HIV and Aging:
How Will We Manage Success?

Melanie Thompson, MD
August 11, 2021

Financial Disclosures

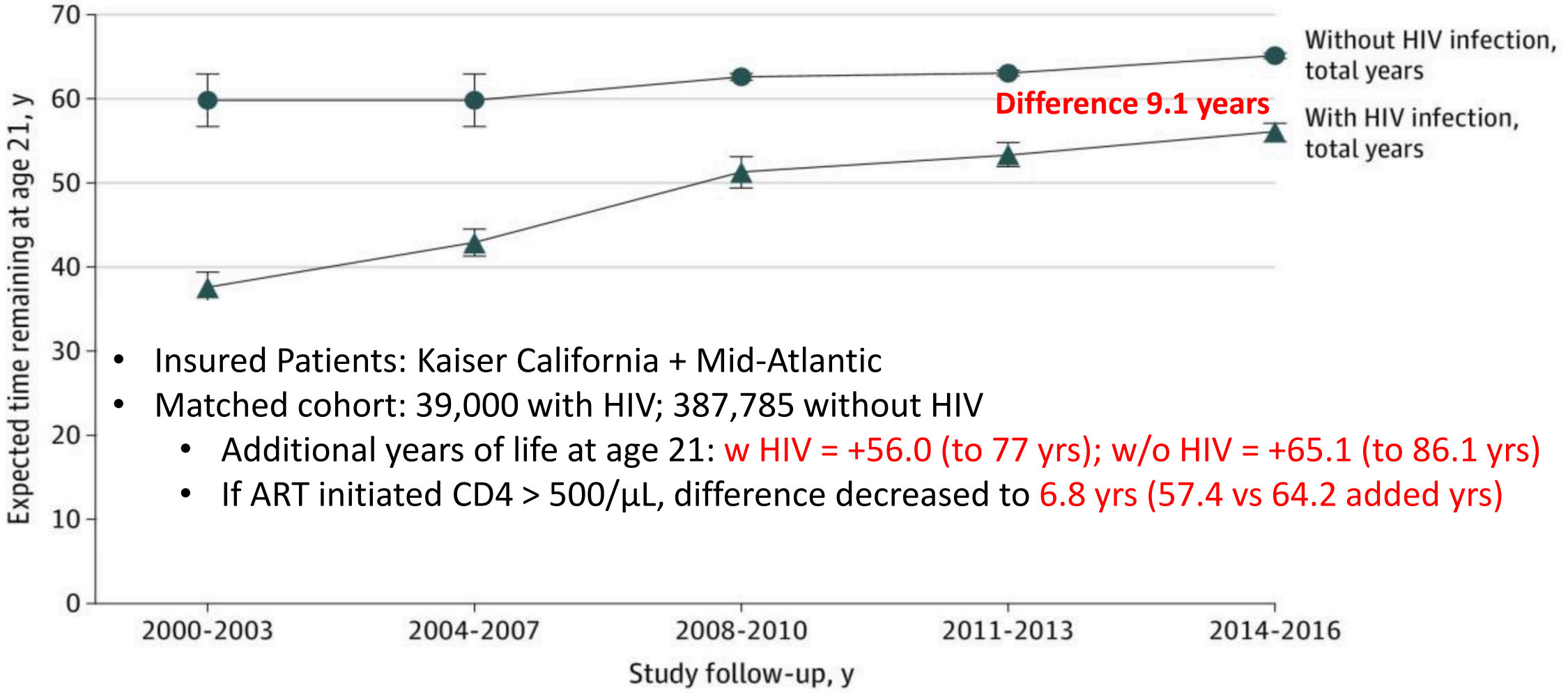
- Support to AIDS Research Consortium of Atlanta for the conduct of clinical trials from:
  - Cepheid, Inc.
  - Cytodyn, Inc.
  - Frontier Biotherapeutics
  - GlaxoSmithKline
  - Gilead Sciences
  - Merck Sharp Dohme
  - ViiV Healthcare
- No direct funding to Dr. Thompson

Learning Objectives

At the conclusion of the webinar, the learner will be able to:

1. Access resources for identifying drug-drug interactions and drugs that may be inappropriate in older persons
2. Describe three tools for assessing frailty
3. Describe HIV-specific risk enhancing factors for cardiovascular disease

People with HIV are Living Longer…

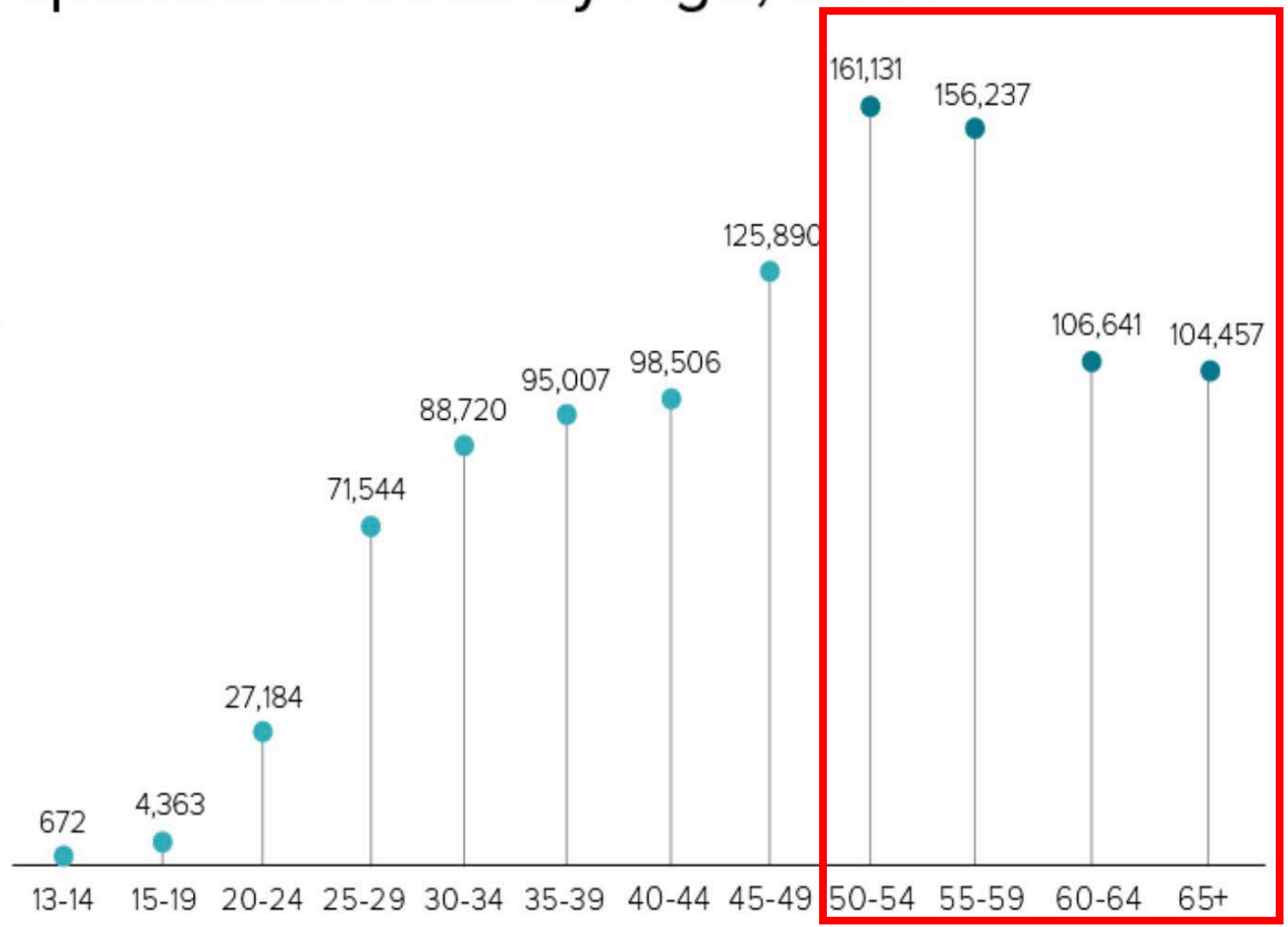


- Insured Patients: Kaiser California + Mid-Atlantic
- Matched cohort: 39,000 with HIV; 387,785 without HIV
  - Additional years of life at age 21: w HIV = +56.0 (to 77 yrs); w/o HIV = +65.1 (to 86.1 yrs)
  - If ART initiated CD4 > 500/µL, difference decreased to 6.8 yrs (57.4 vs 64.2 added yrs)

Marcus et al. JAMA Network Open. 2020 Jun (3)6

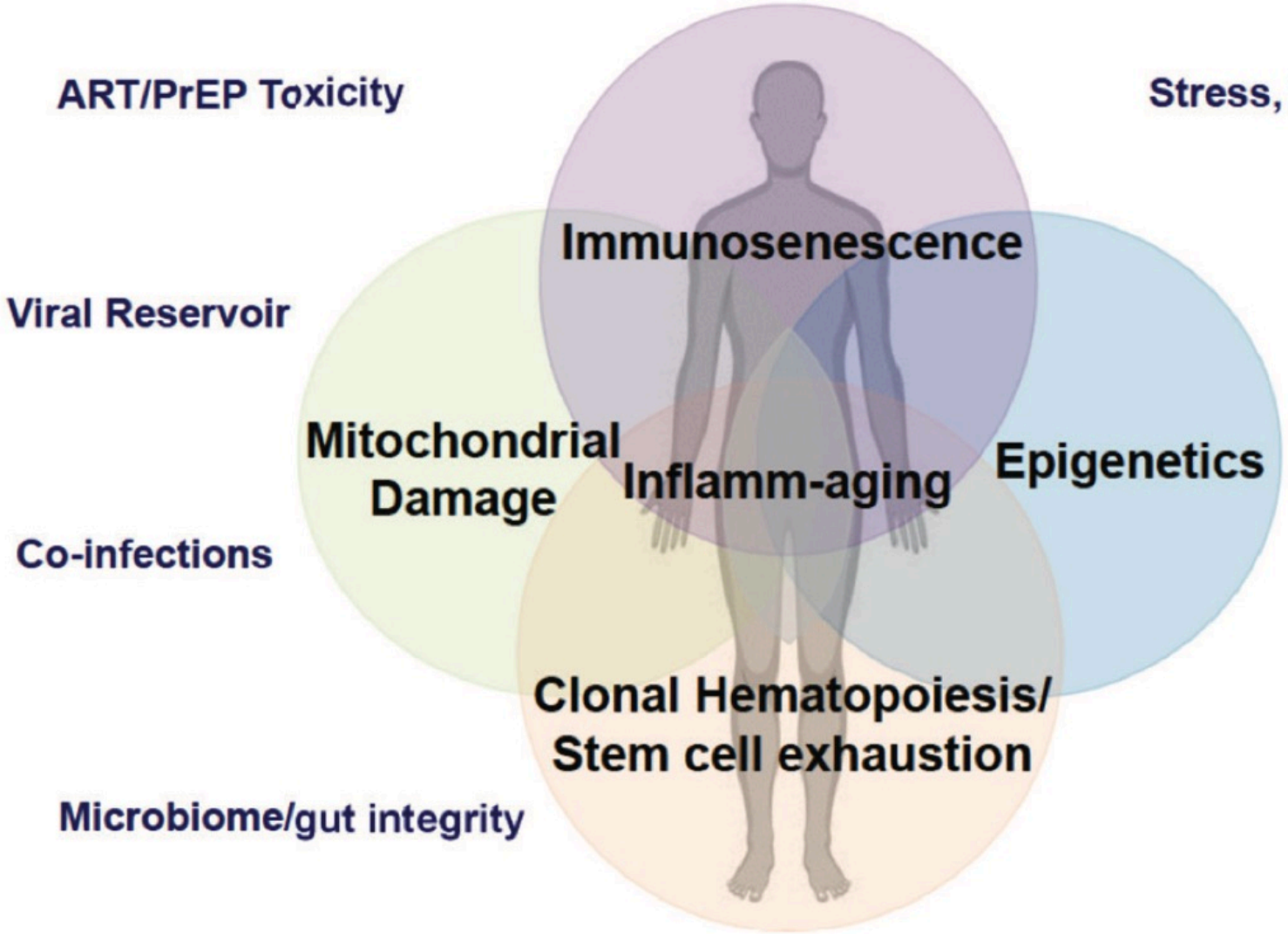
Adults and Adolescents with Diagnosed HIV in the US and Dependent Areas by Age, 2018

Over half of people with diagnosed HIV were aged 50 and older.



