

Women's Health and HIV: Age-related Comorbidities

Caitlin Moran, MD

Associate Professor of Medicine

Division of Infectious Diseases

Emory University School of Medicine



Disclosures

None

In memory

Lauren Collins, MD, MSc



Learning Objectives

1

To describe the impact of aging on the health of women living with HIV

2

To understand cardiometabolic risk factors and prevention strategies associated with HIV and aging

3

To discuss the impact of aging on frailty and cognition in women living with HIV



Aging in Women with HIV

Menopause

Weight gain and obesity

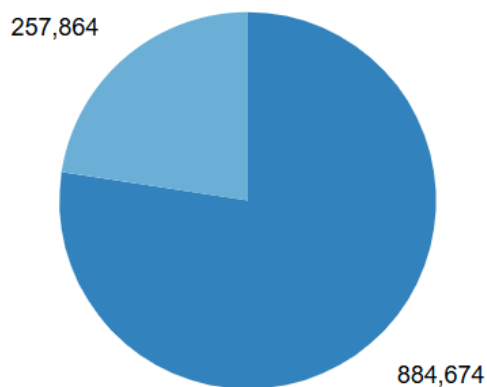
Cardiovascular risk

Frailty and bone disease

Mental health and cognition

Women account for 23% of all PLWH in the US and over 50% of all PLWH worldwide

HIV prevalence | 2024 | Ages 13 years and older | All races/ethnicities | Both sexes | All transmission categories | United States



U.S. CENTERS FOR DISEASE
CONTROL AND PREVENTION

Female
Male



HIV • Hepatitis • STD • TB
• Social Determinants of Health Data

Estimated global numbers of adults and children living with HIV, acquiring HIV and dying from HIV-related causes in 2025^a

	People living with HIV	People acquiring HIV	People dying from HIV-related causes
Total	41.0 million (35.3–47.5 million)	1.2 million (0.95–1.7 million)	570 000 (430 000–780 000)
Adults (≥15 years)	39.7 million (34.1–46.0 million)	1.1 million (0.87–1.5 million)	510 000 (390 000–700 000)
Females (≥15 years)	21.0 million (17.8–24.5 million)	500 000 (360 000–690 000)	220 000 (160 000–310 000)
Males (≥15 years)	18.8 million (16.2–21.6 million)	650 000 (500 000–860 000)	290 000 (220 000–390 000)
Children (0–14 years)	1.3 million (1.0–1.7 million)	93 000 (63 000–140 000)	61 000 (39 000–90 000)

^a 95% uncertainty interval in parentheses.

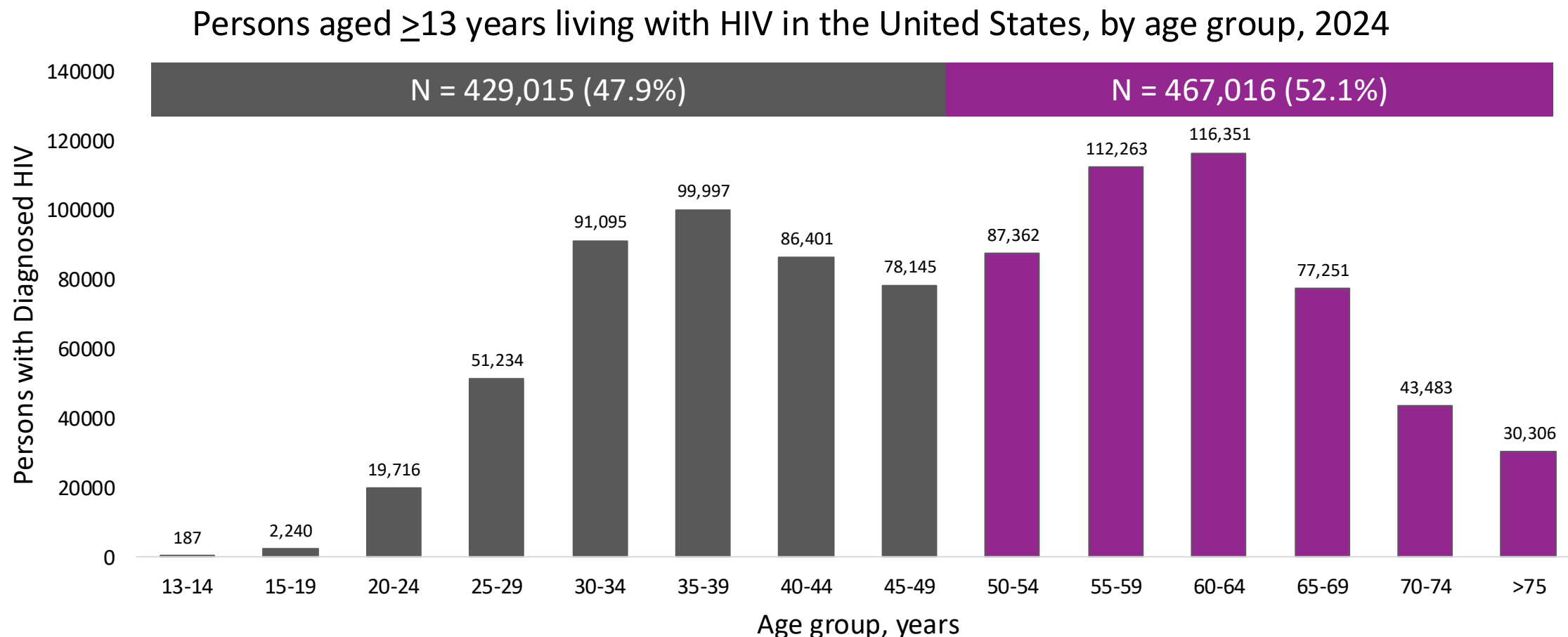
Source: UNAIDS 2026 epidemiological estimates; [AIDSinfo.unaids.org](https://aidsinfo.unaids.org)

Promoting Healthy Aging in Women with HIV

“Being able to do the things we value for as long as possible”



Over 50% of People with HIV in the U.S. are age 50 or older



Source: Centers for Disease Control and Prevention. HIV diagnoses, deaths, and prevalence, 2020–2024. Published May 18, 2026. Accessed September 17, 2026.
<https://www.cdc.gov/hiv-data/nhss/hiv-diagnoses-deaths-prevalence.html>.

