THE UNIVERSITY OF TENNESSEE HEALTH SCIENCE CENTER

Screening for HPV-Related Cancers in Immunosuppressed and Other Vulnerable Groups

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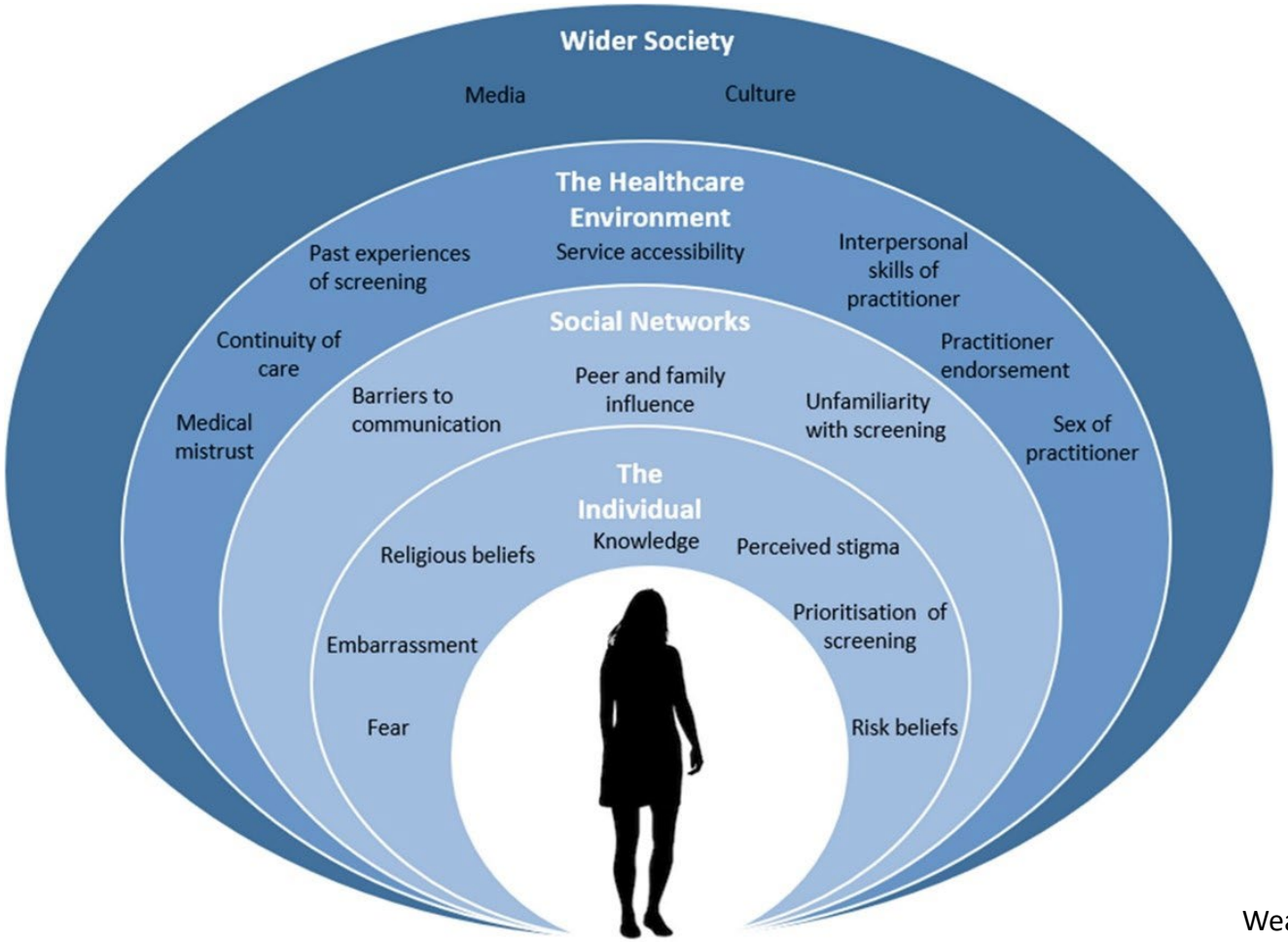
Disclosures

I have no relevant financial relationships to disclose.

Objectives:

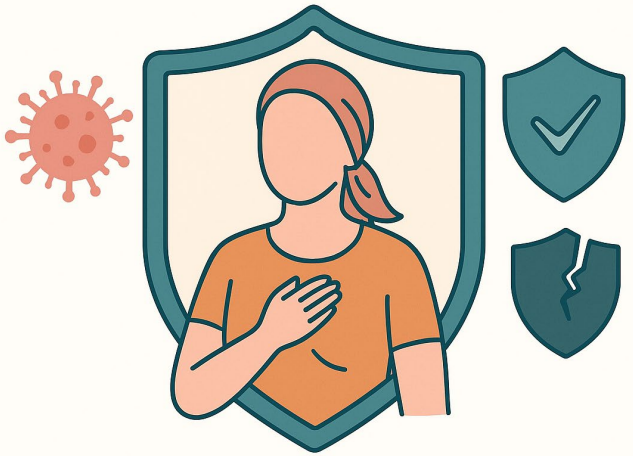
Identify	Identify high-risk groups for cervical and other HPV-related cancers, with emphasis on immunosuppressed individuals.
Compare	Compare screening guidelines for people living with HIV versus those with non-HIV-related immunosuppression
Recognize	Recognize clinical gaps in transplant, autoimmune, and DES-exposed populations.
Describe	Describe screening barriers in transgender, gender-diverse, and underserved groups.
Apply	Apply strategies to improve HPV prevention and screening equity.

