HIV 101: Primary Care for People with HIV

Melanie A. Thompson, MD
Co-chair
HIV Medicine Association/Infectious Diseases Society of America
HIV Primary Care Guidance Panel
Atlanta, GA

2021 Ryan White HIV/AIDS Program CLINICAL CONFERENCE

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

Dr Thompson has received grants for research paid to her institution (ARCA, Atlanta, GA) by Bristol Myers Squibb, Cepheid Inc., Cytodyn Inc, Frontier Biotechnologies, Gilead Sciences, Inc., GlaxoSmithKline, Merck Sharp Dohme, and ViiV Healthcare. (Updated 09/28/21)

Planner/Reviewer Financial Disclosures:
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)

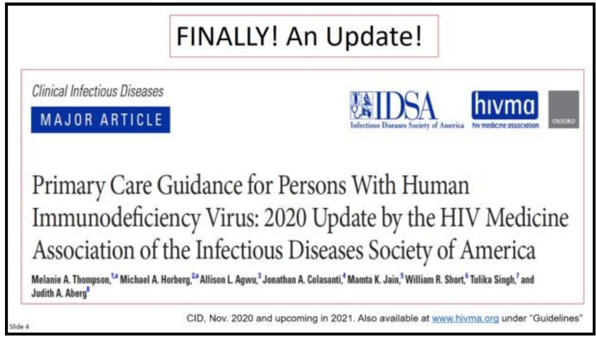
Slide 2

Pretest Question #3

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

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

Slide 3



Vaccinations for Adults with HIV

Slide 5

Routine Vaccinations in Adults with HIV

Generally: Follow CDC Advisory Committee on Immunization Practices (ACIP)[1] and CDC/NIH/HIVMA-IDSA Opportunistic Infection guidelines[2]

- 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

[1]ACIP Recommendations: https://www.cdc.gov/vaccines/hcp/acip-recs/index.html
[2]OI Guidelines, updated 8/13/21: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/Adult_OI.pdf

Slide 6

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/µL[2]
- Repeat HBsAb 1-2 mo after vaccination or at next visit
  - HBsAb level should be ≥ 10 mIU/mL

[1]Prevention of Hepatitis B Virus Infection in US: Recommendations of ACIP. MMWR 2018;67
[2]OI Guidelines, updated 8/13/21: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/Adult_OI.pdf

Slide 7

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

[1]Prevention of Hepatitis B Virus Infection in US: Recommendations of ACIP. MMWR 2018;67
[2]OI Guidelines, updated 8/13/21: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/Adult_OI.pdf

Slide 8

2 vs 3 Dose HBV Vaccine: Heplisav-B®[1] Package Insert

Table 3
Study 1: Seroprotection Rate of HEPLISAV-B and Engerix-B (ages 18 through 55 years)

Timepoint	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)*

Table 4
Study 2: Seroprotection Rate of HEPLISAV-B and Engerix-B (ages 40 through 70 years)

Timepoint	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)
Week 12 (HEPLISAV-B) Week 32 (Engerix-B)	90.1% (88.2, 91.8)	70.5% (65.5, 75.2)	19.6% (14.7, 24.8)*

CI = confidence interval; N = number of subjects in the analysis population in the group; SPR = seroprotection rate (% with anti-HBs ≥ 10 mIU/mL).
* 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%).
Clinical trial number: NCT01005407

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

Slide 9

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 mo[3]

[1]Prevention of Hepatitis B Virus Infection in US: Recommendations of ACIP. MMWR 2018;67
[2]OI Guidelines, updated 8/13/21: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/Adult_OI.pdf
[3]Vargus, et al. JAMA Network Open.2021; 4(8).

Slide 10

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

Slide 11 OI Guidelines, updated 8/13/21: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/Adult_OI.pdf

SARS CoV-2 Vaccination in Persons with HIV

- All approved vaccines are safe and effective for persons with HIV[1]
- All people with HIV aged 12 and older should be vaccinated following CDC/FDA recommendations[1]
- As with other vaccines, response may be less robust if CD4 < 200/µL[1]
  - 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** HIV[3]
    - 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

[1]HIVMA. 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
[2]FDA. 8/12/21: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-additional-vaccine-dose-certain-immunocompromised
[3]CDC. 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…)

[1]FDA. 8/12/21: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-additional-vaccine-dose-certain-immunocompromised
[2]CDC 9/23/21: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

Slide 13

Cancer Screening for People with HIV

Slide 14

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

Slide 15

Cancer Screening for People with HIV

- Prostate, breast, lung, colon cancer screening: follow general population guidelines from USPSTF and American Cancer Society
- Anal cancer screening[1]
  - Digital anorectal exam annually if asymptomatic
  - For those having receptive anal sex: periodic anal cytology by anal Pap test <u>if access to referral and high-resolution anoscopy is available</u>
  - Utility of anal Pap screening being tested in NIH ANCHOR study

