

HPV among Women with HIV

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Learning Objectives

- By the end of the session, the learner will be able to:
 - Describe the pathophysiology of HPV among women with HIV
 - Determine the appropriate screening interval for women with HIV
 - Identify patients that require colposcopy

Disclosures

- I have no financial disclosures.
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Outline

- HPV Epidemiology
- HPV Associated Malignancy
- HPV Vaccine
- Cervical Cancer Screening among Women with HIV

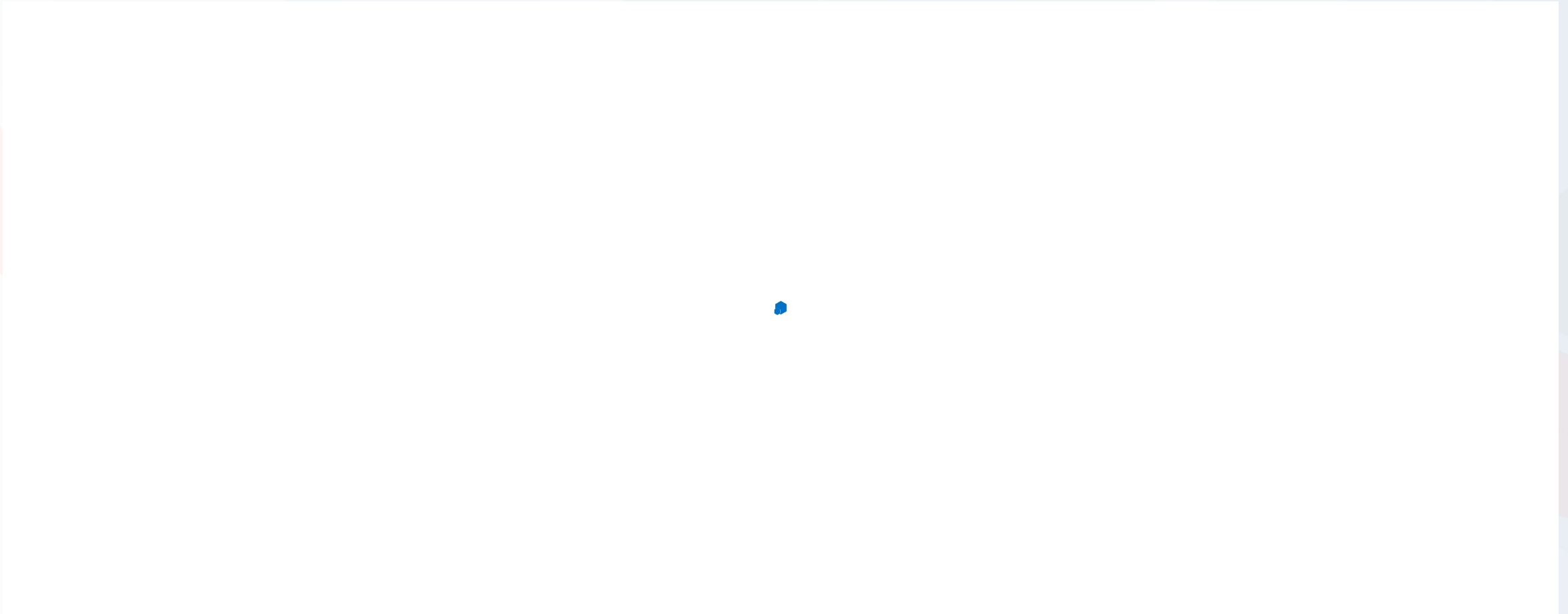
HPV Epidemiology

- HPV is the most common sexually transmitted (STI) infection
- 80% of individuals will be exposed to HPV at some point in their lives
- Cervical cancer is the 4th most common cancer among women globally
 - Estimated 604,000 new cases and 342,000 deaths in 2020
- In the US, about 4000 women die of this cancer and 13,000 new cases of cervical cancer are diagnosed.

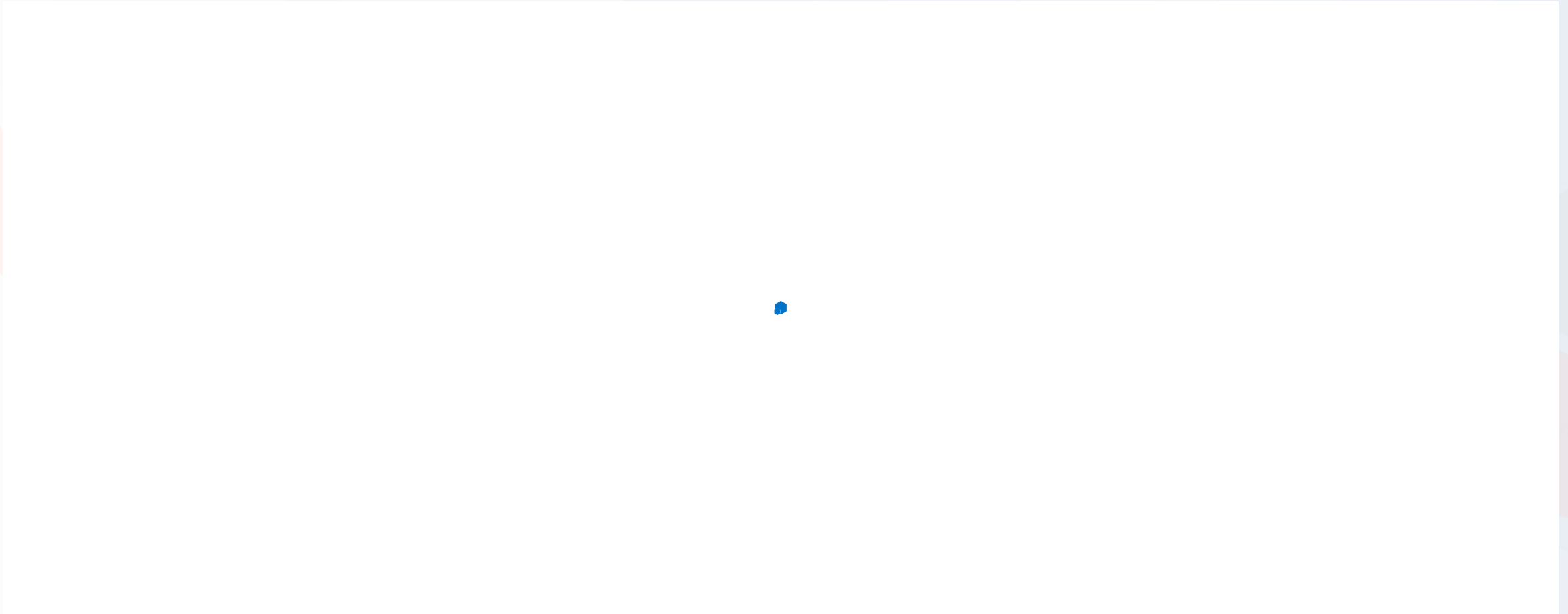
HPV Epidemiology

- Most infections are transient with more than 90% of infected populations clearing the infection
- For women with HIV, it can take only 5-10 years for cervical cancer to develop compared to 15-20 years for women without HIV
- Women with HIV are 6 times more likely to develop cervical cancer compared to women without HIV

