

HPV: Nuovi orientamenti



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HPV: Nuovi orientamenti



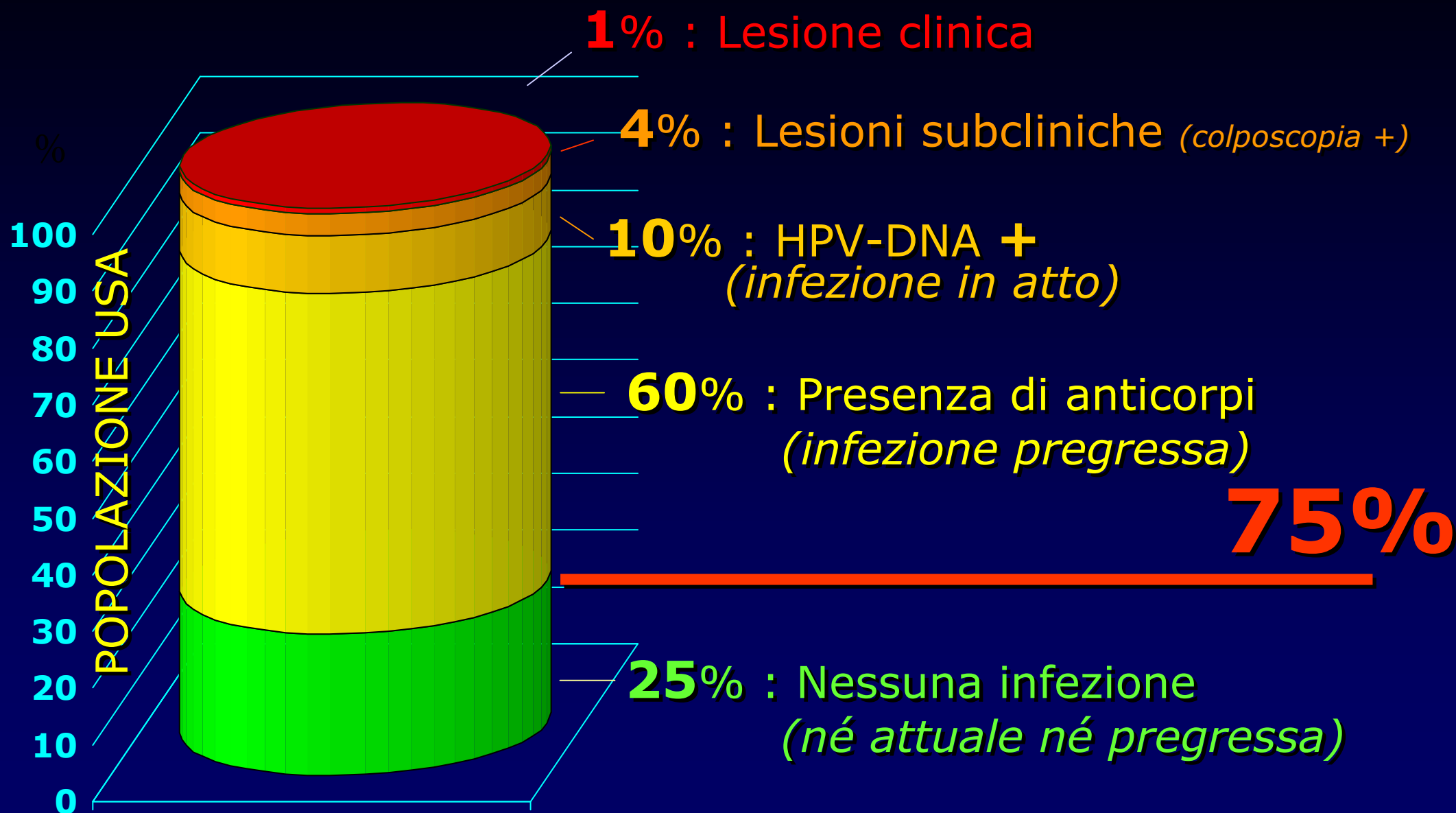
- HPV test, Screening e vaccinazione**
- Ampliamento spettro HPV nei vaccini**
- La vaccinazione nel maschio**

