

Optimizing the clinical value of HPV test

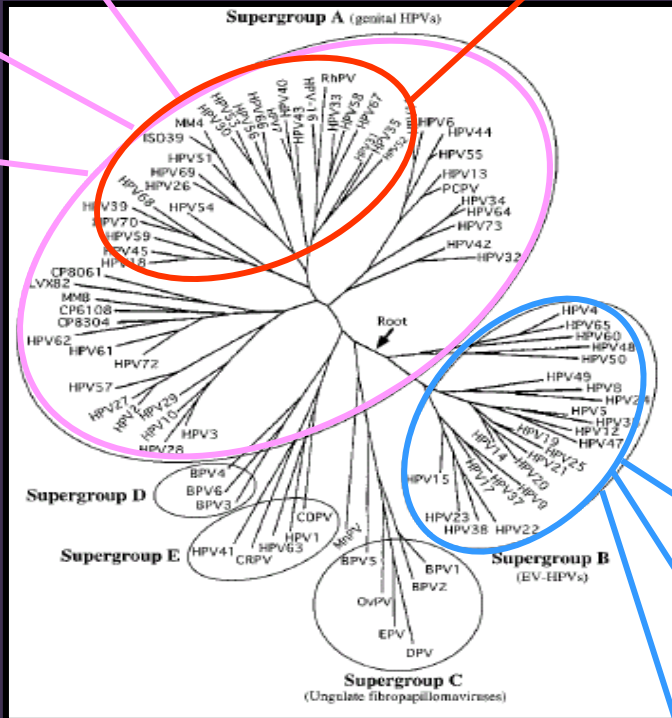
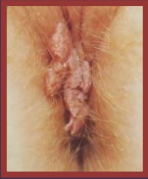
10th Asia-pacific Congress of Medical Virology
15-18 Oct 2015
Taipei

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Faculty of Medicine
The Chinese University of Hong Kong



Estimated contribution of HPV

Cervical cancer: ~ 100%

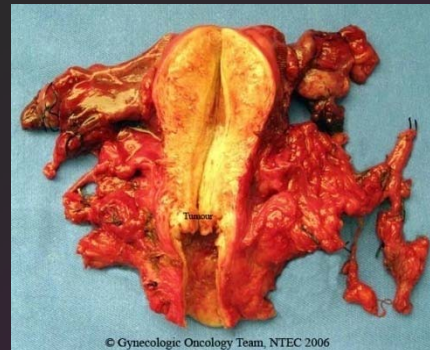
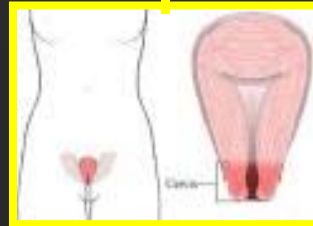
Anal cancer: ~ 90%

Vagina, vulva, penile cancers: ~ 40%

Oropharyngeal cancer: 15-75%



HPV & cervical cancer



Cervical Cytology Screening

Georgios N. Papanikolaou



- Sensitivity ~50%
- Require regular repeat screening
- ~3-5% of low-grade, self-limiting abnormalities

Alternatives / adjuncts to cytology screening



HPV infection

p16^{INK4a}

Ki-67

Topoisomerase IIA

Minichromosome Maintenance 2

Etc.....