Question Time



Question Time

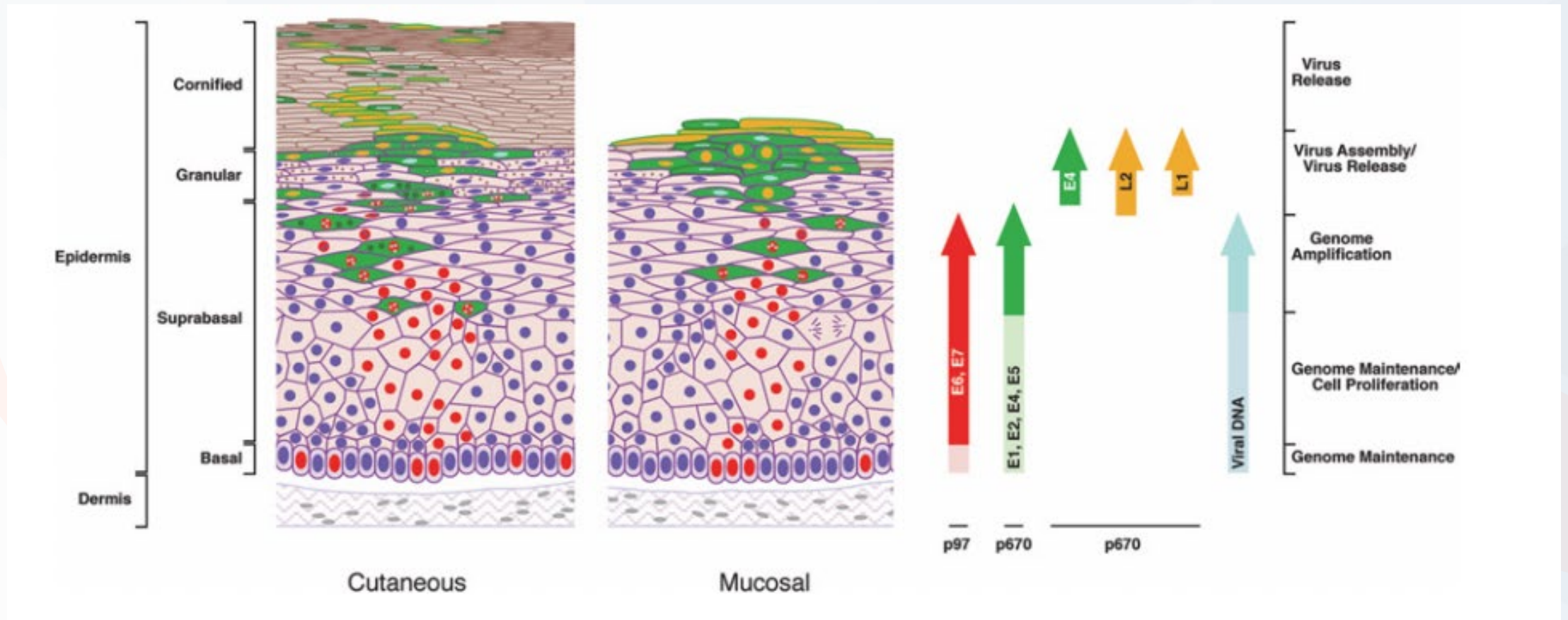


HPV Virology

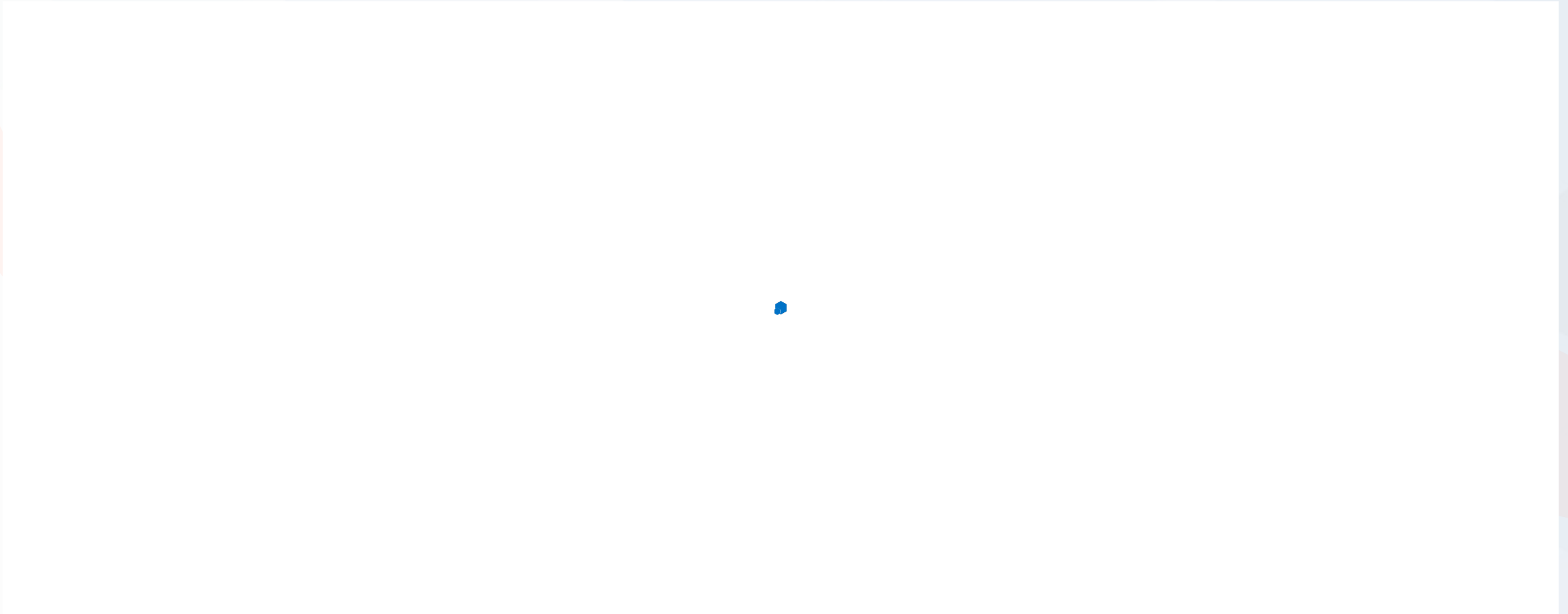
- DS DNA virus
- 13 types known to produce cancer (7 others suspected)
- Types 16 and 18 are responsible for 70% of cervical cancers worldwide
 - 16 causes almost half of invasive cancers