HPV: Nuovi orientamenti

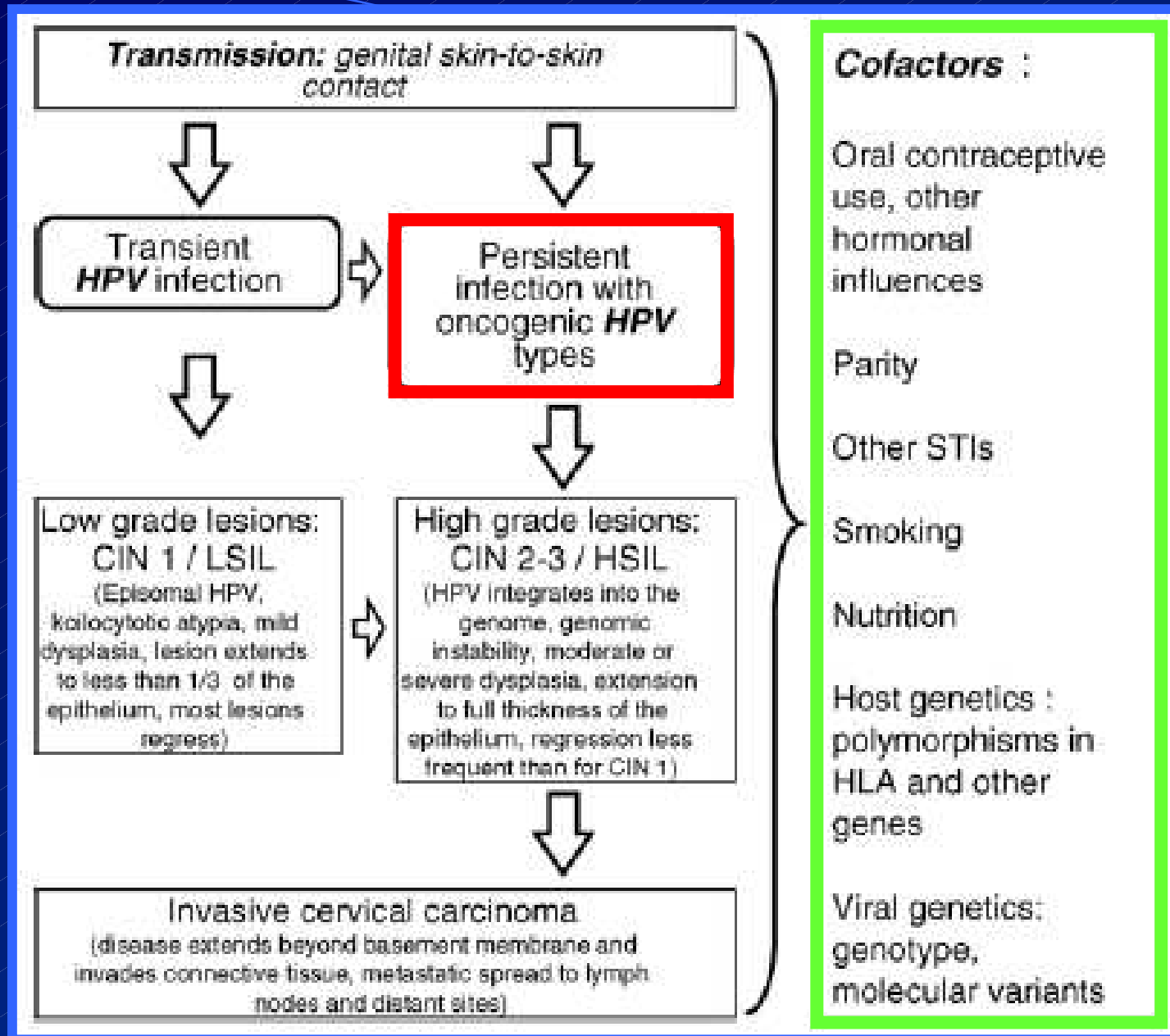


- HPV test, Screening e vaccinazione**

Prevalenza stimata dell'infezione da HPV negli USA



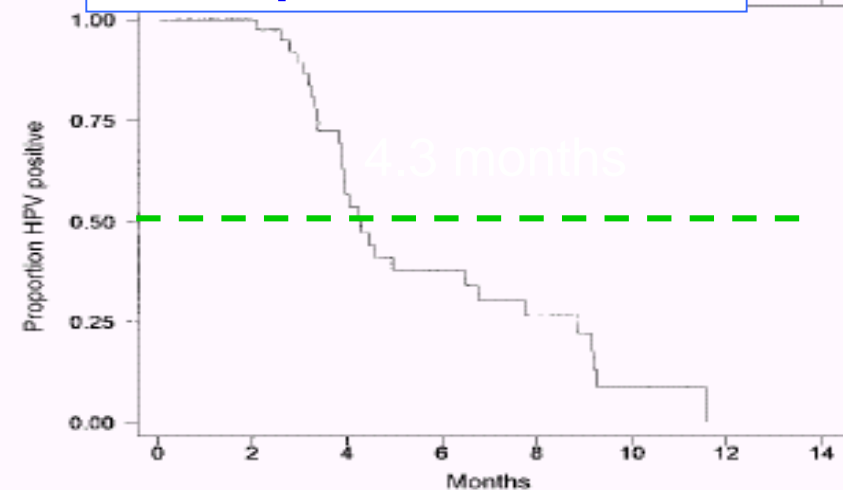
Modificata da Koutsky, 1997



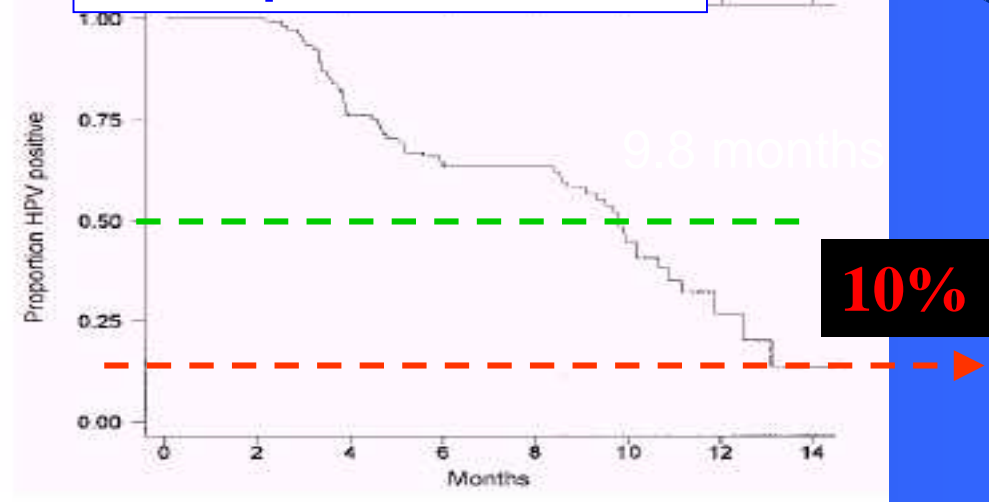
Vaccine, 2006

Tempi di Clearance media dell'infezione in donne immunocompetenti

Sierotipi a basso rischio



Sierotipi ad alto rischio

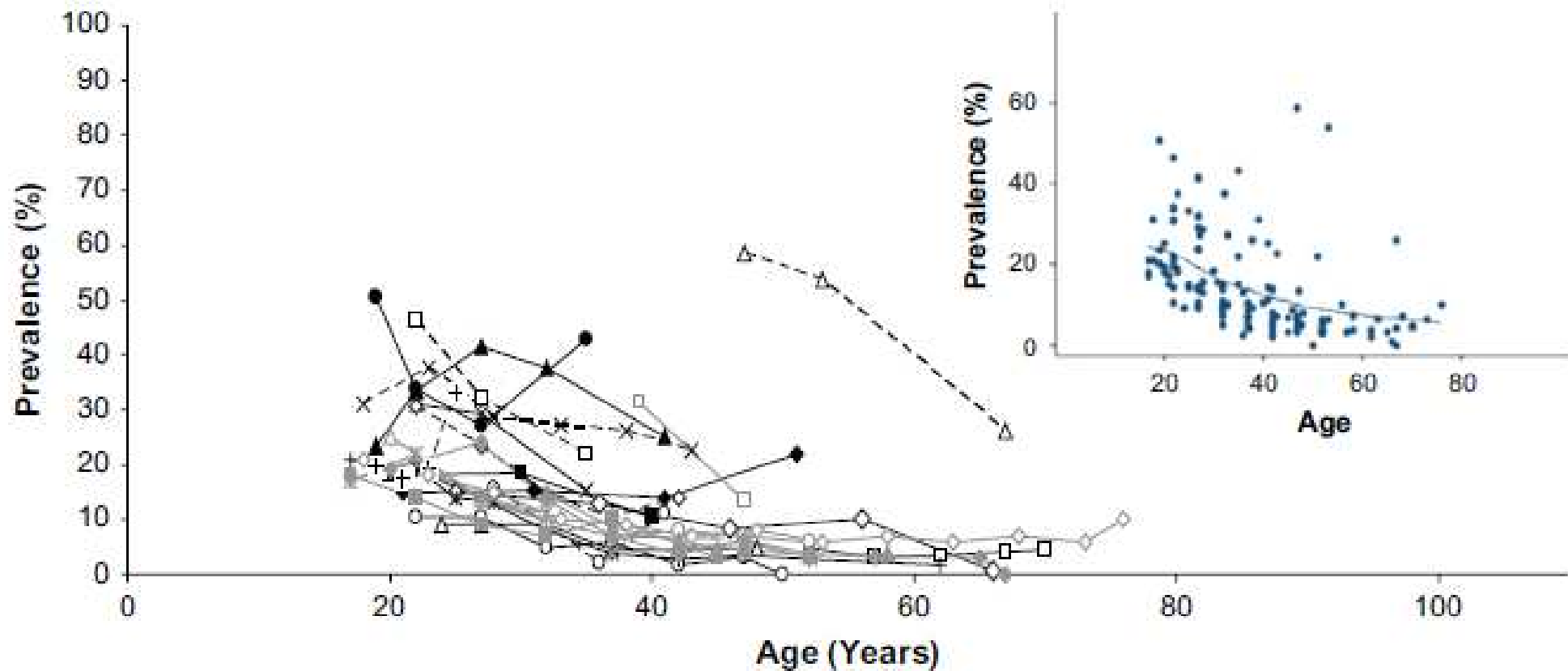


Review article

Age-Specific Prevalence of Infection with Human Papillomavirus in Females: A Global Review

Jennifer S. Smith, Ph.D., M.P.H.^{a,*}, Amy Melendy, D.V.M., M.P.H.^a,
Rashida K. Rana, M.S.^b, and Jeanne M. Pimenta, Ph.D., B.Sc.^b

2008



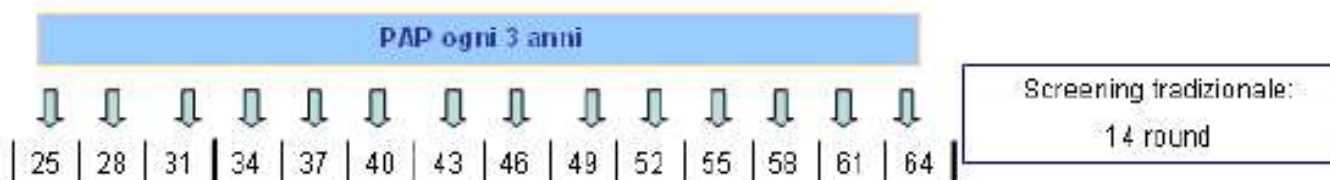
Perchè usare HPV-test come test primario di screening?

- L'infezione persistente con HPV oncogeni è la condizione necessaria per l'evoluzione a carcinoma
 - 12 tipi di HPV causano virtualmente tutti i casi di cancro
- Uno screening basato sulla ricerca di HPV oncogeni come test di screening primario è più efficace dello screening con Pap-test nel prevenire i tumori invasivi cervicali
- Lo screening con HPV non deve iniziare prima dei 30-35 anni (Report HTA italiano: intorno ai 35 anni), sotto questa età è raccomandato lo screening citologico
- L'intervallo di screening con HPV deve essere di almeno 5 anni
- Le donne Positive ad HPV non devono essere inviate direttamente a colposcopia ma effettuano una citologia di triage





- ☐ Nella fascia di età **25-34**: **Pap test triennale** con il test HPV come test di triage nelle citologie ASC-US ,
- ☐ Nella fascia di età **35-64**: **test HPV ogni 5 anni** con il Pap test come test di triage nei soggetti HPV positivi
- ☐ Unico programma quando entreranno nel programma di screening le future coorti di donne sottoposte a vaccinazione anti HPV 16/18 rimanendo il solo test HPV come test di screening



E prima dei 25 anni il problema non esiste??

Early effect of the HPV vaccination programme on cervical abnormalities in Victoria, Australia: an ecological study

Julia M L Brotherton, Masha Fridman, Cathryn L May, Genevieve Chappell, A Marion Saville, Dorota M Gertig

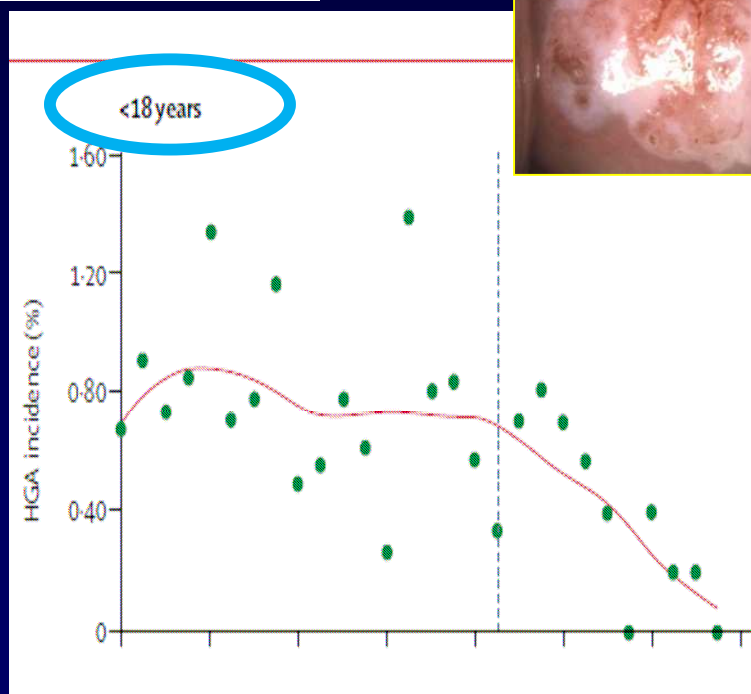
LGA incidence

<18 years	1658 (12.2%)	691 (12.5%)	0.3% (-0.8 to 1.4)	0.6
18-20 years	9465 (11.0%)	5506 (10.9%)	-0.1% (-0.5 to 0.3)	0.6
21-25 years	18671 (7.9%)	11067 (7.3%)	-0.6% (-0.8 to -0.4)	<0.0001
26-30 years	14049 (5.0%)	7810 (4.4%)	-0.6% (-0.7 to -0.5)	<0.0001
≥31 years	44408 (2.5%)	23106 (2.0%)	-0.5% (-0.47 to -0.54)	<0.0001

HGA incidence

<18 years	109 (0.80%)	23 (0.42%)	-0.38% (-0.61 to -0.16)	0.003
18-20 years	1035 (1.20%)	593 (1.17%)	-0.03% (-0.15 to 0.09)	0.7
21-25 years	3639 (1.53%)	2609 (1.71%)	0.18% (0.10 to 0.26)	<0.0001
26-30 years	3561 (1.26%)	2542 (1.43%)	0.17% (0.10 to 0.24)	<0.0001
≥31 years	6320 (0.35%)	4397 (0.37%)	0.02% (0.01 to 0.04)	0.002

Lancet oncol, 2011



Age-specific distribution of Human Papilloma Virus (HPV) mucosal infection among young females

Annalisa Pieralli, Maria Grazia Fallani, Virginia Lozza, Serena Corioni, Manuela Longinotti, Massimiliano Fambrini, Carlo Penna

Table 1. Age-stratified characteristics of HPV-related disease.

	Age 16 - 19 (30 pts)	Age 20 - 25 (55 pts)	P < 0.005
HR HPV	6	47	<0.0001
CO INFECTION	1	11	0.04
CIN 2/3	0	20	< 0.0001
DISEASE RELAPSE	17	9	<0.0001
MULTI SITE DISEASE	13	2	< 0.0001



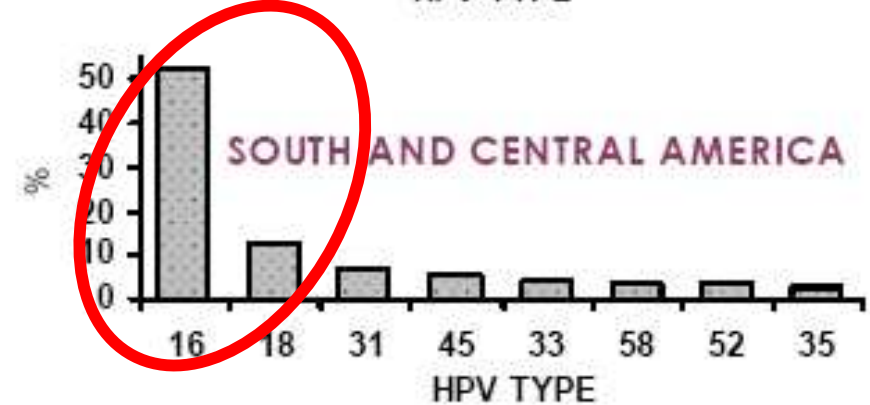
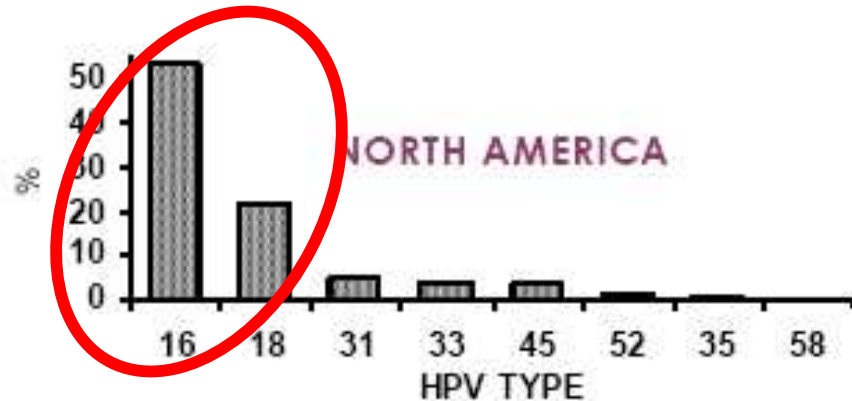
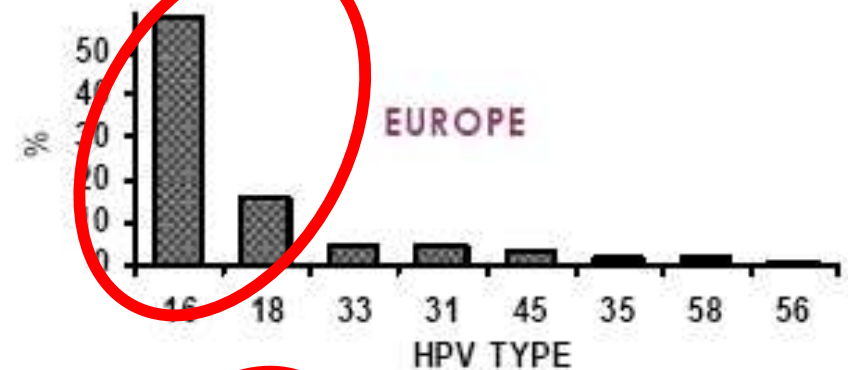
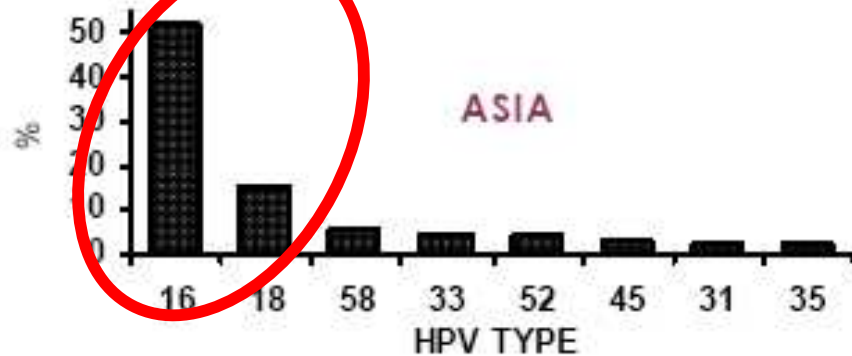
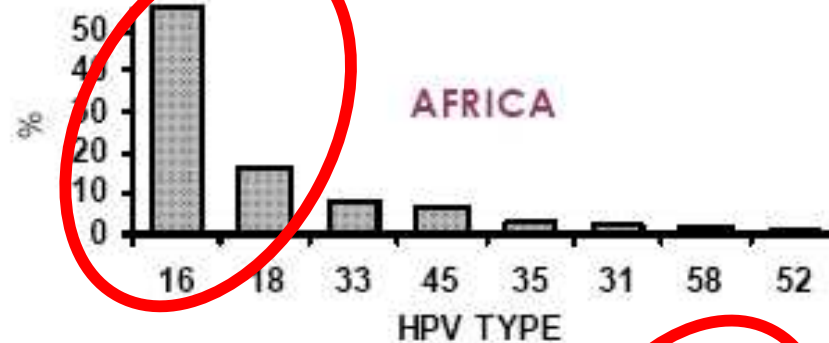
HPV: Nuovi orientamenti



