

RISK FACTORS AND PREVENTION OF CERVICAL CANCER



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- CONFLICT OF INTEREST : NONE



DISCLAIMER

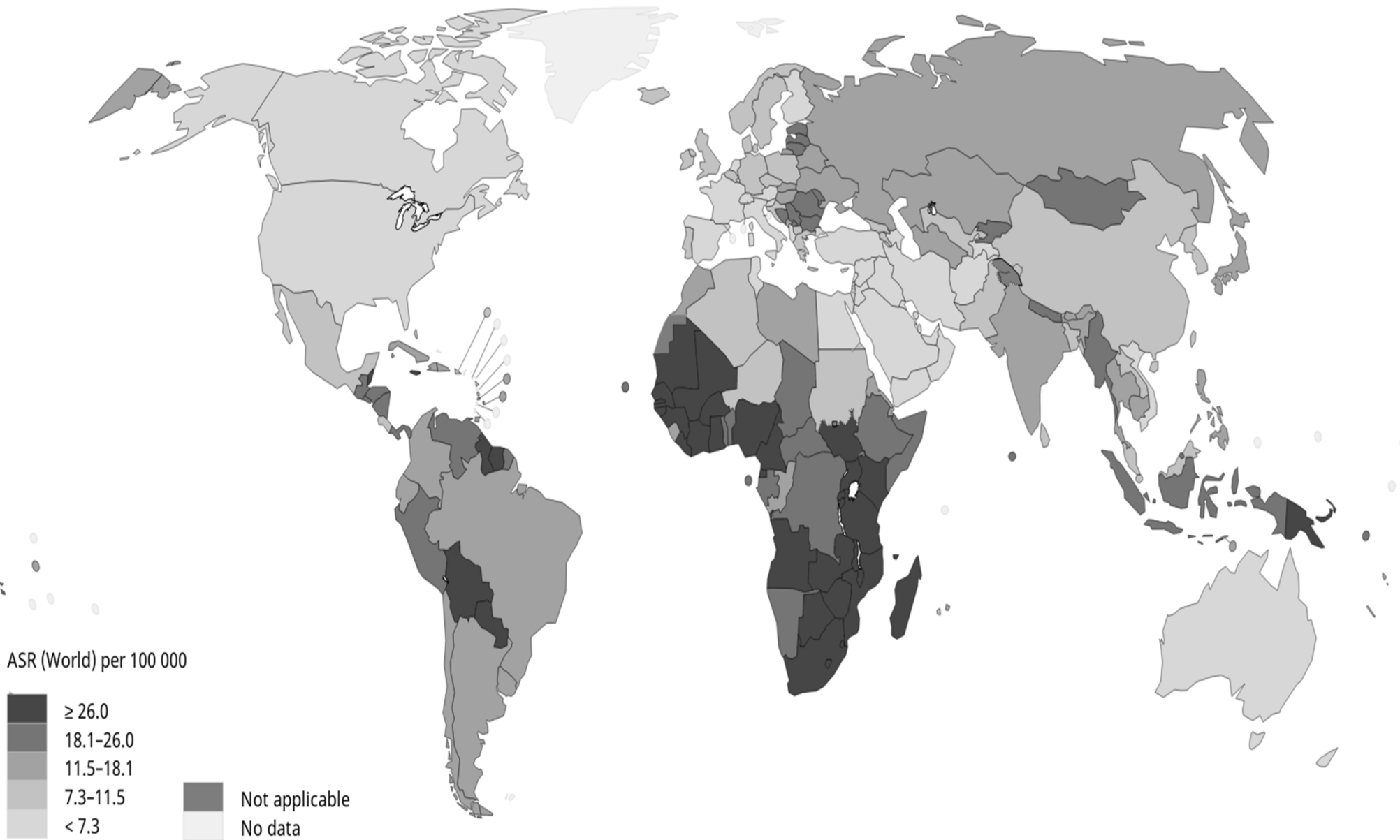
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LEARNING OBJECTIVES

- UNDERSTANDING CERVICAL CANCER
- BURDEN OF DISEASE
- PRIMARY PREVENTION
- SECONDARY PREVENTION



Estimated age-standardized incidence rates (World) in 2018, cervix uteri, all ages



