

HPV infection in women in developing countries

Silvia Franceschi

Infections and Cancer Epidemiology Group

International Agency for Research on Cancer

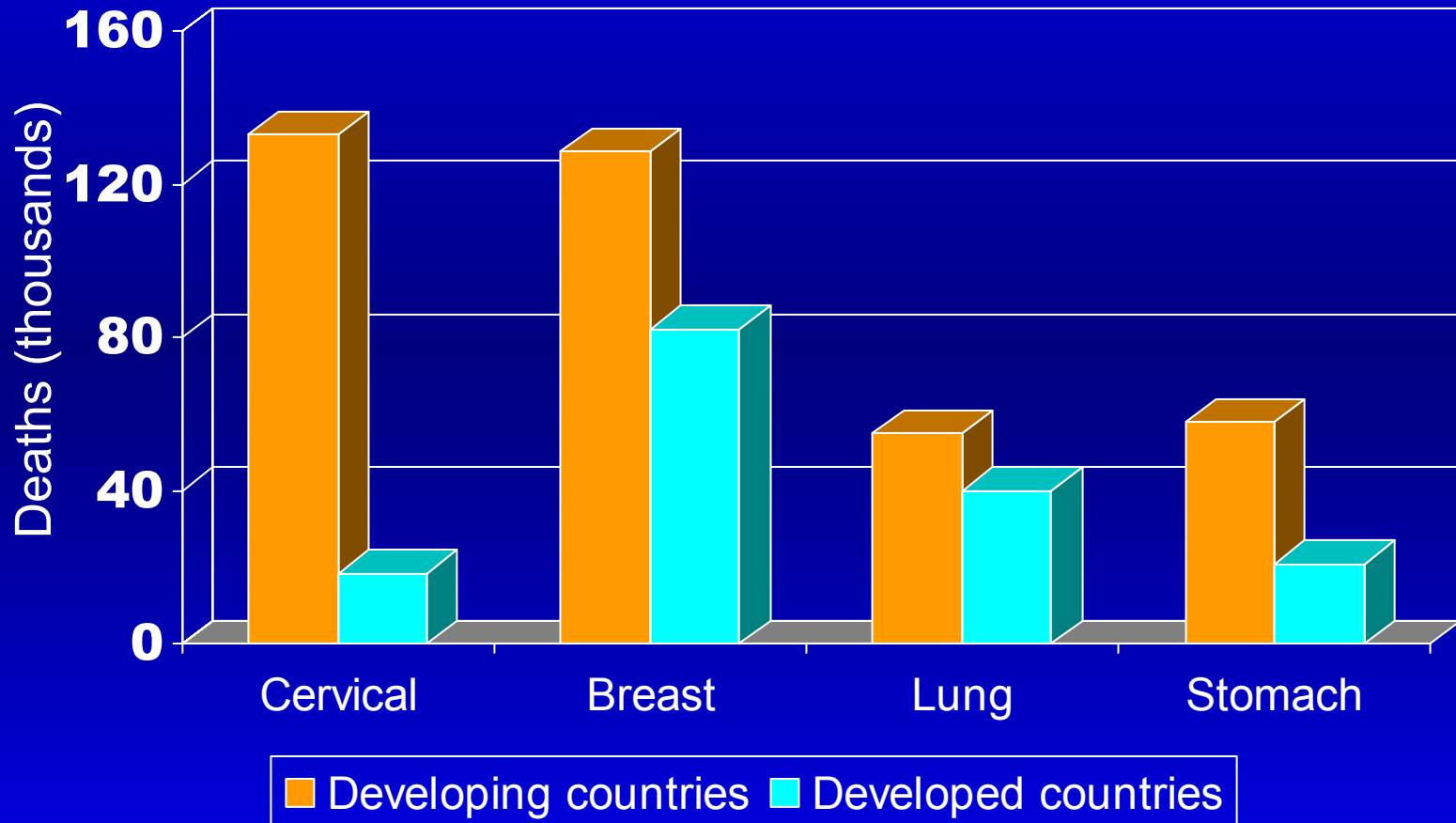
Lyon, France

2nd European Conference on Cervical Cancer Screening

Tubingen, 19-20 September, 2005



Comparison with other cancers: number of deaths among women 25-64 years old



Percentage of female cancer sites attributable to infectious agents

■ HPV ■ other

WORLD

10.7

6.7

**Developed
countries**

5.2

3.2

**Developing
countries**

16.2

9.1

0

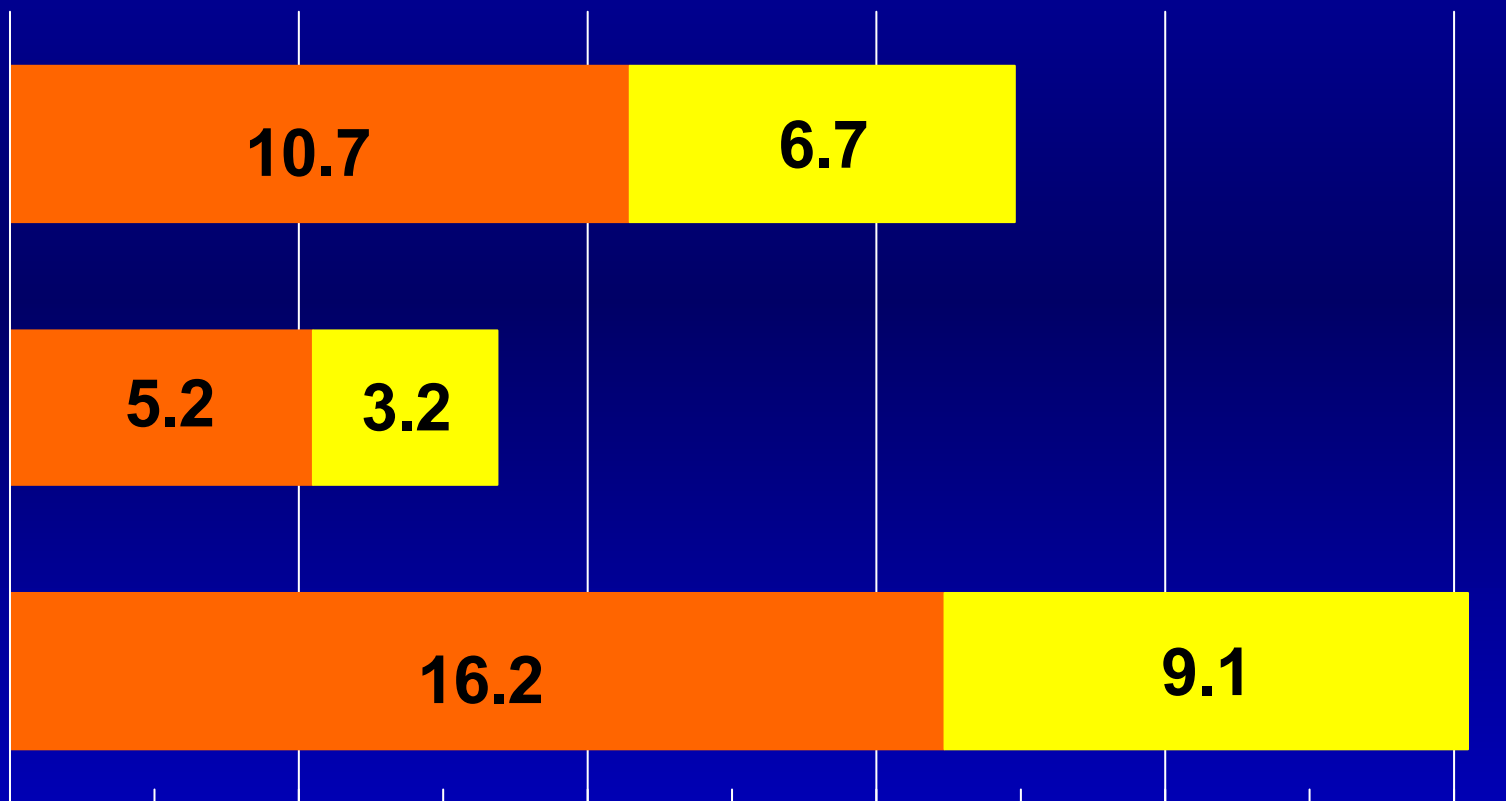
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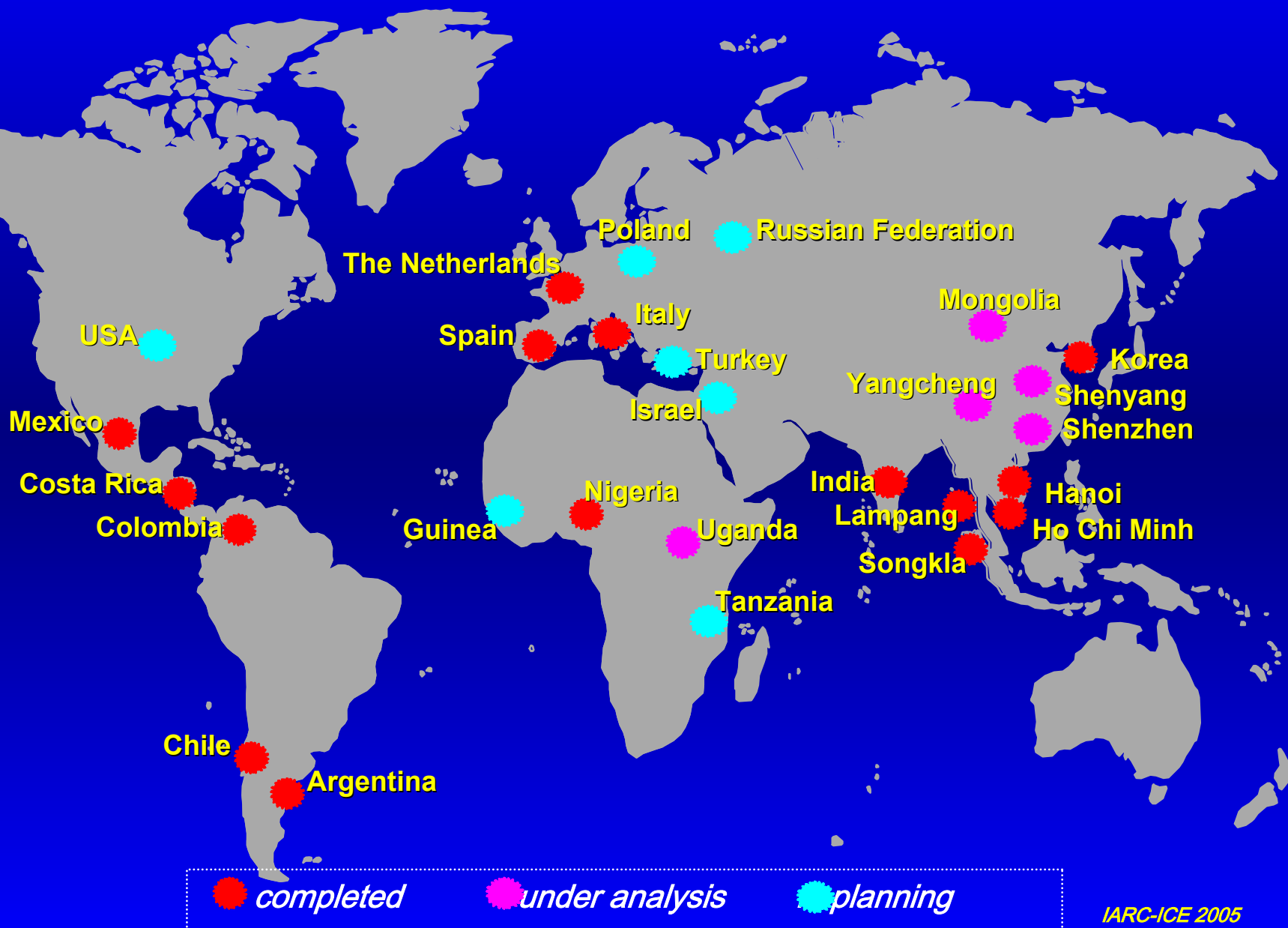
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20

25



IARC Multi-centre HPV Prevalence Surveys



New HPV surveys

Aim :

To expand the IARC population-based HPV survey to areas of the globe where no current information is available in order to compare:

- 1) HPV prevalence in young and old women.
- 2) frequency of high-risk HPV types other than 16 and 18.

Priorities :

1. Areas at high risk for cervical cancer (e.g., sub-Saharan Africa, Eastern Europe).
2. Areas where social changes and/or urbanisation may increase HPV infection among young generations (e.g., China, Mongolia, Turkey).

