Perspective of HPV in women

Deirdre Lyons

MRCOG, PgDip in Digital Healthcare Leadership

Imperial College Healthcare NHS Trust

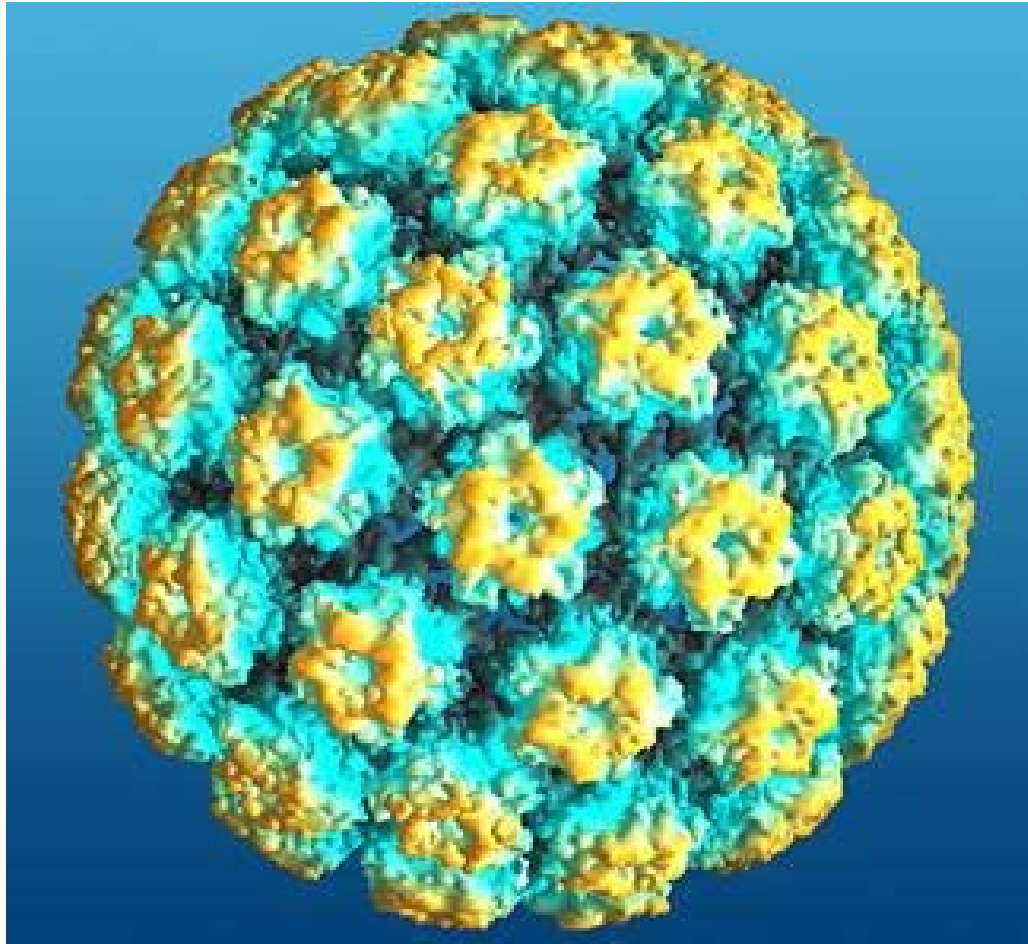President Elect British Society of Colposcopy and Cervical Pathology

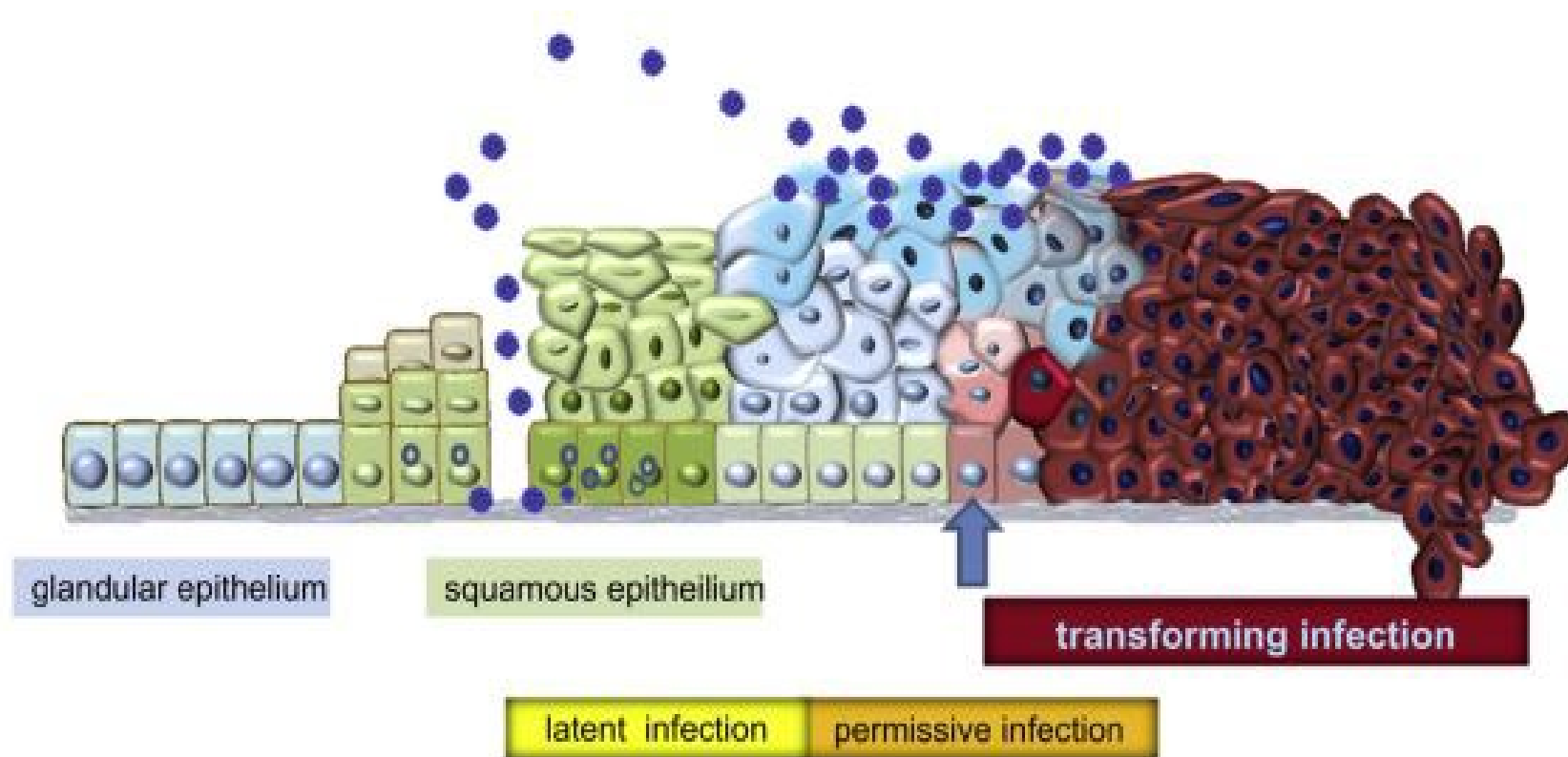# Conflict of Interest

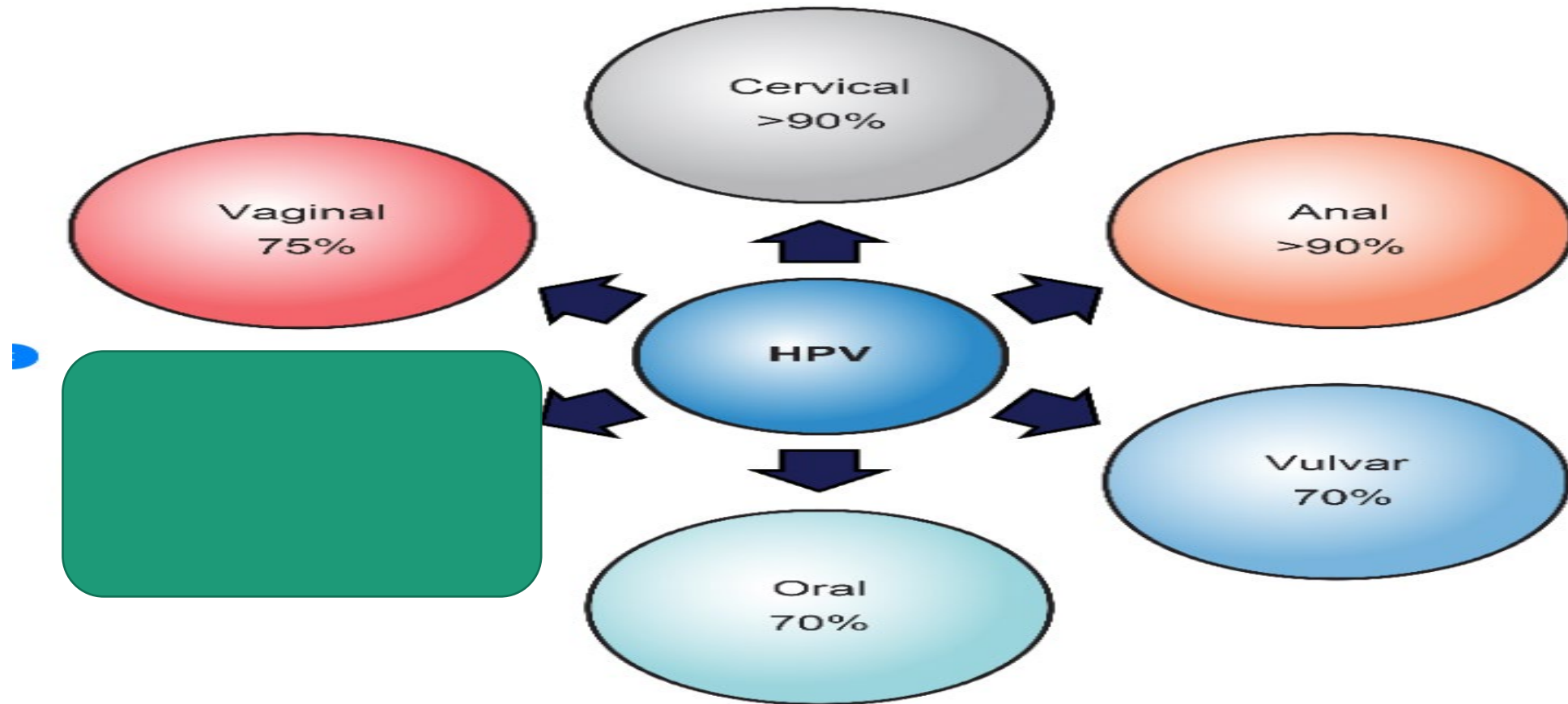I have no conflicts of interest

Perspective of HPV in women

HPV

https://www.thewellproject.org/hiv-information/human-papillomavirus-hpv

- HPV is a double stranded DNA virus from the *Papillomaviridae* family.