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



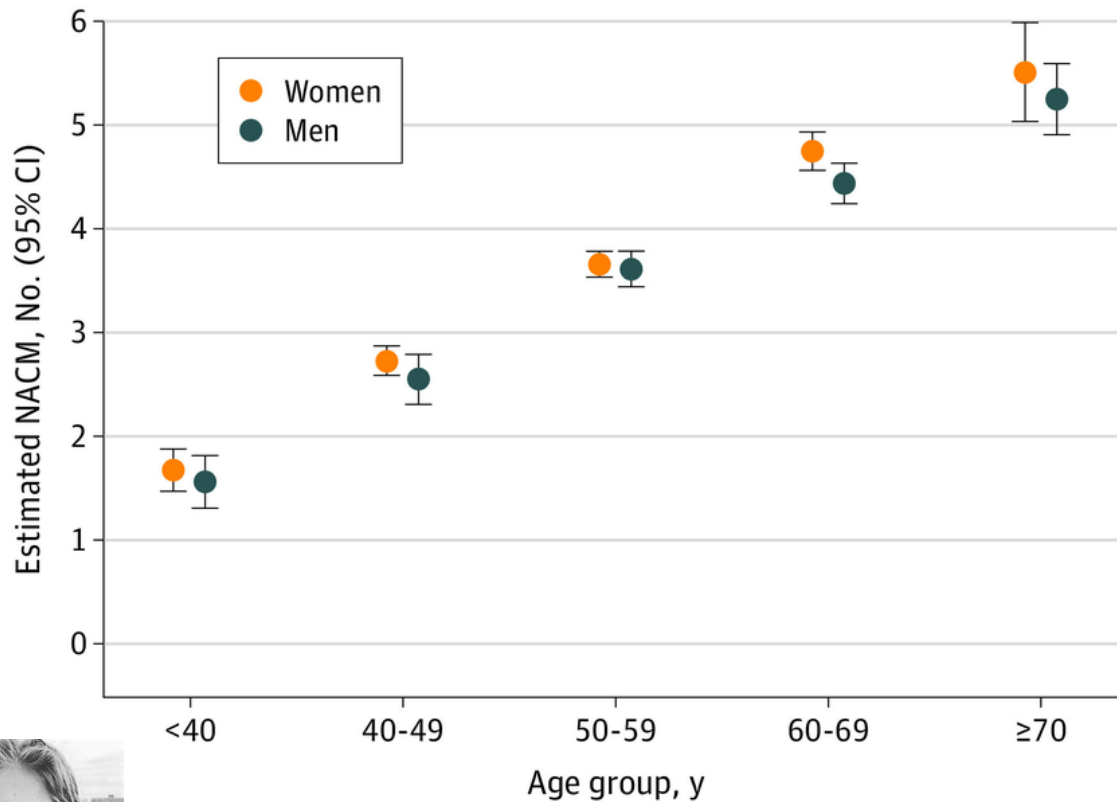


“To suggest that in order to age successfully, one must age in the absence of disease is unrealistic if not ageist, ignoring the diversity that exists in the health of older adults.”

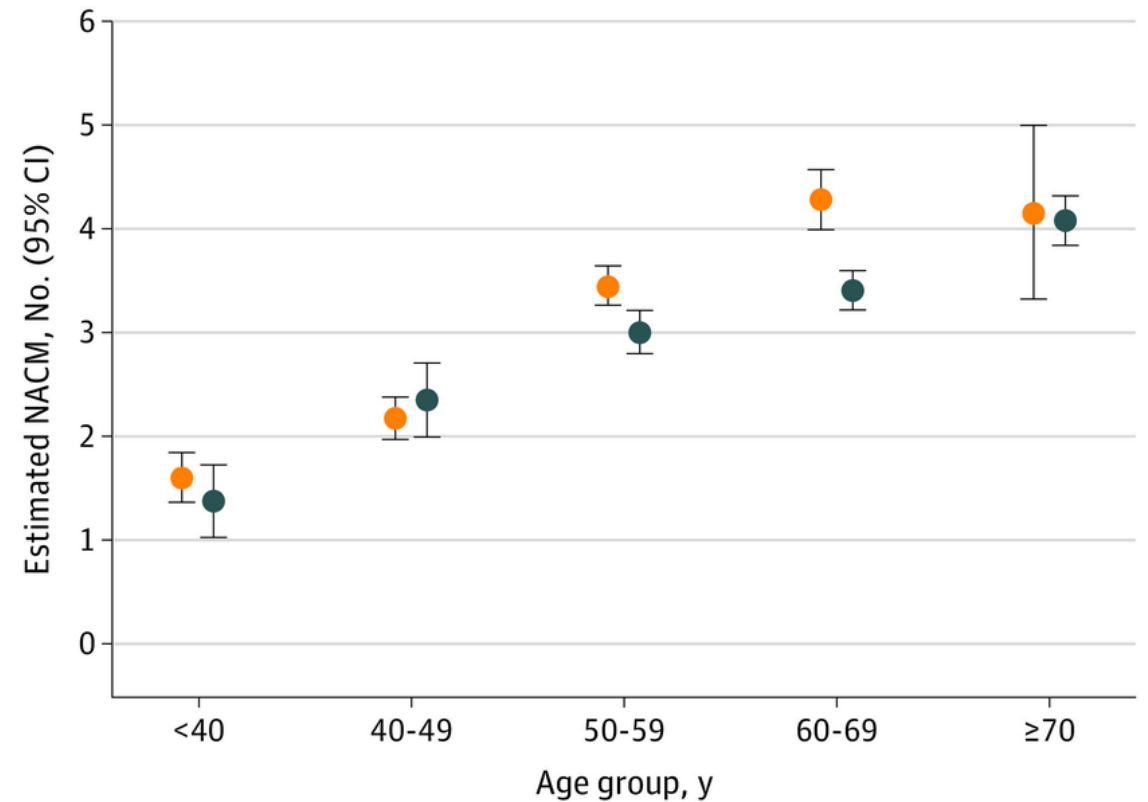
Emlet CA et al. *Ageing and Society*. 2017;37(10):2128-2151

