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USA

Cervical Smears and Culpscopy - Concurrent Workshop Session Repeated

Saturday, 11 June 2011

Start 11:00am

Duration: 55mins

Monet

Start 12:05pm

Duration: 55mins

Monet



Cervical Smears and Colposcopy

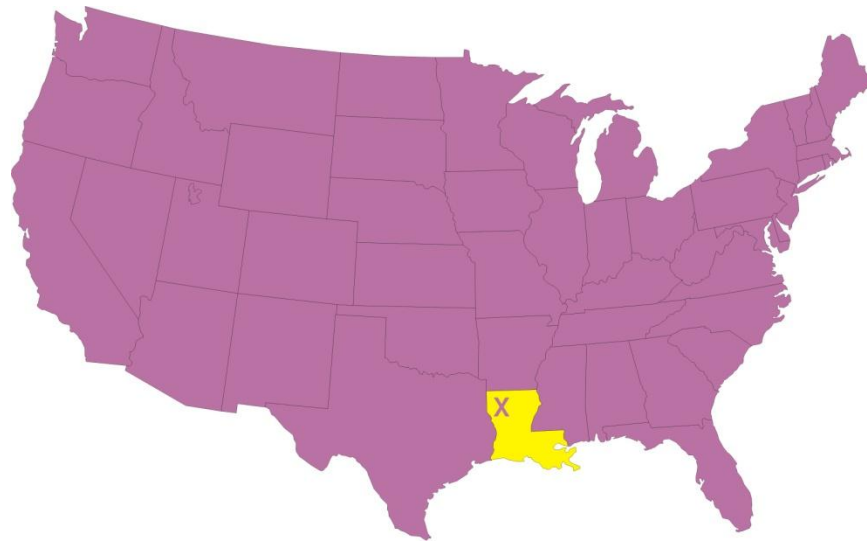
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Shreveport, LA



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

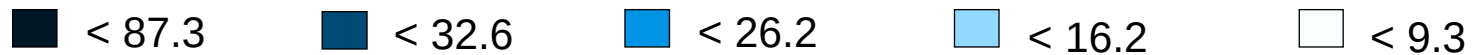
N. AMERICA
14,670

EUROPE
59,931

ASIA
265,884

C-S. AMERICA
71,862

AFRICA
78,897



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

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

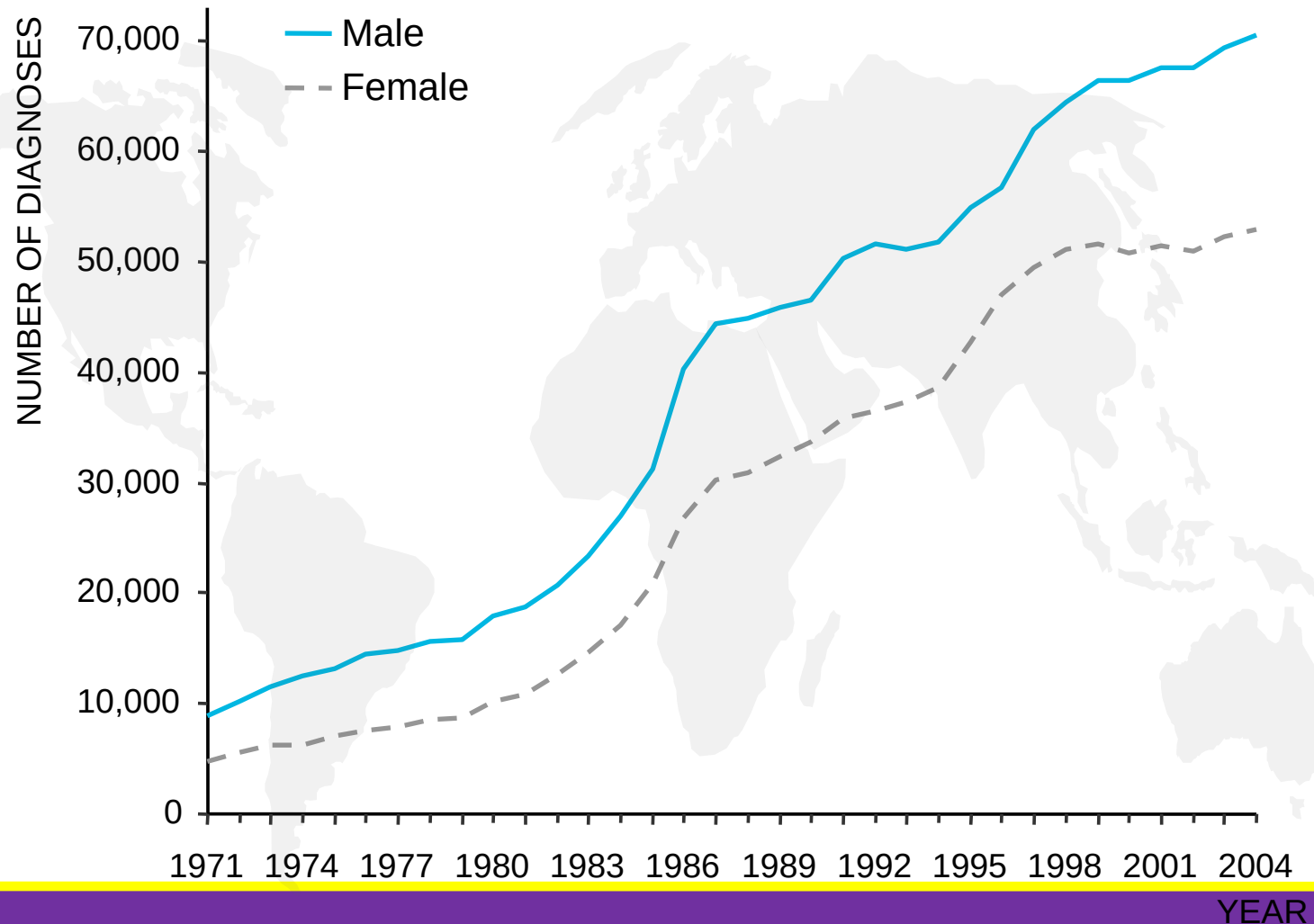
Human Papillomavirus and Related Cancers Summary Report Update: NEW ZEALAND.
September 15, 2010. WHO/ICO Information Centre on HPV and Cervical Cancer (HPV
Information Centre) GLOBOCAN 2010

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	

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

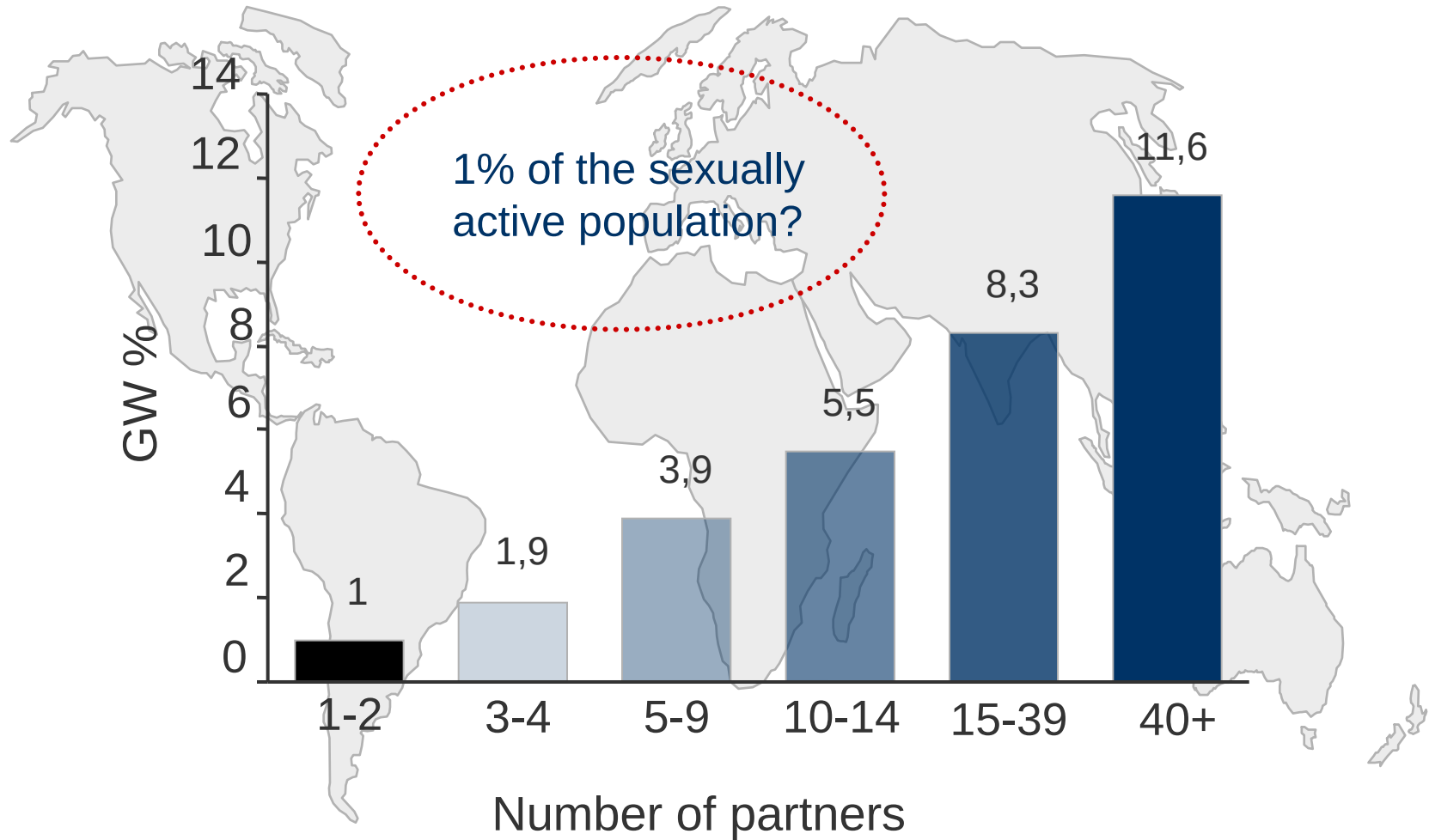


Source: Health Protection Agency, 2006.

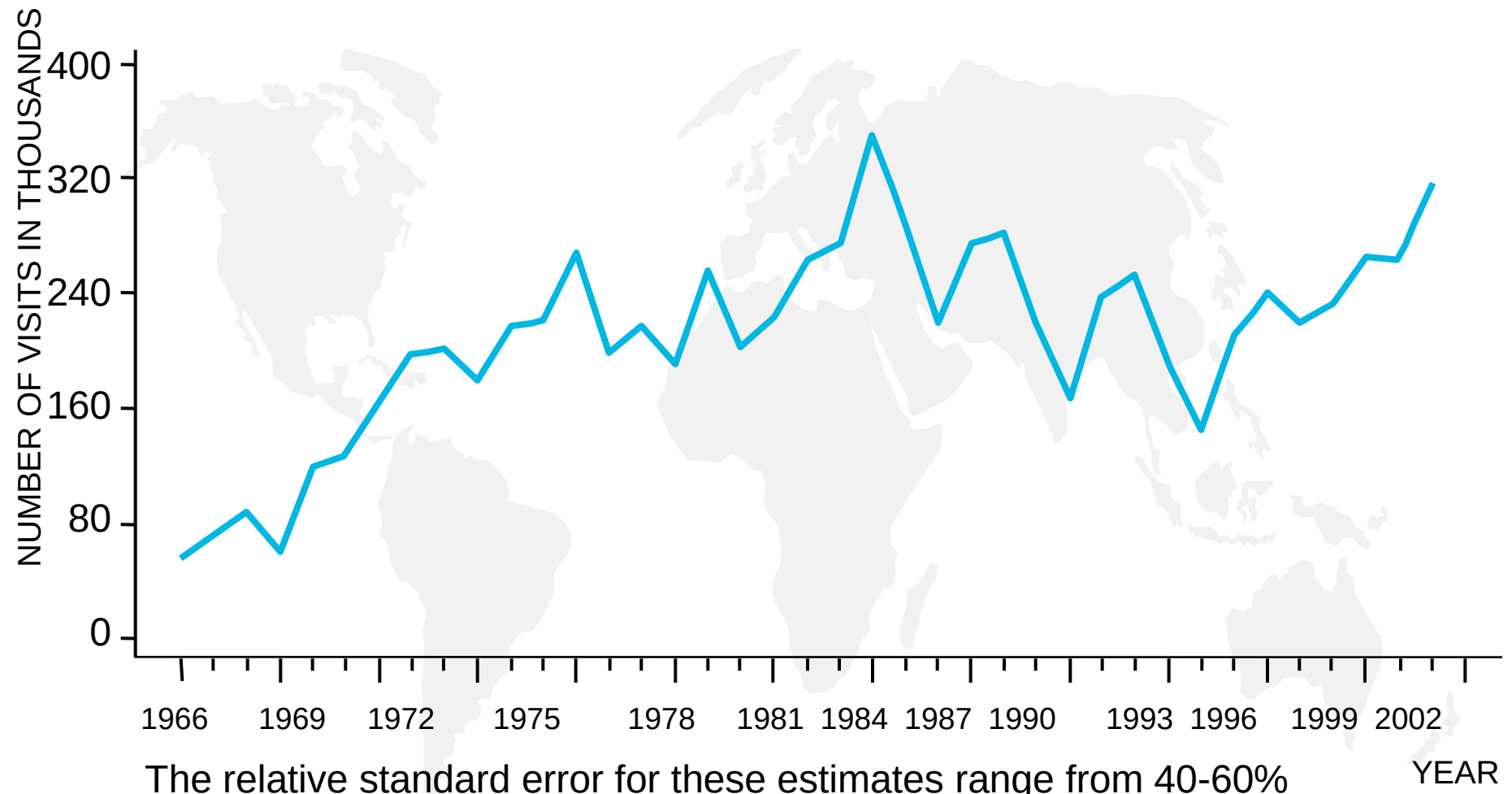
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Number of partners and % of ever GW