- **HPV infection causes up to 4.5% - 5.2% (640,000 cases) of all new cancer cases worldwide**

- HPV is a group of more than 200 related viruses, some of which are spread through 'close intimate' contact. HPV types affecting humans fall into two groups, low risk and high risk.

- Low-risk HPVs mostly cause no disease. However, a few low-risk HPV types can cause warts on or around the genitals, anus, mouth, or throat.

- High-risk HPVs can cause several types of cancer. There are about 14 high-risk HPV types including **HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68**. Two of these, **HPV16 and HPV18**, are responsible for most HPV-related cancers.

Perspective of HPV in women

glandular epithelium

squamous epitheilium

transforming infection

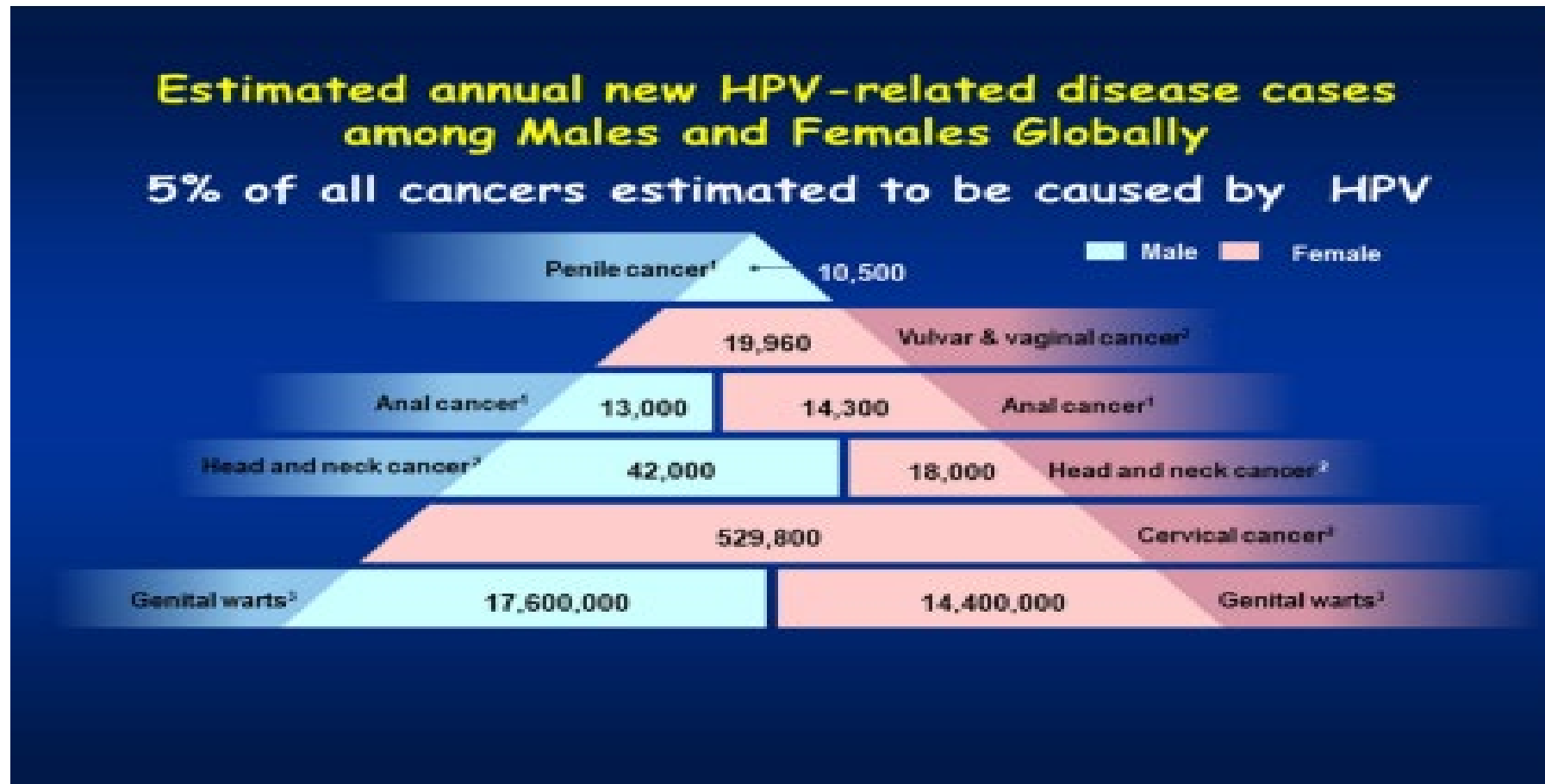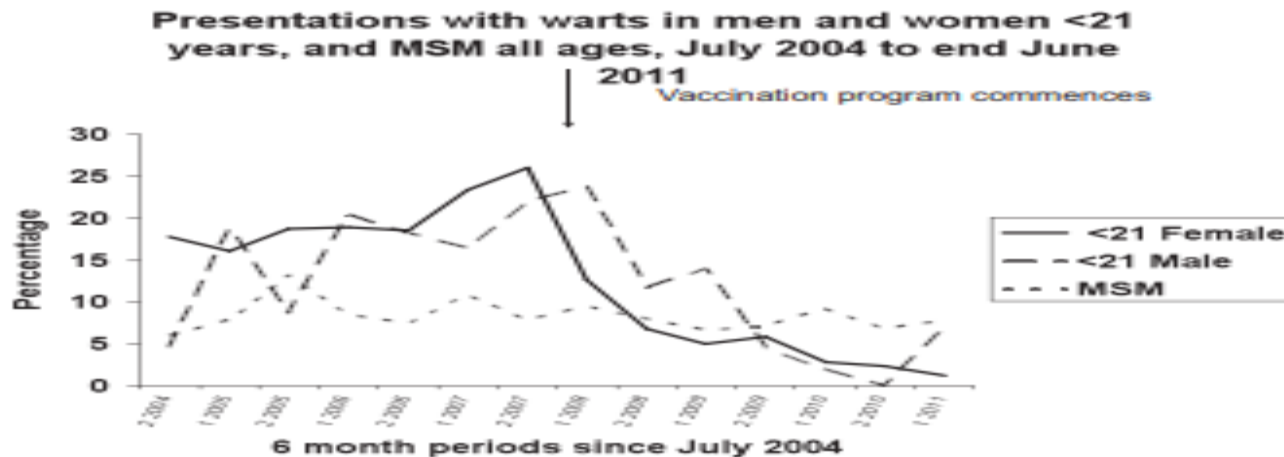latent infection permissive infection

Perspective of HPV in women

HPV-associated cancers. Types of cancer caused by HPV. The percentage of cancers caused by HPVs is from the United States data from the National Cancer Institute.

Perspective of HPV in women

Perspective of HPV in women

- **Genital Warts** - Australia post- HPV vaccine

- 2007/2008 and 2010/2011, GW declined in women < 21 years from 18.6% to 1.9%

- Heterosexual men under 21 years from 22.9% to 2.9%.

Presentations with warts in men and women <21 years, and MSM all ages, July 2004 to end June 2011

Vaccination program commences

Figure 1 Proportion of patients aged <21 years, diagnosed as having genital warts by risk group compared with MSM of all ages: MSM, men who have sex with men, men <21 years excluded MSM, and non-residents excluded.