HPV Life Cycle



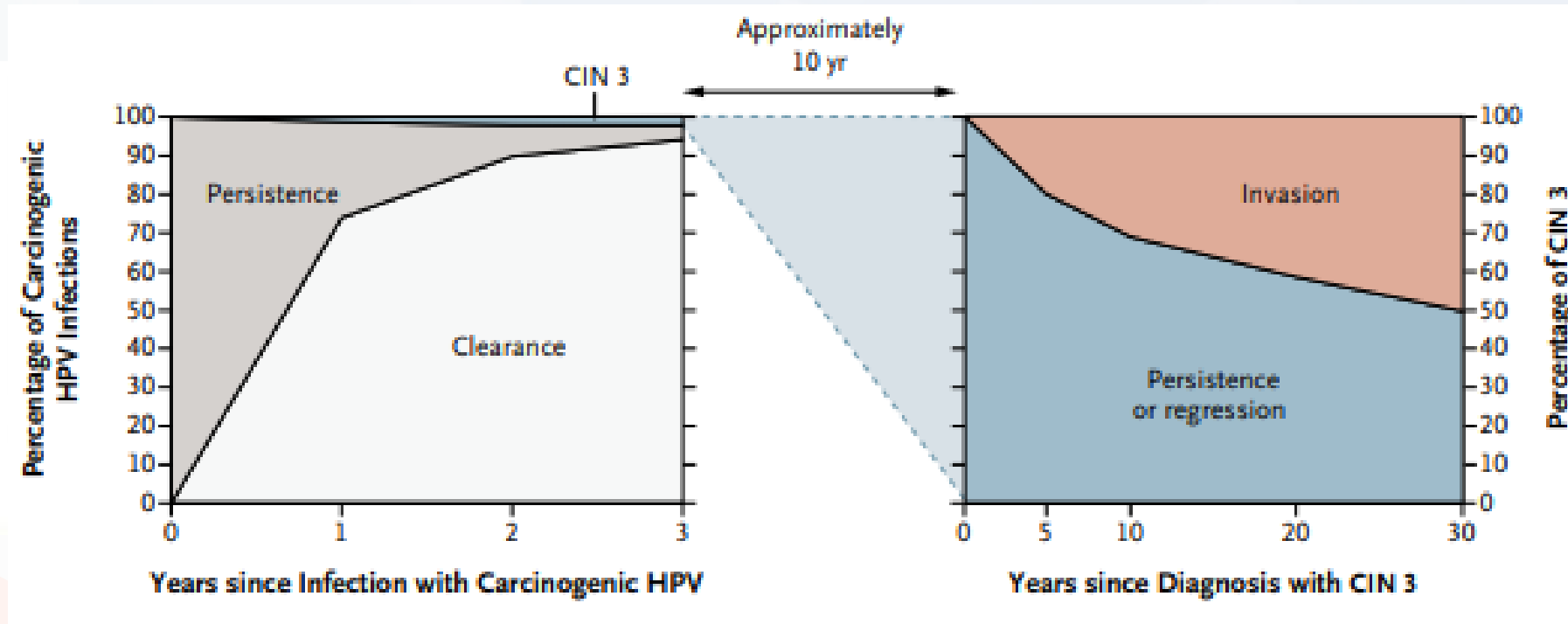
Question Time



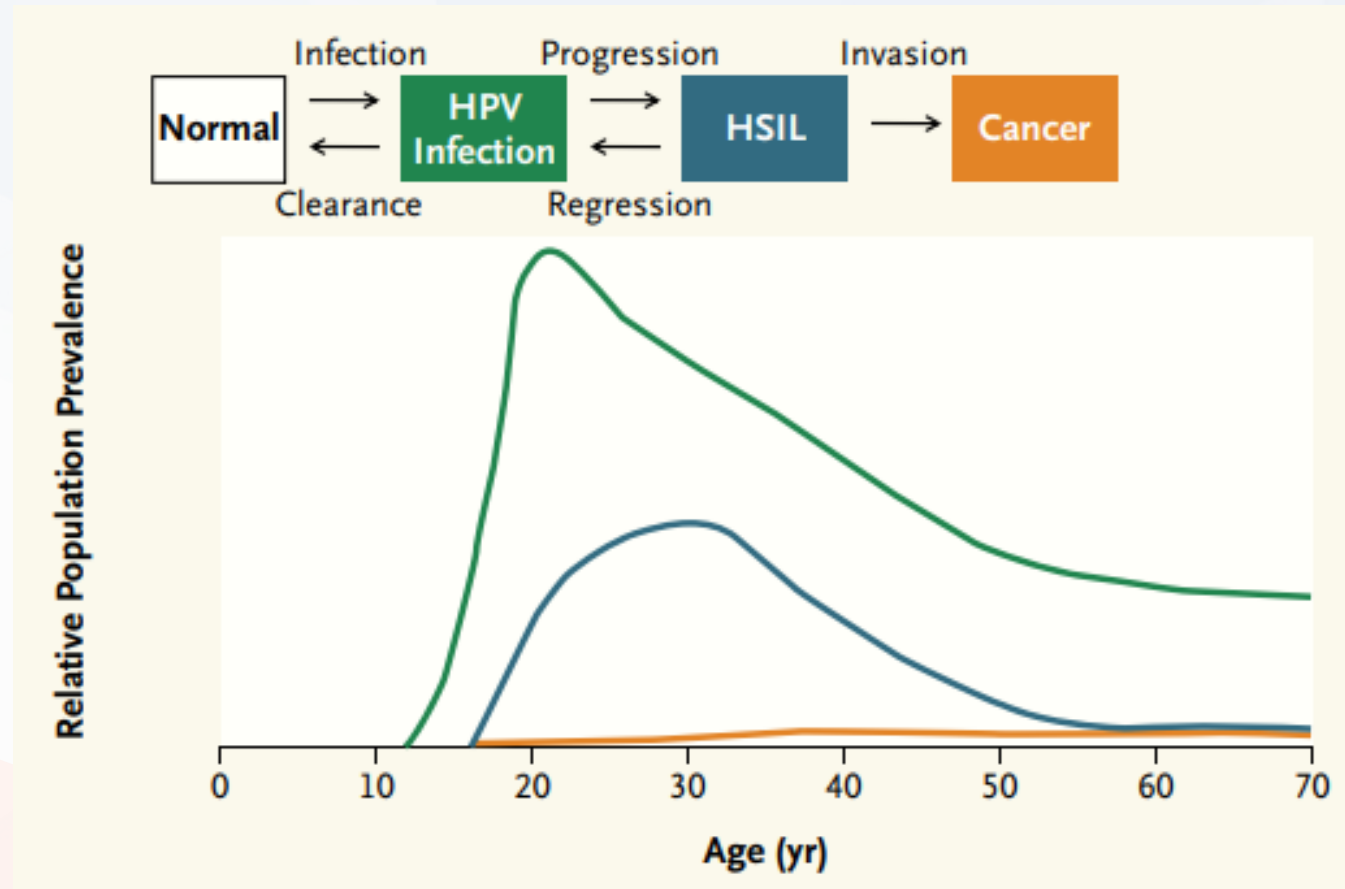
HPV Transmission

- Transmitted by skin-to-skin contact and sexual contact
- Risk factors for HPV infection include:
 - Recent new partners
 - Time having known a partner before sex
 - Sex partner's number of previous partners
 - Inconsistent condom use with new partners

Time Course of HPV Infection

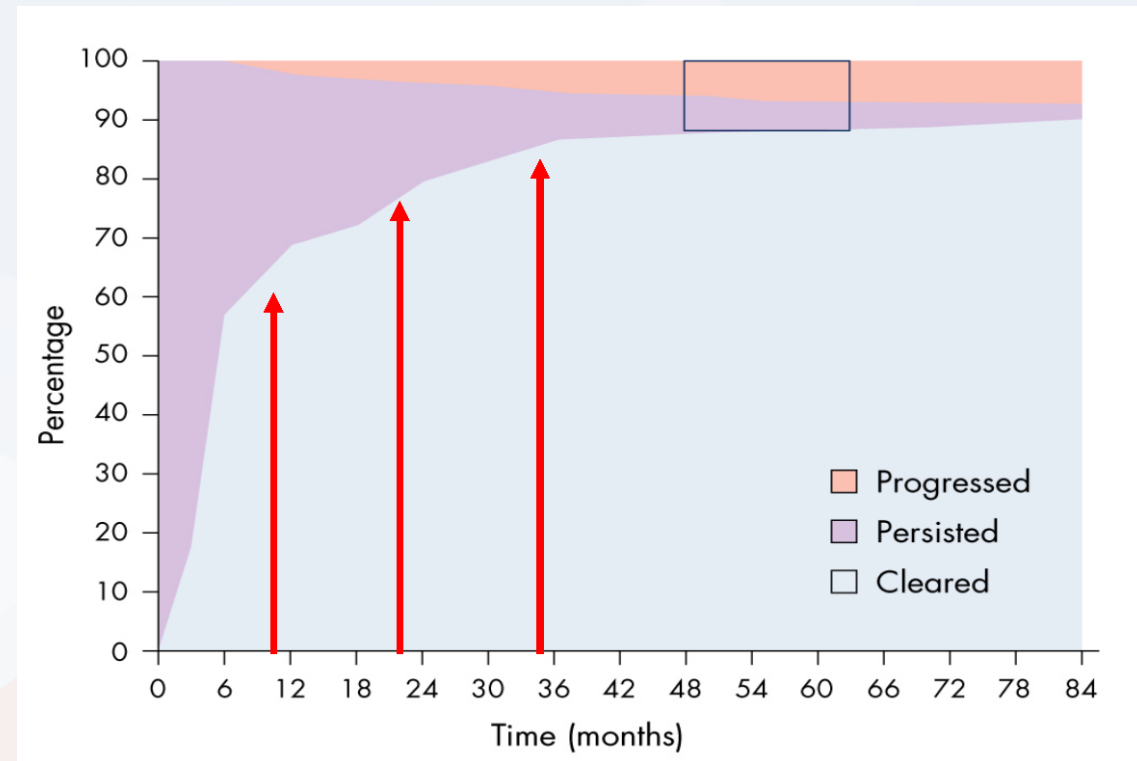


Cervical Carcinogenesis



Natural History of HPV

