

A User-Friendly Guide To Cervical Cancer Prevention

Philip E. Castle, PhD, MPH

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My Disclosures & Potential Conflicts of Interest

- I have received commercial HPV tests for research at a reduced or no cost from Roche, Qiagen, Norchip, and MTM.
- I am a paid consultant for BD and GE Healthcare; I have received a speaker's honorarium from Roche.
- I am a paid consultant for Immunexpress on sepsis diagnostics.
- I am compensated as a member of a Merck Data and Safety Monitoring Board for HPV vaccines.



"I'll have an ounce of prevention."

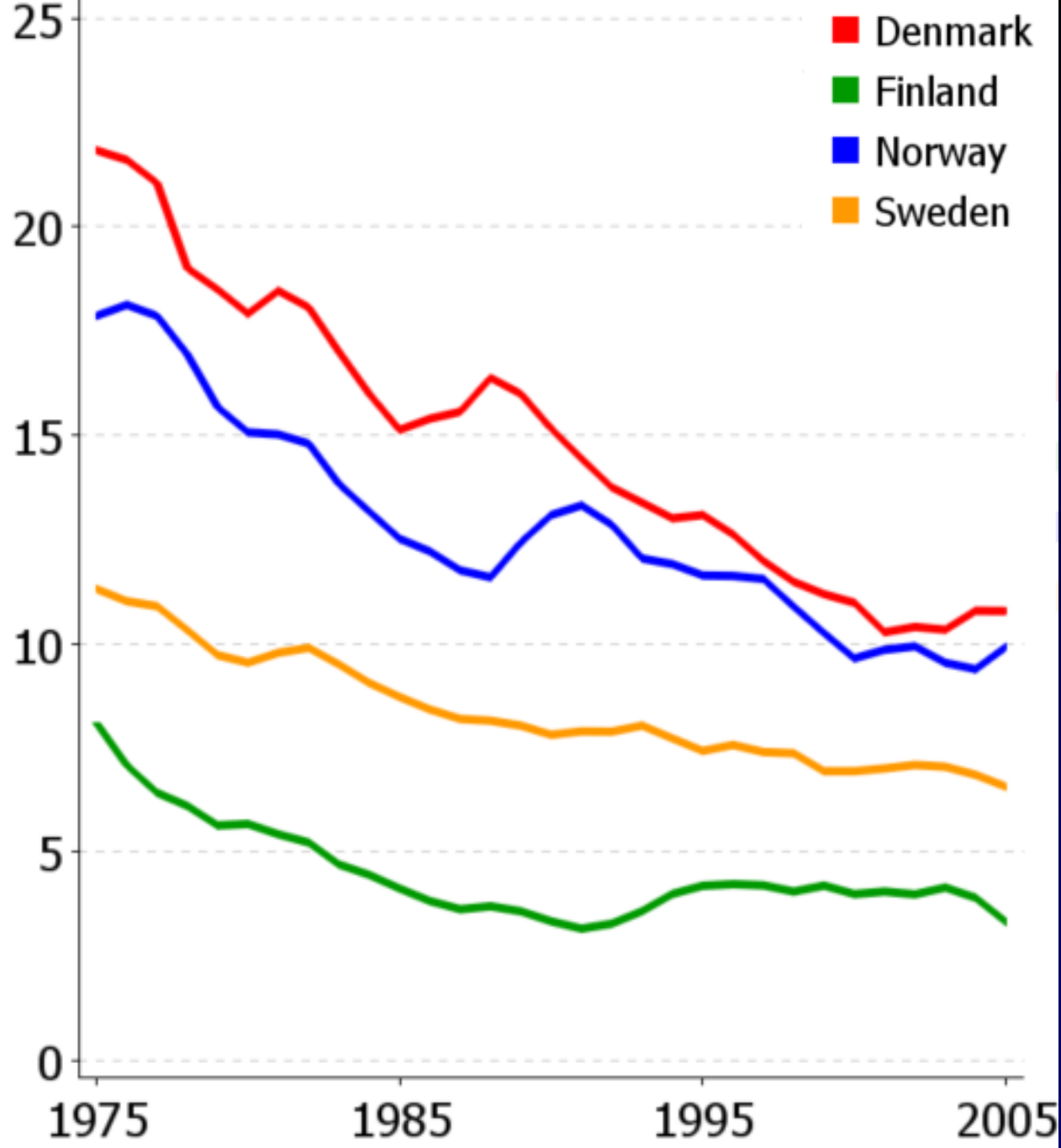
Today's Talk

1. Global Perspective of Cervical Cancer
2. Natural History of HPV: Rational Basis for Cervical Cancer Prevention
3. Targeting the Causal Factor: HPV Vaccines and Testing
4. New Screening Guidelines
5. Reaching the Hard-to-Reach

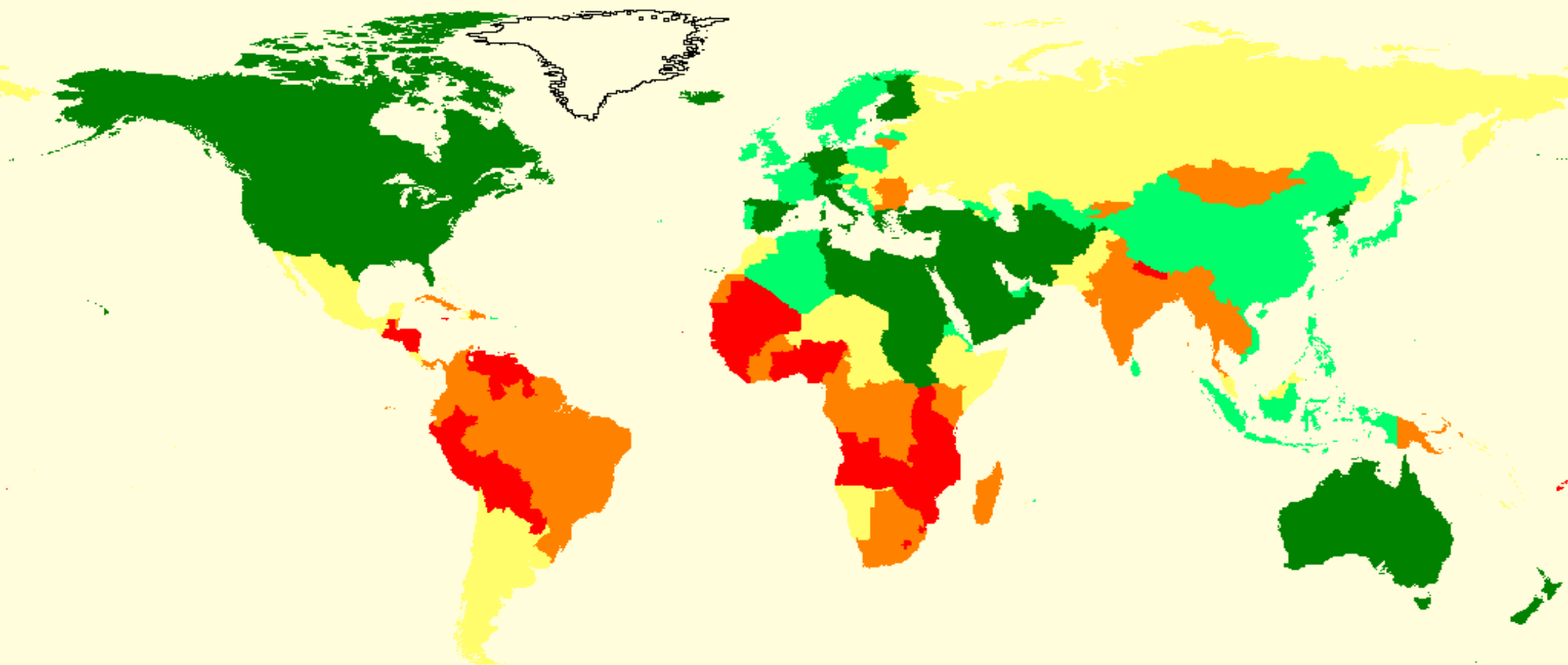
George Papanicolaou (1883-1962): Inventor of the Pap Smear



