Prevention and management of the HPV disease burden, the Finnish perspective

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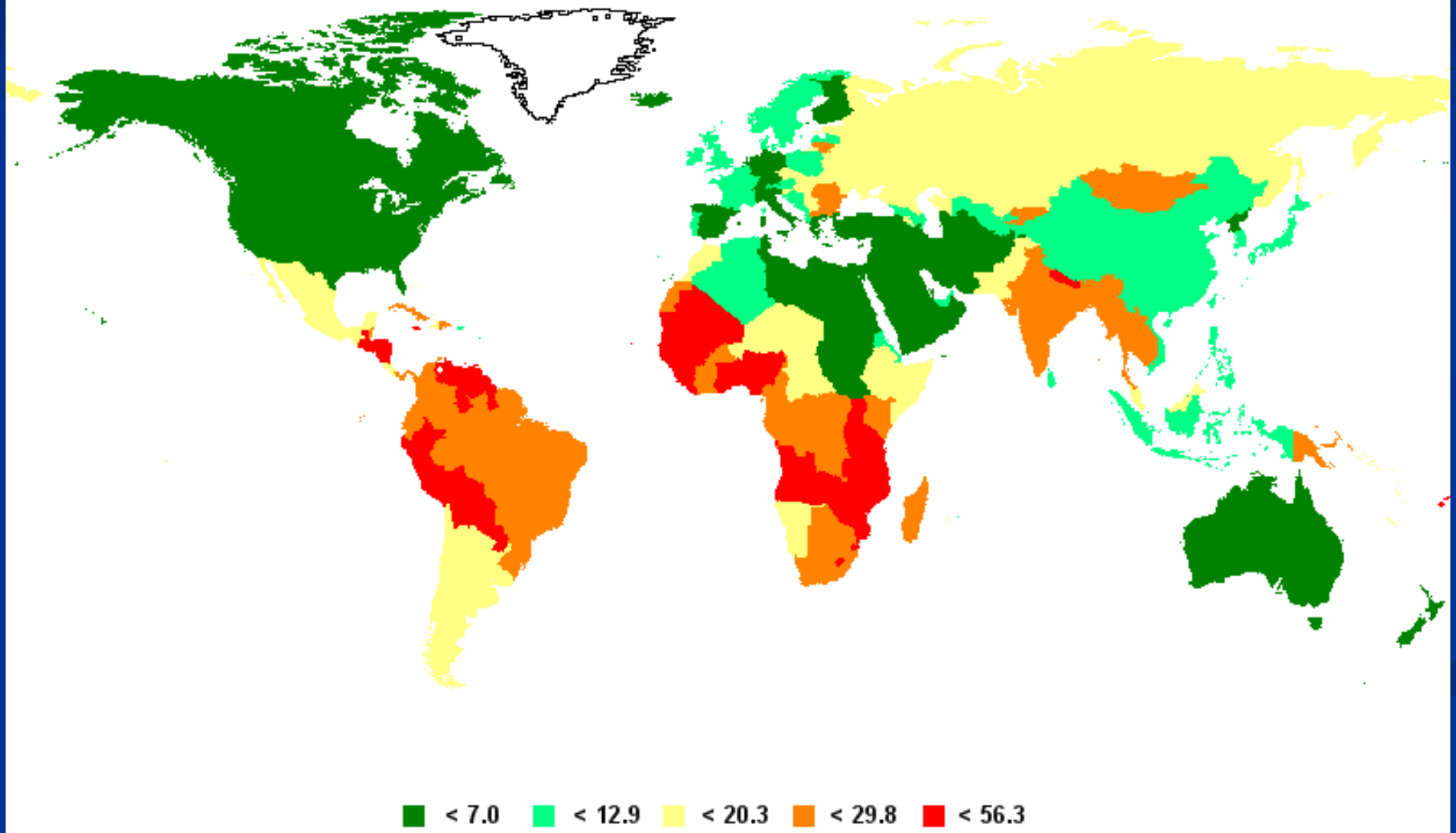
Cervical cancer

- HPV infection needed for cancer development, 70% caused by HPV 16 / 18 (zur Hausen)
- 2nd most common cancer among females in the world
  - about 550 000 new cases and 250 000 deaths, yearly
- In Finland, before organised screening (established in -60's) 3rd most common cancer
- Presently, after 50 years of organised screening, 19th!
- Yearly about 145 new cancers and about 50 cancer deaths in Finland
- Without screening we would have 800-1000 cancers and 4-500 deaths
- Incidence and mortality in Finland among the lowest, 3,7/100 000 and 1.0 /100 000 wy, respectively

Estimated age-standardised incidence rate per 100,000
Cervix uteri, all ages



Prevention of cervical cancer is possible

- Secondary prevention
  - screening (used ~50 years)
- Primary prevention
  - vaccination (implemented recently)

POPULATION-BASED ORGANISED CANCER SCREENING - THE BEST RESULTS

-Prevent mortality from invasive cancer

-Cancer incidence can also be prevented

-Improve quality of life

Less aggressive treatments with early detection of precancer / (cancer)

Limit adverse aspects of testing and management

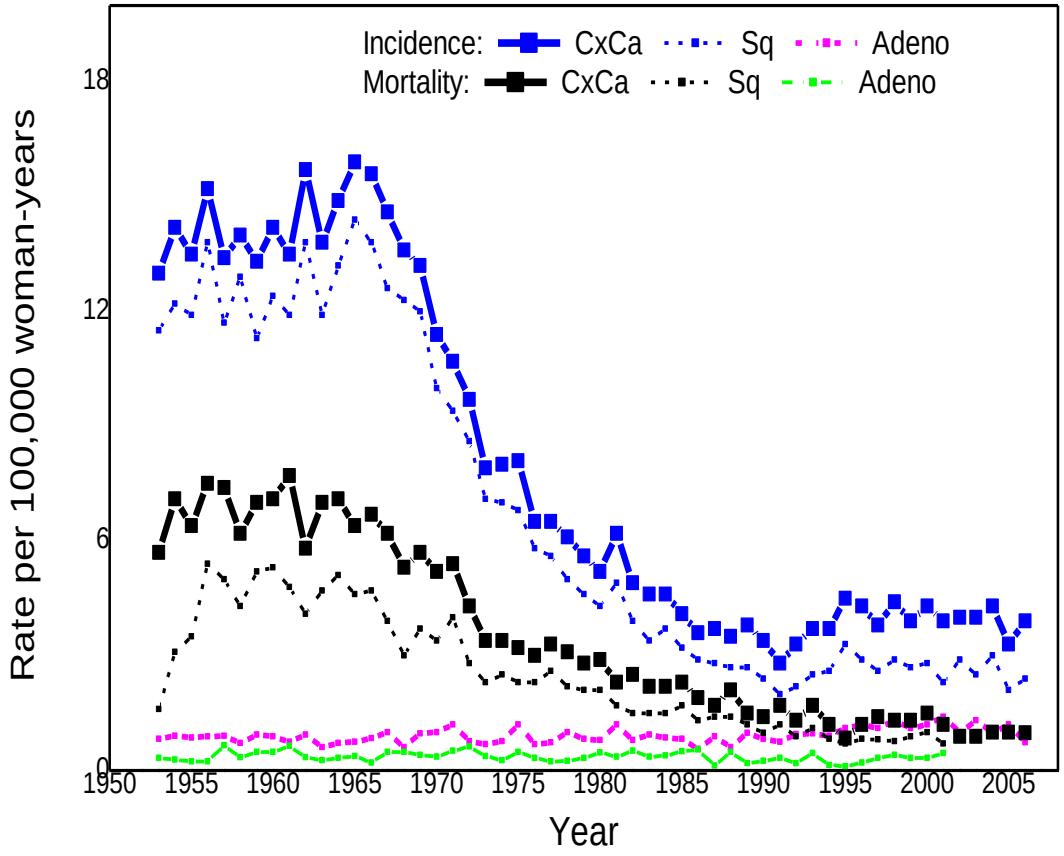
We screen healthy women!

