

**“If I’d Known I Would Live This Long,
I Would Have Moisturized!”:
Aging with HIV**

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

Dr Thompson's institution received research grants from Gilead Sciences, Inc, Merck Sharp Dohme, and ViiV Healthcare. She currently chairs a data safety monitoring board for Excision Biotherapeutics. (Updated 09/01/22)

Slide 2

Learning Objectives

After attending this presentation, learners will be able to:

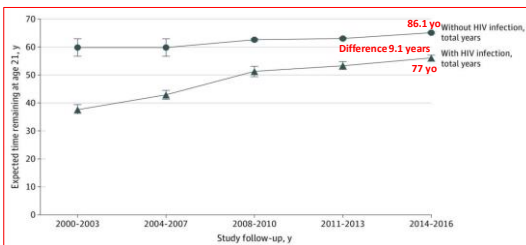
- Use HIV-specific risk enhancers to estimate cardiovascular risk and need for statins
- Screen for and mitigate frailty
- Assess and address polypharmacy

Slide 3

“If I’d Known
I Would Live This Long,
I Would Have Moisturized!”

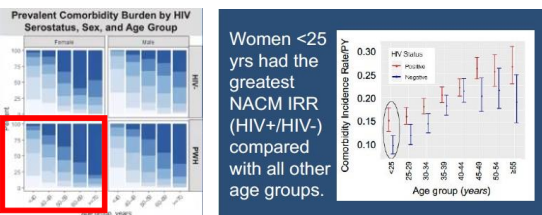
- My Patient, 2005

People with HIV are Living Longer...
But NOT Without Comorbidities (Kaiser California + Mid-Atlantic Matched Cohort)



Marcus et al. JAMA Network Open. 2020 Jun 23;6

Higher Comorbidity Prevalence for Women than
Men with HIV - and Occurring Early (MACS/WIHS Combined)



Collins, L. CROI 2021 & CID, 2021

[illegible]

AIDS 2022

Living with HIV infection: influence on basic aging mechanisms and disease outcomes?

Chronic infection with HIV-1

Biological drivers of aging

Aging disease outcomes

López-Otin et al.
2013 Kennedy et al.
2014

29 July – 2 August | Montreal & virtual
aids2022.org

MADS2022

Montero, M.AIDS 2022

HIV and Aging: A cascade model for loss in reserve with aging

AIDS 2022

Biological reserve and capacities
Increasing multimorbidity

Gero-Drivers:

- Macromolecular Damage
- Senescence
- Inflammation
- Stem cell dysfunction

Homeostatic balance of total organ reserves & capacity

Gero-Protectors:

- Resilience
- Gero-protective compounds
- Exercise modalities
- Behavior interventions

But...no interventions yet for most drivers!

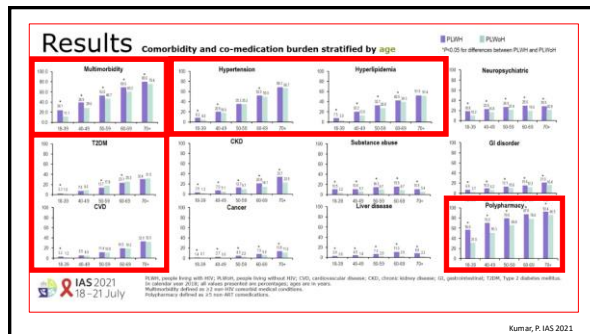
Montano et al, Lancet

29 July - 2 August - Montreal & virtual

AIDS2022

Montano, AIDS 2022

Today's Focus:
Do What We CAN Do!



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

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/lipotoxicity, fatty liver disease
 - Hepatitis C Virus Co-infection

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

Feinstein, Circulation, 2019

2022 USPSTF: Statins for Primary Prevention

Based on Age, Risk Factors, Pooled Cohort Equation (PCE) Score
(Applies to people without known CVD or LDL ≥ 190 mg/dL)

Age	Risk by PCE	Recommendation	Grade
40-75 with ≥ 1 risk factor	$\geq 10\%$	Offer	B
40-75 with ≥ 1 risk factor	7.5% to $< 10\%$	Selectively offer	C
≥ 76 years		Insufficient evidence	I

Risk factors = HTN, DM2, hyperlipidemia, smoking
BUT - HIV Risk Enhancing Factors increase risk by 1.5-2.0- fold, according to AHA/ACC guidelines