The Copenhagen survey: **Ever GW 17%**



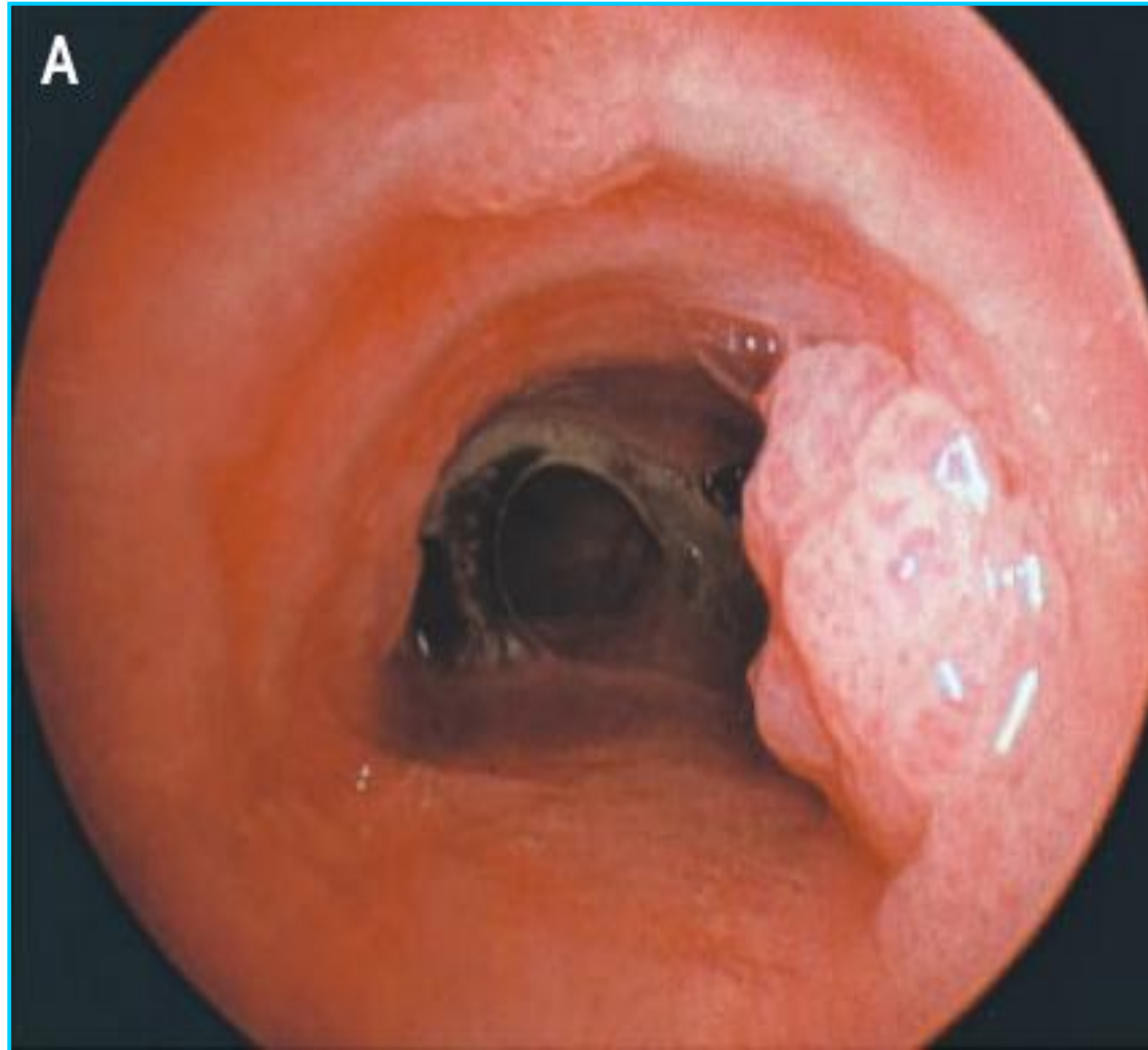
INITIAL VISITS RELATED TO GENITAL WARTS TO PHYSICIANS' OFFICES: UNITED STATES, 1966-2004



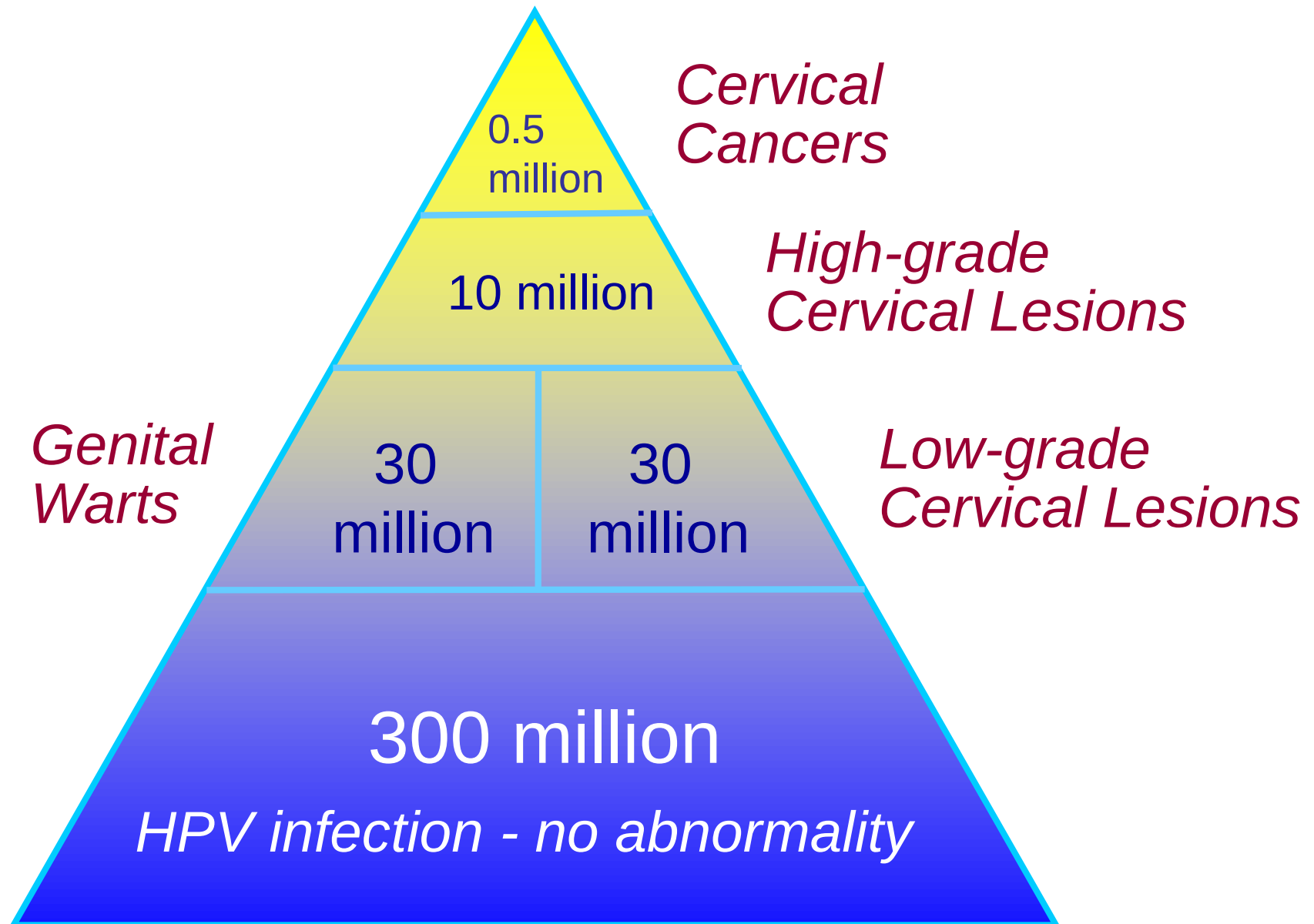
Source: IMS Health, IMS National Disease and Therapeutic Index (tm), 1966-2004. Published 2005.

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



LSU Health Sciences Center – USA

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

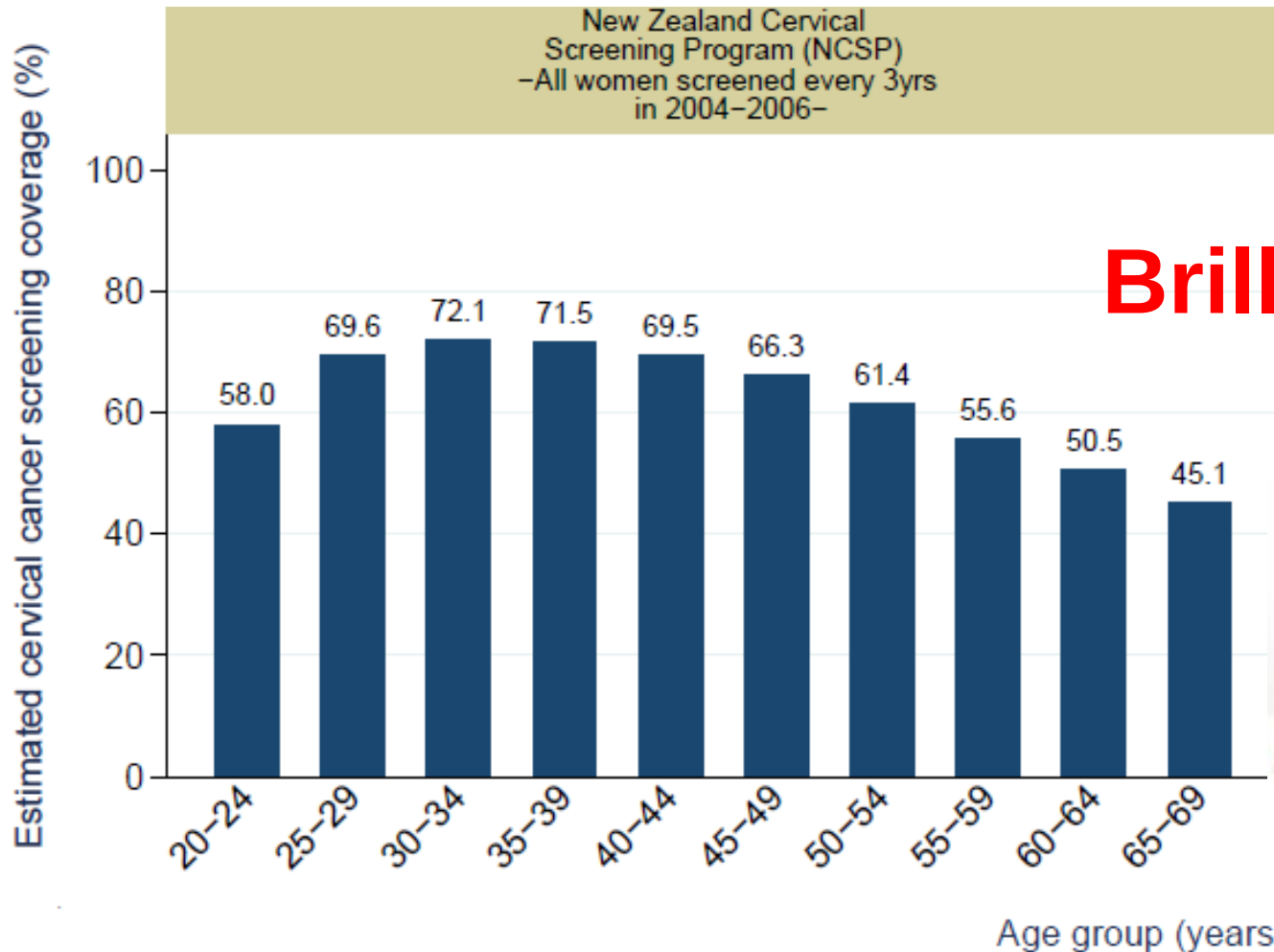
Cervical cancer screening coverage, (reference)	63.5% (New Zealand Cervical Screening Program)
Screening ages (years)	20-69 years
Screening interval (years) or frequency of screens	Every 3 years
First smear, or >5 years since previous smear	A second smear one year after the first, with three-yearly smears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



