AETC AIDS Education & Training Center Program Southeast

Primary Care in People with HIV (PWH)

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Disclosures

- *None*

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- *"Funding for this presentation was made possible by cooperative agreement U1OHA30535 from the Health Resources and Services Administration HIV/AIDS Bureau. The views expressed do not necessarily reflect the official policies of the Department of Health and Human Services nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government. Any trade/brand names for products mentioned during this presentation are for training and identification purposes only."*

Learning Objectives

- Upon completion of this educational activity:
  - Participants will be able to identify drug interactions between ART and commonly prescribed medications in primary care
  - Participants will be able to compare recommended cancer screening and vaccinations for the general population and PWH.
  - Participants will be able to discuss incidence and types of HPV-related cancer with patients
  - Participants will be able to have informed risk/benefit discussion of medication for prevention of cardiovascular disease.
  - Participants will be able to identify which PWH need screening for osteoporosis.

Poll Questions

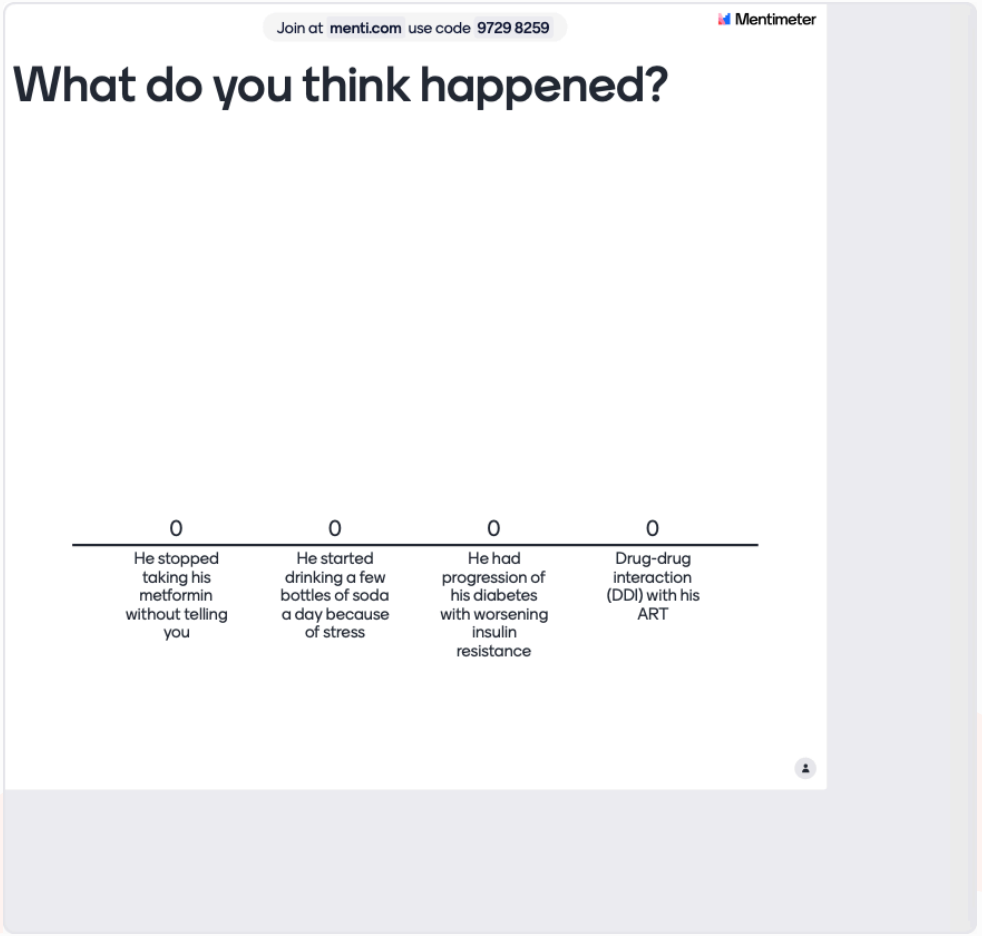
- Join at menti.com
- Code 9729 8259

Poll Question

- 63 yo man with PMH HIV, GERD, OA and DM2 comes to your office reporting increased thirst, frequent urination and fatigue. He's been using his partner's glucometer and has seen readings in the 200s-300s for the last week. His diabetes was previously very well controlled (last a1c 3 months ago was 6.9%).
- Medications:
  - HIV: EVG/COBI/FTC/TAF
  - GERD: famotidine
  - OA: PRN IBU
  - DM2: metformin

What do you think happened?

- A) He stopped taking his metformin without telling you
- B) He started drinking a few bottles of soda a day because of stress
- C) He had progression of his diabetes with worsening insulin resistance
- D) Drug-drug interaction (DDI) with his ART



Drug Interactions

Boosters

- Cobicistat
- Ritonavir
- Both strongly inhibit CYP3A4

Many meds

- Migraines
  - CGRP antagonists (CI) (ubrogepant and rimegepant)
- Men's health
  - PDE5-I (dose reduce)
  - Alpha-blockers (except terazosin)
- Gout
  - Colchicine (dose reduce)

More Drug Interactions with Boosters

- Steroids (glucocorticoids)
  - Oral
  - Nasal sprays (except flunisolide and beclomethasone)
  - Inhalers (see below)
  - Joint injections
  - Eye drops (prolonged use)
- Inhalers
  - LABA: except olodaterol, formoterol
  - ICS: except beclomethasone
- Anticoagulants
  - Rivaroxaban (CI)
  - Apixaban (dose reduce 50%)
  - Coumadin (monitor closely)
  - Dabigatran (monitor closely)
  - No interaction with heparin
- Antiplatelets
  - Clopidogrel (D)
  - Ticagrelor (CI)
  - No interaction with prasugrel
- Mood
  - Buspirone (dose reduce)
- Statins

Drug Interactions

- INSTI
  - Bictegravir
  - Dolutegravir
  - Elvitegravir

- DM2
  - Metformin (dose reduction)
- Polyvalent cations
  - Multivitamin, calcium, magnesium, iron
  - Must be separated or taken together with food

- NNRTI
  - Rilpivirine (PO only)
- PI
  - Atazanavir

- GERD
  - PPI (CI)
  - H2B (must be separated)

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  - OA: PRN IBU
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What do you think happened?

- A) He stopped taking his metformin without telling you
- B) He started drinking a few bottles of soda a day because of stress
- C) He had progression of his diabetes with worsening insulin resistance
- **D) DDI with his ART**

- About two weeks ago, he went to see orthopedic surgery for his osteoarthritis. The same day he received a steroid injection in his right knee
- Unfortunately, he had to be put back on insulin for about 2-3 months until the effect of the steroid wore off

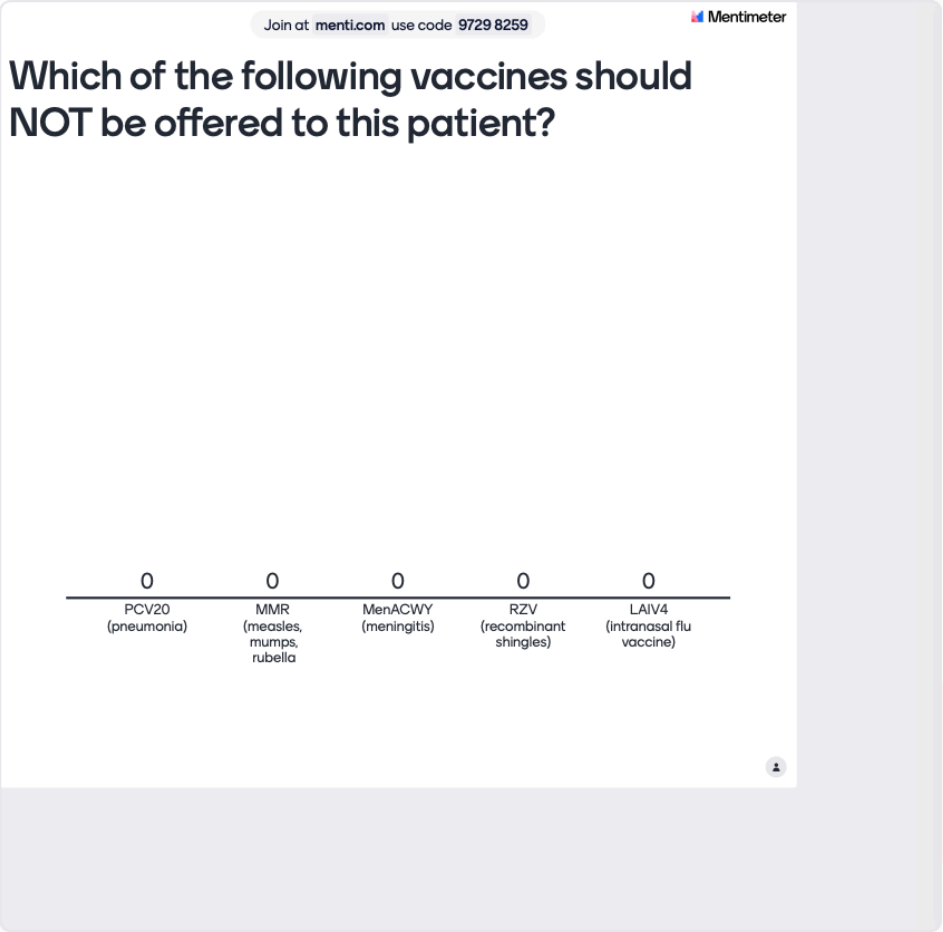
Poll Question

- 42 yo woman with PMH HIV, HTN presents to your office to establish primary care. She recently moved to the US from the DRC. In the process of moving she was diagnosed with HIV and was just started on ART last month. She works as a nurse.