- 777 infections found at enrollment
- The longer a high risk infection persisted, the greater the risk of CIN 2,3

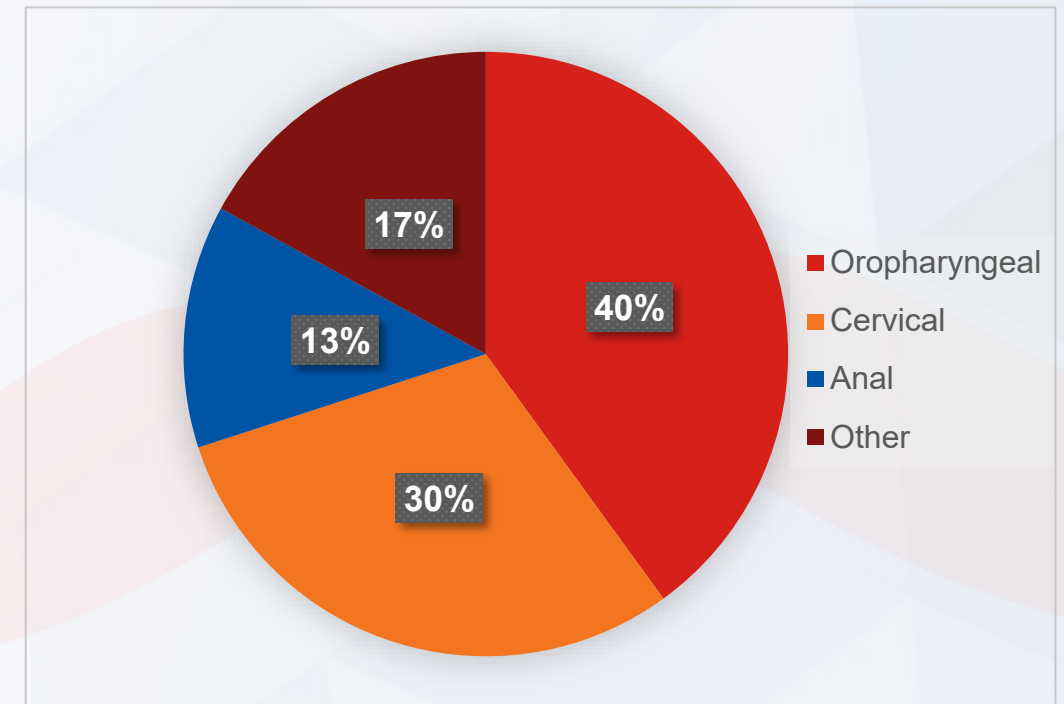


HPV Infection: 3 possibilities

- Sustained Remission
 - Cell mediated immune response contains infection
- Productive Infection
 - In the presence of co-factors, HPV replicates independently relative to host DNA
 - Identified risk factors: smoking, chlamydia, OCPs, immunosuppression
- Neoplastic Transformation
 - Risk established by persistent infection