CDC HIV Surveillance Report 2018 (updated 2020)

Drivers and Mechanisms of Aging with HIV and ART

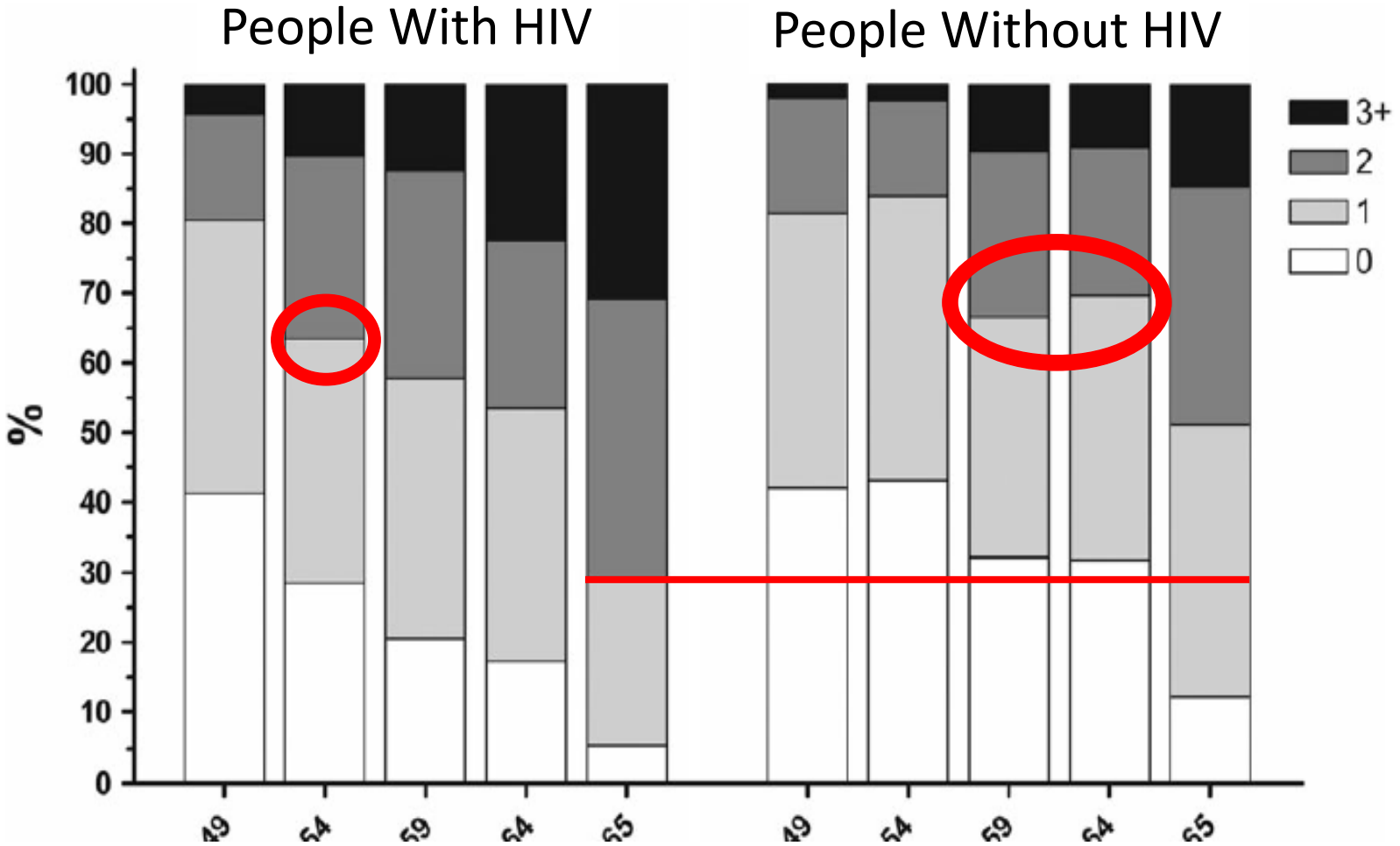


Art: Dr. Leia Novak

Gabuzda D et al. Pathogenesis of Aging and Age-related Comorbidities in People with HIV: Highlights from the HIV ACTION Workshop 2020 Jun 17. doi:10.20411/pai.v5i1.365

Multimorbidity is More Common in PWH… And Occurs Earlier

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



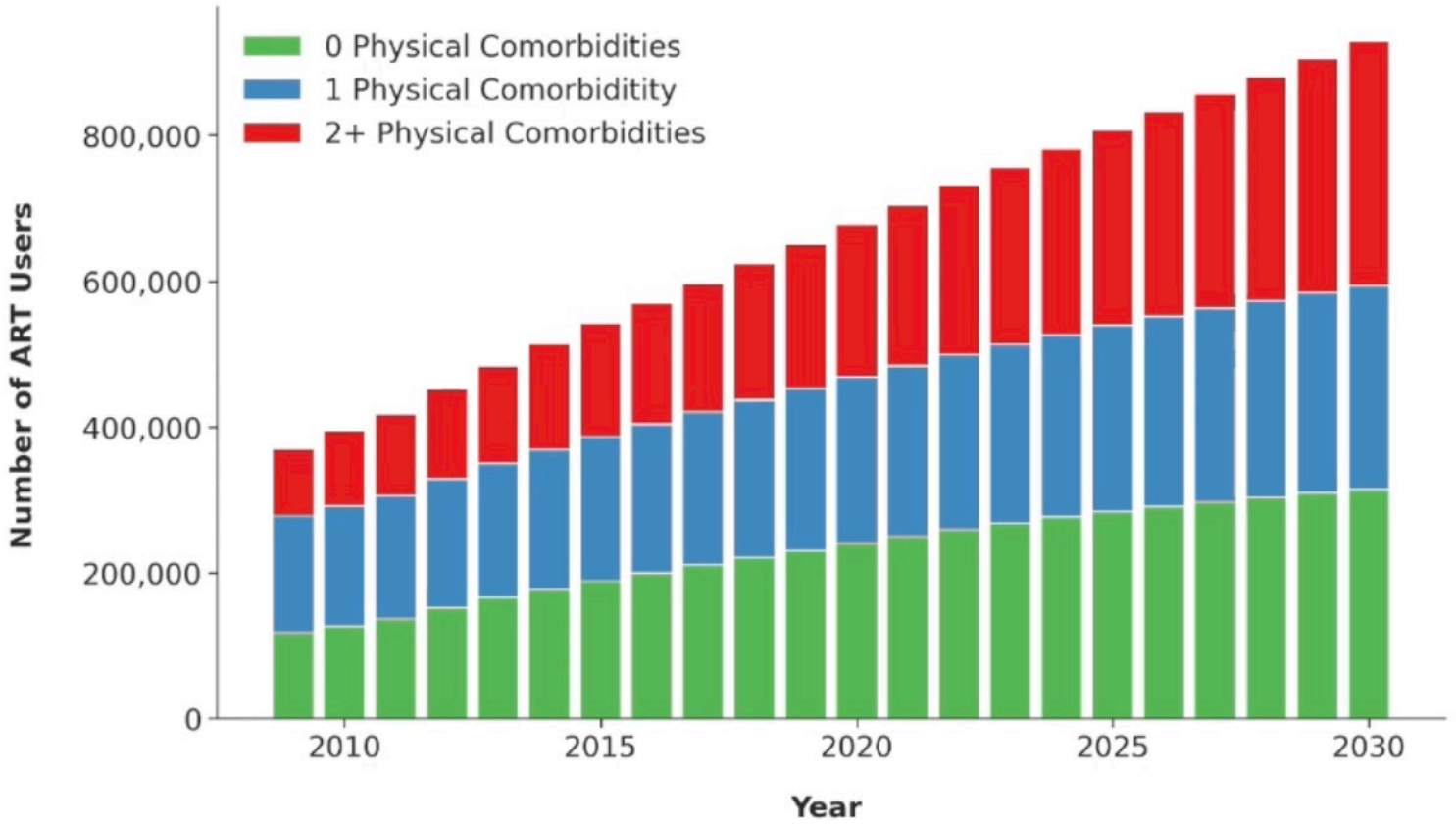
Schouten, CID, 2014

PEARL: Multimorbidity in PWH on ART in the US: 2030 Projections

- The **PEARL** Model: **P**roj**E**cting **A**ge, multimo**R**bidity and po**L**ypharmacy
- NA-ACCORD and CDC surveillance collaboration
- By 2030, 36% will have at least 2 comorbidities
  - Differences by age
  - Greatest increases among gay & bisexual men, esp Black/Hispanic; Hispanic persons who inject drugs & heterosexual women
- Increases in anxiety, depression, chronic kidney ds, DM, MI
- Limitation: excludes transgender & AAPI persons

Kasaie P et al. CROI 2021, Abstract 102.

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



Population with with ≥2 physical comorbidities in addition to HIV in:

2020:
30% (678,000 persons)

2030:
36% (929,000 persons)

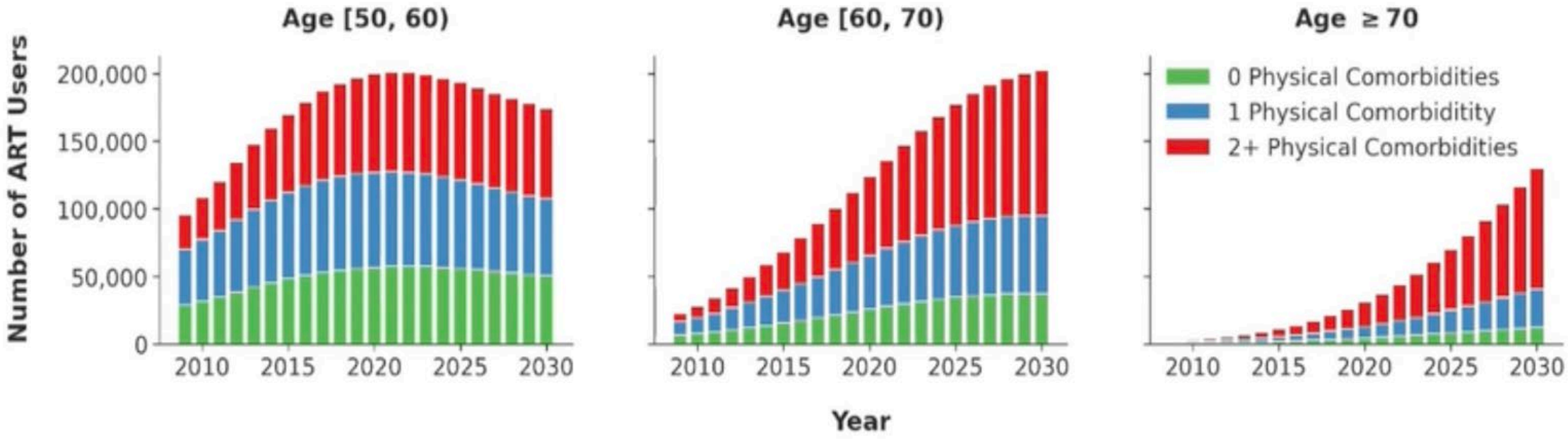
~251,000 additional individuals living with ≥2 physical comorbidities

** Hypertension, Hyperlipidemia, Diabetes, CKD, Cancer, MI & ESLD*

Kasaie P et al. CROI 2021, Abstract 102.

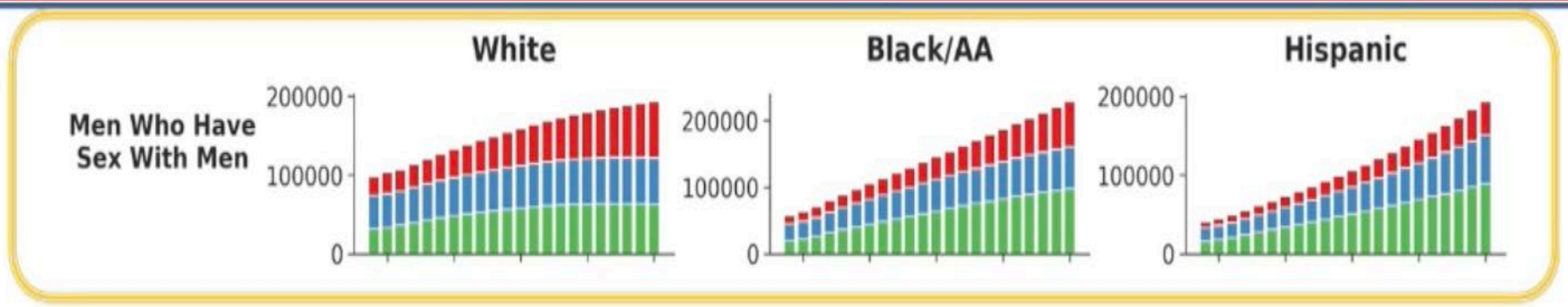
Projected Burden of Multimorbidity by Age, 2030

- Among those ≥ 70yrs, the projected prevalence of multimorbidity increases from 58% (in 2020) to 69% (in 2030), corresponding to an additional 71,000 individuals living with 2+ physical comorbidities beside HIV by 2030



Kasaie P et al. CROI 2021, Abstract 102.

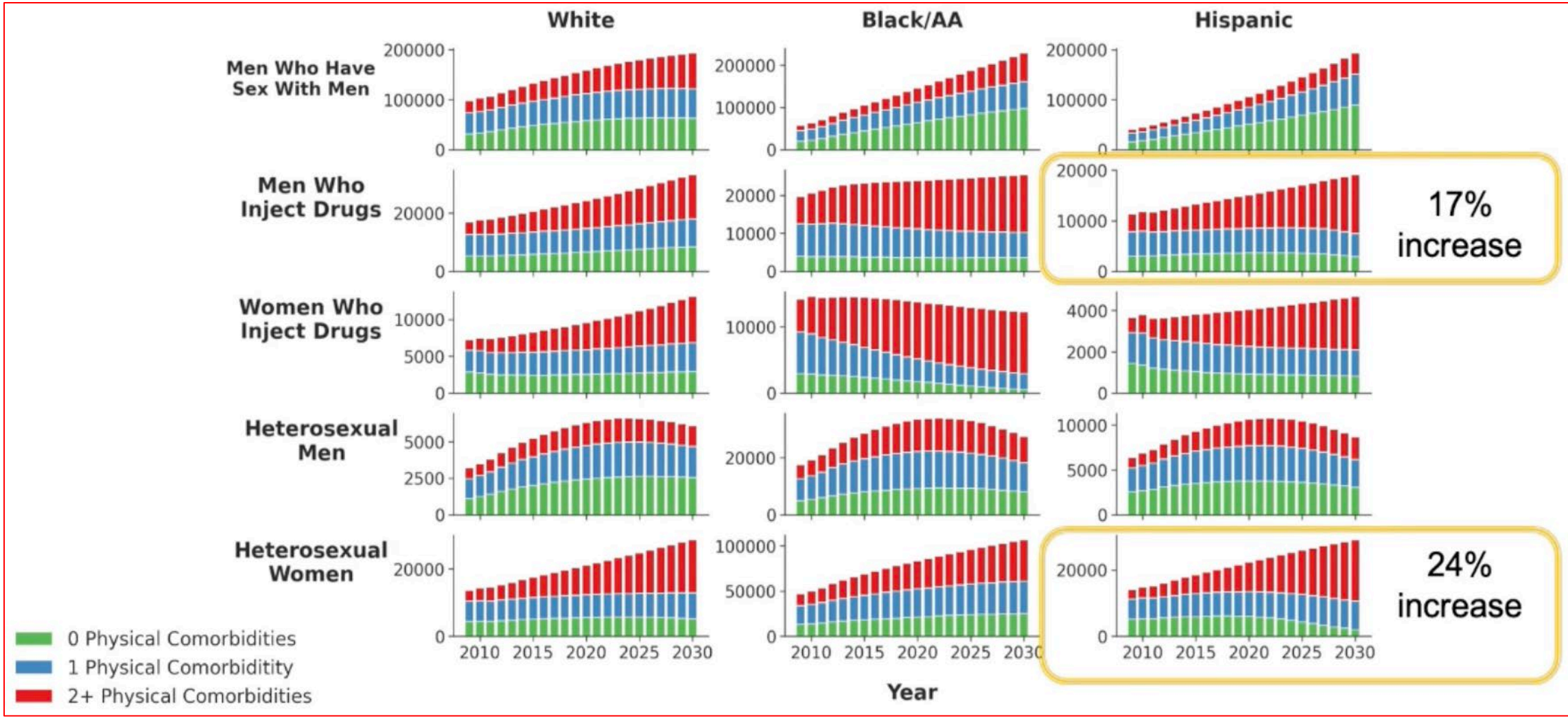
Projected Burden of Multimorbidity by Risk Groups