**TIME TRENDS
IN AGE-
STANDARDIZED
(WORLD)
CERVICAL
CANCER
INCIDENCE IN
FOUR NORDIC
COUNTRIES**



Estimated age-standardised incidence rate per 100,000 Cervix uteri, all ages



< 7.0 **< 12.9** **< 20.3** **< 29.8** **< 56.3**

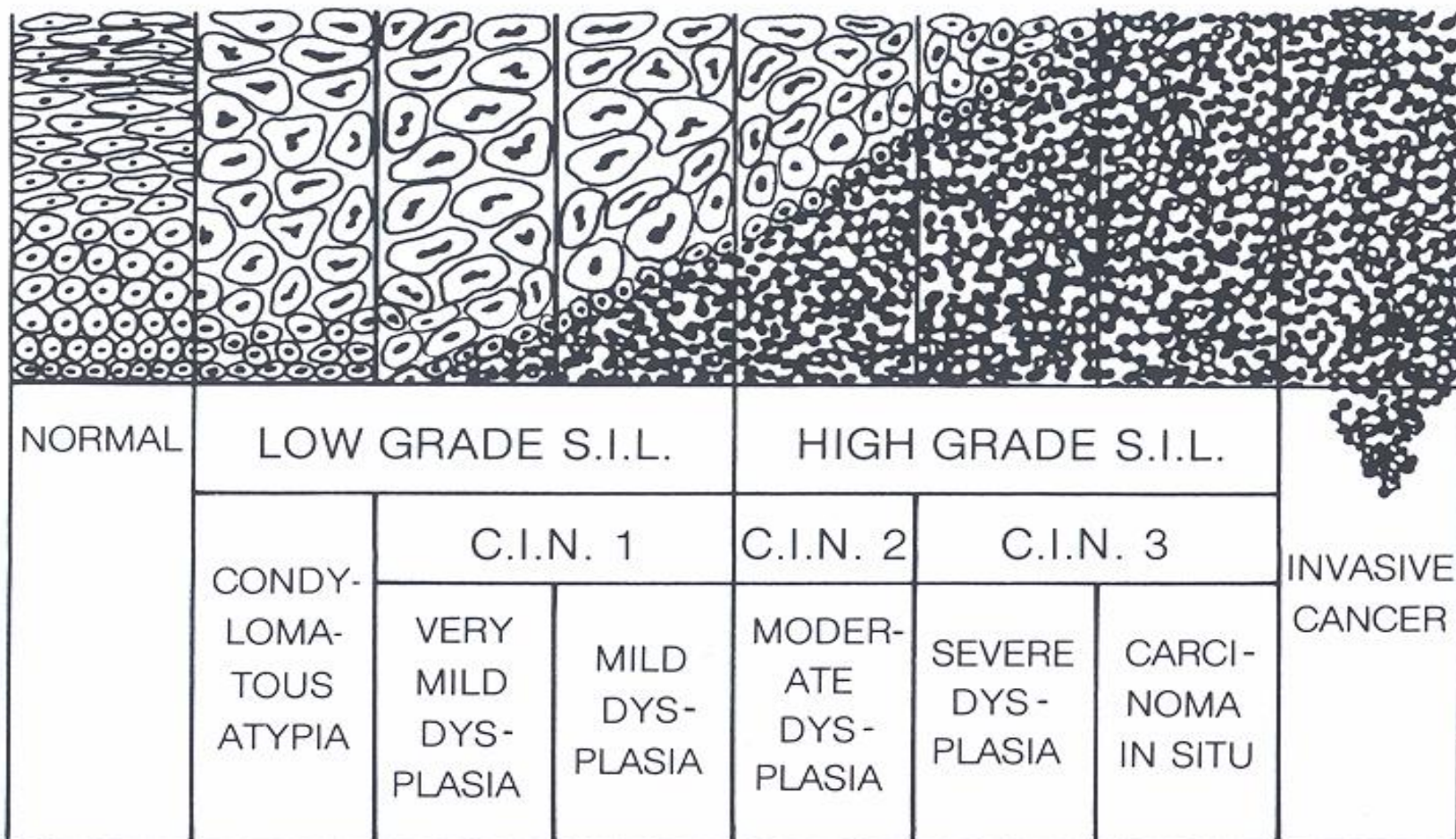
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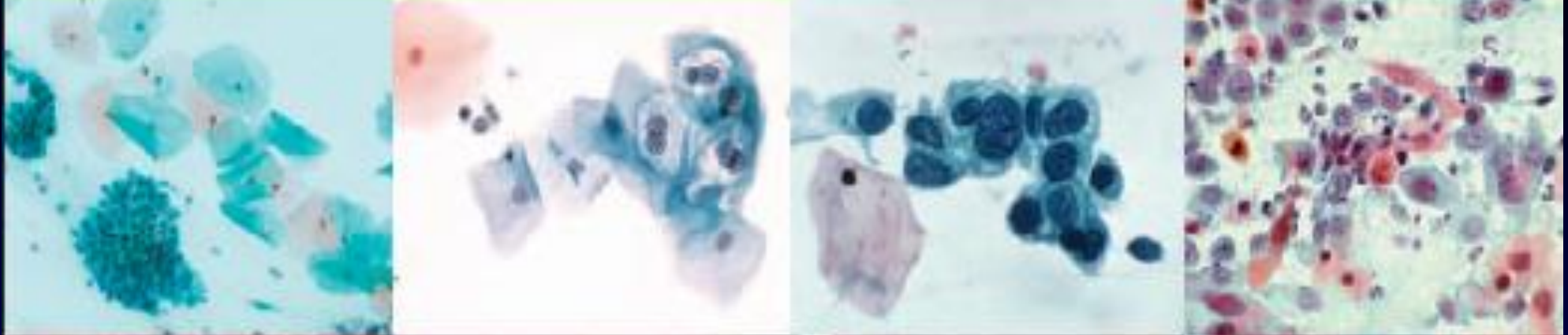
Cervical Cancer Continuum: Old Model of Cervical Carcinogenesis