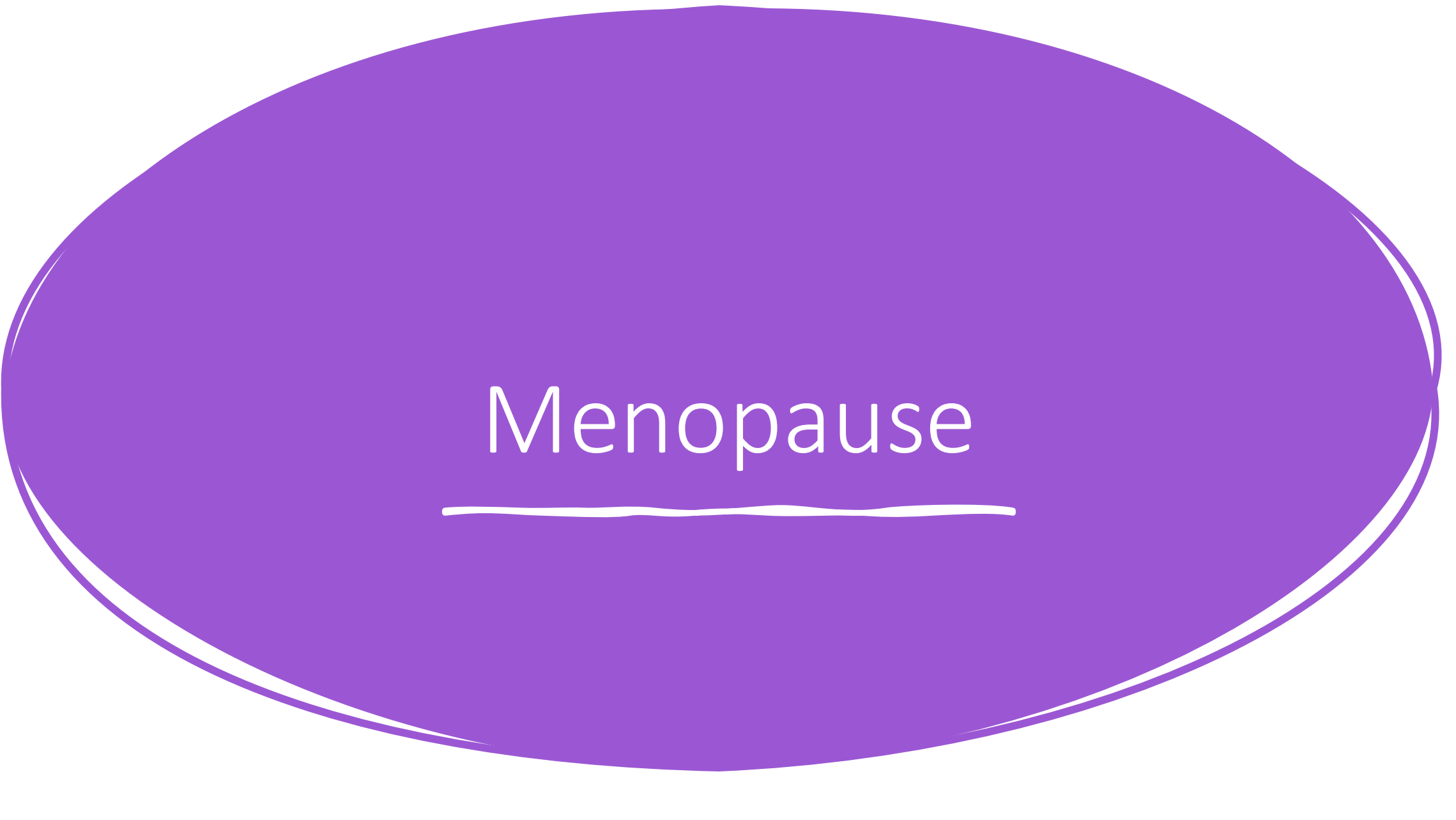
Women living with HIV have a high burden of comorbidities that increases with age