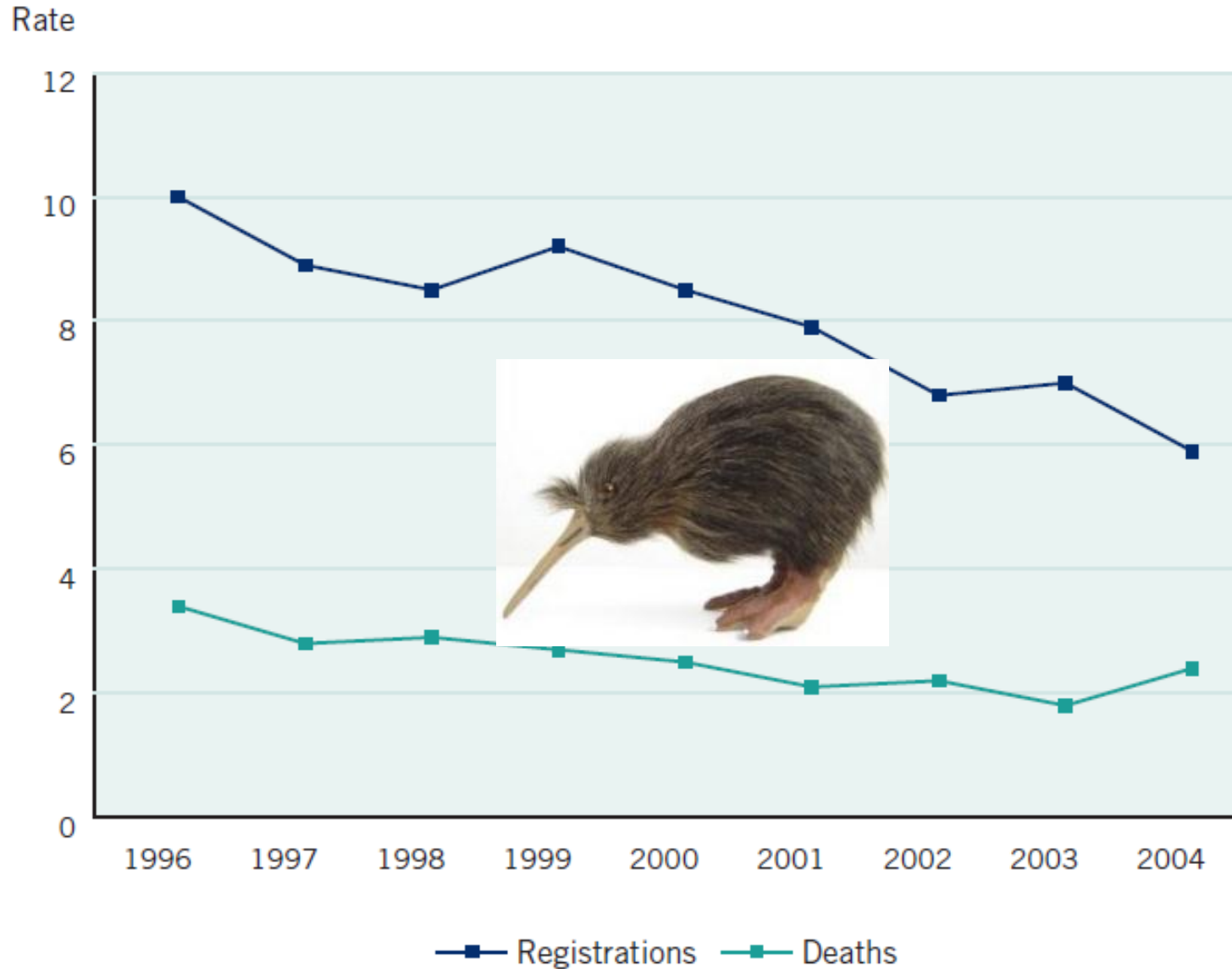
Estimated 2006 Cervical Cancer Screening Coverage in New Zealand



Brilliant!!!!



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



Liquid-based Cytology

- Disadvantages

- Higher cost and decreased specificity

- Advantages

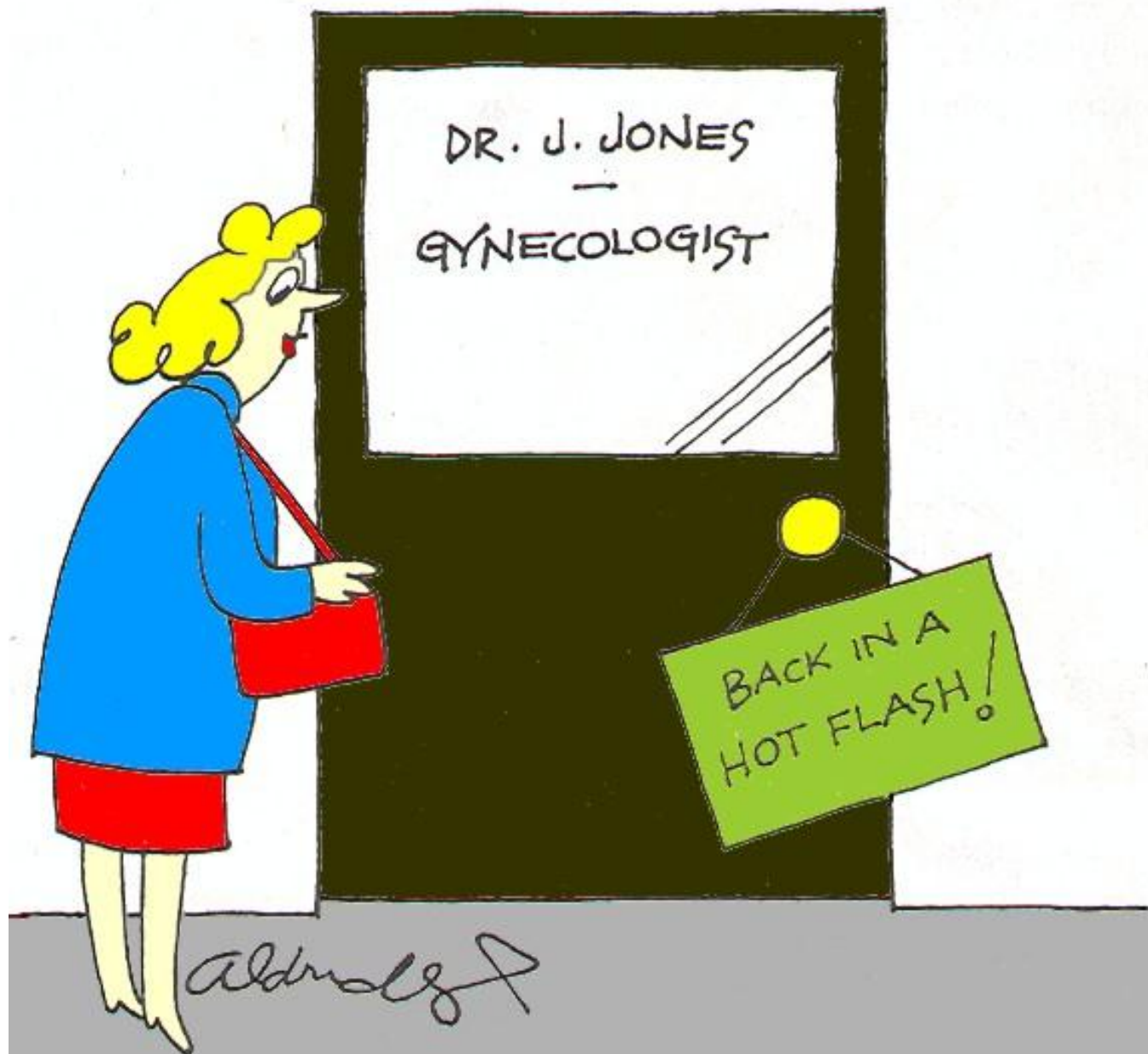
- HPV, gonorrhea, and chlamydia test

- 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.