Sensitivity and specificity are both important

Natural history of CIN and cancer: Important when designing screening

- Length of pre-cancer phase on average 10-12 years; typically between 5 and 15 years
- Progression rates of CIN to invasive cancer (Oortmassen & Habbema, 1991)
  - 16% in lesions in age 18-34 years
  - 60% in lesions in age 35-64 years
- Among 13 – 22 –years old girls and women up to 90 % of pre-cancer lesions regress naturally even in rather short-term follow-up (Moscicki et al. 2004)

Cervical cancer incidence and mortality rates in Finland during 1953-2006, adjusted for age to the world standard population (Finnish Cancer Registry, April 2008)



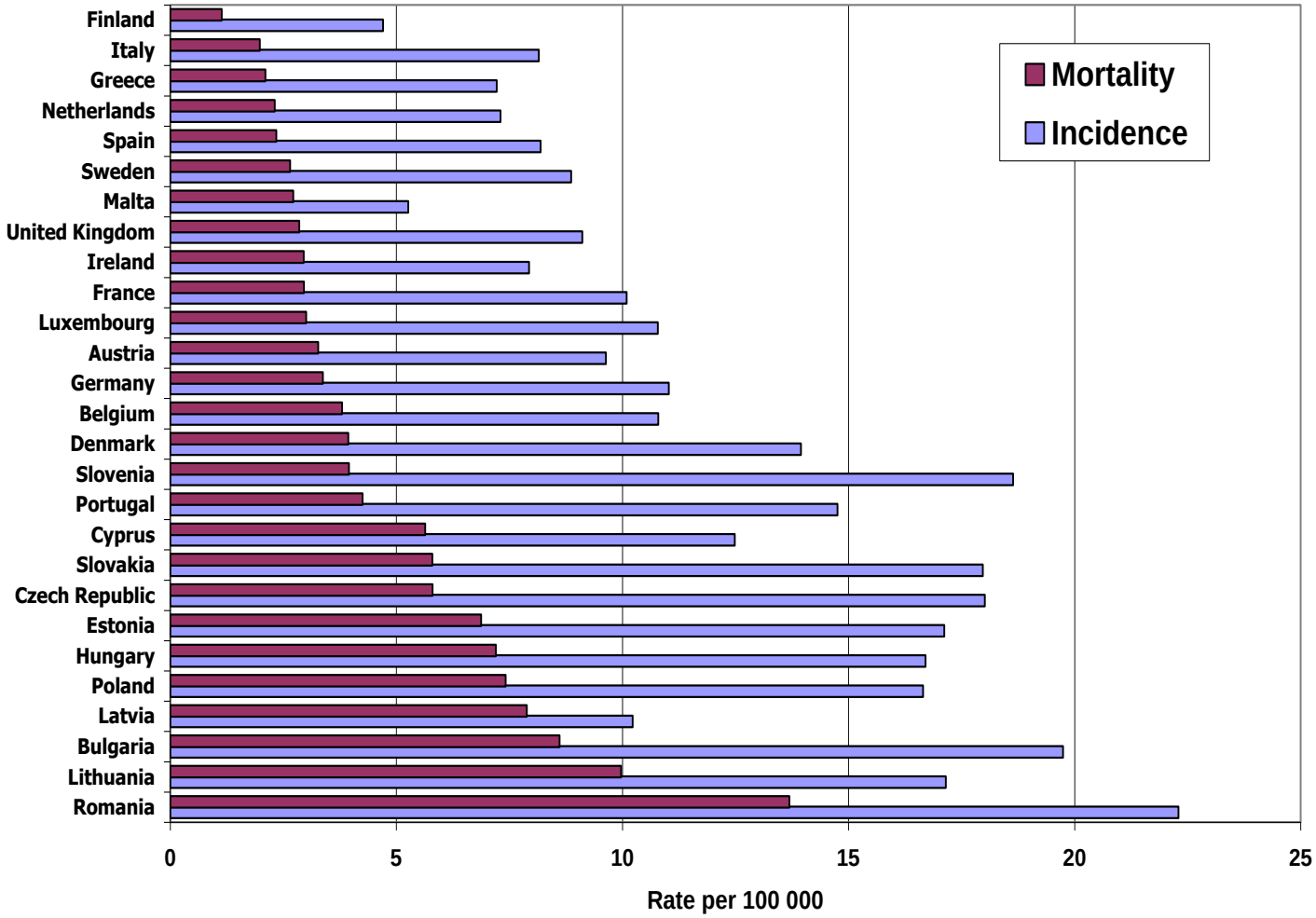
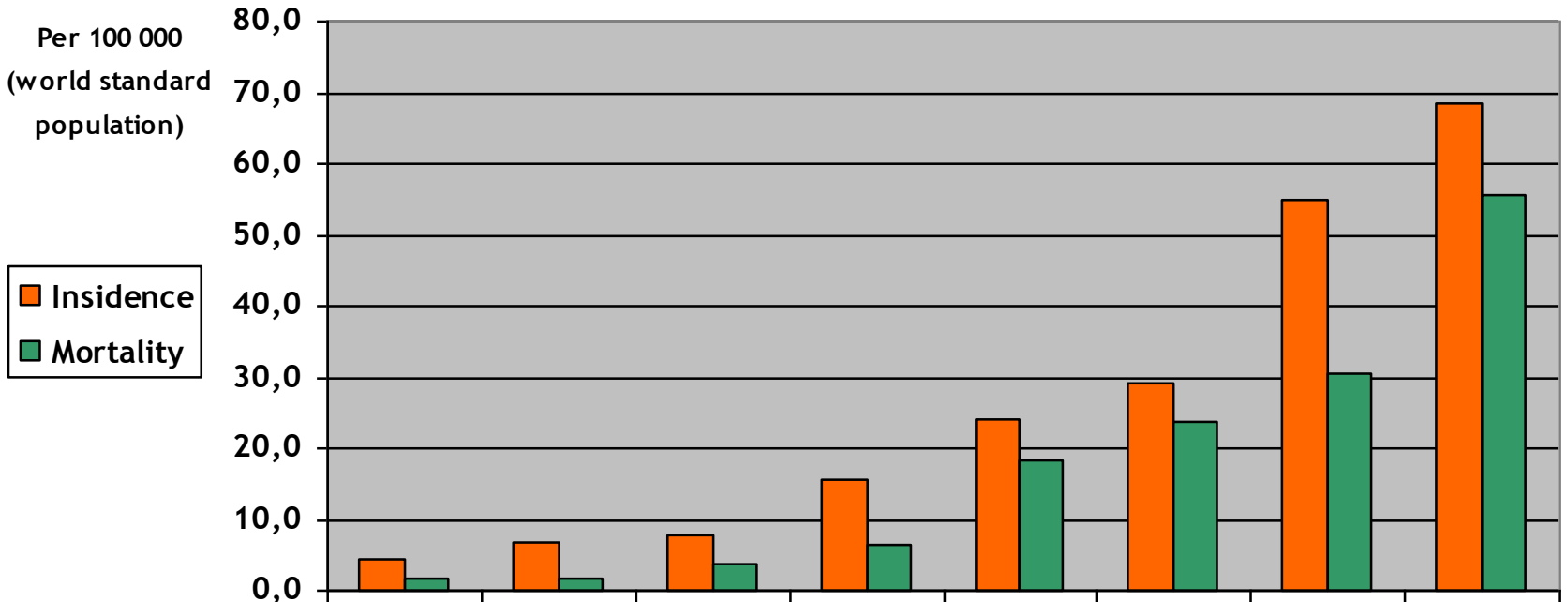


Fig. 1. Age-standardised rated of incidence of and mortality from cervical cancer (/100,000 women-years) in the 27 member states of the European Union, estimates for 2004 (direct standardisation using the World reference population). (derived from Arbyn *et al.*, *Ann Oncol.* 2007b).