Sex Transm Infect 2011;**87**:544—547. doi:10.1136/sextrans-2011-050234

Perspective of HPV in women

Figure 3. Changes in anogenital wart diagnoses between the pre-vaccination and post-vaccination periods (1-4, 5-8 years) in countries using the quadrivalent vaccine
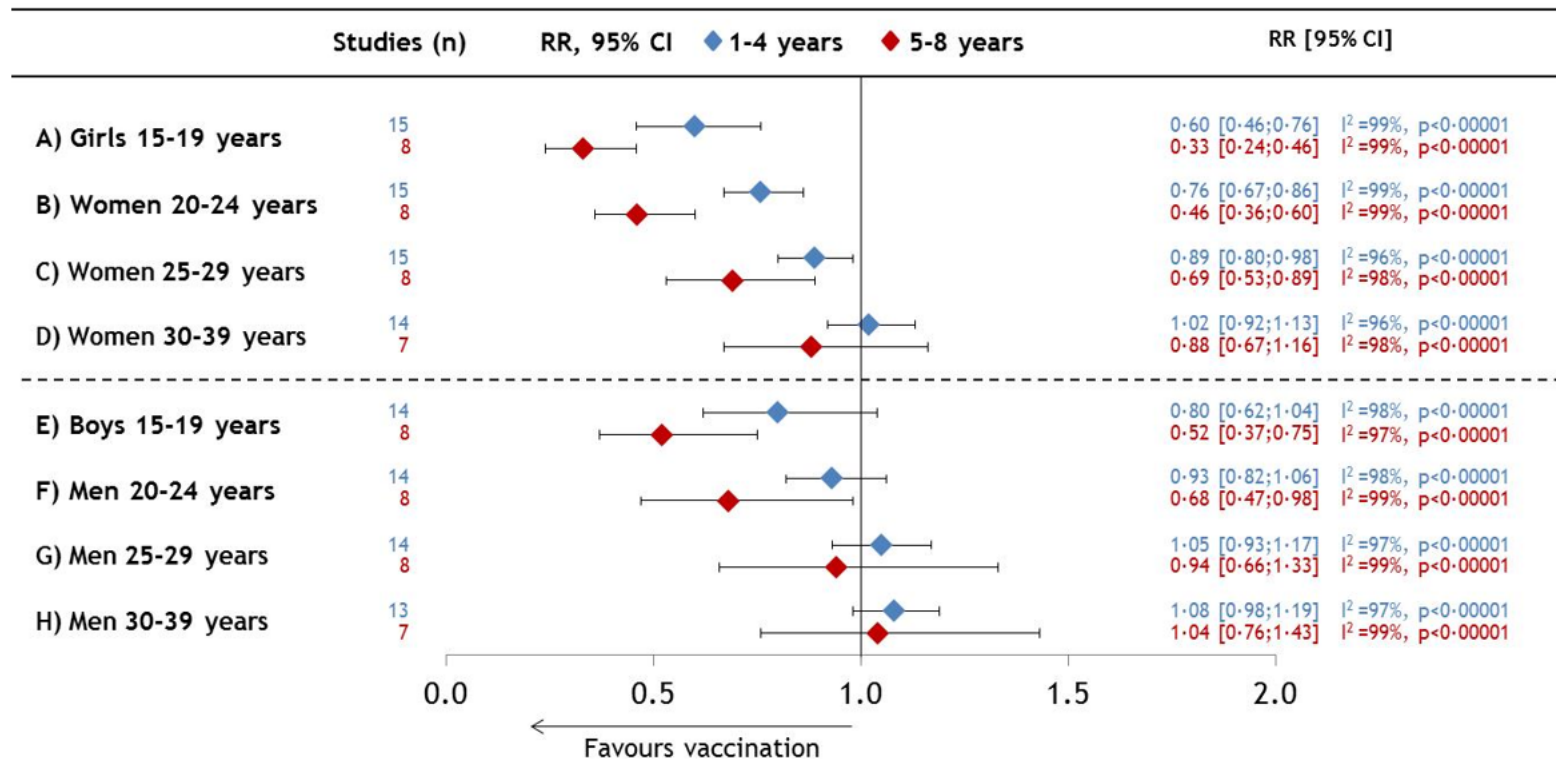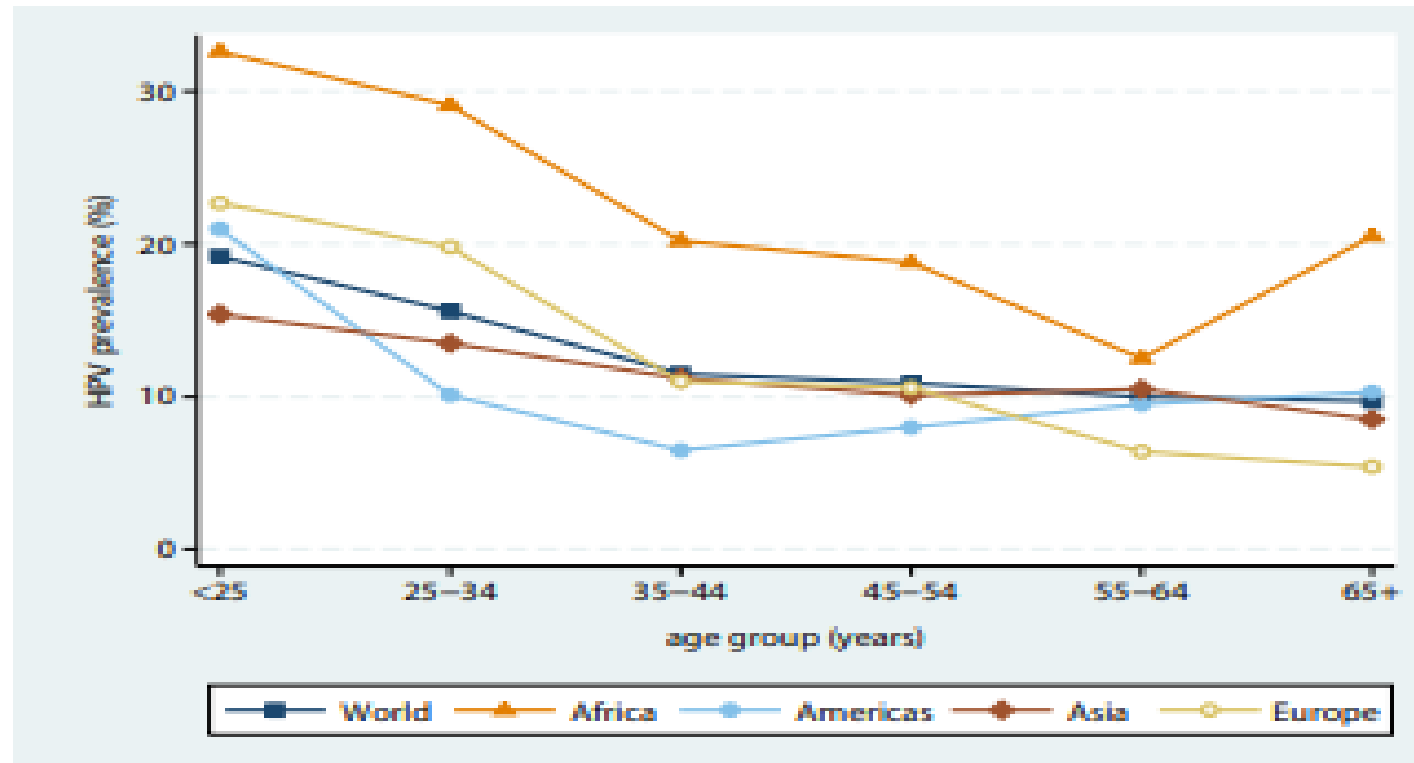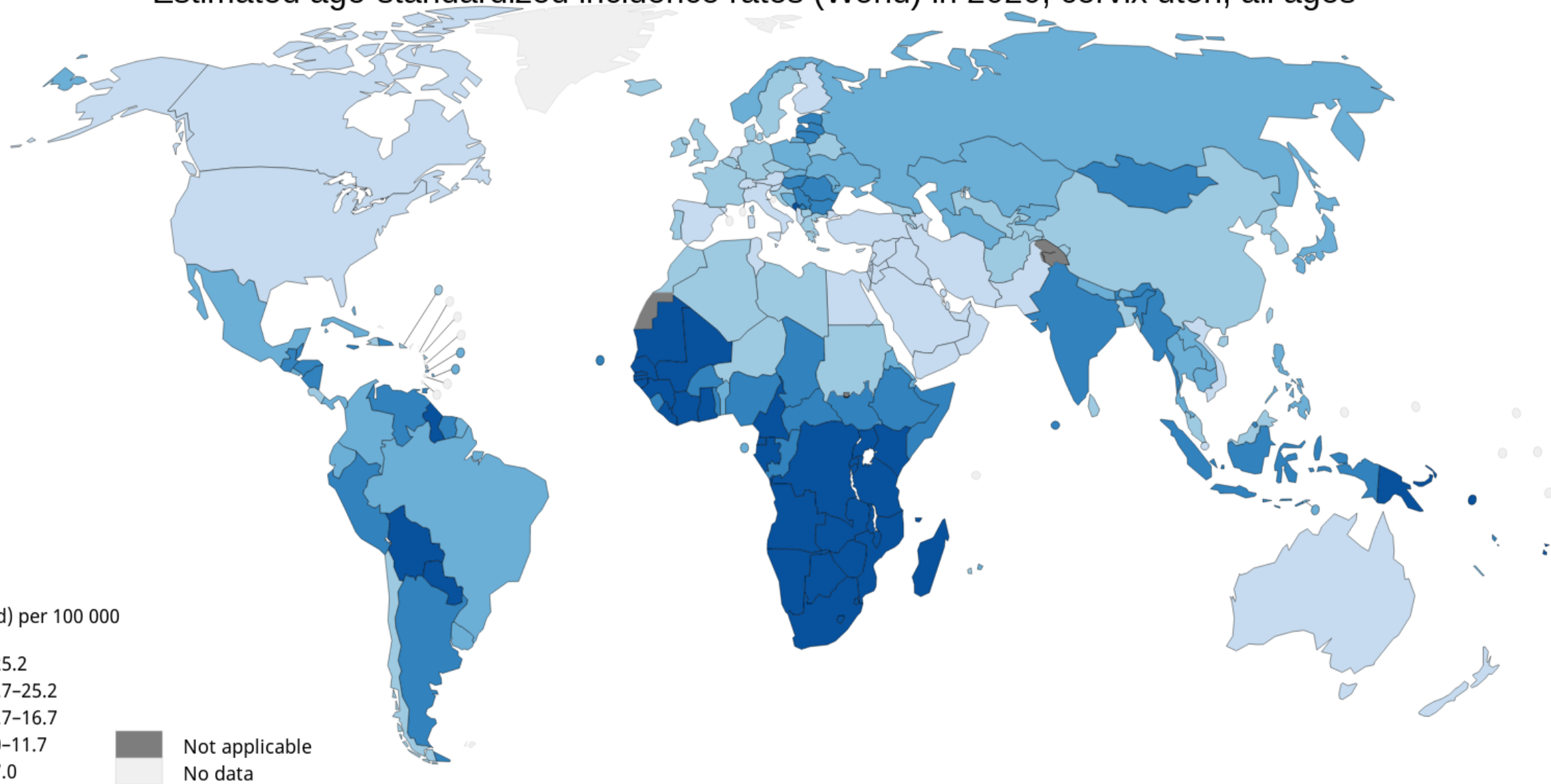
Perspective of HPV in women

. 1. Crude age-specific HPV prevalence (%) in women with normal cervical cytology in the world and its regions.