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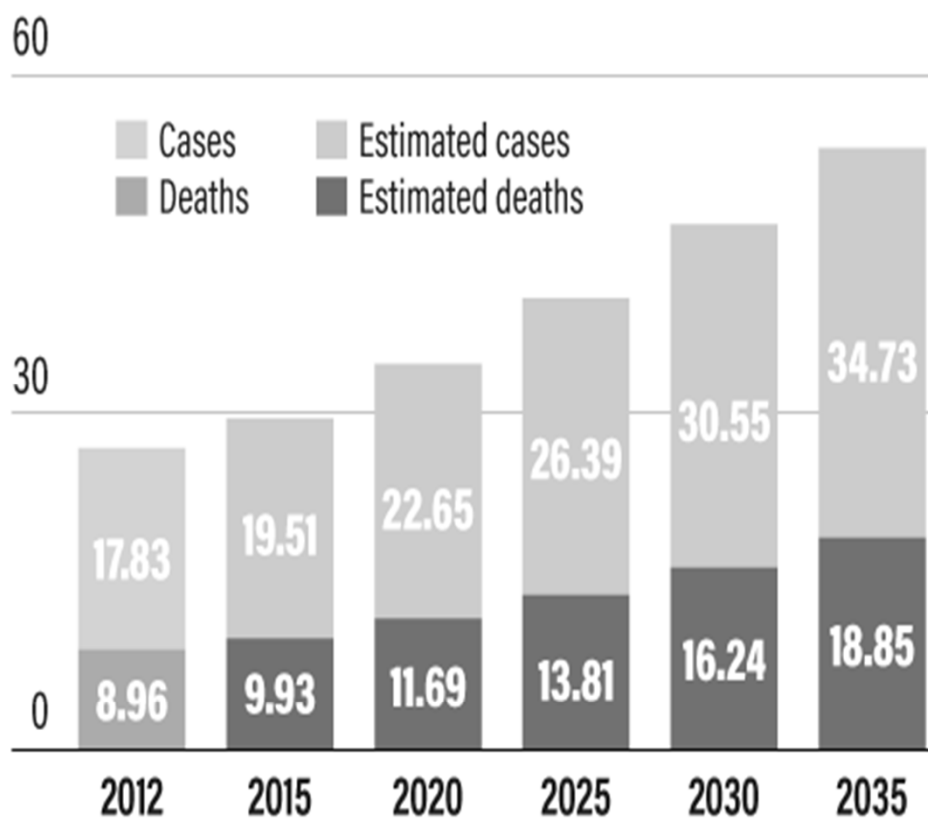
Data source: GLOBOCAN 2018
Graph production: IARC
(<http://gco.iarc.fr/today>)
World Health Organization

Incidence of Cervical Cancer per 100,000 Females in Arab World



Map produced by Prof. Inas Elattar

Cervical cancer deaths are expected to more than double between 2012 and 2035 (thousand)



HPV rates, cervical cancer cases and deaths

Country	HPV prevalence (%)	Cervical cancer cases	Cervical cancer deaths
Morocco	24.5	2,258	1,076
Turkey	13.2	1,686	663
Algeria	6.1	1,288	510
Iraq	15.65	291	142
Tunisia	14.6	265	103
Saudi Arabia	28.6	241	84
Libya	10.7	241	95
Lebanon	10.2	113	42
UAE	3.5	93	28

Sources: who.int, hpvcentre.net, cdc.gov

BURDEN OF CERVICAL CANCER

Annual number of new cases/deaths	108	56
Crude rate	4.1	2.1
Age standardized rate	6.4	4.4
Cumulative risk 0-74(%)	0.7	0.5
Ranking of cervical cancer (all years)	4 th	4 th
Ranking of cervical cancer (15-44y)	4 th	4 th



PRIMARY PREVENTION

HUMAN PAPILLOMA VIRUS

(HPV)



RISK FACTORS FOR CERVICAL CANCER



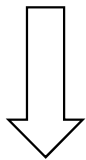
RISK FACTORS

HUMAN PAPILLOMA VIRUS
(HPV)

