Network meeting on Cervical cancer screening in the Nordic countries

Screening women older than 64 years: inviting all, or a selected group?

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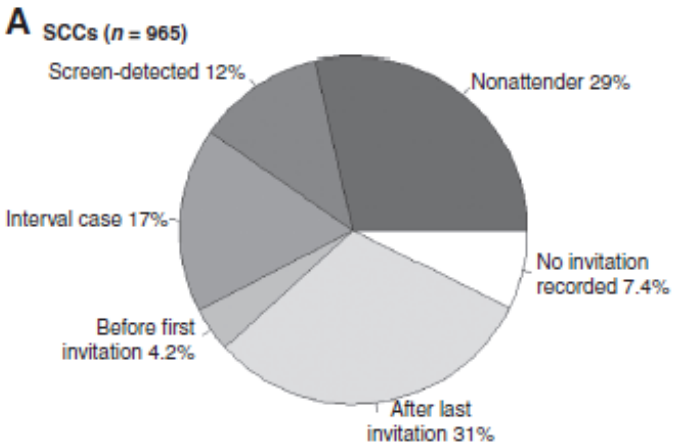
European recommendations on age limit for cervical cancer screening

- Starting at age 25-30 (no later than 30) and continue screening with 3-5 year intervals up to 60 or 65 (Arbyn et al., eds., European guidelines, 2008)
- After the stopping age continue screening those women who had got abnormal findings
  - IARC, 2005: Women who have always tested negative in an organized screening programme should cease screening once they attain the age of 65, as there is little benefit of screening to women over the age of 65 who have had at least two negative tests in the last 10 years
- No systematic evidence available on the different options on the age to start or stop

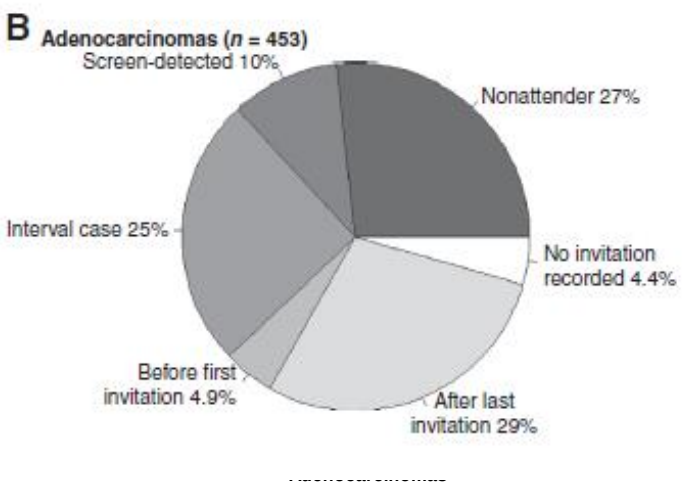
Detection mode of incident cancer and deaths from cervical cancer by major morphology groups, Finland 2000-2009

Lönnberg et al, CEPB 2012 & IJC 2013

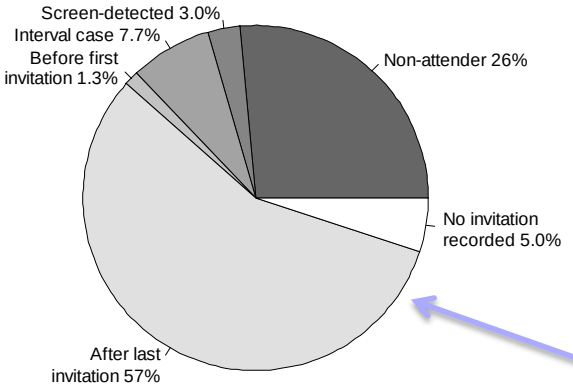


Squamous cell cancers n=299

Incidence



n=148



Mortality

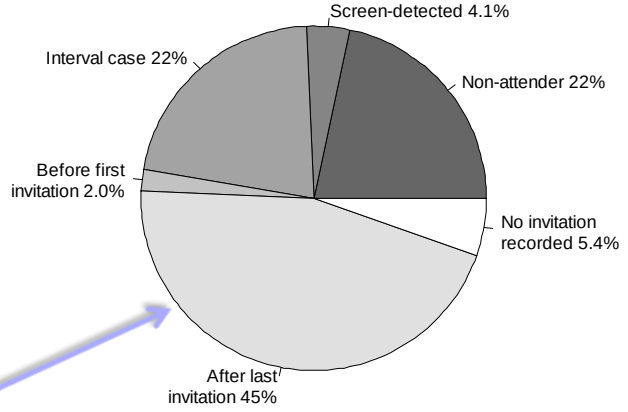


Table 4. Self-selection–corrected ORs showing association of cervical cancer and screening participation by morphology and stage

