

Practice Nurses Programme: HPV

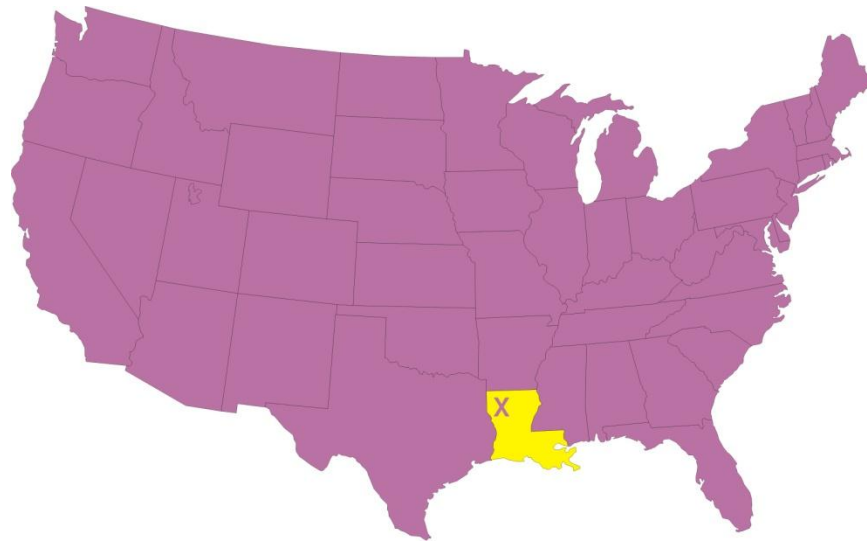
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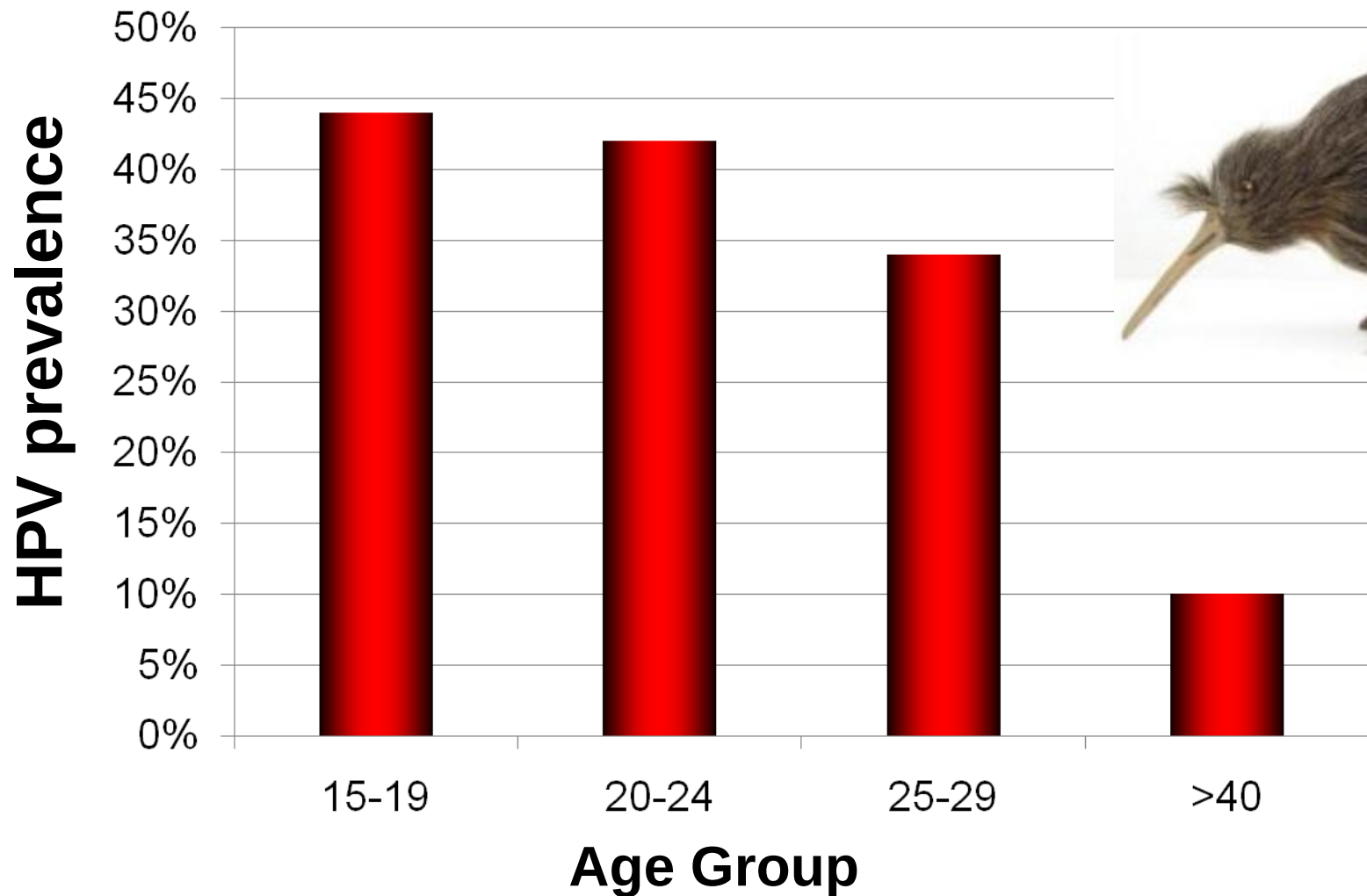


**“According to your chart, Mr. Brown,
apparently what happens in Rotorua
doesn’t always stay in Rotorua.”**

HPV Incidence and Prevalence

- HPV infection is ubiquitous
 - ~75-80% of women acquire (lifetime)
 - 10.5% of women worldwide currently
 - 20-25% around age 20
- Burchell AN, et al. Vaccine. 2006;24(Suppl 3):S52-61.
- Clifford GM, et al. Lancet. 2005 Sep 17-23;366(9490):991-8.

Oceania HPV Study



Common HPV Types

	HPV Types	Disease Manifestations
High risk	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, 82	Low-grade cervical changes ¹ High-grade cervical changes ¹ Cervical cancer ^{1,2} Other anogenital cancers ¹ Head and neck cancer ³
Low risk	6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81	Benign low-grade cervical changes ¹ Genital warts ¹ Recurrent respiratory papillomatosis ⁴

1. Koutsky LA et al. *Epidemiol Rev.* 1988;10:122-163; 2. Muñoz N et al. *N Engl J Med.* 2003;348:518-527; 3. Hansson BG et al. *Acta Otolaryngol.* 2005;125:1337-1344; 4. Wiatrak BJ. *Curr Opin Otolaryngol Head Neck Surg.* 2003;11:433-441.

Factors Associated With Higher Risk

Women

- Age
- Greater number of male partners
- Earlier age of first sexual intercourse
- Sexual behaviors of previous male sexual partners
- Immunological status
 - HPV more likely in immunosuppressed women

