# HIV in Older Adults

Jehan Budak, MD Geriatrics Healthcare Series Winter Quarter January 2024

# Disclosures

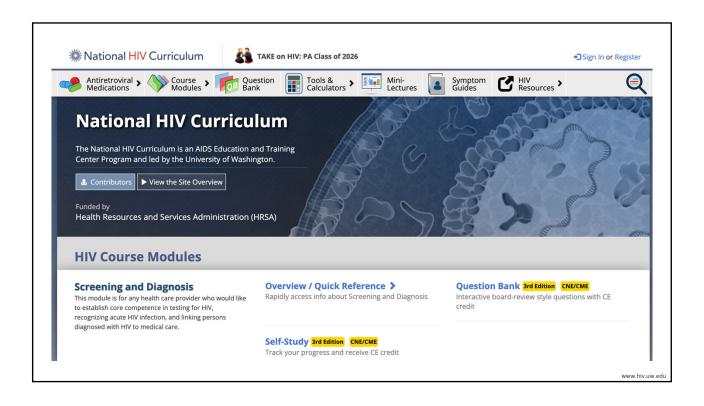
• Disclosures: None

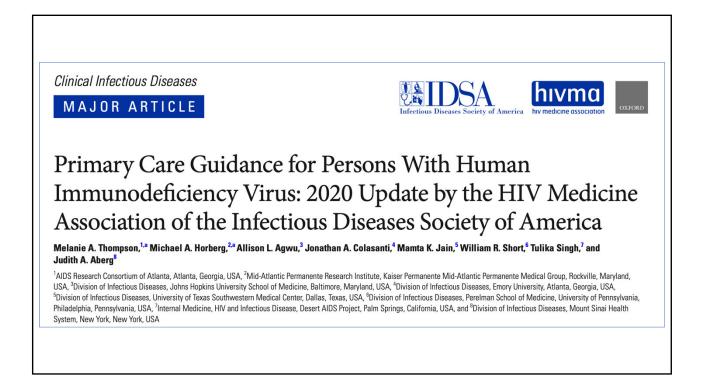
# Objectives

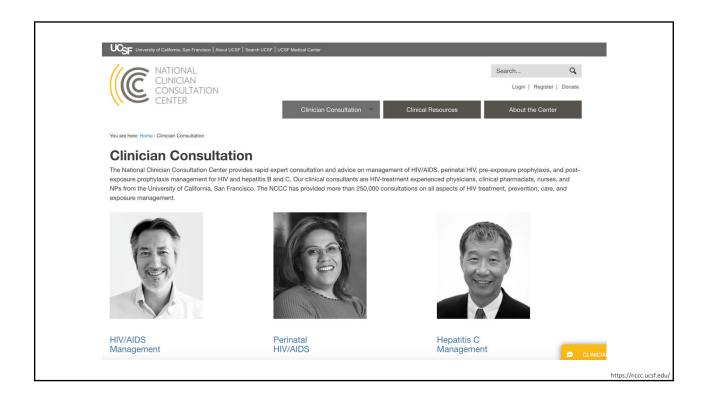
- Identify resources that can be helpful in the care of an older adult with HIV
- Describe the state of HIV epidemiology and a general update on antiretroviral therapy
- Recognize co-morbid conditions that are common in older adults with HIV

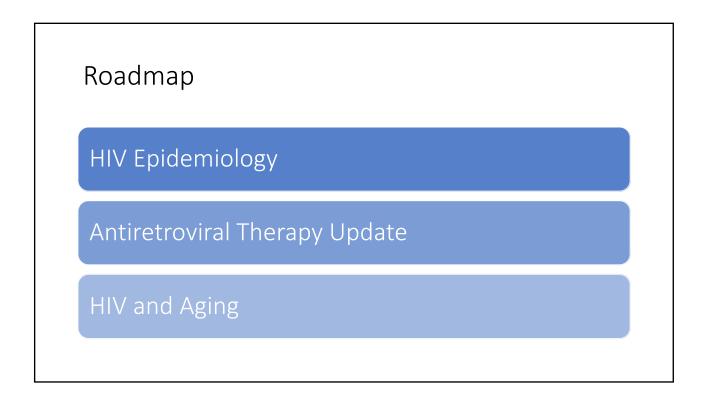
# Resources

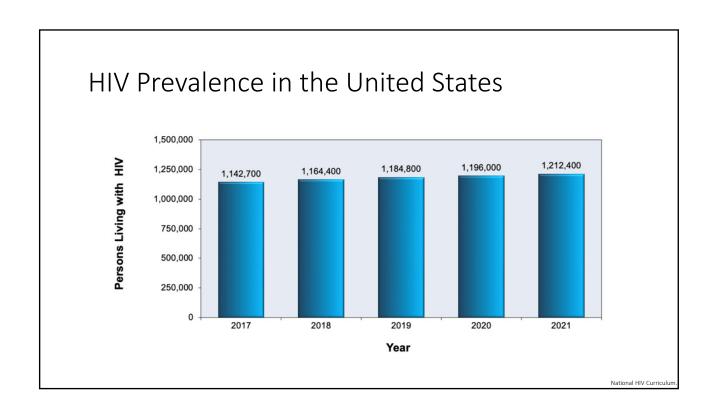
- National HIV Curriculum
- HIVMA Primary Care Guidance
- National Clinician Consultation Center

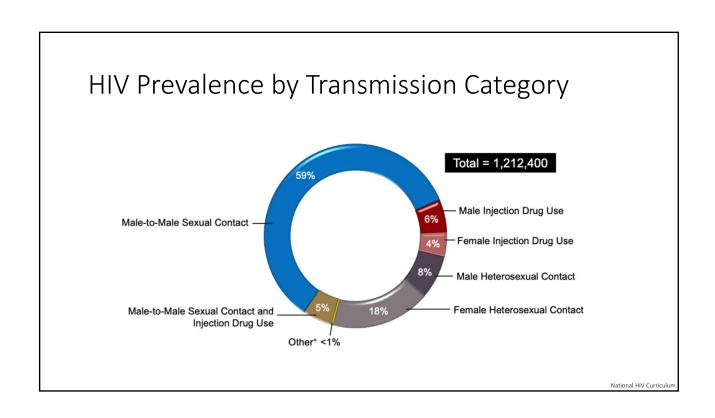




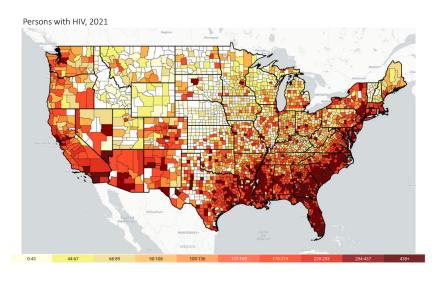








# HIV Prevalence Varies Throughout the US



AIDSVu.or

# The Plan to End the HIV Epidemic in the US

- 1. Focus initially on high incidence geographic areas
- 2. Emphasize early diagnosis, immediate treatment, and engagement
- 3. Rapid and overwhelming response to emerging HIV clusters
- 4. Expand PrEP use to at risk populations by at least 50%

Treatment
as Prevention
(TasP)

Pre-Exposure
Prophylaxis
(PrEP)

auci, JAMA 2019. Fauci, CROI Plenary 3-4-2019.

