Primary HPV screening Current state of the science Europe

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Disclosures

- No financial relationships or conflict of interest to disclose

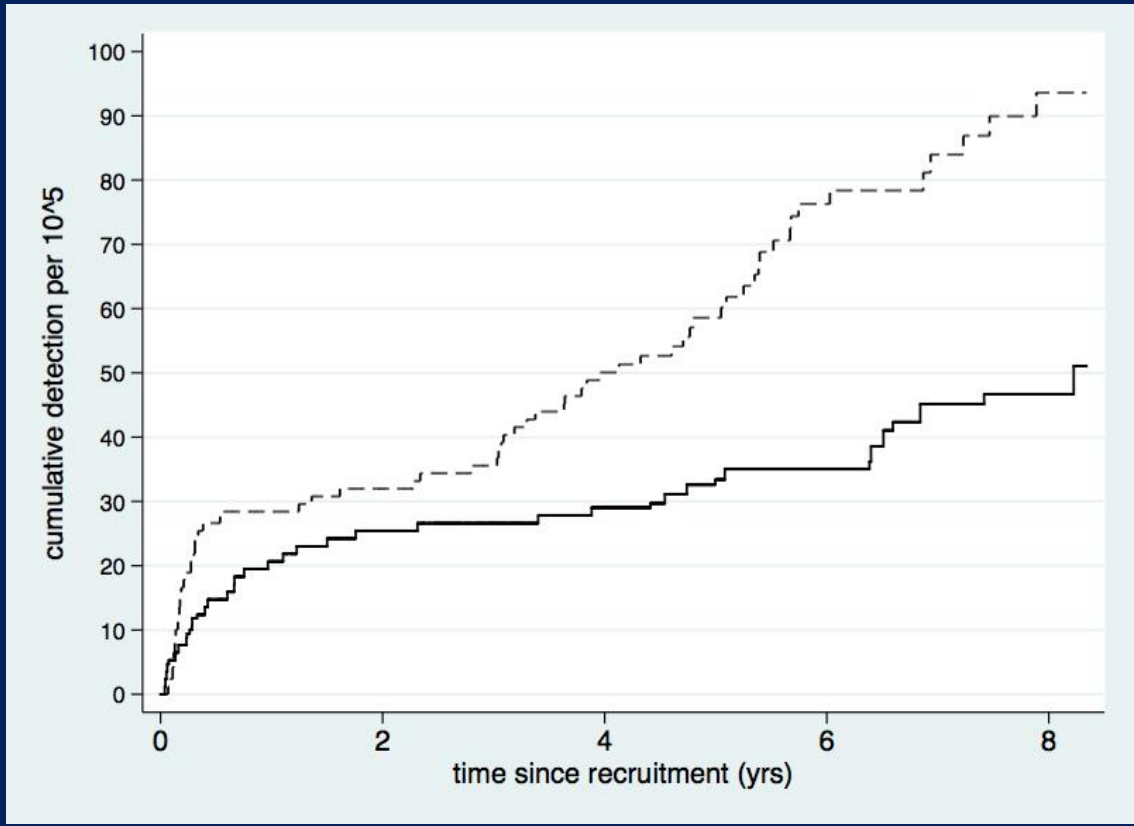
Randomised trials on HPV vs. cytology-based cervical screening with follow-up for 2+ screening rounds

Study	Age	Primary Test Exper. arm	Management HPV+ve women	Primary Test Conv. arm	Screening interval negatives	Management Rounds 2+	# women (ratio)
Swedescreen	29-38	HPV and conv. Cytol.	Cytological triage with HPV repeat	conv. cytol	3 yrs	All as conventional round 1	12,527 (1:1)
POBASCAM	29-61	HPV and conv. Cytol.	Cytological triage with HPV repeat	conv. cytol	5 yrs	All as experimental round 1	44,489 (1:1)
ARTISTIC	20-60	HPV and LBC	Cytological triage with HPV repeat	LBC	3 yrs	As corresponding arm round 1	25,078 (3:1)
NTCC	25-60	Phase1:HPV and LBC Phase 2: stand alone HPV	Colposcopy (cytological triage in phase 1 age 25-34)	conv. cytol	3 yrs	All as conventional round 1	94,730 (1:1)

