Cervical cancer prevention and control

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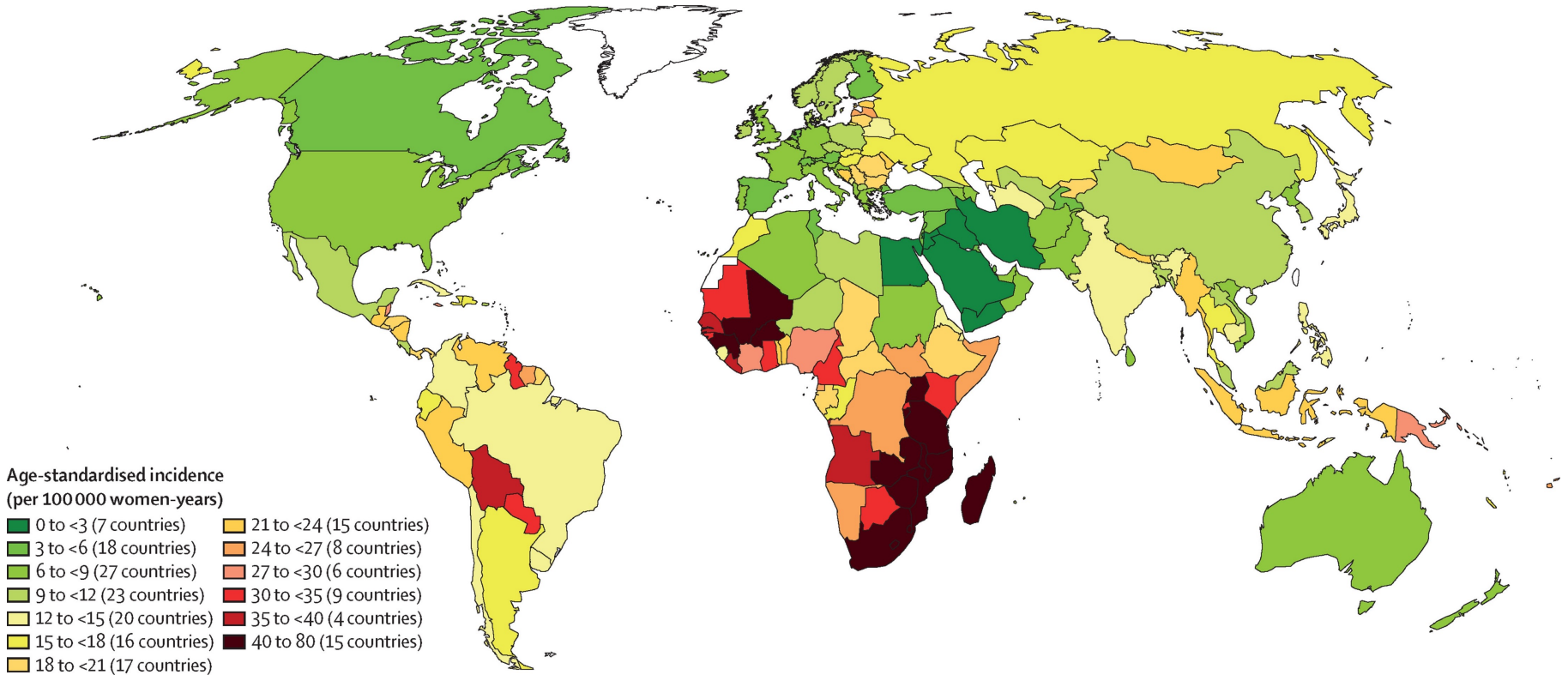
Geographical distribution of world age-standardised incidence of cervical cancer



- **604,127 cases in 2020**
- Deaths **~341,831** per year, >80% in low income/developing countries
- **Access to HPV vaccine, screening and treatment**
- **HIV**

Cervical cancer is one of the most preventable and treatable forms of cancer
=> As long as it is detected early and managed effectively

Arbyn 2020 Lancet Glob Health. 2020 Feb;8(2):e191-e203

Global Cervical Cancer Elimination Threshold & Targets

Threshold for Elimination as a Public Health Problem:
Age-adjusted incidence rate < 4 / 100,000 women

2030 Targets

90%

of girls fully vaccinated with HPV vaccine by 15 years of age

70%

of women are screened with a high-performance test by 35 and 45 years of age

90%

of women identified with cervical disease (precancer or cancer) receive treatment and care

human reproduction programme hrp research for impact
UNDP-UNFPA-UNICEF-WHO-WORLD BANK

World Health Organization

Human Papilloma Virus (HPV)

- HPV - double-stranded DNA within a spherical shell (**capsid**), composed of two proteins, the structural proteins **L1** and **L2**

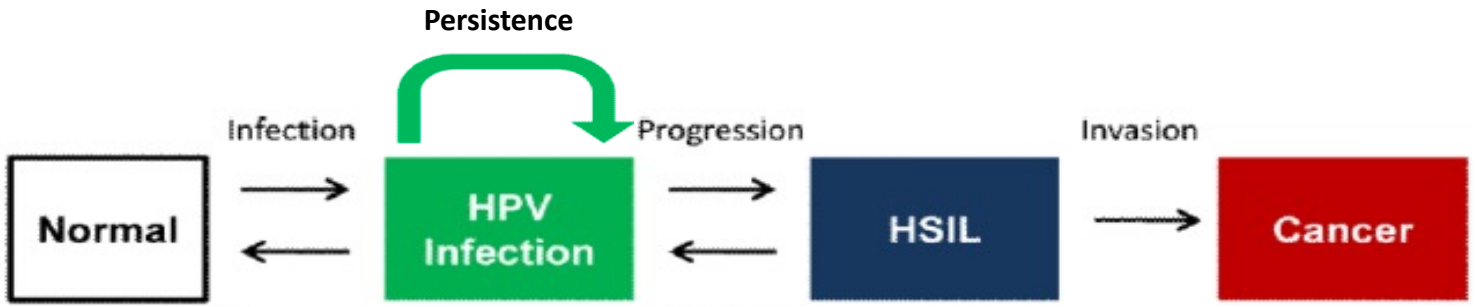
- 40 genotypes infect the genital area, 15 high-risk (HR) oncogenic types,
  => 2 types (**HPV16/18**) linked to 70% of invasive cervical cancer
  => 7 types (**HPV16/18 + 31/33/45/52/58**) linked to >90% of invasive cervical cancer
- HPV6 & 11 linked to anogenital warts (AGW)

- HPV is the most common sexually transmitted infection, **50-80% of women will acquire HPV in their lifetime**
- Most infections will clear; median duration of new infection is approx. 8 month

- Although **new infections decrease** with age, **risk of persistence increases** with age
- HR-HPV persistence increases risk of precancerous lesions and cancer

Burd EM. *Clin Microbiol Rev* 2003; **16**:1–17.