	Age at invitation	Cases screened Y/N[a]	Controls screened Y/N[a]	OR (95% CI)[b]
All cervical cancers	25–69	366/494	3,469/1,813	0.53 (0.46–0.62)
	25–39	122/173	1,028/805	0.81 (0.63–1.05)
	40–54	147/210	1,527/695	0.44 (0.35–0.56)
	55–69	97/111	914/313	0.37 (0.27–0.52)
Squamous carcinoma	25–69	205/327	2,134/1,200	0.50 (0.41–0.61)
	25–39	88/116	703/583	0.91 (0.67–1.24)
	40–54	79/138	931/444	0.40 (0.29–0.54)
	55–69	38/73	500/173	0.23 (0.14–0.37)
Adenocarcinoma	25–69	142/135	1,129/532	0.69 (0.53–0.91)
	25–39	28/51	270/194	0.59 (0.36–0.98)
	40–54	62/59	511/223	0.61 (0.41–0.91)
	55–69	52/25	339/115	0.88 (0.50–1.54)
Stage IA	25–69	95/132	850/562	0.62 (0.46–0.84)
	25–39	44/70	403/339	0.69 (0.45–1.07)
	40–54	34/54	346/179	0.43 (0.27–0.70)
	55–69	17/8	101/44	1.12 (0.41–3.06)
Stage IB+	25–69	234/309	2,269/1,069	0.50 (0.41–0.61)
	25–39	68/86	546/399	0.93 (0.65–1.32)
	40–54	102/132	1,026/445	0.47 (0.35–0.63)
	55–69	64/91	697/225	0.27 (0.18–0.40)
Stage IB+ squamous carcinoma	25–69	114/187	1,275/634	0.44 (0.35–0.56)
	25–39	44/48	329/255	1.04 (0.68–1.58)
	40–54	48/81	573/259	0.39 (0.27–0.56)
	55–69	22/58	373/120	0.19 (0.11–0.32)

