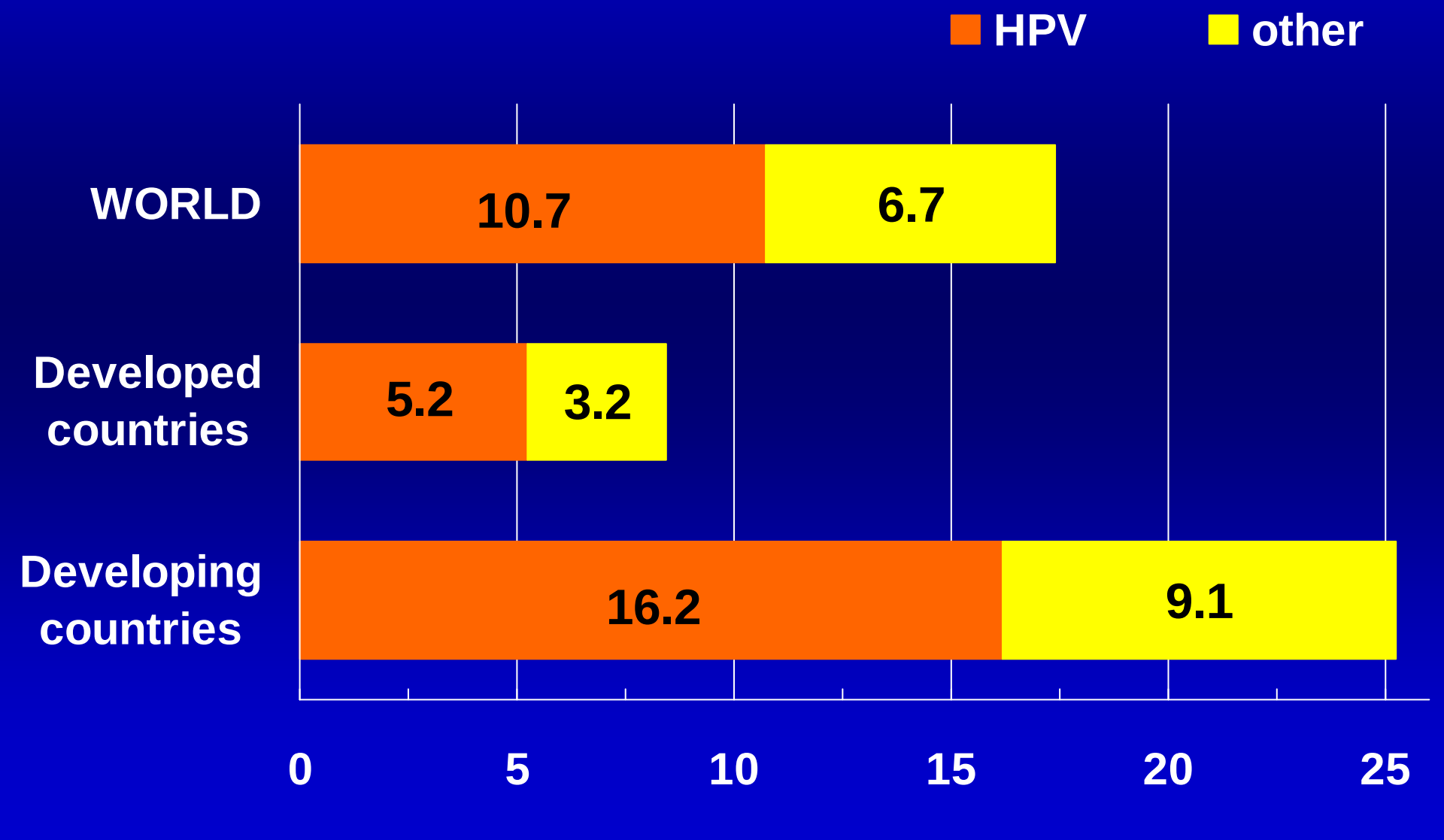
HPV e prevenzione

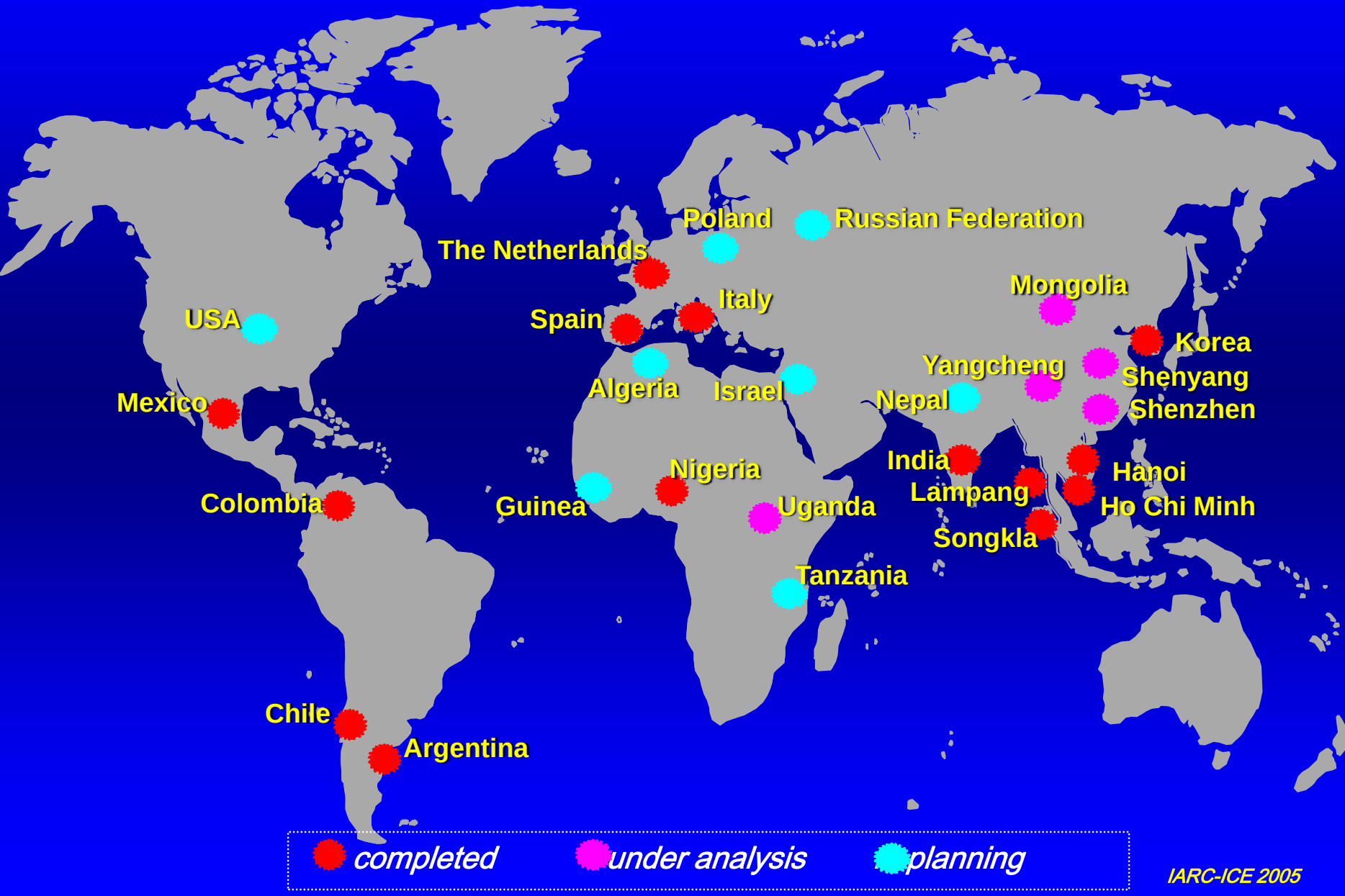
Silvia Franceschi
Infections and Cancer Epidemiology Group
International Agency for Research on Cancer
Lyon, France