- Ampliamento spettro HPV nei vaccini**

16-18

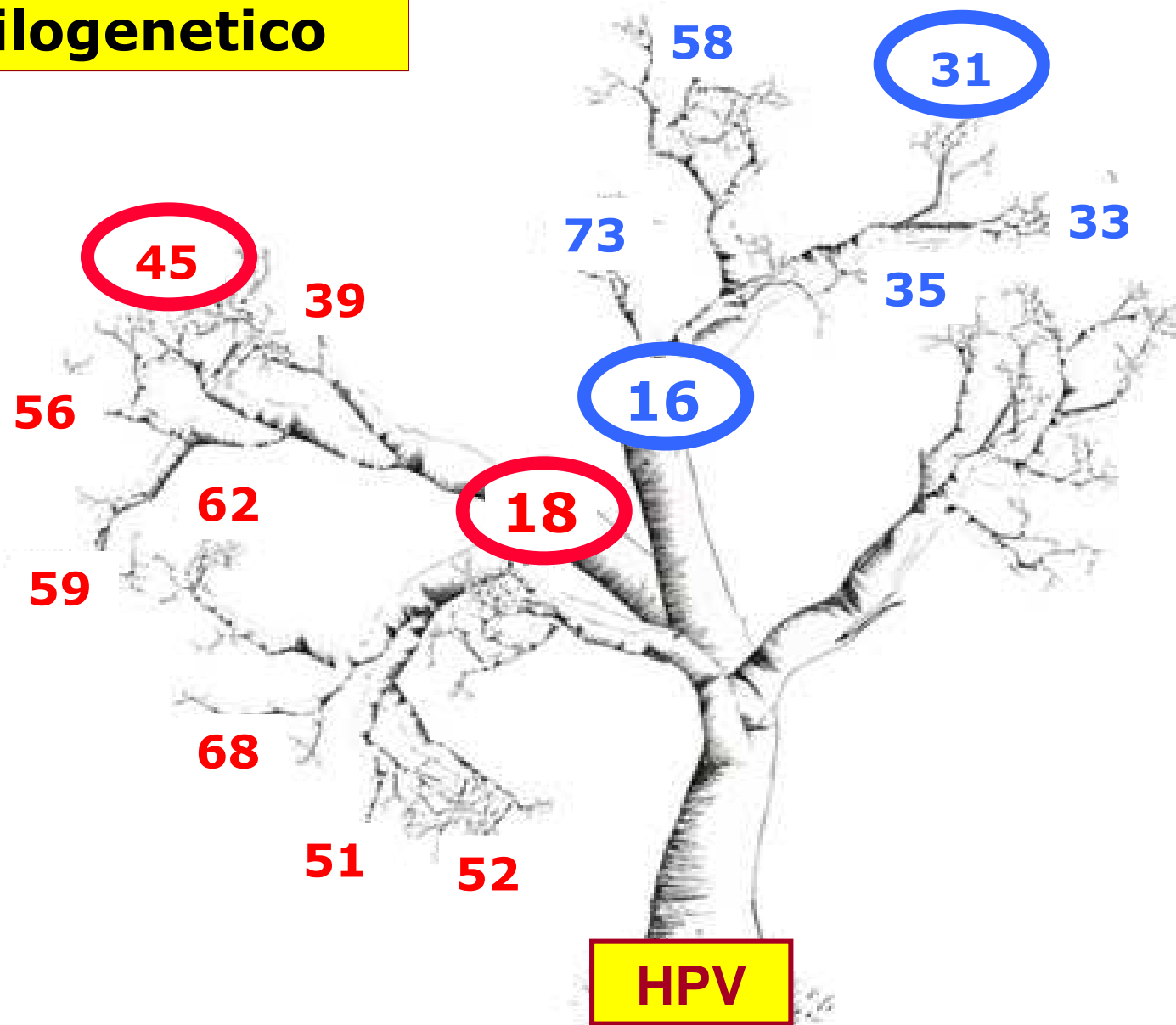
70%



Adapted from Smith, JF, et al. Br J Cancer. Submitted

Br J Cancer, 2007

Albero Filogenetico

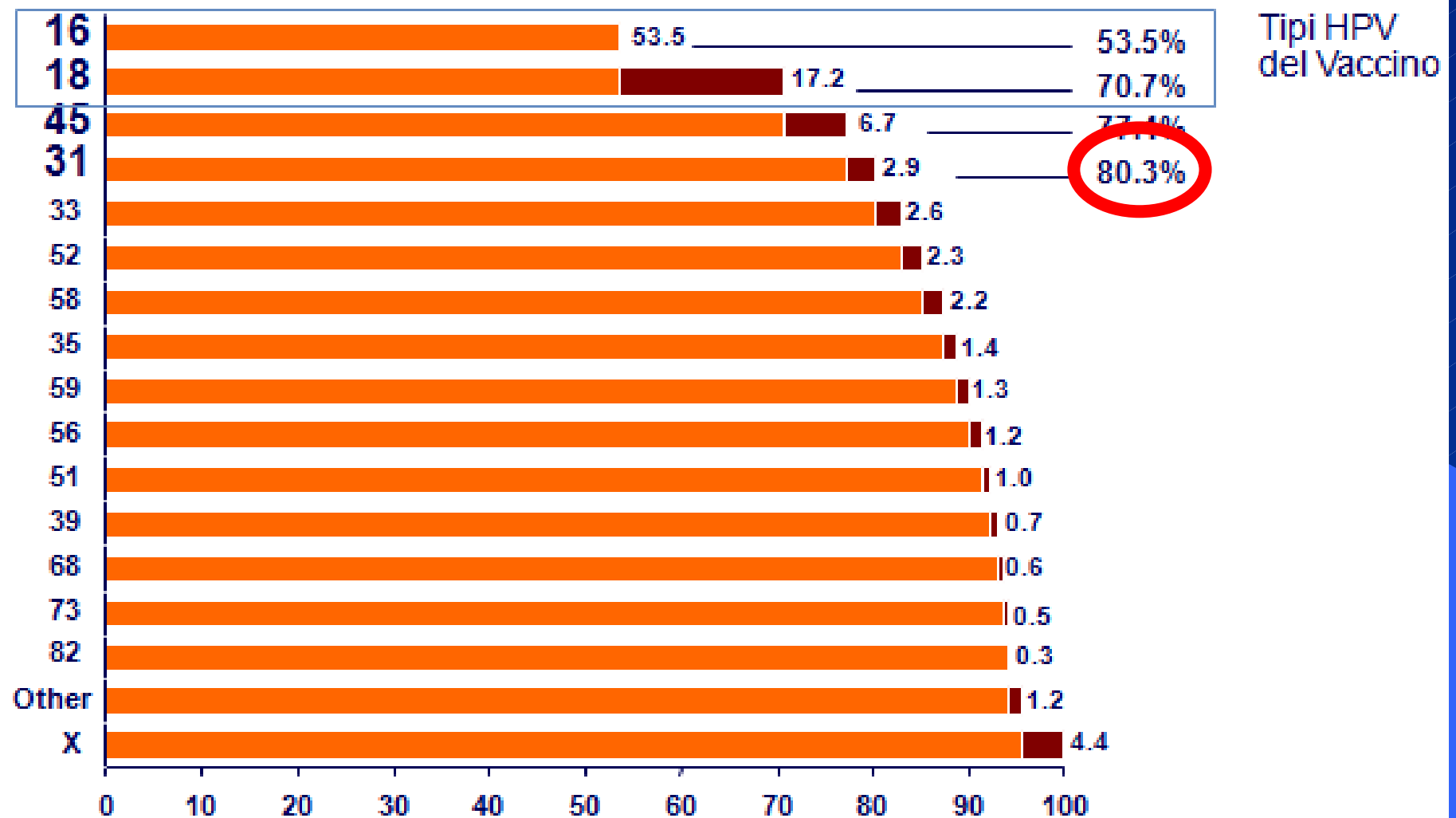


Current Understanding of HPV Vaccines in Females

Attribute	Quadrivalent	Bivalent
Protection against HPV 16/18 related CIN2+*	≥98%	≥93%
Protection against HPV 6/11 related genital lesions	~99%	-
Cross-protection against CIN2+ due to high risk types other than HPV 16,18	Some types phylogenetically related to HPV 16?	Some types phylogenetically related to HPV 16 and 18?
Seroconversion to vaccine types	>99%	>99%
Geometric mean antibody titers	bivalent > quadrivalent	
Duration of protection	Unclear if any differences	
Local reactogenicity	bivalent > quadrivalent	
Cost of vaccine dose	171,64 Euros Private	156,79 Euros Private

*Quadrivalent vaccine - also demonstrated protection against VIN2/3 and VaIN2/3

** <http://www.cdc.gov/vaccines/programs/vfc/cdc-vac-price-list.htm>

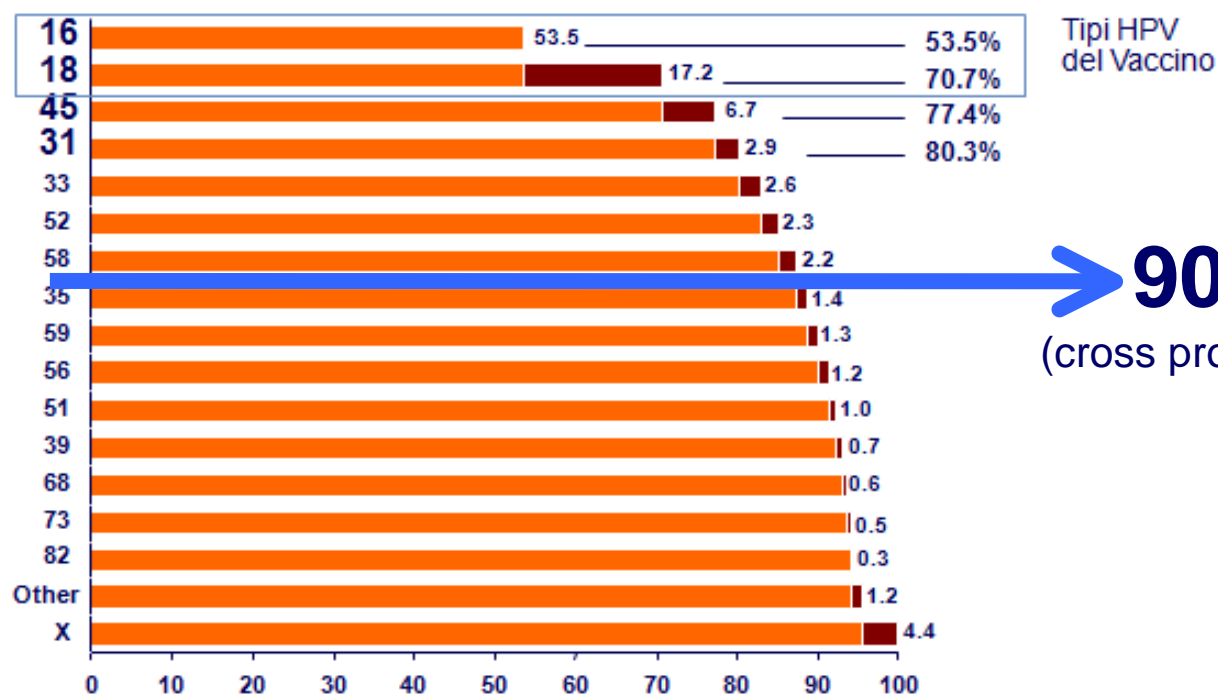


Casi di carcinoma attribuiti ai più frequenti genotipi di HPV (%)