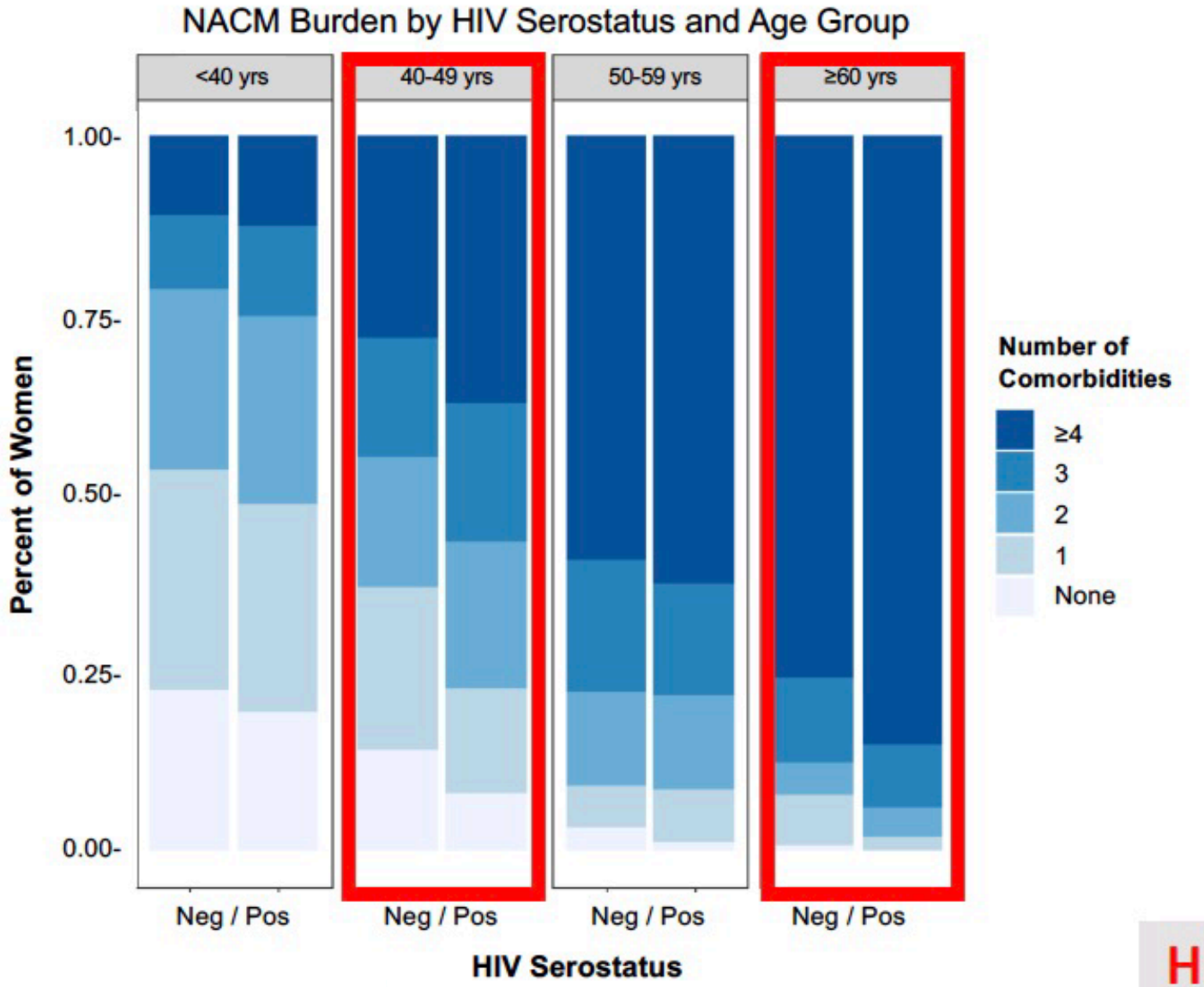
- The Largest increase in number of people with ≥2 physical comorbidities from 2020 to 2030 was projected among MSM, ranging from an additional **34,000 cases among Black/AA MSM** to **21,000 cases among Hispanic MSM**

Kasaie P et al. CROI 2021, Abstract 102.

Projected Burden of Multimorbidity by Risk Groups



Kasaie P et al. CROI 2021, Abstract 102.



Slide: Lauren Collins

Prevalent NACM burden

- Overall, NACM burden was high in the cohort, but higher among WWH
- NACM burden significantly differed by HIV serostatus in certain age groups
- In unadjusted analyses(HIV, age, HIV*age), the effect of HIV on NACM burden was modified by age

HIV*age interaction p=0.0206

Collins L, et al. Clin Infect Dis. 2021 Apr 26;72(8):1301-1311.

Non-AIDS Co-Morbidities in Women with & without HIV

WIHS Women's Interagency HIV Study

- **Prevalence of each NACM increased successively by age group** (<40, 40-49, 50-59, ≥60yrs) in the cohort overall and by HIV serostatus (all $p<0.001$)

- **NACM more prevalent among WWH >> HIV- women** (all $p<0.01$):

	HIV+	HIV-
Psychiatric illness	57%	48%
Liver disease	45%	26%
Hyperlipidemia	40%	35%
Bone disease	40%	33%
Chronic kidney disease	15%	7%
Non-AIDS cancer	11%	7%

- Co-occurrence of HTN & psychiatric illness ranked in top 2 for each HIV-age stratum (60% for women ≥ 60 yrs)
- For WWH, HTN-liver disease was the next most prevalent (33%)

- **No significant difference by HIV serostatus:** HTN, DM2, CVD, lung disease

Collins L, et al. Clin Infect Dis. 2021 Apr 26;72(8):1301-1311.

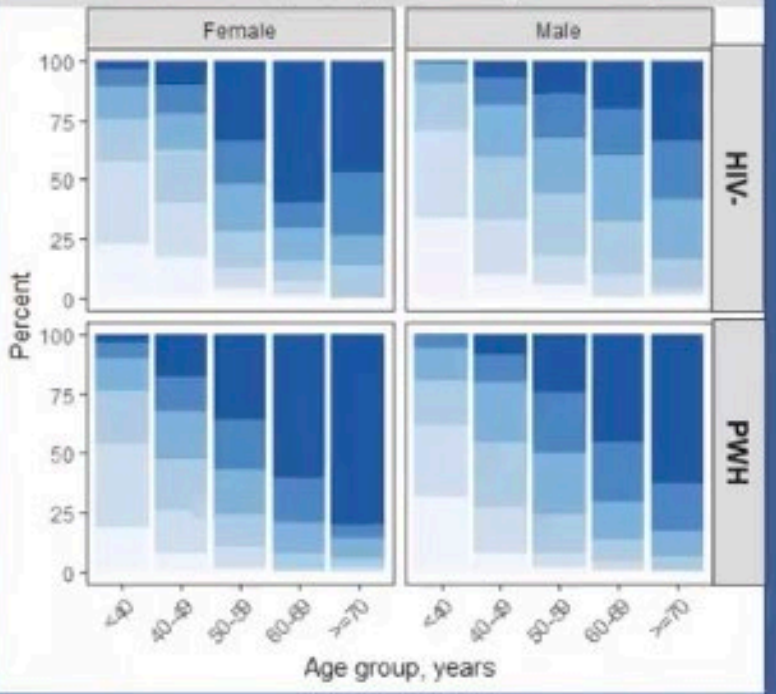
WIHS/MACS Combined Cohort (n=5929): Women Have Higher Burden of NACM Than Men

Characteristics at End of Observation

	Women (n=3238)	Men (n=2691)
Median age, *yrs*	51	58
Median BMI, *kg/m²*	30	26
Black race	65%	25%
Income <150% FPL	78%	32%
Ever smoking	68%	70%
	Women with HIV (n=2316)	**Men with HIV (n=1452)**
Median CD4, *cells/mm³*	620	636
HIV-1 RNA <200 cp/ml	81%	86%
Median time since ART initiation, *yrs*	12.9	15.4

BMI=body mass index; ART = antiretroviral therapy; CVD = cardiovascular disease; FPL = federal poverty level

Prevalent Comorbidity Burden by HIV Serostatus, Sex, and Age Group



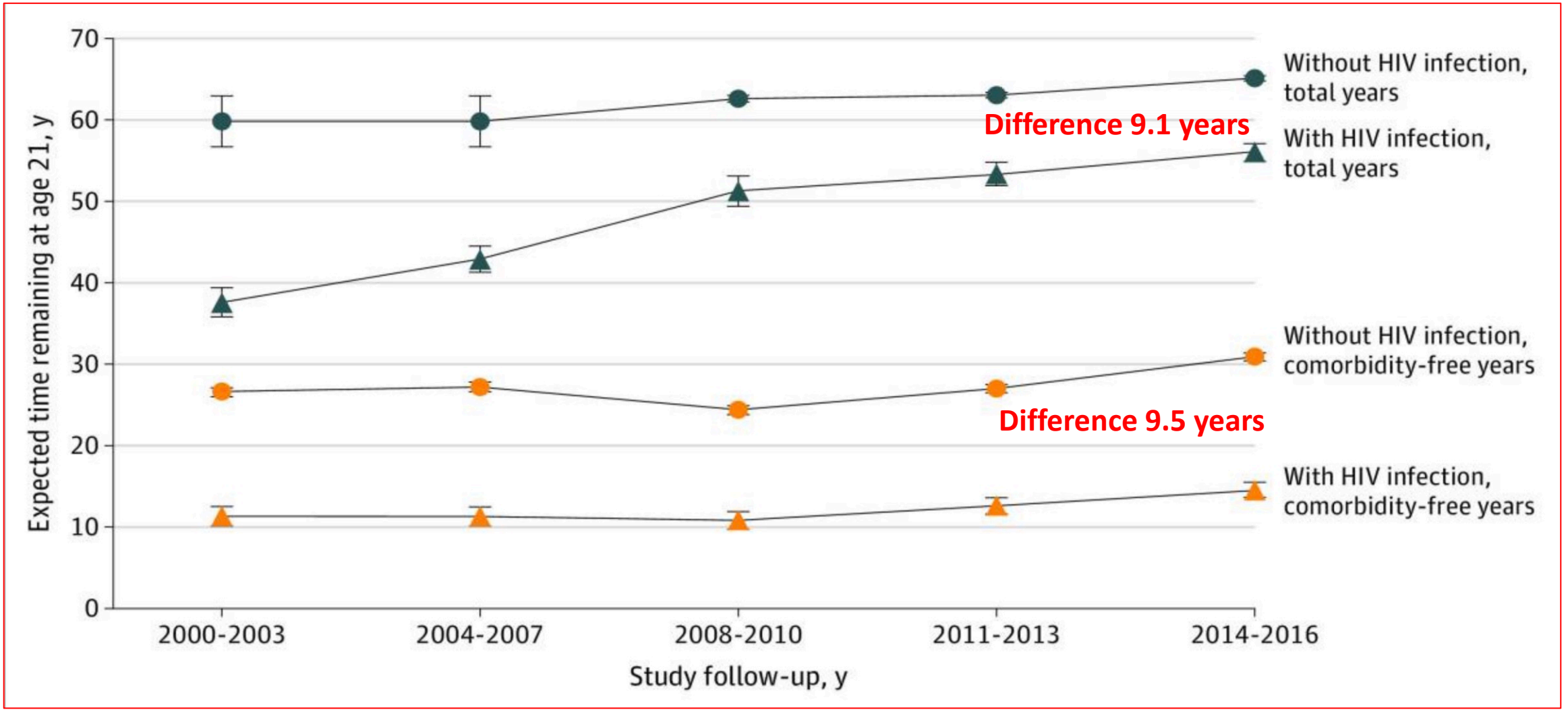
NACM prevalence

	Women	Men
Hypertension	68%	75%
Psych illness	55%	58%
Dyslipidemia	41%	64%
Liver disease	34%	38%
Bone disease	42%	19%
Lung disease	38%	10%
Diabetes	24%	17%
CVD	15%	15%
Kidney disease	14%	15%
Cancer	7%	12%