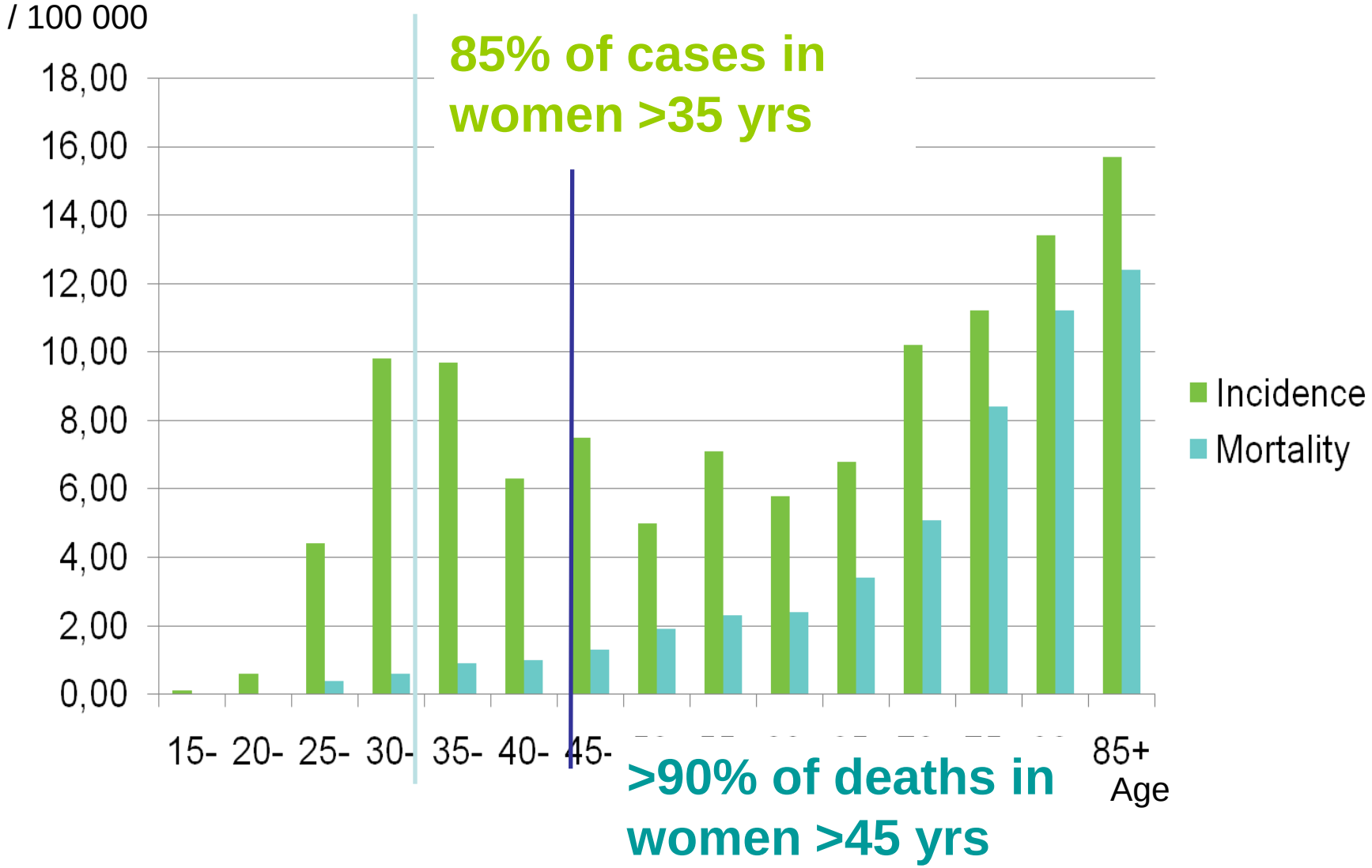
World statistics



	Finland	Australia	USA	Estonia	Romania	Ghana	Bolivia	Tansania
Insidence	4,3	6,9	7,7	15,5	23,9	29,3	55,0	68,6
Mortality	1,8	1,7	3,6	6,6	18,4	23,8	30,4	55,6