Pooled analysis of the Swedescreen, POBASCAM, NTCC and ARTISTIC
Cumulative incidence of ICC by arm. All recruited women

Solid lines:HPV group.
Dotted lines: cytology group

	Overall	≤2.5 yrs from enrolment	>2.5 yrs from enrolment
Pooled RR	**0.60** (0.40-0.89)	**0.79** (0.46-1.36)	**0.45** (0.25-0.81)



Ronco et al. Lancet 2014 modif.

Proportion of women who had biopsy by arm and study and HPV/cytology ratio

	No (%) of women who had biopsy §		ratio* (95%CI)
	Cytology arm	HPV arm	
NTCC	**1127 (2.4)**	**2538 (5.4**	**2.24 (2.09-2.39)**
POBASCAM	**1533 (7.0)**	**1535 (7.0)**	**1.01 (0.94-1.08)**
Swedescreen	**701 (11.2)**	**675 (10.8)**	**0.97 (0.87-1.07)**
ARTISTIC	**528 (8.6)**	**1716 (9.3)**	**1.08 (0.97-1.19**
Pooled RR (Fixed effects)			**1.35 (1.30-1.40**
I^2 (p heterogeneity between studies)			**99.1% (p<0.0001)**
Pooled RR (Fixed effects) NTCC excluded			**1.02 (0.97-1.07)**
I^2 (p heterogeneity between studies)NTCC excluded			**30.7% (p=0.236)**

Ronco et al. Lancet 2014 modif.

NTCC STUDY
WOMEN AGE 25-34

DETECTION OF CIN2 BY STUDY PERIOD

	Women enrolled (invited to round 2)	screening round1 N (%)	screening round2 N (%)	Total over both rounds N (%)
HPV group	12939 (12035)	**126** (0.97%)	**8** (0.07%)	**134** (1.04%)
Cytology group	12596 (12350)	**27** (0.21%)	**15** (0.12%)	**42** (0.33%)
RR (95%CI)		**4.54** (3.00-6.88)	**0.55** (0.23-1.29)	**3.11** (2.20-4.39)
P heterogeneity between phases		**0.65**	**0.66**	**0.60**

Ronco et al. Lancet Oncol 2010 modif

Relative incidence density (RR) of ICC with HPV- vs. cytology-based screening by age at recruitment

	<30$	30-34	35-49	≥50
# cases	5	20	59	25
RR	0.98 (0.19-5.20)	0.36 (0.14-0.94)	0.64 (0.37-1.10)	0.68 (0.30-1.52)
p heterogeneity studies	0.0% (p=0.34)	7.2% (p=0.36)	0.0% (p=0.55)	36.5% (p=0.21)

$ subjects from POBASCAM and Swedescreen excluded

p heterogeneity of HPV effect between age 30-34 and 35+ : 0.13

Ronco et al. Lancet 2013 modif.

Risk of invasive carcinoma after a negative entry test (HPV- in HPV arm and cytology- in cytology arm)