[1]Thompson, 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

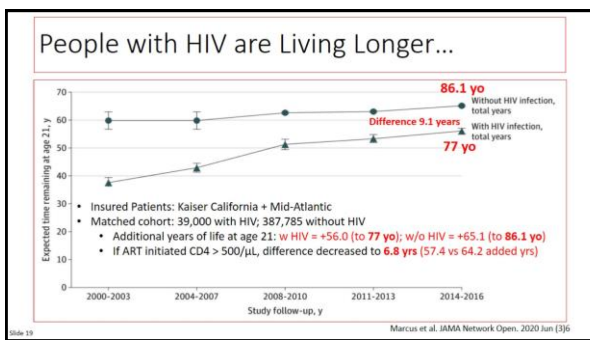
- Cervical cancer screening[1]
  - 1st Pap w/in 1 yr of sexual debut or at HIV dx, at least by 21 yo
  - 21-29 yo: Annual Pap until 3 consecutive normal, then every 3 yrs if normal: HPV testing not recommended
  - ≥ 30 yo: Annual Pap until 3 consecutive normal, then every 3 yrs if normal
    - If HPV 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

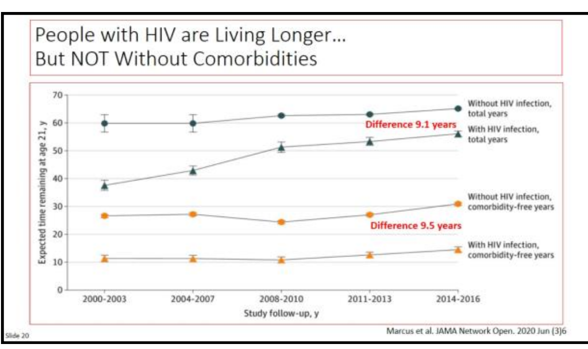
OI Guidelines, updated 8/13/21: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/Adult_OI.pdf

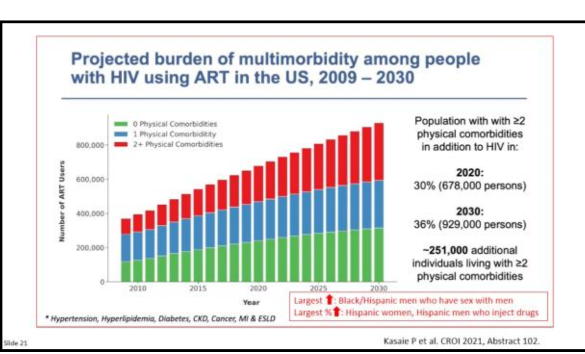
Slide 17

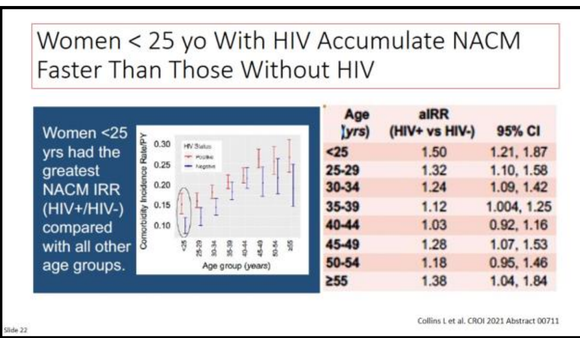
Screening for and Managing Metabolic and Other Noncommunicable Diseases

Slide 18


People with HIV are Living Longer…
86.1 yo
Without HIV infection, total years
Difference 9.1 years
With HIV infection, total years
77 yo
Expected time remaining at age 21, y
Insured Patients: Kaiser California + Mid-Atlantic
Matched cohort: 39,000 with HIV; 387,785 without HIV
Additional years of life at age 21: w HIV = +56.0 (to 77 yo); w/o HIV = +65.1 (to 86.1 yo)
If ART initiated CD4 > 500/µL, difference decreased to 6.8 yrs (57.4 vs 64.2 added yrs)
2000-2003
2004-2007
2008-2010
2011-2013
2014-2016
Study follow-up, y
Marcus et al. JAMA Network Open. 2020 Jun (3)6


People with HIV are Living Longer…
But NOT Without Comorbidities
Without HIV infection, total years
Difference 9.1 years
With HIV infection, total years
Without HIV infection, comorbidity-free years
Difference 9.5 years
With HIV infection, comorbidity-free years
Expected time remaining at age 21, y
2000-2003
2004-2007
2008-2010
2011-2013
2014-2016
Study follow-up, y
Marcus et al. JAMA Network Open. 2020 Jun (3)6