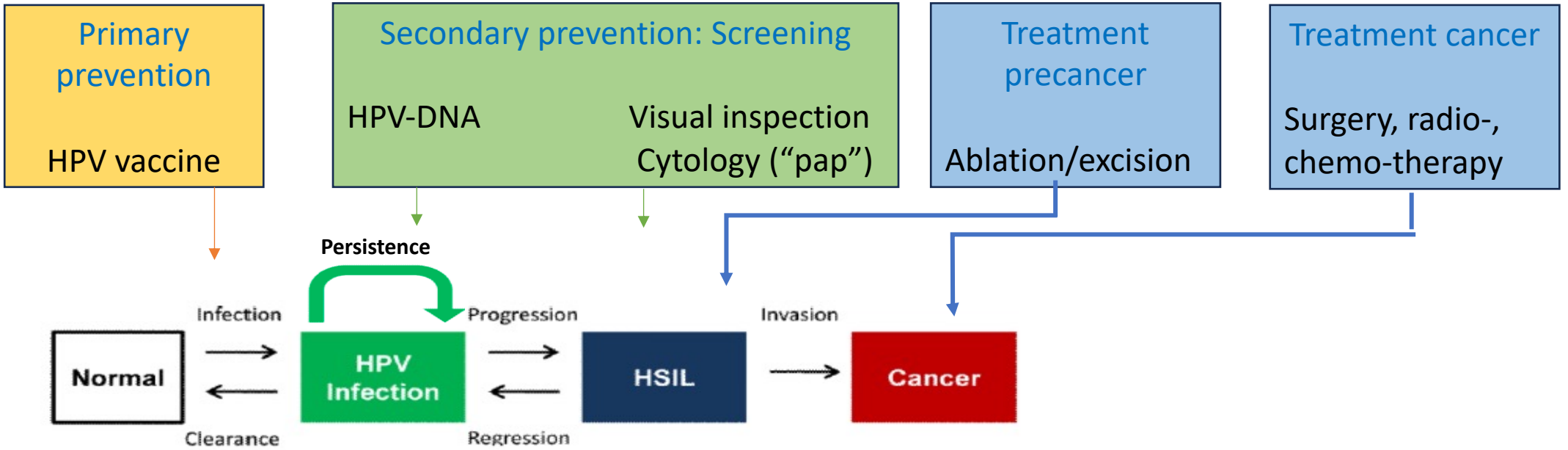
Cervical Cancer Natural History Model
Prevalence of HPV, HSIL & Cancer by Age

