# Cervical Smears and Colposcopy

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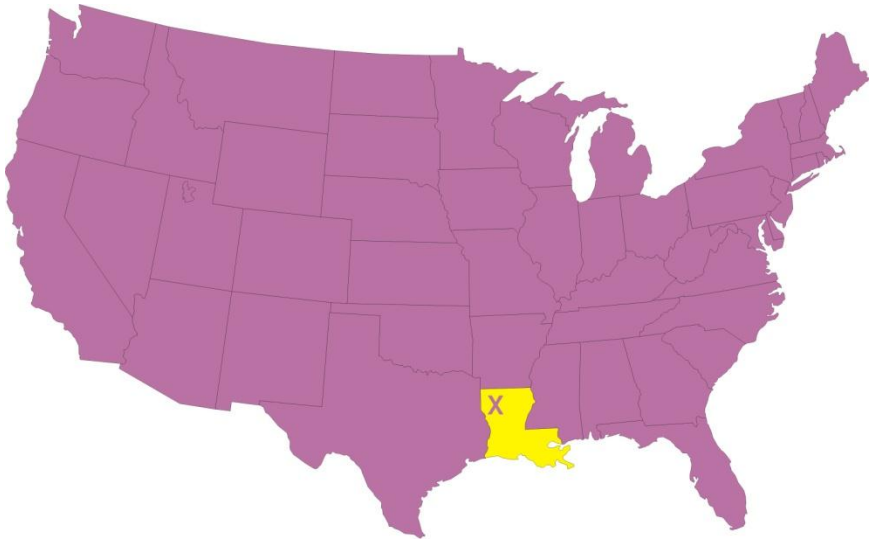
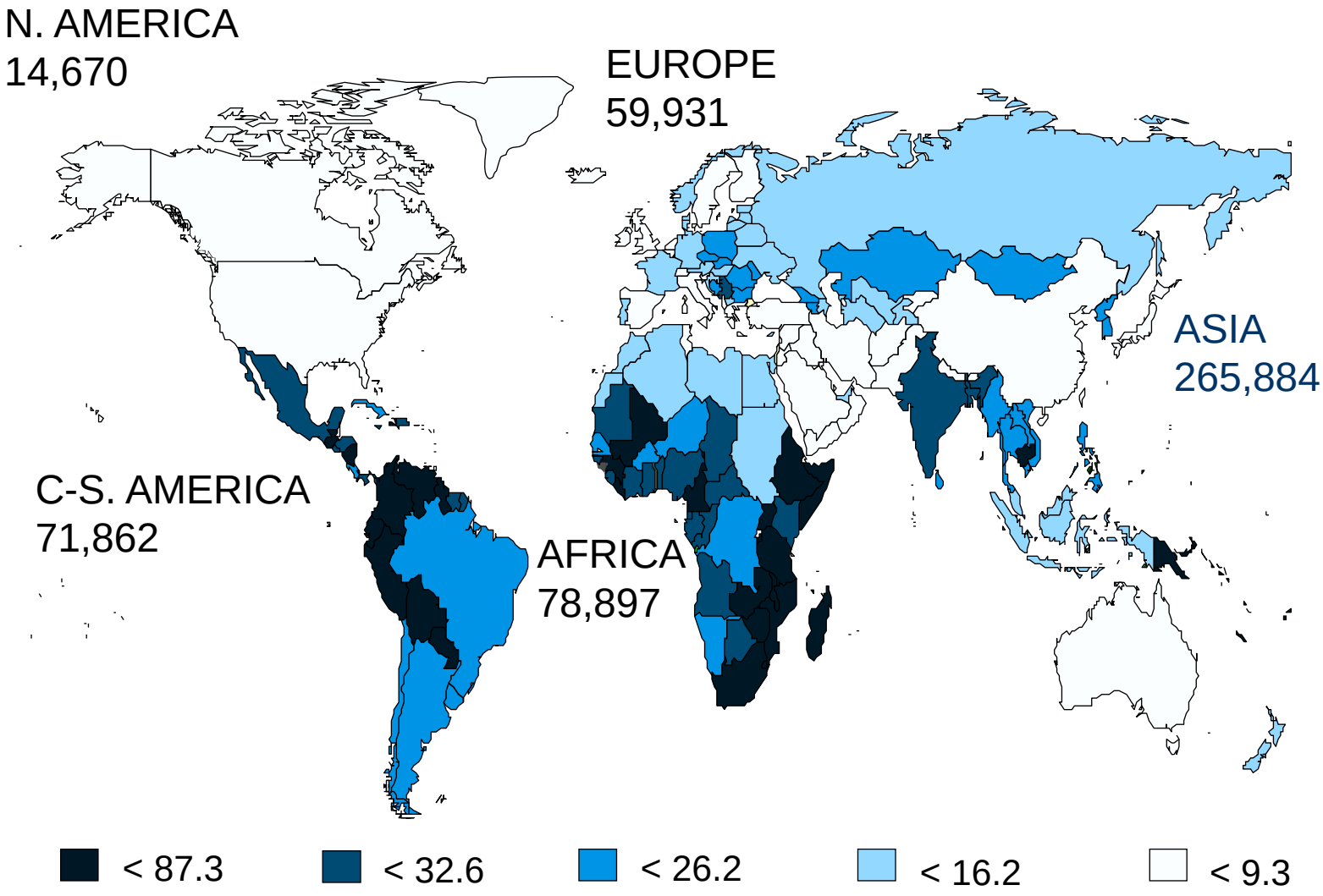


# HPV Worldwide

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

# Estimated Cervical Ca Cases 2002




Age-adjusted incidence rates per 100,000 women per year

# Cervical Cancer Ranking among Cancers in Women Worldwide

| | Less developed regions | | More developed regions | |
|---|---|---|---|---|
| **Ranking** | **N countries** | **%** | **N countries** | **%** |
| 1st | 58 | 45.7 % | 1 | 2.3 % |
| 2nd | 49 | 38.6 % | 27 | 61.4 % |
| 3rd | 7 | 5.5 % | 13 | 29.5 % |
| 4th | 2 | 1.6 % | 3 | 6.8 % |
| 5th | 2 | 1.6 % | 0 | 0.0 % |
| 6 or + | 9 | 7.2 % | 0 | 0.0 % |
| **Total** | **127** countries with data | | **44** countries with data | |

GLOBOCAN 2002

# 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%

# 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 |

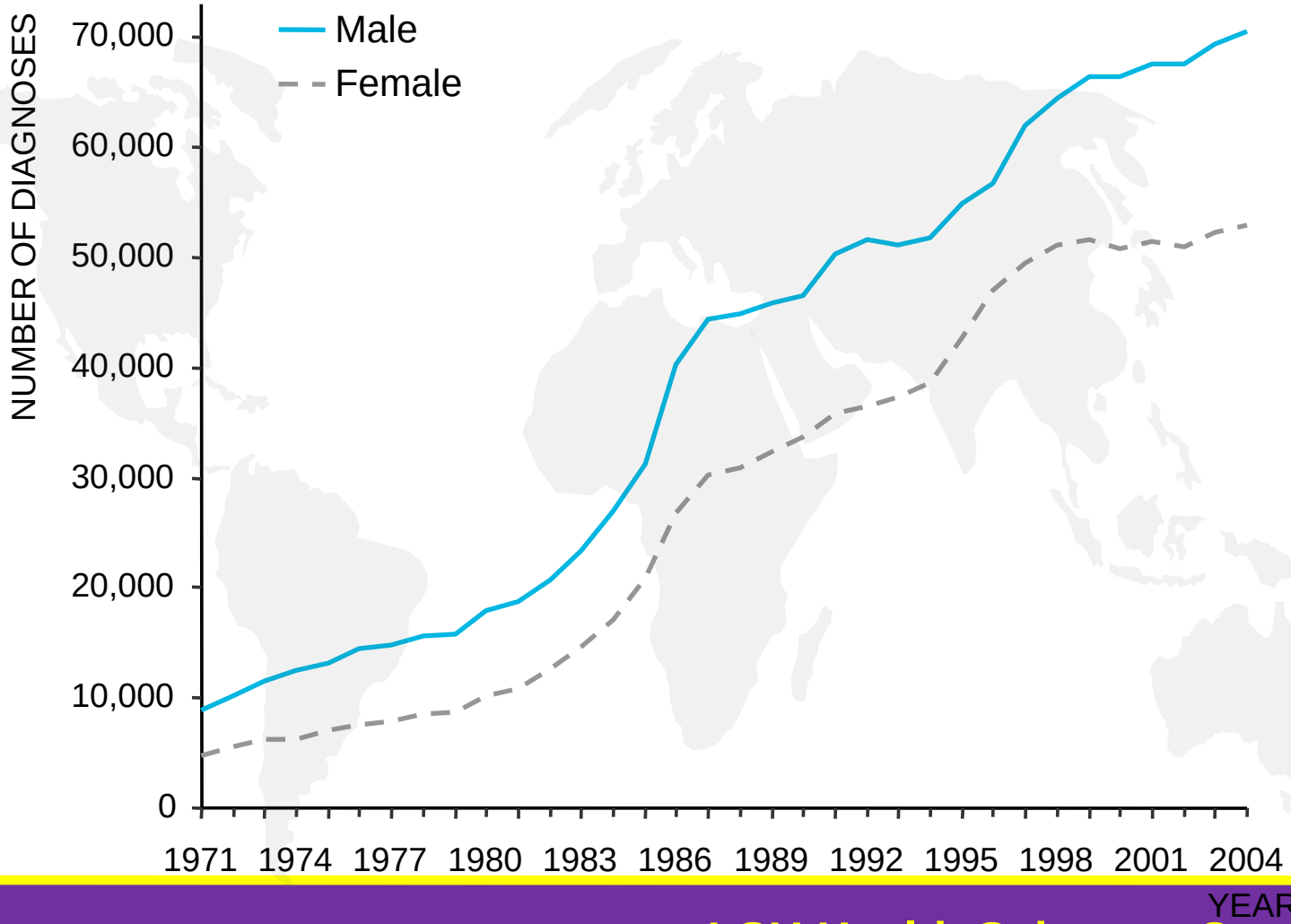
Human Papillomavirus and Related Cancers Summary Report Update: NEW ZEALAND. September 15, 2010. WHO/ICO Information Centre on HPV and Cervical Cancer (HPV Information Centre) GLOBOCAN 2010
http://apps.who.int/hpvcentre/statistics/dynamic/ico/country_pdf/NZL.pdf

# HPV-Attributable Cancers in Women

| SITE | TOTAL cancers | % HPV | Attributable to HPV | Attributable to HPV 16/18 | % of HPV 16/18 |
|---|---|---|---|---|---|
| Cervix | 492,800 | 100 | 492,800 | 344,900 | **70+** |
| Vulva, Vagina | 40,000 | 40 | 16,000 | 12,800 | 80 |
| Anus | 15,900 | 90 | 14,300 | 13,100 | 92 |
| Oropharynx | 9,600 | 11 (60 +) | 1,100 | 1,000 | 91 |
| Mouth | 98,400 | 3 (25 +) | 2,900 | 2,800 | 97 |
| TOTAL | 5,060,700 | 10.4 | 527,100 | 374,600 | |

Adapted from D. M. Parkin, F. Bray, Vaccine 24 Suppl 3, S11 (2006).

