HPV and cervical cancer control
Epidemiological modeling

Barrriers in HPV vaccination & cervical screening programmes
Antwerp, Belgium, 27-28 June 2016

International Agency for Research on Cancer
Lyon, France

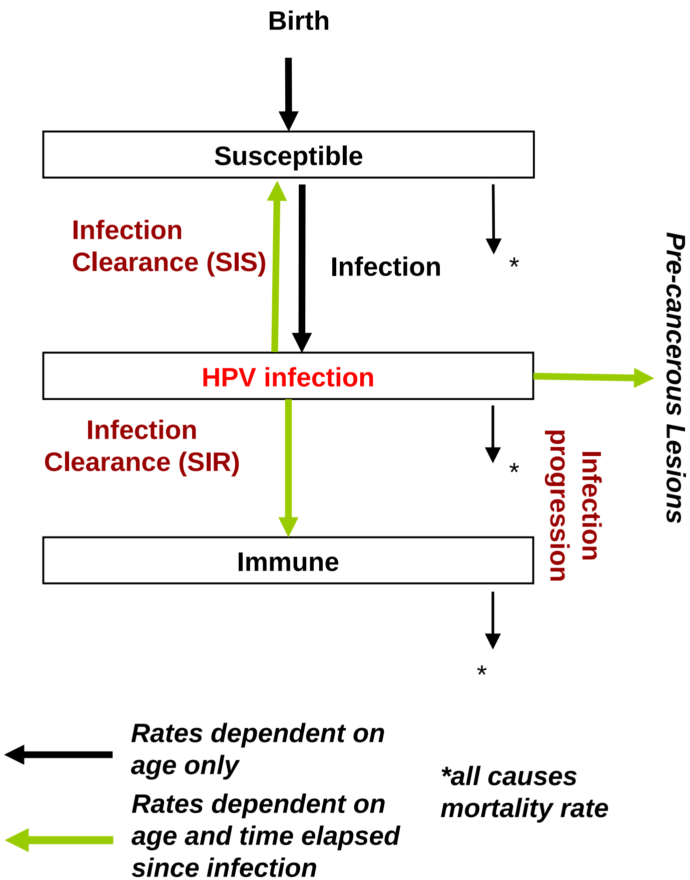
“Cancer research for cancer prevention”

Iacopo Baussano

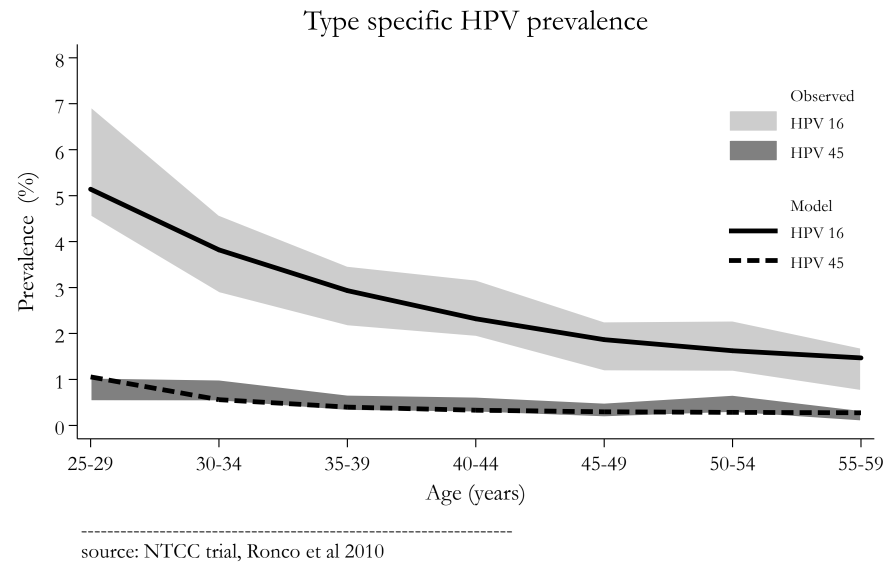
Outline

- Mathematical models of HPV transmission
  - – HPV transmission
  - – HPV progression (not presented)
- Epidemiological modeling (projections & empirical)
  - – Impact of catch-up in High-income countries
  - – Impact of catch-up in Middle/Low-income countries
- Effect of Herd Immunity
  - – HPV prevalence heterogeneity across populations
  - – HPV prevalence heterogeneity within populations
  - – Finnish community randomized vaccination trial

