

Elimination of Cervix Cancer

Novel Options combining Vaccination and HPV Screening

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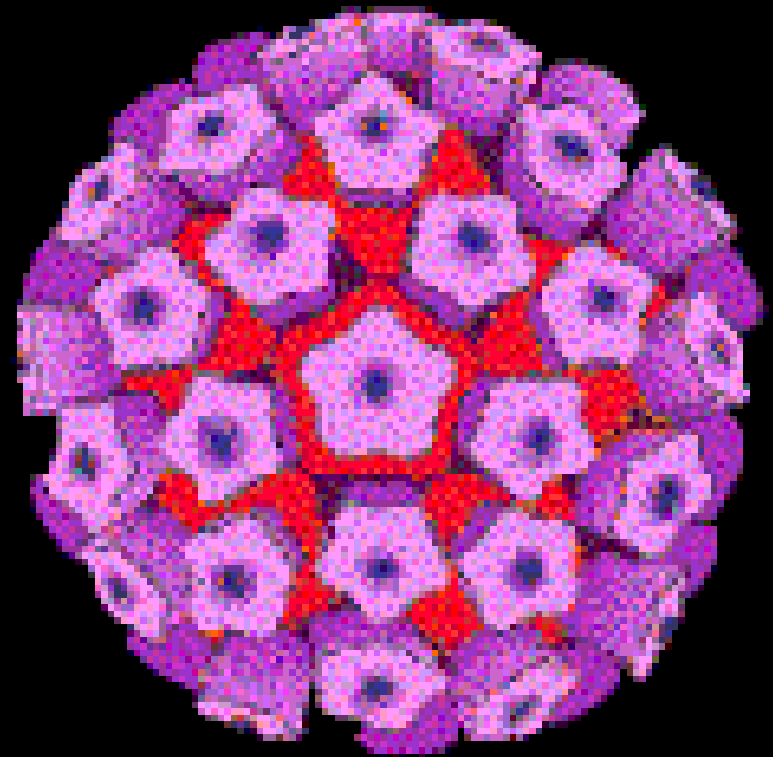
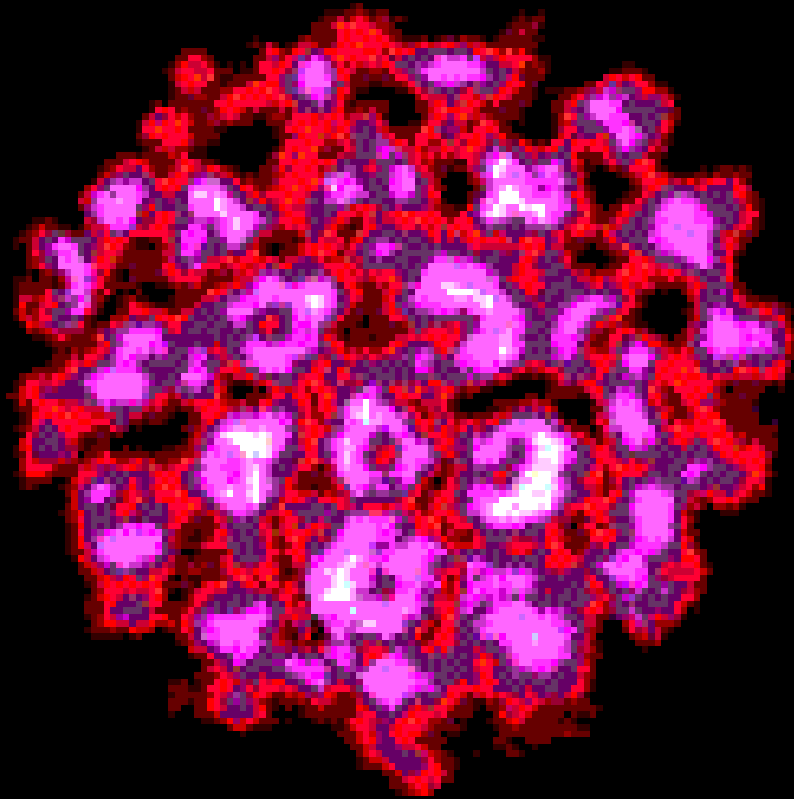
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Disclosure of interests

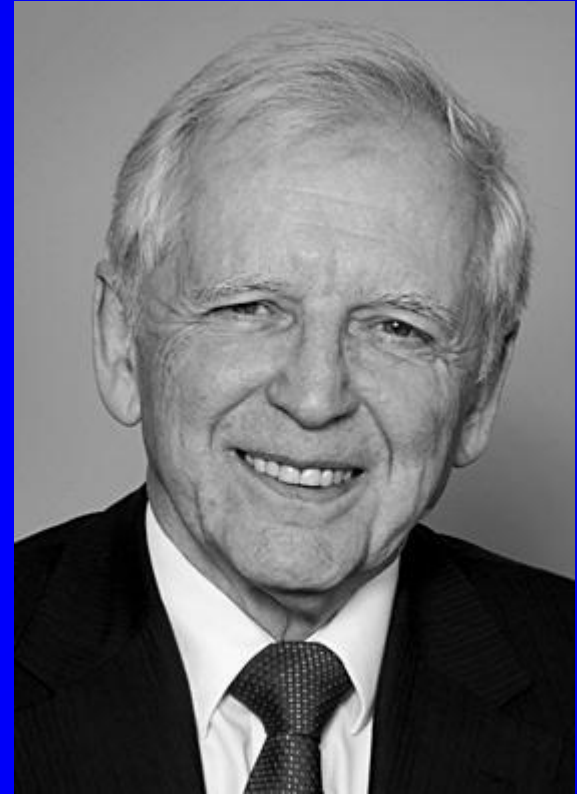
- Jack Cuzick has received honoraria from Qiagen, Roche, Abbott, Becton Dickinson, Gen-Probe, GSK and Merck as a consultant, speaker or advisory board member