No difference in muscle pain or disorders, liver enzyme elevation, or cancer with statin compared with placebo

JAMA online only, Aug 23/30, 2022

Lifestyle + Lipids

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 $>3\times$ the upper limit of normal, or CK $>10\times$ the upper limit of normal

- Watch for drug interactions
- If no response or intolerance, consider alternative agents

Cardiovascular Disease: Screen and Intervene

- Screen for and manage modifiable risk factors
 - **SMOKING!** HTN, dyslipidemia, DM2 (diagnose using plasma glucose, not A1c for PWH)

Screening tools

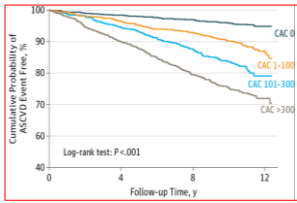
- Increased BMI \rightarrow risk of increased BP, dyslipidemia, DM2, NAFLD
- Waist circumference thresholds adjusted for BMI: predict DM2, MI, frailty, death*

BMI Category kg/m ²	Waist Circ (cm) Women	Waist Circ (cm) Men
Normal (18.5-24.9)	≥ 80	≥ 90
Overweight (25.0-29.9)	≥ 90	≥ 100
Obese I (30.0-34.9)	≥ 105	≥ 110
Obese II-III (≥ 35.0)	≥ 115	≥ 125

- ? Coronary Artery Calcium (CAC) score by CT scan: identify subclinical disease, but only if calcified lesions

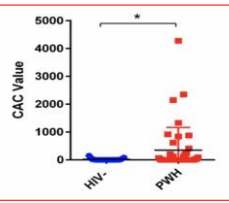
*Ross, et al. Waist circumference as a vital sign in clinical practice: a Consensus Statement from the IAS and ICCR Working Group on Visceral Obesity. Nature Reviews: Endocrinology. March 2020.

Coronary Artery Calcium Categories Predict Time to ASCVD Event



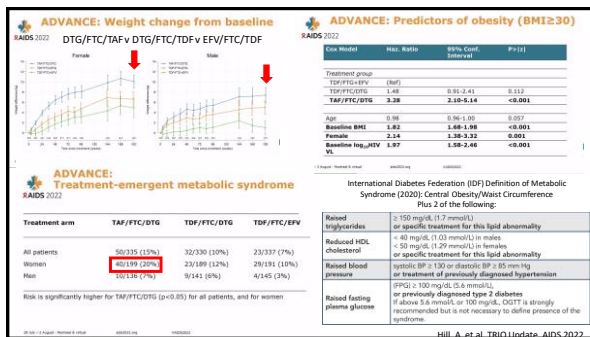
JAMA Cardiol. 2017;2(9):986-994. doi:10.1001/jamacardio.2017.2498

People with HIV Have Higher CAC Scores Than Age-Matched People without HIV

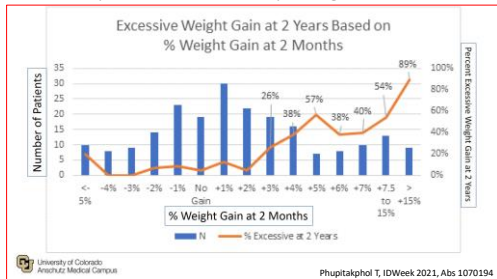


Funderberg N. CROI 2022.

So, What About That Weight Gain Thing?

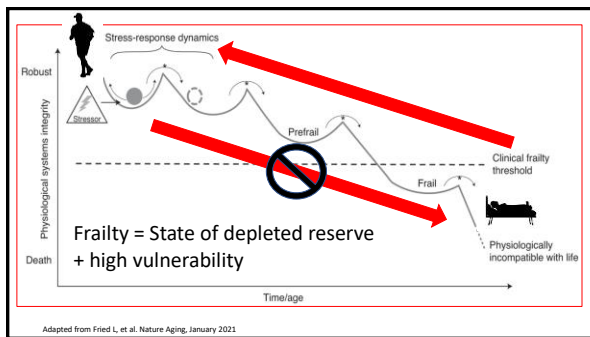


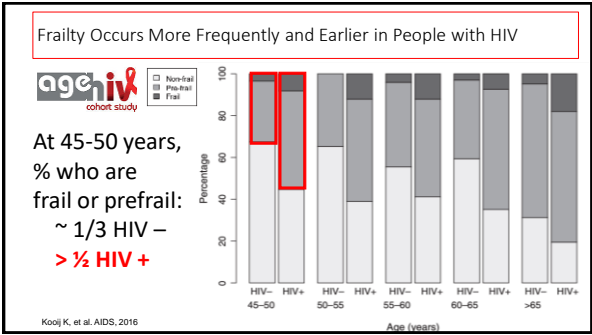
Pay Attention to Early Weight Gain!