A Persons with HIV



B Persons without HIV



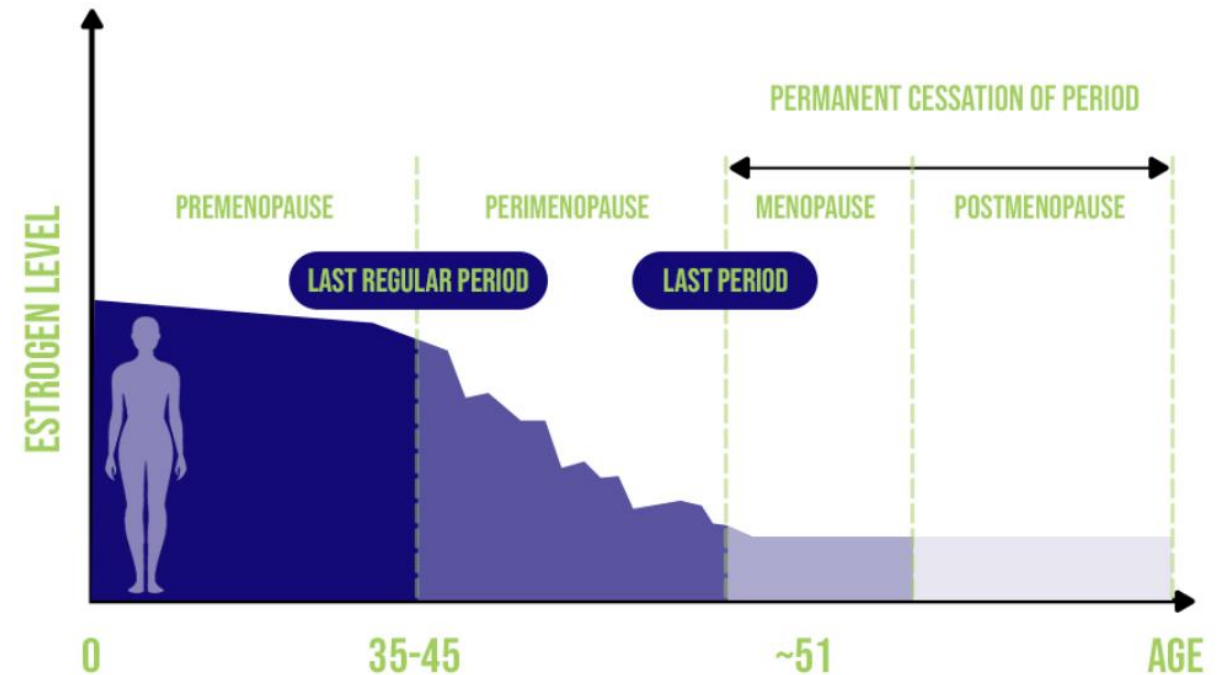


Menopause

Menopause

- 12 months after the final menstrual period
- Average age: 45-55 (possibly younger in women with HIV)
- Ovaries stop producing estrogen
- Results in important health changes
 - Weight gain
 - Cardiovascular risk
 - Bone loss
- Most women with menopausal symptoms do not receive effective, approved, evidence-based therapy

STAGES OF THE MENOPAUSE TRANSITION



Menopause in women with HIV

Biopsychosocial impact

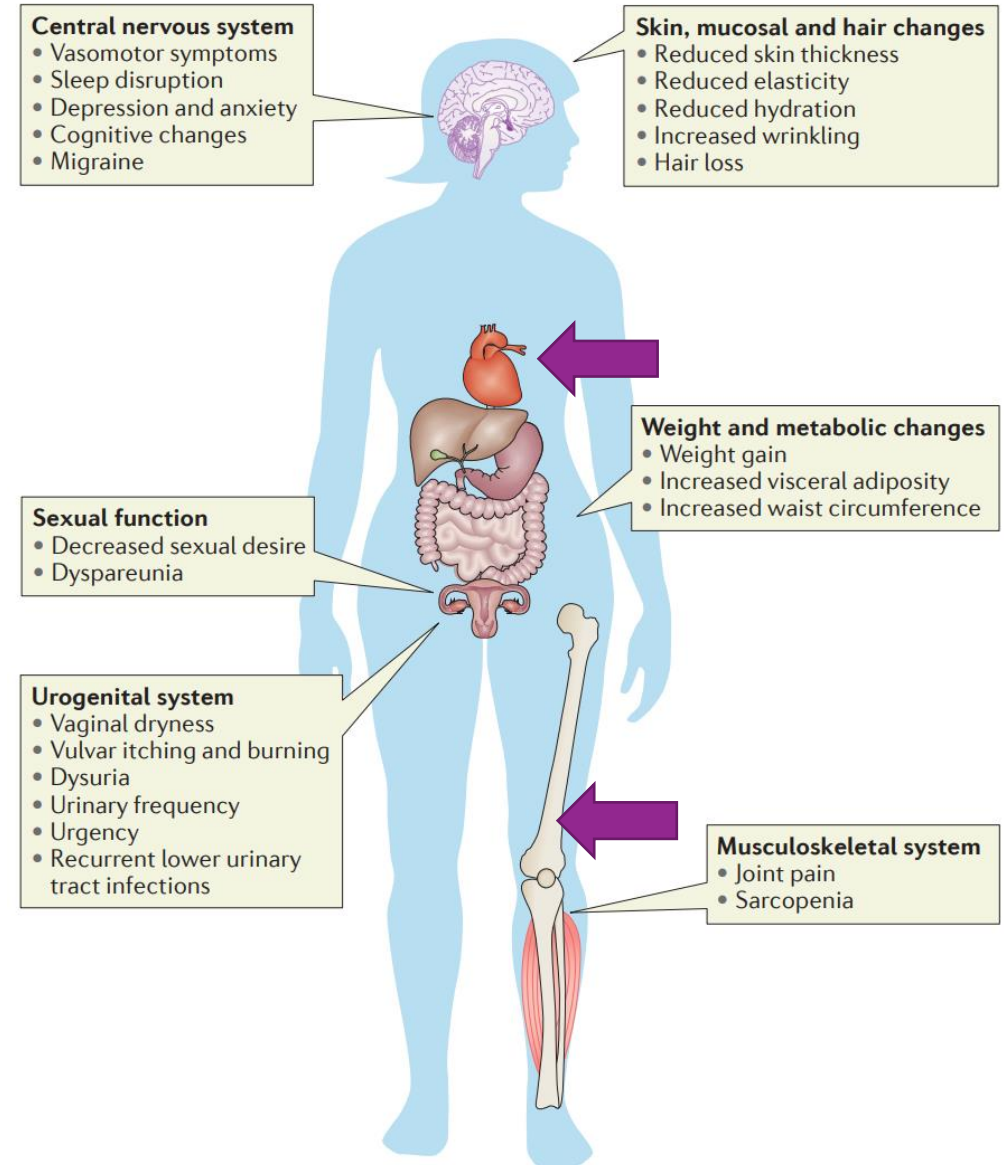
- Comorbidity risk
 - Heart disease
 - Osteoporosis (bone disease)
- Psychological impact
 - Anxiety/depression
 - Irritability
 - Difficulty concentrating