- Initial lab work showed:
  - HIV VL 112,042
  - CD4 359
  - Hep A IgG +
  - Hep B Surface Ab +
  - Hep B Surface Ag -
  - Hep C Ab –
  - Measles Ab +
  - Mumps Ab -
  - Rubella Ab -
  - Varicella Ab +

Which of the following vaccines should NOT be offered to the patient?

- A) PCV20 (pneumonia)
- B) MMR (measles, mumps, rubella
- C) MenACWY (meningitis)
- D) RZV (recombinant shingles)
- E) LAIV4 (intranasal flu vaccine)



Vaccines

Vaccine	19–26 years	27–49 years
COVID-19	2- or 3- dose prim	
Influenza inactivated (IIV4) or **Influenza recombinant** (RIV4) — or — **Influenza live, attenuated** (LAIV4)	1 dose annually — or — 1 dose annually	
Tetanus, diphtheria, pertussis (Tdap or Td)	1 dose Tdap each pregnancy; 1 dose Td/	
	1 dose Tdap, then Td or T	
Measles, mumps, rubella (MMR)	1 or 2 doses depen (if born in 19	
Varicella (VAR)	2 doses (if born in 1980 or later)	
Zoster recombinant (RZV)	2 doses for immunocompromising conditions (see notes)	
Human papillomavirus (HPV)	2 or 3 doses depending on age at initial vaccination or condition	27 through 45 years
Pneumococcal (PCV15, PCV20, PPSV23)	1 dose PCV15 followed b OR 1 dose PCV20 (see n	
Hepatitis A (HepA)	2, 3, or 4 doses de	
Hepatitis B (HepB)	2, 3, or 4 doses dependi	
Meningococcal A, C, W, Y (MenACWY)	1 or 2 doses depending on indication,	
Meningococcal B (MenB)	2 or 3 doses depending on vaccine and indi	
	19 through 23 years	
***Haemophilus influenzae* type b** (Hib)	1 or 3 doses depe	

Recommended vaccination for adults who meet age requirement, lack documentation of vaccination, or lack evidence of past infection

Recommended vaccination for adults with an additional risk factor or another indication

Vaccine	Pregnancy	Immuno-compromise (excluding H infection)	HIV infection CD4 percentage and count	
			<15% or <200 mm³	≥15% and ≥200 mm³
COVID-19			See Notes	
IIV4 or RIV4 — or — LAIV4			traindicated	
Tdap or Td	1 dose Tdap each pregnancy			
MMR	Contraindicated*	Contra	cated	
VAR	Contraindicated*	Contra	cated	
RZV		2 d	at age ≥19 years	
HPV	Not Recommended*	3 dose	rough age 26 years	
Pneumococcal (PCV15, PCV20, PPSV23)				
HepA				
HepB	3 doses (see notes)			
MenACWY		1 or 2 do	depending on indication	
MenB	Precaution		2 or 3 doses depend	
Hib		3 doses HSCT recipients on		

Highlights

- **RSV**: ACIP approved 1 dose of RSV vaccine for adults 60+ at increased risk at June 2023 meeting
- **Mpox**: ACIP approved 2-dose JYNNEOS series at February 2023 meeting for those at risk of mpox during an outbreak
- **Polio**: ACIP recommended primary series with IPV if never vaccinated/incompletely vaccinated. Can consider booster with another dose of IPV if at increased risk of exposure to poliovirus
- **Pneumonia**: PCV15 and PCV20 are now available
- **Shingles**: ACIP recommended RZV in immunosuppressed individuals 19+ yo in fall 2021
- **Hepatitis B**: not a new vaccine but we were only recently able to get Heplisav (with novel adjuvant) and it has worked well for patients who were non-responders to prior series of hepatitis B vaccine
- **Meningitis**: most of our patients are at/past the 5 yr mark since primary series after ACIP recommendation in 2016 and are now due for a booster with MenACWY

Viens LJ, Henley SJ, Watson M, et al. Human papillomavirus-associated cancers - United States, 2008-2012. MMWR Morb Mortal Wkly Rep 2016;65:661-6.

Poll Question

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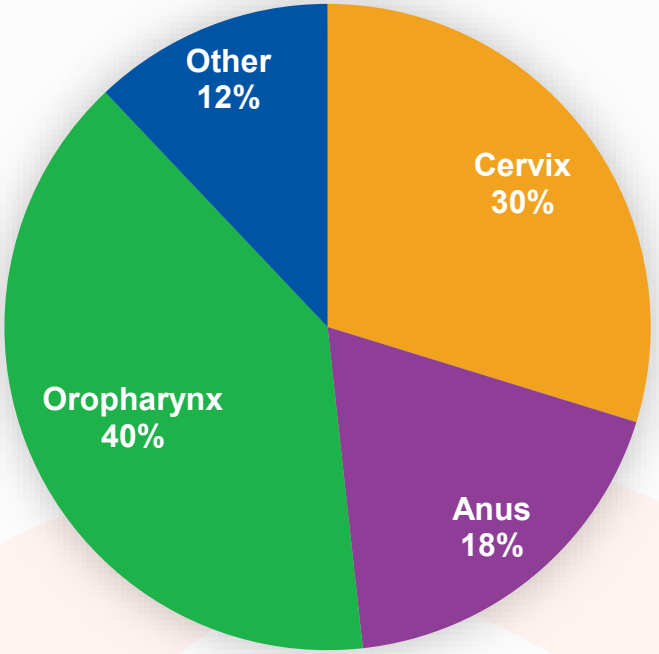
- C) MenACWY (meningitis)
- D) RZV (recombinant shingles)
- **E) LAIV4 (intranasal flu vaccine)**

- Live attenuated influenza vaccine (intranasal) is contraindicated for ALL patients with HIV
- MMR is also live but patients with CD4 >200 and CD4% >15% can receive