Potential impact of a nine-valent vaccine in human papillomavirus related cervical disease

Beatriz Serrano¹, Laia Alemany^{1,2}, Sara Tous¹, Laia Bruni¹, Gary M Clifford³, Thomas Weiss⁴, Francesc Xavier Bosch¹ and Silvia de Sanjosé^{1,2*}

HPV types (HPV 6/11/16/18/31/33/45/52/58)

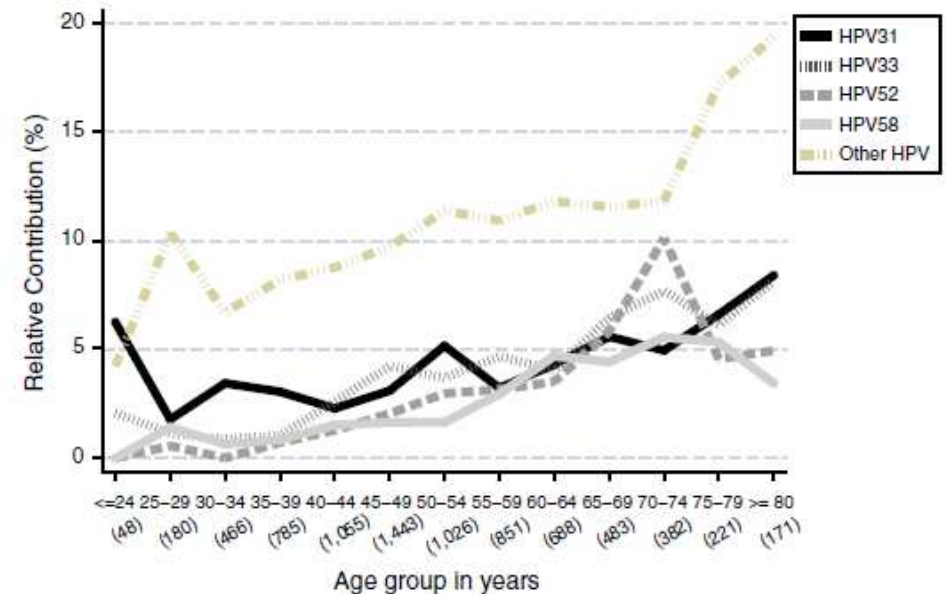
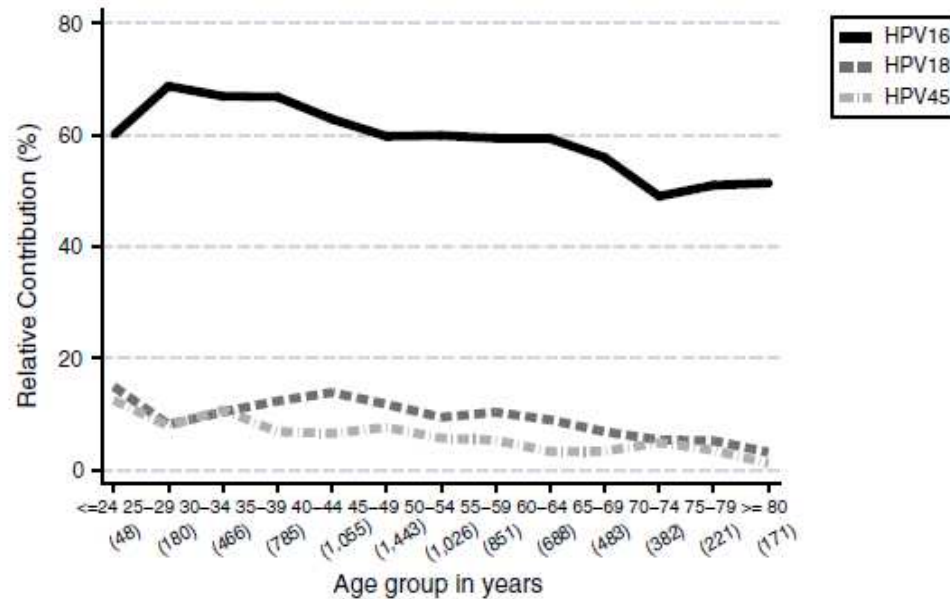


90%
(cross protection?)

Casi di carcinoma attribuiti ai più frequenti genotipi di HPV (%)

Potential impact of a nine-valent vaccine in human papillomavirus related cervical disease

Beatriz Serrano¹, Laia Alemany^{1,2}, Sara Tous¹, Laia Bruni¹, Gary M Clifford³, Thomas Weiss⁴, Francesc Xavier Bosch¹ and Silvia de Sanjosé^{1,2*}



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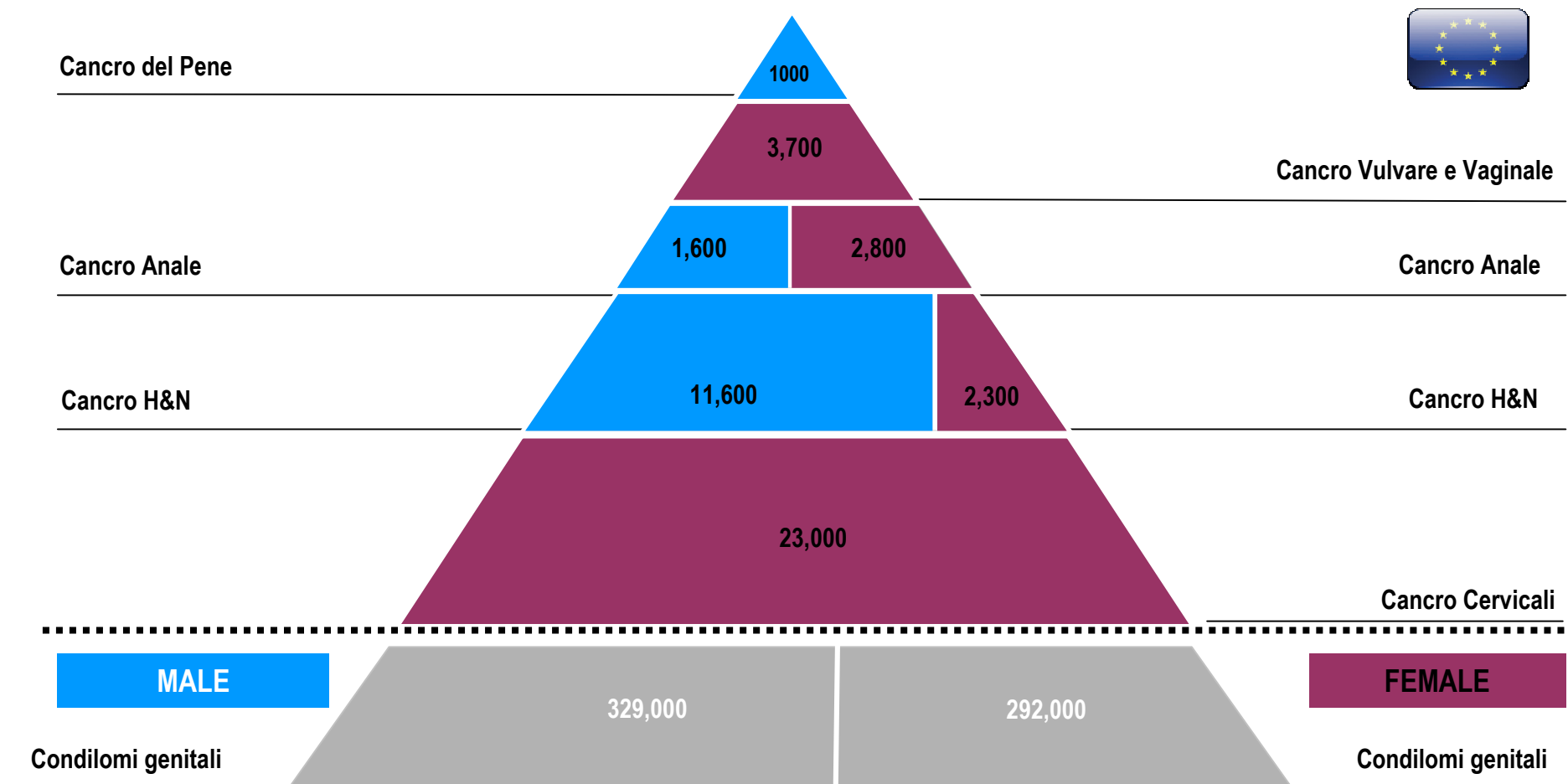


- La vaccinazione nel maschio**

Patologie correlate ad HPV

Cancro del collo dell'utero	100 %
Cancro anale	88 – 94 %
Cancro della vagina	64 – 91 %
Condilomi genitali	90 %
Cancro vulvare	40 %
Cancro del pene	40 %
Cancro della faringe	25 %
Cancro della cavità orale	10 %

Le patologie HPV correlate colpiscono entrambi i sessi



Nuovi casi/anno di cancro e condilomi genitali correlati agli HPV 6, 11, 16 e/o 18 in maschi e femmine in Europa

Annual number of new cancer cases calculated based on crude incidence rates from IARC database (1998-2002) and population estimate Eurostat 2008; estimate Globocan 2008 for cervical cancer; published HPV prevalence rates were applied (for Europe, when available) Genital warts estimates based on incidence rates in UK, HPA 2007

Annual Number of New Cases (2009 estim.) of HPV-Related Cancers in US Men

Anatomic Area	New Cases	% With Detectable HPV	New HPV-Related Cases
Oral cavity and oropharynx	25,240 ¹	25% ²	6,310
Larynx	9,920 ¹	24% ²	2,381
Anus	2,100 ¹	90% ³	1,890
Penis	1,290 ¹	40% ⁴	516
Total	38,550	—	11,097

1. American Cancer Society. Cancer facts & figures 2009. Available at: <http://www.cancer.org/downloads/STT/500809web.pdf>. Accessed January 27, 2010.
2. Kreimer AR et al. *Cancer Epidemiol Biomarkers Prev.* 2005;14:467-475.
3. Ryan DP et al. *N Engl J Med.* 2000;342:792-800.
4. Daling JR et al. *Int J Cancer.* 2005;116:606-616.

Table 1

Total lifetime cost associated with new cases of non-cervical HPV-related disease occurring within a given year (reproduced with permission [7]).

	HPV subtype	Estimated annual incidence	Total lifetime cost (range), US\$ million
Anogenital warts	6, 11 ^a	500,000	171 (71–392)
Anal cancer	16, 18 ^b	4000	92 (44–178)
JORRP	6, 11	1500	82.2 (4.4–900)
Mouth/oropharyngeal cancer	16, 18 ^c	9200/8300	38.1 (17.7–54.1)
Penile cancer	16, 18 ^d	1145	4.4 (2.2–8.6)

HPV, human papillomavirus; JORRP, juvenile onset recurrent respiratory papillomatosis.

^a Assumption that 90% of all anogenital warts are attributable to HPV 6 and 11.

^b Assumption that 82.2% of all anal cancers are attributable to HPV 16 and 18.

^c Assumption that 2.9% of all mouth cancers and 10.7% of all oropharyngeal cancers are attributable to HPV 16 and 18.

^d Assumption that 25.2% of all penile cancers are attributable to HPV 16 and 18.