Sensitivity

No. of patients with POSITIVE result
_____ %

Total no. of patients with disease

Specificity

No. of patients with NEGATIVE result
_____ %

Total no. of patients without disease

Performance of HPV test

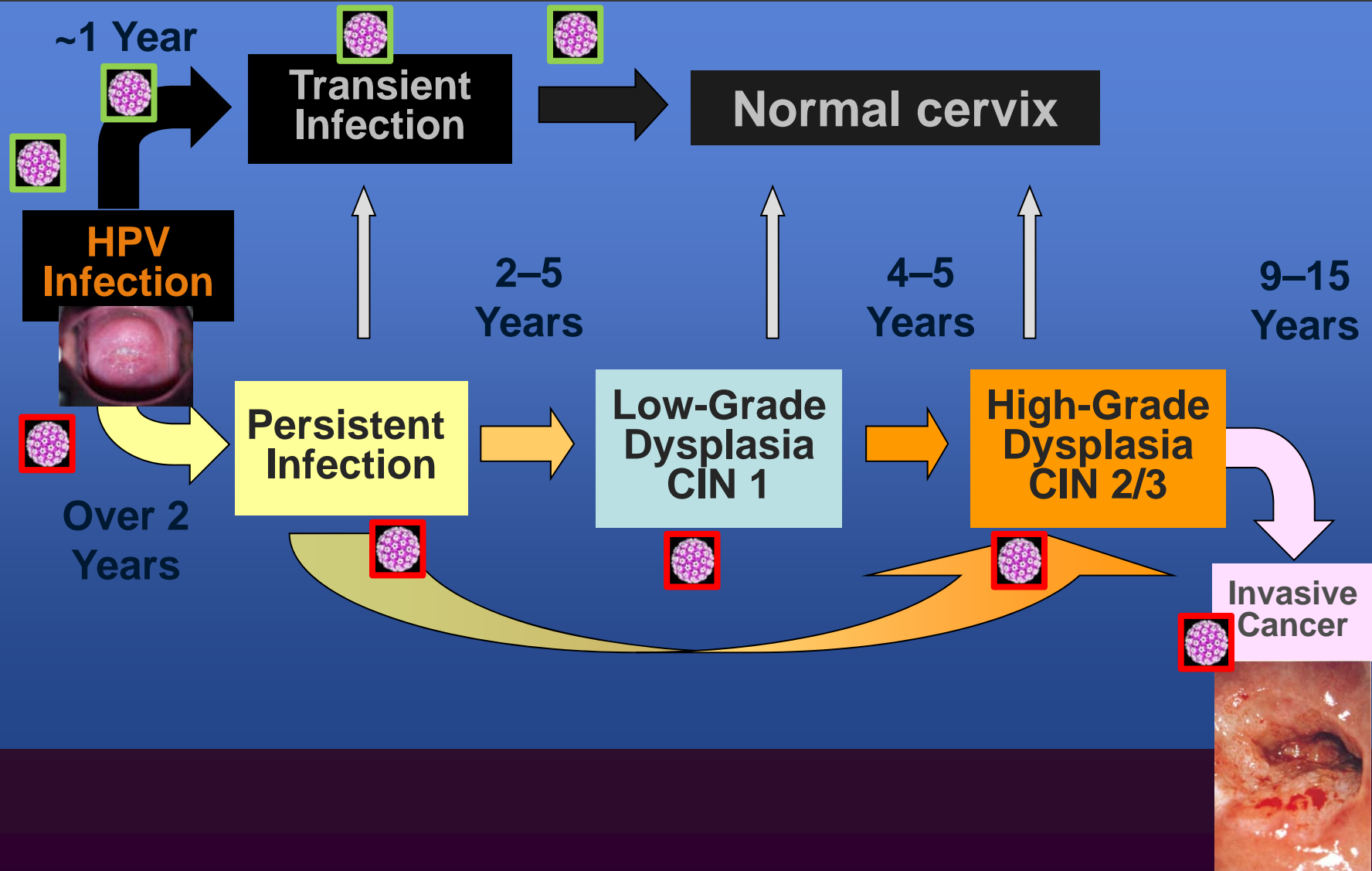


Sensitivity

Specificity



Natural History of High-Risk HPV Infection

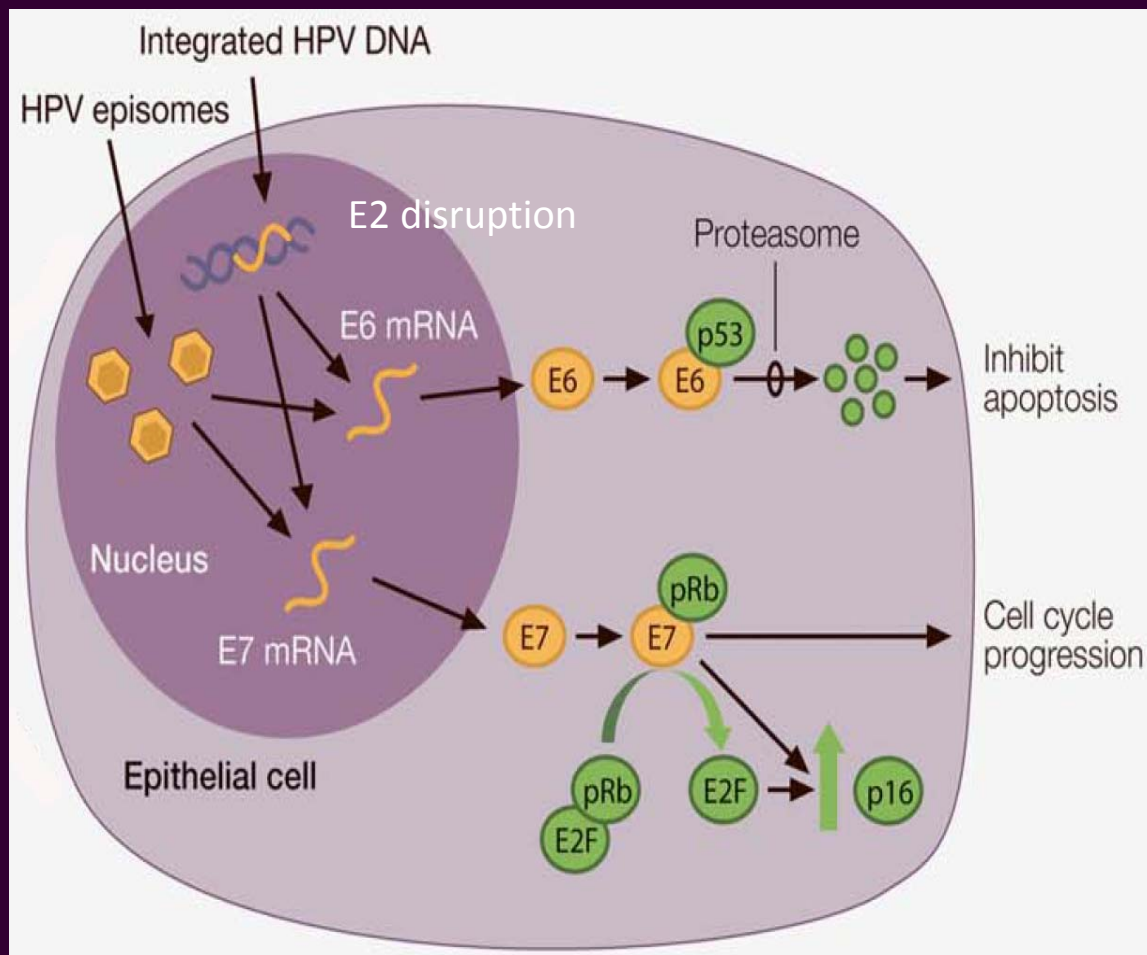




Approaches to improve the clinical performance of HPV tests

1. Transient vs. oncogenic
HPV infection

1. Detect oncogenic phenotype of HPV



HPV DNA

HPV E6 / E7 mRNA +

HPV E6 / E7 protein +/-

E2 disruption / integration ?

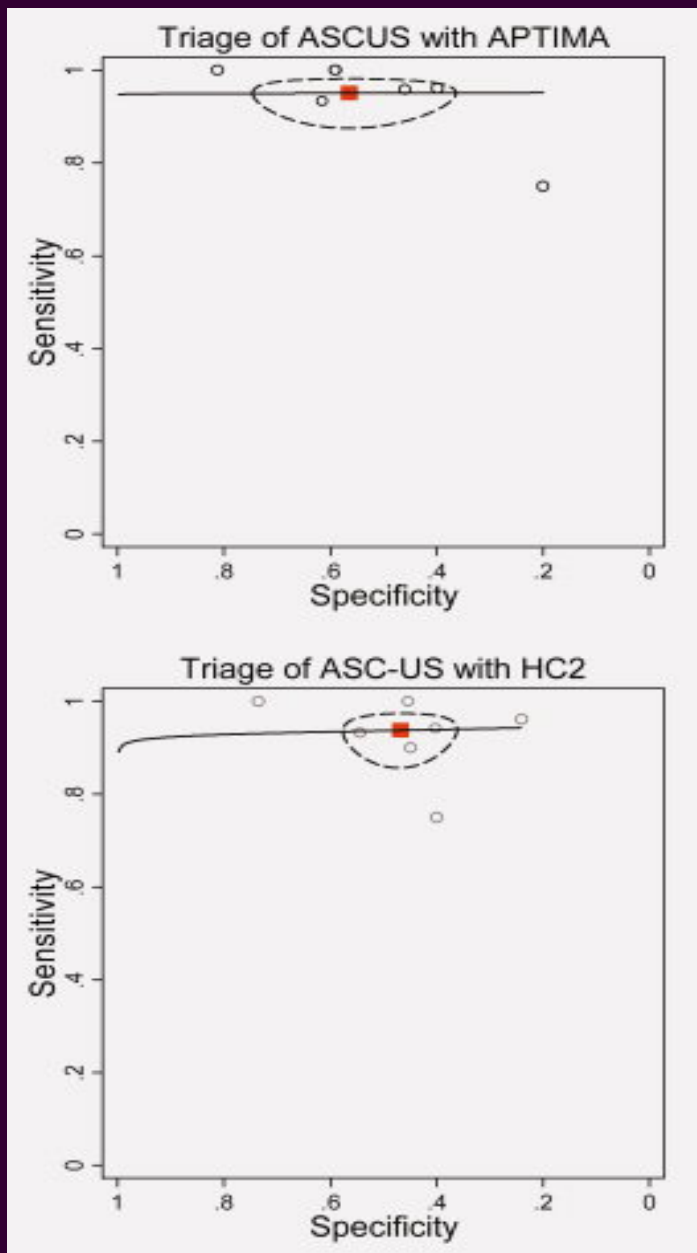
Methylation ?