Median NACM burden among women vs men: 3.4 vs 3.2, *p*=0.015

Collins L, et al. CROI 2021. Abstract 526

People with HIV are Living Longer…
But NOT Without Comorbidities

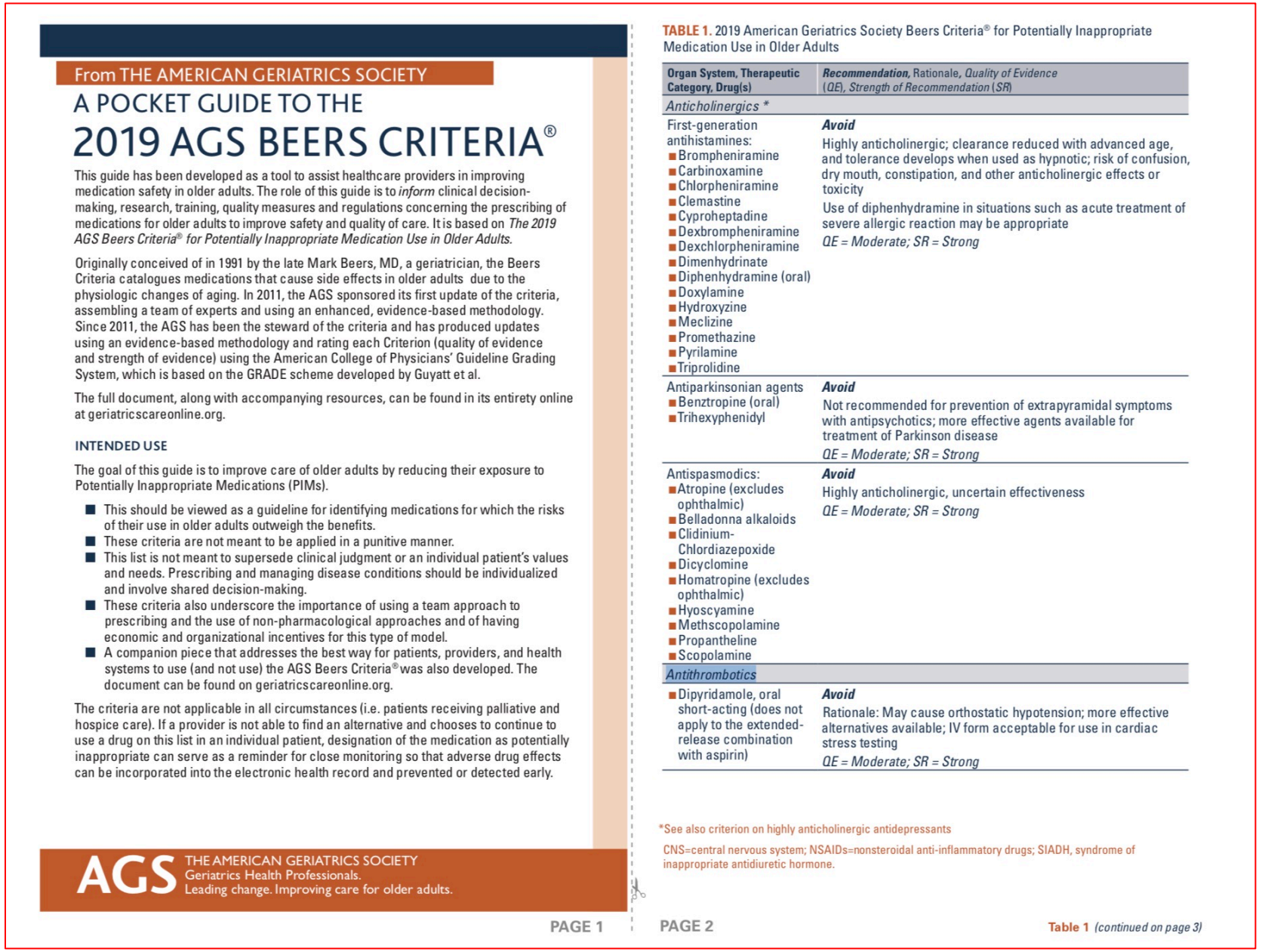


Marcus et al. JAMA Network Open. 2020 Jun (3)6

Issues Associated with Polypharmacy

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

Pocket Guide to Beers Criteria, 2019



From THE AMERICAN GERIATRICS SOCIETY

A POCKET GUIDE TO THE 2019 AGS BEERS CRITERIA®

This guide has been developed as a tool to assist healthcare providers in improving medication safety in older adults. The role of this guide is to *inform* clinical decision-making, research, training, quality measures and regulations concerning the prescribing of medications for older adults to improve safety and quality of care. It is based on *The 2019 AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults.*

Originally conceived of in 1991 by the late Mark Beers, MD, a geriatrician, the Beers Criteria catalogues medications that cause side effects in older adults due to the physiologic changes of aging. In 2011, the AGS sponsored its first update of the criteria, assembling a team of experts and using an enhanced, evidence-based methodology. Since 2011, the AGS has been the steward of the criteria and has produced updates using an evidence-based methodology and rating each Criterion (quality of evidence and strength of evidence) using the American College of Physicians' Guideline Grading System, which is based on the GRADE scheme developed by Guyatt et al.

The full document, along with accompanying resources, can be found in its entirety online at geriatricscareonline.org.

INTENDED USE

The goal of this guide is to improve care of older adults by reducing their exposure to Potentially Inappropriate Medications (PIMs).

- This should be viewed as a guideline for identifying medications for which the risks of their use in older adults outweigh the benefits.
- These criteria are not meant to be applied in a punitive manner.
- This list is not meant to supersede clinical judgment or an individual patient's values and needs. Prescribing and managing disease conditions should be individualized and involve shared decision-making.
- These criteria also underscore the importance of using a team approach to prescribing and the use of non-pharmacological approaches and of having economic and organizational incentives for this type of model.
- A companion piece that addresses the best way for patients, providers, and health systems to use (and not use) the AGS Beers Criteria® was also developed. The document can be found on geriatricscareonline.org.

The criteria are not applicable in all circumstances (i.e. patients receiving palliative and hospice care). If a provider is not able to find an alternative and chooses to continue to use a drug on this list in an individual patient, designation of the medication as potentially inappropriate can serve as a reminder for close monitoring so that adverse drug effects can be incorporated into the electronic health record and prevented or detected early.

AGS THE AMERICAN GERIATRICS SOCIETY
Geriatrics Health Professionals.
Leading change. Improving care for older adults.

PAGE 1

TABLE 1. 2019 American Geriatrics Society Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults

Organ System, Therapeutic Category, Drug(s)	***Recommendation,*** Rationale, *Quality of Evidence (QE), Strength of Recommendation (SR)*
*Anticholinergics **	
First-generation antihistamines: ■ Brompheniramine ■ Carbinoxamine ■ Chlorpheniramine ■ Clemastine ■ Cyproheptadine ■ Dexbrompheniramine ■ Dexchlorpheniramine ■ Dimenhydrinate ■ Diphenhydramine (oral) ■ Doxylamine ■ Hydroxyzine ■ Meclizine ■ Promethazine ■ Pyrilamine ■ Triprolidine	***Avoid*** Highly anticholinergic; clearance reduced with advanced age, and tolerance develops when used as hypnotic; risk of confusion, dry mouth, constipation, and other anticholinergic effects or toxicity Use of diphenhydramine in situations such as acute treatment of severe allergic reaction may be appropriate *QE = Moderate; SR = Strong*
Antiparkinsonian agents ■ Benztropine (oral) ■ Trihexyphenidyl	***Avoid*** Not recommended for prevention of extrapyramidal symptoms with antipsychotics; more effective agents available for treatment of Parkinson disease *QE = Moderate; SR = Strong*
Antispasmodics: ■ Atropine (excludes ophthalmic) ■ Belladonna alkaloids ■ Clidinium-Chlordiazepoxide ■ Dicyclomine ■ Homatropine (excludes ophthalmic) ■ Hyoscyamine ■ Methscopolamine ■ Propantheline ■ Scopolamine	***Avoid*** Highly anticholinergic, uncertain effectiveness *QE = Moderate; SR = Strong*
Antithrombotics	
■ Dipyridamole, oral short-acting (does not apply to the extended-release combination with aspirin)	***Avoid*** Rationale: May cause orthostatic hypotension; more effective alternatives available; IV form acceptable for use in cardiac stress testing *QE = Moderate; SR = Strong*

*See also criterion on highly anticholinergic antidepressants

CNS=central nervous system; NSAIDs=nonsteroidal anti-inflammatory drugs; SIADH, syndrome of inappropriate antidiuretic hormone.

PAGE 2

Table 1 (continued on page 3)

http://files.hgsitebuilder.com/hostgator257222/file/ags_2019_beers_pocket_printable_rh.pdf

Resource: The Beers Criteria

- Potentially inappropriate medications for older adults
  - Due to intrinsic effects
  - Due to **drug-disease, drug-syndrome interactions** that may exacerbate the disease or syndrome
  - To be used with caution in older adults
- Medications that should be avoided or have their dosage reduced with varying levels of kidney function in older adults
- Potentially clinically important drug–drug interactions that should be **avoided** in older adults

American Geriatric Society, 2019

Resource: STOPP and START!

International Journal of Clinical Pharmacology and Therapeutics, Vol. 46 – No. 2/2008 (72-83)

STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment). Consensus validation

P. Gallagher[1], C. Ryan[2], S. Byrne[2], J. Kennedy[2] and D. O'Mahony[3]

[1]Department of Geriatric Medicine, Cork University Hospital, Wilton, Cork, [2]School of Pharmacy and [3]Department of Medicine, University College Cork, Cork, Ireland

Original Investigation | Less Is More

JAMA Network

June 13, 2011

Potentially Inappropriate Medications Defined by STOPP Criteria and the Risk of Adverse Drug Events in Older Hospitalized Patients

Hilary Hamilton, MB, MRCPI; Paul Gallagher, PhD, MRCPI; Cristin Ryan, PhD, MPSI; et al

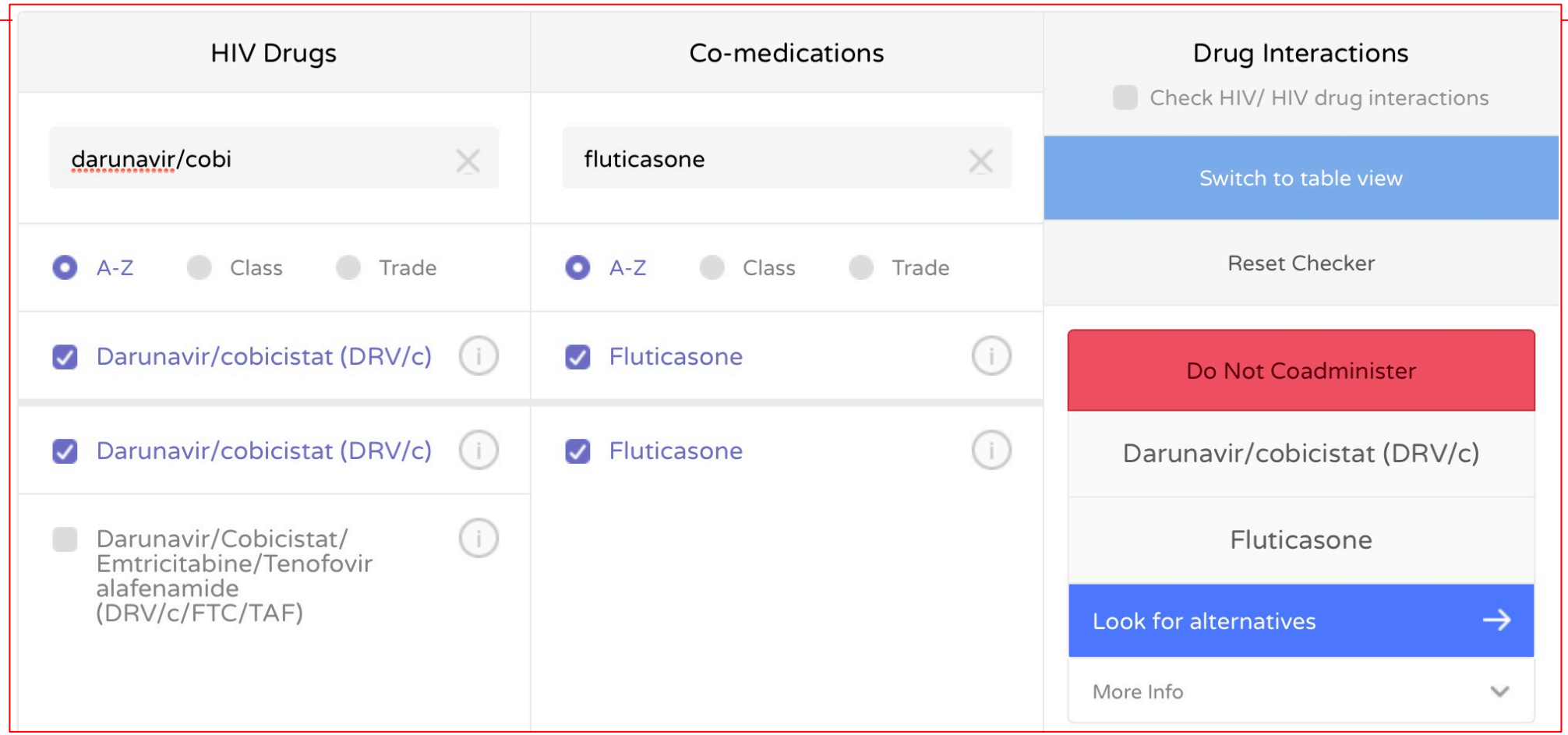
https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/227481

Drug Interactions: Don't Guess!

- Cobicistat, ritonavir: strong CYP3A4 inhibitors, somewhat different interactions (RTV also an inducer)
- PIs: darunavir, atazanavir: lots of interactions
- NNRTIs other than doravirine: CYP3A4 inducers; rilpivirine lowered by PPIs
- INSTIs: Polyvalent cations decrease absorption: Ca, Mg, Fe, Zn, Al especially when given w INSTI on empty stomach
  - Bictegravir: CYP3A4, UGT1A1; dolutegravir: minor CYP3A4, UGT1A1
    - Rifampin/rifabutin (don't use BIC; increase dose with DTG)
    - Metformin increased by BIC and DTG
- Look it up: www.hiv-druginteractions.org

HIV Drug Interactions

UNIVERSITY OF LIVERPOOL



www.hiv-druginteractions.org

Resource: DHHS ART Guidelines: Drug-Drug Interactions Section

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV

Updated June 3, 2021

Developed by the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents – A Working Group of the Office of AIDS Research Advisory Council (OARAC)

Drug-Drug Interactions (Last updated June 3, 2021; last reviewed June 3, 2021)

Overview

Pharmacokinetic (PK) drug–drug interactions between antiretroviral (ARV) drugs and concomitant medications are common and may lead to increased or decreased drug exposure. In some instances, changes in drug exposure may increase the frequency and/or severity of toxicities or affect therapeutic responses. When prescribing or switching one or more drugs in an ARV regimen, clinicians must consider the potential for drug–drug interactions—both those affecting ARVs and those affecting concomitant drugs. A thorough review of concomitant medications in consultation with an expert in ARV pharmacology can help in designing a regimen that minimizes undesirable interactions. Recommendations for managing a specific drug interaction may differ depending on whether a new ARV is being initiated in a patient on a stable concomitant medication

https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf.

