HIV 101: Primary Care for People with HIV

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Planner/Reviewer 1 has no relevant financial affiliations to disclose. (Updated 09/22/21)

Planner/Reviewer 2 has no relevant financial affiliations to disclose. (Updated 09/28/21)

Slide 2

Pretest Question #3

Which is **TRUE** about screening and/or treatment of hyperlipidemia in persons with HIV?

- CD4 count < 200/µL is as strong a risk factor for cardiovascular disease as hypertension
- All persons with HIV should be on a statin, regardless of LDL cholesterol level
- Lovastatin and simvastatin are preferred statins in people taking protease inhibitors
- Prolonged HIV viremia increases cardiovascular risk, and requires adjustment of the risk calculator score

FINALLY! An Update!

Clinical Infectious Diseases

MAJOR ARTICLE







Primary Care Guidance for Persons With Human Immunodeficiency Virus: 2020 Update by the HIV Medicine Association of the Infectious Diseases Society of America

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Vaccinations for Adults with HIV

Routine Vaccinations in Adults with HIV

Generally: Follow CDC Advisory Committee on Immunization Practices (ACIP)¹ and CDC/NIH/HIVMA-IDSA Opportunistic Infection guidelines²

- Influenza annually (inactivated)
- TdAP same as general population
- Meningococcus A,C,W,Y booster every 5 yrs if still at increased risk
- HPV 3 doses!
- Measles, mumps, rubella: if not immune and CD4 ≥ 200/μL; contraindicated < 200/μL
- Varicella zoster: (recombinant) any CD4 but best response CD4 > 200/μL

- Hepatitis A and B
- Pneumococcus
- SARS CoV-2

¹ACIP Recommendations: https://www.cdc.gov/vaccines/hcp/acip-recs/index.html

²OI Guidelines, updated 8/13/21: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/Adult_OI.pdf

Hepatitis B Vaccination in Adults^{1,2}

- Immunize if HBsAg & HBsAb negative or HBsAb < 10 mIU/mL
 - If isolated HBcAb positive, repeat entire series OR give 1 booster and measure response in 1-2 mo (should be >100mIU/mL)²
- Responses may be reduced if CD4 cell count < 200/μL or unsuppressed HIV-1 RNA
 - Decision to delay until CD4 rise or virus suppressed depends on hepatitis risk
 - Ideally vaccinate while CD4 > 350/μL²
- Repeat HBsAb 1-2 mo after vaccination or at next visit
 - HBsAb level should be ≥ 10 mIU/mL

¹Prevention of Hepatitis B Virus Infection in US: Recommendations of ACIP. MMWR 2018;67

²OI Guidelines, updated 8/13/21: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/Adult_OI.pdf

Hepatitis B Vaccines: Dosing^{1,2}

3 doses: give at 0, 1, and 6 mo

- If 4 doses, give at 0, 1, 2, & 6 mo
- Recombivax HB[®] 10, 20, or 40 μg/dose
- Engerix-B[®] 20 or 40 μg/dose

Two doses 1 month apart

 Heplisav-B[®] 20 µg/dose (recombinant, CpG adjuvant)

Twinrix[®]Inactivated hepatitis A 720 EL.U & recombinant hep BsAg 20 μg at 0, 1, & 6 months OR at days 0, 7, 21-30, & 12 mo

¹Prevention of Hepatitis B Virus Infection in US: Recommendations of ACIP. MMWR 2018;67

²OI Guidelines, updated 8/13/21: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/Adult_OI.pdf

2 vs 3 Dose HBV Vaccine: Heplisav-B^{®1} Package Insert

Timepoint	Table 3 Study 1: Seroprotection Rate of HEPLISAV-B and Engerix-B (ages 18 through 55 years)					
	HEPLISAV-B N = 1511 SPR (95% CI)	Engerix-B N = 521 SPR (95% CI)	Difference in SPRs (HEPLISAV-B minus Engerix-B) Difference (95% CI)			
Week 12 (HEPLISAV-B) Week 28 (Engerix-B)	95% (93.9, 96.1)	81.3% (77.8, 84.6)	13.7% (10.4, 17.5)*			
Timepoint	Table 4 Study 2: Seroprotection Rate of HEPLISAV-B and Engerix-B (ages 40 through 70 years)					
	HEPLISAV-B N = 1121 SPR (95% CI)	Engerix-B N = 353 SPR (95% CI)	Difference in SPRs (HEPLISAV-B minus Engerix-B) Difference (95% CI)			

CI = confidence interval; $N = number of subjects in the analysis population in the group; SPR = seroprotection rate (% with anti-HBs <math>\geq 10 \text{ mIU/mL}$).