GISCI 2006
Roma, 20-21 Aprile 2006

Percentage of female cancer sites attributable to infectious agents

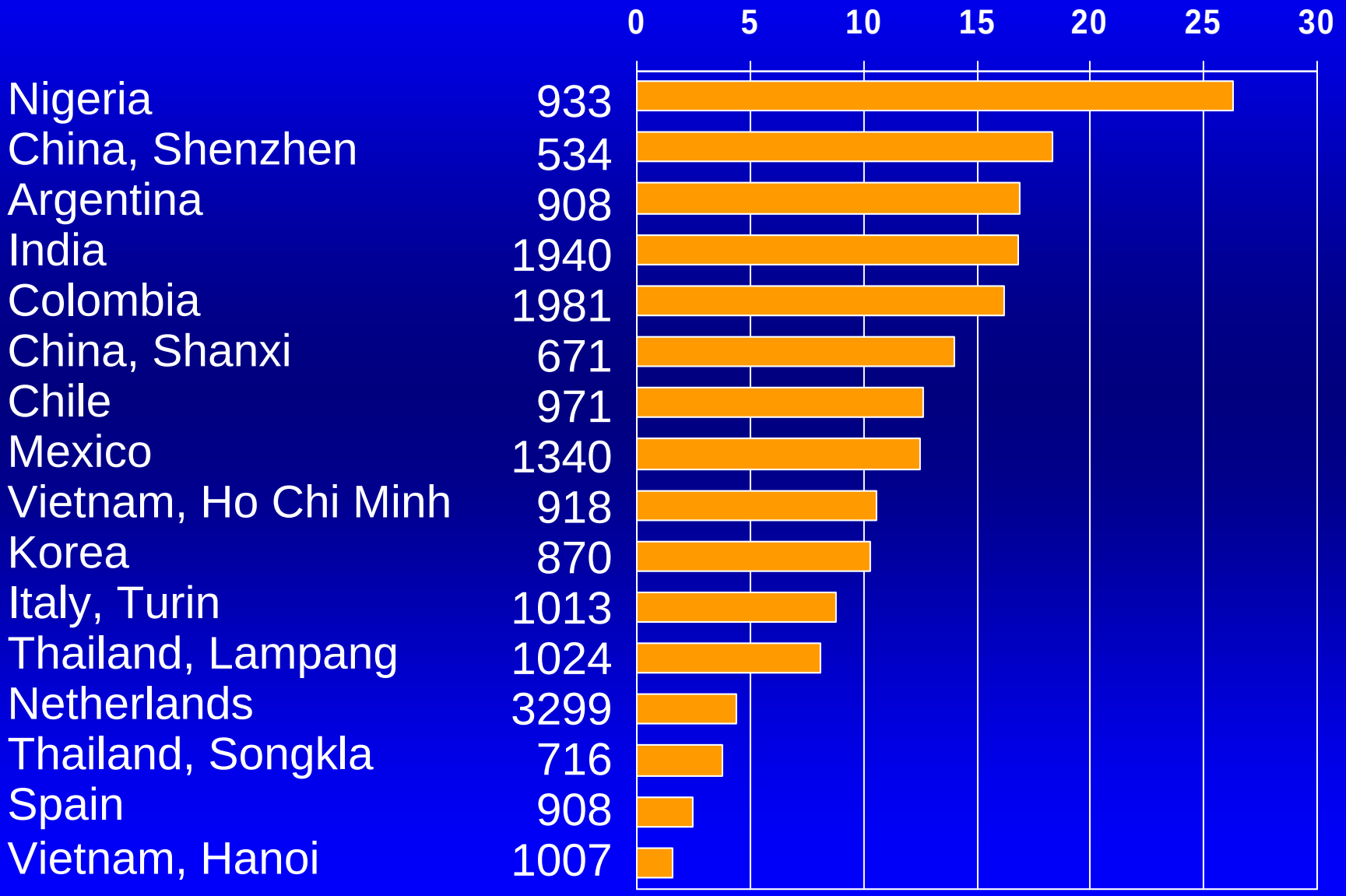