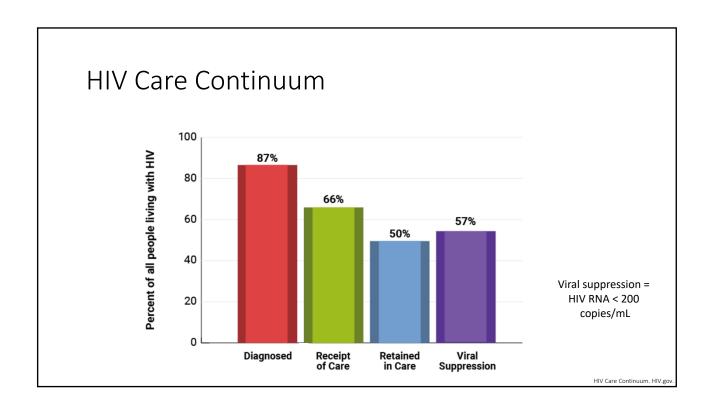
# Pre-Exposure Prophylaxis Prevents HIV

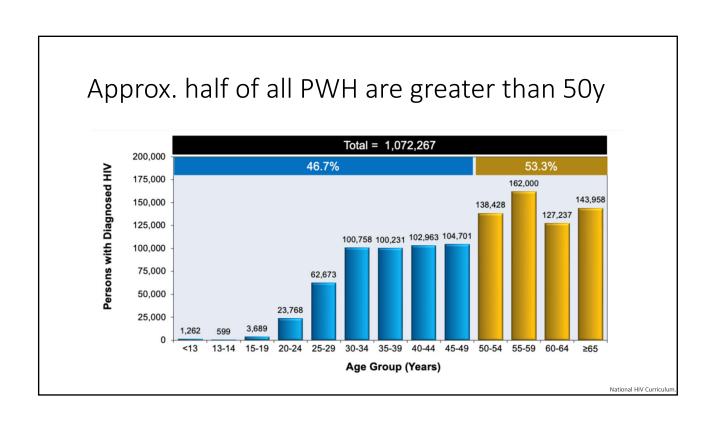
- A strategy of taking anti-retroviral medication(s) to prevent HIV
- A Grade A USPSTF recommendation

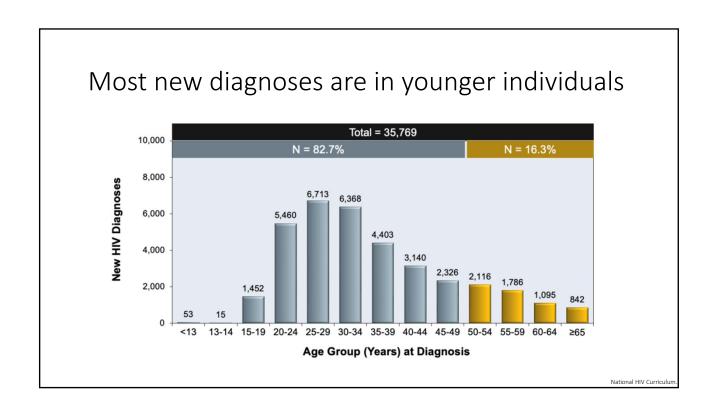
	FDA Approval	Route	Frequency	Drug	Note
1	7/2012	Oral	Daily	Tenofovir DF-emtricitabine ( <i>Truvada</i> ®)	
2	10/2019	Oral	Daily	Tenofovir alafenamide- emtricitabine ( <i>Descovy</i> ®)	NOT for persons having receptive vaginal intercourse
3	12/2021	Injectable	Q2 month	Cabotegravir (Apretude®)	

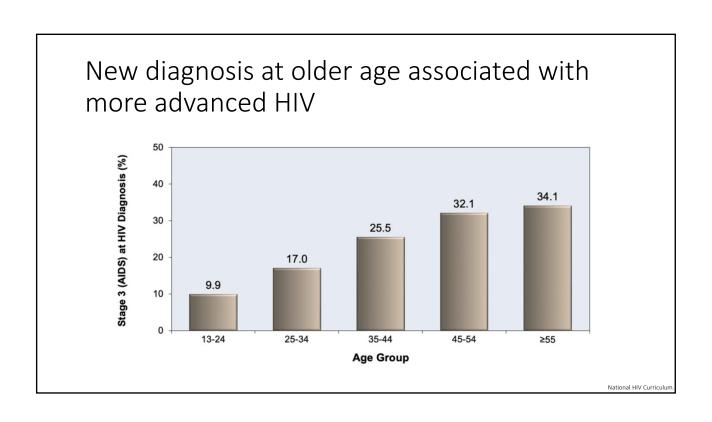
CDC 2021 Update Clinical Practice Guideline – PrEP for the Prevention of HIV Infection in the U

# HIV CARE CONTINUUM: The steps that people with HIV take from diagnosis to achieving and maintaining viral suppression. DIAGNOSED WITH HIV LINKED TO CARE HIV Care Continuum. HIV gov.









# THE LANCET HIV

### Ageing with HIV

# Delayed presentation of HIV among older individuals: a growing problem

Amy C Justice, Matthew B Goetz, Cameron N Stewart, Brenna C Hogan, Elizabeth Humes, Paula M Luz, Jessica L Castilho, Denis Nash, Ellen Brazier, Beverly Musick, Constantin Yiannoutsos, Karen Malateste, Antoine Jaquet, Morna Cornell, Tinei Shamu, Reena Rajasuriar, Awachana Jiamsakul, Keri N Althoff

"Early diagnosis and treatment of HIV for older individuals is particularly challenging because

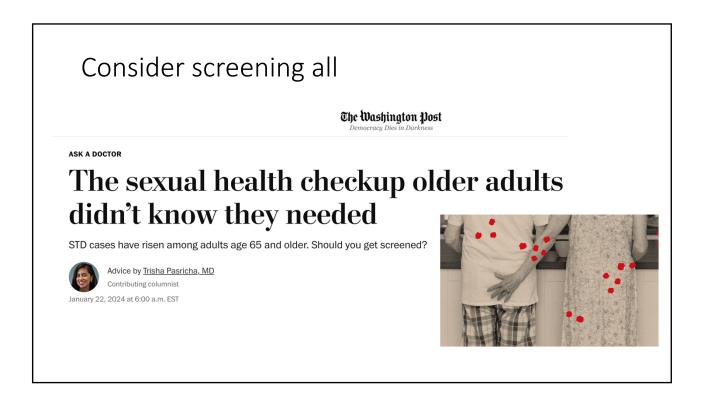
- early signs and symptoms might be attributed to diseases of ageing and because
- neither these individuals or their care providers perceive them to be at risk of HIV infection"

