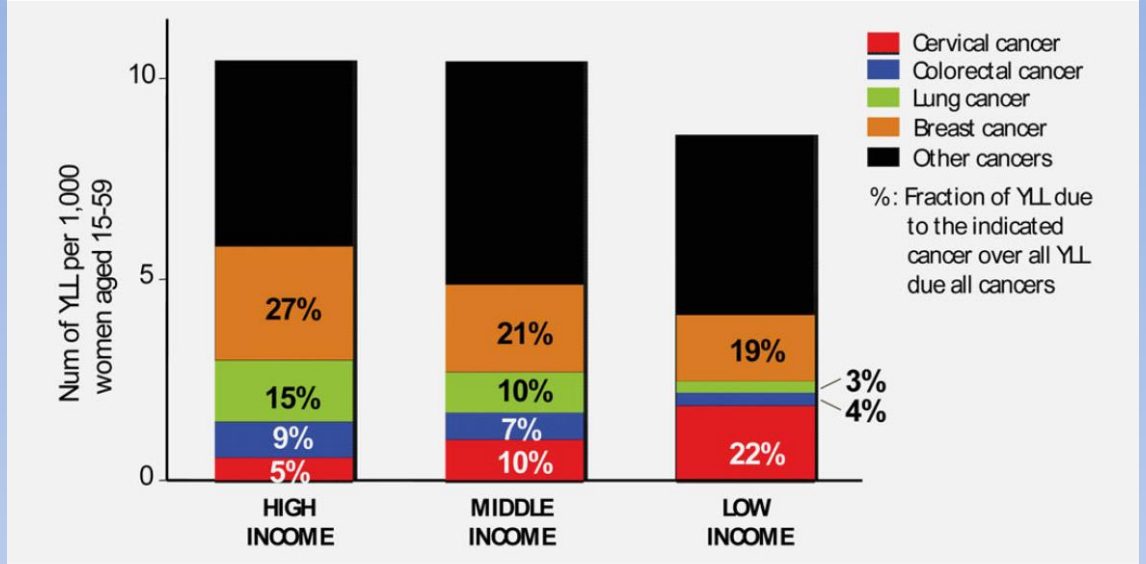

Figure 1. Years of life lost (YLL) to cancer in women aged 15–59 years by income of the country.

Table 1. Cancers associated with high-risk HPV infection and with HPV16 or 18 infection

Site (ICD-10 code)	Attributable to hrHPV	Of which HPV16/18	Number of cancers		
			Total	Attributable to hrHPV	Attributable to HPV16/18
Cervix (C53)	100%[2]	71%[4]	529,500[5]	529,500	375,945
Penis (C60)	47%[6]	74%[6]	26,300[7]	12,361	9,098
Vulva (C51)	40%[8]	93%[8]	30,000[7]	12,000	11,100
Vagina (C52)	70%[8]	93%[8]	15,000[7]	10,500	9,750
Anus (female) (C21)	84%[8]	94%[8]	15,900[7]	13,356	12,561
Anus (male) (C21)	84%[8]	94%[8]	14,500[7]	12,180	11,455
Oro-pharynx (female) (C01, C09-C10)	19%[9, 1]	89.3%[10]	12,600[11]	2,394	2,138
Oro-pharynx (male) (C01, C09-C10)	19%[9, 1]	89.3%[10]	48,900[11]	9,291	8,299
All sites (females)	9.4%	6.8%	6,044,710[11]	567,750	411,494
All sites (males)	0.5%	0.4%	6,617,844[11]	33,832	28,852
All sites (both sexes)	4.8%	3.5%	12,662,554[11]	601,582	440,346

[1]Weighted average of region-specific estimates of hrHPV attributable risk in oro-pharynx cancers, including cancer of tonsils and base of tongue (N.-America 56%, N.-& W.-Europe 39%, E.-Europe 38%, S.-Europe 17%, Australia 45%, Japan 52% and rest of the World 13%, derived from De Martel *et al.*)[9]
Abbreviation: hrHPV: high-risk human papillomavirus.

TABLE 3 **Noninferiority of Seroconversion Response at Month 7 in the PPI Population**

Assay (cLIA)	Girls		Boys		Women		Difference[b] Girls-Women (95% CI)	Difference[b] Boys-Women (95% CI)
	n	Seropositive, %[a]	*n*	Seropositive, %[a]	*n*	Seropositive, %[a]		
Anti–HPV 6	423	100	428	100	320	100	0.0 (−0.9 to 1.3)[c]	0.0 (−1.0 to 1.3)[c]
Anti–HPV 11	423	100	428	100	320	100	0.0 (−0.9 to 1.3)[c]	0.0 (−1.0 to 1.3)[c]
Anti–HPV 16	424	100	427	100	306	100	0.0 (−0.9 to 1.3)[c]	0.0 (−1.0 to 1.4)[c]
Anti–HPV 18	426	100	429	99.7	340	99.1	0.8 (−0.2 to 2.5)[c]	0.6 (−0.6 to 2.4)[c]

[a] Based on a statistical model adjusting for region. Seropositivity determined relative to thresholds of 20, 16, 20, and 24 mMU/mL for HPV 6, 11, 16, and 18, respectively.
[b] Percentage point difference.
[c] Noninferiority $P < .001$.

Table 2. HPV vaccination policies and coverage (for the third dose) of prog

Country	Region	Organization	System	Target group	Period	Vaccine	Definition coverage	Coverage (3rd dose)	Report date	Source
Australia	Whole country	Organized, school-based	Routine	12–15 years	Since 2009	4-valent	12–13 years	73%	Mar/11	http://www.health.gov.au/internet/immunise/publishing.nsf/Content/immunise-hpv
							14–15 years	72%		
		Organized, school-based +GPs+ community providers	Catch-up	16–26 year	2007–2009	4-valent	16–17 years	66%	Mar/11	
							18–19 years	38%		
							20–26 years	30%		
Belgium	Whole country	Opportunistic (partially reimbursed)	On prescription by physician	12–18 years	Since Nov 2007: 12–15 years; since Dec 2008: 12–18 years	2 & 4-valent	Dec 2009		Oct/11	WIV/IMA 2011; Arbyn, Gynecol Obstet Invest 2010;70:152-60, Simoens, Fabri et al, Eurosurveillance 2009; 14 (46)
							C1991	10%		
							C1992	69%		
							C1993	64%		Lefevere, Vaccine 2012 29: 8390-6
							C1994	51%		
							C1995	37%		
	Flemish Community	Organized	Routine	1st year secondary school; (GPs, pediatricians)	Since Sep 2010	4-valent	C1998 (school year 2010–11)	83%	Oct/11	www.zorg-en-gezondheid.be/HPV/
	French Community	Organized	Routine	2nd year secondary school	Planned to start in Sep 2012	2-valent	–	–	–	www.sante.cfwb.be
Canada	British Columbia	Organized	Routine	Grade 6 and 9	Since Sep 2008	4-valent	Grade 6 (2008)	62%	–	
							Grade 9 (2008)	62%		
	Quebec	Organized	Routine	Grade 4 and 9. Doses at months 0 and 2 and year 5	Since Sep 2008	4-valent	Grade 4, 1 st 2 doses (2008)	80%	–	–
							de 9, 3rd e (2008)	81%	–	
								–	–	

TABLE 2 **Noninferiority of GMTs in Girls and Boys Versus Women at Month 7 in the PPI Population**

Assay (cLIA)	Girls		Boys		Women		GMT Ratio (95% CI)	
	n	GMT[a] (mMU/mL)	*n*	GMT[a] (mMU/mL)	*n*	GMT[a] (mMU/mL)	Girls/Women	Boys/Women
Anti–HPV 6	423	959	428	1042	320	575	1.67[b] (1.46–1.91)	1.81[b] (1.58–2.08)
Anti–HPV 11	423	1220	428	1318	320	706	1.73[b] (1.50–2.00)	1.87[b] (1.60–2.17)
Anti–HPV 16	424	4697	427	5638	306	2548	1.84[b] (1.54–2.20)	2.21[b] (1.84–2.66)
Anti–HPV 18	426	916	429	1212	340	453	2.02[b] (1.71–2.39)	2.68[b] (2.24–3.19)

[a] Based on a statistical model adjusting for region.
[b] Noninferiority $P < .001$.