Interventions to Limit/Manage Polypharmacy

1) Complete medication reconciliation: include OTC meds, update each visit

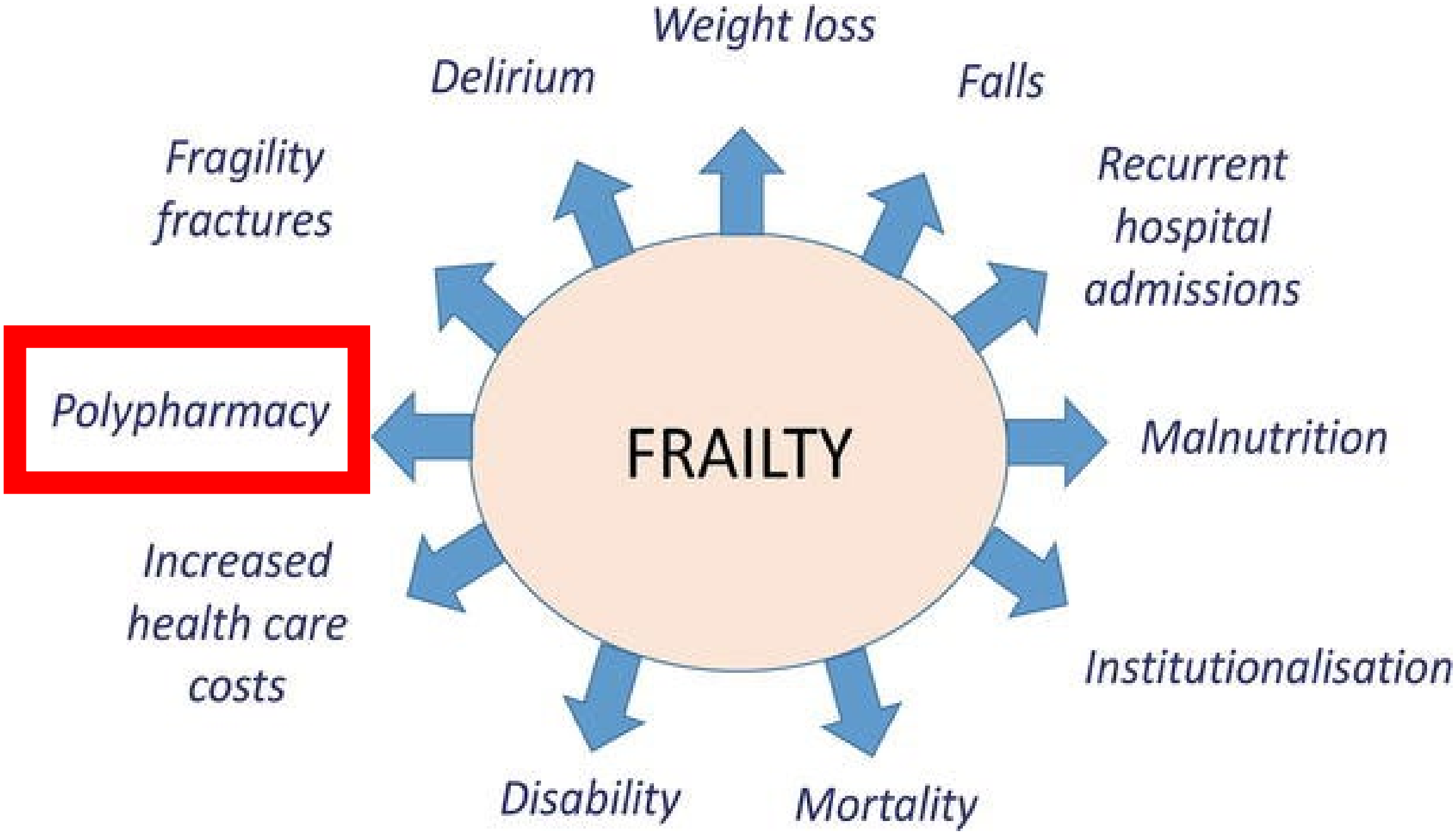
2) Review prescriptions

- Evaluate indication ➔ discontinue unecessary drugs
- Identify meds that are treating adverse effects of other meds
  ➔ discontinue drug that is causing side effect if possible
- Simplify dosing regimen
- Ensure appropriate dosing of medications
- Ensure duration of treatment is appropriate
- Check for drug-drug interactions ➔ use ARV with low DDI potential if possible
- Check for drug-disease interactions
- Check for inappropriate drugs in elderly
- Check for any missing medicine

Beers criteria
STOPP/START criteria

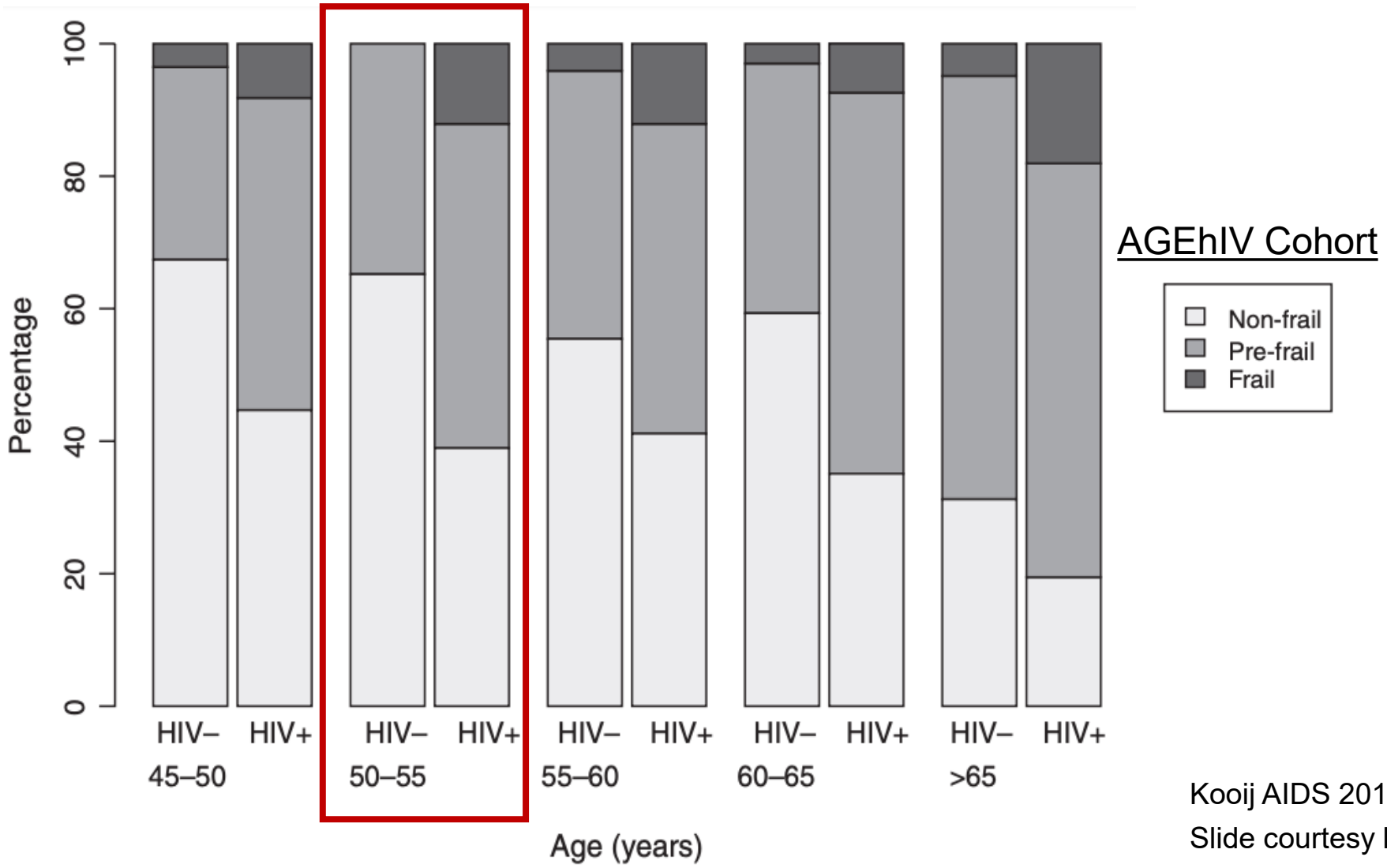
Shah B et al. Clin Geriatr Med 2012, Edelman E et al. Drugs Aging 2013, O'Mahony D et al. Age and Ageing 2015, American Geriatrics Society. J Am Geriatr Soc 2015

Slide courtesy of Charles Flexner



Patel, Epidemiology of Sarcopenia and Frailty, 2016

Frailty Appears to Occur More Frequently… and Perhaps Earlier with HIV



Kooij AIDS 2016

Slide courtesy K. Erlandson

Three 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

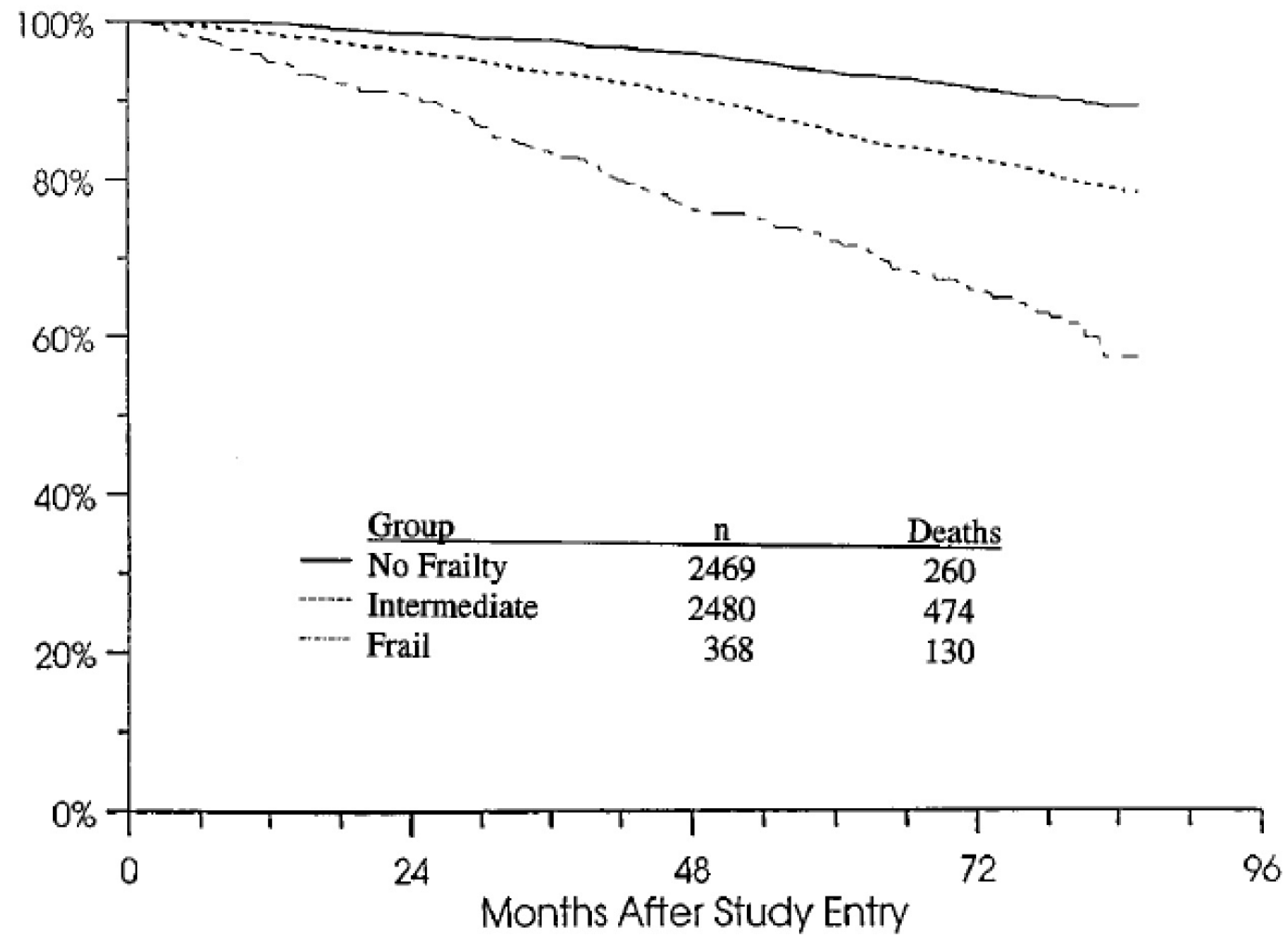
Key. CES-D, Center for Epidemiological Studies Depression; BMI, body mass index.

Fried, J of Gerontology, 2001

Frailty Phenotype as a Predictor

Frailty phenotype predicts

- Death



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**

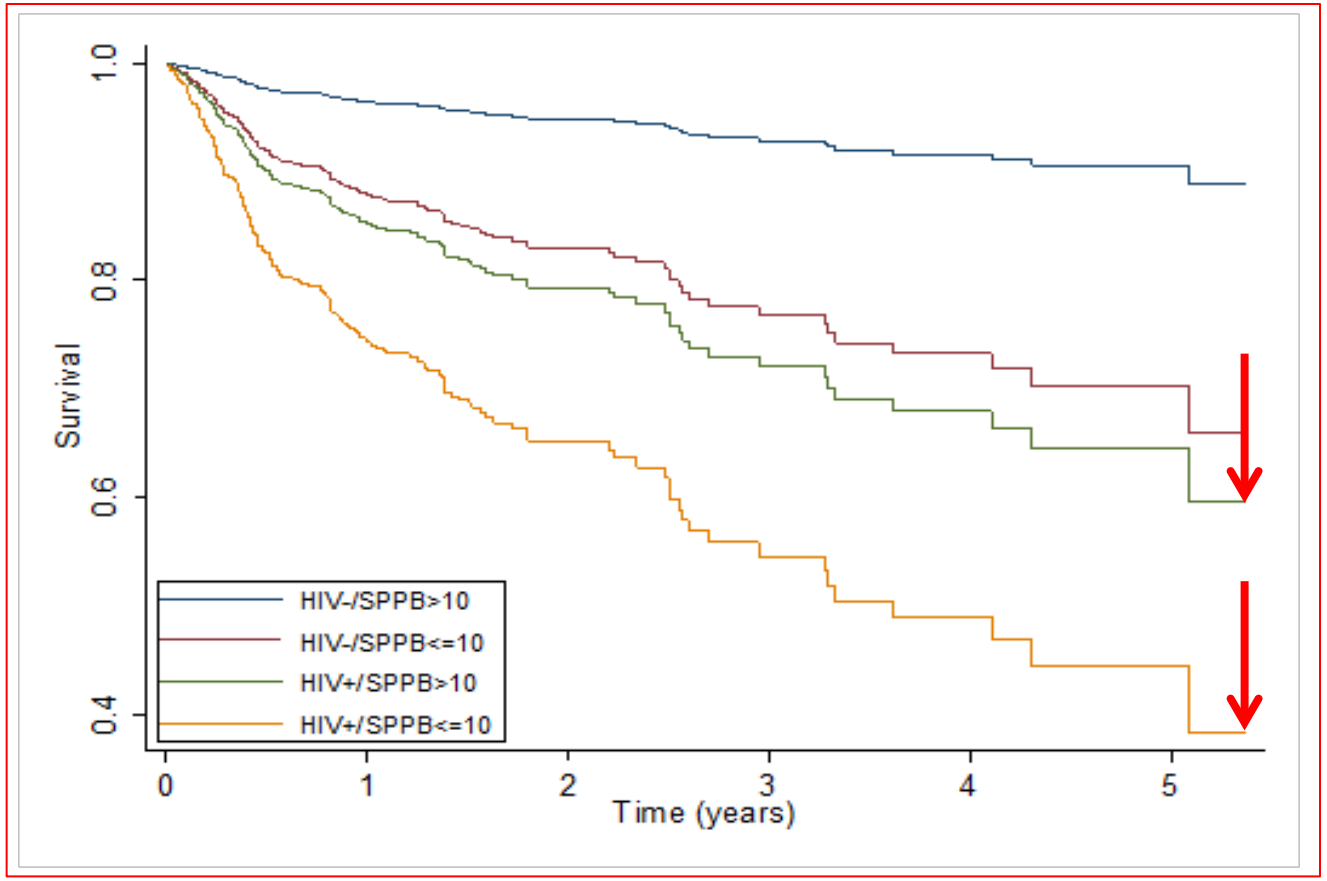
Frailty phenotype was more common in women and African-Americans

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.