Arbyn et al.

Int J Cancer 2013;132:101

Meta-analysis

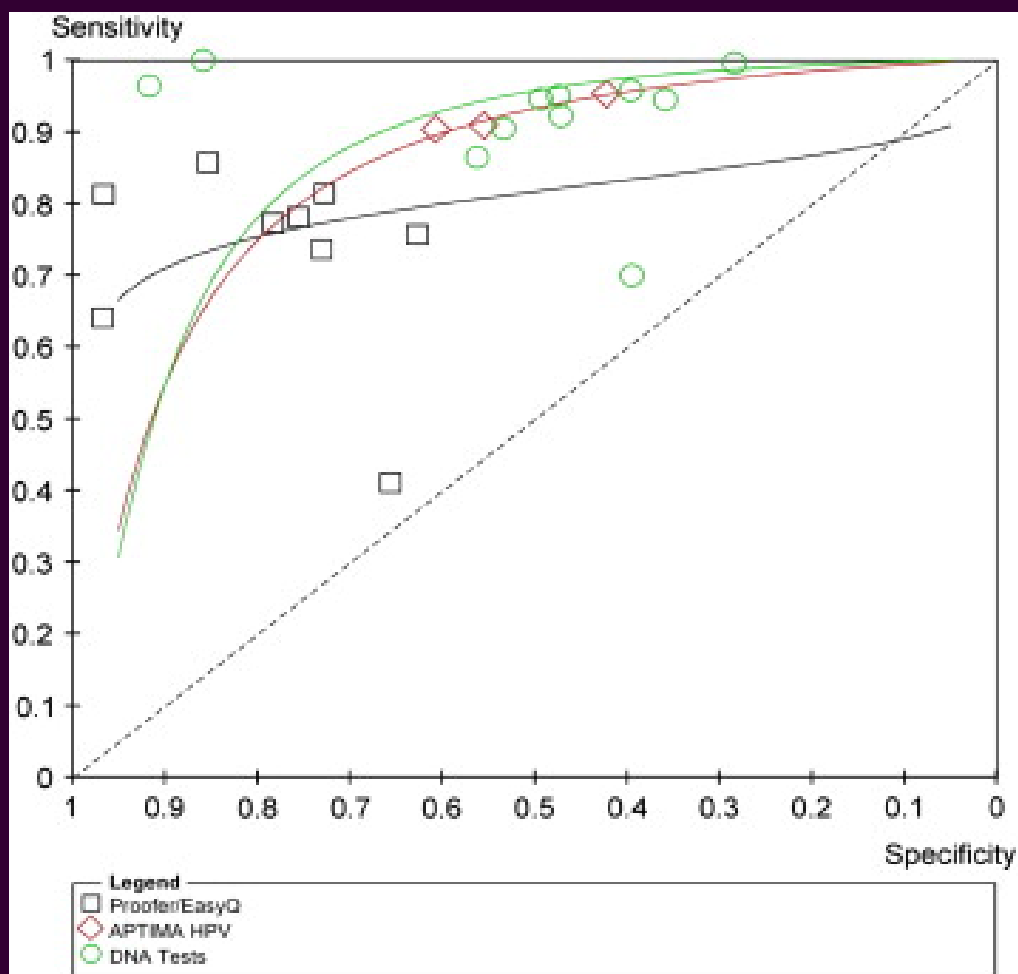
Triage for ASCUS



APTIMA
14 Hr HPV E6/7 mRNA

Hybrid Capture 2
13 Hr HPV DNA

Comparing HPV DNA vs mRNA tests in women with abnormal cytology



Hybrid capture 2 test
13 Hr HPV DNA

APTIMA test
14 Hr HPV E6/7 mRNA

Proofer test
5 Hr HPV E6/7 mRNA
HPV16 / 18 / 31 / 33 / 45

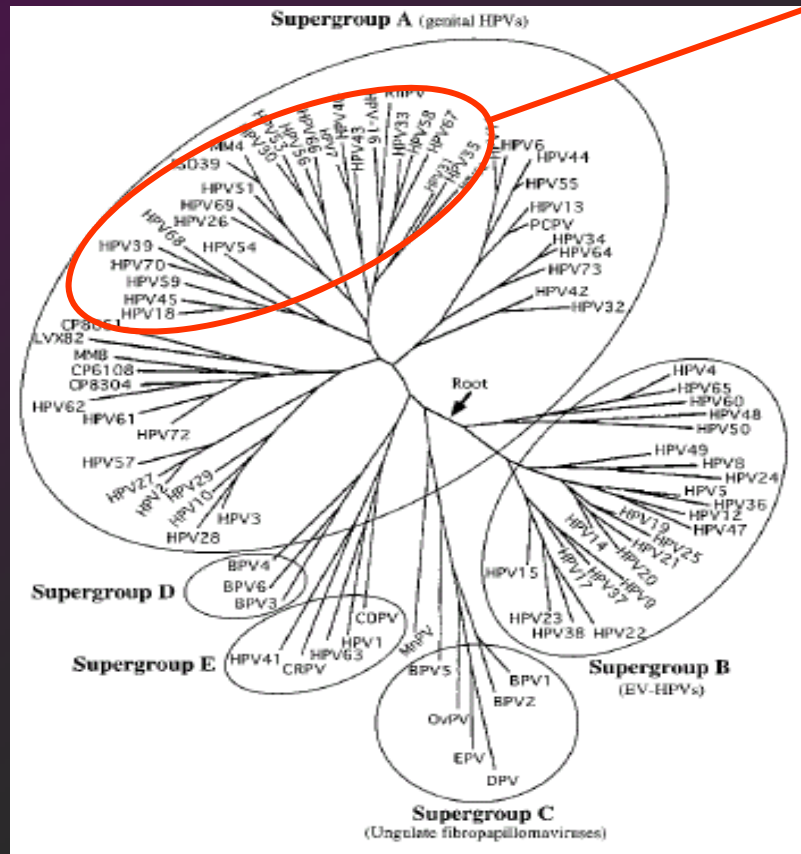
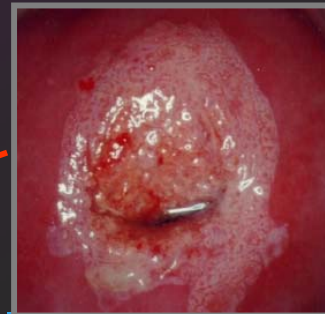
Meta-analysis
12 publications
CIN2+ as outcome
Burger et al. Gynecology Oncology 2011; 120:430.