Men

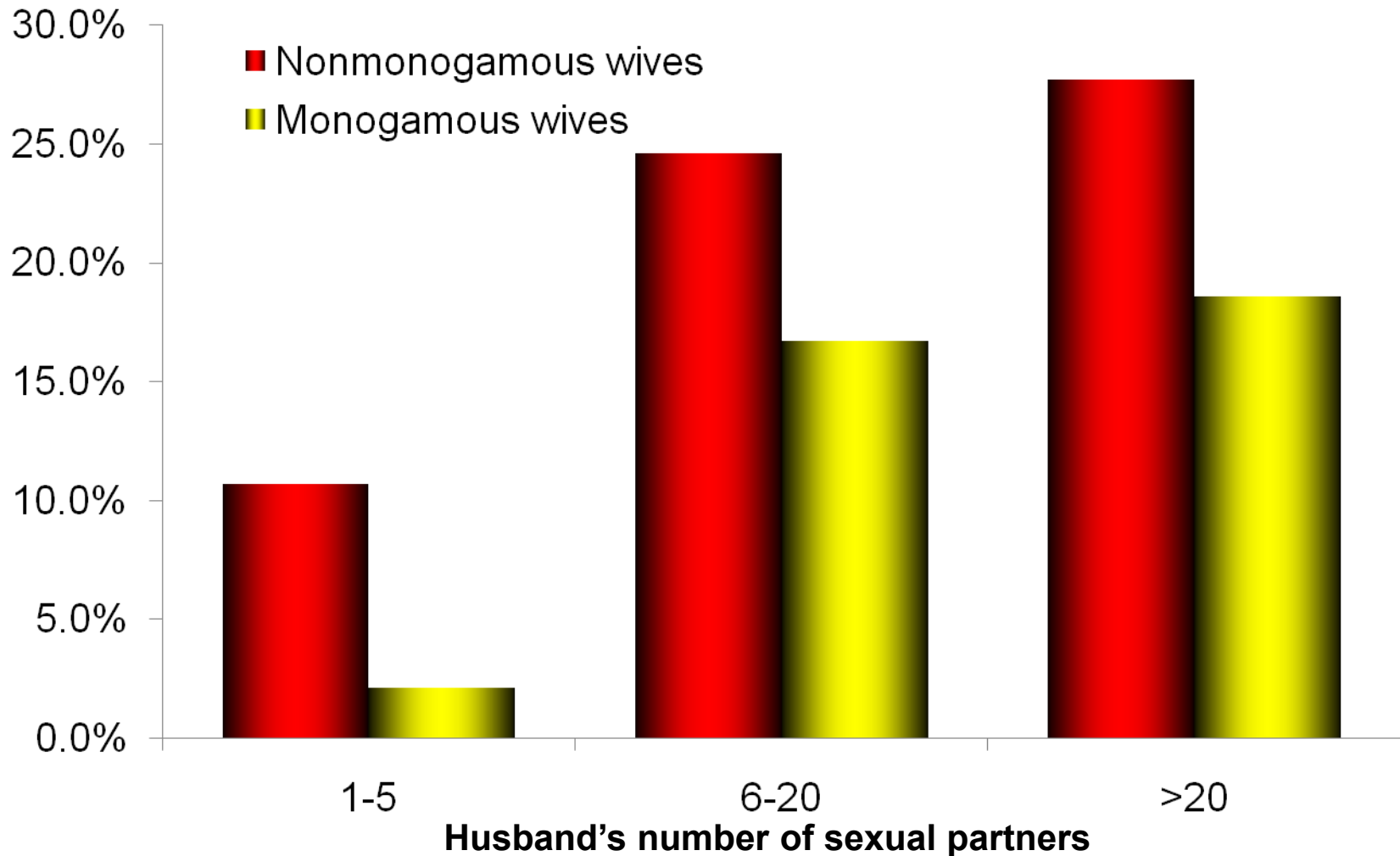
Lifetime number of sexual partners

Number of recent sexual partners

Uncircumcised

Same-sex encounters

Penile HPV-DNA Prevalence by # of Sexual Partners in Spain & Colombia



How to Reduce the Risk of HPV Transmission

- Abstinence from genital contact
- Lifetime mutual monogamy
- Condom use may help reduce risk but is not fully protective.
 - If HPV is present on uncovered skin, transmission is possible.

Dailard C. Understanding 'abstinence': implications for individuals, programs and policies. *Guttmacher Rep Public Policy*. 2003;6:4-6. Anhang R, Goodman A, Goldie SJ. HPV communication: review of existing research and recommendations for patient education. *CA Cancer J Clin*. 2004;54:248-259; Bosch FX. Epidemiology of human papillomavirus infections: new options for cervical cancer prevention. *Salud Publica Mex*. 2003;45 Suppl Manhart LE, Koutsky LA. Do condoms prevent genital HPV infection, external genital warts, or cervical neoplasia? A meta-analysis. *Sex Transm Dis*. 2002;29:725-735.

- **HPV effective condoms....**
- **Condoms decrease transmission but do not prevent transmission where they don't cover**

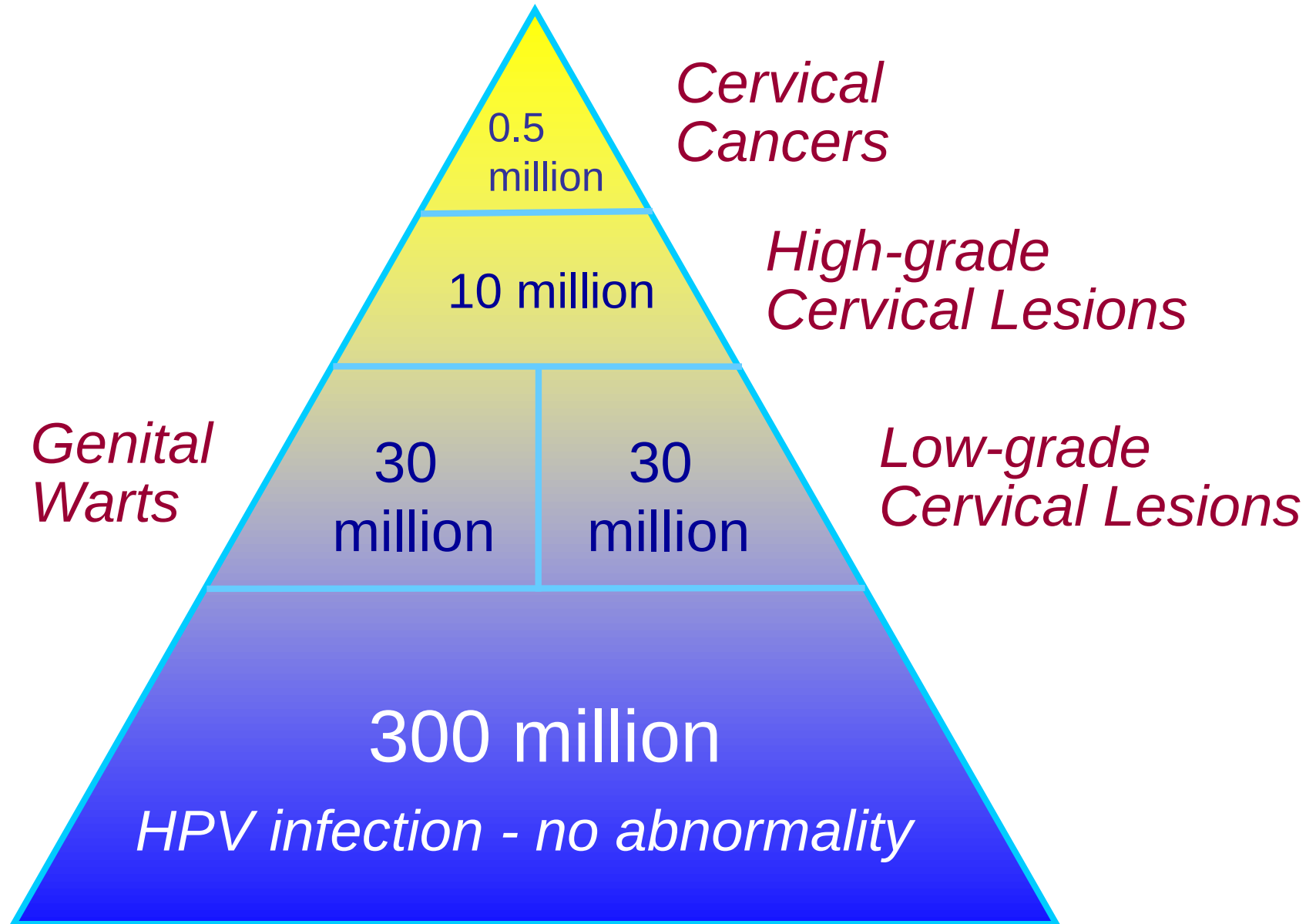


Courtesy of Photobucket

HPV Worldwide

- Likely the #2 human carcinogen
 - After tobacco
- 5% of human cancers
- 10% of cancers in women
- 15% of cancers in women in developing countries

