The Bold and Bright Frontier of Women living with HIV

Lauren Collins, MD, MSc

Assistant Professor of Medicine, Division of Infectious Diseases, Emory University School of Medicine & the Infectious Diseases Program, Grady Memorial Hospital

Disclosures

- None

Learning objectives

1) To describe biologic and psychosocial factors that influence health and disease outcomes among women living with HIV

2) To assess the prevalence and incidence of aging-related non-AIDS comorbidities among women living with HIV as well as the impact of the menopausal transition

3) To appreciate the evolving landscape of HIV care service delivery for women aging with HIV, including novel treatment and prevention modalities


Atlanta
BEST
Wine
Because no great story
started with someone eat
Woodruff Leadership
Academy
THE GAP
The New York Times
AMERICA'S COOKBOOK
CABERNET
GREAT WINE
WINE
ATLAS of WINE

Outline

1) Introduction
2) Aging-related comorbidities in women
3) Impact of the menopausal transition
4) Psychosocial context and considerations
5) Long-acting antiretroviral therapy (ART) for HIV treatment and prevention
6) HIV care infrastructure for aging women

Sex = a biologic trait that is determined by anatomy, which is produced by chromosomes, hormones, and their interactions (male/female)

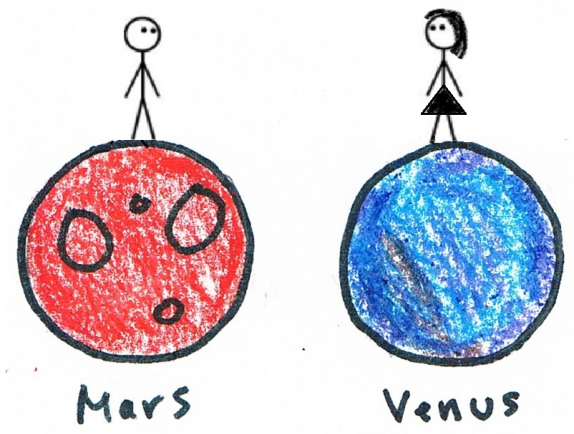
Gender = a social construct related to behaviors and attributes based on labels of masculinity-femininity (man-*spectrum*-woman)

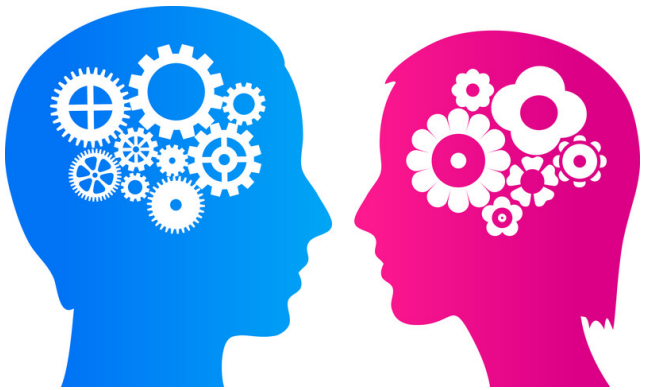
Focus on women

Introduction

WHY WOMEN?

The confluence of female-specific biologic and psychosocial factors, including the disproportionate representation of social determinants of health by sex, impact health and disease outcomes among women





When women rise, we all rise

Women living with HIV (WLWH)

50% of the population with HIV worldwide

19% (U.S.)

Women living with HIV (WLWH)

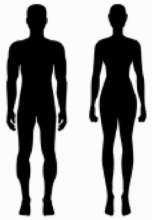
- **How does HIV impact a woman's life experience?**
- **How does female sex impact living with HIV?**

- BIOLOGIC IMPACT

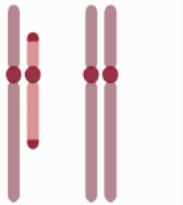
Sex differences in HIV

Sex-specific biologic factors known to affect HIV:

- Acquisition
- Pathogenesis
- Reservoir
- Cure potential
- Responses to antiretroviral therapy (ART) and associated toxicity

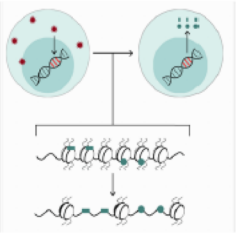


Anatomic Differences:
-Acquisition sites: female genital tract versus rectal mucosa
-Hormonal modulation of risk at the female genital tract
-Drug penetration to mucosal sites



Genetic differences:
-Gene dosage effects of X chromosome encoded genes/ incomplete X inactivation
-Regulatory function of X-encoded microRNAs
-Estrogen responsive elements in promoters of multiple immune active genes

Immune cell phenotypes:
-Higher interferon alpha production from plasmacytoid dendritic cells from women
-Sex differences in the efficacy of vaccines
-Hormone modulation of immune cell function



Latency maintenance:
-Estrogen blockade of HIV transcriptional activation
-Sex specific epigenetic modifications in immune cells

Microbiome:
-Female genital tract and rectal mucosa with distinct microbiome compositions that determine local inflammation and acquisition risk
-Direct effects of the vaginal microbiome on local antiretroviral drug levels
-Sex hormone modulation of the gut microbiota that contributes to systemic inflammation

Scully EP. Curr HIV/AIDS Rep. 2018 Apr;15(2):136-146.

Women living with HIV (WLWH)

- **How does HIV impact a woman's life experience?**
- **How does female sex impact living with HIV?**

- BIOLOGIC IMPACT
  - Among persons living with HIV (PLWH), women versus men have greater immune activation in response to HIV-1 infection
  - How is this impacted by the menopausal transition?

- PSYCHOSOCIAL IMPACT
  - WLWH compared with men living with HIV (MLWH), are at higher risk of sociobehavioral and structural factors (eg, interpersonal violence, economic stability) that may lead to isolation, healthcare underutilization, and poor health outcomes

The experience of *aging* WLWH

Epidemiology

WLWH

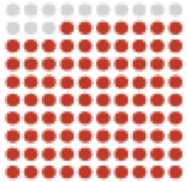
50% of the population with HIV worldwide

19% (U.S.)

Women who don't know they have HIV can't get the care and treatment they need to stay healthy.

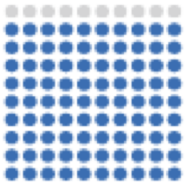
In 2019, an estimated **1.2 million PEOPLE** had HIV.††† **Of those, 263,900 were women.‡‡‡**

For every 100 people with HIV



87 knew their HIV status.

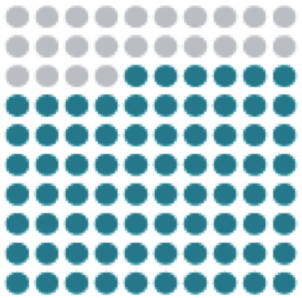
For every 100 women with HIV



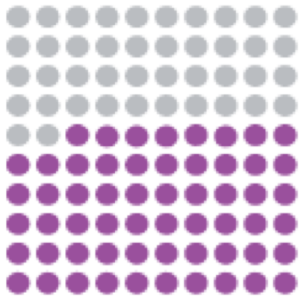
90 knew their HIV status.

It is important for women to know their HIV status so they can take medicine to treat HIV if they have the virus. Taking HIV medicine every day can make the viral load undetectable. People who get and keep an undetectable viral load (or remain virally suppressed) can stay healthy for many years and will not transmit HIV to their sex partners.

Compared to all people with diagnosed HIV, women have lower viral suppression rates. More work is needed to increase these rates. For every **100 women with diagnosed HIV** in 2019: ****



76 received some HIV care



58 were retained in care

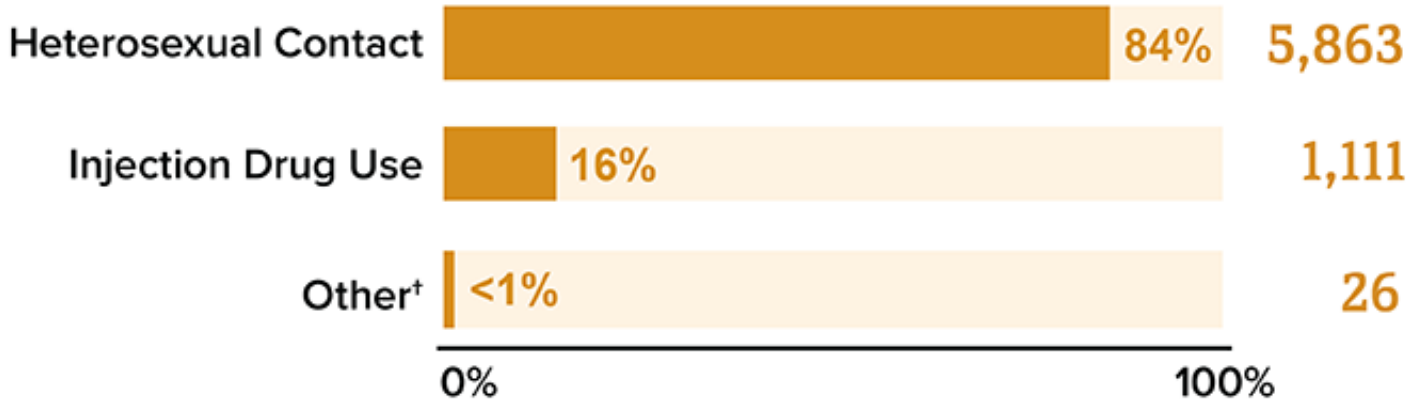
64 were virally suppressed

For comparison, for every **100 people overall** with diagnosed HIV, **76 received some care**, **58 were retained in care**, and **66 were virally suppressed**.

www.cdc.gov/hiv/pdf/group/gender/women [March 2022]

There were 36,801 **new** HIV diagnoses in the U.S. in 2019; 19% (6,999) were among women

Most new HIV diagnoses among women were attributed to heterosexual contact.

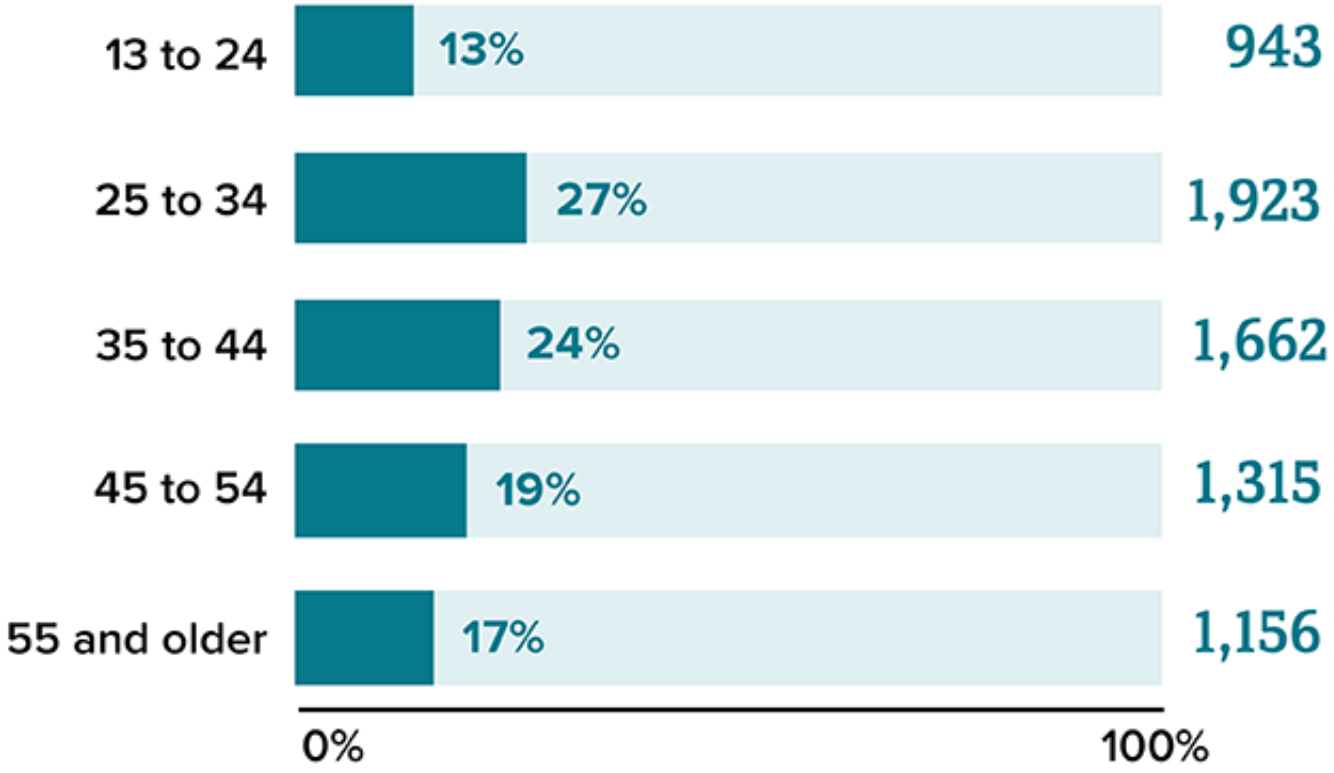


* Based on sex assigned at birth and includes transgender people. For more information about transgender people, visit CDC's HIV and Transgender People web content.
† Includes perinatal exposure, blood transfusion, hemophilia, and risk factors not reported or not identified.

Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2019 . *HIV Surveillance Report* 2021;32.

New HIV Diagnoses Among Women by Age in the US and Dependent Areas, 2019*

Women aged 25 to 34 had the highest number of new HIV diagnoses.



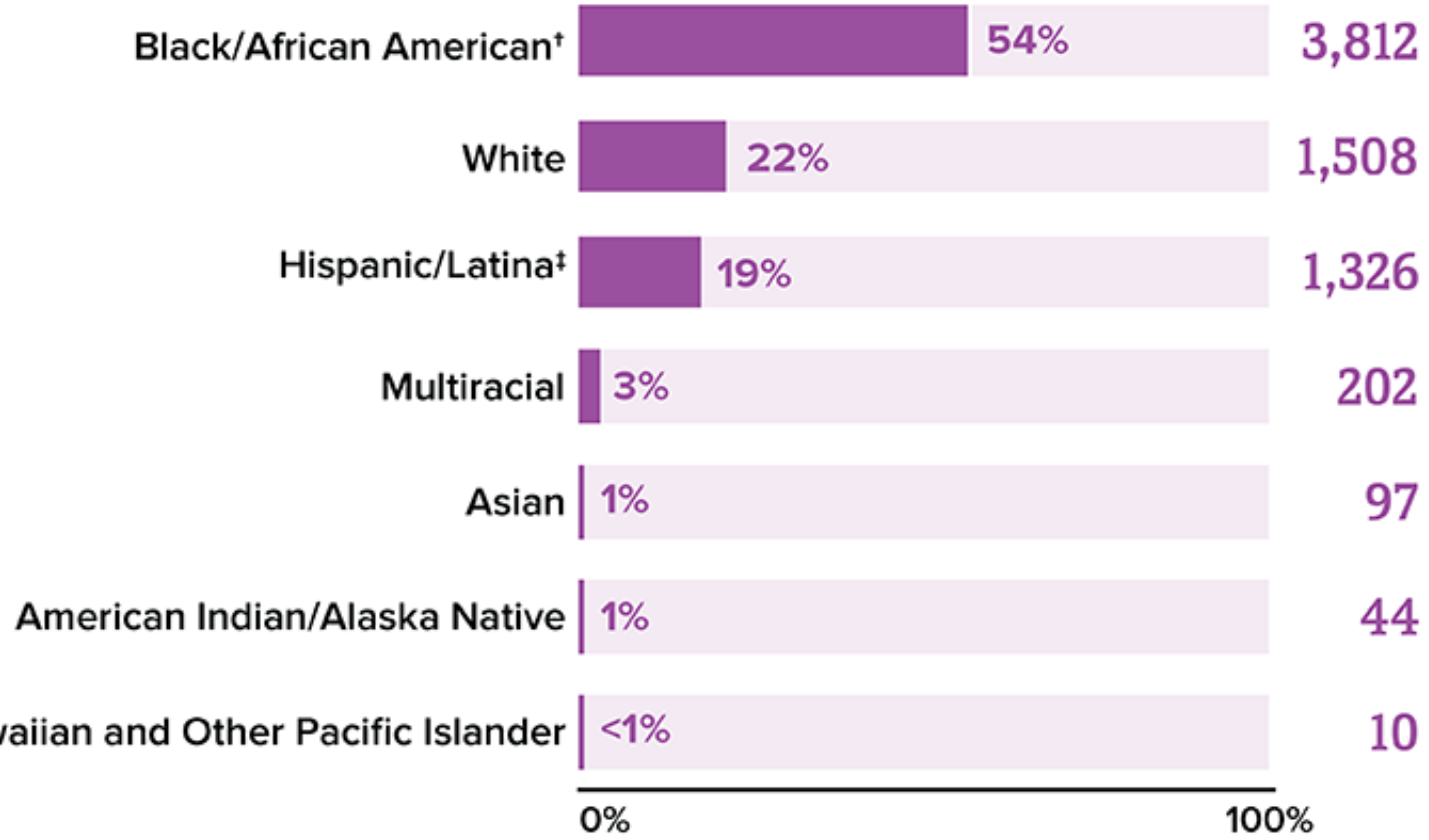
Total may not equal 100% due to rounding.

* Based on sex assigned at birth and includes transgender people. For more information about transgender people, visit CDC's HIV and Transgender People web content.

Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2019. *HIV Surveillance Report* 2021;32.

New HIV Diagnoses Among Women by Race/Ethnicity in the US and Dependent Areas, 2019*

Black/African American women continue to be disproportionately affected by HIV.

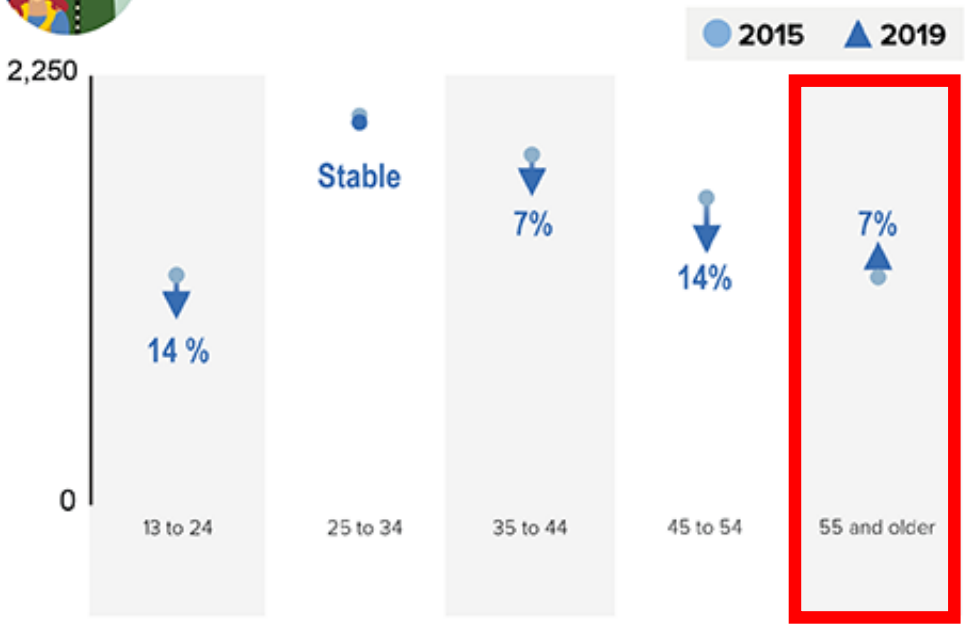


* Based on sex assigned at birth and includes transgender people. For more information about transgender people, visit CDC's HIV and Transgender People web content.
† *Black* refers to people having origins in any of the Black racial groups of Africa. *African American* is a term often used for people of African descent with ancestry in North America.
‡ Hispanic/Latina women can be of any race.

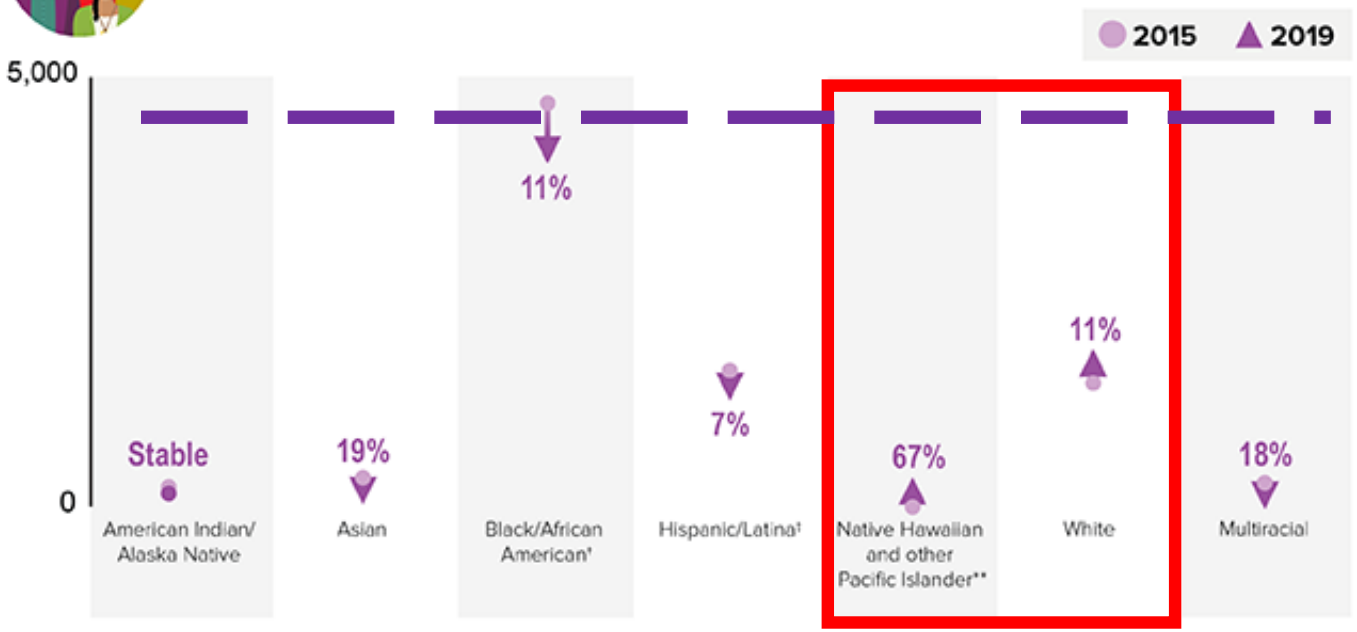
Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2019. *HIV Surveillance Report* 2021;32.

HIV Diagnoses Among Women in the US and Dependent Areas, 2015-2019*

Trends by Age



Trends by Race/Ethnicity



* Based on sex assigned at birth and includes transgender people. For more information about transgender people, visit CDC's HIV and Transgender People web content.
† *Black* refers to people having origins in any of the Black racial groups of Africa. *African American* is a term often used for people of African descent with ancestry in North America.
‡ Hispanic/Latina women can be of any race.
** Changes in subpopulations with fewer HIV diagnoses can lead to a large percentage increase or decrease.