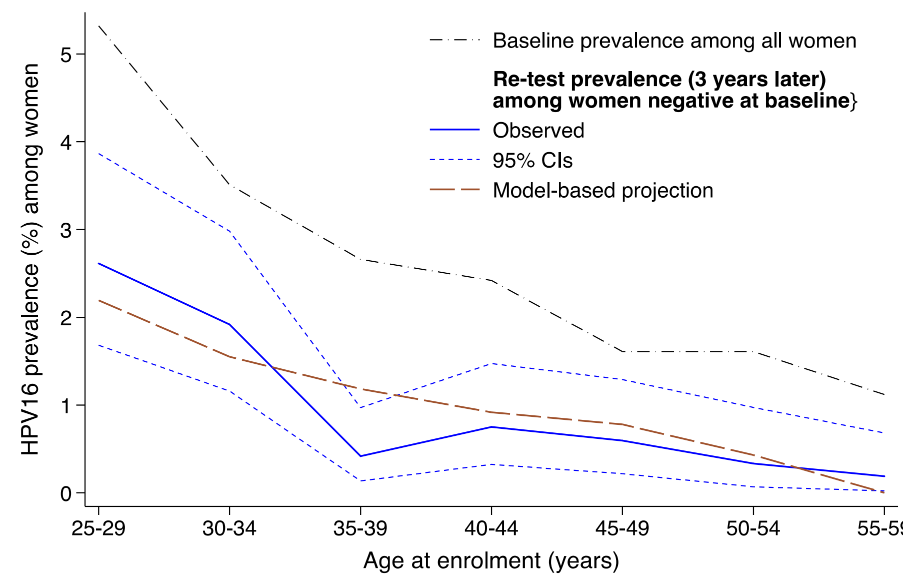
HPV transmission model



Calibration against empirical data from several countries



Cross-validation against independent sets of data from the same countries



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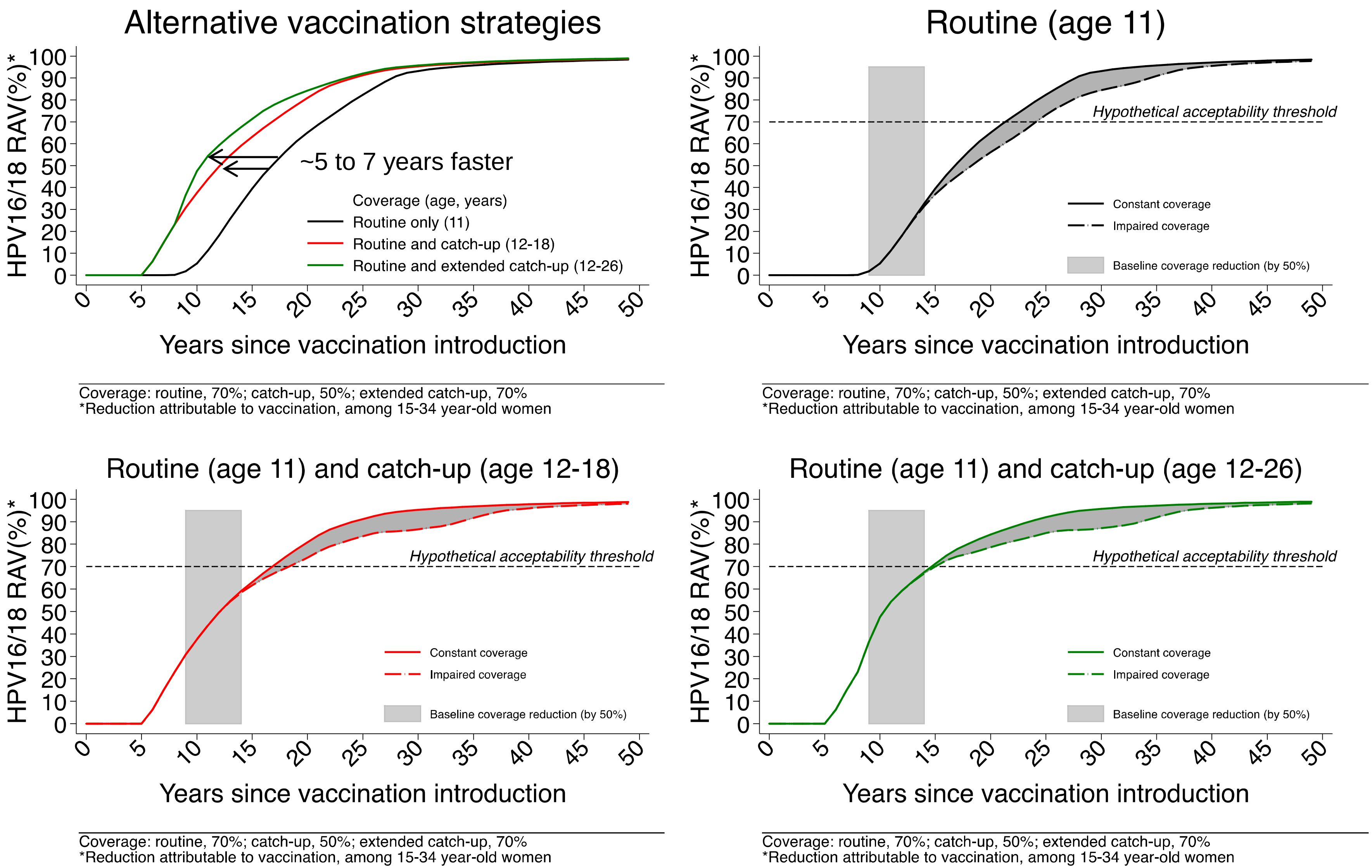
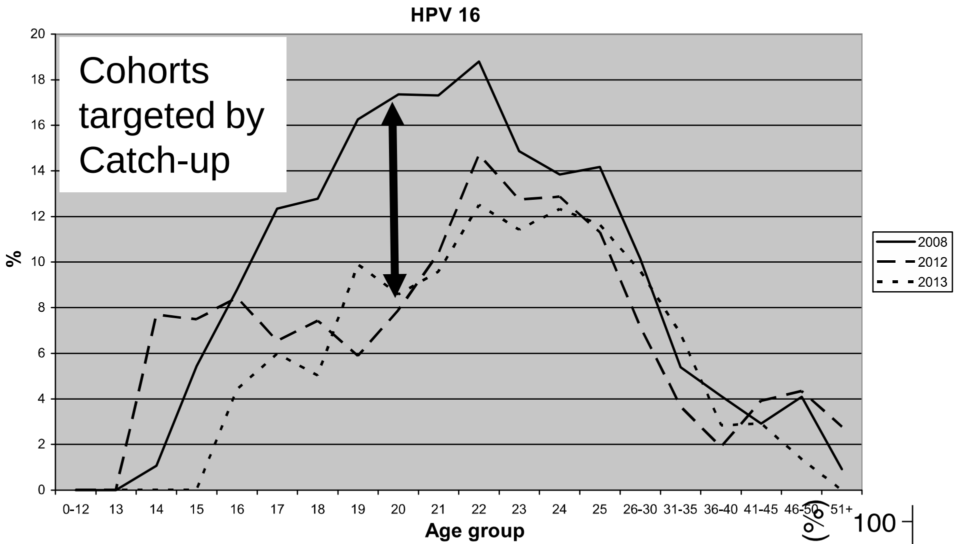
Baussano et al, PloS ONE 2013