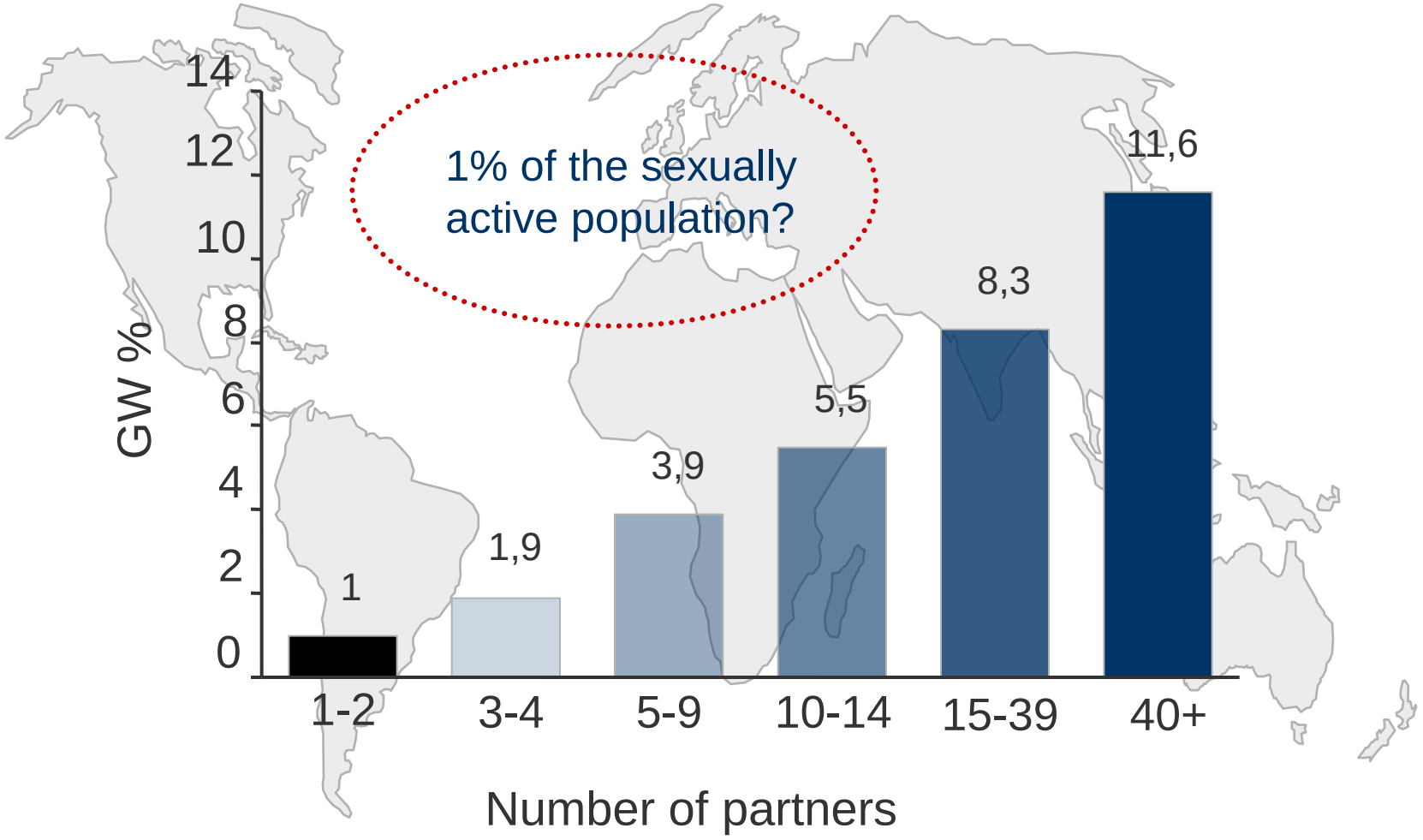
# NUMBER OF DIAGNOSES OF GENITAL WARTS (FIRST, RECURRENT AND RE-REGISTERED EPISODES) BY SEX, SEXUALLY TRANSMITTED DISEASE CLINICS: ENGLAND AND WALES 1971-2004




Source: Health Protection Agency, 2006.

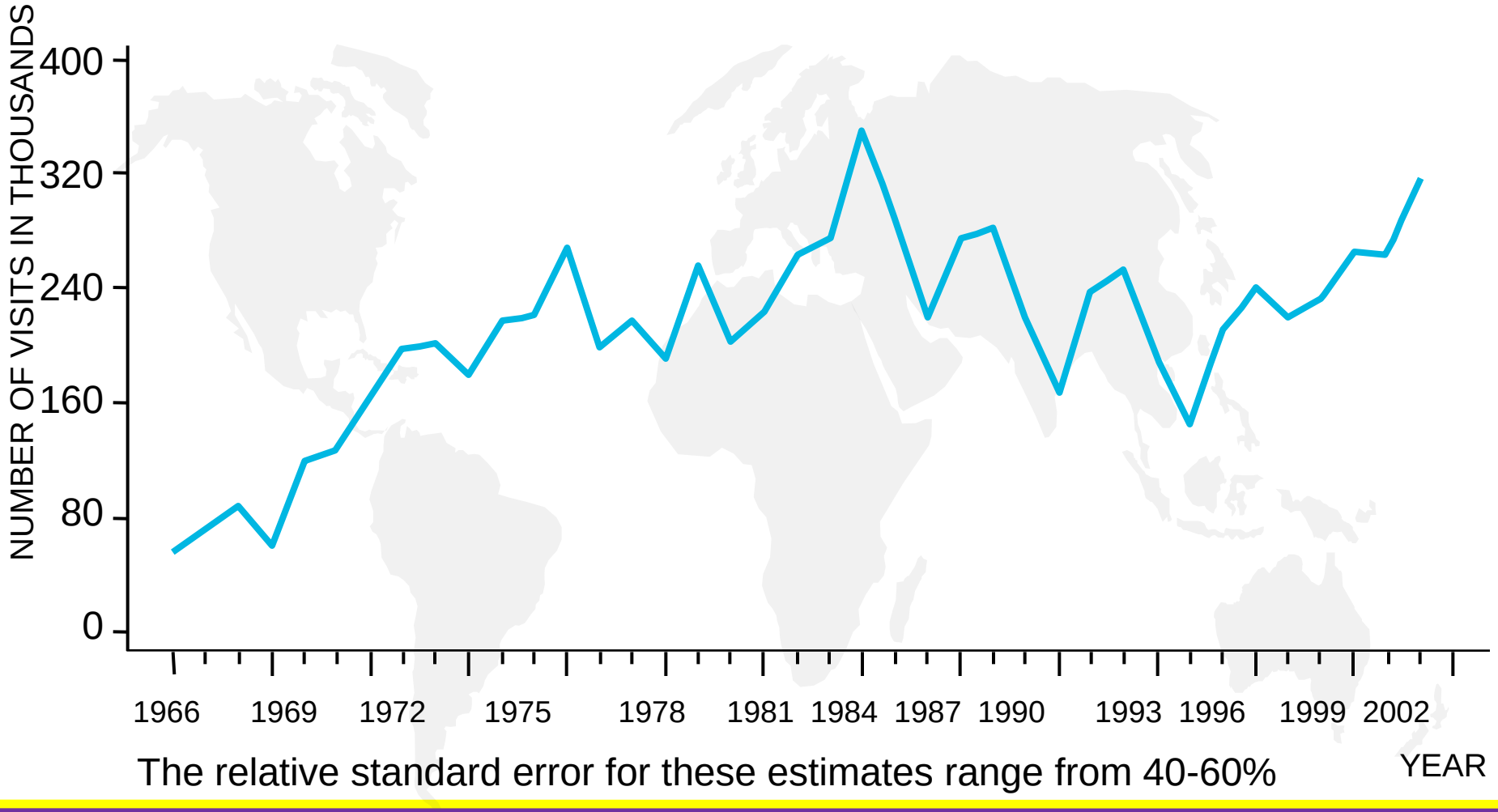
# Number of partners and % of ever GW

## The Copenhagen survey: Ever GW 17%




MUNK C ET AL. *SEX TRANSM DIS.* 1997;24:567-572.