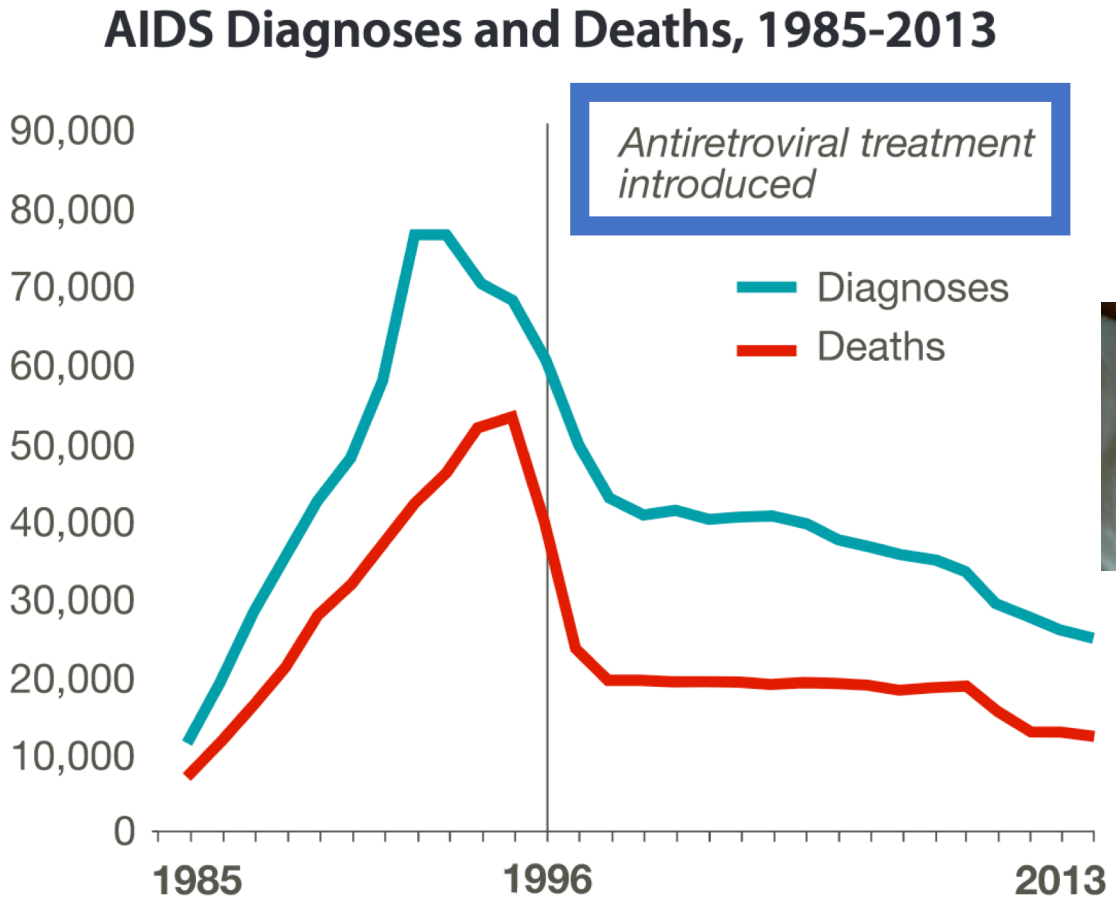
Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2019. *HIV Surveillance Report* 2021;32.

Celebrating aging and recognizing its cost

Aging-related comorbidities in women

BY 2030, UP TO 70% OF PEOPLE WITH HIV WILL BE OVER THE AGE OF 50.

Persons living with HIV (PLWH) are *living longer* and *aging*



= ART

CDC, HIV surveillance report.

Life Expectancy after HIV diagnosis, 2008-2018, United States

(Siddiqi A et al, CROI 2022, abstract #761)

- **Study Population**: National HIV Surveillance Data (persons ≥13 yrs old)
- **Methods**: Survival within or beyond the first year after HIV diagnosis estimated separately. Life expectancy (LE) estimates generated by natal sex, race/ethnicity, disease severity, and transmission category
- **Key Findings**:
  - From 2008–2018, the LE for PLWH increased by an average 1.3% per yr
  - In 2018, LE for males was 3.1 yrs longer [32.7, (95%CI 2.6–32.8)] vs. females [29.6, (95%CI 29.5–29.7)]
  - Males had larger gains (4.0 yrs or 14.1%) vs. females (2.3 yrs or 8.6%)

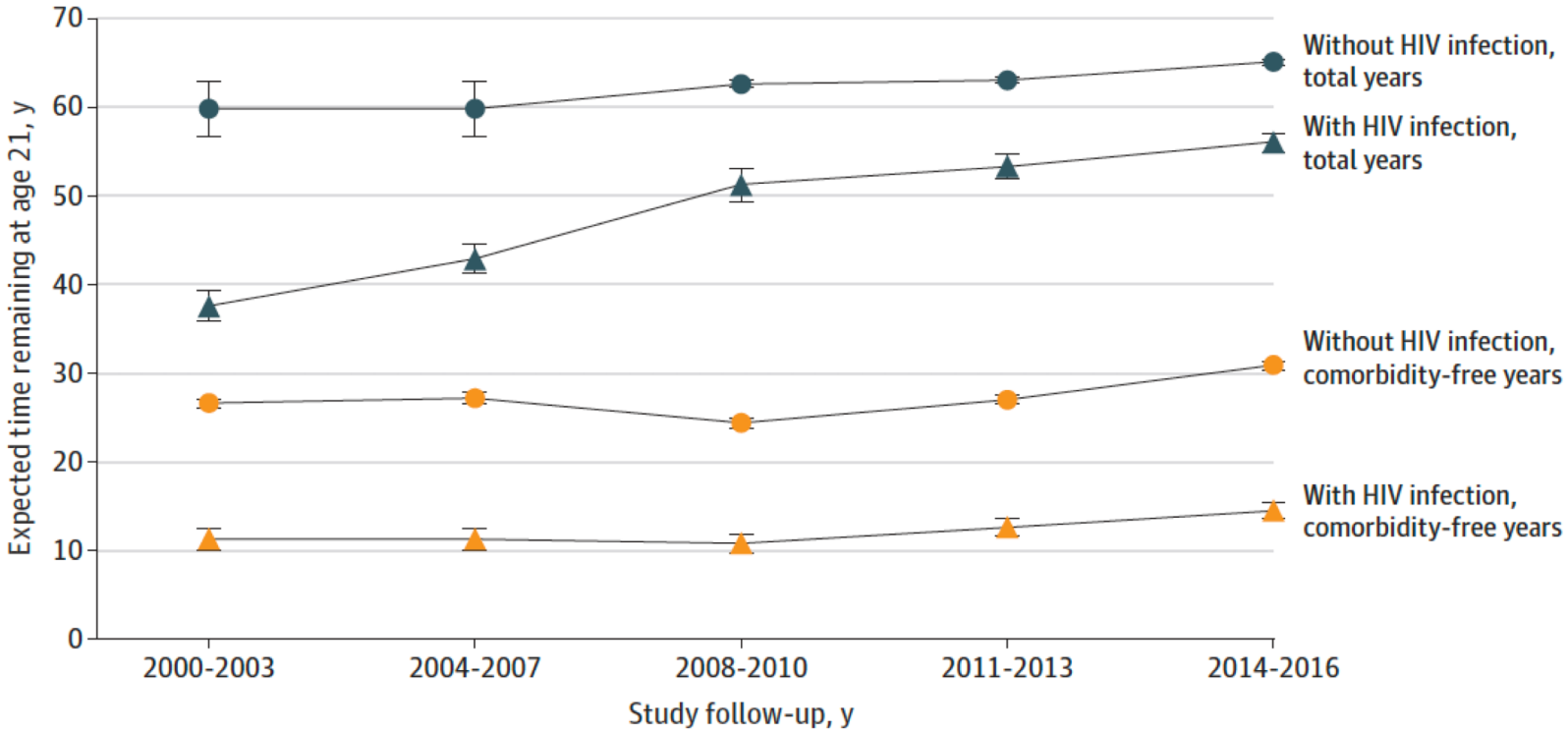
Table: Life expectancy for persons with HIV diagnosed during 2008–2018

		Male			Female		
Year of HIV diagnosis	Overall	Black/African American	Hispanic/ Latino	White	Black/African American	Hispanic/ Latino	White
2008	28.63	26.81	32.69	26.95	26.25	30.73	26.70
2009	29.31	27.87	33.24	27.40	26.54	30.94	27.76
2010	30.41	29.16	33.88	28.02	27.37	31.95	27.87
2011	30.97	29.94	34.34	28.15	28.17	31.73	27.68
2012	31.52	30.37	35.30	28.47	28.12	32.26	27.60
2013	31.83	30.89	35.18	28.32	28.34	32.25	28.02
2014	32.35	31.49	35.48	28.87	28.72	32.99	28.79
2015	32.65	31.64	35.69	29.15	28.76	33.81	28.79
2016	32.67	31.71	35.99	29.17	28.78	31.97	28.78
2017	32.68	31.50	35.67	29.51	28.90	33.08	28.31
2018	32.85	31.53	35.55	29.56	29.08	32.24	28.25

Slide courtesy of Dr. Caitlin Moran

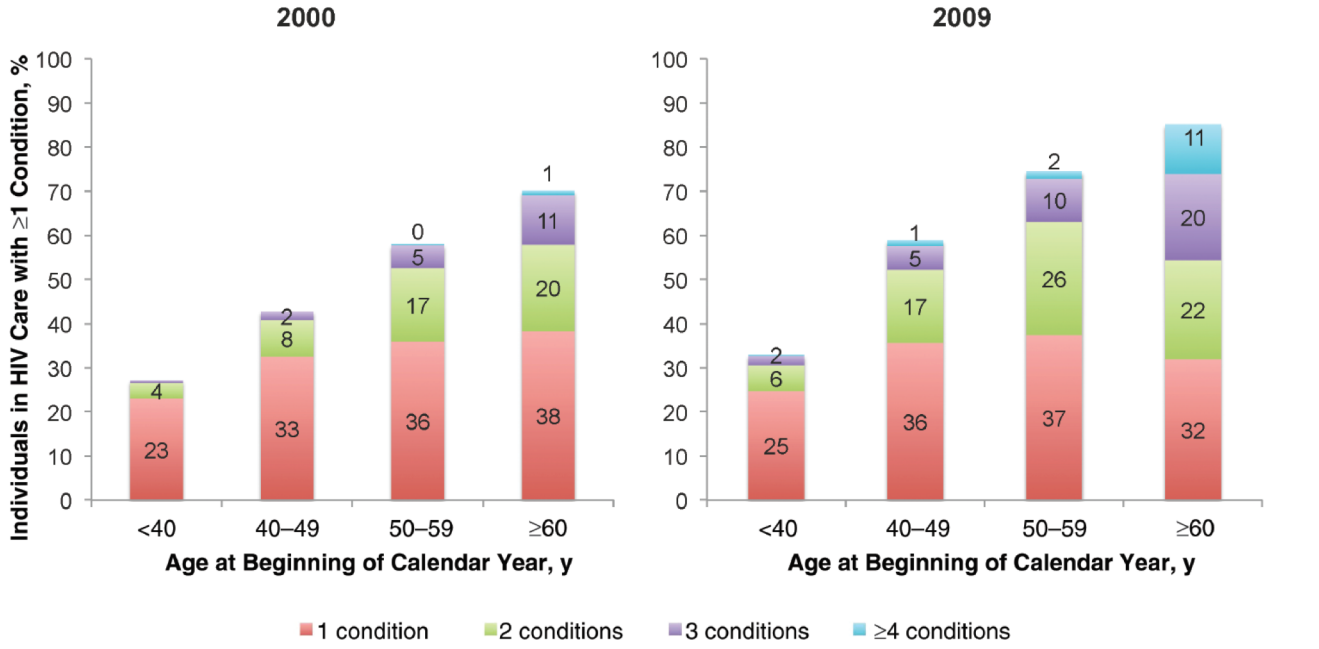
Comorbidity-free life expectancy gap by HIV persists

Figure 1. Overall and Comorbidity-Free Life Expectancy at Age 21 Years for Individuals With and Without HIV Infection, Kaiser Permanente, 2000-2016

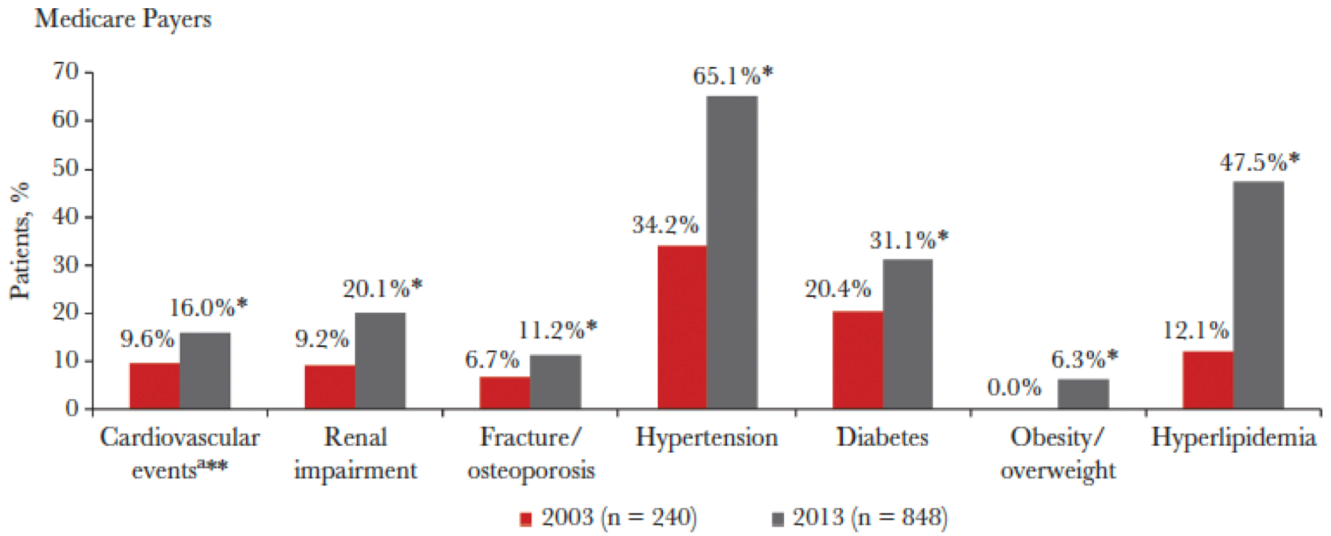


Marcus JL et al. JAMA Network Open. 2020;3(6):e207954

Multimorbidity among PLWH increasing over time



Vascular conditions are common



Wong C et al. Clin Infect Dis. 2018 Apr 3;66(8):1230-1238.
Gallant J et al. J Infect Dis. 2017 Dec 19;216(12):1525-1533.

Non-AIDS comorbidity (NACM) burden

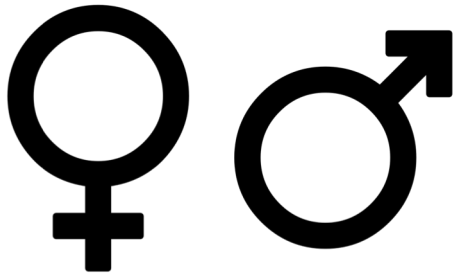
How prevalent are NACM among WLWH? And what is the risk?

- Prior studies had female representation of 13-21%
- Despite evidence suggesting women may be at higher risk of NACM than men (among general population and among PLWH)

HOPS cohort
(PLWH only)
19% female
11 NACM

*Age, **yrs***	**# NACM**
<40	**1.4**
40-49	**2.1**
50-59	**3.0**
≥60	**3.9**
All	**3.5**

3.9 vs 3.4



Palella FJ et al. AIDS. 2019 Dec 1;33(15):2327-2335.

WIHS Women's Interagency HIV Study

- 4 enrollment waves:
  - 1994/95, 2001/02, 2011/12, 2013/15, [2020→]
- ~5K female study participants
- Semiannual visits
- >50K women-years of follow-up

Assessing *prevalent* and *incident* NACM burden in the WIHS

- Women in active follow-up in 2009 (when 80% WLWH reported ART use)

- **Outcomes**
  - **1º = NACM burden**
    Total number of comorbidities (out of 10) per participant
  - **2º = NACM prevalence**
    Individual prevalence of each NACM per cohort

10 NACM evaluated

- Bone disease
- Cancer, non-AIDS
- Cardiovascular disease (CVD)
- Chronic kidney disease
- Diabetes mellitus, type 2 (DM2)
- Hyperlipidemia
- Hypertension (HTN)
- Liver disease
- Lung disease
- Psychiatric illness

Defined using up to 3 data sources:

1. Self-report of diagnosis or medication
2. Laboratory evidence
3. Clinical measurement

CHARACTERISTICS AT END OF WIHS OBSERVATION BY HIV SEROSTATUS

HIV-specific indices (WLWH)

- CD4 current: 615 cells/mm^3
- CD4 nadir: 280 cells/mm^3

- 81% HIV-1 RNA <200 cp/ml
- 12.5yrs on ART

(median or % data are shown above)

Characteristic, *median (Q1-Q3) or n (%)*	WLWH (n=2309)	HIV- women (n=923)	*P* value
Age, *yrs*	51 (44-57)	49 (41-55)	<0.0001
Observation time, *yrs*	15.3 (4-18)	15.3 (4-18)	0.6365
Black race	1486 (64)	622 (67)	0.0478
Annual income <$12K	1091 (50)	424 (49)	0.0198
Substance abuse			
current tobacco	820 (36)	410 (45)	<0.0001
current alcohol	954 (41)	526 (57)	<0.0001
current marijuana	450 (20)	227 (25)	<0.0001
current cr/cocaine	133 (6)	85 (9)	<0.0001
BMI, *kg/m^2*	29 (25-35)	31 (26-37)	<0.0001
SBP, *mmHg*	122 (110-136)	126 (115-141)	<0.0001
eGFR, *ml/min/1.73 m^2*	92 (73-108)	100 (84-114)	<0.0001
Chronic HCV	306 (13)	87 (9)	0.0026
Chronic HBV	56 (2)	10 (1)	0.0148

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

NACM prevalence

- **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%**
Dyslipidemia	**40%**	**35%**
Bone disease	**40%**	**33%**
Chronic kidney disease	**15%**	**7%**
Non-AIDS cancer	**11%**	**7%**

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

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

NACM burden

BY AGE:

- **Mean NACM burden increased with older age** (*p*<0.0001):

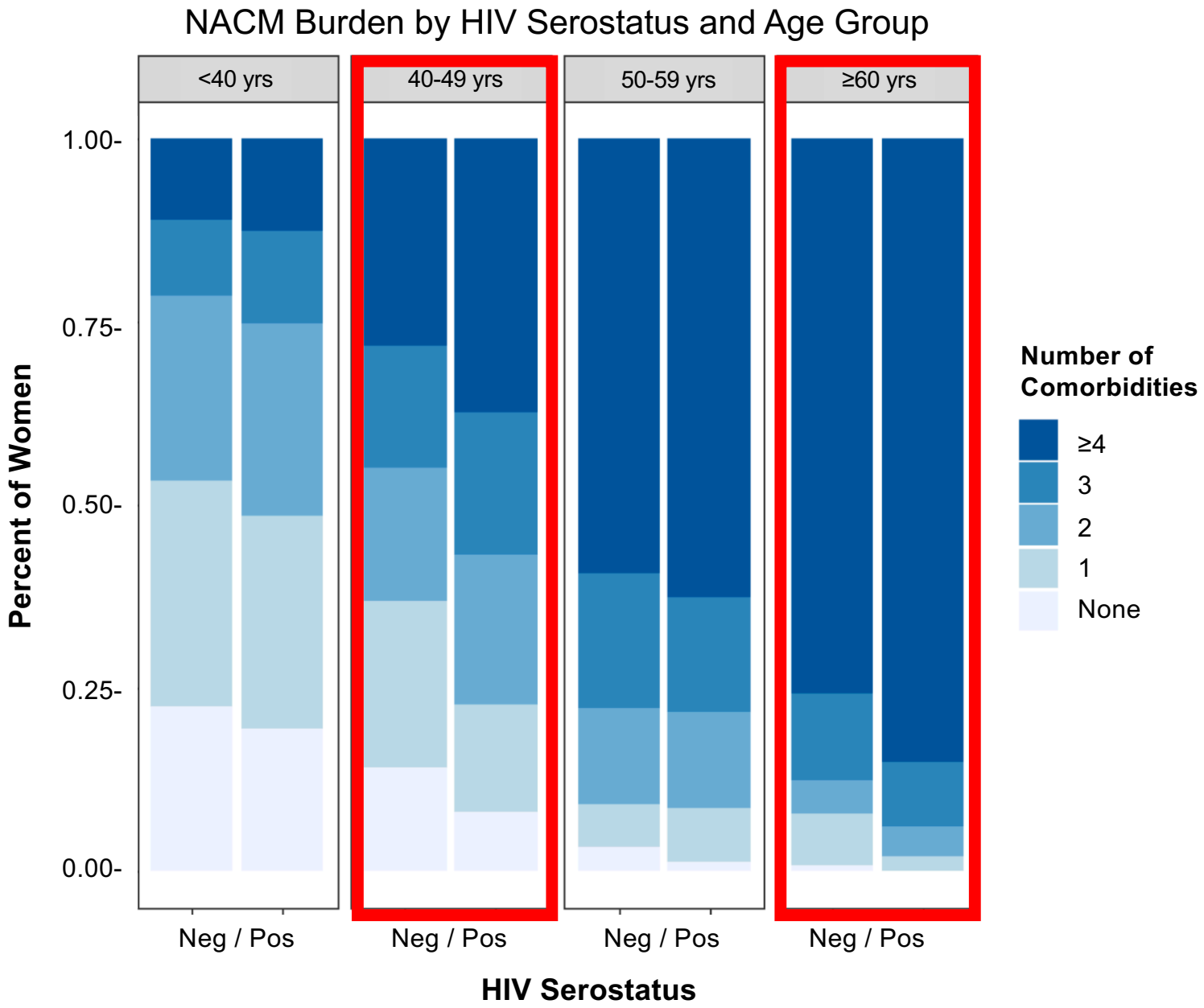
Age, *yrs*	Mean NACM
<40	**1.7**
40-49	**2.7**
50-59	**4.0**
≥60	**5.2**

BY HIV SEROSTATUS:

- **Mean NACM burden higher among WWH >> HIV- women** (*p*<0.0001):

