



## **AIB Technical Meeting**

Strategies for introducing and implementing vaccines for adults into National Immunization Programs in Europe: Exemplary Approaches and Key Insights  
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# **SCIENTIFIC APPROACHES TOWARD IMPROVING CERVICAL CANCER ELIMINATION STRATEGIES**

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# WHAT DO WE MEAN BY ELIMINATION?

## Control

Reduction of disease incidence, prevalence, morbidity, and/or mortality to a locally acceptable level

## Elimination

**Of transmission:** reduction to zero of the incidence of infection caused by a specific pathogen in a defined geographical area, with minimal risk of reintroduction

**As a public health problem** is a term related to both infection and disease.

Achievement of clear, measurable and commonly agreed global targets set by WHO in relation to a specific disease.

*Continued intervention measures needed*

## Eradication

Permanent reduction of a pathogen's prevalence to zero

*Smallpox*

*Intervention measures no longer needed*

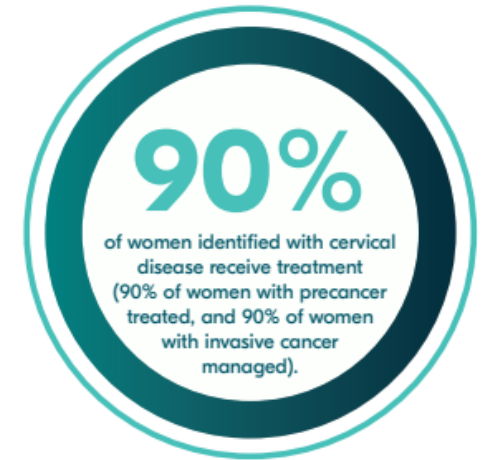
Global strategy to accelerate the elimination of cervical cancer as a public health problem



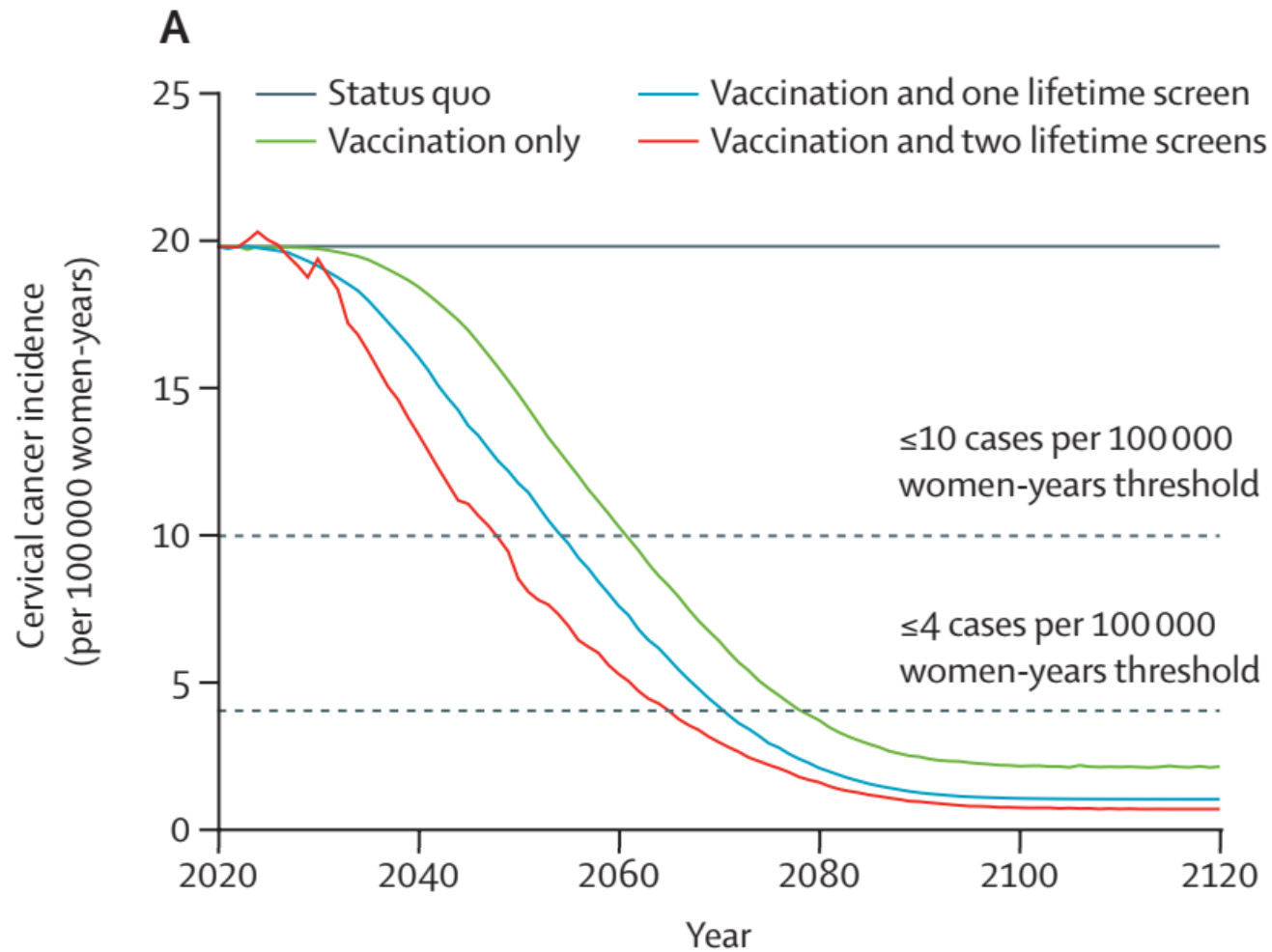
# A TRIPLE INTERVENTION STRATEGY

This global strategy to eliminate cervical cancer proposes:

- a vision of a world where **cervical cancer is eliminated as a public health problem**
- a **threshold of 4 per 100 000 women-years** for elimination as a public health problem
- **the following 90-70-90 targets** that must be met by 2030 for countries to be on the path towards cervical cancer elimination:



# IF IN 2020 WE HAD ALREADY REACHED THE 90-70-90 TARGETS, WHAT WOULD HAPPEN IN THE NEXT 100 YEARS?



**90% HPV vaccination coverage of girls can lead to cervical cancer elimination in most LMICs within the next century**

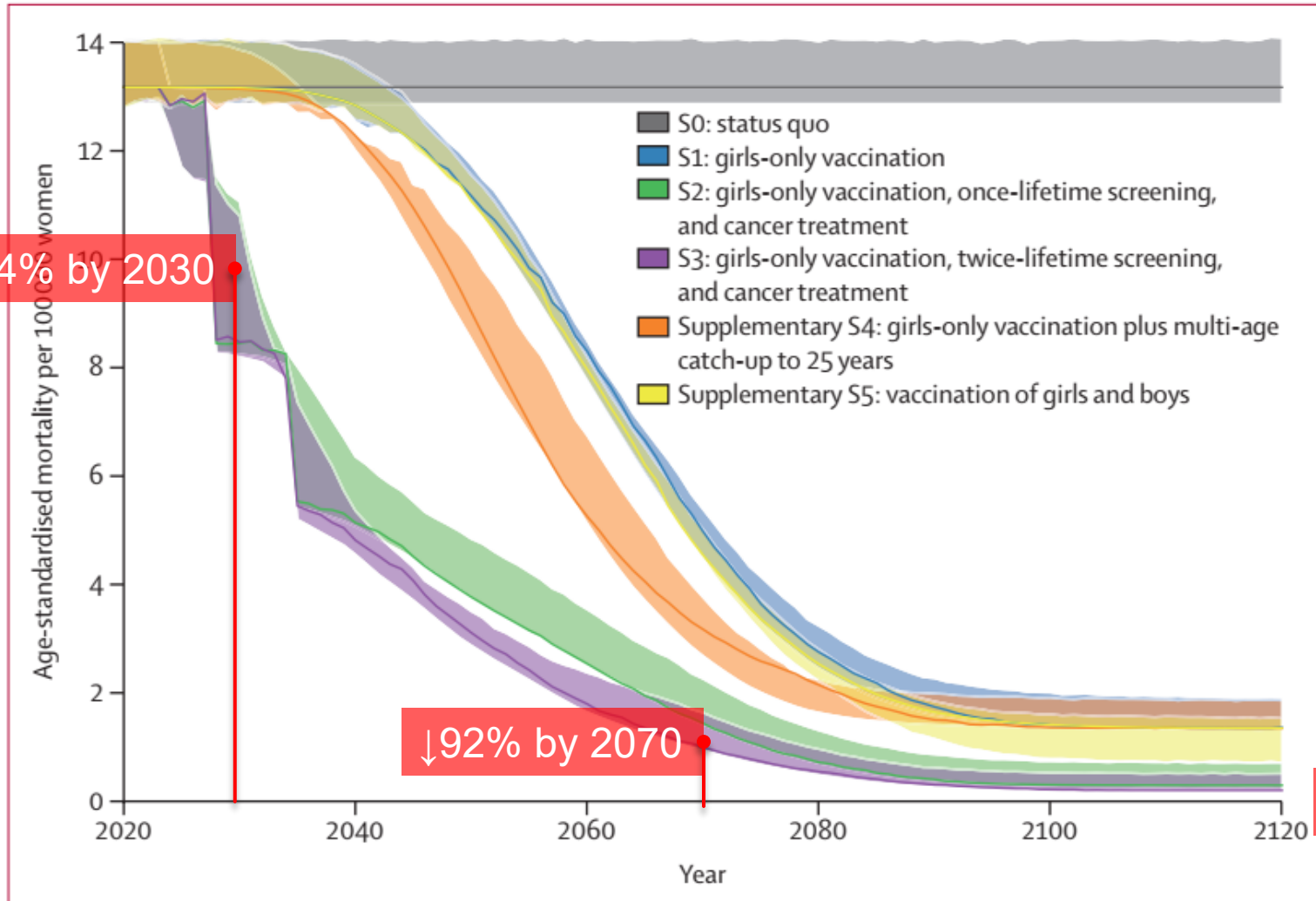
However, countries with the highest cervical cancer incidence might not reach elimination by vaccination alone, although these countries are predicted to have the greatest absolute reductions.

Screening would accelerate elimination by 11–31 years and will be necessary to eliminate cervical cancer in countries with the highest incidence

**HPV vaccination of girls is key for elimination**

Girls only vacc: 61M cases averted  
Adding twice-lifetime screening: extra 12M

# IF IN 2020 WE HAD ALREADY REACHED THE 90-70-90 TARGETS, WHAT WOULD HAPPEN IN THE NEXT 100 YEARS?

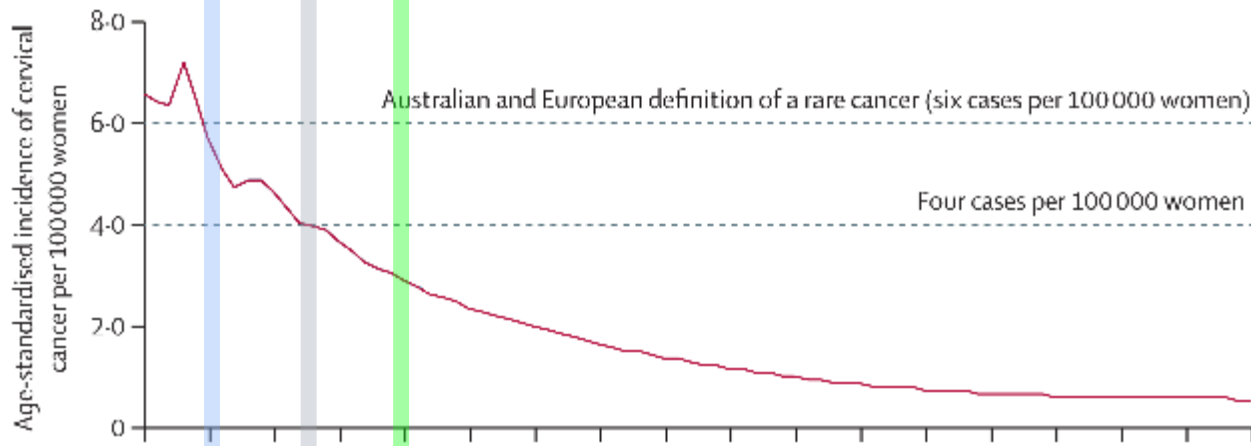


The different strategies move the blue curve (S1, girls only vaccination 90%) to the left in varying degrees but translating into millions of avoided deaths.