Globocan 2002

Cervical cancer by age group in Finland 2001-2007



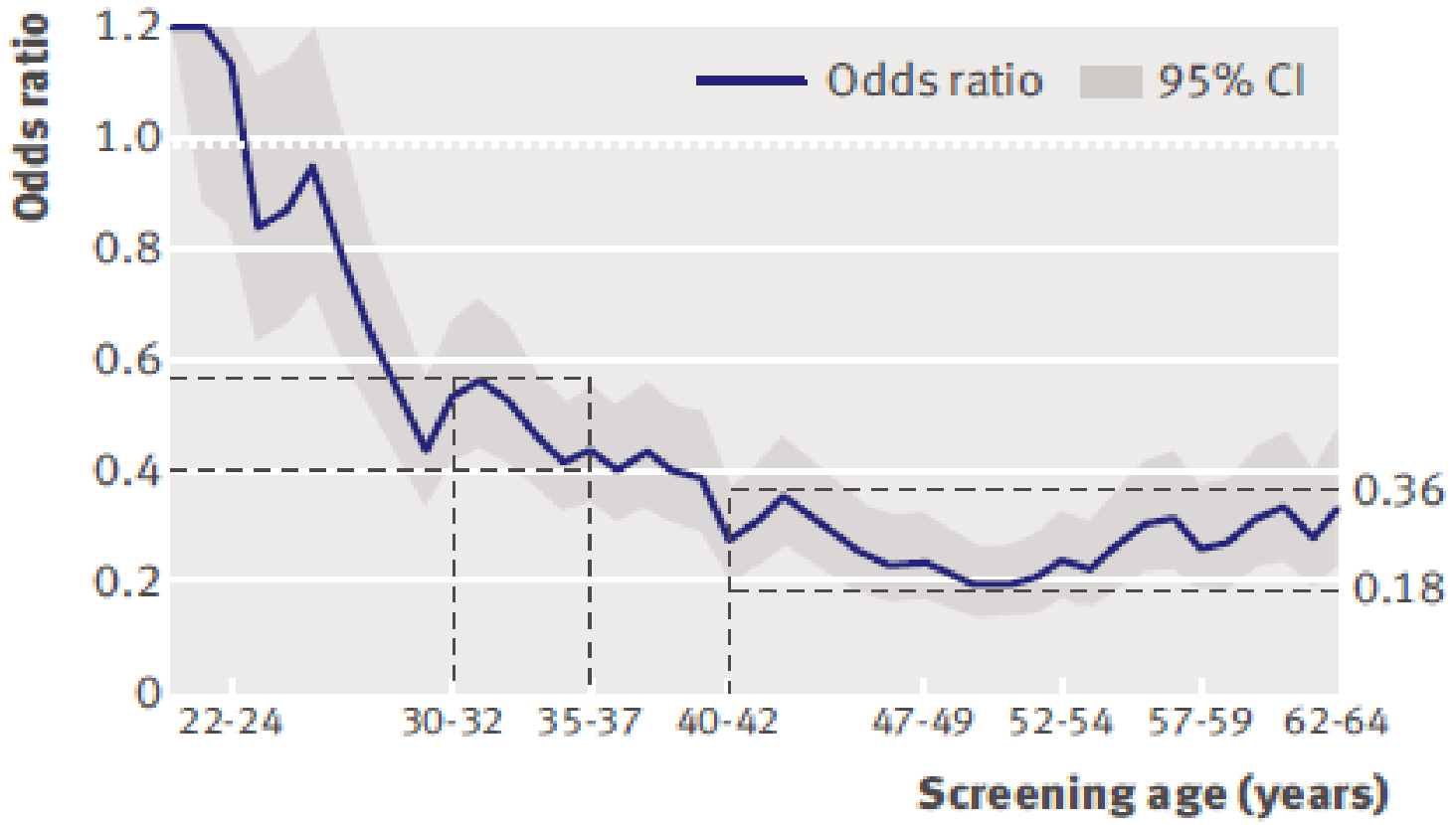


Fig 2 | Odds ratio for developing invasive cervical cancer stage IA or worse (in the next five year interval) in those screened in a given (three year) age band compared with those not screened in that age band (or in two previous years). Odds

Sasieni & Cuzick, BMJ 2009

Why organised screening works?

- Population based
- Defined target ages and groups
- Wide coverage (everybody invited)
  - mode of invitation (personal letter with time and place
- Good compliance (testing, treatment, F-U)
- Evaluation and development
  - screening and cancer registries

New means to prevent HPV disease burden

- HPV vaccines
- Novel screening techniques

- National Institute for Health and Welfare in Finland established a working group in 2008.

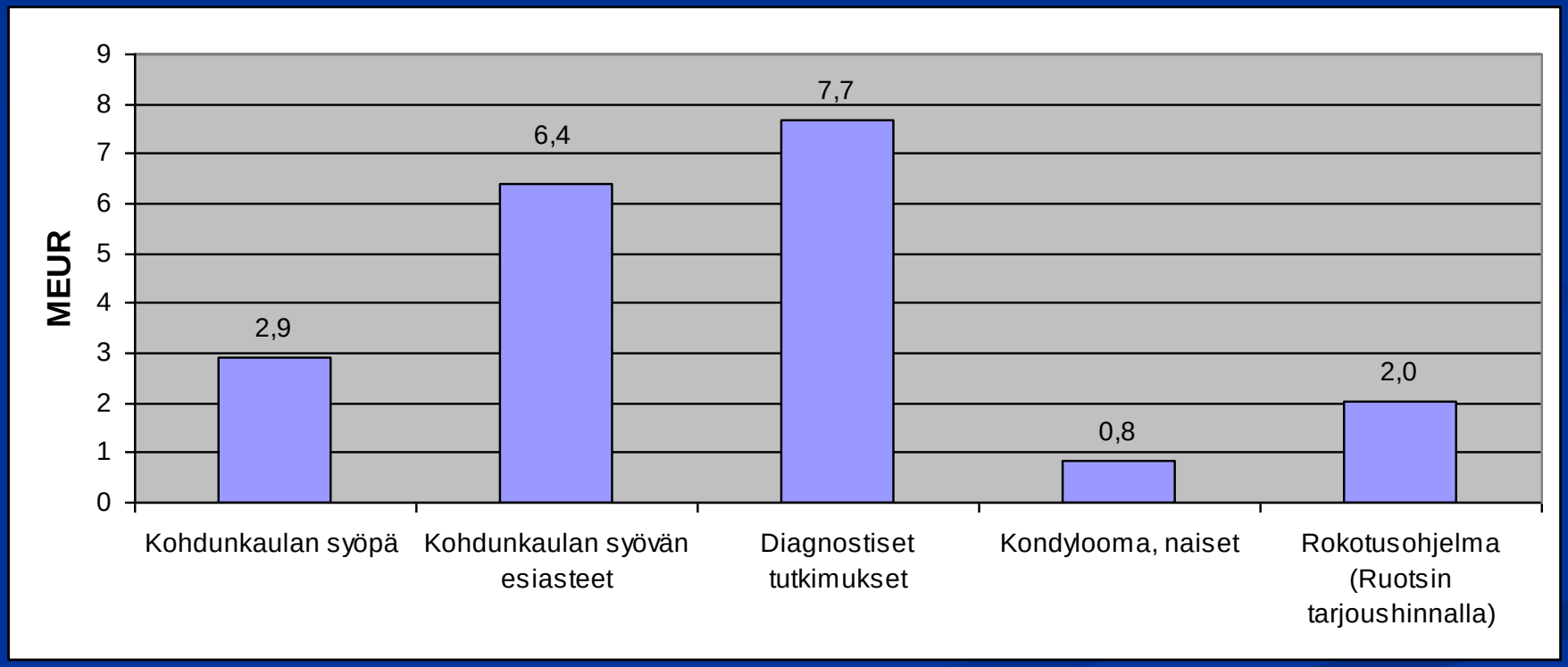
- Modelling the best strategies to prevent HPV diseases in Finland by combining vaccination and screening

HPV-disease burden: yearly costs in Finland

- Population of Finland is 5,3 milj
- 500 000 Pap-tests
- 16 300 colposcopies
- 6 400 condyloma patients
- 2 800 CIN cases
- 150 cervical carcinomas
- Total costs about. 41 milj. €