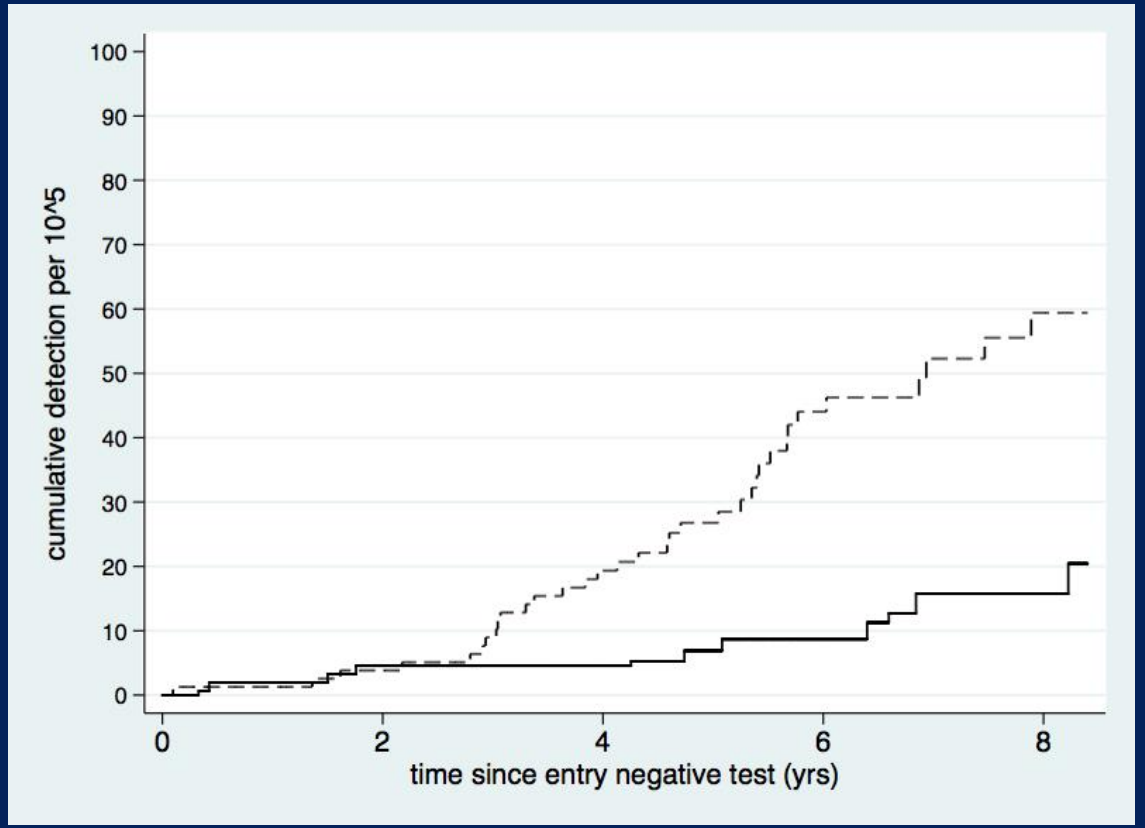
Solid lines: HPV group.
Dotted lines: cytology group