Figure 1: Age-standardised cervical cancer mortality over time for all 78 LMICs

# AUSTRALIA: PREDICTIONS (MODELLING) OF THE IMPACT ON INCIDENCE AND MORTALITY RATES OF THE NEW HPV SCREENING PROTOCOL (2017) + 9vHPV VACCINE

## CERVICAL CANCER INCIDENCE



Maintaining current coverage levels:

2020: incidence < 6 cases per 100,000

2028: incidence < 4 cases per 100,000

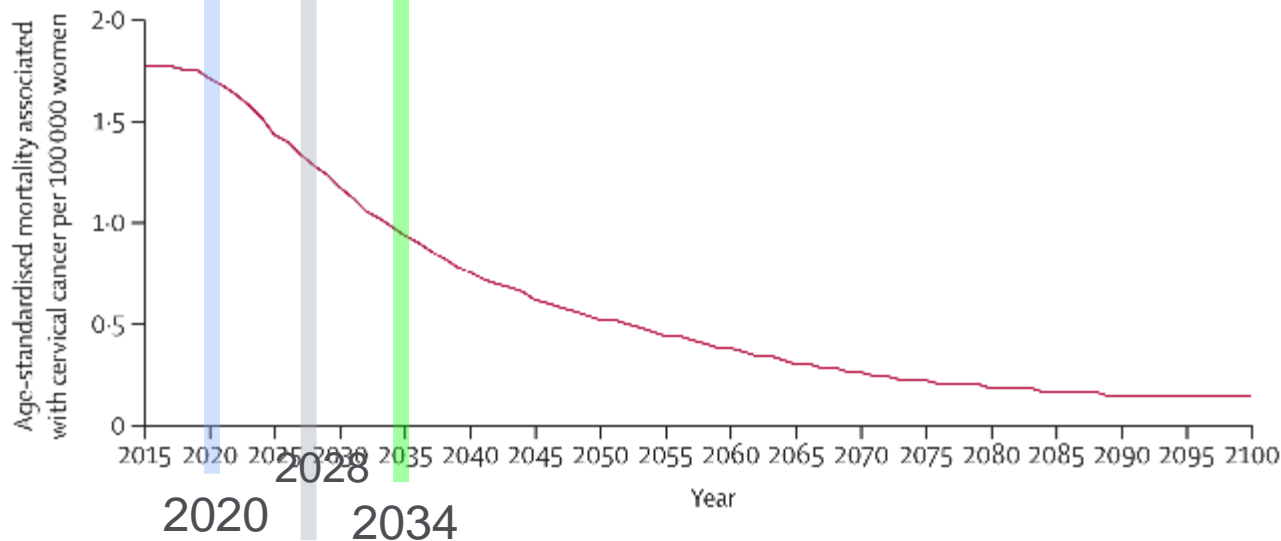
2034: mortality < 1 case per 100,000

2100: incidence 0.57 cases per 100,000

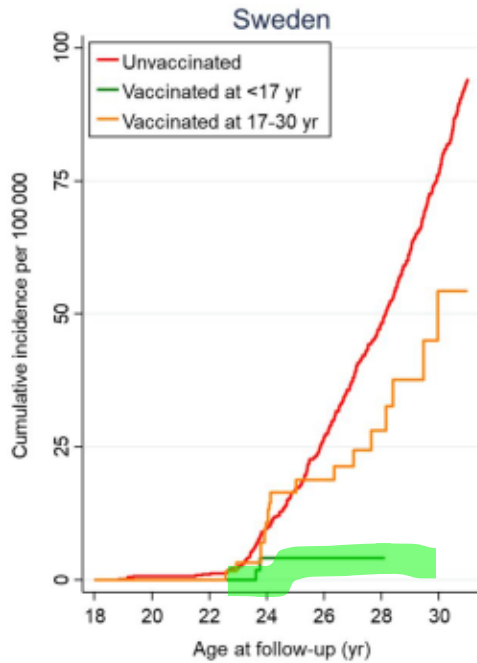
↓ 91%

Mortality 0.15 cases per 100,000

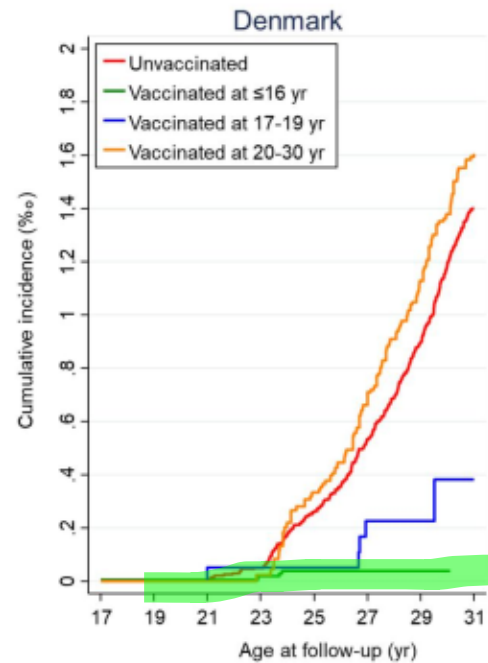
## CERVICAL CANCER MORTALITY



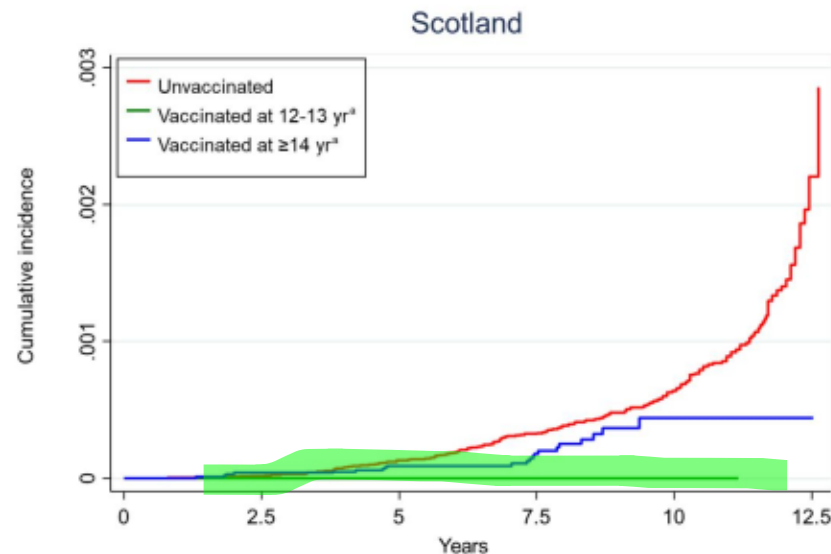
# HPV VACCINATION AT YOUNG AGES STRONGLY REDUCES CERVICAL CANCER INCIDENCE



Lei, N Engl J Med 2020



Kjaer, JNCI 2021



Palmer, JNCI 2024

Reference (Country)	Age at vaccination (years)	VE (95% CI)
Lei, 2020 (14) (Sweden)	<17	81% (35% to 95%)
	17-30	36% (0% to 61%)
Kjaer, 2021 (15) (Denmark)	≤16	87% (59% to 96%)
	17-19	69% (-7% to 91%)
	20-30	-14% (-49% to 13%)
Falcaro, 2021 (16) (England)	12-13	87% (72% to 94%)
	14-16	62% (52% to 71%)
	16-18	34% (25% to 41%)
Palmer, 2024 (1) (Scotland)	12-13 <sup>a</sup>	100% (67% to 100%)
	14-18 <sup>a</sup>	69% (54% to 79%)

**HOWEVER, WE ARE STILL FAR FROM  
REACHING THE 90% TARGET**



# HPV VACCINATION COVERAGE

- Since 2019 WHO/UNICEF publishes annual Estimates of National HPV Immunization Coverage. Also updates the historical series (2010-onwards)
- **Programme performance coverage** : vaccination coverage according to the national schedule and the program's eligibility criteria for each calendar year
- Programme performance is sub-optimal in many countries, including high-income countries with more resources.