HPV-Associated Cancers in US

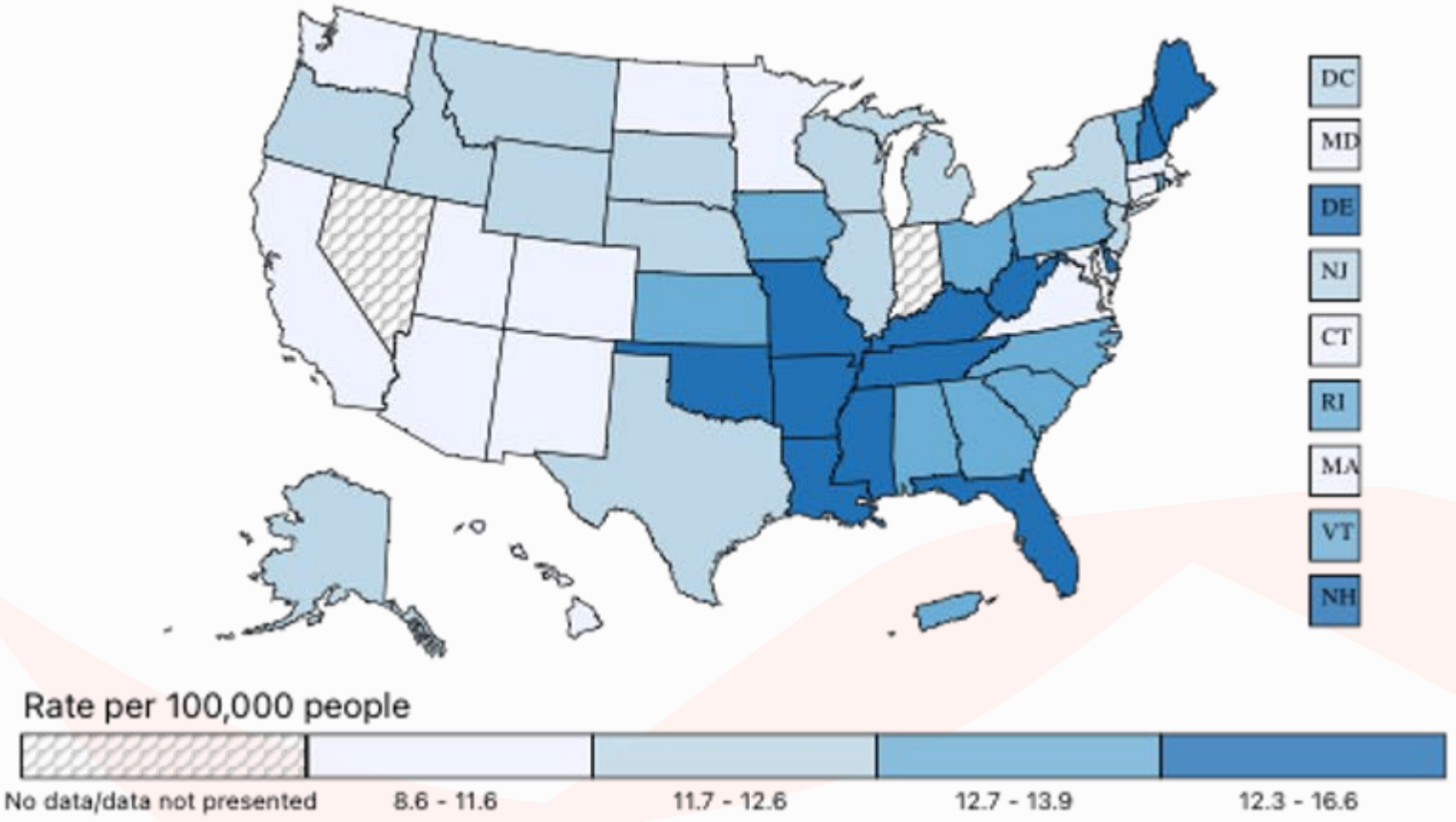
- From 2015-2019, CDC estimated 37,300 new cancers annually that were attributable to HPV
- Oropharyngeal* cancers ~40%
  - Women 1.7 per 100,000
  - Men 9.1 per 100,000
- Cervical cancer ~30%
  - Women 7.2 per 100,000
- Anal/rectal cancer ~18%
  - Women 2.5 per 100,000
  - Men 1.4 per 100,000
- Other cancers ~12%
  - Vulva, vagina, penis



*Oropharyngeal cancers include tongue, tonsils, soft palate, pharynx

National Program of Cancer Registries SEER*Stat Database: U.S. Cancer Statistics Incidence Analytic file 1998–2018. United States Department of Health and Human Services, Centers for Disease Control and Prevention. Released June 2021, based on the 2020 submission.

Rate of New HPV-associated Cancers By State
All HPV-associated Cancers, Male and Female, United States, 2016-2020

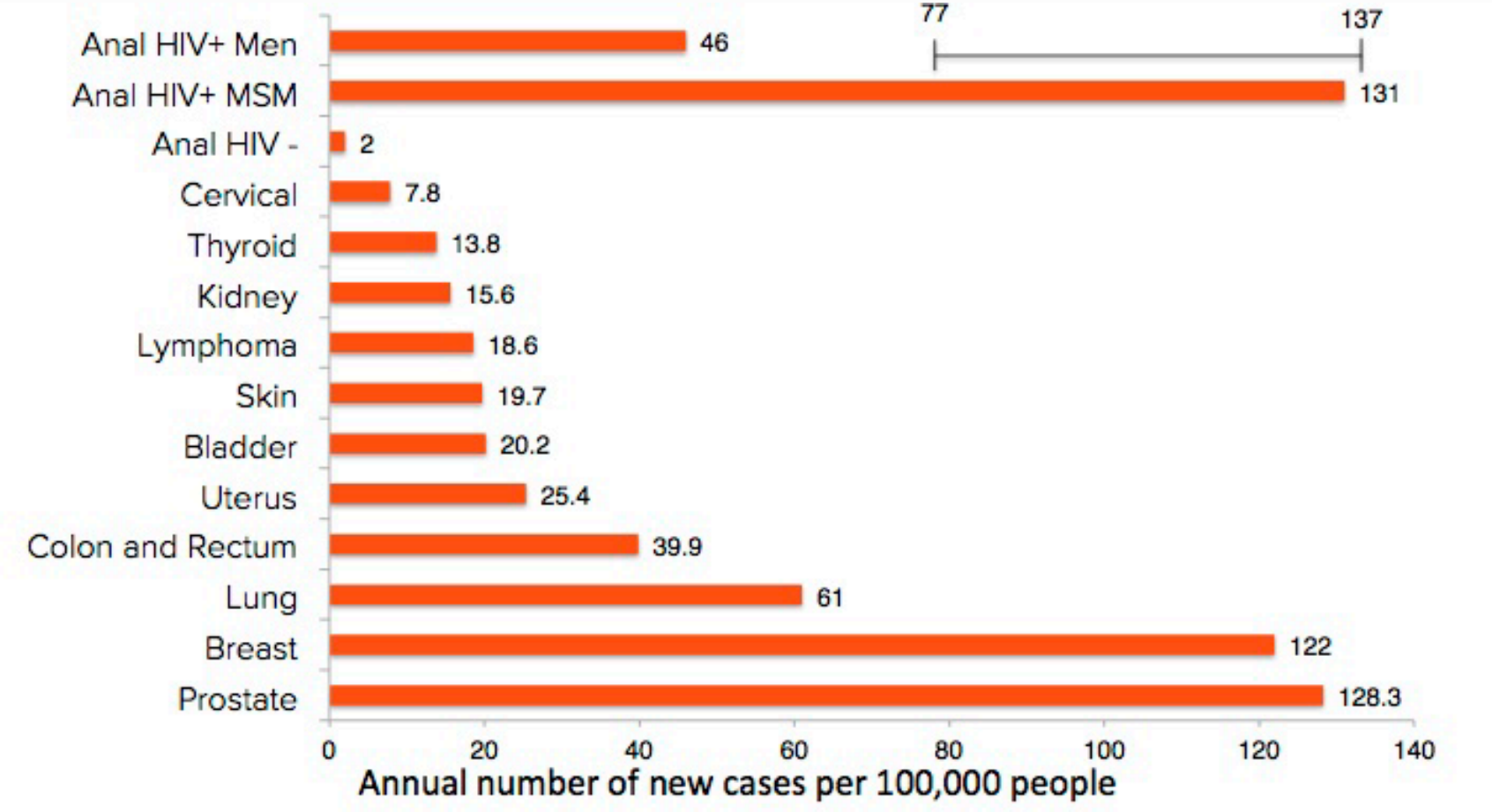


U.S. Cancer Statistics Working Group. U.S. Cancer Statistics Data Visualizations Tool, based on 2022 submission data (1999-2020): U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; https://www.cdc.gov/cancer/dataviz, released in June 2023.

HPV-associated Cancers in PWH

- People with HIV/AIDS have a significantly higher risk of developing an HPV-associated cancer
- Studies have shown a correlation between CD4 count and risk of cervical cancer and anal cancer
- Both HIV and low CD4 count are associated with presence of HPV infection and precancerous cervical lesions
- Despite this, impact of ART on reducing risk of HPV-associated cancer is uncertain
- Screening guidelines for cervical cancer differ from the general population
- No national screening guidelines for anal cancer currently exist

Anal Cancer in PWH



https://anchorstudy.org/anal-cancer-risk-among-hiv-positive-men-and-women

HPV Vaccine

- The current vaccine protects against 9 different strains of HPV
  - HPV 16 and 18- responsible for about 80% 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- responsible for about 10-15% of cervical cancers, small % of other cancers
  - HPV 6 and 11- responsible for ~90% of anogenital warts

Viens LJ, Henley SJ, Watson M, et al. Human papillomavirus-associated cancers - United States, 2008-2012. MMWR Morb Mortal Wkly Rep 2016;65:661-6.

HPV Vaccine

- Current recommendation for general population:
  - Initial vaccine series age 11-12 (2 doses only if 9-14 yo)
  - Catch-up through age 26 if missed (3 doses for 15+ yo)
  - "For adults aged 27 through 45 years, public health benefit of HPV vaccination in this age range is minimal; shared clinical decision-making is recommended because some persons who are not adequately vaccinated might benefit."

Mietes E, Szilagyi PG, Chesson HW, et al. Human papillomavirus Vaccination for Adults: Updated Recommendations of the Advisory Committee on Immunization Practices. MMWR Morb Mortal Wkly Rep 2019;68:698-702.