➢ **3.6 vs 3.0**

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



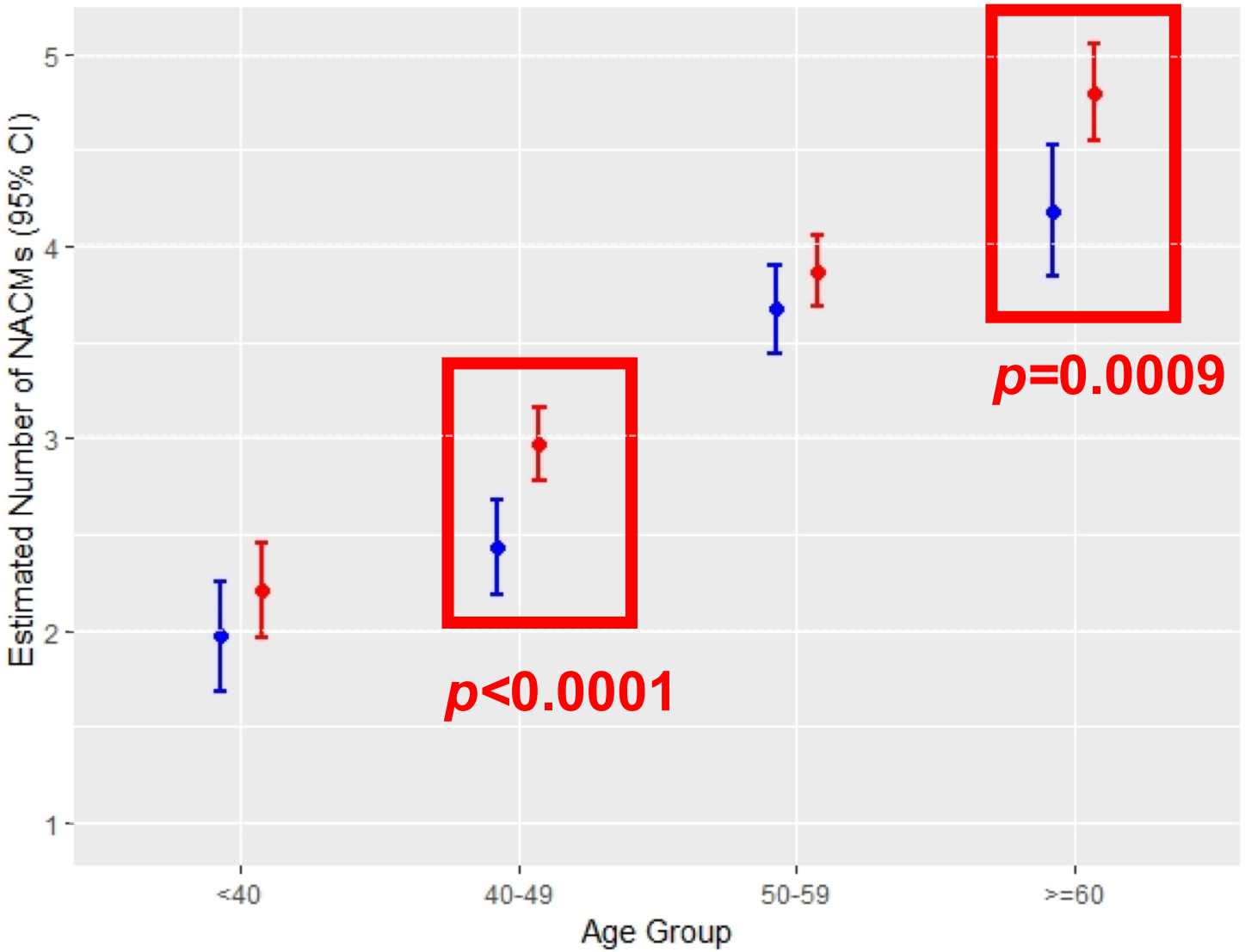
Prevalent NACM burden

- 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 significantly modified by age

HIV*age interaction p=0.0206

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

FULLY-ADJUSTED NACM BURDEN BY HIV AND AGE



Adjusted for:

- HIV, age, HIV*age
- Race
- Body mass index
- Education
- Income
- Marital Status
- Residence
- Substance use (current tobacco, alcohol, crack/cocaine)

HIV Serostatus
Negative
Positive

HIV*age interaction *p*=0.0978

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

Factors associated with NACM burden

- **In adjusted models including <u>all women</u>, higher NACM burden was significantly associated with**:
  - Older age, HIV serostatus, white race, lower income, higher body mass index, tobacco use, crack/cocaine use, alcohol abstinence

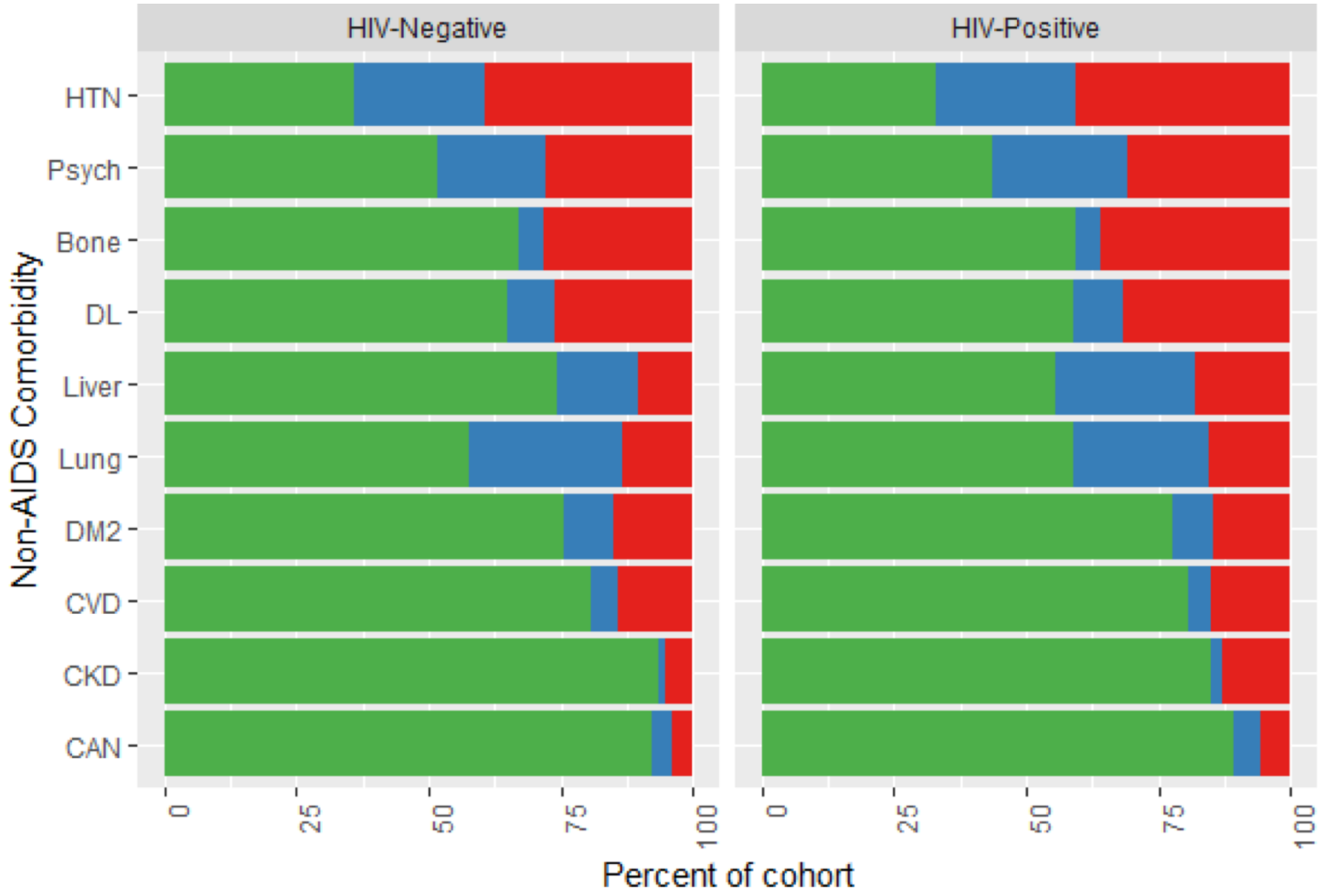
- **In adjusted model including <u>WWH</u>, higher NACM burden was significantly associated with**:
  - Covariates above + recent abacavir use
  - ***<u>NOT</u>*** CD4 count, CD4 nadir, time since ART initiation, proportion visits HIV suppressed, protease inhibitor use

Follow-up longitudinal analysis of the WIHS

- What are the effects of HIV serostatus and age on the **incidence** of NACM among women in the U.S.?

- Included the same cohort of women and assessed the accrual of comorbidities over time:

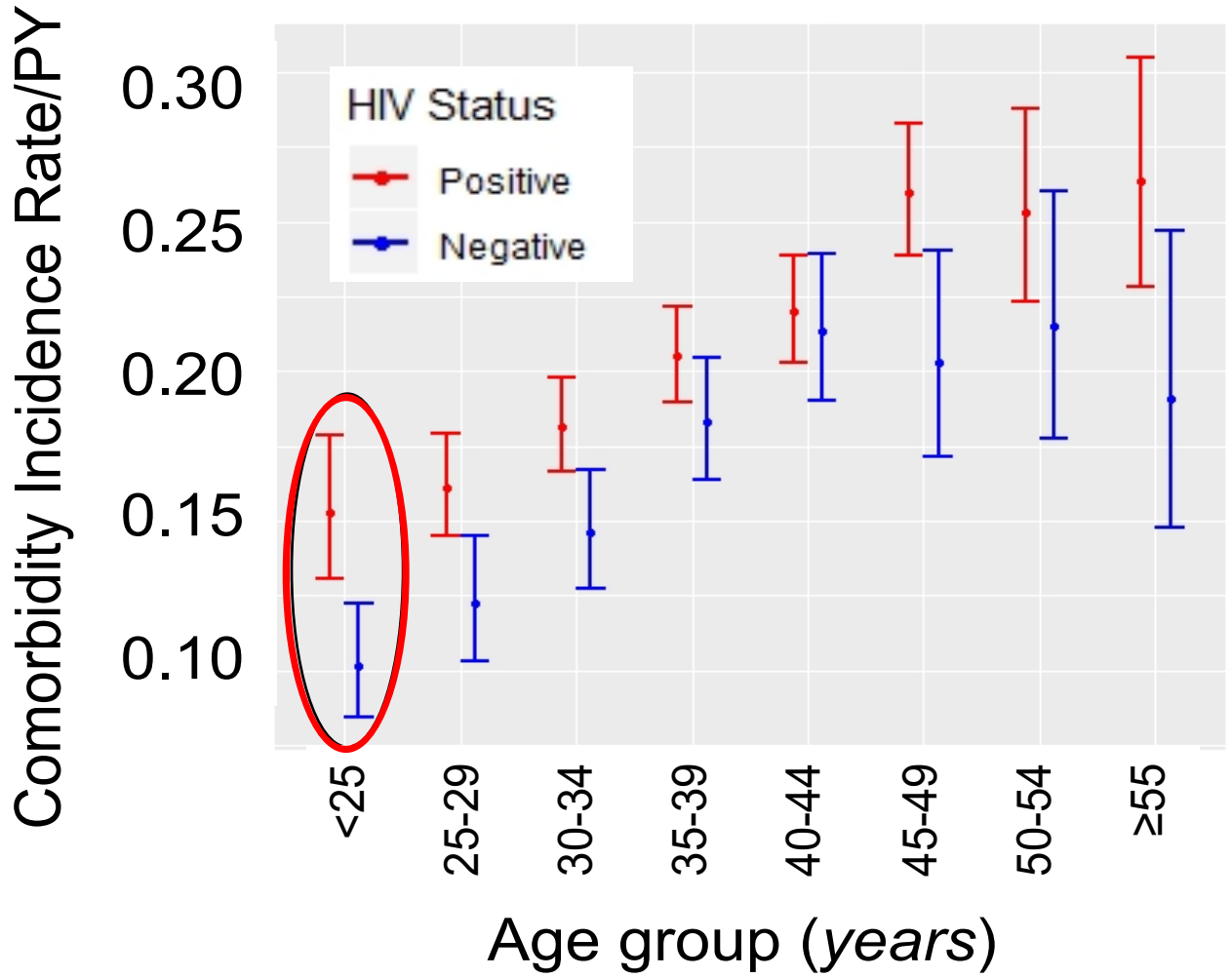
Case distribution of 10 NACM by HIV serostatus



- WLWH had a significantly higher incident NACM rate vs women without HIV (RR 1.36, 95% CI 1.02-1.81)
- HIV*age interaction, *p*=0.0438

Collins LF et al. Clin Infect Dis. 2021 Oct 5;73(7):e2059-e2069.

Adjusted NACM Incidence by HIV and Age

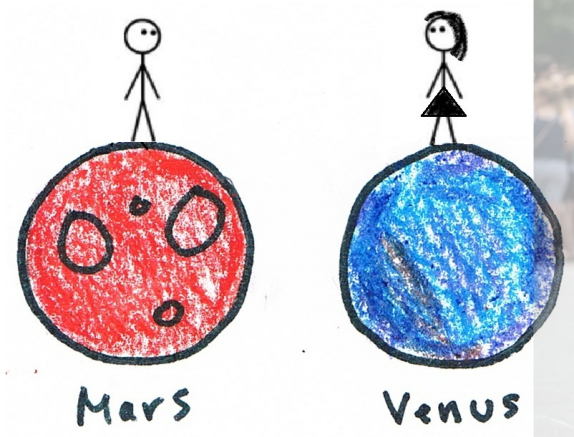


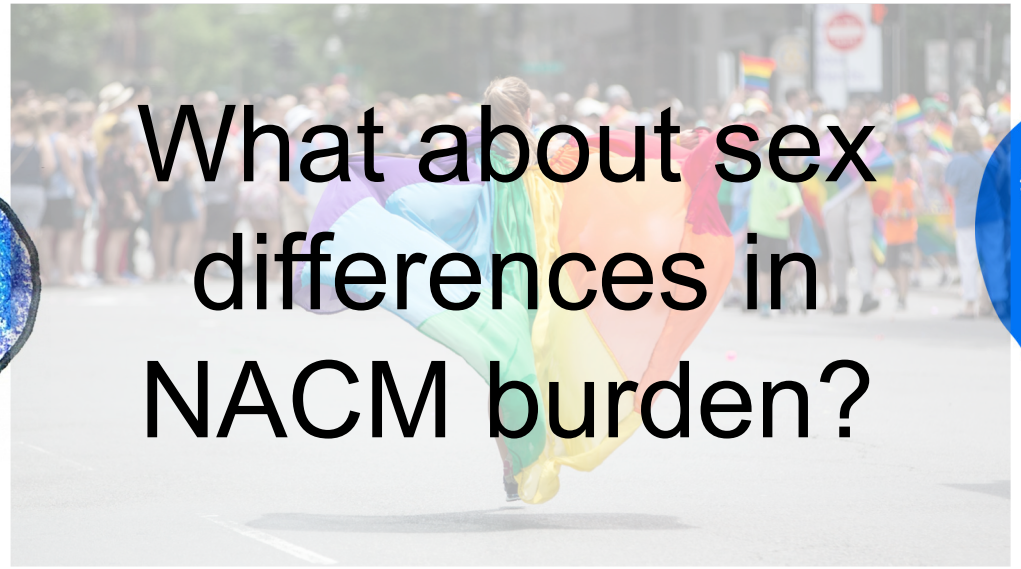
Women aged <25 yrs had the greatest difference in incident NACM burden by HIV serostatus (IRR 1.48, 95% CI 1.19-1.84)

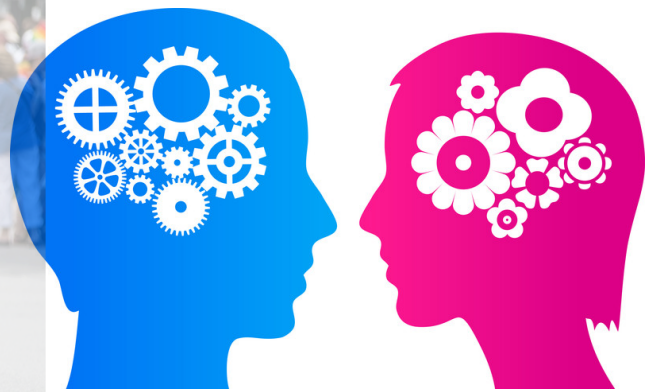
Collins LF et al. Clin Infect Dis. 2021 Oct 5;73(7):e2059-e2069.

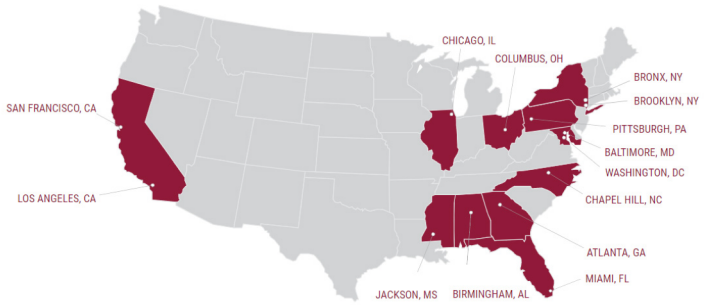
- WLWH have higher prevalence and incidence of NACM burden than women without HIV

- Differences in NACM burden by HIV serostatus begin in the 3rd decade of life



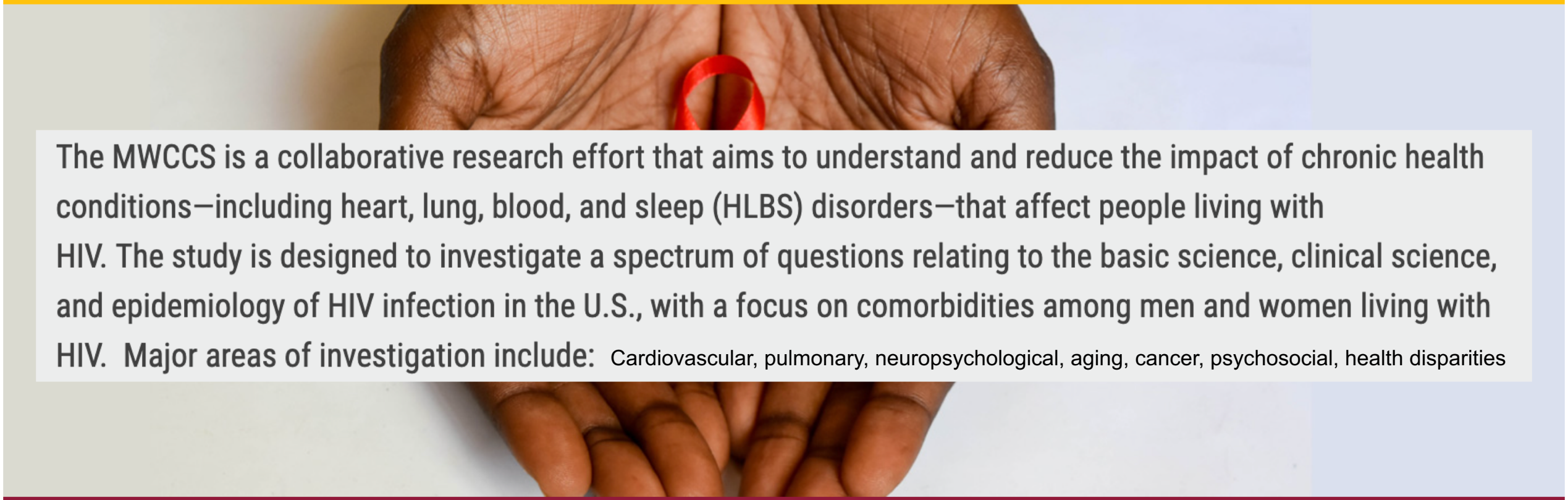






MWCCS

MACS/WIHS COMBINED COHORT STUDY



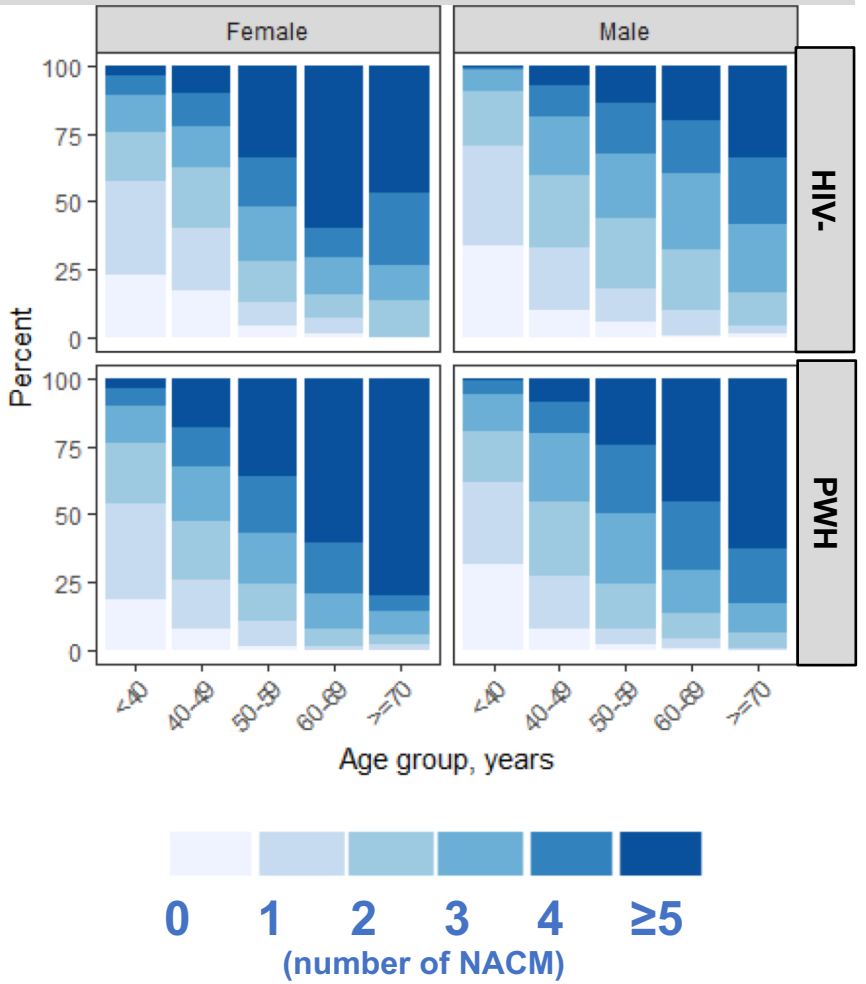
The MWCCS is a collaborative research effort that aims to understand and reduce the impact of chronic health conditions—including heart, lung, blood, and sleep (HLBS) disorders—that affect people living with HIV. The study is designed to investigate a spectrum of questions relating to the basic science, clinical science, and epidemiology of HIV infection in the U.S., with a focus on comorbidities among men and women living with HIV. Major areas of investigation include: Cardiovascular, pulmonary, neuropsychological, aging, cancer, psychosocial, health disparities

Results – cohort profile

Characteristics at End of Observation	Women (n=3238)	Men (n=2691)
Median age, yrs	51	58
Median BMI, kg/m^2	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/mm^3	620	636
HIV-1 RNA <200 cp/ml	81%	86%
Median time since ART initiation, yrs	12.9	15.4

BMI=body mass index; 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%
Cardiovascular disease	15%	15%
Kidney disease	14%	15%
Cancer	7%	12%

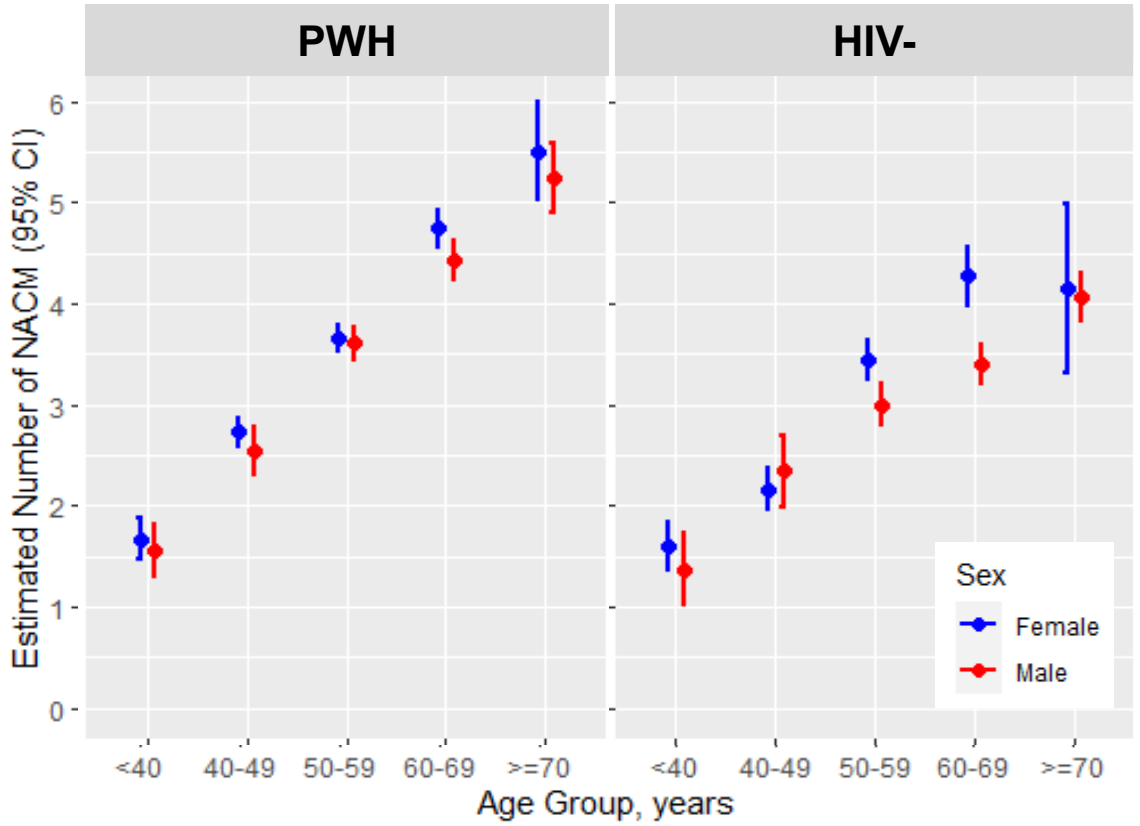
Median NACM burden among women vs men: 3.4 vs 3.2, *p*=0.015

Collins LF et al. Virtual CROI 2021. Science Spotlight.