Catch-up in Sweden: faster & resilient



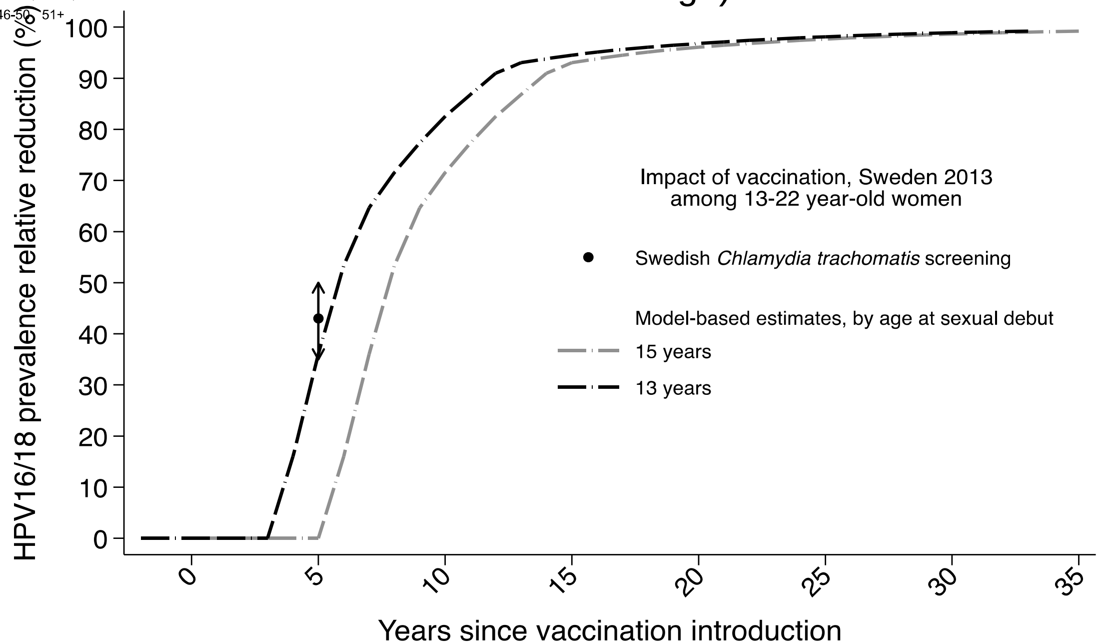
Adapted from Elfström et al, JID, 2015. Bosch FX et al, Nat Rev Clin Oncol. 2015

Evidence of Early Impact: Catch-up



- Chlamydia screening in Sweden
  - Genital swabs or urine samples; PCR with genotyping.
  - Most samples were from women 18 to 23 years of age.
  - Vaccination coverage available for each birth cohort.
  - HPV6/11/16/18 prevalence decline, only among women below 23 years of (high vaccination coverage)

- Model-based projections
  - IARC HPV-transmission model
  - Replicates HPV prevalence
  - Simulated vaccination introduction with realistic coverage
  - Adapted sexual behavior of young birth cohorts