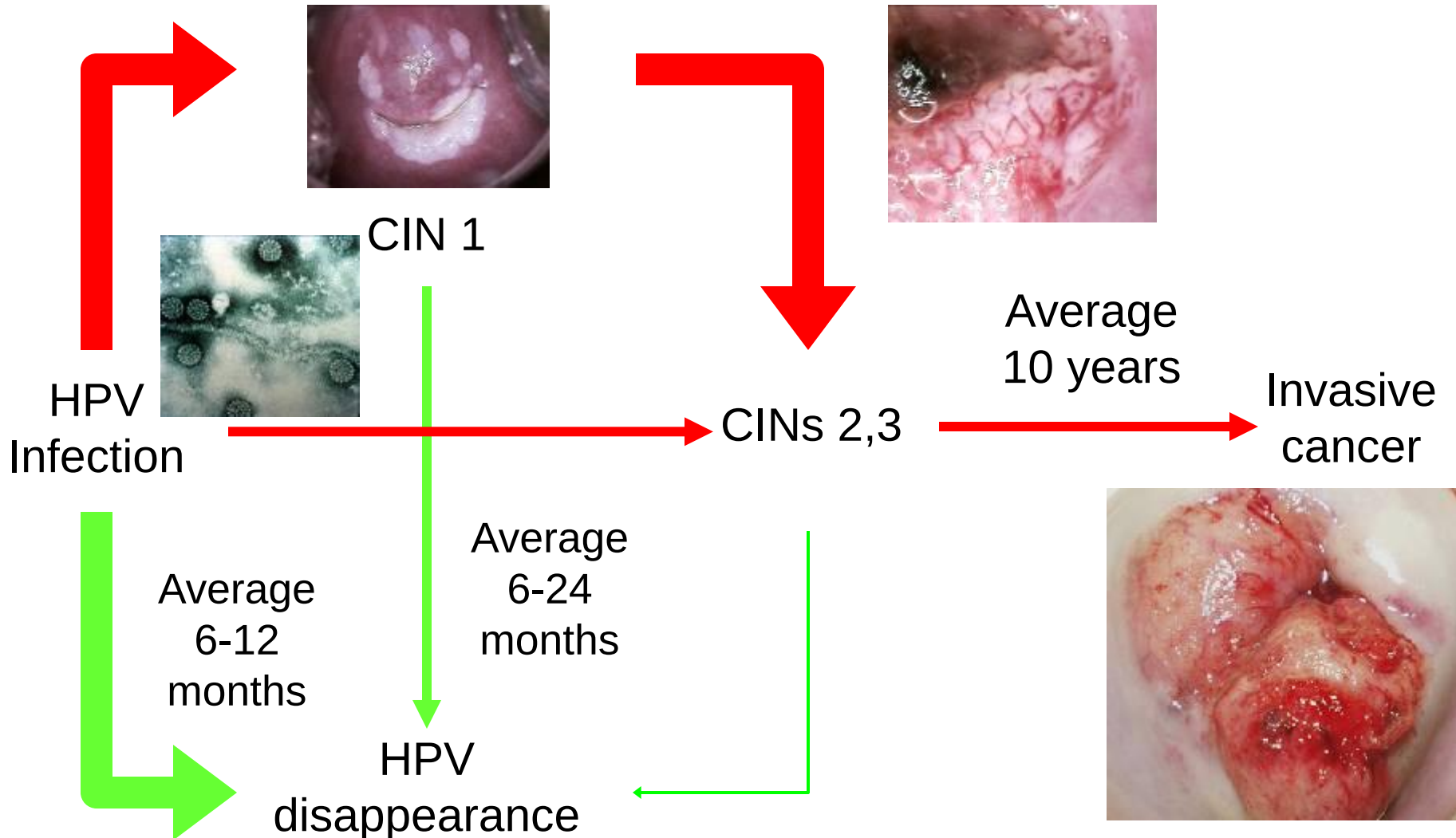
Summary of Worldwide Estimates on the Burden of HPV



HPV Disease in New Zealand

- Women at risk for cervical cancer (Female population aged ≥ 15 yrs) 1.66 millions
 - Annual cervical cancer cases = 140
 - Annual cervical cancer deaths = 53
- Factors contributing to cervical cancer
 - Smoking prevalence, women = 24.3%
 - HIV prevalence (15-49 years) = 0.1%

Natural History of Cervical Neoplasia



Incidence of Cervical Cancer

Indicator	New Zealand	Australia & NZ	World
Crude incidence rate	6.5	6.3	15.8
Age-standardized incidence rate	5.5	5.0	15.3
Cumulative risk (%). Ages 0-74 years	0.5	0.5	1.6
Annual number of new cancer cases	140	799	529,828

Human Papillomavirus and Related Cancers Summary Report Update: NEW ZEALAND.
September 15, 2010. WHO/ICO Information Centre on HPV and Cervical Cancer (HPV
Information Centre) GLOBOCAN 2010

http://apps.who.int/hpvcentre/statistics/dynamic/ico/country_pdf/NZL.pdf



HPV Disease in New Zealand

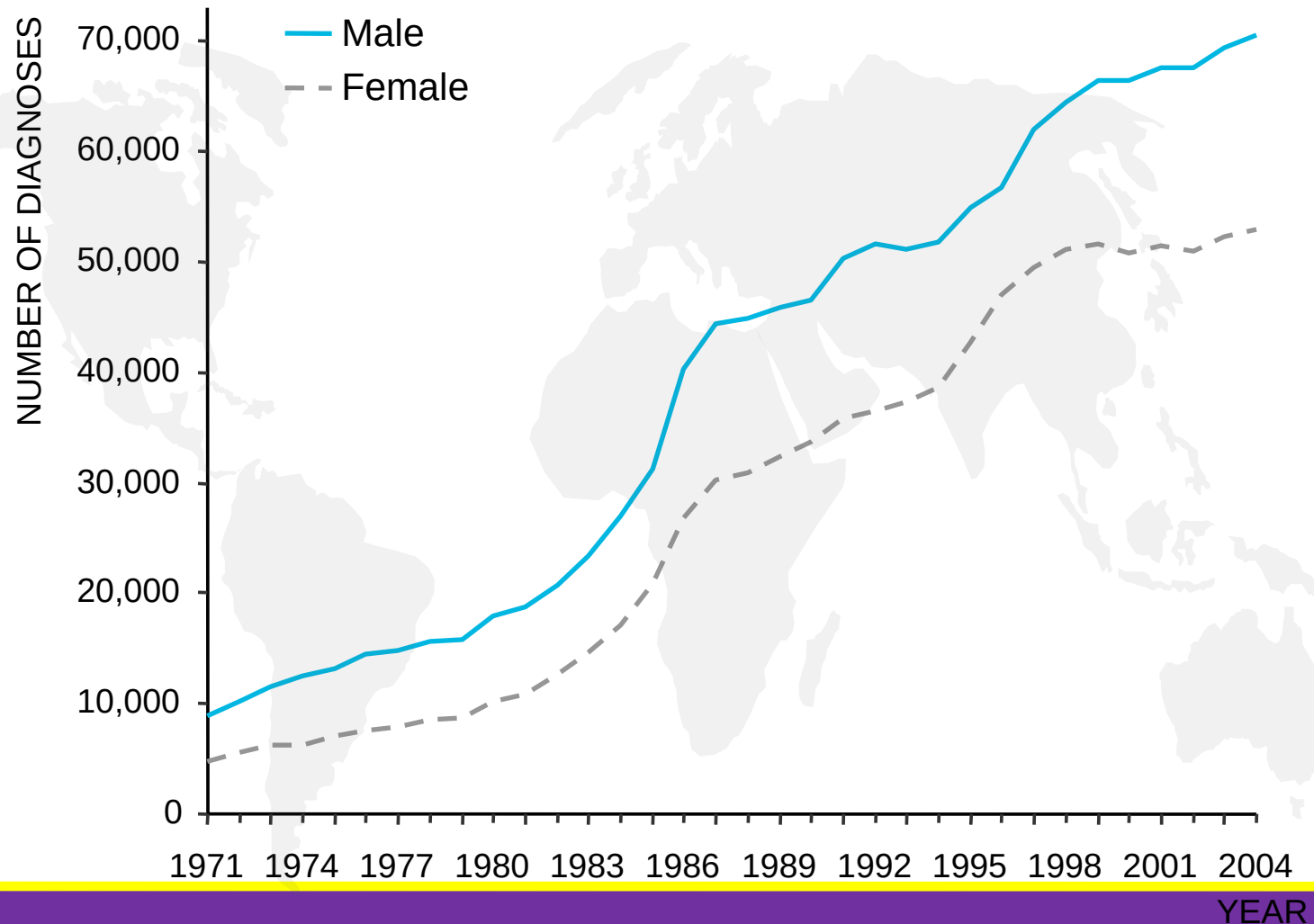


Crude incidence rates per 100,000 population	Male	Female
Cervical cancer	-	6.5
Anal cancer	0.8	1.3
Vulva cancer	-	2.4
Vaginal cancer	-	0.6
Penile cancer	0.7	-
Oral cavity	5.6	3.9
Pharynx (excluding nasopharynx)	2.7	1.0