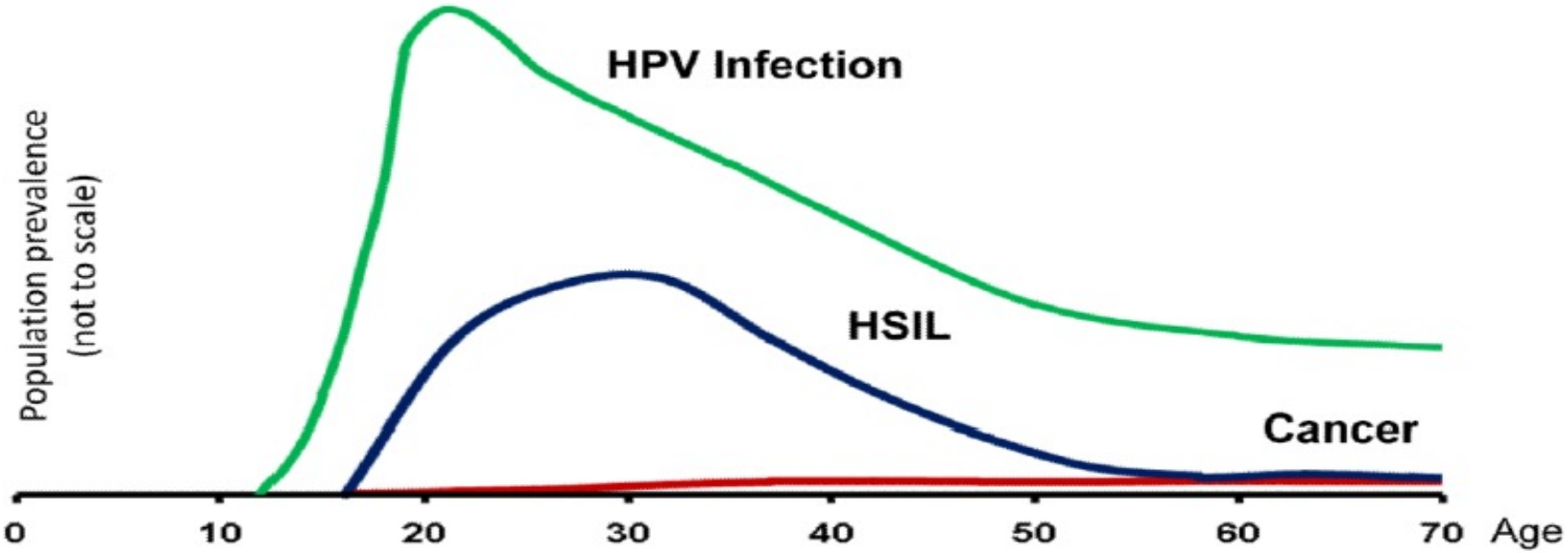


* HR-HPV types: 16, 18, 45, 31, 33, 52, 58, 35, 59, 56, 51, 39, 66 and 68

Schiffman & Wentzensen, CEBP 2013

TOOLS TO PREVENT CERVICAL CANCER

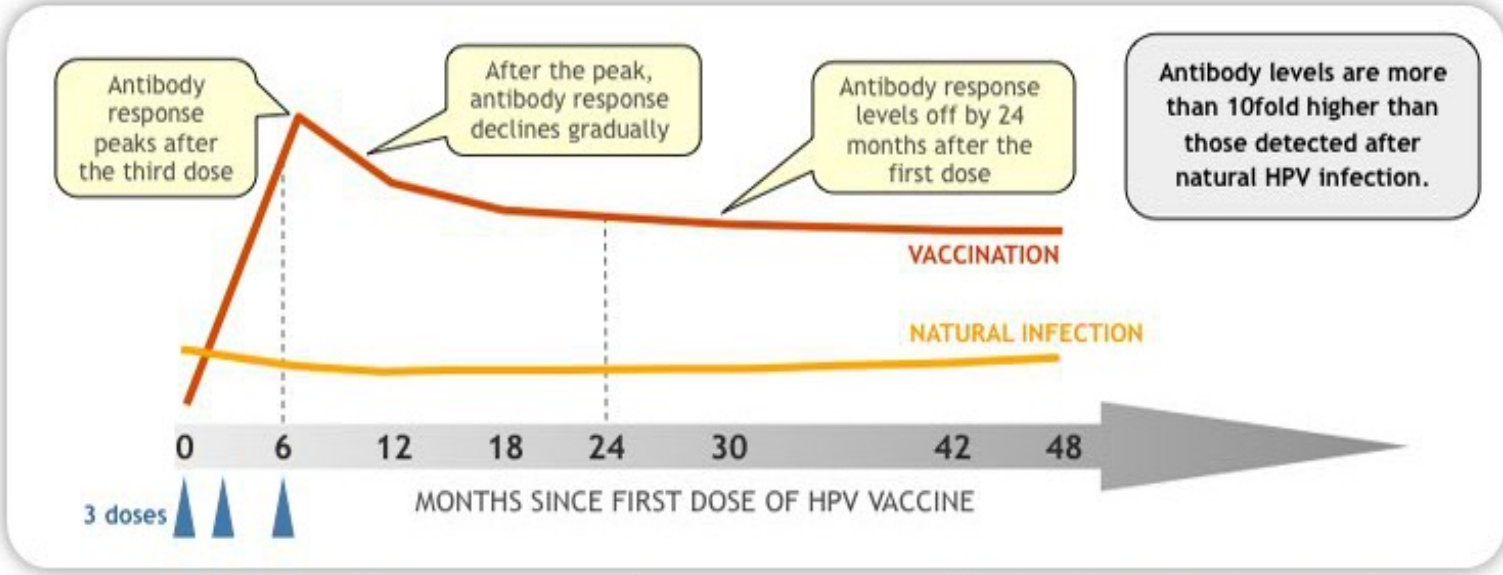




Primary Prevention: HPV vaccines

- Virus-like particle (VLP) vaccines
  - 2-valent: targets 16/18 (Cervarix and Cecolin)
  - 4-valent: targets 6/11 + 16/18 (Gardasil)
  - 9-valent: targets 6/11 + 16/18 + 31/33/52/58 & 45 (Gardasil-9)

- Prevent HPV acquisition, persistence and precancer development (*vaccines are prophylactic, NOT therapeutic*)
- Type specific protection
- Some cross protection



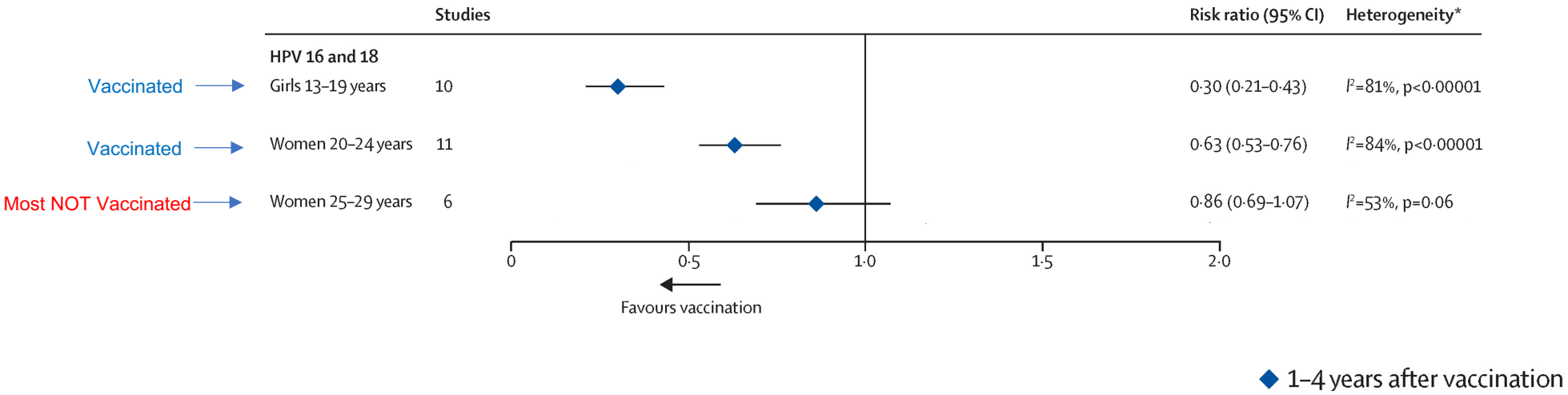
Vaccine effectiveness against HPV infection

Population-level impact and herd effects following the introduction of human papillomavirus vaccination programmes: updated systematic review and meta-analysis

Mélanie Drolet, Élodie Bénard, Norma Pérez, Marc Brisson, on behalf of the HPV Vaccination Impact Study Group

65 articles in 14 high income countries
60 million individuals
8 years post vaccination follow-up

Changes in the prevalence of HPV infections between pre-vaccination and post-vaccination periods



Drolet 2019 Lancet 394 (497-509)

HPV Vaccination and the Risk of Invasive Cervical Cancer

- Over **1.6 million girls and women aged 10 to 30** years from 2006 through 2017 in Sweden .
- 2012 - school-based HPV vaccination program for girls 10 to 12 years of age + free catch-up for girls and women 13-18y
- Population-based, organized cervical cancer screening program, every 3 to 7 years for women 23-64y