HPV-diseases yearly management costs

17,8 M€



Ca

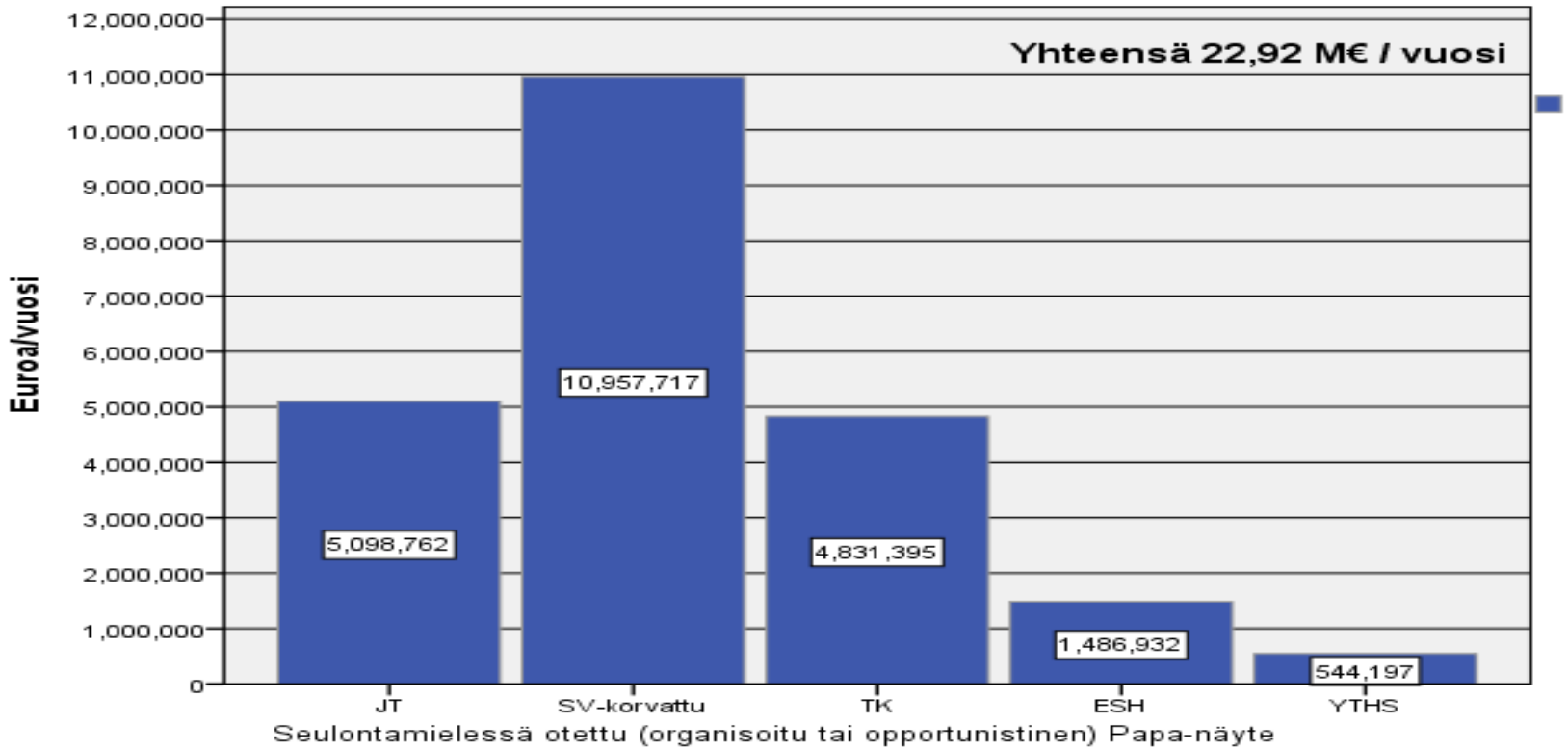
CIN

other colpos etc

condyloma women

vaccination programme

Screening smears (organised and opportunistic) yearly costs 23 M€



organised screening

private, reimbursed

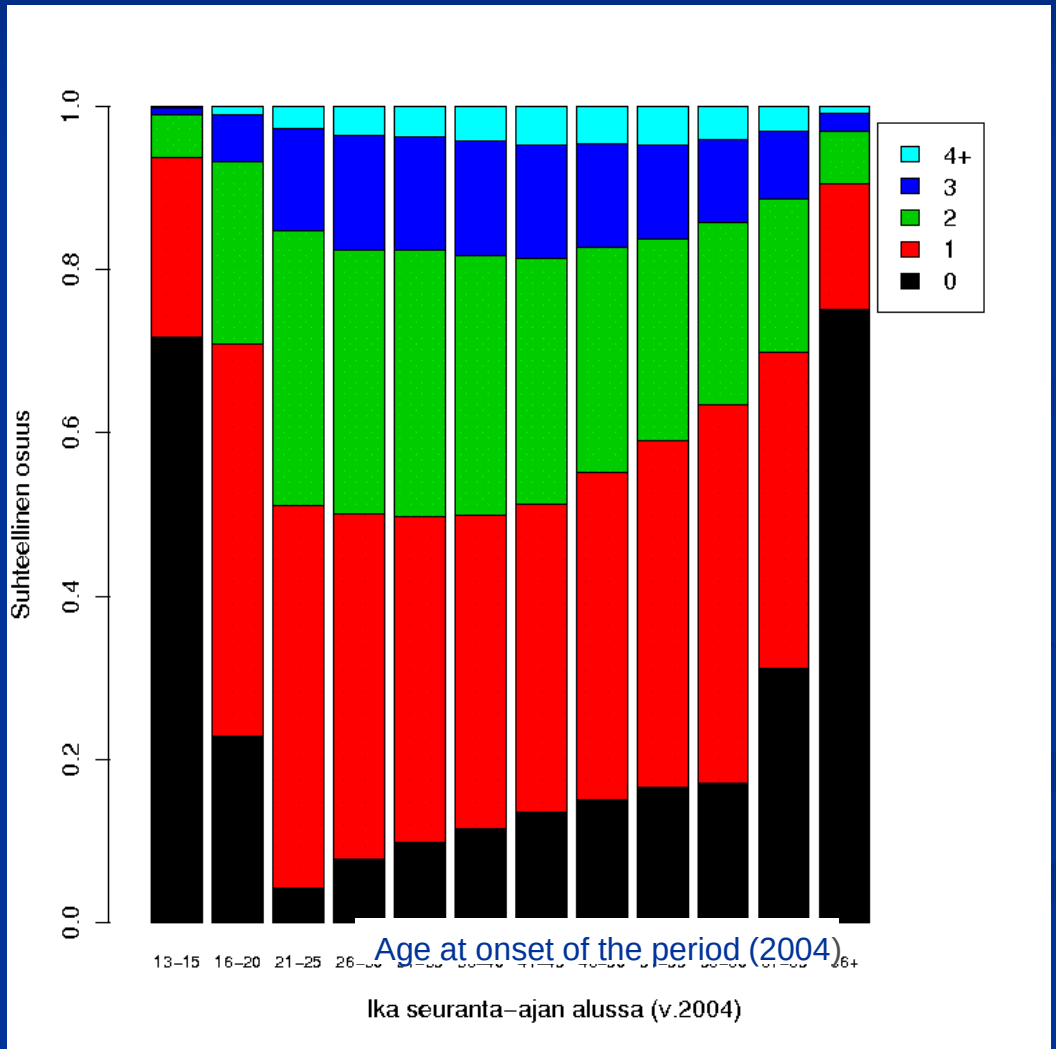
health care centers

hospitals

student health care

Proportion of women with a Pap smear at least once within five years, by age and number of smears within the period. Organised and opportunistic screening (H.Salo, P Nieminen et al. THL, June 2011)