Pooled RR

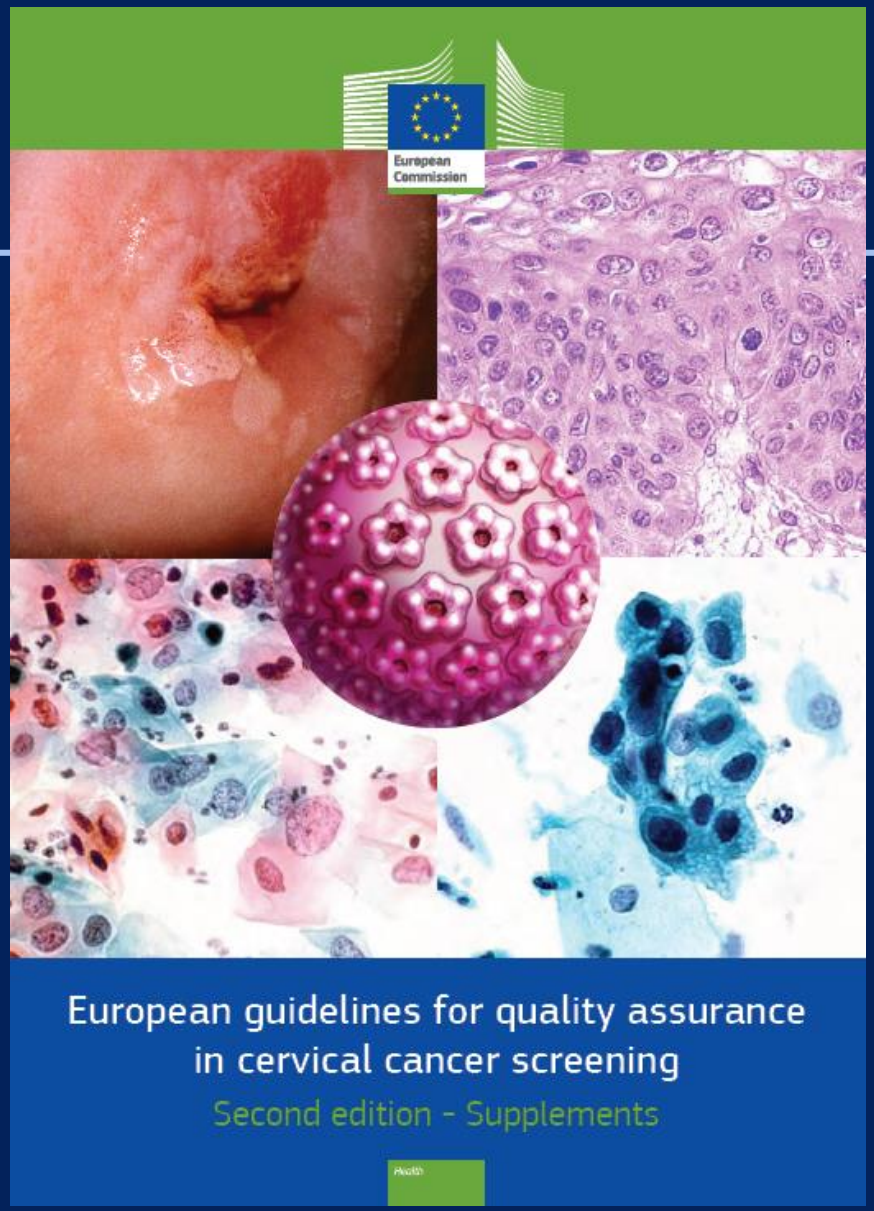
0.30 (0.15-0.60)

	3.5 years	5.5 years
cytology	15.4 (CI 7.9-27.0)	36.0 (23.2-53.5)
HPV	4.6 (1.1-12.1)	8.7 (3.3-18.6)

Ronco et al. Lancet 2014 modif.