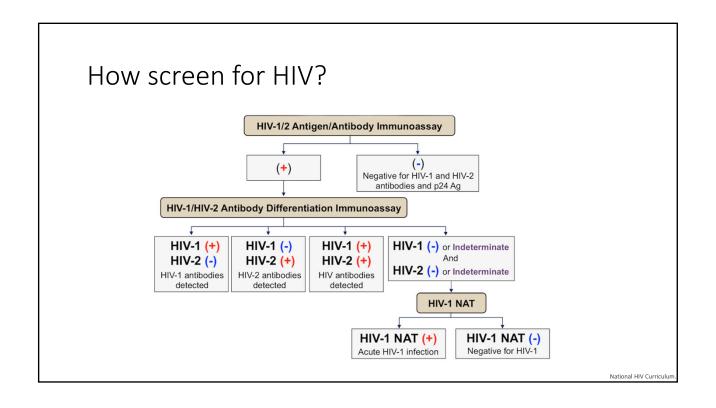
Justice AC, Lancet HIV, 202

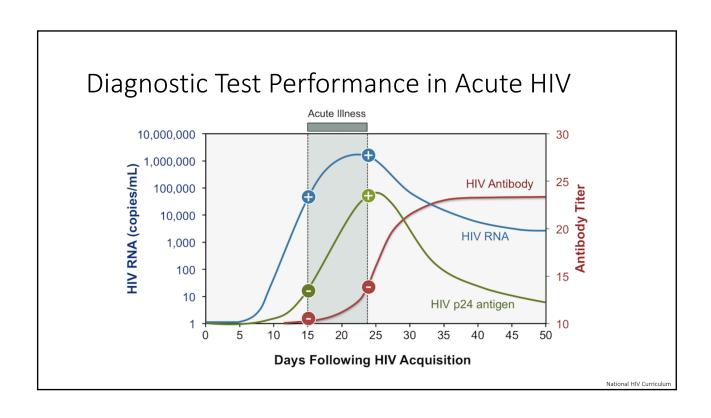
# Screening Recommendations in Older Adults

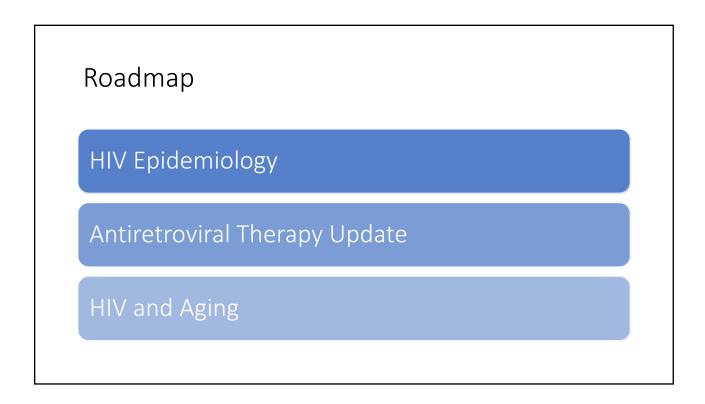
- CDC recommends screening all individuals aged 13-64 for HIV
- USPSTF recommends screening individuals aged 15-65 for HIV

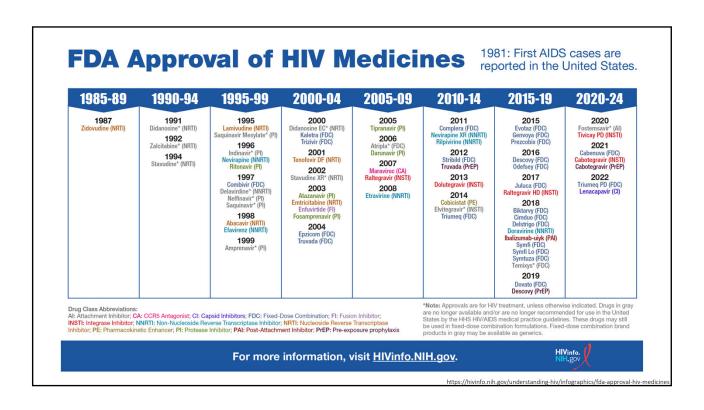
What about screening in individuals over 65?

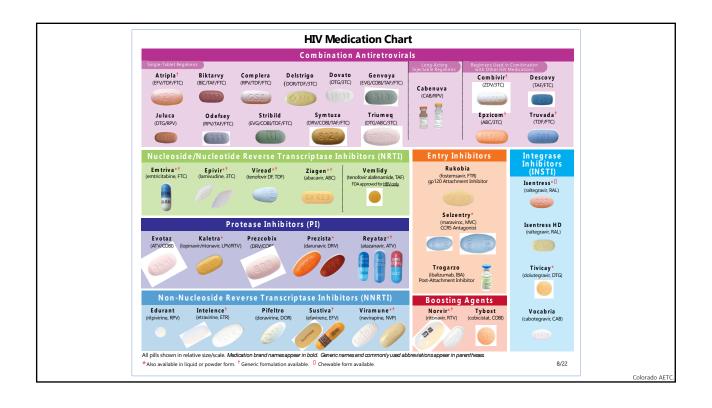


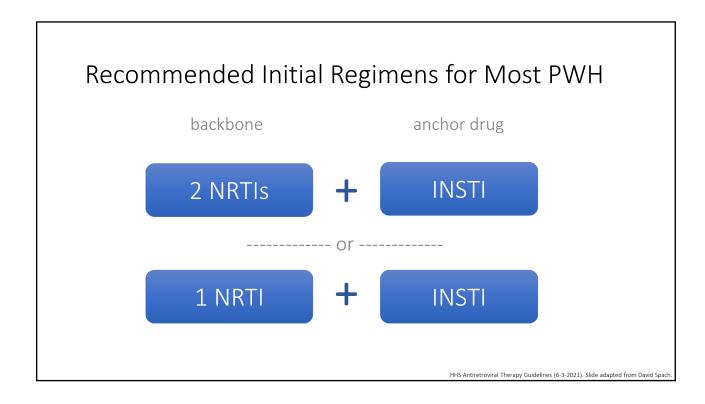












# Recommended Initial Regimens for Most PWH

INSTI + 2 NRTIs	Rating
Bictegravir-TAF-FTC	Al
Dolutegravir-ABC-3TC (if HLA-B*5701 negative)	Al
Dolutegravir + TAF-FTC	Al
Dolutegravir + [TDF-FTC or TDF + 3TC]	Al
INSTI + 1 NRTI	Rating
Dolutegravir-Lamivudine (except: HIV-1 RNA >500,000 copies/mL, HBV, no genotype)	Al