Invisible Risk, Visible Disparities: HPV Prevention in Immunosuppressed and Vulnerable Groups



Wearn & Shepherd, *Psychology & Health*, 2022

Vulnerability and Immunosuppression



Vulnerability in this context refers to **increased biological risk**, **systemic exclusion**, or **both**

Not all vulnerable groups are the same — risk pathways vary:

Immunosuppression → impaired HPV clearance

Social marginalization → decreased access to screening or follow-up

Some populations face **intersectional risk** (e.g., Black women living with HIV, transmasculine people post-transplant)

Types of Vulnerability in HPV-Related Cancer

TYPE	EXAMPLES	KEY RISKS
Biological	PLWH, SOT, SLE, DES	↓ HPV clearance, ↑ progression
Socio-economic	Uninsured, rural, immigrant	Access to care, delayed follow-up language barriers
Sociocultural	Transgender, LGBTQ+	Stigma, mistrust
Intersectional	Black trans woman w/ HIV	Compounded biological + systemic risk

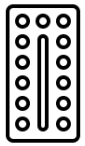
What Increases Risk of HPV-Related Cancer?

HPV Genotype
High-risk types (16, 18, 31, 33, etc.) are strongly associated with malignant transformation

Immunodeficiency
Includes HIV, solid organ transplant (SOT), autoimmune conditions on immunosuppressants, and primary immunodeficiencies

Tobacco Exposure
Carcinogens in tobacco may enhance HPV oncogene (E6/E7) activity

High Parity
Hormonal changes and cervical trauma may promote oncogenic HPV persistence



Oral Contraceptives
Long-term use may be associated with increased risk, though data is mixed

Why Focus on Immunosuppressed Individuals?

Persistent HPV infection is more likely due to impaired immune clearance

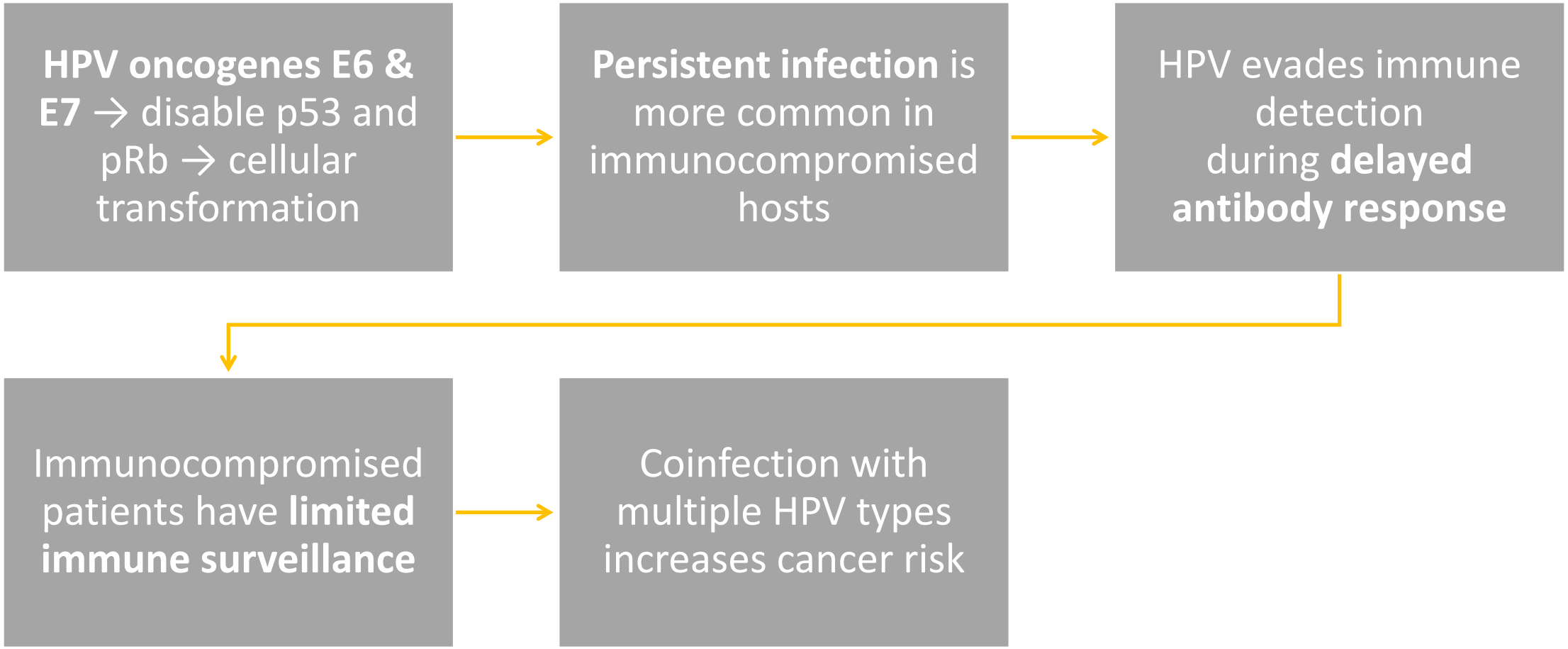
Increased risk of high-grade lesions and invasive cancer