# INITIAL VISITS RELATED TO GENITAL WARTS TO PHYSICIANS´OFFICES: UNITED STATES, 1966-2004

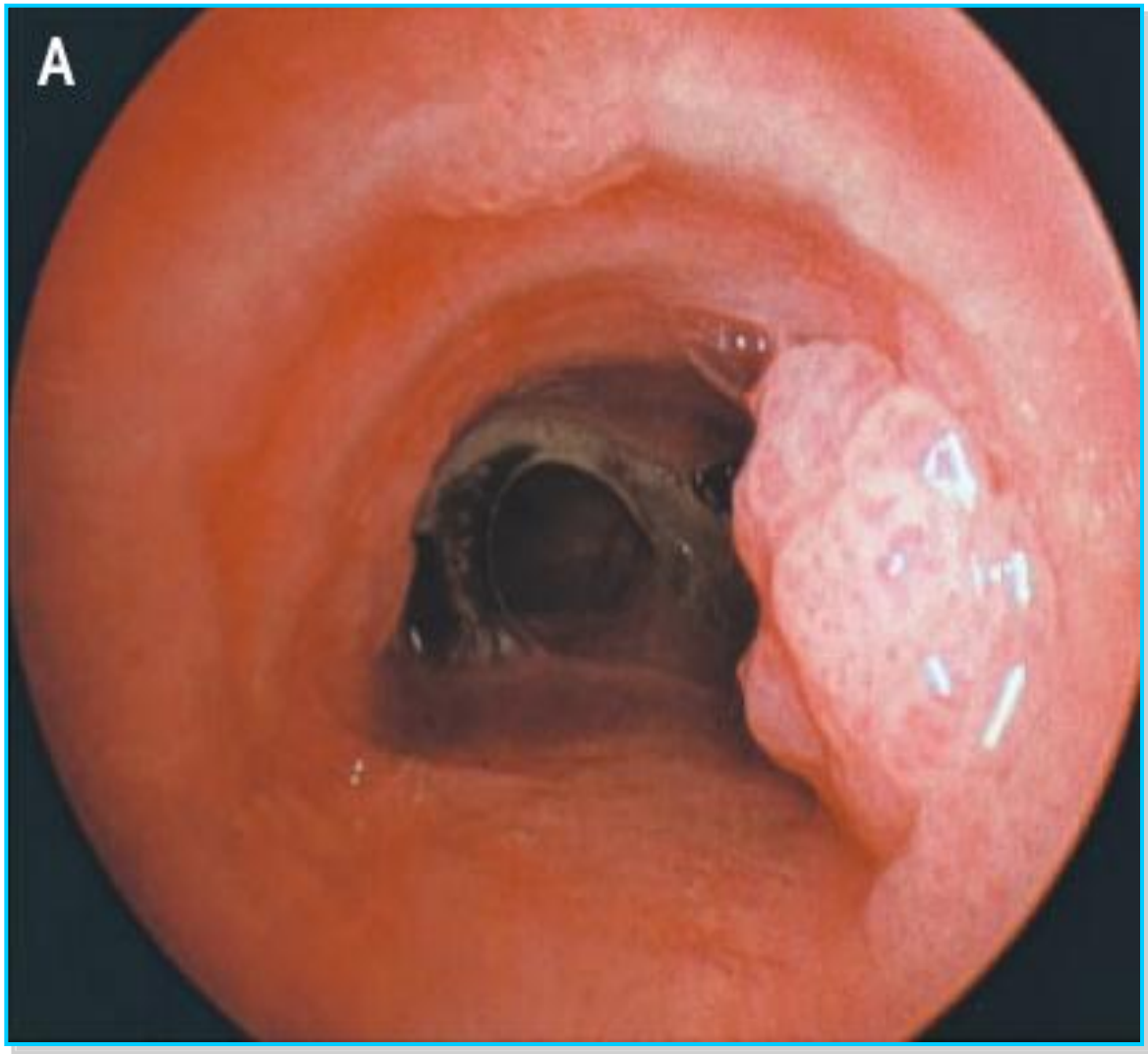



The relative standard error for these estimates range from 40-60%

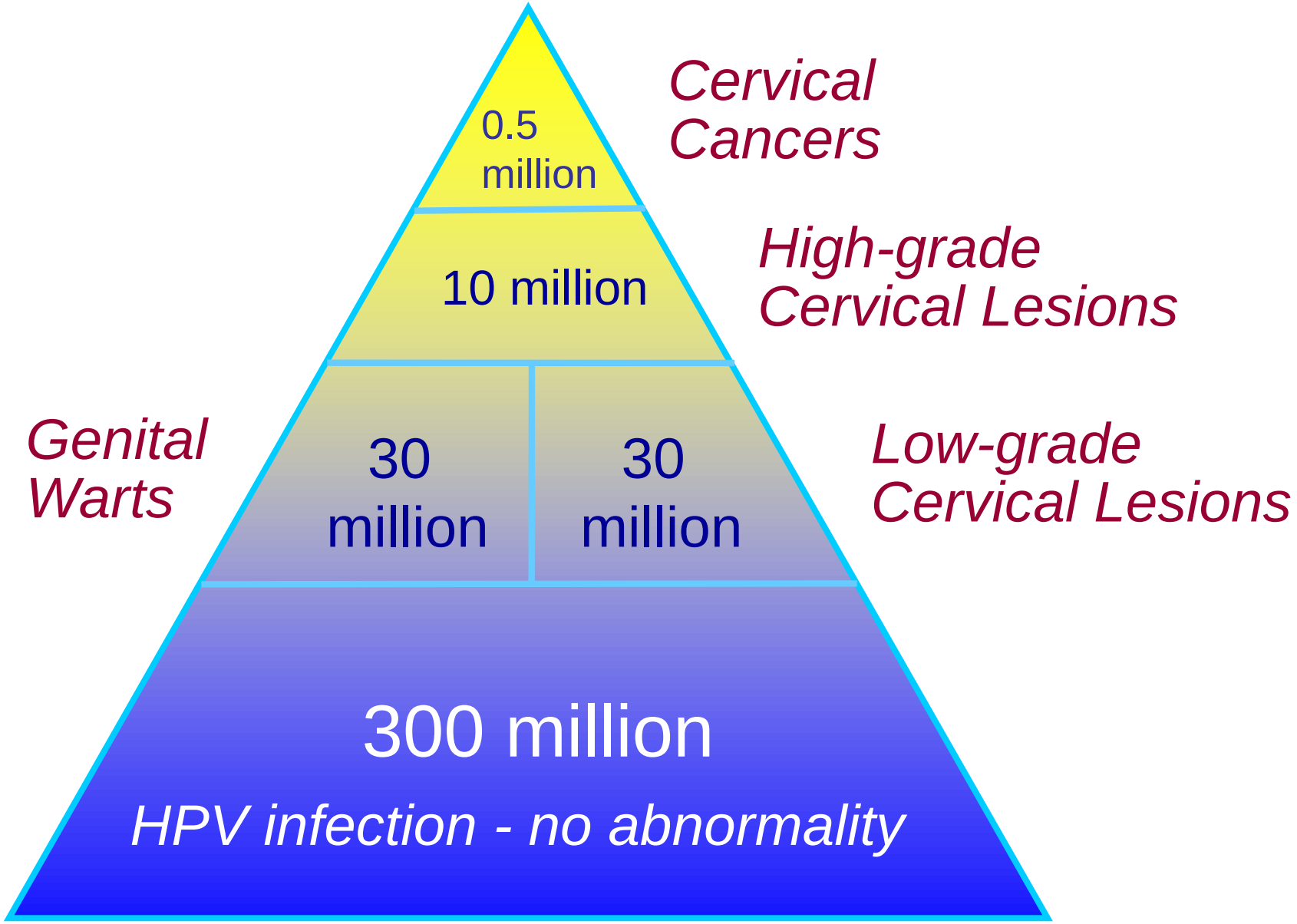
Source: IMS Health, IMS National Disease and Therapeutic Index (tm), 1966-2004. Published 2005.

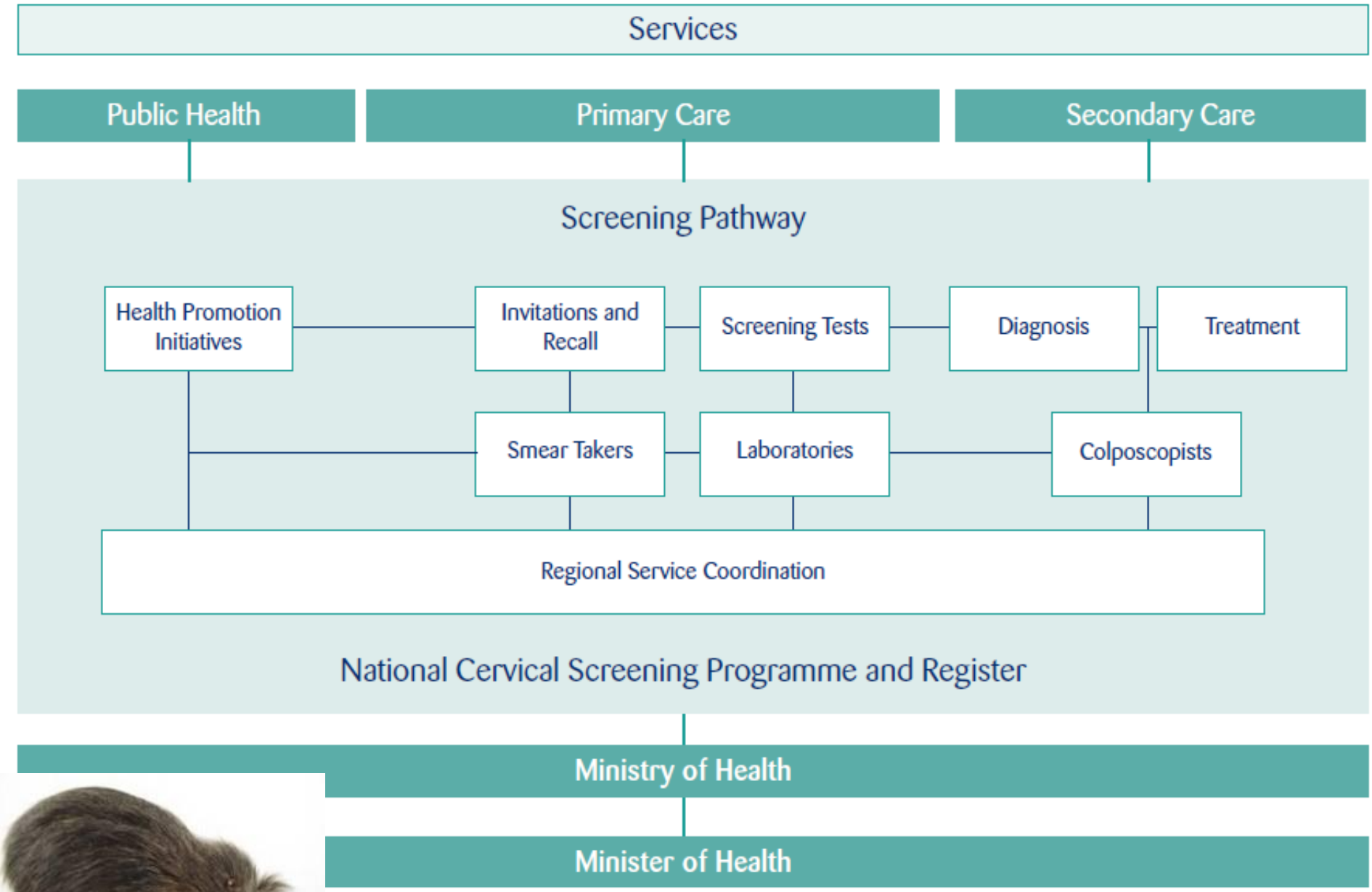
LSU Health Sciences Center – USA

# Laryngeal Papillomatosis



# Summary of Worldwide Burden of HPV Diseases




Services
Public Health
Primary Care
Secondary Care
Screening Pathway
Health Promotion Initiatives
Invitations and Recall
Screening Tests
Diagnosis
Treatment
Smear Takers
Laboratories
Colposcopists
Regional Service Coordination
National Cervical Screening Programme and Register
Ministry of Health
Minister of Health

# Cervical Cytology Techniques

- Liquid-based and conventional methods are acceptable
  - Majority in U.S. liquid-based
- Avoid blood, D/C, and lubricant
- Small amount of lubricant OK

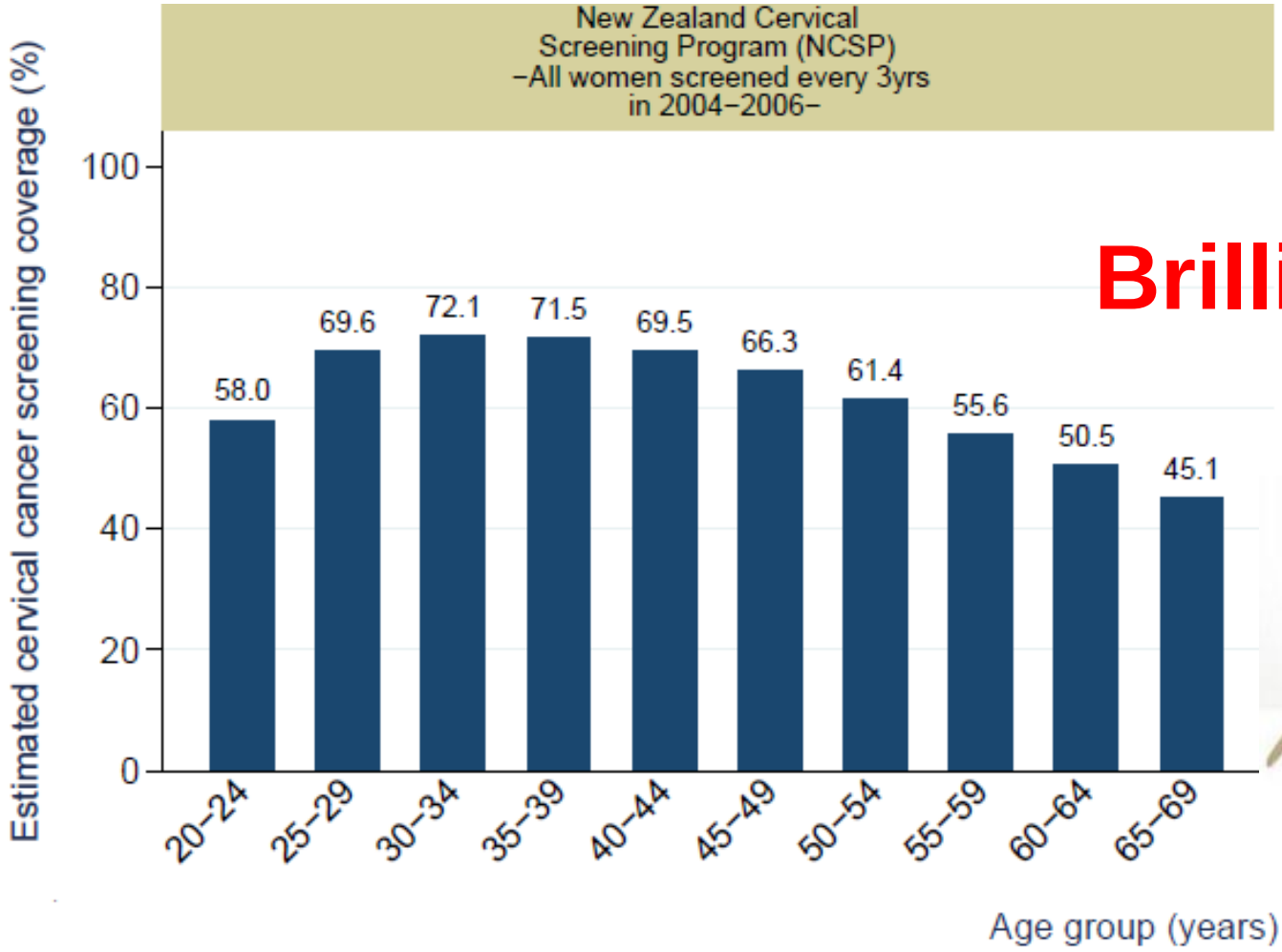

- ACOG Practice Bulletin No. 109. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009: 114:1409-20.

# 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 |

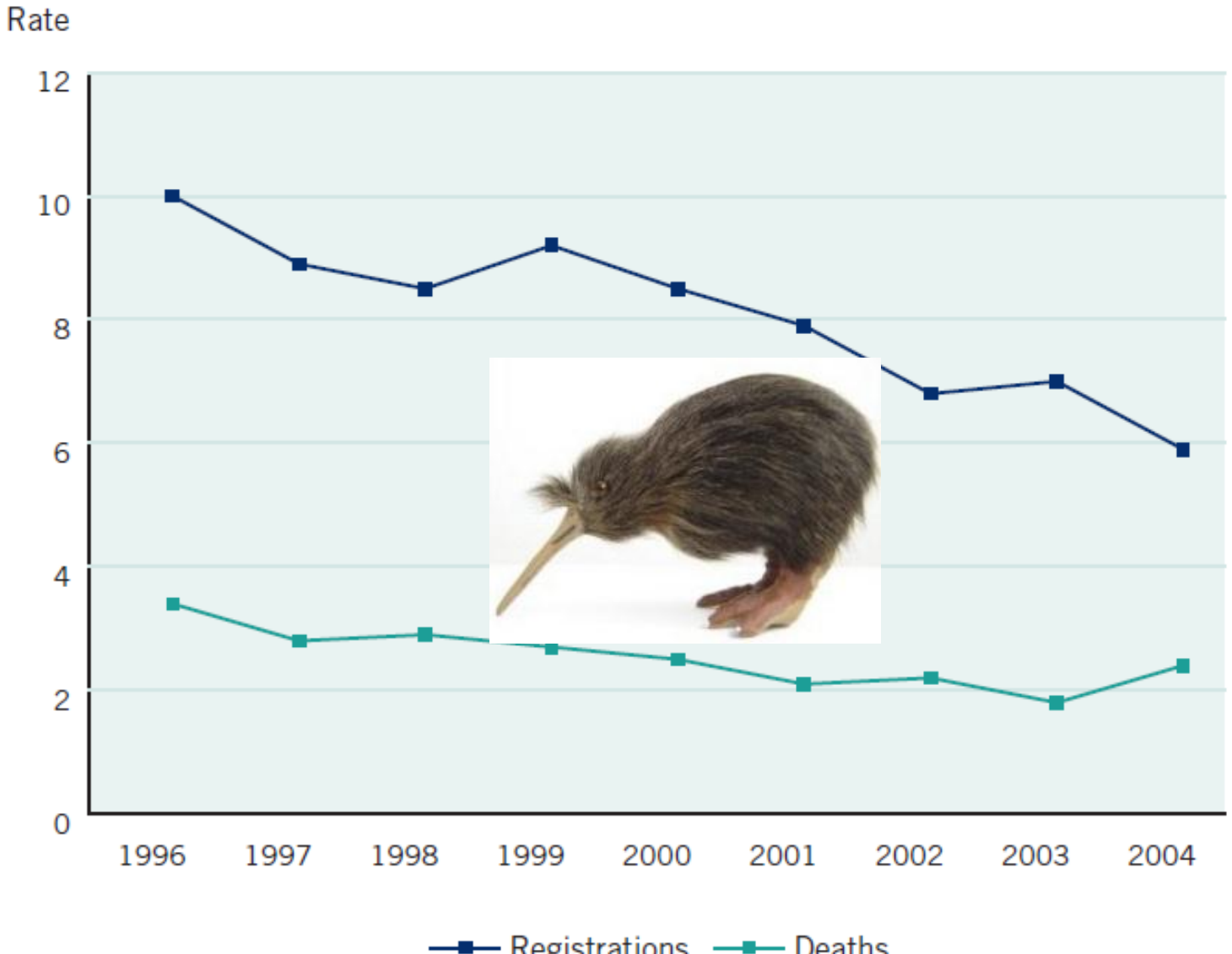
Human Papillomavirus and Related Cancers Summary Report Update: NEW ZEALAND. September 15, 2010. WHO/ICO Information Centre on HPV and Cervical Cancer (HPV Information Centre) GLOBOCAN 2010
http://apps.who.int/hpvcentre/statistics/dynamic/ico/country_pdf/NZL.pdf