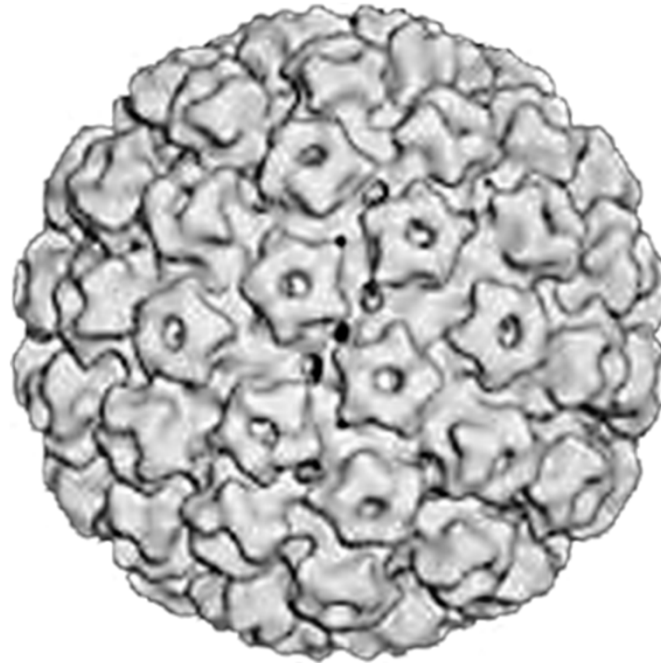
Human Papillomavirus (HPV)

HPV is a necessary cause of cervical cancer – 99.7%⁴

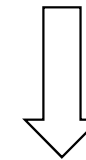
Cancer causing Types^{1,2,4}



HPV



Non-cancer causing types^{1,2}



- >75% of Cervical Cancer⁵
- >50% of Vaginal & Vulvar Cancer⁵

90% of Anogenital warts⁵

1. Schiffman M, Castle PE. *Arch Pathol Lab Med.* 2003;127:930-934. 2. Wiley DJ, Douglas J, Beutner K, et al. *Clin Infect Dis.* 2002;35(suppl 2):S210-S224. 3. Muñoz N, Bosch FX, Castellsagué X, et al. *Int J Cancer.* 2004;111:278-285. Reprinted from *J Virol.* 1994;68:4503-4505 with permission from the American Society for Microbiology Journals Department. 4. Walboomers JM, Jacobs MV, Manos MM, et al. *J Pathol.* 1999;189:12-19. 5. X. Castellsagué, S. de Sanjose, T. Aguado, K. S. Louie, L. Bruni, J. Muñoz, M. Diaz, K. Irwin, M. Gacic, O. Beauvais, G. Albero, E. Ferrer, S. Byrne, F. X. Bosch. HPV and Cervical Cancer in the World. 2007 Report. WHO/ICO Information Centre on HPV and Cervical Cancer (HPV Information Centre). Available at: www.who.int/hpvcentre



Sexual history

- Early coitarche (esp < 18y age)
- Many sexual partners
- One partner with high risk (with HPV or many sexual partners)



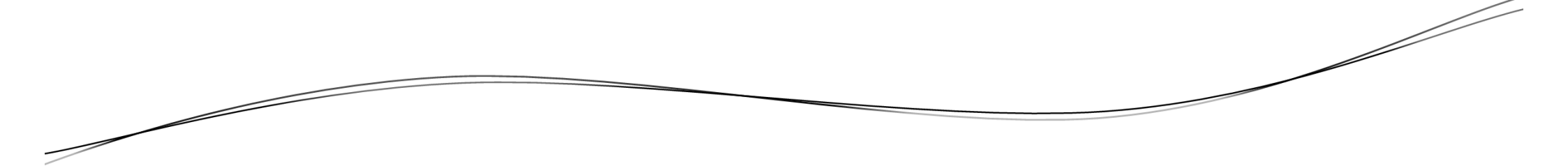
smoking

- Exposure to carcinogens
- Women who smoke twice likely to get cervical cancer
- Makes immune system less effective in fighting HPV