Lönnberg et al. CEBP 2012

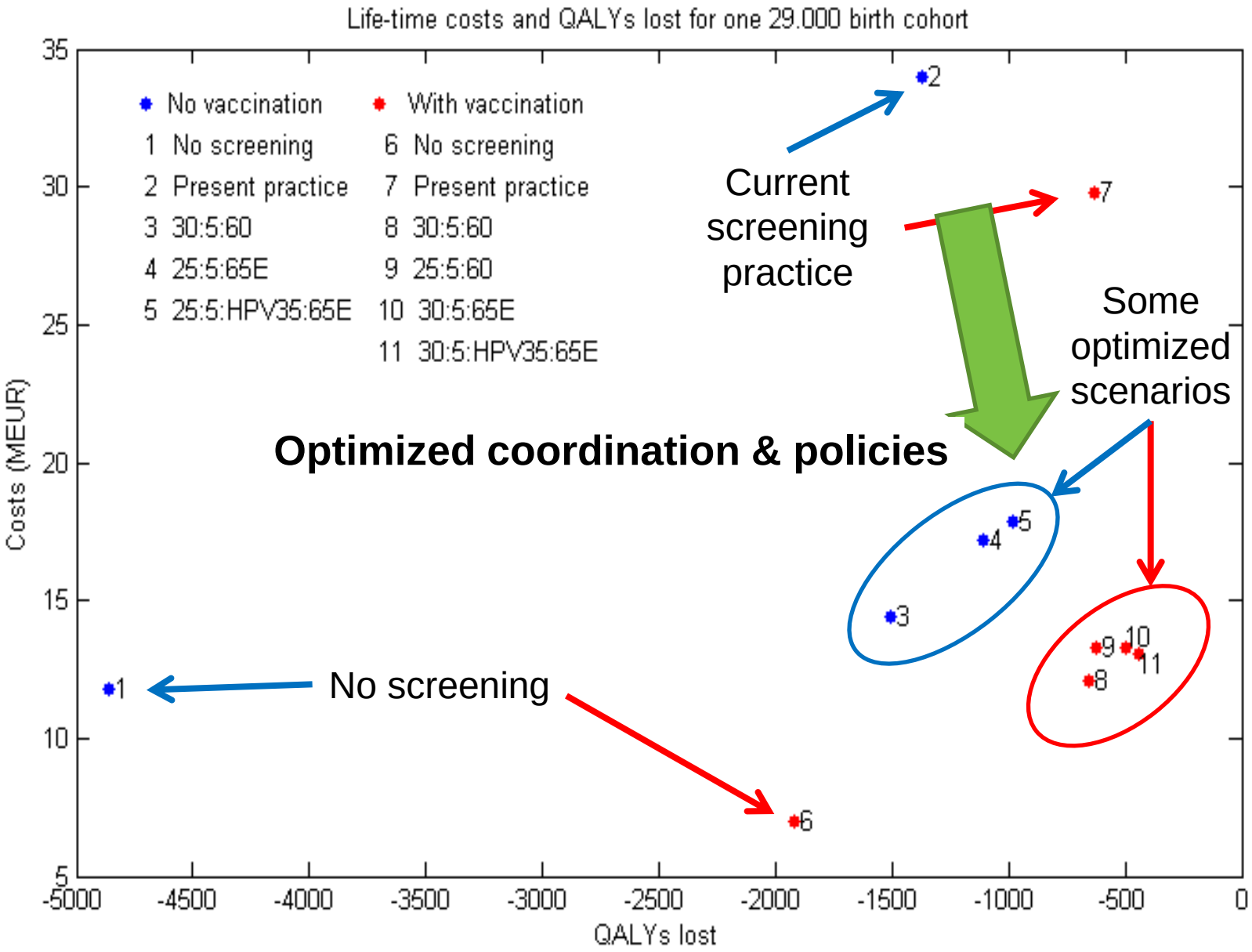
Table 3. Self-selection-corrected ORs showing association of cervical cancer death and screening participation

	Age at invitation	Cases screened Y/N[1]	Controls screened Y/N[1]	Crude OR	Corrected OR (95% CI)[2]
Index invitation					
All cervical cancers	25–69	71/127	876/342	0.19	0.34 (0.14–0.49)
	25–39	13/22	133/78	0.44	0.70 (0.33–1.48)
	40–54	29/59	388/154	0.18	0.33 (0.20–0.56)
	55–69	29/46	355/110	0.15	0.29 (0.16–0.54)
Squamous cell carcinomas	25–69	26/83	489/200	0.12	0.22 (0.13–0.36)
	25–39	10/12	78/49	0.61	0.97 (0.39–2.41)
	40–54	7/45	228/94	0.06	0.11 (0.05–0.28)
	55–69	9/26	183/57	0.09	0.17 (0.07–0.44)
Adenocarcinomas	25–69	37/33	297/122	0.42	0.75 (0.43–1.31)
	25–39	2/6	29/23	0.32	0.50 (0.09–2.76)
	40–54	19/12	133/55	0.65	1.21 (0.53–2.75)
	55–69	16/15	135/44	0.28	0.55 (0.23–1.35)

Lönnberg et al. IJC 2013

Effectiveness of screening older women than 64 years

- OR of CxCa incidence **0.41 (0.23–0.74)** and of CxCa mortality **0.41 (0.23–0.74)** for participating to screening in age 65, vs not participating; *follow-up age 66-84 years* [Lönnberg et al. 2012 and 2013, Finnish programme]
- OR of CxCa mortality **0.5 (0.4-0.8)** for screening at age 65 years, follow-up 60 months [Vicus et al. 2014, Canada]
- OR of CxCa incidence **0.33 (0.12–0.92)** and of CxCa mortality **0.47 (**0.14-1.63) estimated from cancers diagnosed at age >65 years [Kamineni et al. 2013, Rustagi et al. 2014; Seattle, USA]. The study did not assess impacts by age at screen, even though a large part of the screening tests had been taken after age 64
- No studies available on continuing screening in women with earlier abnormal findings only compared with continuing screening in all, e.g. at age 70+