# Estimated 2006 Cervical Cancer Screening Coverage in New Zealand




**Brilliant!!!!!**

# NZ Cervical cancer incidence and mortality trends, total population, 1996–2004




– USA

# Liquid-based Cytology

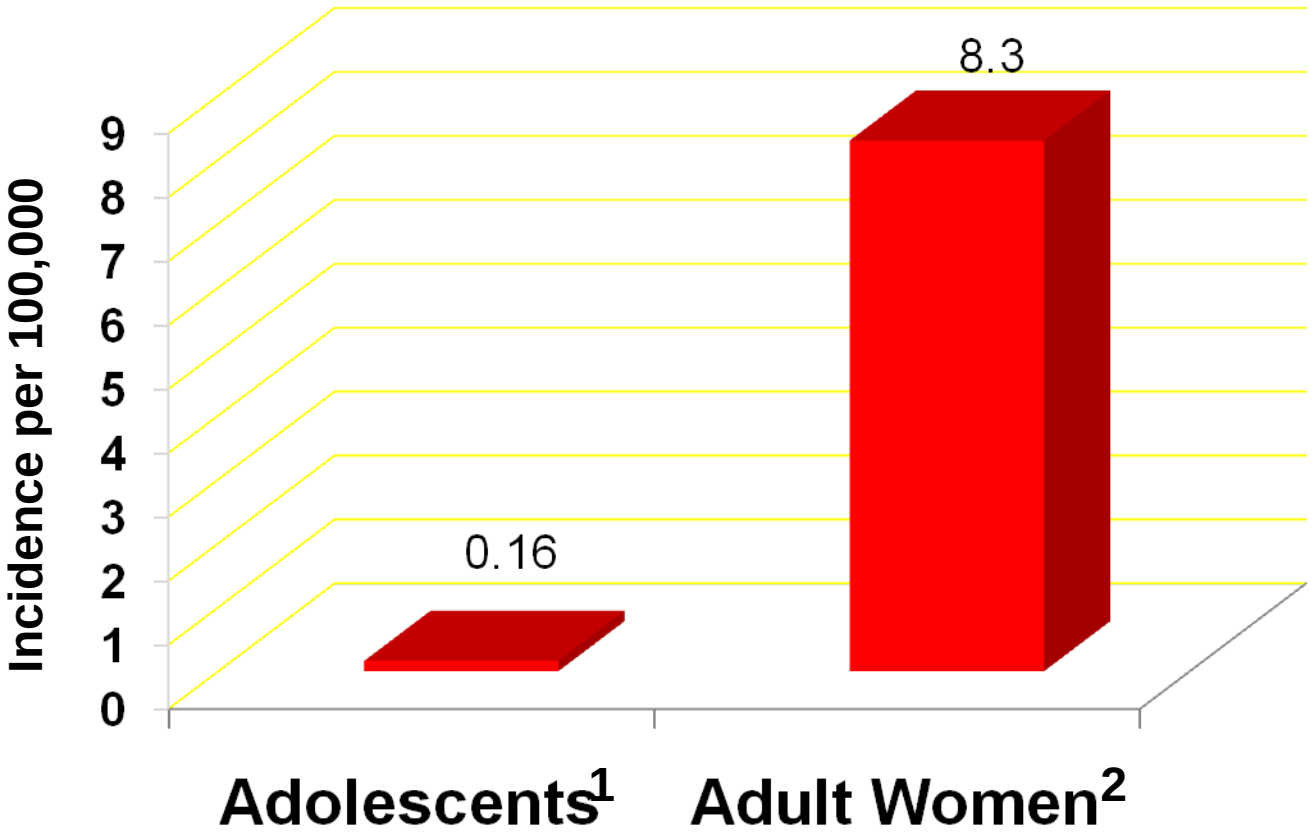
- Disadvantages
  - Higher cost and decreased specificity
- Advantages
  - HPV, gonorrhea, and chlamydia test
  - Eliminates air drying artifact
  - Easier to read
  - Less blood/inflammation problem


- ACOG Practice Bulletin No. 109. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009: 114:1409-20.

# 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

# Cervical Cancer Incidence




1. Chan PG, Sung HY, Sawaya GF. Obstet Gynecol 2003; 102:765.
2. Cancer Statistics, 2004. CA Cancer J Clin 2004;54:8-29

# CIN3/Ca Rare in Adolescents

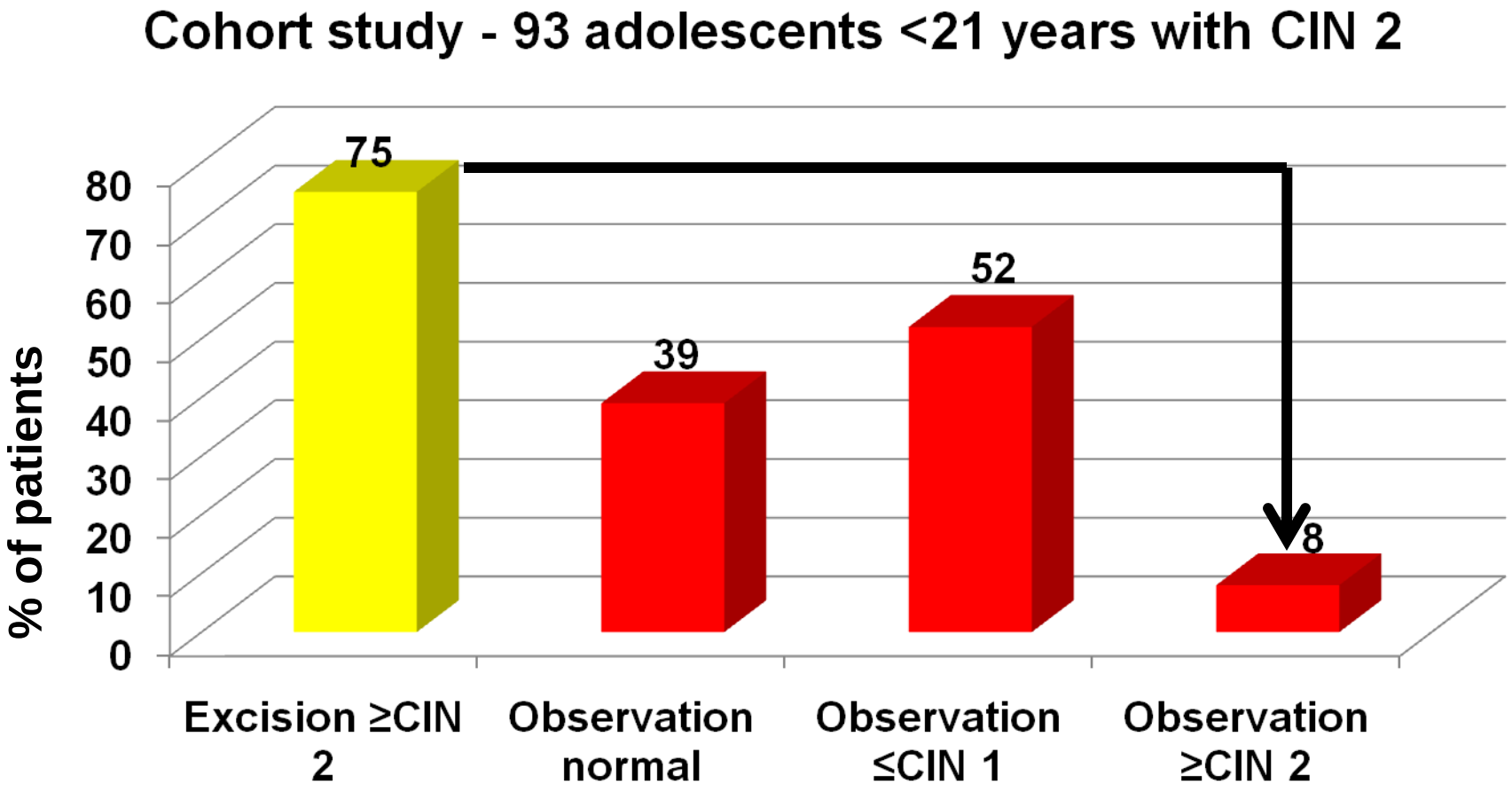
- 622 women 13-24 yrs with abnl Pap
  - Colpo and biopsy if needed
- Multinomial logistic regression analysis
  - ASCUS 231, ASC-H 30
  - LSIL 314, HSIL 11
  - CIN-3 in 6.6% and no cancers

- Moscicki AB, et al. Obstet Gynecol. 2008 December ; 112(6): 1335–1342

# ↓ Sensitivity of Pap Screening

- 4,012 British women 20-69 years with invasive cancer
- Cytology screening in 3 years prior to diagnosis
  - 80% reduction at 64 years
  - 60% at age 40 years
  - no significant reduction @ 20 - 24 yrs
- Pap doesn't detect disease
- Sasieni P, et al. BMJ 2009;339:b2968.