Clinical trial number: NCT01005407

^{*} Noninferiority was met because the lower bound of the 95% confidence interval of the difference in SPRs was greater than -10%. The SPR following HEPLISAV-B was statistically significantly higher than following Engerix-B (lower bound of the 95% confidence interval of the difference in SPRs was greater than 0%).

¹Heplisav-B = Recombinant HBsAg + CpG 1018 (cytosine phosphoquanine oligonucleotide, a TLR 9 agonist)

Hepatitis B Re-vaccination in Adults^{1,2}

- If HBsAb level < 10 mIU/mL at least 1 mo after full series
 - Give second series of 3 doses of recombinant vaccine using standard or 40 mcg doses at 0, 1, and 6 mo; OR
 - Give second series 4 doses of recombinant vaccine using standard or 40 mcg doses at 0, 1, 2, and 6 mo
 - Give 2 dose recombinant CpG adjuvant vaccine at 0, 1 mo
- Small study showed better response rate, higher antibody levels when using recombinant vaccine 40 mcg vs 20 mcg, both given at 0, 1, 2 mo³

¹Prevention of Hepatitis B Virus Infection in US: Recommendations of ACIP. MMWR 2018;67

²OI Guidelines, updated 8/13/21: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/Adult_OI.pdf
³Vargus, et al. JAMA Network Open.2021; 4(8).

Pneumococcal Vaccination in Adults

Two vaccines

- Pneumococcal conjugate (PCV13)
- Pneumococcal polysaccharide (PPV23 or PPSV23)
- Give PCV13 upon diagnosis regardless of CD4 count
- Give PPV23 at least 8 weeks after PCV13
 - Can wait until CD4 > 200/μL on ART
- Give 2nd dose of PPV23 five years later
- Give 3rd & final PPV23 dose after age 65, at least 5 yrs after last dose
- If 1st dose was PPV23 rather than PCV13, give PCV 13 at least 1 year after PPV23

SARS CoV-2 Vaccination in Persons with HIV

- All approved vaccines are safe and effective for persons with HIV¹
- All people with HIV aged 12 and older should be vaccinated following CDC/FDA recommendations¹
- As with other vaccines, response may be less robust if CD4 < 200/μL¹
 - \bullet On Aug. 12, FDA amended Pfizer, Moderna EUAs to recommend 3rd mRNA dose for people with moderate-severe immune compromise 2 including "advanced or uncontrolled HIV" 3
 - Moderna or Pfizer: 3rd doses for PWH with advanced or uncontrolled HIV³
 - If Pfizer series, 3rd dose of Pfizer (age ≥ 12 yrs), ≥ 28 days after 2nd vaccine
 - If Moderna series, 3rd dose of Moderna (age ≥18 yrs), ≥ 28 days after 2nd vaccine
 - If J & J primary: wait for further recommendations

¹HIVMA. COVID19 Vaccines and People with HIV FAQ. 8/23/21: https://www.idsociety.org/globalassets/idsa/public-health/covid-19/covid-19-vaccines-hiv-faq.pdf
²FDA. 8/12/21: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-additional-vaccine-dose-certain-immunocompromised

³CDC. 9/2/21: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/immuno.html Slide 12

Boosters for People with HIV as of 9/30/21

- Pfizer recipients ONLY: eligible for Pfizer booster ≥ 6 mo after 2nd vaccine
 - ≥ 65 years old or those in long-term care settings: **SHOULD** get booster
 - PWH aged 50-64 yo: SHOULD get booster [underlying medical condition]
 - PWH aged 18-49 yo: MAY get booster [underlying medical condition]
 - If Moderna or J & J primary vaccination: wait for future recs [soon, please!]
- OMG! What a great topic to chat about in the Q & A!!! (Hint...)

¹FDA. 8/12/21: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-additional-vaccine-dose-certain-immunocompromised

²CDC 9/23/21: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

Cancer Screening for People with HIV

Smoking and Cancer in People with HIV

- Smoking: up to ¾ of PWH, in some studies
- Cancer burden attributable to smoking
 - Lung cancer: 94%
 - Other 'smoking related' cancers (esophageal, oral, etc.): 31%
- ◆ Anal cancer: 32%
 - All cancer: 9%
- Low dose chest CT scan according to USPSTF recommendations



Altekruse, AIDS, 2018

Cancer Screening for People with HIV

- Prostate, breast, lung, colon cancer screening: follow general population guidelines from USPSTF and American Cancer Society
- Anal cancer screening¹
 - Digital anorectal exam annually if asymptomatic
 - For those having receptive anal sex: periodic anal cytology by anal Pap test if access to referral and high-resolution anoscopy is available
 - Utility of anal Pap screening being tested in NIH ANCHOR study