HS Antiretroviral Therapy Guidelines (6-3-2021). Slide adapted from David Spach

# FDA-Approved Two-Drug Regimens

- DTG-3TC (Dovato®)
  - Dolutegravir + Lamivudine
- DTG-RPV (Juluca®)
  - Dolutegravir + Rilpivirine
- IM CAB-RPV (Cabenuva®)
  - Cabotegravir + Rilpivirine



NRTI

**INSTI** 

INSTI + NNRTI

National HIV Curriculur

# Long acting injectables are the future!

- Three long acting injectables are FDA approved to treat & prevent HIV
- Treatment
  - Cabotegravir-Rilpivirine (Cabenuva®) IM every 2 months
  - Lenacapavir (Sunlenca®) SQ every 6 months with orals for multidrug resistant HIV
- Prevention
  - Cabotegravir (Apretude®) IM every 2 months

# Undetectable = Untransmittable (U=U)

• Concept that an individual with an undetectable HIV VL cannot transmit HIV infection to their sexual partners

STUDY	FINDINGS
HPTN-052	96% reduction in infections among heterosexual couples when the partner with ${\rm HIV}\ {\rm started}\ {\rm ART^1}$
PARTNER-1	Of 58K condomless sex acts in 888 serodiscordant couples (40% MSM, partner with HIV with UD VL), no new HIV infections phylogenetically linked <sup>2</sup>
PARTNER-2	972 serodiscordant MSM who are coupled had 76K condomless sex acts, no HIV infections phylogenetically linked $^{\rm 3}$

1-Cohen NEJM 2016, 2-Rodger JAMA 2016, 3-Rodger Lancet 201

# Roadmap

HIV Epidemiology

Antiretroviral Therapy Update

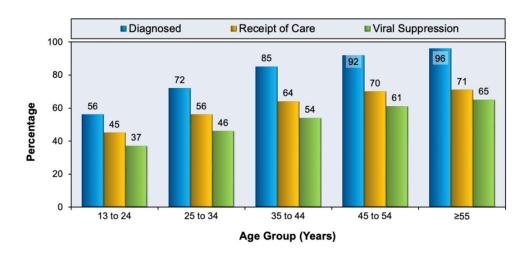
HIV and Aging

# Principles about HIV in the Older Adult

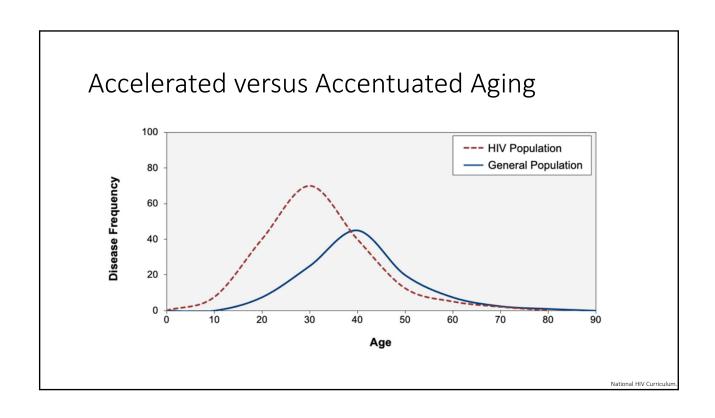
- 1. Older PWH have greater risk of developing non-AIDS complications than younger PWH.
- 2. Older PWH often have a blunted immunologic response to ART.
- 3. Chronic HIV may cause accelerated development of comorbid conditions that are common in older persons.
- 4. Persons > 50 may have a significant risk of HIV transmission due to unfavorable changes in mucosal surfaces and infrequent use of condoms.
- 5. ART substantially reduces AIDS-related and non-AIDS related mortality in older PWH.