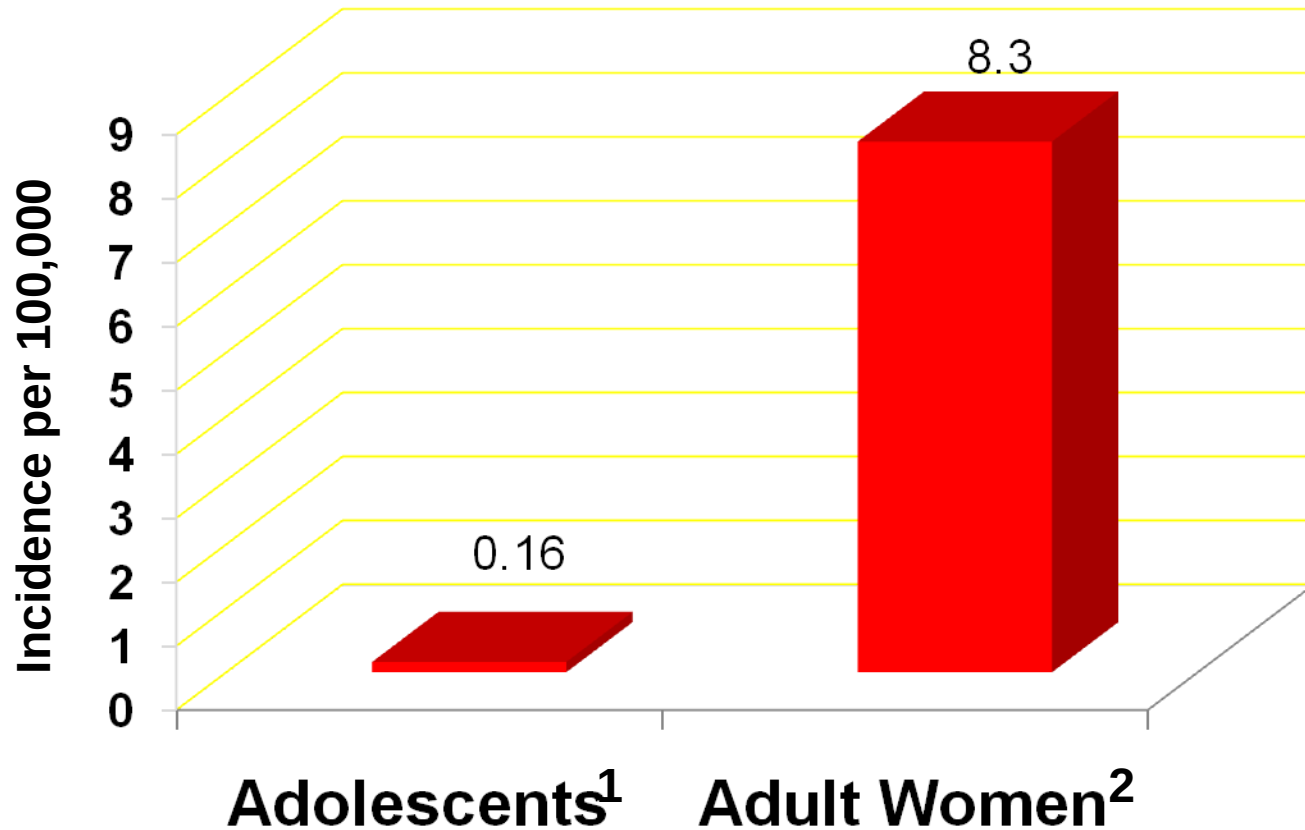


When to Begin Screening

- 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

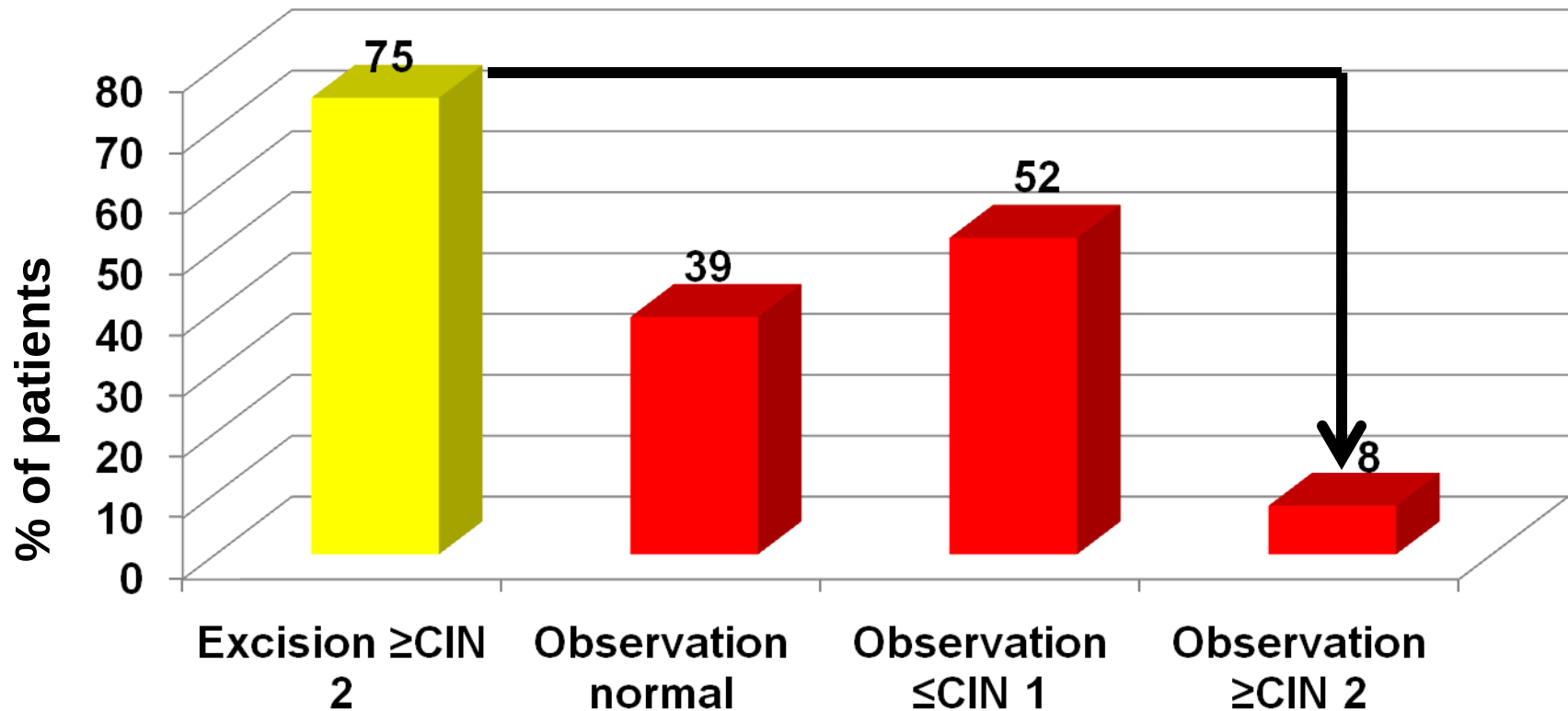
- 622 women 13-24 yrs with abnl Pap
 - Colpo and biopsy if needed
- Multinomial logistic regression analysis
 - ASCUS 231, ASC-H 30
 - LSIL 314, HSIL 11
 - CIN-3 in 6.6% and no cancers
- Moscicki AB, et al. Obstet Gynecol. 2008 December ; 112(6): 1335–1342

↓ 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

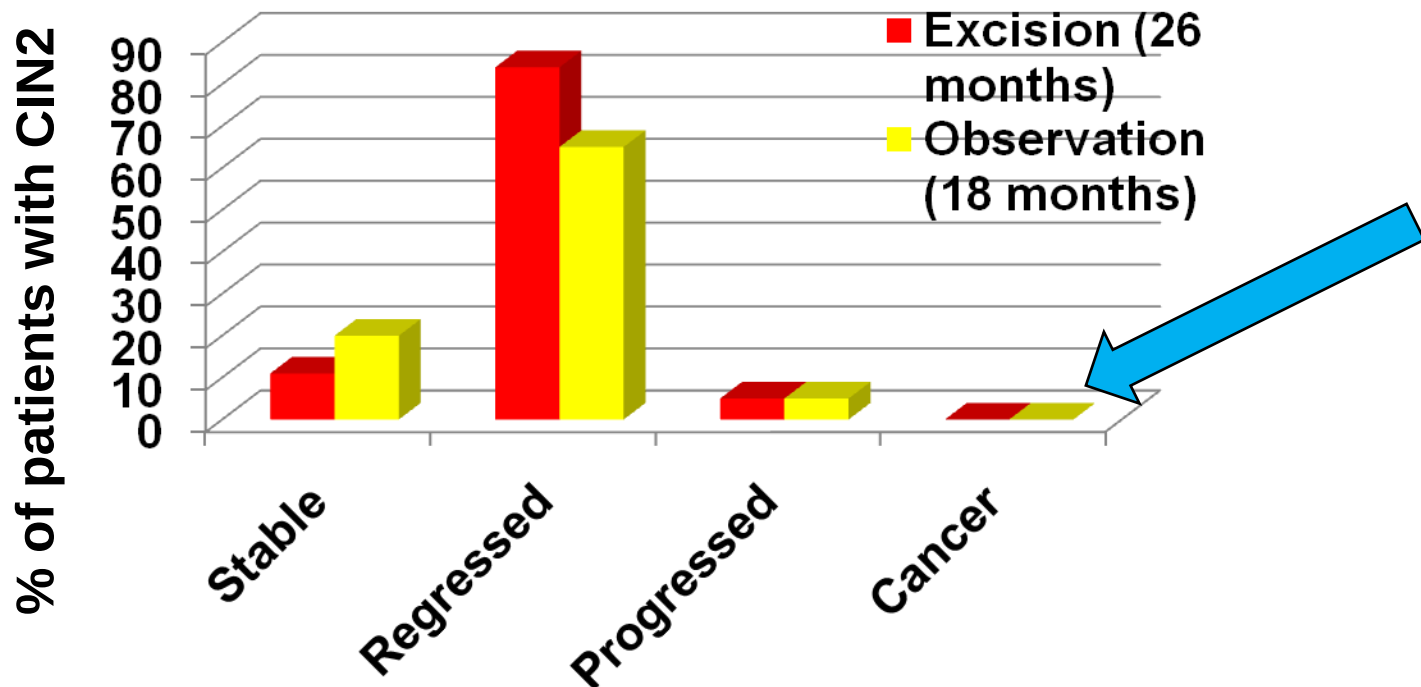
Cohort study - 93 adolescents <21 years with CIN 2



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

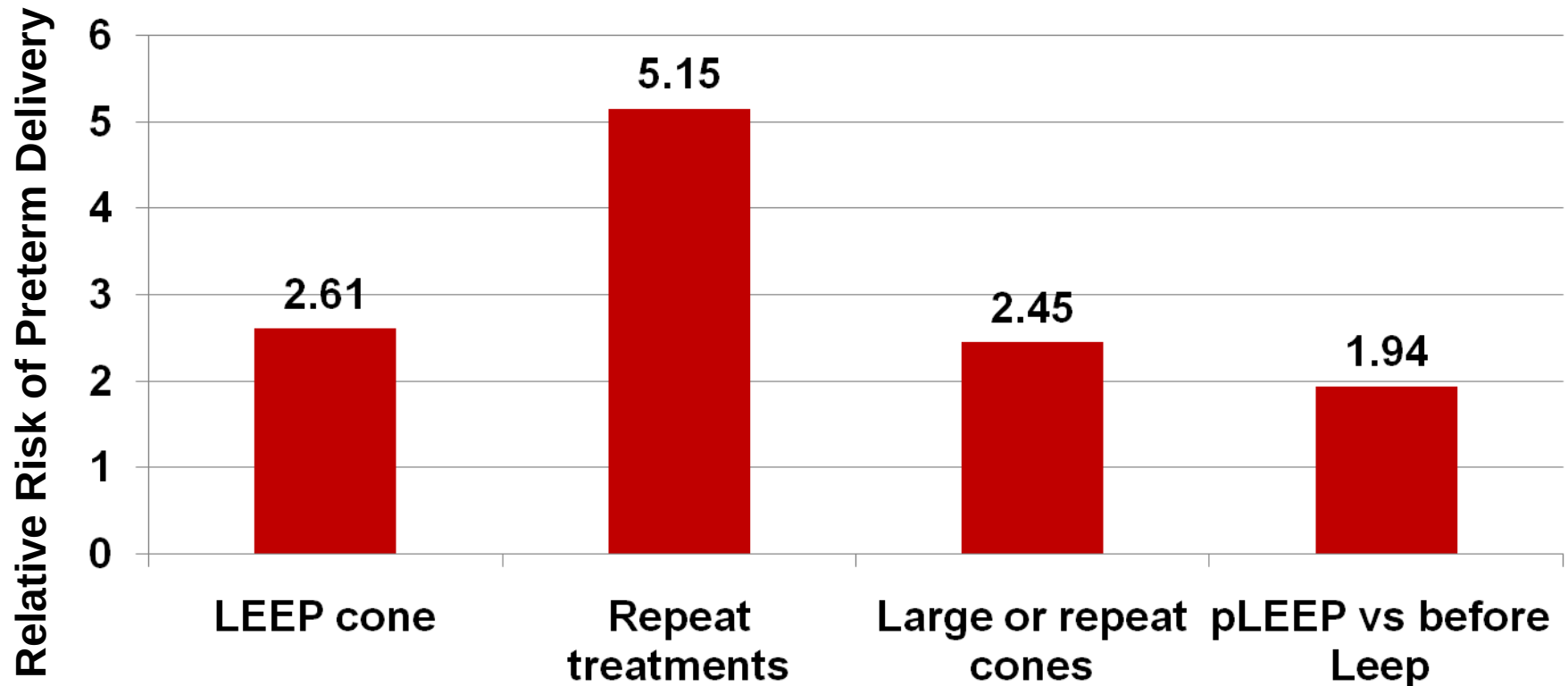
Chart review of 501 patients. 324 (65%) had $\leq$ CIN 1 and 177 patients (35%) had $\geq$ CIN2



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

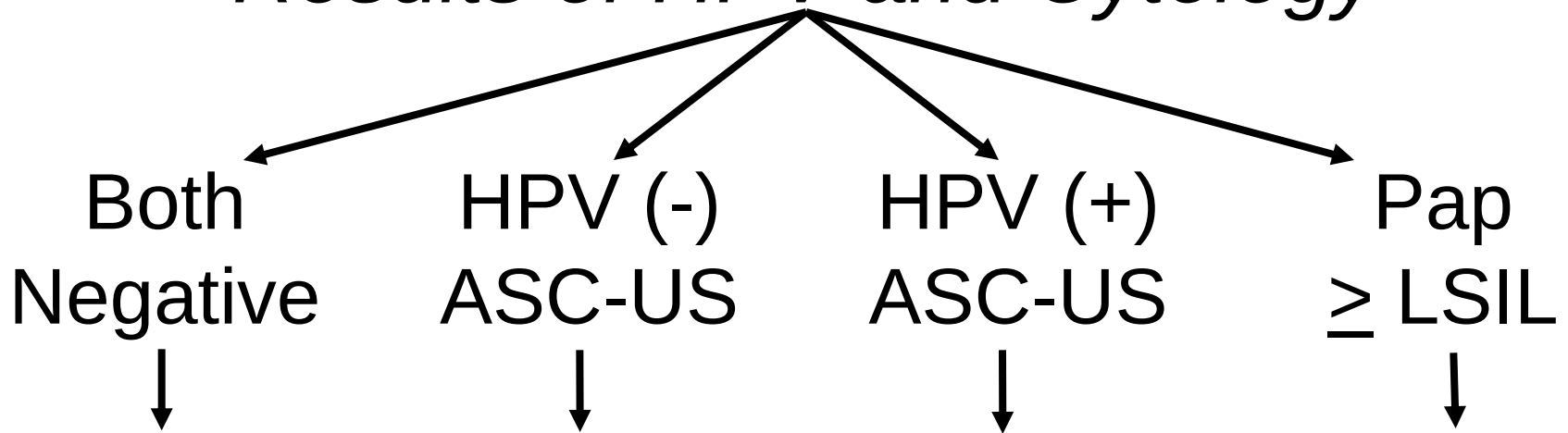
Screening frequency (yr)	Woman-years of life	Dollars
1	17,551	29,471,000
2	17,140	12,531,000
3	16,964	7,042,000
4	16,501	4,309,000
5	16,161	2,788,000
6	15,412	1,860,000
7	14,868	1,152,000
8	14,073	736,000
10	12,773	349,000