HPV-Associated Cancers

- Approximately, 45,000 HPV associated cancers are diagnosed annually in the US
 - 60% in women and 40% in men



Burden of Cervical Cancer

- Most common cancer in adult females in developing countries
- Greatest cause of years-of-life lost in adult females
 - South-central Asia, Latin America and Sub-Saharan Africa
- In the US:
 - 13,800 new cases annually
 - 4290 deaths
 - 18th in incidence and mortality

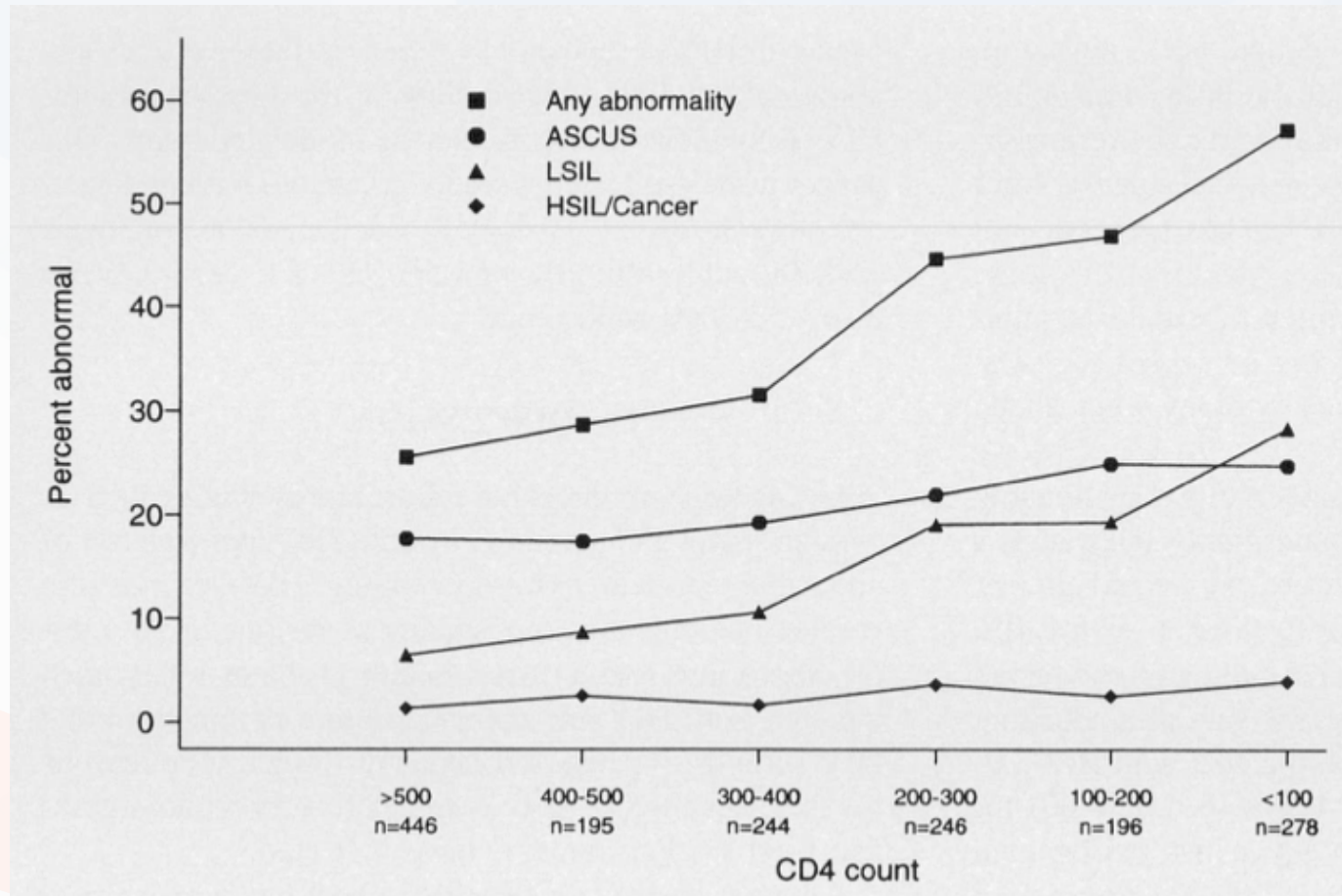
Strength of Cancer Risk Association

- White male smoker vs. non-smoker
 - Relative Risk of Lung Cancer: 8
- Postmenopausal individuals on combined HRT vs. no HRT
 - RR of breast cancer: 1.3
- HPV 16 positive vs. HPV 16 negative
 - RR of cervical cancer: 434