IARC Multi-centre HPV Prevalence Surveys

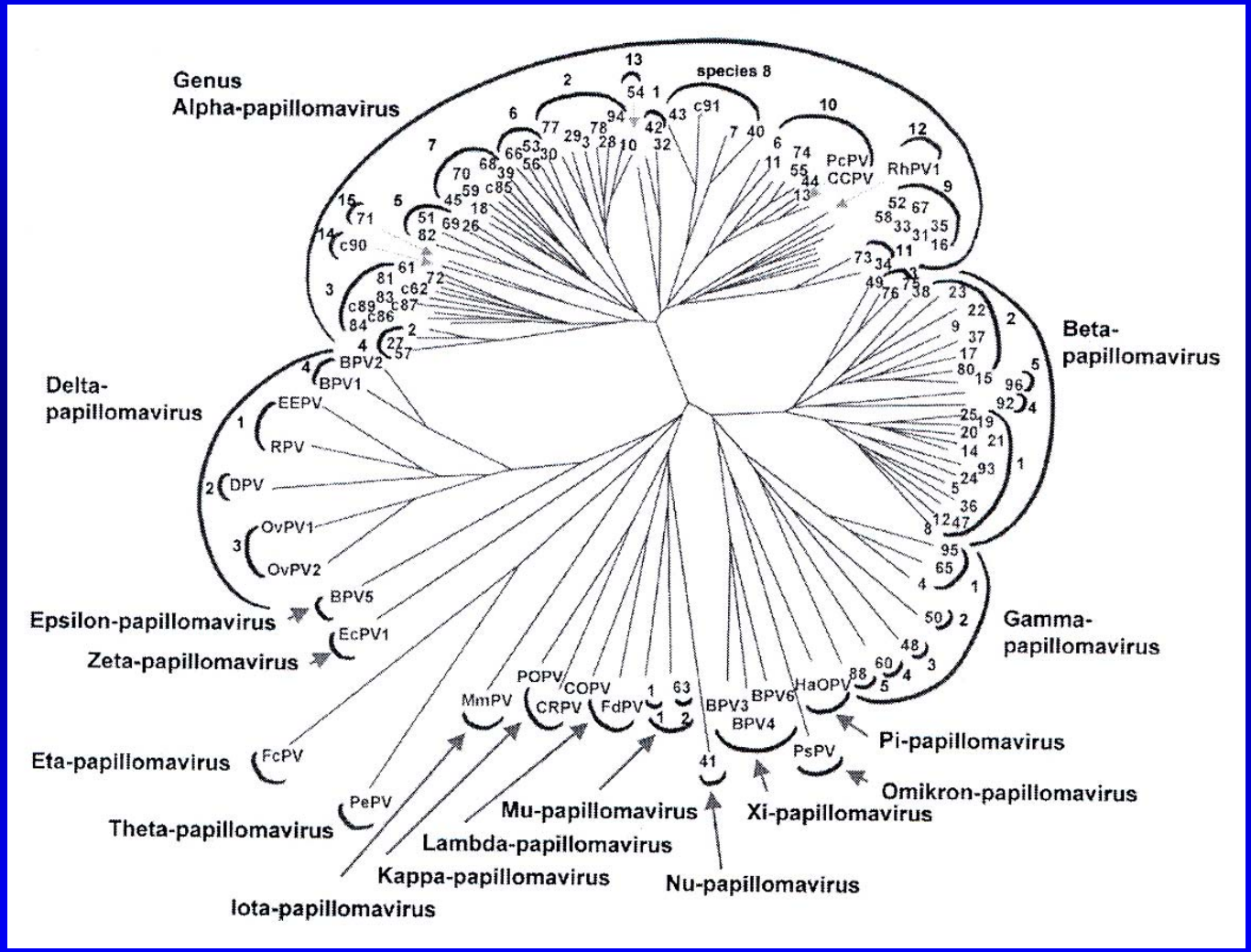


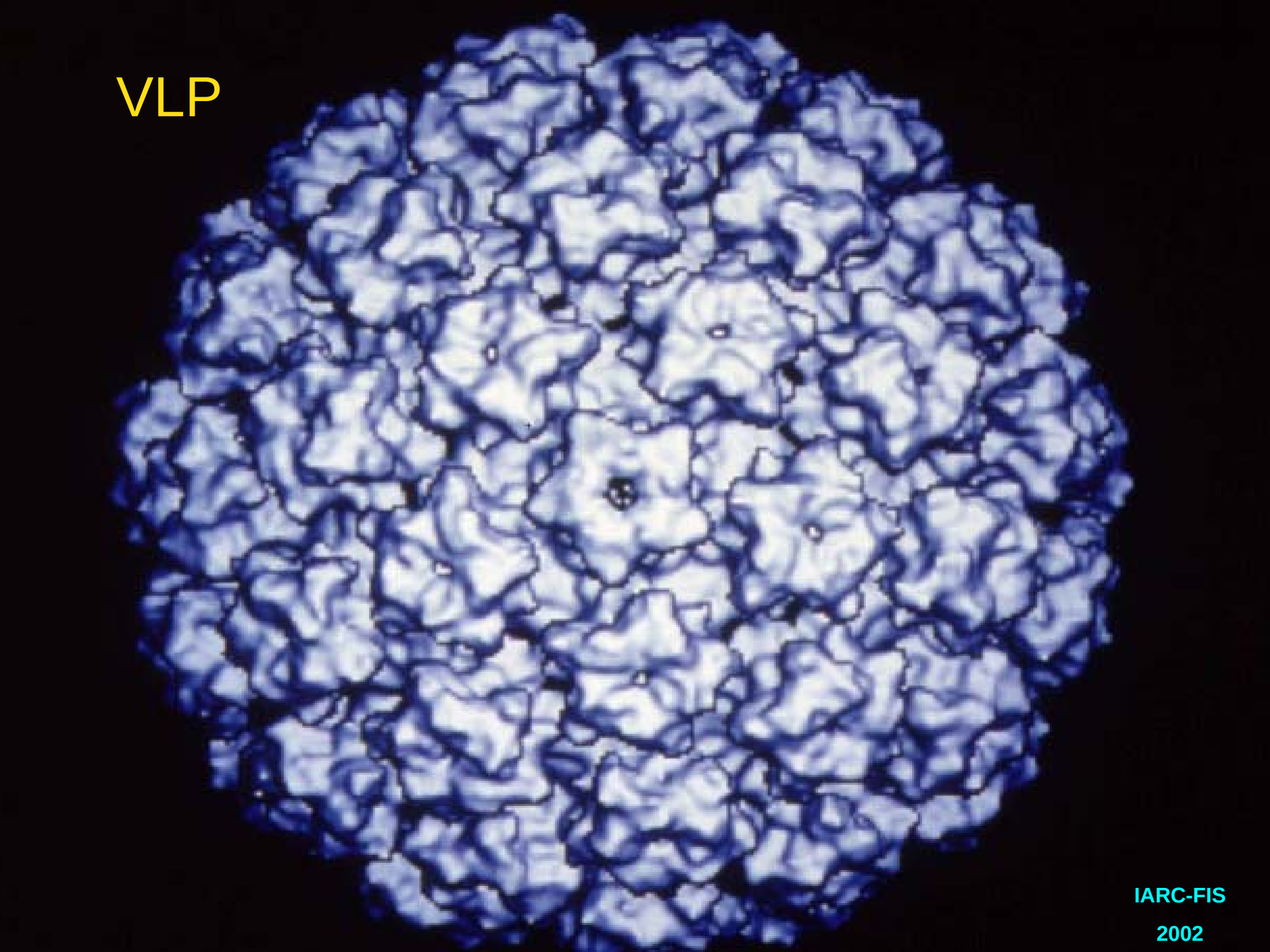
Prevalence of cervical HPV DNA in sexually active women

