2020 Ryan White HIV/AIDS Program CLINICAL CONFERENCE

Screening for and Managing Comorbidities in Older Adults with HIV Infection

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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)
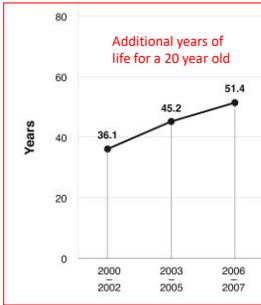

Learning Objectives

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

People With HIV Are Living Longer!

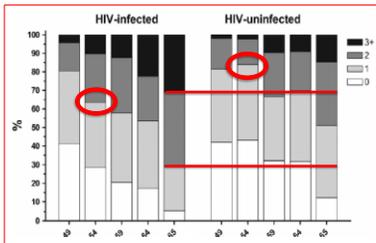Additional years of life for a 20 year old

Samji, PLOS One, 2013

Multimorbidity is More Common in PLWH

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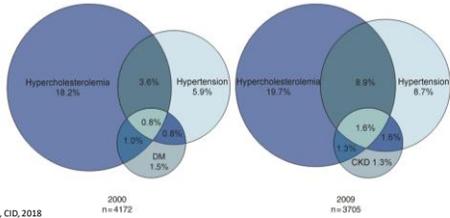- ✧ Osteoporosis
- ✧ Malignancy
- ✧ Depression

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

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Cardiovascular Disease in PLWH
Population Attributable Fraction Globally

Legend
<0.07%
0.07% to 0.16%
0.17% to 0.30%
0.31% to 0.51%
0.52% to 1.04%
1.05% to 2.51%
2.52% to 24.36%

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

Hypercholesterolemia 18.2% 3.6% Hypertension 5.9%
0.8%
1.0% 0.8%
DM 1.5%
2000 n=4172

Hypercholesterolemia 19.7% 8.8% Hypertension 8.7%
1.6% 1.0%
1.3%
CKD 1.3%
2009 n=3705

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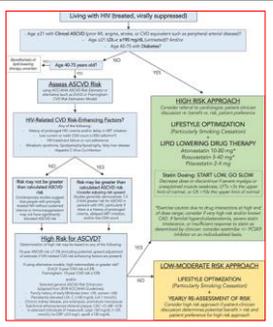
- Recognizes increased risk of ASCVD in persons living with HIV
- Addresses pathophysiology, screening, treatment
- Includes link to patient perspective from PLWH

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
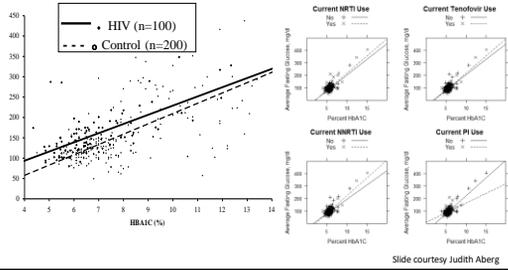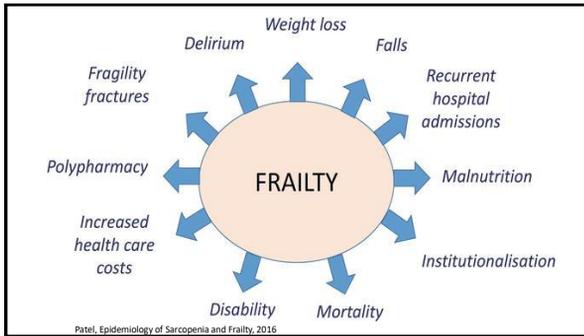
Smoking and Cancer in PLWH

- 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

Weight loss

Delirium   **Falls**

Fragility fractures

Recurrent hospital admissions

Polypharmacy   **FRAILTY**   **Malnutrition**

Increased health care costs

Institutionalisation

Disability   **Mortality**

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. Ohl, 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