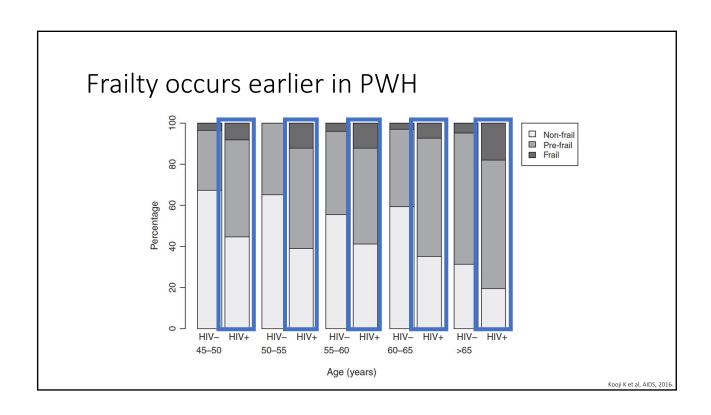
National HIV Curriculum

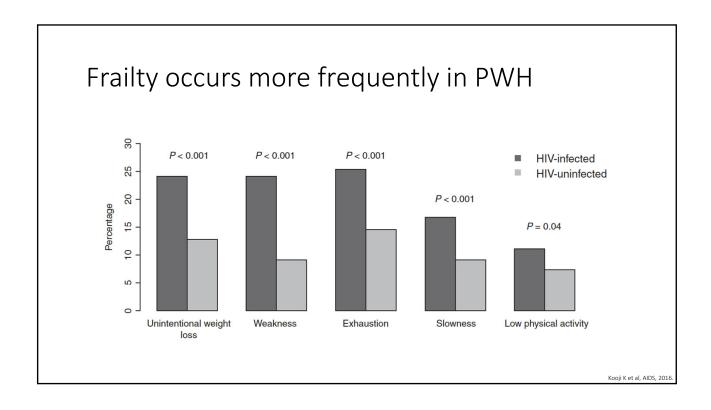
# Viral Response to ART in Older Adults

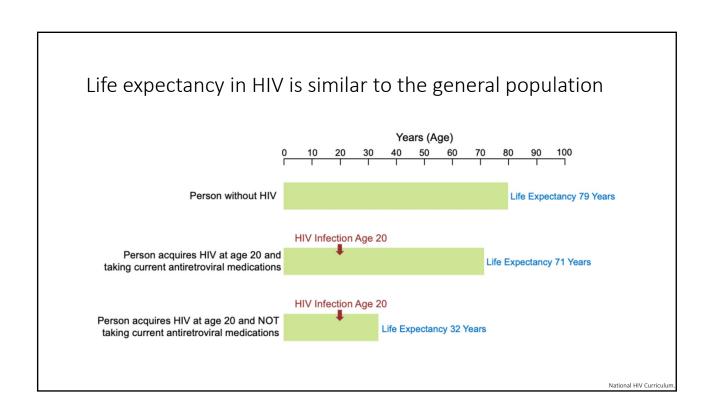


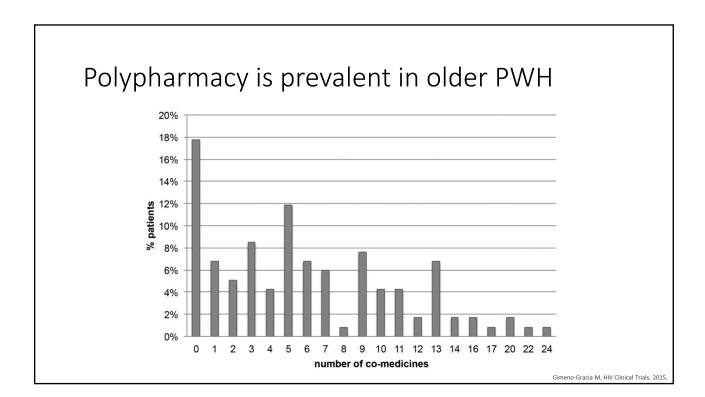
National HIV Curriculum





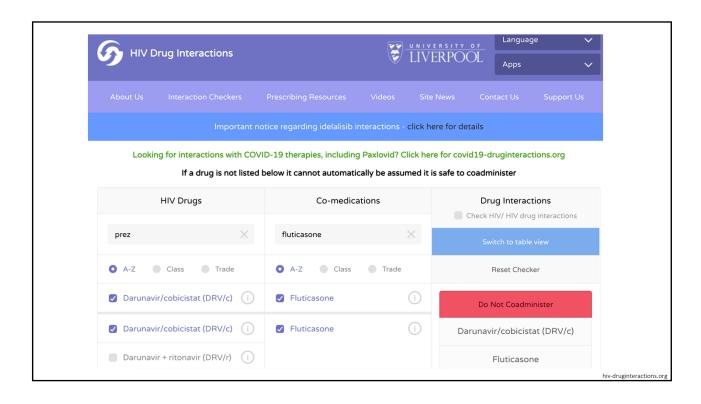






# Examples of ART drug-drug interactions

- Cations
  - Polyvalent cations can bind to and chelate certain INSTIs
- Antacids
  - H2 blockers and PPIs can inactivate rilpivirine, which requires an acidic environment for absorption
- Pharmacologic boosters needed with protease inhibitors
  - Ritonavir and cobicistat inhibits CYP 3A4

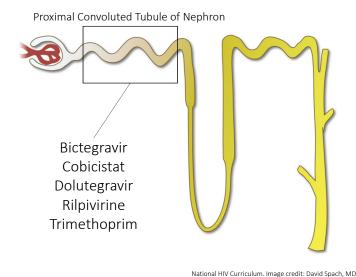


## ARVs have adverse effects

- Tenofovir disoproxil fumarate (TDF) NRTI class
  - Bone demineralization
  - Nephrotoxicity
  - Less bone and kidney issues with tenofovir alafenamide (TAF), prodrug of TDF
- Weight gain INSTI class, TAF
- Cardiovascular risk Abacavir (NRTI class)
- Hyperlipidemia TAF, Darunavir (Protease inhibitor class)

# Benign Effects of ART on Creatinine

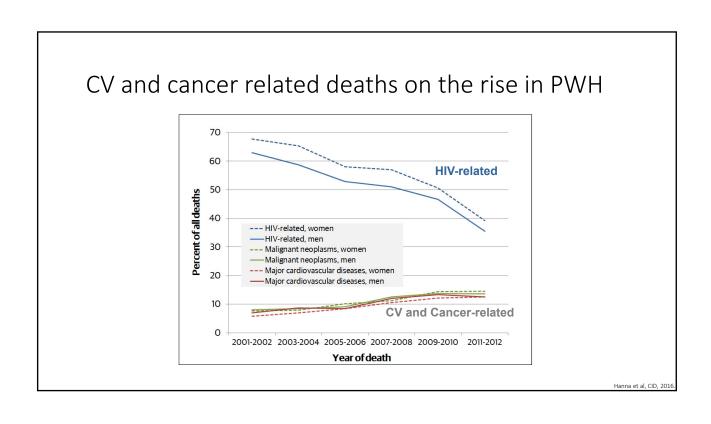
- BIC, DTG, RPV, cobicistat, and TMP inhibit proximal tubular secretion of creatinine (Cr), which may increase the serum Cr without changing the GFR
- May expect a 10-20% (or 0.1-0.2 mg/dL) increase in Cr, usually within first few weeks of therapy, then plateaus
- Check a Cr level one month after starting any of these medications to establish a new baseline

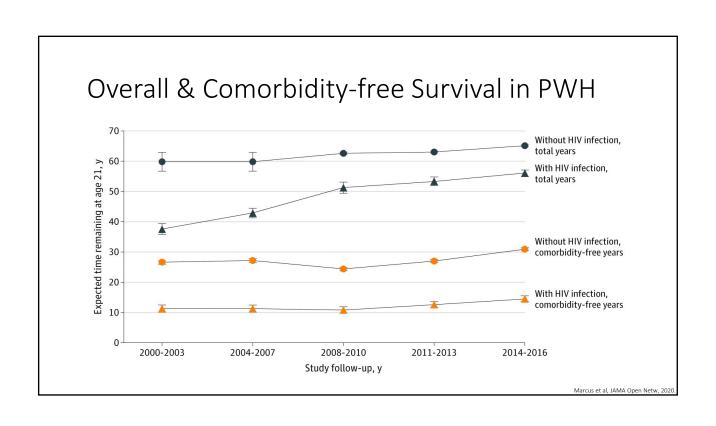


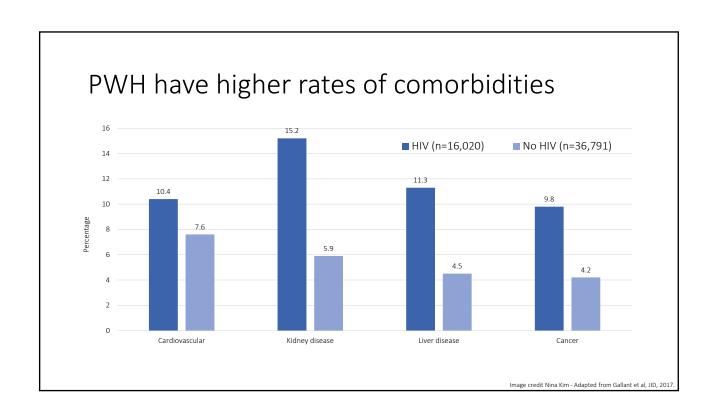
PWH tend to have more risk factors for comorbidity