RACCOMANDAZIONI INTERNAZIONALI: VACCINAZIONE DI ROUTINE NEL MASCHIO



**US_Advisory Committee in
Immunization Practices (ACIP)
(MMWR_23/12/2011)
Vaccinazione universale (m+f)**

**-Vaccinazione di routine per i
bambini di 11 o 12 anni**

- + catch-up dai 13 ai 21 anni

**Australia_Pharmaceuticals Benefits
Advisory Committee (PBAC)
(19/12/2011)
Raccomandazione positiva**

**-Vaccinazione nelle scuole per i
ragazzi di 12-13 anni**

**- + 2 anni di catch-up per i
ragazzi di 14-15 anni**

**Canada_National Advisory
Committee on Immunization (NACI)
(CCDR_Gennaio 2012)
Raccomandazione Grado A**

**- Vaccinazione per i maschi dai 9
ai 26 anni (vaccinazione di
routine tra i 9 e i 13 anni)**



**Nel mese di agosto 2011, l'European Medicines Agency (EMA)
ha dato parere positivo all'estensione delle indicazioni del vaccino quadrivalente nei maschi fino a
26 anni**

Vaccinazione nel maschio

L'utilità di una vaccinazione nel maschio in termini di costo/efficacia dipende da alcune variabili che possono essere scomposte ed analizzate:

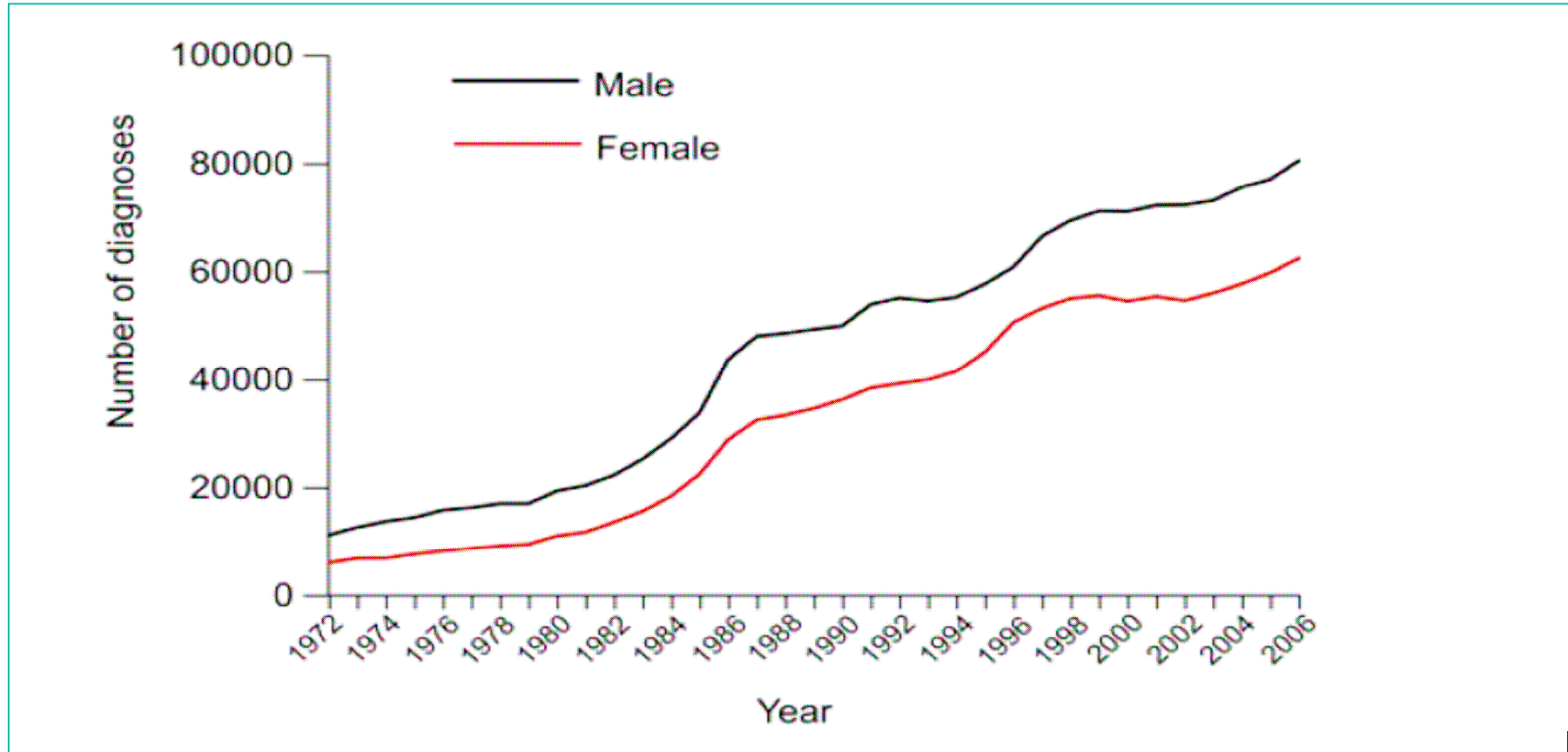
Tipo di patologia: condilomi genitali, PIN-penil cancer, anal cancer

Tipo di popolazione: eterosex, MSM



Condilomi genitali

England and Wales (1971–2006)

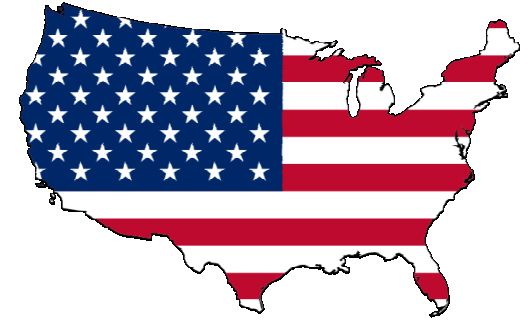


Cancro del pene

1290 casi/anno negli USA

HPV correlato nel 40% circa dei casi

516 casi/anno di tumore HPV correlato negli USA (tipo 16 = 60%; tipo 18 = 15%)



condilomi genitali, PIN-penil cancer

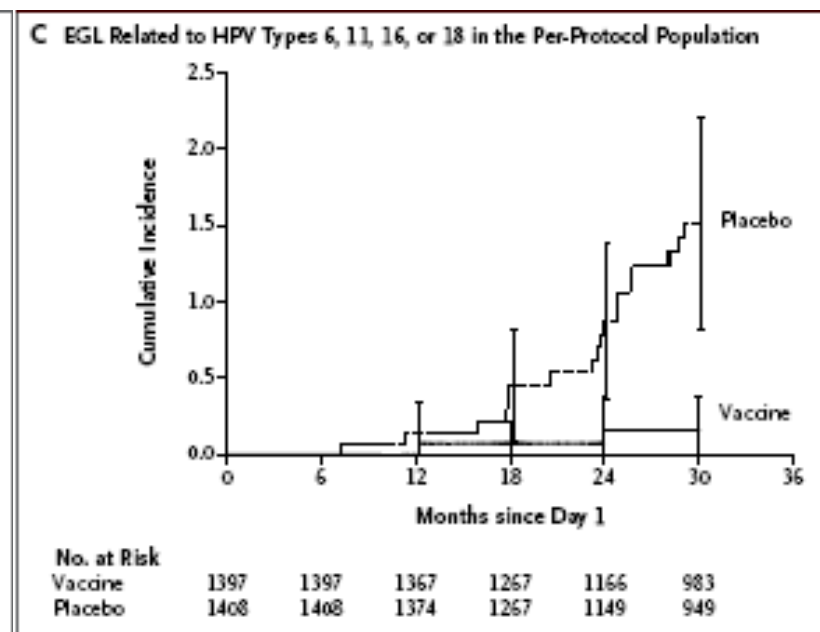
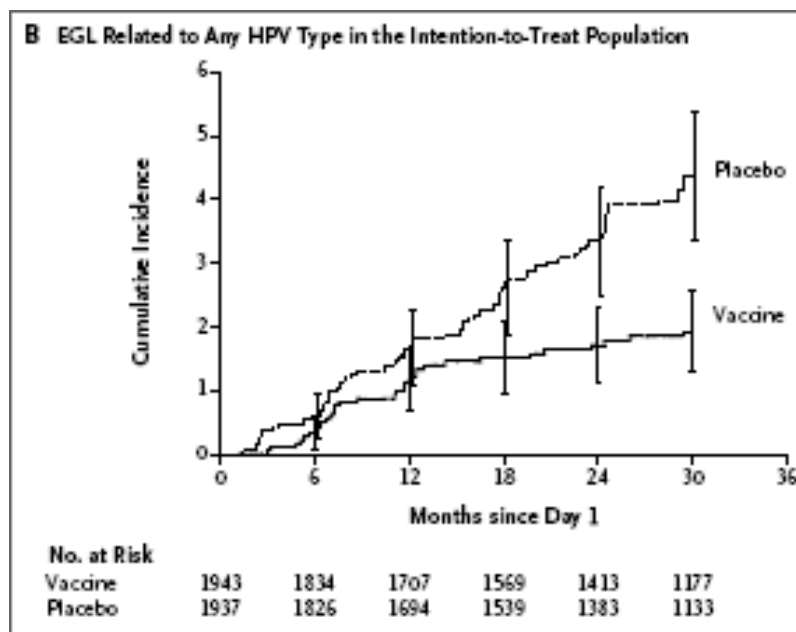
Patologie HPV correlate

a trasmissione prevalentemente eterosessuale

Tabella 5. Efficacia di Gardasil contro le lesioni genitali esterne nella popolazione PPE* di uomini di età compresa tra 16 e 26 anni di età.

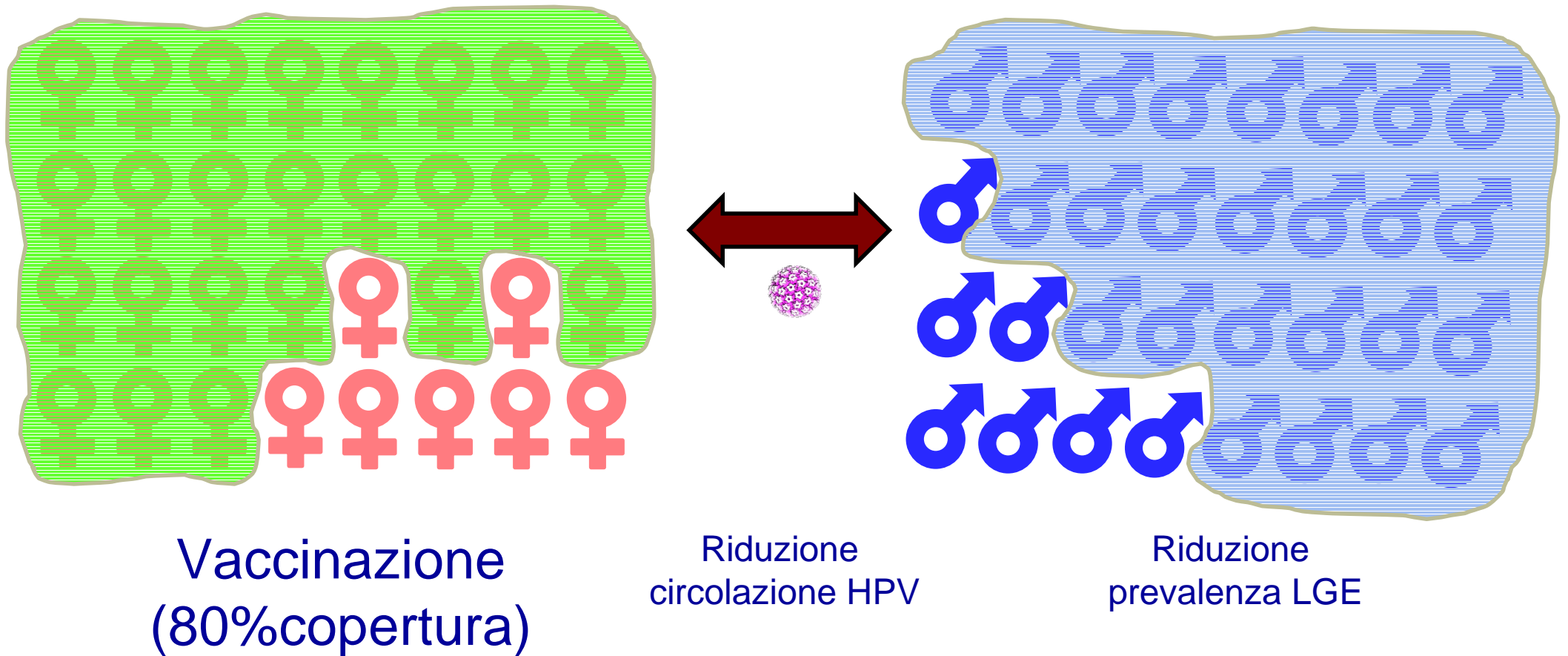
Endpoint	Gardasil		Placebo		% Efficacia (95% IC)
	N	Numero di casi	N	Numero di casi	
Lesioni genitali esterne correlate ad HPV 6/11/16/18					
Lesioni genitali esterne	1394	3	1404	32	90,6 (70,1 - 98,2)
Condilomi genitali	1394	3	1404	28	89,3 (65,3 - 97,9)
PIN 1/2/3	1394	0	1404	4	100,0 (-52,1 - 100,0)