HPV Vaccine

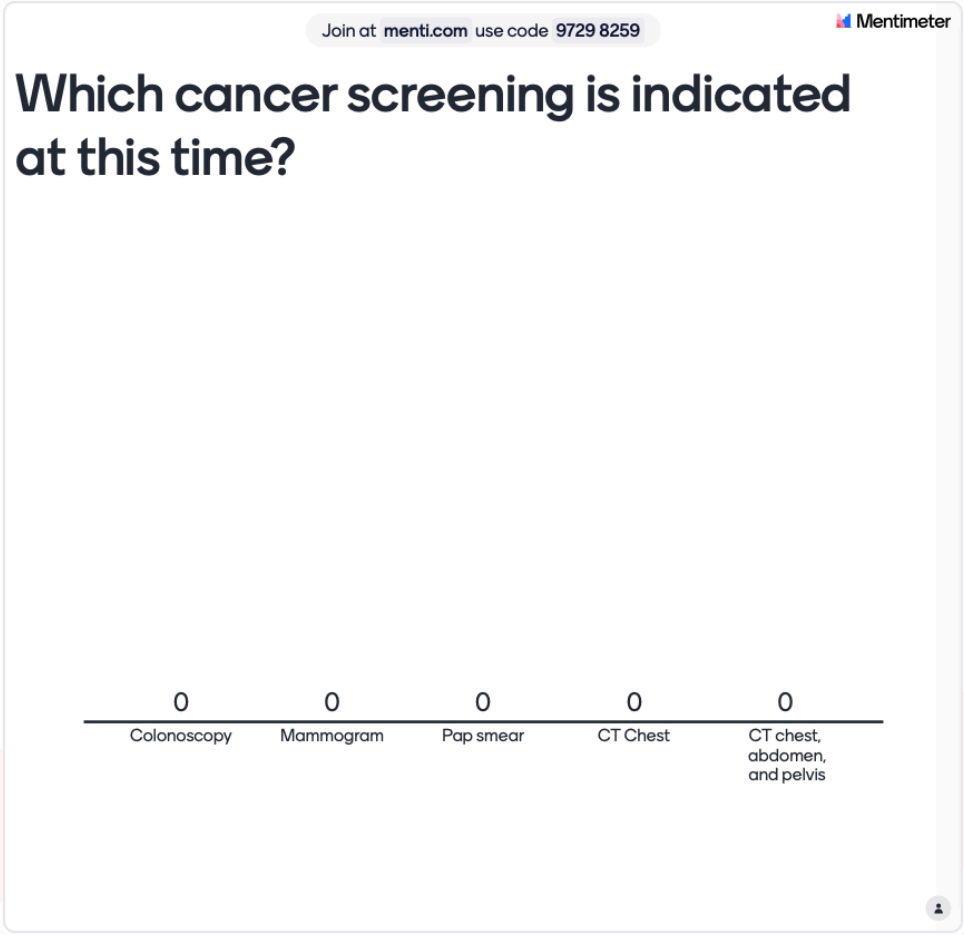
- If people previously received the 2v or 4v vaccine, there is no official recommendation to give the 9v vaccine, but it is likely safe
- While we have effective screening for cervical cancer with guidelines for follow-up and treatment of pre-cancerous lesions, this does not exist for the majority of HPV-associated cancers
- Educate your patients so they can make an informed decision!

Poll Question

- 46 yo woman with HIV and no other medical history presents to your office to establish care. She was recently diagnosed with HIV after sexual assault 6 months ago
- Social hx: smokes 1 ppd since age 20, rare alcohol use, no substances. Monogamous with 1 sexual partner for past 6 months, does not use condoms
- Her only colonoscopy was done last year. No polyps found. Her mom was diagnosed with colon cancer at age 56
- Last mammogram was done earlier this year, normal. No FH of breast cancer. No hx of abnormal mammograms.
- Her last pap smear was done 2 yrs ago. She reports normal paps her whole life.
- She has had no other testing/screening

Which cancer screening is indicated at this time?

- A) Colonoscopy
- B) Mammogram
- C) Pap smear
- D) CT chest
- E) CT chest +abdomen/pelvis



Cancer Screening

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

*Though not specifically stated, all of these recommendations are based on assuption that patient has life expectancy >10 yrs and would desire treatment/intervention if cancer were found

Cervical Cancer Screening

Recommendations for Cervical Cancer Screening for Women with HIV

Women with HIV Aged <30 Years

- WWH aged 21 to 29 years should have a Pap test following initial diagnosis of HIV.
- Pap test should be done at baseline and every 12 months **(BII)**.
- If the results of three consecutive Pap tests are normal, follow-up Pap tests can be performed every 3 years **(BII)**.
- Co-testing (Pap test and HPV test) is not recommended for women younger than 30 years.

Women with HIV Aged ≥30 Years

Pap Testing Only

- Pap test should be done at baseline and every 12 months **(BII)**.
- If the results of three consecutive Pap tests are normal, follow-up Pap tests can be performed every 3 years (**BII**).

Or

Pap Test and HPV Co-Testing

- Pap test and HPV co-testing should be done at baseline **(BII)**.
- If the result of the Pap test is normal and HPV co-testing is negative, follow-up Pap test and HPV co-testing can be performed every 3 years **(BII)**.

ANCHOR Study

Background:

- 4446 PWH with biopsy-proven anal HSIL (high-grade squamous intraepithelial lesions)
  - 35 yrs or older
- Multisite randomized controlled trial
- Intervention: randomized 1:1 to treatment or active monitoring
  - Treatments included topical fluorouracil or imiquimod, office-based ablation, or ablation or excision under anesthesia
- Follow-up: median follow-up 25.8 months
- Primary outcome: progression to anal cancer (time-to-event analysis)

Palefsky JM, Lee JY, Jay N, et al. Treatment of anal high-grade squamous intraepithelial lesions to prevent anal cancer. *N Engl J Med.* 2022; 386(24):2273-82.

ANCHOR Study

Findings:

- 9 participants in treatment group and 21 participants in active monitoring group were diagnosed with anal cancer
- Rate of progression was 173 per 100,000 person-years in treatment group and 402 per 100,000 person-years in active monitoring group
- Serious adverse events were more common in treatment group though rare

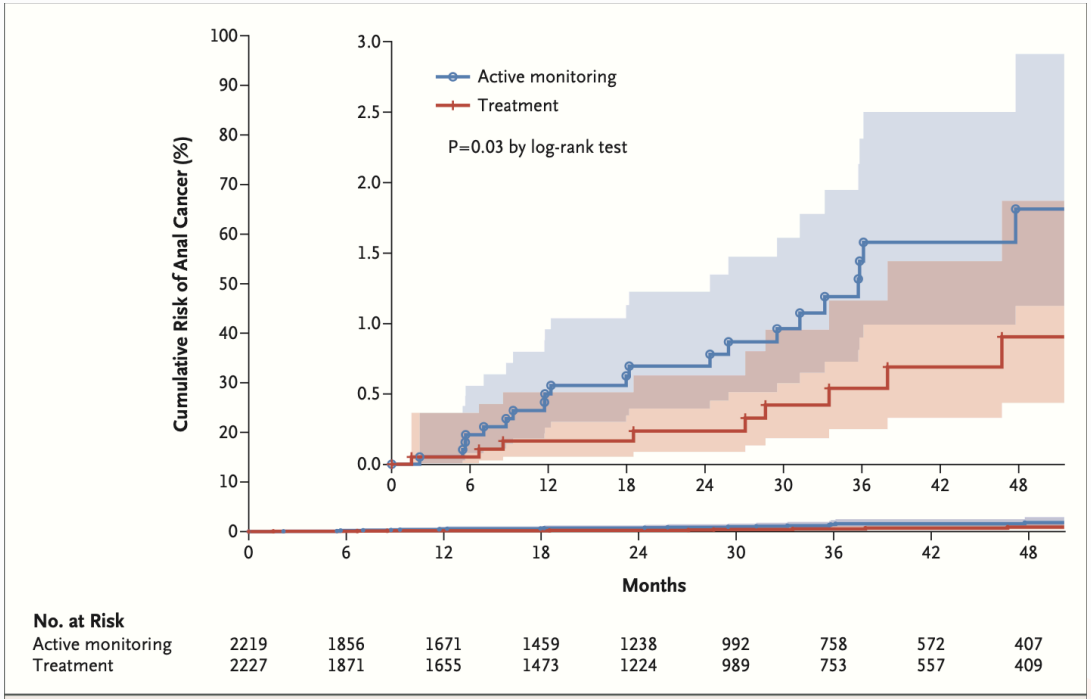


Figure 2. Kaplan–Meier Curve of the Time to Progression to Anal Cancer.
The inset shows the data on an expanded y axis. The shaded areas represent 95% confidence intervals.