Gates Foundation HPV Vaccine Grants:

a coordinated strategy for exploring how to make HPV vaccines available, acceptable, and affordable to those most in need

Harvard University (2005-2009)

- Decision models for population impact and cost-effectiveness

IARC (2005-2010)

- Epidemiological data in low-resource settings in Asia, Africa, Eastern Europe

WHO Initiative for Vaccine Research (2005-2010)

- HPV Laboratory Network
- Guidelines for Introduction
- Information Centre for HPV and Cervical Cancer (ICO, Barcelona)

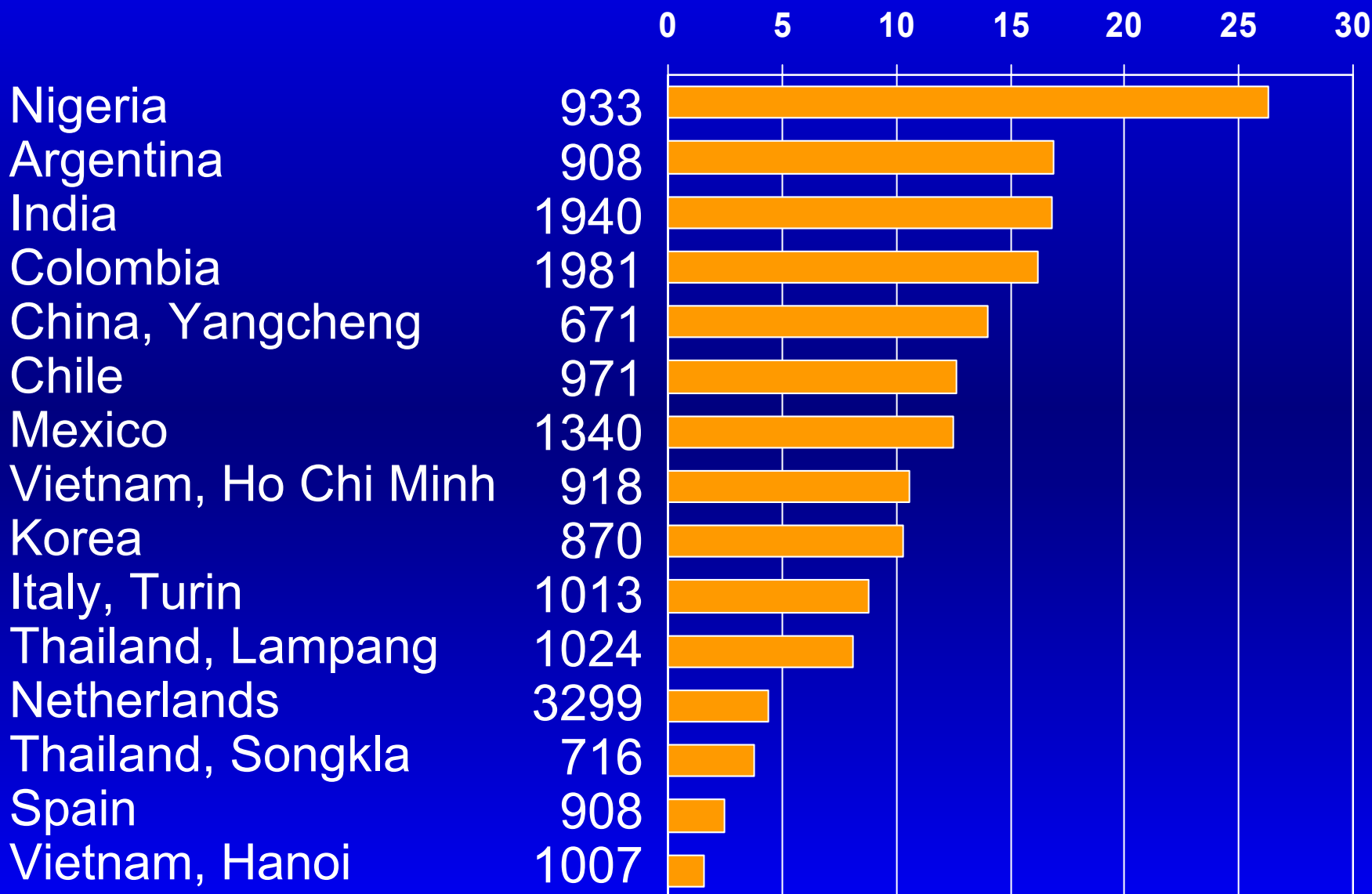
PATH – planning grant (4/05-3/06)

IARC Multi-centric HPV Prevalence Survey

- 15 centres in 13 countries already completed
- low-, intermediate- and high-risk areas represented
- Population-based samples of approx. 1000 women
- 100 women per 5-year age group
- Standardised risk factor questionnaire
- Testing for 36 HPV types using GP5+/GP6+ PCR