Results – estimated NACM burden

Estimated Mean Difference in NACM burden†				
Women vs men	**PWH**		**HIV-**	
<40 yrs	+0.33	p=0.03	+0.52	p=0.01
40-49 yrs	+0.37	p<0.01	-0.07	p=0.72
50-59 yrs	+0.38	p<0.01	+0.88	p<0.01
60-69 yrs	+0.66	p<0.01	+1.39	p<0.01
≥70 yrs	+0.62	p=0.03	+0.33	p=0.46

†Unadjusted linear regression model including HIV, age, sex and all interaction terms in the model: HIV*age *p*=0.0002, HIV*sex *p*=0.3040, age*sex *p*<0.0001, HIV*age*sex *p*=0.0014



In the adjusted model†, findings were attenuated but HIV and age still significantly modified the estimated mean NACM burden by sex (HIV*age*sex, *p*=0.038)

†Including covariates in the unadjusted linear regression model plus race, body mass index, smoking, drinking, cocaine, socioeconomic status

Conclusions

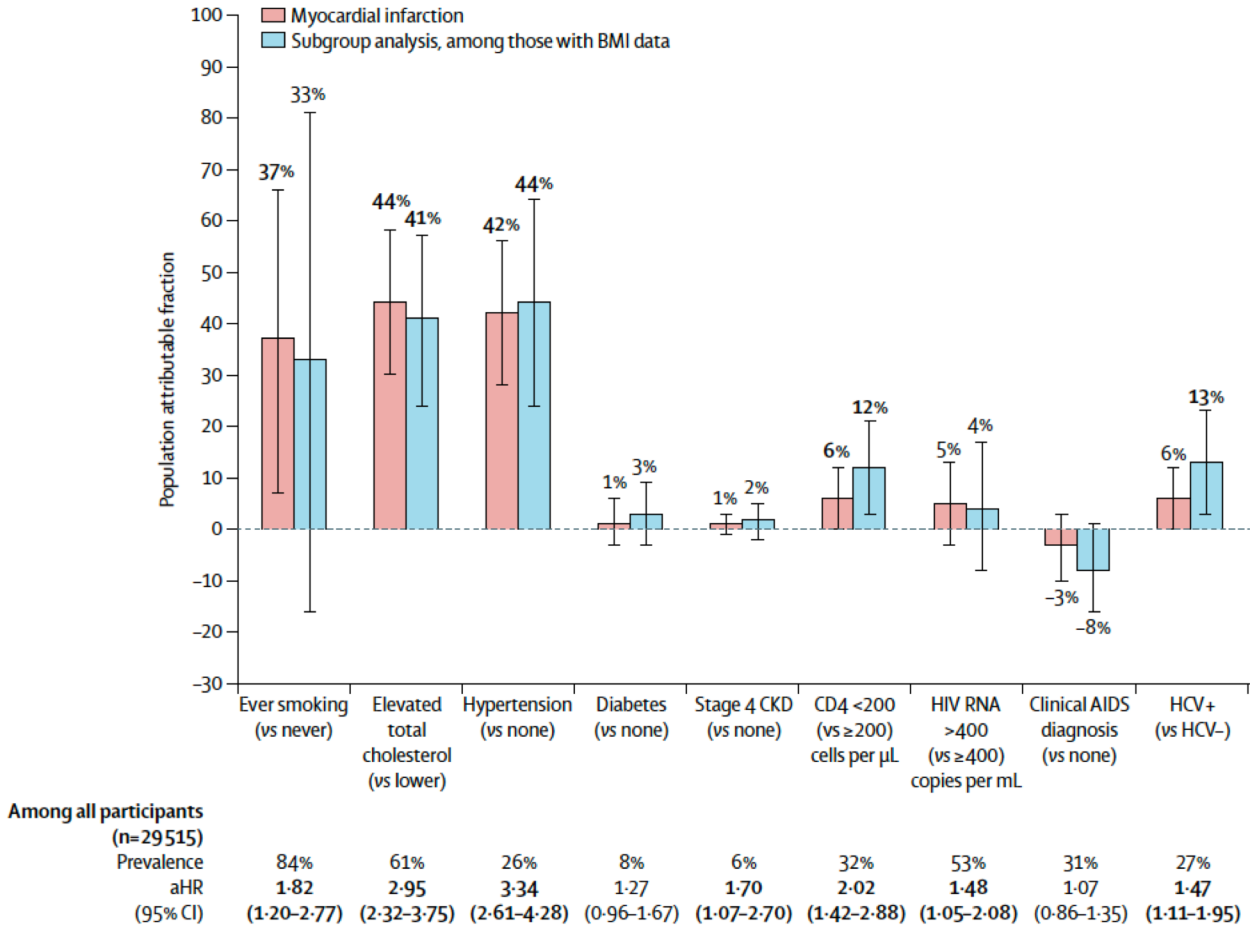
- The prevalence and burden of NACM was high in the MWCCS among men and women with or at-risk for HIV
  - Particularly for hypertension, psychiatric illness, dyslipidemia, liver, and bone disease

- NACM burden was higher among women vs men, particularly among PWH, and varied by age category
  - The distribution of specific NACM prevalence differed by sex

- Given HIV is associated with differential effects on age-related comorbidities by sex, HIV serostatus- and sex-specific strategies for NACM screening and prevention are needed

What is the role of traditional vs HIV-related risk factors in mediating NACM burden?

Traditional risk factors commonly associated with multimorbidity



- A substantial proportion of myocardial infarctions, end-stage liver disease, end-stage renal disease and non-AIDS cancer could be prevented with interventions on traditional risk factors (eg, smoking)
- Elevates the importance of screening for these risk factors and improving the effectiveness of prevention/modification among aging PLWH

Althoff KA. Lancet HIV. 2019 Feb;6(2):e93-e104.

What about HIV-related indices, are we capturing robustly enough?

Multimorbidity (≥2 of 5 NACM):

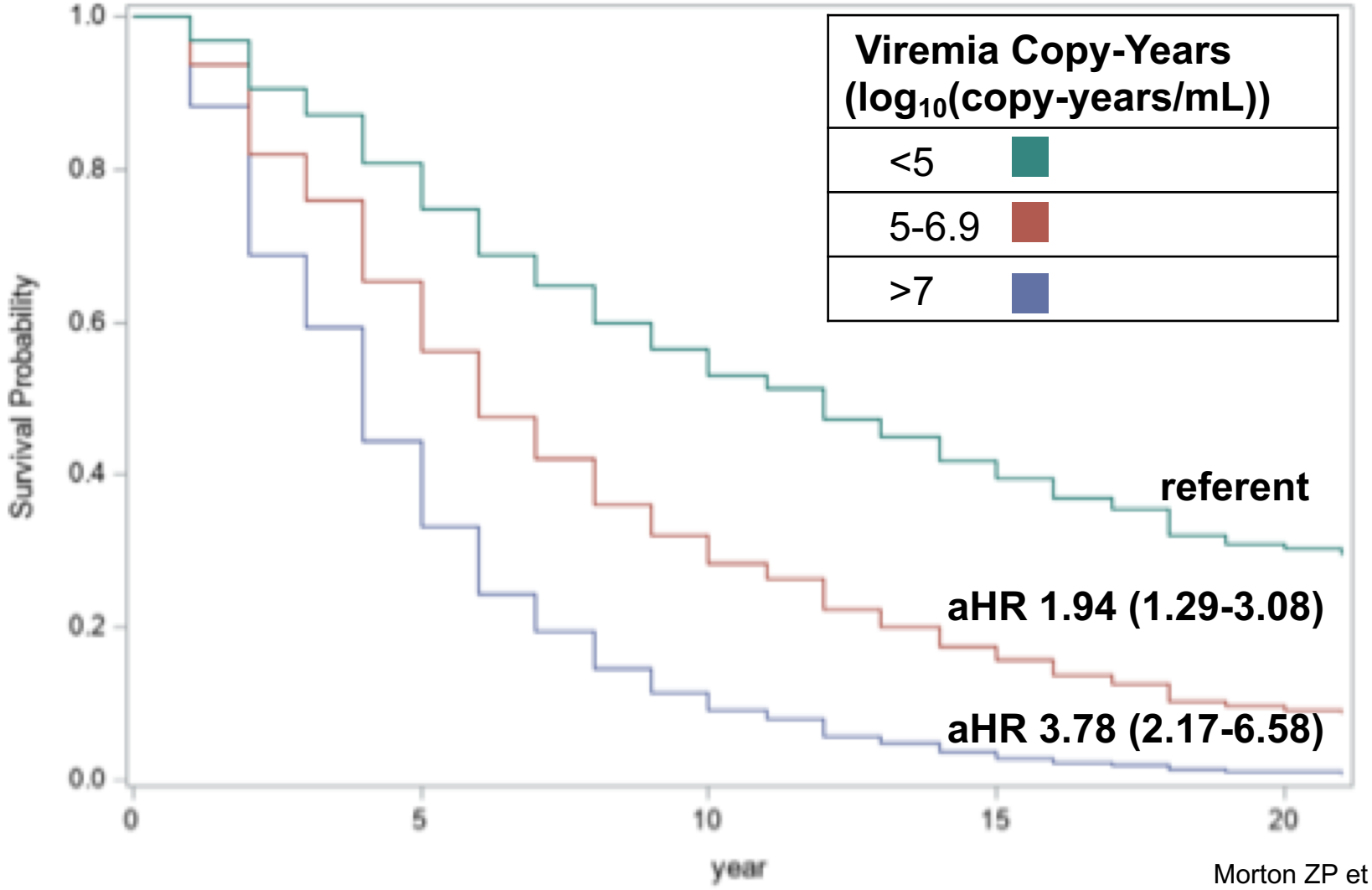
Hypertension
Dyslipidemia
Diabetes
Kidney disease
CVD

> ¼ of WLWH developed multimorbidity

- Among 806 women, at baseline, median age was 39 years, 56% were Black, 62% ever smoked, and median CD4 count was 534 cells/mm^3
- Of 211 (26%) WLWH who developed **multimorbidity:**
  - 162 (77%) had hypertension
  - 133 (63%) had dyslipidemia
  - 60 (28%) had diabetes
  - 52 (25%) had CVD
  - 32 (15%) had kidney disease

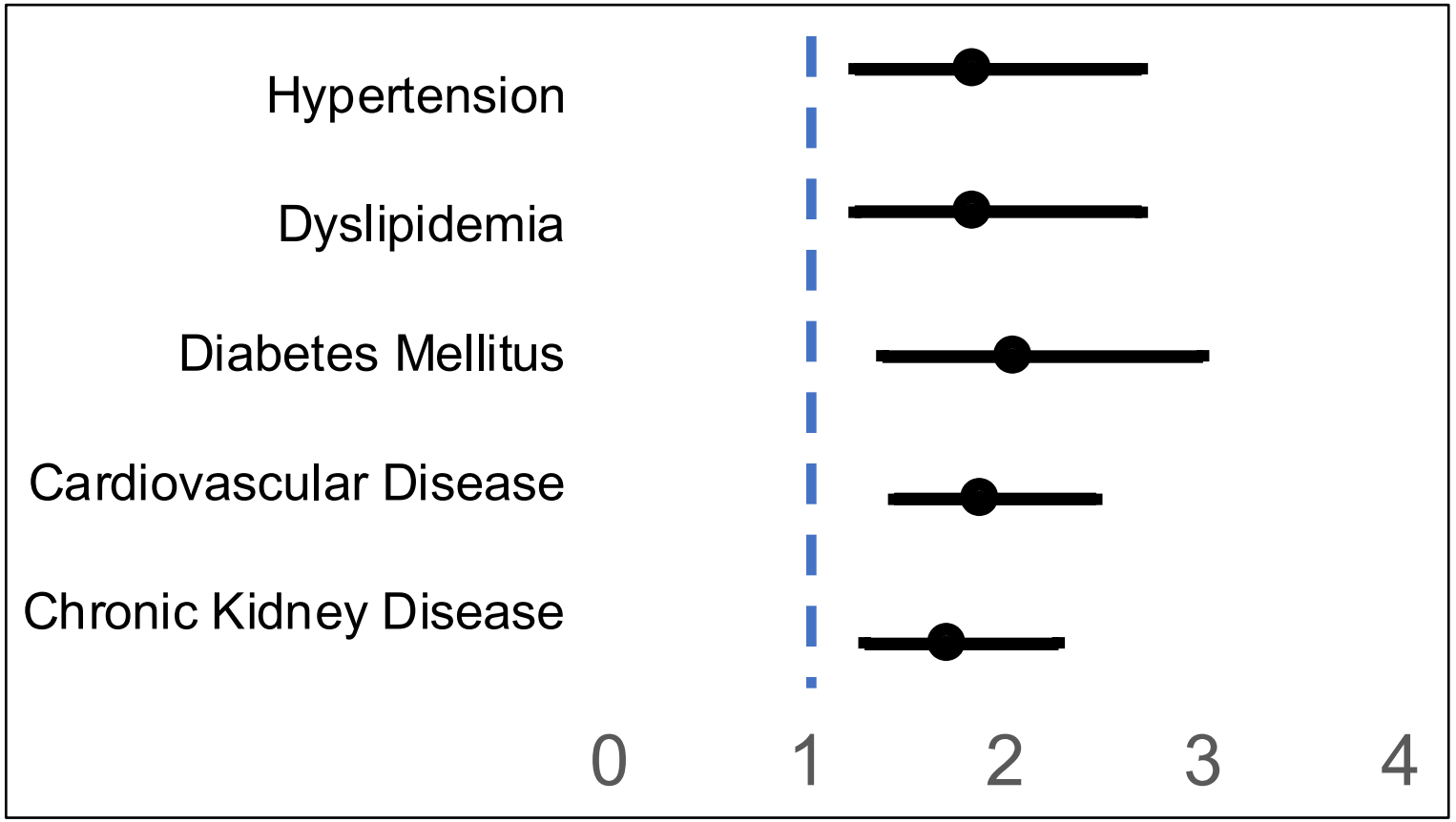
Morton ZP et al. AIDS 2022, accepted abstract.

VCY increases hazard of multimorbidity in a dose-dependent manner



Morton ZP et al. AIDS 2022, accepted abstract.

VCY associated with increased risk of each individual NACM



Morton ZP et al. AIDS 2022, accepted abstract.

Both traditional and HIV-related factors play a role in development of NACM among PLWH (W > M).

Routine screenings for comorbidities underperform among PLWH, perhaps related to HIV indices not being accounted for? And/or under-capture of social determinants of health?

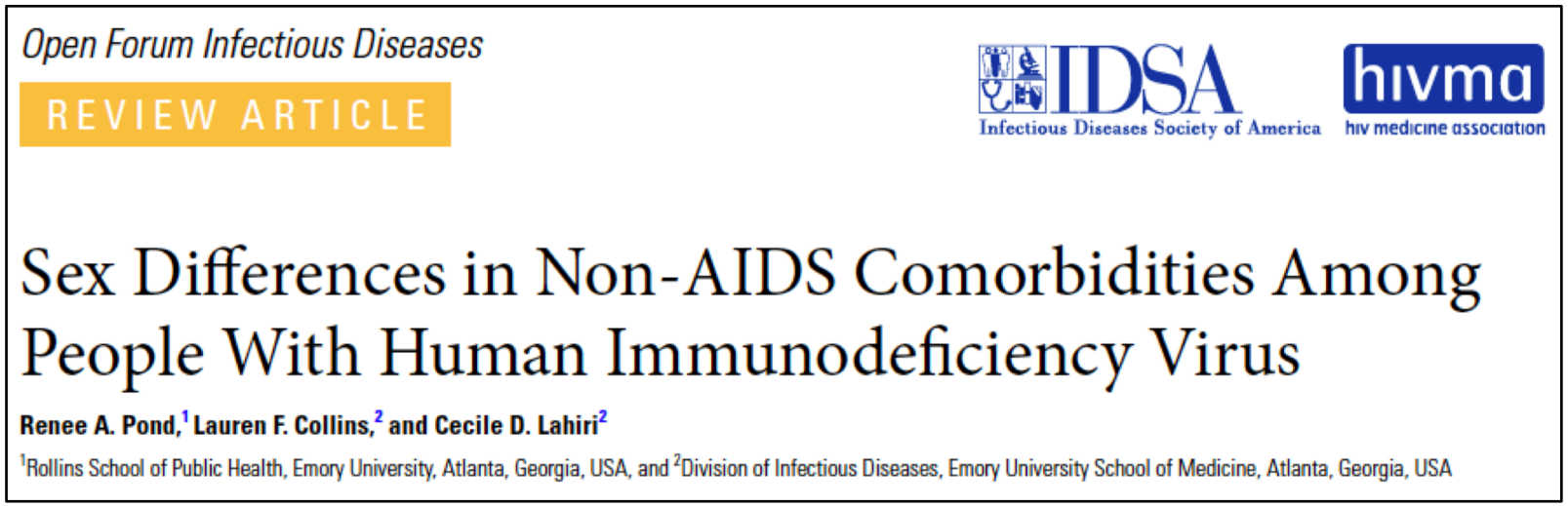
Individual comorbidities

Data and guidance on selected NACM

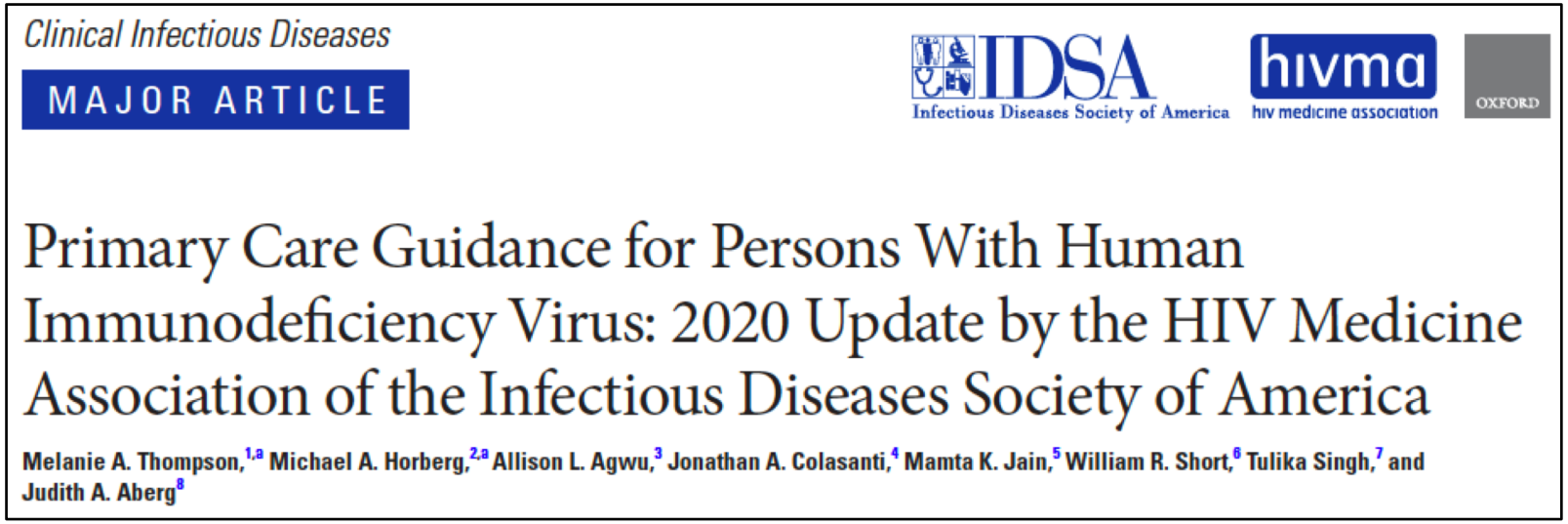
- Cardiovascular disease (CVD)
- Metabolic dysfunction
- Bone disease
- Neurocognitive impairment
- HPV-associated disease

Pond RA et al. Open Forum Infect Dis. 2021 Nov 3;8(12):ofab558.

Data on sex-differential risk and related mechanisms



HIVMA/IDSA **guidance** on screening and prevention



Thompson MA et al. Clin Infect Dis. 2021 Dec 6;73(11):e3572-e3605.