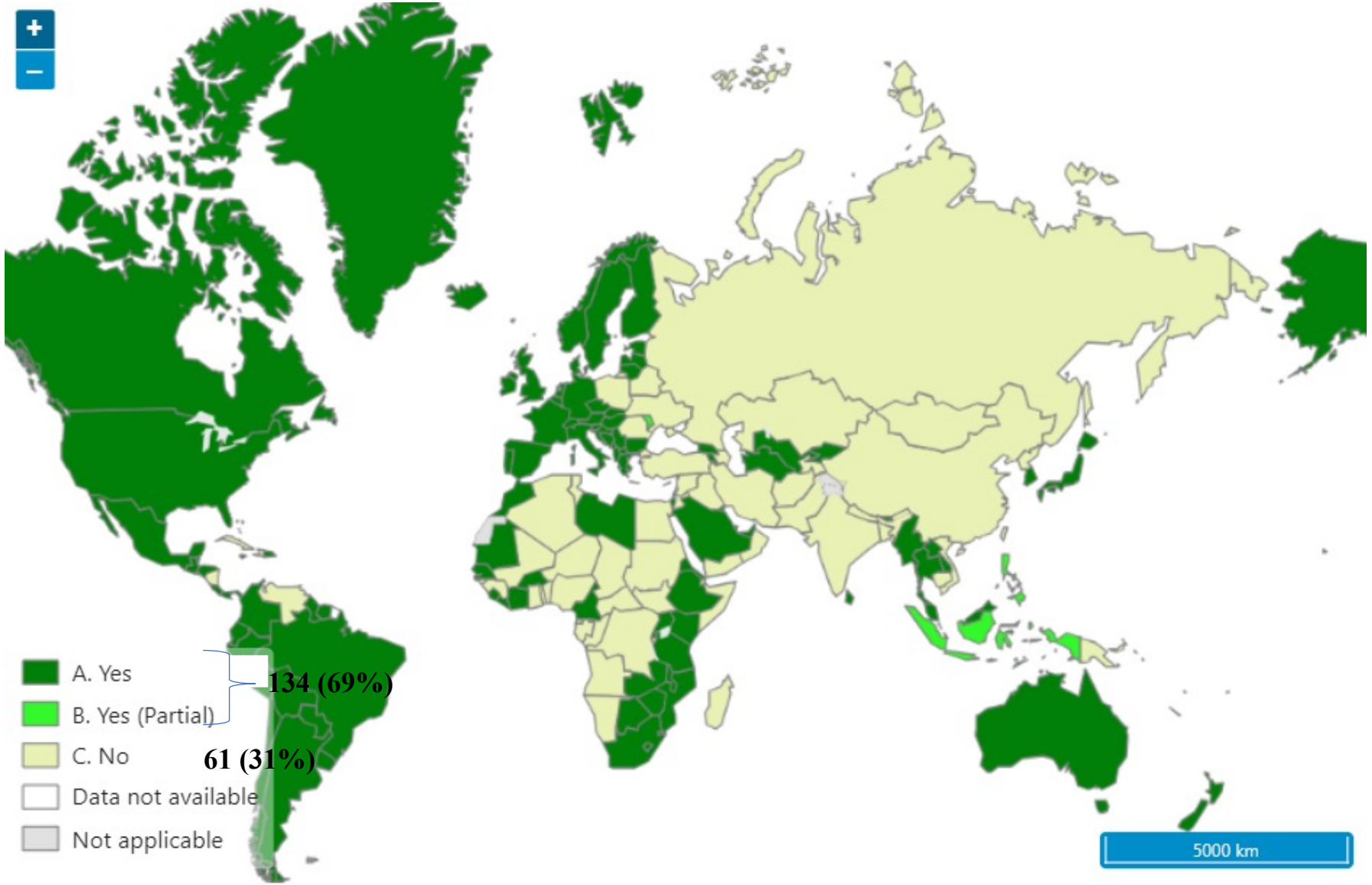
- **88% reduction in cervical cancer incidence** among women vaccinated <17 years

Table 2. HPV Vaccination and Invasive Cervical Cancer.

HPV Vaccination Status	No. of Cases of Cervical Cancer	Crude Incidence Rate per 100,000 Person-Yr (95% CI)	Age-Adjusted Incidence Rate Ratio (95% CI)	Adjusted Incidence Rate Ratio (95% CI)*
Unvaccinated	538	5.27 (4.84–5.73)	Reference	Reference
Vaccinated	19	0.73 (0.47–1.14)	0.51 (0.32–0.82)	0.37 (0.21–0.57)
Status according to age cutoff of 17 yr				
Vaccinated before age 17 yr	2	0.10 (0.02–0.39)	0.19 (0.05–0.75)	0.12 (0.00–0.34)
Vaccinated at age 17–30 yr	17	3.02 (1.88–4.86)	0.64 (0.39–1.04)	0.47 (0.27–0.75)

Lei J, Ploner A, N Engl J Med. 2020 Oct 1;383(14):1340-1348

HPV vaccination programmes worldwide



134 Countries have HPV vaccine in national programme

2030 Target: 194 countries

Date of slide: May. 2023
Map production: Immunization Vaccines Biologicals (IVB), World Health Organization
Data Source: WHO HPV vax Intro Dashboard

Power BI

HPV vaccine programme, by gender

- By 2019, **15% of girls 9-14 yrs and 4% of boys 9-14 yrs** were vaccinated with the full course of vaccine
  - **20% of girls and 5% of boys** received <u>at least one dose</u> of HPV vaccine

- Almost **one third** of the programs were “gender neutral” (GN)

  => both girls and boys receive the vaccine

- Mostly in high income settings vs. upper-middle-income countries

Cumulative number of countries that have introduced HPV vaccination by sex, year and income level.