Projected burden of multimorbidity among people with HIV using ART in the US, 2009 – 2030
0 Physical Comorbidities
1 Physical Comorbidity
2+ Physical Comorbidities
Number of ART Users
Year
Population with with ≥2 physical comorbidities in addition to HIV in:
2020:
30% (678,000 persons)
2030:
36% (929,000 persons)
~251,000 additional individuals living with ≥2 physical comorbidities
Largest ⬆: Black/Hispanic men who have sex with men
Largest % ⬆: Hispanic women, Hispanic men who inject drugs
* Hypertension, Hyperlipidemia, Diabetes, CKD, Cancer, MI & ESLD
Kasaie P et al. CROI 2021, Abstract 102.

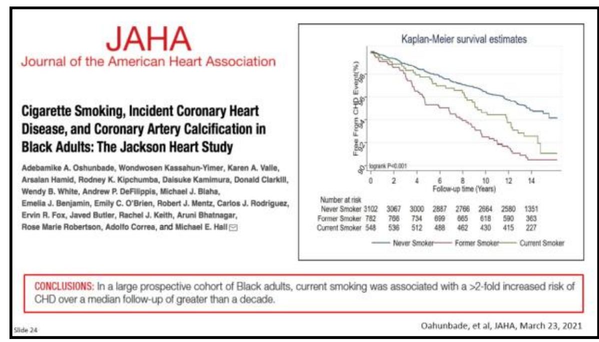


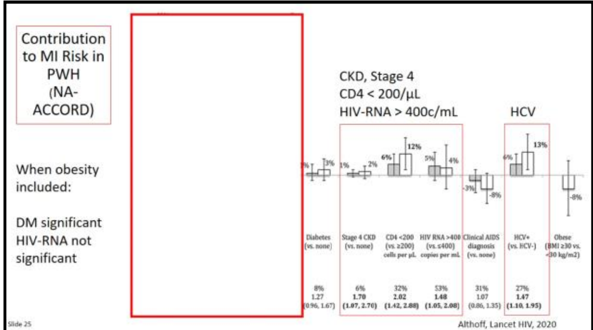
Age (yrs)	aIRR (HIV+ vs HIV-)	95% CI
<25	1.50	1.21, 1.87
25-29	1.32	1.10, 1.58
30-34	1.24	1.09, 1.42
35-39	1.12	1.004, 1.25
40-44	1.03	0.92, 1.16
45-49	1.28	1.07, 1.53
50-54	1.18	0.95, 1.46
≥55	1.38	1.04, 1.84

Approach to Comorbidities: Increased Awareness, Early Intervention

- Smoking
- SMOKING
- SMOKING
- SMOKING
- SMOKING!

Slide 23





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

Feinstein, et al. Circulation, 2019. 140:e98–e124 https://doi.org/10.1161/CIR.0000000000000695

Slide 26

ASCVD Risk Assessment and Treatment

Two approaches

- High risk
- Low-moderate risk

Living with HIV (treated, virally suppressed)

Assess ASCVD Risk

HIV-Related CVD Risk-Enhancing Factors?

High Risk for ASCVD?

HIGH RISK APPROACH

LIFESTYLE OPTIMIZATION

LIPID LOWERING DRUG THERAPY

LOW-MODERATE RISK APPROACH

LIFESTYLE OPTIMIZATION

YEARLY RE-ASSESSMENT OF RISK

Feinstein, Circulation, 2019

Slide 27

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.*

Slide 28

Feinstein, Circulation, 2019

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/mm^3)
- 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