Cardiovascular disease

SCREENING & PREVENTION

- No validated CVD risk assessment tools for use among PLWH
- Pooled cohort equations from the 2013 ACC/AHA guidelines (default)
  - Underestimates risk by 12-20% especially among *women*
- HIV recognized as an independent risk enhancer (2018 ACC/AHA) multispecialty cholesterol guidelines
- Weight, blood pressure at every visit

RISK-MODIFICATION INTERVENTIONS

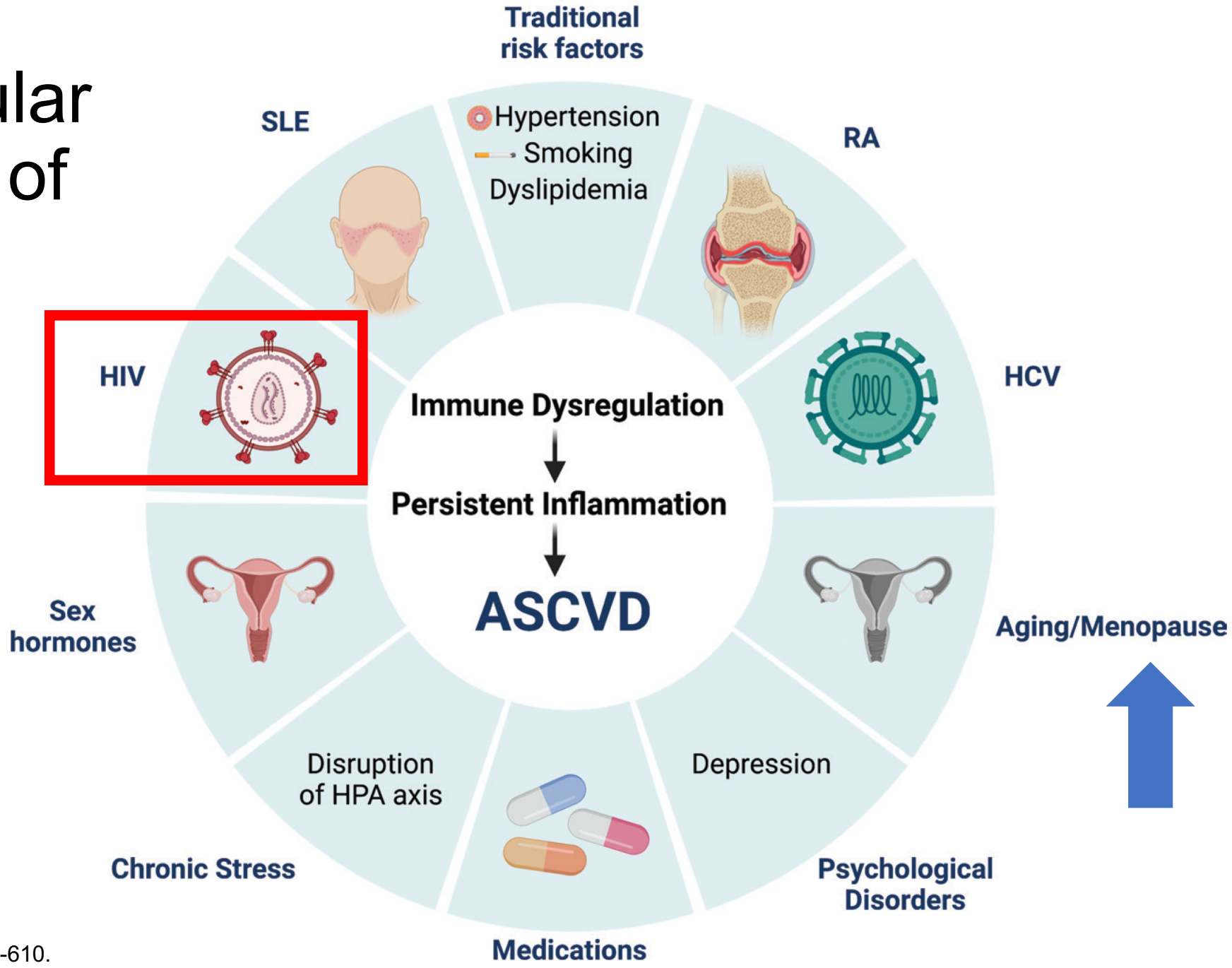
Statins; weight loss; aggressive BP, lipid, glucose control; smoking cessation

Consider drug-drug interactions with ART

- **WLWH vs MLWH**:
  - 2x greater risk of heart risk
    - Non-calcified plaque more common
  - 40% higher pulmonary arterial hypertension risk
  - Mixed data on hypertension
  - 2-3x higher stroke risk [young WLWH]
- **Mechanism**:
  - HIV-related immune activation
  - ART-associated dyslipidemia and other toxicities
  - Overrepresentation of traditional risk factors

Cardiovascular implications of immune disorders in women

Immune dysregulation plays a prominent role in chronic systemic inflammation, a key driver of atherosclerotic CVD



Moran CA et al. Circ Res. 2022 Feb 18;130(4):593-610.

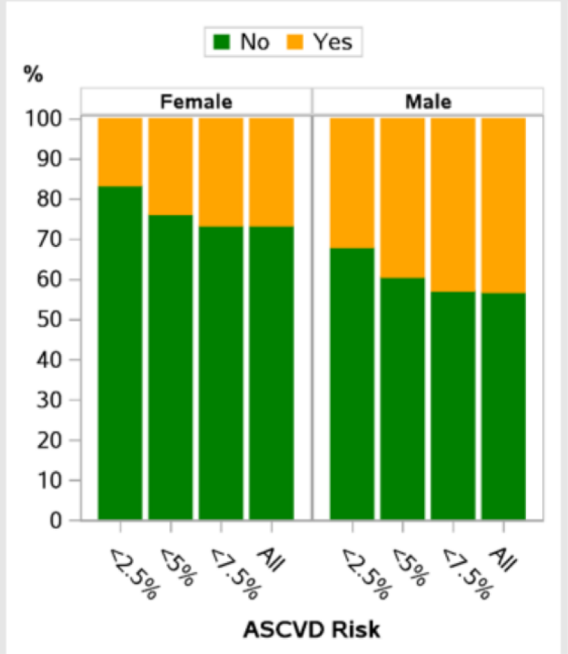
Subclinical Atherosclerosis and Immune Activation among U.S. females and males with HIV

(Zanni MV et al, CROI 2022, abstract #577)

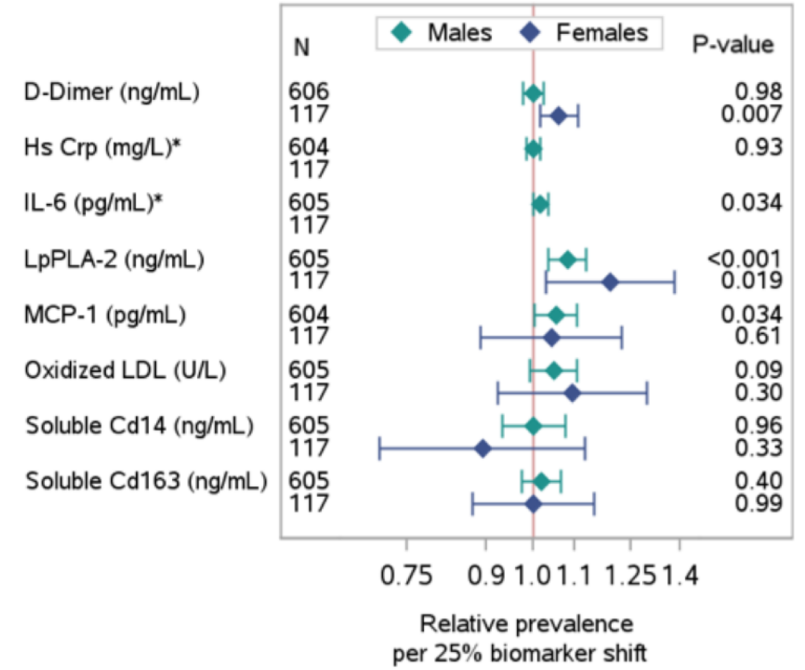
REPRIEVE
Randomized Trial to Prevent Vascular Events in HIV

- **Study Population**: REPRIEVE cohort participants. PWH ages 45-75 on ART, no known CAD
- **Methods**: subset of U.S. REPRIEVE participants underwent CCTA +/- immune phenotyping at study enrollment. Immune-plaque relationships compared by sex.
- **Key Findings**:
  - 631 males, 124 females; median age 51
  - Plaque prevalence lower for females than males [aRR 0.67 (95% CI 0.50-0.92)]
  - Among those with any plaque, vulnerable plaque features did not differ by sex
  - Females vs. males showed:
    - Higher levels of IL-6, hsCRP, and D-Dimer and lower levels of LpPLA-2 (P<0.001 for all).
    - A lower percentage of total monocytes and a shift toward a higher percentage of inflammatory/ intermediate (CD14+CD16+) and patrolling/ non-classical (CD14-CD16+) vs. classical (CD14+CD16-) monocyte subsets (P<0.001 for all)

A. Prevalence of Plaque with Visible Noncalcified Portions or Vulnerable Features by ASCVD Risk Group among Females vs. Males with HIV



B. Relationships between Systemic Immune Indices and Plaque with Visible Noncalcified Portions or Vulnerable Features by Sex



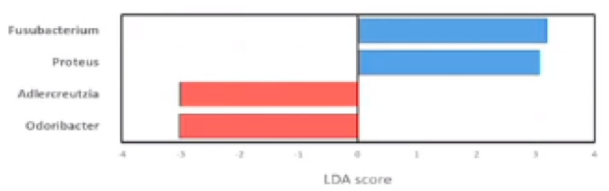
Slide courtesy of Dr. Caitlin Moran

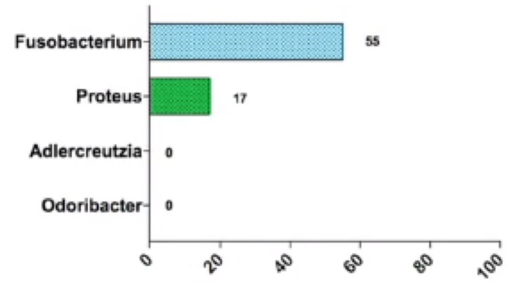
Gut Microbiota, Plasma Metabolomics, and Atherosclerosis in HIV Infection

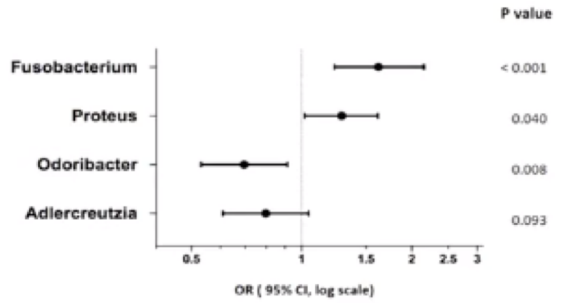
(Wang Z et al, CROI 2022, abstract #37)

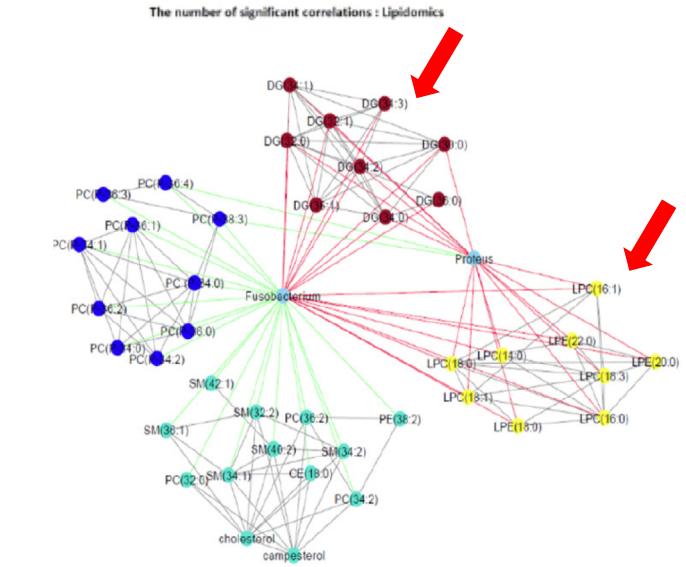
MWCCS
MACS/WIHS COMBINED COHORT STUDY

- **Study Population**: Women (WIHS) with or at-risk for HIV (cross-sectional) and women and men (MACS) with or at-risk for HIV (longitudinal)
- **Methods**:
  - Cross-sectional: gut microbiota features (diversity, taxonomy) with prevalent carotid artery (CA) plaque in women; 2017-2019
  - Longitudinal: gut bacteria-associated lipidomic and metabolomic profiles with incident CA plaque over median 7-year follow-up; 2004-2013
- **Key Findings**:
  - 361 WIHS women; 737 WIHS/MACS participants
  - Proteus and Fusobacterium are associated with prevalent and incident CA plaque









Lysophosphatidylcholines(LPCs), lysophosphatidylethanolamines (LPEs) and diglycerides(DGs) were longitudinally associated with increased risk of carotid artery plaque

Slide courtesy of Dr. Caitlin Moran

Metabolic dysfunction

SCREENING & PREVENTION

- Lipid levels prior to and within 1-3 months after starting ART; every 5 years if normal
  - Monitor q6-12 mo if abnl/high risk
- Random/fasting glucose and HgbA1c prior to starting ART
  - Screen with glucose annually (dx)
  - Monitor with HgbA1c q6mo
  - Urine microalbumin/Cr ratio q6mo
- BMI, waist circumference, etc.

INTERVENTIONS

Statins, antiglycemics, weight loss, increased exercise, dietary modification

- **WLWH vs MLWH**:
  - Mixed data on DM2
  - Gain more weight post-ART
  - Accelerated liver disease post-menopause
- **Mechanism**:
  - HIV-associated inflammation and immune activation
  - ART effects on glucose and lipid metabolism
  - Adipose tissue disorders
  - Insulin resistance

HBV/HCV coinfection may compound impact

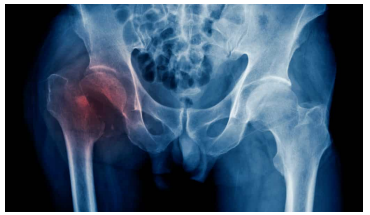
Bone disease

SCREENING & PREVENTION

- Baseline bone densitometry (DXA) in postmenopausal women and men aged ≥50 years
- FRAX (10-yr probability of fracture) is insensitive among PLWH; may be used in resource-limited settings

INTERVENTIONS

- Vitamin D, calcium, bisphosphonates
- Regular exercise
- Smoking cessation and minimize alcohol consumption



- **WLWH vs MLWH**:
  - BMD lower pre-ART
  - ART initiation exacerbates sex difference:
    - 3x more likely to experience ≥5% BMD loss at lumbar spine after 5yrs
    - 3x fracture rate among those initiating TDF, occurrence 123 vs 1438 days
  - Menopause further exacerbates risk

- **Mechanism**:
  - HIV-1 direct viral effects
  - ART-associated immune reconstitution
  - ART toxicity
  - High prevalence of substance use

Neurocognitive impairment

SCREENING & PREVENTION

- No specific diagnostics for HIV-associated neurocognitive dementia (HAND); ranges asx to dementia
- Rule out other etiologies:
  - Neurologic/neurodegenerative
  - Substance use
  - Primary psychiatric illness
  - Polypharmacy

RISK-MODIFICATION INTERVENTIONS

- HIV control, ie, ART adherence!
- Optimize CVD risk factors
- Manage comorbid psych/substance use
- Ensure personal safety

- **WLWH vs MLWH**:
  - Greater risk of global neurocognitive impairment
  - Scored lower on learning and memory; information processing speed; motor function
  - Associated w/ psychiatric illness

- **Mechanism**:
  - CD4 nadir, HIV-1 viremia
  - Inflammation and associated vascular and metabolic abnormalities
  - Traditional CVD risk factors

Cervical (and anal) cancer

- **PLWH vs persons without HIV**:
  - 4-5x risk of cervical intraepithelial neoplasia
  - Those with history of receptive anal intercourse, abnormal cervical pap, genital warts should be screened with anal pap (*if appropriate follow-up available*) due to increased risk of anal cancer
- **Mechanism**: HPV infection (via sex); 16/18

SCREENING

Cervical cancer screening:

Age <21 years: Pap within 1 year of sexual activity, no later than age 21

Age 21–29 years: Pap at diagnosis of HIV, repeat yearly × 3, then if all normal, Pap every 3 years

Age <30 years: no HPV testing unless abnormalities are found on Pap test

Age ≥30 years: Pap only, same as 21–29 years or Pap with HPV testing, if both negative then Pap with HPV every 3 years.

Note: In general, continue screening past 65 years.

FOLLOW-UP

Colposcopy or high-resolution anoscopy

PREVENTION

- Vaccination decreases incidence of infection with high-risk HPV types associated w/ cervical/anal cancer (most effective before sexual debut)
- Per ACIP, recommended for all males and females, aged 9-26 yrs; shared decision making for catch-up 27-45yrs

Treatment of Anal High-Grade Squamous Intraepithelial Lesions to Prevent Anal Cancer

- Phase 3 trial, 25 U.S. sites
- PLWH ≥35 yrs old with biopsy-proven anal HSIL
- 1:1 randomization
  - Active monitoring
  - Treatment: office-based ablative procedures, ablation or excision under anesthesia, administration of topical 5-FU or imiquimod
- Median age 51, **16% female**
- Primary outcome: progression to anal cancer (time to event analysis)

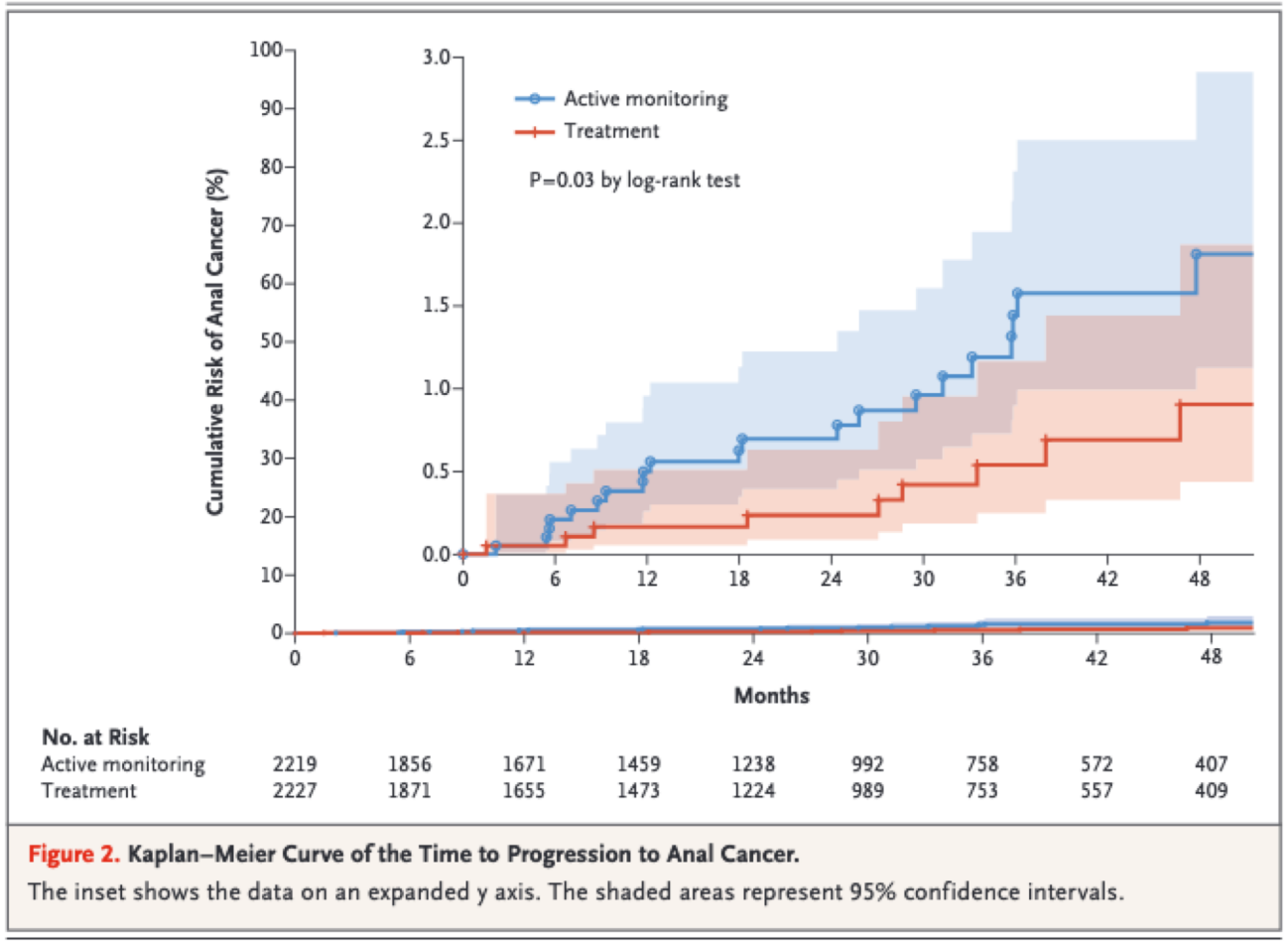


Figure 2. Kaplan–Meier Curve of the Time to Progression to Anal Cancer.
The inset shows the data on an expanded y axis. The shaded areas represent 95% confidence intervals.

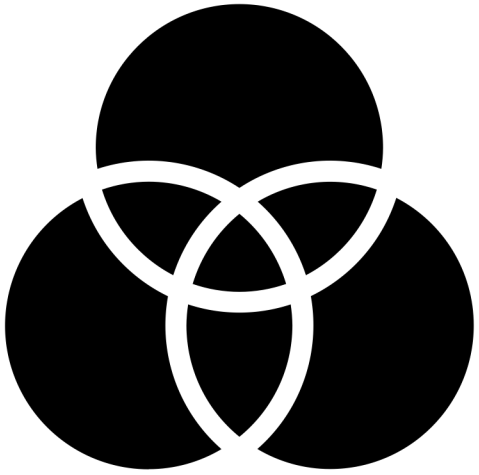
Palefsky JM et al. N Engl J Med. 2022 Jun 16;386(24):2273-2282.