HPV



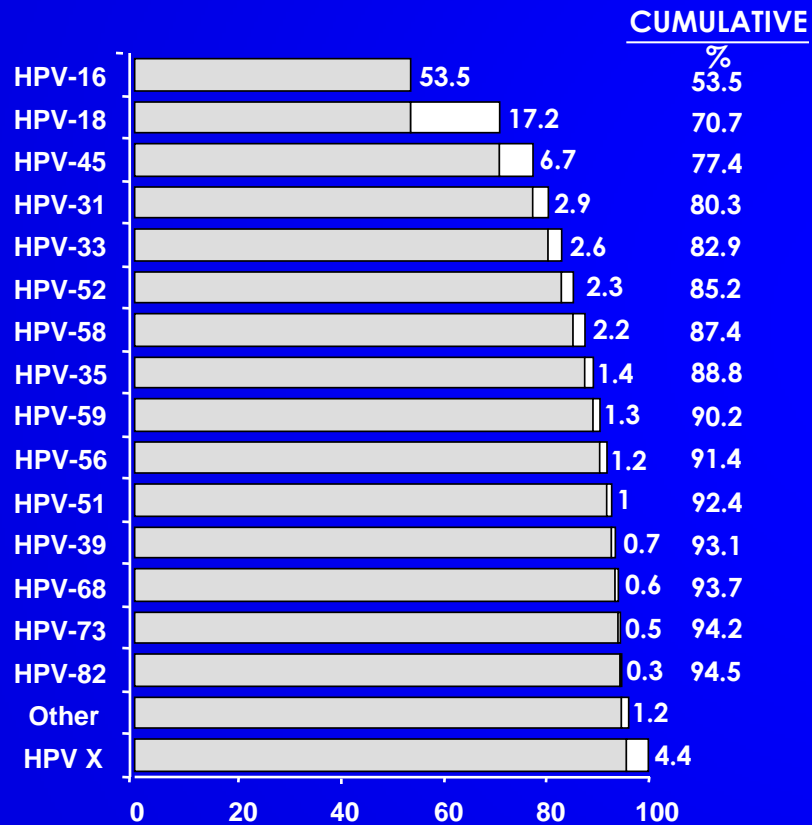
Recognition of Importance of HPV

The Nobel Prize in Physiology or Medicine 2008 was divided, one half awarded to Harald zur Hausen *"for his discovery of human papilloma viruses causing cervical cancer"*, the other half jointly to Françoise Barré-Sinoussi and Luc Montagnier *"for their discovery of human immunodeficiency virus"*