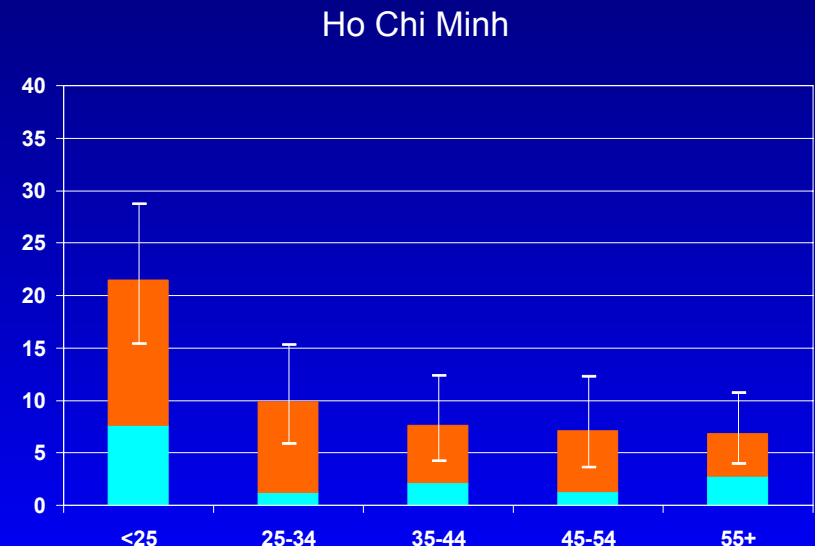
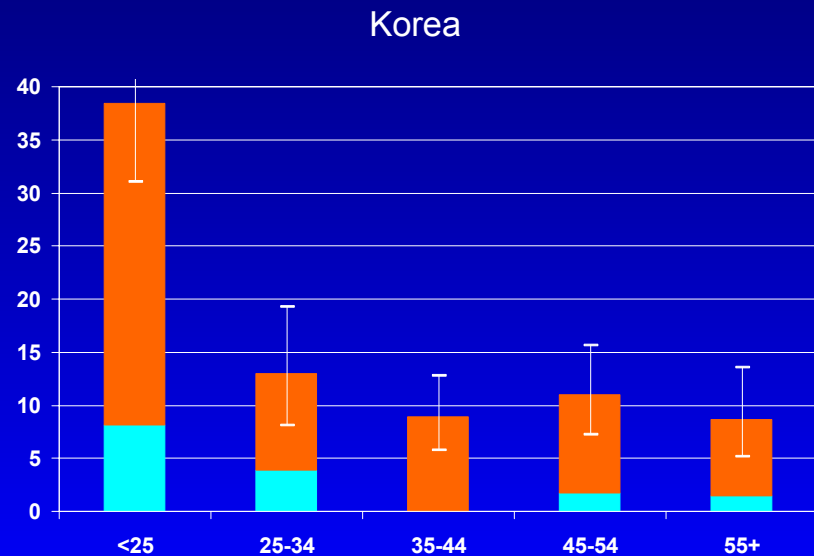
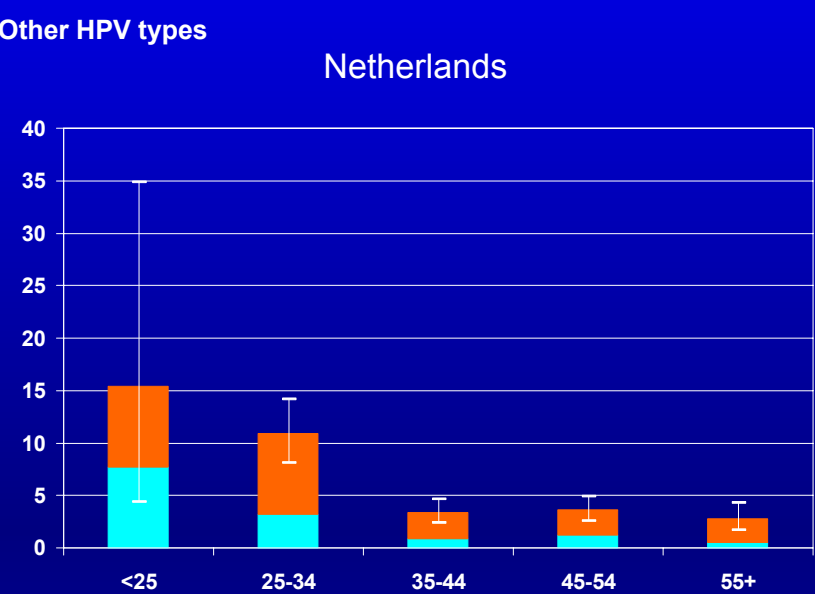
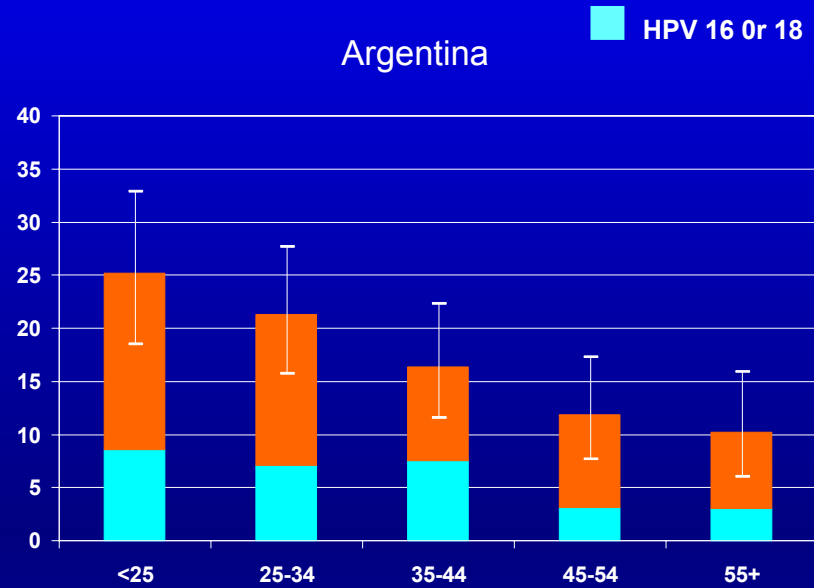
Prevalence of cervical HPV DNA in sexually active women

IARC Multi-centre HPV Prevalence Survey, 1995-2002



Prevalence of cervical HPV DNA by age and HPV type

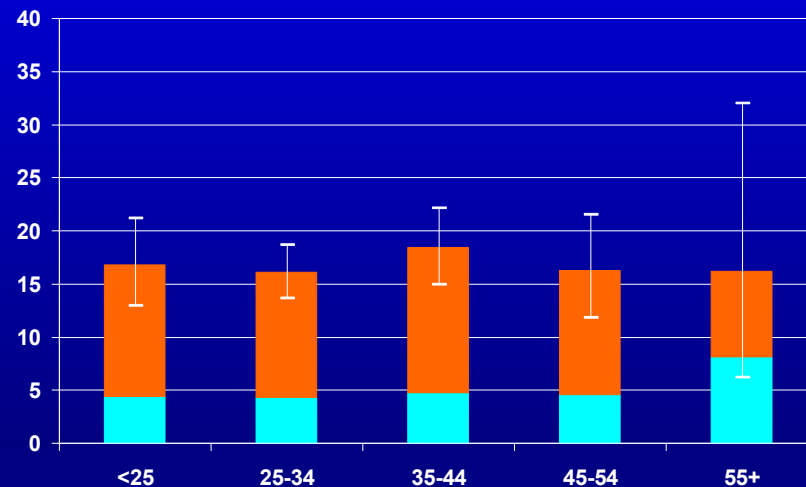
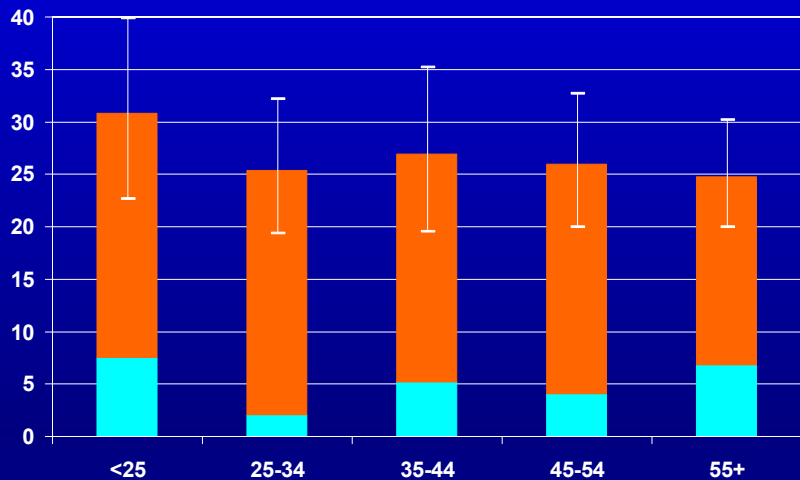
IARC Multi-centre HPV Prevalence Survey