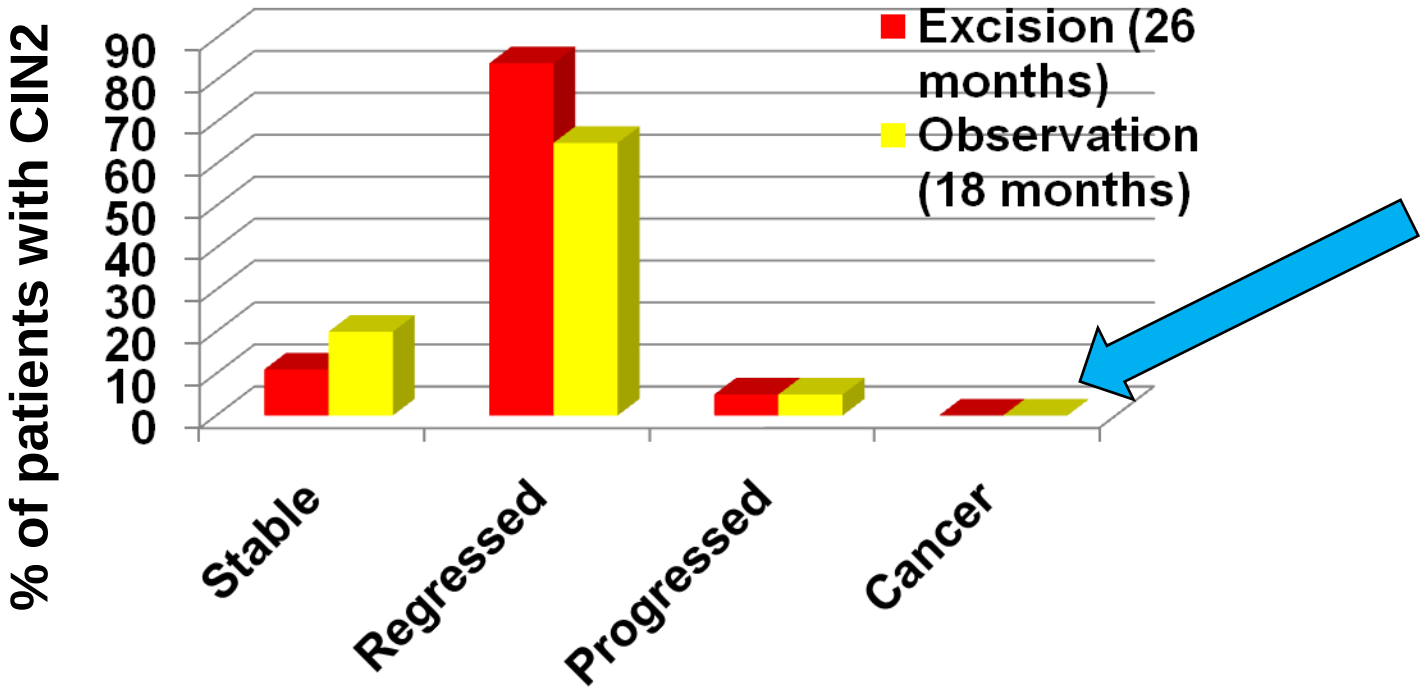
# Regression Common in Adolescents




Fuchs K, Weitzen S, Wu L, Phipps MG, Boardman LA. Management of Cervical Intraepithelial Neoplasia 2 in Adolescent and Young Women. J Pediatr Adolesc Gynecol (2007) 20:269e274

# CIN 2 Treatment Vs Observation

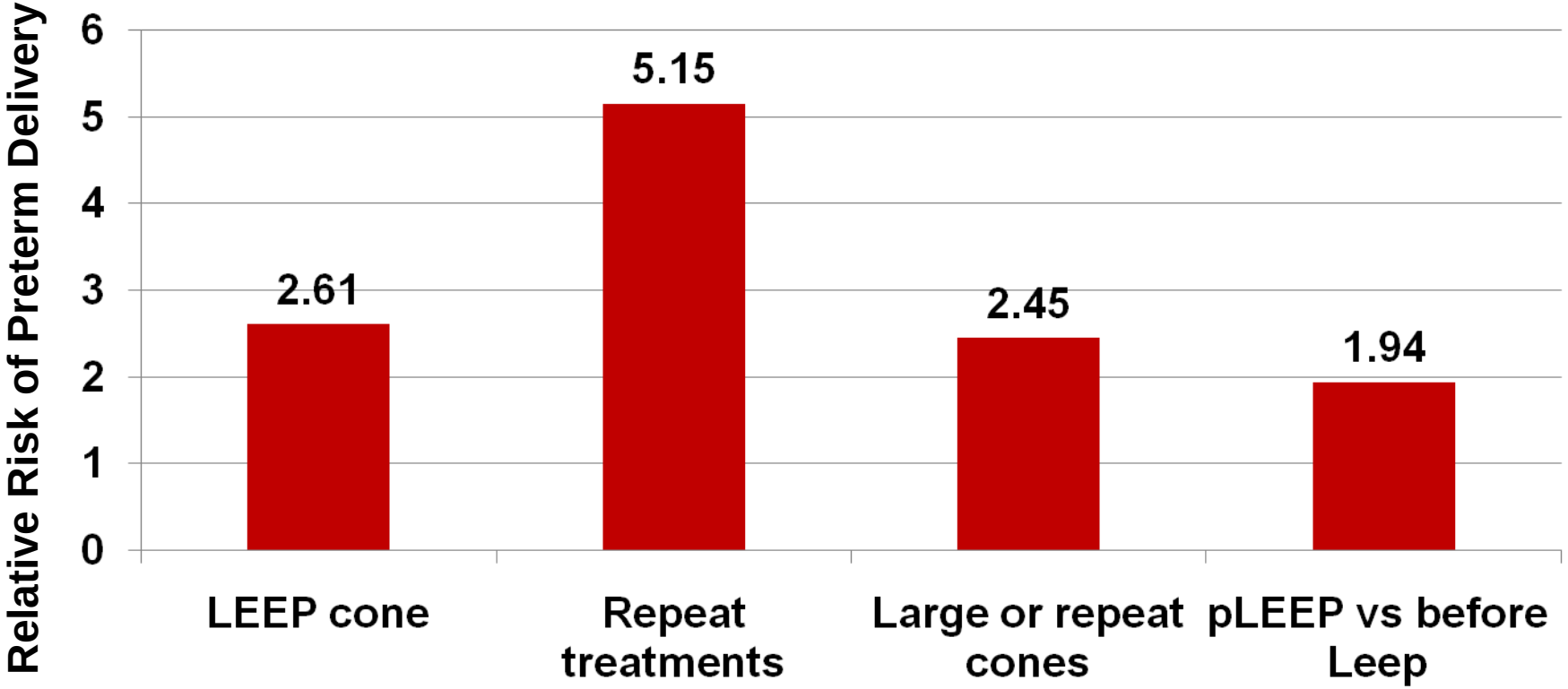
**Chart review of 501 patients. 324 (65%) had ≤CIN 1 and 177 patients (35%) had ≥CIN2**




Moore K, et al. Am J Obstet Gynecol 2007;197:141.e1-141.e6.

# Tx ↑ Risk Preterm Delivery

**Retrospective cohort study from 1997 - 2003 with a follow-up until 2006 of 624 women delivered after LEEP cone**




Jakobsson M, et al. Obstet Gynecol 2009;114:504–10.

# Tx ↑ Risk of pPROM

- **Retrospective cohort study comparing delivery outcomes**
  - **No significant increase in risk of preterm delivery for any treatment in this study**
  - **pPROM risk significantly ↑ following laser cone (aRR, 2.7) or LEEP (aRR, 1.9)**
  - **Risk of pPROM and total preterm delivery ↑ with ↑ height of tissue removed**


- **Sadler L, Saftlas A, Wang W, et al. Treatment for Cervical Intraepithelial Neoplasia and Risk of Preterm Delivery. JAMA. 2004;291(17):2100-2106**

# 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 3 years in NZ
- 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]

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

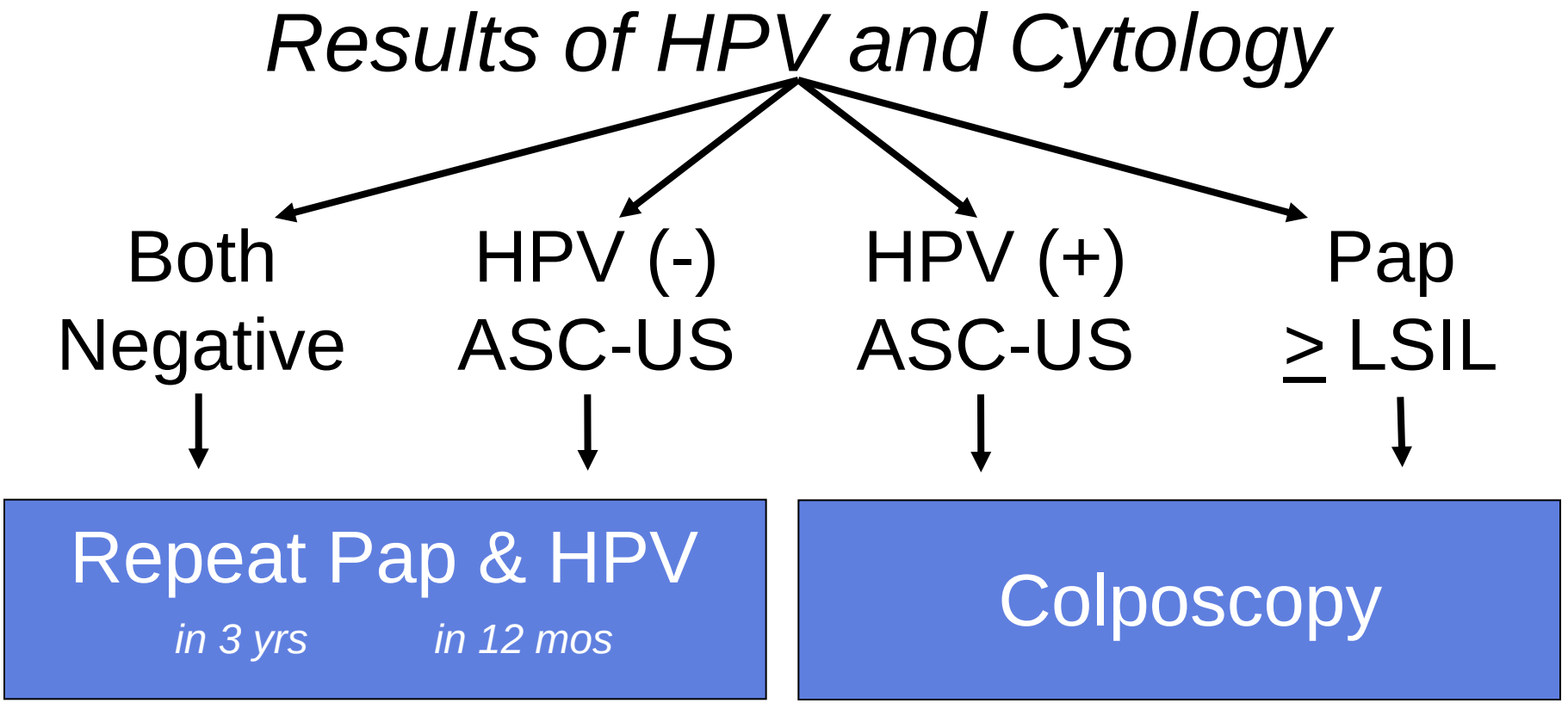
| Screening frequency (yr) | Woman-years of life | Dollars |
|---|---|---|
| 1 | 17,551 | 29,471,000 |
| 2 | 17,140 | 12,531,000 |
| 3 | 16,964 | 7,042,000 |
| 4 | 16,501 | 4,309,000 |
| *5* | 16,161 | 2,788,000 |
| 6 | 15,412 | 1,860,000 |
| 7 | 14,868 | 1,152,000 |
| 8 | 14,073 | 736,000 |
| 10 | 12,773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

# Optimal Screening > Age 30 US

- HPV DNA testing is more sensitive than cervical cytology in detecting CIN 2 and CIN 3
- Women with negative concurrent test results have a risk of unidentified CIN 2,3 or cervical cancer of only ~1 in 1,000 [Level A]

- ACOG Practice Bulletin (2005) Human Papillomavirus

# Optimal Screening > Age 30 in Low-risk Women



# 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

# After Hysterectomy

- For benign indications and no prior high-grade CIN, routine cytology testing should be discontinued
- With a history of CIN 2,3 – continue screening [Level A]
- Undocumented Hx – continue screening [Level A]


- ACOG Practice Bulletin No. 109. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009: 114:1409-20.