In 2019, programmes worldwide had an average performance coverage of:

- **67%** for the first dose of vaccine
- **53%** for the full recommended schedule.

In 2022, programmes worldwide had an average performance coverage of:

- **55%** for the first dose of vaccine
- **44%** for the full recommended schedule.

- The **performance of the HPV vaccination programme during the first two years appears to be a strong predictor** of the level of vaccine coverage in subsequent years

# 2022 –AVERAGE PROGRAMME COVERAGE BY WHO REGION

AFR: African region  
 AMR: Americas region  
 EMR: Eastern Mediterranean Region  
 EUR: European Region  
 SEAR: South-East Asia region  
 WPR: Western Pacific region

## First dose

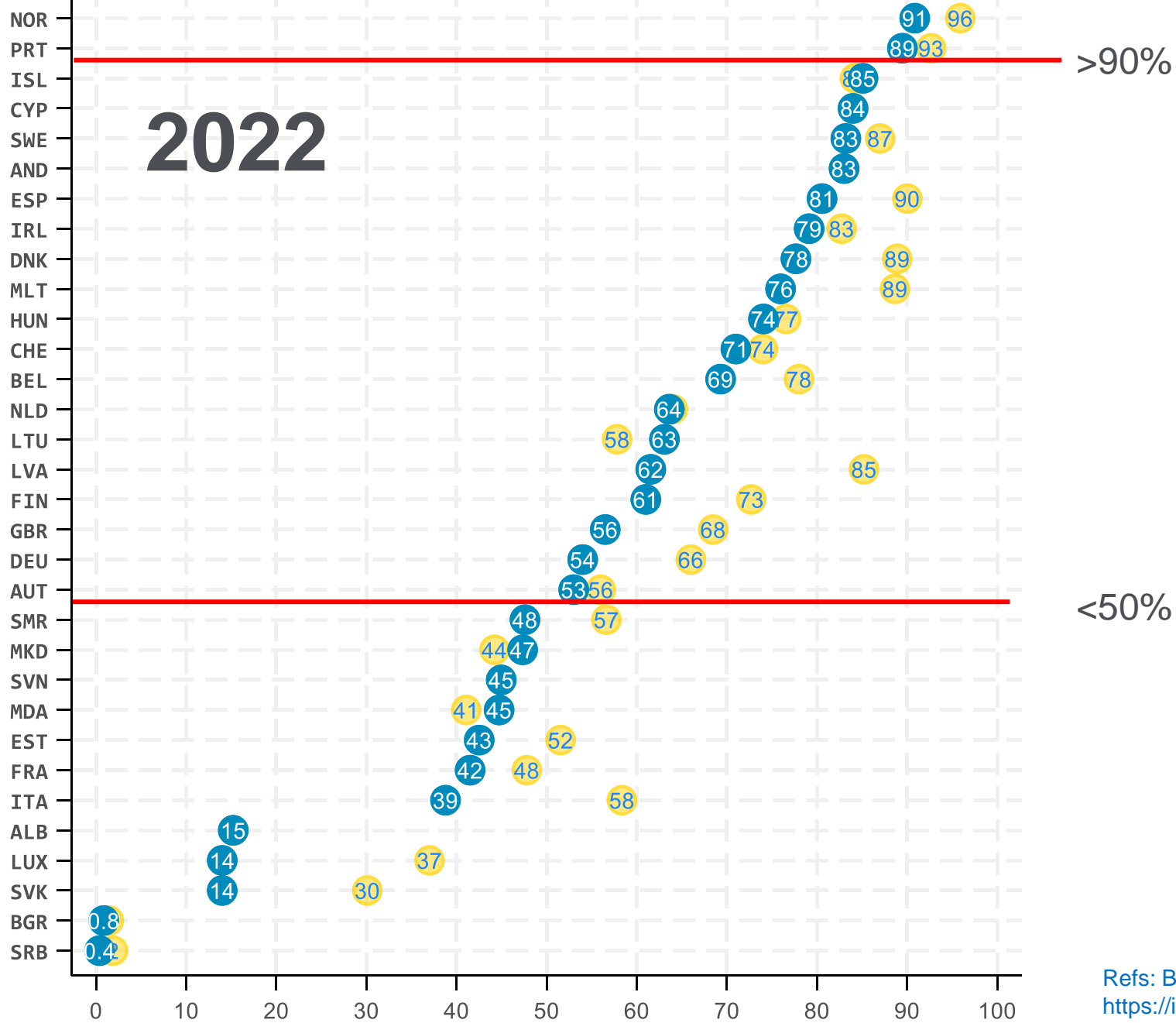
Mean of programme coverage in the region/world

Region	HPV1 (%)
AFRO	51
AMRO	45
EMRO	43
EURO	65
SEARO	45
WPRO	57
Global	HPV1 (%)
Global	55