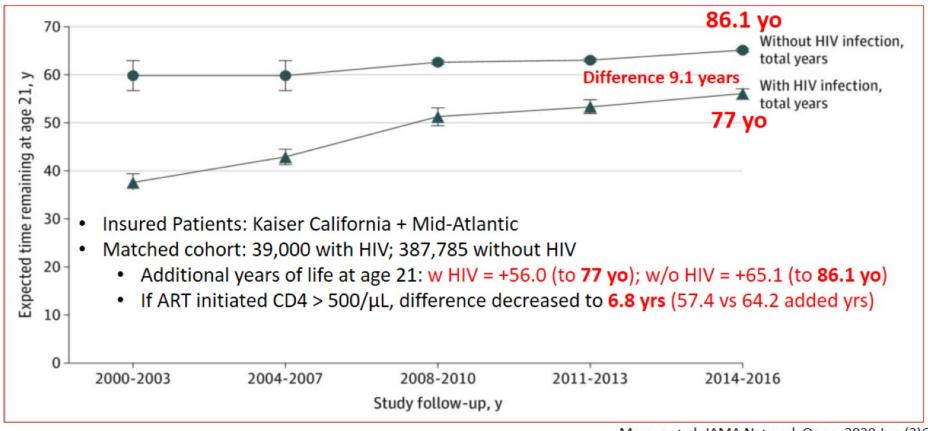
¹Thompson, et al. Primary Care Guidance for Persons With HIV: 2020 Update: Available at HIVMA.org under Guidelines Slide 16

Cancer Screening for People with HIV

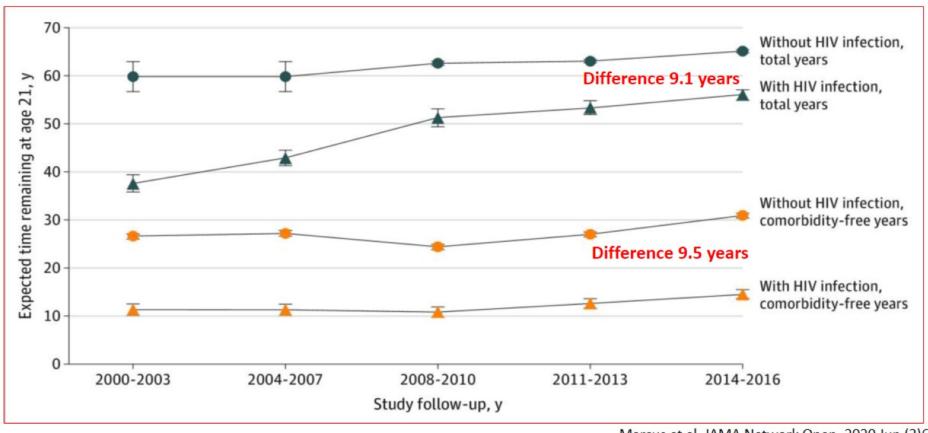
- Cervical cancer screening¹
 - 1st Pap w/in 1 yr of sexual debut or at HIV dx, at least by 21 yo
 - 21-29 yo: Annual Pap until 3 consecutive normal, then every 3 yrs if normal: HPV testing not recommended
 - ≥ 30 yo: Annual Pap until 3 consecutive normal, then every 3 yrs if normal
 - If HPV co-testing done with Pap and both are negative, Pap with HPV can be done every 3 years after a single Pap test
 - Colposcopy if abnormal Pap or normal Pap + persistent positive HPV
 - No upper age for stopping Pap testing in persons with HIV

Screening for and Managing Metabolic and Other Noncommunicable Diseases

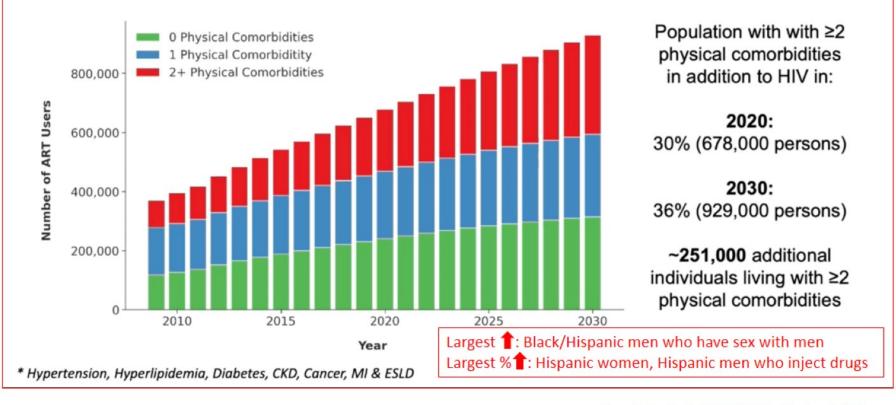
People with HIV are Living Longer...