# Discontinuing Screening

- Primary vaginal cancer is rare
- Women who have had a hysterectomy and have no history of CIN are at very low risk of developing vaginal cancer [Level A]
  - Continued cytology in such women are not cost-effective and causes anxiety and over-tx
- ACOG - may discontinue screening

# 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.

# Guidelines for Cervical Screening in New Zealand

Incorporating the Management of Women with Abnormal Cervical Smears

National cervical SCREENING PROGRAMME

New Zealand Government

– USA

# 2006 ASCCP National Consensus Conference

- **ASCCP 2006 National Consensus Conference for the Management of Women with Cervical Cytological Abnormalities and Cervical Cancer Precursors**
  - **National Institutes of Health in Bethesda, Md on September 18-19, 2006**
  - **Guidelines for managing abnormal cytology, CIN, AIS, and screening tests for high-risk HPV DNA**

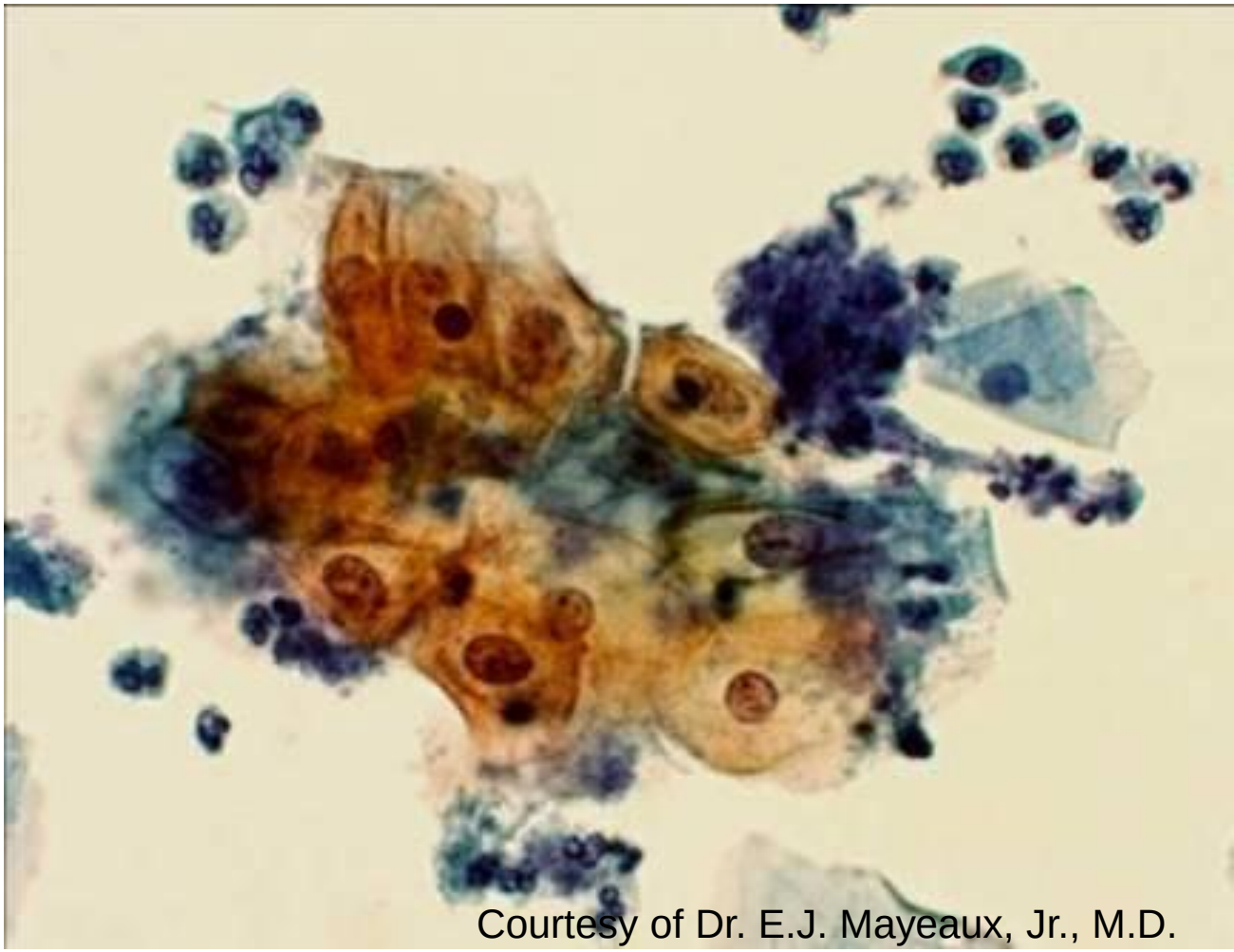
# NZ and ASCCP Algorithms Sources

- **Cervical Cytology Algorithms**
  - **Wright TC, et al. Am J Obstet Gynecol 2007; 197(4):346-355 www.asccp.org**
- **CIN Treatment Algorithms**
  - **Wright TC, et al. Am J Obstet Gynecol 2007; 197(4):340-345 www.asccp.org**
- **Guidelines for Cervical Screening in New Zealand. National Screening Unit, Ministry of Health. www.nsu.govt.nz**

# National Consensus Conference

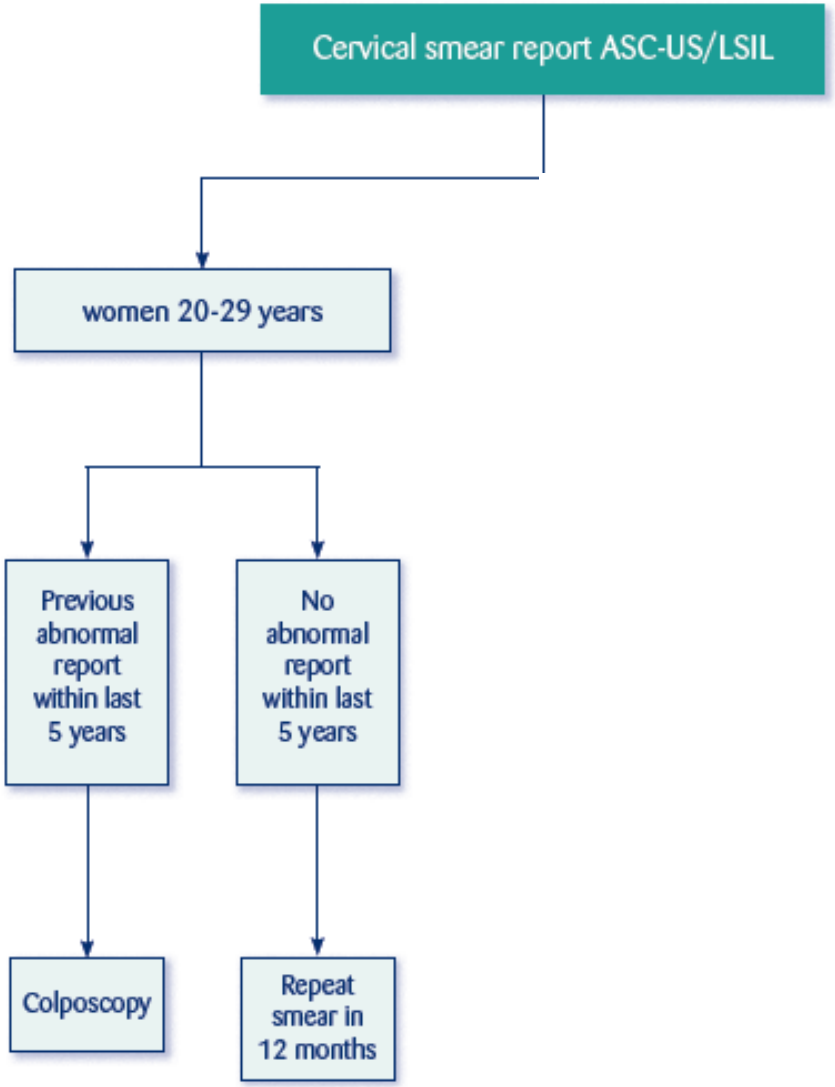
- **Guidelines are based on best available evidence**
  - **Highest quality evidence not available for all questions**
- **Guidelines should never substitute for clinical judgment**

# ASCUS/LSIL



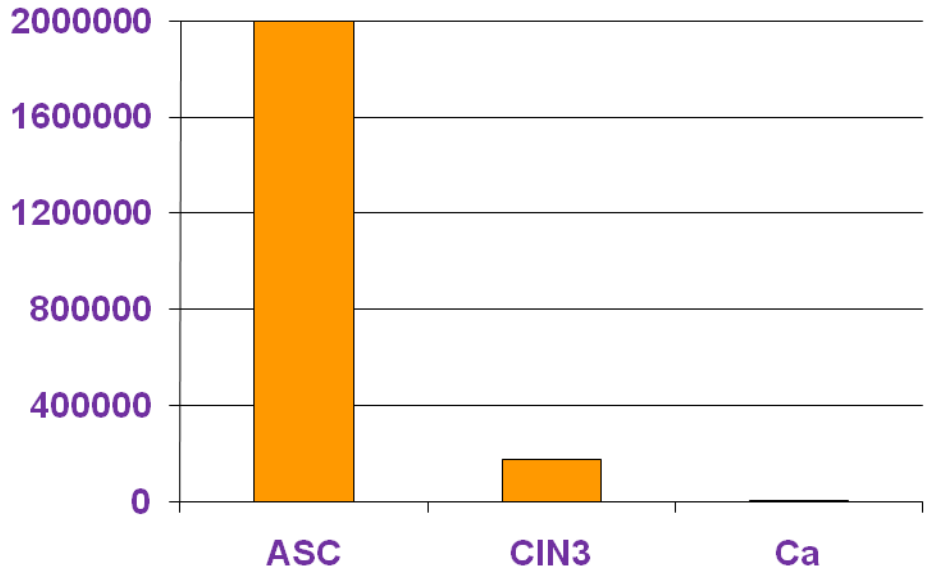
Courtesy of Dr. E.J. Mayeaux, Jr., M.D.

# Management of women with low-grade abnormalities: ASC-US or LSIL

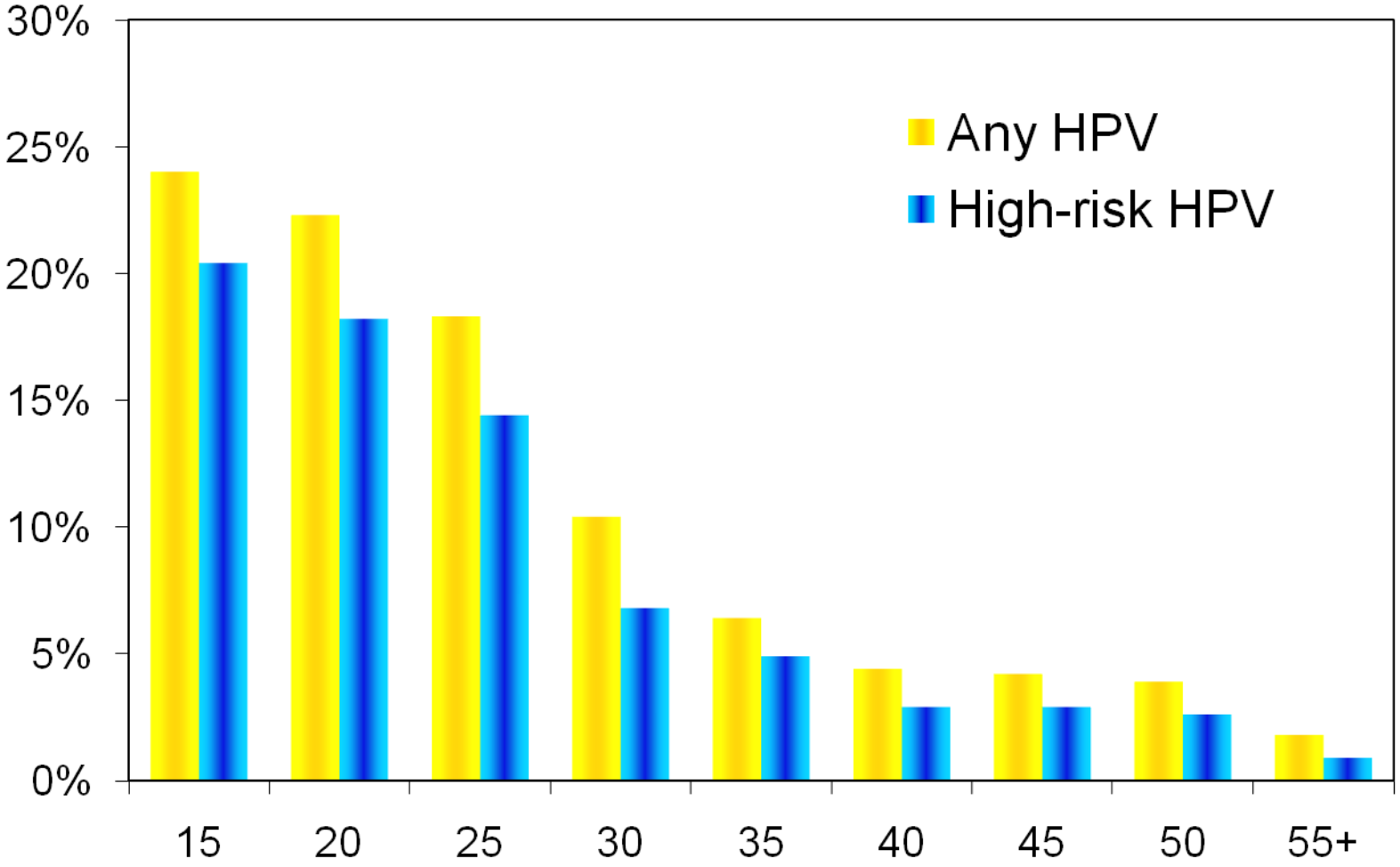



# Estimated CIN 3+ from ASCUS in U.S.

- 2,000,000 ASC-US Pap smears in the U.S. per year
- 176,000 CIN 3 detected in ASC-US follow-up per year
- Approximately 2000 cancers
  - 1/1000 already have cancer