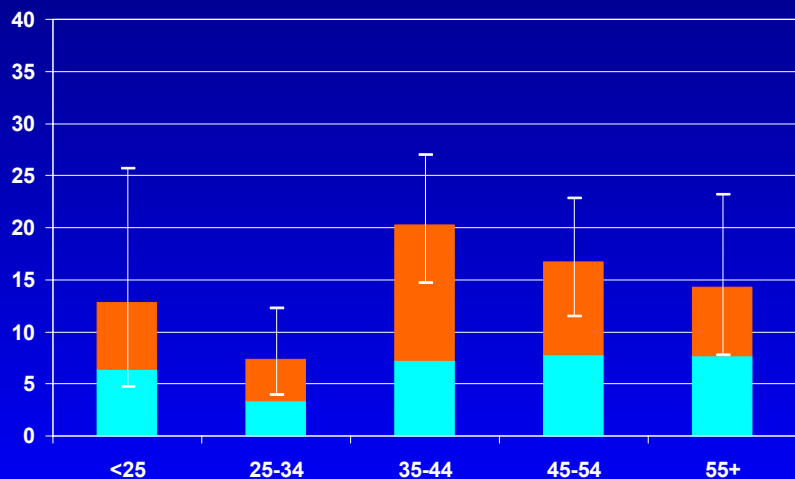
Prevalence of cervical HPV DNA by age and HPV type

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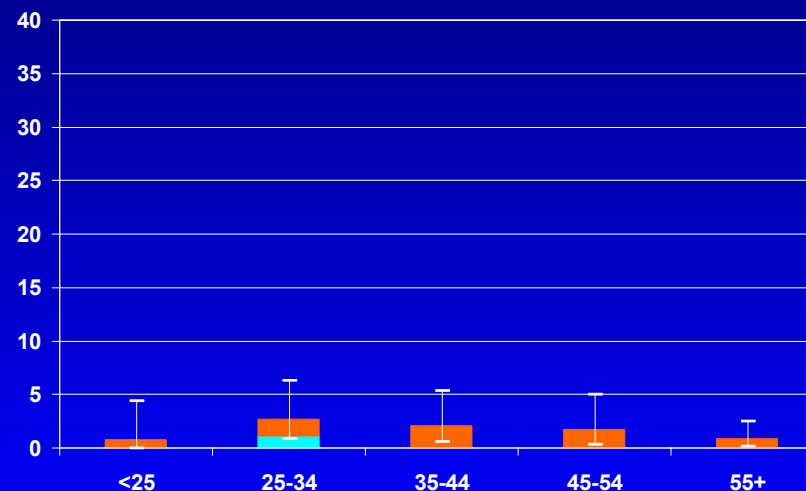
Nigeria ■ HPV 16 Or 18 ■ Other HPV types India



China, Yangcheng



Vietnam, Hanoi

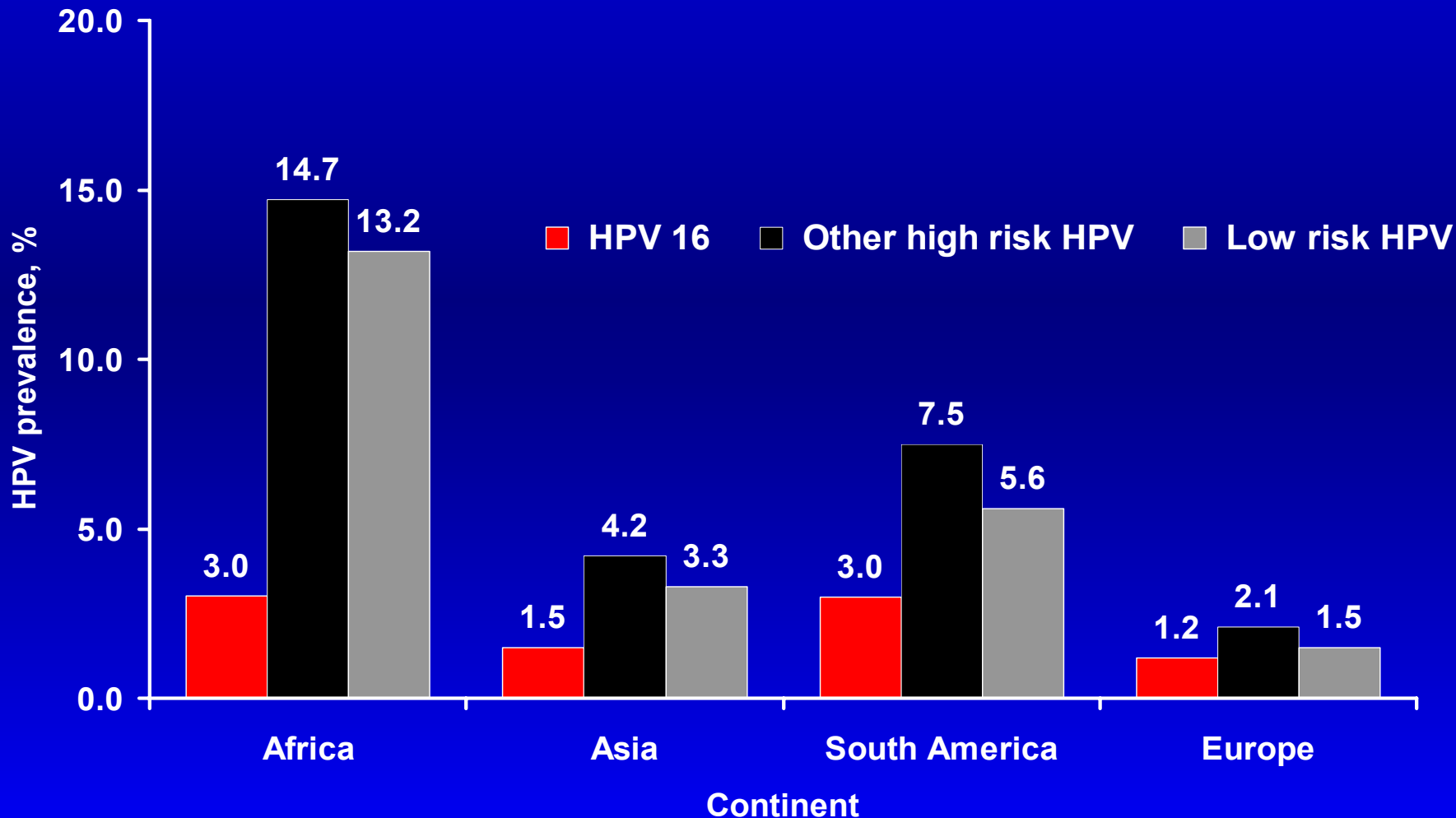


Why does the age curve of HPV prevalence vary from one country to another?