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

Kuniholm M. CROI 2021, Abstract 538

Factors associated with Frailty in PLHIV 70+: the ANRS SEPTAVIH Study

% or median	Robust n=111, 23.4%	Pre-frail n=300, 63.1%	Frail n=64, 13.5%	P-value
Age, years	**72**	**73**	**76**	**<0.001**
Male	79.3	82.3	73.4	0.85
College education level	**48.6**	**36.3**	**35.9**	**0.02**
Homeowner	**70.3**	**60.0**	**45.3**	**0.03**
Baseline CD4/mL	623	565	498	0.05
Nadir CD4/mL	185	187	155	0.53
HIV-RNA≤50c/mL at baseline	96.4	94.3	85.9	0.42
Duration of HIV infection, years	22.5	22.8	23.3	0.84
Comorbidities	**2**	**3**	**3**	**0.04**
Deprived socioeconomic status	**20.7**	**32.7**	**48.4**	**<0.001**
Cognitive impairement	**44.1**	**63.3**	**60.9**	**<0.001**

Allevena C. CROI 2021, Abstract 537

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

STEADI Algorithm for Fall Risk Screening, Assessment, and Intervention among Community-Dwelling Adults 65 years and older

START HERE

1 SCREEN for fall risk yearly, or any time patient presents with an acute fall.

Available Fall Risk Screening Tools:

- **Stay Independent: a 12-question tool**
  [at risk if score ≥ 4]
  Important: If score < 4, ask if patient fell in the past year
  (If **YES** → patient is at risk)

- **Three key questions** for patients [at risk if **YES** to any question]
  Feels unsteady when standing or walking?
  Worries about falling?
  Has fallen in past year?
  » If **YES** ask, "How many times?" "Were you injured?"

SCREENED NOT AT RISK

PREVENT future risk by recommending effective prevention strategies.

- Educate patient on fall prevention
- Assess vitamin D intake
  If deficient, recommend daily vitamin D supplement
- Refer to community exercise or fall prevention program
- Reassess yearly, or any time patient presents with an acute fall

SCREENED AT RISK

2 ASSESS patient's modifiable risk factors and fall history.

Common ways to assess fall risk factors are listed below:

Evaluate gait, strength, & balance	Common assessments: •30-Second Chair Stand •Timed Up & Go •4-Stage Balance Test
Identify medications that increase fall risk	(e.g., Beers Criteria)
Ask about potential home hazards	(e.g., throw rugs, slippery tub floor)
Measure orthostatic blood pressure	(Lying and standing positions)
Check visual acuity	Common assessment tool: •Snellen eye test
Assess feet/footwear	
Assess vitamin D intake	
Identify comorbidities	(e.g., depression, osteoporosis)

3 INTERVENE to reduce identified risk factors using effective strategies.

Reduce identified fall risk

- Discuss patient and provider health goals
- Develop an individualized patient care plan (see below)

Below are common interventions used to reduce fall risk:

Poor gait, strength, & balance observed	•Refer for physical therapy •Refer to evidence-based exercise or fall prevention program (e.g., Tai Chi)
Medication(s) likely to increase fall risk	•Optimize medications by stopping, switching, or reducing dosage of medications that increase fall risk
Home hazards likely	•Refer to occupational therapist to evaluate home safety
Orthostatic hypotension observed	•Stop, switch, or reduce the dose of medications that increase fall risk •Educate about importance of exercises (e.g., foot pumps) •Establish appropriate blood pressure goal •Encourage adequate hydration •Consider compression stockings
Visual impairment observed	•Refer to ophthalmologist/optometrist •Stop, switch, or reduce the dose of medication affecting vision (e.g., anticholinergics) •Consider benefits of cataract surgery •Provide education on depth perception and single vs. multifocal lenses
Feet/footwear issues identified	•Provide education on shoe fit, traction, insoles, and heel height •Refer to podiatrist
Vitamin D deficiency observed or likely	•Recommend daily vitamin D supplement
Comorbidities documented	•Optimize treatment of conditions identified •Be mindful of medications that increase fall risk

FOLLOW UP with patient in 30-90 days.

Discuss ways to improve patient receptiveness to the care plan and address barrier(s)

https://www.cdc.gov/steadi/index.html

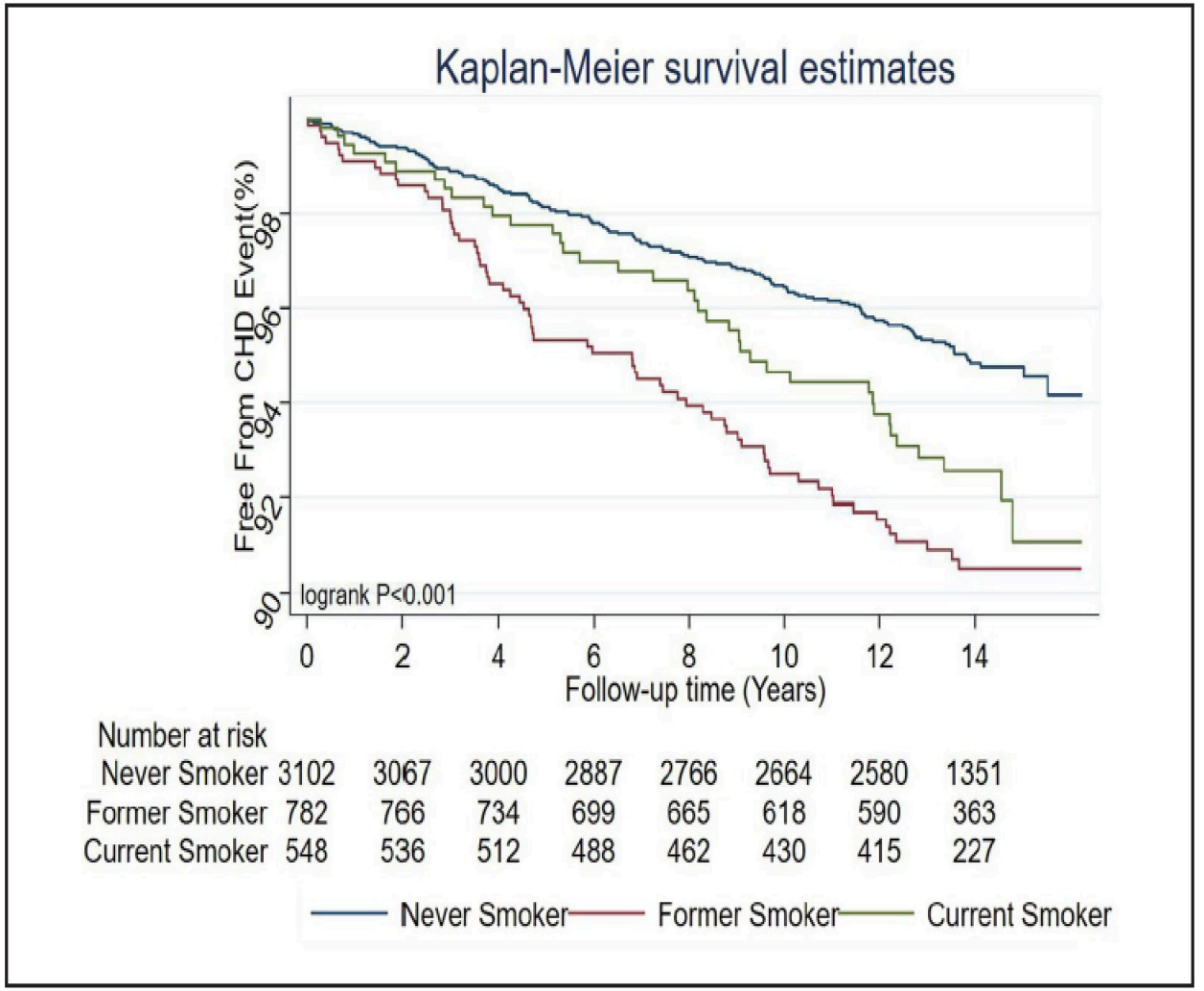
Approach to Comorbidities: Increased Awareness, Early Intervention

- Smoking
- SMOKING
- SMOKING
- SMOKING
- SMOKING!

JAHA
Journal of the American Heart Association

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



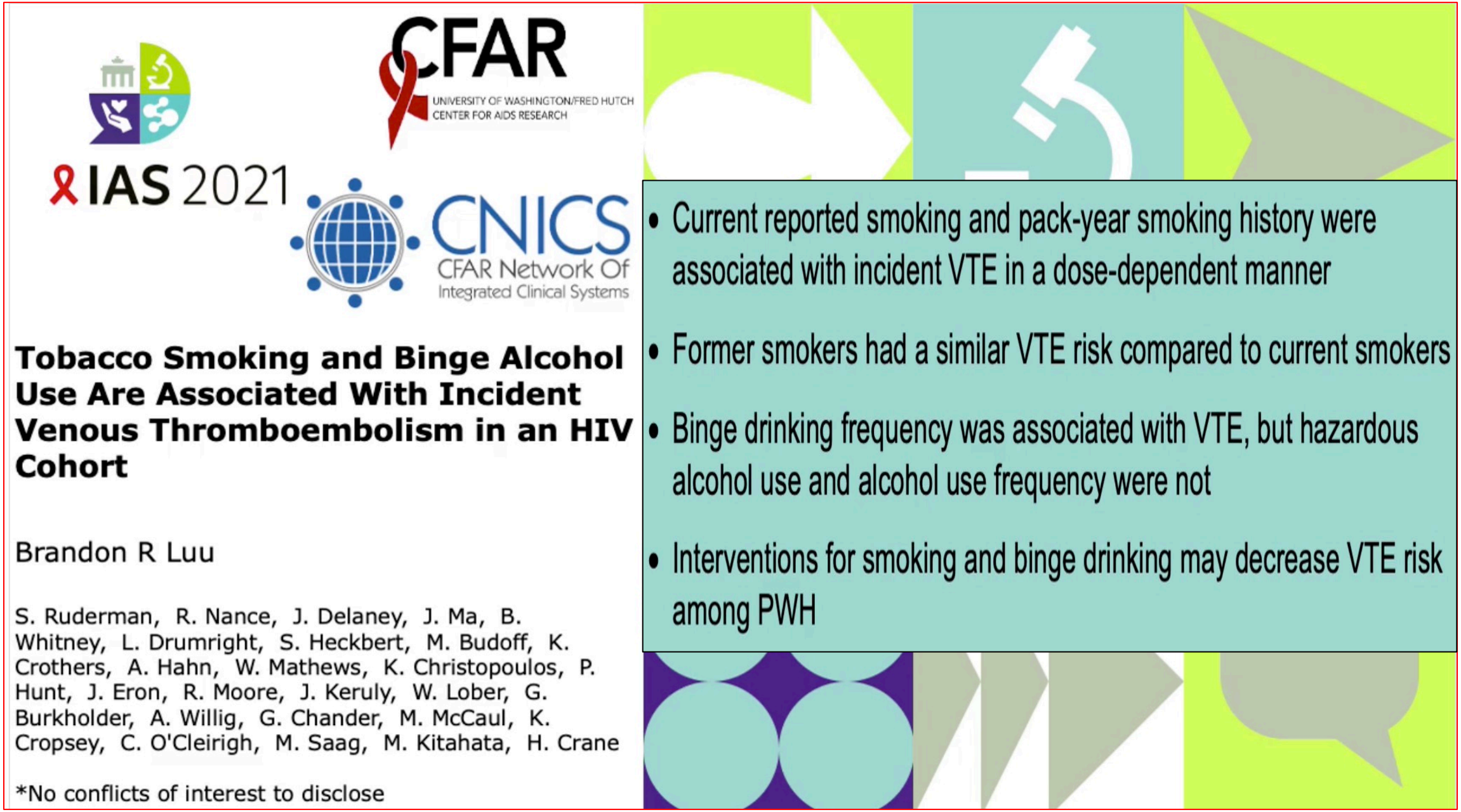
CONCLUSIONS: In a large prospective cohort of Black adults, current smoking was associated with a >2-fold increased risk of CHD over a median follow-up of greater than a decade.