# Risk of HPV in Adolescents




Peto et al Br J Cancer 2004:91:942-53

# Management of ASC - US

- Cancer is rare In the young

| | |
|---|---|
| ***15-19 yrs*** | **<0.3 per 100,000** |
| ***20-24 yrs*** | **2.6 per 100,000** |
| ***25-29 yrs*** | **7.8 per 100,000** |
| ***30-34 yrs*** | **11.4 per 100,000** |
| ***35-39 yrs*** | **14.4 per 100,000** |

*SEER 1992-1996 all races, MMWR*

# LSIL and Neoplasia

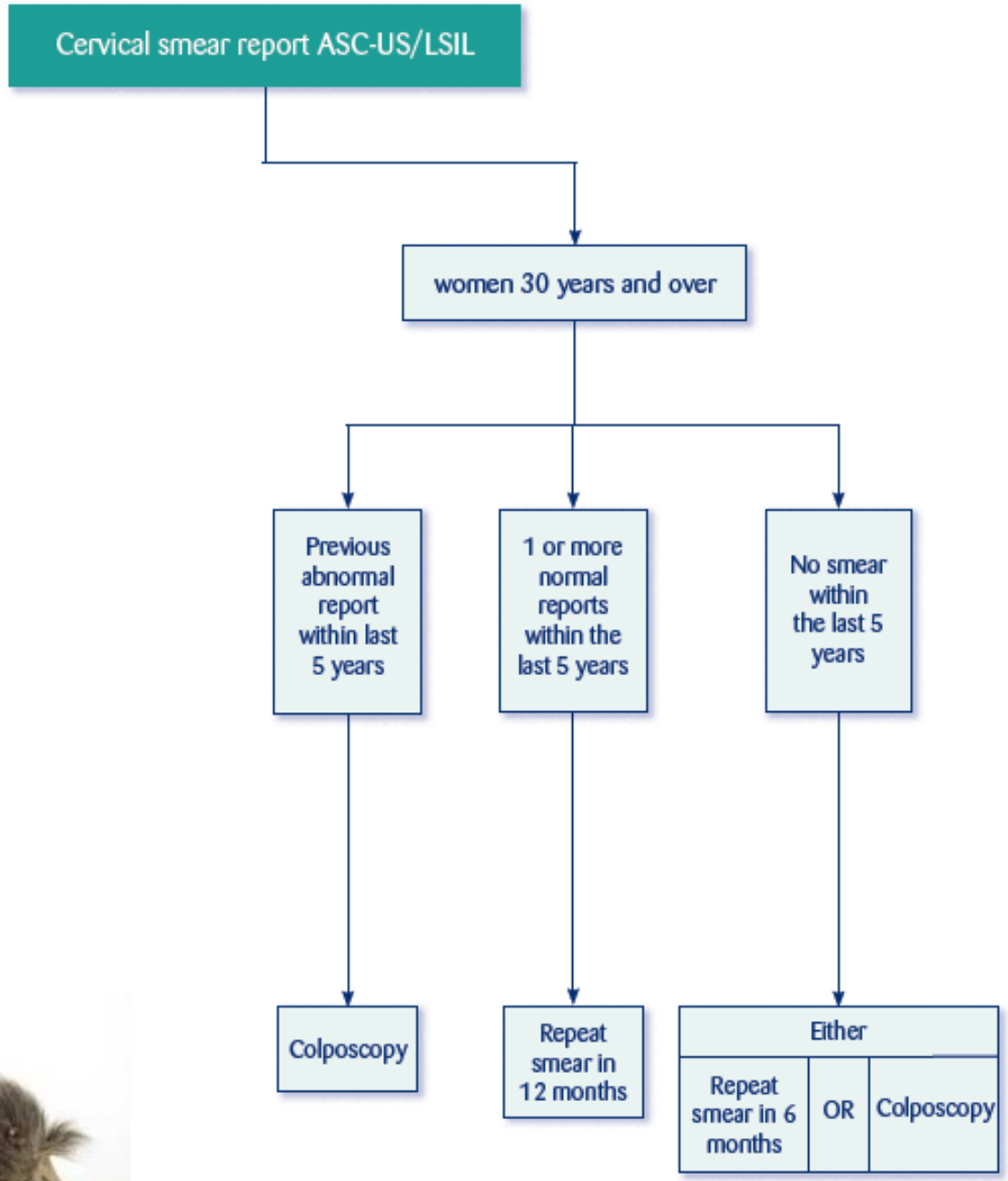
- **LSIL is highly predictive of HPV infection**
  - **76.6% with LSIL are HR HPV DNA+**
  - **Doesn't discriminate risk level**
  - **Postmenopausal women are an exception, with lower HPV prevalence after an LSIL result**

- **Wright TC, et al. Am J Obstet Gynecol 2007; 197(4):346-355**
  **www.asccp.org**

# LSIL and Neoplasia

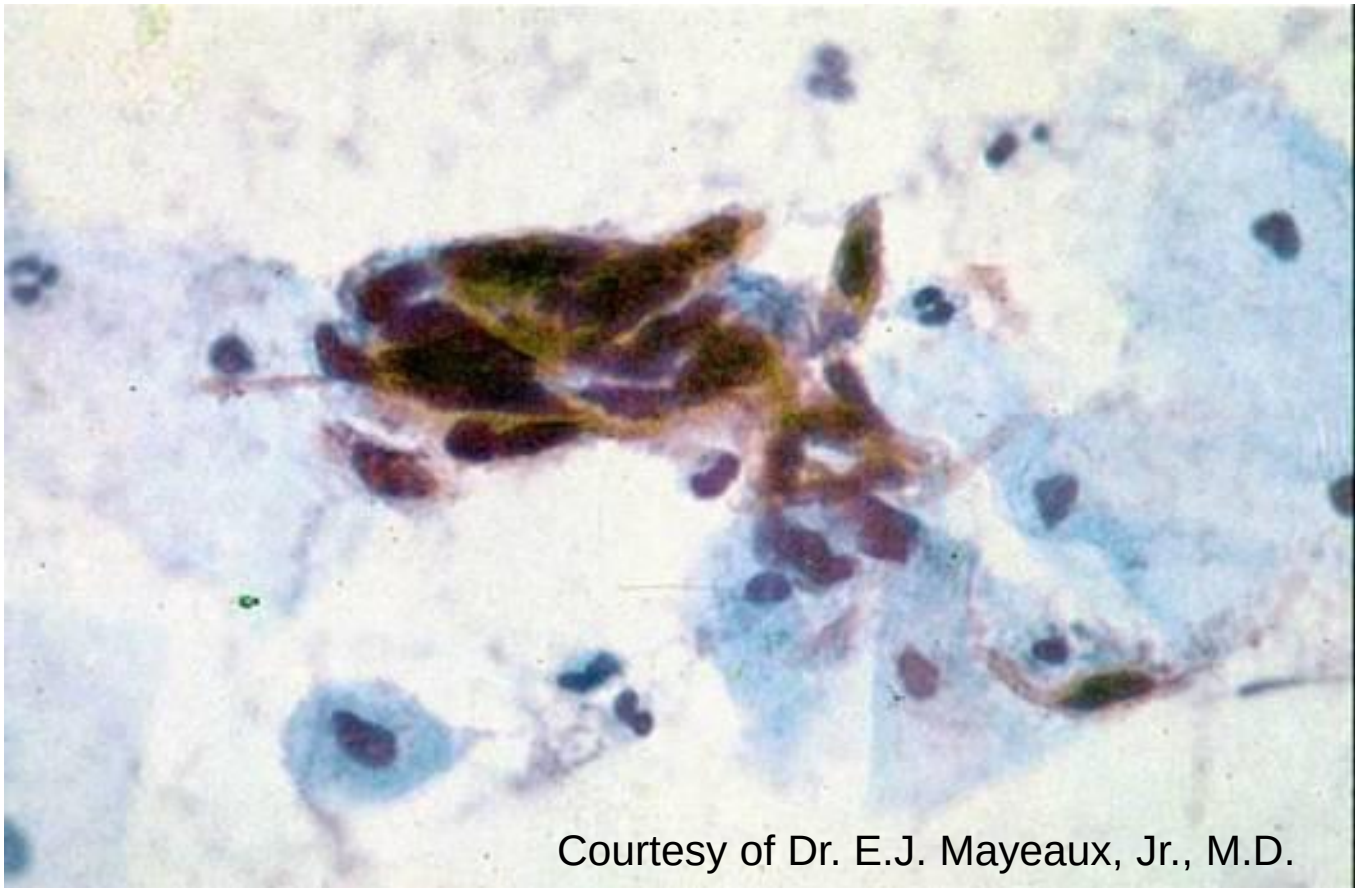
- **Some 85% of women with LSIL will be found at colposcopy to have a biopsy-confirmed CIN**
  - **14% have no lesion**
  - **67% have CIN1 or HPV**
  - **18% have CIN2,3**
  - **0.3% have invasive cervical cancer**
- **Wright TC, et al. Am J Obstet Gynecol 2007; 197(4):346-355 www.asccp.org**

# Management of women with low-grade abnormalities: ASC-US or LSIL



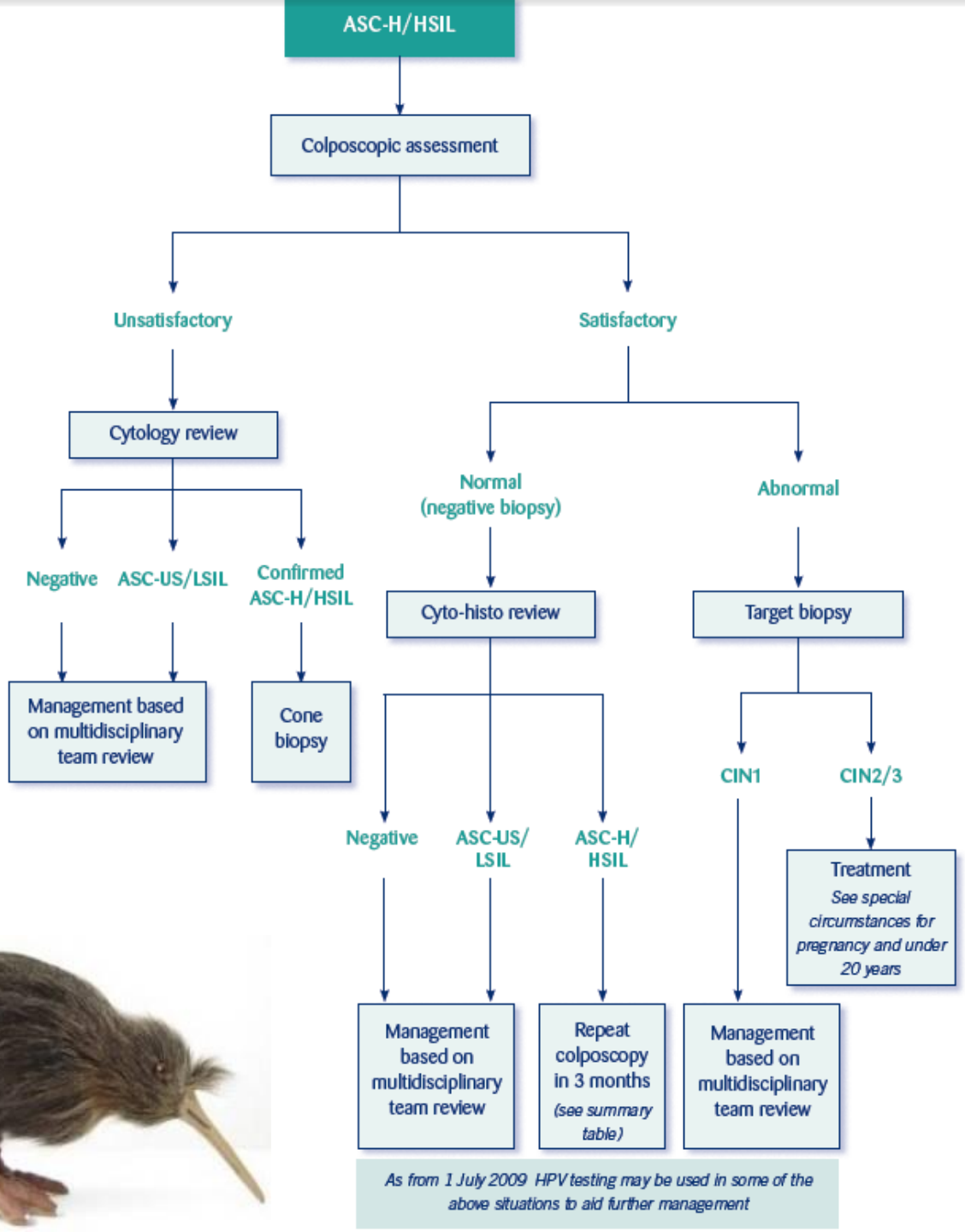

*As from 1 July 2009 triage with HPV testing as per NCSP Best Practice Guidance on HPV Testing*

# HSIL/ASC-H



Courtesy of Dr. E.J. Mayeaux, Jr., M.D.