Rate of progression to cancer was lower in treatment group by 57% (95% CI 6-80, p = 0.03)

Palefsky JM, Lee JY, Jay N, et al. Treatment of anal high-grade squamous intraepithelial lesions to prevent anal cancer. *N Engl J Med.* 2022; 386(24):2273-82.

What's next?

- What's the best method of treating HSIL to prevent progression to anal cancer?
- What's the best method to screen for HSIL?
  - Anal pap and HPV-only testing both have major limitations
- What's the appropriate population to screen for HSIL?
- What's the optimal age to start screening?
- What's the optimal interval for screening?

Anal Cancer Screening

- USPSTF: recommendation in progress
- 2020 HIV Primary Care Guidelines: recommends for patients with abnormal cervical pap smear, presence of genital warts, and/or history of receptive anal sex
- Some states and some experts recommend screening but no data and no consensus
- Everyone agrees that you should only screen patients if you have referral access to provider who can do high-resolution anoscopy to follow-up abnormal anal paps.

Thompson MA, Horberg MA, Agwu AL, et al. Primary care guidance for persons with human immunodeficiency virus: 2020 update by the HIV Medicine Association of the Infectious Diseases Society of America. *Clin Infect Dis.* 2021; 73(11):e3572-605.

Colon Cancer Screening (A/B/C)

- US Preventive Services Task Force (USPSTF) (2021)
  - Average risk people 50-75 yrs old (A)
  - Average risk people 45-49 yrs old (B)
  - Discuss 76-85 yrs old (C)
- American College of Physicians (ACP): screening for everyone at average risk should start at age 50 (2023)
- American Cancer Society (ACS): screening for everyone at average risk should start at age 45
- Many methods of screening, colonoscopy is gold standard but any screening is better than none

Lung Cancer Screening (B)

- Everyone 50-80 yrs old who:
  - Has ≥ 20 pack-yr history AND
  - Current smoker OR quit within last 15 yrs
- Stop screening if/when:
  - ≥ 15 yrs since quit smoking
  - Life expectancy is limited
  - Patient not willing/able to undergo surgery
- Screen with LDCT- low dose CT chest
  - “CT Lung Cancer Screening” in our EMR routes to the screening program coordinator

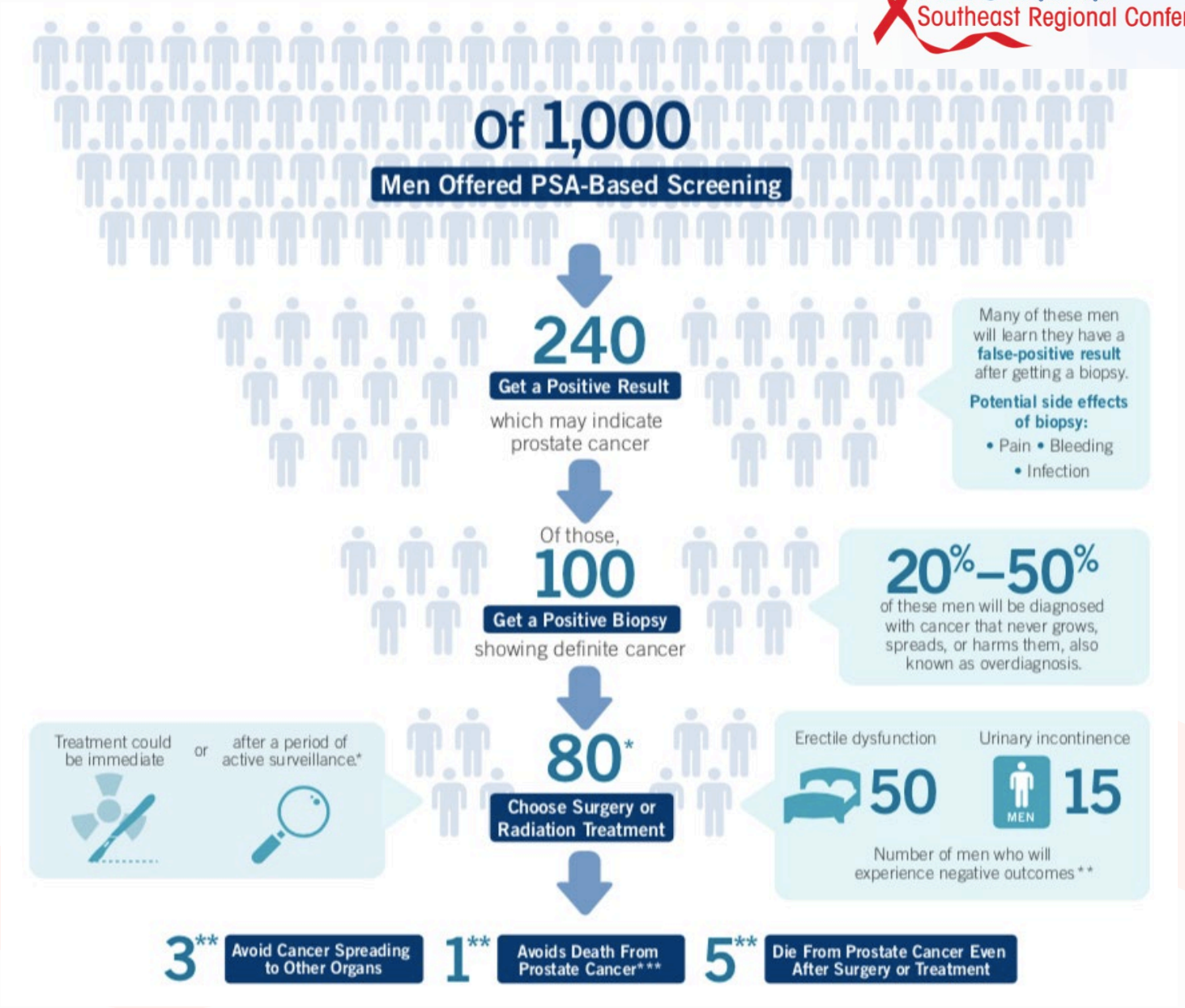
Breast Cancer Screening (B/C)

- USPSTF/ACP:
  - Biennial mammogram for average-risk women 50-74 yo (B)
  - Discuss risks/benefits for average-risk women 40-49 yo (C)
- ACS:
  - Annual mammogram for average-risk women 45-54 yo
  - Mammogram every 1-2 yrs for average-risk women 55+ yo
  - Discuss risks/benefits for average-risk women 40-45 yo
- American College of Obstetricians and Gynecologists (ACOG) and American College of Radiology (ACR) agree about at least biennial screening for women 50-75
- Bottom line: Women should start mammograms no later than 50 yo and continue every 1-2 yrs

Prostate Cancer Screening (C/D)

- USPSTF:
  - Discuss risks/benefits for men 55-69 yo (C)
  - Do not screen men 70+ yo (D)
- ACS:
  - Discuss risks/benefits for average-risk men 50+ yo
  - Discuss risks/benefits for high-risk men 45-49 yo
    - African American men and men with 1st degree relative diagnosed with prostate cancer <65 yo
  - Discuss risks/benefits for very-high-risk men 40-44 yo
    - Men with more than one 1st-degree relative diagnosed with prostate cancer at early age (undefined)
- Screening with PSA (prostate-specific antigen) blood test

Prostate Cancer Screening (C/D)



https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/prostate-cancer-screening1

Skin Cancer Screening

- USPSTF (I)
  - Insufficient evidence to recommend screening for skin cancer
- Not mentioned in 2020 update of Primary Care Guidance for Persons with HIV by HIVMA/IDSA
- PWH have a higher rate of non-melanoma skin cancer (NMSC) than the general population
- I counsel my patients about appropriate sun protection and have a low threshold to biopsy suspicious lesions/refer to dermatology

Omland SH, Ahlström MG, Gerstoft J, et al. Risk of skin cancer in patients with HIV: A Danish nationwide cohort study. *J Am Acad Dermatol.* 2018; 79(4):689-695.

Poll Question

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- Social hx: smokes 1 ppd since age 20, rare alcohol use, no substances. Not sexually active since HIV diagnosis
- Her only colonoscopy was done last year. No polyps found. Her mom was diagnosed with colon cancer at age 56
- Last mammogram was done earlier this year, normal. No FH of breast cancer. No hx of abnormal mammograms.
- Her last pap smear was done 2 yrs ago. She reports normal paps her whole life.
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Which cancer screening is indicated at this time?

- A) Colonoscopy
- B) Mammogram
- **C) Pap smear**
- D) CT chest
- E) CT chest +abdomen/pelvis

- Pap smear is recommended at time of HIV diagnosis

Screening for Transgender People

Transgender Women

- If prostate intact, can discuss screening in appropriate age group
- Screening for breast cancer with mammography is appropriate starting at 50 yo if completed at least 5 yrs of estrogen and/or progesterone therapy

Transgender Men

- If cervix intact, routine pap smears are indicated
- If breast tissue remains (pt hasn't had mastectomy), routine mammograms are indicated
- Both are regardless of testosterone treatment

Deutsch, MB. Screening for breast cancer in transgender women. UCSF Transgender Care. June 17, 2006.