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

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

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.*

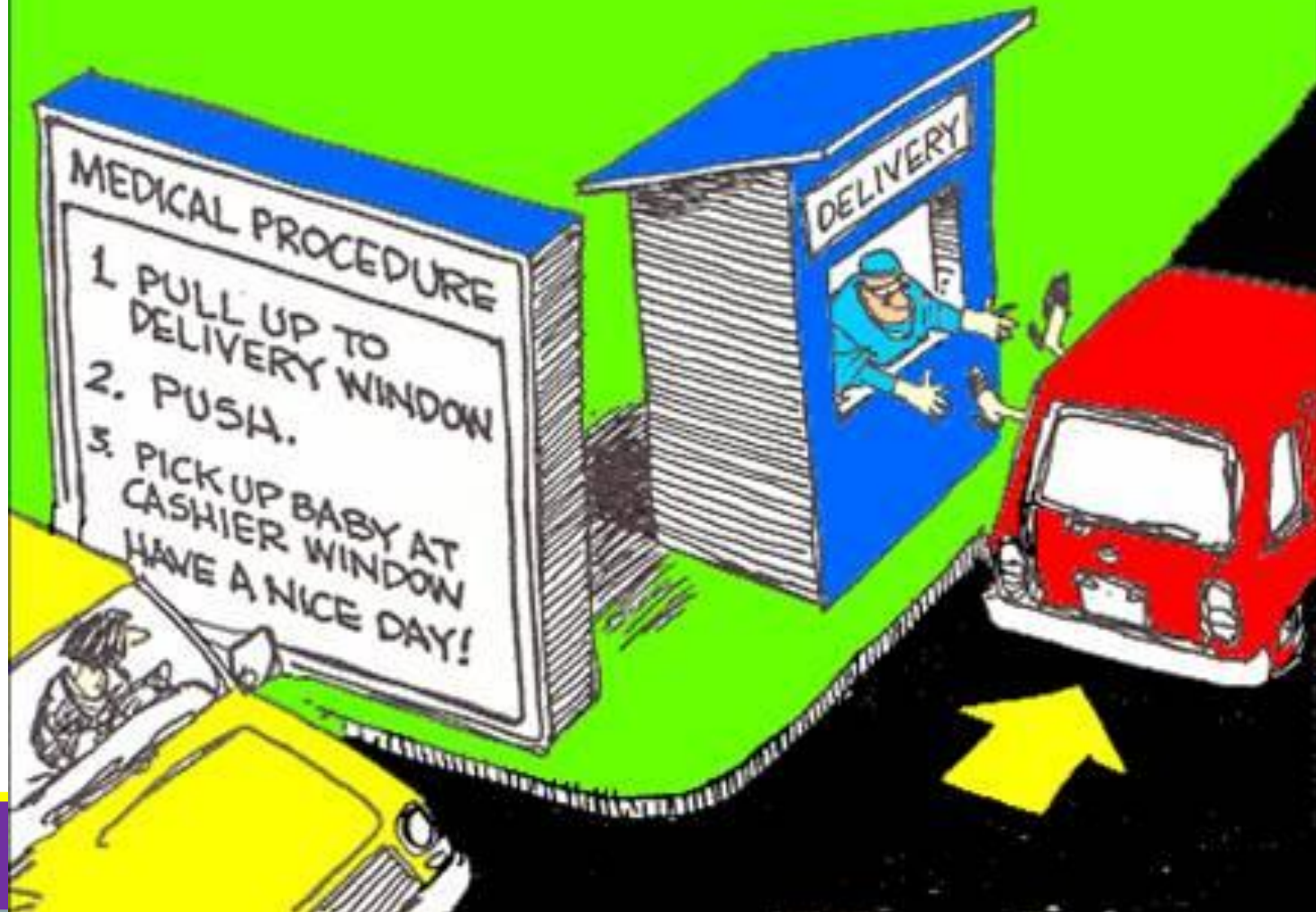
FINDING	NO. OF SMEARS (%)	NO. OF WOMEN	NO. REFERRED FOR COLPOSCOPY	NO. WITH VAIN ON BIOPSY
Atypical squamous cells of undetermined significance	52 (0.5)	47	5	1
Low-grade squamous intraepithelial lesion	44 (0.5)	30	15	2
High-grade squamous intraepithelial lesion	6 (0.1)	6	6	3
Squamous-cell carcinoma	2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

The H.M.O. MATERNITY WARD



Guidelines for Cervical Screening in New Zealand

Incorporating the Management of Women with Abnormal Cervical Smears



New Zealand Government

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**

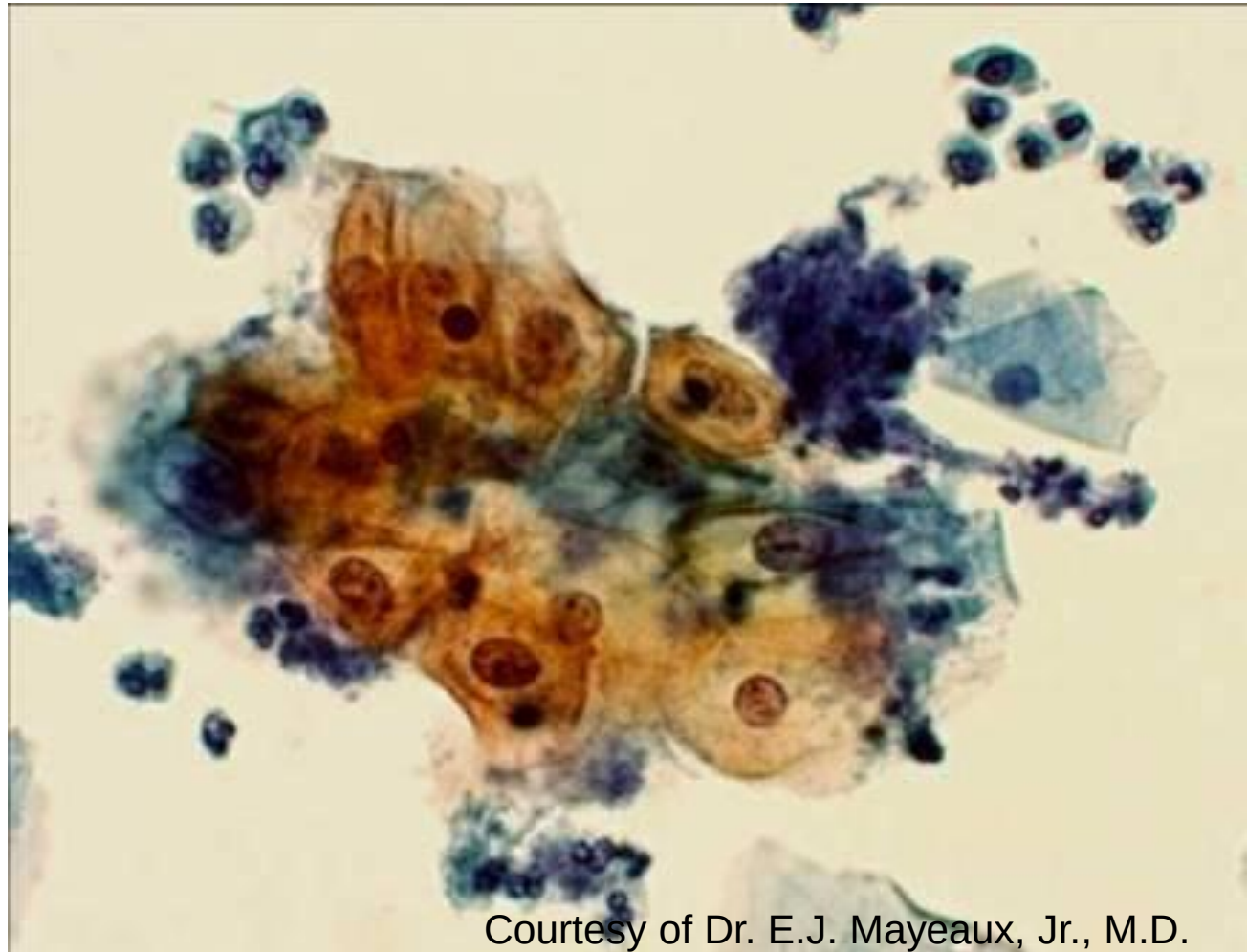
HARD WORK IS
ITS OWN REWARD!



OKAY, OKAY!
GIMME THE
PUNCH LINE!

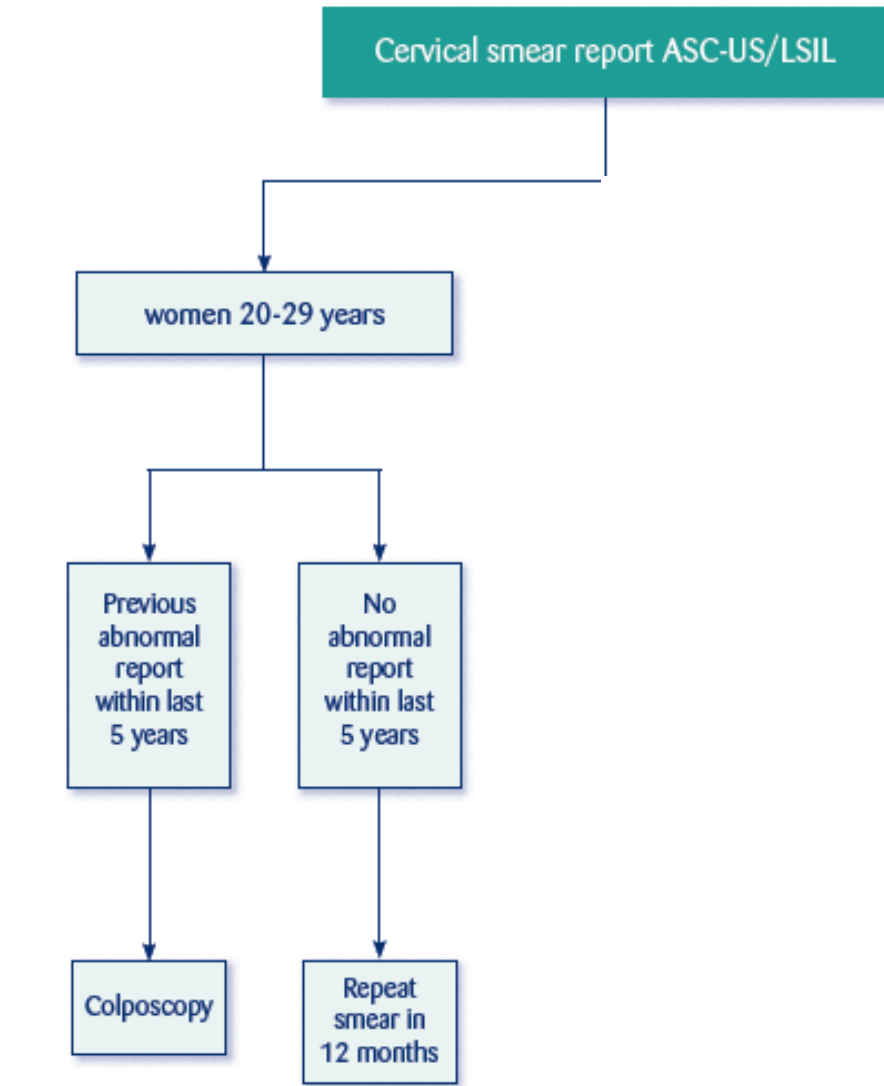


ASCUS/LSIL



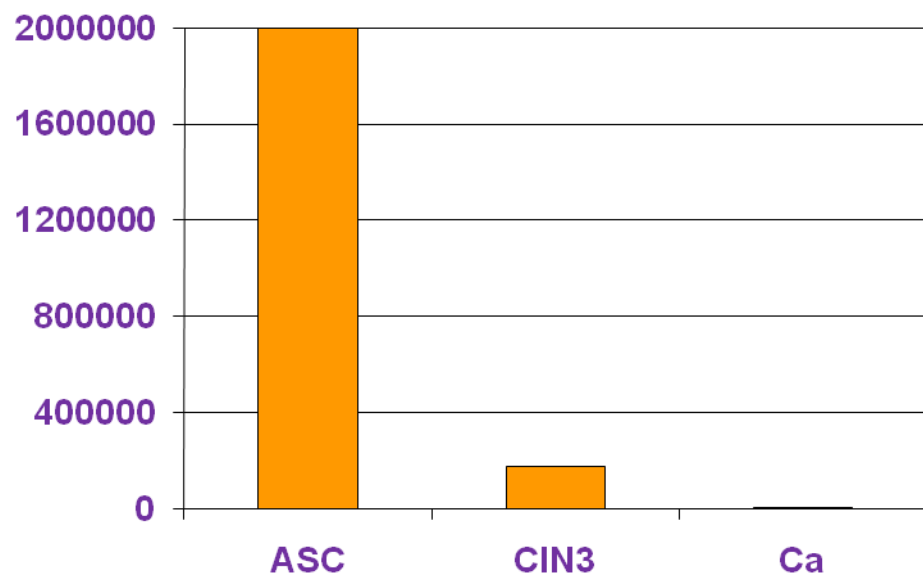
Courtesy of Dr. E.J. Mayeaux, Jr., M.D.