observations censored 2.5 yrs after CIN2 or CIN3 detection, if any



Screening for cervical cancer with primary testing for human papillomavirus

Authors
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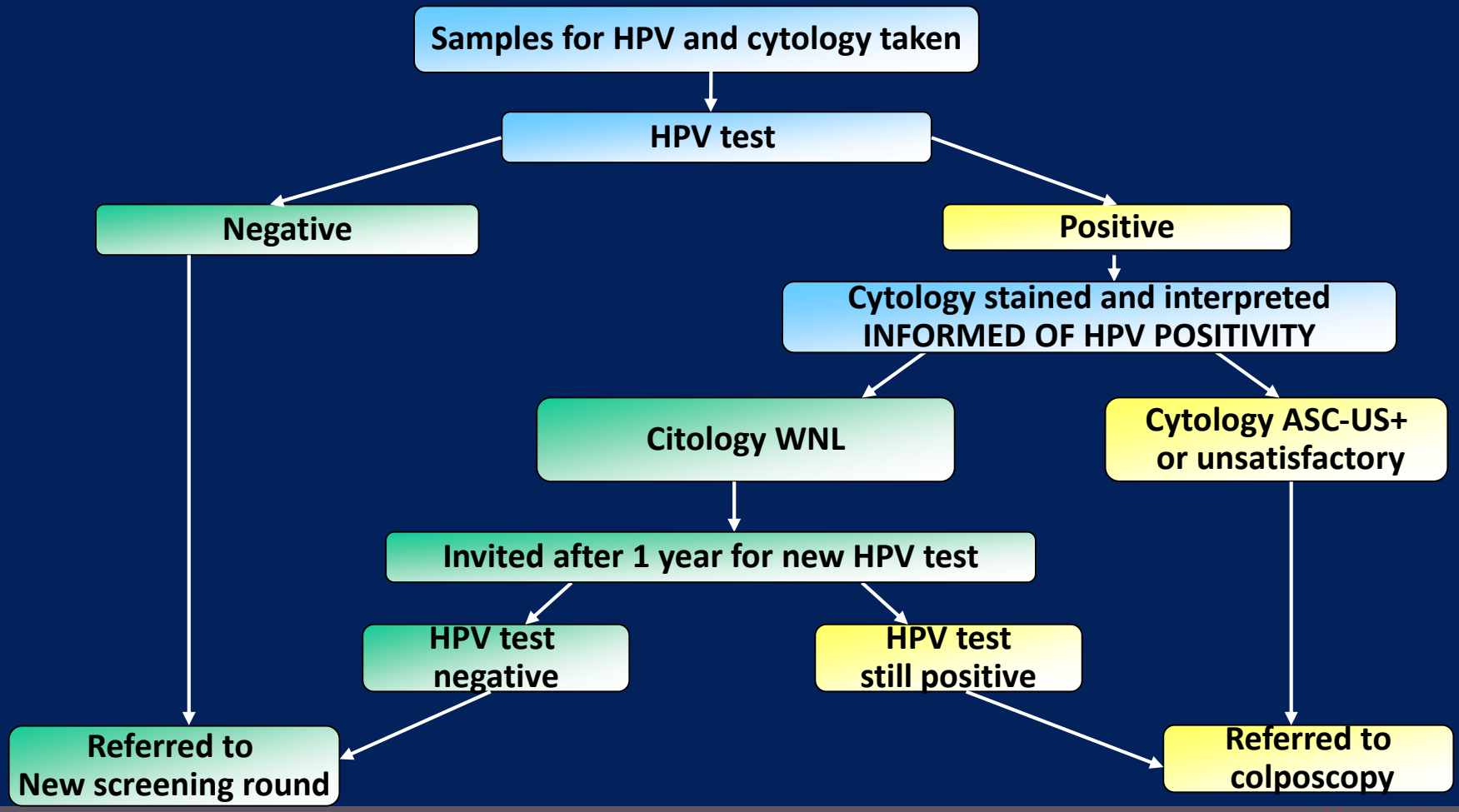
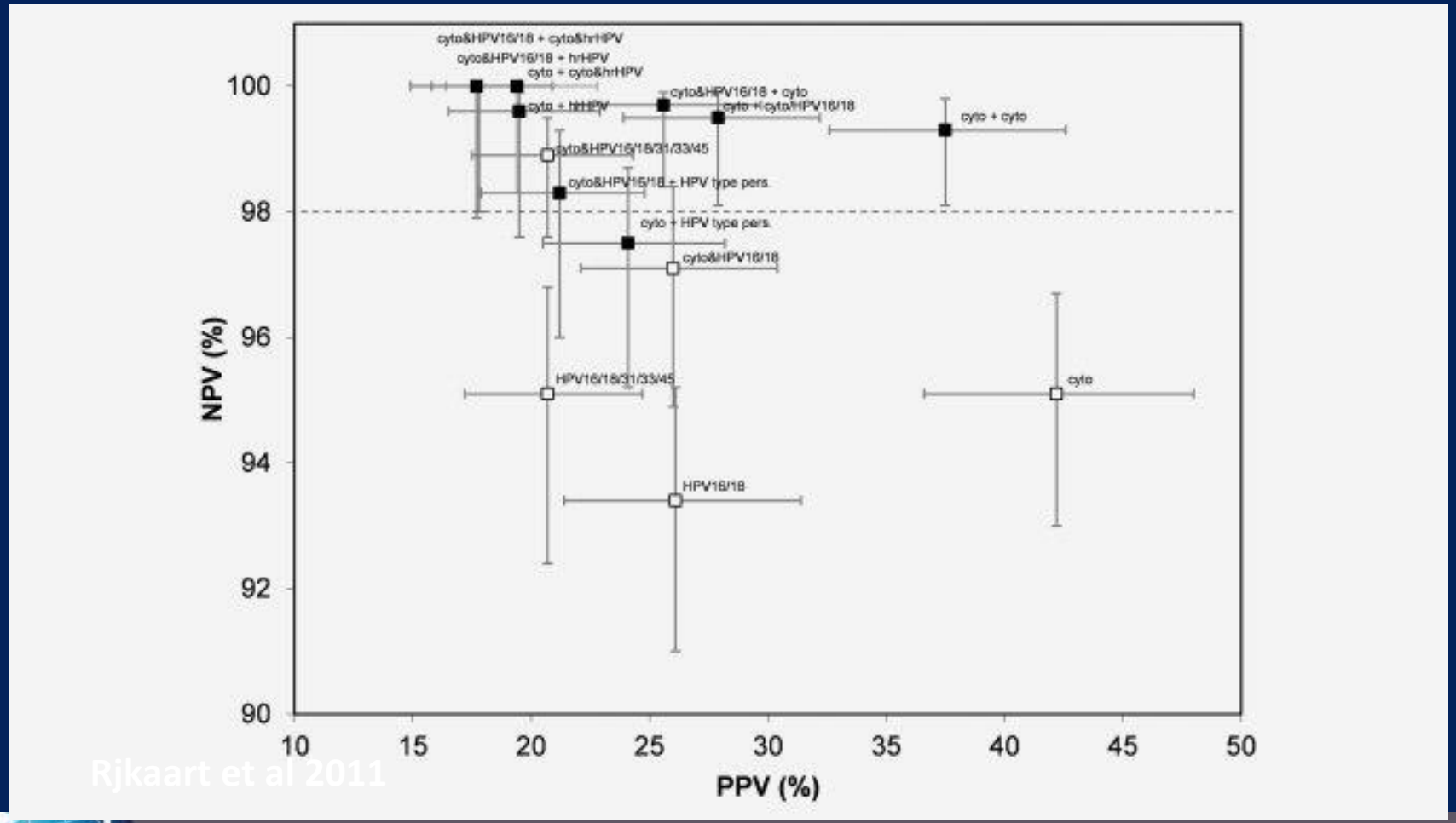
Main Recommendations