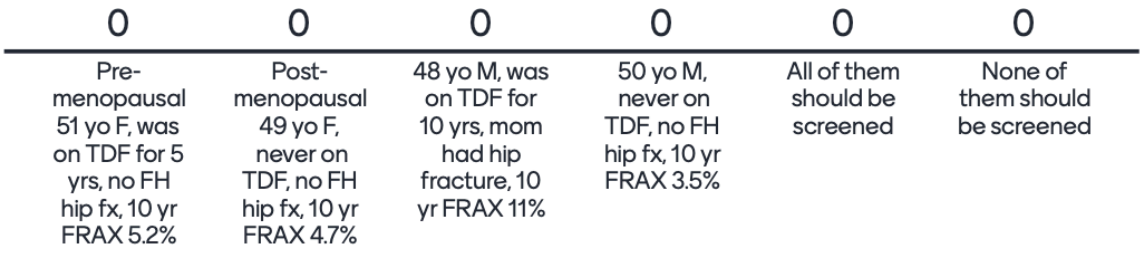
Poll- Which of these patients should NOT be screened for osteoporosis at this time?

- A) Pre-menopausal 51 yo F, was on TDF for 5 yrs, no FH hip fx, 10 yr FRAX 5.2%
- B) Post-menopausal 49 yo F, never on TDF, no FH hip fx, 10 yr FRAX 4.7%
- C) 48 yo M, was on TDF for 10 yrs, mom had hip fracture, 10 yr FRAX 11%
- D) 50 yo M, never on TDF, no FH hip fx, 10 yr FRAX 3.5%
- E) All of them should be screened
- F) None of them should be screened

Join at menti.com use code 9729 8259

Mentimeter

Which of these patients should NOT be screened for osteoporosis at this time?



Osteoporosis Screening

- Why do we screen?
  - HIV is associated with Vitamin D deficiency which is an independent risk factor for osteoporosis
  - Initiation of ART is associated with a 2-6% decrease in bone mineral density (BMD) in the first two years, depending on regimen used
    - Greatest with TDF and boosted PI regimens

Allavena C, Delpierre C, Cuzin L, et al. High frequency of vitamin D deficiency in HIV-infected patients: effects of HIV-related factors and antiretroviral drugs. J Antimicrob Chemother. 2012 Sep;67(9):2222-30.

Brown TD, Hoy J, Borderi M, et al. Recommendations for Evaluation and Management of Bone Disease in HIV, *Clinical Infectious Diseases*, Volume 60, Issue 8, 15 April 2015, Pages 1242–1251

Osteoporosis in PWH

Who to Screen?

- Men ≥ 50
- Post-menopausal women
- Anyone with fragility fracture regardless of age
- Many other RFs...
- People with high FRAX score

How to Screen?

- DEXA scan (preferably same machine every time)

Who to Treat?

- Anyone with osteoporosis
- Osteopenia with high FRAX score

FRAX® Fracture Risk Assessment Tool

Home | Calculation Tool | Paper Charts | FAQ | References | English

Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: US (Caucasian) Name/ID: About the risk factors

Questionnaire:

1. Age (between 40 and 90 years) or Date of Birth
   Age: 55 Date of Birth: Y: M: D:
2. Sex — Male / Female
3. Weight (kg) 63.5
4. Height (cm) 177.8
5. Previous Fracture — No / Yes
6. Parent Fractured Hip — No / Yes
7. Current Smoking — No / Yes
8. Glucocorticoids — No / Yes
9. Rheumatoid arthritis — No / Yes
10. Secondary osteoporosis — No / Yes
11. Alcohol 3 or more units/day — No / Yes
12. Femoral neck BMD (g/cm^2)
    T-Score -2

Clear Calculate

BMI: 20.1
The ten year probability of fracture (%)
with BMD

Major osteoporotic	6.6
Hip Fracture	2.2

If you have a TBS value, click here: Adjust with TBS

Weight Conversion
Pounds → kg
140 Convert

Height Conversion
Inches → cm
70 Convert

07722142
Individuals with fracture risk assessed since 1st June 2011

Osteoporosis Risk Factors

Previous fracture	A previous fracture denotes more accurately a previous fracture in adult life occurring spontaneously, or a fracture arising from trauma which, in a healthy individual, would not have resulted in a fracture. Enter yes or no (see also notes on risk factors).
Parent fractured hip	This enquires for a history of hip fracture in the patient's mother or father. Enter yes or no.
Current smoking	Enter yes or no depending on whether the patient currently smokes tobacco (see also notes on risk factors).
Glucocorticoids	Enter yes if the patient is currently exposed to oral glucocorticoids or has been exposed to oral glucocorticoids for more than 3 months at a dose of prednisolone of 5mg daily or more (or equivalent doses of other glucocorticoids) (see also notes on risk factors).
Rheumatoid arthritis	Enter yes where the patient has a confirmed diagnosis of rheumatoid arthritis. Otherwise enter no (see also notes on risk factors).
Secondary osteoporosis	Enter yes if the patient has a disorder strongly associated with osteoporosis. These include type I (insulin dependent) diabetes, osteogenesis imperfecta in adults, untreated long-standing hyperthyroidism, hypogonadism or premature menopause (<45 years), chronic malnutrition, or malabsorption and chronic liver disease
Alcohol 3 or more units/day	Enter yes if the patient takes 3 or more units of alcohol daily. A unit of alcohol varies slightly in different countries from 8-10g of alcohol. This is equivalent to a standard glass of beer (285ml), a single measure of spirits (30ml), a medium-sized glass of wine (120ml), or 1 measure of an aperitif (60ml) (see also notes on risk factors).

Osteoporosis Treatment

- Bisphosphonates
  - Oral (weekly) and IV (annually)
  - Both formualations have been studied in PWH
- Monoclonal antibodies
  - Denosumab and romosozumab
  - Limited data in PWH but used clinically
- Parathyroid hormone analogs
  - Teriparatide and abaloparatide
  - Limited data in PWH but used clinically

Osteoporosis Treatment

- Bisphosphonates can be managed by primary care
- Other treatments are usually managed by bone clinic

- Who to refer?
  - Ineligible for bisphosphonate
  - Severe osteoporosis (t-score < -3)
  - New fractures or worsening bone density on bisphosphonate therapy
  - CKD with GFR <35

Osteoporosis Management

- Consider a change in ART regimen if on TDF or PI
- Plus treating vitamin D to maintain level >30, ensuring adequate dietary calcium intake or calcium supplement (separating from INSTI if applicable)

Brown TD, Hoy J, Borderi M, et al. Recommendations for Evaluation and Management of Bone Disease in HIV, *Clinical Infectious Diseases*, Volume 60, Issue 8, 15 April 2015, Pages 1242–1251

Poll- Which of these patients should NOT be screened for osteoporosis at this time?