Human Papillomavirus and Related Cancers Summary Report Update: NEW ZEALAND.
September 15, 2010. WHO/ICO Information Centre on HPV and Cervical Cancer (HPV
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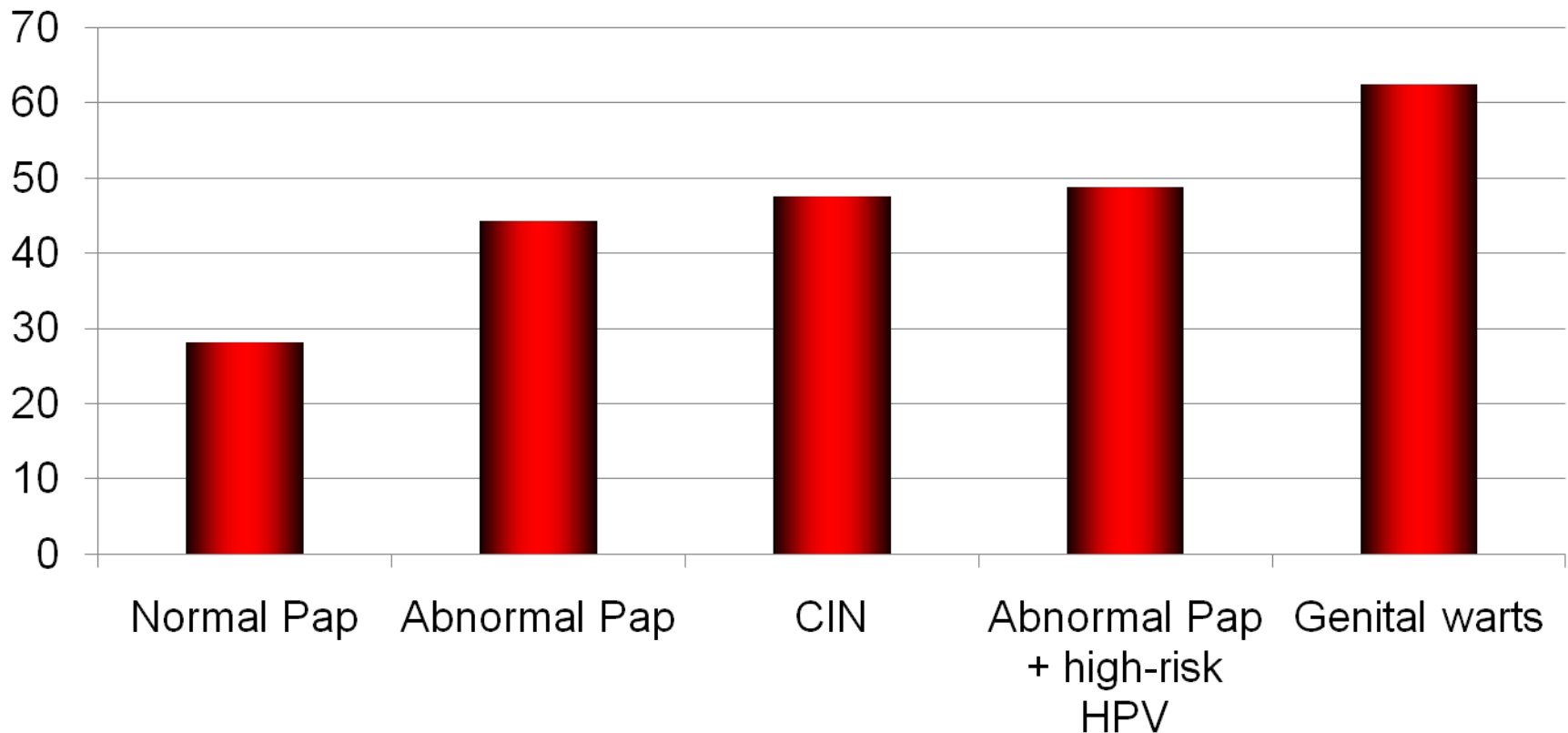
NUMBER OF DIAGNOSES OF GENITAL WARTS (FIRST, RECURRENT AND RE-REGISTERED EPISODES) BY SEX, SEXUALLY TRANSMITTED DISEASE CLINICS: ENGLAND AND WALES 1971-2004



Source: Health Protection Agency, 2006.

LSU Health Sciences Center – USA

Psychological Impact of HPV Related Illness



Women with genital warts had the highest psychological impact scores



Guidelines for Cervical Screening in New Zealand

Incorporating the Management of Women with Abnormal Cervical Smears



New Zealand Government

Liquid-based Cytology

- Disadvantages
 - Higher cost and decreased specificity
- Advantages
 - HPV, gonorrhea, and chlamydia test
 - Eliminates air drying artifact
 - Easier to read
 - Less blood/inflammation problem
- ACOG Practice Bulletin No. 109. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009; 114:1409-20.

Cervical Screening in New Zealand

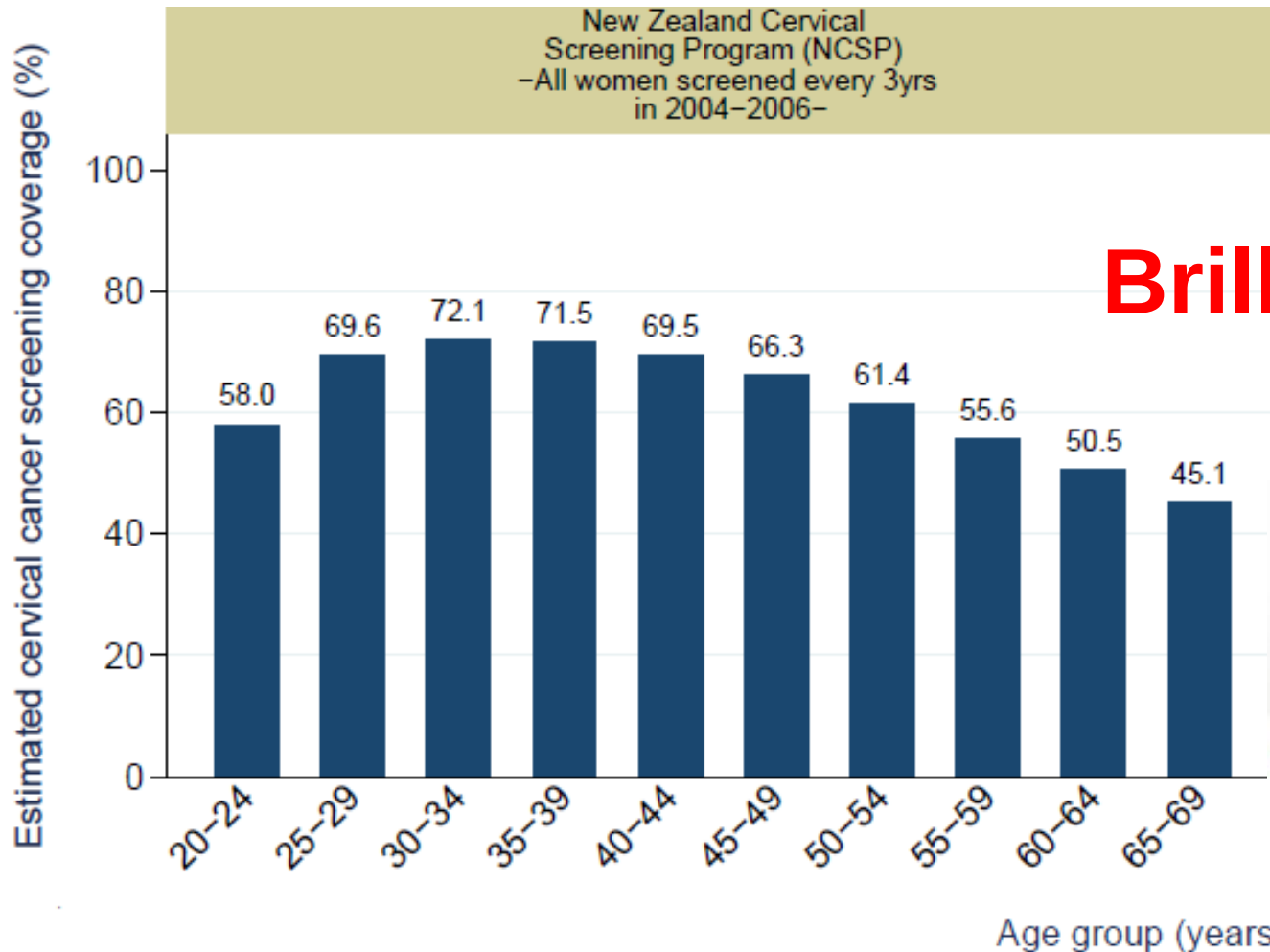
Cervical cancer screening coverage, (reference)	63.5% (New Zealand Cervical Screening Program)
Screening ages (years)	20-69 years
Screening interval (years) or frequency of screens	Every 3 years
First smear, or >5 years since previous smear	A second smear one year after the first, with three-yearly smears thereafter

Human Papillomavirus and Related Cancers Summary Report Update: NEW ZEALAND. September 15, 2010. WHO/ICO Information Centre on HPV and Cervical Cancer (HPV Information Centre) GLOBOCAN 2010

http://apps.who.int/hpvcentre/statistics/dynamic/ico/country_pdf/NZL.pdf



Estimated 2006 Cervical Cancer Screening Coverage in New Zealand



Brilliant!!!!