Life-time costs and QALYs lost for one 29.000 birth cohort
No vaccination
With vaccination
1 No screening
2 Present practice
3 30:5:60
4 25:5:65E
5 25:5:HPV35:65E
6 No screening
7 Present practice
8 30:5:60
9 25:5:60
10 30:5:65E
11 30:5:HPV35:65E
Current screening practice
Some optimized scenarios
Optimized coordination & policies
No screening
Costs (MEUR)
QALYs lost
35
30
25
20
15
10
5
-5000
-4500
-4000
-3500
-3000
-2500
-2000
-1500
-1000
-500
0

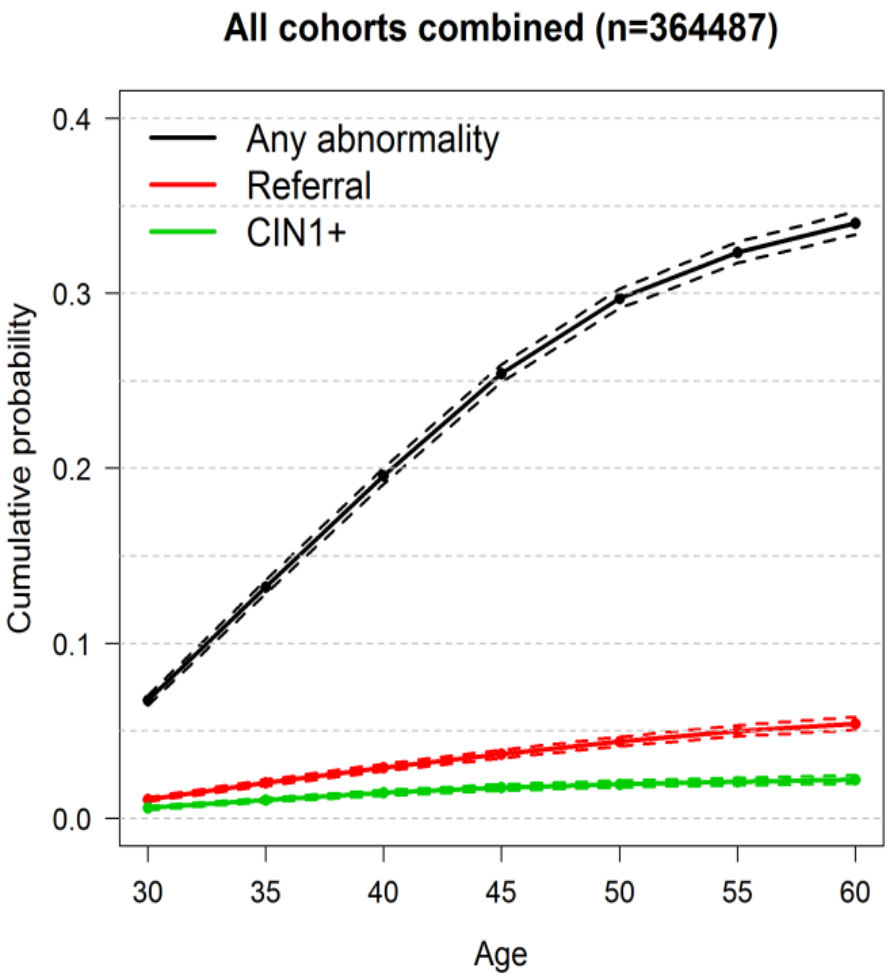
Screening women older than 64 years, how?

1. Up to which age to invite *all* women?
   - 64? 69? 74? Older?
2. When to stop, and how to continue? At least 3 strategies:
   1. Invite if *ever* lifetime abnormal, referral or CIN?
   2. Invite if not attended regularly; or abnormal finding at least once during the last 10 years
      - ✓ Exclude if regularly screened and all test results normal/negative
   3. Invite if HPV test was positive in the last round (THL 2011) or earlier?

Screening women older than 64 years, how?