*I soggetti inclusi nella popolazione PPE hanno ricevuto tutte e 3 le vaccinazioni entro 1 anno dall'arruolamento, non hanno avuto nessuna deviazione maggiore dal protocollo di studio ed erano naïve nei confronti dei relativi tipi di HPV prima della dose 1 e fino ad 1 mese dopo la dose 3 (Mese 7).



condilomi genitali, PIN-penil cancer (LGE)

*Patologie HPV correlate
a trasmissione prevalentemente eterosessuale*

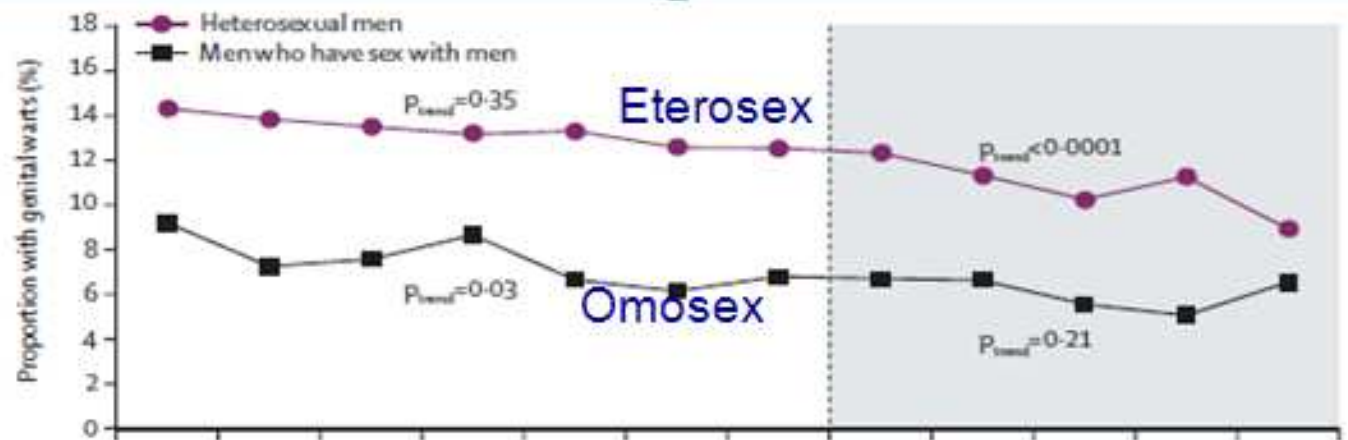
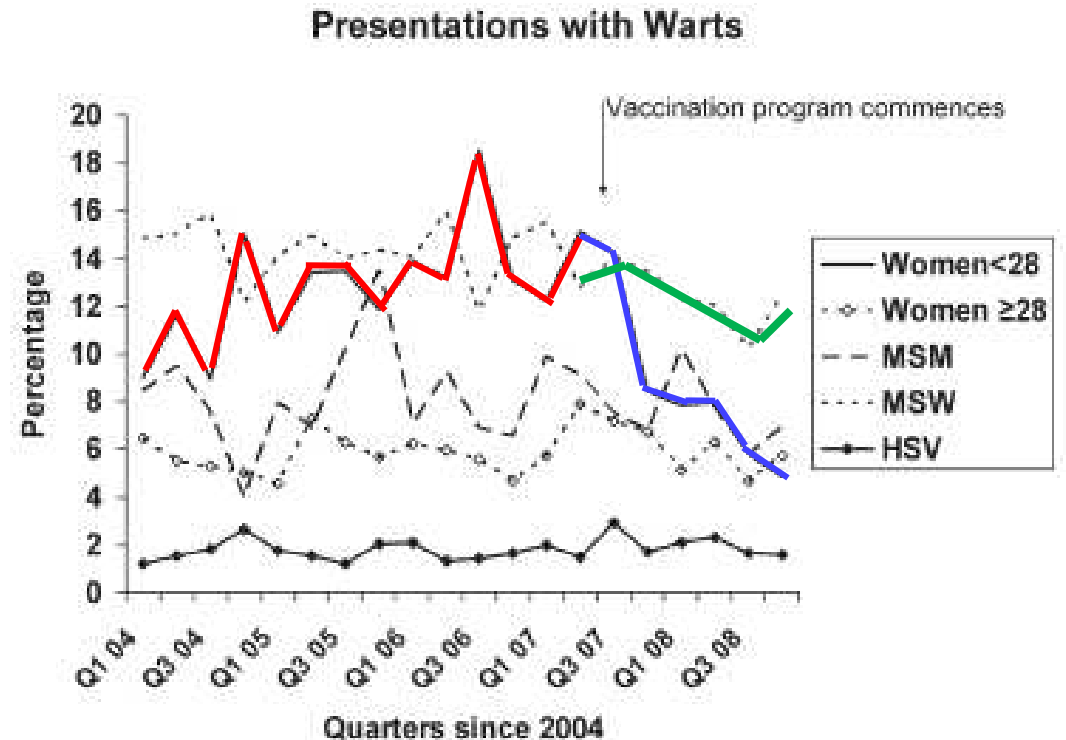


Rapid decline in presentations of genital warts after the implementation of a national quadrivalent human papillomavirus vaccination programme for young women

C K Fairley,¹ J S Hocking,² L C Gurrin,³ M Y Chen,¹ B Donovan,⁴ C S Bradshaw⁵

Sex Transm Infect, 2009

Quadrivalent human papillomavirus vaccination and trends in genital warts in Australia: analysis of national sentinel surveillance data



Lancet, 2010

condilomi genitali, PIN-penil cancer (LGE)

*Patologie HPV correlate
a trasmissione prevalentemente eterosessuale*

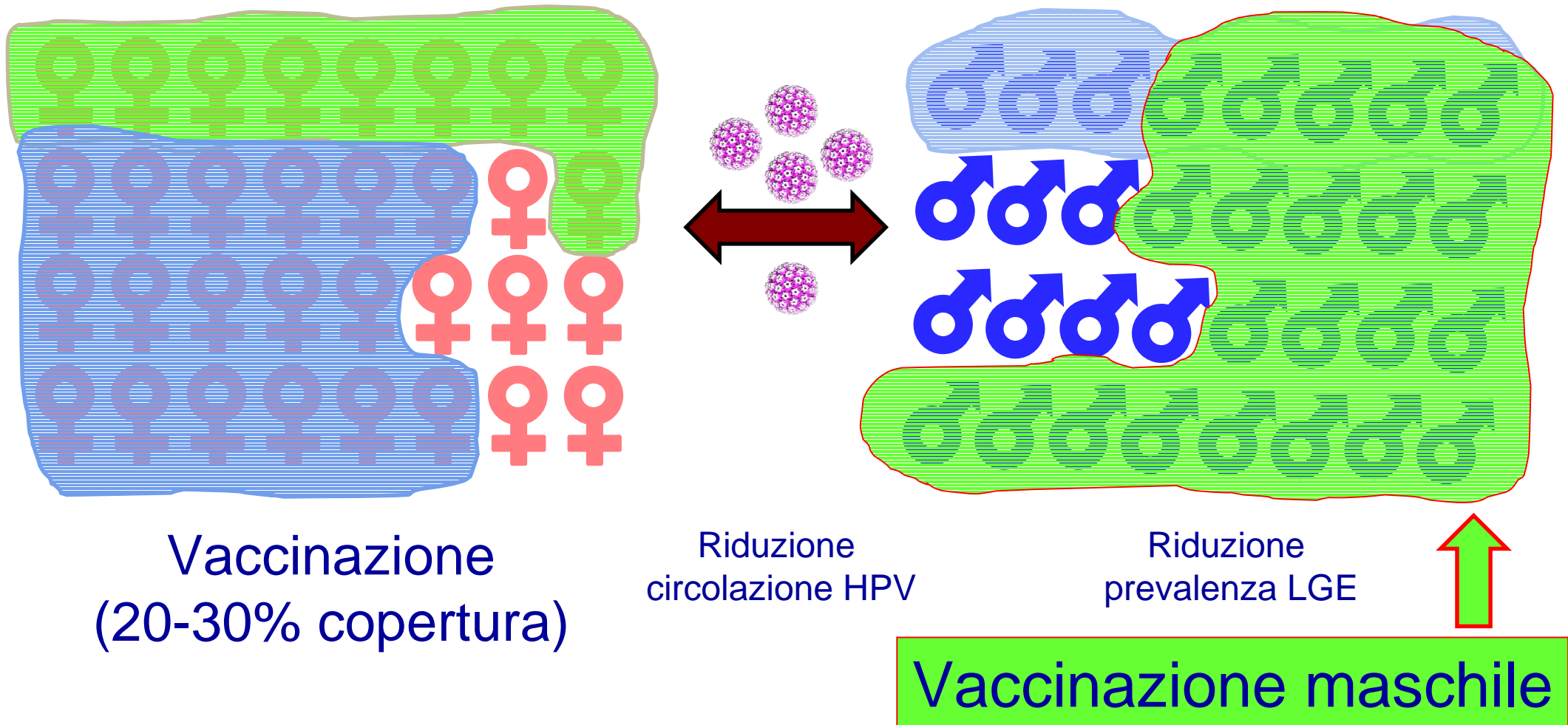
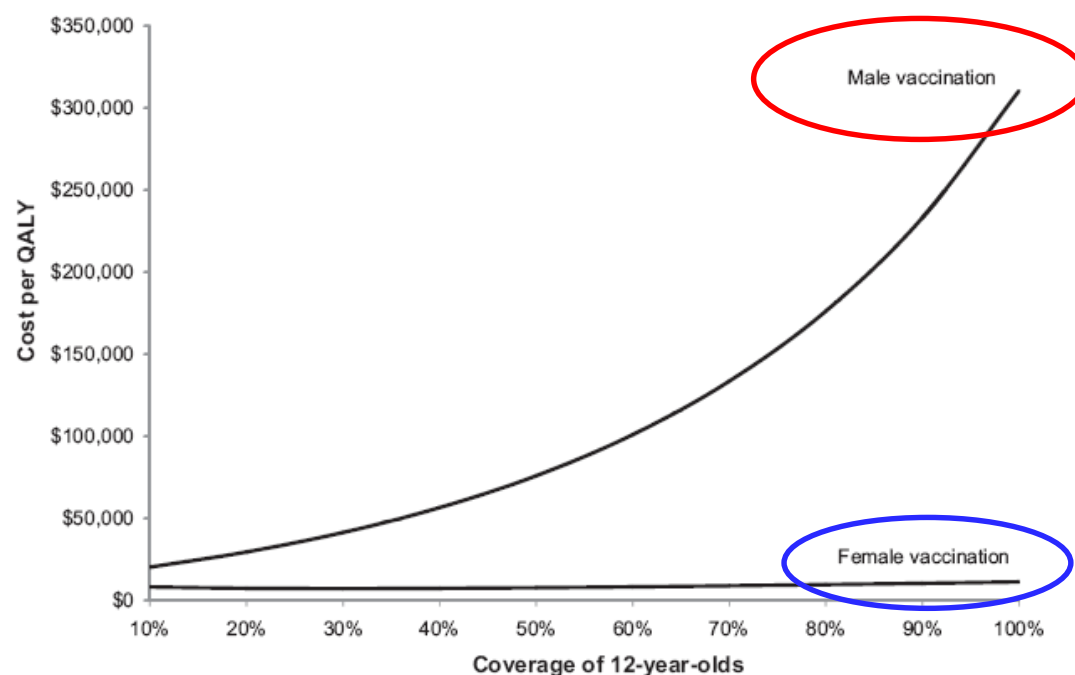


Table 3

Base case results: incremental cost per quality-adjusted life year (QALY) gained by HPV vaccination, by health outcomes included in analysis, for three coverage scenarios.