Oahunbade, et al, JAHA, March 23, 2021

Smoking and Cancer in PLWH

- Smoking: up to ¾ of PLWH, 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%

Altekruse, AIDS, 2018



Luu B, et al. IAS 2021, Abstract PEB114

AHA SCIENTIFIC STATEMENT

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

A Scientific Statement From the American Heart Association

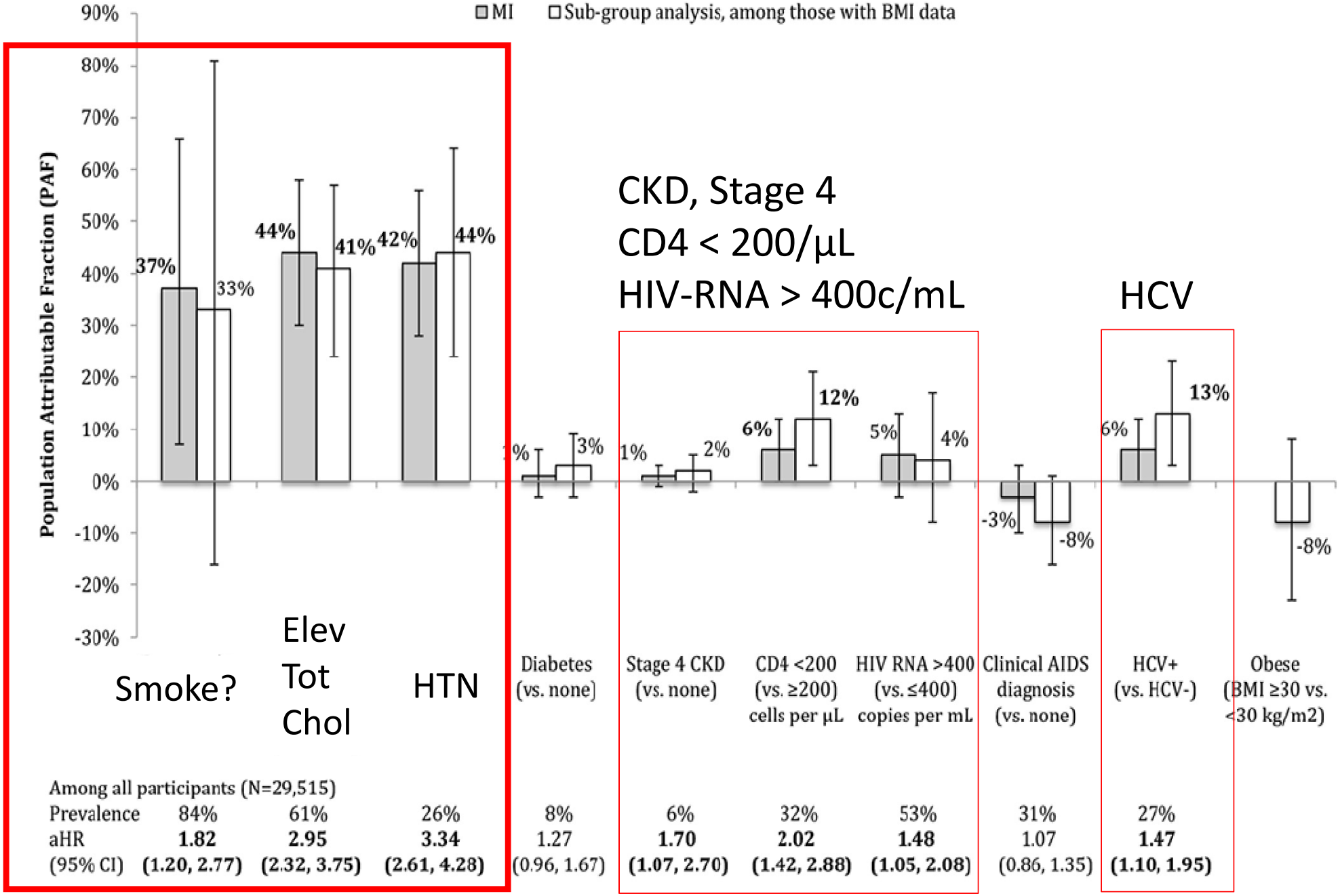
- Recognizes increased ASCVD risk in persons with HIV
  - 1.5-2x increase in MI, stroke, heart failure
  - Increased pulmonary HTN, blood clots, sudden death
- Addresses pathophysiology, screening, treatment
- Includes link to patient perspective from PLWH

Feinstein, Circulation, 2019

Contribution to MI Risk in PWH (NA-ACCORD)

When obesity included:

DM significant
HIV-RNA not significant

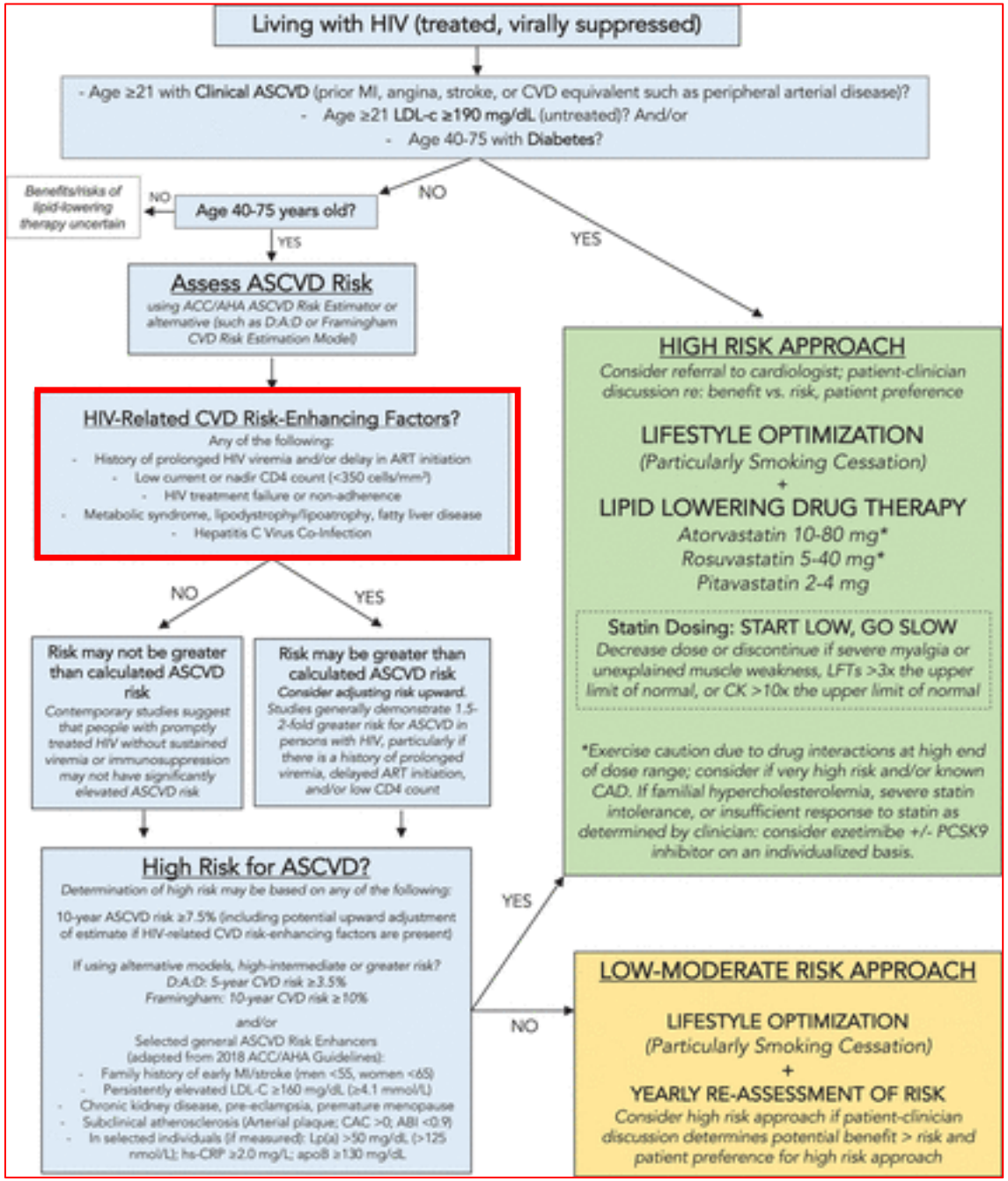


Althoff, Lancet HIV, 2020

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.*

Feinstein, Circulation, 2019

HIV-Related CVD Risk-Enhancing Factors?

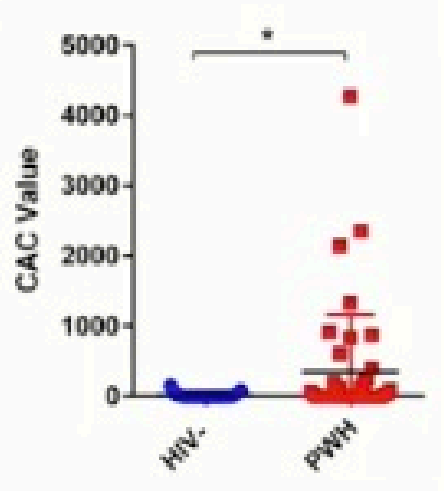
Any of the following:

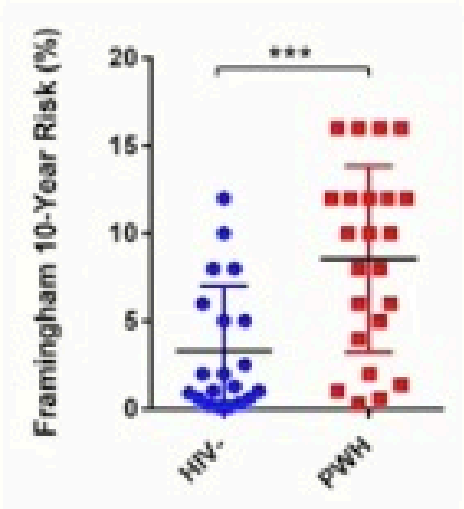
- History of prolonged HIV viremia and/or delay in ART initiation
- Low current or nadir CD4 count (<350 cells/mm^3)
- HIV treatment failure or non-adherence
- Metabolic syndrome, lipodystrophy/lipoatrophy, fatty liver disease
- Hepatitis C Virus Co-Infection

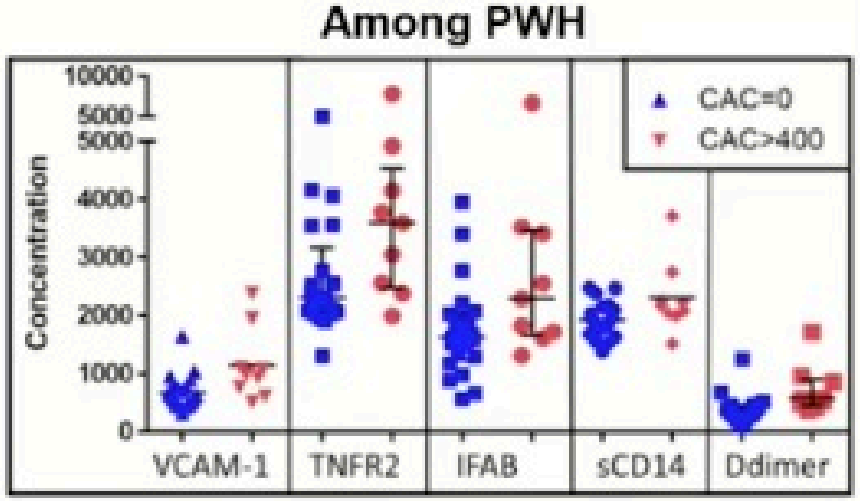
If YES: Consider adjusting risk upward; may be 1.5-2x higher

Feinstein, Circulation, 2019

PWH have increased coronary calcium scores and arterial ages compared to a demographically similar group of people without HIV

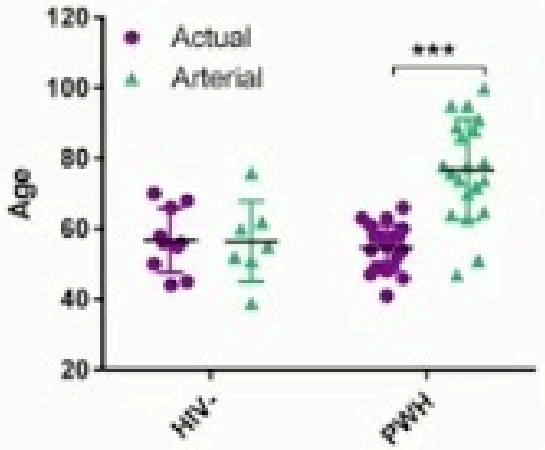


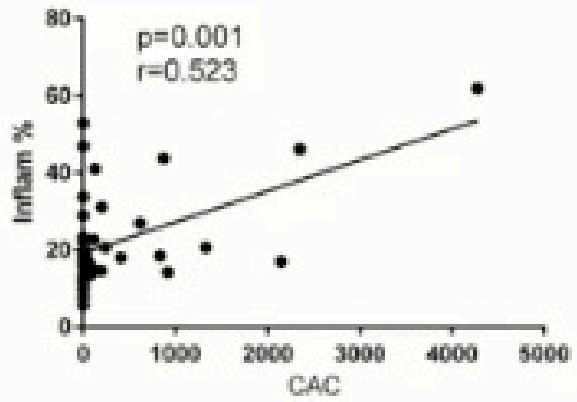




Arterial Age Calculation Factors

- Coronary Artery Calcium Score
- Age
- Sex
- Total Cholesterol
- HDL
- Systolic Blood Pressure
- Smoking Status
- Use of Anti-Hypertensive Meds





McClelland et al *Am J Cardiol* 2009

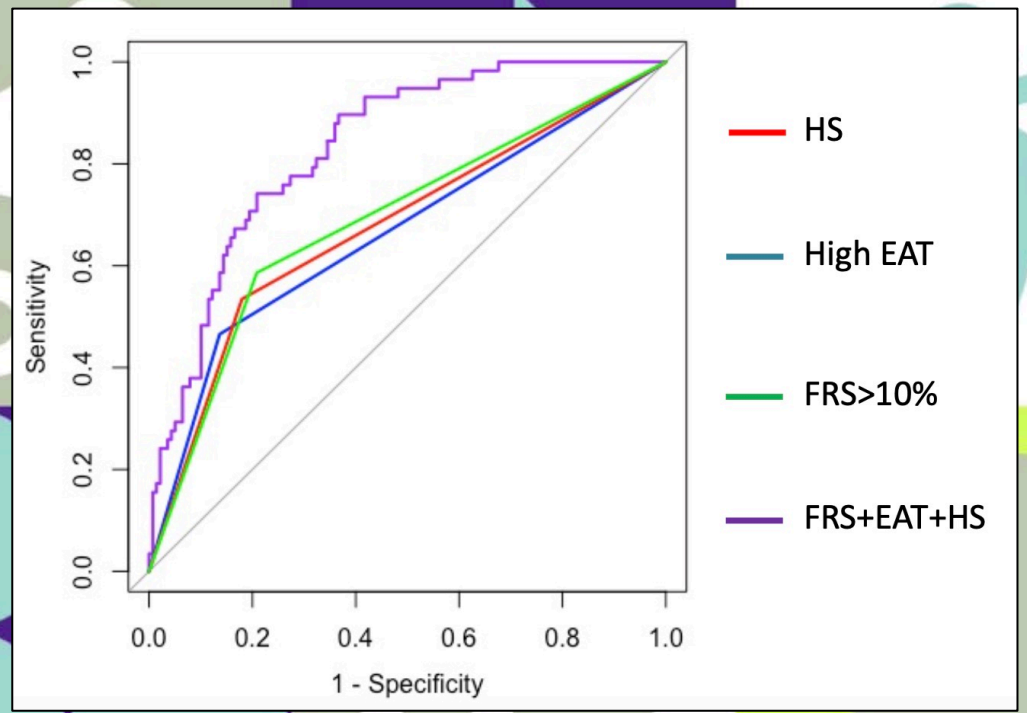
The Ohio State University
Wexner Medical Center

Slide: N. Funderberg, IAS 2021

IAS 2021

The Association of Coronary Calcification with Visceral Adiposity in people living with HIV. Results from the Liverpool HIV-Heart Collaberation

- The discriminatory ability of FRS to detect coronary calcification was modest (area under the receiver operator curve [AUC] 0.689).
- The addition of HS and EAT volume improved the discriminatory ability of the model significantly (AUC:0.833).