Lower vaccine efficacy and immunogenicity

Often **excluded** or underrepresented in screening guidelines

Require **more frequent screening** and individualized care

HPV Carcinogenesis and Immunosuppression



People living with HIV

Impact of ART on HPV Progression

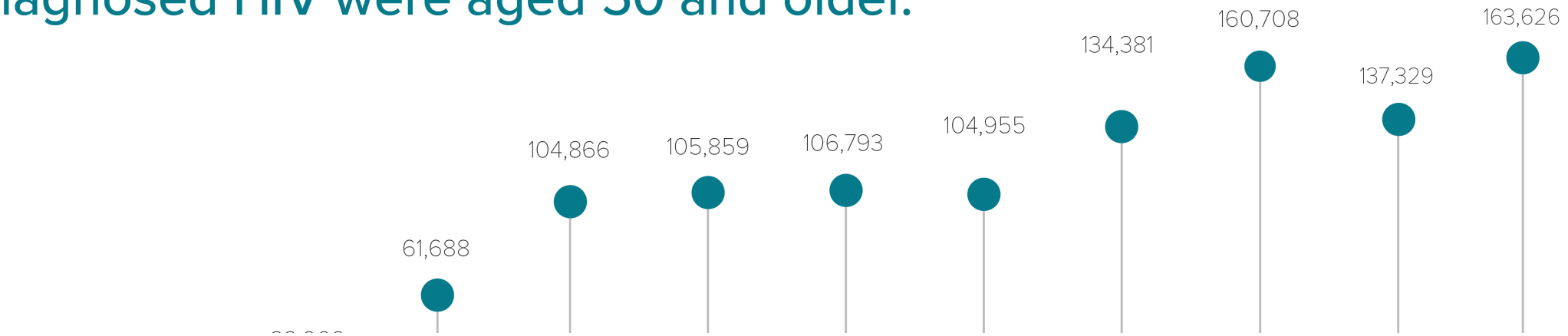
- Effective ART **reduces** HPV persistence and progression.
- Women on consistent ART show **lower rates of CIN and ICC**.
- HPV clearance improves with **restored CD4+ cell counts**.

ART is not only life-saving—it's cancer-preventing in the context of HPV.

Increasing the lifespan in PLWH

People with diagnosed HIV in the US and 6 territories and freely associated states by age, 2022

People with diagnosed HIV are living longer, healthier lives because of effective HIV treatment. At the end of 2022, over half of people with diagnosed HIV were aged 50 and older.



Primary Prevention – HPV Vaccination

- 🛡️ HPV vaccination is a major advance in cervical cancer prevention that has the potential to greatly reduce HPV-related malignancies.

In people living with HIV:

✓Vaccines are **safe**

✓Trigger a **robust initial immune response**

? **Antibody titers are lower** than in the general population

? **Long-term protection** remains unclear

Staadegaard et al., EClinicalMedicine, 2022

Primary Prevention – 9-Valent HPV Vaccine

🧬 **FDA-approved** for preventing:

- Cervical, vaginal, vulvar, and anal cancers
- Genital warts
- Head and neck cancers (including oropharyngeal)

💉 **Vaccination Schedule**:

- Recommended at ages 11–12
- 3-dose series at 0, 1–2, and 6 months
- **2-dose series not recommended** for people with HIV
- 🚫 Not recommended during pregnancy

