An Update on Screening for Non-AIDS-Defining Cancers

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Learning Objectives

After attending this presentation, learners will be able to:

- Describe overall trends in non-AIDS-defining cancers for people with HIV
- List non-AIDS-defining cancers with increased incidence in people with HIV
- Implement appropriate screening for non-AIDS-defining cancers for people with HIV

Financial Relationships With Ineligible Companies (Formerly Described as Commercial Interests by the ACCME) Within the Last 2 Years

Dr Wilkin has received grants paid to his institution from Merck & Co, Inc., and Viiv Healthcare. He has served as a consultant to Merck & Co, Inc. (Updated 10/04/21)
Cancer has been linked to HIV since the beginning of the epidemic in the U.S.

HIV therapy restoring immunity has resulted in lower rates of AIDS-defining cancers

Increased life expectancy due to HIV therapy has also impacted the cancer burden

- HIV infection does not increase the risk of every cancer type.
- However, if more PHIV survive to ages >50, then more PHIV are alive to develop cancer.
However, cancer risk remains elevated in people living with HIV (PLWH)

Standardized Incidence Ratios (SIRs) for cancer in PLWH (1996-2012), compared to the general U.S. population

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Observed Cases</th>
<th>SIR (95% CI)*</th>
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</thead>
<tbody>
<tr>
<td>All cancers</td>
<td>27,594</td>
<td>1.69 (1.67-1.72)</td>
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<tr>
<td>AIDS-defining cancers</td>
<td>6,384</td>
<td>14.0 (13.6-14.3)</td>
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<tr>
<td>Kaposi sarcoma</td>
<td>1,564</td>
<td>4.66 (4.15-5.21)</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>2,298</td>
<td>3.06 (2.81-3.33)</td>
</tr>
<tr>
<td>Cervical cancer</td>
<td>2,042</td>
<td>2.96 (2.69-3.23)</td>
</tr>
<tr>
<td>Non-AIDS cancers (NADC)</td>
<td>14,344</td>
<td>1.21 (1.19-1.23)</td>
</tr>
<tr>
<td>Non-viral NADC</td>
<td>9,339</td>
<td>6.01 (5.69-6.44)</td>
</tr>
<tr>
<td>Viral NADCs</td>
<td>4,144</td>
<td>3.39 (3.23-3.55)</td>
</tr>
<tr>
<td>Anus</td>
<td>297</td>
<td>1.45 (1.14-1.84)</td>
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<tr>
<td>Liver</td>
<td>1,104</td>
<td>3.21 (2.93-3.51)</td>
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<tr>
<td>Merkel cell carcinoma</td>
<td>118</td>
<td>2.56 (1.84-3.47)</td>
</tr>
<tr>
<td>Vagina</td>
<td>25</td>
<td>3.05 (2.36-4.24)</td>
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<tr>
<td>Vulva</td>
<td>101</td>
<td>4.25 (3.10-5.83)</td>
</tr>
<tr>
<td>Penis</td>
<td>114</td>
<td>5.30 (4.38-6.40)</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>875</td>
<td>7.70 (7.06-8.37)</td>
</tr>
</tbody>
</table>

Viral NADCs are increased 5 fold in PLWH (e.g. HPV, HBV, HCV and EBV cancers)
Non-viral NADCs are not increased in HIV (e.g. breast, colorectal, prostate)

Exception: Lung cancer is increased 2 fold in PLWH

Non-AIDS cancer is now a leading cause of death in PLWH

- The D:A:D study (11 HIV cohorts) reported that NADCs were the leading cause of non-AIDS death (1999-2011) @ 15% (Smith Lancet 2014)
- NA-ACCORD (>20 HIV cohorts) reported cancer as a leading cause of non-AIDS death (1995-2009) @ 10% (Engels CID 2017)
  - Approximately 7% of deaths due to NADCs
- The HIV/AIDS Cancer Match (HACM) Study reported population attributable fractions for cancer mortality (PAF%) in PHIV between 2001-2015.
  - PAF% increased from 7% to 12% for NADCs
  - PAF% held steady at 5% over time for ADCs