When to Begin Screening

- Age 20 in NZ
- Age 21 years In US
 - Regardless of the age of onset of sexual intercourse [A]
 - “Risk outweighs benefits”
 - Adolescents clear most HPV within 1-2 years without neoplastic changes
 - ↑ anxiety, morbidity, and expense from test and overuse of procedures



Sexually Active Adolescents

- Counsel and test for sexually transmitted infections
 - May be carried out without cervical cytology screening and, in the asymptomatic patient, without the use of a speculum
- Counsel regarding safe sex and contraception

Optimal Screening Frequency

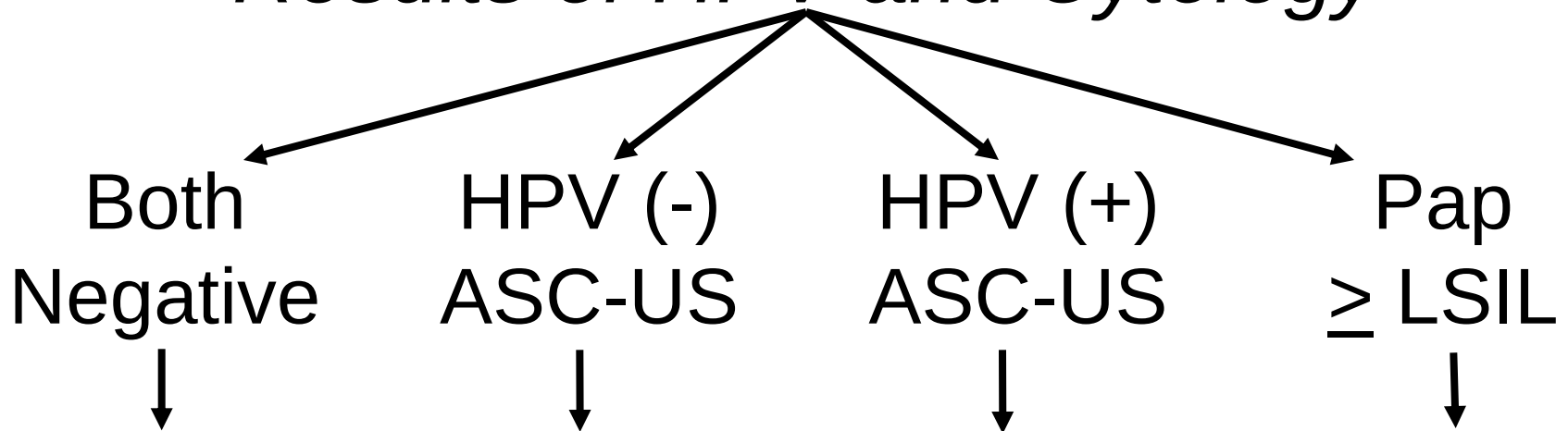
- Every 2 years for women aged 21-29 years, with conventional or liquid-based cytology [Level A]
- Every 3 years for women ≥ 30 years with 3 consecutive negative Pap results [Level A]
- Every 3 years in NZ

Effect on Woman-Years of Life and Costs of Screening 100,000 Women

Screening frequency (yr)	Woman-years of life	Dollars
1	17,551	29,471,000
2	17,140	12,531,000
3	16,964	7,042,000
4	16,501	4,309,000
5	16,161	2,788,000
6	15,412	1,860,000
7	14,868	1,152,000
8	14,073	736,000
10	12,773	349,000

Optimal Screening > Age 30 in Low-risk Women

Results of HPV and Cytology



Repeat Pap & HPV
in 3 yrs *in 12 mos*

Colposcopy

Use **Annual** Screening

- Women who are infected with HIV
- Immunosuppression
- Exposure to diethylstilbestrol (DES) in utero
- Previously treatment for CIN 2, CIN 3, or cancer
 - For at least 20 years
- ACOG Practice Bulletin No. 109. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009; 114:1409-20.

Discontinuing Screening



- **NZ** – Age 69
- **ACS** - 70 years in low-risk women after 3 consecutive negative Paps
- **USPSTF** - age 65 years
- **ACOG** - either of the above and no abnormal test results in past 10 years
- Annual screening if at risk

Out of 10,595 Paps

Pearce KF, Haefner HK, Sarwar SF, Nolan TE. Cytopathological findings on vaginal Papanicolaou smears after hysterectomy for benign gynecologic disease. N Engl J Med 1996; 335: 1559-62.

TABLE 2. FOLLOW-UP OF ABNORMAL PAPANICOLAOU SMEARS IN WOMEN WHO HAD UNDERGONE HYSTERECTOMY FOR BENIGN GYNECOLOGIC DISEASE.*

FINDING	NO. OF SMEARS (%)	NO. OF WOMEN	NO. REFERRED FOR COLPOSCOPY	NO. WITH VAIN ON BIOPSY
Atypical squamous cells of undetermined significance	52 (0.5)	47	5	1
Low-grade squamous intraepithelial lesion	44 (0.5)	30	15	2
High-grade squamous intraepithelial lesion	6 (0.1)	6	6	3
Squamous-cell carcinoma	2 (<0.1)	1	1	1
Total	104 (1.1)	79†	27	5‡

*The estimated total number of Papanicolaou smears in women with benign gynecologic disease was 9610. VAIN denotes vaginal intraepithelial neoplasia.

†Three women each had Papanicolaou smears classified as abnormal in two categories, and one had a smear classified as abnormal in three categories.

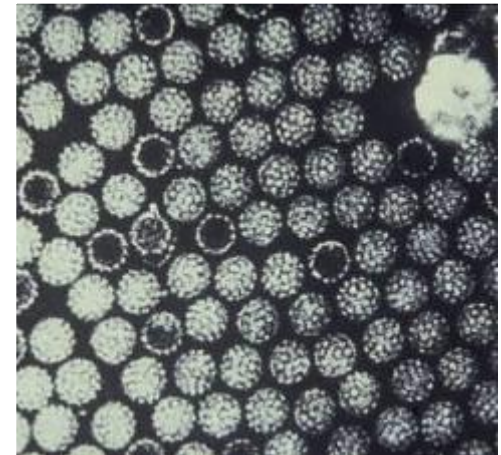
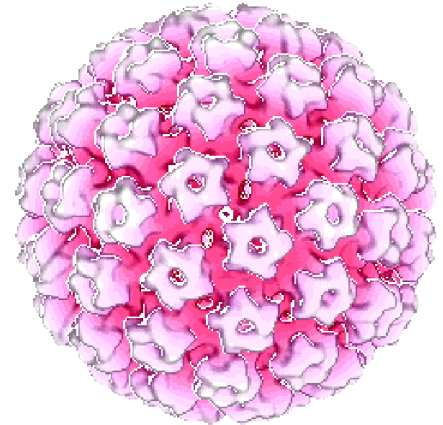
‡One woman had Papanicolaou smears classified as abnormal in three categories, so the abnormal biopsy results were from only five women.



"All we gotta do is place them on
the waiting room chairs."

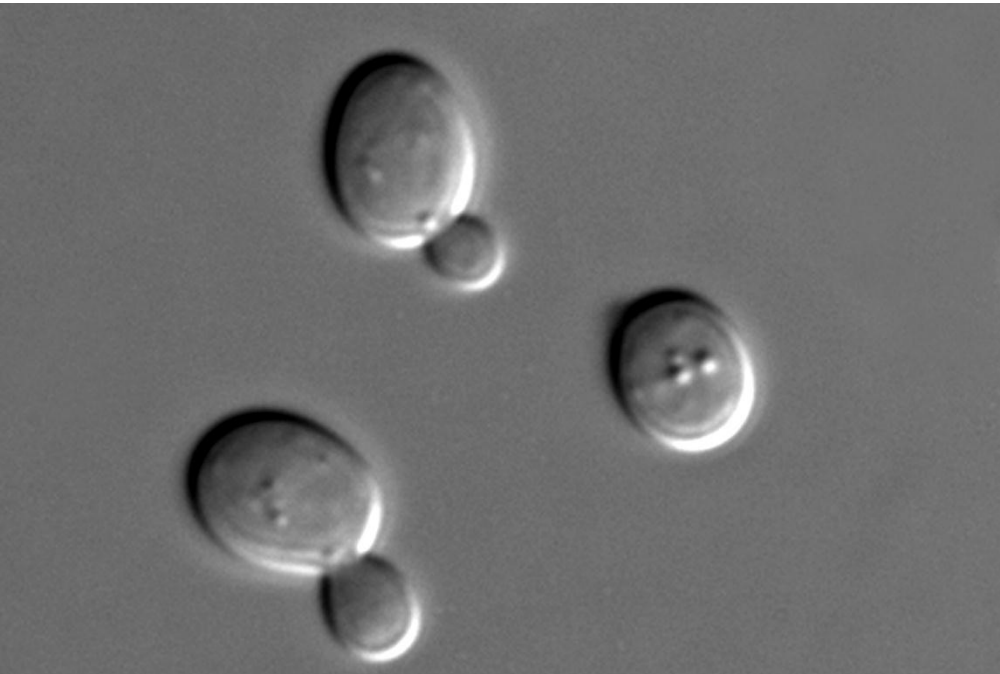
Immunization Against HPV

- Epidemiologic studies suggested type-specific immunity to HPV.
 - ?Some cross-protection within families
 - Outcome data lacking
- Type-specific neutralizing antibodies
- Virus-like particles (VLP) are recombinant viral capsids that induce type-specific neutralizing antibodies
- VLPs are highly immunogenic.