## Last dose

Mean of programme coverage in the region/world

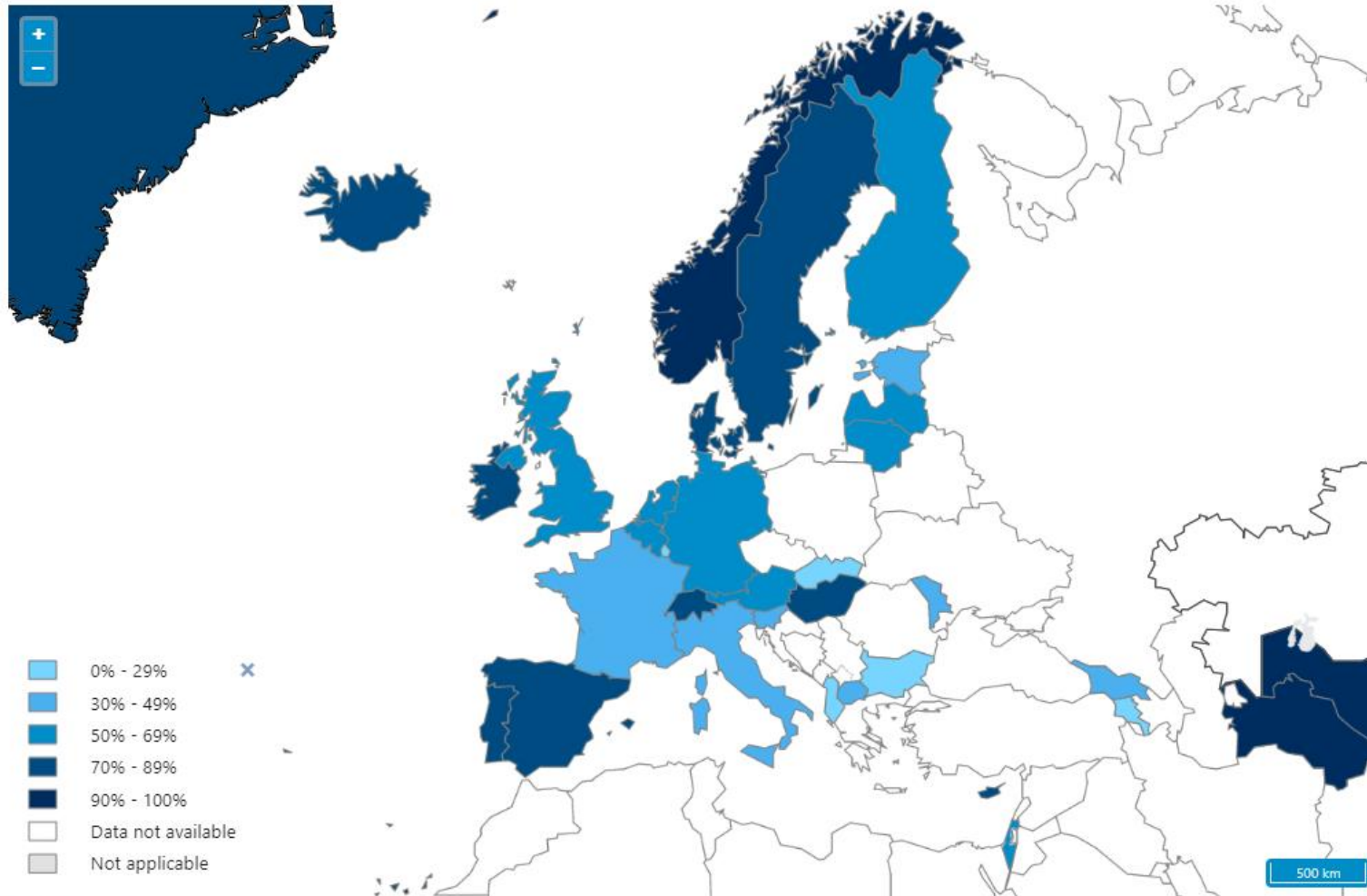
Region	HPVc (%)
AFRO	38
AMRO	31
EMRO	34
EURO	60
SEARO	36
WPRO	44
Global	HPVc (%)
Global	44



# COUNTRY-SPECIFIC HPV VACCINE COVERAGE ESTIMATES (PERFORMANCE COVERAGE) IN EUROPE

Refs: Bruni et al 2021 Prev Med, [WHO Immunization Data portal: https://immunizationdata.who.int/](https://immunizationdata.who.int/)