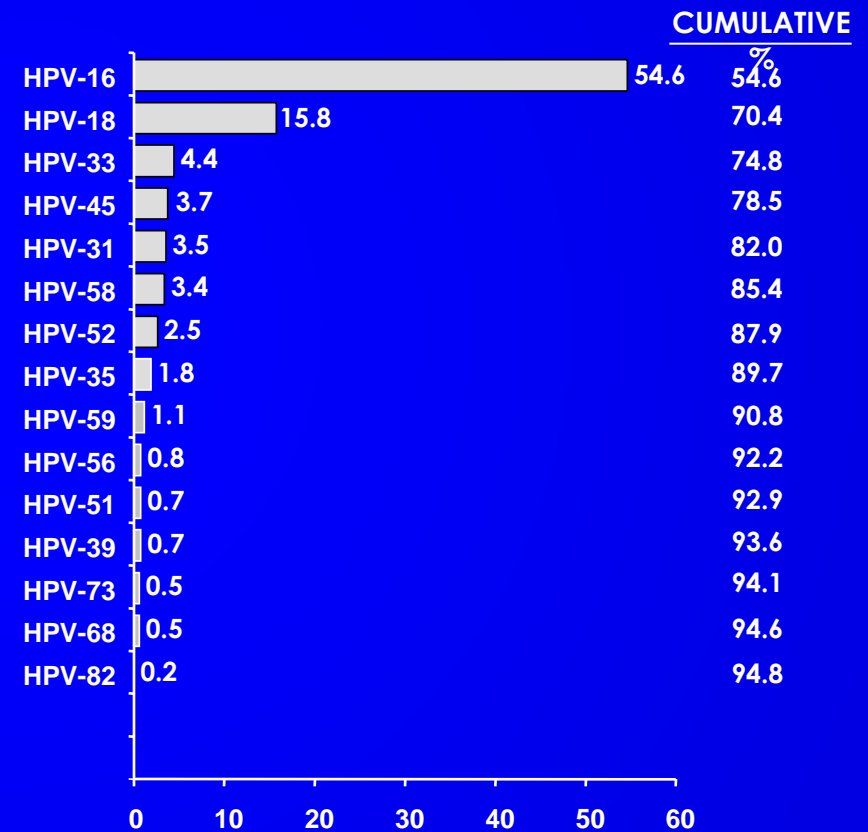


PERCENTAGES OF CERVICAL CANCER CASES ATTRIBUTED TO THE MOST FREQUENT HPV TYPES IN ALL WORLD REGIONS COMBINED

(A) IARC ANALYSIS OF 3,085 CASES

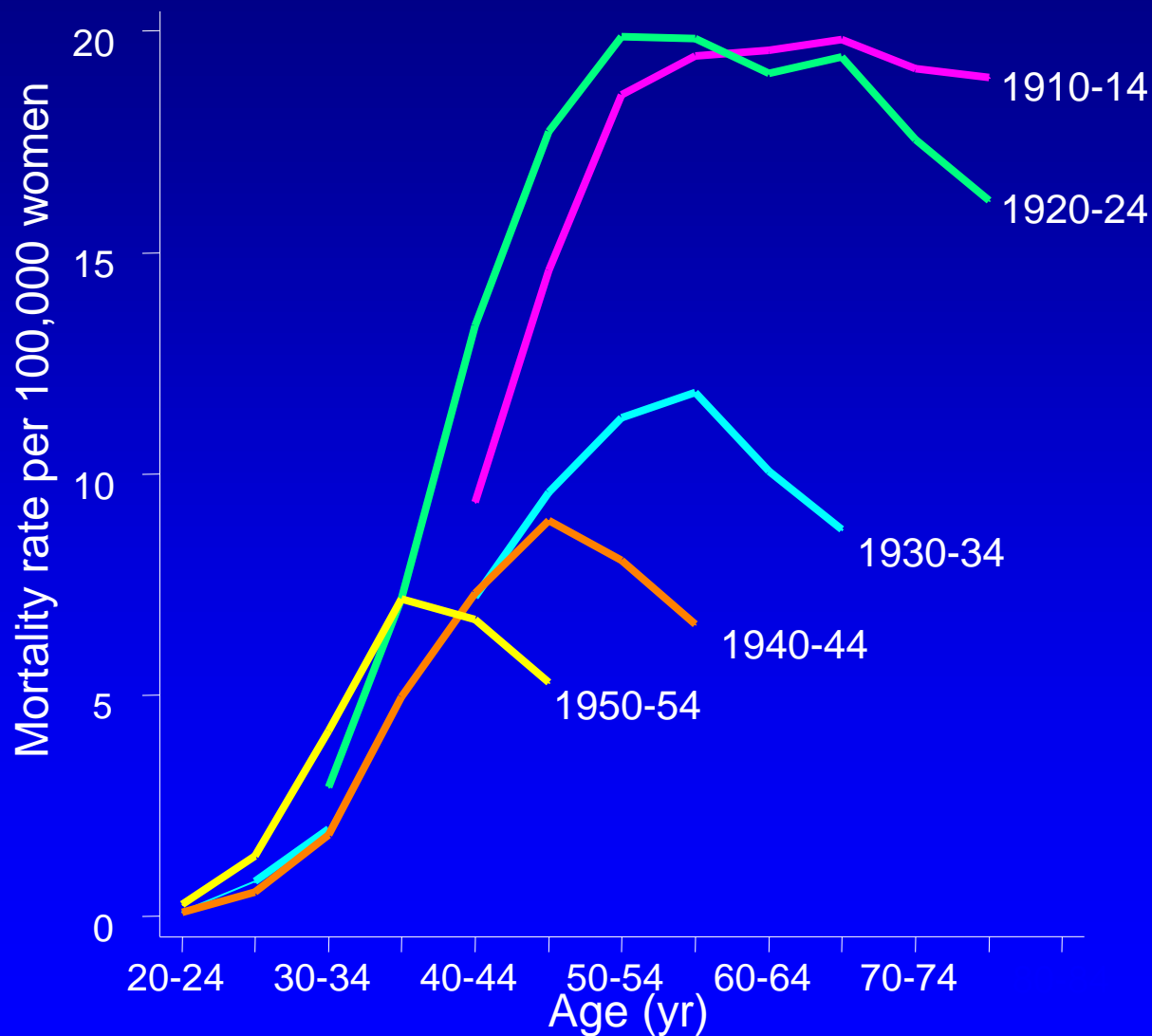


B) META-ANALYSIS OF 14,500 CASES



Screening

Age – Specific mortality rates by birth cohort, England and Wales, 1950-1998



UK audit - cases

- 62% of women with fully invasive cancer (age <70) had been screened within 5 years of diagnosis: 60% of squamous, 70% of adenocarcinoma.
- 10% of cases under age 65 were diagnosed >6 months after positive cytology.
- 52% had only negative smears