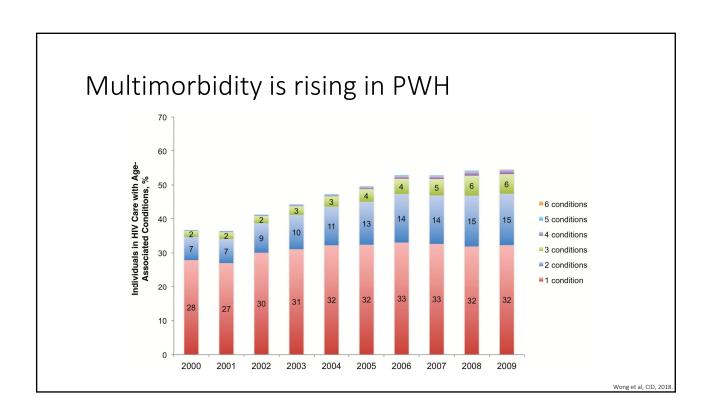
- Depression/anxiety
- Substance use (smoking, alcohol, meth, opiates, etc)
- Health disparities
- Co-infections (hepatitis B and C, for example)
- Side effects from ART
- Stigma and impact of living with a chronic disease

Adapted from Nina Kim.









# Multimorbidity in HIV, especially those aging

- Weight Gain
- Cardiovascular Disease
- Renal Disease
- Neurocognitive Decline
- Cancer
- Osteoporosis
- Testosterone deficiency

# ART and Weight Gain: A Chronology

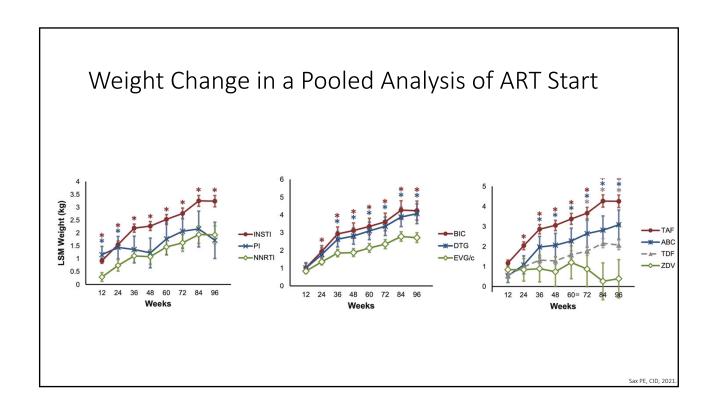
- CROI 2019 – An association between INSTIs & weight gain is reported, perhaps more so with DTG<sup>1-4</sup>

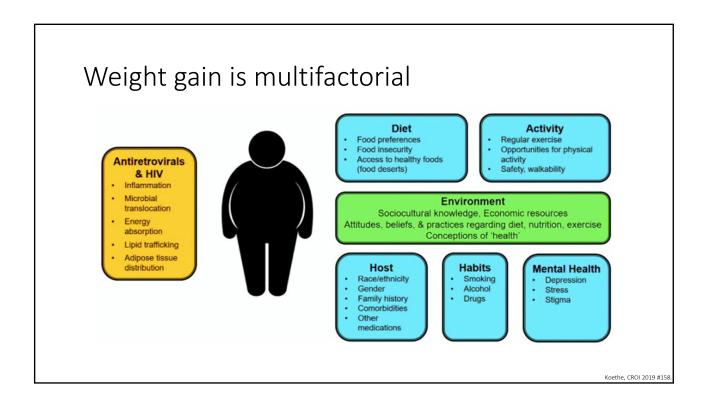
- ADVANCE Study 2019 - RCT in Sub-Saharan Africa, combination of TAF/FTC + DTG led to the most weight gain<sup>5</sup>

IAS 2020 – OPERA cohort demonstrated weight gain in PWH switching from TDF to a TAF-containing regimen, most pronounced in the  $1^{\rm st}$  nine months after switch<sup>6</sup>

ID Week 2020 – A cohort study finds switch from TDF to TAF associated with more weight gain than switch from ABC to  $TAF^7$ 

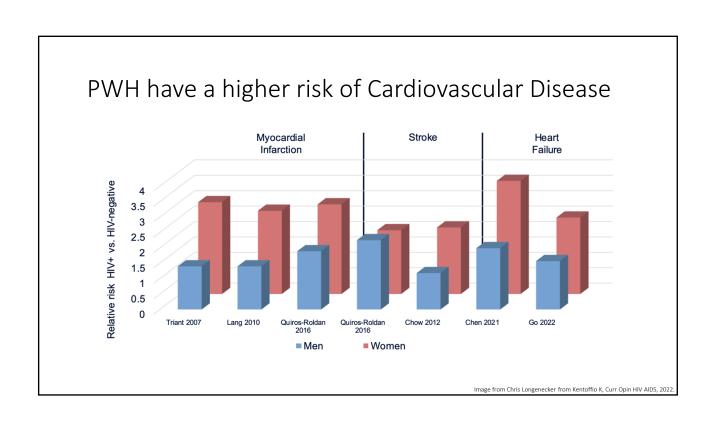
1-Lake, CROI 2019 #669. 2-Bourgi, CROI 2019 #670. 3-McComsey, CROI 2019 #671. 4-Kerchberger, CROI 2019 #672. 5-Venter WDF et al. NEJM. 2019. 6-Mallon, AIDS 2020 # OAB0604. 7-McComsey GA, ID Week 2020



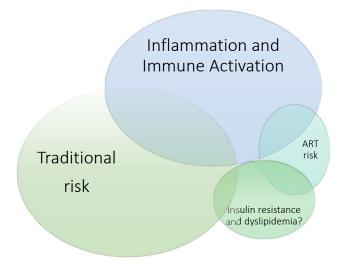


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## Increased Risk of CVD in PWH is Multifactorial



Adapted from Chris Longenecker and Hillary Lis

### Circulation

Volume 140, Issue 2, 9 July 2019; Pages e98-e124 https://doi.org/10.1161/CIR.000000000000000695



### AHA SCIENTIFIC STATEMENT

### Characteristics, Prevention, and Management of Cardiovascular Disease in People Living With HIV: A Scientific Statement From the American Heart Association

Matthew J. Feinstein, MD, MSc, FAHA, Chair, Priscilla Y. Hsue, MD, Vice Chair, Laura A. Benjamin, PhD, Gerald S. Bloomfield, MD, MPH, FAHA, Judith S. Currier, MD, Matthew S. Freiberg, MD, MSc, Steven K. Grinspoon, MD, Jules Levin, MS, Chris T. Longenecker, MD, FAHA, and Wendy S. Post, MD, MS On behalf of the American Heart Association Prevention Science Committee of the Council on Epidemiology and Prevention and Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; and Stroke Council

# Management of CV risk in PWH

- Start ART as soon as possible
- Check lipids
  - 2020 HIVMA PC Guidance suggests at baseline, then q5y if normal or q6-12m if abnormal or CV risk factors are present
- Calculate ASCVD and start statin if appropriate, perhaps at lower %s
  - Beware PIs and NNRTIs with statins
  - In general, atorvastatin, pitavastatin, and rosuvastatin OK
- Discuss smoking cessation, BP control, diet, and exercise

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The NEW ENGLAND JOURNAL of MEDICINE

### **REVIEW ARTICLE**

Julie R. Ingelfinger, M.D., Editor

# Kidney Diseases Associated with Human Immunodeficiency Virus Infection

Scott D. Cohen, M.D., M.P.H., Jeffrey B. Kopp, M.D., and Paul L. Kimmel, M.D.

