Screening in the nonavalent vaccine era: What do we know and what do we need to know?

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When can we stop screening highly vaccinated birth cohorts?

-Birth cohorts who do not propagate HPV16/18 have an about 70% reduced background risk for cervical cancer.

-Birth cohorts who do not propagate HPV16/18/31/33/45/52/58 have an about 90% reduced risk for cervical cancer.

We currently offer 12 lifetime screens –
If all birth cohorts were highly vaccinated against HPV16/18, two lifetime screens would be enough.

If all birth cohorts were highly vaccinated against HPV16/18/31/33/45/52/58 one lifetime screen would be enough.

When to stop screening highly vaccinated birth cohorts?

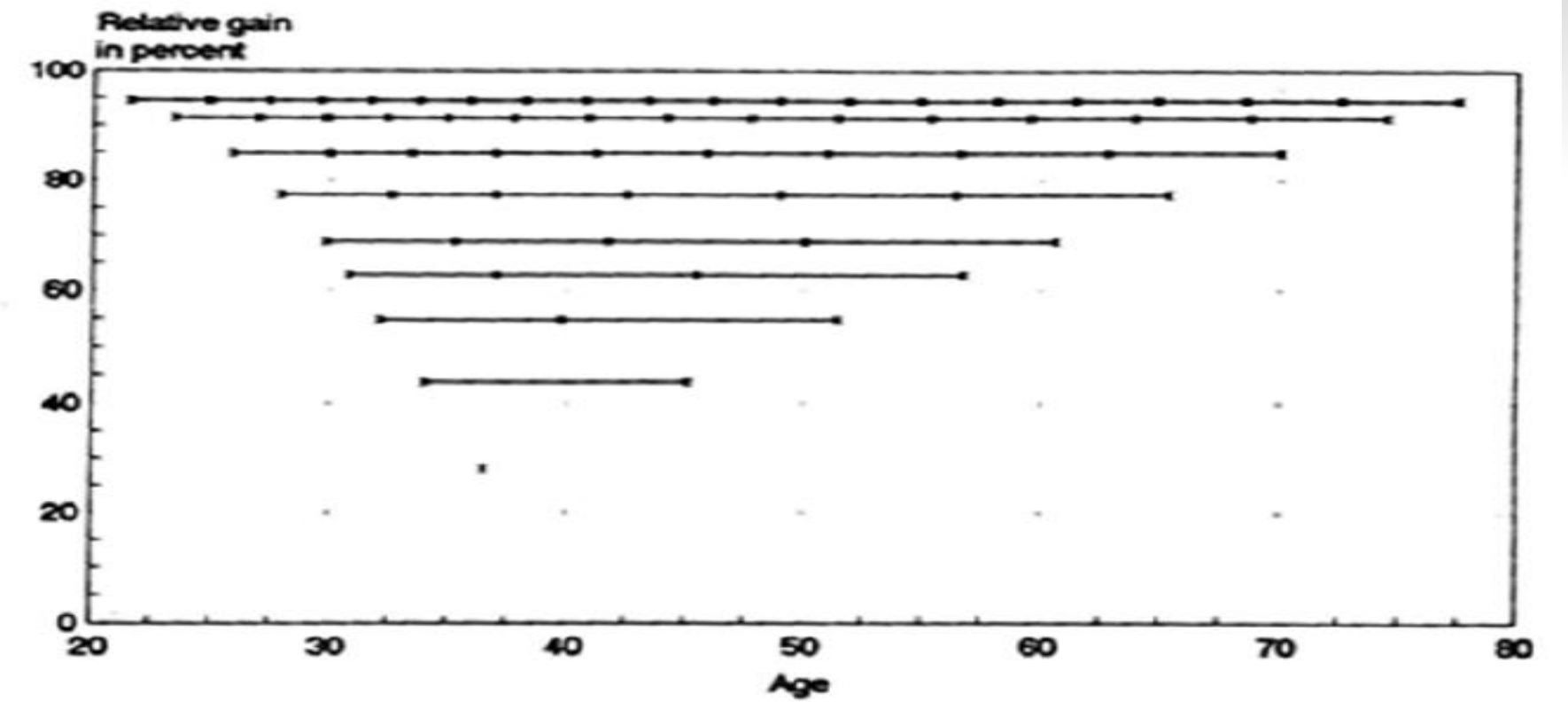
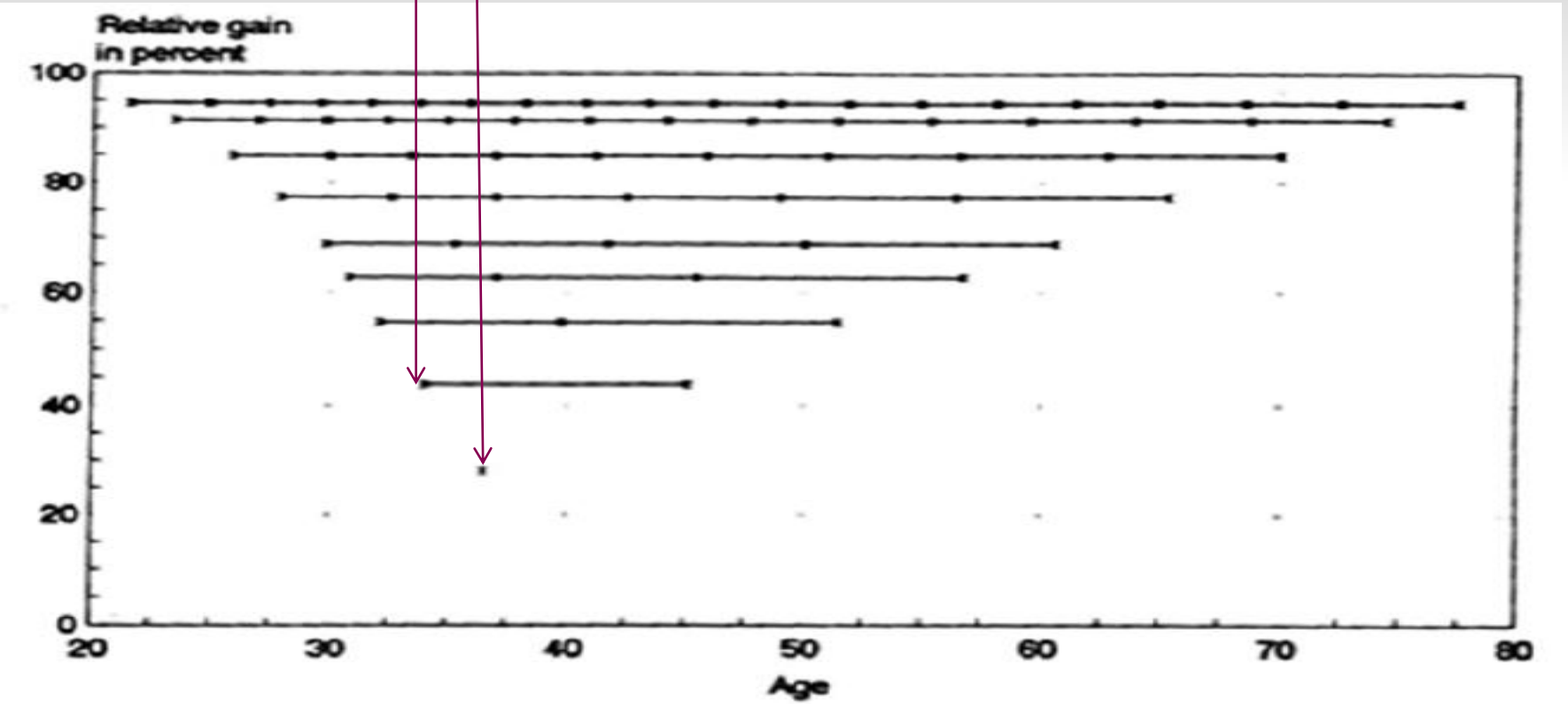


Figure 5. The schedule and reduction in the lifetime probability of developing invasive cervical cancer with optimal scheduling of programs with a total of 1, 2, 3, 4, 5, 7, 10, 15, and 20 screenings with 75% of all prevalent cases of cancer *in situ* eliminated at each round (efficiency 0.75). For two screenings, for example, an optimal schedule at ages 34 and 45, give a relative gain of 44%.