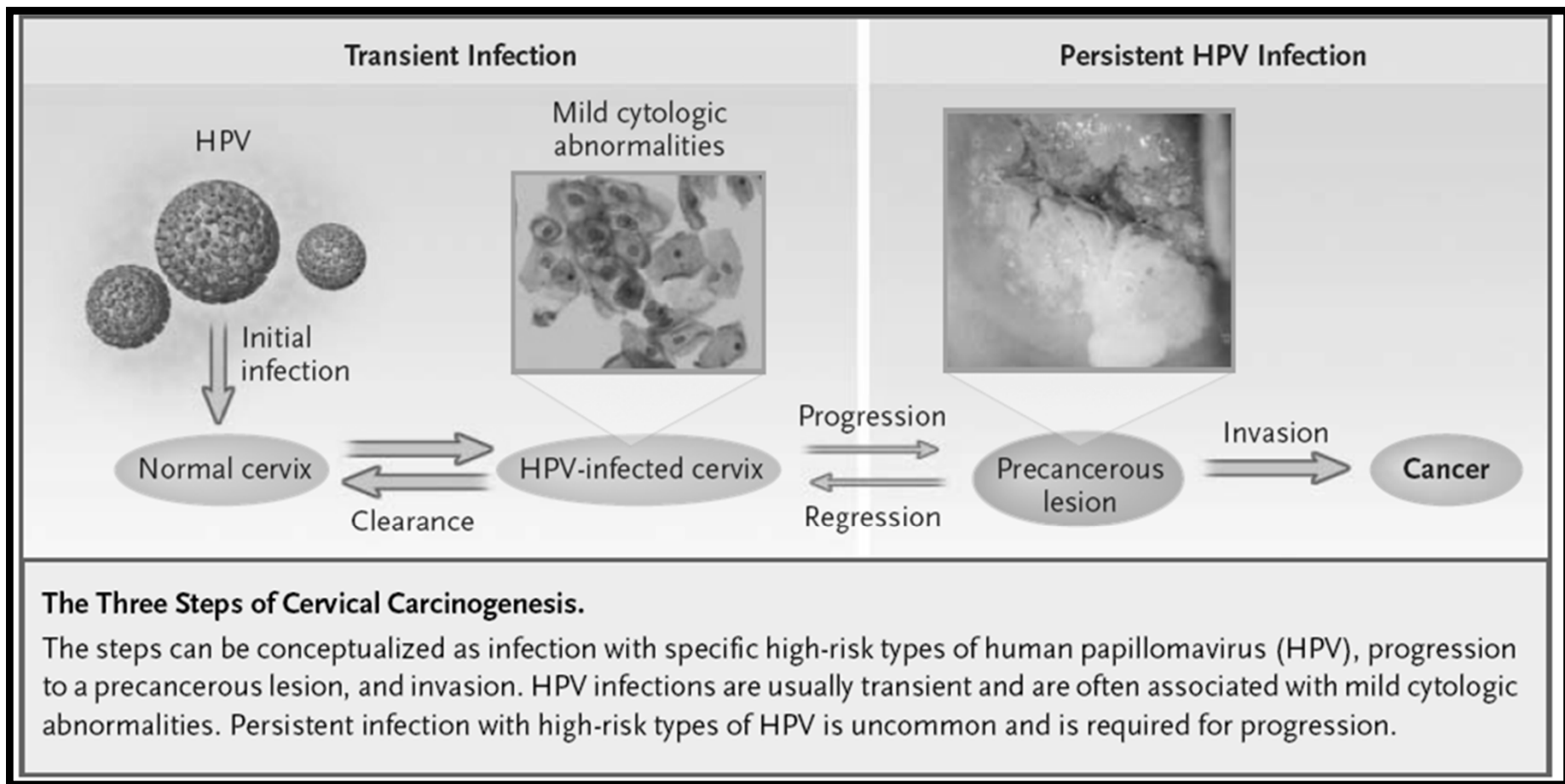


Low immune status

- HIV
- Autoimmune diseases
- Organ transplant

- 
- Chlamydia infection
 - Long term use of oral contraceptives
 - Multiple full term pregnancies
 - Young age at first full term pregnancy
 - Economic status
 - Diet low in fruits and vegetables
 - Diethylstilbestrol exposure
 - Family history of cervical cancer

Cervical Carcinogenesis



High and Low Risk HPV

Oncogenic Potential	Clinical Manifestations	Types
Low	CIN I Genital warts	6, 11
Low	CIN I	40,42,43,44,54 55,57,61,84
High	CIN I-III carcinoma	16,18,31,33,35, 39,45,51,52,56, 58,59,68,73,82