# Common Causes of CKD in PWH

- The usual causes, including non-ART medication side effects
- Hepatitis B or C
- HIV-associated nephropathy (HIVAN)
  - Nephrotic range proteinuria not on ART (low CD4, high VL)
- Tenofovir-associated nephrotoxicity

Cohen SD, NEJM, 2017

# Tenofovir-Associated Nephrotoxicity

- Due to TDF more often than TAF
- May or may not reverse with drug discontinuation
- Higher risk with ritonavir-boosted medications, caution with cobicistat
- Use of tenofovir can lead to any of the following:
  - 1. GFR decline
  - 2. Proteinuria
  - 3. Proximal tubulopathy
  - 4. Fanconi syndrome (a type II renal tubular acidosis)

Cohen SD, NEJM, 2017. Hamzah L, J Infect, 2017. Cattaneo D, JAIDS, 2018

# Diagnostic Workup of Cr Elevation in PWH

CONSIDER BENIGN
ART EFFECT

Did the patient recently start an ART which can lead to an elevation in serum Cr and is the increase < 20% from baseline? If yes, continue medication.

CONSIDER TENOFOVIR EFFECT

Recall TDF >> TAF more likely implicated. If concerned, obtain UA and send urine protein:creatinine ratio. Send urine Cr, urine  $PO_4$ , serum Cr, and serum PO4 to calculate a  $FePO_4$ . If elevated, refer to nephrology.

CONSIDER NON-HIV RELATED CAUSES

Comorbid conditions, such as HTN and DM, are increasingly common in PWH. Screen for Hep B and Hep C. Review medication list for nephrotoxic meds.

SEND OTHER
DIAGNOSTIC WORKUP

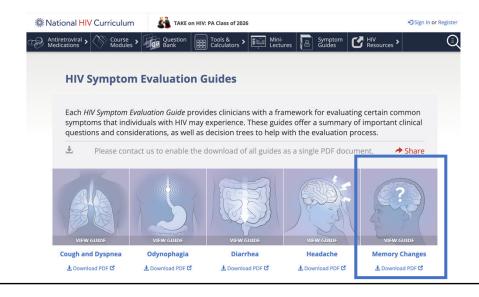
If FePO4 < 20%, patient is not on tenofovir-containing ART, patient has proteinuria, or high suspicion remains, consider renal ultrasound, post-void residual, and nephrology consultation.

# Multimorbidity in HIV, especially those aging

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# Neurocognitive Decline is Multifactorial in PWH | Sepression | Sepres

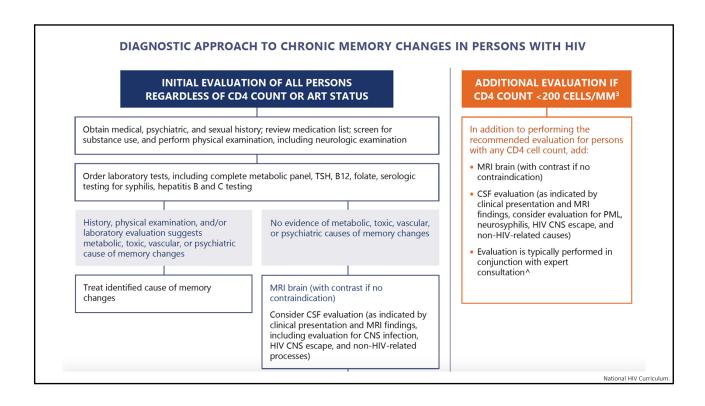
# Evaluation of Memory Changes in HIV

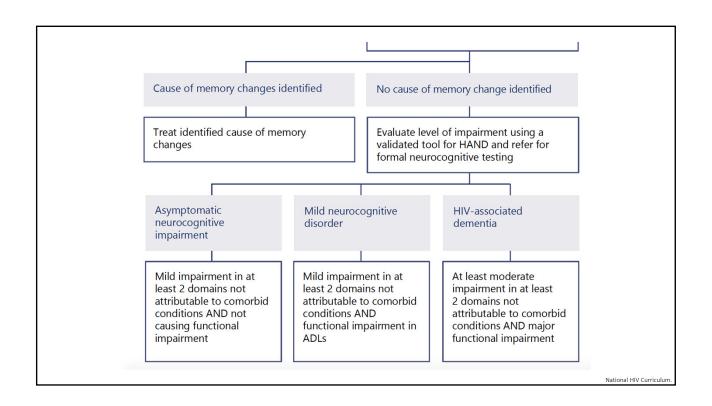


Evaluation of Memory Changes in PWH

- What is the most recent CD4 cell count?
- Is the person taking a medication known to cause neurologic or cognitive side effects?
- Has syphilis testing been performed?
- Are there associated symptoms that suggest a metabolic, toxic, or psychiatric disorder?
- Are there signs or symptoms that suggest obstructive sleep apnea?
- Could HIV infection be the cause?

National HIV Curriculum.