# 2022 FULL DOSE HPV PROGRAMME COVERAGE



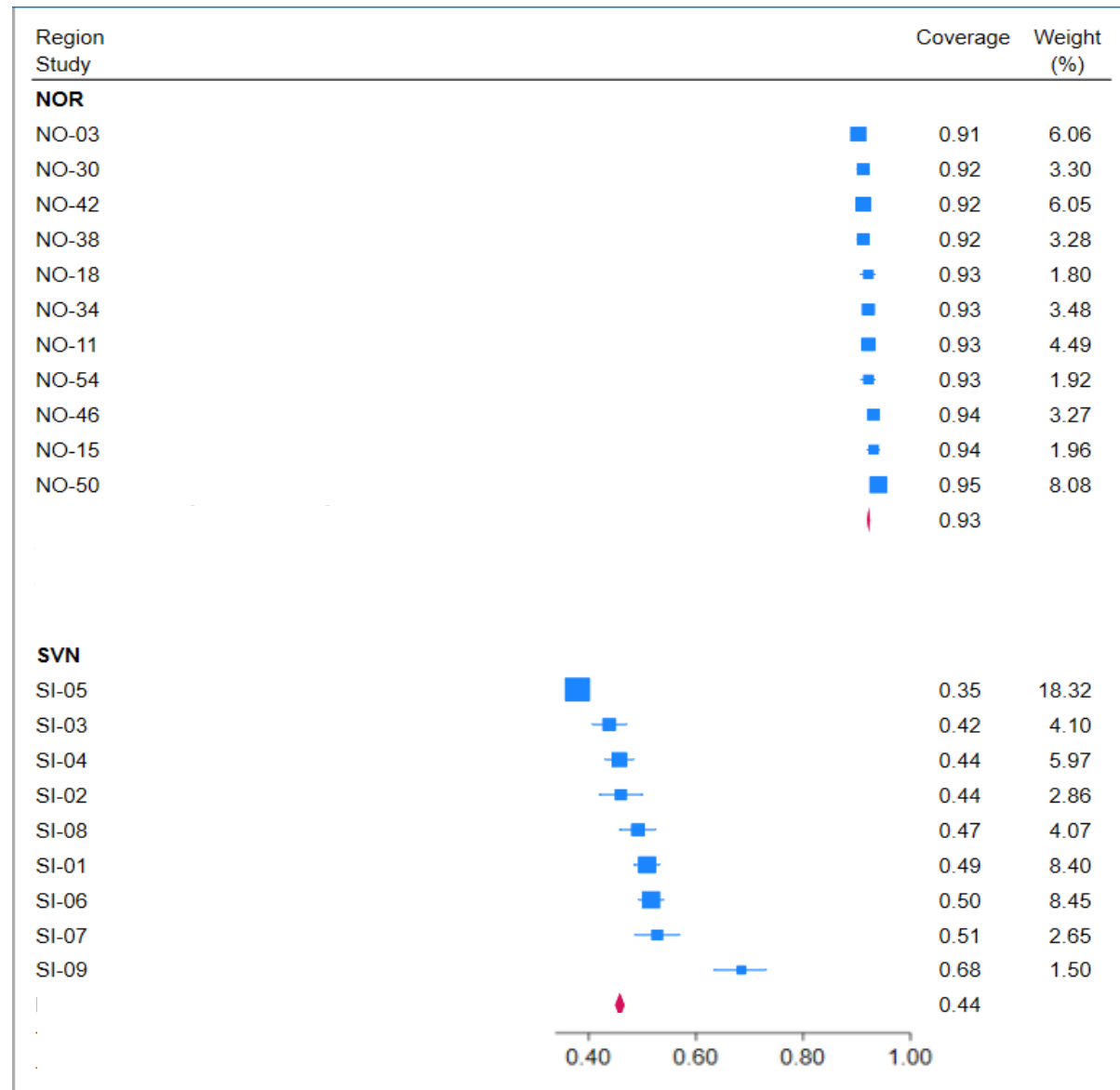
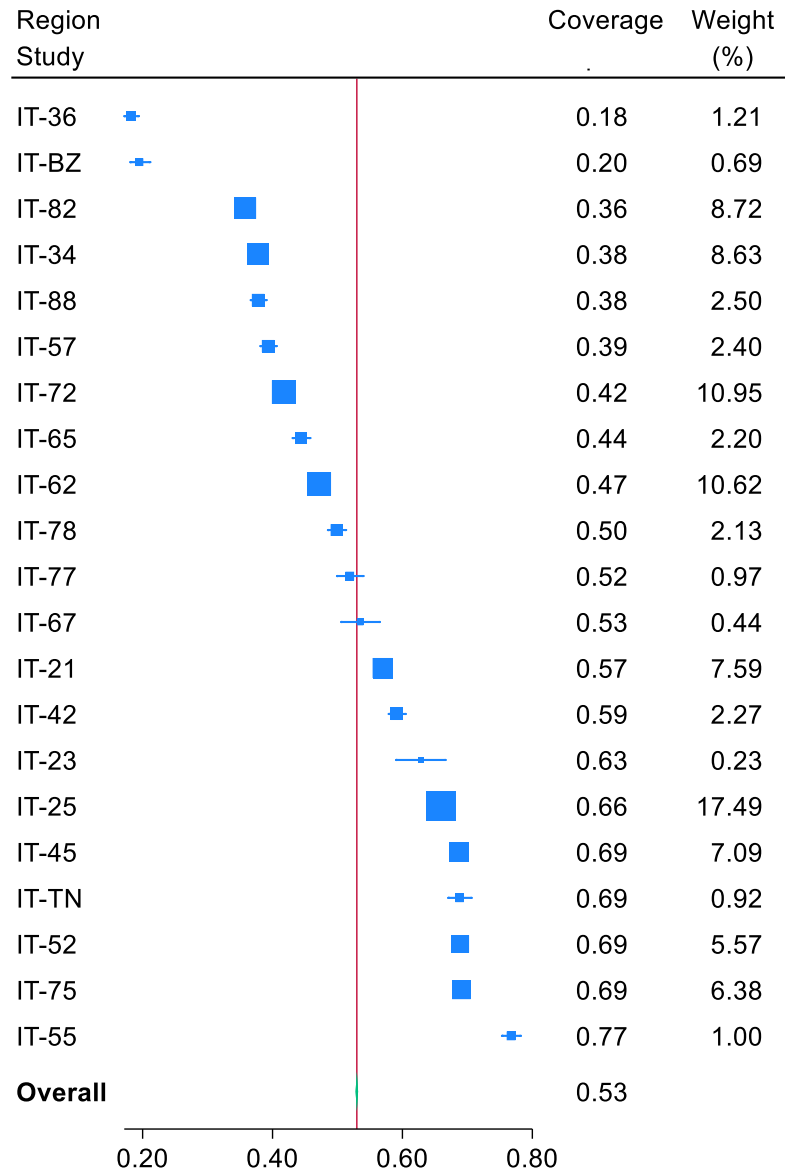
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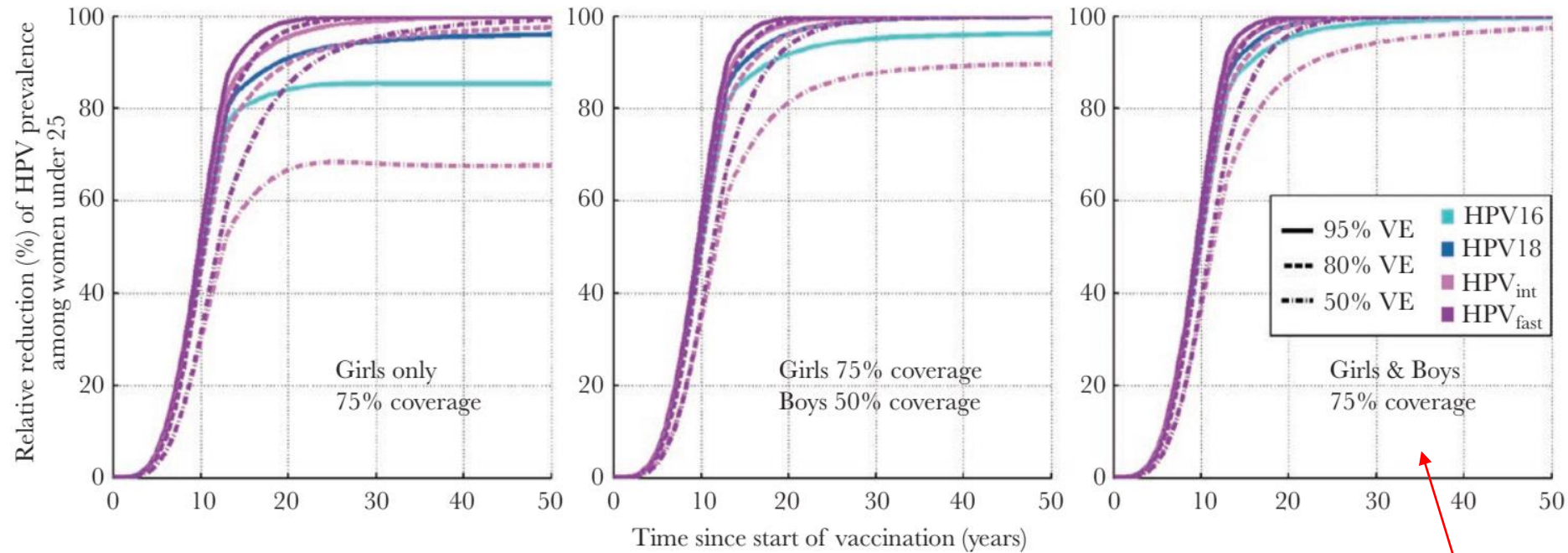
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# SUBNATIONAL DIFFERENCES



# **THE IMPORTANCE OF HERD PROTECTION AND UNIVERSAL VACCINATION**

# GENDER-NEUTRAL VACCINATION IS SUPERIOR FOR ELIMINATION OF ONCOGENIC HPV<sub>s</sub>



The degree of vaccine-induced herd protection is dependent on vaccination coverage, the population, and the distribution of HPV types

**Figure 3.** Modeled eradication of human papillomavirus (HPV) types 16 [■], 18 [■], and oncogenic HPV types with moderate (31 of 33) [■] or fast (35) [■] clearance rates by vaccine efficacy ([VE] 95%/80%/50%), with 75% girls-only vaccination coverage, with 50% boys and 75% girls vaccination coverage, and with 75% gender-neutral vaccination coverage.