A holistic approach to comorbidities

Emerging multimorbidity phenotype among women > men living with HIV

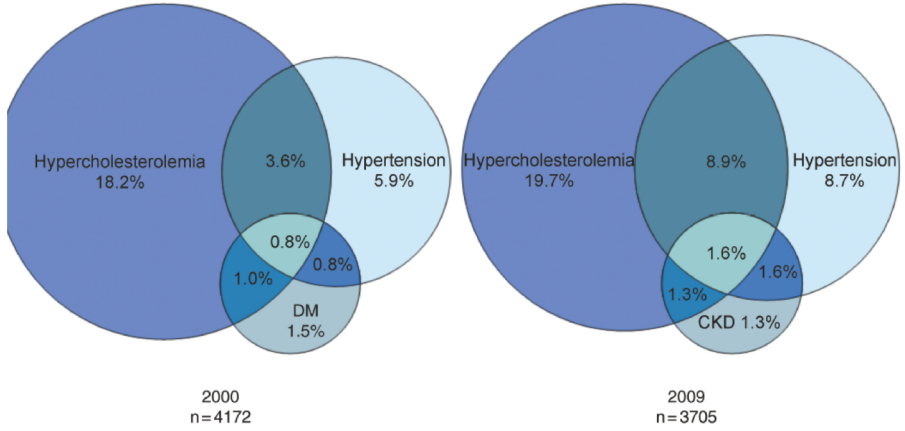
- NACM co-occurrence is common (and non-random)

NACM occur in non-random patterns



NA-ACCORD

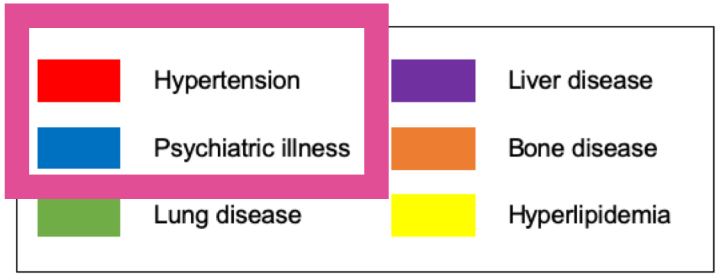
- 23K PWH; 21% female
- 2000 → 2009, multimorbidity prevalence = 8% → 22% (*p*-trend <0.001)
- HTN-hyperlipidemia most commonly co-occurred



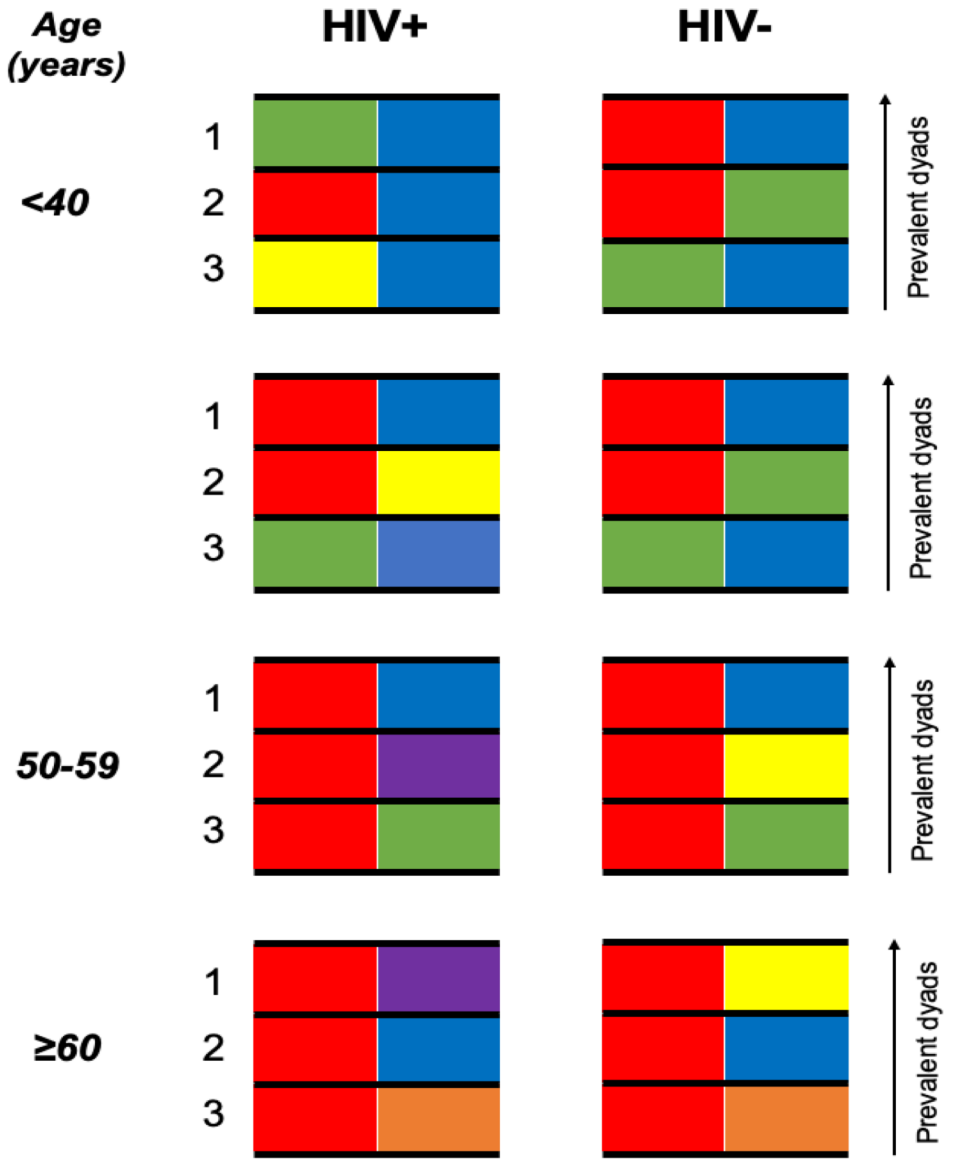
Assessment of co-occurring NACM (i.e. dyads, triads, etc) may provide useful insights into shared pathophysiology and/or risk factors among NACM and suggest possible uniting screening/prevention strategies

Wong et al. Clin Infect Dis. 2018 Apr 3;66(8):1230-1238.

NACM dyads



The dyad of **hypertension-psychiatric illness** is represented in each stratification of HIV serostatus and age.



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

Emerging multimorbidity phenotype among women > men living with HIV

- NACM co-occurrence is common and non-random
  - May be driven by shared risk factors (eg, smoking, coinfections, etc)
  - And/or common mechanisms:
    - Inflammation and immune activation ←→ ongoing HIV-1 viremia
    - Microvascular disease
    - Sex hormone effects
    - Microbial gut translocation

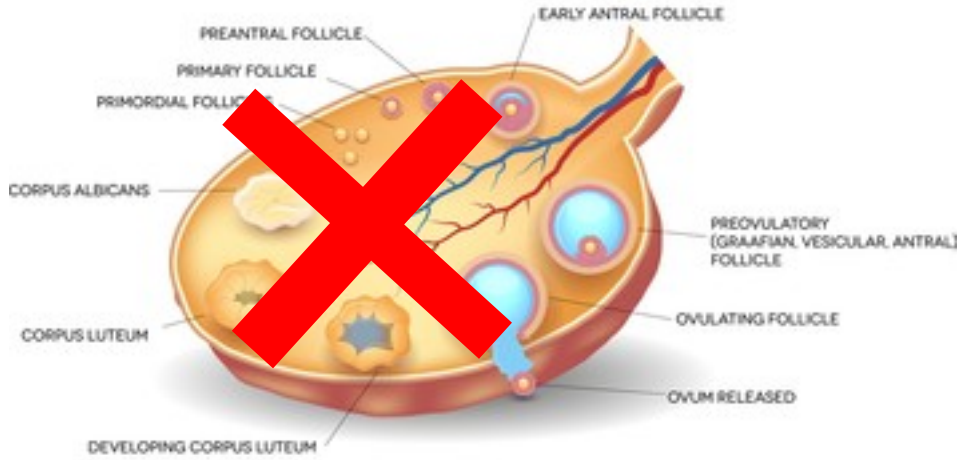
Need to think about more holistic strategies for screening and prevention of NACM, including HIV-specific and sex-differential tools targeting common mechanisms and risk factors, inclusive of **social determinants of health**

It’s getting hot in here…

Impact of the menopausal transition

As PLWH are aging, a growing number of women are entering menopause

- **Menopause**: ≥ 12 months without menses with no other obvious pathologic or physiologic cause



Ovarian follicular depletion

- Low estrogen
- Increased FSH

Mean age (U.S.): 51 yrs

What about for WLWH?

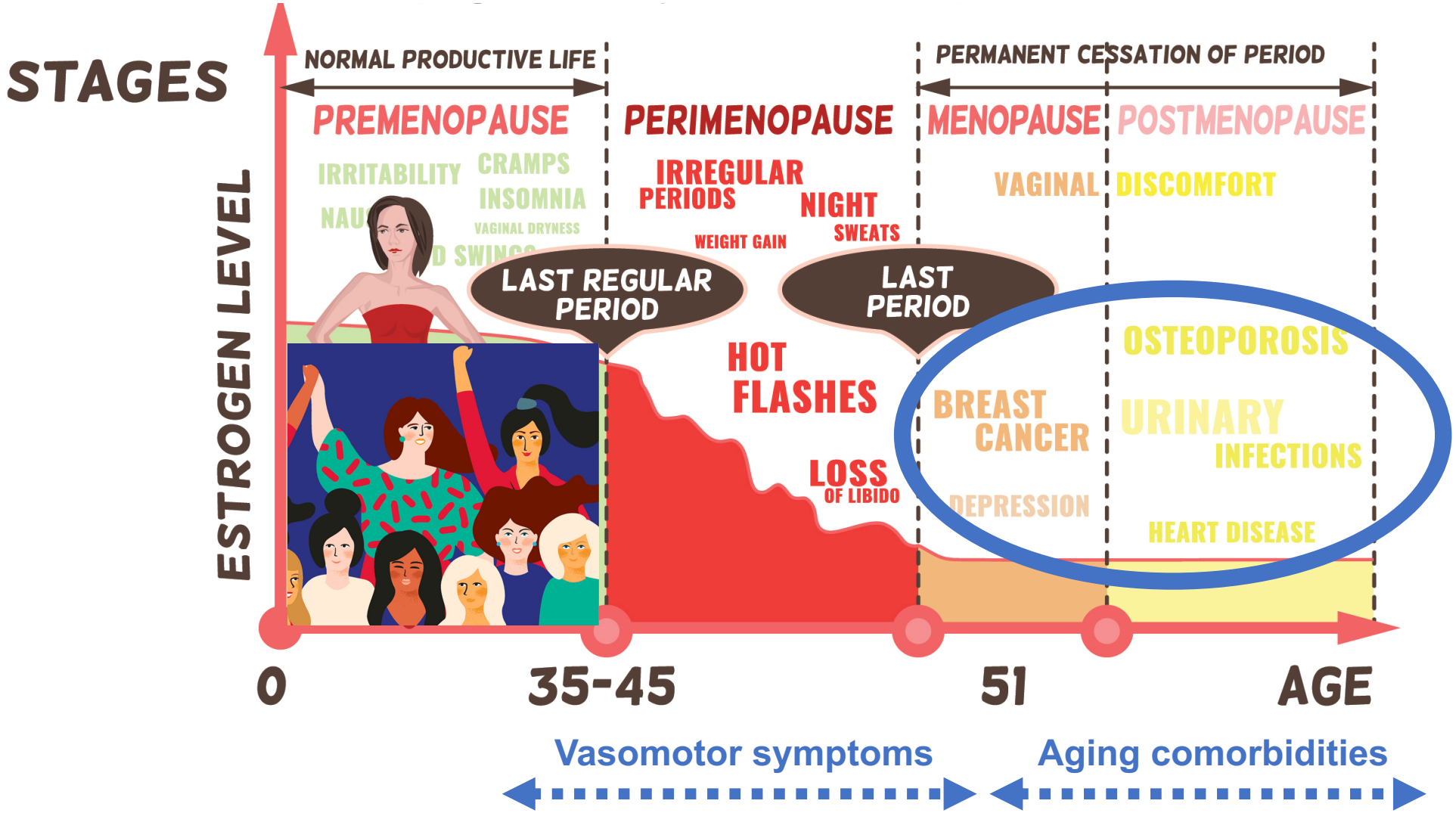
Menopause ≠ amenorrhea

- 1431 women (1139 WWH, 292 women without HIV)
- Menopause=ovarian failure: amenorrhea >1yr + FSH >25 milli-IU/ml

- >50% of WLWH with amenorrhea >1yr did not have ovarian failure
- When adjusted for age, WLWH were 3x more likely than women without HIV to have prolonged amenorrhea without ovarian failure
- BMI, serum albumin, and parity were all negatively associated with ovarian failure among WLWH

Cejtin HE et al. Obstet Gynecol. 2006;108(6):1423.

The menopausal transition



What treatments are available?

- **Menopause hormone therapy (MHT)**
  - Estrogen + Progestin (E+P) — *Uterus*
  - Estrogen (E) — *No uterus*

  } **Primary goal:** alleviate hot flashes

  - Low-dose vaginal estrogen → *Vulvovaginal atrophy*

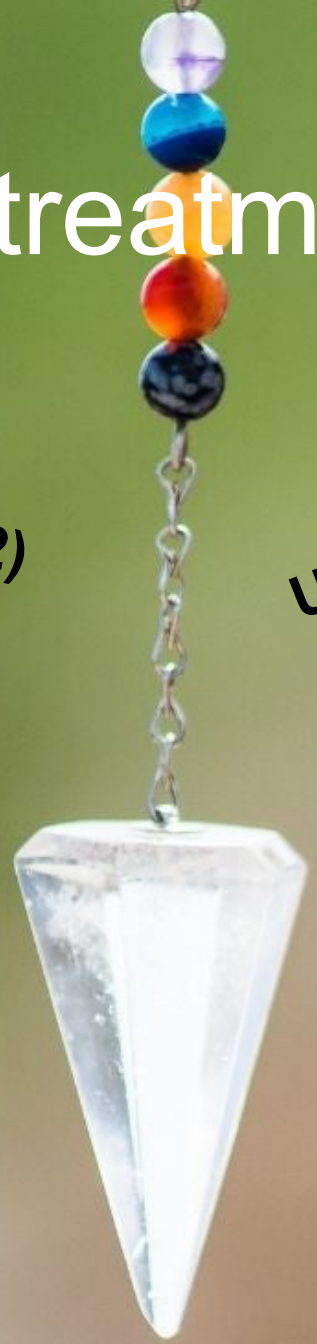
- Non-hormonal options:
  - SSRIs, SNRIs, gabapentin; pregabalin, clonidine

- **Secondary goals**: mitigating sleep disturbances, mood lability/depression, +/- joint aches and pains

For whom are treatments available?

Initial WHI results (2002)

- 27,000 women
- Mean age 63
- Indication: chronic disease prevention
- Risks > benefits
- Adverse outcomes: excess risk of CVD, stroke, VTE, breast cancer



Uptake of MHT among peri-menopausal women dropped significantly

USPSTF 2017 recommends against use of MHT for prevention of chronic conditions

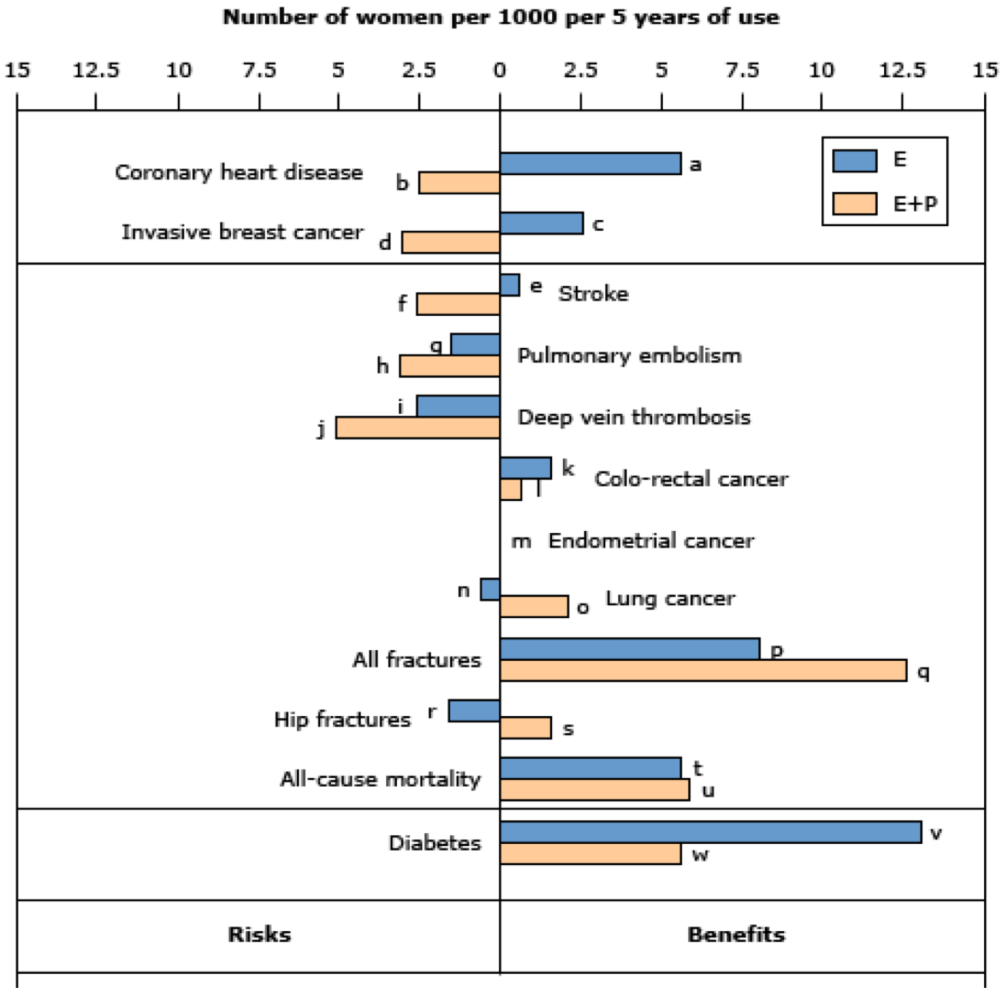
For whom are treatments NOT available?

Contraindications
Hx breast cancer
CVD
Stroke or TIA
Prior VTE event
Active liver disease
Unexplained vaginal bleeding
High-risk endometrial cancer

Excess risks and benefits of MHT

- Sub-analysis of Women's Health Initiative data
- Postmenopausal women aged *50-59 years*

Emerging consensus:
benefits > risks of MHT for the *relief of symptoms* in women who have recently undergone menopause and are not at risk of breast cancer and CVD



Santen et al. J Womens Health (Larchmt). 2014 Apr;23(4):281-5.

An individualized approach

10-year CVD risk	<10 years since menopausal onset
Low (<5%)	MHT okay
Moderate (5-10%)	MHT okay – transdermal
High (>10%)*	Avoid MHT

*Includes heart attack, stroke, peripheral arterial disease, etc

Similar guidance available for breast cancer risk assessment

Consider the following:

- Age
- Years post-menopause
- Presence of symptoms
- Comorbidities
- Risk of adverse outcomes
- E vs E+P
- Route of administration
- Duration of MHT

Quality of life gains!

Manson et al. Fertil Steril 2014; 101:916.
Stuenkel et al. J Clin Endocrinol Metab 2015; 100:3975.

WLWH and the menopausal transition

- WLWH may experience menopause ***earlier*** and ***more severely*** than women without HIV
  - Data are conflicting and inconclusive
  - Confounding factors:
    - Substance use, HCV coinfection
    - CD4 count, ART use

- The effect of HIV on the neuro-endocrine axis may play a role, potentially mediated by HIV-associated inflammation

Scherzer R et al. Am J Obstet Gynecol. 2017 Jan;216(1):46.e1-46.e11.
Merlini E et al. Medicine (Baltimore). 2021; 100, e27157.

How WLWH are affected by the menopausal transition…

- Reduced ART adherence
- Poor cognitive performance
- Elevated markers of inflammation
- Increased comorbidity burden
- Low uptake of MHT

Peters BA. J Infect Dis. 2022 Jan 18;225(2):295-305.

HIV impacts NACM burden most in the pre/peri-menopausal phases

- N=2,716 women
- STRAW +10 principal criteria used to classify menopausal status
- HIV, age, menopausal status all independently associated with menopausal status

Among WLWH vs women without HIV, post-menopausal status was:

- <40 yrs, 10% vs 6% (*p*=0.0939)
- 40-49 yrs, 34% vs 21% (*p*=0.0004)
- 50-59 yrs, 86% vs 85% (*p*=0.9706)

	WLWH versus women without HIV*		
Age	**Pre-menopausal**	**Peri-menopausal**	**Post-menopausal**
40-49 yrs	+0.22 (-0.13-0.58)	+0.52 (-0.26-1.31)	-0.22 (-1.39-0.95)
50-59 yrs	+0.50 (+0.18-0.84)	+0.43 (-0.10-0.95)	+0.25 (-0.25-0.75)
60-69 yrs	+0.52 (-0.60-1.63)	+0.47 (-0.22-1.17)	+0.18 (-0.07-0.43)

*3-way interaction (age, menopausal status, HIV), *p*=0.9580
(also adjusted for race, BMI, smoking status)

Collins LF et al. Clin Infect Dis. 2022 Jun 10:ciac465.

Patient and provider education and engagement needed for MHT uptake

WIHS Women's Interagency HIV Study

TABLE 2. *Prevalence of hormonal medication use during menopause by participant and by visit, Women's Interagency HIV Study, 2008 to 2020*

	Menopause before 41 *N (%)*		Menopause 41-45 *N (%)*		Menopause 46-50 *N (%)*	
	Participant[a] ($N=35$)	Visits ($N=255$)	Participant[b] ($N=101$)	Visits ($N=775$)	Participant[c] ($N=442$)	Visits ($N=1,548$)
Hormone use						
Vaginal estrogen[d]	0 (0)	0 (0)	16 (16)	134 (17)	3 (1)	25 (2)
Menopausal hormone therapy[e]	5 (14)	10 (4)	16 (16)	49 (6)	29 (7)	57 (4)
Hormonal contraception[f]	13 (37)	37 (15)	10 (10)	34 (4)	2 (0)	2 (0)
Any oral hormones[g]	18 (51)	47 (18)	24 (24)	82 (11)	30 (7)	59 (4)

[a]Median [interquartile range] of visits between premature menopause before age 41 and age 51 was 5 [2,9].
[b]Median [interquartile range] of visits between premature menopause between ages 41 and 45 and age 51 was 5 [2,9].
[c]Median [interquartile range] of visits between premature menopause between ages 46 and 50 and age 51 was 2 [1,4].
[d]Self-reported use of prescription drug that was classified as vaginal estrogen.
[e]Self-reported use of hormone therapy or self-reported use of prescription drug that was classified as hormonal therapy.
[f]Self-reported use of oral contraceptives, implants, Depo Provera, or hormonal IUDs or self-reported use of a prescription drug that was classified as hormonal contraception.[8]
[g]Includes hormone therapy and hormonal contraceptives.

Bullington BW. Menopause. 2022 Jun 1;29(6):741-747.

Why may WLWH be undertreated for premature or early menopause?