# Management of women with high-grade abnormalities: ASC-H or HSIL



# Rates of CIN2 with ASCUS-H

| Author-Year | No | HPV (+) | CIN 2,3 |
|---|---|---|---|
| Duncan 2005 | 99 | 74% | 40% |
| Srodan 2005 | 96 | 67% | 40% |
| Liman 2005 | 48 | 79% | 46% |
| Sherman 2006 | 101 | 84% | 50% |

# HSIL Management

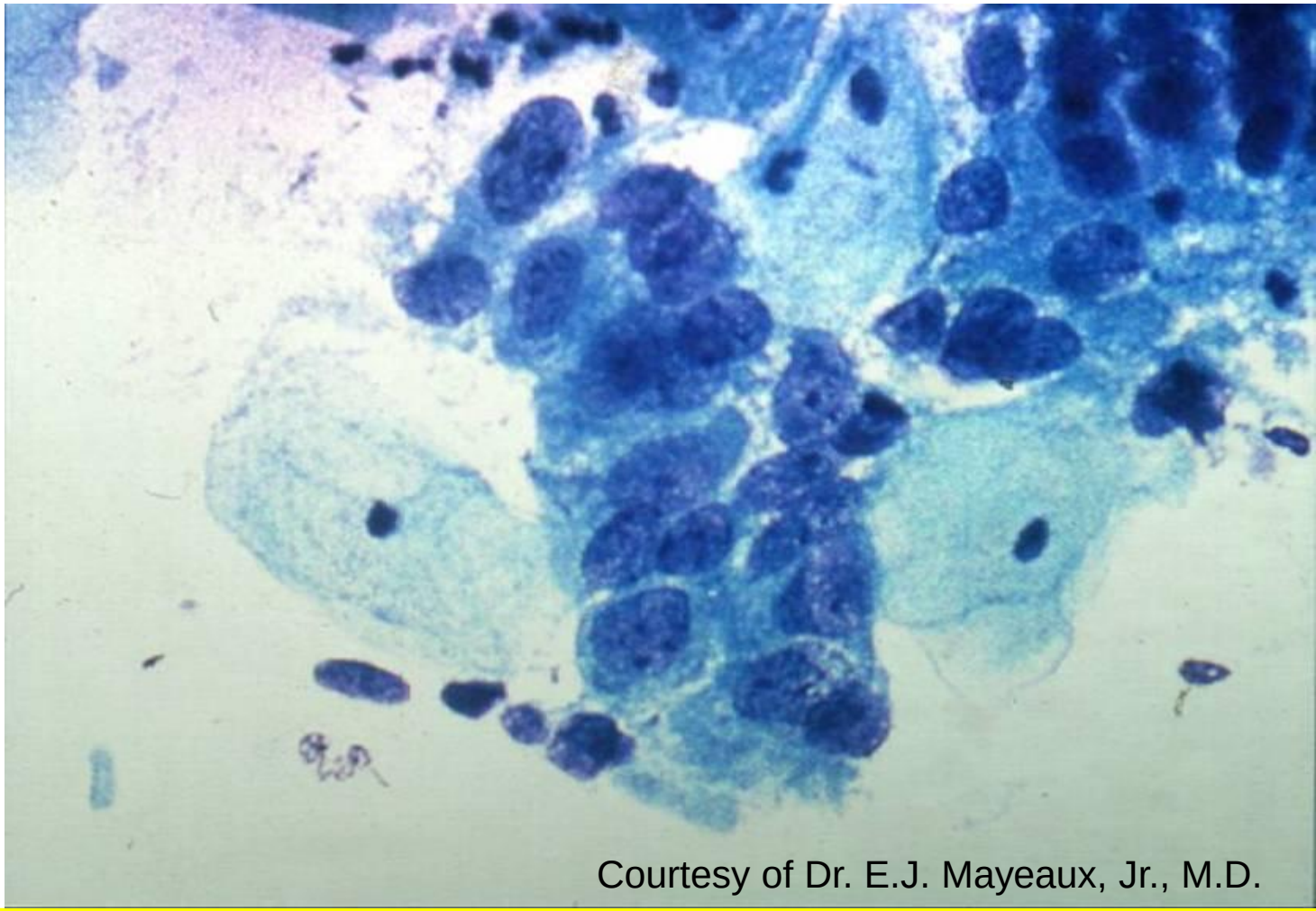
- **Some 70-75% of adult women with HSIL will have a biopsy-confirmed CIN 2,3 at colposcopy**
  - **7% have no lesion**
  - **16% have CIN1**
  - **1-2% have invasive cervical cancer**

- **Wright TC, et al. Am J Obstet Gynecol 2007; 197(4):346-355**
  **www.asccp.org**

# HSIL 2006 Changes

- **Immediate loop excision and colpo with ECC/B = weight**
  - **Rationale: Prospective studies showing high yield of CIN2,3 with lower cost and fewer women lost to follow-up**
  - **ALTS, only 54% of CIN3 found at colpo**
- **Wright TC, et al. Am J Obstet Gynecol 2007; 197(4):346-355**
  **www.asccp.org**

# AGC



Courtesy of Dr. E.J. Mayeaux, Jr., M.D.

# AGC and AIS

- **In New Zealand, and internationally, glandular lesions are now ~15–20% of cervical cancers**
- **Cervical screening is less effective**
- **HrHPV associated with cervical adenoCa and AIS in approximately 90% of cases**
- **Associated with adenocarcinoma of the cervix, endometrium, ovary and salpinx**
- **All women with glandular abnormalities should be referred to colposcopy**

# AGC and AIS

- **It is common for both squamous and glandular lesions to co-exist**
- **May find either a squamous or coexisting squamous/glandular lesion**
- **Because of the high incidence of neoplasia and poor sensitivity of testing methods, diagnostic excisional procedures may be necessary**
- **HrHPV testing may have an ancillary role**

# Atypical glandular cells

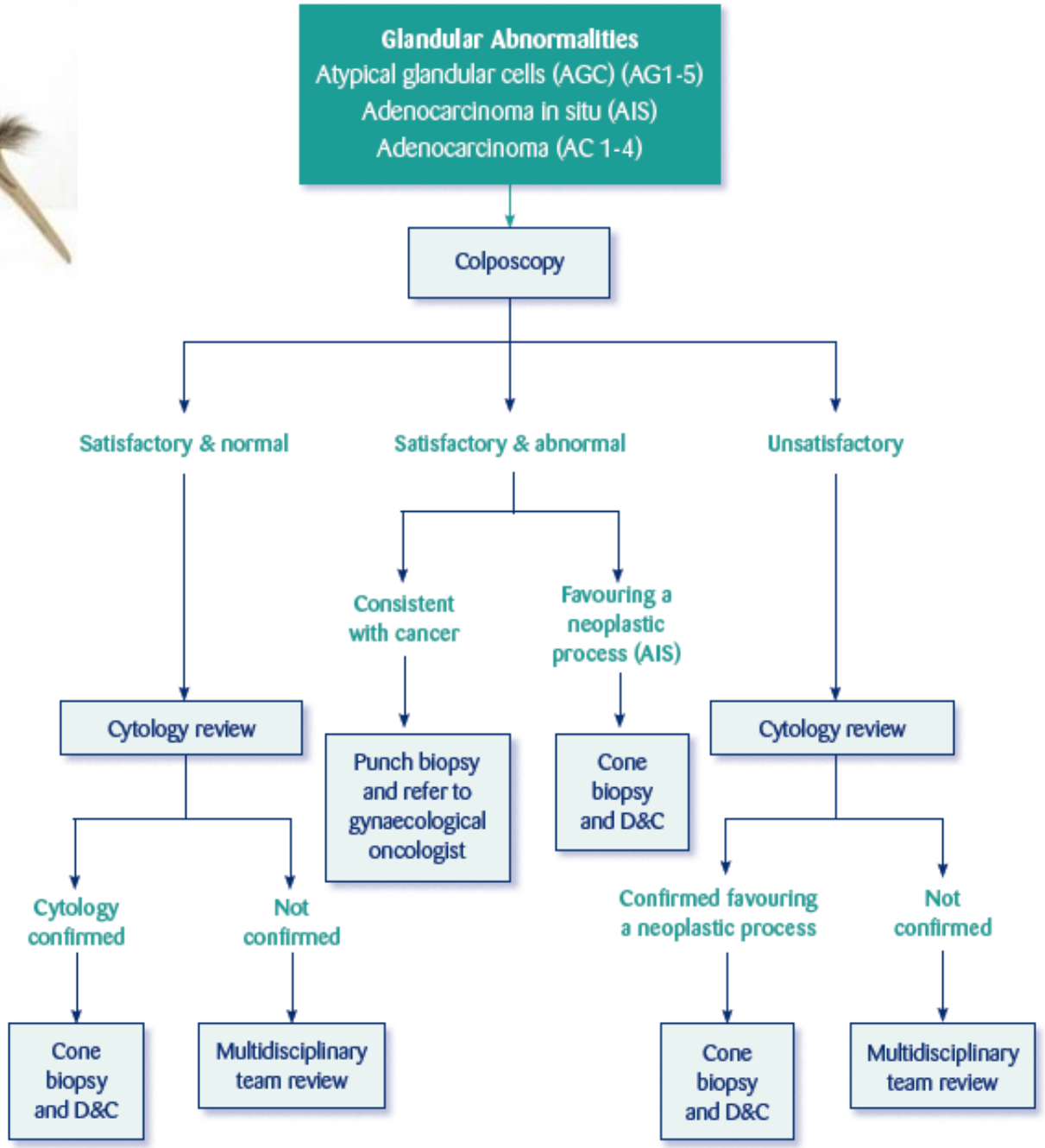
- **HG CIN is most common after AGC**
- **Gyn cancers more common >35 yrs**

| | |
|---|---|
| **CIN1/HPV** | **8.5%** |
| **CIN 2,3** | **11.1%** |
| **AIS** | **2.9%** |
| **Endometrial hyperplasia** | **1.4%** |
| **Cancer** | **5.2%** |

# US AGC 2006 Changes

- **If not already obtained, HR-HPV testing at the time of colposcopy is preferred with AGC-NOS (CIII)**
- **The use of HPV DNA testing alone or repeat cervical cytology alone is unacceptable for the initial triage of all subcategories of AGC and AIS (EII)**


- **Wright TC, et al. Am J Obstet Gynecol 2007; 197(4):346-355**




Guidelines for Cervical Screening in New Zealand. National Screening Unit, Ministry of Health. www.nsu.govt.nz

# Pregnant Women

# NZ Cytology in Pregnancy

- **Routine screening**
- **No contra-indication to smear-taking during pregnancy**
- **Routine smears may be delayed**
  - **Unless the woman is well overdue**
  - **Previous smear was abnormal**

# Colposcopy in Pregnancy

- **Low Risk of progression of CIN 2/3 to invasive cancer during pregnancy**
- **High probability that a HG lesion persists**
- **Need colposcopic/cytological surveillance during the pregnancy (at about 20–30 weeks) and postpartum (after 6 weeks)**

# Colposcopy in Pregnancy

- **Treatment during pregnancy**
  - **Associated with complications**
  - **High rate of recurrence or persistence**
- **Only indication for treatment in pregnancy is invasive cancer**
- **Assessment of pregnant women with HSIL be undertaken by a colposcopist experienced in assessing the pregnant cervix**

# Colposcopy in Pregnancy

- **Goal of colpo in pregnancy is identification of invasive cancer**
- **Among 146 women with LSIL in 3 series who had pregnancy bx,**
  - **133 (91%) had no lesion or CIN1**
  - **13 (9%) had CIN2,3**
  - **No cancer**
- **Murta EF, et al. Eur J Gynaecol Oncol. 2004;25(5):600-602.**

# US Pregnancy 2006 Changes

- **Colposcopy is preferred for pregnant, non-adolescent women with LSIL cytology (BII)**
- **Deferring initial colpo until at least 6 weeks postpartum is acceptable (BIII)**
- **ECC is unacceptable (EIII)**


- Wright TC, et al. AJOG 2007;197(4):346-355.

# Pregnancy 2006 Changes

- **Complicated by vascular and epithelial changes**
- **Bx = pain, cost, bleeding**
- **Failure to biopsy associated with missed cancers postpartum**
- **Risk of cancer postpartum <10%**
- **Many oncologists follow with Stage I cancer to viability**

# lib-sh.lsuhsc.edu/fammed/default.html

# www.asccp.org