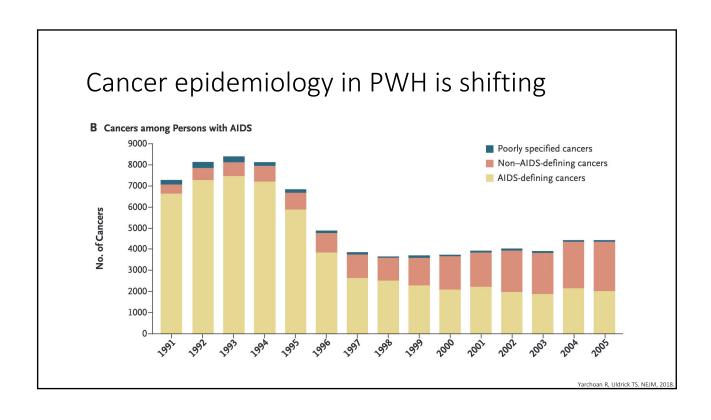
# HIV-Associated Neurocognitive Disorders (HAND)

- A spectrum of disorders due to HIV that can cause cognitive decline
- HIV-associated Dementia (HAD) is the most severe of HAND<sup>1</sup>
  - International HIV Dementia Scale (IHDS) can be used in diagnosis
- In 2023, International HIV Cognition Working Group suggested moving away from HAND alone toward HABI (HIV-associated brain injury), which would include HAND and HAD and incorporates multimorbidity<sup>2</sup>
- Management includes treating HIV
  - Current ART have excellent CNS penetration
  - No data to support intensifying ART if already suppressed<sup>3</sup>

1-National HIV Curriculum. 2-Nightingale S et al, Nature Reviews Neurology, 2023. 3-Letendre SL, CID, 2023

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# Cancer Screening in PWH

Disease	Approach	Notes
Anal CA	ANCHOR study shows benefit to screening for anal dysplasia	TBD
Colon CA	C-scope q10yrs or FIT yearly age 45-75	Same as for without HIV
Lung CA	Annual low dose CT chest if age 50-80 and 20 pack- year smoking hx and smoked within last 15yrs and would be candidate for curative resection (grade B)	Same as for without HIV
Prostate CA	Ages 55-69 should make an individual decision about prostate CA screening with their clinician (do not screen if $\geq$ 70yo)	Same as for without HIV
Breast CA	Mammogram q1-2 yrs in age 50-75	Same as for without HIV
Cervical CA	See next slide	Different in HIV

Table modified from David Sears

# Cervical Cancer Screening in PWH

Age	Recommendation
<21	Pap within 1 yr of sexual activity, no later than age 21
21-29	Pap at diagnosis of HIV, repeat yearly x 3, then if all normal, Pap every 3 years
<30	No HPV testing unless abnormalities are found on Pap
≥30	Pap with HPV cotesting; if both negative consecutively x 3, then Pap with HPV q 3 years

### **Key Points:**

- Most will need Pap with HPV co-test
- Never stop screening (i.e. in women without HIV recommendation is to stop screening at age 65 but women with HIV continue)
- Abnormal Pap and/or HPV follow-up is different too

National HIV Curriculum. 2020 HIVMA Primary Care Guidance

# Multimorbidity in HIV, especially those aging

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# Relationship between HIV and Osteoporosis

- $\bullet$  Osteoporosis is more common in PWH compared to age-matched individuals without  ${\rm HIV^1}$ 
  - PWH have a higher risk of low bone mineral density (BMD) and fragility fractures<sup>2</sup>
- Reasons are multifactorial
  - ART contributes as well, specifically TDF and protease inhibitors
  - ART initiation leads to 2-6% loss in BMD during the first 2 years of therapy<sup>3</sup>
  - HIV-1 can infect osteoclast precursors and increase bone resorption<sup>4</sup>
- Increased risk of osteoporosis with HCV, commonly seen in PWH<sup>5</sup>
- Unrelated to osteoporosis, PWH are at increased risk of avascular necrosis

1-Todd Brown, Ryan White Provider Conference, 2020. 2-McComsey GA, CID, 2010. 3-Brown TT, CID, 2015. 4-Raynaud-Messina B, PNAS, 2018. 5-Wijarnpreecha K, Saudi J Gastroenterol, 2017.

### Etiologies of Bone Loss in HIV are Multifactorial Smoking/alcohol Weight loss Lipodystrophy Glucocorticoids Decreased activity CKD **HCV** infection Hypogonadism Vitamin D deficiency Host Direct effect of viral Direct effect on bone cells proteins on bone cells Inadequate mineralization Immune activation Immune reconstitution **Virus** ART Brown TT, HIV and the Bo

# Recommendations for Evaluation and Management of Bone Disease in HIV

Todd T. Brown,<sup>1</sup> Jennifer Hoy,<sup>2</sup> Marco Borderi,<sup>3</sup> Giovanni Guaraldi,<sup>4</sup> Boris Renjifo,<sup>5</sup> Fabio Vescini,<sup>6</sup> Michael T. Yin,<sup>7</sup> and William G. Powderly<sup>8</sup>

<sup>1</sup>Division of Endocrinology, Diabetes and Metabolism, Johns Hopkins University School of Medicine, Baltimore, Maryland; <sup>2</sup>Department of Infectious Diseases, Alfred Hospital and Monash University, Melbourne, Australia; <sup>3</sup>Infectious Diseases Unit, Department of Medical and Surgical Sciences, Alma Mater Studiorum University of Bologna, and <sup>4</sup>Department of Medical and Surgical Sciences for Children and Adults, University of Modena and Reggio Emilia, Modena, Italy; <sup>5</sup>Global Medical Affairs Virology, Global Pharmaceutical Research and Development, AbbVie, North Chicago, Illinois; <sup>6</sup>Endocrinology and Metabolism Unit, University Hospital "Santa Maria della Misericordia," Udine, Italy; <sup>7</sup>Department of Medicine, Columbia University Medical Center, New York, New York; and <sup>8</sup>Division of Infectious Diseases, Washington University School of Medicine, St Louis, Missouri

Brown TT, CID, 201

# Management of Bone Disease in PWH

- DXA screening in men with HIV ≥ 50 and postmenopausal women
- Optimize ART if possible
  - If osteopenia or osteoporosis, avoid PIs and TDF if possible
  - Switching from TDF to TAF leads to improvements in BMD
    - Over 48 weeks, can improve BMD by +1.5 to +2.31
  - In osteoporosis, OK to use TAF or can switch to a TFV-sparing regimen entirely
- Treat for osteopenia or osteoporosis similar to how is done for general population

Pozniak, JAIDS, 2017

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# Testosterone Deficiency in PWH

- Background
  - In 1988, 50% of a small cohort of men with AIDS had a lab diagnosis of low T<sup>1</sup>
  - In a US study of 530 men, laboratory-confirmed low T found in 9.3% of PWH, as compared to 7.2% in matched HIV-negative controls<sup>2</sup>
  - Among PWH who initiated T, only 24% had laboratory-confirmed T deficiency<sup>3</sup>
- When screen? In men with HIV if symptoms are suggestive of low T
- How screen? Fasting AM blood draw of free AND total testosterone
  - HIV can increase SHBG concentrations, which can lead to falsely elevated total T

1- Dobs AS, Am J Med, 1988. 2- Monroe AK, AIDS Res Ther, 2014. 3- Bhatia R, AIDS, 201

# Conclusions

- People with HIV are living longer and growing older
- Greater than 50% of PWH are over 50
- Do not forget to screen older adults for STIs and HIV
- PWH may have accelerated and accentuated aging, more frailty, more multimorbidity, and polypharmacy