Baseline Results of HPV Testing in European & North American Screening Studies

Jack Cuzick

Christine Clavel, Ulli Petry, Peter Sasieni

Chris Meijer, Sam Ratnam

Philippe Birembaut, Anne Szarewski

Shalini Kulasingam, Heike Hoyer

Thomas Iftner



Barts and The London
Queen Mary's School of Medicine and Dentistry

Int J Cancer 119:1095-1101,2006



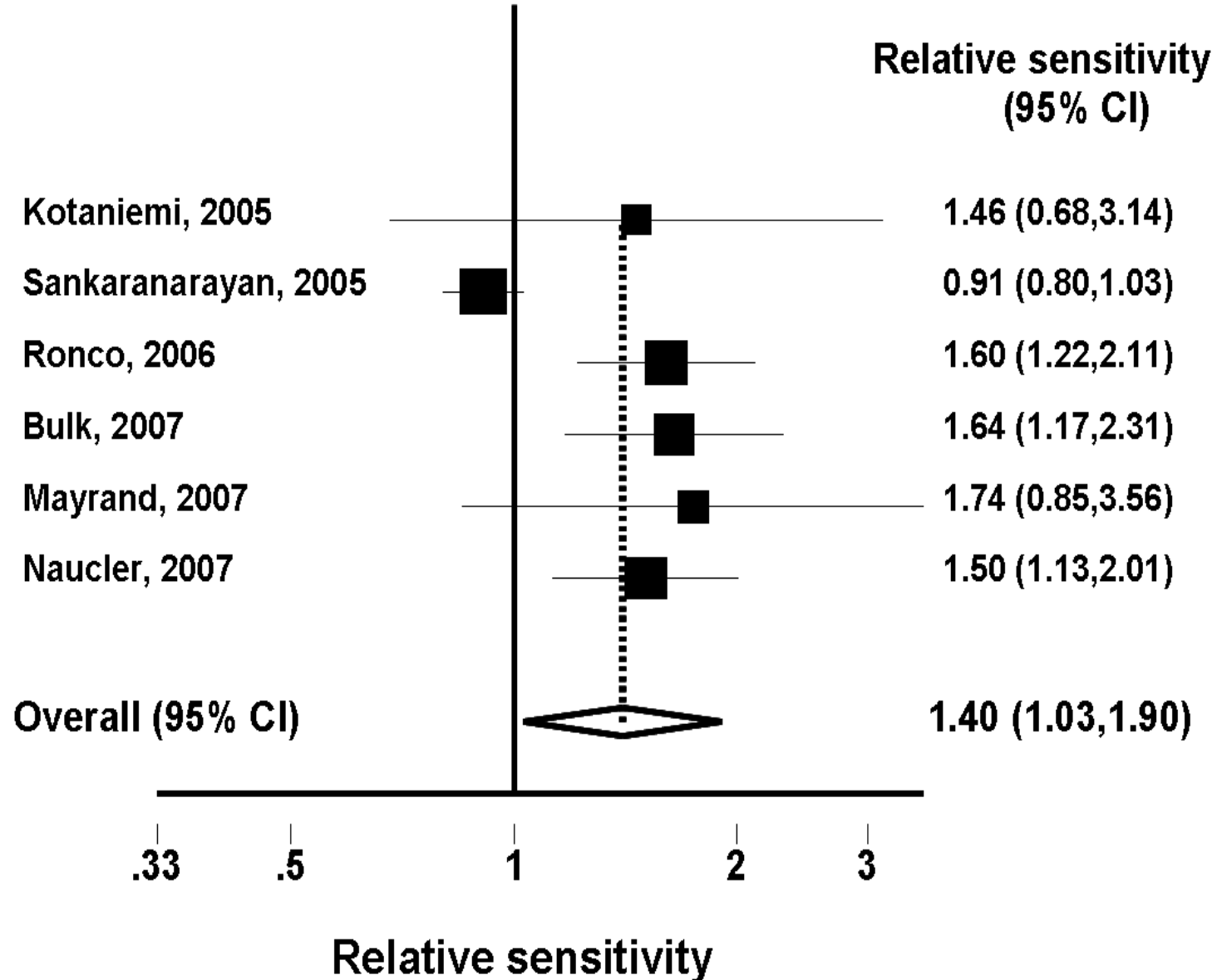
Summary

	Sensitivity	Specificity
HPV	96%	92%
CYTOLOGY	53%	97%

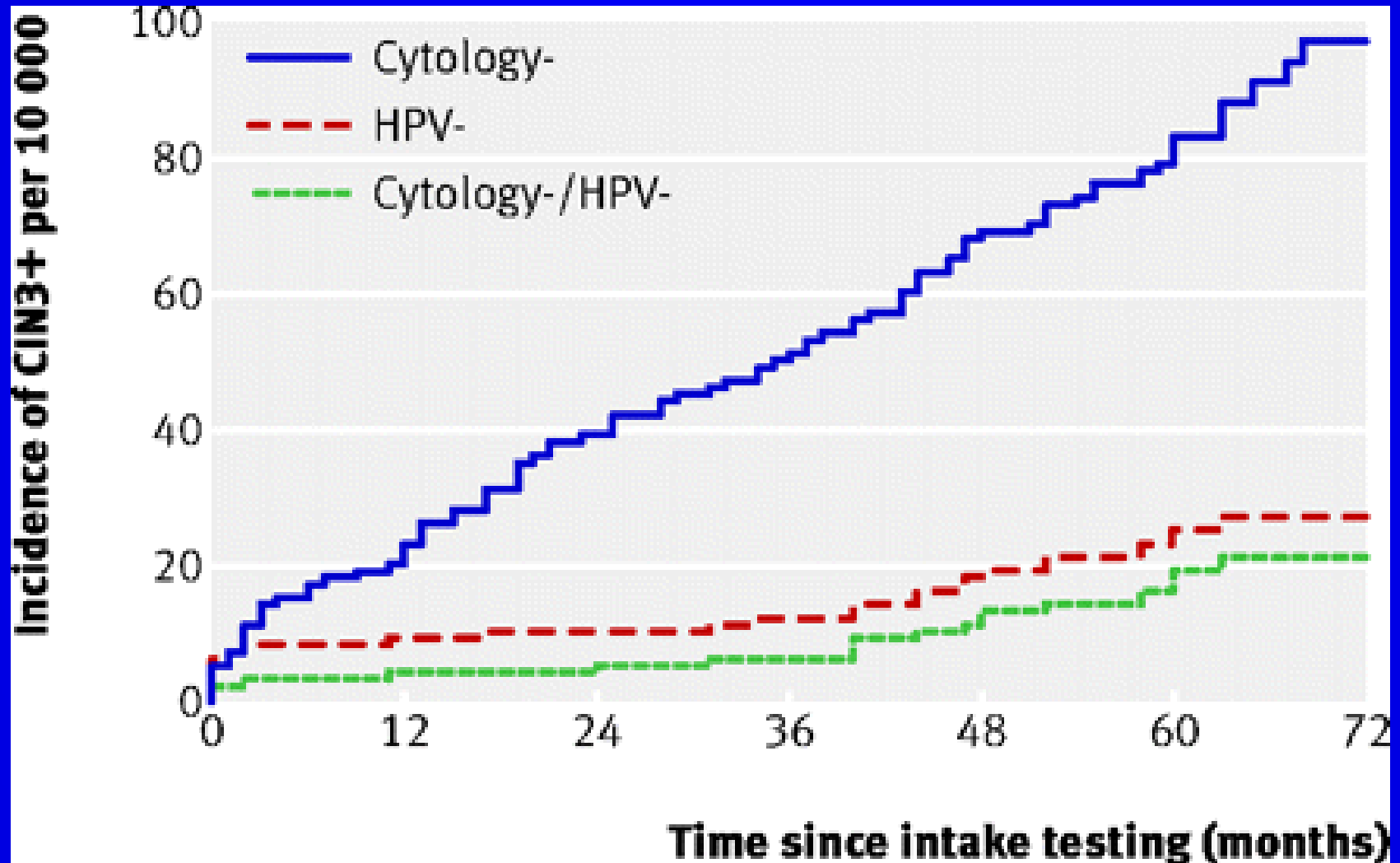
Double-testing studies after overview

		Sensitivity	Specificity
Italian Phase I	HPV	97.3	93.2
(experimental arm)	Cytology	74.0	94.8
Canadian	HPV	94.6	94.1
	Cytology	55.4	96.8