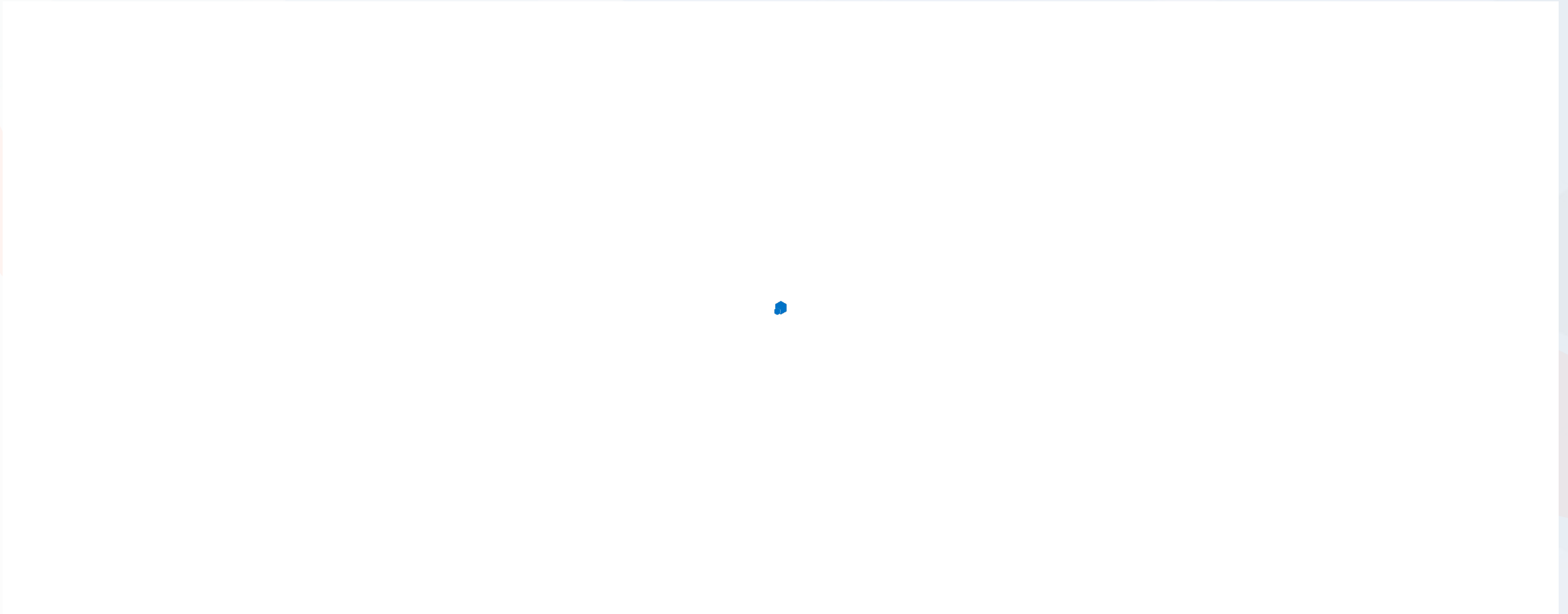
HPV-Associated Cancer in PWH

- PWH have a significantly higher risk of developing an HPV-associated cancer
- HIV+ women have a threefold higher risk of abnormal cervical cytology compared to HIV- women.
- There is a correlation between CD4 count and risk of cervical cancer and anal cancer
- PWH are more likely to have a higher prevalence of genital oncogenic HPV infection than women without HIV

CD4 Count and Abnormal Cervical Cytology



Question Time



ART and Incidence of HPV Infection

Influence of Adherent and Effective Antiretroviral Therapy Use on Human Papillomavirus Infection and Squamous Intraepithelial Lesions in Human Immunodeficiency Virus–Positive Women

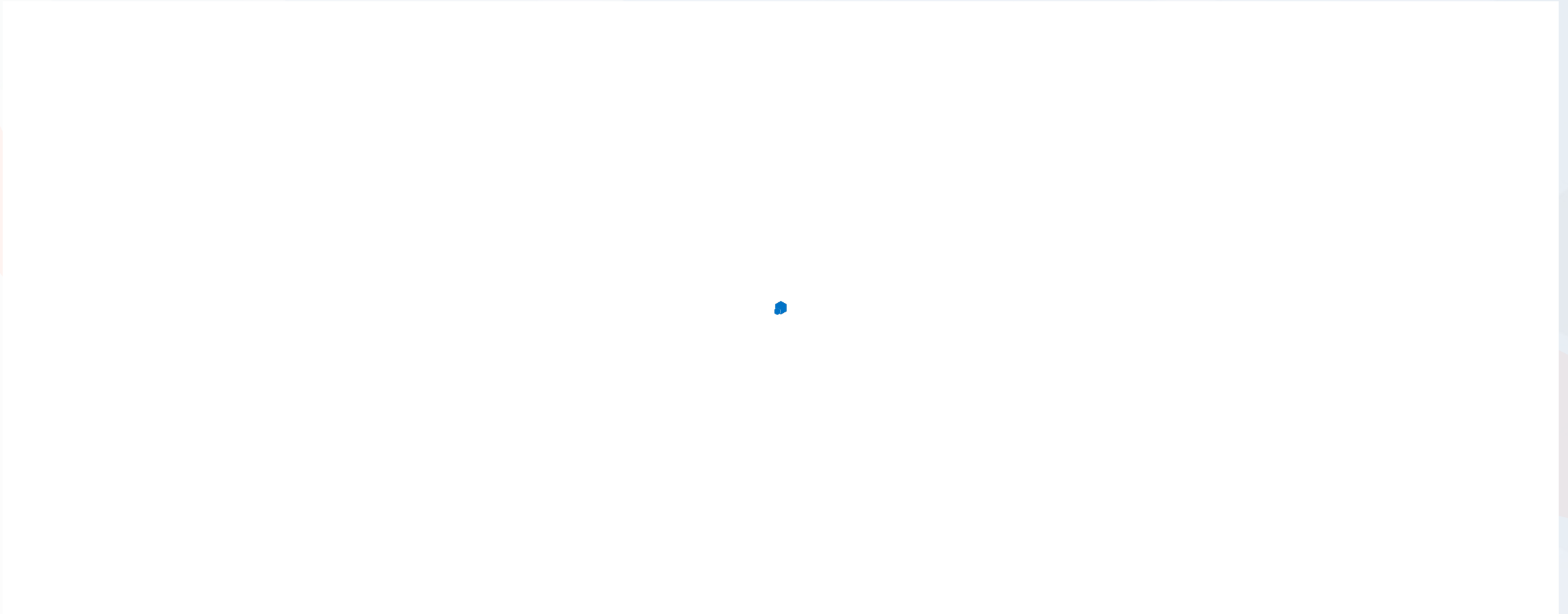
Howard Minkoff,¹ Ye Zhong,² Robert D. Burk,² Joel M. Palefsky,⁴ Xiaonan Xue,² D. Heather Watts,⁶ Alexandra M. Levine,⁵ Rodney L. Wright,³ Christine Colie,⁸ Gypsyamber D'Souza,⁷ L. Stewart Massad,⁹ and Howard D. Strickler²

- ART initiation was associated with a significant reduction in prevalence of HPV (OR 0.60 [95% CI, 0.44-0.81], $p=0.001$), incident of oncogenic HPV infection (HR, 0.49 [95% CI 0.30-0.82], $p=0.006$)

HPV Vaccine

- The HPV vaccine was approved in 2006 for women and 2009 for men
- Provides protection against 90% of cervical-cancer causing strains of HPV
- The vaccine was originally approved for cervical cancer prevention, but in 2020 the FDA expanded its approval to include prevention of oropharyngeal cancer and other head and neck cancers.