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Review

Reframing Cervical Cancer Prevention. Expanding the Field Towards Prevention of Human Papillomavirus Infections and Related Diseases

F. Xavier Bosch[a,*], Vivien Tsu[b], Alex Vorsters[c], Pierre Van Damme[c], Mark A. Kane[d]

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[b] PATH, Seattle, WA, USA
[c] Centre for the Evaluation of Vaccination, Vaccine & Infectious Disease Institute, University of Antwerp, Belgium
[d] Consultant on Immunization Policy, Mercer Island, WA, USA

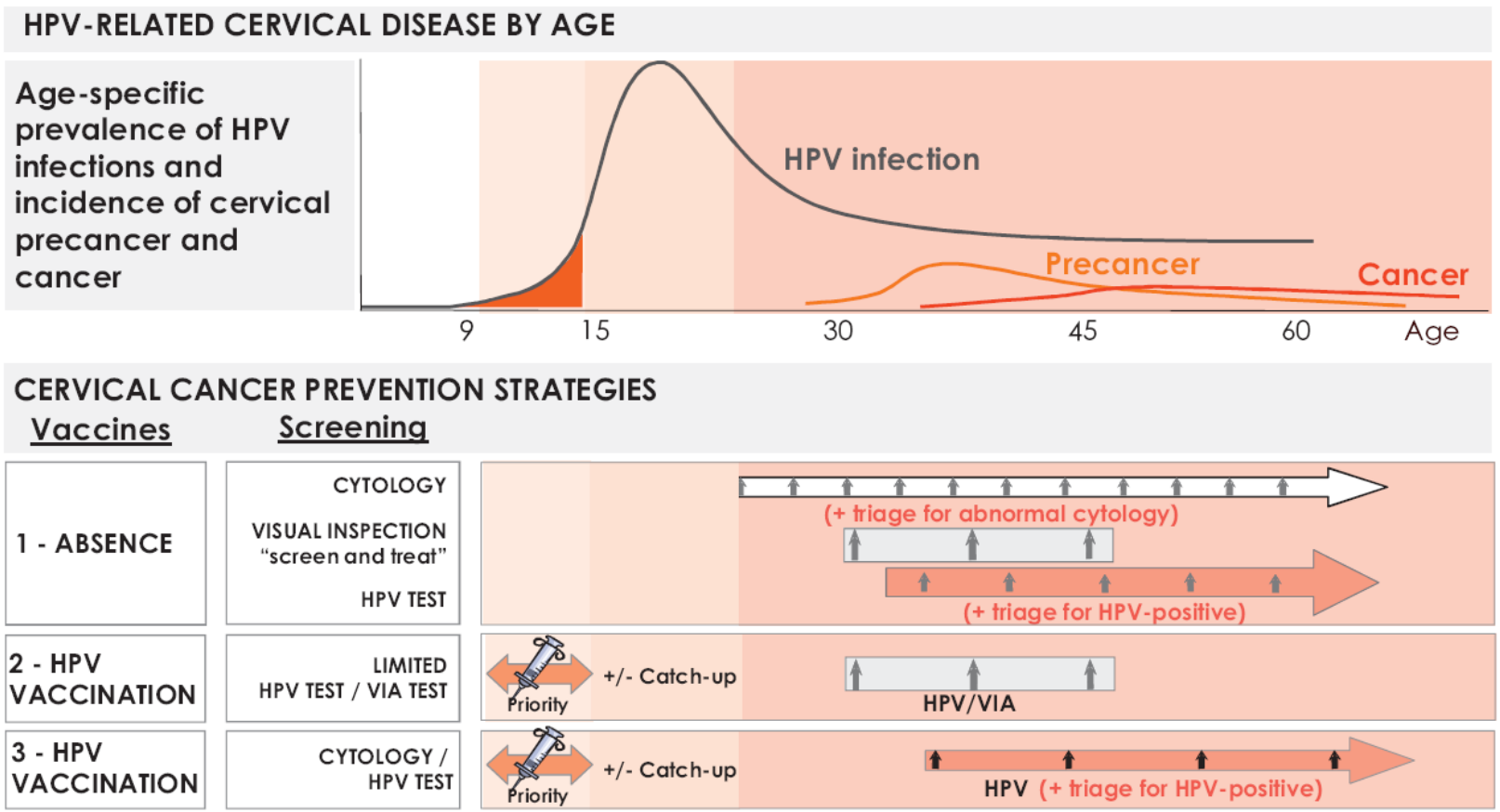


Figure 1. Natural history and HPV-based prevention strategies according to age. Adapted with modification from reference [9]. VIA: Visual inspection with acetic acid.

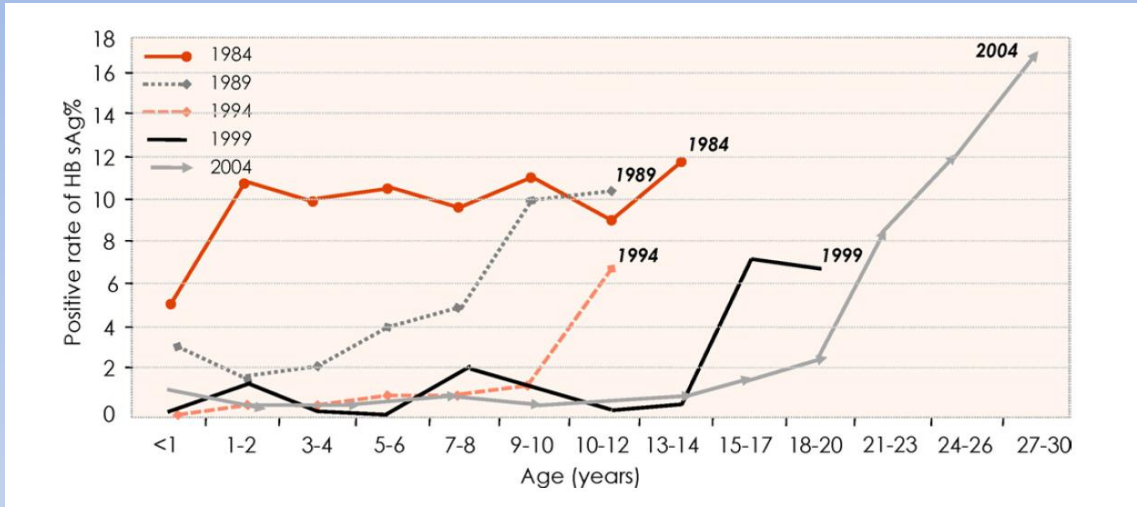


Table 2
Selected results on HBV infections and disease reduction following HBV vaccination.

Country	Endpoint	Pre-vaccination (year)	Post-vaccination (year)	Notes	Ref.
Taiwan	HBsAg prevalence	9.8% (1984)	0.6% (2004)	In <20 year-olds	[47]
	Liver cancer incidence per 100,000	0.7 in children 14 yrs (1981–86)	0.15 (2004)	Children 6–9	[47]
			0.19	Children 10–14	
			0.16	Children 15–19	
The Gambia	HBsAg prevalence	10% (1983)	0.6% (2003)	Vaccination of newborns	[48]
Malaysia	HBsAg prevalence	1.6% (1997)	0.3% (2003)	Children 7–12	[49]
Alaska	Acute hepatitis B cases per 100,000	19 (1981–82)	No cases since 1992	In children <20 years	[50]
	Liver cancer incidence per 100,000	3 (1984–88)	No cases since 1999		
	Number of HbsAg positives	657 (1987)	2 (2008)		
Hawai	HBsAg		97% reduction from 1990 to 2004		[51]
	Acute hepatitis B per 100,000	4.5 (1990)	0 (2004)		

HBsAg: Hepatitis B surface antigen; HBV: Hepatitis B virus.

Table 4
Summary of the differences between the HBV and HPV vaccines.

The HPV spectrum of viral type protection:
The hepatitis plasma-derived vaccine and later the recombinant vaccines provide protection against all HBV genotypes. The situation is quite different for HPV where up to 15 HPV types can induce malignancies. Although there are reports of mid-term cross-protection, not all HPV high-risk type infections will be prevented by the current generation of vaccines.
Duration of response:
For HBV, it has clearly been shown that most persons who displayed a good immune response after three doses of HBV vaccine have an immune memory even without detectable antibodies. Current long-term follow-up studies for HBV immunization show very few break-through infections and no chronic viral hepatitis B was observed in a fully vaccinated individual 20-30 years after vaccination. Based on the current evidence, the now documented long-term protection induced by the HBV vaccine cannot be extrapolated to the HPV vaccine. HPV vaccination induces high titers of genotype-restricted neutralizing antibodies which are thought to be primary, if not the only, immune effectors of protections following vaccination [55]. The observed waning of antibody levels after vaccination, apparently less relevant for protection against HBV infection must be taken into account when developing an optimal HPV prevention program -especially when setting up universal programs targeting children early in life- until more is known about other potential protective immune responses.
Immune memory:
It has been clearly shown that anamnestic responses (a rapid rise in antibody levels) occur following an HPV challenge (a fourth dose) with both vaccines, but it is unclear if an exposure with wild HPV virus will elicit an anamnestic response and protect against chronic infection and disease as is the case with HBV.
The value of serological monitoring of prevention programmes:
The correlates of protection for HBV infections, especially for long-term follow-up, are not ideal. However, HBV serological testing can be applied to test for pre-vaccination exposure, initial protection, anamnestic response and post-vaccination exposure. For HPV, the utility of serological assays is less well understood and complicated by the absence of consensus and standardisation.
Primary target in the young adolescent age groups:
Reaching adolescents will be challenging in most countries, but school-based programmes have been shown feasible in several countries [53, 54]. Alternatively strategies such as national immunization days or campaign-style programs can be considered. Alternatives to adolescent HPV immunization should be explored; for instance, by incorporating the HPV vaccine into childhood or Expanded Program on Immunization (EPI) programmes. As most countries, even the poorest ones, are highly effective at reaching children below two years of age, such alternative would guarantee very high rates of coverage.
Require adapted vaccine prices and support from donors:
Monovalent HBV vaccine is now available for approximately US $ 0.20 per dose for public sector programs in developing countries, although it was introduced into industrial countries at more than US $ 100 per dose for a three-dose series in 1982. Although high prices for HPV vaccine persist in industrial countries, GAVI has been offered a price of US $ 5 for quadrivalent HPV vaccine. Wealthier developing countries are offered a "tiered" price dependent on their per capita GNP depending on tender and bid or negotiation with the manufacturers.
Require increased collaboration:
Require Increased collaboration of the HPV and cancer community with primary prevention experts to draft national integrated control plans of vaccination, screening and treatment.

GAVI: Global Alliance for Vaccines and Immunisation; GNP: Gross national product.

Table 6
Summary of the major elements of paradigm change for HPV prevention.