Relative Sensitivity of HPV vs cytology for CIN2+ in randomised trials



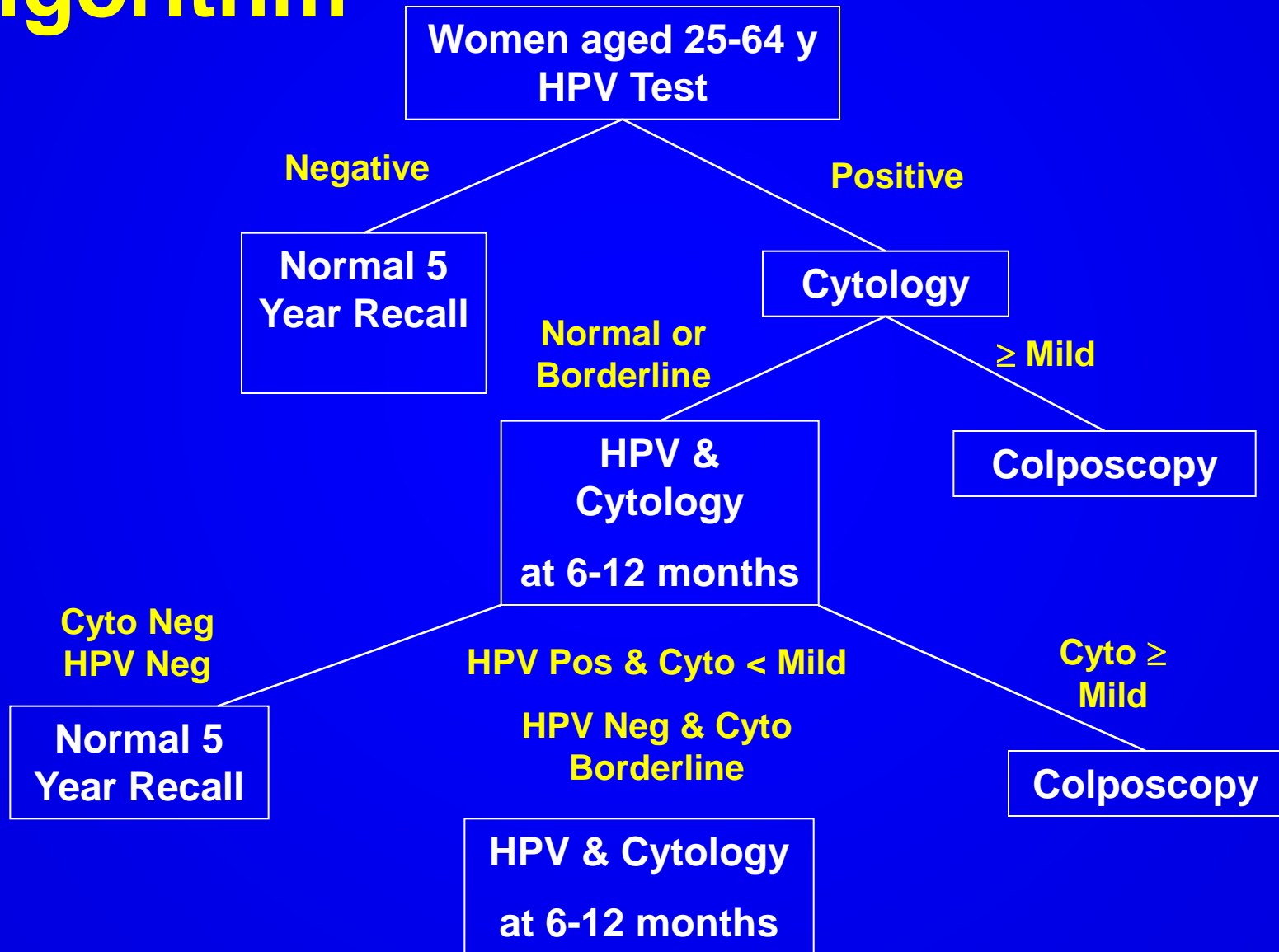
Cumulative incidence rate for CIN3+ according to baseline test results excluding Denmark and Tübingen



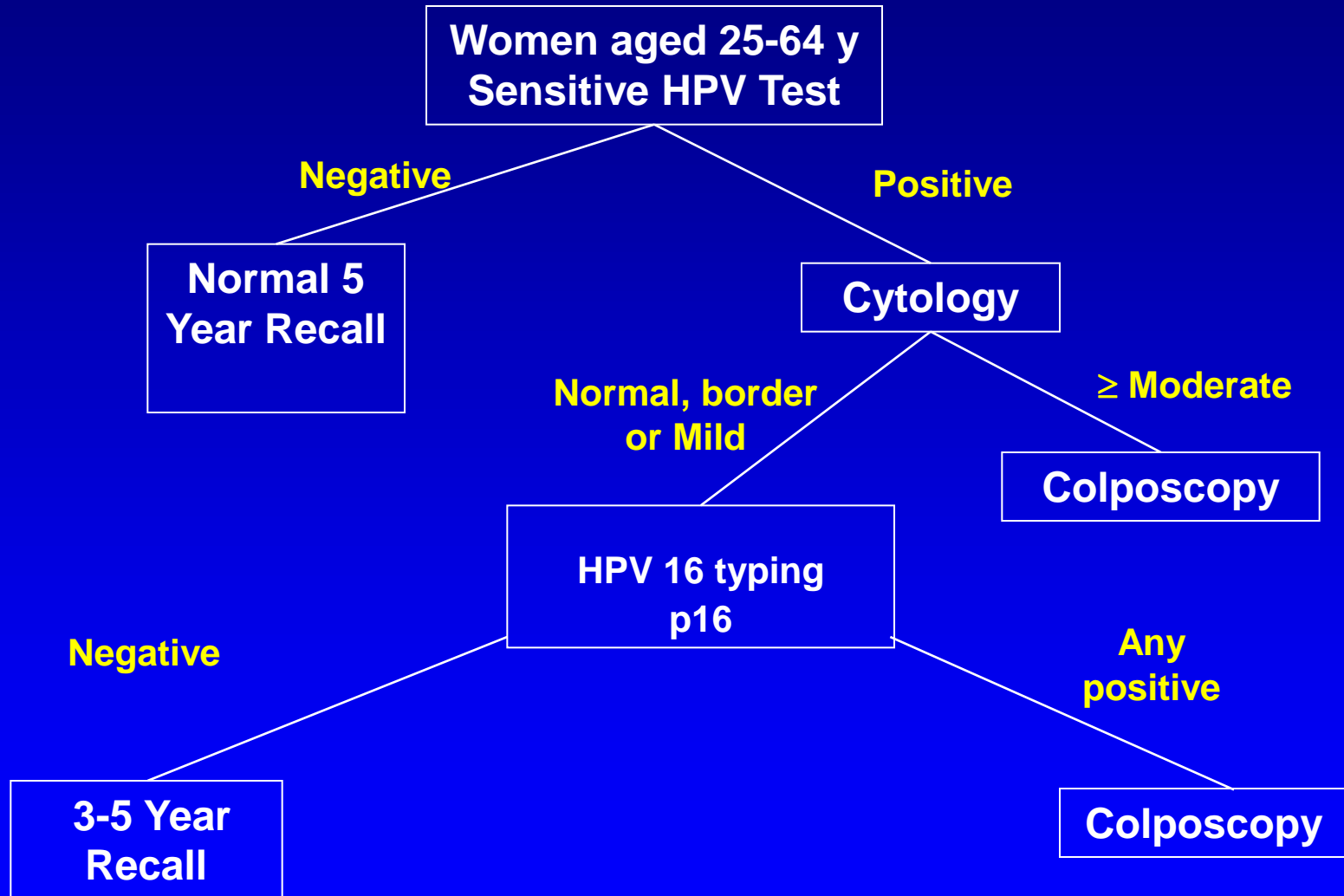
NTCC - INVASIVE CERVICAL CANCER

	HPV group	Cytology group	p value
Screening round one	7	9	0.62
Screening round two	0	9	0.004
Total over first two rounds	7	18	0.028