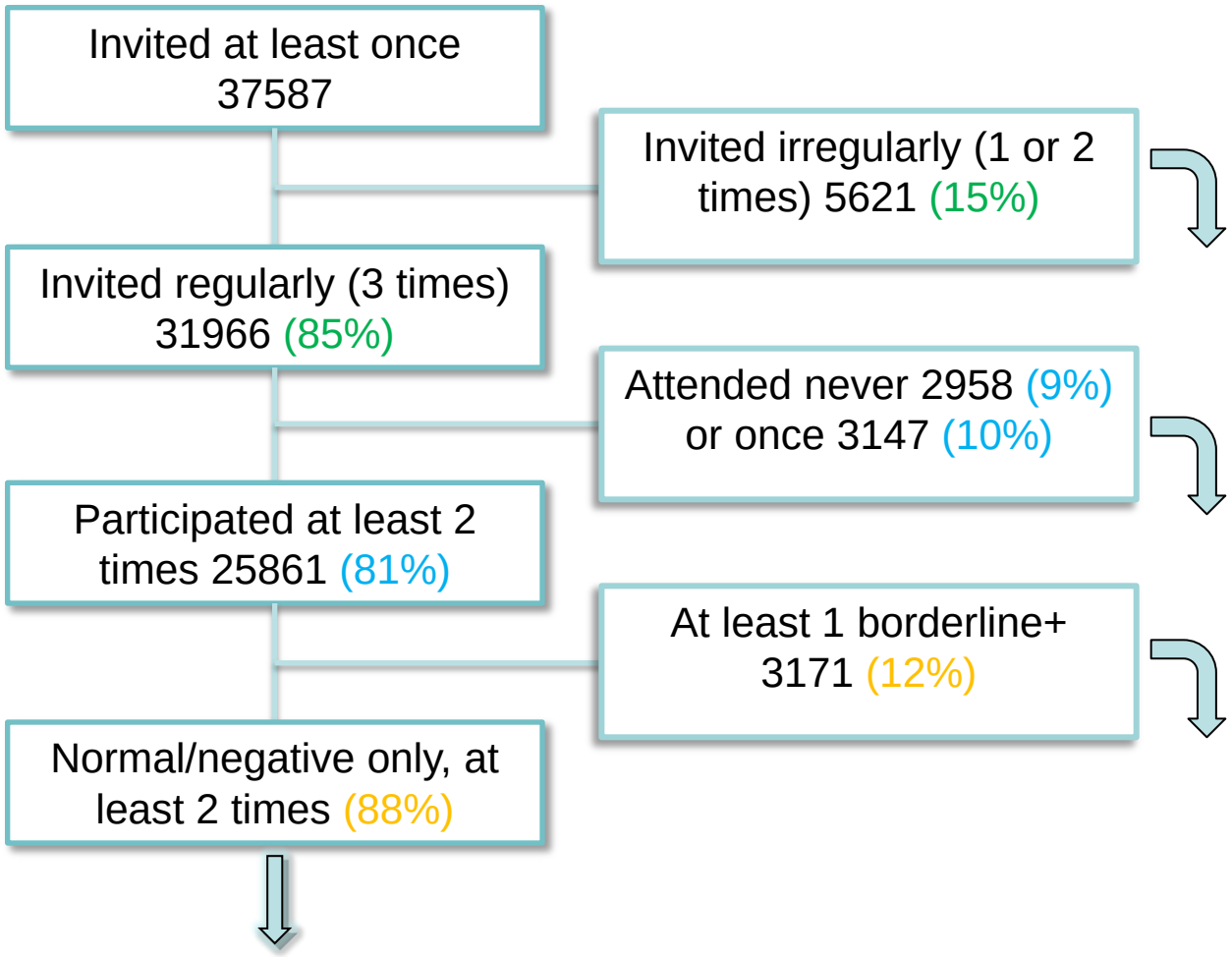
- How to obtain evidence of what could be the best option: potential for Nordic collaboration
  - We have screening databases over sufficiently long periods
  - Linkable to cancer incidence and mortality records
    - Cause-specific mortality and all-cause mortality (life expectancy) also essential
  - Retrospective assessments would provide key results faster than longitudinal new trials (c.f. long period to satisfy the evaluation condition, and adequate duration of follow-up)
  - If planning for prospective interventions, also then knowing screening histories is highly beneficial

Option 1: cumulative borderline+ probability in age 30 to 60, Finnish programme (Pankakoski et al., submitted)



Option 2: Birth cohort –wise example

Birth-cohort 1952, aged 50, 55 or 60 in 2002-2012



Discussion and conclusions

1. Benefit of screening women older than 64 years demonstrated
2. Better description of screening policies in our countries, and a new generation of linkage studies needed
3. Considerations of health-economic and QoL perspectives should be based on effectiveness
4. How we could collaborate on this topic?