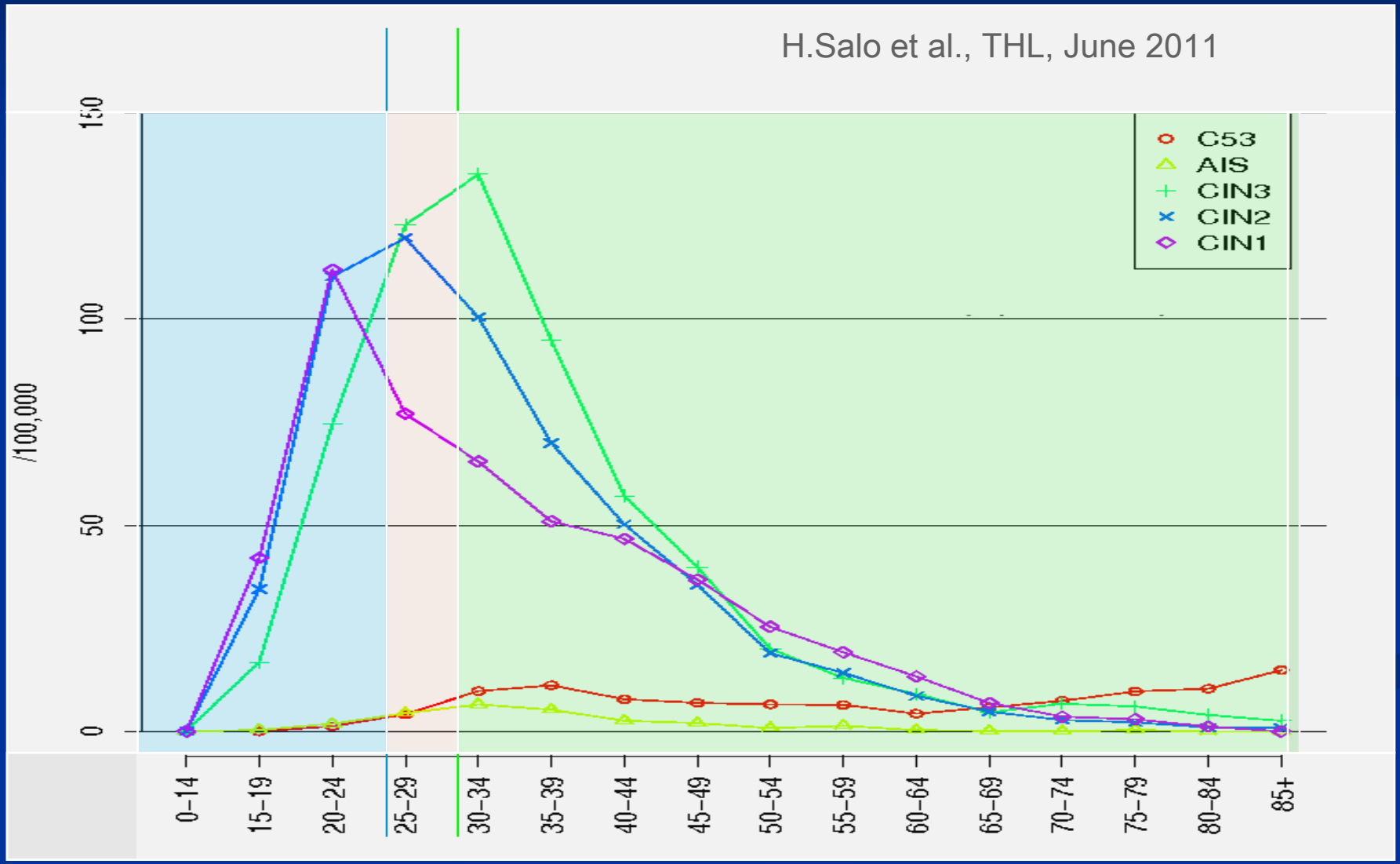
% of women



no of smears

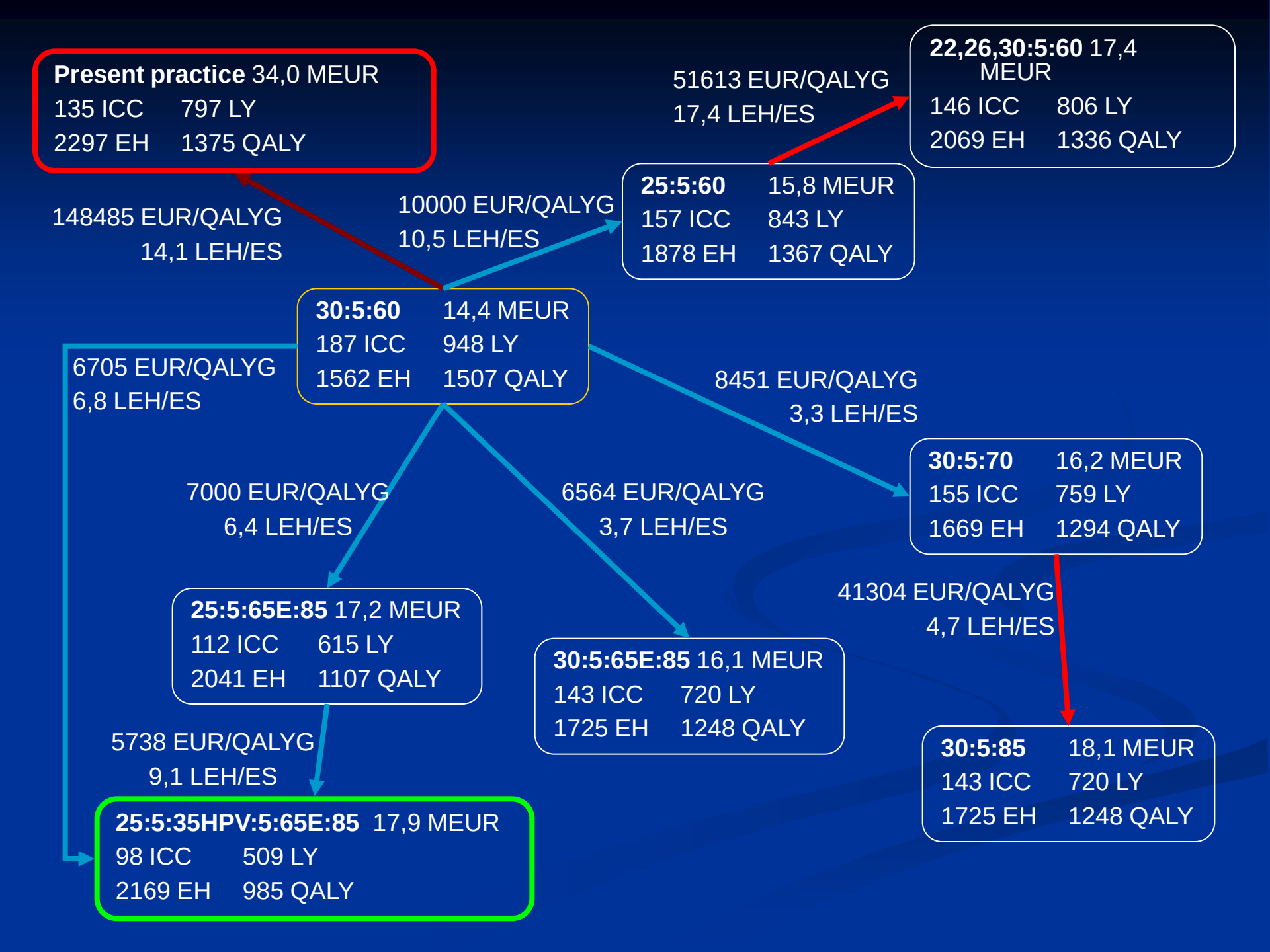
Age-specific rates of cervical cancers and pre-cancers in Finland

Finnish Cancer Registry and Hospital/Outpatient Treatment Register 2004-2008



Mathematical modelling of HPV disease burden in Finland

- Data collected from every registries available
  - Cancer registry
  - Screening registry
  - Diagnosis and procedures registry
  - Other registries in health care
- Modelling with dynamic methods (National Institute of Health and Welfare 2011):
  - screening
  - vaccination
- **To find cost-effective methods for prevention**


Present practice 34,0 MEUR
135 ICC 797 LY
2297 EH 1375 QALY
148485 EUR/QALYG
14,1 LEH/ES
10000 EUR/QALYG
10,5 LEH/ES
51613 EUR/QALYG
17,4 LEH/ES
22,26,30:5:60 17,4 MEUR
146 ICC 806 LY
2069 EH 1336 QALY
25:5:60 15,8 MEUR
157 ICC 843 LY
1878 EH 1367 QALY
30:5:60 14,4 MEUR
187 ICC 948 LY
1562 EH 1507 QALY
6705 EUR/QALYG
6,8 LEH/ES
8451 EUR/QALYG
3,3 LEH/ES
7000 EUR/QALYG
6,4 LEH/ES
6564 EUR/QALYG
3,7 LEH/ES
30:5:70 16,2 MEUR
155 ICC 759 LY
1669 EH 1294 QALY
41304 EUR/QALYG
4,7 LEH/ES
25:5:65E:85 17,2 MEUR
112 ICC 615 LY
2041 EH 1107 QALY
30:5:65E:85 16,1 MEUR
143 ICC 720 LY
1725 EH 1248 QALY
5738 EUR/QALYG
9,1 LEH/ES
30:5:85 18,1 MEUR
143 ICC 720 LY
1725 EH 1248 QALY
25:5:35HPV:5:65E:85 17,9 MEUR
98 ICC 509 LY
2169 EH 985 QALY

Mathematical cost-effectiveness analysis of simultaneous control strategies for HPV-induced disease burden