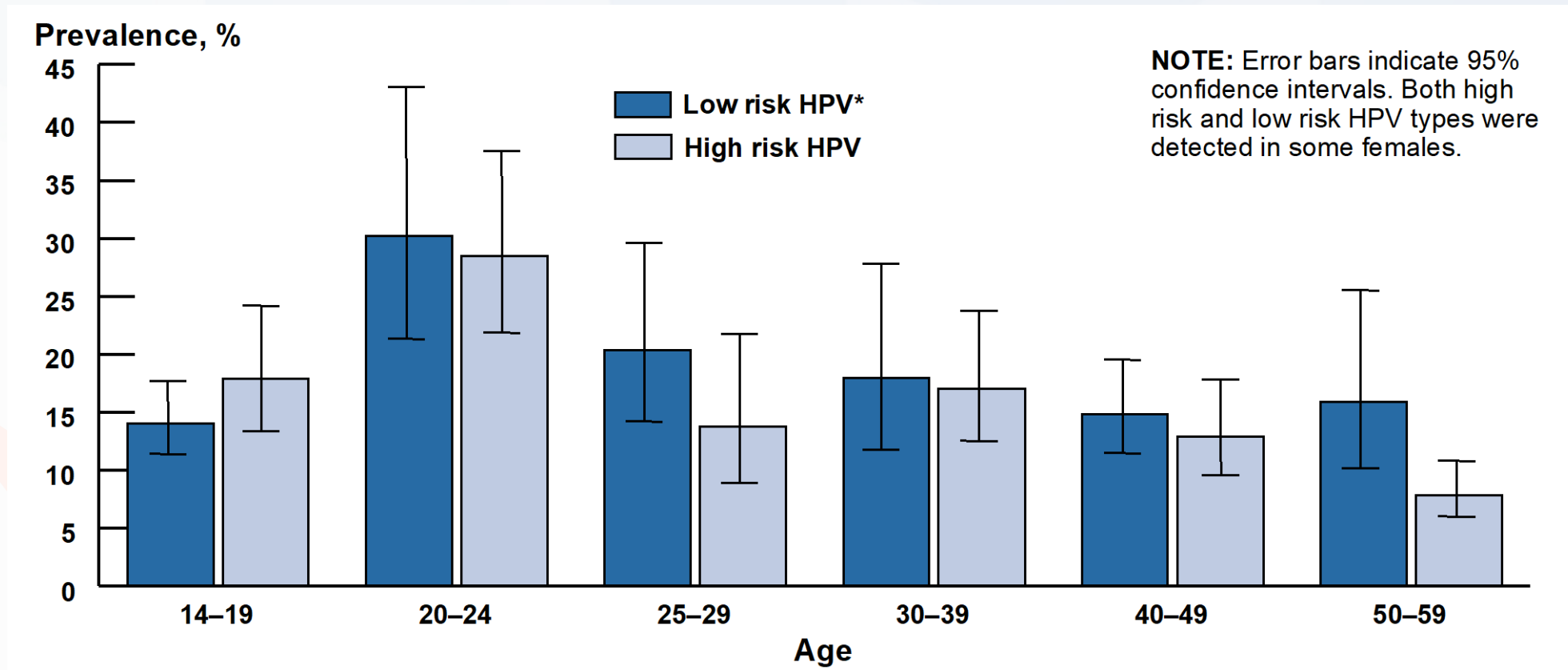
Question Time



HPV Vaccine

- Current vaccine protects against 9 different strains of HPV
- HPV 16 and 18 are responsible for about 80% of HPV-associated cancers, about 66% of cervical cancers and majority of other HPV-associated cancers in women and men
- HPV 31, 33, 45, 52, 58: cause about 10-15% of cervical cancers
- HPV 6 and 11 cause anogenital warts

Prevalence of High and Low Risk HPV among women



Who is eligible for the HPV Vaccine?

- Recommended at age 11-12 years (can start at age 9)
- Age 9-14 years at initial vaccination: 2 dose series at 0, 6-12 months
- Age 15 years or older at initial vaccination: 3 dose series at 0, 1-2 months, 6 months
- If vaccination schedule is interrupted, then do NOT need to restart series
- For adults age 27 through 45 years, vaccination based upon shared decision making







Immunogenicity and Safety of the 9-Valent Human Papillomavirus Vaccine in Solid Organ Transplant Recipients and Adults Infected With Human Immunodeficiency Virus (HIV)

Lise Boey,^{1,2} Ans Curinckx,¹ Mathieu Roelants,^{1,2} Inge Derdelinckx,^{2,3} Eric Van Wijngaerden,^{2,3} Paul De Munter,^{2,3} Robin Vos,⁴ Dirk Kuypers,^{2,5} Johan Van Cleemput,⁶ and Corinne Vandermeulen¹

- Phase III study including 100 PWH age 18-45 years and 171 SOT recipients (age 18-55 years)
- All HIV-infected participants seroconverted for all HPV types
- Seroconversion ranged from 46 to 72% among SOT

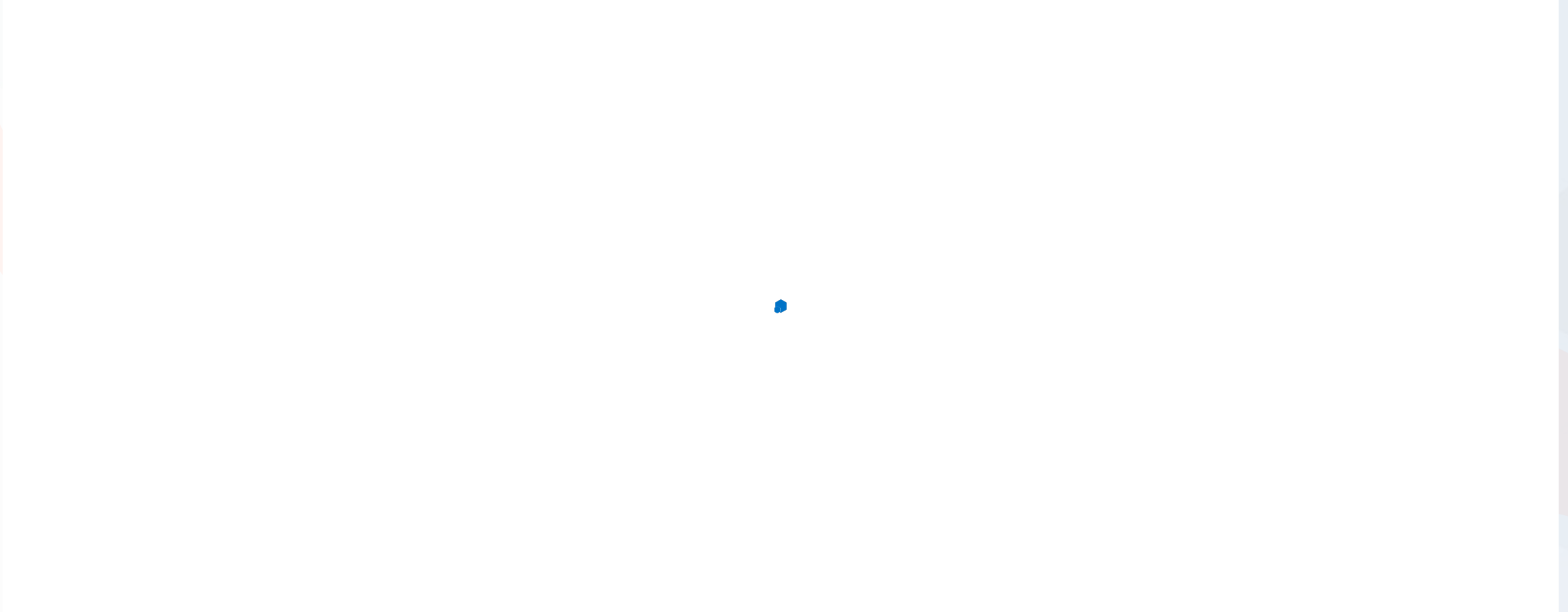
Review

Adjuvant HPV Vaccination to Prevent Recurrent Cervical Dysplasia after Surgical Treatment: A Meta-Analysis