Surface of epithelium

Basal epithelium



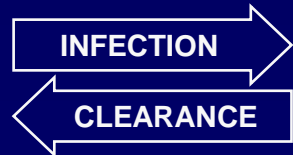
New Model of Cervical Carcinogenesis



Transient infection

Persistent HPV

Normal cervix



HPV-infected cervix

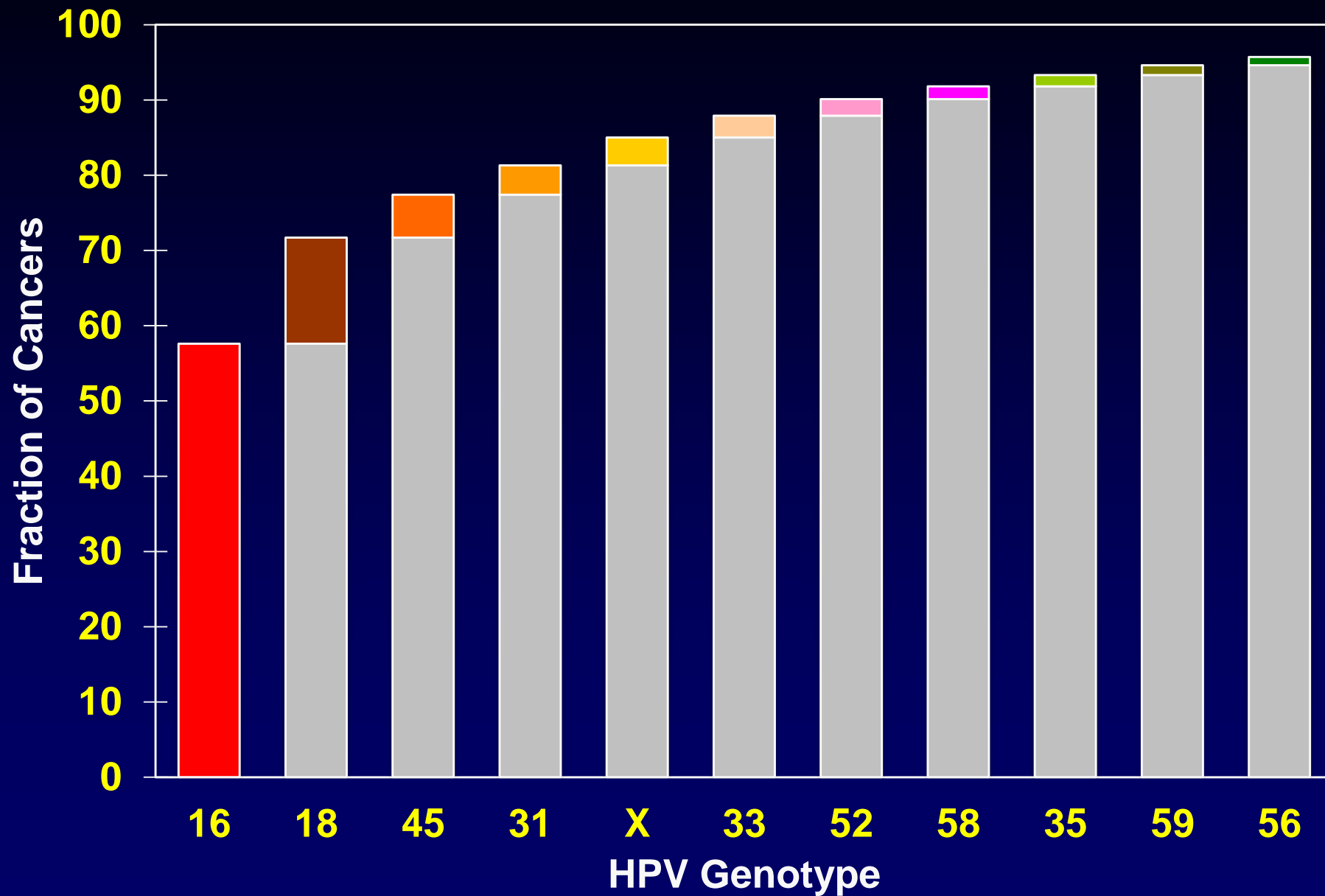


Precancer

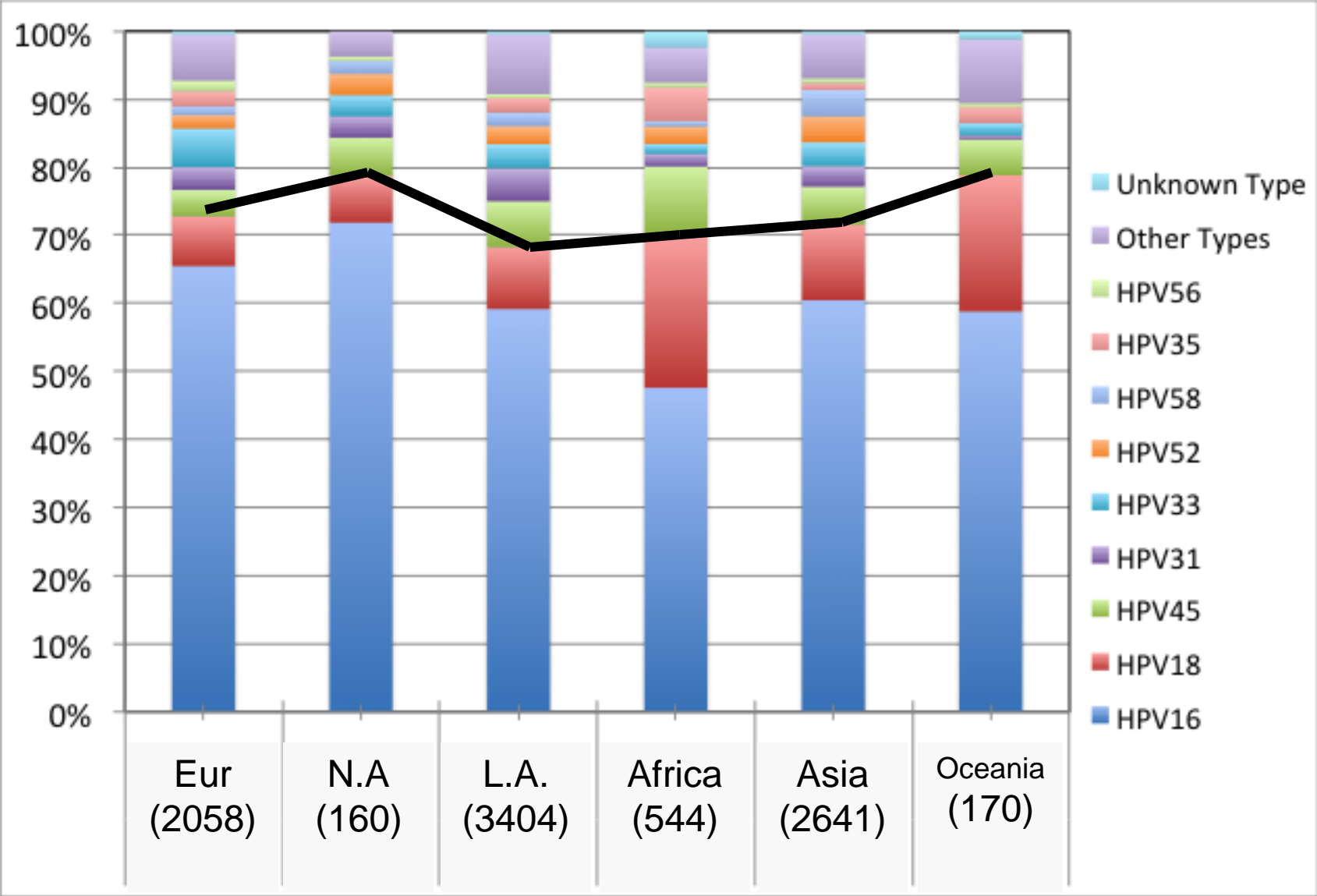


Cancer

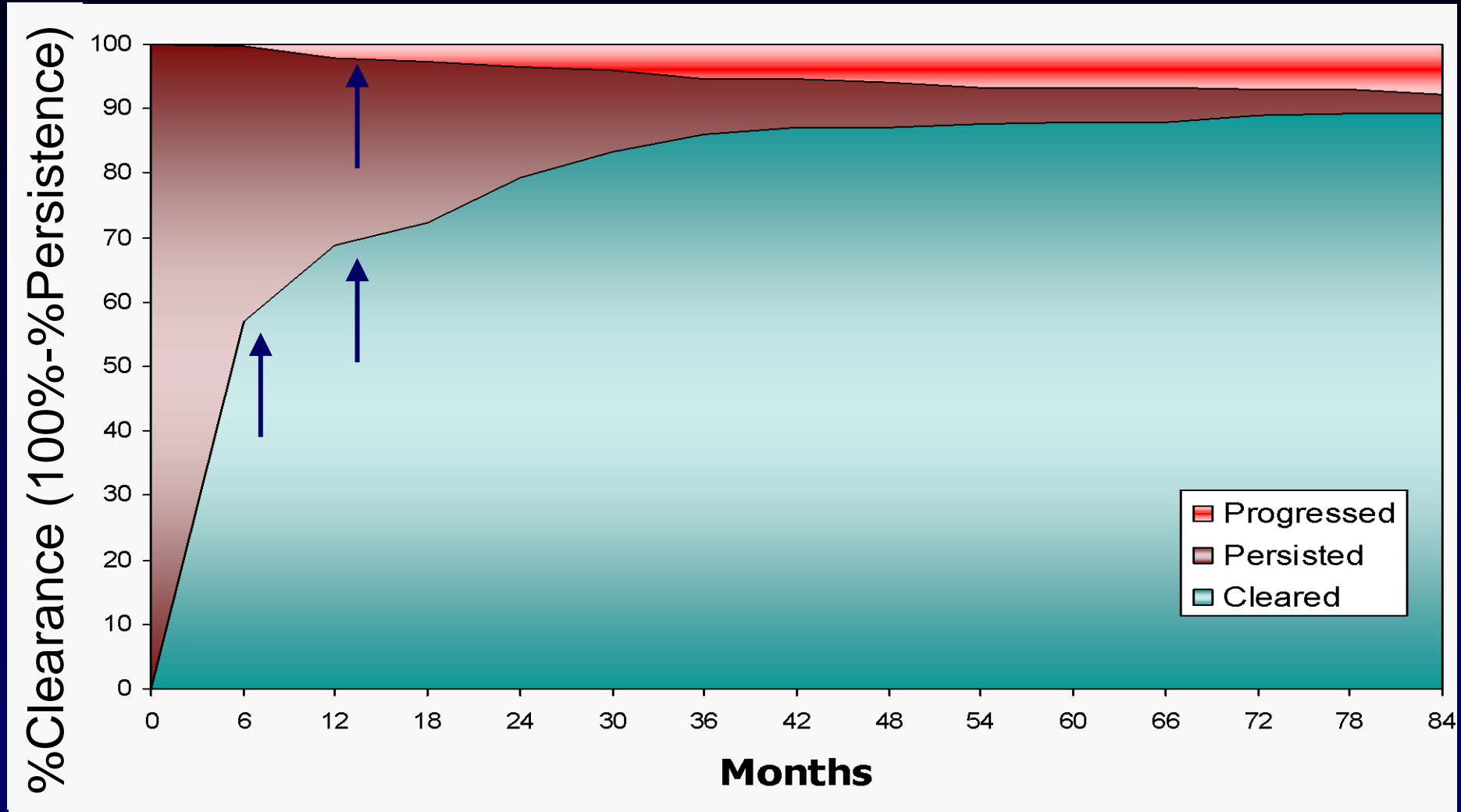
Etiologic Contribution of HPV Genotypes



Regional Variation of HPV Genotypes in CxCa



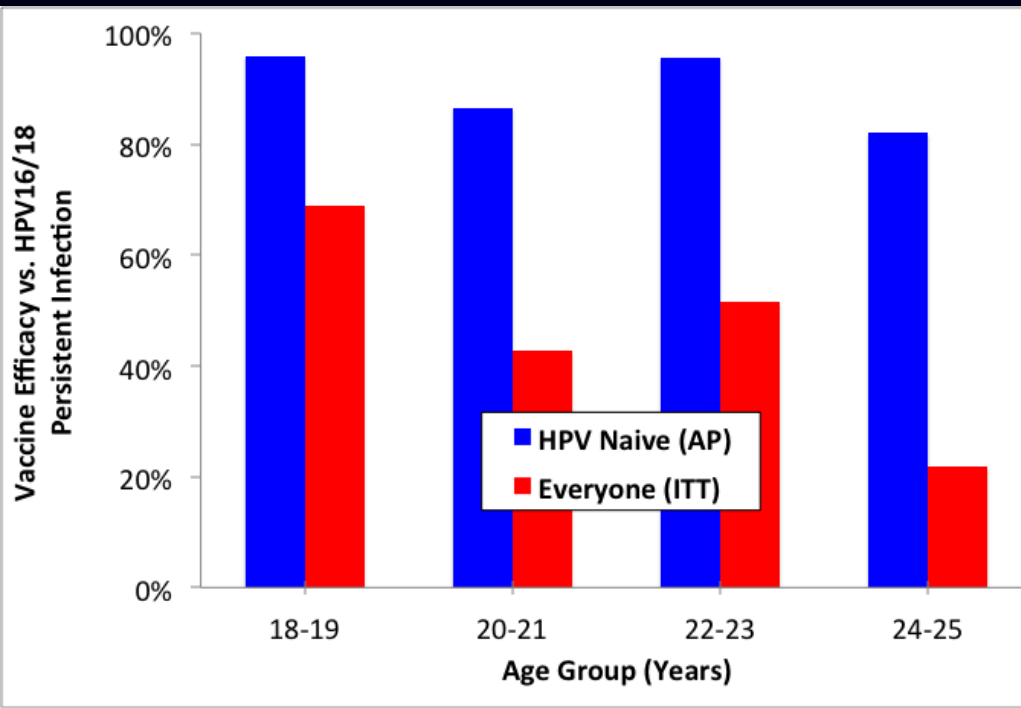
Natural History Profile of Prevalent HPV



Today's Talk

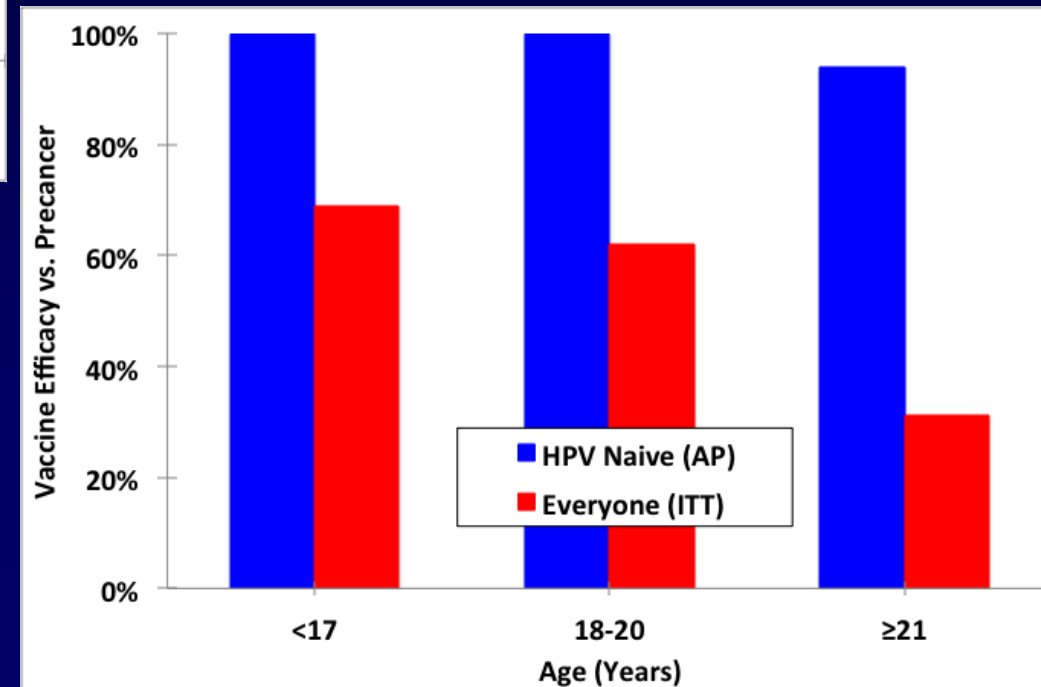
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Impact of Age on Vaccine Efficacy