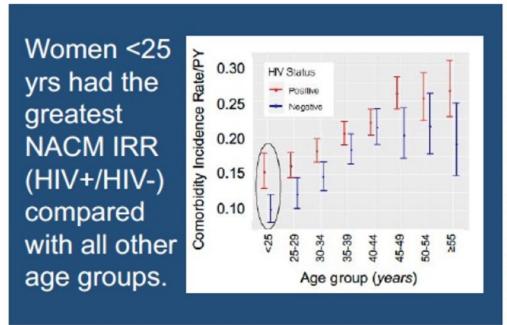
People with HIV are Living Longer... But NOT Without Comorbidities



Projected burden of multimorbidity among people with HIV using ART in the US, 2009 – 2030



Women < 25 yo With HIV Accumulate NACM Faster Than Those Without HIV



Age (yrs)	alRR (HIV+ vs HIV-)	95% CI
<25	1.50	1.21, 1.87
25-29	1.32	1.10, 1.58
30-34	1.24	1.09, 1.42
35-39	1.12	1.004, 1.25
40-44	1.03	0.92, 1.16
45-49	1.28	1.07, 1.53
50-54	1.18	0.95, 1.46
≥55	1.38	1.04, 1.84

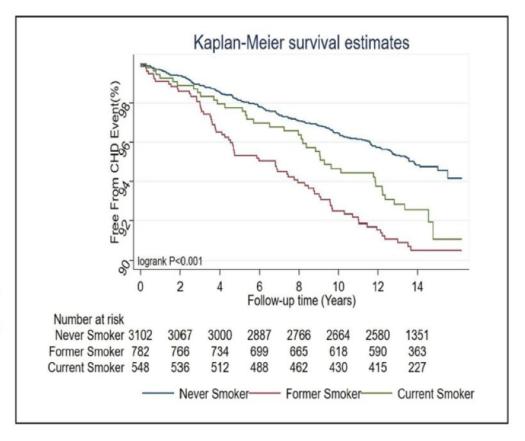
Approach to Comorbidities: Increased Awareness, Early Intervention

- Smoking
- SMOKING
- SMOKING
- SMOKING
- SMOKING!



Cigarette Smoking, Incident Coronary Heart Disease, and Coronary Artery Calcification in Black Adults: The Jackson Heart Study

Adebamike A. Oshunbade, Wondwosen Kassahun-Yimer, Karen A. Valle, Arsalan Hamid, Rodney K. Kipchumba, Daisuke Kamimura, Donald ClarkIII, Wendy B. White, Andrew P. DeFilippis, Michael J. Blaha, Emelia J. Benjamin, Emily C. O'Brien, Robert J. Mentz, Carlos J. Rodriguez, Ervin R. Fox, Javed Butler, Rachel J. Keith, Aruni Bhatnagar, Rose Marie Robertson, Adolfo Correa, and Michael E. Hall

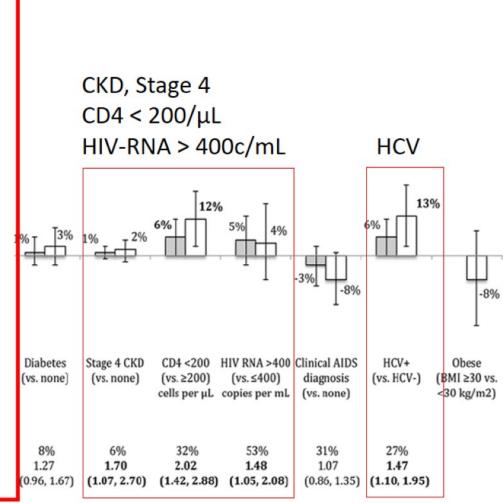


CONCLUSIONS: In a large prospective cohort of Black adults, current smoking was associated with a >2-fold increased risk of CHD over a median follow-up of greater than a decade.