IARC Multi-centre HPV Prevalence Survey, 1995-2002



Phylogenetic tree of HPV genotypes




VLP
IARC-FIS
2002

Étude d'Efficacité Combinée Phases II/III
Résultats d'efficacité (vaccin quadrivalent SPMSD)

Population ITTM
Suivi moyen de 25 Mois (à partir de J30 après la 1ere dose)

Endpoint	Cas Vaccin HPV † (N=9,342)	Cas Placebo † (N=9,400)	Efficacité Vaccinale	Intervalle de Confiance 95%
CIN 2/3 ou + associés à HPV 16/18	1	81	99%	93%,100%
CIN 2/3 ou + associés à HPV 16	1	68	99%	92%,100%
CIN 2/3 ou + associés à HPV 18	0	18	100%	77%,100%
CIN 2 associés à HPV 16/18	1	55	98%	89%,100%
CIN 3/AIS associés à HPV 16/18 *	0	52	100%	93%,100%

† Les sujets sont comptés une fois par ligne. Un sujet peut apparaître sur plus d'une ligne.

*CIN 3/AIS = Cancer Cervical Stade 0 FIGO

IARC-ICE 2005

Vaccine efficacy for persistent infection up to 4.5 years (intention-to-treat)

	Placebo women	Event rate	Vaccine women	Efficacy % (95%CI)
HPV 16	470	2.3	481	93.4 (74.0-99.2)
HPV 18	470	0.6	481	100.0 (42.8-100.0)
HPV 16/18	470	2.7	481	94.4 (78.2-99.4)

Harper et al, 2006

Vaccine efficacy for incident infection up to 4.5 years (intention-to-treat)

	Placebo women	Event rate	Vaccine women	Efficacy % (95%CI)
HPV 31	516	2.1	528	54.5 (11.5-77.7)
HPV 45	518	1.2	528	94.2 (63.3-99.9)

Harper et al, 2006

Other important long-efficacy HPV vaccine trials

Study	Randomisation (age)	Women	Vaccine	Follow-up
Guanacaste, NCI	2004-5 (18-25 yrs)	7,467	GSK HPV 16/18 vs HAV	1/year x 4
Nordic country trial	2002-3 (18-23 yrs) 2004-5 (18-23 yrs)	7,320 4,875	MSD HPV 16/18/6/11 vs placebo GSK HPV 16/18 vs HAV	2/year x 4 2/year x 4
Nordic country cohort	2002-5 (18-19 yrs) 2003-5 (18-25 yrs)	6,790 10,300	- -	Registries (Cancer, Screening, Pharmacy)
Finland, phase IV	Planned (13-14 yrs)	>35,000	HPV girls + HBV boys vs HPV girls & boys vs HBV girls & boys	Finnish Maternity Cohort, Registries

Efficacy in women with evidence of current

or previous infection with vaccine HPV types

From Eliav Barr

Does GARDASIL® alter the course of HPV infection?

	Seronegative	Seropositive
PCR(-)	Prophylactic efficacy in HPV-naïve women; ≥95% reduction in incidence of HPV 6/11/16/18-related disease	Prevention of recurrence of infection; 100% reduction in incidence of HPV 6/11/16/18-related disease (low recurrence rates)
PCR(+)	Post exposure prophylaxis in women with early infection; 28% reduction in progression to CIN 2/3	Treatment of chronic HPV infection; No vaccine efficacy

From Eliav Barr

The E

- *"Cerv*
  Effect
- *"Cerv*
  A Yea

The E

- *"Coul*
  (Daily
- *"New*
  smea

HPV Vaccines: The Challenges!

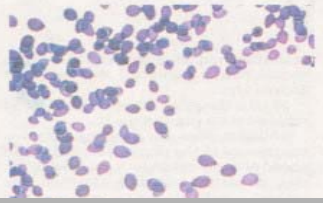
The Guardian | Saturday October 8 2005

Schools may offer cervical cancer vaccination to all girls

Sarah Boseley
Health editor

Vaccination against cervical cancer could become as common in schools as jabs against meningitis are now, following the dramatic results of the latest clinical trials. The breakthrough is generally seen as a real victory against one of the commonest cancers and may eliminate it in the UK.

The good news comes as steady but much slower progress is being made



Progress report

Bowel cancer The first national screening programme begins in April, offering hope of early detection. Two biological agents are being assessed for general use in the NHS, and chemotherapy is showing good results alongside surgery.

Breast cancer Screening and better drugs have brought down the death

who are sexually active become infected with HPV at some time, so girls as young as 10 to 13 will be the target population.

The demise of the smear test, offered to all women every few years from the age of 25, is not imminent. The NHS national screening programme's director, Julietta Patnick, said it could be more than half a century before all sexually active women have been vaccinated as children. By that time, there will probably be an even better vaccine. This one protects against HPV 16 and HPV 18, but not strains responsible for the other 30% of cervical cancers.

Peter Stern of the immunology group at the Paterson Institute for Cancer Research at Manchester's Christie hospital, funded by Cancer Research UK, said it would probably be possible to create a vaccine that would protect against all strains of HPV. "Everything is feasible if you have enough money to pay for it," he said. But a better solution might be to find and attack what the strains have in common.