Herrero *et al.*, Cancer Discov, 2012

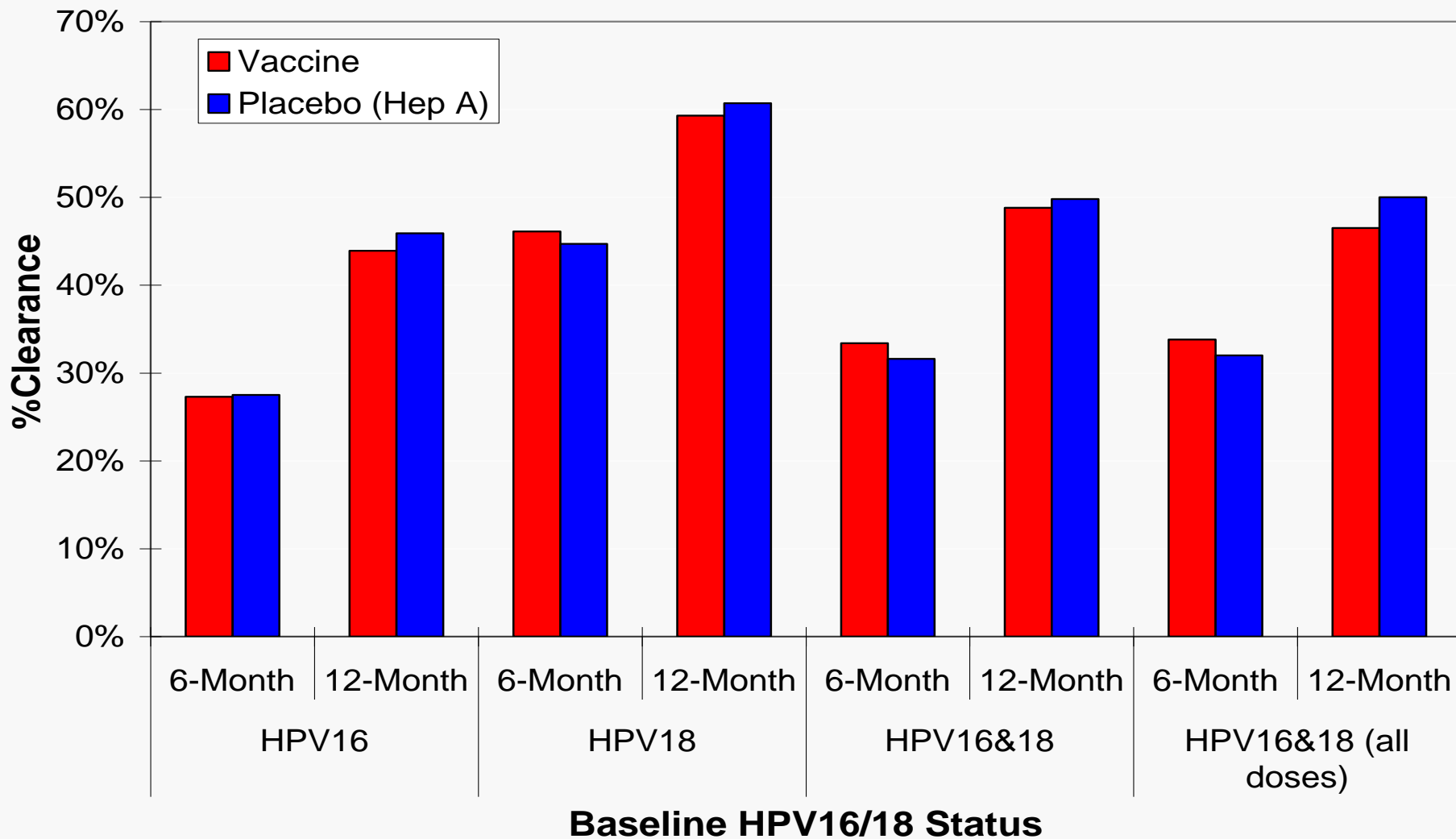
Kjaer, Cancer Prev Res, 2009



HPV-16/18 Clearance by Trial Arm



C
V
T



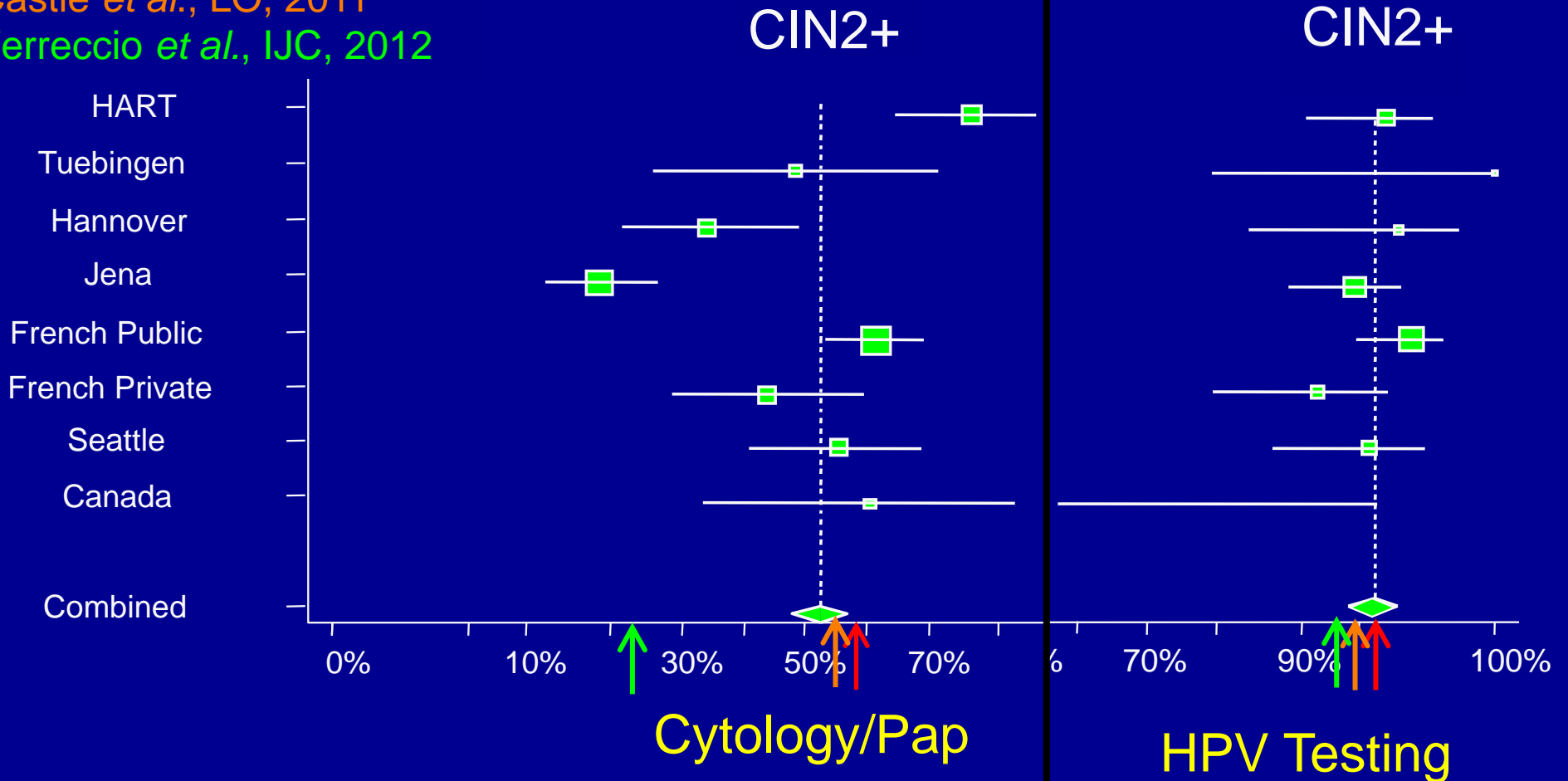
Sensitivity: CIN2+

Cuzick *et al.*, IJC, 2006

Mayrand *et al.*, NEJM, 2007

Castle *et al.*, LO, 2011

Ferreccio *et al.*, IJC, 2012



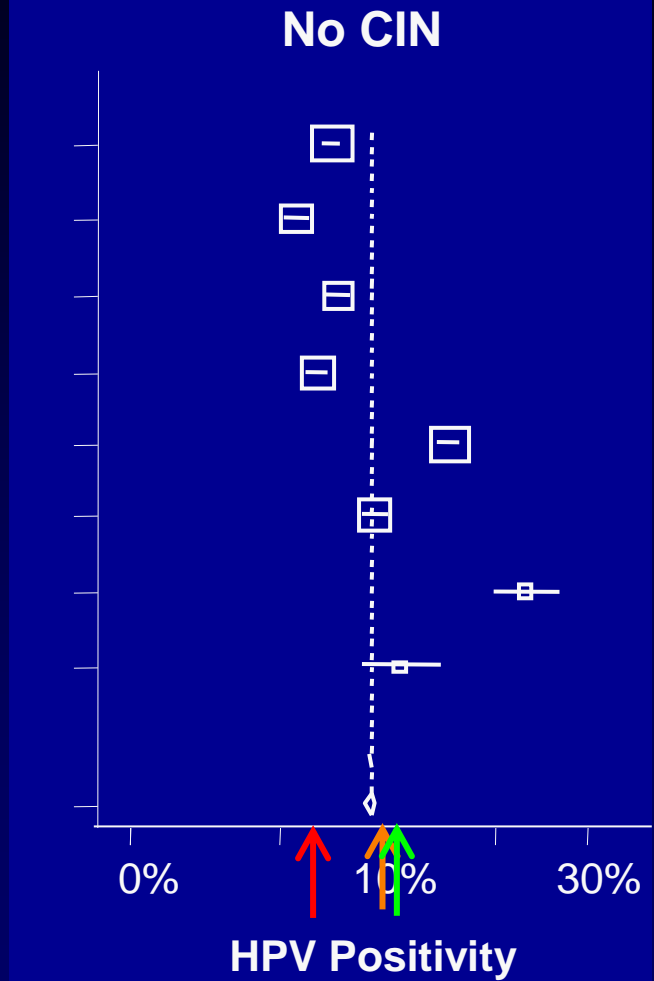
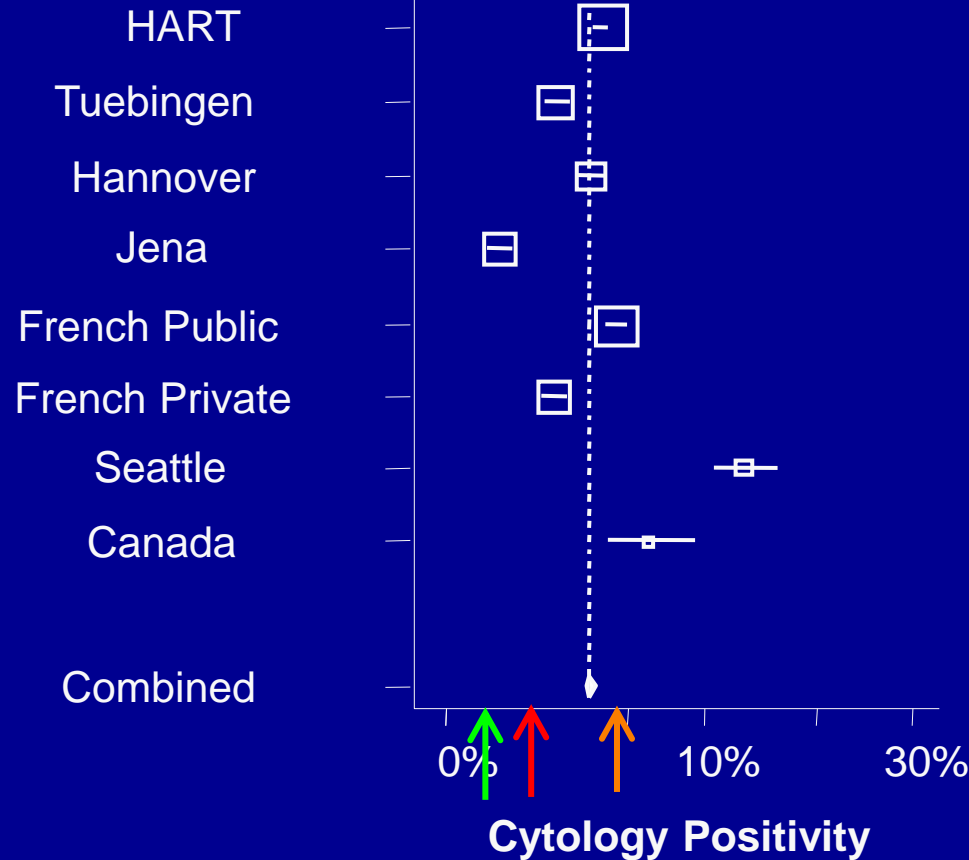