- Under recognition of menopause in this population (vs amenorrhea)
- Provider hesitancy to prescribe
  - Potential interactions with older classes of ART (PIs, cobi/r, NNRTIs)
  - Perception that relative contraindications (eg, HTN) are absolute, especially in the setting of other comorbidities or substance use
- WLWH may decline due to medication burden/ perceived side effects
- Disparities in care access related to social determinants of health, including current/past substance use

Consequences of undertreatment

- Insufficiently managed symptoms
- Worsening health disparities in aging-related comorbidities (eg, CVD, osteoporosis, etc)
- Negative impact on quality of life and overall mortality

Need to provide additional training in menopausal medicine to providers; educate and empower patients; provide risk-assessment, counseling, and treatment of distressing symptoms to improve QoL (and mortality)

Lean in

Psychosocial context and considerations

Barriers to care for WLWH

CONCRETE

- Childcare
- Transportation
- Housing
- Food insecurity
- Lack of insurance

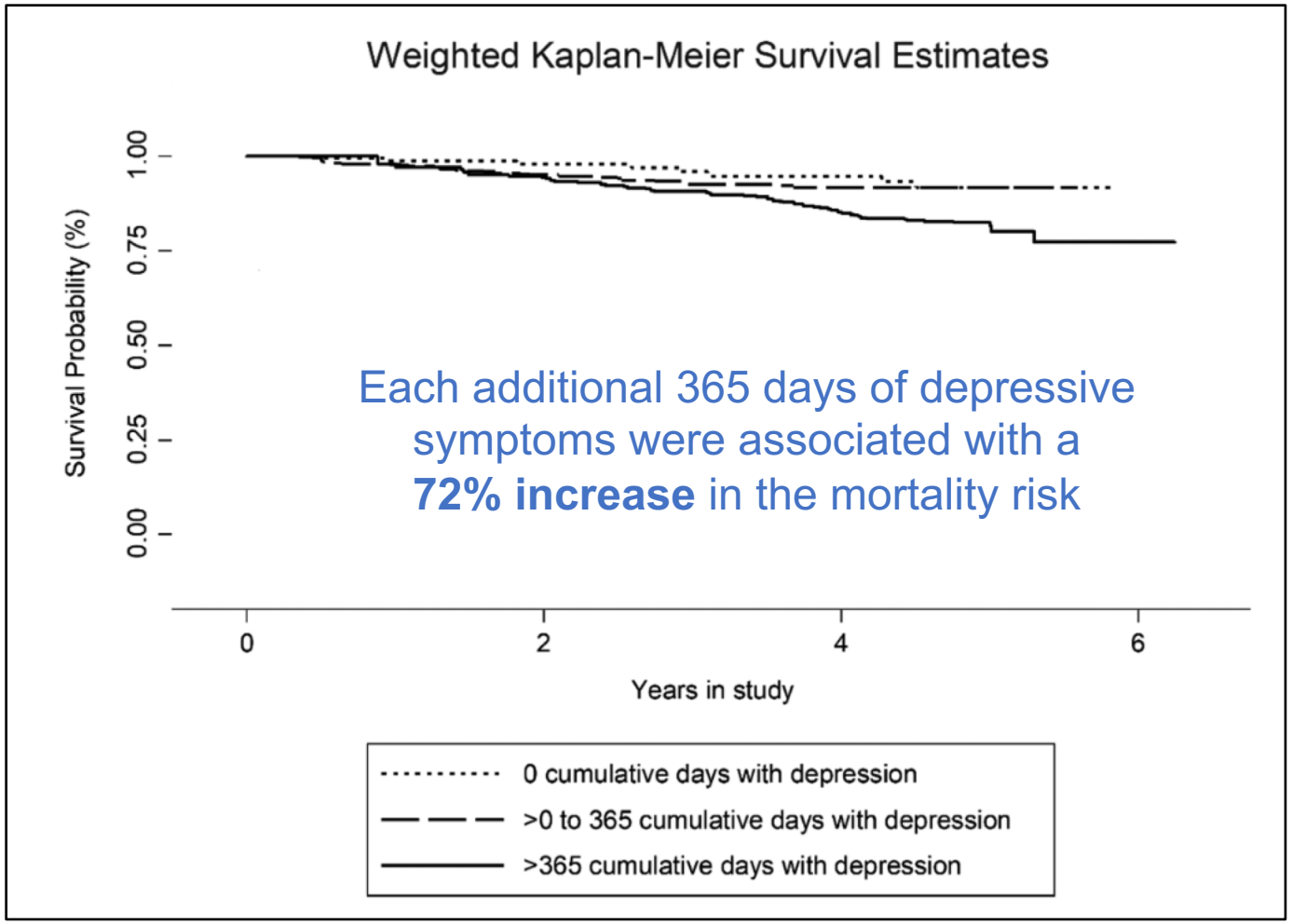
PSYCHOSOCIAL

- Fear of disclosure
- Denial
- Intimate partner and other violence
- Cultural mistrust of the healthcare system

WLWH often provide primary care for family members who may include children or other patients with HIV/AIDS

Depression is common among WLWH

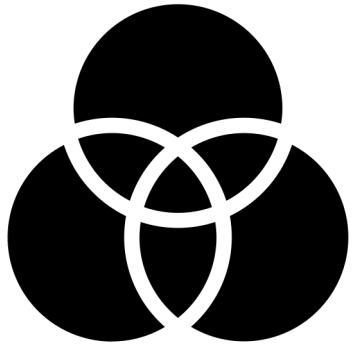
- >800 WLWH
- Median 5yr follow-up
- There was a dose-related association between cumulative days with depression and mortality



Mills JC et al. Clin Infect Dis. 2018 Oct 30;67(10):1575-1581

Implications of food insecurity among WLWH

- Associated with:
  - 2x higher HIV-1 VL and lower CD4 count (-42.1, 95%CI -81.2, -3.0)
  - Elevated inflammation regardless of HIV control
  - Higher odds of current illicit substance abuse
  - Depressive symptoms and internalized HIV stigma
  - Sexual, physical, psychological violence



- Multilevel interventions are needed to improve health and disease among WLWH that entail a syndemics approach

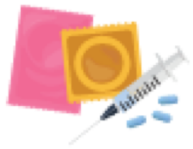
Spinelli MA et al. AIDS Behav. 2017 Dec;21(12):3473-3477.

There are several challenges that place some women at higher risk for HIV.

Racism, Discrimination, and HIV Stigma

Racism, discrimination, and stigma may affect whether some women seek or receive high-quality health services.

Unaware of Partner's Risk Factors



Some women don't know their male partner's risk factors for HIV (such as injection drug use or having sex with men) and may not use a condom or medicine to prevent HIV.

Risk of Exposure

Because receptive sex is riskier than insertive sex, women are more likely to get HIV during vaginal or anal sex than their sex partner.

Intimate Partner Violence (IPV)

Women who have been exposed to IPV may be more likely to engage in risky behaviors or be forced to have sex without a condom or medicines to prevent or treat HIV.

Biology of HIV (risk, control, etc) is intertwined in psychosocial context

www.cdc.gov/hiv/pdf/group/gender/women [March 2022]

A new landscape for ART delivery

Long-acting antiretroviral therapy for HIV treatment and prevention

Long-acting ART has the potential to improve clinical outcomes & patient experience:

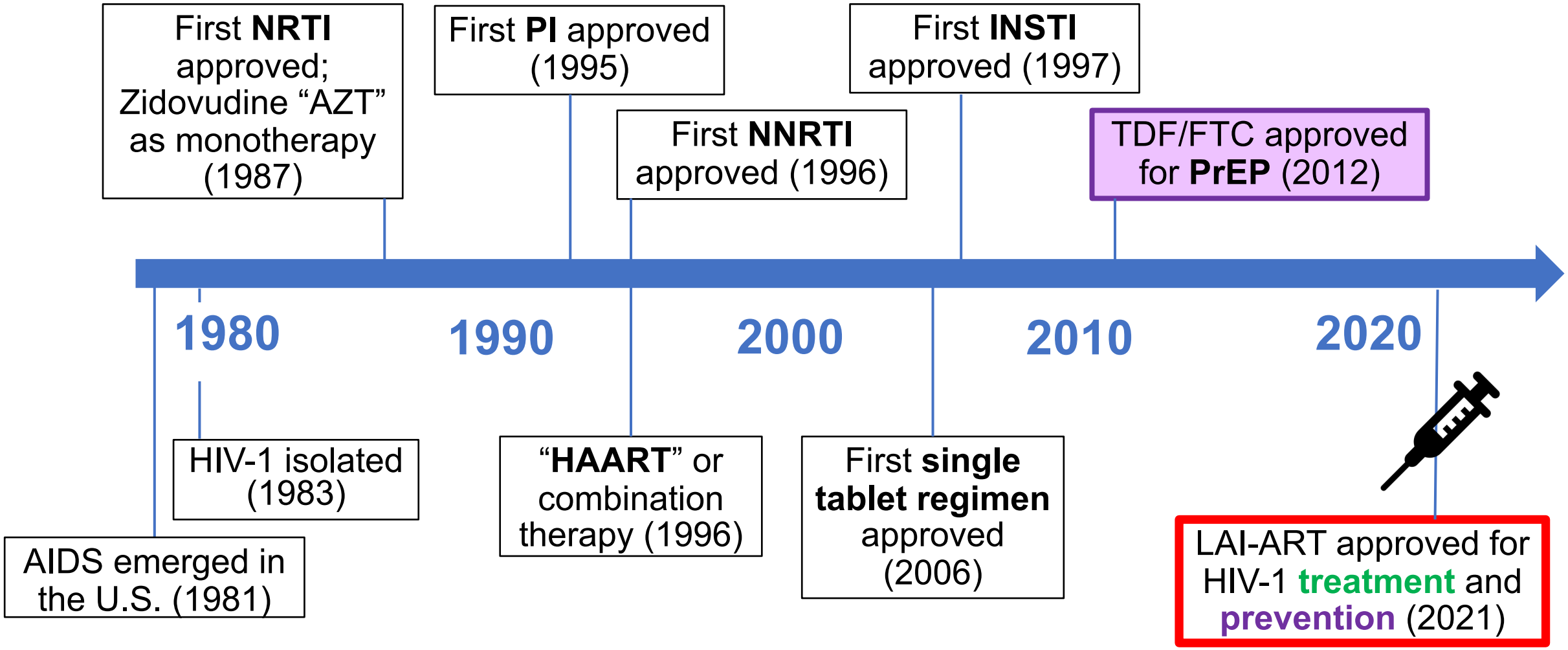
- Alleviate pill fatigue
- Improve adherence
- Reduce stigma

Provide *more accessible* and *equitable* care for persons with HIV (PWH) & those at risk

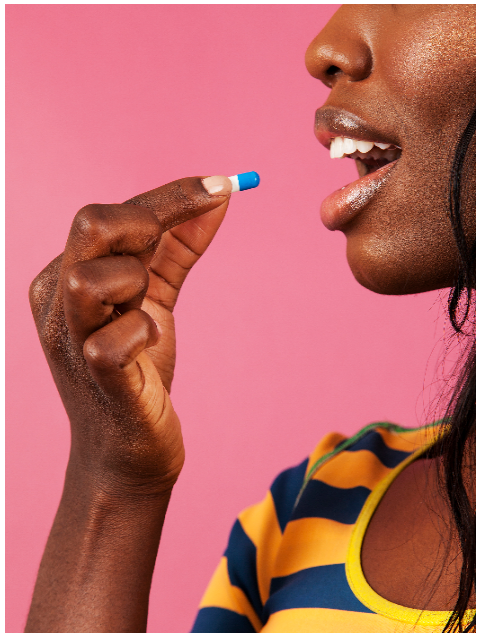
Drugs

HAART: highly-active ART
INSTI: integrase strand transfer inhibitor
NRTI: nucleoside reverse transcriptase inhibitor
NNRTI: non-NRTI
PI: protease inhibitor
PrEP: pre-exposure prophylaxis

History of ART



CAB/RPV (Cabenuva): 1st injectable for HIV-1 maintenance treatment, administered q1-2mo



Oral lead-in
2 pills/day x 30d

Injectable phase
2 IM intra-gluteal injections x1-2 mo

CABENUVA
cabotegravir 200 mg/mL; rilpivirine 300 mg/mL
extended-release injectable suspensions

6 months of HIV-1 virologic suppression on oral ART

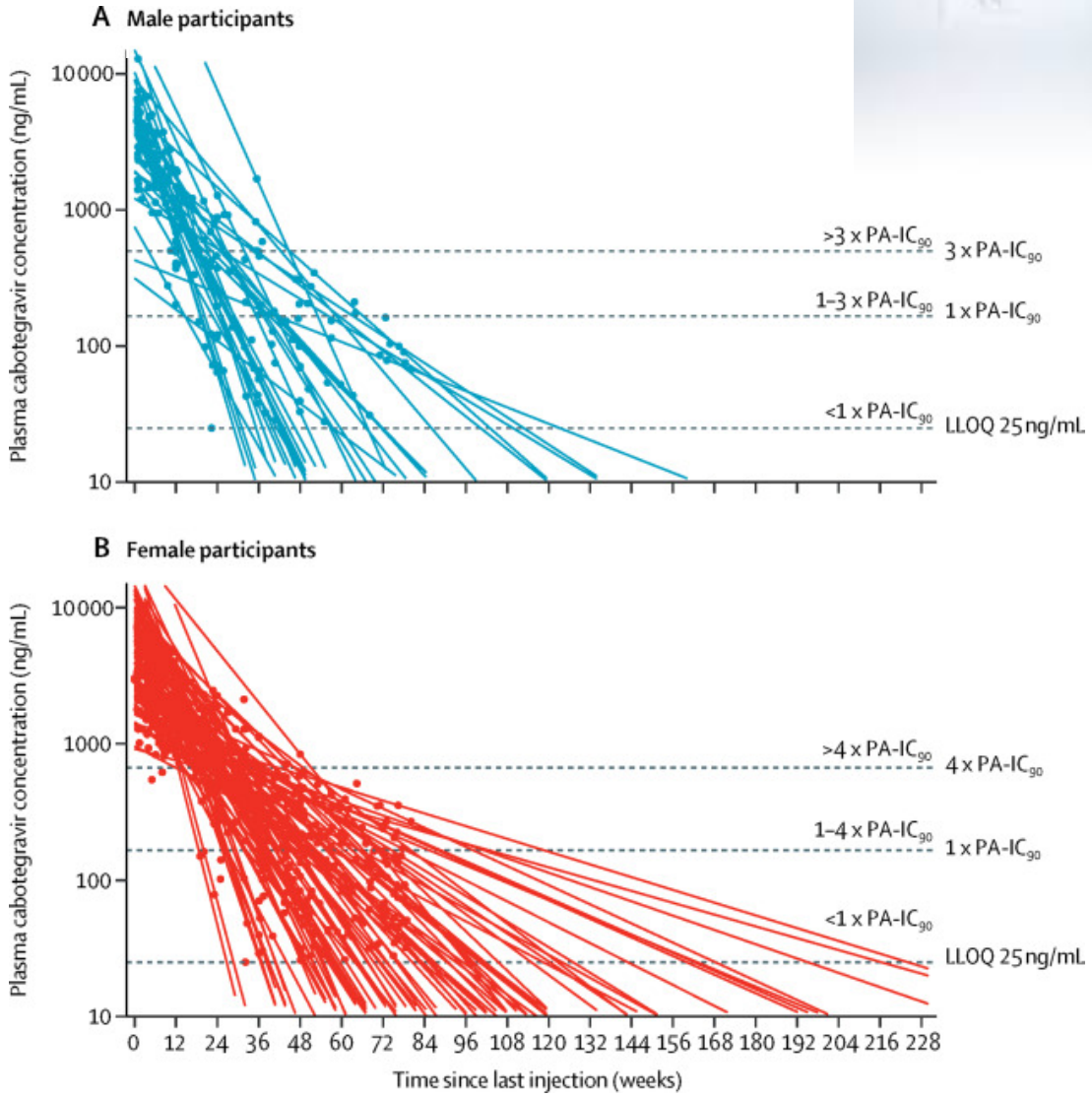
Manufactured by ViiV Healthcare

CAB: cabotegravir (INSTI)
RPV: rilpivirine (RPV)

What's a tail got to do with it?

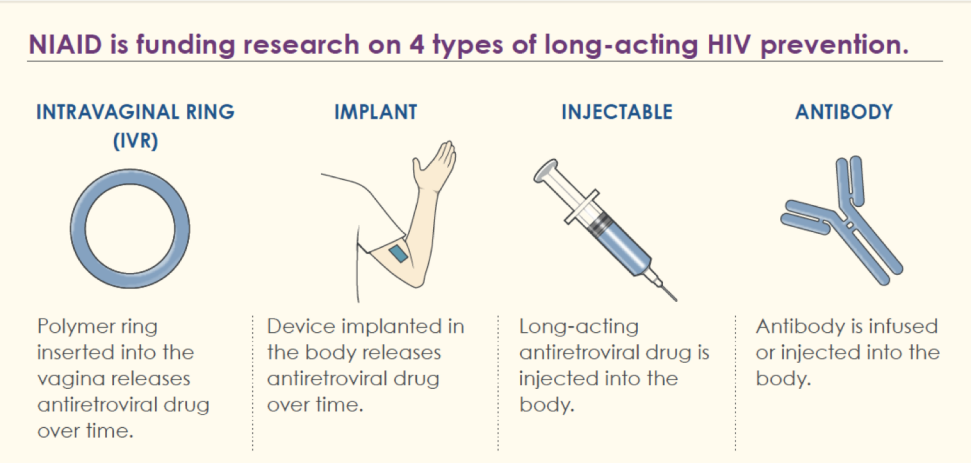
LAI-CAB (PrEP)

- HPTN 077
- At 76wk follow-up post-injection, 13% vs 42% of male vs female participants, respectively, had detectable CAB
- Female (vs male) sex and higher (vs lower) BMI were strong predictors of terminal phase ½ life



Landovitz RJ et al. Lancet HIV. 2020 Jul;7(7):e472-e481.

Additional alternatives to daily oral ART for treatment/prevention:



- **Lenacapavir** SQ injection (q6mo, capsid inhibitor)
  - Tx: phase 3 trial for MDR HIV (NEJM 2022)
  - PrEP: FDA lifted hold on phase 3 trial (vial compatibility issue, May 2022)
- **Ibalizumab** IV (biweekly, anti-CD4 domain 2 monoAb)
  - Tx: FDA approved for MDR HIV
- **Islatravir** pill (monthly)/ implant (NRTTI)
  - Partial (Tx, phase 3) and full (PrEP, phase 2) clinical hold given decreased total lymphocytes and CD4
- **Dapivirine** intravaginal ring (monthly, NNRTI)
  - PrEP: ~30% reduction in HIV acquisition (up to 85%)
  - EMA approved, application withdrawn by FDA

Treatment

First of its kind

Scientific advancement of HIV-1 treatment

Most PWH treated with 3 total drugs (2 NRTIs + 1 anchor drug), ideally in one daily pill

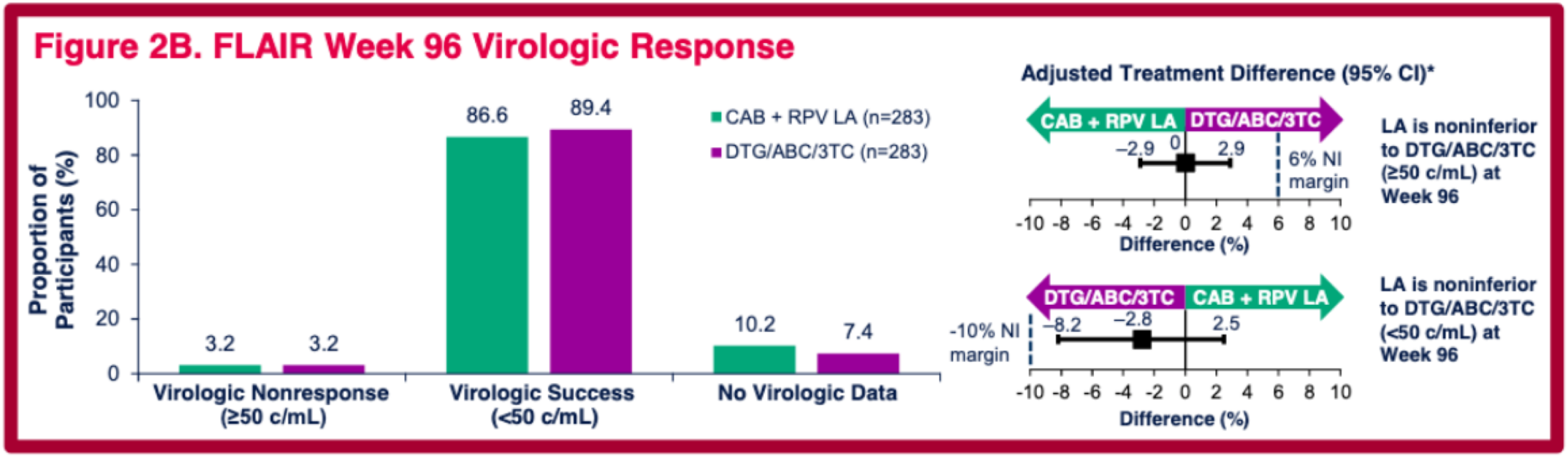
1980 1990 2000 2010 2020

Multiple pills, multiple times per day

>30 FDA-approved antiretroviral options

Two injections monthly or bimonthly (2 drugs)

LAI-CAB/RPV is efficacious, safe, and preferred (vs oral ART) in clinical trials



*Adjusted for sex and baseline HIV-1 RNA (< vs ≥100,000 c/mL).

Among participants in **FLAIR** (ART-naïve), non-inferiority met and patient satisfaction high despite 88% reporting injection-site reactions; similar results observed in **ATLAS** (ART-experienced)/**2M**

Orkin C et al. Lancet HIV. 2021; 8: e185-e196.

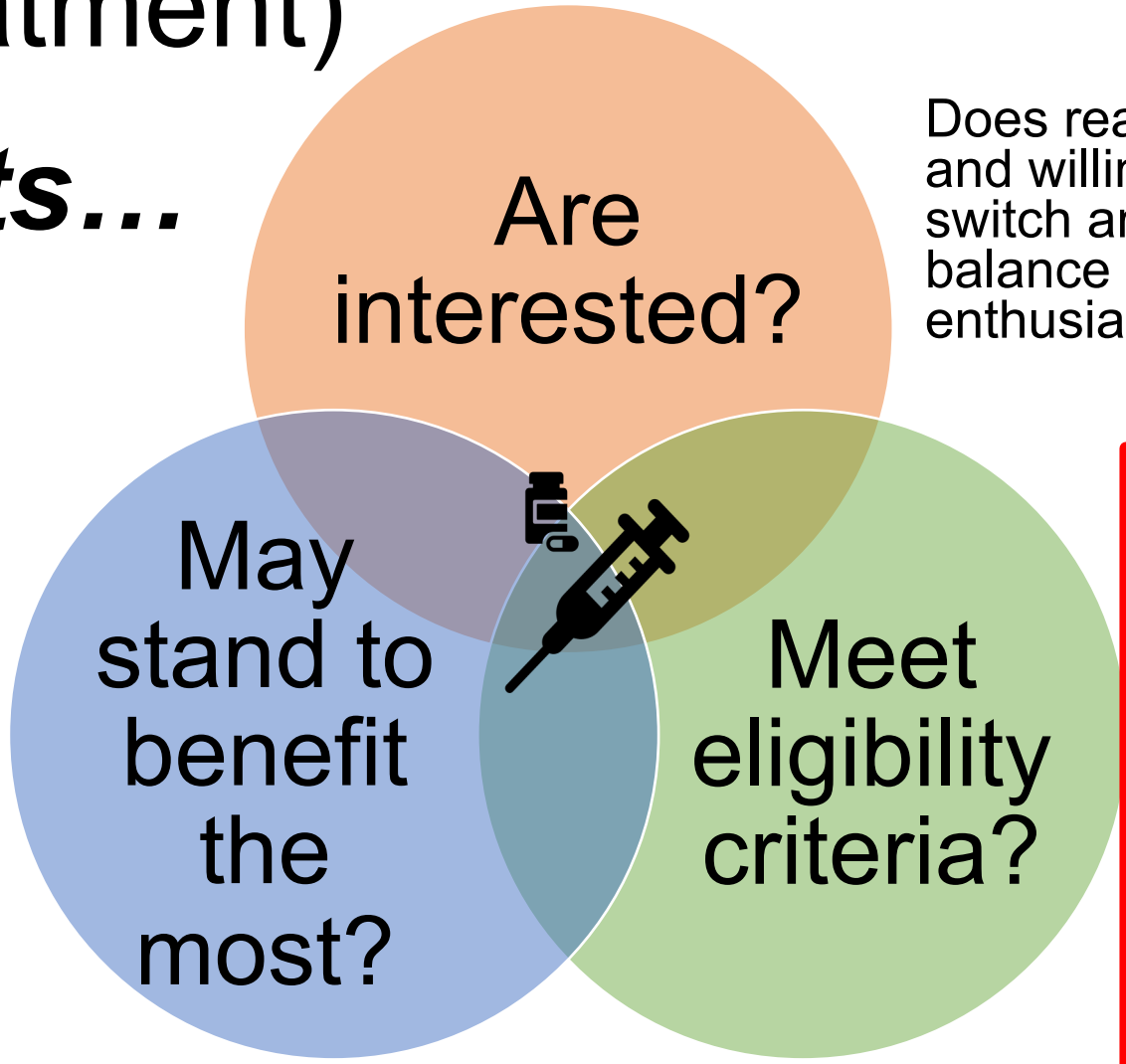
Swindells S et al. AIDS. 2022; 36: 185-94.