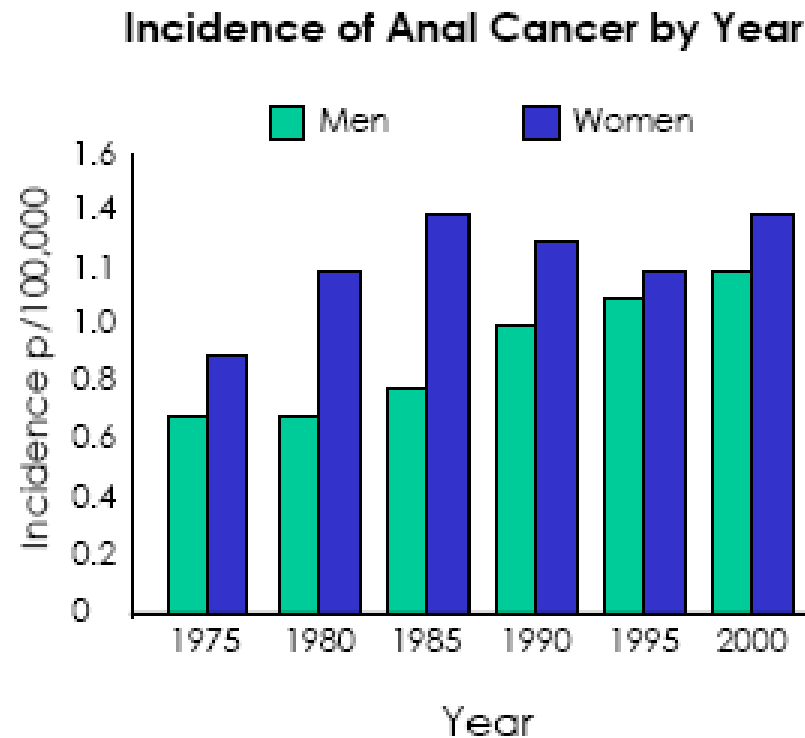
	Cervical outcomes only	Cervical outcomes and genital warts	Cervical outcomes and other HPV-associated cancers	All outcomes: cervical outcomes, other HPV-associated cancers, genital warts, RRP
20% coverage scenario				
Female vaccination	\$18,300	\$14,000	\$8800	\$5700
Male and female vaccination	\$69,600	\$52,100	\$29,700	\$23,600
30% coverage scenario				
Female vaccination	\$21,300	\$16,500	\$10,500	\$7200
Male and female vaccination	\$121,700	\$89,100	\$50,800	\$41,400
75% coverage scenario				
Female vaccination	\$28,400	\$22,000	\$14,500	\$10,500
Male and female vaccination	\$741,300	\$436,000	\$229,600	\$184,300

H.W. Chesson et al. / Vaccine 29 (2011) 8443–8450



Anal Cancer Incidence and Association With HPV

- Annual incidence among males in the United States is 2,020¹
- 80% to 90% of cases are HPV related²
- 73% of all tumors associated with HPV 16³
- Incidence of anal cancer is increasing⁴



1. American Cancer Society. *Cancer Facts and Figures 2008*. 2. International Agency for Research on Cancer. *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*. 2007;90. 3. Daling JR et al. *Cancer*. 2004;101:270-280. 4. Partridge JM et al. *Lancet Infect Dis*. 2006;6:21-31.

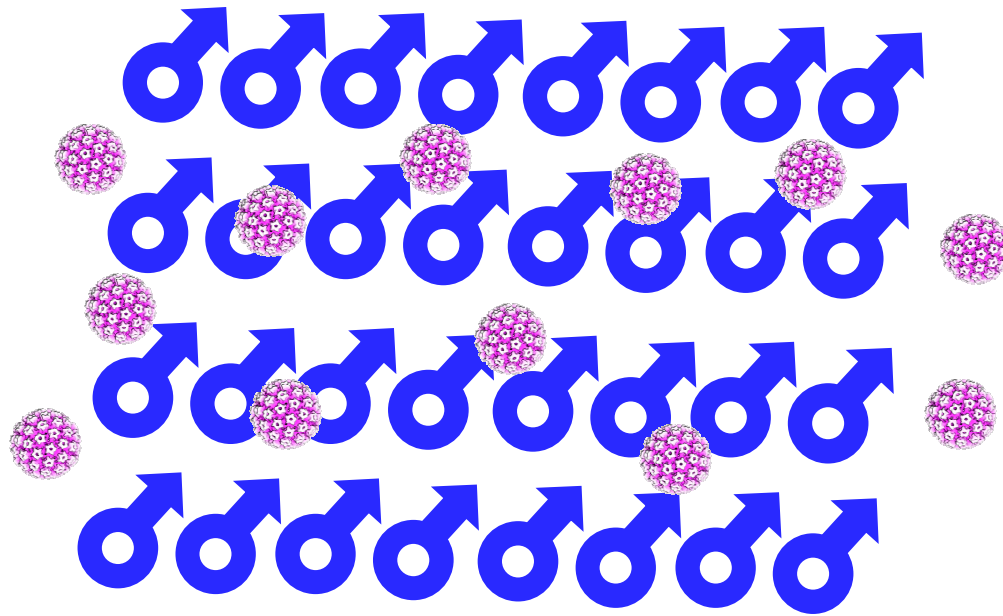
Incidenza del Cancro Anale In Italia

Donne	2.1 per 100,000
Uomini (tutti)	2.1 per 100,000 ←
Uomini (omosessuali)	35 per 100,000 ←
Uomini (HIV & Omosex)	70 per 100,000



Anal cancer

*Nel maschio patologia HPV correlata
a trasmissione prevalentemente omosessuale*



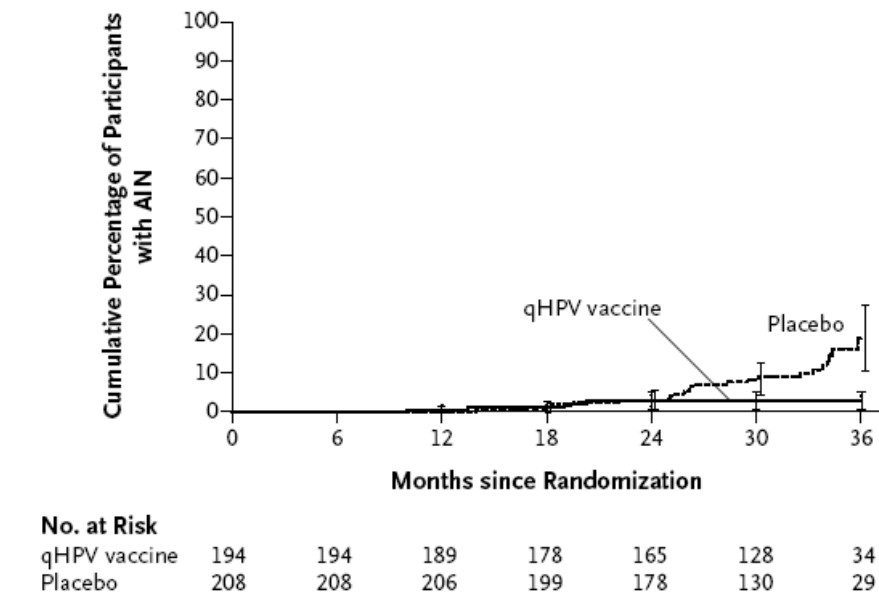
HPV Vaccine against Anal HPV Infection and Anal Intraepithelial Neoplasia

Joel M. Palefsky, M.D., Anna R. Giuliano, Ph.D., Stephen Goldstone, M.D.,

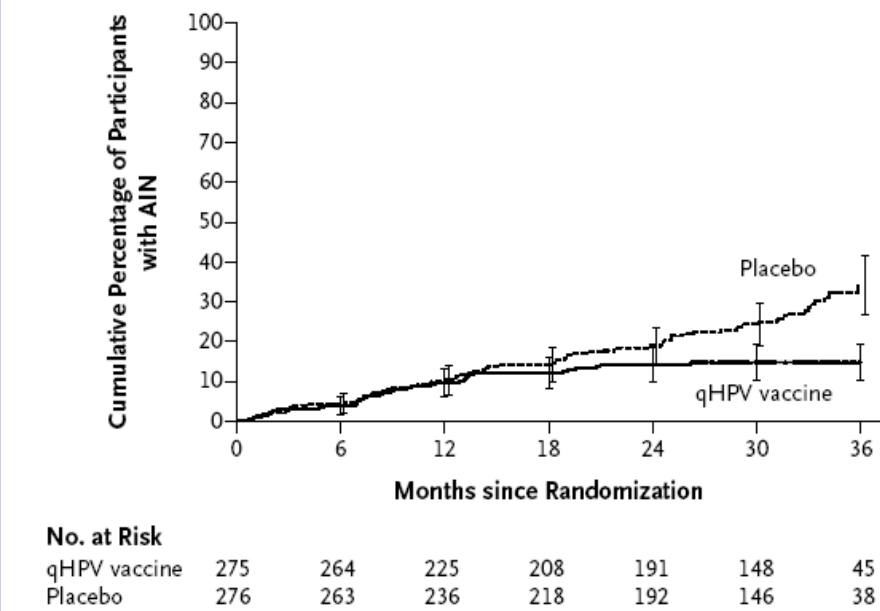
602 healthy men who
have sex with men, 16 to 26 years of age

NEJM, 2011

A HPV-6, 11, 16, or 18–Related AIN in the PPE Population



B HPV-6, 11, 16, or 18–Related AIN in the ITT Population



CONCLUSIONS

Use of the qHPV vaccine reduced the rates of anal intraepithelial neoplasia, including of grade 2 or 3, among men who have sex with men. The vaccine had a favorable safety profile and may help to reduce the risk of anal cancer. (Funded by Merck and the National Institutes of Health; ClinicalTrials.gov number, NCT00090285.)

Targeted human papillomavirus vaccination of men who have sex with men in the USA: a cost-effectiveness modelling analysis

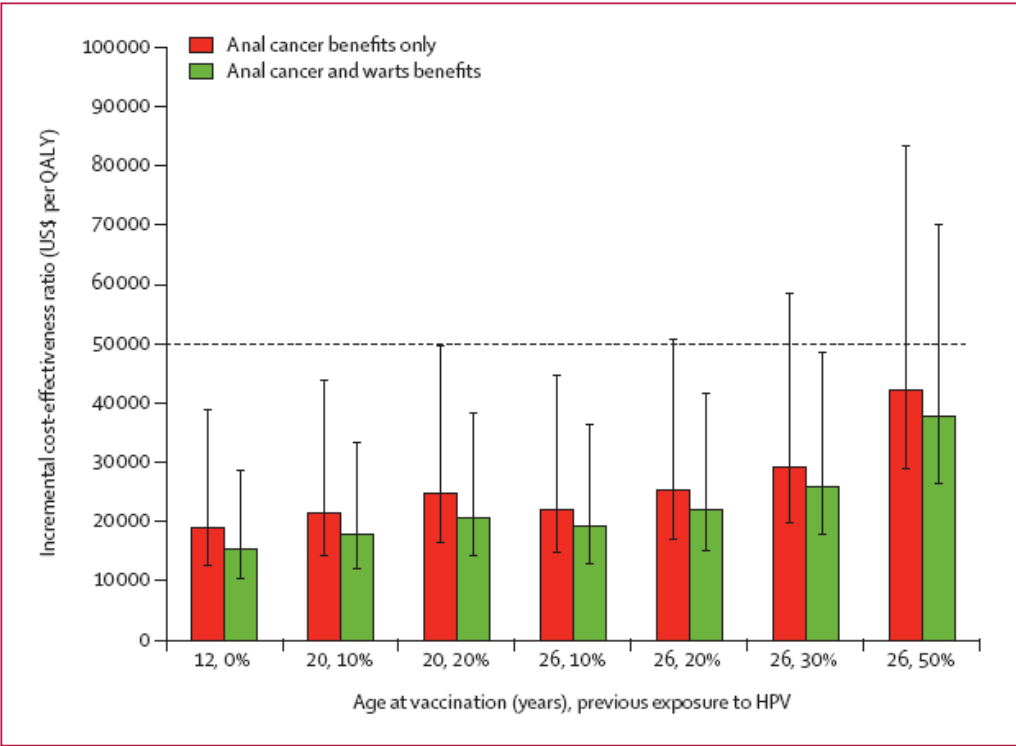


Figure: Effect of age at vaccination and previous exposure to vaccine-targeted HPV types on cost-effectiveness ratios of HPV vaccination of MSM

Kim JJ, Lancet 2010

What men who have sex with men think about the human papillomavirus vaccine

D Simatherai,¹ C S Bradshaw,² C K Fairley,^{1,3} M Bush,³ S Heley,³ M Y Chen^{1,3}

vaccine course. A total of 93% indicated that they would be willing to disclose that they were MSM to a health professional in order to obtain the vaccine for free, but not until a median age of 20 years: 2 years after the median age of sexual debut (18 years) and after a median of 15 sexual partners. If the HPV vaccine is targeted to MSM, the challenge will be for MSM to be vaccinated before they acquire HPV infection.