Bruni et al, Preventive Medicine 144 (2021) 106399

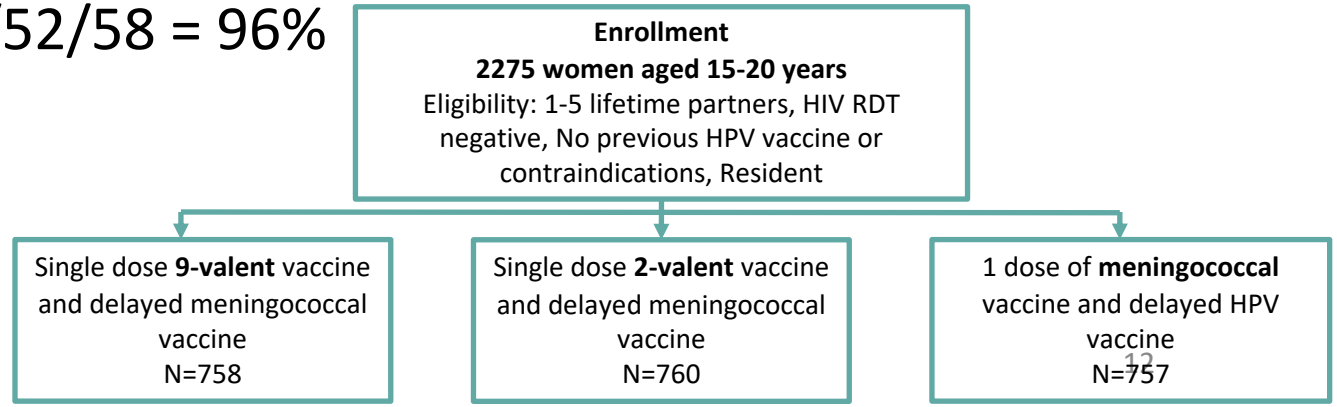
How to increase coverage?

- Multi-dose schedule expensive and complex to deliver, especially for LMIC

  => Reduce doses?

- Single dose could reduce costs of vaccine supply and delivery, increase access and sustainability of HPV vaccine programmes

- Observational studies - data suggest 1 dose could be enough
- KEN-SHE Individual randomized, double-blind, control, three group trial
- **Efficacy of 99% (nonavalent) and 98% (bivalent)** against persistent vaccine type specific HPV infection (HPV16/18) over 3 years ,
- Nonavalent VE for HPV 16/18/31/ 33/45/52/58 = 96%



Barnabas, **NEJM Evid 2022;1(5);** Barnabas, Nat Med 2023 Dec;29(12):3224

New WHO recommendations on HPV vaccine schedules can optimize vaccine coverage

Primary target : girls 9 to 14 years of age

2-dose schedule for all ages starting from 9 years old

Option: 1-dose schedule for 9 to 20-year-olds

Prioritize the vaccination of Immunocompromised/HIV+ populations – also at ages beyond primary target - with at least 2 doses, ideally 3

"Current evidence suggests that a single dose has comparable efficacy and duration of protection as a 2-dose schedule and may offer programme advantages, be more efficient and affordable, and contribute to improved coverage. From a public health perspective, the use of a single dose schedule can offer substantial benefits that outweigh the potential risk"

2022, 97, 645–672 No 50

World Health Organization
Organisation mondiale de la Santé

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

16 DECEMBER 2022, 97th YEAR / 16 DÉCEMBRE 2022, 97e ANNÉE
No 50, 2022, 97, 645–672
http://www.who.int/wer

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Human papillomavirus vaccines: WHO position paper (2022 update)

Introduction

In accordance with its mandate to provide normative guidance to Member States on health policy matters, WHO issues a series of regularly updated position papers[1] on vaccines and combinations of vaccines against diseases that have an international public health impact. These papers are concerned primarily with the use of vaccines in large-scale vaccination programmes.

The vaccine position papers are drafted by the WHO SAGE Secretariat; they summarize essential background information on diseases and vaccines and conclude with the current WHO position on the use of the vaccines worldwide. Before finalization, the position papers are reviewed by a large group of external subject-matter experts and end-users. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) and the evidence-to-recommendation tables are published alongside the position paper. The methods followed by SAGE[2] and the processes[3] for preparation of vaccine position papers are described on the WHO website. The position papers are intended for use by national public health officials and managers of immunization programmes. They may also be of interest to vaccine advisory groups, international funding agencies, health professionals,

Vaccins contre les papillomavirus humains: note de synthèse de l'OMS (mise à jour de 2022)

Introduction

Conformément à son mandat, qui prévoit qu'elle fournisse aux États Membres des orientations à caractère normatif en matière de politique sanitaire, l'OMS publie une série de notes de synthèse[1] régulièrement mises à jour sur les vaccins et les associations vaccinales contre les maladies ayant une incidence sur la santé publique internationale. Ces notes portent principalement sur l'utilisation des vaccins dans le cadre de programmes de vaccination à grande échelle.

Les notes de synthèse sur les vaccins sont rédigées par le secrétariat du SAGE de l'OMS; elles résument les informations essentielles sur les maladies et les vaccins associés et présentent en conclusion la position actuelle de l'OMS concernant l'utilisation de ces vaccins à l'échelle mondiale. Avant leur mise en forme définitive, elles sont examinées par un large groupe d'experts externes et d'utilisateurs finals. Les résultats de l'évaluation GRADE (Grading of Recommendations Assessment, Development and Evaluation) et les tableaux des données à l'appui des recommandations sont publiés en même temps que la note de synthèse. Les méthodes employées par le SAGE[2] et la procédure suivie[3] pour élaborer les notes de synthèse sur les vaccins sont décrites sur le site Web de l'OMS. Les notes de synthèse sont destinées aux responsables nationaux de la santé publique et aux administrateurs des programmes de vaccination, mais elles peuvent également présenter un intérêt pour les

[1] WHO vaccine position papers. Geneva: World Health Organization (www.who.int/teams/immunization-vaccines-and-biologicals/policies/position-papers, accessed August 2022).

[2] Guidance for the development of evidence-based vaccine-related recommendations. Geneva: World Health Organization; 2017 (www.who.int/publications/m/item/guidance-for-the-development-of-evidence-based-vaccine-related-recommendations, accessed August 2022).

[3] WHO position paper process. Geneva: World Health Organization; 2020 (www.who.int/publications/m/item/who-position-paper-process, accessed August 2022).

[1] WHO vaccine position papers. Genève: Organisation mondiale de la santé (www.who.int/teams/immunization-vaccines-and-biologicals/policies/position-papers, consulté en août 2022).

[2] Guidance for the development of evidence-based vaccine-related recommendations. Genève: Organisation mondiale de la santé; 2017 (www.who.int/publications/m/item/guidance-for-the-development-of-evidence-based-vaccine-related-recommendations, consulté en août 2022).

[3] WHO position paper process. Genève: Organisation mondiale de la santé; 2020 (www.who.int/publications/m/item/who-position-paper-process, consulté en août 2022).