Estimated age-standardized incidence rates (World) in 2020, cervix uteri, all ages

ASR (World) per 100 000

- ≥ 25.2
- 16.7–25.2
- 11.7–16.7
- 7.0–11.7
- < 7.0

- Not applicable
- No data

Data source: GLOBOCAN 2020
Graph production: IARC
(http://gco.iarc.fr/today)
World Health Organization

World Health Organization

Estimated age-standardized mortality rates (World) in 2020, cervix uteri, all ages
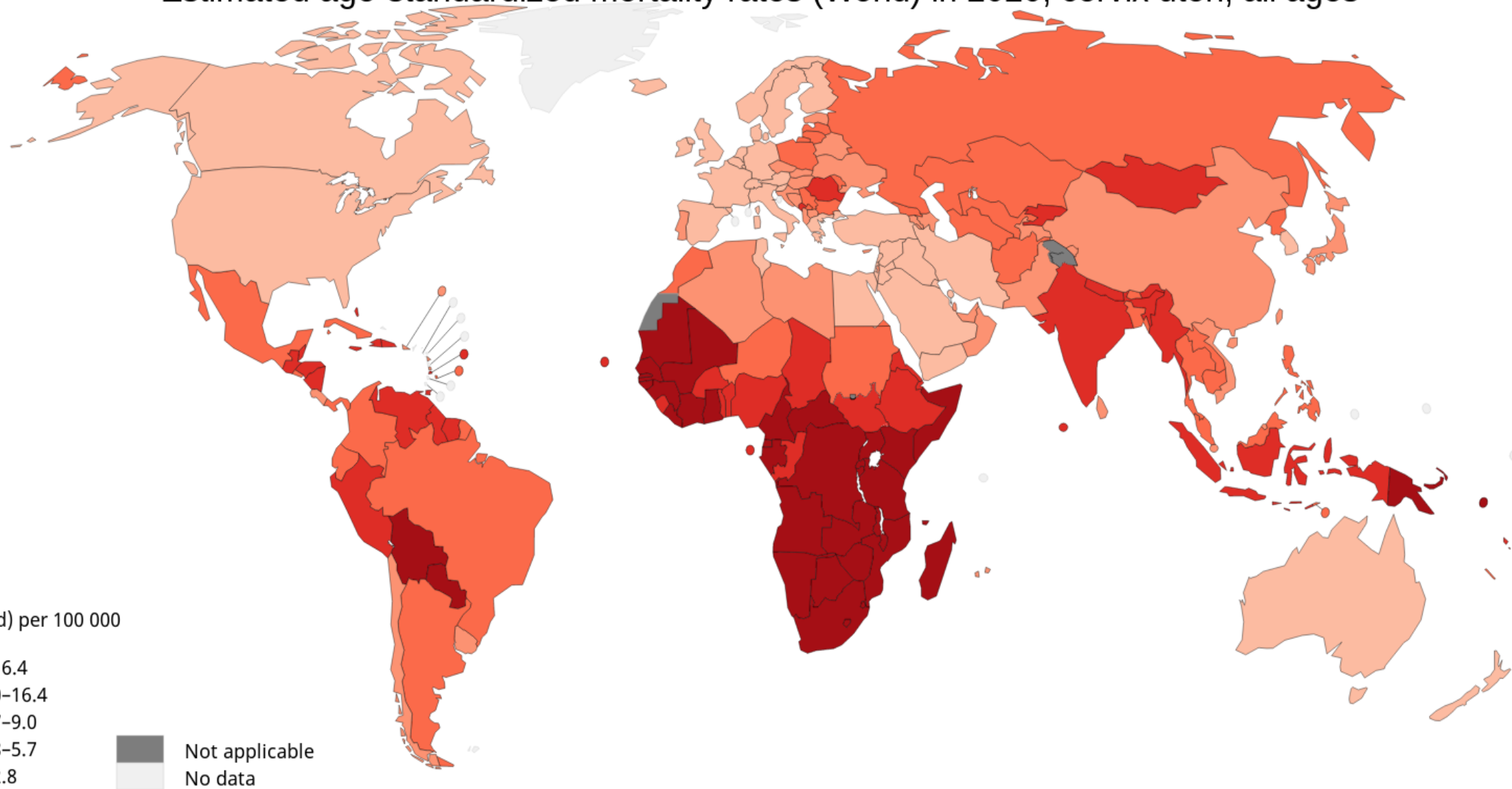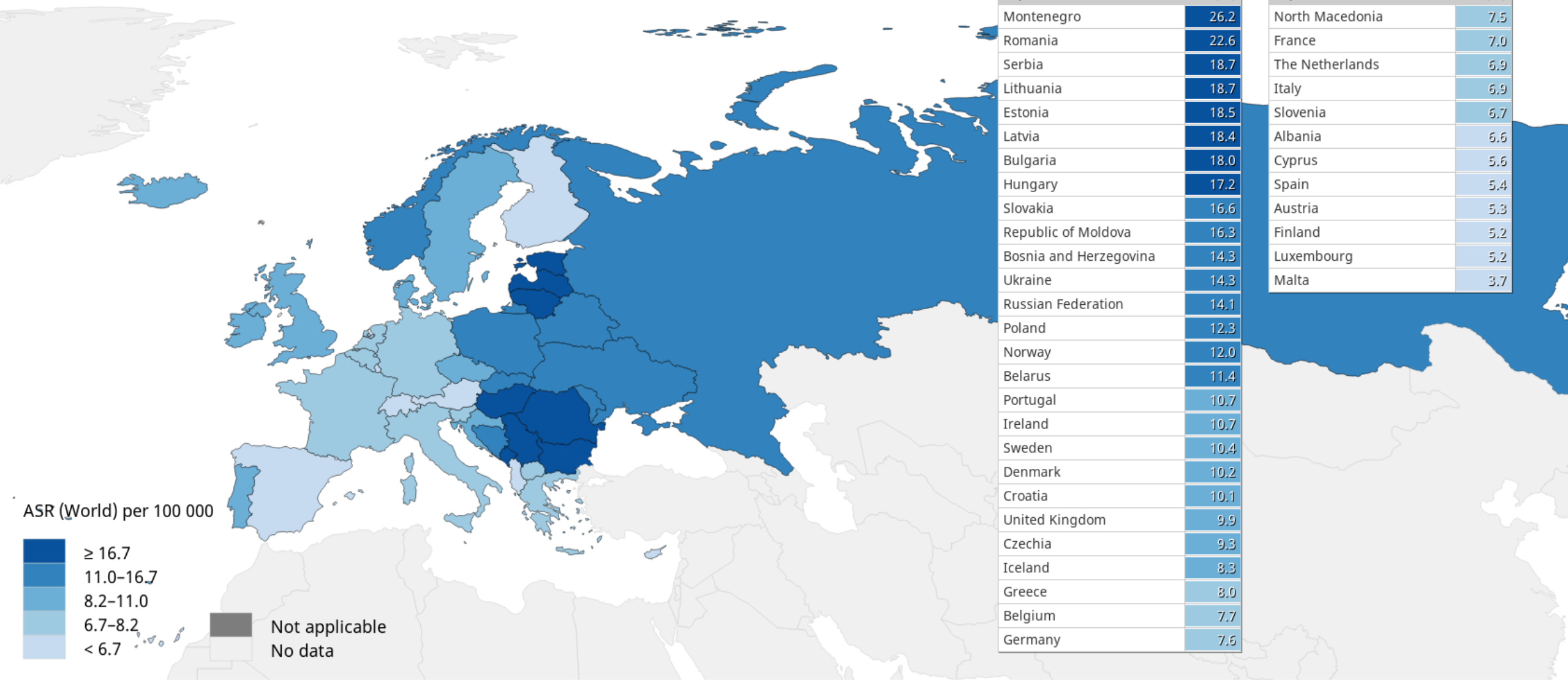
ASR (World) per 100 000

- ≥ 16.4
- 9.0–16.4
- 5.7–9.0
- 2.8–5.7
- < 2.8
- Not applicable
- No data

Data source: GLOBOCAN 2020
Graph production: IARC
(http://gco.iarc.fr/today)
World Health Organization

World Health Organization

Ranking (Cervix uteri), estimated number of new cases in 2020, ages 20-44

■ 1st (23)	
■ 2nd (93)	
■ 3rd (36)	
■ 4th (13)	
■ 5th (8)	
■ 6th - 10th (10)	■ Not applicable
■ >= 11th (2)	■ No data

World Health Organization

© International Agency for Research on Cancer 2021

Estimated age-standardized incidence rates (World) in 2020, cervix uteri, all ages,