Sources: Soderlund-Strand A et al. 2014, CEPB & Elfstrom KM et al. 2015, JID

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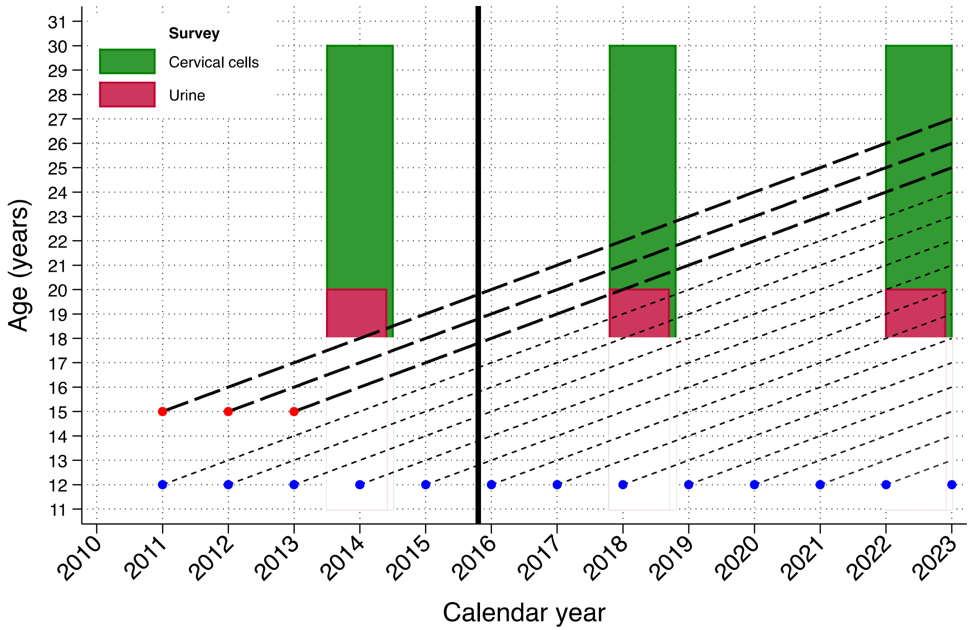
Monitoring HPV vaccination in Rwanda



- **Surveys.**

Cytology: general population, n. 2,508, aged 18–69, 20% HIV positive.

Urine: school-based, n. 912, aged 17-22

Rwanda, 2011 (Gardasil; MoH MSD)

Cumulative human papillomavirus vaccination coverage, by vaccination round

Coverage	Round 1	Round 2	Round 3
Girls vaccinated in school, no.	91 752	89 704	88 927
Girls vaccinated outside school, no.	2 136	3 066	3 180
Total no. of girls vaccinated	93 888	92 770	92 107
Cumulative coverage (%)	**95.04**	**93.90**	**93.23**

- **Prevalence**

- Any HPV =34%
- HR-HPV =22%
- HPV16/18 =7 %

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Adapted from Ngabo et al BMC Infect Dis, 2016 & Binagwaho et al. Bull World Health Organ 2012

Urine survey: effect of vaccination

Choice of test for HPV prevalence monitoring from urine sensitivity versus specificity

Vaccinated	N	HPV6/11/16/18-pos	Adjusted[1] PR (95% CI)
Bhutan			
GP5+/6+	973		
No	77	2 (2.6)	**1**
Yes	896	6 (0.7)	**0.32 (0.06-1.64)**
E7-MPG (IARC)	973		
No	77	1 (1.3)	**1**
Yes	896	11 (1.2)	**0.86 (0.11-6.77)**
Rwanda			
GP5+/6+	912		
No	519	21 (4.1)	**1**
Yes	393	2 (0.5)	**0.12 (0.03-0.51)**
E7-MPG (IARC)	912		
No	519	33 (6.4)	**1**
Yes	393	11 (2.8)	**0.45 (0.23-0.90)**