PRIMARY PREVENTION

VACCINATION

TABLE 1**FDA-approved HPV Vaccines**

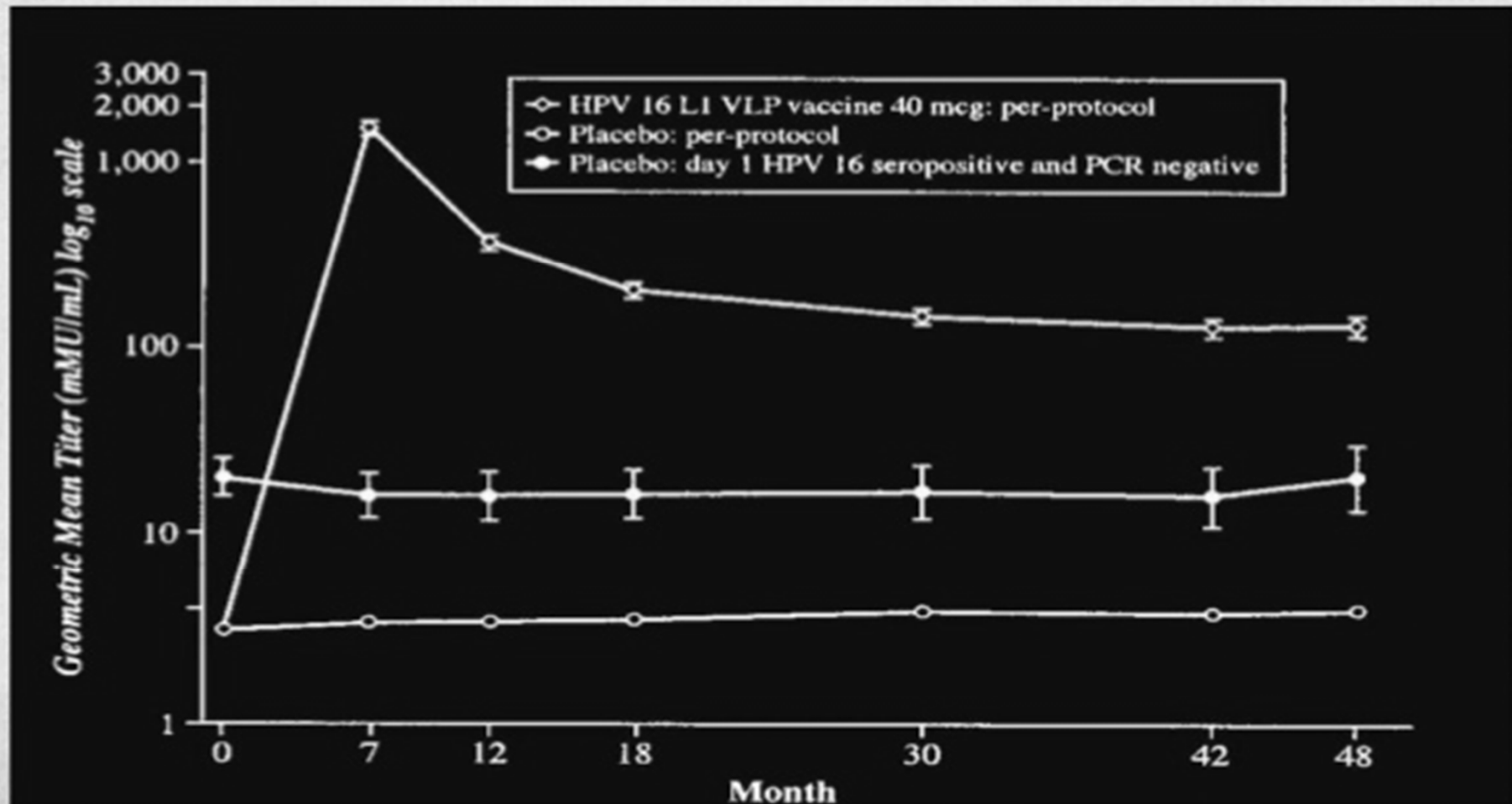
Vaccine	Coverage (HPV types)	Gender and age range
Cervarix (bivalent HPV vaccine)*	HPV 16 and 18	Females, 9-25 y
Gardasil (quadrivalent HPV vaccine)	HPV 6, 11 (genital warts), 16, and 18	Males and females, 9-26 y
Gardasil 9 (9-valent HPV vaccine)	HPV 6, 11 (genital warts), 16, 18, 31, 33, 45, 52, and 58	Males and females, 9-26 y

*Recently taken off the market in the United States.