%Cytology and HPV Positive: No CIN

Cuzick *et al.*, IJC, 2006

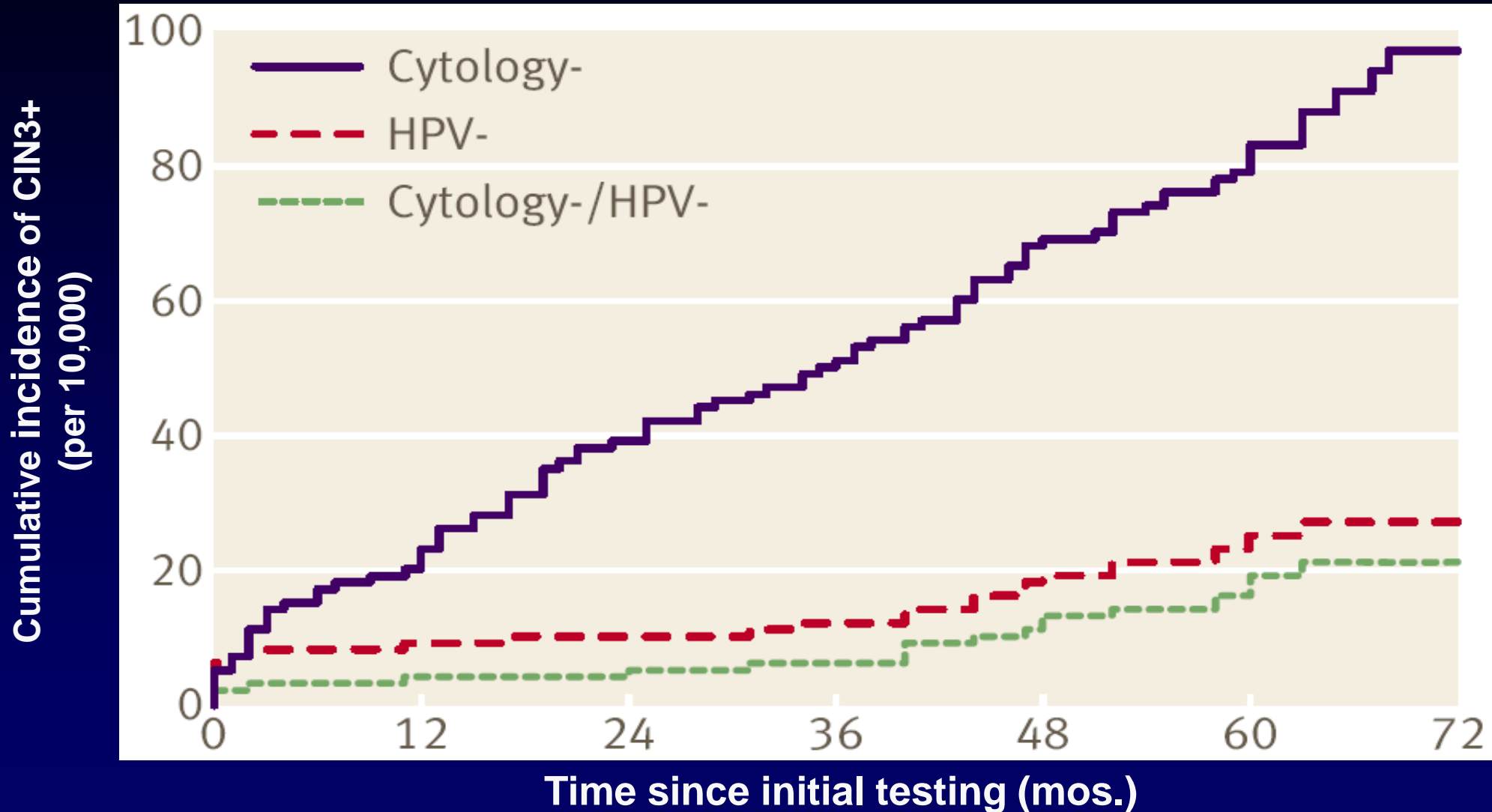
Mayrand *et al.*, NEJM, 2007

Castle *et al.*, LO, 2011

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CIN3+ Risk Following a Negative Screening Test



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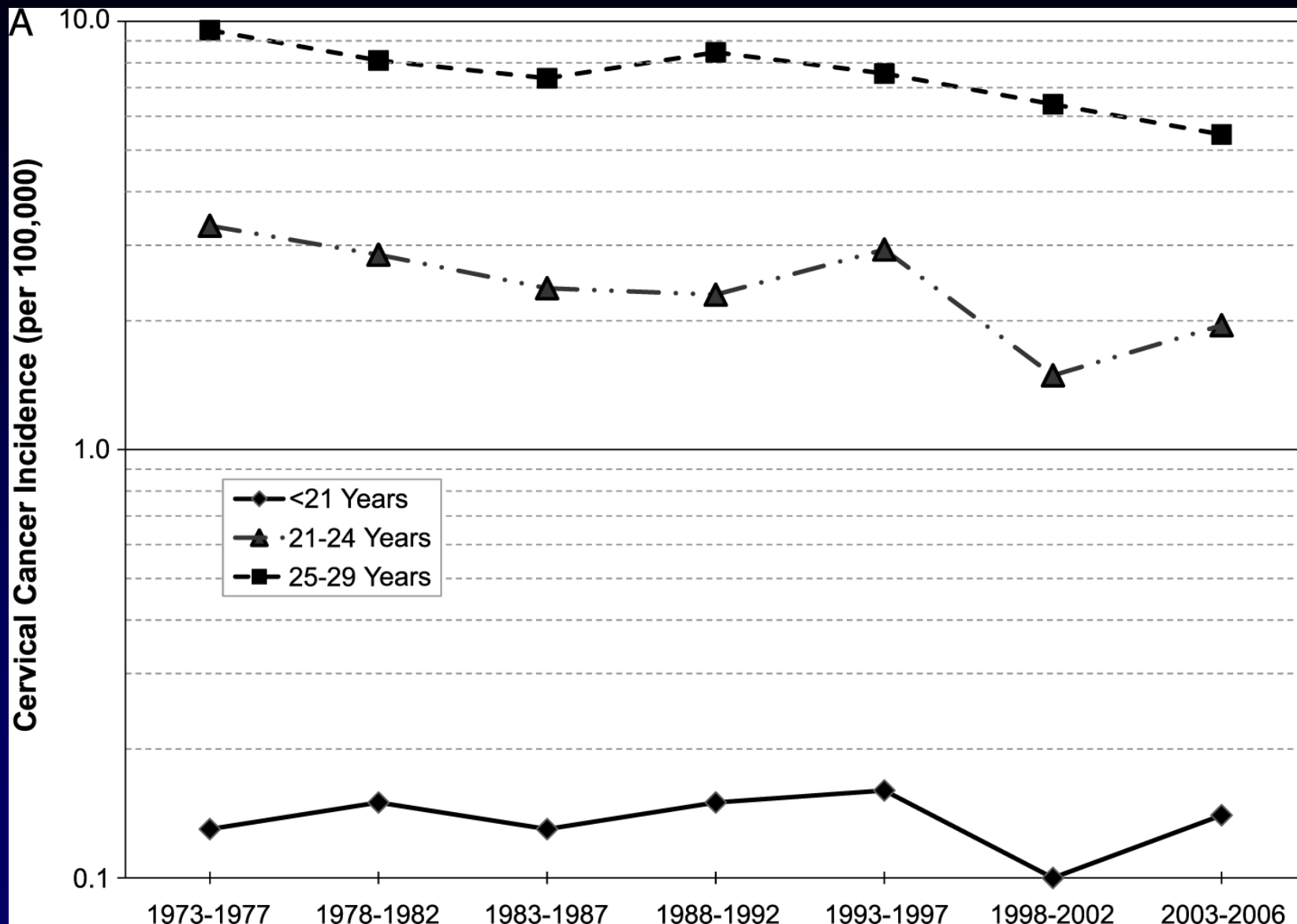
Benefits vs. Harms