Population	ASR(W)
Montenegro	26.2
Romania	22.6
Serbia	18.7
Lithuania	18.7
Estonia	18.5
Latvia	18.4
Bulgaria	18.0
Hungary	17.2
Slovakia	16.6
Republic of Moldova	16.3
Bosnia and Herzegovina	14.3
Ukraine	14.3
Russian Federation	14.1
Poland	12.3
Norway	12.0
Belarus	11.4
Portugal	10.7
Ireland	10.7
Sweden	10.4
Denmark	10.2
Croatia	10.1
United Kingdom	9.9
Czechia	9.3
Iceland	8.3
Greece	8.0
Belgium	7.7
Germany	7.6

Population	ASR(W)
North Macedonia	7.5
France	7.0
The Netherlands	6.9
Italy	6.9
Slovenia	6.7
Albania	6.6
Cyprus	5.6
Spain	5.4
Austria	5.3
Finland	5.2
Luxembourg	5.2
Malta	3.7

ASR (World) per 100 000

- ≥ 16.7
- 11.0–16.7
- 8.2–11.0
- 6.7–8.2
- < 6.7
- Not applicable
- No data

World Health Organization

© International Agency for Research on Cancer 2021

HPV contribution to cancer
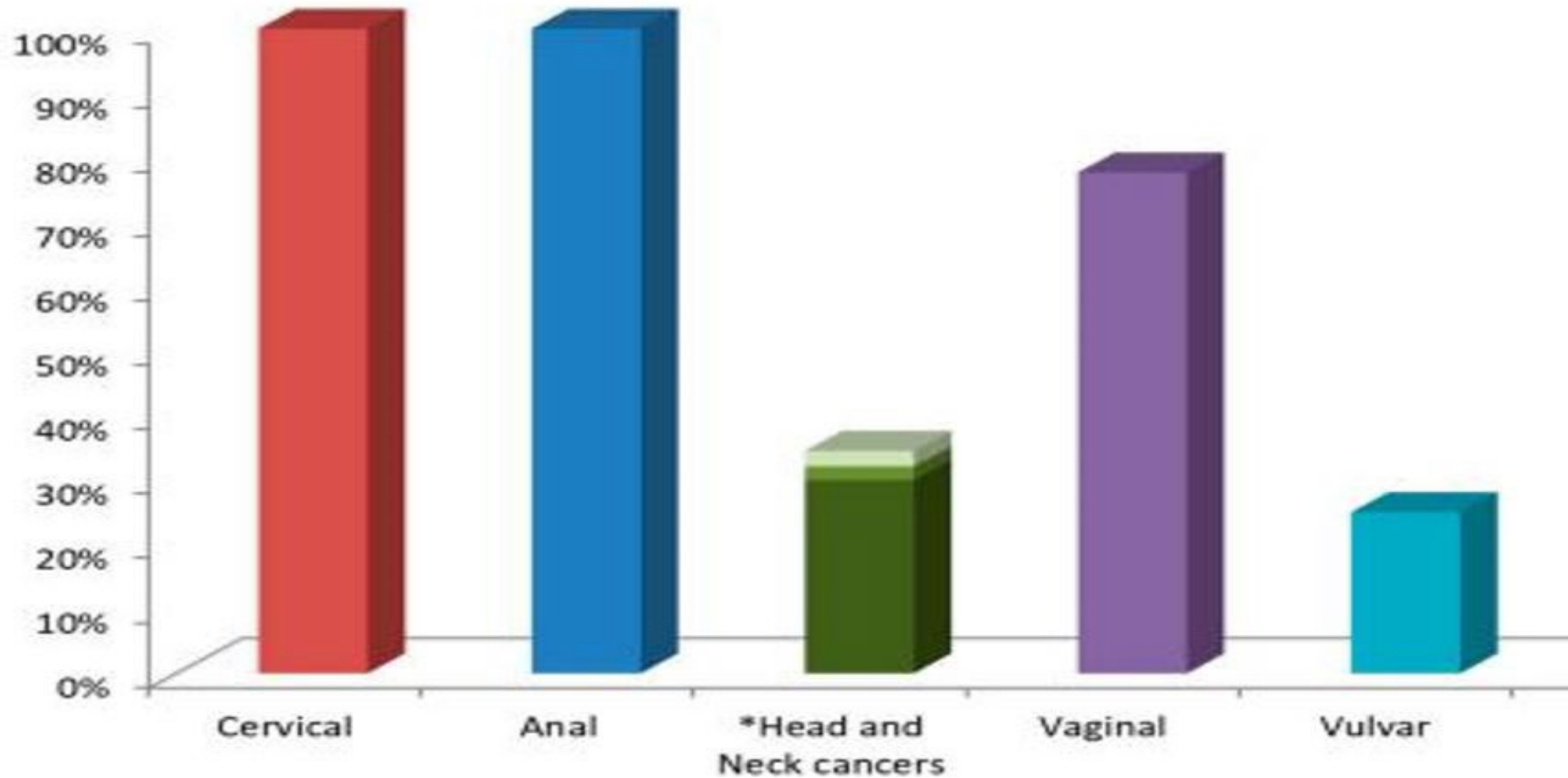
Perspective of HPV in women
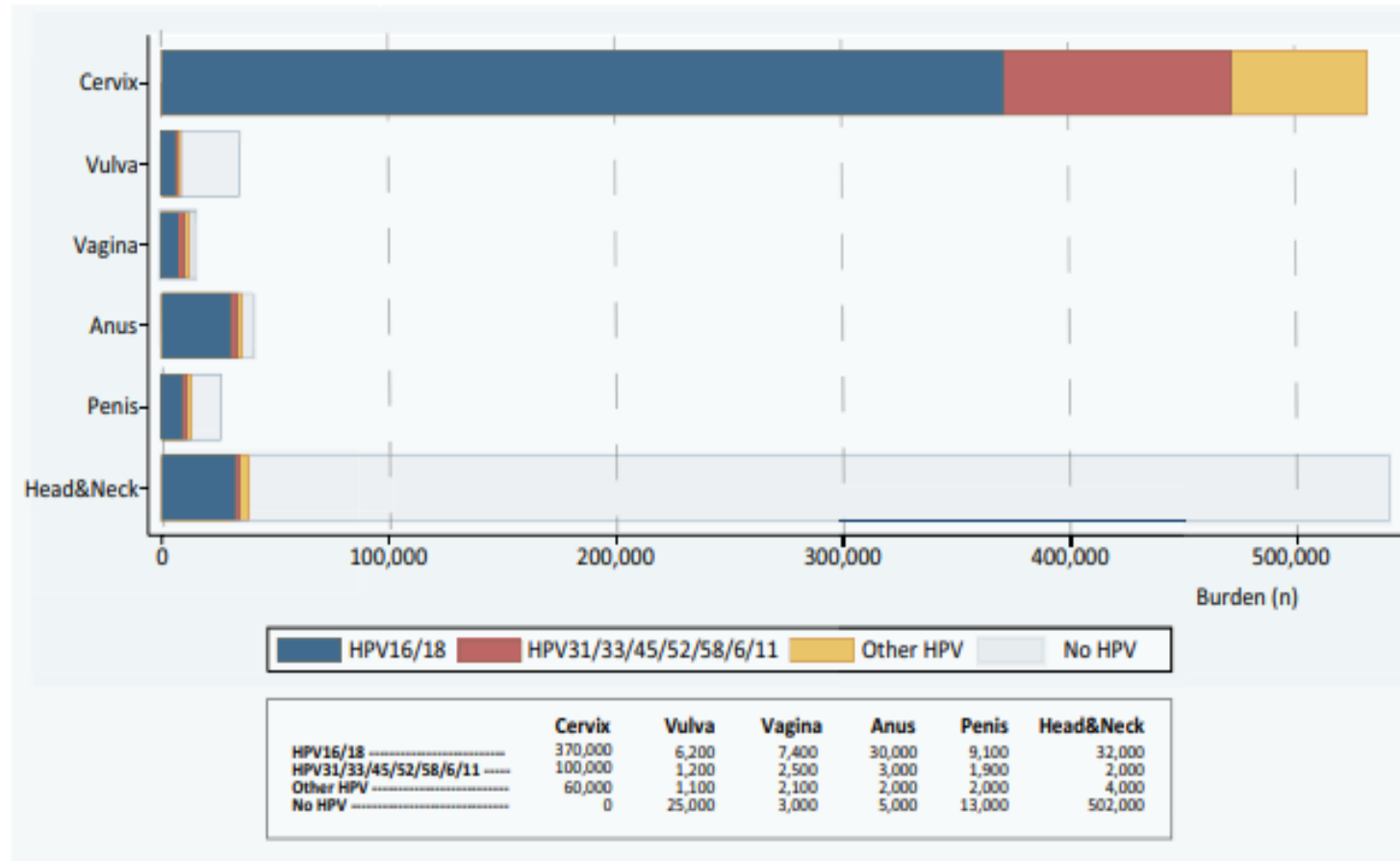
Fig. 4. Burden of HPV-related cancer cases attributable to HPV infection by cancer site and HPV vaccine. HPV: Human papillomavirus. Adapted from *de Martel et al., Int J Cancer 2017* [7].