Creation of VLPs

Saccharomyces cerevisiae
(Brewer's yeast)



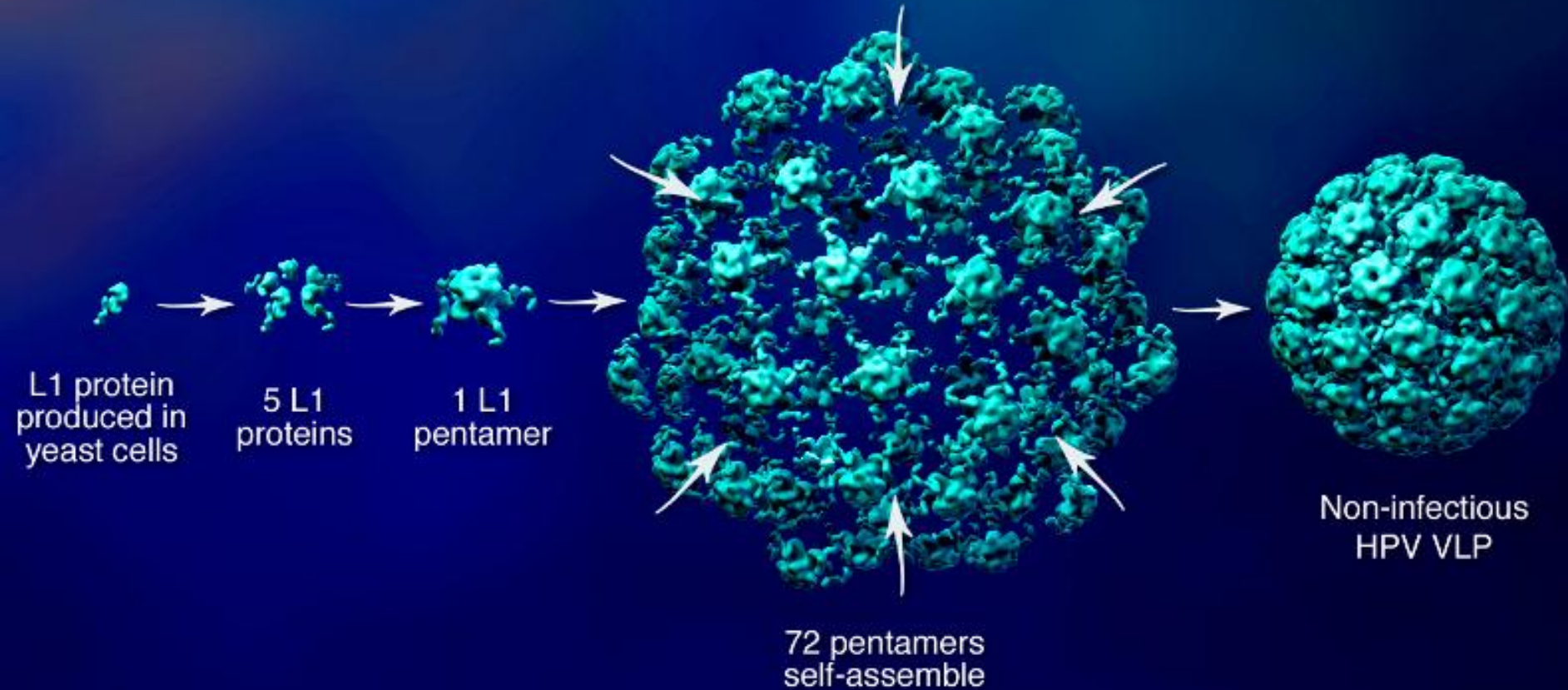
Courtesy of Masur,
Wikimedia Commons

Trichoplusia ni
(Cabbage Looper moth)



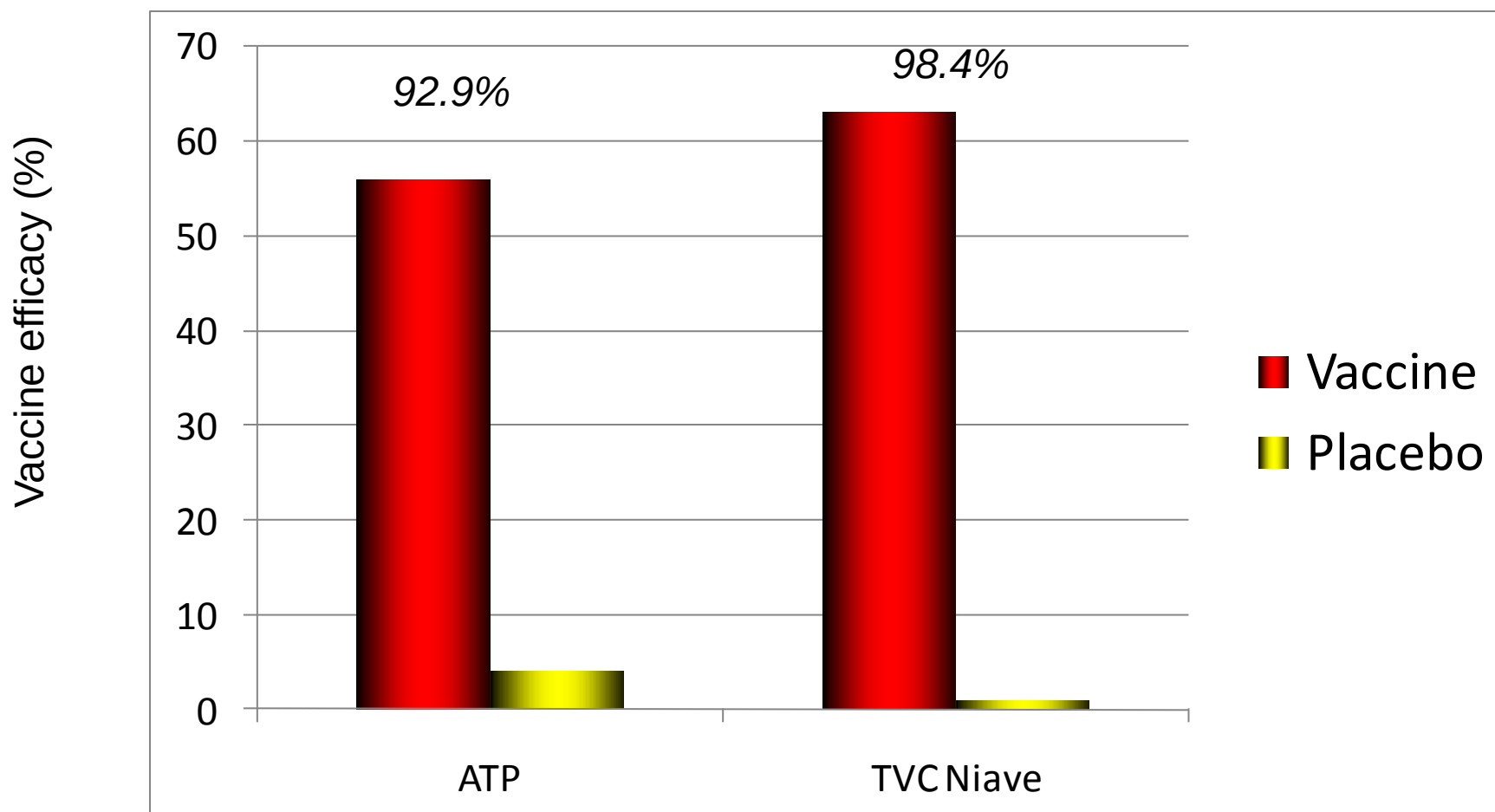
Courtesy of Alton N. Sparks, Jr.,
Wikimedia Commons