Abbreviation: HPV, human papillomavirus.

Sources: Markowitz et al. *MMWR Recomm Rep*. 2014²; ACOG. 2017⁶; Meites et al. *MMWR Morb Mortal Wkly Rep*. 2016.⁷

IMMUNOGENICITY RESULTS (PER PROTOCOL POPULATION): HPV; VLP; PCR



Efficacy Against Incident Infection by Other High Risk HPV Types

HPV16/18 Vaccine: ITT Analysis

HPV Type	# Vaccine	# Placebo	Efficacy (95%CI)
16	1	16	94 (53-99)
18	0	5	100 (24-100)
45	1	17	94 (63-100)
31	14	30	54 (11-78)
33	12	13	1 (<0 - 61)
52	40	48	19 (-27 - 48)
58	14	16	14 (-88 - 61)

Table. HPV vaccines currently licensed in the United States³

	Bivalent 2vHPV (Cervarix)	Quadrivalent 4vHPV (Gardasil)	9-Valent 9vHPV (Gardasil 9)
Manufacturer	GlaxoSmithKline	Merck	Merck
Year licensed and for whom	October 2009, females	June 2006, females; October 2009, males	December 2014, females and males
HPV types included	16, 18	6, 11, 16, 18	6, 11, 16, 18, 31, 33, 45, 52, 58
Contraindications	Hypersensitivity to latex*	Hypersensitivity to yeast	Hypersensitivity to yeast
Dosing schedule	3-dose series: 0, 1, 6 months	3-dose series: 0, 2, 6 months	3-dose series: 0, 2, 6 months

*Only contained in pre-filled syringes, not single-dose vials.

TABLE. 2019 HPV VACCINATION RECOMMENDATIONS FROM ACIP¹³

Age	Gender	Regimen	Schedule
Initial Vaccination			
9-14 years	Females and males	2 doses	0, 6 to 12 months
Catch-up Vaccination			
15-26 years	Females and males	3 doses	0, 2, 6 months
27-45 years ^a	Females and males	3 doses	0, 2, 6 months

ACIP indicates Advisory Committee on Immunization Practices; HPV, human papillomavirus.

^aBased on shared clinical decision making between patient and practitioner.



Practice Advisory: FDA Approval of 9-valent HPV Vaccine for Use in Women and Men Age 27-45

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Practice Advisory: FDA Approval of 9-valent HPV Vaccine for Use in Women and Men Age 27-45

On October 5, 2018 the FDA approved the use of the 9-valent HPV vaccine in women and men aged 27 through 45 years¹. Although this approval opens the possibility for expanded protection against HPV disease in women and men, further review of the available data, including cost-effectiveness, is needed. The Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices (ACIP) is reviewing the available data, and ACOG is working closely with the CDC to determine if changes in clinical guidance and recommendations are appropriate.

In the meantime, members are advised that *Committee Opinion 704, Human Papillomavirus Vaccination*, remains in effect². As outlined in the guidance, obstetrician-gynecologists and other health care providers are encouraged to welcome conversations with women older than 26 years who are interested in receiving the HPV vaccine². In patients aged 27 to 45 years, their decision to be vaccinated should be individually based using shared decision making and clinical judgment based on those patients' circumstances, preferences, and concerns. The vaccine is safe and is effective in preventing new infections with HPV in women aged 27-45 years³.

This Practice Advisory was developed by the American College of Obstetricians and Gynecologists' Immunization, Infectious Disease, and Public Health Preparedness Expert Work Group with Linda O'Neal Eckert, MD, and Kevin Ault, MD.