Proposed New Screening Algorithm



Potential Future Screening Algorithm

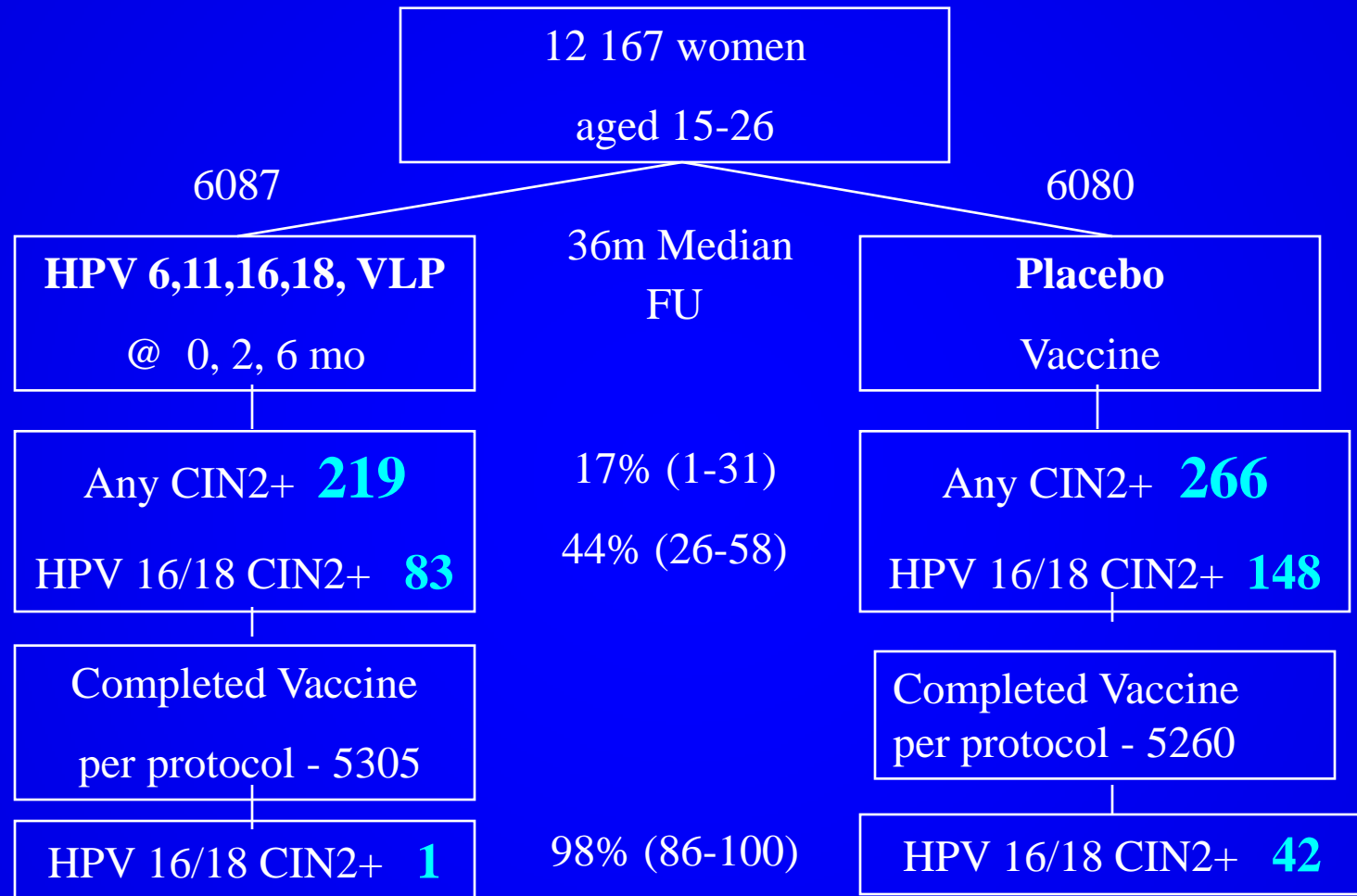


Vaccination

Merck Vaccine trials

Protocol	005 Proof of Principle	007	013 FUTURE I	015 FUTURE II
Phase	Ila	Ilb	III	III
No entered	2409	552	5455	12167
Sites	USA	International	International	International
HPV types	16	6,11,16,18	6,11,16,18	6,11,16,18
Age	16-23	16-23	16-23	16-26
No Sex partners	0-5	0-4	0-4	0-4
Average FU	3.5y	2.5y	2.5y	2.5y