Clinicalinfo.HIV.gov

Catch-up HPV Vaccination in People with HIV

Ages 13–26

- If not previously vaccinated:
  → 3-dose series at 0, 1–2, and 6 months

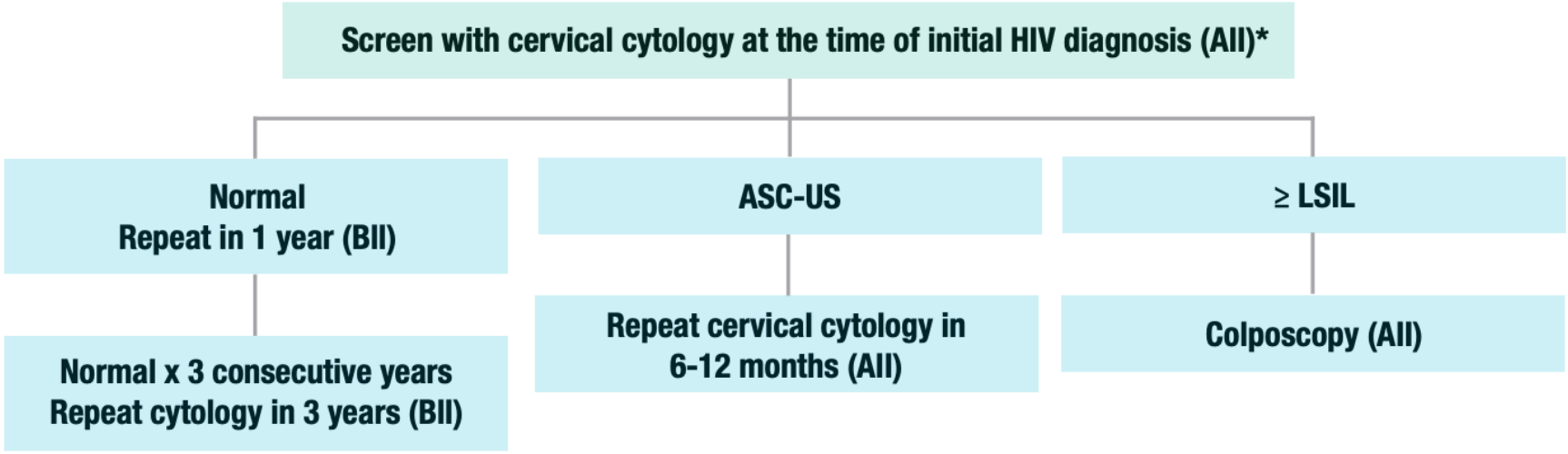
Ages 27–45

- Not routinely recommended
- Shared decision-making for those at risk of new HPV infection

Previously vaccinated with bivalent or quadrivalent vaccine?

→ Consider **9-valent HPV vaccination**

Screening algorithm for cervical cancer in people living with HIV aged 21-29 years



* Please see text for guidance regarding hr-HPV screening in persons aged 25-29 years

Key: ASC-US = atypical squamous cells of undetermined significance; hr-HPV = high-risk human papillomavirus; LSIL = low-grade squamous intraepithelial lesion

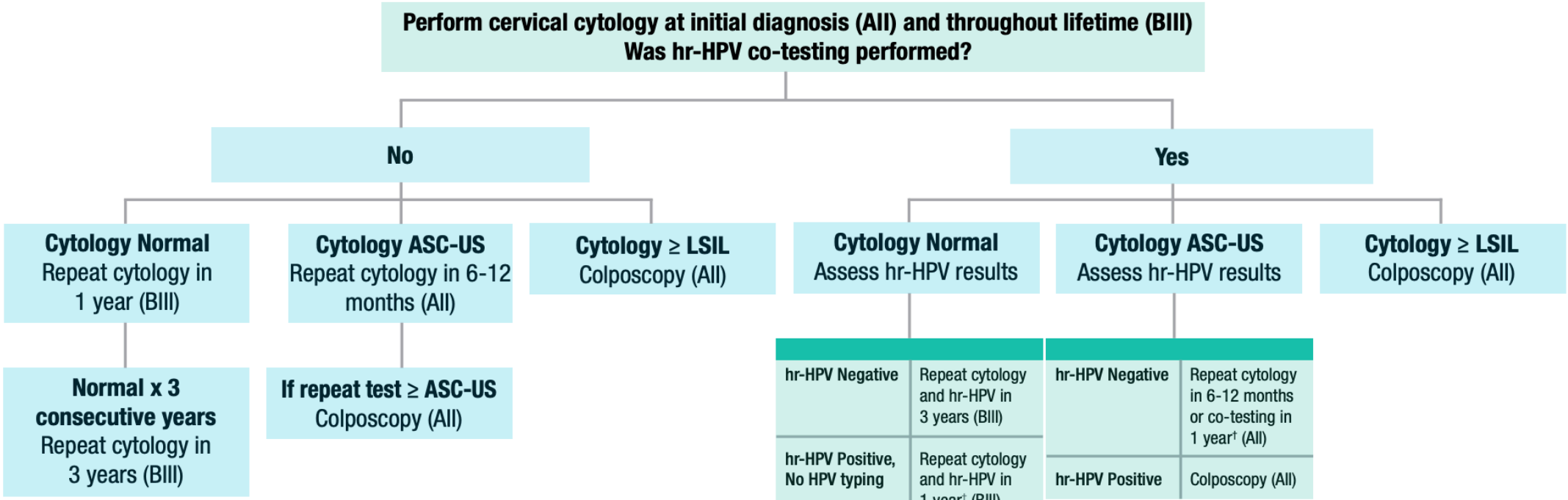
HIV.org- Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV

Cervical Cancer Screening: Patients with HIV <30 Years

Recommendation	Details
Start Screening	At age 21, regardless of sexual activity
Ages 21–29	Cytology at baseline and every 12 months
After 3 Normal Annual Cytologies	Screen every 3 years
HPV Co-testing	Not recommended for <30 years
If ASCUS/HPV+ or LSIL or worse	Refer to colposcopy
If ASCUS HPV- or no HPV test	Repeat cytology in 6–12 months
If repeat abnormal	Refer to colposcopy

Moscicki et al. J Low Genit Tract Dis 2025

Screening algorithm for cervical cancer in people with HIV aged 30 years and older