645

Source: https://www.who.int/publications/i/item/who-wer9750-645-672

Secondary prevention: Screening

Diagnostic accuracy of screening for detection of cervical precancerous lesions (HSIL-CIN2+)

	General population (2-5% HSIL-CIN2+)		
	Sensitivity	**Specificity**	
Visual Inspection (VIA) [1]	**22-90%**	**49-98%**	"Screen and treat" Requires frequent training & supervision Improves treatment rates in WLHIV in South Africa
Cervical cytology (≥ASCUS) [2]	**73%**	**90%**	Observer-dependent++ Can be automated (LBC)
HPV-DNA (clinician collected)[2]	**90%**	**90%**	Single round halved rate of advanced cervical cancer (HR 0.47) and death from ICC (HR 0.52) compared to VIA and vs. cytology in Europe

HPV-DNA (PCR-based) similar accuracy using self-collected as clinican collected[4]
=> Potential for increased coverage in LMIC

[1]Arbyn et al (unpublished); [2]Koliopoulos et al, *Cochrane Database of Systematic Reviews* 2017, Issue 8. [4]*Arbyn et al, BMJ* 2018; 363

Summary Recommendations
WHO suggests using the following strategy for cervical cancer prevention

For the general population of women

Screen and Treat OR Screen, Triage and Treat

- HPV DNA as primary screening test
- Starting at age 30
- Every 5 to 10 years screening interval

For women living with HIV

Screen, Triage and Treat

- HPV DNA as primary screening test
- Starting at age 25
- Every 3 to 5 years screening interval

* Where HPV DNA testing is not yet operational, use a regular screening interval of every 3 years when using VIA or cytology as the primary screening test among WLHIV

When providing HPV DNA testing, WHO suggests using either provider or self-collected samples

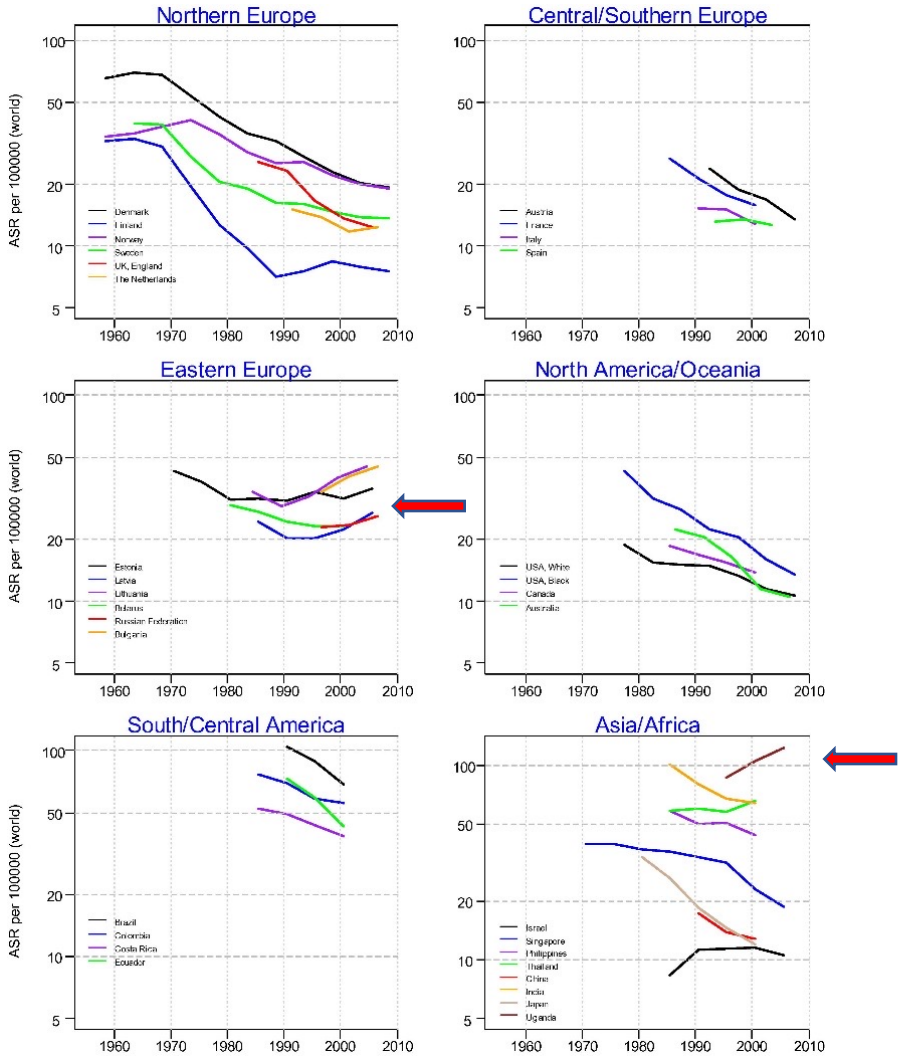
Impact of screening programmes on invasive cervical càncer over time

- Downward trends : Europe/North America, South America and Oceania, Asia

- Successful screening and treatment programmes
- HPV vaccination
- Changes in disease risk factors

- Increasing incidence rates Eastern European and Sub-Saharan Africa (Uganda)