Merck- Quadrivalent HPV Vaccination Trial FUTURE II



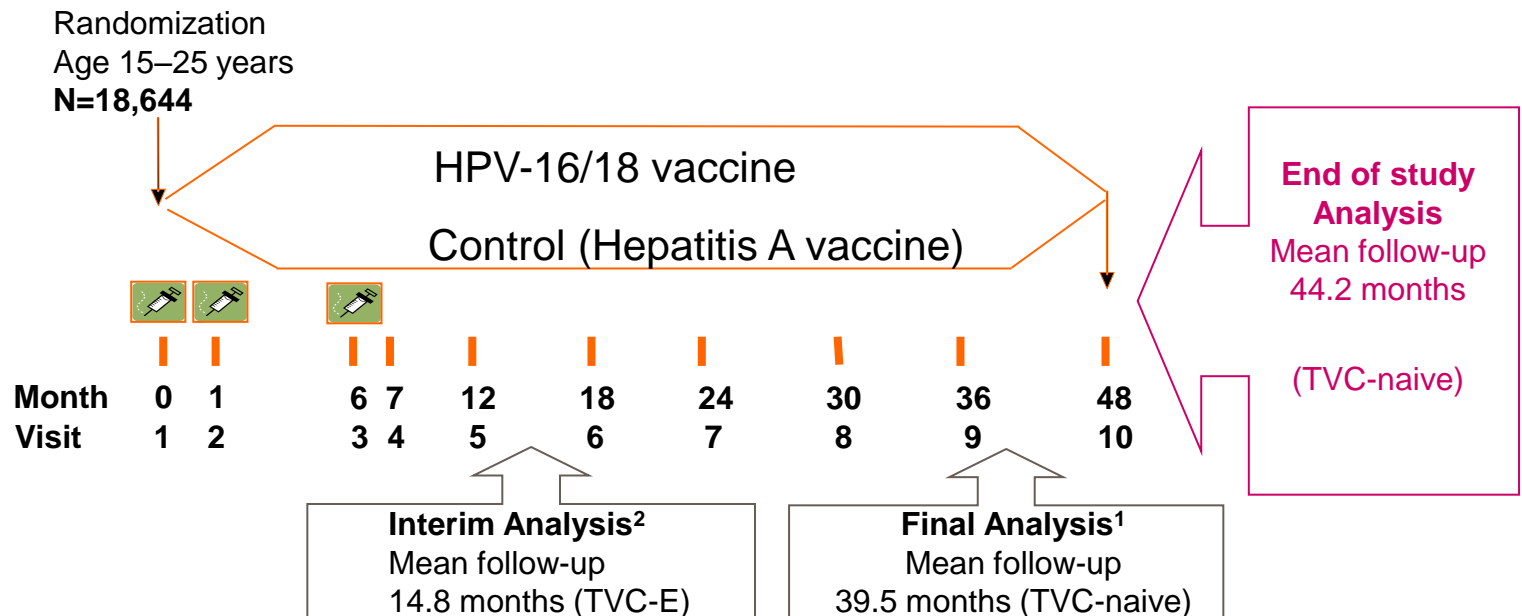
- **Nonavalent Vaccine in late development by Merck**
 - HPV16,18
 - HPV 6,11 (genital warts)
 - 5 new oncogenic types – 31,33,45,52,58

GSK Phase 3 Study - PATRICIA

(Papilloma TRIal against Cancer In young Aadults)

End of Study Analysis

- Phase III efficacy trial* conducted in 14 countries¹ from: Europe, Asia-Pacific, North America, Latin America

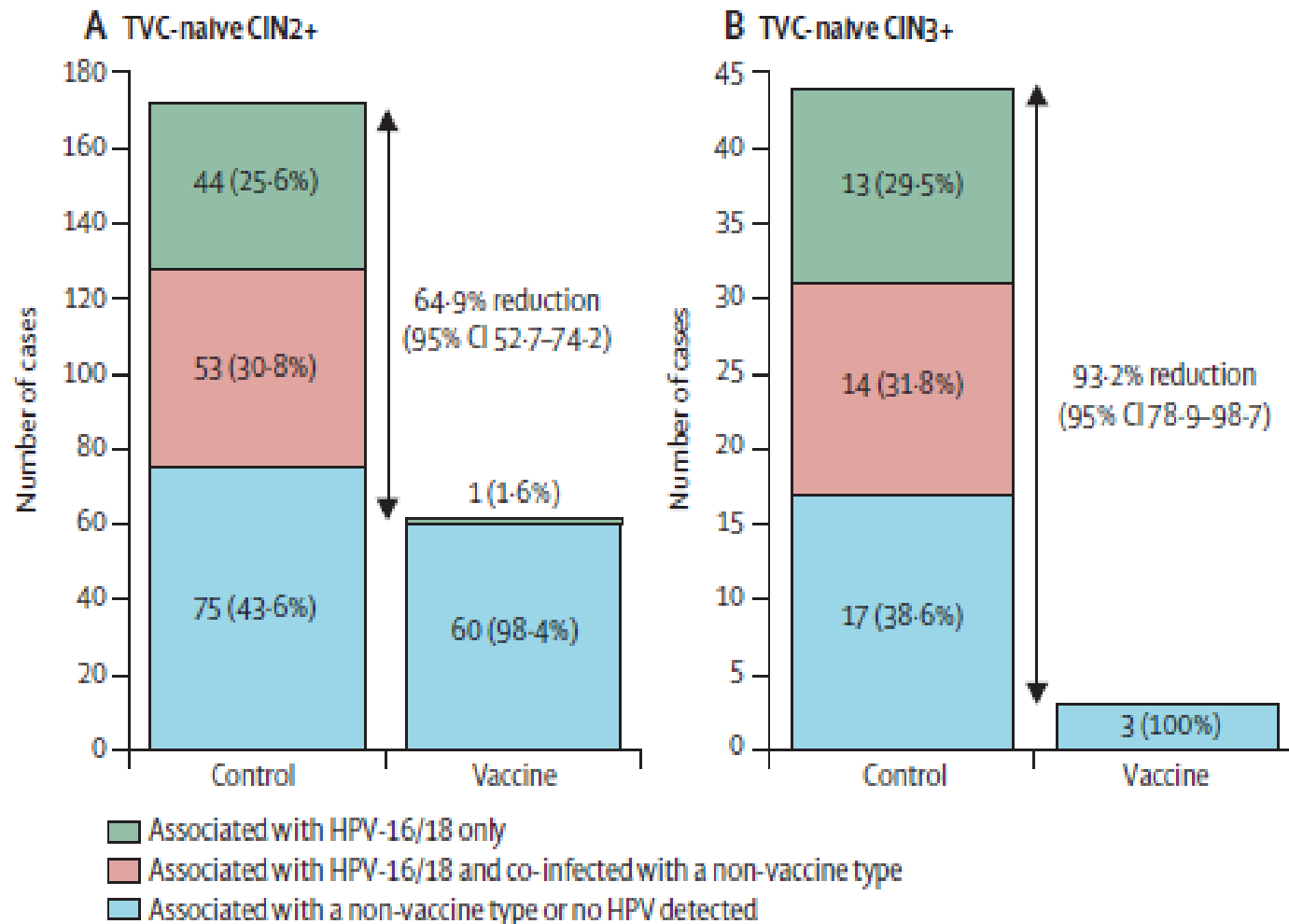


¹ Paavonen J et al. *Lancet* 2009; 374: 301-314

² Paavonen J et al. *Lancet* 2007; 369: 2161–70

*Study HPV-008 -NCT00122681

Number of cases of CIN2+ and CIN3+ associated with vaccine and non-vaccine types in the TVC-naïve