	Benefits	Harms
Actual	✧ Cervical cancer prevention	<ul style="list-style-type: none">➤ Anxiety associated with a positive screening test➤ Potential stigmatization from the diagnosis of a sexually transmitted infection➤ Discomfort from additional diagnostic and treatment procedures➤ Bleeding from treatment➤ Increased risk of pregnancy complications such as preterm delivery due to treatment.
Surrogate	Early detection of CIN3	Number of colposcopic referrals

Current ACS Cervical Cancer Screening Guidelines (2012)

<u>Age (Years)</u>	<u>Recommended Screening</u>
<21	No Screening!!!!
21-29	Cytology (3 Year)
30-64	HPV and Cytology Cotesting (5 Year) (Preferred) Cytology (3 Year) Acceptable)
65 and Older	No Screening with a 10-Year Negative Screening History

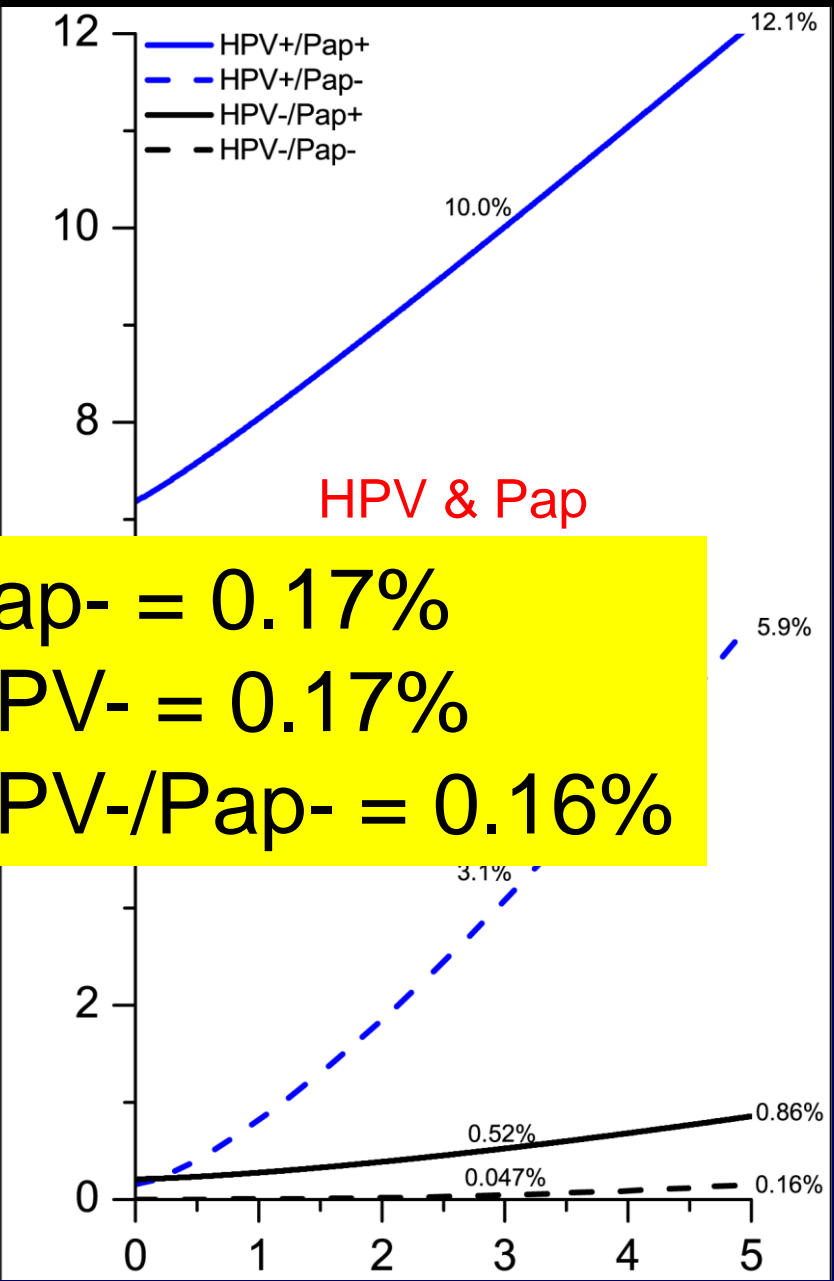
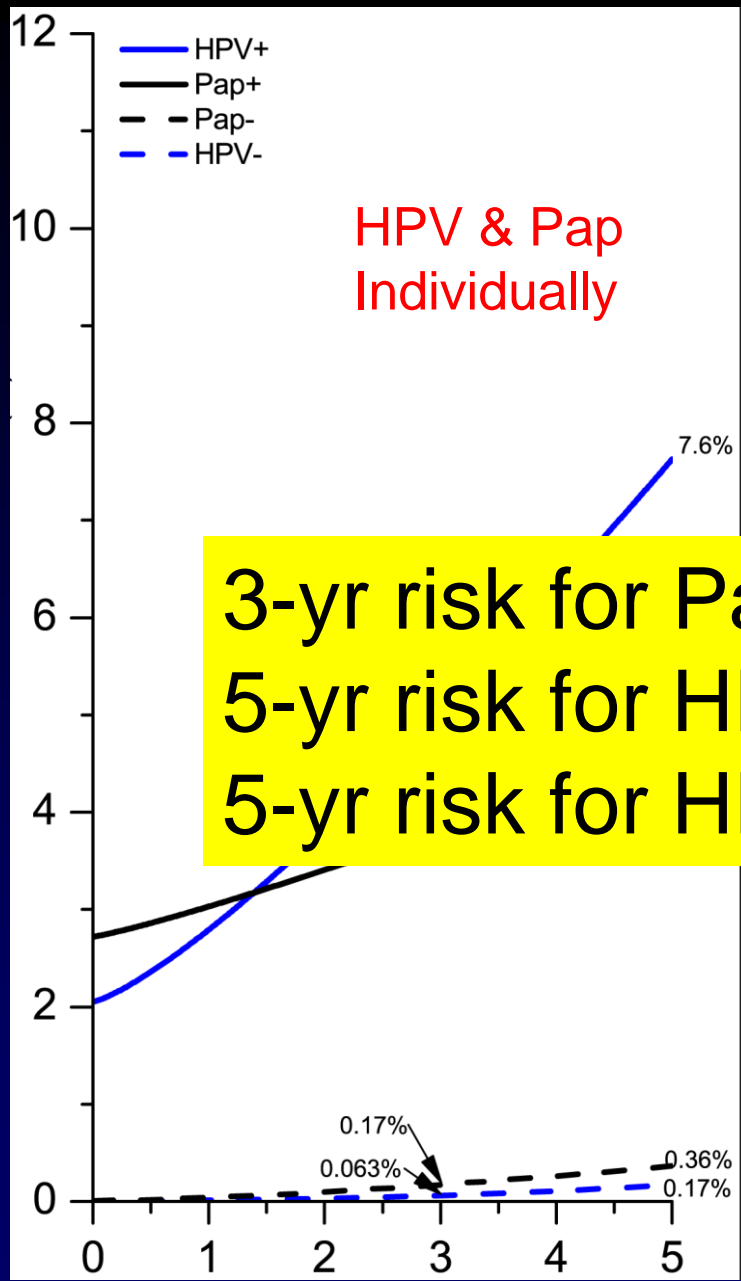
Cervical Cancer Incidence by Age (USA)



Cytology Screening Interval: Cancer Risk vs. Colposcopy

	Lifetime (per 1,000)	
	Cancer Risk	Number of Colposcopies
Every Year	3	2000
Every 2 Years	4 to 6	1080
Every 3 Years	5 to 8	760

Cumulative Incidence of CIN3+



3-yr risk for Pap- = 0.17%
 5-yr risk for HPV- = 0.17%
 5-yr risk for HPV-/Pap- = 0.16%

Real World Performance

Years Since Enrollment

Katki et al., Lancet Oncol, 2011

Algorithm for Cotesting in Women 30-64 Y.O.