Per FDA label, LAI-CAB/RPV is indicated as a complete HIV-1 treatment regimen:

- As a replacement for current ART in those who are:
  - Virologically suppressed (HIV-1 RNA <50 cp/ml) on a stable ART regimen
  - With no history of treatment failure
  - With no known or suspected resistance to either CAB or RPV
  - With no hypersensitivity to either agent
- No additional contraindications (active HBV infection unless otherwise treated; pregnancy; drug-drug interactions)

Clinical considerations for use of LAI-CAB/RPV (treatment)

Which patients…



Does real world interest and willingness to switch among PWH balance clinical trial enthusiasm?

PWH who have:

- Pill aversion, intolerance, or fatigue?
- Malabsorption?
- Populations with lower rates of viral suppression +/- clinic vist adherence?
  - Unstable housing
  - Transactional sex workers
  - Suffering from stigma
  - Comorbid mental/ psychosocial issues

Current label use may not match those PWH with greatest needs

LAI-ART interest among U.S. Women

- 6 sites of the Women's Interagency HIV Study (WIHS), 2017-2018
- 59 women with HIV, 30 women without HIV participated in focused interviews
- Women's prior experiences with injections occurred primarily through **substance use, physical comorbidities, birth control, or flu vaccines**.

- Four primary categories of women emerged; those who
  - (1) received episodic injections and had few LAI-related concerns;
  - (2) required frequent injections and would refuse additional injections;
  - (3) had a history of injection drug use, of whom some feared LAI might trigger a recurrence, while others had few LAI-related concerns; and
  - (4) were currently injecting drugs and had few LAI-related concerns.
- ***Most women with a history of injectable medication would prefer LAI, but those with other frequent injections and hx of injection drug use might not***.

Philbin MM et al. AIDS Patient Care STDS. 2021 Jan;35(1):23-30.

Prevention

The toolkit expands

PrEP Coverage Among Women in the US, 2019*†

PrEP is highly effective for preventing HIV from sex or injection drug use.

ONLY

of women who could benefit from PrEP were prescribed PrEP in the US in 2019.

* Based on sex assigned at birth.
† Among people aged 16 and older.

Source: CDC. Monitoring selected national HIV prevention and care objectives by using HIV surveillance data—United States and 6 dependent areas, 2019. *HIV Surveillance Supplemental Report* 2021;26(2).

Scientific advancement of HIV-1 prevention

One injection bimonthly
(1 drug)

2010

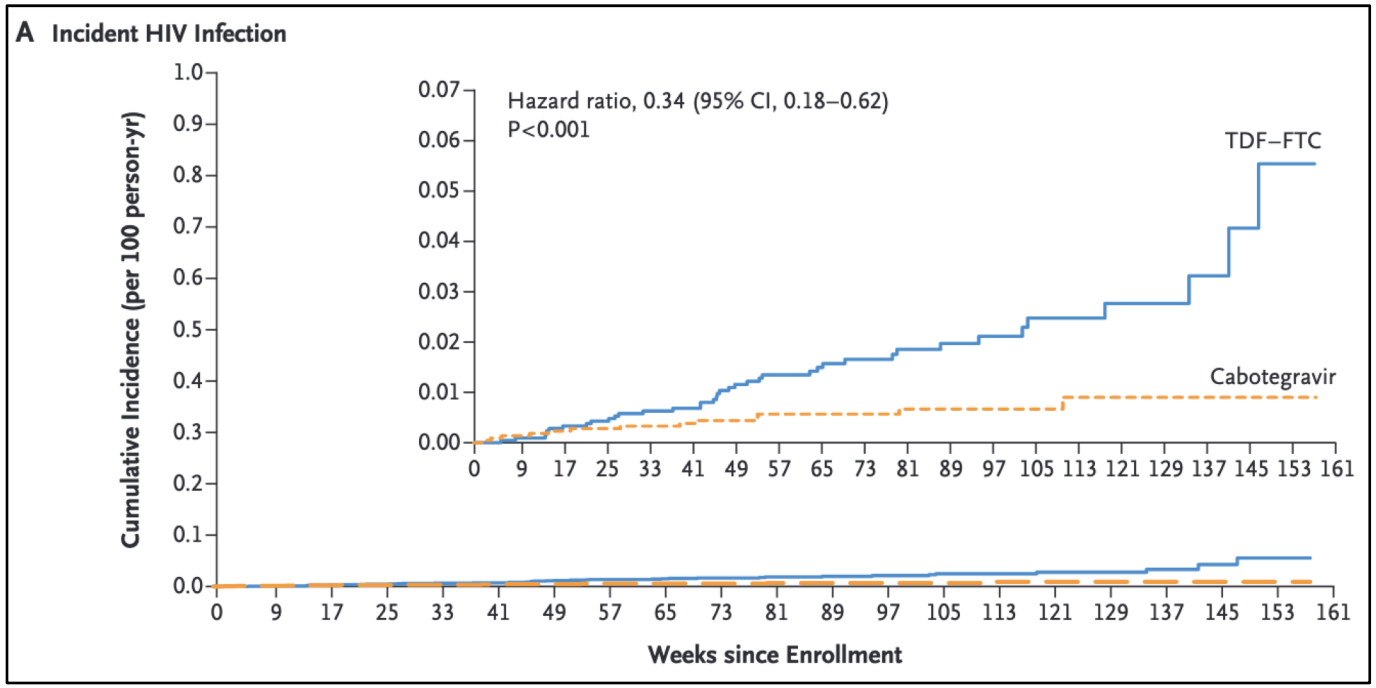
2020

TDF/FTC (**Truvada**)
approved (2012)

TAF/FTC (**Descovy**)
approved (2019)

2 single pill daily options (2 drugs) reduce the risk of getting HIV from sex by 99% when taken *as prescribed*

RCTs of LAI-CAB for **HIV prevention** stopped early due to efficacy



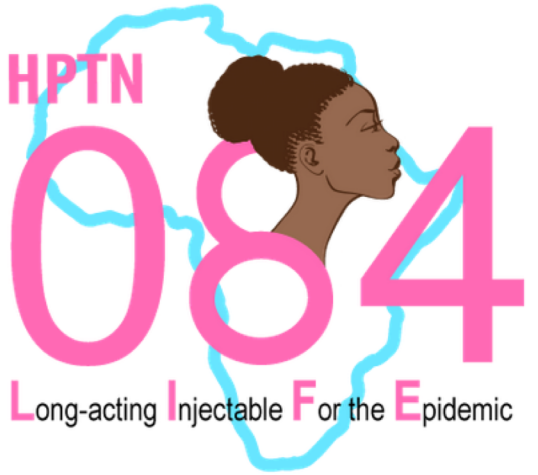
Among cisgender men and transgender women who have sex with men in **HPTN 083** (shown) and among cisgender women in **HPTN 084** (next slide), LAI-CAB was superior to TDF/FTC

FDA approved for use in at-risk adults and adolescents (≥35kg) for PrEP to reduce risk of sexually acquired HIV

(Oral lead-in optional)

Landovitz R et al. NEJM. 2021; 385(7): 595-608.

HPTN 084: sub-Saharan Africa



- HIV incidence 1/100 PY
- +2 kg/yr in both arms
- Despite long-acting contraception requirement, 49 pregnancies (29 CAB); no known NTD or congenital anomalies
- LAI-PrEP preferred by women
- Familiarity with injectable contraception
- Need to prioritize study in younger women

Delany-Moretlwe et al. Lancet. 2022 May 7;399(10337):1779-1789.

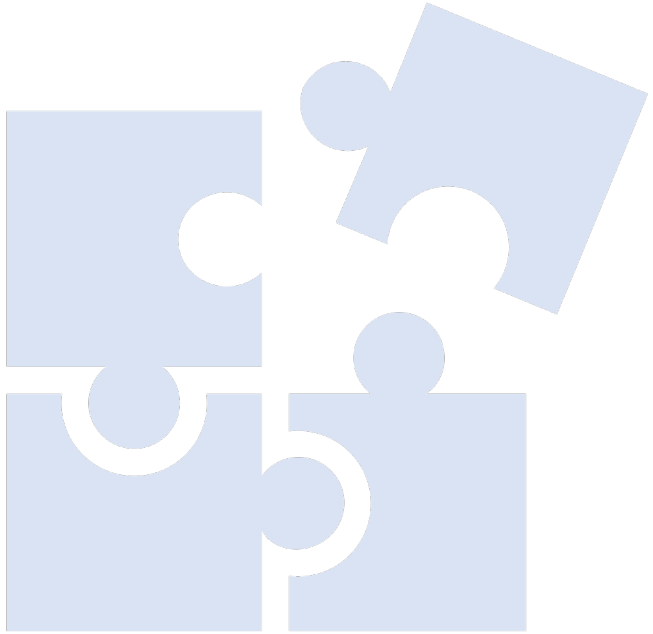
Clinical considerations for use of LAI-CAB (prevention)

- In the participants in whom HIV infection was diagnosed *after* exposure to LAI-CAB:
  - INSTI resistance was detected
  - Delays in detection of HIV infection occurred
- Boxed warning: to not use drug unless negative HIV test confirmed prior to each use

Performance of HIV tests differs among those who acquire infection on ART vs not (ie, lagged HIV Ab/Ag positivity compared with HIV-1 RNA testing)

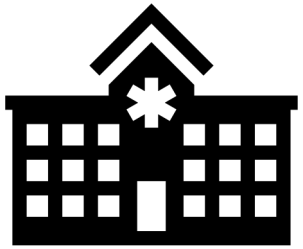
CDC: Clinicians' WARM LINE for PrEP-related dx dilemmas (1-800-933-3413)

Marzinke M et al. J Infect Dis. 2021 Nov 16;224(9):1581-1592



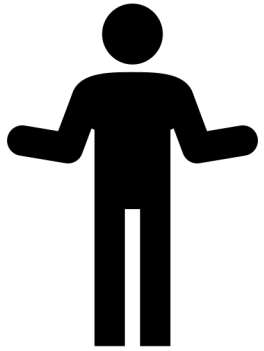
Implementation of LAI-ART

Building the infrastructure, considering the patient, accessing the drug



Building an administration infrastructure

- Medication cold-chain supply and storage required
- Trained personnel for IM administration, ideally in private space
- Dedicated staff for intensive patient tracking and monitoring

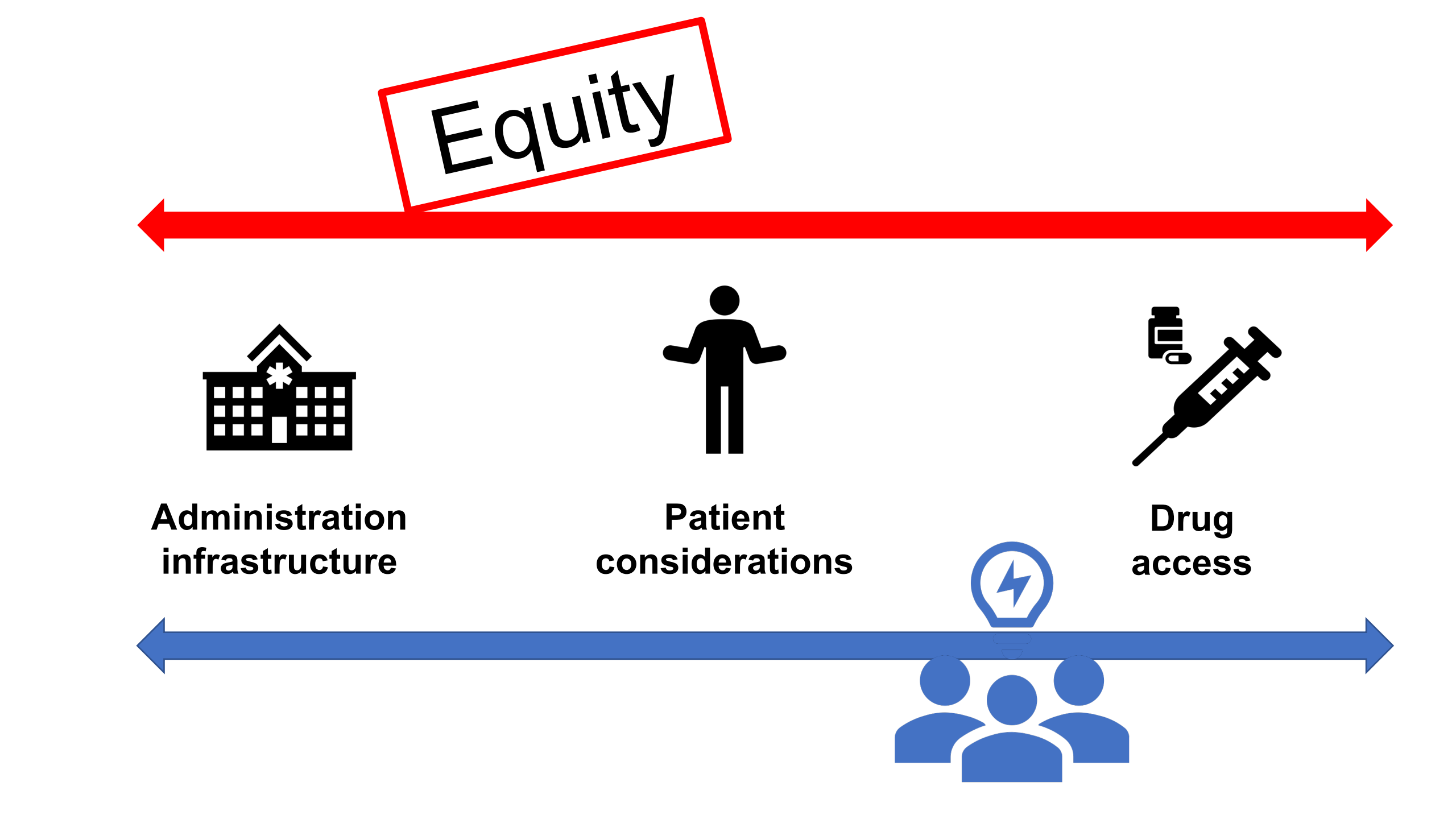


Considering the patient

- LAI-ART has the *potential* to make a great impact for many types of patients in many ways

Accessing the drug

- Different processes for oral lead-in vs IM procurement
- Coverage as medical vs pharmacy benefit differs by payor source; not yet on formulary of all payor sources


Equity
Administration infrastructure
Patient considerations
Drug access

ATLAS baseline characteristics

Table 1. Baseline Characteristics of Participants in the Intention-to-Treat Exposed Population.*

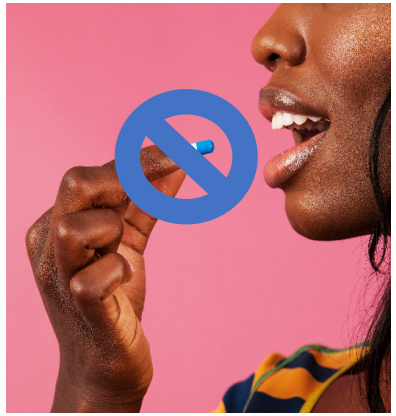
Characteristic	Long-Acting Therapy (N = 308)	Oral Therapy (N = 308)	Overall (N = 616)
Median age (range) — yr	40 (21–74)	43 (18–82)	42 (18–82)
Age group — no. (%)			
<35 yr	80 (26)	80 (26)	160 (26)
35–49 yr	162 (53)	132 (43)	294 (48)
≥50 yr	66 (21)	96 (31)	162 (26)
Female sex — no. (%)	99 (32)	104 (34)	203 (33)
Median body-mass index (range)†	26 (15–51)	26 (18–58)	26 (15–58)
Race — no. (%)‡			
White	214 (69)	207 (67)	421 (68)
Black	62 (20)	77 (25)	139 (23)
Asian	22 (7)	13 (4)	35 (6)
Other	10 (3)	11 (4)	21 (3)
CD4+ lymphocyte count — no. (%)			
<350/mm^3	23 (7)	27 (9)	50 (8)
350–499/mm^3	56 (18)	57 (19)	113 (18)
≥500/mm^3	229 (74)	224 (73)	453 (74)
Median time since first ART (range) — mo	52 (7–222)	52 (7–257)	52 (7–257)

ACTG Protocol 5359

ACTG LATITUDE

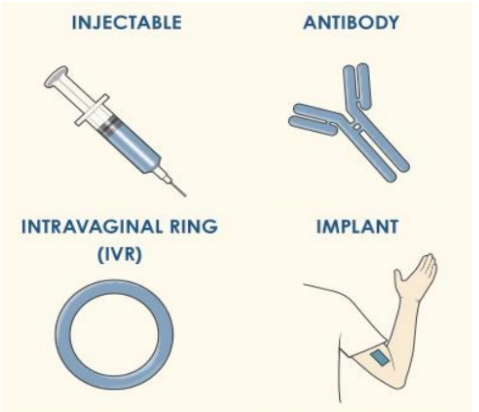
- Registered Sites: 31 ACTG, 4 IMPAACT (U.S + Puerto Rico)
- Screened: 592
- Enrolled in Step 1: 277
  - 63% Black/African-American
  - 18% Hispanic/Latinx Ethnicity
  - 30% Female Sex at Birth
  - 6% Age 18-24 years
  - 5% Transgender
  - 5% Current injection substance use
  - Median CD4 count 268 cells/mm^3
  - Median time since HIV diagnosis 13 yrs

Realizing the full potential of LAI-ART: being able to offer this treatment equitably



ACTG LATITUDE

ACTG Protocol 5359



https://www.niaid.nih.gov/diseases-conditions/long-acting-forms-hiv-prevention

We should act now to capitalize on this unique opportunity of LAI-ART to improve care delivery and outcomes for all PWH and those at risk

Reimagining service delivery

HIV care infrastructure for aging women

Improving the care infrastructure for aging PLWH

- Common gaps in care
  - Access to affordable hearing aids, glasses, dental care
  - Failure to assess functional or cognitive status and depression
  - Limited awareness of decreased vaccine responses due to aging
  - Failure to address sexual health – competing comorbidities or perception of limited sexual activity
- Valid assessments exist for above

What Is a Geriatric Multidisciplinary Approach to Health Care?

It is a health care approach involving physicians, nurses, medical case managers, occupational therapists, social workers, and others to manage the care of people aging with HIV. Together, the health care team establishes patient-centered goals by addressing the domains of medical problems, cognitive and functional abilities, psychiatric disorders, and social circumstances and maximizes the use of community resources and referrals.

https://ryanwhite.hrsa.gov/sites/default/files/ryanwhite/grants/aging-guide-new-elements.pdf

Specific to WLWH

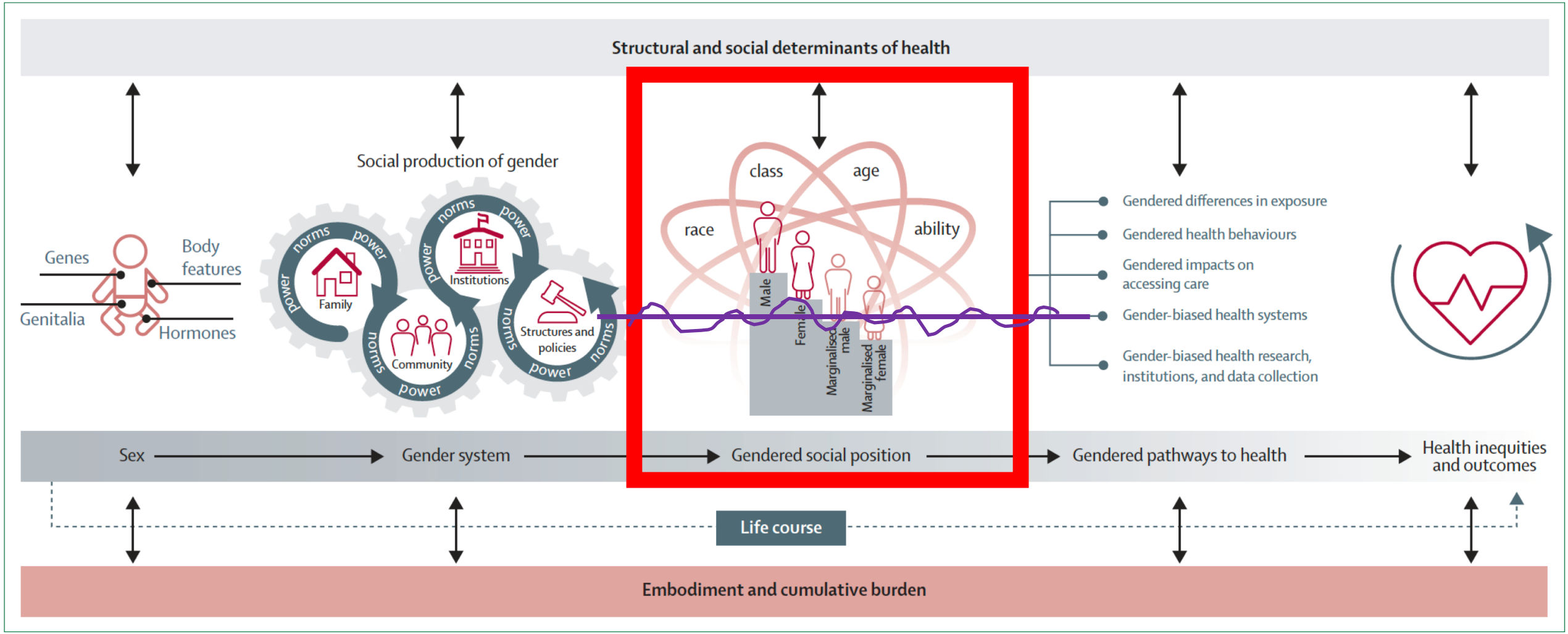
- Educate providers (and patients) about menopause
- Provide infrastructural support to women– prioritize education; make childcare more accessible; ask about food insecurity, violence, mood, and develop programs that address social determinants of health to improve care engagement and outcomes
- Investigate novel, HIV-specific and sex-tailored NACM screening and preventions strategies to identify those at highest risk in need of targeted, aggressive risk-modification

Stevenson J. Womens Health (Lond). 2022 Jan-Dec;18:17455057221095911.

Gender Equality, Norms, and Health 1

Gender inequality and restrictive gender norms: framing the challenges to health

Lori Heise, Margaret E Greene*, Neisha Opper, Maria Stavropoulou, Caroline Harper, Marcos Nascimento, Debrework Zewdie, on behalf of the Gender Equality, Norms, and Health Steering Committee†*



Heise L et al. Lancet. 2019 Jun 15;393(10189):2455-2468.

Embracing bold and bright

- **Knowledge is power**
  - **ACTG**: "Estrogen versus Escitalopram (EVE) for Peri- and Postmenopausal Women with HIV"
  - Ongoing studies at Emory:

- **Community heals**
  - Participatory qualitative study (London, UK) exploring women's experiences aging with HIV:

"Women ageing with HIV countered the 'violence of invisibility' through forming community with other women living with HIV, rejecting stigma, and enacting a personal form of advocacy through care for others."

Stevenson J. Womens Health (Lond). 2022 Jan-Dec;18:17455057221095911.

Acknowledgements

- Study participants
- Colleagues and collaborators
- Mentors and mentees
- Funding sources/ sponsors

MWCCS
MACS/WIHS COMBINED COHORT STUDY

CFAR
Emory Center for AIDS Research

Emory University School of Medicine
Division of Infectious Diseases

NIH National Heart, Lung, and Blood Institute

Grady

NATAP NATIONAL AIDS TREATMENT ADVOCACY PROJECT

Georgia CTSA
Georgia Clinical & Translational Science Alliance

SCORE
SPECIALIZED CENTER OF RESEARCH EXCELLENCE ON SEX DIFFERENCES

Thank you all for your interest and attention!

@lfcollins_md