Contribution to MI Risk in PWH (NA-ACCORD)

When obesity included:

DM significant HIV-RNA not significant



Althoff, Lancet HIV, 2020

AHA SCIENTIFIC STATEMENT

Characteristics, Prevention, and Management of Cardiovascular Disease in People Living With HIV

A Scientific Statement From the American Heart Association

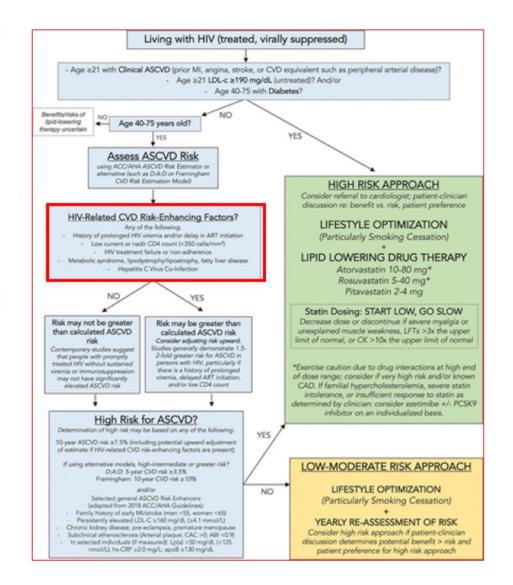
- Recognizes increased ASCVD risk in persons with HIV
 - 1.5-2x increase in MI, stroke, heart failure
 - Increased pulmonary HTN, blood clots, sudden death
- Addresses pathophysiology, screening, treatment
- Includes link to patient perspective from PLWH

ASCVD Risk Assessment and Treatment

Two approaches

- High risk
- Low-moderate risk

Feinstein, Circulation, 2019



High Risk Approach

- Known clinical ASCVD, or
- LDLc ≥ 190 mg/dL (untx) and/or
- Age 40-75 with diabetes mellitus

OR

- Calculated high ASCVD risk by risk calculator tools
- Presence of HIV-related or 2018 ACC/AHA "risk enhancers"

HIGH RISK APPROACH

Consider referral to cardiologist; patient-clinician discussion re: benefit vs. risk, patient preference

LIFESTYLE OPTIMIZATION

(Particularly Smoking Cessation)

LIPID LOWERING DRUG THERAPY

Atorvastatin 10-80 mg* Rosuvastatin 5-40 mg* Pitavastatin 2-4 mg

Statin Dosing: START LOW, GO SLOW

Decrease dose or discontinue if severe myalgia or unexplained muscle weakness, LFTs >3x the upper limit of normal, or CK >10x the upper limit of normal

*Exercise caution due to drug interactions at high end of dose range; consider if very high risk and/or known CAD. If familial hypercholesterolemia, severe statin intolerance, or insufficient response to statin as determined by clinician: consider ezetimibe +/- PCSK9 inhibitor on an individualized basis.

HIV-Related CVD Risk-Enhancing Factors?

Any of the following:

- History of prolonged HIV viremia and/or delay in ART initiation
 - Low current or nadir CD4 count (<350 cells/mm³)
 - HIV treatment failure or non-adherence
- Metabolic syndrome, lipodystrophy/lipoatrophy, fatty liver disease
 - Hepatitis C Virus Co-Infection

If YES: Consider adjusting risk upward; may be 1.5-2x higher

But also...

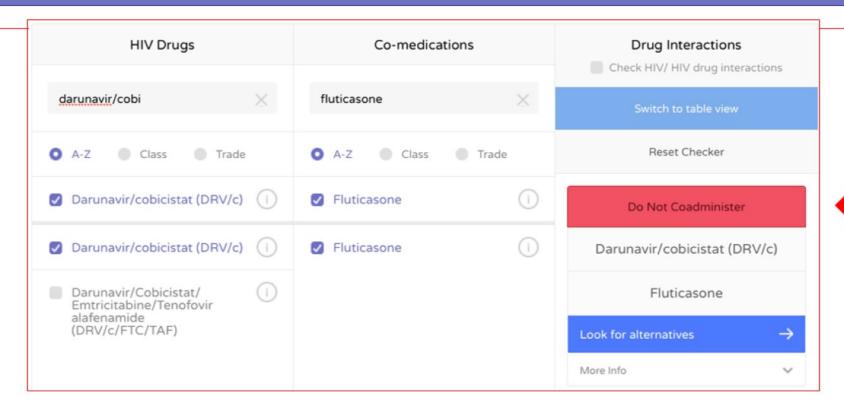
- Control risk factors other than lipids
 - Smoking, smoking, smoking!
 - Diabetes mellitus
 - Hypertension
 - Obesity encourage exercise and diet: education!
- Statin (without hyperlipidemia)?
 - Wait for REPRIEVE trial...

Issues Associated with Polypharmacy

- Inappropriate drugs, doses: review at EVERY visit
- Drug interactions: DON'T GUESS LOOK IT UP!
- Additive toxicities: nephrotoxicity, exacerbation of depression, etc.
- Risk of forgetting doses
- Risk of missing prescriptions/skipping refills due to cost
- Expense
- "Overwhelmed" feeling of just too many pills!