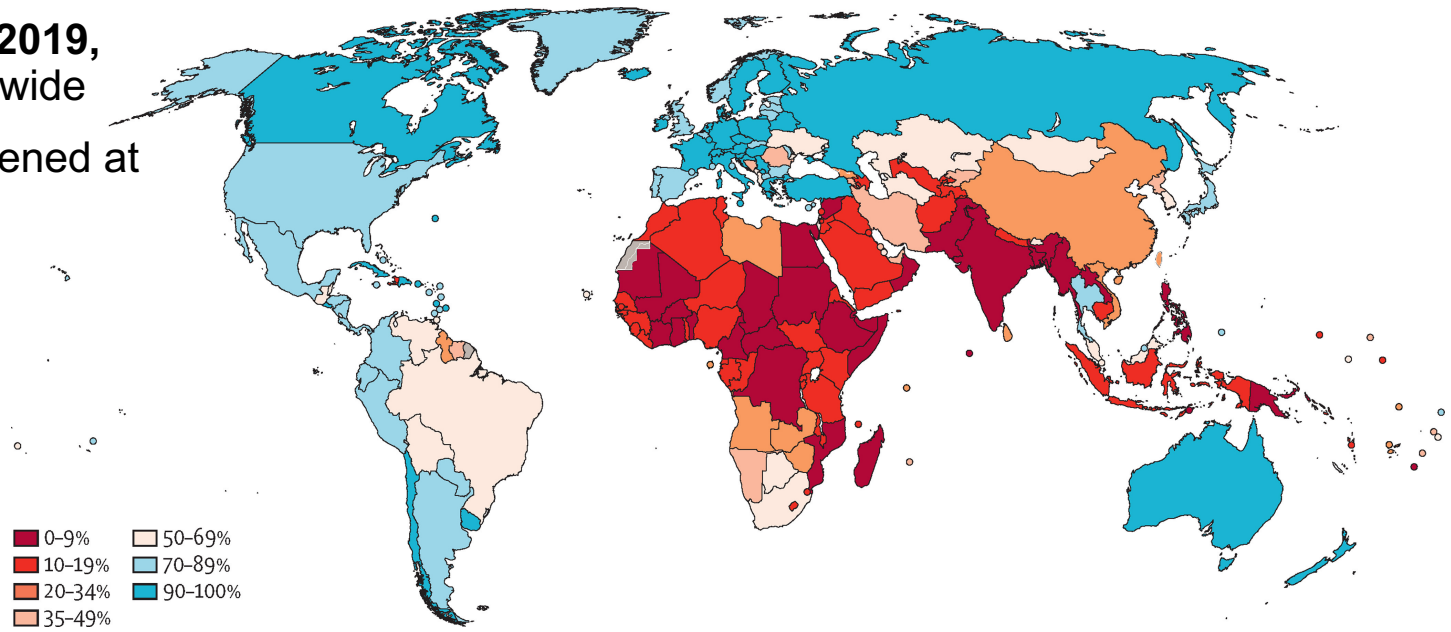
- Shorter duration and quality of screening programmes
- Changes in disease risk factors – increased exposure to HPV
- Impact of HIV (Africa)



Vaccerella 2013; European J Cancer. 49, 3262– 3273

Coverage of cervical cancer screening

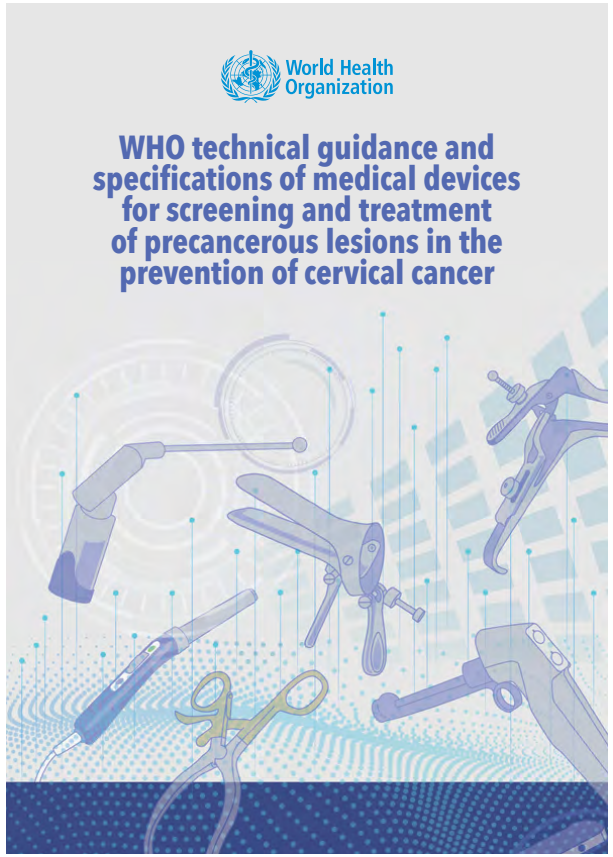
- Estimated cervical cancer screening coverage in **2019,** women **aged 30-49** years in **127 countries** worldwide
- **38%** of women aged 30-49 years have been screened at least once in their lifetime;
- **88%** in high-income settings
- **15%** in low-income countries