Kevin Harrington of the Institute of Cancer Research, a clinical oncologist at the Royal Marsden hospital in London, said it was possible the vaccine could stamp out cervical cancer in developed countries. "All the excitement is entirely justified," he said. "Cervical cancer could be eradicated." There are 3,300 cases a year in the UK and 1,300 women die, although screening has reduced the toll enormously. It is a far greater problem in south-east Asia and India, he said. "Often

Campaigners release balloons, each one representing a woman who has died of cervical cancer

cases and is being investigated. Research into targeted drugs similar to Herceptin is also under way.

women are presenting at a late stage and they are not curable." As with Aids drugs, it is likely the vaccine will not be affordable where it is most needed.

Other cancers may also succumb to a vaccine against HPV, he said, as the virus also causes penile cancer, anal cancer and cancer of the vulva, and is possibly involved in some head and neck cancers.

John Toy, the medical director of Cancer Research UK, said the breakthrough was "almost a one-off". But he added: "We are beginning to understand the biology of cancer – what it is that differentiates the cancer cell." This has allowed the development of drugs for breast cancer and acute myeloid leukaemia which target cancer cells and avoid the destruction caused by chemotherapy.

Professor Stern said immunology could provide the tools to make still greater advances. "There has been a revitalisation of optimism about being able to harness the immune response to treat cancer," he said. Immunologists hope to teach the immune system to recognise the enemy within – the cancerous cell – and attack it before it causes potentially fatal disease.

SocietyGuardian.co.uk/cancer »

Routine vaccination
Proposed recommendations

Advisory Committee on Immunization Practices (ACIP) recommends routine vaccination of females 11-12 years of age with three doses of quadrivalent HPV vaccine. The vaccination series can be started as young as 9 years* of age at the discretion of the physician.