BURDEN OF DISEASE IN BOTH GENDERS	• *The HPV viral etiology has been established for significant fractions of cancers of the vulva, vagina, anus in both genders and penile cancer. A significant fraction of oropharyngeal cancer in both genders is highly associated with HPV infection [61].* • *In several industrialized countries with ongoing screening programs, data suggests that the actual number of cases of anal and oropharyngeal cancers are on the increase and may have already (or will soon) exceed that of cervical cancer [62].* • *There has been an increased understanding of the HPV co-morbidity that occurs with HIV as well as the realization that the highest mortality from both diseases tends to occur in the same countries, often in sub-Saharan Africa [63].* • *Data on the high rates of anal cancer in men who have sex with men, and the very high rates in HIV positive individuals [64].*
VACCINE EFFICACY IN MEN	• *Early data from Australia is already showing high efficacy in prevention of genital warts in immunized cohorts of females and significant but lower efficacy in unimmunized males from the same population, a significant example of the impact of herd immunity [65].* • *Data from male efficacy studies of HPV vaccines are showing high efficacy against HPV-related anal pre-cancerous lesions and anal cancer as well as high efficacy in preventing genital warts [25].*
VACCINE ACCESSI-BILITY	• *The GAVI Alliance has included HPV in the list of vaccines to be supported financially in eligible countries opening the possibility of affordable immunization in the developing world. Vaccine prices for the quadrivalent vaccine is being offered at 5$/dose. Many other multinational organizations (i.e., OPS/PAHO revolving fund) and national procurement offices have negotiated prices that facilitate the development of HPV vaccination public programs.* • *Economic analyses are being redone to reflect this level of vaccine price, since the developing countries themselves will initially have to co-pay a fraction of this price.*

Table 5
Summary of HPV prevention framework in the initial years of HPV vaccines.

Initial clinical trials were planned and implemented in women only, as was the initial licensing in 2006. Clinical trials for efficacy in men are only now coming to completion and licensing has been first granted in 2011-12.
Early health economic models conceptualized investment in HPV vaccines from the point of view of preventing cervical disease in women, and sometimes included genital warts. Only recently have economic models begun to study the costs and benefits of controlling non cervical disease in both sexes [60].
Non-oncogenic genital lesions are sometimes dismissed as being less important since they are largely self-limiting; however, they have become increasingly difficult to ignore in the industrial world because the large number of health provider visits triggered by genital warts incurs significant costs and much suffering. The burden of genital warts in developing

Table 1. Subsites and ICD-O-3 codes for oral cavity and oropharynx.

Site	Subsites	ICD-O-3 codes
Oral cavity	Lips (internal*)	C00.3–C00.9
	Tongue	C02.0–C2.3; C02.8–9
	Gum	C03.0–1, C03.9
	Floor of the mouth	C04.0–1, C04.8–9
	Hard palate	C05.0, C05.8–9
	Cheek mucosa	C06.0
	Vestibule of mouth	C06.1
	Retromolar area	C06.2
	Mouth (overlapping)	C06.8
	Mouth, NOS	C06.9
Oropharynx	Base of tongue	C01.9
	Lingual tonsil	C02.4
	Soft palate	C05.1
	Uvula	C05.2
	Tonsils	C09.0–1, C09.8–9
	Oropharynx†	C10.0–C10.4, C10.8–9

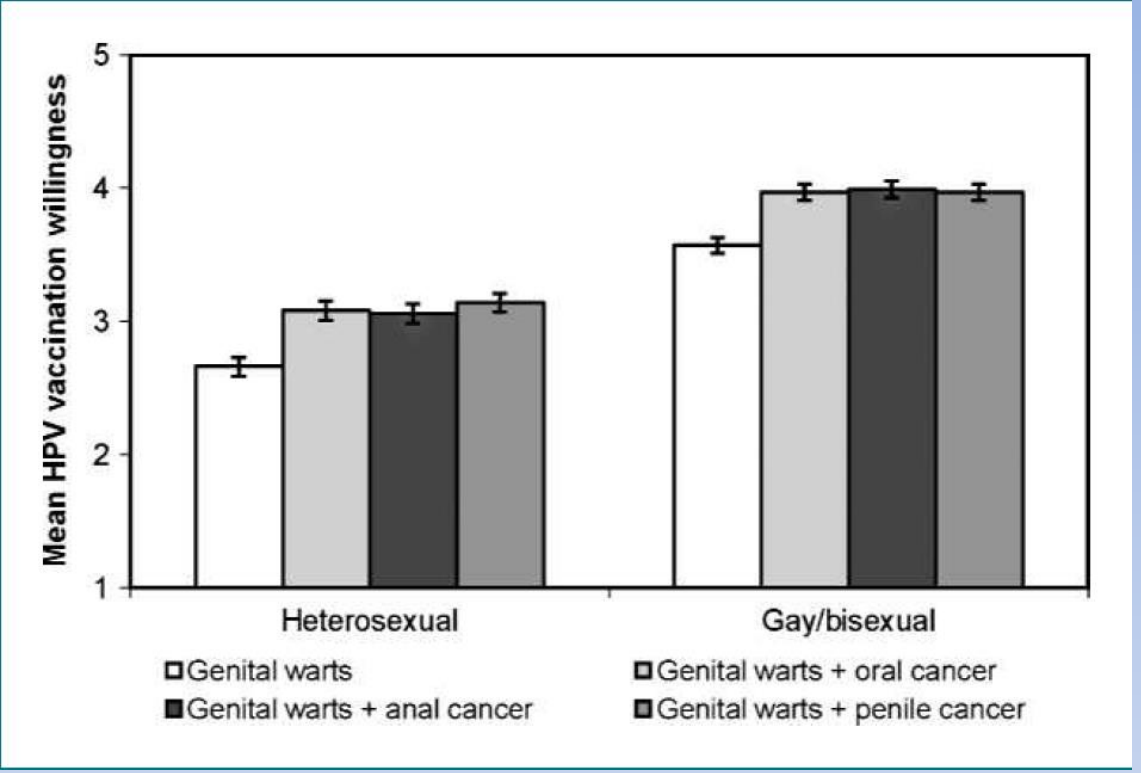
Cancer Epidemiology, Biomarkers & Prevention

AACR

Does Framing Human Papillomavirus Vaccine as Preventing Cancer in Men Increase Vaccine Acceptability?

Annie-Laurie McRee, Paul L. Reiter, Kim Chantala, et al.

Cancer Epidemiol Biomarkers Prev 2010;19:1937-1944. Published OnlineFirst July 20, 2010.



Human Vaccines & Immunotherapeutics 8:2, 201–207; February 2012; © 2012 Landes Bioscience

The burden of hospitalizations for anus and penis neoplasm in Spain (1997–2008)

Ruth Gil-Prieto,[1,*] Pablo Viguera Ester,[1] Alejandro Álvaro-Meca,[1] María San Martín Rodríguez[2] and Ángel Gil De Miguel[1]

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Table 1. Hospitalization rates, rate of death and case-fatality rate of anus and penis neoplasm in Spain

		N	Hospitalization rate (per 100,000 inhabitants) CI (95%)	Deaths	Rate of Death (per 100,000 inhabitants) CI (95%)	Case-fatality rate* (%) CI (95%)	Average length of stay (days (SD))	Cost (euros)
Anus	Male	6973	2.84 (2.77–2.91)	738	0.30 (0.28–0.32)	10.58 (9.86–11.31)	14 (16)	6,968
	Female	4992	1.97 (1.91–2.02)	488	0.19 (0.17–0.21)	9.78 (8.95–10.60)	14 (16)	6,692
Penis		7643	3.11 (3.04–3.18)	530	0.22 (0.20–0.23)	6.93 (6.36–7.50)	10 (13)	6,381

Notes: *, %; **, per 100,000.

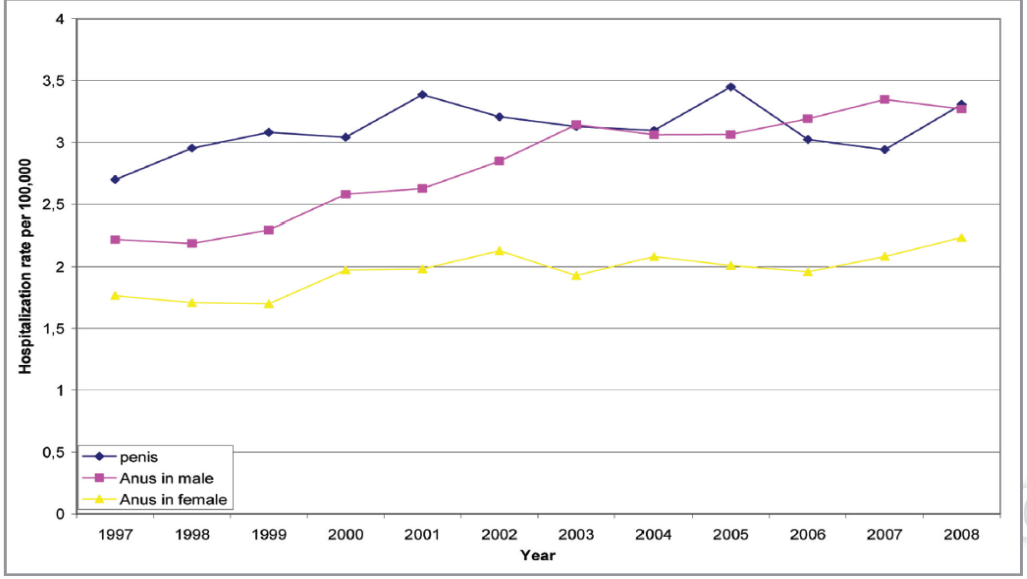

Figure 1. Hospitalization rate related to anus and penis malignant neoplasm in Spain (1997–2008).