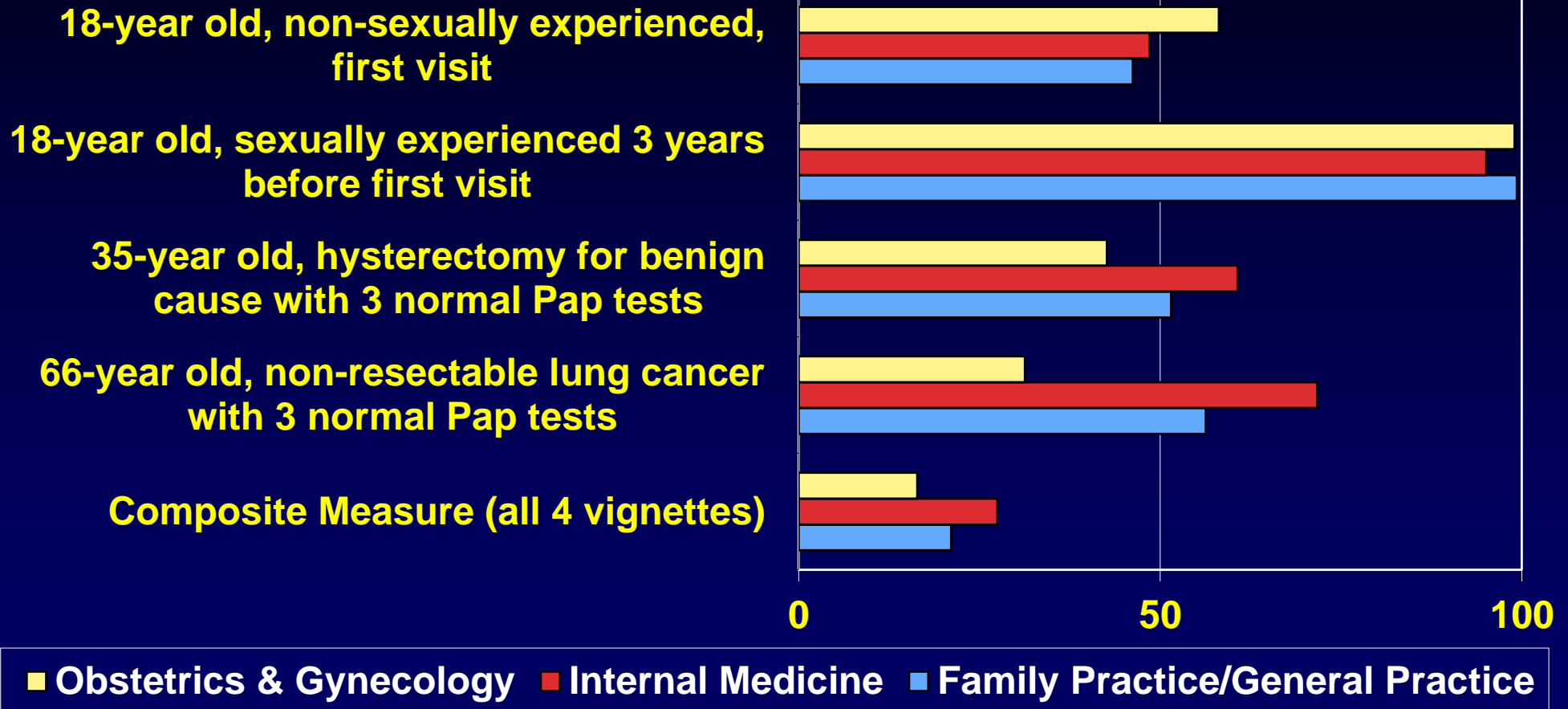
Current Screening Guidelines

HPV+Pap Cotesting
Every 5 Years*

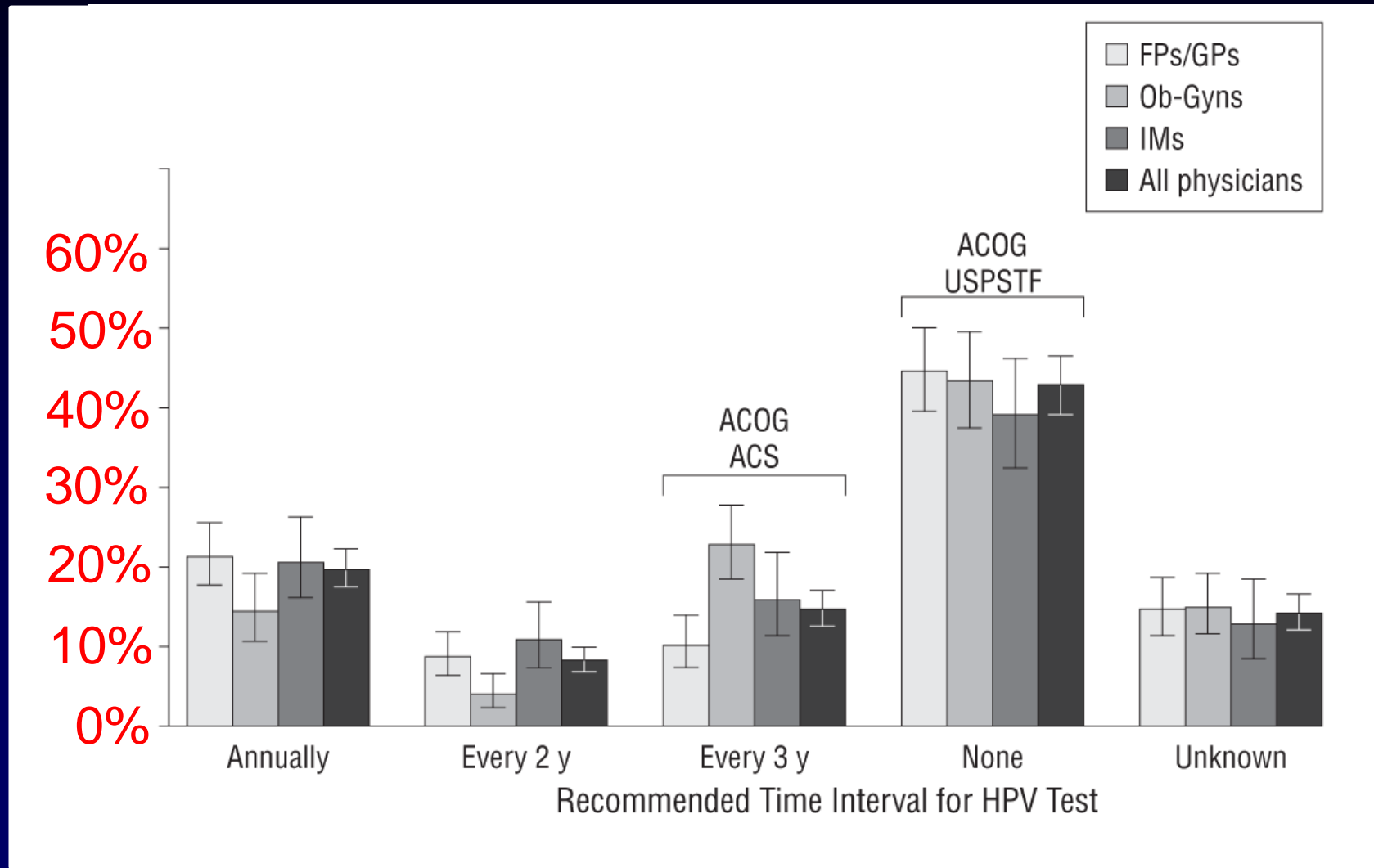


Guideline Failures

Percentage With Guideline-Consistent Recommendations



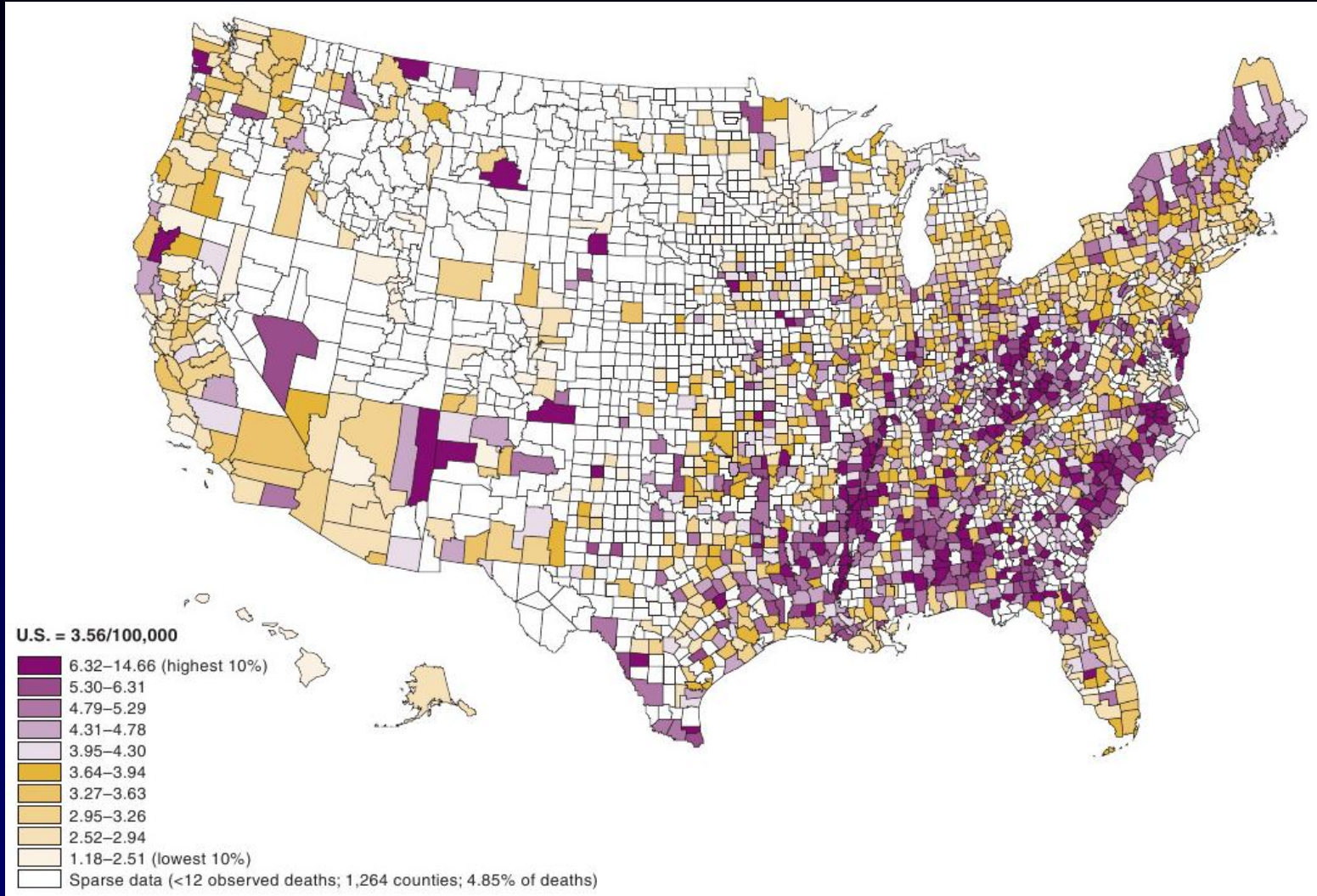
When Would Next HPV Test? 35 years, Pap Normal and HPV Negative?