- Assessment of HPV in young women is difficult
- Age-curve is not “natural history” of HPV.
- Differences in age-specific patterns of infection/clearance of HPV infection
- Cohort effects (epidemic in young women)

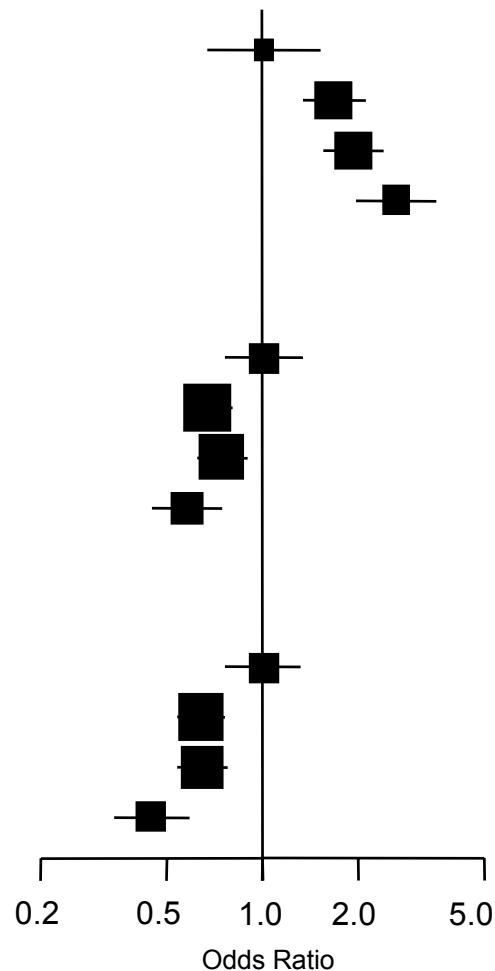
Prevalence of HPV16, high risk HPV and low risk HPV among women with normal cytology – by continent

IARC multi-centre HPV prevalence survey, 1995-2002



Odds ratios for infection with selected HPV types among HPV-positive women with normal cytology

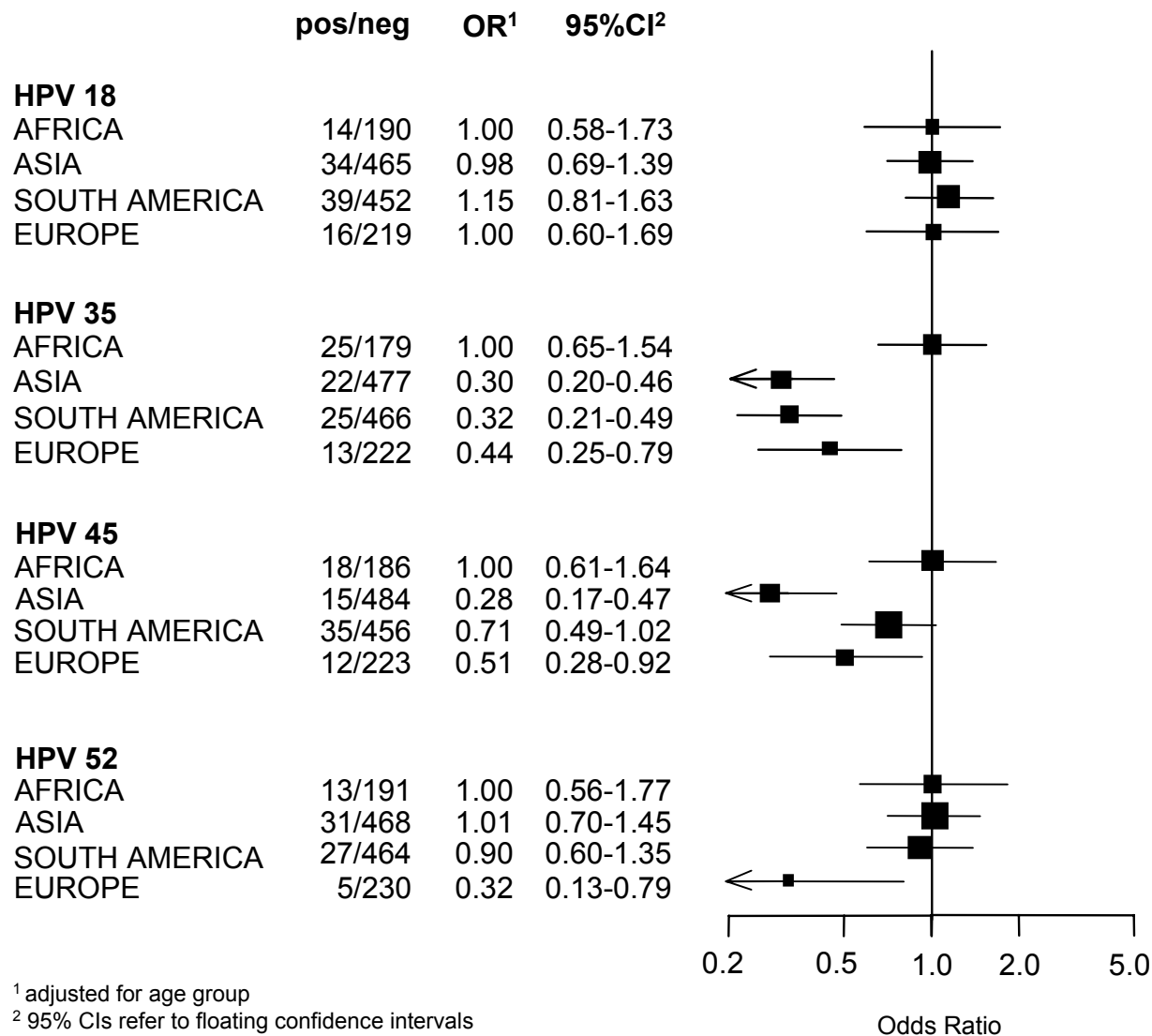
| | pos/neg | OR ¹ | 95%CI ² |
|---------------------|---------|-----------------|--------------------|
| HPV16 | | | |
| AFRICA | 25/179 | 1.00 | 0.66-1.52 |
| ASIA | 92/407 | 1.68 | 1.34-2.10 |
| SOUTH AMERICA | 105/386 | 1.92 | 1.53-2.41 |
| EUROPE | 60/175 | 2.64 | 1.95-3.58 |
| Other HR HPV | | | |
| AFRICA | 121/83 | 1.00 | 0.75-1.33 |
| ASIA | 253/246 | 0.66 | 0.56-0.79 |
| SOUTH AMERICA | 267/224 | 0.74 | 0.61-0.89 |
| EUROPE | 106/129 | 0.57 | 0.44-0.74 |
| LR HPV | | | |
| AFRICA | 109/95 | 1.00 | 0.76-1.32 |
| ASIA | 200/299 | 0.63 | 0.53-0.76 |
| SOUTH AMERICA | 198/293 | 0.64 | 0.53-0.77 |
| EUROPE | 75/160 | 0.44 | 0.33-0.58 |