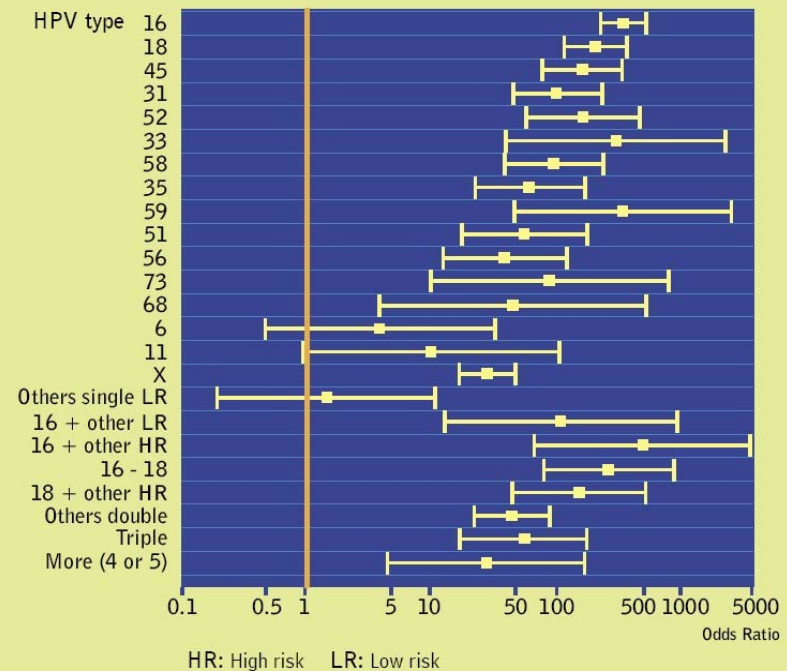
Approaches to improve the clinical performance of HPV tests

2. High-risk vs. super high-risk
HPV infection

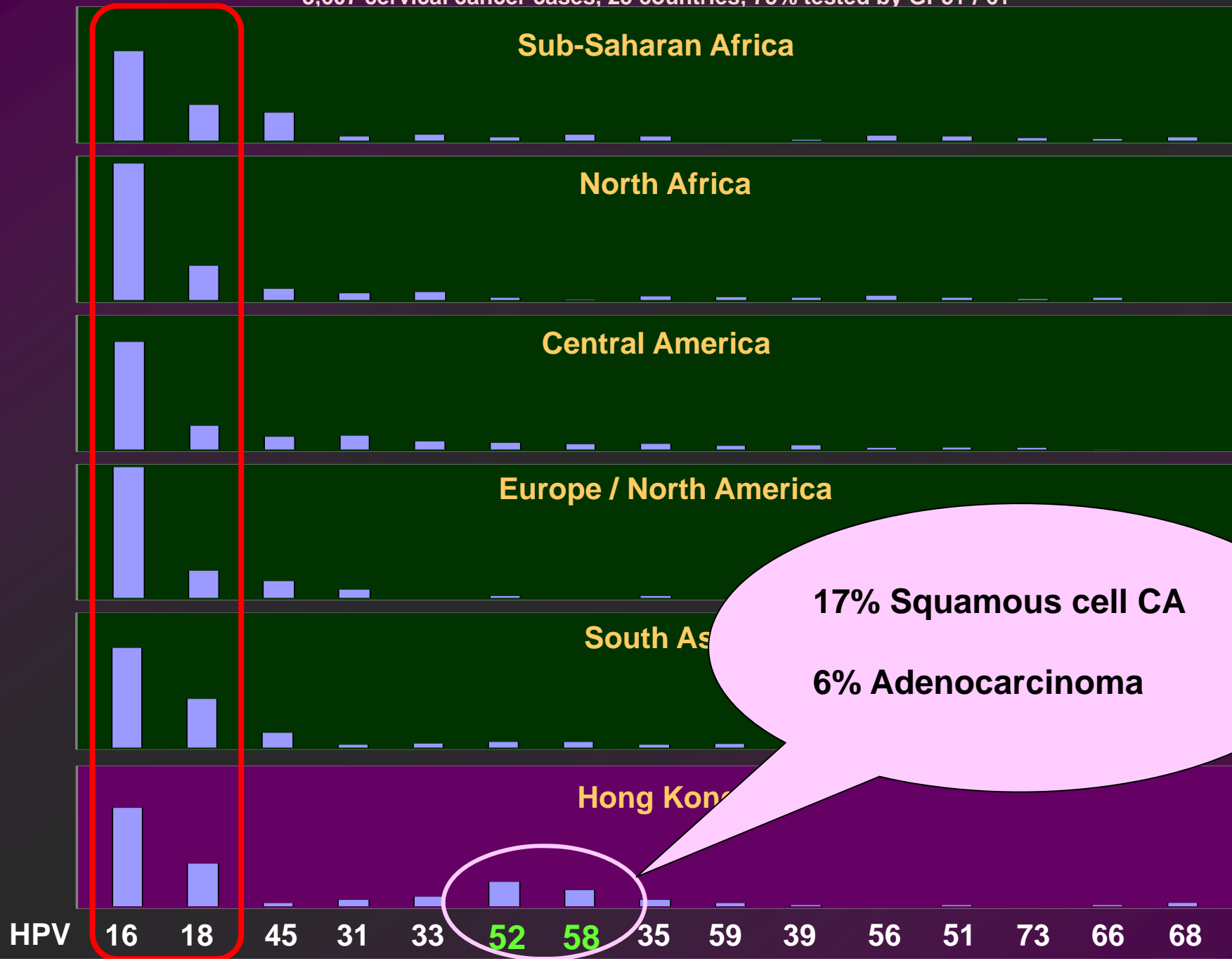
2. Detect “super” high-risk HPV types



HPV TYPE-SPECIFIC RISK ESTIMATES FOR CERVICAL CANCER



Munoz et al. Int J Cancer 2004; 111: 278-5
3,607 cervical cancer cases, 25 countries, 75% tested by GP5+ / 6+



17% Squamous cell CA
6% Adenocarcinoma

Meta-analysis on attribution of HPV58 in cervical cancers (worldwide)

