2020 Ryan White HIV/AIDS Program CLINICAL CONFERENCE

Screening for and Managing Comorbidities in Older Adults with HIV Infection

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AIDS Research Consortium of Atlanta
Atlanta, Georgia

Financial Relationships With Commercial Entities

Dr Thompson's institution has received grants for research from CytoDyn, Inc, Cepheid, Inc, Kowa Pharmaceuticals America, Inc, Frontier Biotechnologies, Gilead Sciences, Inc, GlaxoSmithKline, Merck & Co, Inc, and ViiV Healthcare. (Updated 08/6/20)

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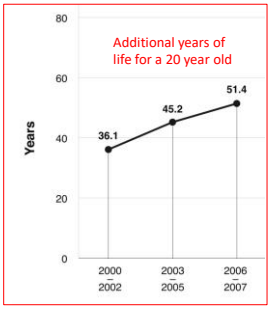
Learning Objectives

After attending this presentation, learners will be able to:

- Assess risk for cardiovascular disease in people ;living with HIV (PLWH)
- Diagnose diabetes mellitus in PLWH
- Assess frailty in older PLWH

Slide 3 of 55

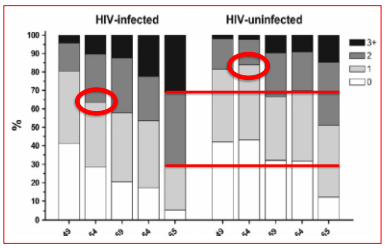
People With HIV Are Living Longer!



Samji, PLOS One, 2013

Multimorbidity is More Common in PLWH

- Cardiovascular
- Diabetes mellitus
- Chronic kidney ds
- Neurologic
- Osteoporosis
- Malignancy
- Depression



Schouten, CID, 2014

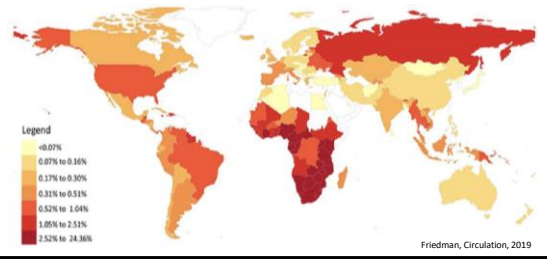
Aging is…

"Being nibbled to death by goldfish"
- My father in law, Richard Morris

Considerations for Aging with HIV

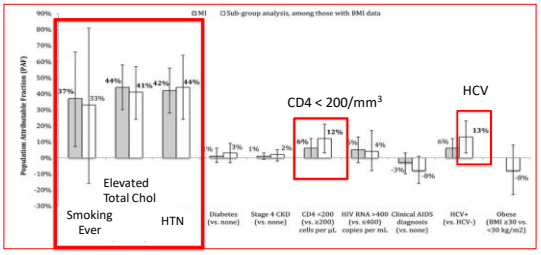
- Multimorbidity
  - Co-morbidities including ASCVD, DM, frailty
  - Mental health/substance use issues
  - Organ demise: Hearing/vision loss, incontinence
- Polypharmacy
- Social isolation and loneliness
- Stigma
- Financial and housing insecurity; impact of social determinants of health

Cardiovascular Disease in PLWH
Population Attributable Fraction Globally



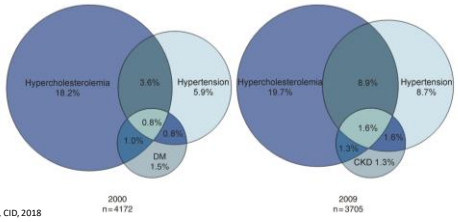
Friedman, Circulation, 2019

Risk of MI in PLWH – NA-ACCORD



Althoff, Lancet HIV, 2020

NA-ACCORD: Most Common Age-Associated Conditions Among ART-Experienced PLWH 2000 and 2009



Wong, CID, 2018

Cardiovascular Disease More Common in PLWH

- Myocardial infarction, heart failure, stroke: 1.5-2 fold higher than for HIV negative
- Pulmonary hypertension
- Blood clots
- Sudden death