FRS = Framingham Risk Score; HS = hepatosteatosis; EAT = epicardial adipose tissue

Heseltine, IAS 2021, Abstract PEB115

INSTI Switch/Add Study

WIHS Women's Interagency HIV Study

- 61% Black, mean age 49yrs, BMI 31 kg/m^2, CD4 count 669 cells/mm^3

- **Body measurements**
  - INSTI group had significantly greater INCREASE in body weight, BMI, body fat % and circumference of waist, hip, thigh, arm
    - No difference by INSTI drug type (RAL, EVG, DTG)
  - Risk factors for weight gain in the INSTI group: ≥50 years old, minority race/ethnicity, baseline BMI <30, CD4 ≥350, HIV-1 RNA ND, TAF use

- **Cardiometabolic profiling**
  - INSTI group had worsening of blood pressure and hemoglobin A1c risk categories and decreased HDL
  - No significant differences in incident T2DM or HTN

Kerchberger, et al, CID 2020; 71(3): 593-600.
Summers, et al, JAIDS 2020;85(3):355-62.
Lahiri, et al, ARHR 2021, epub ahead of print.

Slide courtesy: Lauren Collins

Prevention of Multimorbidity

- 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…
- Consider role of mental health in being able to address general health issues: holistic approach needed

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

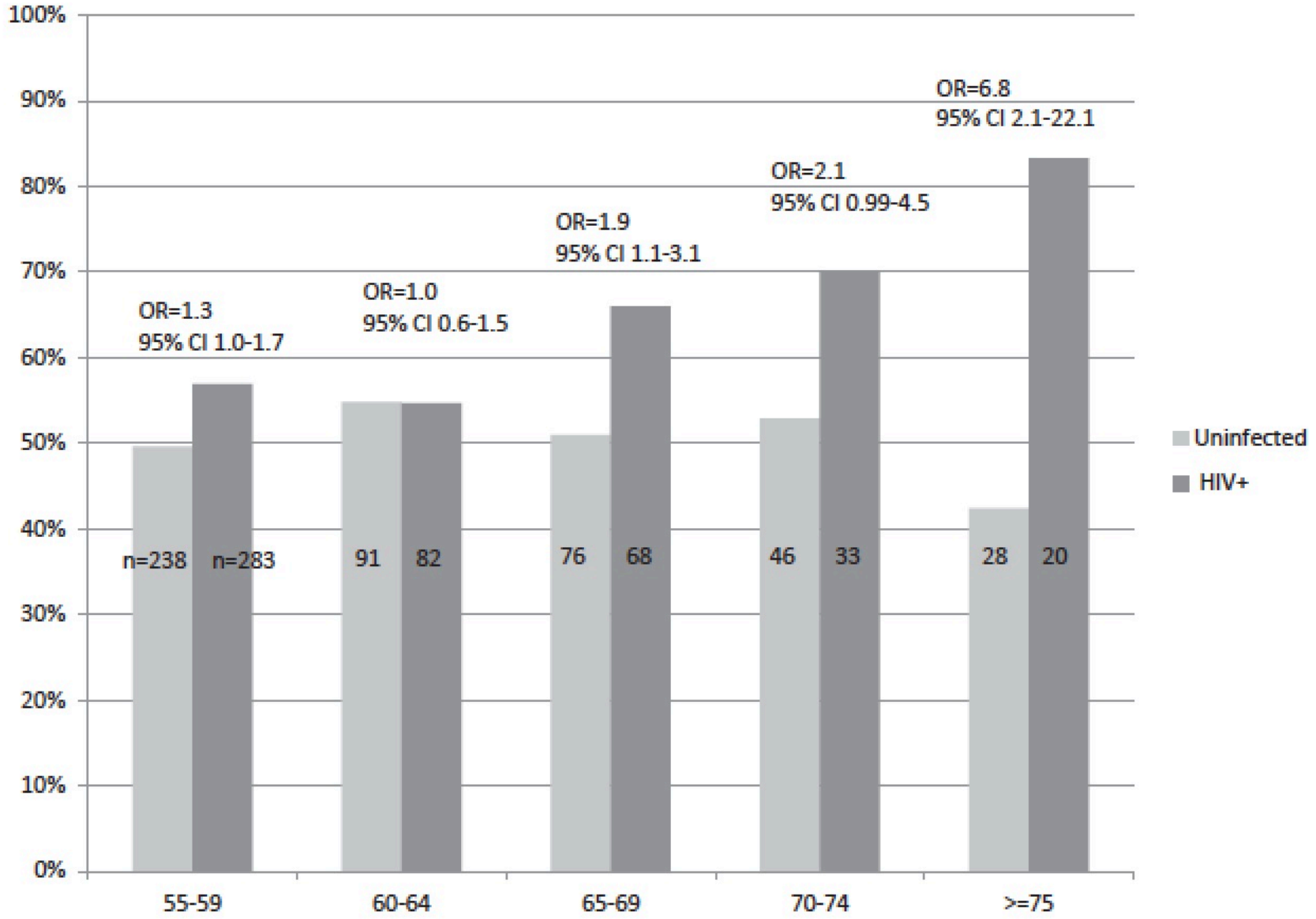
S. Ryan Greysen, MD, MHS, MA, Leora I. Horwitz, MD, MHS,† Kenneth E. Covinsky, MD, MPH,‡§ Kirsha Gordon, MS,¶ Michael E. Ohl, MD, MSPH,‖ and Amy C. Justice, MD, PhD†¶*

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

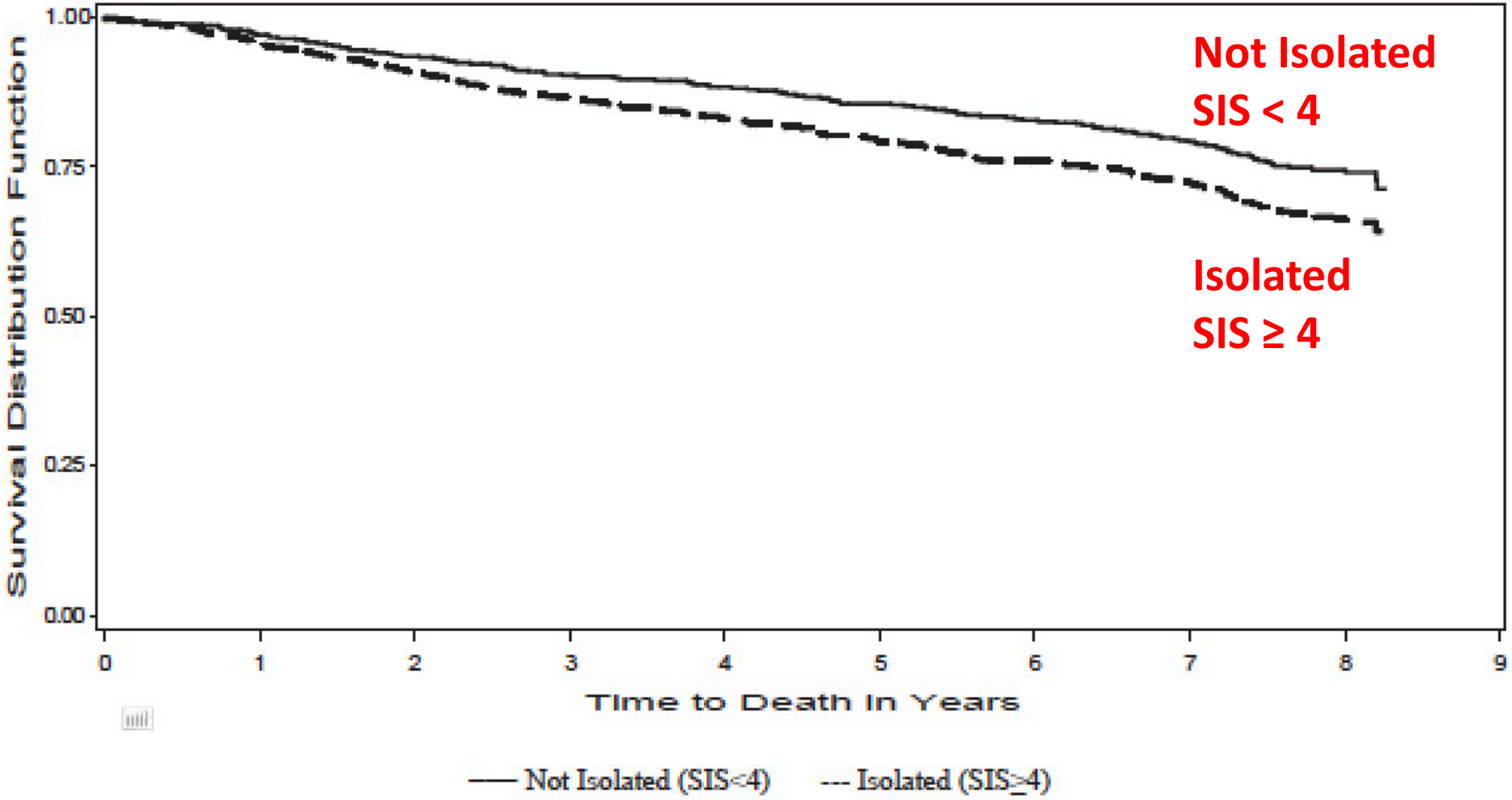
PLWH ≥ 65 yo are 2-7 times more likely to experience social isolation than those who are HIV -



* 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

Social Isolation Is Associated with Increased Mortality



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

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

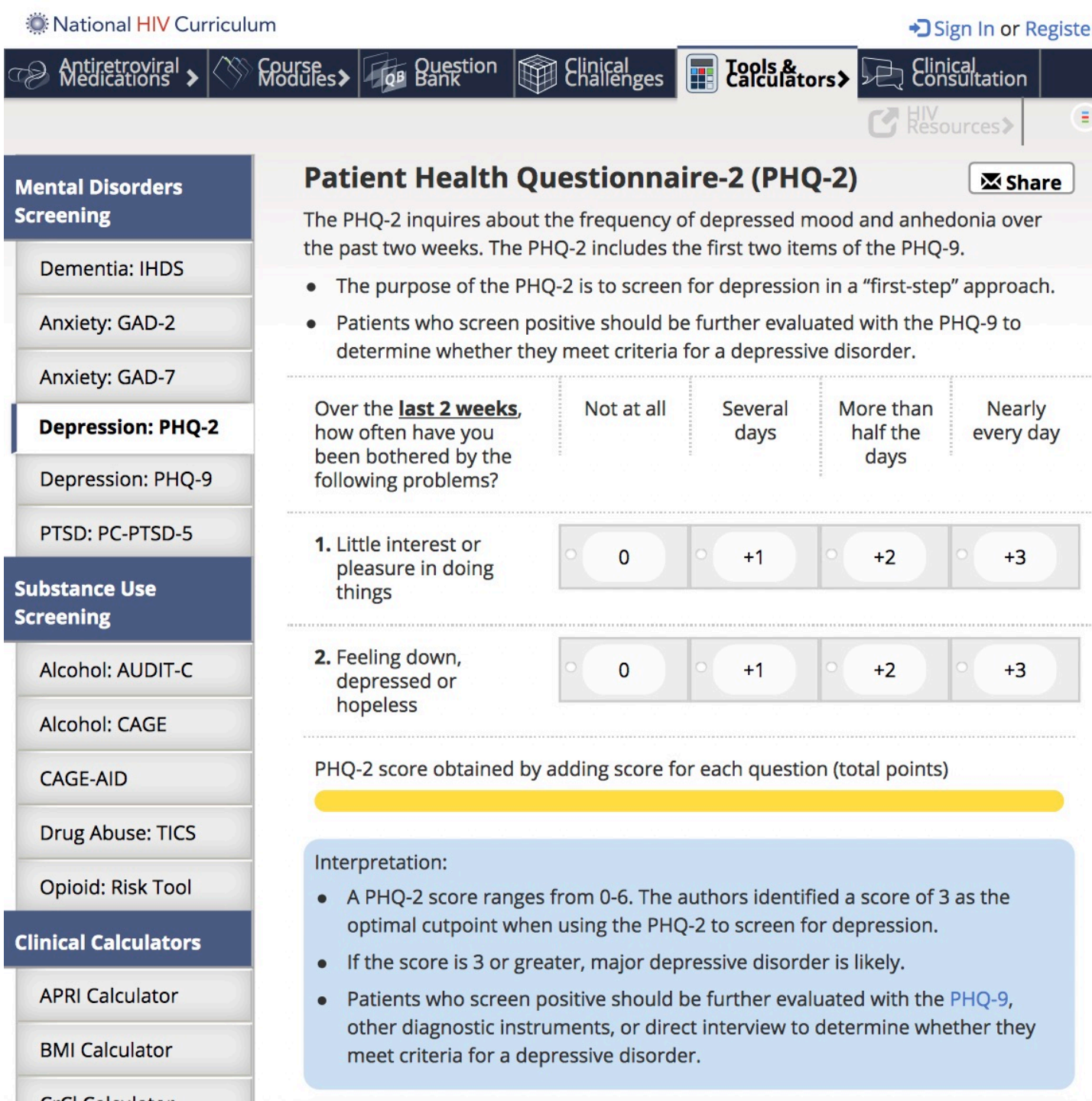
National HIV Curriculum: https://www.hiv.uw.edu/page/mental-health-screening/phq-2

Screening Resources

National HIV Curriculum

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

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



Stigma Kills!

- HIV status
- LGBTQ+ discrimination
- Ageism
- Substance use
- Race/ethnicity

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

Melanie A. Thompson,[1,a] Michael A. Horberg,[2,a] Allison L. Agwu,[3] Jonathan A. Colasanti,[4] Mamta K. Jain,[5] William R. Short,[6] Tulika Singh,[7] and Judith A. Aberg[8]

Thompson M, et al. www.hivma.org under "Guidelines"

Acknowledgements

- People with – and without – HIV whose data are included
- Researchers whose data (and slides) were included
- My patients – who have allowed me to grow older along with them and whose wisdom and resilience inspires me