No. of Studies

No. of Patients

2

129

10

1732

44

9845

10

1498

5

599

Total

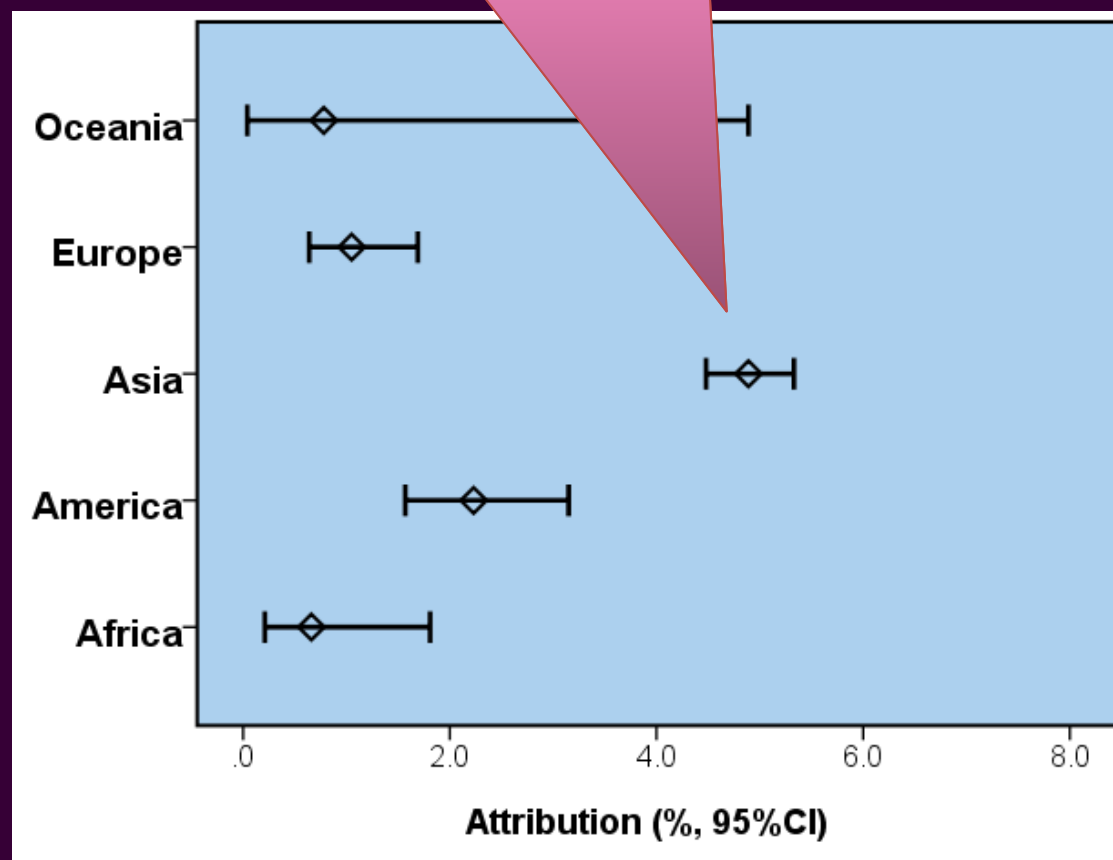
71

13803

HPV58 in HPV-positive cervical cancers

4.9 (4.5-5.3)% in Asia

Significantly higher than Americas, Europe and Africa, $P < 0.001$



Meta-analysis on attribution of HPV58 in cervical cancer (Asia)