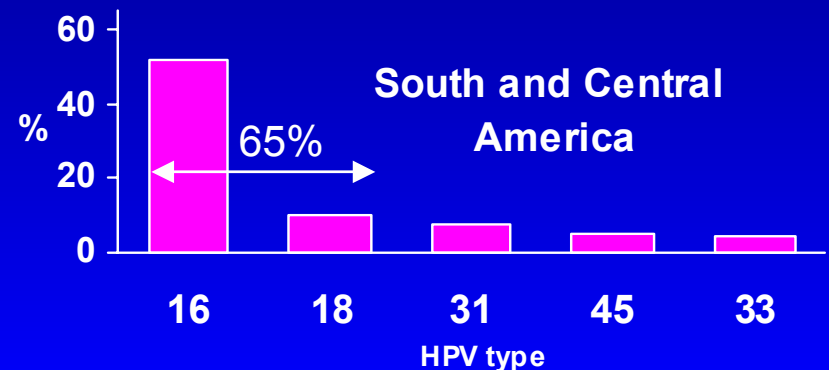
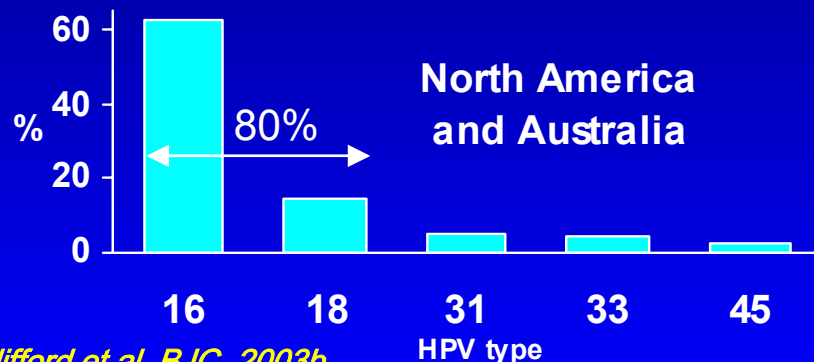
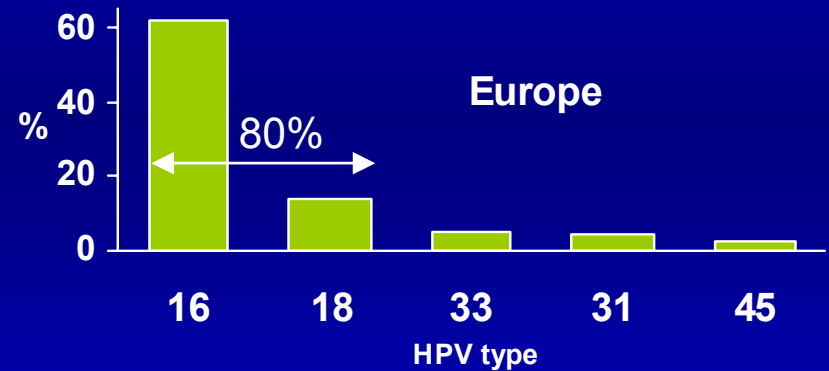
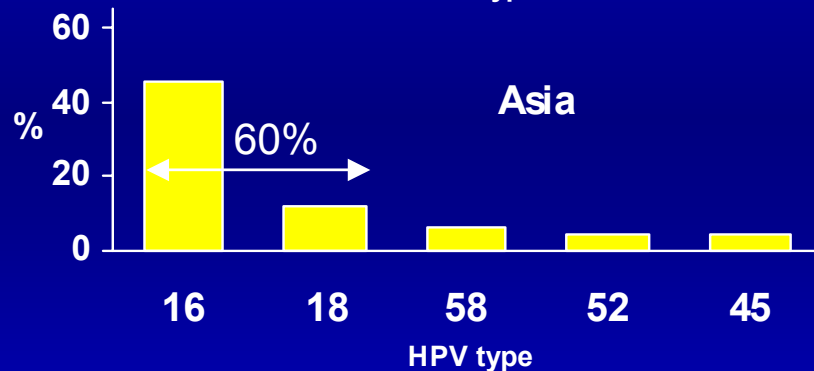
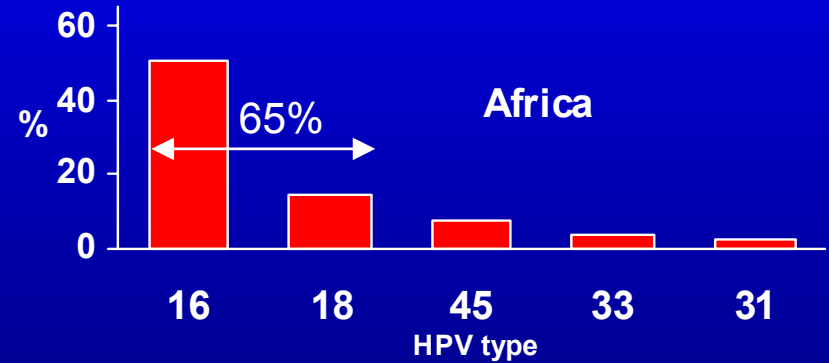
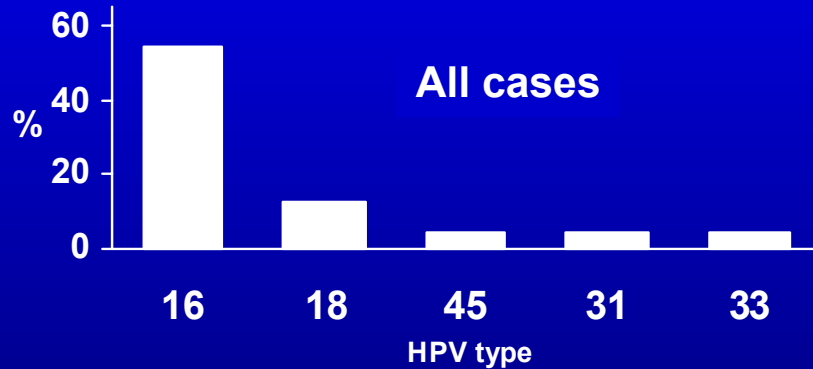
¹ adjusted for age group

² 95% CIs refer to floating confidence intervals

Odds ratios for infection with selected HPV types among HPV-positive women with normal cytology