H.Salo, S.Vänskä, P.Nieminen & WORKGROUP, THL June 2011

Policy scenario	CIN1 cases	CIN2 cases	CIN3 AIS cases	CxCa cases	QALY loss	Cost million euro	Δ cost million euro	ICE euro /QALY gain
Organised throughout 30 to 60 (5y) (by-law)	260	417	885	187	1507	14.4	baseline	baseline
Organised throughout 25 to 60 (5y)	367	552	959	157	1367	15.8	+1.4	10,000
Organised throughout 30 to 70 (5y)	278	445	946	155	1294	16.2	+1.8	8,451
Organised throughout Cyto: 25-34 (5y) HPV: 35 to 65 (5y) +HPV Exit test at 65	459	675	1035	98	985	17.9	+3.5	6,705
Current organised and non-organised	621	775	901	137	1375	34.0	+19.6	148,485

New recommendation for screening:

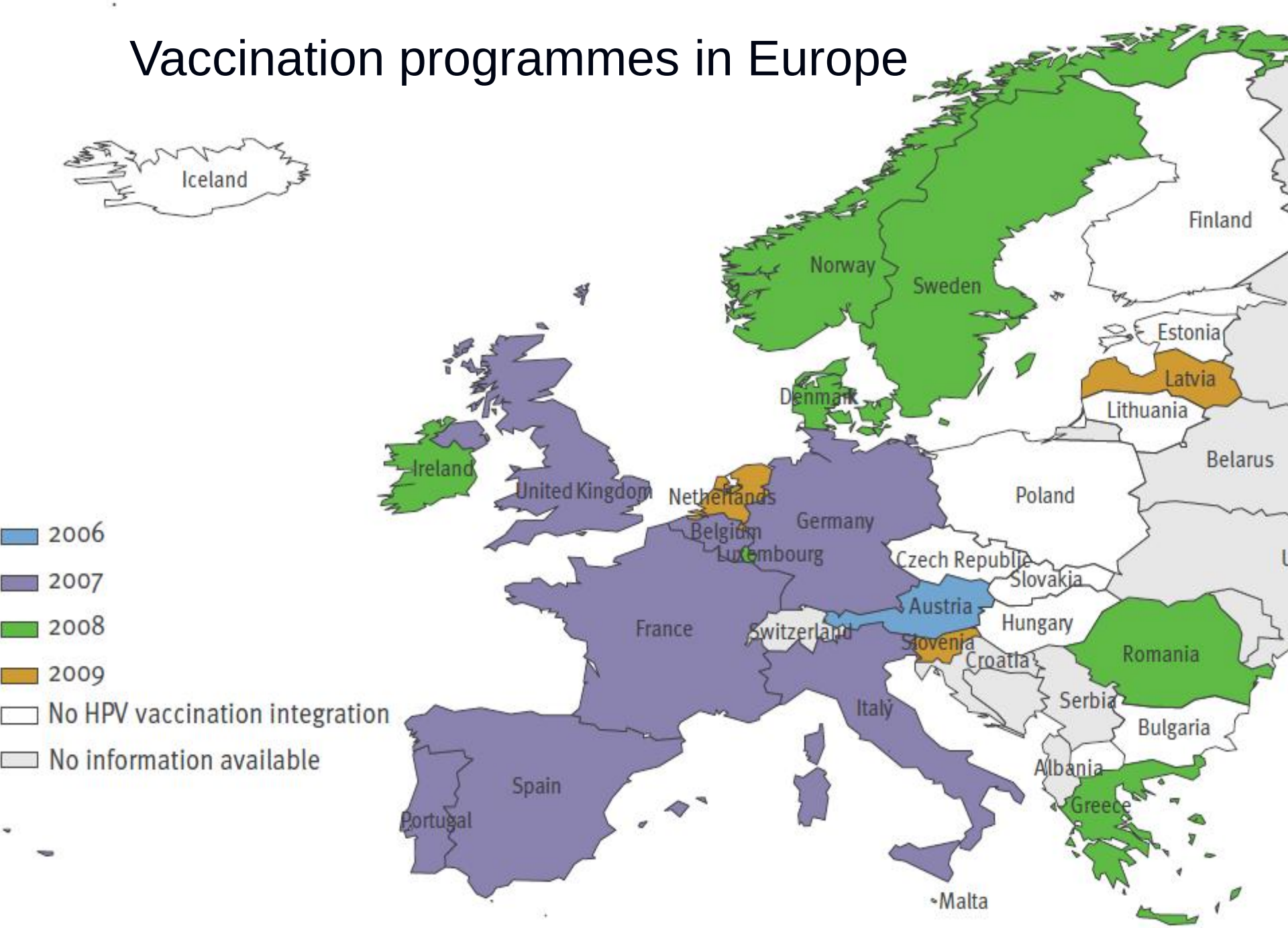
25-65 –years old women, 5-year interval, HPV-test instead of Pap-test for women 35-years and older

	Present		New recommendation	Change
	2008	model population*		
Carcinomas	**150**	**135**	**98**	**-27 %**
CIN	**2800**	**2300**	**2170**	**-6 %**
Lost life years	**1000**	**800**	**510**	**-36 %**
M€	**41,0**	**34,0**	**17,9**	**-47 %**

*Model population, age cohort of 29 000 girls

Vaccination schemes

Vaccination programmes in Europe



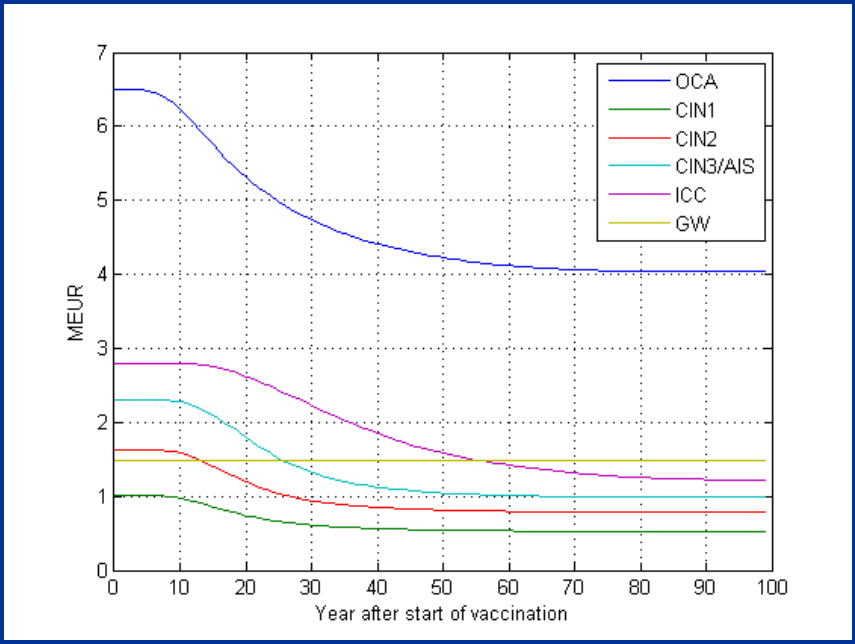
Protective effect in ATP cohorts :

HPV	Cervarix	Gardasil
16	95 %	95 %
18	95 %	95 %
31	80 %	50 %
33	50 %	0 %
45	80 %	0 %
6, 11	0 %	95 %
Muut	0 %	0 %