Vaccine - Issues

- Need for 3 doses
- Cross - protection
- Durability of protection
- Age groups – focus adolescent girls
- Vaccination of boys
- More rugged vaccines not needing careful cold chain storage
- Not effective after HPV infection

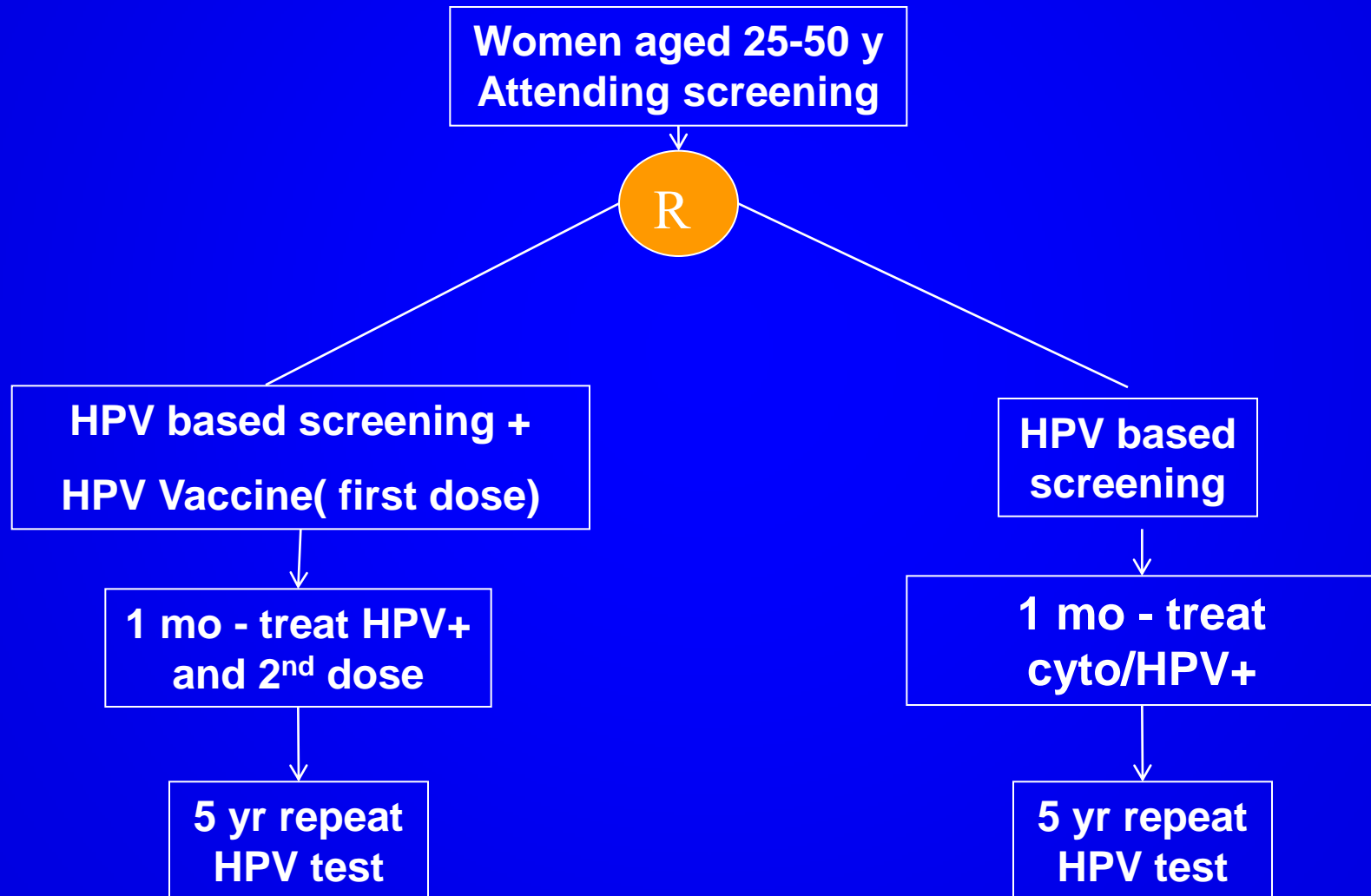
Potential future opportunities for HPV vaccination

- **Cervical cancer prevention: improved vaccination coverage**
 - Extending the age range for vaccination (paediatrics and adult women)
 - Alternative dose schedules, e.g. two doses¹
- **Vaccinate and screen algorithms for older women**
 - Screen to remove all current disease
 - Vaccine esp with polyvalent vaccines to prevent future disease
- **Next-generation HPV vaccines**
 - Polyvalent L1 virus-like particle (VLP) vaccines²
 - L2 peptide vaccines²
 - Chimeric L1/L2 VLP HPV vaccines³
 - Combined prophylactic and therapeutic HPV vaccination²

1. Kreimer AR, et al. *IPvC* 2010; Abstract;

2. Stanley M. *Curr Opin Infect Dis* 2010; **23**:70–75; 3. Kanda T & Kondo K. *Hum Vaccin* 2009; **5**:43–45.

Screen and Vaccinate Trial Schema



Cervical cancer is preventable!

- **Cervical cancer is the only cancer with a single, known cause: the human papillomavirus (HPV)**
- **Vaccination can prevent infection, but not eliminate it or subsequent cancer once it occurs**
- **Screening can identify precursor lesions which are treatable and HPV testing has a sensitivity approaching 100%**
- **Combined screening and vaccination in women aged 25-50 offers the best chance of rapid elimination of cervix cancer**