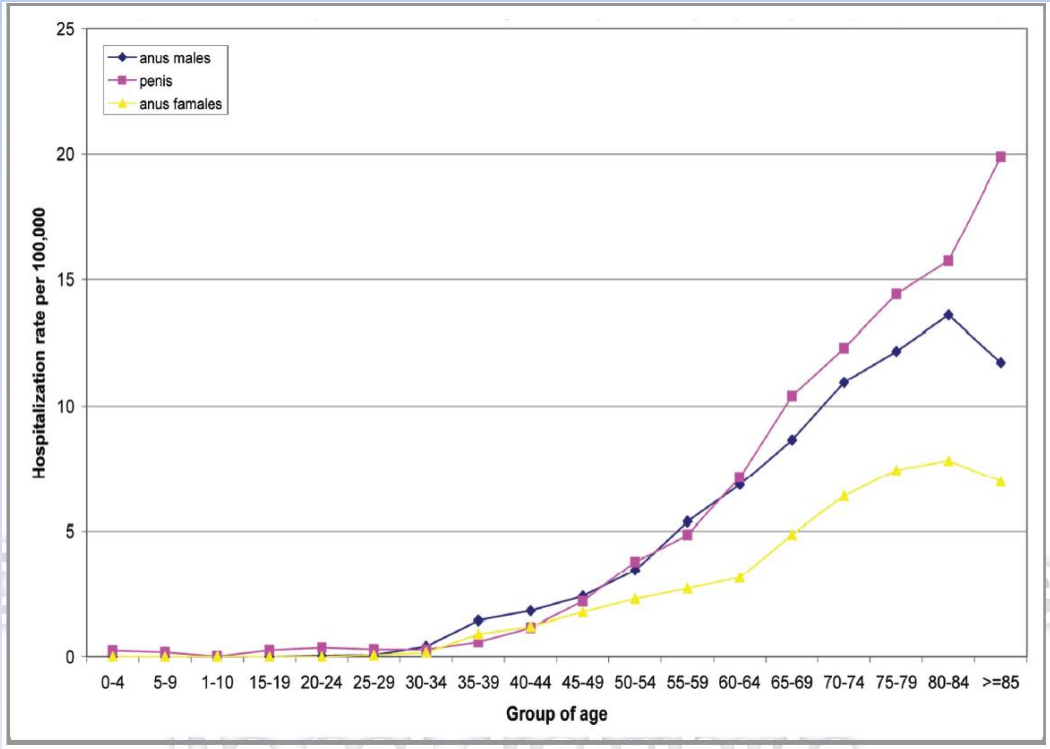

Figure 2. Hospitalization rate of penis and anus malignant neoplasm by group of age in Spain (1997–2008).

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 3, 2011 VOL. 364 NO. 5

Efficacy of Quadrivalent HPV Vaccine against HPV Infection and Disease in Males

Anna R. Giuliano, Ph.D., Joel M. Palefsky, M.D., Stephen Goldstone, M.D., Edson D. Moreira, Jr., M.D., Mary E. Penny, M.D., Carlos Aranda, M.D., Eftyhia Vardas, M.D., Harald Moi, M.D., Heiko Jessen, M.D., Richard Hillman, M.D., Yen-Hwa Chang, M.D., Daron Ferris, M.D., Danielle Rouleau, M.D., Janine Bryan, Ph.D., J. Brooke Marshall, Ph.D., Scott Vuocolo, Ph.D., Eliav Barr, M.D., David Radley, M.S., Richard M. Haupt, M.D., and Dalya Guris, M.D.

Table 1. Efficacy of Quadrivalent Vaccine against the Development of External Genital Lesions in the Intention-to-Treat Population.*

Variable	Quadrivalent HPV Vaccine			Placebo			Observed Efficacy (95% CI)
	Cases of EGL	Person-Yr at Risk	Rate	Cases of EGL	Person-Yr at Risk	Rate	
	no.		*no./100 person-yr at risk*	*no.*		*no./100 person-yr at risk*	%
HPV type							
Any type	36	4612.6	0.80	89	4538.6	2.00	60.2 (40.8 to 73.8)
Type 6, 11, 16, or 18†	27	4625.7	0.58	77	4556.5	1.69	65.5 (45.8 to 78.6)
Type 6	21	4635.8	0.45	51	4576.0	1.11	59.4 (31.2 to 76.8)
Type 11	6	4663.7	0.13	25	4606.6	0.54	76.3 (40.8 to 92.0)
Type 16	3	4663.1	0.06	10	4621.9	0.22	70.3 (−15.5 to 94.7)
Type 18	2	4670.0	0.04	3	4627.9	0.06	33.9 (−476.7 to 94.5)
Sexual orientation‡							
Heterosexual males	21	4153.9	0.51	57	4087.5	1.39	63.7 (39.3 to 79.1)
Males who had sex with male partners	6	471.8	1.27	20	469.0	4.26	70.2 (23.0 to 90.2)
Lesion type							
Condyloma acuminatum§	24	4635.4	0.52	72	4558.8	1.58	67.2 (47.3 to 80.3)
All PIN lesions	6	4658.7	0.13	5	4628.2	0.11	−19.2 (−393.8 to 69.7)
PIN grade 1	3	4666.1	0.06	4	4629.7	0.09	25.6 (−339.9 to 89.1)
PIN grade 2 or 3	3	4663.1	0.06	2	4628.6	0.04	−48.9 (−1682.6 to 82.9)
Penile, perianal, or perineal cancer	0	4670.6	0.00	0	4630.5	0.00	—

Contents lists available at SciVerse ScienceDirect

Vaccine

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

Quadrivalent HPV vaccine efficacy against disease related to vaccine and non-vaccine HPV types in males☆

Stephen E. Goldstone[a,*], Heiko Jessen[b], Joel M. Palefsky[c], Anna R. Giuliano[d], Edson D. Moreira Jr.[e], Eftyhia Vardas[f,g], Carlos Aranda[h], Richard J. Hillman[i], Daron G. Ferris[j], Francois Coutlee[k], J. Brooke Marshall[l], Scott Vuocolo[l], Richard M. Haupt[l], Dalya Guris[l], Elizabeth Garner[l]

CVI
Journals.ASM.org

Immunogenicity of the Quadrivalent Human Papillomavirus (Type 6/11/16/18) Vaccine in Males 16 to 26 Years Old

Richard J. Hillman,[a] Anna R. Giuliano,[b] Joel M. Palefsky,[c] Stephen Goldstone,[d] Edson D. Moreira, Jr.,[e] Eftyhia Vardas,[f] Carlos Aranda,[g] Heiko Jessen,[h] Daron G. Ferris,[i] Francois Coutlee,[j] J. Brooke Marshall,[k] Scott Vuocolo,[k] Richard M. Haupt,[k] Dalya Guris,[k] and Elizabeth I. O. Garner[k]

TABLE 4 Summary of anti-HPV seroconversion over time among HM and MSM subjects[a]

		Vaccinated HM (N = 1,726)			Vaccinated MSM (N = 299)		
cLIA (mMU/ml)	Study time	n	Seroconversion (%)	95% CI	n	Seroconversion (%)	95% CI
HPV-6 (≥20)	Day 1	978	0.0	0.0, 0.4	114	0.0	0.0, 3.2
	Mo 7	978	99.2	98.4, 99.6	114	96.5	91.3, 99.0
	Mo 24	851	91.3	89.2, 93.1	90	86.7	77.9, 92.9
	Mo 36	792	89.5	87.2, 91.6	55	80.0	67.0, 89.6
HPV-11 (≥16)	Day 1	978	0.0	0.0, 0.4	114	0.0	0.0, 3.2
	Mo 7	978	99.4	98.7, 98.4	114	97.4	92.5, 99.5
	Mo 24	851	95.5	93.9, 96.8	90	96.7	90.6, 99.3
	Mo 36	792	94.3	92.5, 95.8	55	89.1	77.8, 95.9
HPV-16 (≥20)	Day 1	999	0.0	0.0, 0.4	136	0.0	0.0, 2.7
	Mo 7	999	99.4	98.7, 99.8	136	94.1	88.7, 97.4
	Mo 24	869	99.2	98.3, 99.7	110	98.2	93.6, 99.8
	Mo 36	811	98.3	97.1, 99.1	66	93.9	85.2, 98.3
HPV-18 (≥24)	Day 1	1,032	0.0	0.0, 0.4	142	0.0	0.0, 2.6
	Mo 7	1,032	98.4	97.5, 99.1	142	89.4	83.2, 94.0
	Mo 24	897	62.9	59.6, 66.0	114	57.9	48.3, 67.1
	Mo 6	836	57.3	53.9, 60.7	69	53.6	41.2, 65.7

[a] Abbreviations: N, number of subjects randomized to the respective vaccination group who received at least 1 injection; n, number of subjects contributing to the analysis.

Vaccine 30S (2012) F168–F174

Contents lists available at SciVerse ScienceDirect

Vaccine

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

Review

Human Papillomavirus, Human Immunodeficiency Virus and Immunosuppression

Lynette A. Denny[a,*], Silvia Franceschi[b], Silvia de Sanjosé[c,d], Isabelle Heard[e], Anna Barbara Moscicki[f], Joel Palefsky[g]

Clinical trials designed to evaluate the safety and immunogenicity of HPV vaccines in HIV-infected infants and females (ClinicalTrials.gov, January 2, 2012).