Perspective of HPV in women

The life-course approach for cervical cancer prevention and control

Perspective of HPV in women

Khairkhah, N., Bolhassani, A.,Najafipour, R. Journal of Molecular Medicine (2022) 100:829–845. https://doi.org/10.1007/s00109-022-02199-y
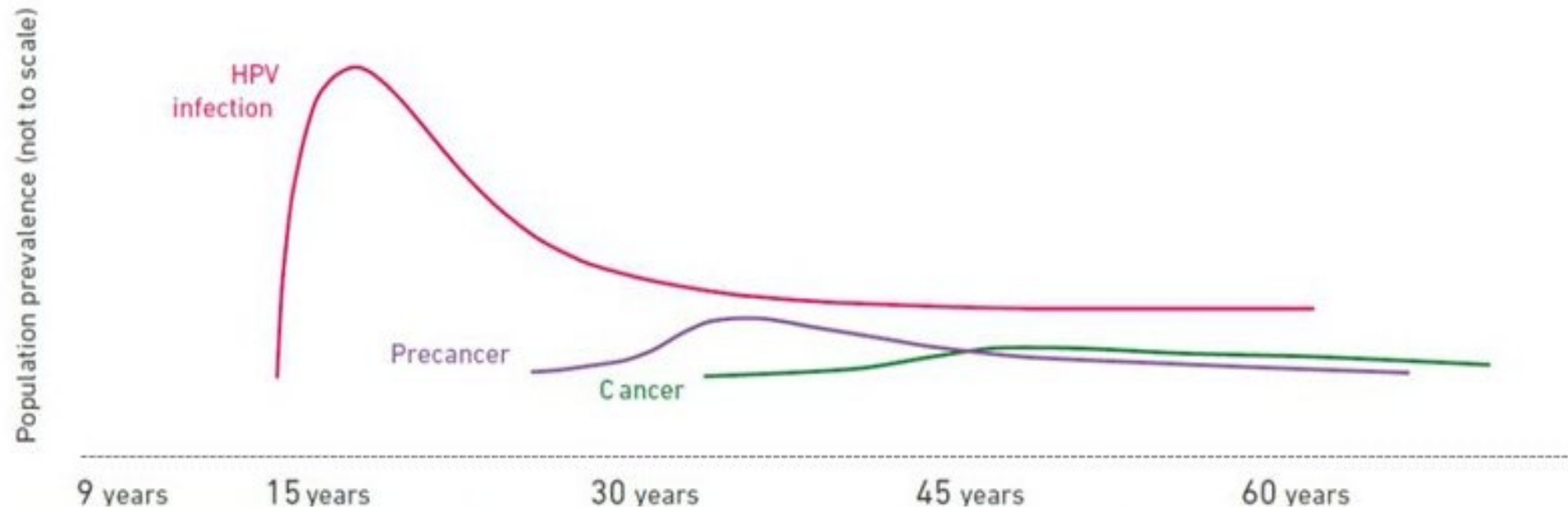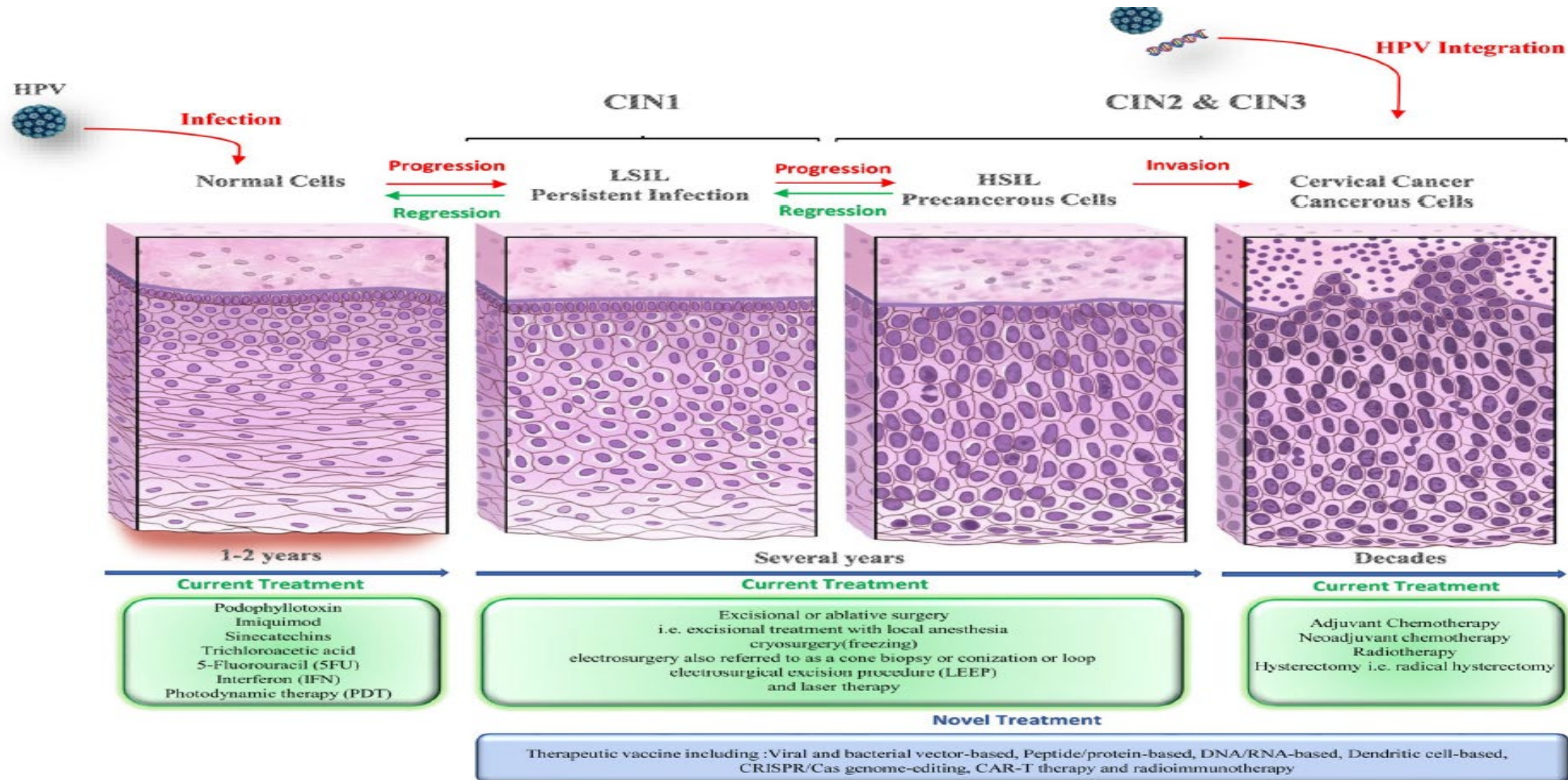
Perspective of HPV in women

- The anus and cervix share embryologic and anatomical characteristics
- They may respond similarly to malignant changes induced by persistent hrHPV infection
- Women with cervical HPV infection are 8 times more likely to have anal HPV infection and anal lesions
- 50% of women with anal HPV infection have cervical HPV infection.
- 80% of women with concurrent anal and cervical infections show genotype concordance.
- This finding is important for women with cervical HPV-16 or HPV-18 infections because these HPV types are also drivers of high-grade anal disease.

Vegunta et al. Screening Women for Anal Cancers: Guidance for Health Care Professionals. Am J Gastroenterol 2021;116:509–516. https://doi.org/10.14309/ajg.0000000000001186

Perspective of HPV in women

- CIN AND AIN
- Study by Sehnal et al[1] - : Concurrent anal and cervical HR HPV infection was found in nearly half of women with CIN 2+.
- The dominant genotype found in both anatomical locations was HPV 16

- Valari et al[2] - 235 women included
- HPV DNA, high-risk HPV DNA, high-risk mRNA was detected in 45%, 31% and 8% of the anal smears and in 56%, 39% and 25% of the cervical smears respectively. Concordance 74%.
- Logistic regression analysis revealed risk factors for the presence of anal HPV DNA (>3 lifetime sexual partners and presence of cervical hr HPV DNA and hr mRNA (presence of cervical hr mRNA).
- Twelve months after LLETZ 53% of women were cervical HPV negative, **but 25% of those were still HPV positive in the anus.**

[1]B. Sehnal et al. / Journal of Clinical Virology 59 (2014) 18–23
[2]O. Valari et al. / Gynecologic Oncology 122 (2011) 505–508

Perspective of HPV in women

Table 4. Different Grades of Lower Genital Tract Intraepithelial Lesion by Anal Lesion

Lower genital tract intraepithelial neoplasia, n = 481 (100%)	AIN Positive, n = 126 (26%) High grade, n = 28 (20.9%)	AIN Positive, n = 126 (26%) Low grade, n = 106 (79.1%)	p^a	Negative, n = 355 (74%)	p^b	OR (95% CI)
Cervical						
HSIL (CIN 2, 3)	7 (25)	13 (12.3)	0.121	94 (27.2)	0.039	1.91
LSIL (CIN 1)	6 (21.4)	29 (27.4)		86 (24.9)		(1.1–3.6)
Vaginal						
High-grade VAIN (VAIN 2, 3)	3 (10.7)	4 (3.7)	0.358	15 (4.2)	0.567	1.35
Low-grade VAIN (VAIN 1)	3 (10.7)	24 (22.4)		43 (12.1)		(0.5–3.7)
Vulvar						
VIN	10 (35.7)	8 (6.5)	<0.001	26 (7.3)	0.155	1.69
Condyloma	9 (32.1)	77 (72)		102 (28.7)		(0.8–3.4)
Perineal						
High-grade PEIN (PEIN 2, 3)	6 (21.4)	1 (0.9)	<0.001	7 (2)	0.107	2.69
Low-grade PEIN (PEIN 1)	3 (10.7)	32 (29.9)		13 (3.7)		(0.8–9.1)