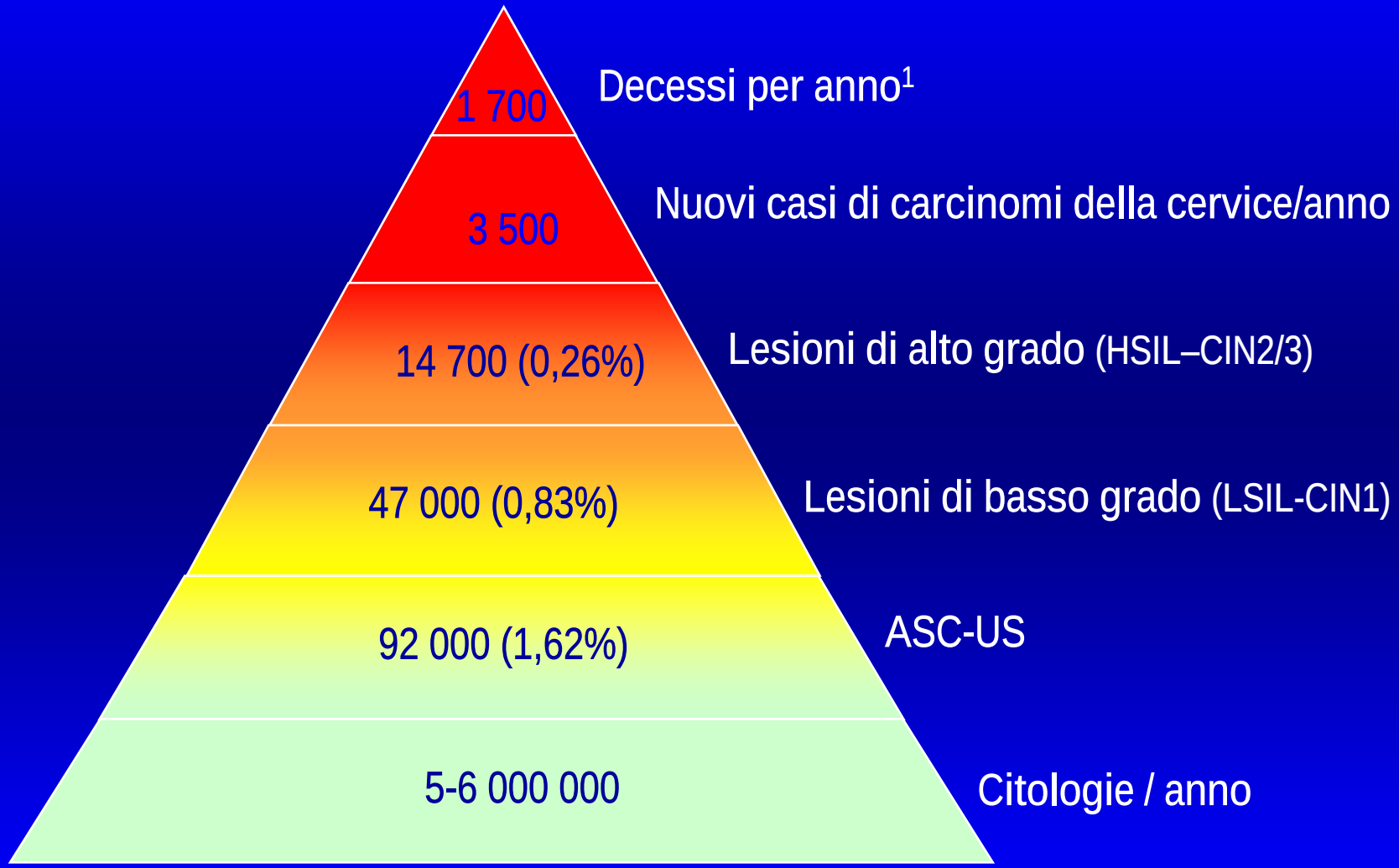
**** Depends on FDA indication***

From Lauri Markowitz

Research Agenda

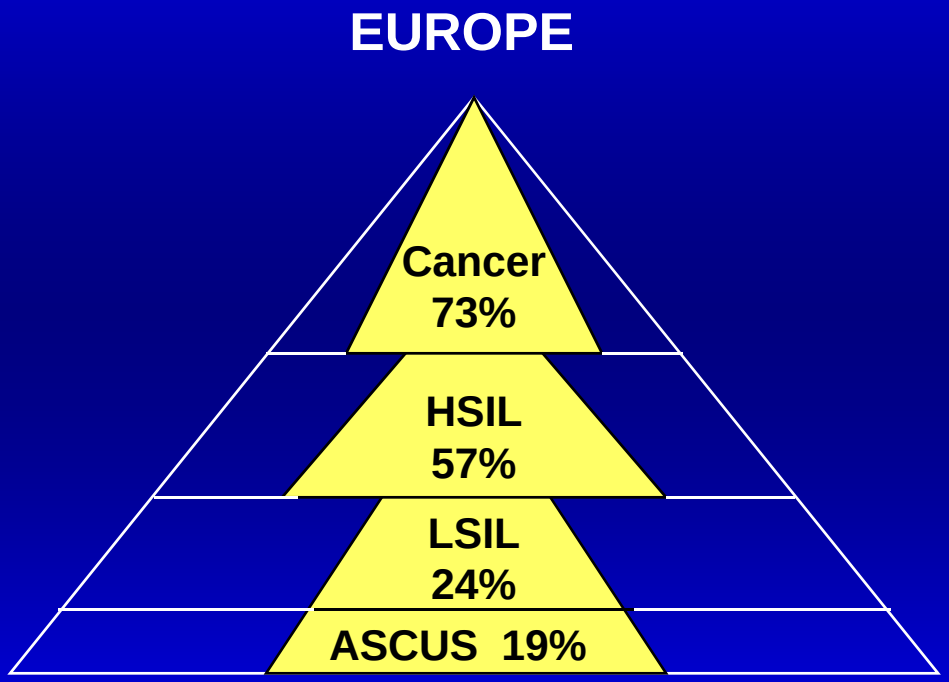
- Will the vaccine change morbidity and mortality (epidemiological impact)?
- What is required for vaccine delivery and what its effect on other services (system impact)?
- What are the necessary investments, costs and savings (economic impact)?

3% degli esami citologici presentano anomalie che necessitano ulteriori esami/trattamento. Italia, anni 2004 (Franceschi&Ronco)



IARC-ICE 2005

Fraction of cervical lesions prevented by HPV 16/18 vaccine in Europe and approximate number prevented per year in Italy (assuming no protection against other types)



ITALY

Cancer : 2,500

HSIL : 8,400

LSIL : 11,300

ASCUS : 17,500

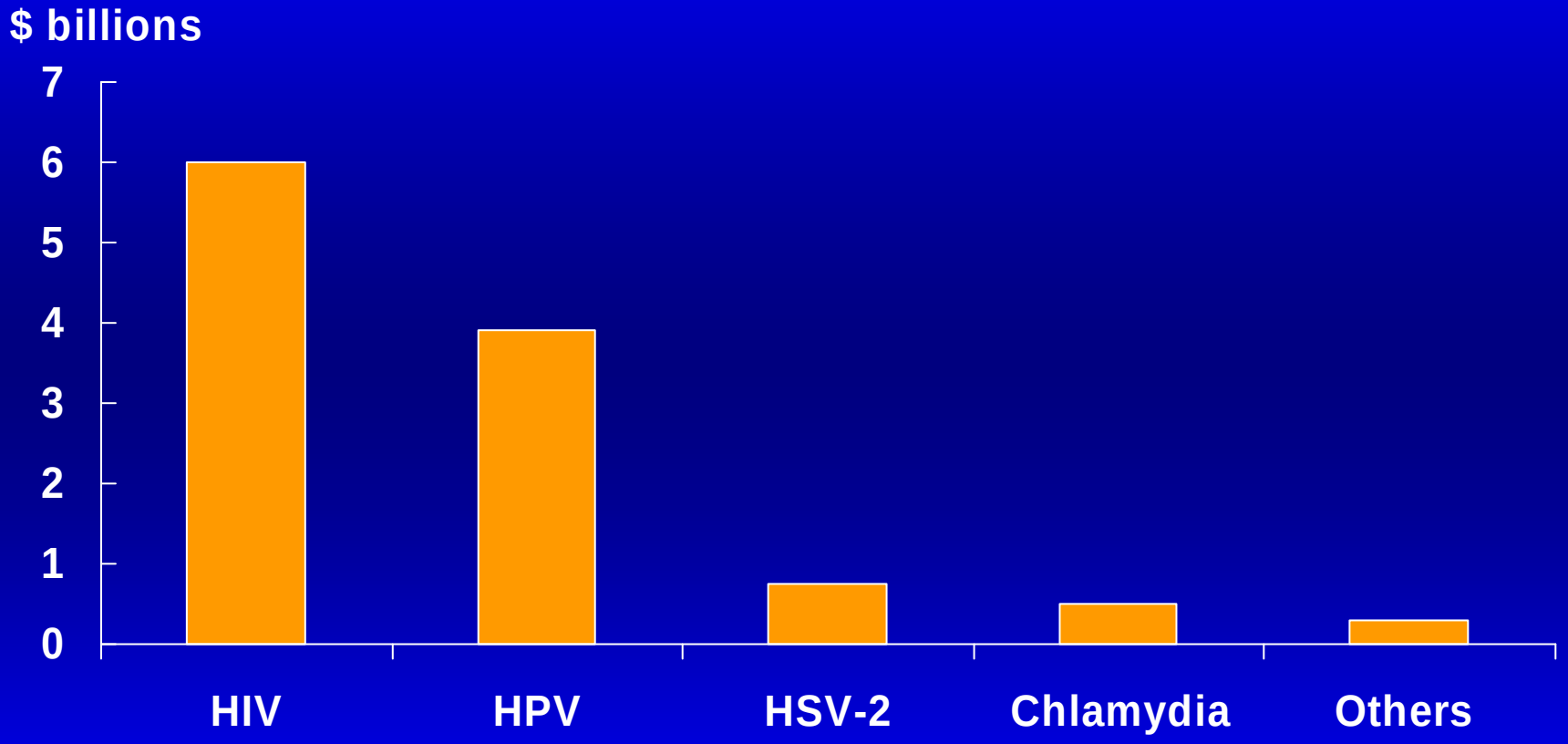
Taken from Mirieia Diaz

Background: HPV-associated conditions
HPV types 16, 18, 6, 11

HPV 16, 18	**Estimated attributable %**
– Cervical cancer	70 %
– High grade cervical abnormalities	50 %
– Low grade cervical abnormalities	30 %
– Anal cancer	~70 %
– Vulva / Vagina / Penile	~40 %
– Head and neck cancers	~10 %
HPV 6, 11	
– Low grade cervical abnormalities	10 %
– Genital warts	90 %
– Recurrent respiratory papillomatosis (RRP)	90 %