- Start age 30/35, stop as with cytology
- At least 5-year intervals
- Stand-alone HPV
- Cytological triage of HPV+ women
- Use validated tests
- Self sampling for non attenders
- Use just in organised settings

HPV based screening - Italy



PPV and NPV of different triage strategies in VUSA Screen study (Rijkaart et al.2011)

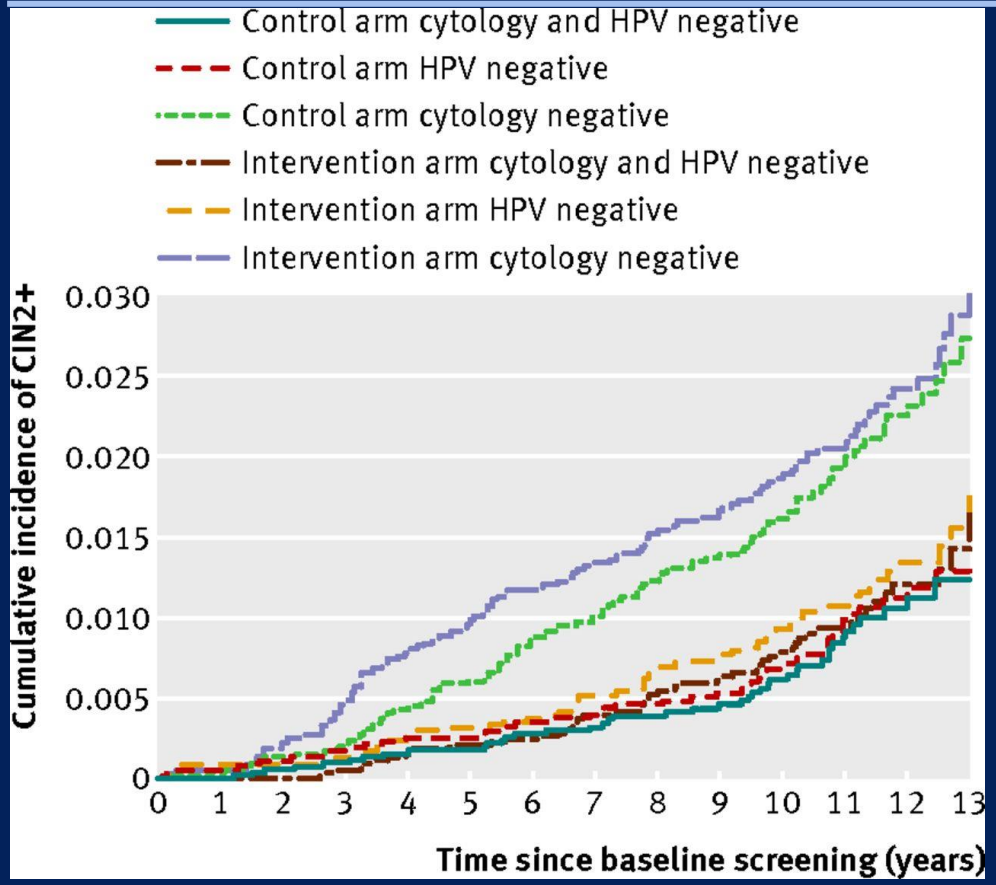


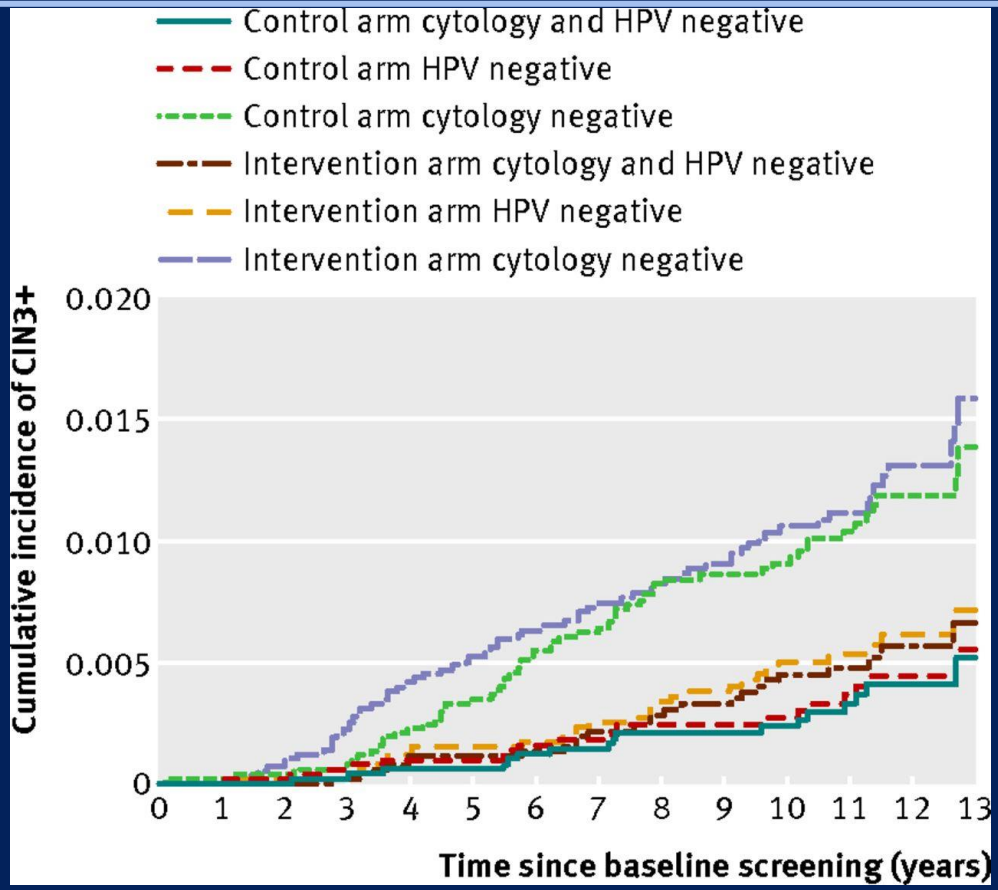
Rjkaart et al 2011

Dutch triage protocol

If triage negative repeat cytology after 6 months

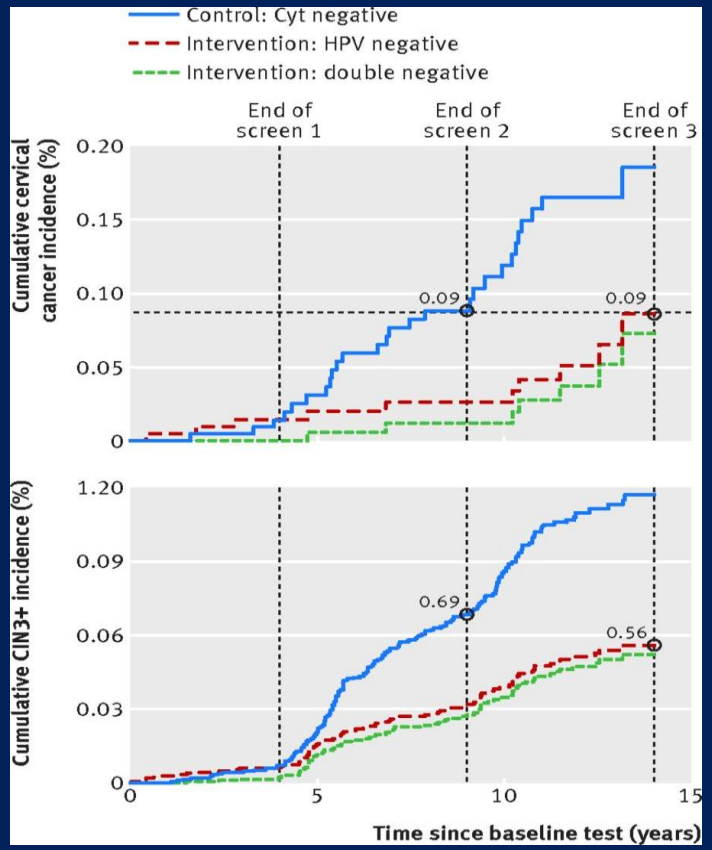
Long term follow-up Swedescreen





Elfström et al. BMJ 2014

Long term follow-up POBASCAM



Dijkstra et al. BMJ 2016

Screening interval with HPV

HPV CYTOLOGY

Netherlands

Age 30-49: 5 years Age 30-60: 5 years

Age 50+ : 10 years.

Italy

Age 30-64: 5 years Age 25-64: 3 years

COHEAHR PROJECT

- FURTHER POOLED ANALYSES OF RCTS (Age effects, triage methods, biological parameters for modelling)
- META-ANALYSES
- SCREENING IN VACCINATED WOMEN (RCT in Finland, cohort-based Sweden and Italy)
- SELF SAMPLING WITH MOLECULAR TRIAGE (RCT Netherlands)
- MODELLING
- FASTER PROJECT (Increased vaccination age for rapid eradication, feasibility)