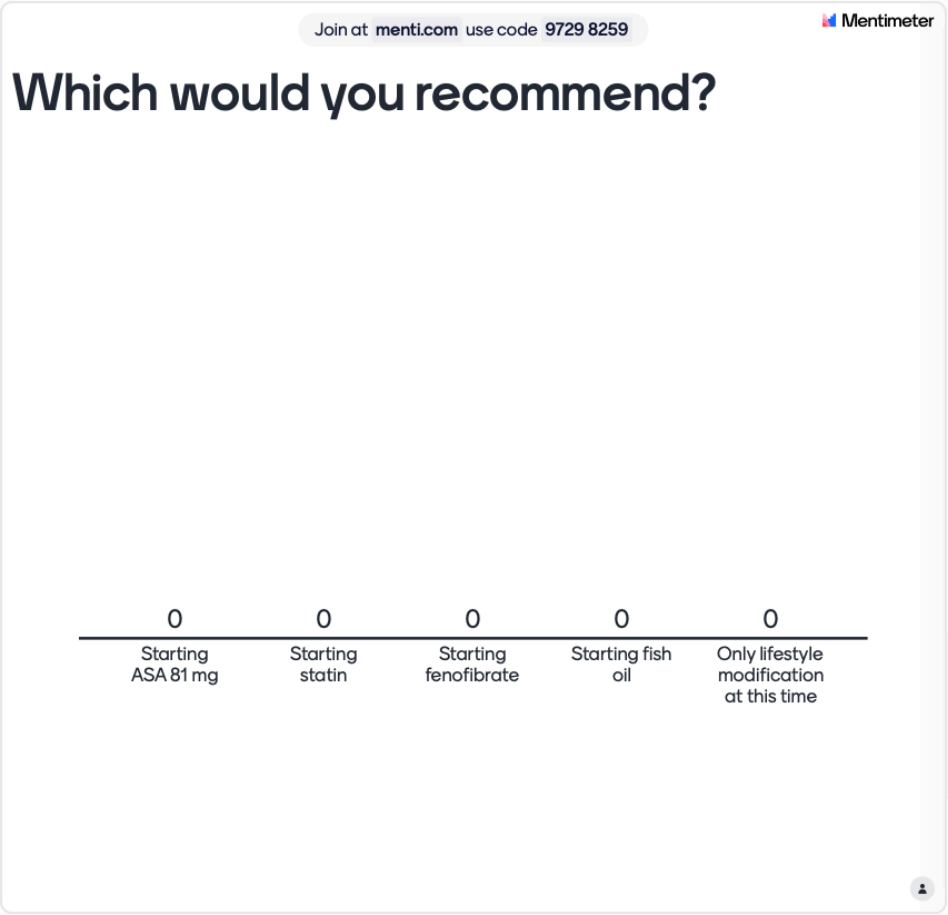
- **A) Pre-menopausal 51 yo F, was on TDF for 5 yrs, no FH hip fx, 10 yr FRAX 5.2%**
- B) Post-menopausal 49 yo F, never on TDF, no FH hip fx, 10 yr FRAX 4.7%
- C) 48 yo M, was on TDF for 10 yrs, mom had hip fracture, 10 yr FRAX 11%
- D) 50 yo M, never on TDF, no FH hip fx, 10 yr FRAX 3.5%
- E) All of them should be screened
- F) None of them should be screened

Poll Question

- 48 yo man with PMH HIV, HTN comes to your office for routine follow-up. He reveals that his mom recently had a heart attack (she's in her 70s). He wants to know what he can do to lower his chances of having a heart attack in the future.
- Social hx: he smoked ½ ppd but quit last week, occasional alcohol use, he runs on treadmill 45 min 4-5 days per week before work
- Vitals: HR 68, BP 115/79, BMI 24
- Medications:
  - HIV: BIC/FTC/TAF
  - HTN: amlodipine
- Lipids: Total Cholesterol 215, HDL 43, LDL 107, TG 325
- 10-yr ASCVD risk is 3.6%

Besides counseling on importance of remaining quit from cigarettes and discussing heart healthy diet, what would you recommend?

- A) Starting ASA 81 mg
- B) Starting statin
- C) Starting fenofibrate
- D) Starting fish oil
- E) Only lifestyle modification at this time



Cardiovascular Disease (CVD)

- Relative risk of CVD 1.5-2x times higher in PWH
- Includes not only myocardial infarction, but also stroke, heart failure, pulmonary arterial hypertension
- Absolute burden of disease continues to increase as PWH are living longer
- When imaged, PWH have more subclinical atherosclerosis
- Coronary artery calcium (CAC) has been shown to progress more rapidly in PWH
- Co-infection with Hepatitis C may increase stroke risk even more

Feinstein MJ, Hsue PY, Benjamin LA, et al. Characteristics, Prevention, and Management of Cardiovascular Disease in People Living With HIV: A Scientific Statement From the American Heart Association, *Circulation.* 2019; 140(2):e98-e124.

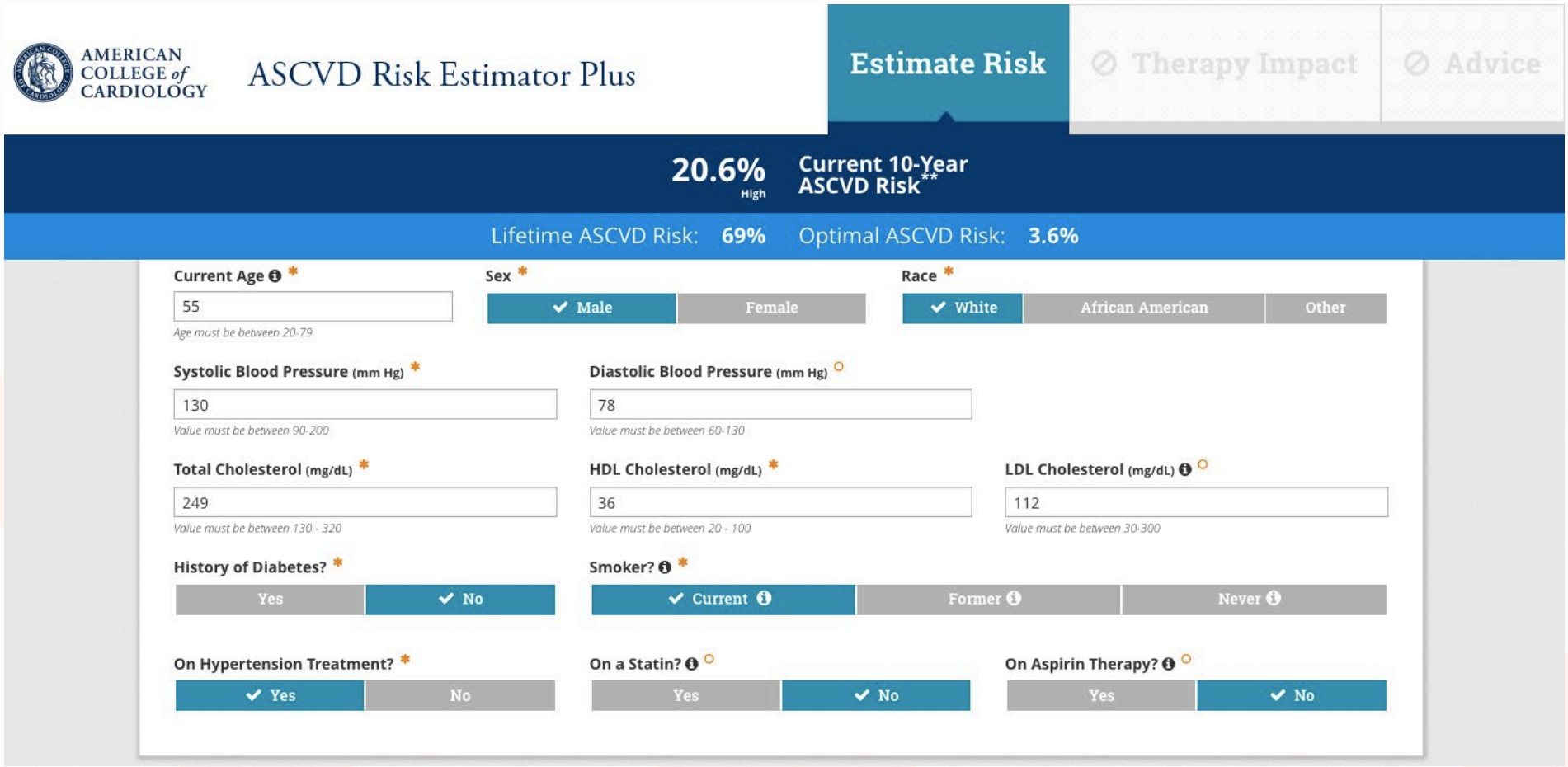
Risk Factors

- Multifactorial
- Traditional risk factors all still apply (diabetes, obesity, smoking, etc.)
- Rate of smoking is higher in PWH

- HIV-specific
  - Low current or nadir CD4
  - History of sustained viremia or untreated HIV
  - ART
    - PIs (except atazanavir)
    - Abacavir
  - Chronic inflammation/ immune activation even when virally suppressed

Feinstein MJ, Hsue PY, Benjamin LA, et al. Characteristics, Prevention, and Management of Cardiovascular Disease in People Living With HIV: A Scientific Statement From the American Heart Association, *Circulation.* 2019; 140(2):e98-e124.

Calculating Risk



- Many calculators/models exist but all underestimate risk in HIV

Statins

- Consider earlier in PWH
- Per American Heart Association Scientific Statement in 2019, we should consider starting in PWH with an ASCVD risk ≥7.5%
- Best choices:
  - High intensity: atorvastatin, rosuvastatin
    - Atorvastatin has lower maximum dose (20 mg) with DRV/r, DRV/COBI, and EVG/COBI
    - Rosuvastatin may require dose adjustment or close monitoring
  - Moderate intensity: pitavastatin, pravastatin
    - Pitavastatin does not require dose adjustment
    - Pravastatin may require close monitoring at higher doses
- AVOID:
  - Lovastatin and simvastatin (CI with all PIs and EVG/COBI)
- When in doubt, start low and go slow while titrating

Feinstein MJ, Hsue PY, Benjamin LA, et al. Characteristics, Prevention, and Management of Cardiovascular Disease in People Living With HIV: A Scientific Statement From the American Heart Association, *Circulation.* 2019; 140(2):e98-e124.