Elimination of HPVs 18, 31, 33 and eventually HPV16 from the young adult population can occur respectively within 20 and 30 years with a feasible 75% vaccination coverage

# FOR EACH HPV TYPE THERE IS A CRITICAL VACCINATION COVERAGE THRESHOLD AT WHICH THE HPV TYPE MAY BE ELIMINATED

- If the vaccination coverage within a defined geographic population is greater than this **coverage threshold**, then the herd immunity will result in the elimination of HPV infection in that population.
- This coverage threshold is dependent on:
  - the HPV vaccine efficacy
  - the  $R_0$ , of the HPV type, which is both HPV type specific and population-specific.
- The  $R_0$  and resulting critical vaccination coverage is higher for **HPV16**, the most oncogenic HPV type, than for other high-risk HPV types.



# THE ELIMINATION OF HPV16 FROM A POPULATION WILL BE THE SOUNDEST WAY TO PROTECT THE HPV UNVACCINATED WOMEN AND THE MOST VULNERABLE

Lehtinen et al, state that the following requirements should now guide the implementation of HPV vaccination:

- **Gender-Neutral Approach**
- **Equitable Delivery:**  
*Consider free-of-charge school-based vaccination.*
- **Critical Immunization Threshold:**  
*Vaccination coverage should meet or exceed the country-specific critical immunization threshold.*
- **Comprehensive Strategy for Immigrants and Migrants:**  
*Tailor cervical cancer prevention strategies to include HPV vaccination and screening for all immigrants and migrants.*

## **VACCINATION BEYOND AGE 15**

**ELIMINATION OF CERVICAL CANCER BY  
STRATEGICALLY COMBINING HPV VACCINATION  
AND HPV SCREENING: THE “EVEN-FASTER” MODEL**

# TO ACHIEVE FASTER CERVICAL CANCER ELIMINATION, OFFERING HPV VACCINATION TO WOMEN ATTENDING SCREENING HAS BEEN PROPOSED (THE SO-CALLED FASTER CONCEPT)

Sweden in 2021 launched a nationwide population-based study offering all females in the country who are aged 23–28 concomitant HPV-vaccination and HPV-screening (NCT04910802).

- Sweden: For age  $\geq 25$  years the  $R_0$  was 1.3, for age  $\geq 30$  years it was 1.1 and for age  $\geq 35$  years it was 0.4
- If a Faster-type campaign focuses on age groups with an  $R_0 > 1$ , accelerated HPV clearance would be expected.
- The results suggest that, for elimination, HPV vaccination is unnecessary above age 35 and may not even be necessary above age 30
- Although  $R_0$  estimates are from Sweden and  $R_0$  depends on the contact mixing pattern in the population, the concept of using  $R_0$  to design focused and accelerated HPV elimination campaigns can be applied to any population in which  $R_0$  can be calculated.

Faster concept: Bosch 2015 Nat Rev Clin Oncol  
Even Faster: Dillner 2021 Prev Med

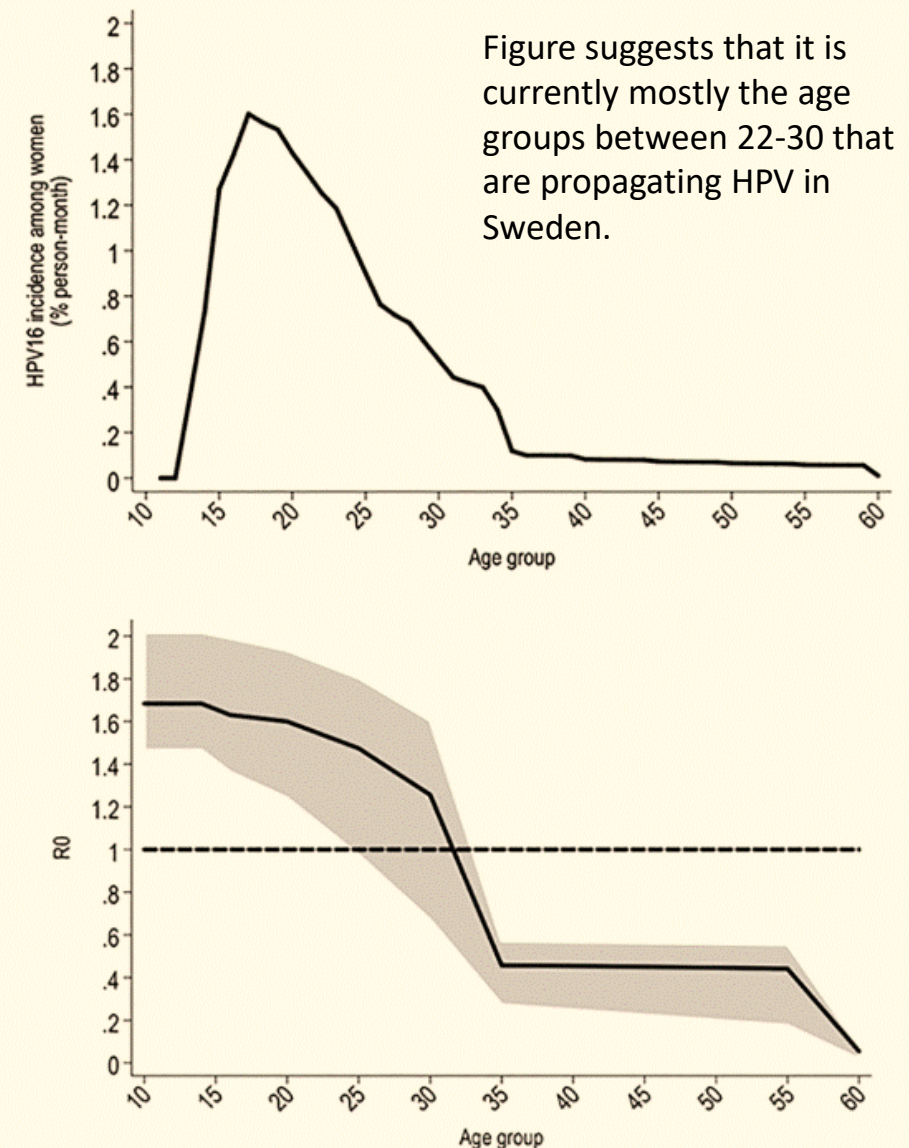


Figure suggests that it is currently mostly the age groups between 22-30 that are propagating HPV in Sweden.

Fig. 1. HPV16 age-specific incidence (top panel) and basic reproductive number ( $R_0$ ) (bottom panel) among unvaccinated women (% person-month) as estimated using a population-based, single-type, HPV transmission model fitted to Swedish data (2-4). Please observe that incidence is calculated for each age cohort, whereas the  $R_0$  is calculated using a “cut-off age” with no spread among women younger than the cut-off age. The shaded area in the bottom panel corresponds to the 95% confidence interval of the  $R_0$  estimates.