Friedman, Circulation, 2019

AHA SCIENTIFIC STATEMENT

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

A Scientific Statement From the American Heart Association

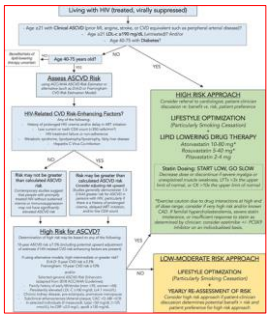
- Recognizes increased risk of ASCVD in persons living with HIV
- Addresses pathophysiology, screening, treatment
- Includes link to patient perspective from PLWH

Feinstein, Circulation, 2019

Screening and Treatment

Two approaches
- High risk
- Low-moderate risk

Friedman, 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 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.*

High Risk Approach

- Consider cardiology referral after risk-benefit discussion with patient
- Lifestyle optimization, particularly smoking cessation
- Lipid lowering therapy
- Start low – go slow
  - Decrease dose or stop if severe myalgia, unexplained muscle weakness, LFT > 3x ULN, CK > 10x ULN

Friedman, Circulation, 2019

Lipid Lowering Therapy[1]

- Atorvastatin 10-80 mg
- Rosuvastatin 5-40 mg
- Pitavastatin 2-4mg
  - INTREPID study in HIV+: pitavastatin superior to pravastatin in reduction of LDL-c & non-HDL apolipoprotein B at 12 & 52 weeks; fewer drug-drug interactions; no glucose effect[2]
- Simvastatin & lovastatin contraindicated with PIs or cobicistat
- Statin toxicity or insufficient response
  - Consider adding ezetemibe +/-PCSK9 inhibitor

1. Friedman, Circulation, 2019; 2.Aberg, Lancet HIV, 2017

Low-Moderate Risk Approach: Use Calculators

High Risk for ASCVD?

Determination of high risk may be based on any of the following:

10-year ASCVD risk ≥7.5% (including potential upward adjustment of estimate if HIV-related CVD risk-enhancing factors are present)

If using alternative models, high-intermediate or greater risk?
D:A:D: 5-year CVD risk ≥3.5%
Framingham: 10-year CVD risk ≥10%

Friedman, Circulation, 2019

ASCVD Risk Assessment Tools

- Tools: AHA/ACC calculator; D:A:D; Framingham
- Traditional risk assessment tools may **underestimate** risk in PLWH **by 1.5 -2 fold**, especially if
  - Hx of prolonged viremia: delayed ART initiation, treatment failure, non-adherence
  - Nadir or current CD4 < 350/mm^3
  - Metabolic syndrome: lipodystrophy, fatty liver
  - Hepatitis C

Friedman, Circulation, 2019; http://www.cvriskcalculator.com; https://chip.dk/Tools-Standards/Clinical-risk-scores;

Low Risk Approach: Risk Enhancers

Selected general ASCVD Risk Enhancers
(adapted from 2018 ACC/AHA Guidelines):

- Family history of early MI/stroke (men <55, women <65)
- Persistently elevated LDL-C ≥160 mg/dL (≥4.1 mmol/L)
- Chronic kidney disease, pre-eclampsia, premature menopause
- Subclinical atherosclerosis (Arterial plaque; CAC >0; ABI <0.9)
- In selected individuals (if measured): Lp(a) >50 mg/dL (>125 nmol/L); hs-CRP ≥2.0 mg/L; apoB ≥130 mg/dL

Friedman, Circulation, 2019

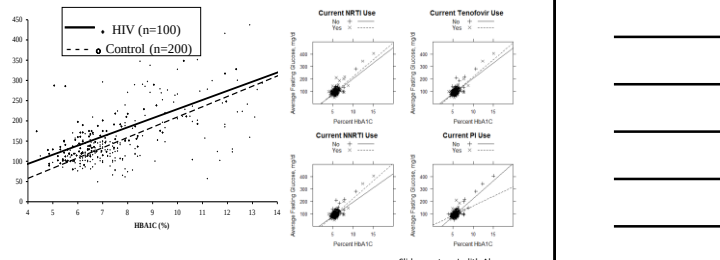
But also…

- Control risk factors other than lipids
  - Smoking, smoking, smoking!
  - Diabetes mellitus – 2.4x increased risk of MI
  - Hypertension – 35% prevalence in tx-experience
  - Obesity: encourage exercise and diet: education!
- Aspirin prophylaxis? Not studied in PLWH
- Statin (without hyperlipidemia)?
  - Wait for REPRIEVE trial…