When to stop screening highly vaccinated birth cohorts?

Probably no screening required before 33 for HPV16/18 vaccinated cohorts and not before 36 for nonavalent vaccine vaccinated cohorts



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Disease burden to estimate benefit:

The data exists!

Virology 445 (2013) 224–231

HPV type	IARC classification	Normal		ASCUS		LSIL		HSIL		CIN1		CIN2		CIN3		ICC	
		N tested	%pos	N tested	%pos	N tested	%pos	N tested	%pos	N tested	%pos	N tested	%pos	N tested	%pos	N tested	%pos
Any		263971	12.6	13178	52.1	19456	75.2	7727	85.3	10030	74.2	4809	85.4	11679	92.4	41101	89.5[a]
HPV16	1	263971	2.6	13178	12	19456	19.5	7727	40.5	10030	19.2	4809	34	11679	53.8	41101	55.8[a]
HPV18	1	263702	1	13161	4.7	19447	6.3	7711	8.2	9883	7	4735	8.7	11583	6.9	41164	14.3[a]
HPV45	1	243656	0.6	11591	2.9	14957	3.3	5901	3.9	8527	3	4344	4.3	10030	3.4	33997	4.8[a]
HPV33	1	254120	0.6	12218	3	18617	4.9	7431	7.1	9176	3.7	4617	7.1	11121	8.5	37700	4.0[a]
HPV58	1	247990	0.8	11790	3.9	15052	5.5	6108	6.9	8762	7.1	4420	10.3	10322	8.4	35539	4.0[a]
HPV31	1	252392	1	12191	4.7	18546	7.9	7293	9.4	9193	6.8	4754	10	11254	10.8	36769	3.5[a]
HPV52	1	239298	1	10288	5.4	13016	6.5	5268	8.6	8546	10.1	4486	14.1	10399	9.6	34939	3.2[a]

Disease burden: We need interpreted data.
AP= S*1-1/RR. Particularly important for low grade lesions