REPRIEVE Trial

Background:

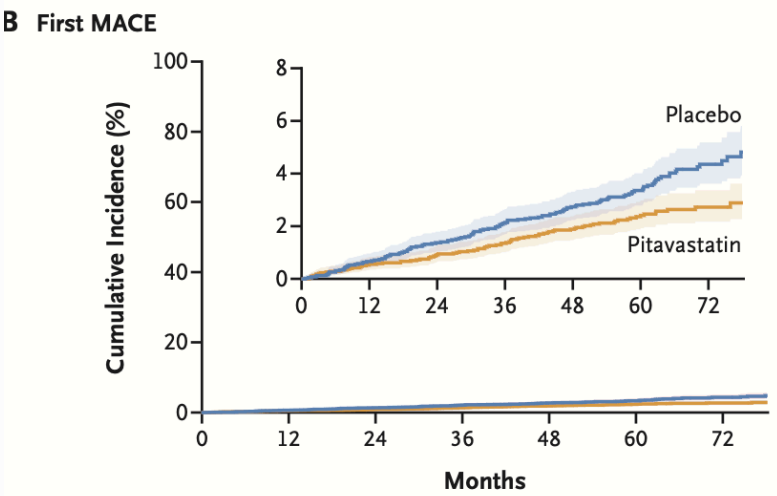
- 7769 PWH on ART at low to moderate risk of ASCVD
  - 40-75 yrs old
  - ASCVD risk 0-15% using 2013 ACC calculator
- Multi-site international trial
- Randomized 1:1 to pitavastatin 4 mg (moderate intensity) vs placebo
- Median follow-up 5.1 yrs
- Primary outcome: occurrence of MACE (major adverse cardiovascular event)
- Study stopped early for benefit

Grinspoon SK, Fitch KV, Zanni MV, et al. Pitavastatin to prevent cardiovascular disease in HIV infection. *N Engl J Med.* Published online July 23, 2023. doi: 10.1056/NEJMoa2304146

REPRIEVE Trial

Findings:

- "Pitavastatin to Prevent Cardiovascular Disease in HIV Infection" published online in NEJM on 7/23/23
- LDL effect was not as large as expected
- Hazard reduction was greater than expected
- NNT 106 over 5 yrs



Cumulative Incidence of Event (%)							
Placebo	0.00	0.66	1.38	2.14	2.74	3.36	4.36
Pitavastatin	0.00	0.56	0.95	1.35	1.89	2.41	2.73
No. at Risk							
Placebo	3881	3693	3506	3356	2997	2182	959
Pitavastatin	3888	3647	3475	3364	2997	1947	1052

HR 0.65 (CI 0.48-0.90)

Grinspoon SK, Fitch KV, Zanni MV, et al. Pitavastatin to prevent cardiovascular disease in HIV infection. *N Engl J Med.* Published online July 23, 2023. doi: 10.1056/NEJMoa2304146

What's next?

- Does the benefit seen in this trial extend to all statins?
- Should we offer a statin to all PWH 40-75 yrs of age?
- Will ACC publish a new scientific statement or guideline for PWH?
- How can we better predict which PWH will have a future cardiovascular event?
- Are there other therapies that may further reduce risk of CVD?

PCSK9 Inhibitors

- Alirocumab and evolocumab
- Biweekly injections
- Approved for patients with CVD or hyperlipidemia as adjunct to lifestyle changes and alone/in addition to other therapies
- No DDI with ART

- EPIC-HIV Trial
  - Effect of PCSK9 Inhibition on Cardiovascular Risk in Treated HIV Infection
  - Started 2018
  - Ends 2025
  - Primary outcome is arterial inflammation and endothelial dysfunction

Poll Question

- 48 yo man with PMH HIV, HTN comes to your office for routine follow-up. He reveals that his mom recently had a heart attack (she's in her 70s). He wants to know what he can do to lower his chances of having a heart attack in the future.
- Social hx: he smoked ½ ppd but quit last week, occasional alcohol use, he runs on treadmill 45 min 4-5 days per week before work
- Vitals: HR 68, BP 115/79, BMI 24
- Medications:
  - HIV: BIC/FTC/TAF
  - HTN: amlodipine
- Lipids: Total Cholesterol 234, HDL 35, LDL 110, TG 445
- 10-yr ASCVD risk is 5.2%

Besides counseling on importance of remaining quit from cigarettes and discussing heart healthy diet, what would you recommend?

- A) Starting ASA 81 mg
- **B) Starting statin**
- C) Starting fenofibrate
- D) Starting fish oil
- E) Only lifestyle modification at this time

Diabetes mellitus (DM)

- DM is more common in PWH than general population
- We commonly use HgbA1c to diagnose and monitor DM
- **HgbA1c underestimates hyperglycemia in PWH** (tends to be falsely low) leading to underdiagnosis and undertreatment

- Multifactorial issue
  - Mild anemia
  - Elevated MCV
  - ART (no consistent data as to which drug classes are responsible)
- Not the same in every patient
- Bottom line: use your clinical judgement, may need to use more FSBG or CGM

Could you test me for low T?

- Only test men who are symptomatic and eligible for treatment
- ACP Guidelines- 2020
  - Treatment may improve sexual function. If it doesn't, stop treatment
  - Very little/no benefit for energy, vitality, cognition, physical function- DON'T PRESCRIBE
- Order free testosterone level or panel because HIV affects sex hormone binding globulin (SHBG)
- Lab should be drawn between 8-10 am, ideally fasting
- If low, it should be repeated at least once to confirm

Qaseem A, Horwitch CA, Vijan S, et al. Testosterone Treatment in Adult Men With Age-Related Low Testosterone: A Clinical Guideline From the American College of Physicians, *Ann Intern Med.* 2020;172(2):126-133.

STI Screening

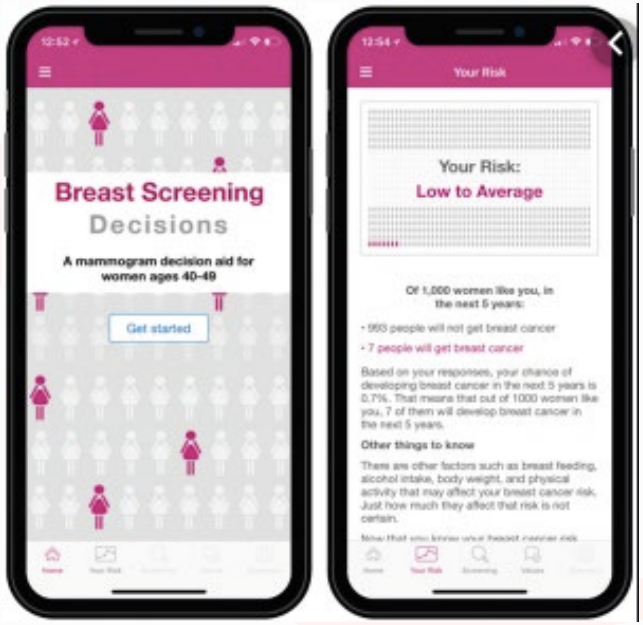
- If you use it, swab it for gonorrhea and chlamydia
- Not everyone has sex the same way
- Ask if any new partners, sexual contacts at every visit
- At minimum, test for STIs at least annually
  - For people with vaginas, this includes trichomonas
- Syphilis is the great imitator- any rash/skin lesion that I'm not 100% confident about the diagnosis, I test for syphilis
- For MSM and people who inject drugs, test for hepatitis C on a regular basis

Take Home Points

- Check for drug interactions before prescribing new med!
- There is an increased risk of HPV-associated cancers in PWH
  - Discuss HPV vaccine in individuals 27-45 if appropriate
  - Offer anal pap smears if able to refer for anoscopy
- Transgender individuals: screen organs that are present
  - Transgender women- start mammograms at 50 if ≥ 5 yrs on hormone therapy
- Screen for osteoporosis with DEXA (men 50+, women post-menopausal)
- Calculate ASCVD risk in PWH ≥ 40 yo, discuss statin for everyone?? (at minimum PWH and ASCVD >7.5%), smoking cessation for all

There's an app for that!

Guided decision making tool for mammograms for women 40-49



ASCVD PLUS

CV Risk Calculator

ASCCP

Pap smear follow-up

CDC

Vaccine Schedule

ePSS

USPSTF Recs

Other Resources

- AIDSInfo- by NIH (app)
- Advisory Committee on Immunization Practices (ACIP)
  - CDC Vaccines App
- US Preventive Services Task Force (app)
- Lexicomp (also in UpToDate Drug Interaction Checker)
- Liverpool HIV Drug Interaction Checker (also includes illicit substances)

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

Questions?