Menopause timing

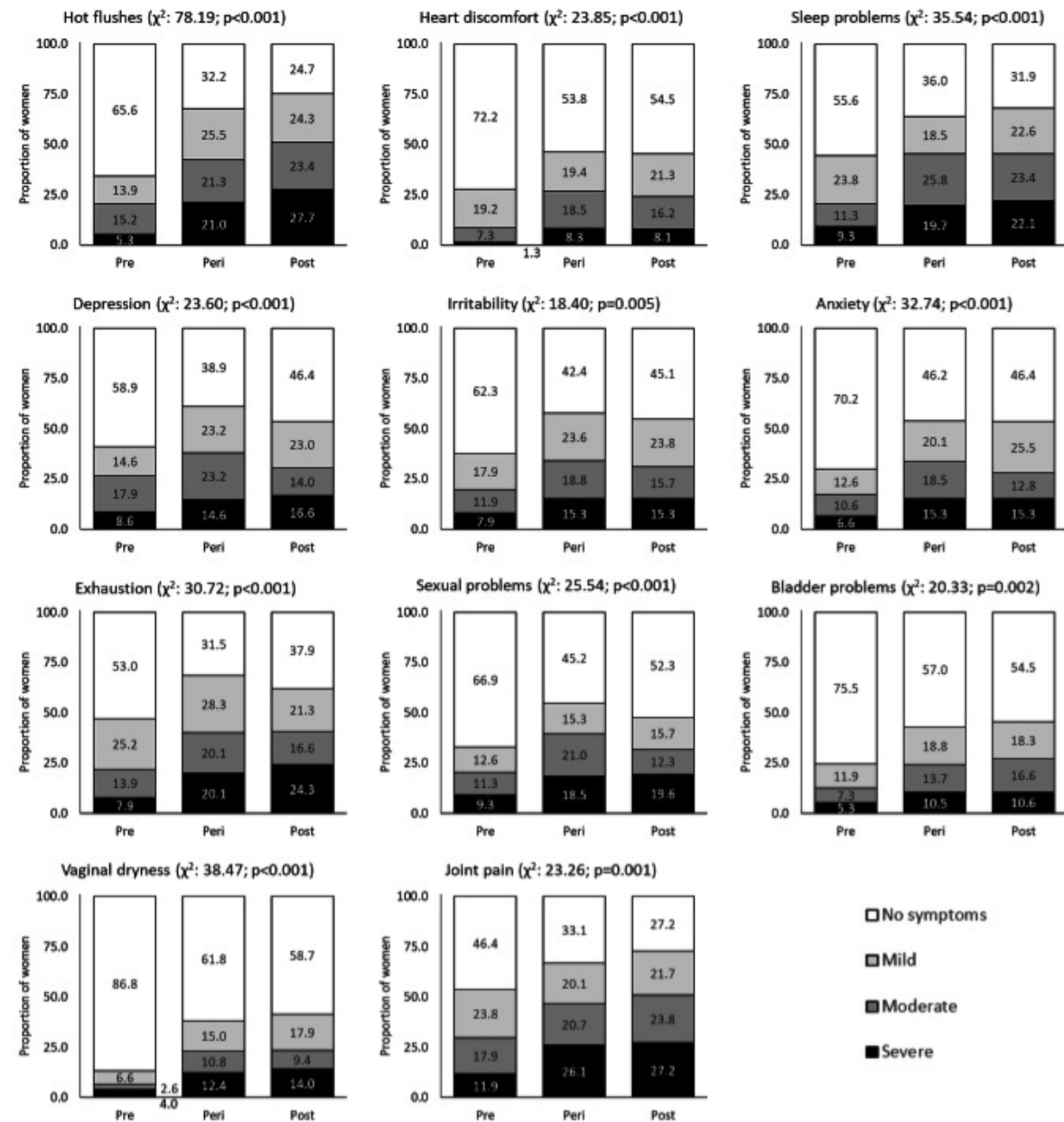
- Smoking
- Detectable HIV viral load
- Hepatitis C virus coinfection