References

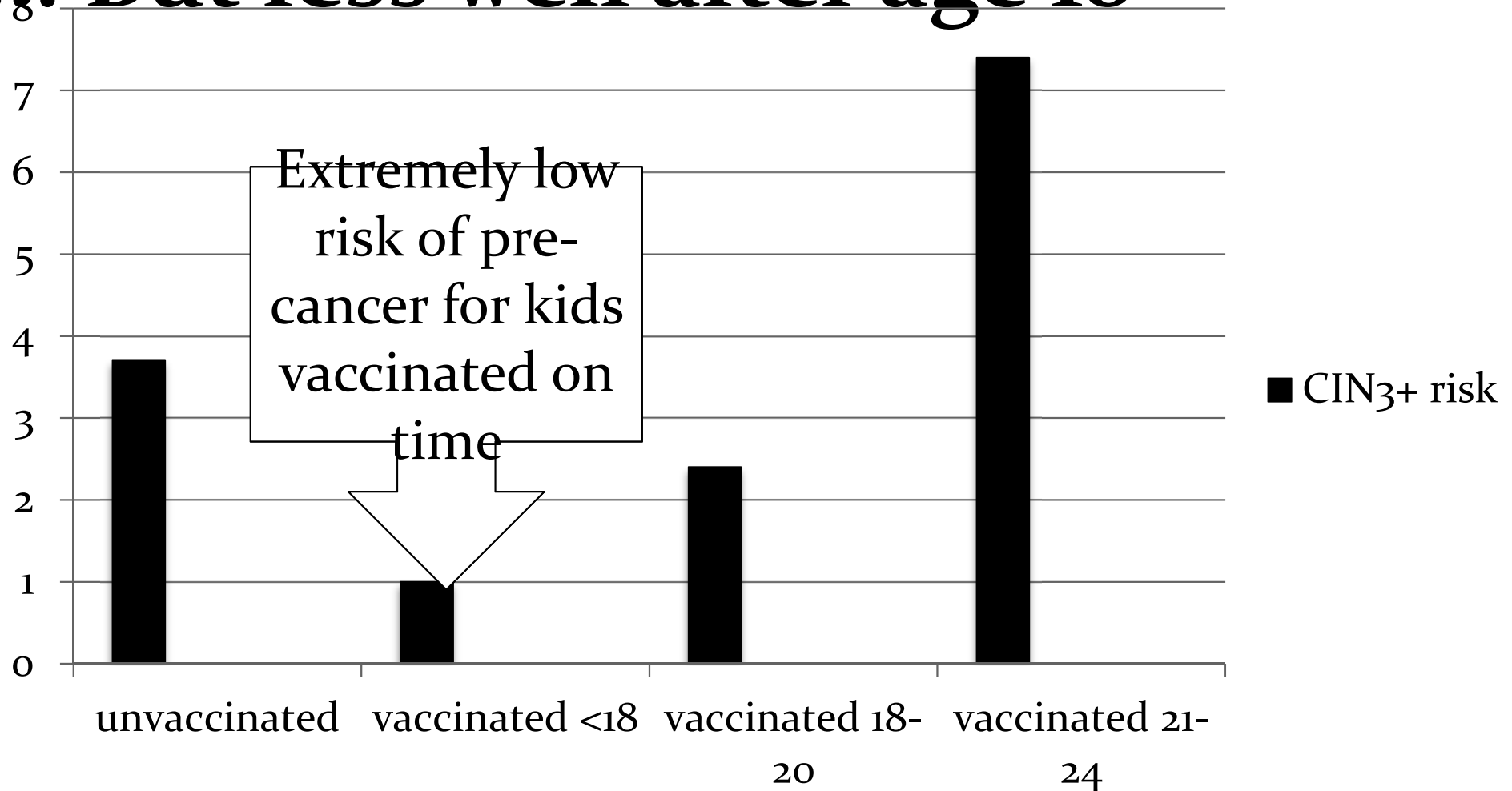
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Timeline