[1]Adjusted for age and sexual behavior

Franceschi et al. Submitted 2015

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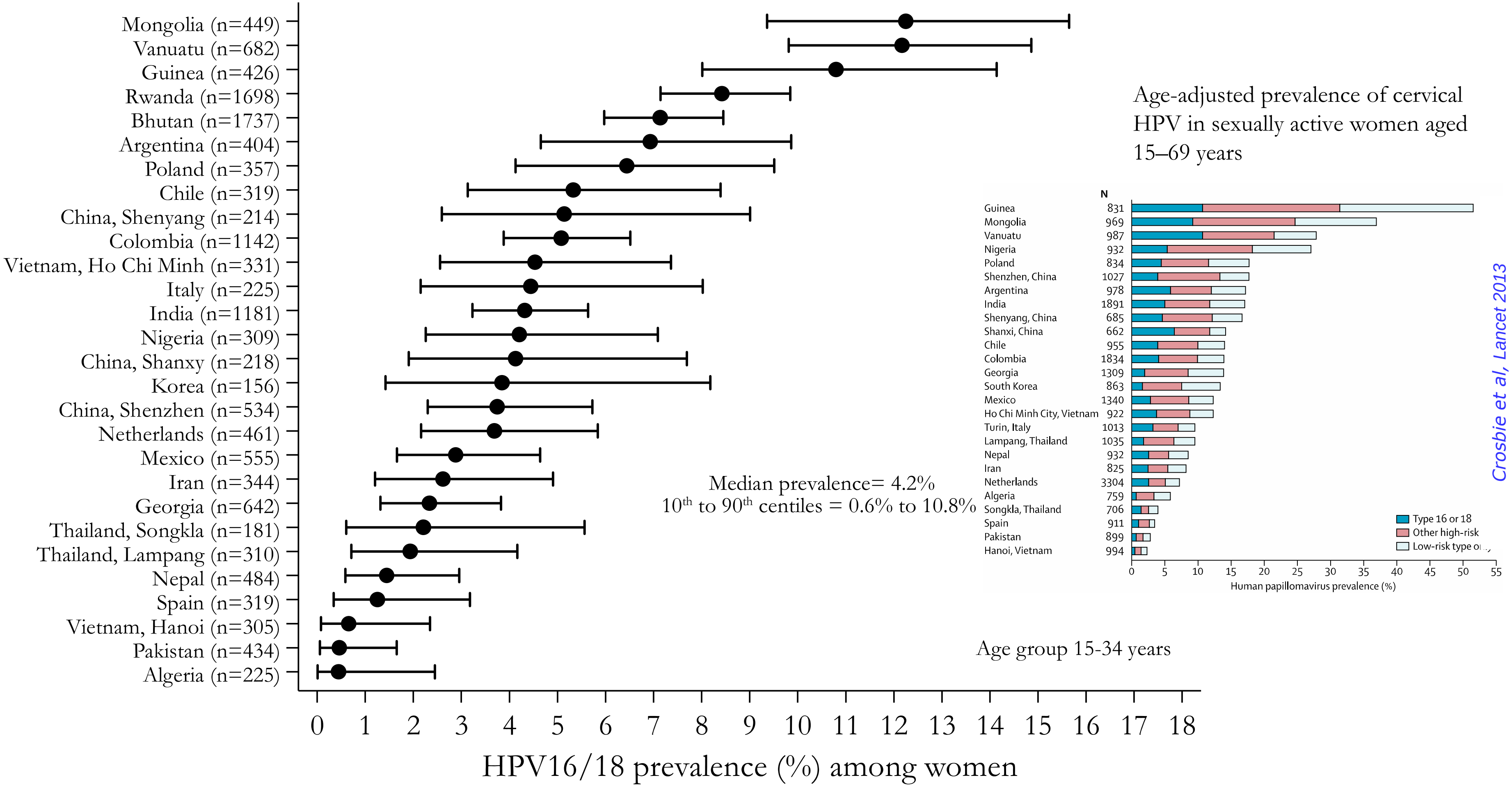
HPV Prevalence* heterogeneity

Mostly attributable to different sexual activity patterns (i.e. ≠ incidence)



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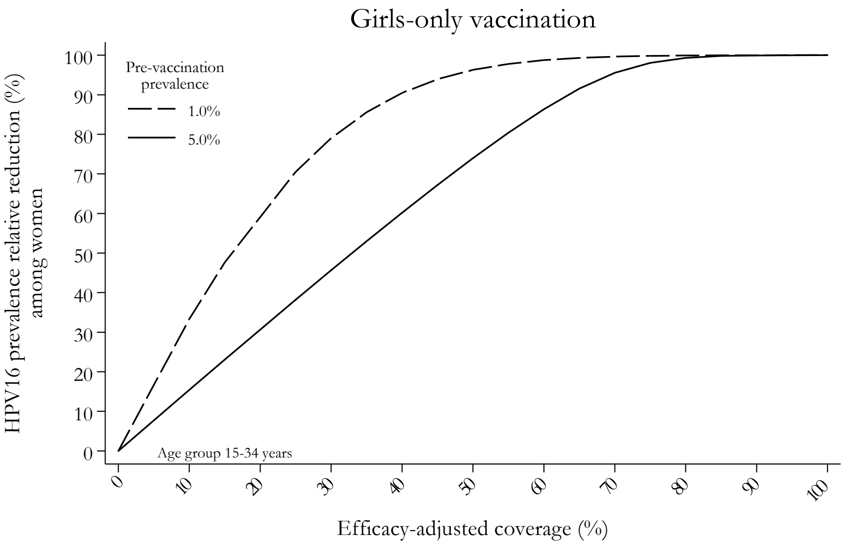
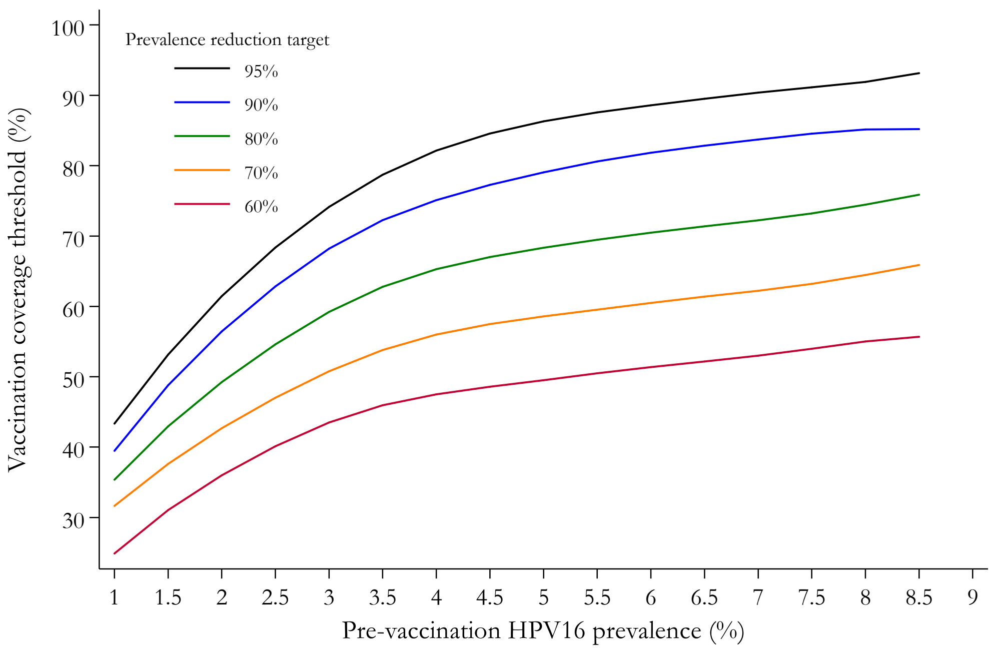
***Pre-vaccination prevalence, source: IARC Multi-centre HPV Prevalence Surveys, 1995-2016**