Participants	Clinicaltrials.gov identifier	Sponsor	Location	Vaccine	Status	Study
180 HIV-infected girls and boys aged 9–14 years	NCT01446718	Nelly R Mugo	Kenya	Quadrivalent	Not yet recruiting	Immunogenicity and safety of the quadrivalent vaccine
105 HIV-infected and HIV-negative adolescents and young adults aged 12–26 years	NCT00798265	National Cancer Institute	USA, Maryland	Quadrivalent	Recruiting	Safety and immunogenicity on HIV-infected compared to HIV-negative persons of the same age
99 HIV-infected women aged 16–23 years	NCT00710593	NICHD	USA Puerto Rico	Quadrivalent	Completed	Immunogenicity, safety, tolerability, and behavioral impact Participants divided in two arms according to immune status and duration and efficacy of antiretroviral therapy
282 HIV-infected women aged 13–45 years	NCT00604175	NIAID	USA Brazil Puerto Rico South Africa	Quadrivalent	Ongoing, not recruiting	Phase II study to evaluate safety, tolerability, and immunogenicity of HPV vaccine Participants will be divided in 3 arms according to level of immunosuppression
150 HIV-infected females aged 18 years or older	NCT00667563	AIDS Malignancy Clinical Trials Consortium	India	Quadrivalent	Ongoing, not recruiting	To assess the safety of the quadrivalent vaccine in women without prior exposure to at least one of the HPV types in the vaccine Only study with clinical endpoints: prevalence and incidence of cervical intraepithelial neoplasia in patients and description of the spectrum of cervical HPV types at baseline, 9 months, and 1 year after vaccination
120 HIV-infected adult females aged 18–25 years and 30 HIV-negative females	NCT00586339	GlaxoSmithKline	South Africa	Bivalent	Completed	To evaluate safety and immunogenicity of the Bivalent vaccine. Double blinded, randomized for HIV-positive subjects and open for HIV-negative subjects
600 HIV-infected females aged 15–25 years	NCT01031069	GlaxoSmithKline	Brazil India Thailand	Bivalent Quadrivalent	Ongoing, not recruiting	Phase IV, observer-blind study designed to evaluate the safety and immunogenicity of the bivalent vaccine as compared to the quadrivalent vaccine

Lenzi *et al. BMC Public Health* 2013, **13**:117
http://www.biomedcentral.com/1471-2458/13/117

BMC Public Health

CORRESPONDENCE Open Access

Rome consensus conference - statement; human papilloma virus diseases in males

Andrea Lenzi[1*], Vincenzo Mirone[2], Vincenzo Gentile[3], Riccardo Bartoletti[4], Vincenzo Ficarra[5], Carlo Foresta[6], Luciano Mariani[7], Sandra Mazzoli[8], Saverio G Parisi[9], Antonio Perino[10], Mauro Picardo[11] and Carla Maria Zotti[12]

Interpretation

Since our data show a reduction of anal HPV infection rates in vaccinated women, it suggests that, in the future, women who receive the prophylactic HPV vaccines before exposure to the virus will possibly have less anal cancer.

Conclusions: The Jury made Recommendations based on the scientific evidence presented by the Scientific Committee. Accordingly, for prevention purposes and social fairness and equality, as both sexes are affected by the disease, the vaccination of 12-year-old males against HPV should be recommended in order to guaranty protection to everyone. Aspects related to healthcare policy and economic sustainability, are to be discussed by respective public system representatives. More campaigns to raise awareness through all institutional channels are needed, not only regarding anogenital warts, but for HPV-related diseases in general in males in accordance to new scientific evidences.

Based on the previous statements and data, HPV DNA sero status seem to play a fundamental role in HPV transmission and diseases development between partners. In males, there are several risk factors that play a fundamental role in HPV infection and development of the disease such as immunodeficiency disease.

Conclusive considerations of the consensus panel

➢ Awareness campaigns should be implemented not only for anogenital warts but for HPV-related diseases in general, through all institutional channels, in order to increase HPV knowledge and reduce, when possible, HPV transmissibility at a population level

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Table 2 Main prevalence studies conducted using the PCR method

Population type (n° males examined)	Country	Prevalence of positive HPV DNA (PCR test)	Prevalence of positive HPV DNA tests (high-risk genotypes)
Population (290) Giuliano et al., 2007 [7]	USA	30.0%	16.6%
Military recruits (285) Hippelainen et al., 1993 [8]	Finland	16.5%	- -
University students (317) Weaver et al., 2004 [9]	USA	32.8%	14.5%
Students and industrial workers (114) Lazcano-Ponce et al., 2001 [10]	Mexico	36.0%	16.7%
Military recruits (337) Kjaier et al., 2005 [11]	Denmark	33.8%	- -
Military men (1030)	Mexico	44.6%	34.8

Question no. 3: What method of prevention of HPV-related diseases could significantly reduce their impact on the male population?

Question conclusion

Vaccination on males, according to recent data, seems to be effective with the quadrivalent vaccine as it is in women. Vaccination is the most effective measure to reduce HPV related diseases impact in males with efficacy rates around 90%. Condom usage seems to be also effective in reducing at least in 50% the risk of transmission when used

Question conclusions

Although herd immunity exist, primary vaccination exclusively of males or females doesn't seem to be effective when coverage rates are less than high in reducing HPV related disease on partners in a significant way. In Italy coverage rates are not high, only 53% of 12 years old females have been vaccinated with 3 doses. Social equity right to get the vaccine in males and higher risk groups, as well as social burden (including psychological burden) should be taken into consideration as they seem relevant.

ary prevention of HPV-related
V-related diseases in their

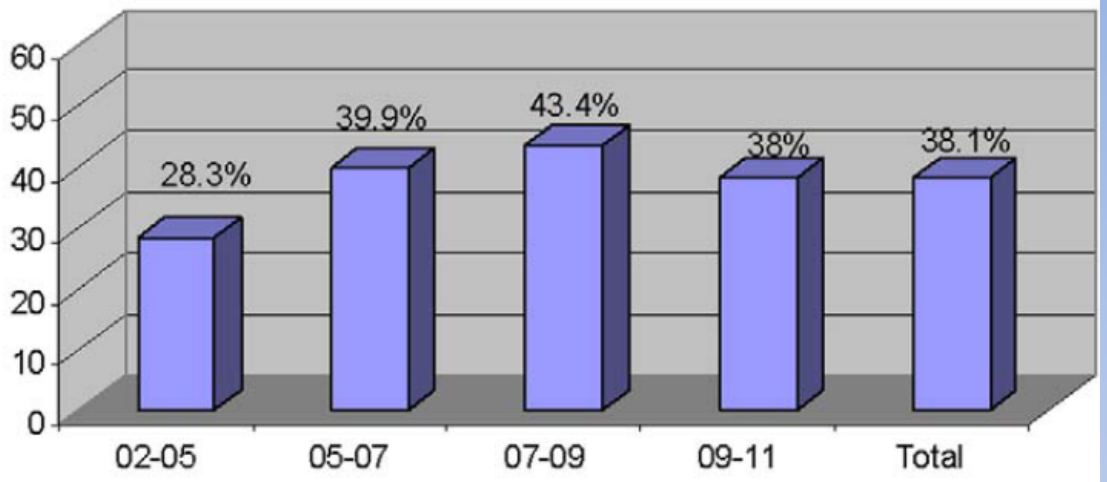


Figure
doi:10.1

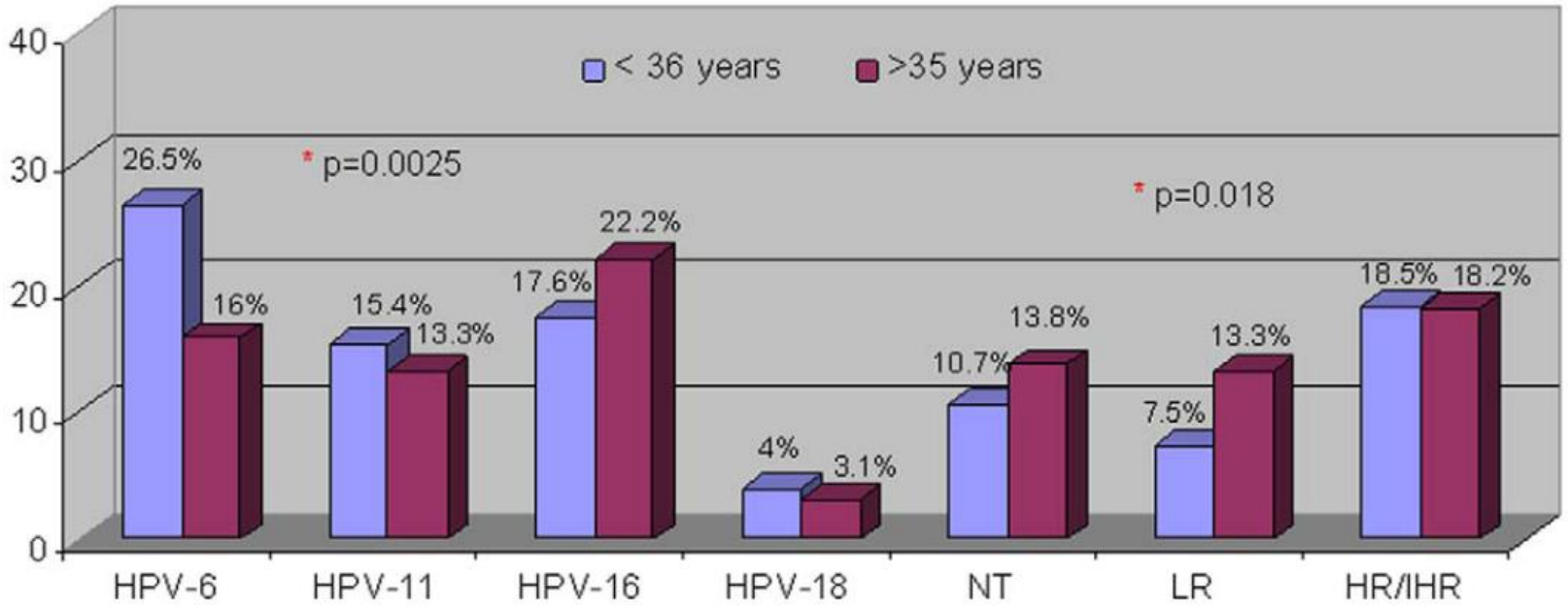


Figure 3. Detected genotype distribution according to age.
doi:10.1371/journal.pone.0054375.g003

Table 2. Association of the different factors with HPV infection in males. HPV +/− (%).