Symptom burden and severity

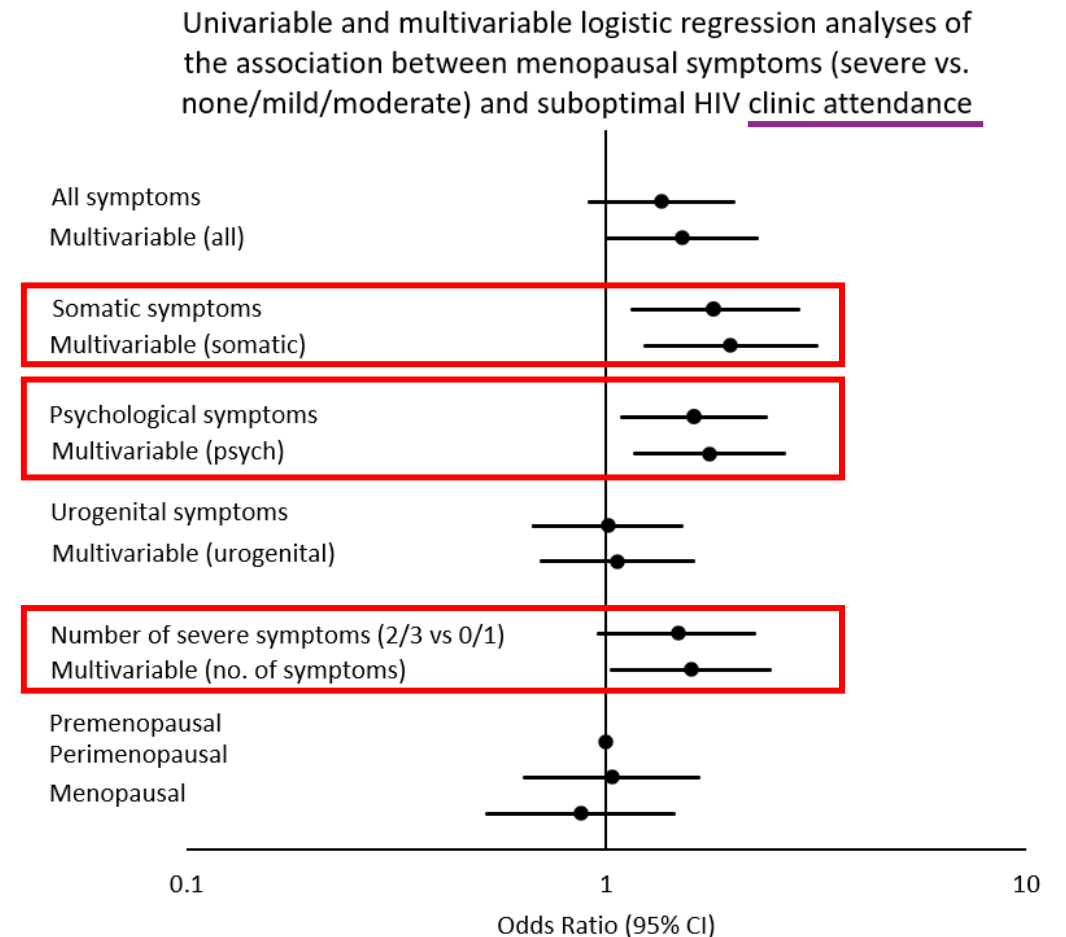
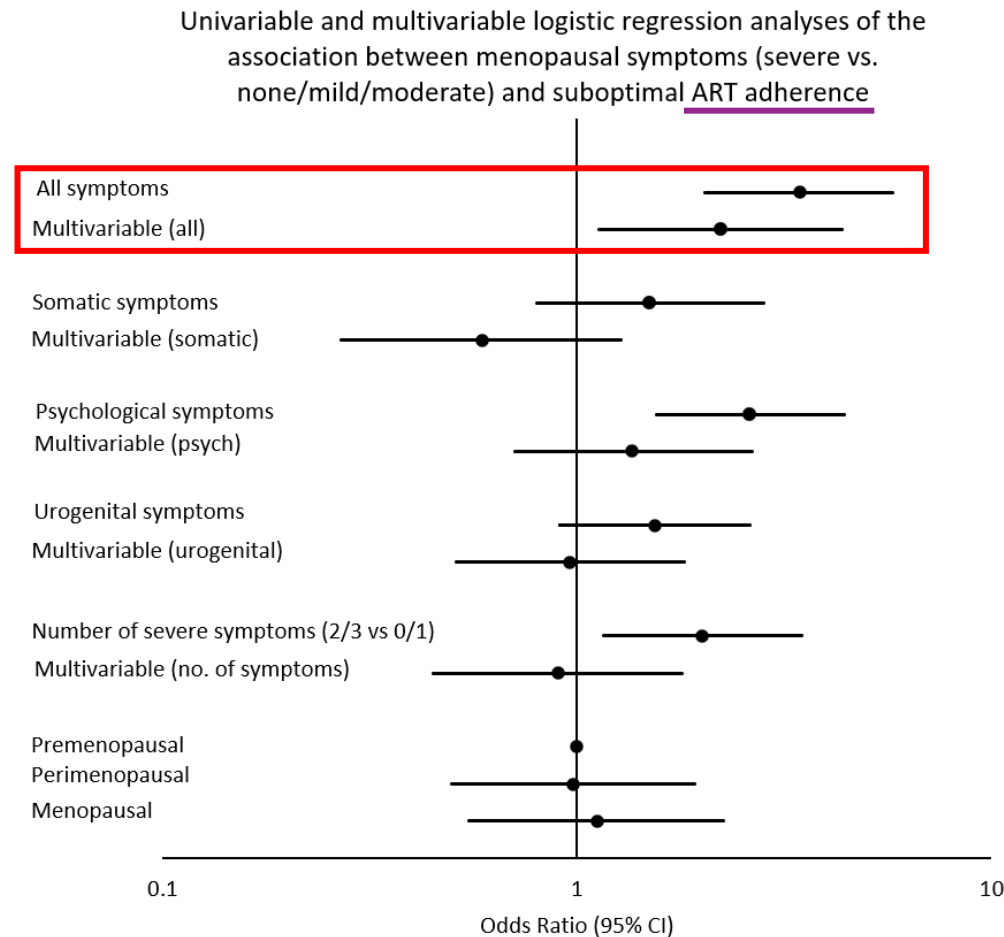
- Hot flashes
- Fatigue
- Muscle aches/joint pains
- Insomnia
- Sexual health and well-being



Menopause symptoms are common in women with HIV



Severe menopause symptoms are associated with reduced quality of life, poorer mental health, and poorer engagement in HIV care



Solomon D et al. *AIDS Care*. 2021;33(1):101-108

Haag K et al. *Menopause*. 2022;29(4):421-429

Okhai H et al. *Women's Health (Lond)*. 2022;18:17455065211068722.

Treatment options for menopause symptoms



Systemic menopause hormone therapy

- Estrogen (no uterus)
- Estrogen + progestin (uterus)