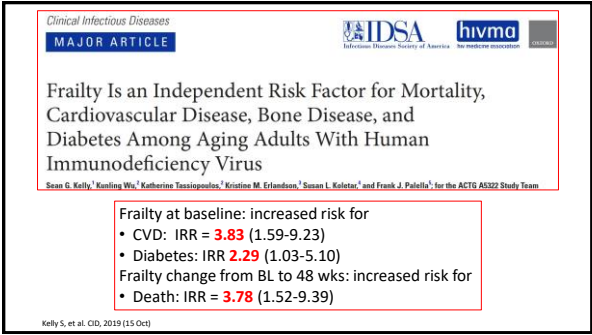


Common Comorbidities: Prevent, Screen, and Intervene

- Vaccinate: SARS CoV-2, monkeypox (if appropriate), pneumococcus, meningococcus, HPV, HAV/HBV, Tdap, Herpes zoster, travel vaccines
- Liver disease: screen for HBV, HCV; NAFLD (EACS guidelines algorithm)
- Osteopenia, osteoporosis
 - Assess bone density in those at risk using DEXA; treat as appropriate
 - Address modifiable risk factors, secondary causes: **smoking**, alcohol, sedentary lifestyle, TDF, thyroid/parathyroid ds, steroids
- Cancer: lung, colon, anal/cervical, breast, prostate
- STIs: syphilis, chlamydia, gonorrhea, trichomonas, HPV
- Depression: PHQ-2 or PHQ-9: **easy and reimbursable!**
 - Role of stigma, social isolation
- Substance use: alcohol, pain meds, non-prescription drugs









OMG More Screening!
I Do NOT Have Time for This!



PS. It's the system – not you!

Journal of Gerontology, MEDICAL SCIENCES
2015, Vol. 70, No. 3, 309–316

Copyright 2015 by The Gerontological Society of America

Frailty in Older Adults: Evidence for a Phenotype

Linda P. Fried,¹ Catherine M. Tangen,² Jeremy Walston,¹ Anne B. Newman,³ Calvin Hirsch,⁴
John Gottdiner,⁵ Teresa Seeman,⁶ Russell Tracy,⁷ Willem J. Kop,⁸ Gregory Burke,⁹
and Mary Ann McBurnie² for the Cardiovascular Health Study
Collaborative Research Group

Frailty indicator	Measure
Weight loss	ounds or recorded weight loss of $\geq 5\%$ per annum
Self-reported exhaustion	ion score (3–4 days per week or most of the time)
Low energy expenditure	s) or <270 KCal/week (females)
Slow gait speed	stratified for sex and height
Weak grip strength	Requires dynamometer
Key: CES-D, Center for Ep	mass index.



\$436.89 (+ tax)

A "clinical judgement" tool for people ≥ 65 yo

Very mild frailty = 4
• Not dependent on others for daily help
• Often symptoms limit activities
• "Slowing down"
• Daytime tiredness

Validated using the Canadian Study of Health and Aging Cohort

CLINICAL FRAILTY SCALE

- 1 VERY FIT**
People who are robust, active, energetic and resilient. They tend to exercise regularly and are among the fittest for their age.
- 2 FIT**
People who have no active disease symptoms but are less fit than category 1. Often, they exercise or are very active occasionally, e.g., occasionally.
- 3 BORDERING WELL**
People whose medical problems are well contained, even if occasionally symptomatic, but often are not regularly active beyond routine walking.
- 4 BORDERING FRAILTY**
Previously "robustness" this category marks early transition from complete independence. While not dependent on others for daily help, often symptoms limit activities, a common complaint is being "slowed up" and/or being tired during the day.
- 5 BORDERING FRAILTY**
People who often have more evident slowing, and need help with high order instrumental activities of daily living (finances, transportation, heavy housework). Typically, need help progressively in more shopping and walking outside home, need prescription medications and begins to exhibit slight housework.
- 6 BORDERING FRAILTY**
People who need help with all available activities and with keeping house. Inside, they often have problems with stairs and need help with bathing and night care. Outside, they are unable to walk safely without a cane or walking stick.
- 7 BORDERING FRAILTY**
Completely dependent for personal care, from whatever cause (physical or cognitive). Seen as they are unable and not at high risk of dying (within 6 months).
- 8 BORDERING FRAILTY**
Completely dependent for personal care and approaching end of life. Typically, they could not move even from a minor illness.
- 9 BORDERING FRAILTY**
Approaching the end of life. This category applies to people with a life expectancy of 6 months, who are not otherwise living with severe frailty (Many terminally ill people can still move, so are not very close to death).