≠ HPV prevalence across populations

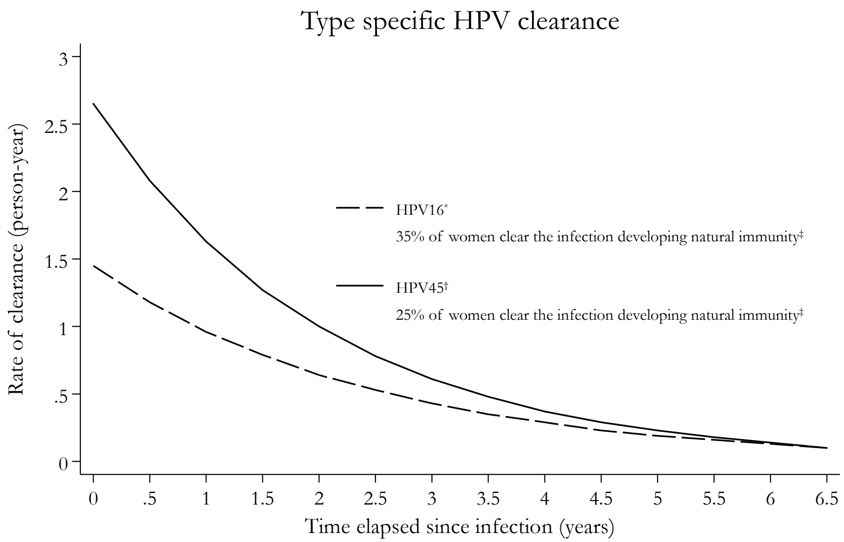


- Assuming same vaccination coverage & efficacy
  - ≠ HPV16 prevalence (i.e. 1% vs. 5%).
  - Women ≤ 35 years of age.
  - For any level of coverage impact of vaccination is larger in population 1% prevalence.
  - Same direct effect across populations, different herd immunity effect
  - Larger HI in populations with lower prev.

- HPV control thresholds
  - Same vaccination coverage are likely to meet ≠ prevalence reduction targets according to the pre-vaccination prevalence.
  - Crucial difference with most vaccine-preventable infections, elimination threshold (p_c) assumed as constant across populations.
  - HPV R_0 range ~1.8 to 5.0 → P_c= to 45% to 80%