Diabetes Mellitus: ADA Definition (2019)

- Hemoglobin A1C ≥ 6.5%
  - "In conditions associated with an altered relationship between A1C and glycemia, such as …HIV….**only plasma blood glucose criteria** should be used to diagnose DM." Only applies when on ART
- Fasting plasma glucose ≥ 126 mg/dL, confirmed by repeat
- Plasma glucose ≥ 200 mg/dL 2 hrs after 75 g oral glucose tolerance test
- Random plasma glucose ≥ 200 mg/dL with polyuria and polydipsia

A1C May Under- or Overestimate Depending on ART



Slide courtesy Judith Aberg

Smoking and Cancer in PLWH

- Smoking: up to ¾ of PLWH
- Cancer burden attributable to smoking
  - Lung cancer: 94%
  - Other 'smoking related' cancers (esophageal, oral, etc.): 31%
  - Anal cancer: 32%
  - All cancer: 9%

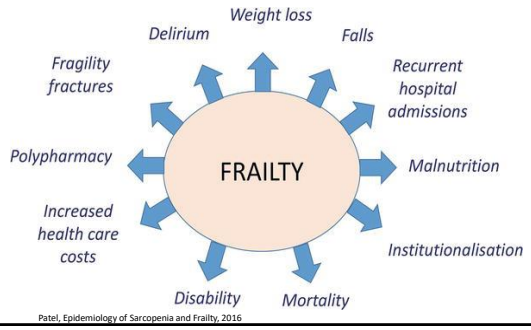


Altekruse, AIDS, 2018

Issues Associated with Polypharmacy

- Drug interactions: **DON'T GUESS – LOOK IT UP!**
  - Cobicistat, ritonavir: strong CYP3A4 inhibitors
  - PIs: darunavir, atazanavir: check interactions
  - NNRTIs other than doravirine: CYP3A4 inducers; lowered by PPIs
  - INSTIs: polyvalent cations; bictegravir: CYP3A4, UGT1A1: rifampin/rifabutin; metformin (increased 40%!); atazanavir contraindicated
- Additive toxicities: nephrotoxic drugs, etc.
- Inappropriate drugs
- Risk for forgetting doses
- Risk for forgetting prescriptions
- Expense

https://www.hiv-druginteractions.org



Patel, Epidemiology of Sarcopenia and Frailty, 2016

Tools for Assessing Frailty

- Fried's Frailty Phenotype
  - 5 physical variables
- Short Physical Performance Battery (SPPB)
  - 3 physical tasks
- Frailty Index
  - 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

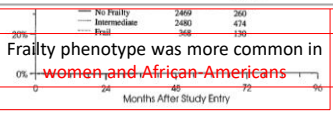
Key. CES-D, Center for Epidemiological Studies Depression; BMI, body mass index.

Fried, J of Gerontology, 2001

Frailty Phenotype as a Predictor

Frailty phenotype predicts
- Death
- Worsening disability
- Incident fall
- 1st hospitalization

	Hazard Ratios* Estimated Over 3 Years Frail*** (Versus Not Frail)
Worsening mobility disability	1.50**
Worsening ADL disability	1.98**
Incident fall	1.29**
First hospitalization	1.29**
Death	2.24**

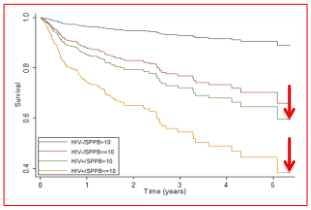


Frailty phenotype was more common in women and African-Americans

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



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

Searle, BMC Geriatrics, 2008.