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Cervical Cancer Mortality Map for The U.S.



Freeman HP, Wingrove BK. Excess Cervical Cancer Mortality: A Marker for Low Access to Health Care in Poor Communities. Rockville, MD: National Cancer Institute, Center to Reduce Cancer Health Disparities, May 2005. NIH Pub. No. 05–5282.

Cervical Cancer in Maryland

TABLE 3.6

Female Uterine Cancer Incidence and Mortality by Race in Maryland, 2002-2006

RACE/ETHNIC GROUP	INCIDENCE	MORTALITY
African American/Black	20.0	7.1
White	23.9	3.7
Hispanic/Latino	19.8	N/A
Asian/Pacific Islander	10.6	N/A
American Indian/Alaska Native	N/A	N/A

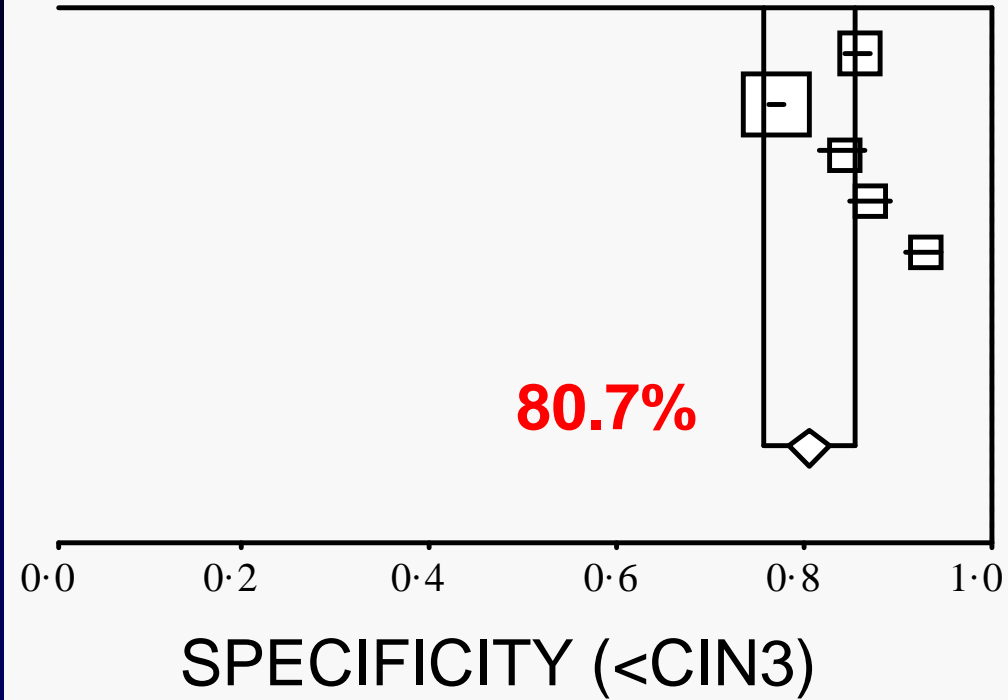
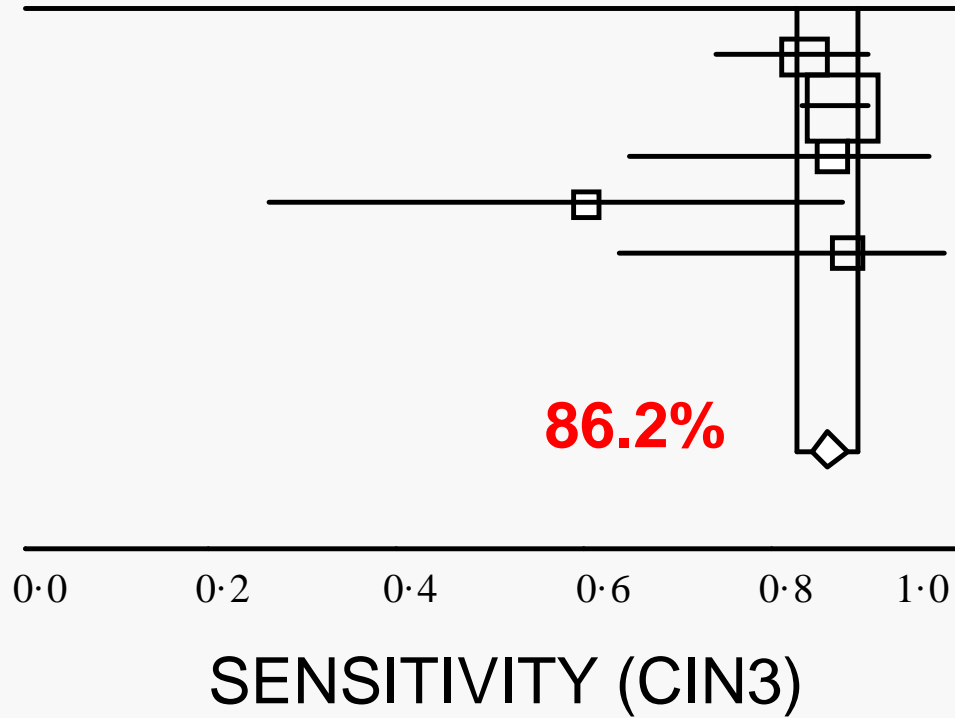
Rates are per 100,000 and are age-adjusted to the 2000 US standard population.

Source: United States Cancer Statistics: 1996-2006 Incidence and Mortality Web-based Report.

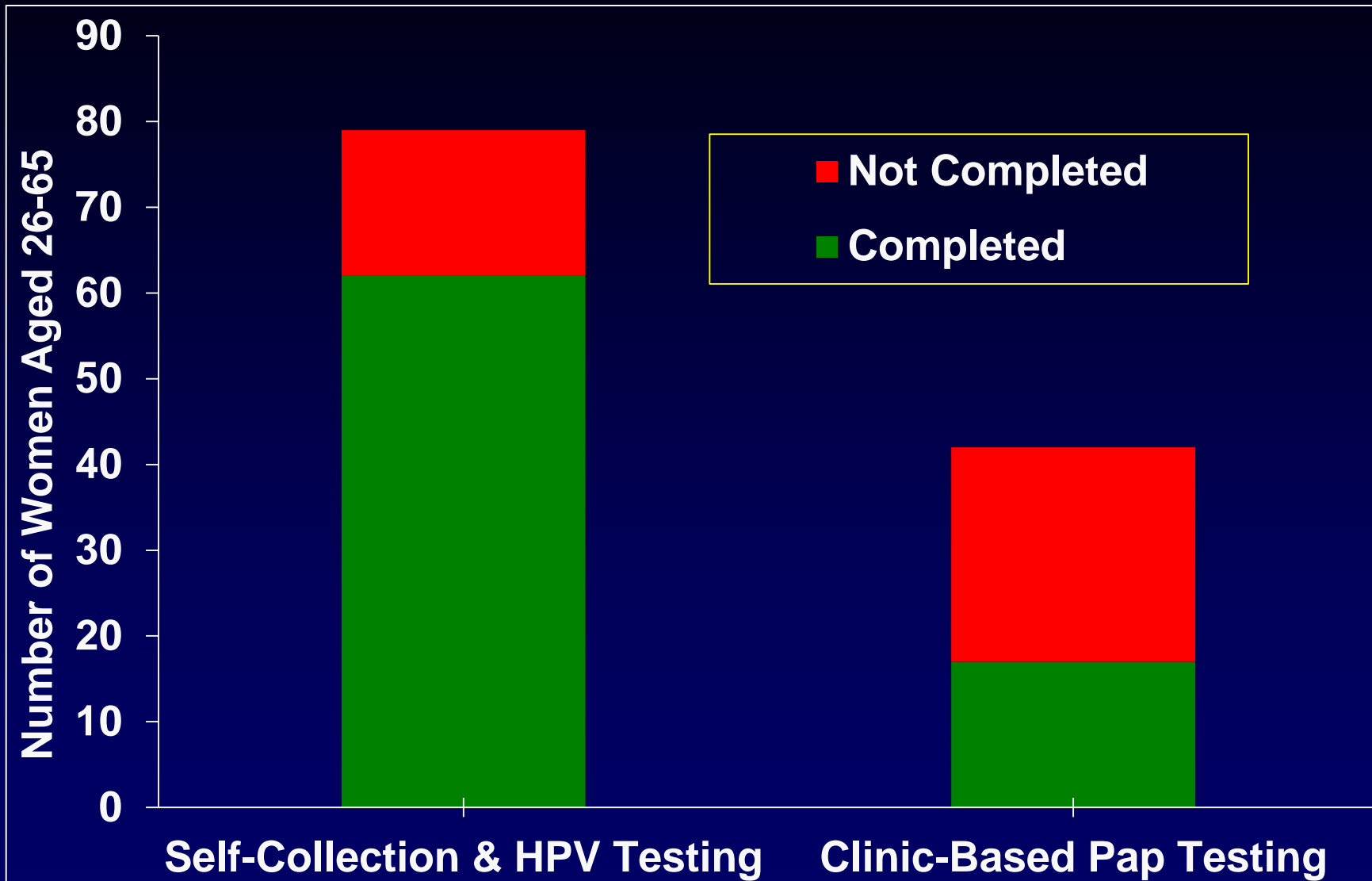
N/A means rates were suppressed if counts were fewer than 16 or if the population of the specific category (race, ethnicity) is less than 50,000.

US Incidence:
~8 per 100,000

Self Collection and HPV Testing in China



Screening in the Mississippi Delta



Final Comments

- HPV is the necessary but infrequent cause of cervical cancer.
- HPV vaccines and tests can be highly effective if used in an age-appropriate manner. HPV vaccines will prevent cancer and clinically important disease from occurring in the future. Screening prevents cancer *now*.
- Current screening guidelines are based on two basic principles:
 - Benefits to the few at-risk women must outweigh the harms to the generally healthy population.
 - Equal Risk = Equal Care

Final Comments

- It is impractical and very costly, and potentially very harmful, to screen women excessively in an attempt to prevent ALL cervical cancer.
- The greatest gains in cancer prevention will be achieved by reaching those not currently getting services.