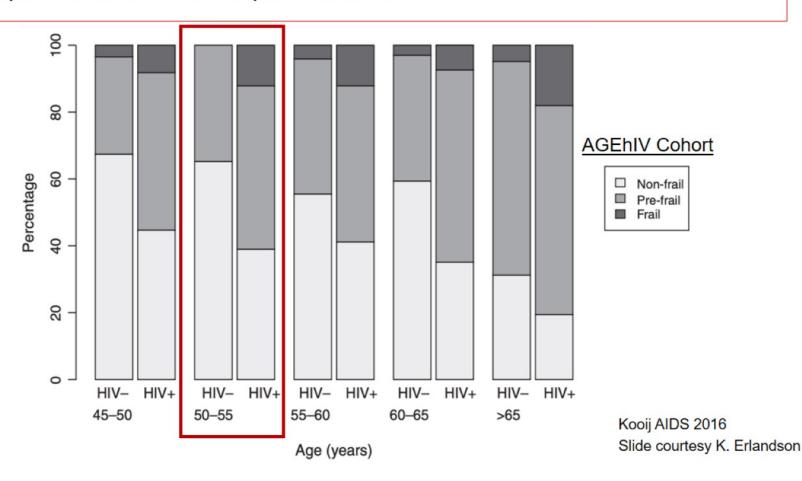






www.hiv-druginteractions.org

Frailty Occurs More Frequently... and Perhaps Earlier in People with HIV



Slide 33

Frailty is Associated with Cardiovascular Risk by ACC/AHA 2013 Pooled Cohort Equation for Men & Women

- WIHS and MACS Cohorts
- Framingham Risk Score and ACC/AHA Pooled Cohort Equation for CVD risk
- Outcome: Fried's frailty phenotype

Repeated measures logistic regression of cardiovascular risk scores with frailty								
	Women				<u>Men</u>			
	HIV- (3,526 visits) HIV+ (8,889 visits)		HIV- (19,500 visits)		HIV+ (19,846 visits)			
ATP-III FRS	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Low risk (<10%)	Ref		Ref		Ref		Ref	
Moderate risk (10-20%)	NS		NS		1.51	1.32, 1.74	1.33	1.18, 1.50
High risk (>20%)	NS		NS		2.31	1.74, 3.07	2.07	1.65, 2.60
ACC/AHA PCE								
Low risk (<7.5%)	Ref		Ref		Ref		Ref	
High risk (≥7.5%)	1.41	1.11, 1.80	1.43	1.20, 1.70	2.12	1.78, 2.51	1.43	1.25, 1.63

Adjusted for education, income, cholesterol medication use, HCV serostatus, and in HIV+ participants, CD4 count, ART therapy and suppressed HIV viral load

Three Tools for Assessing Frailty

- Fried's Frailty Phenotype¹
 - 5 physical variables
- Short Physical Performance Battery (SPPB)^{2,3}
 - 3 physical tasks
- Frailty Index⁴
 - 40 physical, psychological, social/functional variables

Fried's Frailty Phenotype

Frailty indictor	Measure		
Weight loss	Self-reported weight loss of more than 10 pounds or recorded weight loss of ≥ 5% per annum		
Self-reported exhaustion	Self-reported exhaustion on CES-D depression score (3-4 days per week or most of the time)		
Low energy expenditure	Energy expenditure <383 KCal/week (males) or <270 KCal/week (females)		
Slow gait speed	Standardised cut-off times to walk 15 feet, stratified for sex and height		
Weak grip strength	Grip strength, stratified by sex and BMI Requires dynomometer		

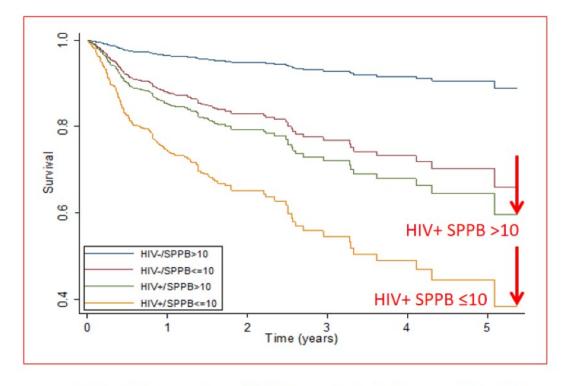
Key. CES-D, Center for Epidemiological Studies Depression; BMI, body mass index.

Frailty is associated with survival!