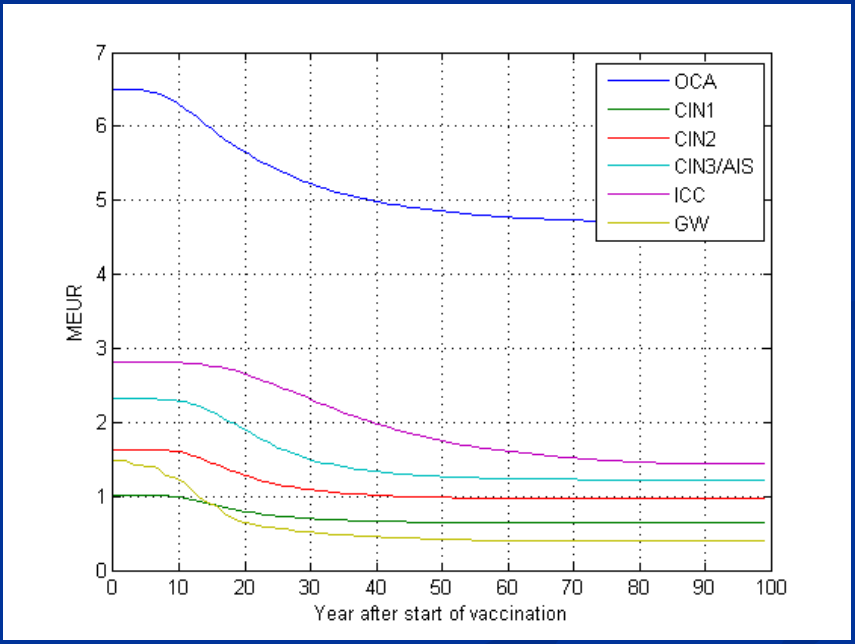
Protective effect towards different end-points within originally HPV negative girls, regardless of the HPV types (real life)

	CIN1+,	CIN2+	CIN3+
Gardasil	30 %	43 %	43 %
Cervarix	50 %	70 %	87 %

Undiscounted costs by HPV vaccination in base case programme (girls aged 12 years, no catch-up programme, 80%vaccine coverage, 100 year time horizon) over time following the introduction of HPV vaccination assuming vaccine protection lasts an average of 20 years.

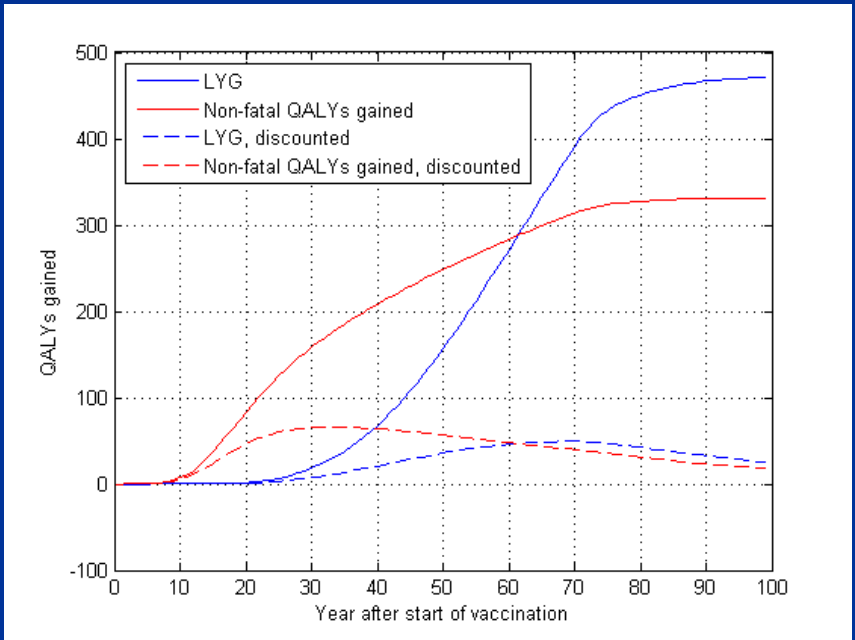


Cervarix

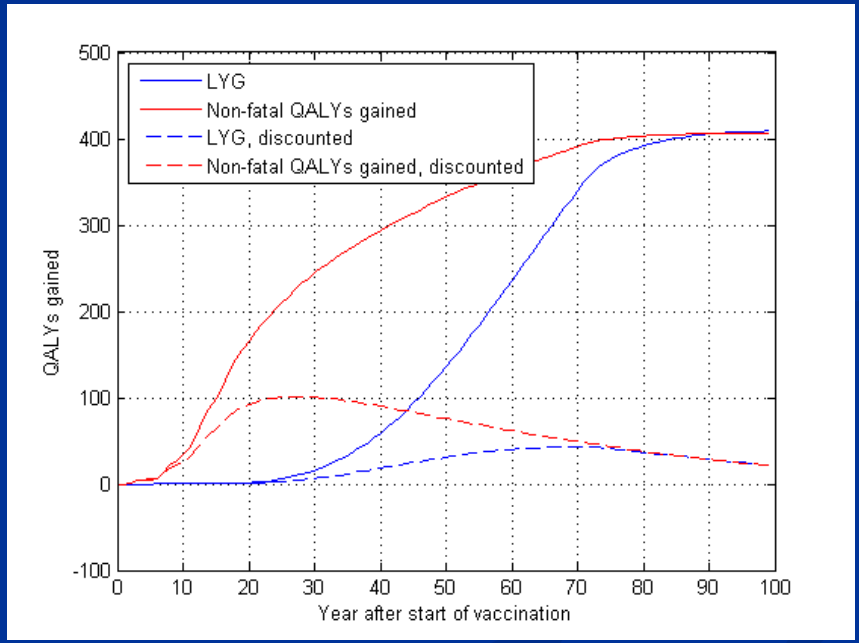


Gardasil

Estimated undiscounted and discounted QALYs and life-years gained (LYG) in base case programme (girls aged 12 years, no catch-up programme, 80% vaccine coverage, 100 year time horizon, and 3 % discount rate) over time following the introduction of HPV vaccination



Cervarix



Gardasil

Basic analysis with different prices

Girls, vaccination programme (80 % coverage) vs. no vaccination
Cervical Ca and condylomas (view point)
Protection years 20 + 20

Price	MEUR	EUR/QALYG
75	-41,3	HCC saving
100	-22,4	HCC saving
125	-3,5	HCC saving
150	15,4	1958

No vaccination

Girls 80 %

Price	MEUR	EUR/QALYG
75	-40,6	HCC saving
100	-21,7	HCC saving
125	-2,8	HCC saving
150	16,0	2524

GARDASIL
2142 LYG, 7866 addit QALYs

CERVARIX
2468 LYG, 6339 addit QALYs

HCC= health care costs saving = Cost savings from the prevented cases are bigger than the costs of the vaccination programmme

Parameter	Cervarix	Gardasil
Costs (MEUR) saved / 100 yrs		
Reduction in other cytological abnormalities	39.1	28.2
Reduced CIN1-3	42.6	34.5
Cancers prevented	16.4	14.3
Warts prevented	0	21.6
Total cost savings (MEUR)	**98.1**	**98.6**
QALYs gained / 100 yrs		
Reduction in other cytological abnormalities	949	689
Reduced CIN1-3	1 785	1 443
Cancers prevented	936	817
Warts prevented	0	2 608
Life years gained	2 549	2 210
Total QALYs gained	**6 219**	**7 767**

When implementing vaccination

- Vaccine coverage important (like scr)
- School based programmes have succeeded best (UK, Australia)
- Implementaton to population based vaccination programmes (like scr) perform significantly better than opportunistic programmes

While the vaccination is increasing

- It does not replace organised screening
- Improving and developing organised screening is necessary
- There are obvious synergies between screening and vaccination
  - Vaccination prevents CIN3+ cases of younger women, (<35 years), sooner, while screening is not very effective in those age groups
  - older women protected effectively by screening