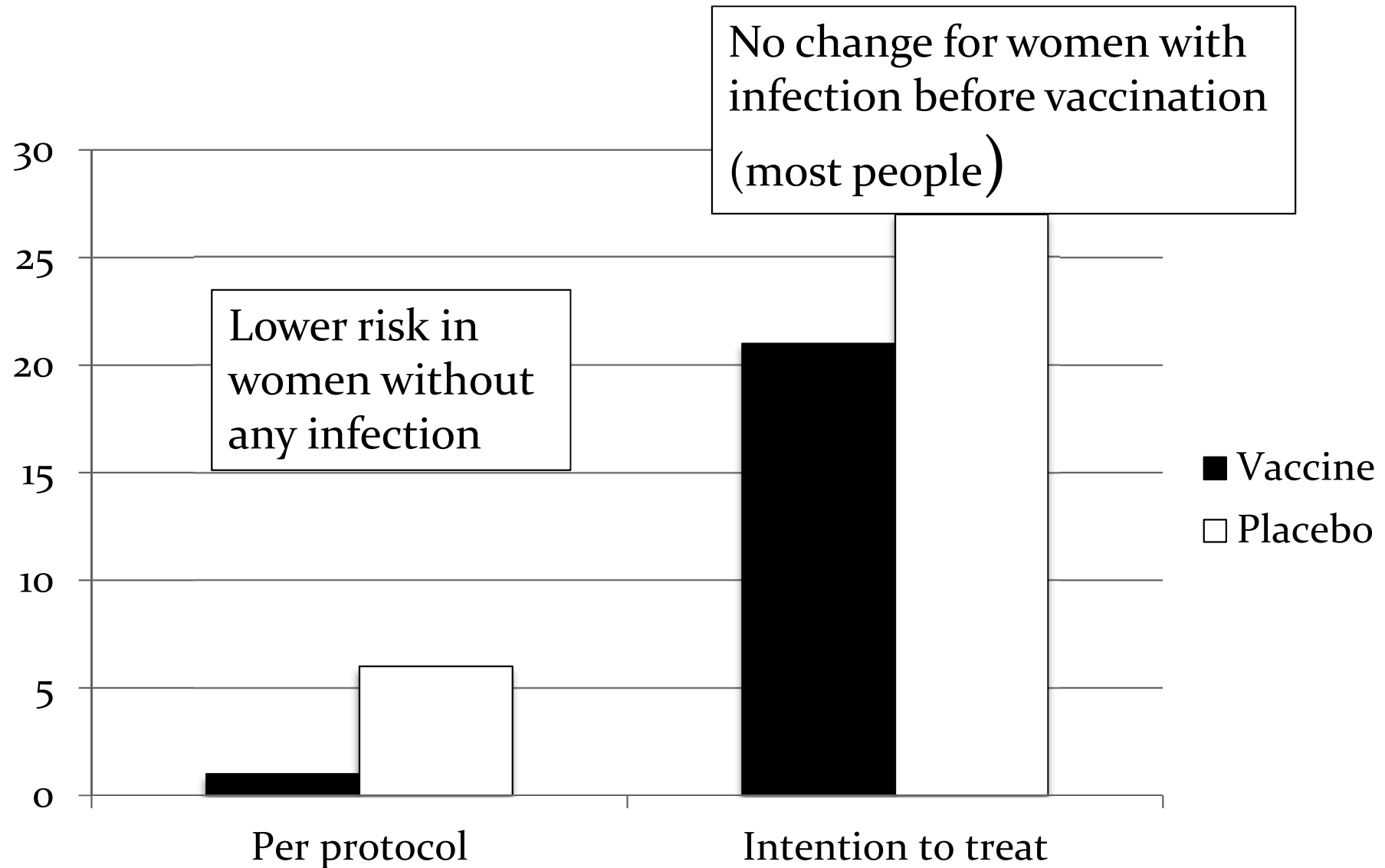
- ❑ October 5th, 2018: FDA approved Gardasil 9 for men and women ages 27-45 years
- ❑ October 25th, 2018: ACIP presentations on evidence, cost-effectiveness, potential impact, and policy options
- ❑ February 27-28, 2019: ACIP presentations on additional evidence and economic analysis, potential vote

HPV vaccination works REALLY WELL for kids....

... But less well after age 18



Not much cervical pre-cancer was prevented by vaccination in 27-45 year old women



Castellague et al Br J Cancer, 2011



SECONDARY PREVENTION

PAP SMEAR TEST

- LIQUID BASED CYTOLOGY
- CONVENTIONAL SLIDE PREPARATION

HPV TESTING



COMBINED HPV AND PAP SMEAR TESTING



SUMMARY

- RISK FACTORS
- PRIMARY PREVENTION – HPV and vaccine
- SECONDARY PREVENTION
pap smear and or HPV testing