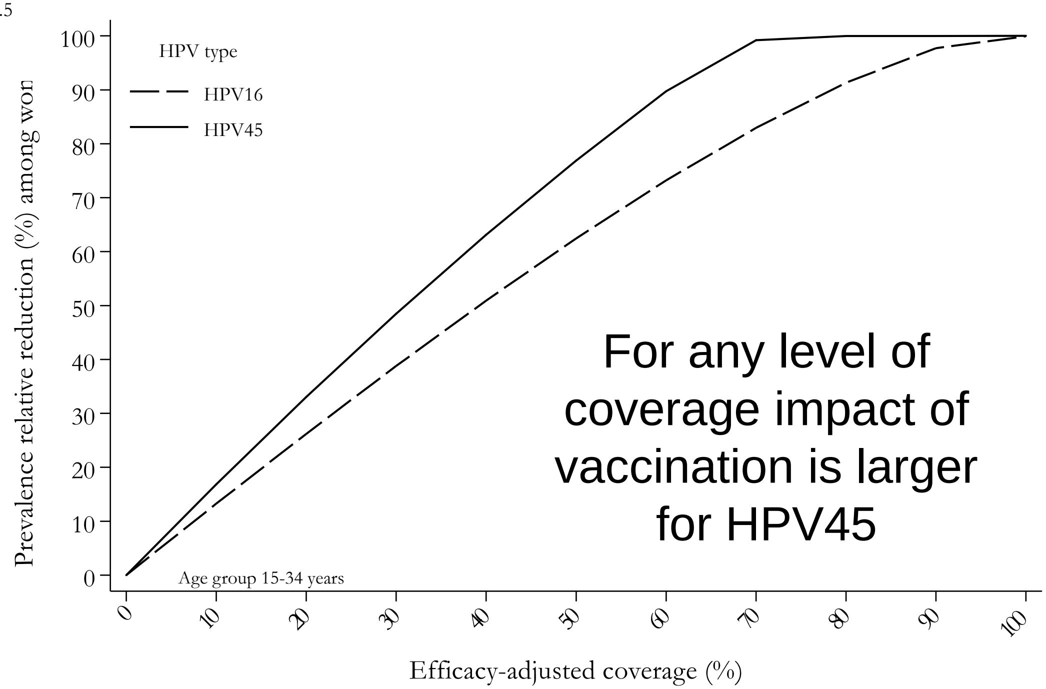


≠ HPV prevalence within populations



- HPV16 vs. HPV45
  - Share the transmission network
  - Prevalence determined by their ≠ biology (in particular Infection Duration)
  - Infection duration is inversely related to R_0→ directly related to P_c

- Implications to project the impact of HPV vaccination against types other than HPV16/18
  - HI estimated for HPV16 is a conservative estimate of the HI expected for other types
  - Impact of vaccination is proportional to the fraction of cancer attributable to each HPV type



For any level of coverage impact of vaccination is larger for HPV45

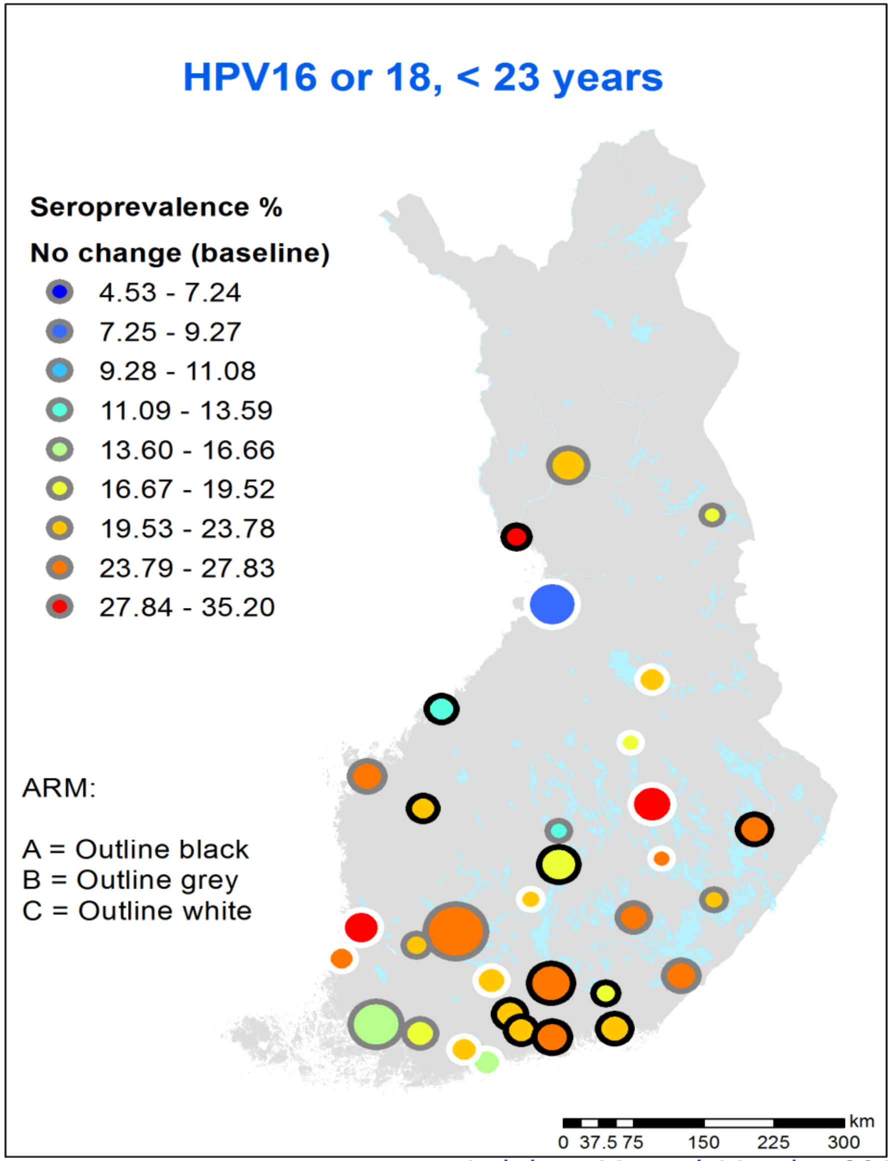
Finnish effectiveness trial

Arm A communities (n.11): 90% of participating girls and boys were assigned receive HPV-16/18 vaccine

Arm B communities (n.11): 90% of girls were assigned to receive HPV-16/18 vaccine, boys were assigned to receive hepatitis B-virus (HBV) vaccine

Arm C communities (n.11): all were assigned to receive HBV-vaccine.