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

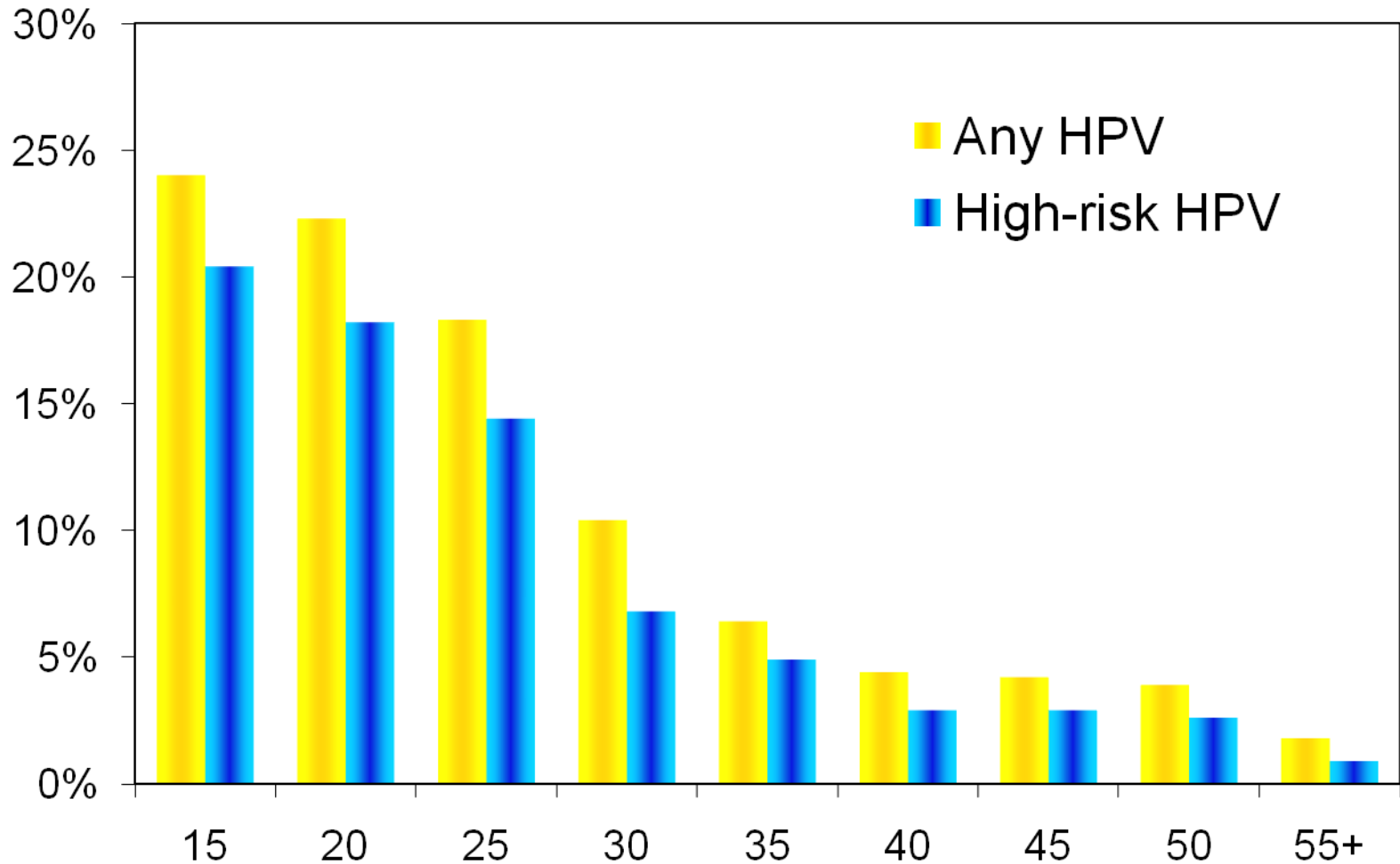


Estimated CIN 3+ from ASCUS in U.S.