† If at repeat testing either cytology is ≥ ASC-US or any hr-HPV is detected, refer for colposcopy (AII)

Key: ASC-US = atypical squamous cells of undetermined significance; HPV = human papillomavirus; hr-HPV = high-risk HPV; LSIL = low-grade squamous intraepithelial lesion

Cervical Cancer Screening: Patients with HIV ≥30 Years Old

- **Cytology testing only:**
  - Baseline and every 12 months after HIV diagnosis
  - After 3 normal tests, every 3 years
  - Abnormal results: follow-up as for <30 years

- **Cytology + HPV cotesting:**
  - Baseline cotest at diagnosis
  - If both normal and HPV negative: cotest every 3 years
  - If cytology normal but HPV positive:
    - Repeat cotest in 1 year
    - If repeat abnormal or HPV+, refer to colposcopy
  - Or HPV genotyping:
    - If HPV 16/18+, refer to colposcopy
    - If HPV 16/18-, repeat cotest in 1 year

- **HPV 16 or 16/18 specified in cotesting:**
  - Baseline cotest at diagnosis
  - If normal and HPV 16/18 negative: cotest every 3 years
  - If HPV 16 or 16/18+, refer to colposcopy

Overview of Cervical Cancer Screening Guidelines

	<21 Years	21–24 Years	25–29 Years	≥30 Years
NIH OAR Adult and Adolescent OI Guidelines (specific to people with HIV)	No screening recommended	**Cytology Only** • Cytology yearly If normal cytology on 3 consecutive annual tests, adjust to every 3 years	**Cytology Only** • Cytology yearly If normal cytology on 3 consecutive annual tests, adjust to every 3 years	**Co-testing** • Co-testing yearly If normal cytology and hr-HPV negative on 3 consecutive years, adjust to every 3years **Cytology Only** • Cytology yearly • If normal cytology on 3 consecutive years, adjust to every 3 years
USPSTF (2018) (no HIV-specific guidance)	No screening recommended	Cytology every 3 years	Cytology every 3 years	**Cytology Only** • Every 3 years **hr-HPV Testing Only** • Every 5 years **Co-testing** • Every 5 years
ACS (2020) (no HIV-specific guidance)	No screening recommended		**Preferred** • Primary HPV test every 5 years **Acceptable** • Co-testing every 5 years • Cytology alone every 3 years	**Preferred** • Primary HPV test every 5 years **Acceptable** • Co-testing every 5 years • Cytology alone every 3 years
WHO (2021) (HIV-specific guidance)	No screening recommended	No screening recommended	**Preferred** • Primary HPV test (provide-obtained or self-collection) every 3–5 years	**Preferred** • Primary HPV test (provider-obtained or self-collection) every 3–5 years

Beyond the Cervix – Other HPV-Related Cancers in PLWH

Higher incidence of:

1. **Anal cancer** (especially in MSM)
2. **Oropharyngeal cancers**
3. **Vulvar, vaginal, penile cancers**

📌 Anal cancer risk still high even **after age 50**.

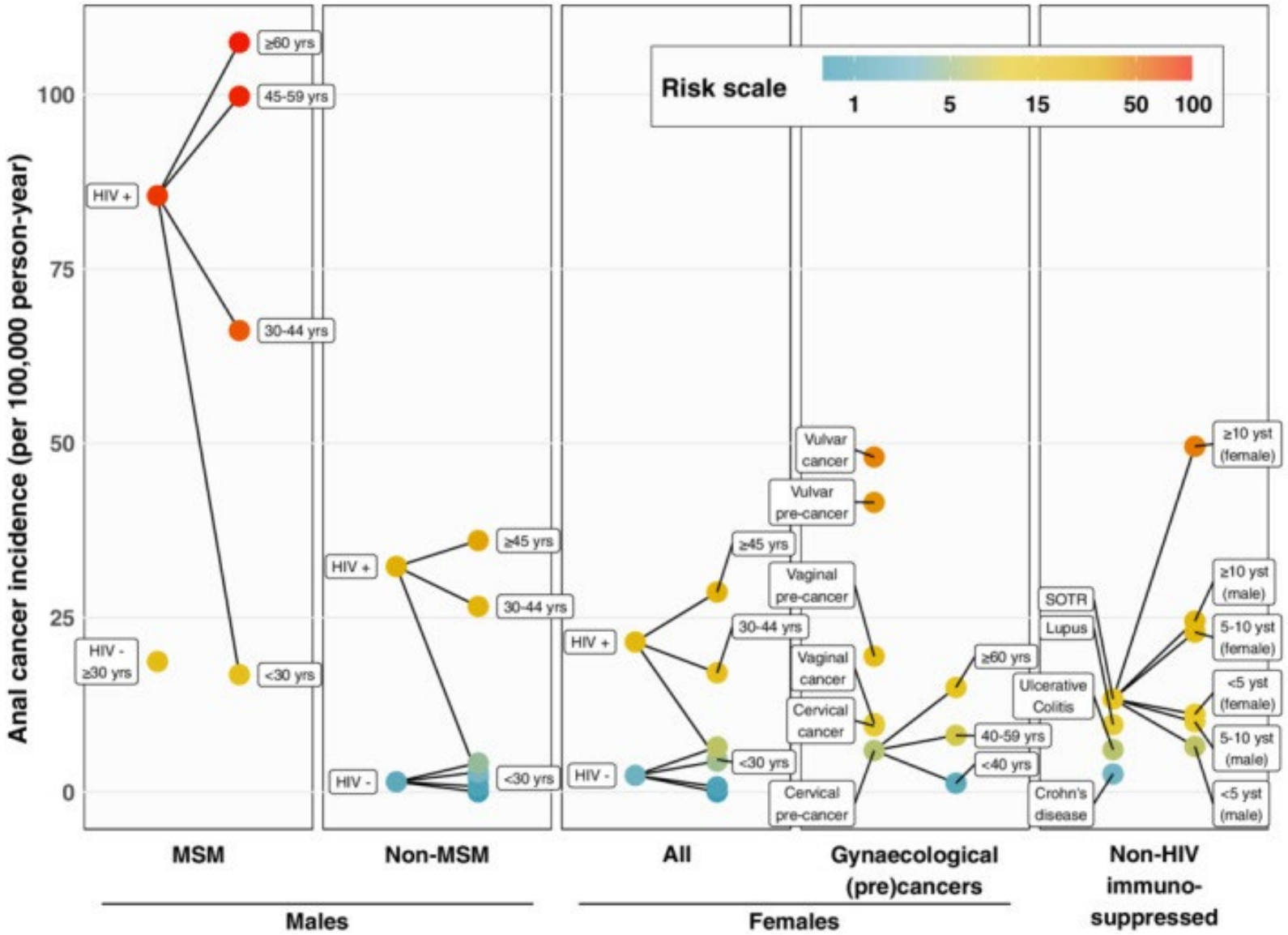
• Risk Factors:

CD4 <200 cells/μL

Lack of HPV vaccination

Co-infection with other STIs

Anal Cancer incidence



Anal Cancer screening

Anal Cancer Screening Guidelines

Immunosuppressed Women Without HIV Infection

Increased Screening regardless of immunosuppressant use

Follow CDC HIV Cervical Cancer Screening Guidelines:

- **Solid Organ Transplant (SOT) recipients**
- **End-Stage Renal Disease (ESRD)** patients on dialysis
- **Hematopoietic Stem Cell Transplant (HSCT)** recipients
- **Systemic Lupus Erythematosus (SLE)** — whether or not on immunosuppressants

Recommend Increased Screening If on Immunosuppressive Therapy:

- **Rheumatoid Arthritis (RA)**
- **Inflammatory Bowel Disease (IBD)**
- **Multiple Sclerosis (MS)**

.

Patients on Disease-Modifying Therapies (DMTs) or Monoclonal Antibodies (MABs)

- Due to potential effects on HPV persistence and cervical dysplasia, although data is mixed.
- Shared decision-making is recommended

Summary of Cervical Cancer (CC) Screening and Vaccination recommendations

	General Population CC screening	Increased screening with immunosuppressant use	Increased screening regardless of immunosuppressant use	HPV Vaccination
Solid organ transplant			X	X
End-stage renal disease			X	X
Hematopoietic stem cell transplant			X	X
Systemic lupus erythematosus			X	X
Rheumatoid arthritis	X	X		X
Inflammatory bowel disease	X	X		X
Multiple sclerosis	X	X		X
Disease-modifying therapies or monoclonal antibodies	X	X		X

HPV Vaccine Recommendations in Immunosuppressed Populations

Routine vaccination starting at age **9**, catch-up to **26**, shared decision up to **45**.

3-dose series recommended for all immunosuppressed patients.

Solid Organ Transplant (SOT):

- Complete series **before transplant** if possible.
- If not, give **1 dose pre-transplant**, resume **6 months post-transplant**.

Hematopoietic Stem Cell Transplant (HSCT):