Infection factors (HPV+)	YES	NO	p
PDA	4/8 (33.3)	158/264 (37.4%)	ns
STD	89/86 (50.8%)	133/138 (49%)	ns
Promiscuity	86/164 (34.4%)	97/157 (38.2%)	ns
Marital Status			
Single	119/179 (39.9%)		
Divorced	17/26 (39.5%)		0.05
Married	35/112 (23.8%)		
Progression factors (E6/E7+)	**YES**	**NO**	
Alcohol	32/62 (34%)	20/43 (31.7%)	ns
Tobacco usage			

PDA: Parenteral drug ad
doi:10.1371/journal.pone.

Marty *et al. BMC Cancer* 2013, **13**:10
http://www.biomedcentral.com/1471-2407/13/10

BMC Cancer

RESEARCH ARTICLE Open Access

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

Rémi Marty[1*], Stéphane Roze[1], Xavier Bresse[2], Nathalie Largeron[2] and Jayne Smith-Palmer[3]

Conclusions: In Europe, the vaccination of 12-year old boys and girls against HPV 6, 11, 16 and 18 would be associated with substantial additional clinical benefits in terms of reduced incidence of HPV-related genital warts and carcinomas versus girls-only vaccination. The incremental benefits of adding boys vaccination are highly dependent on coverage in girls. Therefore, further analyses should be performed taking into account the country-specific situation. In addition to clinical benefits, substantial economic benefits are also anticipated and warrant further investigation as do the social and ethical implications of including boys in vaccination programs.

Table 4 Incremental benefit of a boys and girls vaccination strategy against HPV 6,11,16,18 vs. girls-only vaccination (results presented in a steady state situation, at 50 and 100 years; results from base case analysis)

Gender	Disease	Annual number of HPV 6/11/16/18 cases	Annual number of cases avoided with girls only vaccination		Incremental number of cases avoided due to GNV (vs. girls only)		Relative reduction in remaining burden: GNV vs. girls only (%)	
			At 50 years	At 100 years	At 50 years	At 100 years	At 50 years	At 100 years
Female	Genital warts	288,959	227,388	228,724	34,936	35,164	−56.7	−58.4
	Cervical cancer	23,254	13,848	19,728	958	1,362	−10.2	−38.6
	Vulvar cancer	2,702	873	2,286	67	157	−3.7	−37.8
	Vaginal cancer	1,146	406	981	31	66	−4.2	−39.9
	Anal cancer	2,929	821	2,330	80	258	−3.8	−43.0
	Head/neck cancer	2,531	701	2,020	67	220	−3.7	−43.0
	Total cancers	**32,562**	**16,649**	**27,345**	**1,203**	**2,062**	**−7.6**	**−39.5**
Male	Genital warts	325,722	202,671	202,587	85,740	87,900	−69.7	−71.4
	Penile cancers	1,091	93	197	156	542	−15.6	−60.6
	Anal cancers	1,699	313	1,067	180	402	−13.0	−63.6
	Head/neck cancers	12,707	2,555	8,203	1,449	2,967	−14.3	−65.9
	Total cancers	**15,497**	**2,961**	**9,467**	**1,784**	**3,911**	**−14.2**	**−64.9**
Female + Male	**Genital warts**	614,681	430,059	431,311	120,676	123,064	−65.4	−67.1
	Total cancers	48,059	19,610	36,812	2,987	5,973	−10.5	−53.1

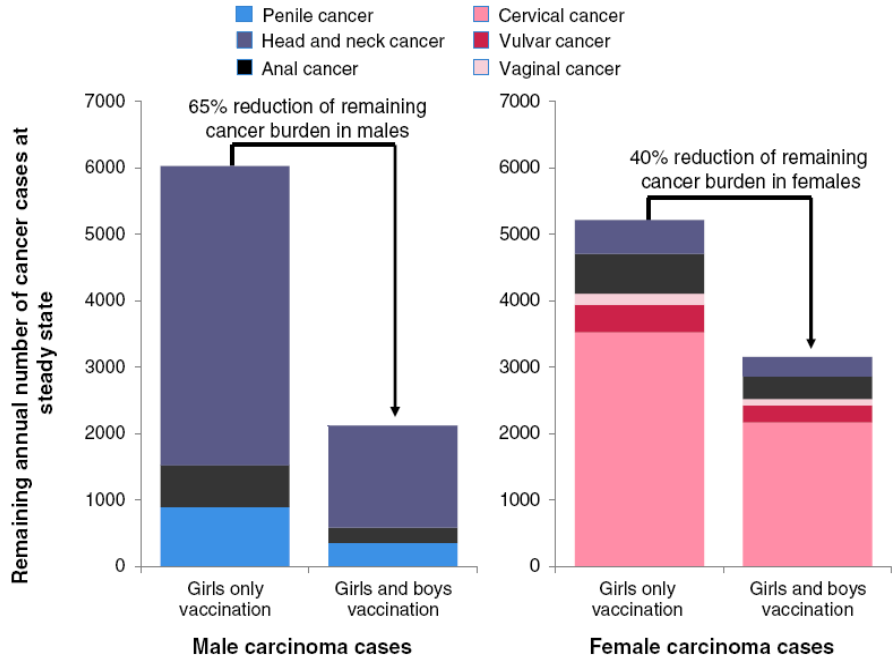


Figure 1 Annual number HPV 16/18 related carcinoma cases among males and females when considering a vaccination strategy of boys and girls aged 12 versus girls only vaccination aged 12 (70% vaccine coverage rates assumed for all cohorts) - base case analysis **presented at steady-state, 100 years.** The remaining annual burden of male HPV-related carcinomas is shown in the chart on the left side; remaining burden of female HPV-related carcinomas is shown in the chart on the right hand side.

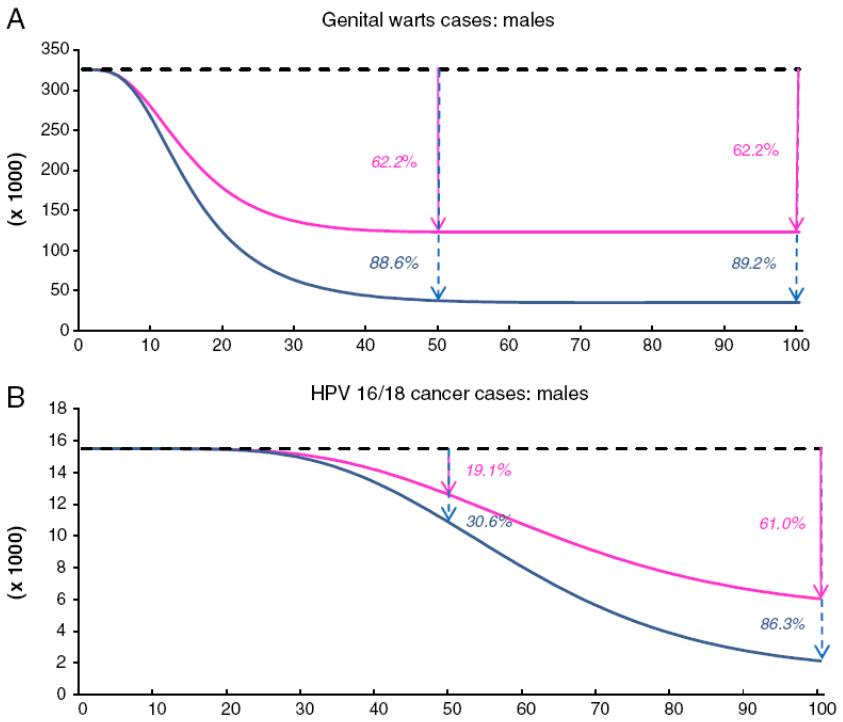


Figure 2 Estimated annual remaining burden over the years 2012–2112 of HPV-related diseases when vaccinating 12-year old boys and girls versus girls only vaccination aged 12 (cumulative vaccination coverage rate 70%, lifetime duration of protection).