Topical hormone therapy

- Low-dose vaginal estrogen
 - For vaginal dryness
 - Prevents recurrent UTIs



Non-hormonal medication

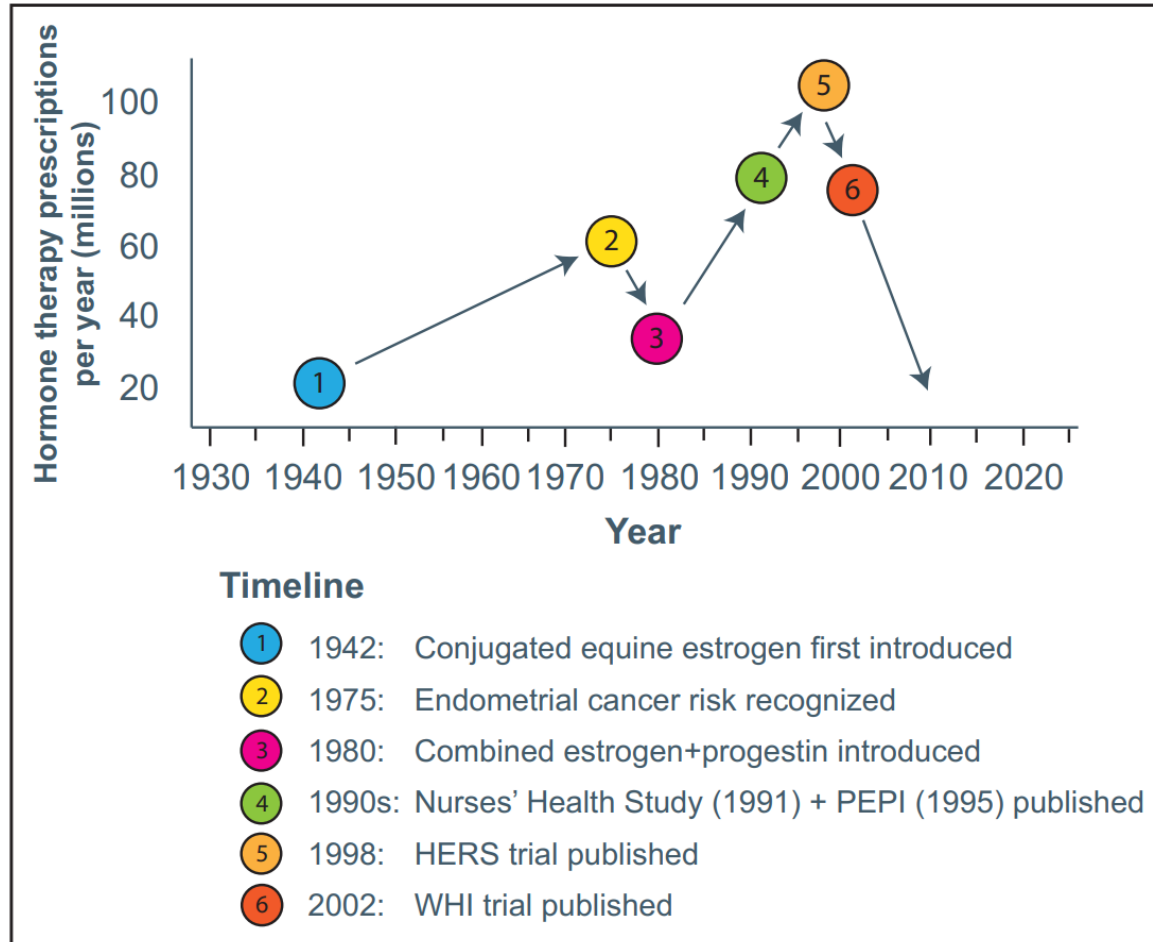
- Sleep aids
- Antidepressants (citalopram, venlafaxine, paroxetine)
- Gabapentin
- Clonidine
- Oxybutynin
- Neurokinin B receptor antagonists



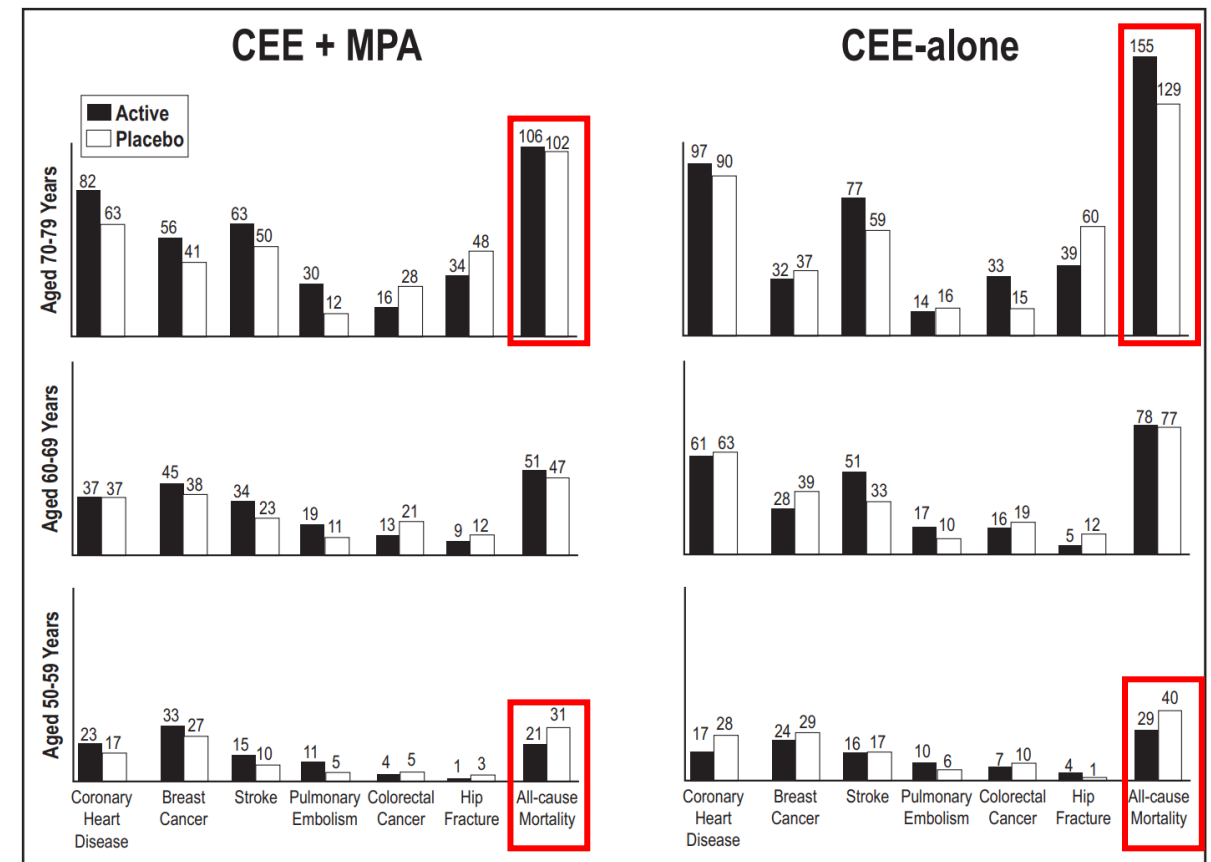
Non-pharmacologic treatments

- Cognitive behavioral therapy
- Hypnotherapy
- Acupuncture

A brief history of menopausal hormone therapy



The Timing Hypothesis



Menopause hormone therapy was effective at reducing VMS without increasing CVD risk in younger women