SCORING FRAILTY IN PEOPLE WITH DEMENTIA

The degree of frailty generally corresponds to the degree of dementia. Common symptoms and instrumental activities of daily living (finances, transportation, heavy housework). Typically, need help progressively in more shopping and walking outside home, need prescription medications and begins to exhibit slight housework.

DALHOUSIE UNIVERSITY
www.geriatrics.dal.ca

Short Physical Performance Battery (SPPB)

3 physical tasks:

- Timed chair stands (sit then stand x 5)
- Timed 3 or 4-meter walk
- 3 balance tests

Score < 10 associated with higher risk of death

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

Balance: stand for 10 sec

- Side-by-side
- Semi-tandem
- Tandem



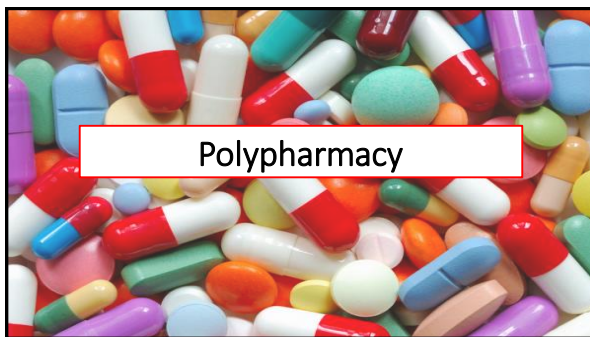
And If You Like Numbers...

Clinical Infectious Diseases
MAJOR ARTICLE

Discrimination and Calibration of the Veterans Aging Cohort Study Index 2.0 for Predicting Mortality Among People With Human Immunodeficiency Virus in North America

- 13 variables: usually available in the EHR; online calculator (mdcalc.com)
 - Age, sex, BMI
 - Hepatitis C (yes/no)
 - HIV RNA, CD4
 - WBC, hemoglobin, platelets
 - Estimated GFR, AST, ALT, albumin

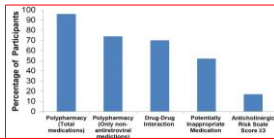
McGinnis KA, et al. Discrimination and Calibration Of The Vacs Index 2.0 For Predicting Mortality Among People With HIV In North America. CID. 2021 Oct 5;ciab883. doi: 10.1093/cid/ciab883. <https://www.mdcalc.com/veterans-aging-cohort-study-vacs-2.0-index>



Polypharmacy

What is Polypharmacy and Why is it Bad?

- Polypharmacy = 5+ drugs; hyperpolypharmacy = 10+ drugs
- Polypharmacy is driven by multimorbidity
- Associated with polypharmacy:
 - Increased drug-associated adverse effects
 - Increased drug interactions
 - Potentially inappropriate meds
 - Prescribing "cascades"
 - Missed doses, missed refills
 - Increased cost



Management of Polypharmacy

- Go through the drug list EVERY visit (👁️) (esp after hospitalizations, consults)
- 🚫 for new or unnecessary drugs (including OTC), wrong dose or duration
- 🚫 for prescribing cascades: drugs treating side effects of other drugs
- 🚫 for drugs with overlapping toxicities, drug-disease interactions, intrinsic toxicities (anticholinergics; sedatives)
- 🚫 for drug-drug interactions, esp ARV (DON'T GUESS – LOOK IT UP!)
- Remember alcohol, recreational substances, OTC drugs & supplements

Helpful tools: STOPP and START screeners¹, Beers Criteria²
HIV-druginteractions.org