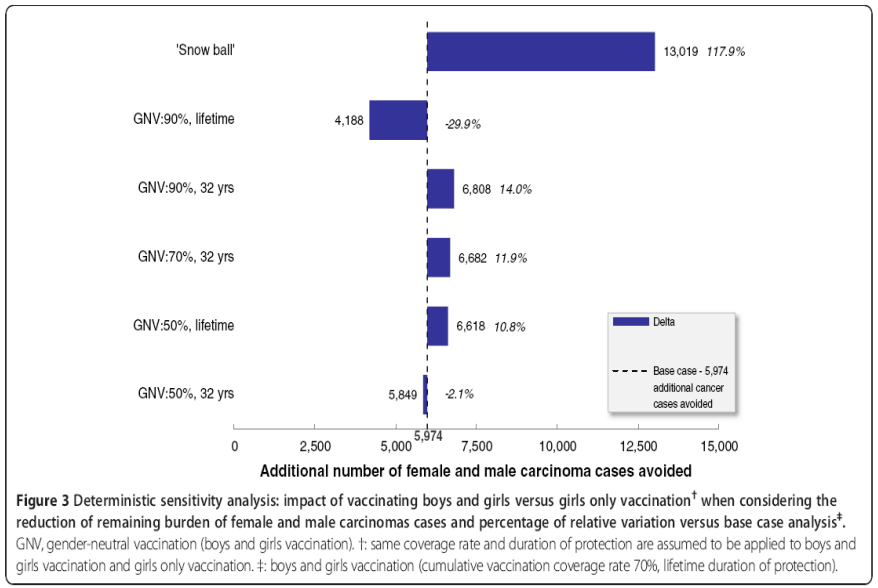


Figure 3 Deterministic sensitivity analysis: impact of vaccinating boys and girls versus girls only vaccination† when considering the reduction of remaining burden of female and male carcinomas cases and percentage of relative variation versus base case analysis‡. GNV, gender-neutral vaccination (boys and girls vaccination). †: same coverage rate and duration of protection are assumed to be applied to boys and girls vaccination and girls only vaccination. ‡: boys and girls vaccination (cumulative vaccination coverage rate 70%, lifetime duration of protection).

Contents lists available at SciVerse ScienceDirect

Vaccine

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

Review

Human Papillomavirus and Diseases of the Upper Airway: Head and Neck Cancer and Respiratory Papillomatosis

Maura L. Gillison[a,*], Laia Alemany[b,c], Peter J.F. Snijders[d], Anil Chaturvedi[e], Bettie M. Steinberg[f], Steve Schwartz[g], Xavier Castellsagué[b,c]

Molecular criteria in support of a causal association.

Criterion	Feature	References
Molecular pathology	Regular presence in tumors	Kreimer AR *et al.* [6]
	Clonally related to tumors	Niedobitek G *et al.* [9] Gillison M *et al.* [10] Begum S *et al.* [11]
	Persistence in tumors	Yeudall WA *et al.* [150] Ferris RL *et al.* [12] Steenbergen RD *et al.* [13]
	Viral oncogene activity	Van Houten VM *et al.* [15] Jung A *et al.* [16] Hoffmann M *et al.* [17]
	Biological evidence on the basis of known viral oncogene functions	Gillison M *et al.* [10] Klussman JP *et al.* [24] Braakhuis BJ *et al.* [19] Westra W *et al.* [27] Hoffmann M *et al.* [17]
In vitro models	Capacity to transform respective target cells	Park NH *et al.* [35] Sexton CJ *et al.* [36] Chen RW *et al.* [38] Smeets SJ *et al.* [37] Lace MJ *et al.* [20]
	Dependence of transformed phenotype on functions exerted by viral oncogenes	Rampias T *et al.* [14]
Animal models	Capacity to induce respective tumors in transgenic mice	Strati K *et al.* [40] Strati and Lambert [151]

Table 8
Selected studies of incidence trends for head and neck cancers.

Country	Reference	Years	Incidence trends for oropharyngeal cancers		Incidence of oropharyngeal cancers by age	Incidence trends for other head and neck cancers	
			Men	*Women*		*Men*	*Women*
Australia	Hocking J *et al.* [81]	1982–2005	Increase (APC = 1.4[a])	Increase (APC = 1.0[a])	Younger, 45–59 years	Decrease (APC = 1.7[a])	Stable
Canada	Auluck A *et al.* [82]	1980–2006	Increase (APC = 0.8[a])	Increase (APC = 0.6[a])	Younger, 55–64 years	Decrease (APC = 0.6[a])	Stable
Denmark	Blomberg M *et al.* [83]	1978–2007	Increase (APC = 4.4[a])	Increase (APC = 4.1[a])	Younger, <60 years	Increase (0.7[a])	Increase (0.9[a])
England	Reddy VM *et al.* [84]	1985–2006	Increase (APC = 2.5[a] to 6.7[a])	Increase (APC = 2.6[a] to 6.5[a])	Younger, 40–69 years	Increase (APC = 1.7[a])	Increase (APC = 2.8[a])
Japan	Ioka A *et al.* [86]	1965–1999	Increase (3.6-fold)	Increase (3-fold)	NR	Increase	Stable
The Netherlands	Braakhius BJ *et al.* [87]	1989–2006	Increase (APC = 2.6[a])	Increase (APC = 3.0[a])	Younger ages among men	Stable	Increase (APC = 2.0[a])
Norway	Mork J *et al.* [88]	1981–2005	Increase (APC = 5.0[a])	Increase (APC = 4.2[a])	Recent birth cohorts	Decrease	Stable/decrease
Sweden	Hammarstedt L *et al.* [90]	1970–2002	Increase (2.6- fold)	Increase (3.5-fold)	NR	NR	NR
USA	Chaturvedi AK *et al.* [91]	1973–2004	Increase (APC = 1.3[a])	Decrease	Younger, 40–59 years	Decrease	Decrease

NR: Not reported; APC: Annual percent change in incidence.
[a] Statistically significant at $p < 0.05$.

Contents lists available at SciVerse ScienceDirect

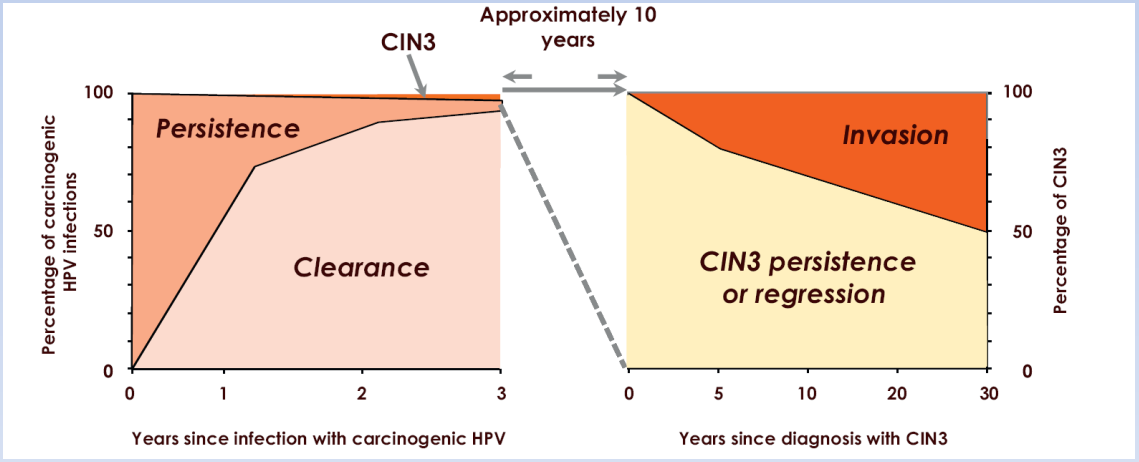
Vaccine

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

Review

Updating the Natural History of Human Papillomavirus and Anogenital Cancers

Anna-Barbara Moscicki[a,*], Mark Schiffman[b], Ann Burchell[c], Ginesa Albero[d,e], Anna R. Giuliano[f], Marc T. Goodman[g], Susanne K. Kjaer[h,i], Joel Palefsky[j]



7 de agosto de 2013

GSK solicita a la UE la autorización para la administración de Cervarix con un esquema de vacunación de dos dosis

GlaxoSmithKline (GSK) ha solicitado a la Unión Europea la autorización de administración con un esquema de dos dosis en niñas entre 9 y 14 años para su vacuna frente al cáncer de cérvix, Cervarix [vacuna bivalente frente al virus del papiloma humano (tipos 16 y 18), recombinante].

Journal section: Oral Medicine and Pathology
Publication Types: Review

doi:10.4317/medoral.18419
http://dx.doi.org/doi:10.4317/medoral.18419

Oral cancer, HPV infection and evidence of sexual transmission

Fátima Martín-Hernán [1], Juan-Gabriel Sánchez-Hernández [1], Jorge Cano [2], Julián Campo [2], Jorge del Romero [3]

[1] DDS, Universidad Complutense de Madrid. Private practice. Madrid
[2] DDS, PhD, Department of Medicine and Orofacial Surgery. Universidad Complutense de Madrid

Table 1. Differences between oropharyngeal cancer HPV + and HPV -.