No. of studies

No. of Patients

2

371

5

895

8

1622

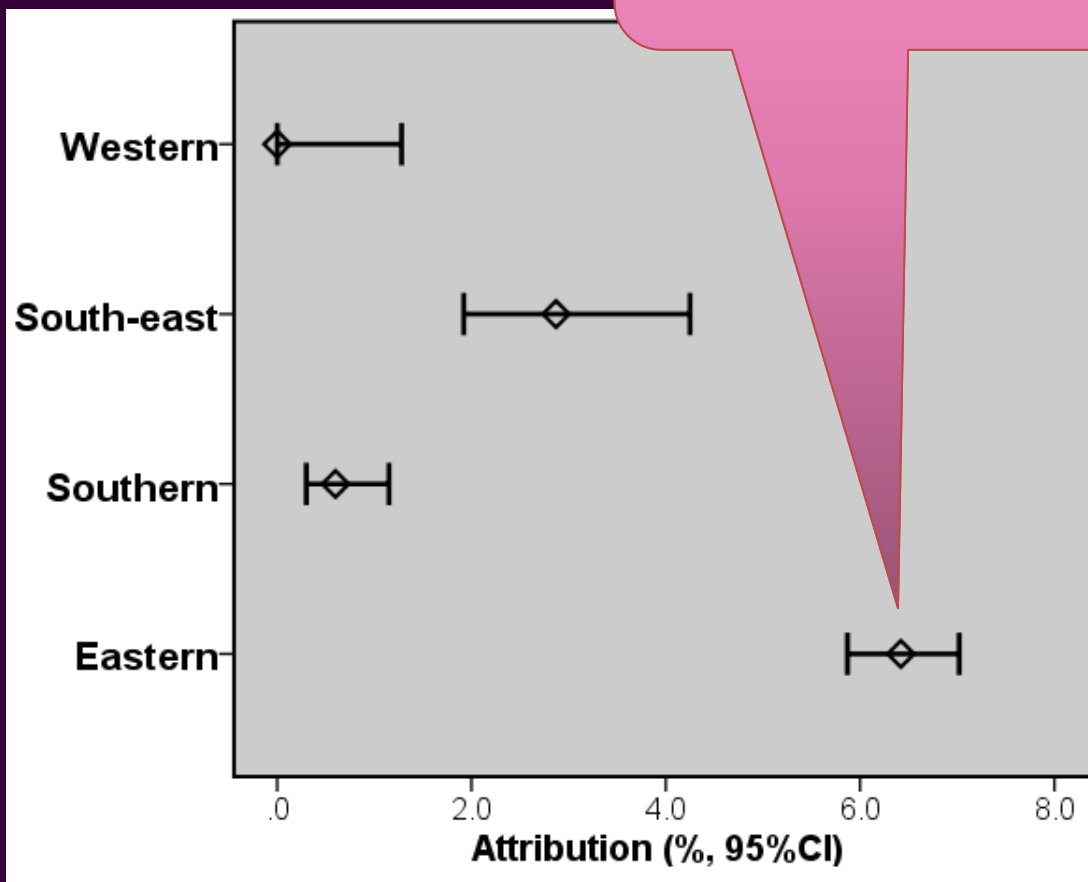
29

6957

Total

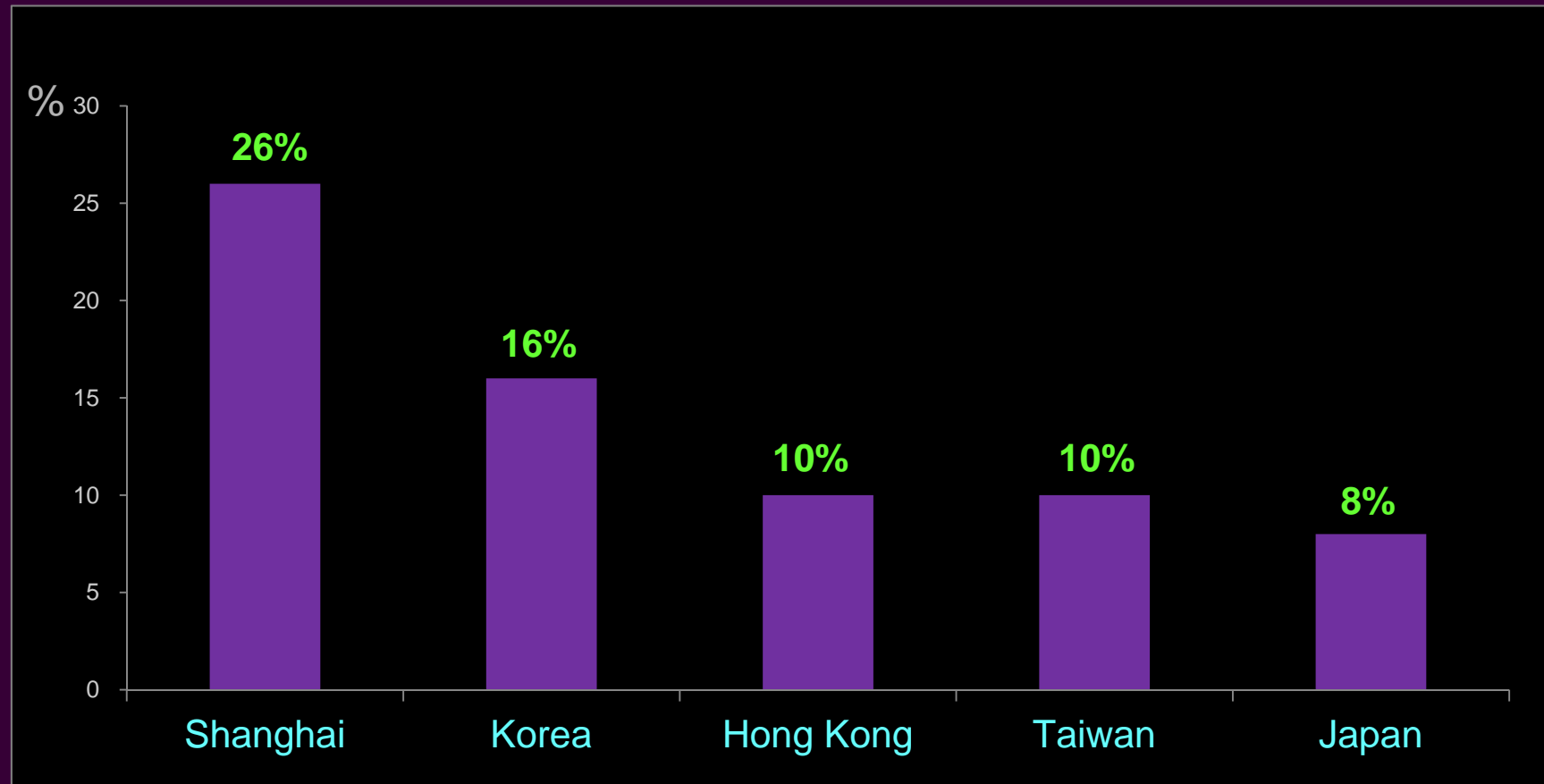
44

9845



HPV58 in HPV-positive cervical cancers
 6.4 (5.9-7.0)% in Eastern Asia
 Significantly higher than others, P <0.001

Prevalence of HPV58 in cervical cancer (SCC) in East Asia



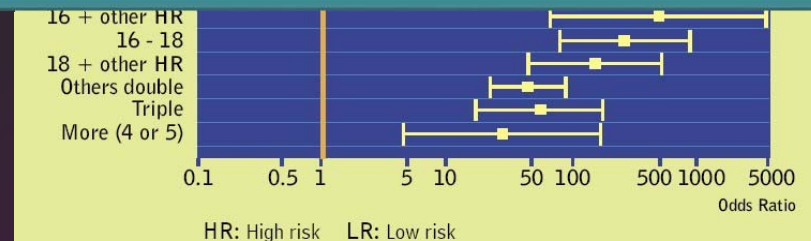
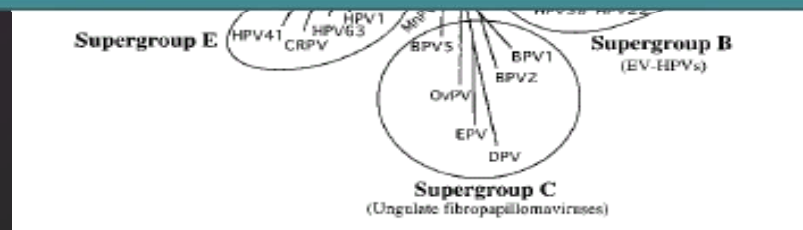
2. Detect “super” high-risk HPV types