PLWH experience higher, stage-adjusted cancer-specific mortality
Summary: Evolving cancer burden in PHIV

- Rates of AIDS-defining cancers (e.g., Kaposi sarcoma) have declined with widespread effective HIV therapy in the U.S.
- Despite effective HIV therapy, PLWH remain at higher risk for many cancers, particularly infection-associated cancers.
- Non-AIDS-defining cancers not linked to infections are now more common in PLWH, reflecting the aging of the HIV population due to effective HIV therapy.
- One result of this changing cancer profile is that non-AIDS-defining cancers are now a leading cause of death in PHIV.

Screening for non-AIDS cancers

- US Preventive Health Task Force recommends cancer screening for
  - Breast cancer (same as those without HIV)
  - Cervical cancer (closer follow-up)
  - Colorectal cancer (same as those without HIV)
  - Lung cancer screening (same as those without HIV)
- Some groups recommend prostate screening after counseling

Lung cancer screening

- Active screening diagnoses lung cancer at earlier stages
- Earlier stages have better survival
- Who should be screened?
  - 55 and older
  - Current or former smoker (within 15 years of quitting)
  - 30 pack year history
  - No signs of lungs cancer

Journal of Thoracic Oncology 2017 12: 1109-1121
National Lung Cancer Screening Trial

- Randomized 50K pts to 3 yearly low-dose CT scans vs. CXRs
- Abnormalities concerning for possible cancer evaluated further
- Most abnormalities (>95%) were not cancer

CT screening arm diagnosed more cancers at an earlier stage allowing curative therapy

CT screening arm had a lower risk of death from lung cancer

Screen 320 to prevent one death
Other cancer prevention activities per USPTH/ACIP

- Hepatocellular carcinoma
  - Vaccination against hepatitis B and other prevention practices
  - Treatment of hepatitis B and C
  - Screening for hepatocellular carcinoma
- Human papillomavirus-related cancers
  - 9-valent HPV vaccination for prevention of anal, cervical, oropharyngeal, penile, vaginal and vulvar cancers
- Smoking cessation
- Aspirin use for prevention of colorectal cancer in those with >10% ASCVD risk for MI
- Breast CA medication, BRCA screening in selected groups

Anal Cancer is common among PLWH

HPV Infection and Progression to Anal Cancer

- **Initial HPV Infection**
- **Continuing Infection**
- **Anal HSIL**
- **Anal LSIL**

Cleared HPV Infection

Decreased cell-mediated immunity

Prevention of Anal Cancer

- **Initial HPV Infection**
- **Continuing Infection**
- **Anal HSIL**

Cleared HPV Infection

**Anal cancer prevention**

Goal is to identify pre-cancerous areas of the anus that can be removed to prevent invasive cancer

- **SCREEN** with cytology or HPV testing
- **DIAGNOSE** with High Resolution Anoscopy
- **TREAT** HSIL with ablation or topical therapy

Anal cancer is treated with combined chemotherapy and radiation

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**ANCHOR Trial**

- Screen > 17,385
- Enroll 5,058
- Retain for 5-8 years
- Estimated < 50 develop cancer
ACIP HPV Vaccine Recommendations

- Children and adults age 9-26
  - Routine vaccination of 11-12 girls
  - Catch-up vaccination up to age 26

- Adults age 27-45
  - Shared decision making

HPV vaccine efficacy at non-cervix sites

Costa Rica Vaccine Trial
One-time detection of HPV16/18 infection 4 yrs. after vaccination

Summary: Reducing NADC in PLWH

- Implement screening for NADC
  - Breast, cervical, colorectal, lung
  - Lung cancer screening identifies cancer at earlier stages where treatment is curative

- Evolving data on screening for anal cancer will say whether this should be standard of care.

- HPV vaccination for prevention of HPV-associated cancers
  - Prevents anal, cervical, penile, vaginal, vulvar cancers
  - Existing data suggests preventions against HPV-associated oropharyngeal cancer