¹STOPP and START: Gallagher, et al. Int J Clin Pharm & Therapeutics, 2006; Hamilton, et al. JAMA Int Med, 2011
²Beers Criteria: http://files.hqpharmacy.com/hospital/257222/NoSign_2019_beers_pocket_printable_r1.pdf

Contraindicated Drugs: Ritonavir

- Alpha 1- Adrenoreceptor Antagonist : alfuzosin
- Antianginal: ranolazine
- Antiarrhythmics: amiodarone, dronedarone, flecainide, propafenone, quinidine

Look It Up!
HIV-druginteractions.org



- PDE5 Inhibitor: sildenafil (Revatio®) when used for the treatment of pulmonary arterial hypertension
- Sedative/Hypnotics: triazolam, orally administered midazolam
- Anticancer Agents: apalutamide
- Herbal Products: St. John's Wort (hypericum perforatum)

https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/020659s072,022417s024,209512s0071bl.pdf

Important Paxlovid™ interactions

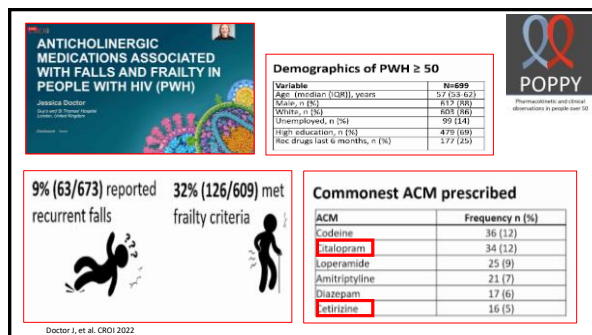
Look It Up!

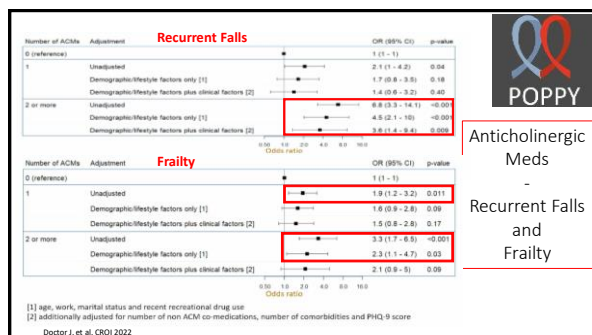
HIV-druginteractions.org

COVID19-druginteractions.org

U of Waterloo Drug Interactions

https://www.accessdata.fda.gov/drugatfda_docs/label/2020/020659s072_022417s024_209512s0071bl.pdf





Principles of Frailty Prevention and Intervention

Minimize aggregating factors

- Maintain access to **routine healthcare**
 - Address age-related deficits: vision, hearing, dentition
 - Routine cancer screening, vaccinations, STI screening
- Screen for, prevent, & manage **comorbidities**
 - Including mental health & substance use!
- Address **polypharmacy**
- Prevent **falls**

Increase factors promoting health and resiliency

- Physical **activity**
- Social **interaction**

Think about **frailty** as part of the assessment!

Fried L, et al. Nature Aging. January 2021

We've put more effort into
helping folks reach old age than
into helping them enjoy it.

— Frank Howard Clark

Question-and-Answer Session



Screening for Cognitive Impairment in Older Adults

US Preventive Services Task Force Recommendation Statement

- Mini Mental Status Exam = most evaluated instrument (30 studies)
- MMSE for detection of **dementia**: sensitivity 0.89 (95% CI, 0.85 to 0.92) specificity 0.90 (95% CI, 0.86 to 0.93)
- Across all instruments, sensitivity and specificity were higher to detect dementia compared with Mild Cognitive Impairment.

No single tool excels to detect MCI.

USPSTF. JAMA. 2020;323(8):757-763. doi:10.1001/jama.2020.0435



Original Investigation | Infectious Diseases

Evaluation of Computerized Cognitive Training and Cognitive and Daily Function in Patients Living With HIV

A Meta-analysis

- 12 RCTs with CCT Interventions
- BrainHQ.com
 - Cogmed
 - GT Racing 2
 - Captain's Log MindPower Builder
 - Luminosity
 - InSight

Significant improvement in **6 of 8 domains**:

- Abstraction and executive function
- Attention and working memory
- Memory
- Motor skills
- Speed of information processing
- Daily function

Wei et al. JAMA Network Open. 2022;5(3):e220970. doi:10.1001/jamanetworkopen.2022.0970