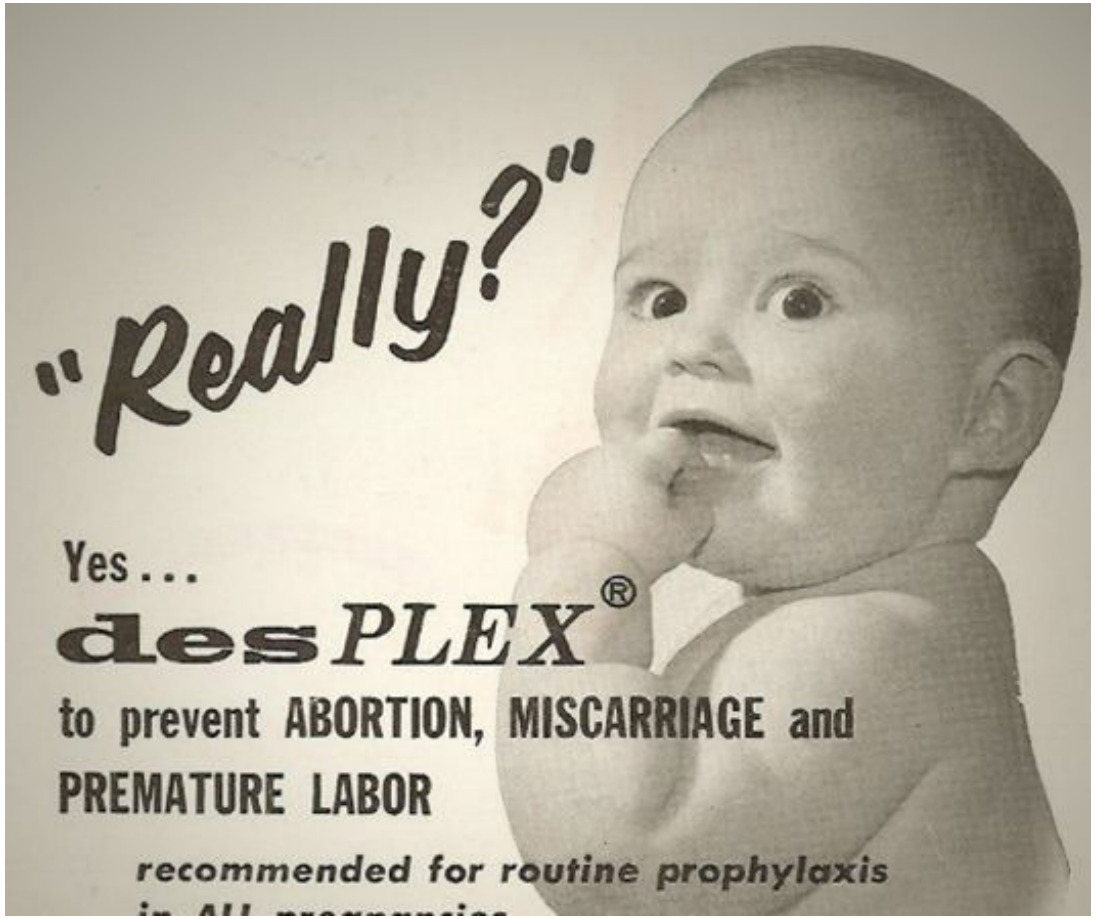
- **Re-vaccinate** post-transplant (up to age 45).

Disease-Modifying Therapy (DMT)/Monoclonal Antibody (MCA):

- Begin **before starting immunosuppressive treatment**.

- Moscicki et al. J Low Genit Tract Dis 2025

People Exposed to Diethylstilbestrol (DES) In Utero



Legacy of DES Exposure: A Unique Cancer Risk

DES is an orally active nonsteroidal estrogen administered for a wide range of obstetric and gynecological conditions from 1938 to 1971.

In utero exposure is associated with a **significantly increased risk** of clear cell adenocarcinoma (CCA) of the cervix and vagina.

Risk remains **elevated into older age**, but **absolute incidence is low**.

DES-exposed individuals are excluded from routine screening cessation at age 65

Continue **vaginal and cervical cytology** annually until age 65

Screening can continue beyond 65 via **shared decision-making**, considering lack of strong evidence and potential harms.

Marcus et al. J Low Genit Tract Dis 2024

HPV-Related Cancer Risks in Transgender Individuals

- Face barriers to care due to provider bias, systemic discrimination, and limited access to inclusive services.
- Insurance often fails to cover hormone therapy, mental health support, or gender-affirming procedures.
- These barriers contribute to disparities in cancer screening and preventive care.

Transmasculine Individuals

Cervical cancer screening should be performed according to age-related guidelines.

Transmasculine individuals have a 10-fold higher rate of unsatisfactory Pap tests compared with cisgender individuals

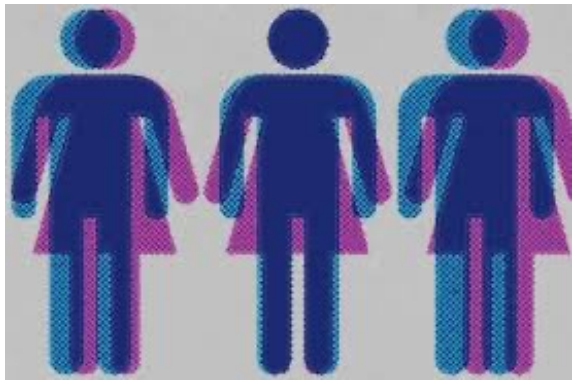
Inadequate Pap tests have been shown to cause increased anxiety in non-transgender females, which is associated with lower likelihood of returning for a repeat test within the recommended time frame

Long-term testosterone therapy induces vaginal and cervical atrophy that can alter Pap results and make the exam more difficult.

Clinicians should receive training in increasing comfort for FTM patients during the exam

Peitzmeier et al., JGIM, 2014

Transfeminine Individuals



A neovagina does not require routine cytologic screening.