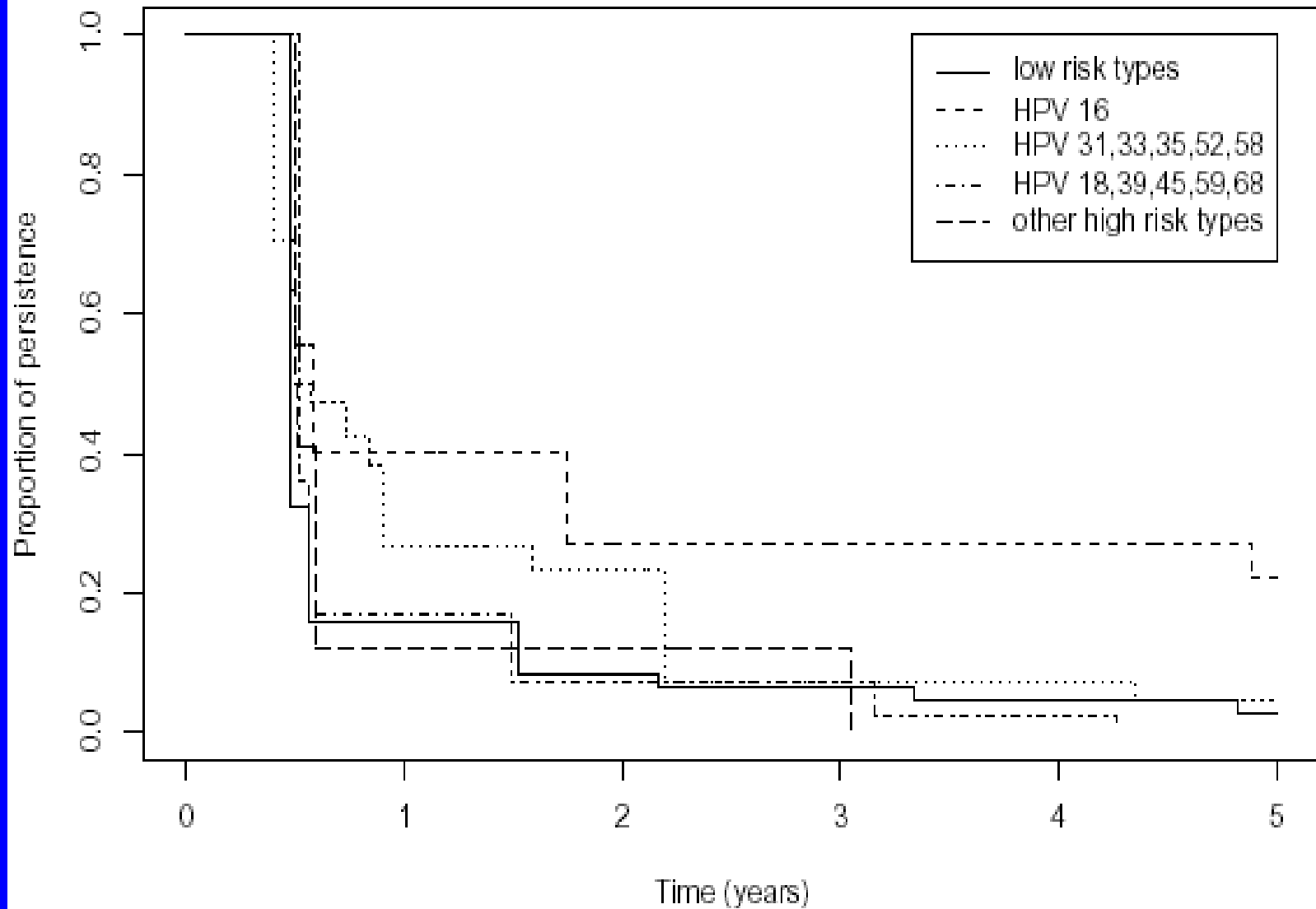
5 most common HPV types in squamous cell carcinoma by region



Cohort studies of IARC HPV Studies in Asia

| Center/Country | No. | % HPV positivity (age-standard.) |
|---------------------|------|----------------------------------|
| Busan/Korea | 1448 | 14.7 |
| Lampang, Thailand | 1024 | 8.9 |
| Songkla, Thailand | 716 | 3.9 |
| Ho Chi Min, Vietnam | 918 | 10.3 |
| Hanoi, Vietnam | 1007 | 1.6 |
| Yangcheng, China | 671 | 14.8 |
| Shenzhen, China | 1153 | 14.0 |
| Shenyang, China | 1000 | In progress |
| Total | 7937 | |

HPV types (phylogenetic groups)



Main risk factors of HPV incidence and clearance, Thailand

| | Incidence | Clearance |
|--------------------------|------------------|------------------|
| Age | | |
| <35 | 1 | 1 |
| 35-54 | 0.39 (0.17-0.94) | 0.54 (0.31-0.95) |
| ≥55 | 0.25 (0.09-0.68) | 0.52 (0.28-0.97) |
| HSV2 serostatus | | |
| Negative | 1 | 1 |
| Positive | 1.83 (0.84-3.99) | 0.79 (0.49-1.30) |
| Oncogenicity type | | |
| HPV16 | -- | 1 |
| HPV18 | -- | 2.06 (0.60-7.05) |
| Others HR types | -- | 2.29 (0.95-5.50) |
| LR types | -- | 3.11 (1.20-8.07) |


Adjusted for age

Open issues

- Follow up for HPV new infection/clearance requires repeated gynecological examinations. **How often?**
- **Frequent visits** (6-to-12 mos): better for natural history studies, but expensive and not without dangers (e.g., overtreatment of cervical abnormalities)
- **Less frequent visits** (2-to-5 yrs): more “pragmatic” approach, may reflect screening schedules.

State of the Art

HPV Vaccine Efficacy Trials

| Manufacturer | Vaccine | Location | Participants | Projected End |
|--|--|--|----------------------------------|---------------|
| Merck  | VLPs of L1 protein from HPV 6/11/16/18, made in yeast, aluminum adjuvant | U.S., S. America, Europe | 17,800 women, 16 to 26 years old | 2007 |
| | | U.S., S. America, Europe, Asia | 3800 women, 24 to 45 years old | 2008 |
| | | U.S., S. America, Europe, Asia, Africa | 3700 men, 16 to 24 years old | 2008 |
| GSK | VLPs of L1 protein from HPV 16/18, made in baculovirus, AS04 adjuvant | U.S., S. America, Europe, Asia Pacific | 18,000 women, 15 to 25 years old | 2010 |
| | | Costa Rica (run by NCI) | 12,000 women, 18 to 25 years old | 2010 |

Challenges to introduction in developing countries

1. Some regions and groups underrepresented in clinical trials
2. Socio-cultural barriers to HPV vaccine unclear
3. Health delivery strategies/systems for reaching adolescent girls limited
4. Vaccine affordability and financing not yet known
5. Demand for/uptake of vaccine not yet known, so supply is hard to predict
6. Timing and extent of long-term impact hard to predict
7. Screening/treatment programs are only just emerging
8. Accurate and accessible information on HPV generally not available
9. Competition with other new vaccines and health needs

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