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 HIV-Associated Neurocognitive Disorders

Screening tools have variable sensitivity/specificity

- Mini-mental state examination (MMSE)
- International HIV dementia scale (IHDS)
- Montreal cognitive assessment (MoCA)
- Simioni symptom questionnaire (SSQ)
- Cognitive assessment tool-rapid version (CAT-rapid)

Joska, AIDS Behavior, 2016

Screening for HIV-Associated Neurocognitive Disorders

Screening for HIV dementia

- IHDS + CAT-rapid = most sensitive/specific

Screening for asymptomatic/mild HAND

- No screener had adequate sensitivity/specificity: need full neuropsych testing

Don't forget reversible causes … syphilis, thyroid disease, B12 deficiency, depression

Joska, AIDS Behavior, 2016

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: CAGE and AUDIT
- Drug Use: TICS; opioid risk tool

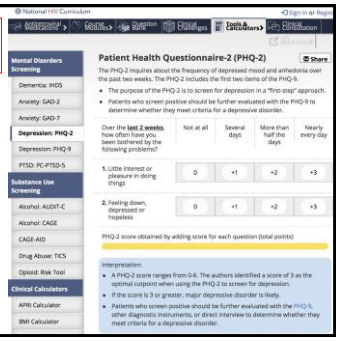
National HIV Curriculum: https://www.hiv.uw.edu/page/mental-health-screening/phq-2

Tools for Screening

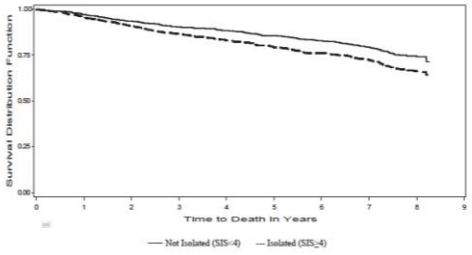
National HIV Curriculum

- https://www.hiv.uw.edu

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

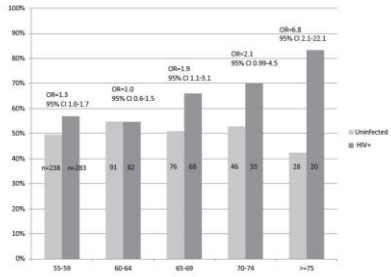


Social Isolation Is Associated with Increased Mortality



Greysen et al., Journal of American Geriatrics Society, 2013

PLWH ≥ 65 yo are 2-7 times more likely to experience social isolation than those who are HIV -



* Odds ratios are unadjusted and demonstrate the likelihood of isolation (SIS≥4) for HIV+ vs. uninfected patients in each age bracket

Greysen et al., Journal of American Geriatrics Society, 2013

Does Social Isolation Predict Hospitalization and Mortality Among HIV+ and Uninfected Older Veterans?

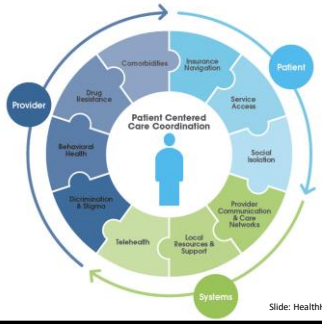
S. Ryan Greysen, MD, MHS, MA,* Leora I. Horwitz, MD, MHS,† Kenneth E. Covinsky, MD, MPH,‡§ Kirsha Gordon, MS,‖ Michael E. Obl, MD, MSPH,‖ and Amy C. Justice, MD, PhD¶#

The Social Isolation Score (SIS)

- ✧Visits from close family
- ✧Visits from close friends
- ✧Number of close family/friends
- ✧Use of self-help or support group in last year
- ✧Volunteer work or involvement in community organization
- ✧Frequency of attendance to religious events
- ✧Relationship status
- ✧Living alone

Greysen et al., Journal of American Geriatrics Society, 2013

Patient Centered Care Coordination for Older PLWH



Slide: HealthHIV

IDSA GUIDELINES

Primary Care Guidelines for the Management of Persons Infected With HIV: 2013 Update by the HIV Medicine Association of the Infectious Diseases Society of America

2020 UPDATE COMING!!

Aberg, CID, 2014

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Question-and-Answer Session