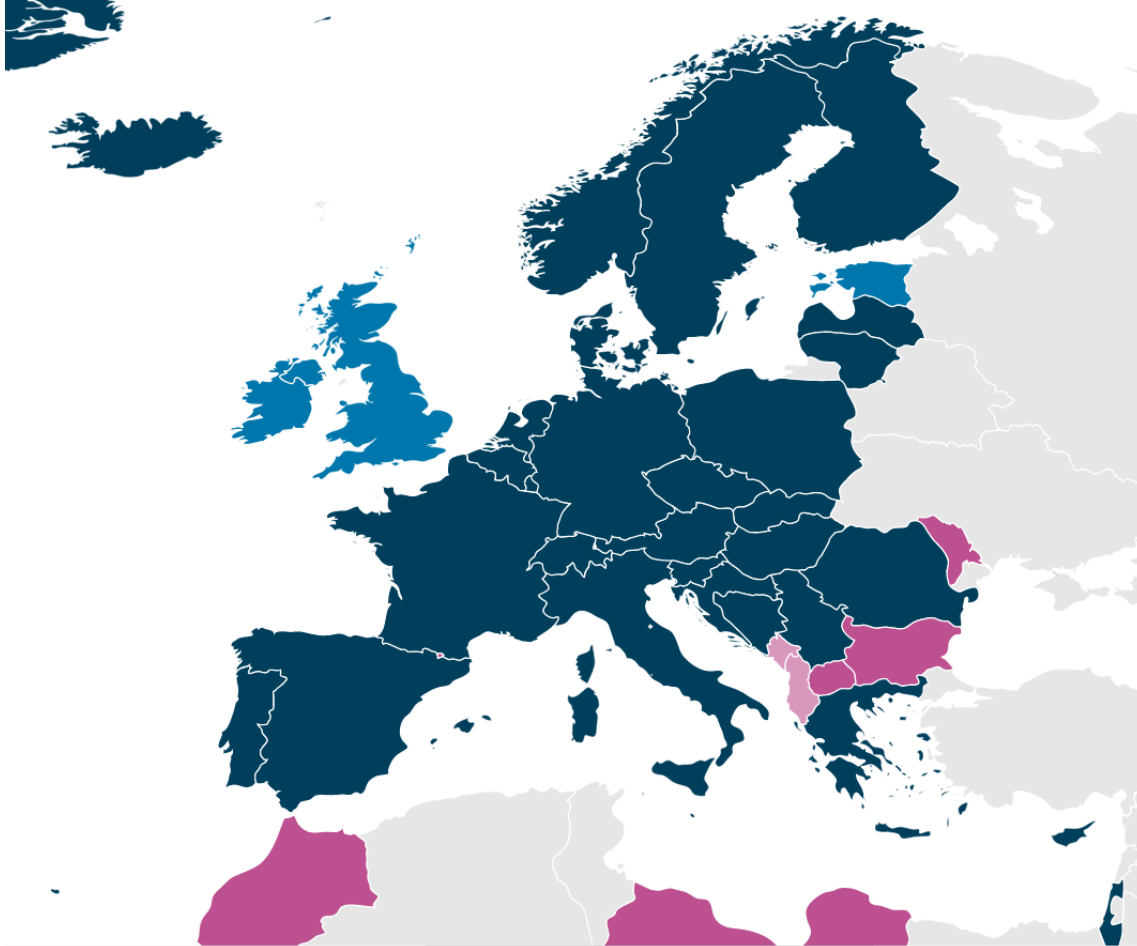
# **SINGLE DOSE RECOMMENDATION**

[Human papillomavirus vaccines: WHO position paper, December 2022](#)

Weekly Epidemiological Record No 50, 2022, 97, 645–672

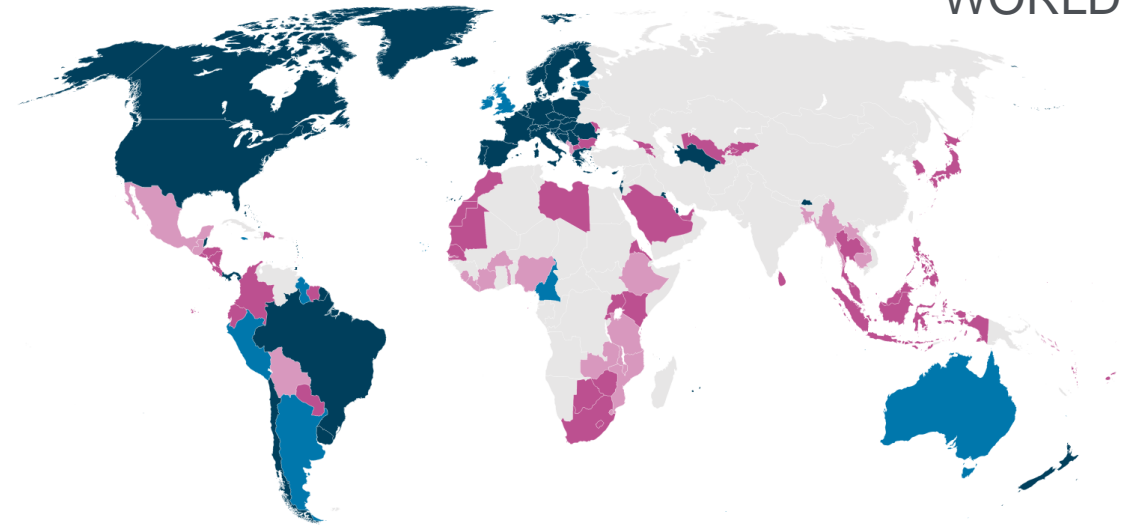
# HPV VACCINE INTRODUCTION AND THE SWITCH TO SINGLE DOSE VACCINATION

## EUROPE



- Girls and boys / ■ Single-dose strategy
- Only girls / ■ Single-dose strategy

## WORLD



- 37 countries in the world are switching to single dose
- In Europe: Albania, Estonia, Ireland, Montenegro, UK

# SUMMARY

- There are huge differences not only in HPV vaccination coverage by world regions, but also in programmes performance between and within countries.
- In 2022, the average HPV vaccination programme coverage in Europe was 65% for the first dose and 60% for the second dose.
- To meet the 90% target, we need not only to speed up introductions worldwide, but also to improve HPV vaccination programmes performance.
- The single-dose recommendation, gender-neutral vaccination (even with moderate coverage), extended catch-up, and the faster strategies combining HPV vaccination with screening in older cohorts, and the outreach to vulnerable groups, have the potential to accelerate the road to cervical cancer elimination by leveraging both the direct and indirect effects of HPV vaccination.

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