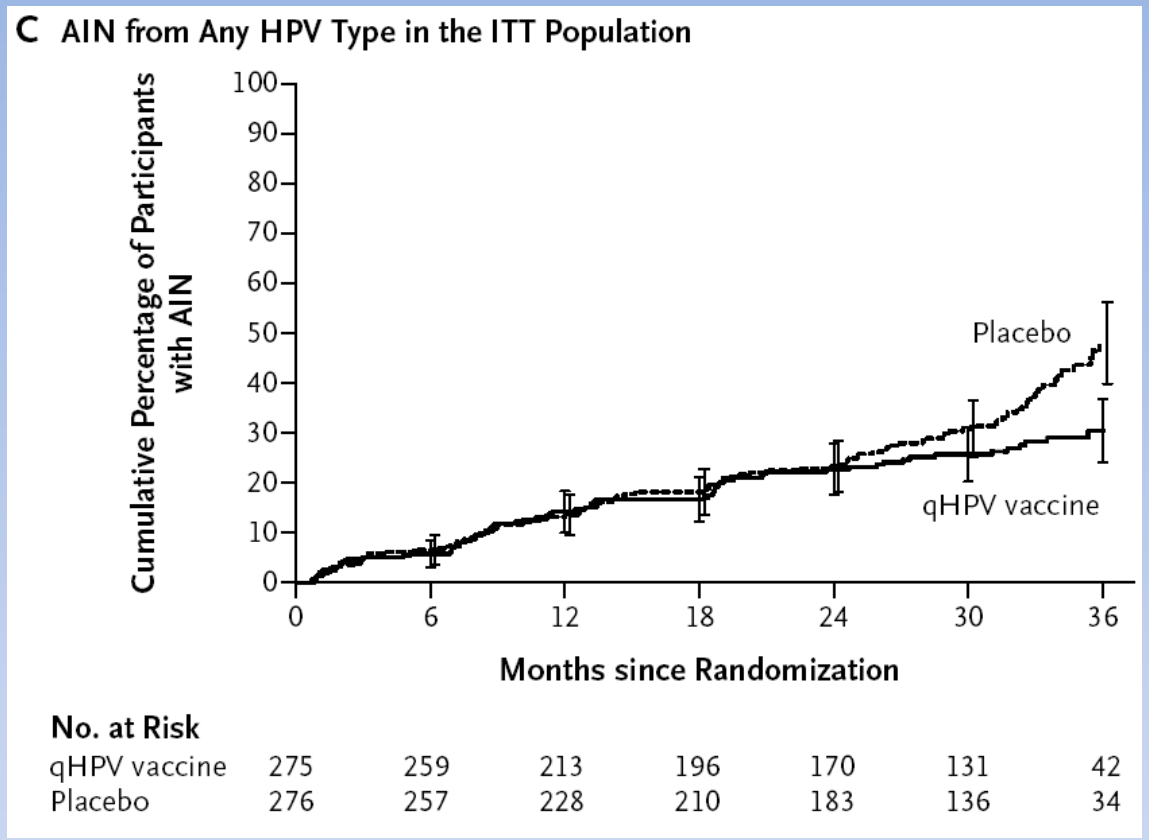
	HPV-positives	HPV-negatives
Age	Younger individuals (30-50)	Older individuals (50-70)
Risk factor	Oral sex, French kiss, high number of sexual partners, history of STI	Long history of tobacco and/or alcohol consumption
Incidence	Increasing	Decreasing
Localization	Tongue base, amygdalae	Oral mucosa
Field cancerization	No	Yes
Histology	Poorly differentiated - basaloid	Clearly differentiated
Stage at diagnosis	T3-4; N2-3	Variable
Biomarkers	Over-expressed P16; Inactivation of P16 and pRb	Loss of P16; P53 and pRb mutation; cyclin-D1, EGFR and survivine over-expression
Chromosomal mutations	Less frequent	Frequent
Prognosis	Very good, increased sensitivity to radiotherapy and chemotherapy	Poor
Distant metastasis	Rare	Frequent
Second primaries	Rare	Frequent
Five year survival rate	60%-90%	20%-70%

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

HPV Vaccine against Anal HPV Infection and Anal Intraepithelial Neoplasia

Joel M. Palefsky, M.D., Anna R. Giuliano, Ph.D., Stephen Goldstone, M.D., Edson D. Moreira, Jr., M.D., Carlos Aranda, M.D., Heiko Jessen, M.D., Richard Hillman, M.D., Daron Ferris, M.D., Francois Coutlee, M.D., Mark H. Stoler, M.D., J. Brooke Marshall, Ph.D., David Radley, M.S., Scott Vuocolo, Ph.D., Richard M. Haupt, M.D., M.P.H., Dalya Guris, M.D., and Elizabeth I.O. Garner, M.D., M.P.H.



Vaccine 30S (2012) F24–F33

Contents lists available at SciVerse ScienceDirect

Vaccine

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

Review

Updating the Natural History of Human Papillomavirus and Anogenital Cancers

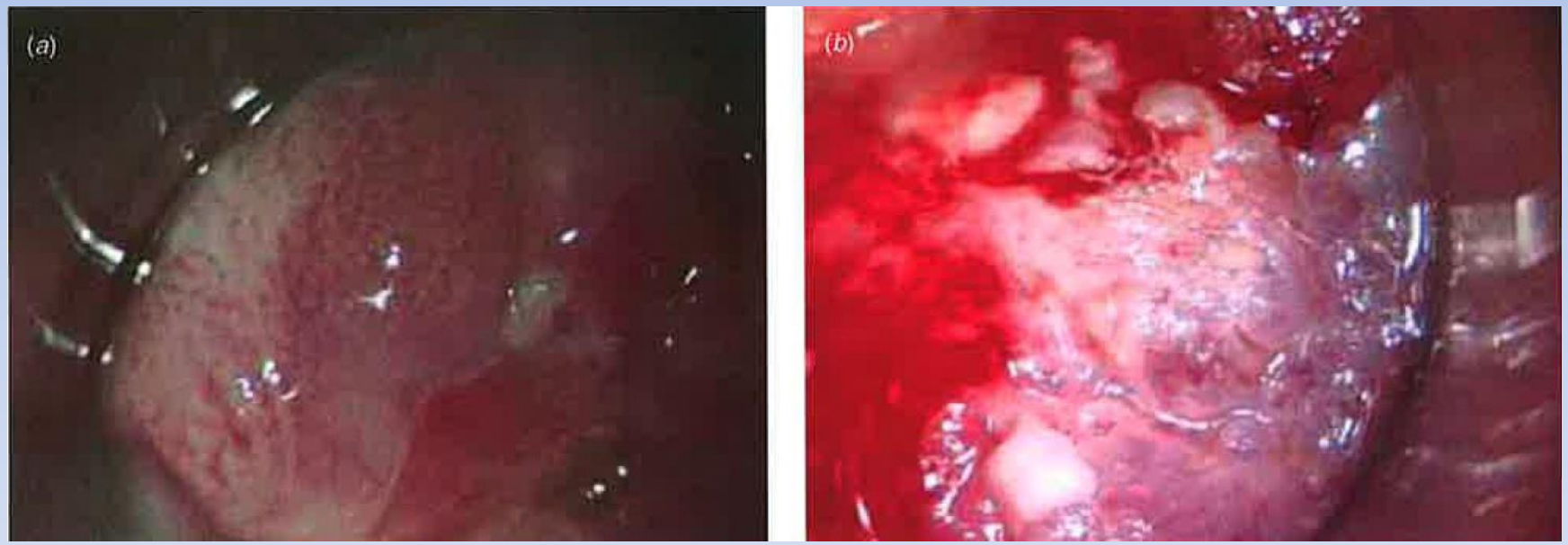
Anna-Barbara Moscicki[a,*], Mark Schiffman[b], Ann Burchell[c], Ginesa Albero[d,e], Anna R. Giuliano[f], Marc T. Goodman[g], Susanne K. Kjaer[h,i], Joel Palefsky[j]

Sexual Health, 2012, **9**, 580–586
http://dx.doi.org/10.1071/SH12045

Practising high-resolution anoscopy

Joel M. Palefsky

University of California, San Francisco, CA 94143, USA. Email: Joelp@medicine.ucsf.edu



PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Safety, Tolerability, and Immunogenicity of Gardasil Given Concomitantly With Menactra and Adacel

Keith S. Reisinger, Stan L. Block, Michelle Collins-Ogle, Colin Marchant, Melissa Catlett, David Radley, Heather L. Sings, Richard M. Haupt, Elizabeth I.O. Garner and for the Protocol 025 Investigators

WHAT'S KNOWN ON THIS SUBJECT: Previous studies have shown that co-administered Gardasil and Recombivax HB and co-administered Gardasil and Repevax were generally well tolerated and did not interfere with the immune responses to the respective vaccines.

WHAT THIS STUDY ADDS: We have demonstrated that co-administration of Gardasil, Menactra, and Adacel, vaccines which are currently recommend by the ACIP for routine vaccination of adolescents, does not compromise the safety, tolerability, and immunogenicity of the individual vaccines.

J Hyg (Lond). 1983 April; 90(2): 259–325. PMCID: PMC2134248

Vaccination against rubella and measles: quantitative investigations of different policies.

R. M. Anderson and R. M. May

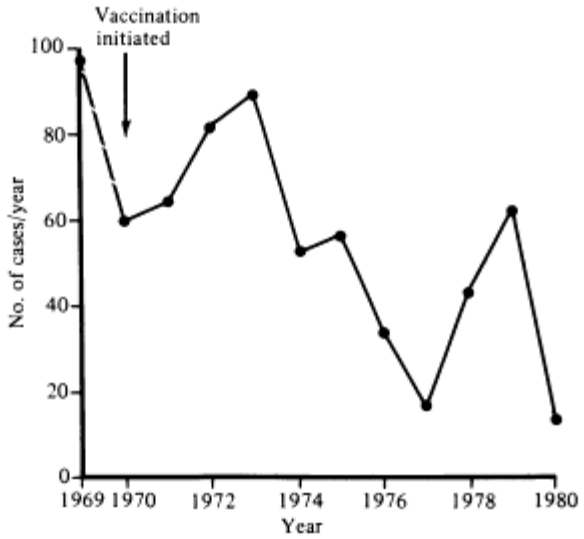


Fig. 12. The annual number of reported cases of congenital rubella syndrome in the years 1970–80 in England, Scotland and Wales. For a given year the total number of cases is based on diagnoses up to 4 years after the birth of the child (the figures for 1979 and 1980 are therefore only provisional values). The figure for 1969 is a rough estimate based on reported cases in the previous 4 years (data from Dr W. C. Marshall, The Hospital for Sick Children, Great Ormond Street, London).