Creation of VLPs

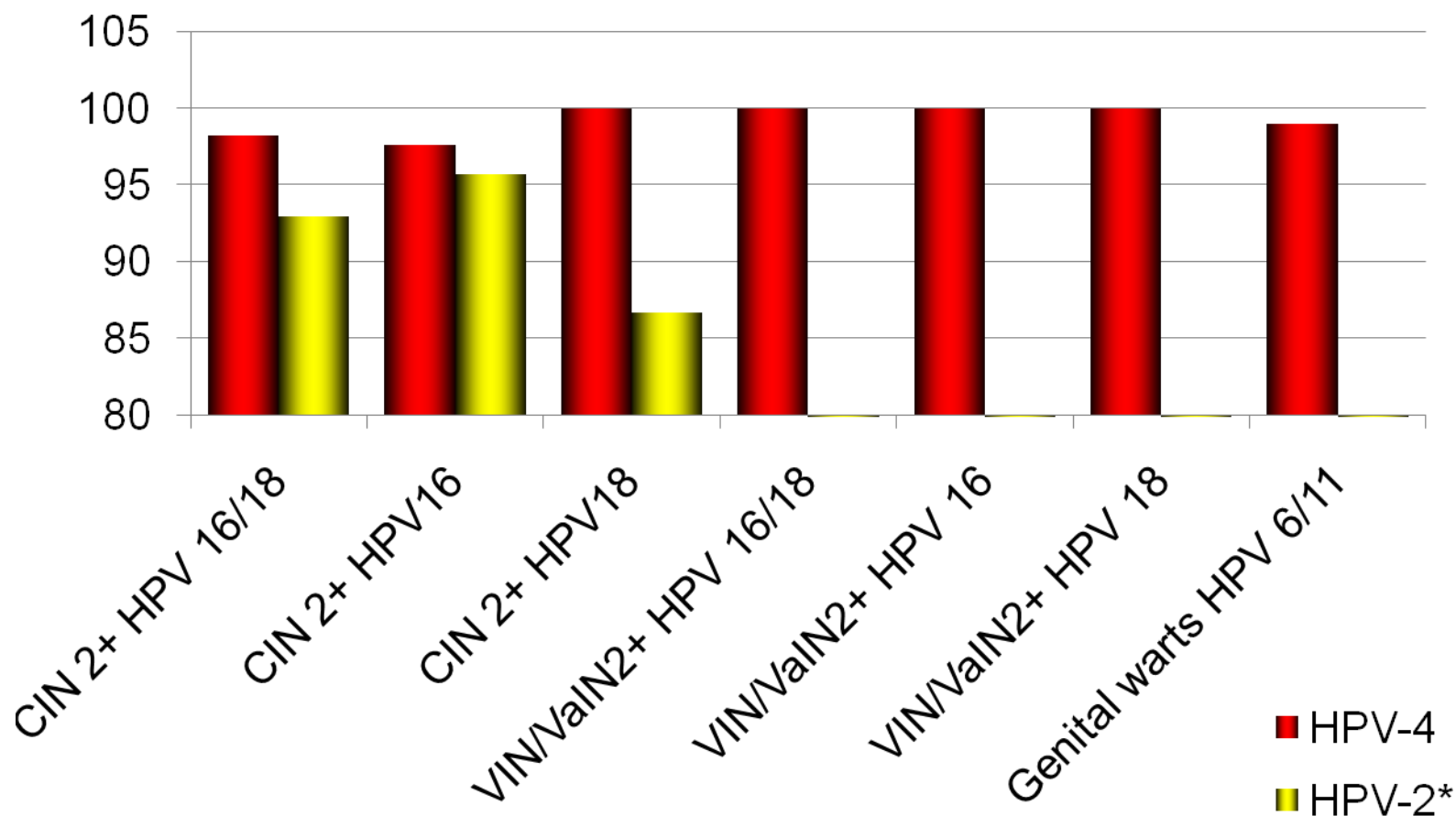


1. Berzofsky JA et al. *J Clin Invest.* 2004;114:450–462. 2. Kirnbauer R et al. *Proc Natl Acad Sci USA.* 1992;89:12180–12184. 3. Modis Y et al. *EMBO J.* 2002;21:4754–4762.

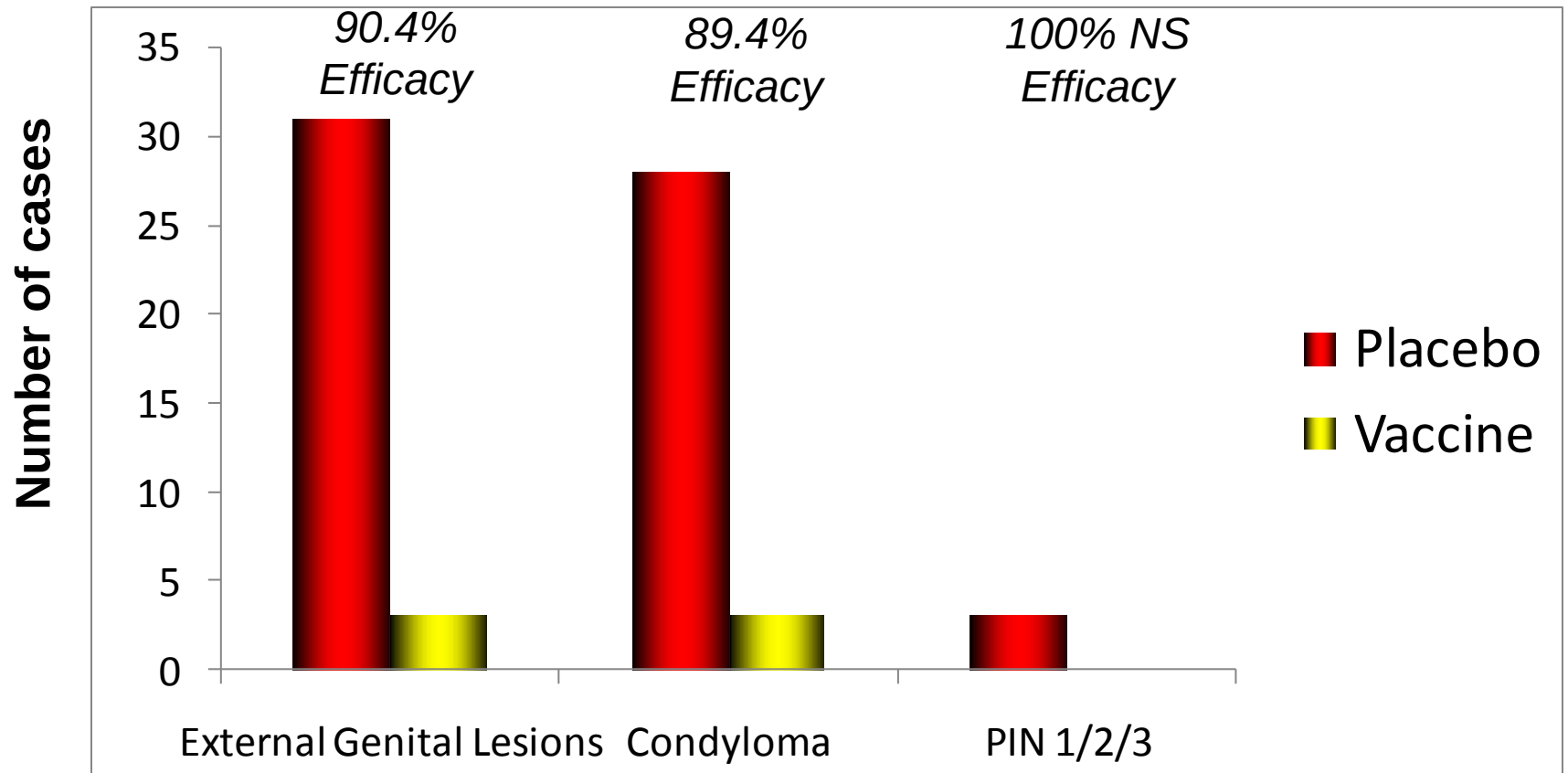
Phase 3 HPV 16/18 Vaccine Efficacy @ 39 Mo



Phase III Per-protocol End of Trial Data



HPV 16/18/6/11 Vaccine: 2.3 Year Efficacy Results for Males Aged 16-26



Gardasil Prescribing Information

HPV-2 Vaccine: Phase 3 Adverse Events

<u>Injection site symptoms*</u>	<u>Vaccine Group</u> (n=3077)	<u>Control Group</u> (n=3080)
Pain	2786 (90.5%)	2402 (78.0%)
Redness	1348 (43.8%)	841 (27.6%)
Swelling	1292 (42.0%)	609 (19.8%)
<u>General symptoms*</u>		
Fatigue	1771 (57.6%)	1652 (53.6%)
Headache	1665 (54.1%)	1579 (51.3%)
Myalgia	1606 (52.2%)	1382 (44.9%)
Gastrointestinal	850 (27.6%)	841 (27.3%)
Arthralgia	633 (20.6%)	551 (17.9%)
Raised temperature†	381 (12.4%)	337 (10.9%)
Rash	312 (10.1%)	258 (8.4%)
Urticaria	298 (9.7%)	244 (7.9%)

*Participants who reported a specified symptom within 7 days of vaccine injection.

†Defined as axillary or oral temperature $\geq 37.5^{\circ}\text{C}$.

Paavonen J et al. *Lancet*. 2007;369:2161-70.

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HPV-4 Vaccine: Phase 3 AEs

	HPV-4	Placebo
Pain	83.9	75.4
Swelling	25.4	15.8
Erythema	24.7	18.4
Pyrexia	13.0%	11.2%
Nausea	6.7%	6.6%
Nasopharyngitis	6.4%	6.4%
Dizziness	4.0%	3.7%
Diarrhea	3.6%	3.5%
Vomiting	2.4%	1.9%
Myalgia	2.0%	2.0%
Cough	2.0%	1.5%
Toothache	1.5%	1.4%
Upper respiratory tract infection	1.5%	1.5%

Perceived Challenges to Adult Vaccination

Health Care Provider Perceptions	Patient Reasons
• Side effects • Dislike of needles • Lack of insurance coverage • Lack of knowledge about disease prevention	• Doctor hasn't told me I need it • Not knowing when to get it • The belief that a healthy person doesn't need it • Financial concerns were not a deterrent for most