Clifford, BJ Ca 2003; Munoz Int J Cancer 2004; Brown J Clin Micro 1993; Carter Cancer Res 2001; Clifford Cancer Epi Biomarkers Prev 2005; Gissman Proc Natl Acad Science 1983; Kreimer Cancer Epidemiol Biomarkers Prev 2005

Estimated annual direct medical cost of specific sexually transmitted infections, US, 2000

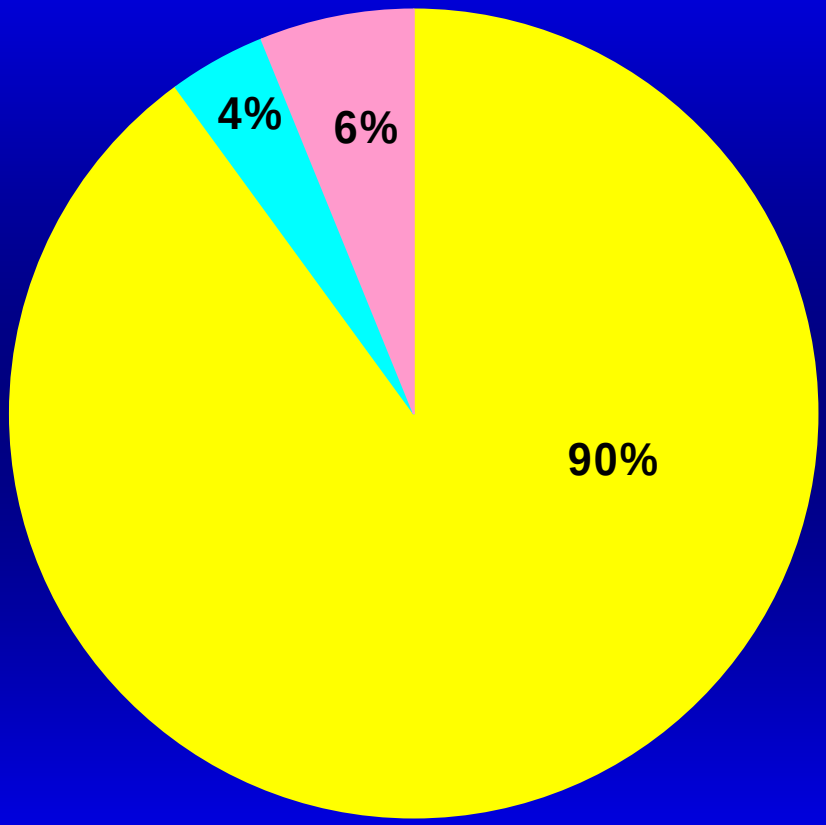


Based on estimated incidence rates in 2000, in 2000 SUS

Modified from Chesson et al. Perspectives on Sexual Reproductive Health 2004, 36(1):11-19

Weinstock et al. perspectives on Sexual and reproductive health 2004, 36(1):6-10

Components of total cost burden of HPV US, 2000



Modified from Chesson et al. Perspectives on Sexual Reproductive Health 2004, 36(1):11-19

Summary of base-case cost-effectiveness ratios for female vaccination (cost per QALY)

Markov	$ 24,300
models	$ 22,800
Dynamic	$ 14,600
models	$ 700 (includes HPV 6/11 benefits)

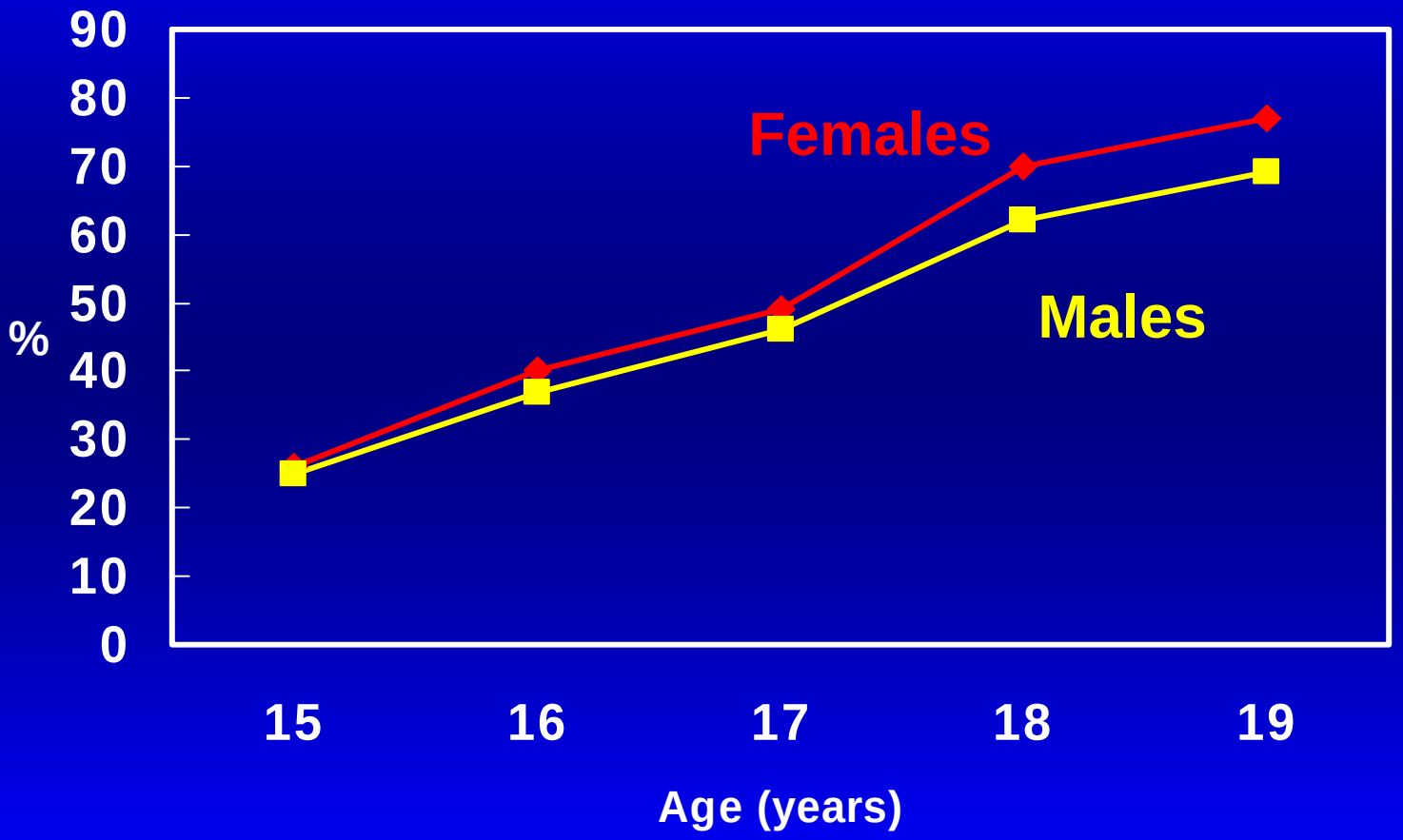
These are base-case estimates; the cost-effectiveness can vary substantially (from <$0 to >$100,000 per QALY) when base-case parameter values and assumptions are modified.