The vagina is lined by skin, not mucosa

Vaginal exams, however, may be indicated to screen for sexually transmitted infections and to address certain pelvic issues after vaginoplasty

Barriers to HPV Screening and Prevention in Vulnerable Population

- **Limited awareness** of HPV-related cancer risks in immunosuppressed populations
- **Stigma and discrimination** (e.g., HIV status, gender identity, incarceration history)
- **Lack of provider training** on non-standard guidelines for vulnerable groups
- **Inadequate access** to specialized care (e.g., colposcopy, follow-up)
- **Disrupted care continuity** during transitions (e.g., release from incarceration, changes in insurance)
- **Low HPV vaccination uptake**, especially in older adults and high-risk groups
- **Psychosocial barriers**, including medical mistrust, trauma, and fear of procedures
- **Cost and insurance coverage limitations** for preventive services

Call to Action: Advancing Equity in HPV Cancer Prevention

1

Recognize risk beyond the general population
Identify and prioritize screening for individuals with HIV, transplant recipients, autoimmune disease, and those with DES exposure.

2

Apply tailored screening guidelines
Integrate updated, population-specific recommendations into clinical practice—especially for immunosuppressed individuals.

3

Advocate for access and system-level change
Support policies expanding access to HPV vaccination, screening, and follow-up care—especially in carceral, rural, and underserved communities.

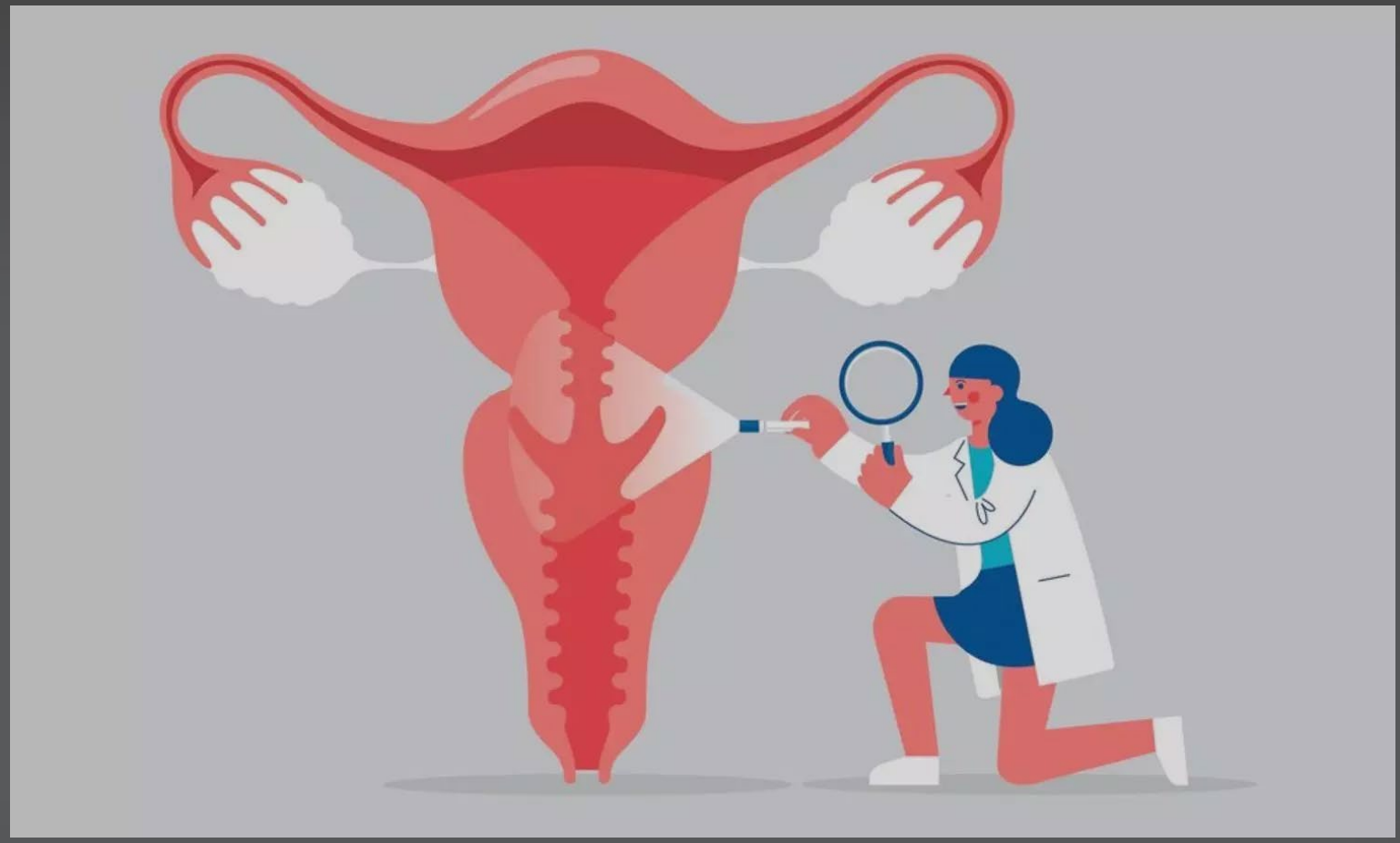
4

Empower through education
Engage patients in shared decision-making, emphasizing culturally sensitive, trauma-informed communication.

5

Strengthen care coordination
Build interdisciplinary partnerships across infectious disease, oncology, and primary care to ensure seamless follow-up and treatment.

Questions?



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