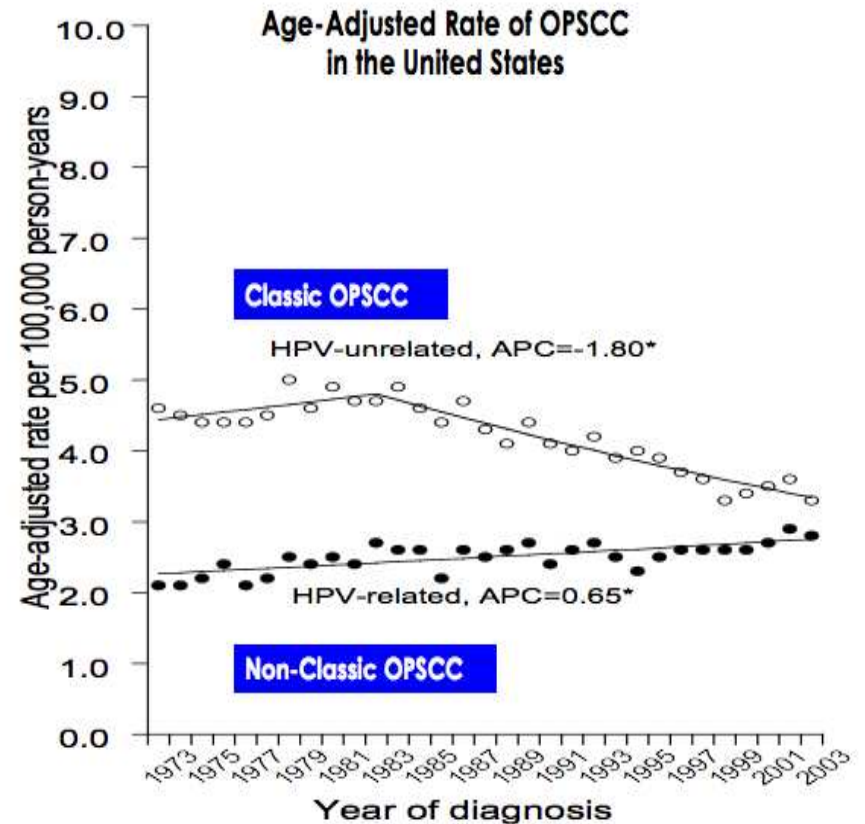
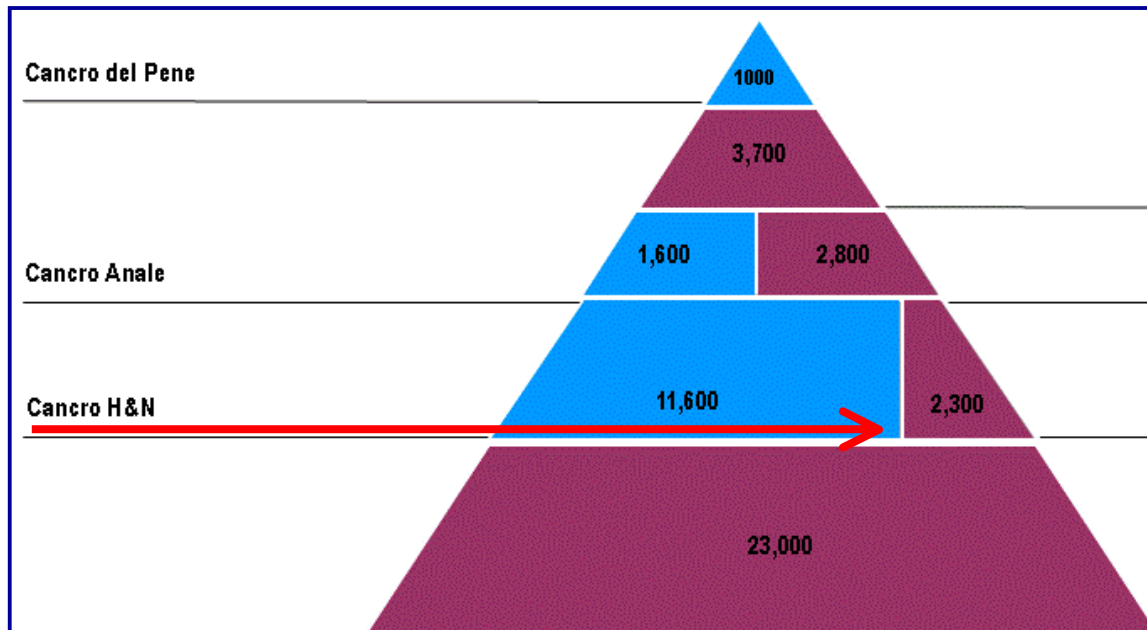
Table 1 Median age of male sexual health service attendees when they first engaged in specified sexual activities with another man

Sexual activity	Median age (y)
Insertive oral sex	18
Receptive oral sex	18
Insertive anal sex	20
Receptive anal sex	20
Insertive fingering	20
Receptive fingering	19
Insertive penile–anal contact	18
Receptive penile–anal contact	18

Oropharyngeal Cancer

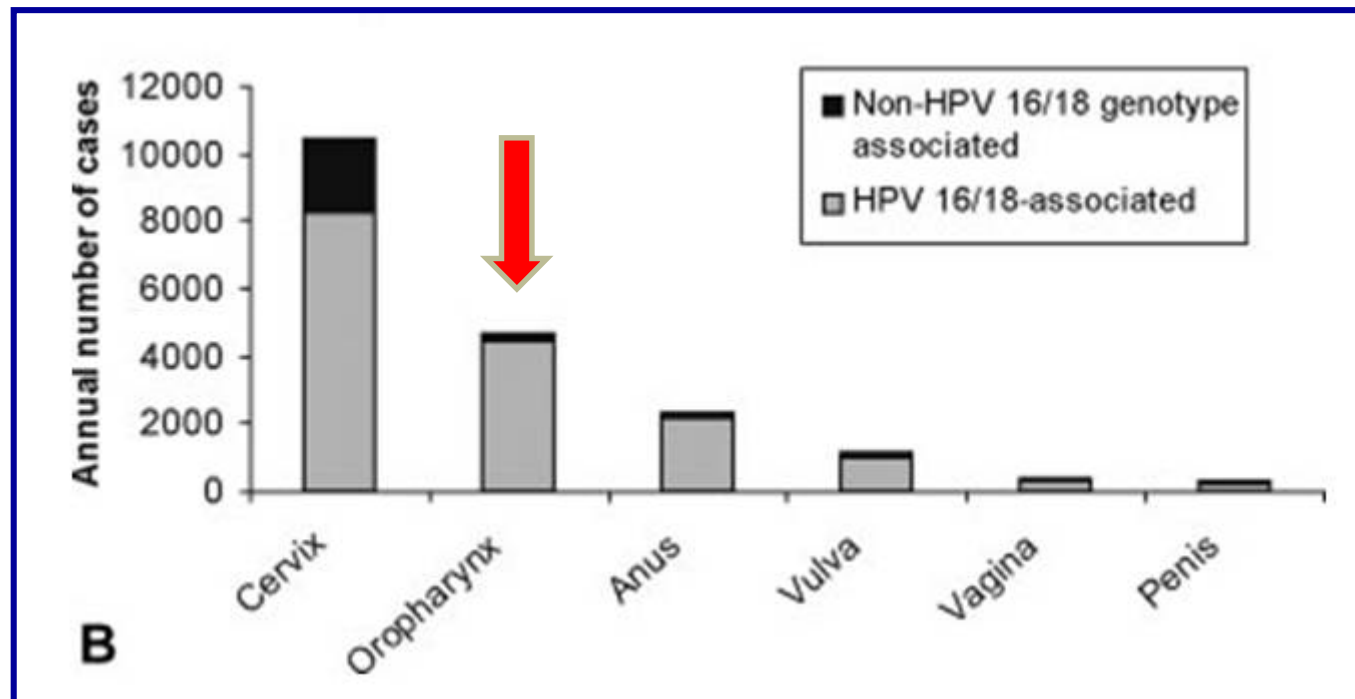
■ Changing Epidemiology

- ➔ Classic: bad teeth, smoker, drinker, > 65 year old male
- ➔ Non-classic: no traditional risks, < 55 year old male – **HPV related**
- ➔ Non-classic cancer >50% of new OPSCC cases (2008 onward)
- ➔ Risk related oral sex



DSouza G, NEJM 2007

Oropharyngeal Cancer




HPV 16 in > 90% of cases

Vaccino nei maschi: è costo/efficace??

PubMed


▼

hpv vaccine cost effectiveness

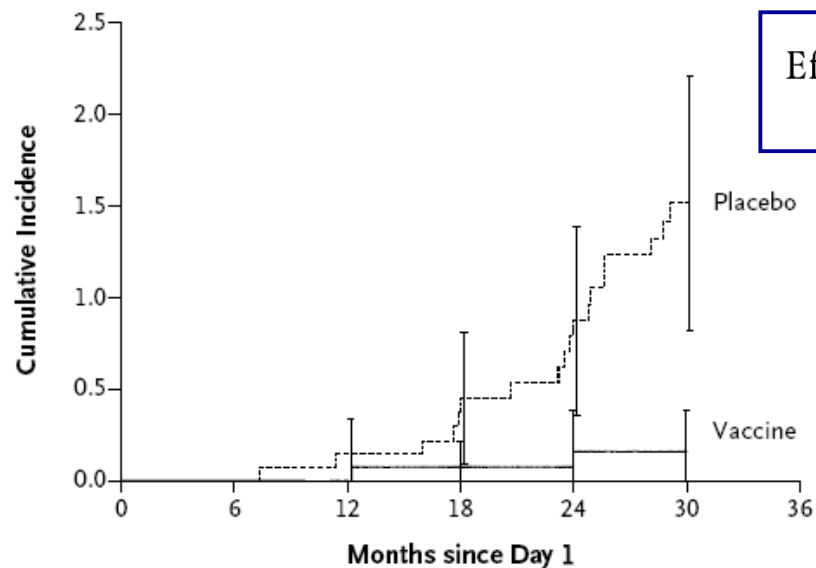
 [RSS](#) [Save search](#) [Advanced](#)

Display Settings: ☒ Summary, 20 per page, Sorted by Recently Added

Results: 1 to 20 of 252 [<< First](#)

 Filters activated: published in the last 5 years [Clear all](#)

C EGL Related to HPV Types 6, 11, 16, or 18 in the Per-Protocol Population



No. at Risk

Vaccine	1397	1397	1367	1267	1166	983
Placebo	1408	1408	1374	1267	1149	949

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

Giuliano et al, NEJM 2011

HPV Type	Proporzione casi HPV correlati
16 and 18	<ul style="list-style-type: none"> ■ 70% cancro dell'ano and AIN ■ 30-40% cancro del pene ■ 20-30% cancro orofaringeo ■ Trasmissione
6 and 11	<ul style="list-style-type: none"> ■ 90% dei condilomi genitali ■ Trasmissione