Tatti et al. Anal Intraepithelial Lesions in Women With Human Papillomavirus Related Disease. Journal of Lower Genital Tract Disease, Volume 16, Number 4, 2012, 454 - 459
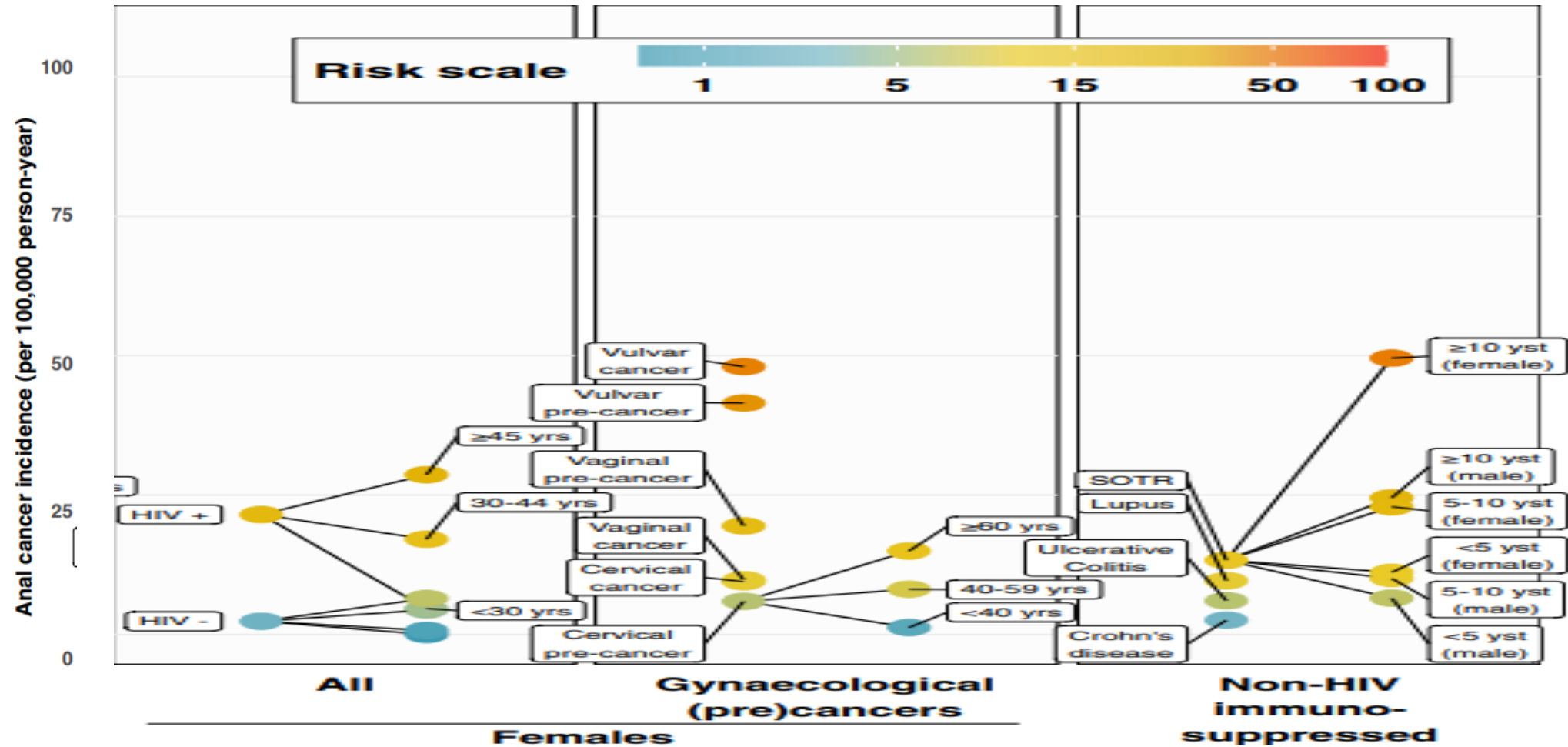
Perspective of HPV in women

- Women with high-grade cervical intraepithelial neoplasia (CIN 2, 3) had 2 times the odds of developing AIN compared with women with low-grade CIN (CIN 1) (odds ratio = 1.91, 95% CI = 1.1-3.6) [1]

- Anal cancer IRs were substantially higher for vulvar (reaching an IR close to 50), than for vaginal and cervical cancer (closer to 10) [2].

- HIV women – between 20- 30 per 100,000 (Age dependent)

- Anal cancer IRs were 10 (95% CI = 5-19), 6 (95% CI = 3-11) and 3 (95% CI = 2-4) for systemic lupus erythematosus, ulcerative colitis and Crohn's disease, respectively [2]

[1]. Tatti et al. Anal Intraepithelial Lesions in Women With Human Papillomavirus Related Disease. Journal of Lower Genital Tract Disease, Volume 16, Number 4, 2012, 454 - 459
[2]. Clifford et al. A meta-analysis of anal cancer incidence by risk group: Toward a unified anal cancer risk scale. Int. J. Cancer. 2021;148:38–47.

Perspective of HPV in women

Clifford et al. A meta-analysis of anal cancer incidence by risk group: Toward a unified anal cancer risk scale. Int. J. Cancer. 2021;148:38–47

Perspective of HPV in women

Table 1. Example patient populations and corresponding incidence rates of ASCC

Population	Approximate ASCC incidence per 100,000 persons
Human immunodeficiency virus–positive men who have sex with men	70–144
Women with VIN3+ (69)	35–44
Women with human immunodeficiency virus (55)	30
Women who receive a solid-organ transplant	20
Women with CIN3+ diagnosed at age <30 yr (Evans, 2003 #87)	15
Women in the general population	2

ASCC, anal squamous cell cancer; CIN3+, cervical intraepithelial neoplasia grade 3 or cancer; VIN3+, vulvar intraepithelial neoplasia grade 3 or cancer.

Vegunta et al. Screening Women for Anal Cancers: Guidance for Health Care Professionals. Am J Gastroenterol 2021;116:509–516.
https://doi.org/10.14309/ajg.0000000000001186

Perspective of HPV in women

Clinical relevance of HPV status in distinct anatomical locations.

Anatomic location	High-grade intraepithelial neoplasia	Cancer
Anus	Early detection in high-risk populations	Prognostic marker
Cervix	Early detection*	Early detection*
Penis	Unclear	Unclear, possibly prognostic marker
Vagina	Unclear	Unclear, possibly prognostic marker
Vulva	Unclear	Unclear, possibly prognostic marker
Oropharynx	No HPV-associated high-grade intraepithelial neoplasia known	Prognostic marker
Non-oropharynx head and neck	No HPV-associated high-grade intraepithelial neoplasia known	Unclear, possibly prognostic marker

* At the uterine cervix virtually all high-grade intraepithelial neoplasias (IN) and invasive cancers are causally attributable to HPV. Consequently, not the mere association with HPV but the stage of the infection (i.e. non-transforming vs. transforming) is diagnostically important in cervical IN (CIN). Similarly, the infection stage may be important in the diagnosis of high-grade IN at non-cervical sites.

Perspective of HPV in women

- **Anchor Study**
- 1822 women
- 860 HSIL
- 346 – Treatment arm
- 365 – Monitoring Arm
- 4 developed cancer
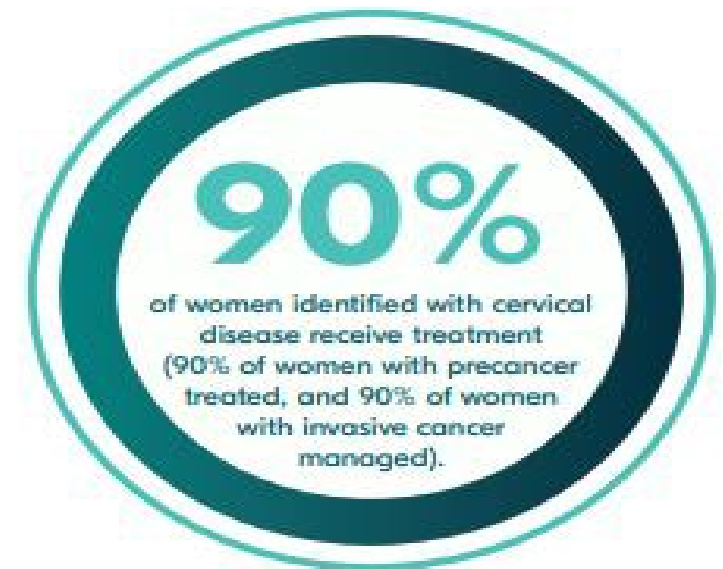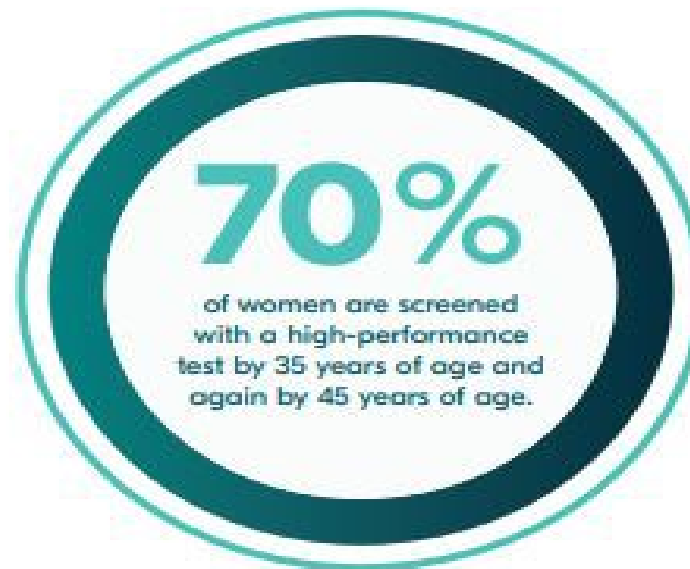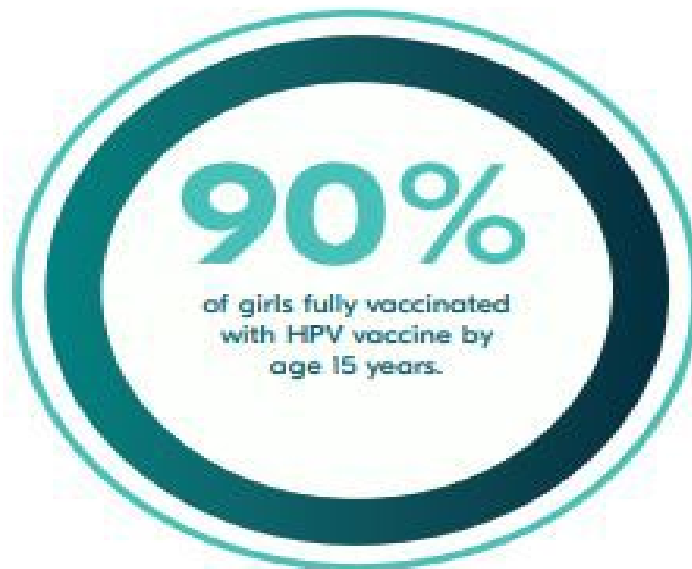- 707 – did not develop cancer
- Co-existent 'IN'