Frailty: Short Physical Performance Battery (SPPB)

3 physical tasks:

- Repeated chair stands (sit then stand 5 times)
- Balance tests
- 4-meter (10-foot)
 walk test



geriatrictoolkit.missouri.edu/SPPB-Score-Tool.pdf; Greene, AIDS, 2014

Frailty Index

- Relates deficit accumulation to risk of death
- 40 variables
 - Physical: e.g. walk outside < 3d/wk; wt loss > 5 kg/yr
 - Comorbid diseases, without regard to severity
 - Psychological: feel depressed, happy, lonely, etc.
 - Social/Functional: help bathing, dressing, eating, etc.
- Scored between 0-1 = deficits/variables
 - < 0.08 = robust; ≥ 0.25 = frail

Frailty is Dynamic! Interventions to Prevent Frailty

- Exercise, strength and balance training
- Social interaction
- Healthy diet
- Preventative health care and screening
- Management of medications
- Smoking cessation

Screening for Mental Health and Substance Use Issues

- Depression and substance use are common; screening is uncommon
- Easy screening tools available (and reimbursable!)
- Depression PHQ 2 and 9; Anxiety GAD-2 and 7
 - PHQ-2: Over the last 2 weeks, how often have you been bothered by the following: (score 0-3)
 - Little interest or pleasure in doing things
 - · Feeling down, depressed or hopeless
- Alcohol Use: CAGE and AUDIT
- Drug Use: TICS, opioid risk tool

Screening Resources

National HIV Curriculum

https://www.hiv.uw.edu

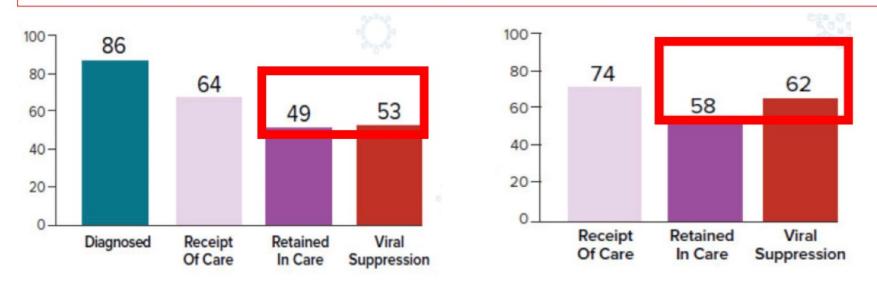
◆ Sign In or Registe Tools & Calculators> Resources> Patient Health Questionnaire-2 (PHQ-2) **Mental Disorders** Screening The PHQ-2 inquires about the frequency of depressed mood and anhedonia over the past two weeks. The PHQ-2 includes the first two items of the PHQ-9. Dementia: IHDS • The purpose of the PHQ-2 is to screen for depression in a "first-step" approach. Anxiety: GAD-2 • Patients who screen positive should be further evaluated with the PHQ-9 to determine whether they meet criteria for a depressive disorder. Anxiety: GAD-7 Over the last 2 weeks. Not at all Several More than Nearly Depression: PHQ-2 how often have you half the every day days been bothered by the days Depression: PHQ-9 following problems? PTSD: PC-PTSD-5 1. Little interest or pleasure in doing **Substance Use** things Screening 2. Feeling down, Alcohol: AUDIT-C depressed or hopeless Alcohol: CAGE PHQ-2 score obtained by adding score for each question (total points) CAGE-AID Drug Abuse: TICS Interpretation: Opioid: Risk Tool • A PHQ-2 score ranges from 0-6. The authors identified a score of 3 as the optimal cutpoint when using the PHQ-2 to screen for depression. Clinical Calculators • If the score is 3 or greater, major depressive disorder is likely. APRI Calculator Patients who screen positive should be further evaluated with the PHQ-9, other diagnostic instruments, or direct interview to determine whether they **BMI Calculator** meet criteria for a depressive disorder. C-Cl C-l--l-t-

National HIV Curriculum

https://www.hiv.uw.edu/page/mental-health-screening/phq-2

What is Needed to End the Epidemic? Engagement in Care: "It's Complicated"

Half of all PWH in US have suppressed virus; slightly more among those diagnosed **Worse** among multiple subpopulations that vary regionally **Structural** as well as individual barriers must be addressed = "social determinants"