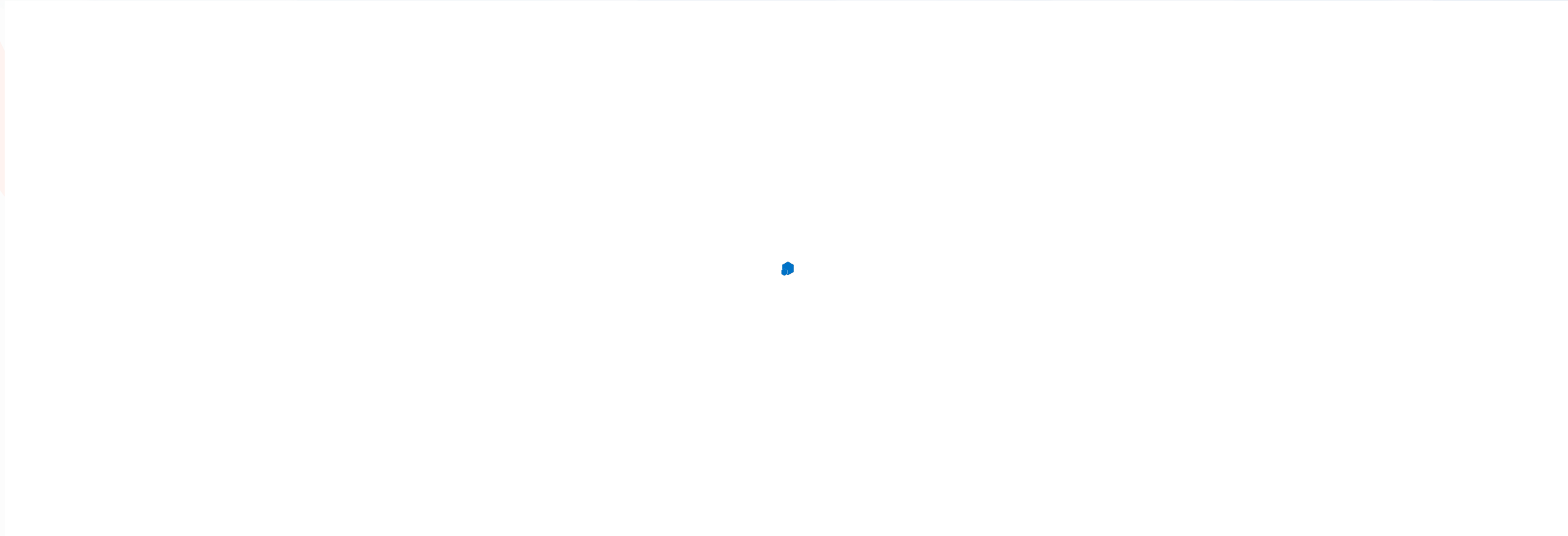
Violante Di Donato ¹, Giuseppe Caruso ^{1,*}, Marco Petrillo ^{2,3}, Evangelos Kontopantelis ⁴,
Innocenza Palaia ¹, Giorgia Perniola ¹, Francesco Plotti ⁵, Roberto Angioli ⁵, Ludovico Muzii ¹,
Pierluigi Benedetti Panici ¹ and Giorgio Bogani ⁶

- Administration of prophylactic HPV vaccine (shortly before or after treatment of CIN 2+ may reduce the risk of recurrence
- Unclear mechanism as HPV vaccines elicit the development of neutralizing antibodies against HPV-like particles and prevent virus particles from entering host cells so they should not be effective in clearing preexistent infections
- In this meta-analysis of eleven studies, they found that using prophylactic HPV vaccination as an adjunct to surgical excision for CIN2+ reduces the risk of recurrent disease (OR 0.36; 95% CI 0.22-0.57; $p < 0.0001$).

Question Time



29 y.o. F with newly diagnosed HIV presents to clinic. Her only risk factor is heterosexual sex with 2 male partners since sexual debut at age 18. She has never received the HPV vaccine. Which one of the following is TRUE regarding cervical cancer screening?



Cervical Cancer Screening

- Cervical pap smear should be performed at diagnosis if between 21 and 29 years and if not performed within the last year
- PWH with a uterus and aged 21-29 years
 - Annual cytology
 - After 3 negative results, then can space out to every 3 years
- PWH with a uterus and ≥ 30 years
 - Pap test and HPV testing should be performed at baseline
 - If normal, then co-testing should be performed every 3 years
- Annual cytology for WWH aged 21-29 years
 - After 3 negative results, then triennial cytology
- HPV testing is NOT recommended if less than 30
- Screening should be continued indefinitely for women with an intact uterus instead of ending at age 65

The Abnormal Pap

ASCUS

Negative
Cytology with
+HPV

Colposcopy
or Cotesting
in 1 year

What goes to colposcopy?

- Negative cytology BUT + HRHPV 16 or 18
- ASC-H
- Atypical glandular cells
- LSIL or HSIL
- Squamous carcinoma

QUESTIONS?

AETC Program National Centers and HIV Curriculum

- **National Coordinating Resource Center** – serves as the central web –based repository for AETC Program training and capacity building resources; its website includes a free virtual library with training and technical assistance materials, a program directory, and a calendar of trainings and other events. Learn more: <https://aidsetc.org/>
- **National Clinical Consultation Center** – provides free, peer-to-peer, expert advice for health professionals on HIV prevention, care, and treatment and related topics. Learn more: <https://nccc/ucsf.edu>
- **National HIV Curriculum** – provides ongoing, up –to-date HIV training and information for health professionals through a free, web –based curriculum; also provides free CME credits, CNE contact hours, CE contact hours, and maintenance of certification credits. Learn more: www.hiv.uw.edu