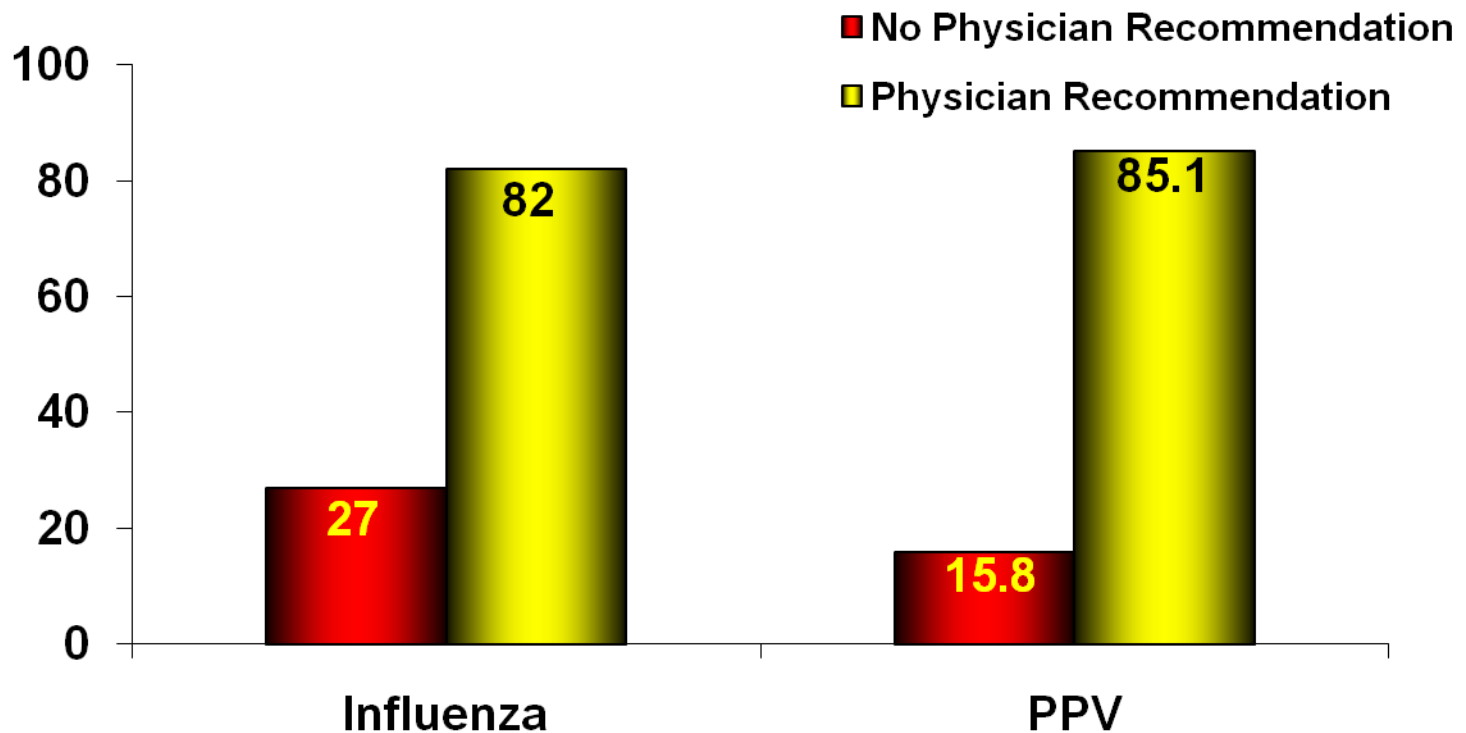
Most patients indicated that they were likely to receive a vaccination if their health care provider recommended it.

Consumers (N=2,002) and health care providers (N=200) completed structured telephone interviews, e-mails, or faxes

Johnson DR et al. Am J Med. 2008;121(7 Suppl 2):S28—S35.

Provider Recommendation Can Overcome Negative Attitudes

Vaccination Rates Among High-Risk Patients With Negative Attitudes



Family/Parent Issues

- **Fears about vaccine safety**
 - Fears are sometimes increased by anti-vaccine groups
 - Fear (incorrectly) that vaccines are riskier for their children than non-immunization
 - No credible evidence that vaccines cause autism, diabetes, other problems
 - No mercury in vaccine
- **Trails show high degree of safety**

CRITICS CLAIM
HPV VACCINATION
WILL LEAD TO
PROMISCUITY

I AM SO
TURNED ON
RIGHT NOW.



ANNE TEAL

7/8/06

Women's eNews

Cultural Issues

- **Patients indicate they are not more comfortable engaging in high risk sexual behaviors after getting the vaccine ¹**
- **Most parents (93.5%) do not think the HPV vaccine would actually encourage sexual activity in their children ²**
 - **Health care providers can be less hesitant in recommending the vaccine to young sexually naive girls**

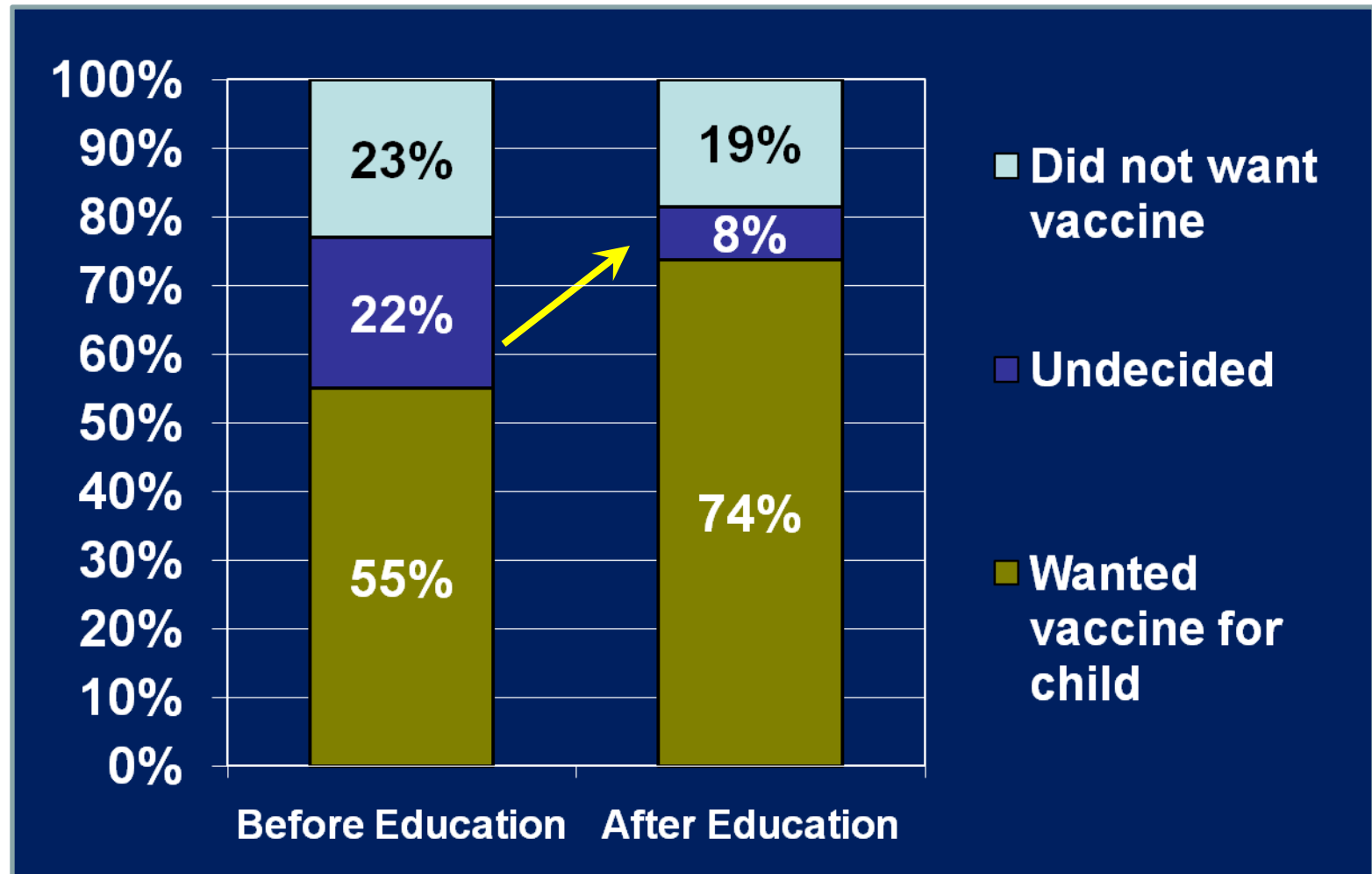
1. Kahn JA, Rosenthal SL, Hamann T, Bernstein DI. *Int J STD AIDS*. 2003;14:300-6.

2. Ferris DG, Cromwell L, Waller JL, Horn L. *J Lower Genital Tract Disease*, 2010; 14:179-184.

Family/Parent Issues

- Patients should ideally be vaccinated prior to being exposed to the virus.
- Parental permission and support needed
- Major factors that determine the acceptability of an HPV vaccine:
 - Vaccine efficacy
 - Endorsement by physicians
 - Cost of the vaccine

Impact of Education on Adolescents Parents Decision to Get HPV Vaccine





Hell



"OK, folks! ... It's a wrap!"