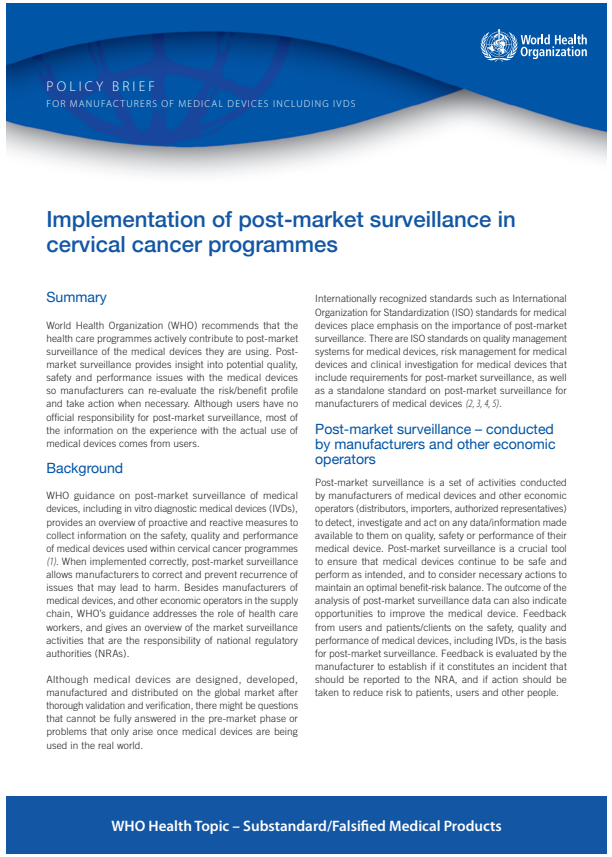


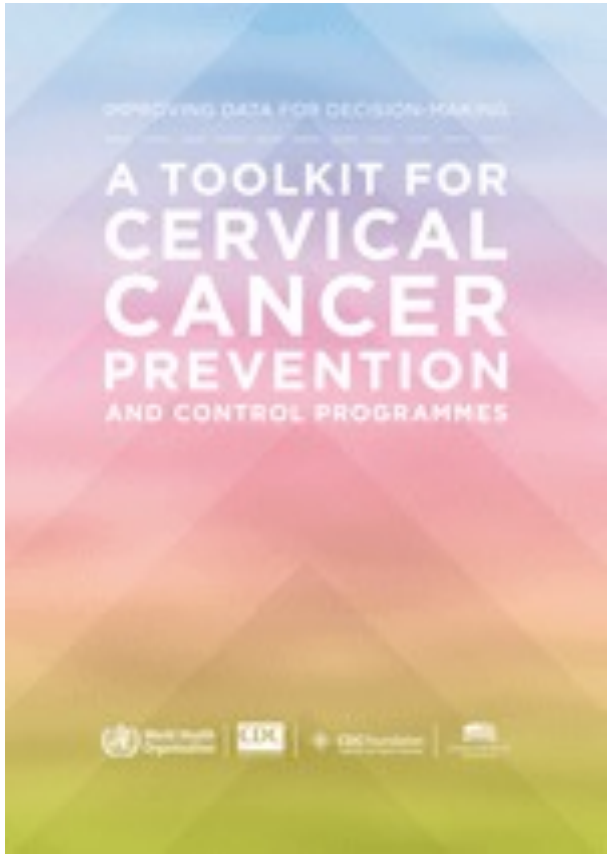
- **Cytology (95%) or HPV DNA test (45%)** most common in HIC
- **VIA (72%)** was the most used in LMIC

Bruni, 2022 Lancet Glob Health. 2022 Aug;10(8):e1115-e1127

WHO guidance to support the introduction and scale-up of screening and treatment guideline

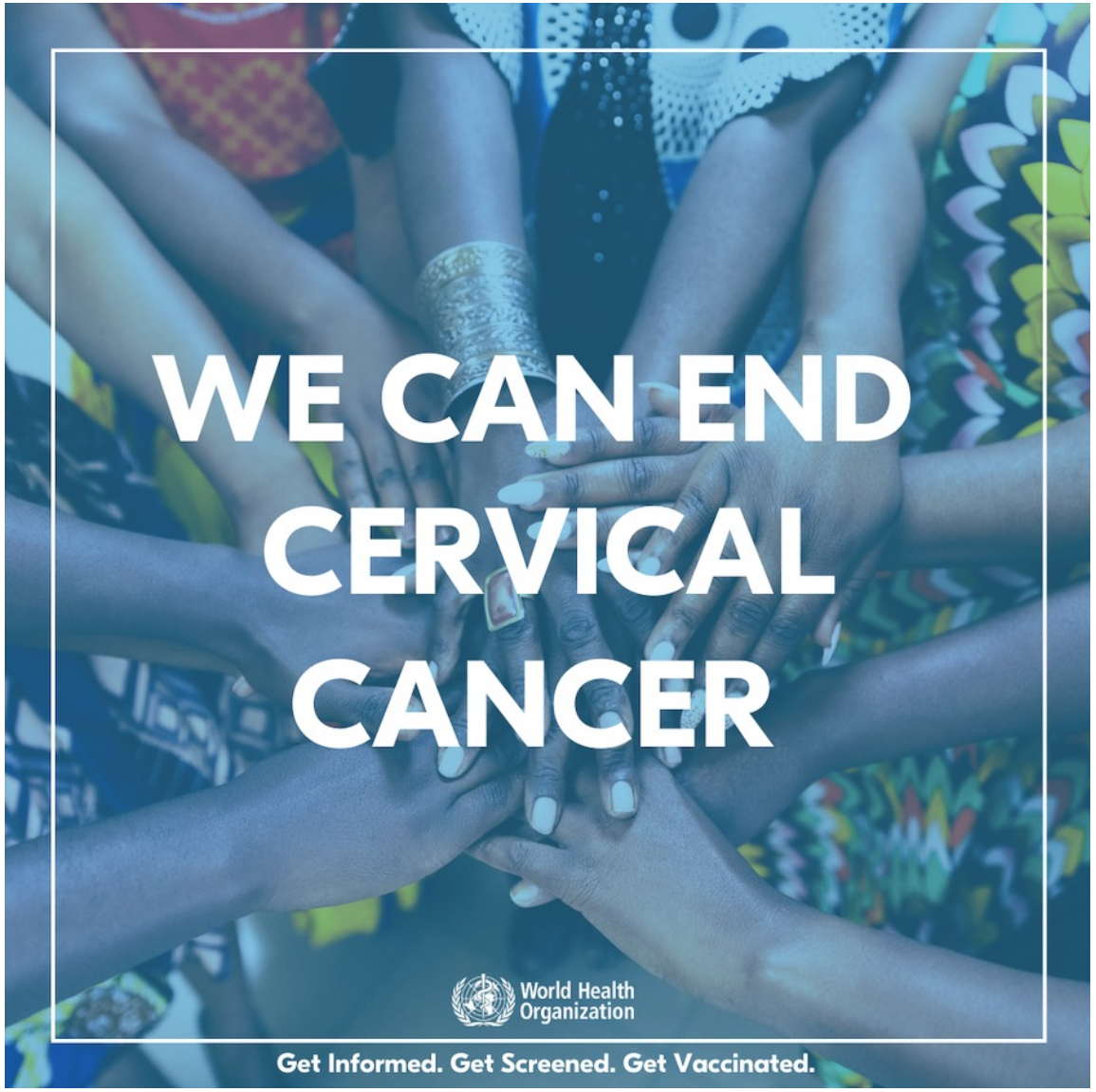






Focus Now: Policy & program implementation

- **Support ministries of health in adopting guidelines**
  - Increase country-level impact to reduce cervical cancer incidence and mortality across the 3 pillars (prevention, screening, treatment)
- **Bi-directional integration of HIV and cervical cancer services**
  - Improve service provision in settings with high HIV prevalence
  - Facilitate referrals between programs
- **Strengthen facility-based monitoring of cervical cancer screening & treatment**
- **Further strengthen links with the community**
  - Advocate for better counselling, patient education, availability of treatment and screening tests
  - Involve community of women and community of PLHIV in all aspects of programme development
- **Address knowledge gaps with living guidelines and implementation science**



Outline

1. Epidemiology of Human papillomavirus (HPV) & cervical cancer

2. Natural history of HPV & cervical cancer

3. Control and prevention
   - HPV vaccination
   - Screening for cervical cancer