Choose “supra” high-risk types

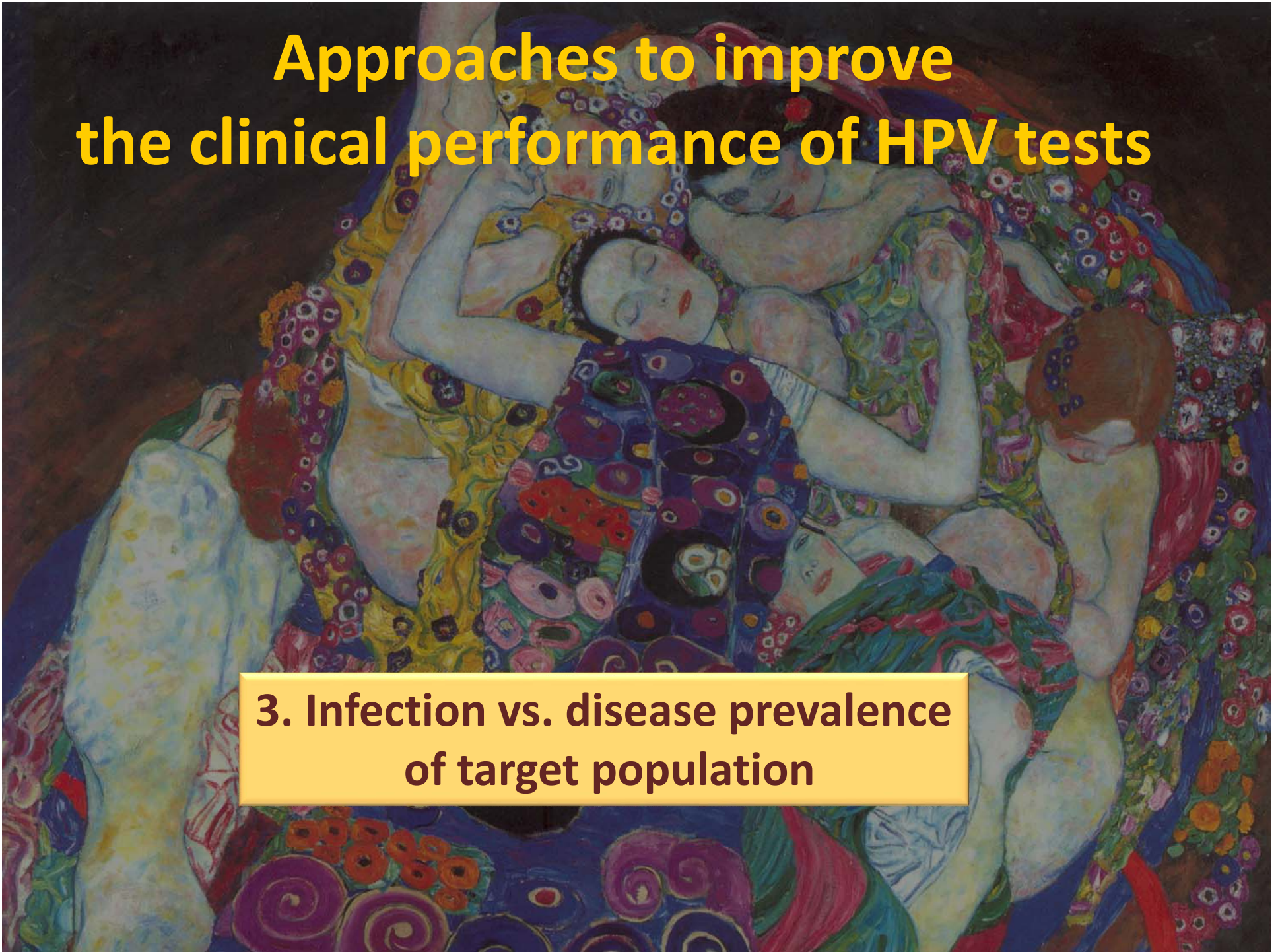
based on

contextual-specific epidemiological data



Approaches to improve the clinical performance of HPV tests

**3. Infection vs. disease prevalence
of target population**



Sensitivity

No. of patients with POSITIVE result
_____ %

Total no. of patients with disease

Specificity

No. of patients with NEGATIVE result
_____ %

Total no. of patients without disease

Positive & Negative Predictive Value

Probability of a test result correctly indicates
the presence / absence of disease