Notably, sample size calculations allowed for herd immunity effect and were obtained using an HPV transmission model



Lehtinen M. et al, Vaccine 2015

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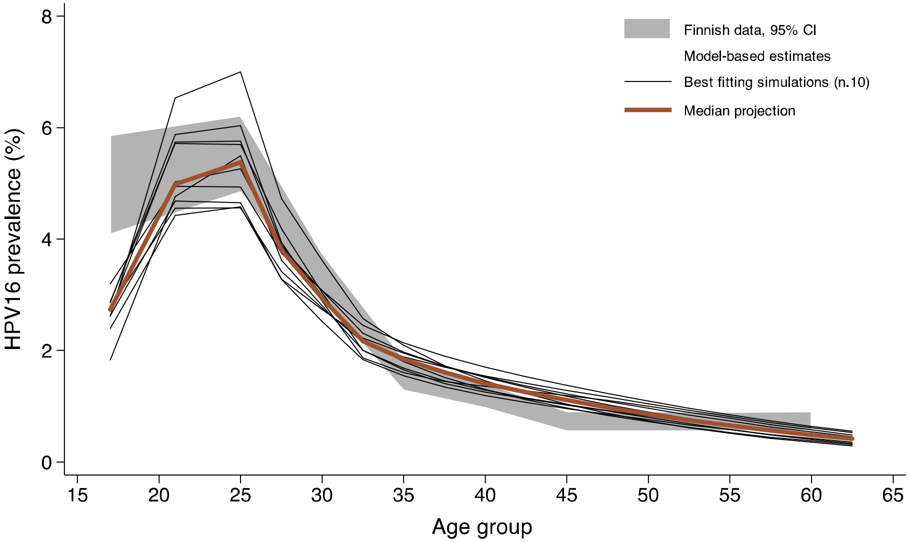
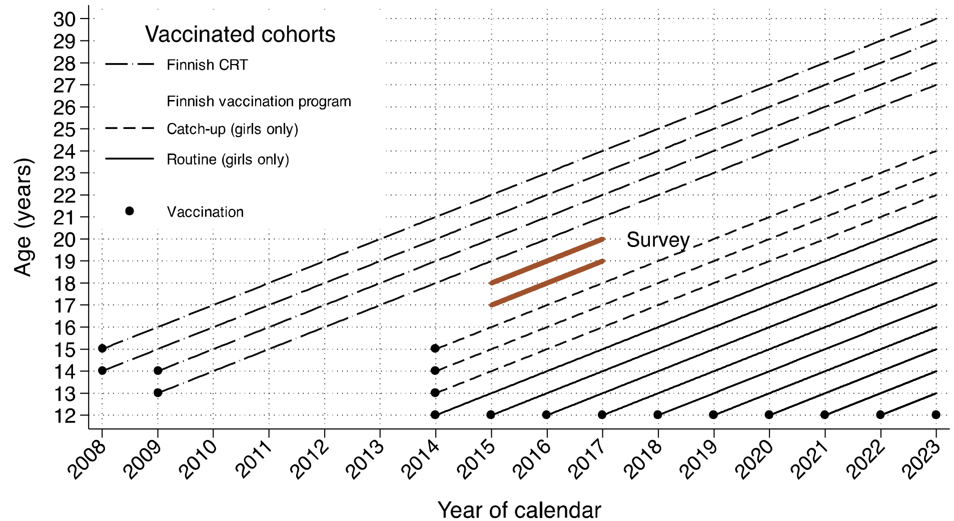
HPV vaccination in Finland





Birth cohort/Calendar year	ICL/IARC model[a]			
	BC-92/2011	BC-93/2012	BC-94/2013	BC-95/201
Vaccine coverage				
♀ 45.5% (Arm B)				
Prevalence	n.a.	4.0%	3.6%	3.5%
Reduction	n.a.	15%	22%	24%
♀ 47.5%/♂ 19.8% (Arm A)				
Prevalence	n.a.	3.7%	3.2%	3.2%
Reduction	n.a.	22%	30%	31%

Lehtinen M. et al, Vaccine 2015

Conclusions – Future developments

- Catch-up
  - Accelerate direct protection against HPV (and consequently cervical cancer) among cohort of sexually active women at vaccination.
  - Accelerate indirect protection against HPV (and consequently cervical cancer) among unvaccinated and sexually active women.
  - Modeling and empirical results are consistent

- Herd immunity effect
  - Is not constant across populations and HPV types
  - Is directly dependent from HPV prevalence in absence of vaccination
  - Populations with different HPV prevalence need different coverage to reach the same HPV control threshold
  - In the same population vaccination coverage may generate ≠ HI vs. ≠ HPV types
  - Finnish trial will provide empirical data to test the model-based findings

Acknowledgments

IARC

- Infection and Cancer section
- Cancer Surveillance section

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