From Harrell Chesson

Social impact

- What will be the reaction of various constituencies (community impact)?
- What will happen to special groups (e.g., HIV+)?

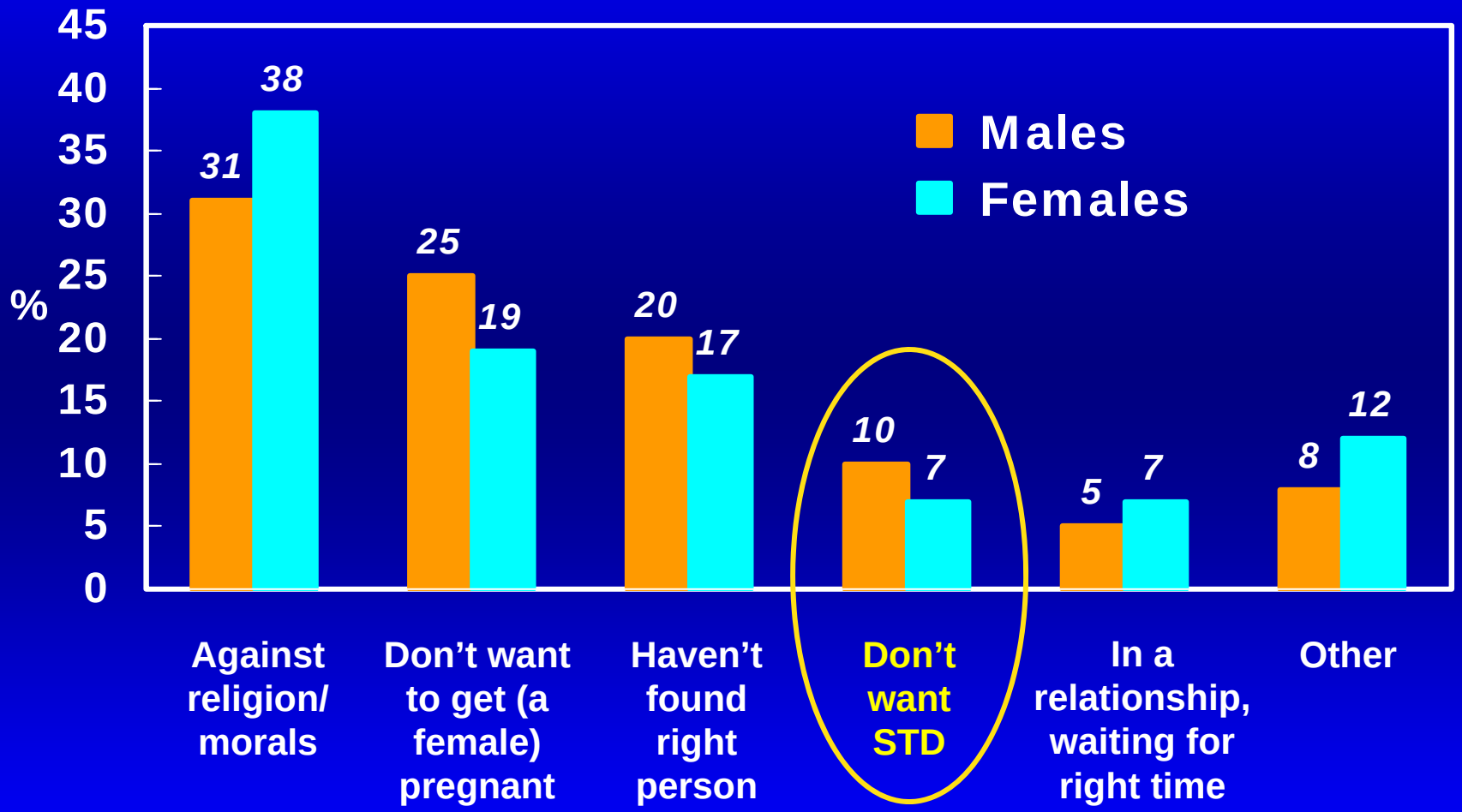
Percentage of young adults who have had vaginal sex by gender and age: NSFG 2002



Mosher et al, 2005; Vital and Health Statistics No 362.

From Nicole Liddon

Main reason for not having sex among adolescents who have never had sex: NSFG 2002



Abma et al, 2004; Vital and Health Statistics, Series 23, No 24.

From Nicole Liddon

Rate of new male sex partners in Merck North American HPV vaccine trial participants (n=4,879)

	Number of new sex partners per person year	
Time period	Estimate	95% CI
Last 6 month (prior to day 1)	0.73	(0.70 - 0.76)
Day 1 to month 7	0.58	(0.55 – 0.61)
Post-month 7	0.52	(0.51 – 0.54)

Merck research laboratories, unpublished data

From Nicole Liddon

Conclusions

- Adolescent sexual behaviour indicates an opportunity during early adolescence for HPV vaccine delivery
- Unlikely sexual behavioural disinhibition will result from HPV vaccine:
  - Multiple other factors associated with adolescent sexual risk
  - Fear of STD not apparent major motivation for abstinence
  - No evidence of behavioral disinhibition in other similar fields
- Monitoring efforts
  - Ongoing national data collection efforts
  - Other potential projects

From Nicole Liddon