Performance of HPV test



Sensitivity

Specificity



Positive Predictive Value

Negative Predictive Value



2080 women enrolled for cervical screening

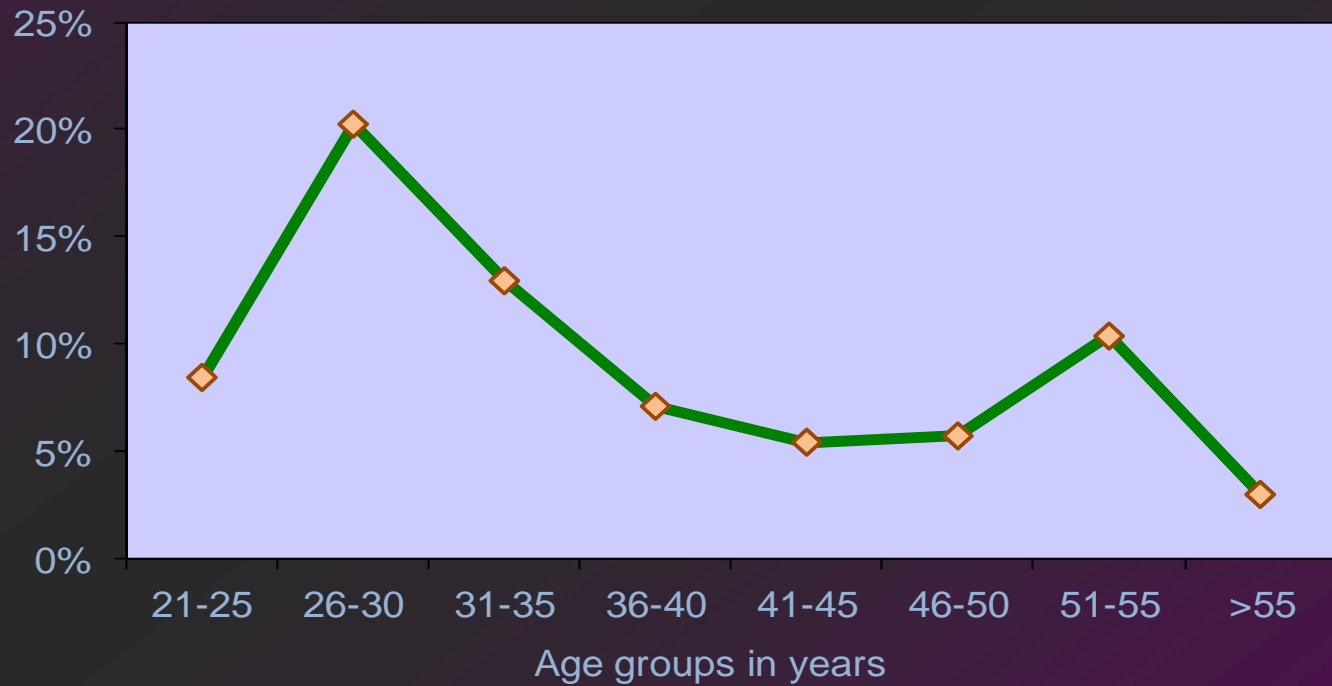
Hong Kong



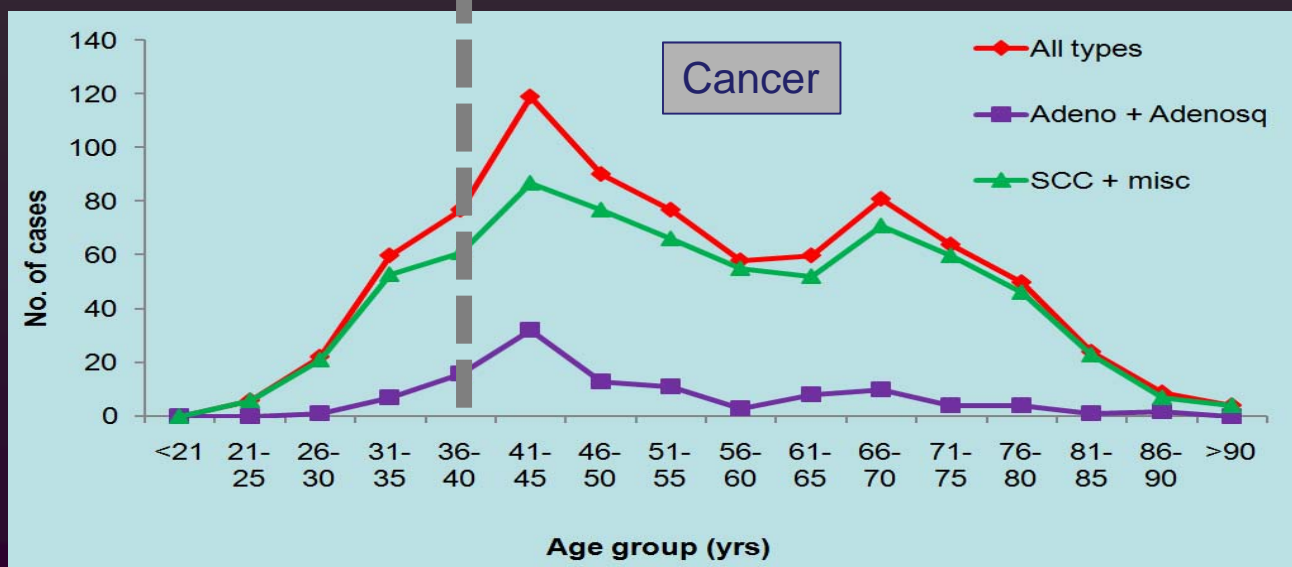
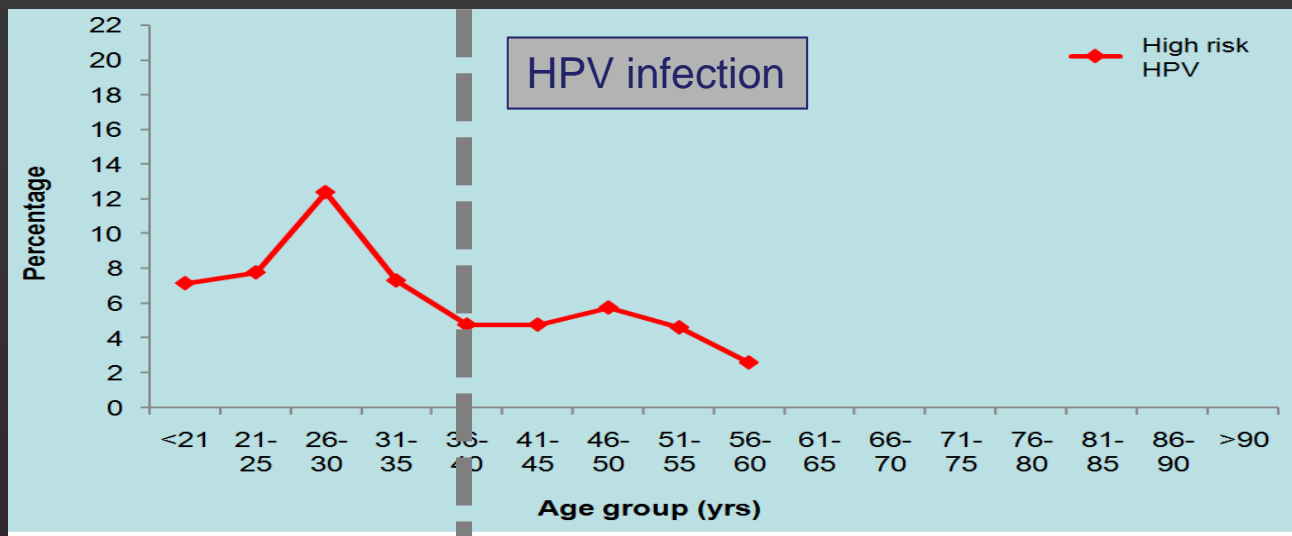
Average for 21-45 yr : 10.8%

~ 1 / 10

Any HPV



3. Select target population





Approaches to improve the clinical performance of HPV tests

4. Positive vs. negative predictive value

Performance of HPV test



Sensitivity

Specificity



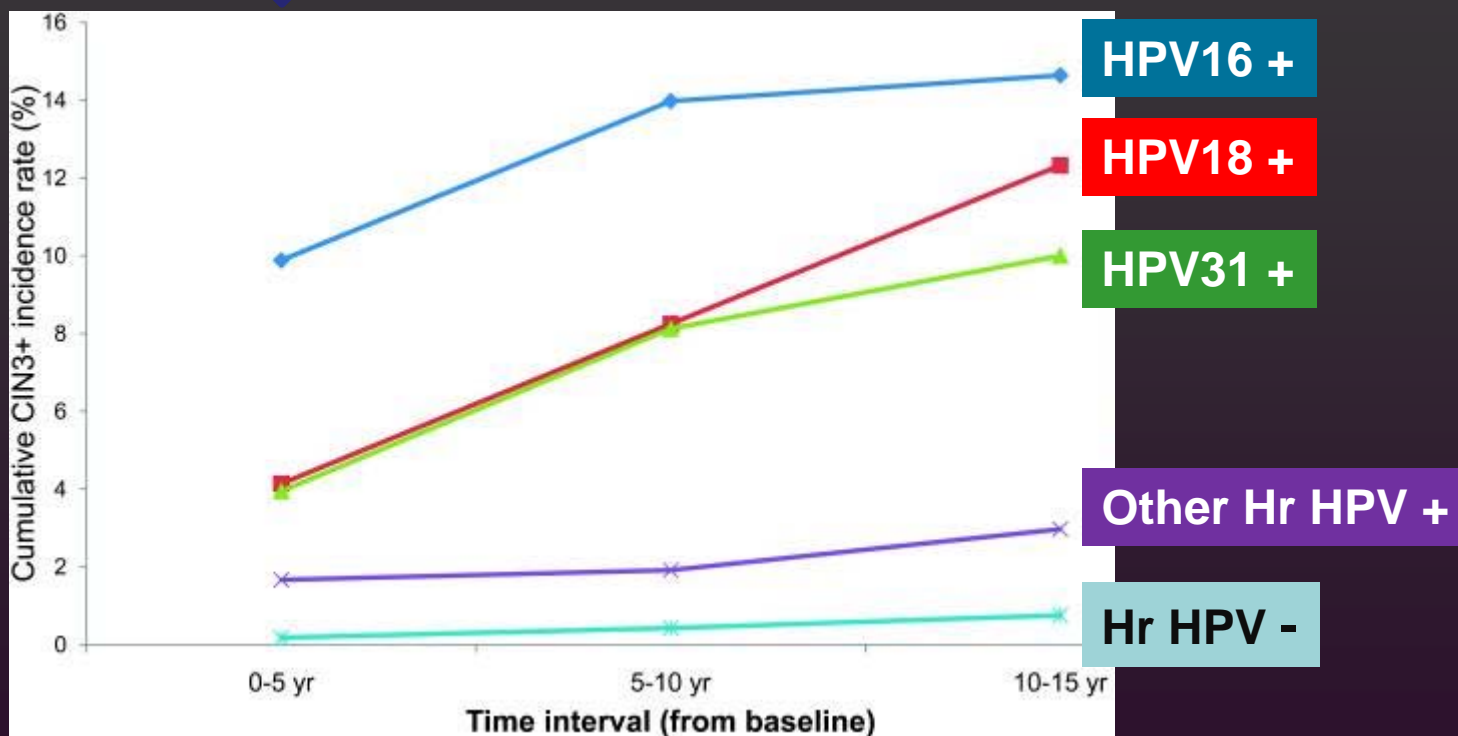
Positive Predictive Value

Negative Predictive Value



4. Make use of “long-lasting” negative-predictive value

Single HPV DNA test



20 000 women

Khan et al. JNCI 2005; 97: 1072

Schiffman et al. JNCI 2011; 103: 368.

Considerations for applying HPV test

S

Sensitivity

S

Specificity

S

Savings

S

Stigmata

8th APCMV 2009 Hong Kong





Thank you