- 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

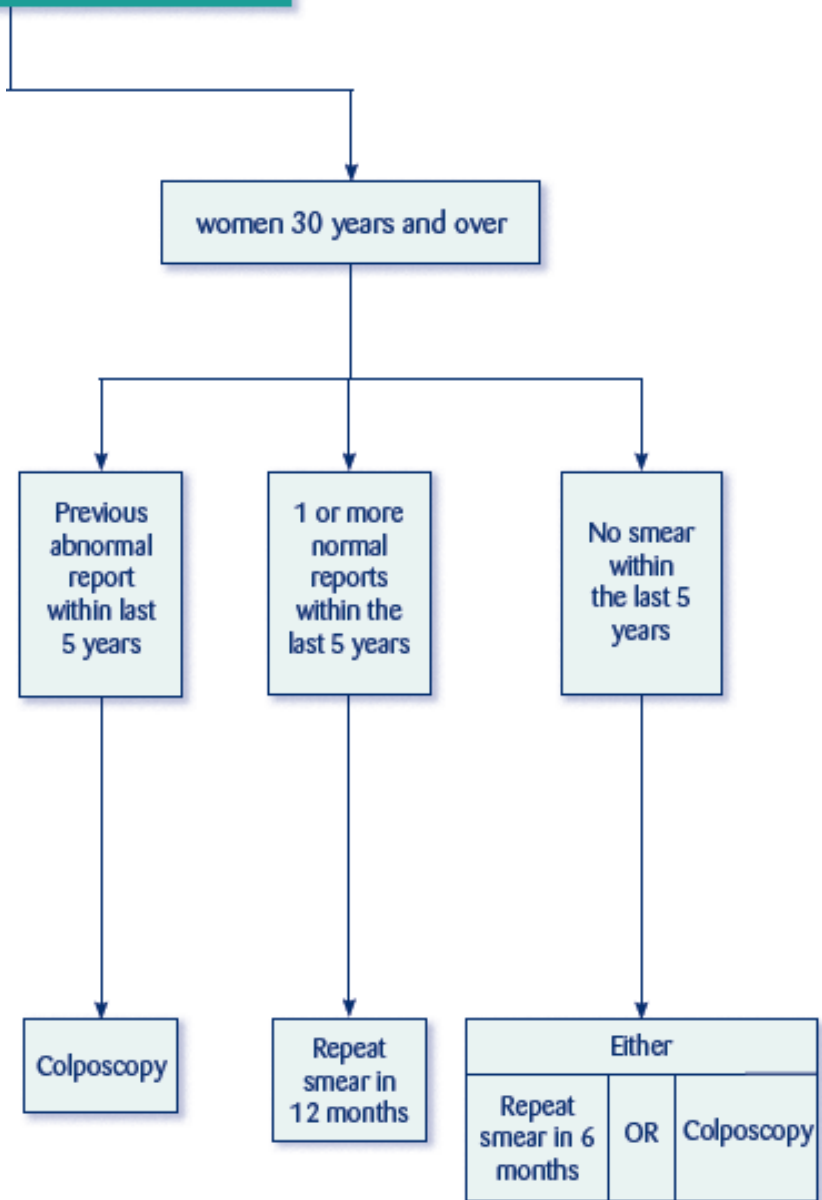
LSIL and Neoplasia

- **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



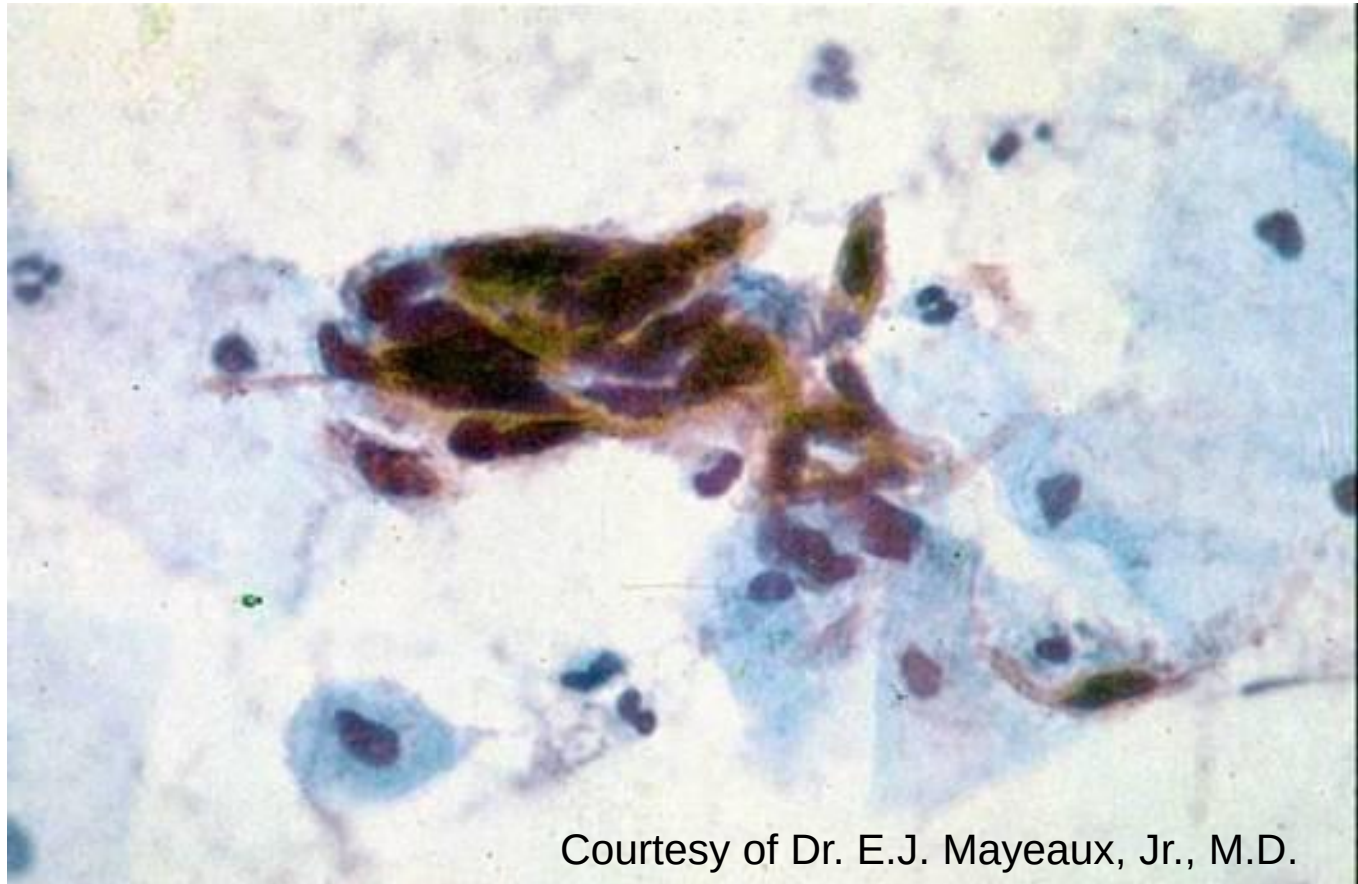
Cervical smear report ASC-US/LSIL



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

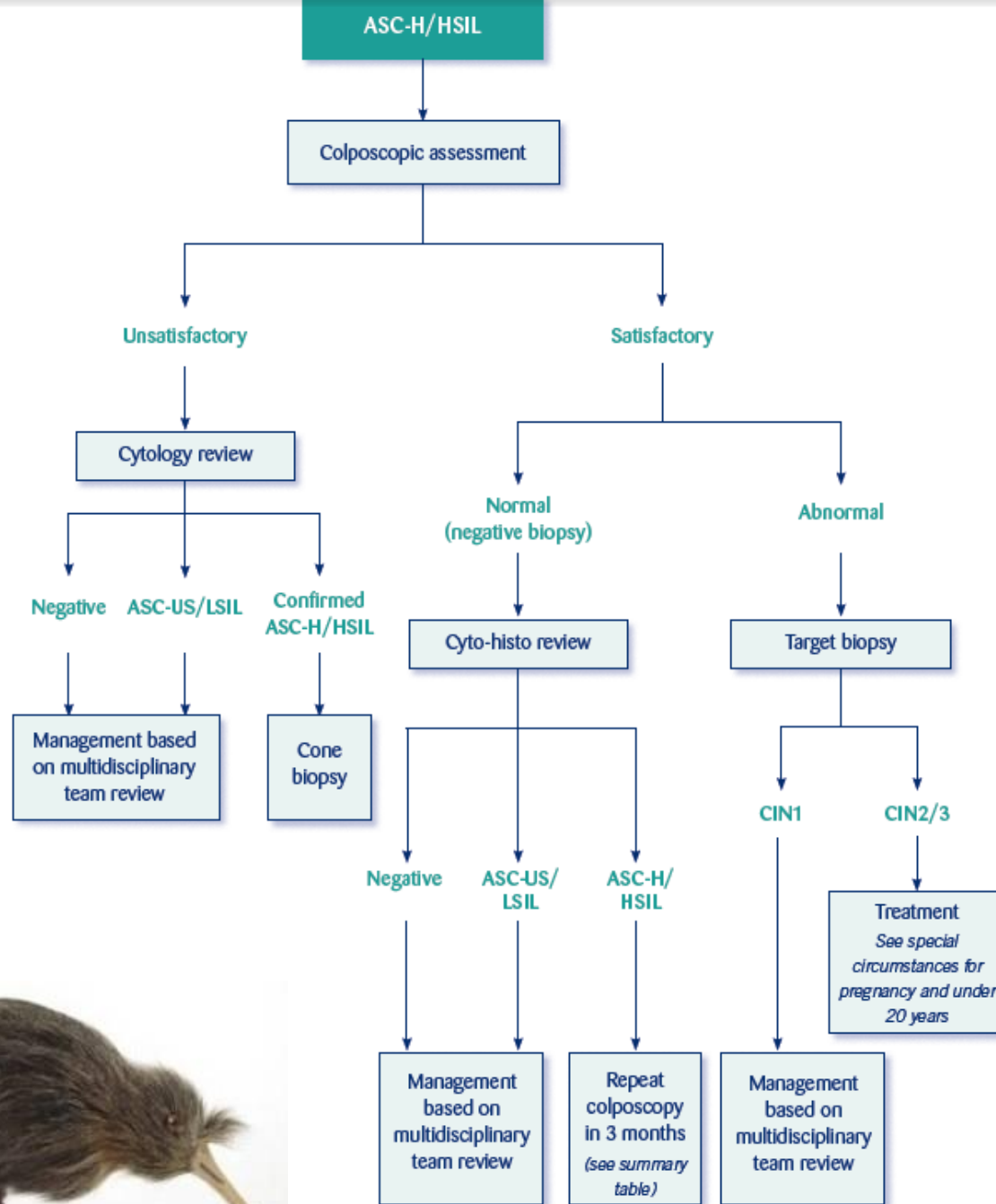


HSIL/ASC-H



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

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



As from 1 July 2009 HPV testing may be used in some of the above situations to aid further management

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%

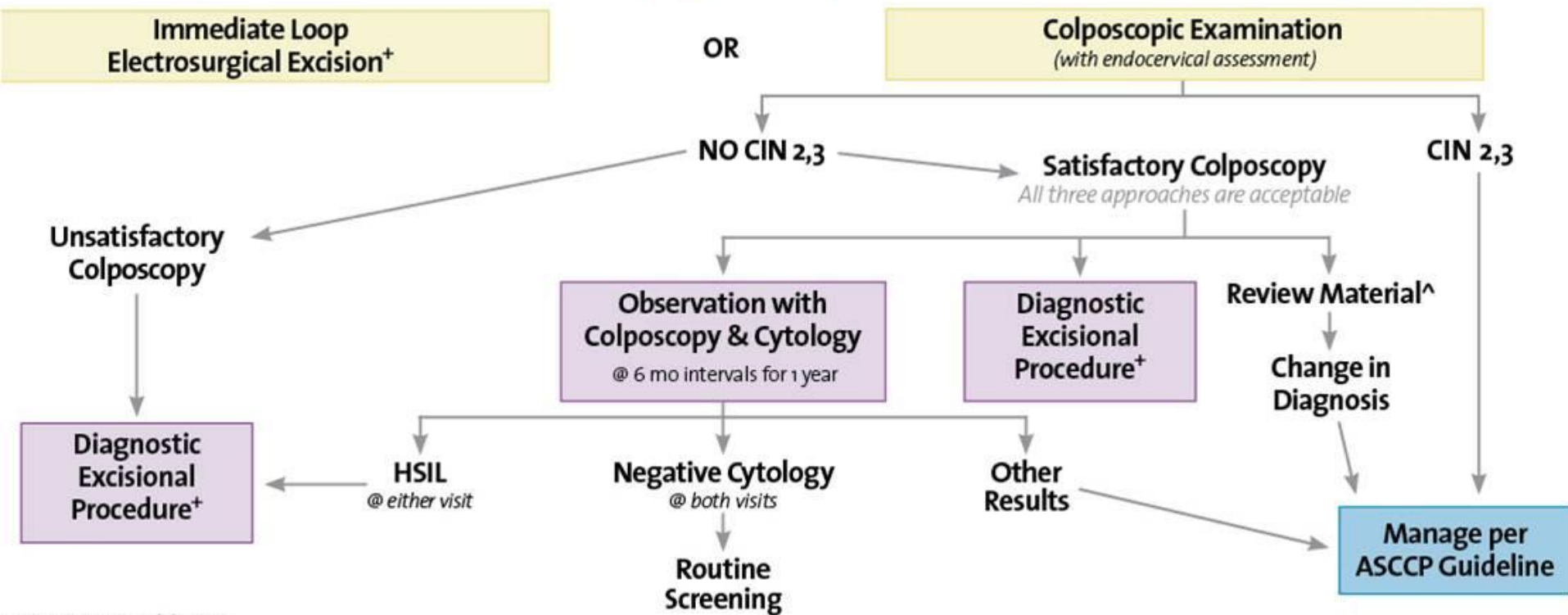
HSIL Management

- 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

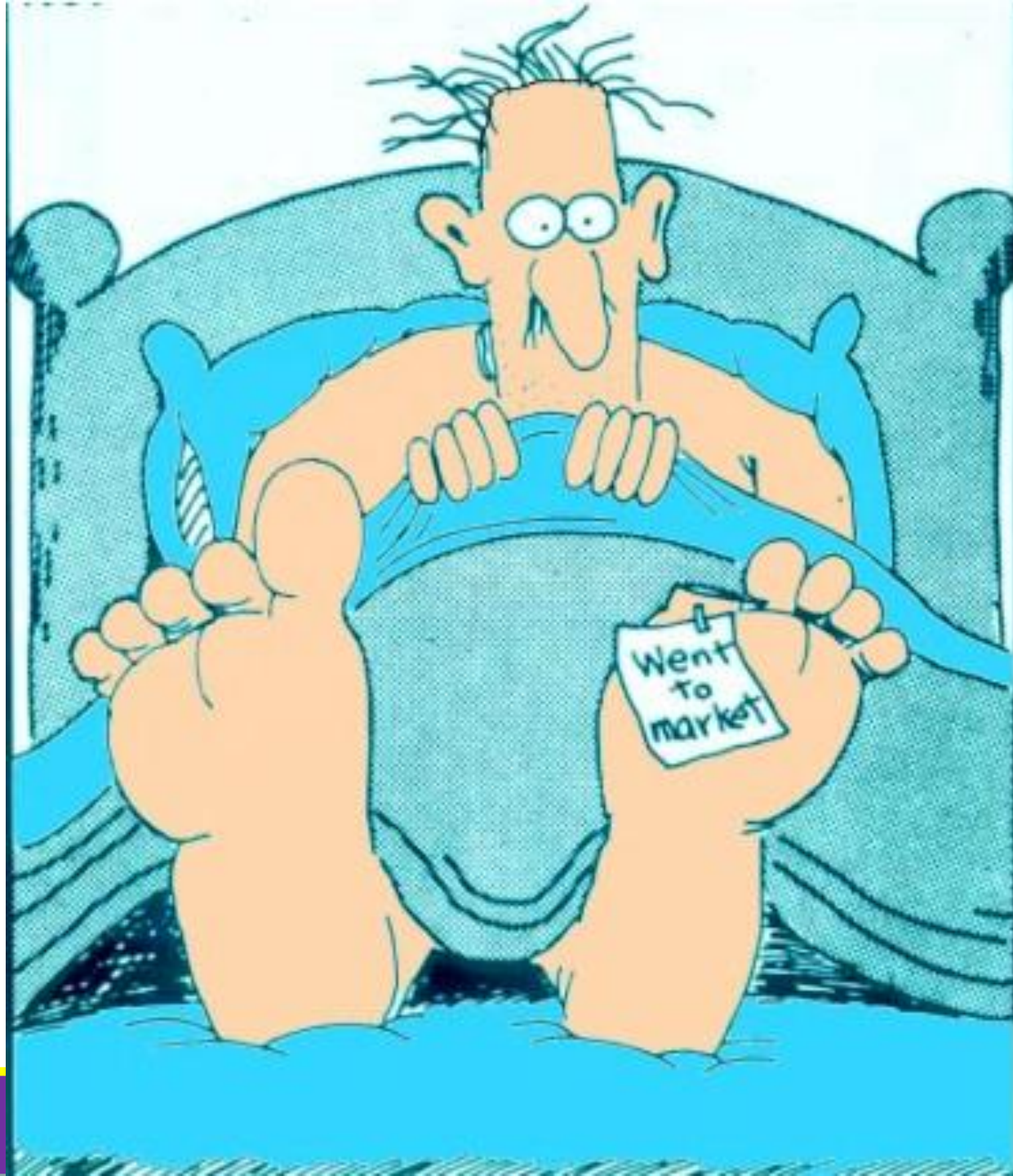
- **Immediate loop excision and colpo with ECC/B = weight**
 - **Rationale: Prospective studies showing high yield of CIN2,3 with lower cost and fewer women lost to follow-up**
 - **ALTS, only 54% of CIN3 found at colpo**
- Wright TC, et al. Am J Obstet Gynecol 2007; 197(4):346-355
www.asccp.org