ANCHOR STUDY OUTCOMES

Figure 2. Kaplan–Meier Curve of the Time to Progression to Anal Cancer.
The inset shows the data on an expanded y axis. The shaded areas represent 95% confidence intervals.
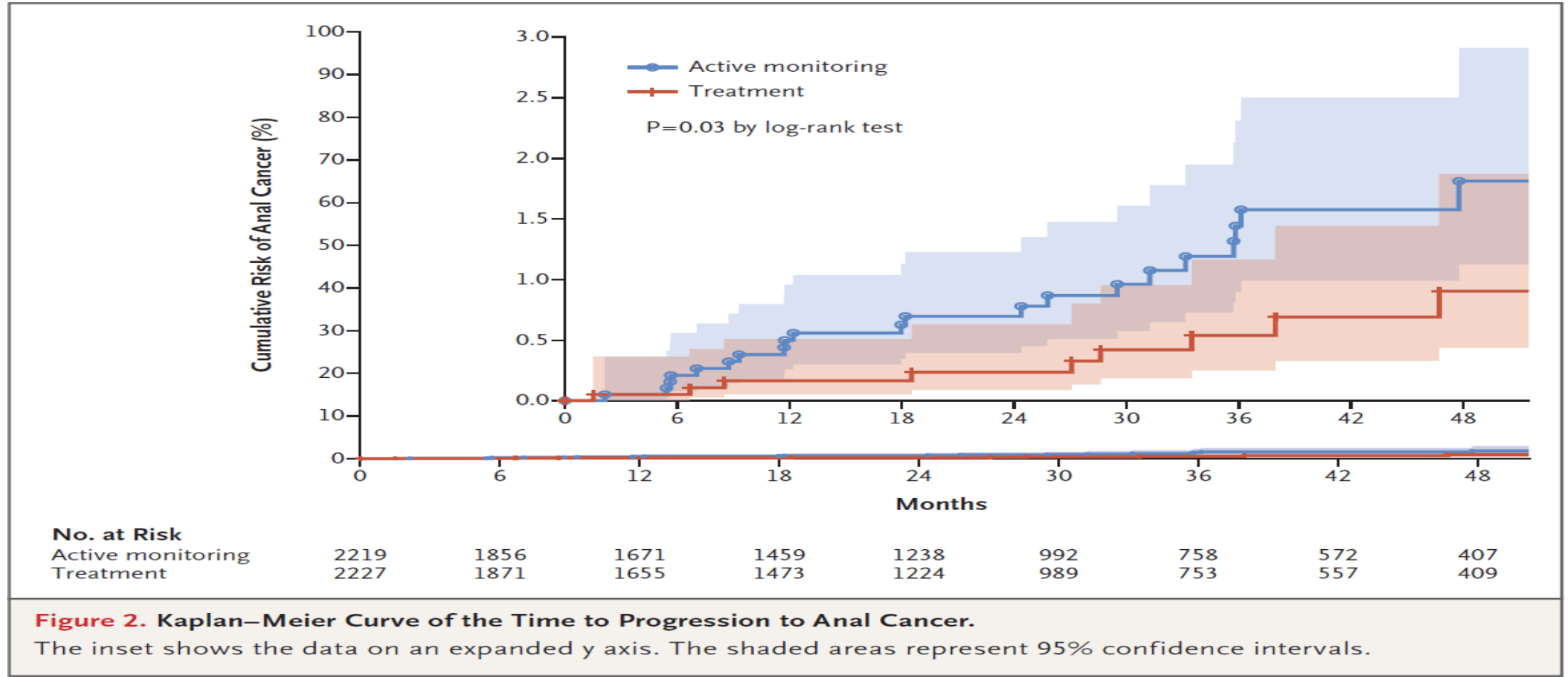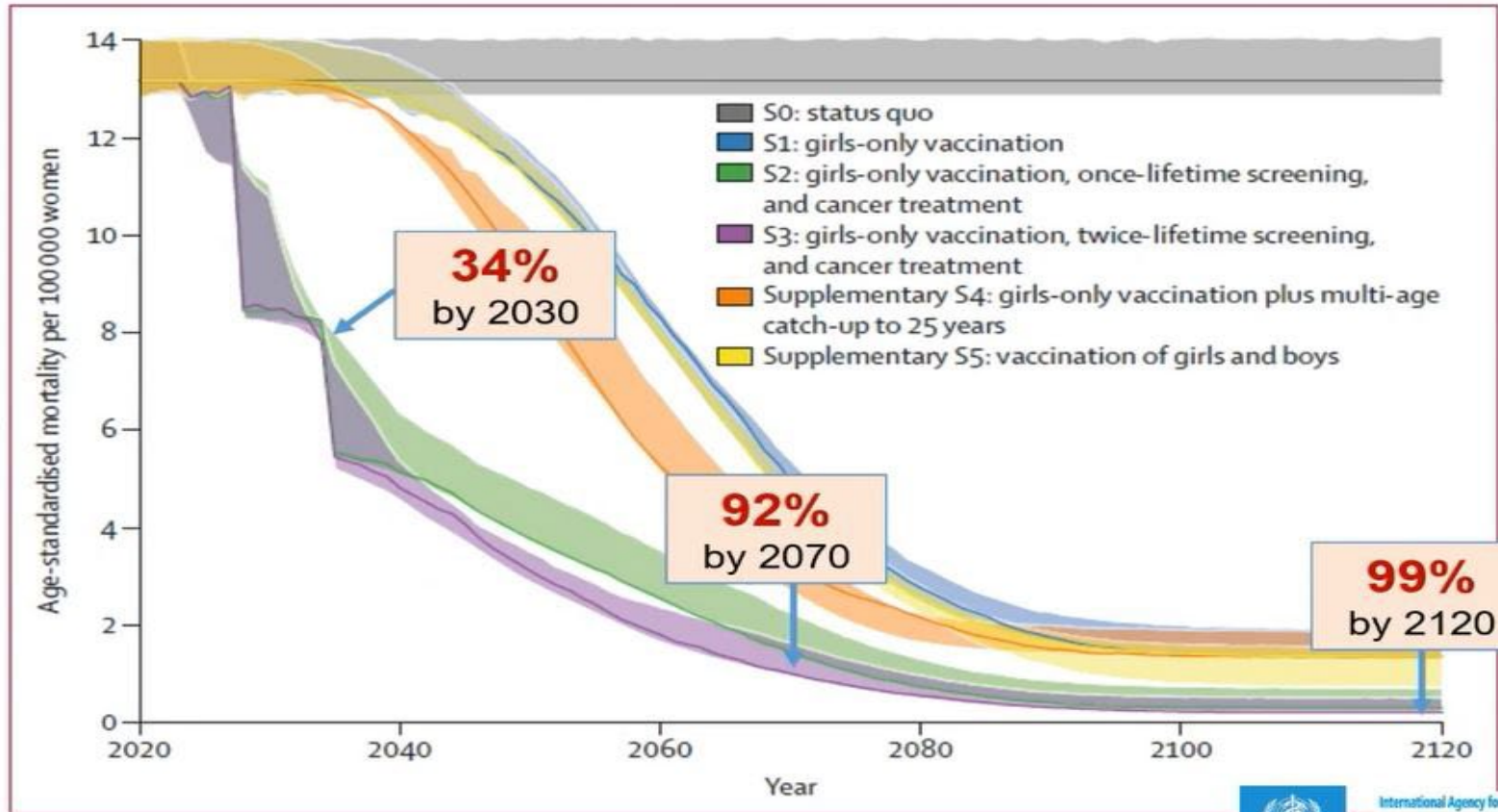
Perspective of HPV in women

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:

90% of girls fully vaccinated with HPV vaccine by age 15 years.

70% of women are screened with a high-performance test by 35 years of age and again by 45 years of age.

90% of women identified with cervical disease receive treatment (90% of women with precancer treated, and 90% of women with invasive cancer managed).

Global strategy to accelerate the elimination of cervical cancer as a public health problem : WHO 2020

Perspective of HPV in women

Canfell K/Kim JJ/Brisson M et al., Lancet Jan 30 2020

Perspective of HPV in women

- What can we do to decrease risk of anal SCC in women
- Identify women at higher risk of anal carcinoma
- 'Screen' high risk women for AIN/ SCC
- Improve availability of anal screening
- Suitable test for AIN
- Improve HRA access
- Formal training in HRA – Diagnostic and Treatment
- Formal training in multizonal disease?
- HPV Vaccination

Perspective of HPV in women

- Thank you for your attention