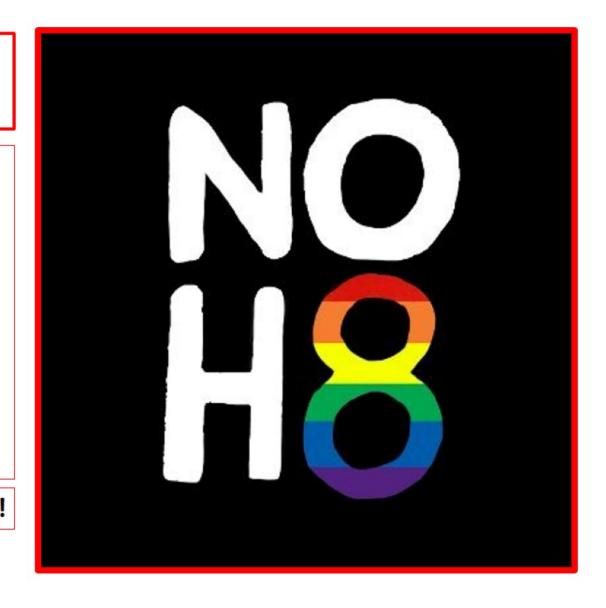


CDC: Understanding the HIV Care Continuum, July 2019. https://www.cdc.gov/hiv/pdf/library/factsheets/cdc-hiv-care-continuum.pdf

Stigma Kills!

- HIV status
 - HIV Criminalization Laws
- LGBTQ+ discrimination
- Ageism
- Substance use
- · Mental health
- Race/ethnicity
- Socioeconomic status

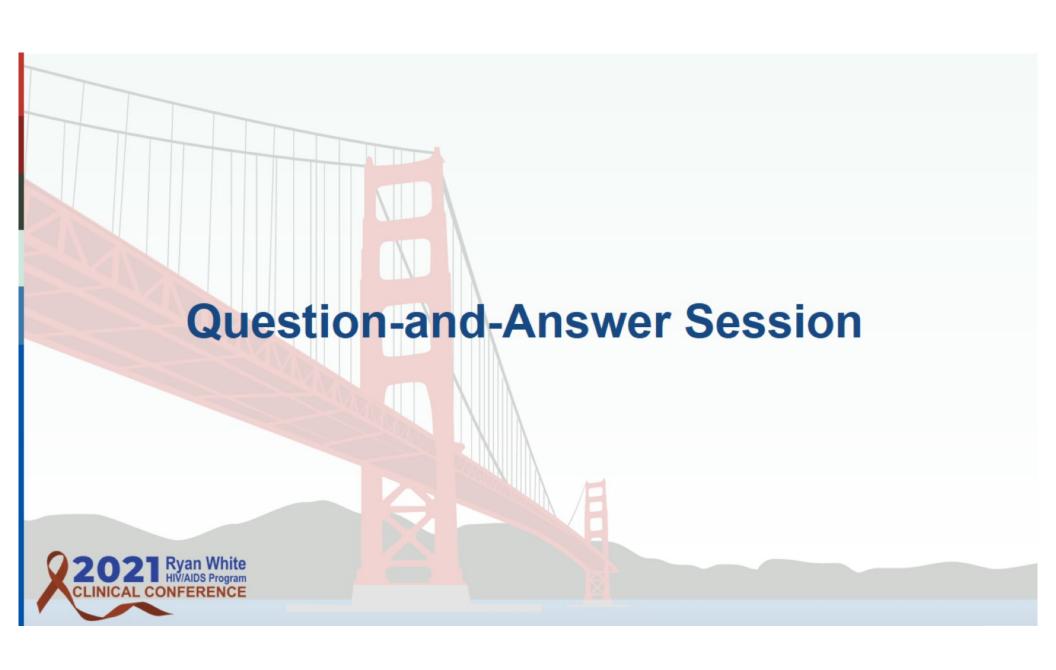
Advocacy by clinicians is needed!



Posttest Question #3

Which is **TRUE** about screening and/or treatment of hyperlipidemia in persons with HIV?

- CD4 count < 200/µL is as strong a risk factor for cardiovascular disease as hypertension
- All persons with HIV should be on a statin, regardless of LDL cholesterol level
- Lovastatin and simvastatin are preferred statins in people taking protease inhibitors
- Prolonged HIV viremia increases cardiovascular risk, and requires adjustment of the risk calculator score



Back Up

Boosters: FDA Emergency Use Authorization¹ and CDC Recommendations²

- Applies only to Pfizer-BioNTech vaccine
- Booster to be given at least 6 months after 2nd dose of primary series
- Should receive a booster:
 - People ≥ 65 yo and residents in long-term care settings
 - People aged 50-64 with underlying medical conditions (including HIV)
- May receive a booster, based on individual benefits and risks
 - People aged 18-49 with underlying medical conditions (including HIV)
 - People aged 18-64 years who are at increased risk for COVID-19 exposure and transmission because of occupational or institutional setting

¹FDA. https://www.fda.gov/news-events/press-announcements/fda-authorizes-booster-dose-pfizer-biontech-covid-19-vaccine-certain-populations
https://www.fda.gov/news-events/press-announcements/fda-authorizes-booster-dose-pfizer-biontech-covid-19-vaccine-certain-populations
https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html