Management of Women with High-grade Squamous Intraepithelial Lesion (HSIL) *

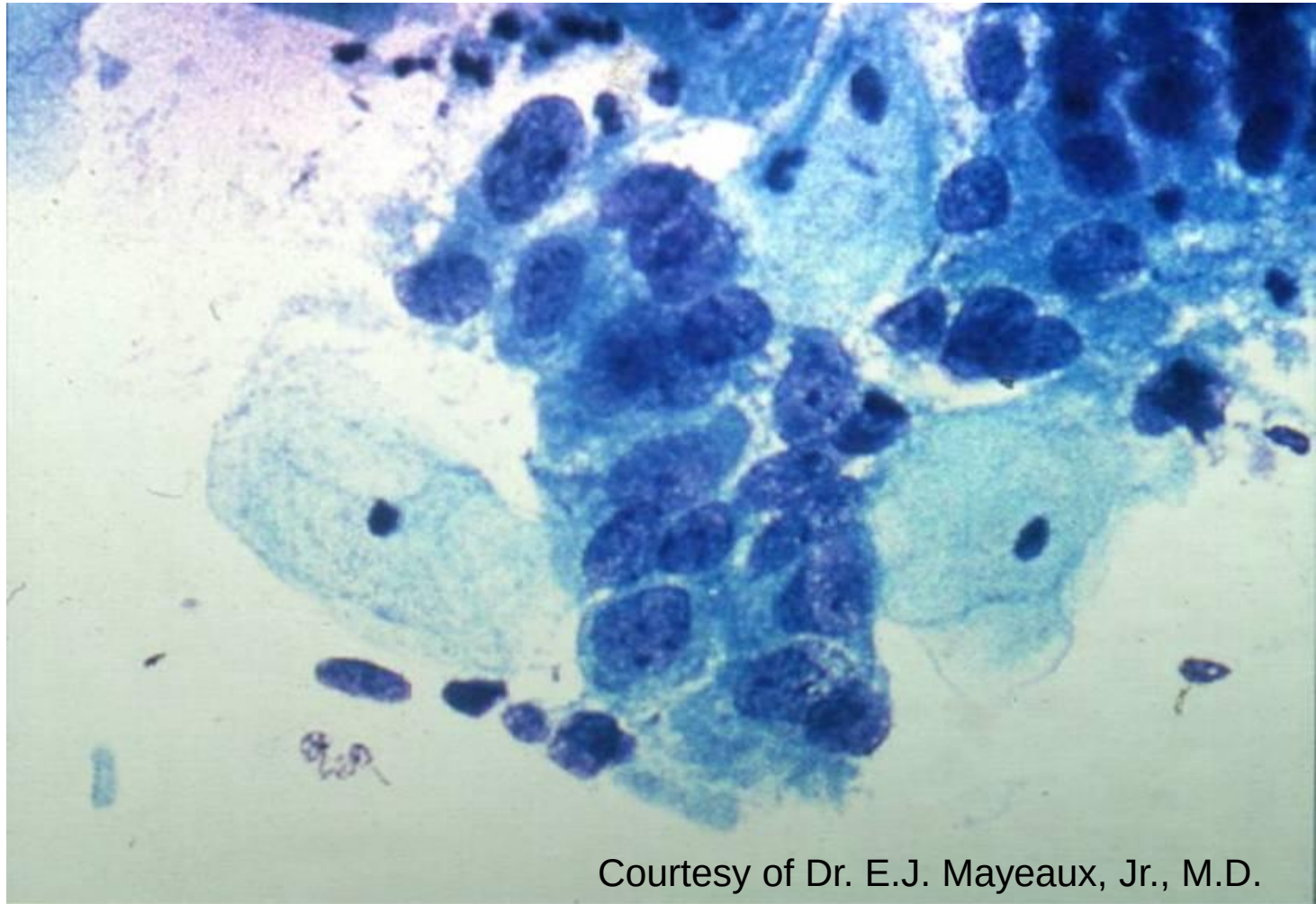


** For pregnant or an adolescent woman, management options may vary if the woman is pregnant, postmenopausal, or an adolescent*

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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**

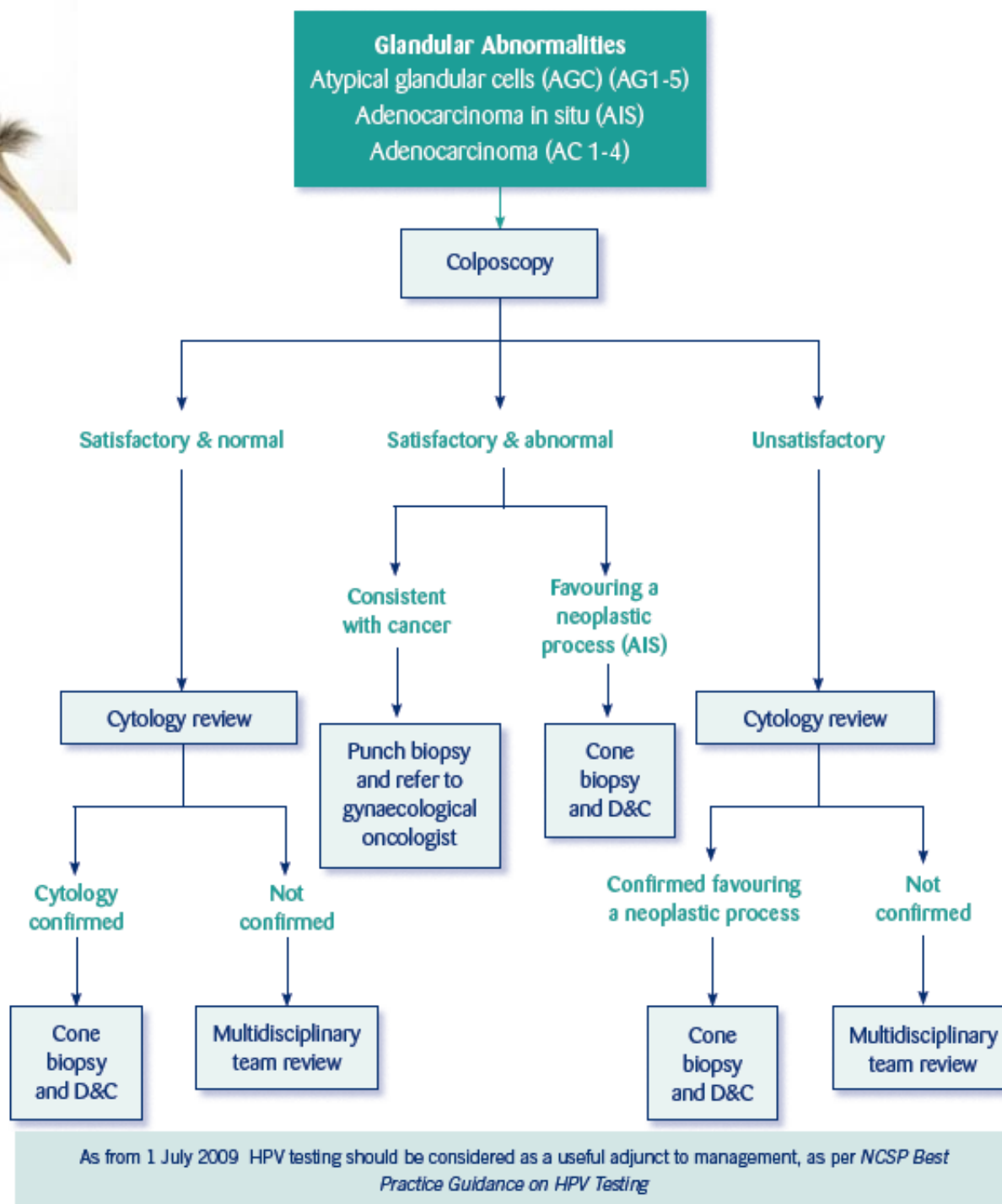
Atypical glandular cells

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

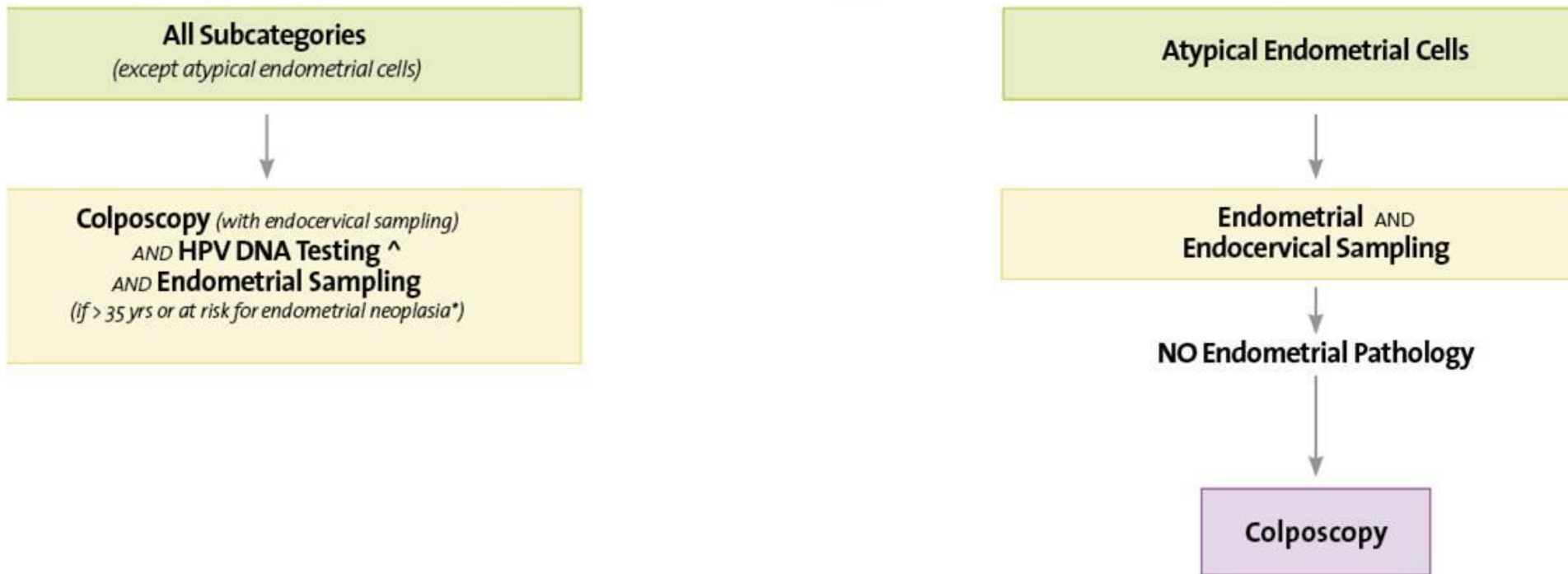
CIN1/HPV	8.5%
CIN 2,3	11.1%
AIS	2.9%
Endometrial hyperplasia	1.4%
Cancer	5.2%

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



Initial Workup of Women with Atypical Glandular Cells (AGC)



dy obtained. Test only for high-risk (oncogenic) types.
explained vaginal bleeding or conditions suggesting chronic anovulation.

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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.

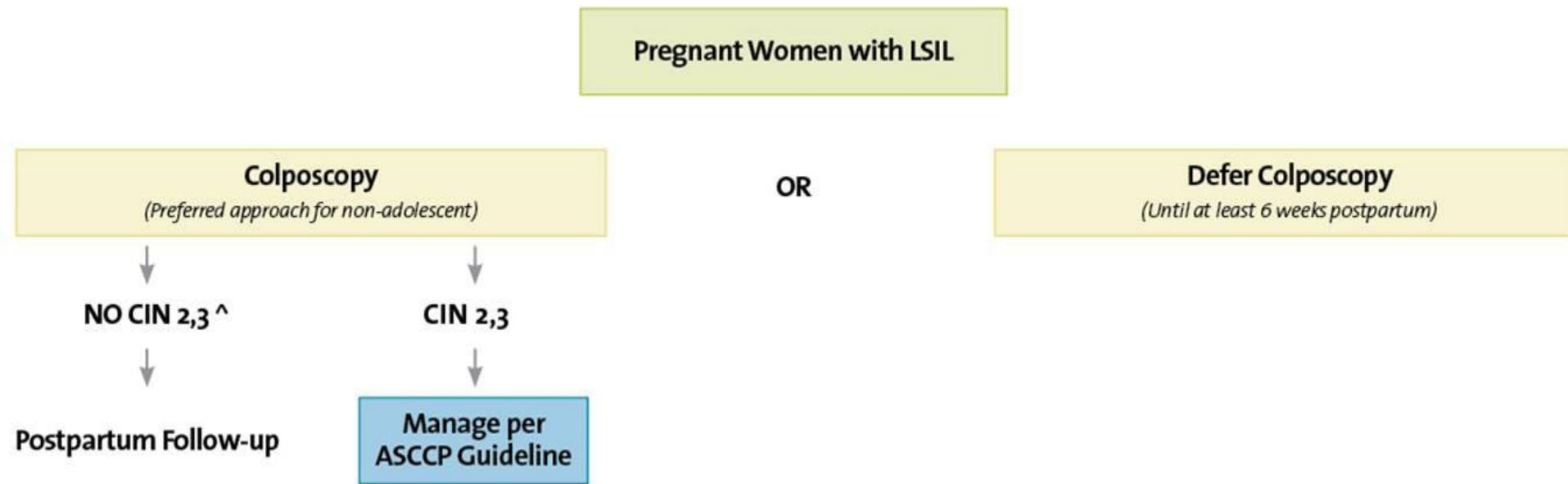
US Pregnancy 2006 Changes

- **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**

Management of Pregnant Women with Low-grade Squamous Intraepithelial Lesion (LSIL)



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[^] In women with no cytological, histological, or colposcopically suspected CIN 2, 3.

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IN CASE OF EMERGENCY