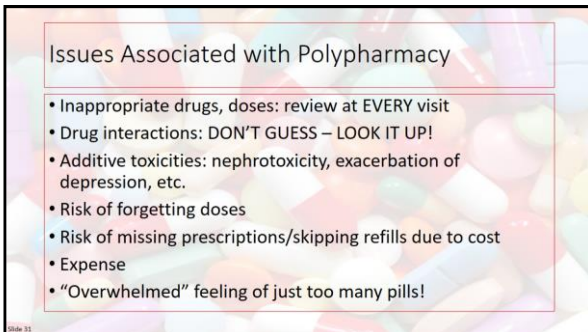
Slide 29

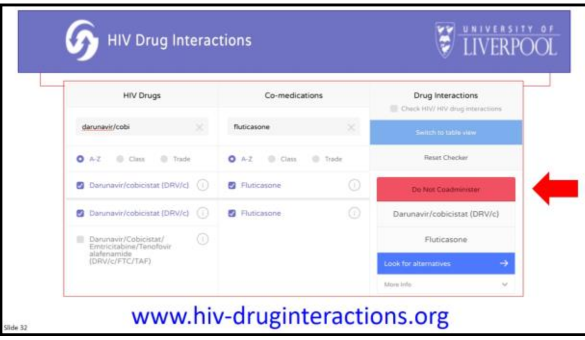
Feinstein, Circulation, 2019

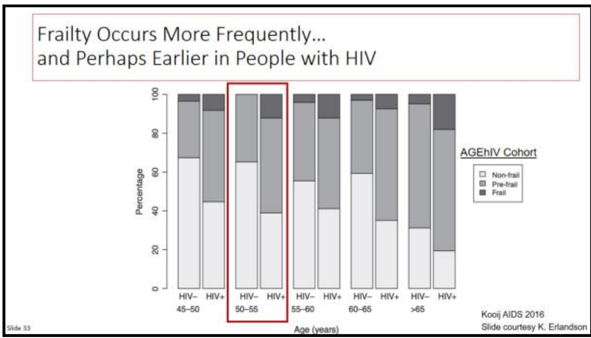
But also…

- 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…

Slide 30


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!
Slide 31


HIV Drug Interactions
UNIVERSITY OF LIVERPOOL
HIV Drugs
Co-medications
Drug Interactions
darunavir/cobi
fluticasone
Reset Checker
Darunavir/cobicistat (DRV/c)
Fluticasone
Do Not Coadminister
Darunavir/cobicistat (DRV/c)
Fluticasone
Darunavir/Cobicistat/Emtricitabine/Tenofovir alafenamide (DRV/c/FTC/TAF)
Darunavir/cobicistat (DRV/c)
Fluticasone
Look for alternatives
www.hiv-druginteractions.org
Slide 32


Frailty Occurs More Frequently…
and Perhaps Earlier in People with HIV
Percentage
0
20
40
60
80
100
HIV– HIV+
45–50
HIV– HIV+
50–55
HIV– HIV+
55–60
HIV– HIV+
60–65
HIV– HIV+
>65
Age (years)
AGEhIV Cohort
Non-frail
Pre-frail
Frail
Kooij AIDS 2016
Slide courtesy K. Erlandson
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				Men			
	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

Slide 34

Kuniholm M. CROI 2021, Abstract 538

Three Tools for Assessing Frailty

- Fried's Frailty Phenotype[1]
  - 5 physical variables
- Short Physical Performance Battery (SPPB)[2,3]
  - 3 physical tasks
- Frailty Index[4]
  - 40 physical, psychological, social/functional variables

Slide 35

[1]Fried, J of Gerontology, 2001; [2]Greene, AIDS, 2014; [3]geriatrictoolkit.missouri.edu/SPPB-Score-Tool.pdf; [4]Searle, BMC Geriatrics, 2008.

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!

Slide 36

Fried, J of Gerontology, 2001

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

HIV+ SPPB >10

HIV+ SPPB ≤10

Survival

Time (years)

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

Slide 37

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

Searle, BMC Geriatrics, 2008.

Slide 38

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

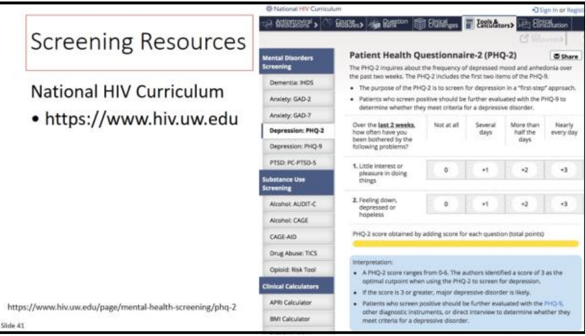
Slide 39

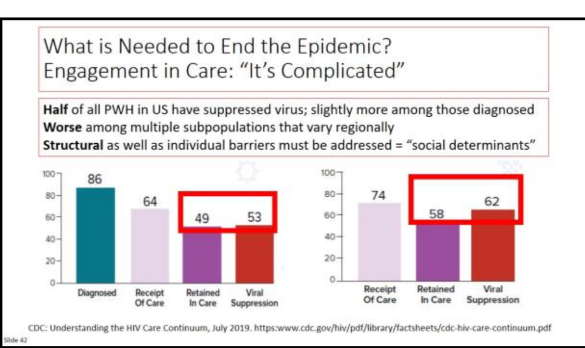
Screening for Mental Health and Substance Use Issues

- 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

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

Slide 40





Posttest Question #3

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

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

Slide 44

Back Up

Slide 46

Boosters: FDA Emergency Use Authorization[1] and CDC Recommendations[2]

- 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

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