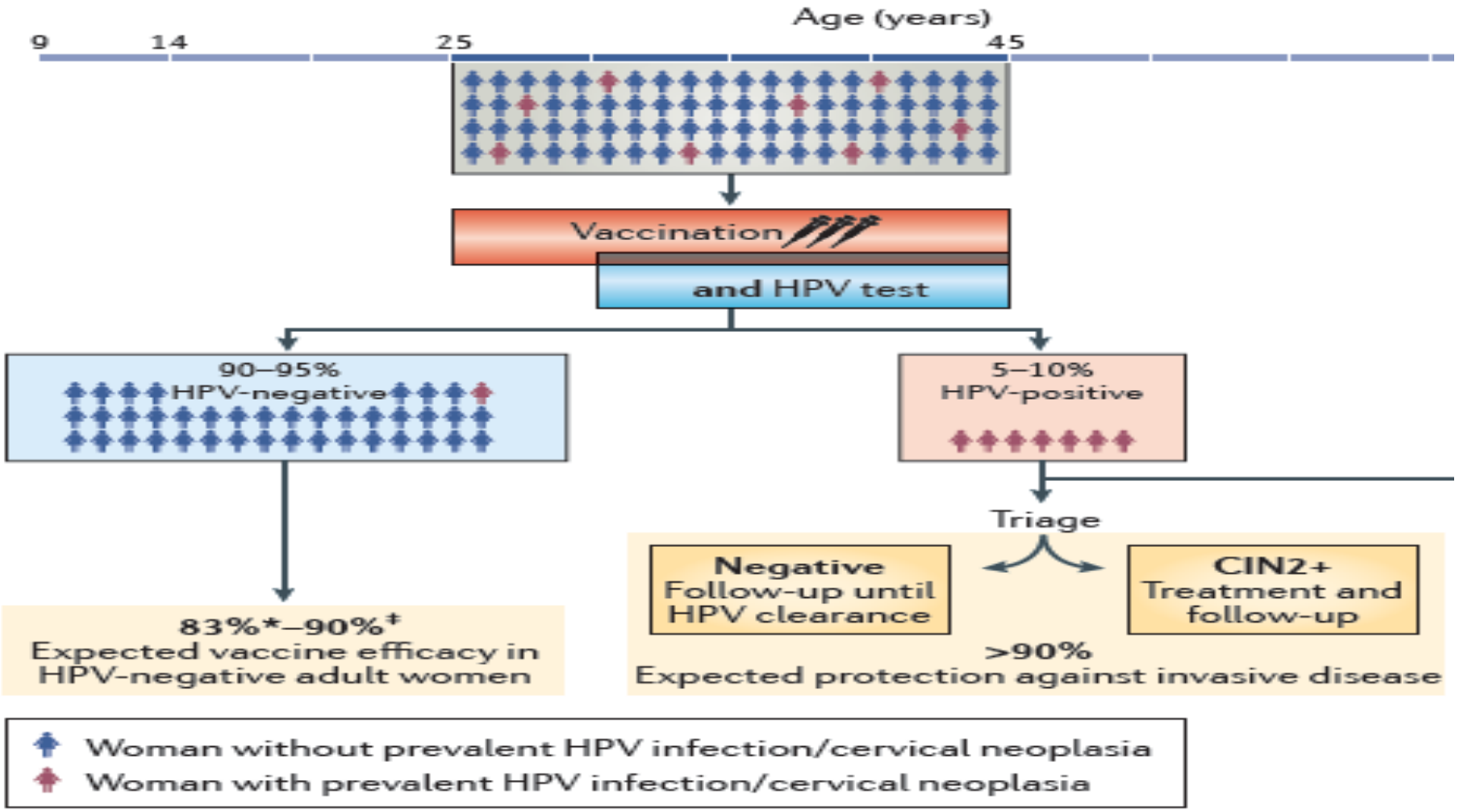
Long-term HPV type-specific risks for ASCUS and LSIL: A 14-year follow-up of a randomized primary HPV screening trial

K. Miriam Elfström[1], Vitaly Smelov[2], Anna L.V. Johansson[1], Carina Eklund[2], Pontus Naucler[3,4], Lisen Arnheim-Dahlström[1] and Joakim Dillner[1,2]

Table 5. Type-specific population attributable proportion for the 1st screening round 0 to ≤3 years, study arms combined

	Population attributable proportion (95% CI)	
HPV type	ASCUS	LSIL
HR HPV negative	–	–
HPV 16	15.5 (9.7–20.9)	14.7 (8.0–20.9)
HPV 18	4.2 (1.1–7.2)	6.7 (2.3–11.0)
HPV 31	8.4 (4.2–12.5)	11.6 (6.0–16.8)
HPV 33	3.2 (0.4–5.8)	3.4 (0.1–6.5)
HPV 35	1.7 (0.0–3.7)	1.8 (0.0–4.1)
HPV 39	1.7 (0.0–3.7)	2.5 (0.0–5.1)
HPV 45	5.9 (2.2–9.4)	4.4 (0.5–8.1)
HPV 51	3.8 (0.9–6.7)	3.0 (0.0–6.1)
HPV 52	6.5 (2.7–10.1)	4.0 (0.3–7.5)
HPV 56	0.8 (0.0–2.3)	4.2 (0.7–7.7)
HPV 58	2.0 (0.0–4.2)	5.1 (1.3–8.8)

One-time effort with combined HPV vaccination and HPV screening for rapid cervical cancer control (The FASTER concept: Bosch et al, Nature Reviews in Clinical Oncology 2015)



The HPV FASTER concept:

-Which design of a FASTER vaccination campaign is likely to be most efficient?

-Could we settle for just one dose of the nonavalent vaccine?

-What is the meaning (if anything) of low-level HPV DNA positivity in previously exposed persons?