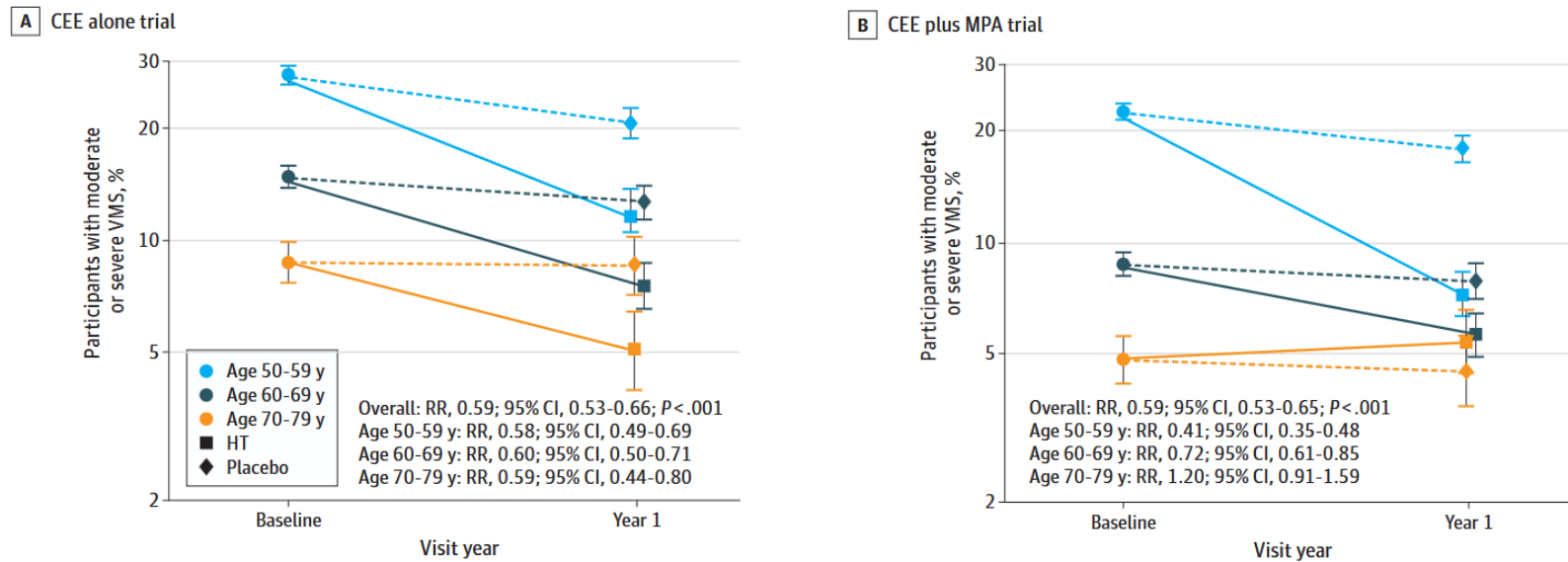


Figure 3. Overall Effect of Hormone Therapy (HT) on Atherosclerotic Cardiovascular Disease and Select Subgroups

Subgroup	Patients in the CEE alone trial, No. (annualized %)		Difference in absolute risk per 10000 PY	Favors HT	Favors placebo	P value ^a	Patients in the CEE plus MPA trial, No. (annualized %)		Difference in absolute risk per 10000 PY	Favors HT	Favors placebo	P value ^a
	HT	Placebo					HT	Placebo				
Main effect	704 (1.98)	658 (1.79)	19			.07	573 (1.22)	534 (1.21)	1			.74
Moderate or severe VMS												
No	567 (1.95)	540 (1.80)	15			.37	495 (1.22)	462 (1.21)	1			.69
Yes	129 (2.14)	108 (1.73)	40				71 (1.20)	59 (1.10)	10			
Age at randomization, y												
50-59	98 (0.82)	119 (0.98)	-16			.10	86 (0.52)	83 (0.53)	-2			.59
60-69	348 (2.23)	307 (1.88)	35				266 (1.28)	251 (1.29)	-1			
70-79	258 (3.22)	232 (2.82)	40				221 (2.39)	200 (2.23)	15			
Time since menopause, y ^b												
<10	55 (0.87)	52 (0.83)	4			.87	104 (0.58)	103 (0.62)	-4			.49
10 to <20	201 (1.70)	172 (1.41)	29				238 (1.28)	225 (1.29)	-1			
≥20	448 (2.58)	435 (2.37)	21				231 (2.22)	207 (2.07)	15			
VMS by age, y												
No												
50-59	64 (0.75)	78 (0.89)	-14			.31	64 (0.50)	60 (0.50)	0			.76
60-69	278 (2.09)	252 (1.81)	27				232 (1.23)	212 (1.20)	4			
70-79	225 (3.11)	210 (2.84)	27				199 (2.26)	190 (2.25)	0			
Yes												
50-59	34 (1.04)	38 (1.17)	-13			.03	20 (0.54)	20 (0.60)	-6			.02
60-69	64 (3.00)	52 (2.26)	74				30 (1.64)	32 (2.04)	-40			
70-79	31 (4.77)	18 (2.60)	217				21 (5.44)	7 (1.62)	382			

Rossouw JE et al. *JAMA Intern Med.* 2025 Nov 1;185(11):1330-1339.

The New York Times

F.D.A. Will Remove Black Box Warnings From Hormone Treatments for Menopause

CNN Health

HEALTH • 7 MIN READ

‘Black box’ safety warning to be removed from hormone therapy for menopause

UPDATED NOV 10, 2025

By Jacqueline Howard, Brenda Goodman

npr

FDA reverses decades of guidance on hormone therapy for menopause

NOVEMBER 10, 2025 • 6:04 PM ET

<https://www.fda.gov/drugs/drug-alerts-and-statements/fda-requests-labeling-changes-related-safety-information-clarify-benefit-risk-considerations>

<https://www.fda.gov/news-events/press-announcements/fda-approves-labeling-changes-menopausal-hormone-therapy-products>

Changes to MHT product labeling requested by FDA (11/20/2025):

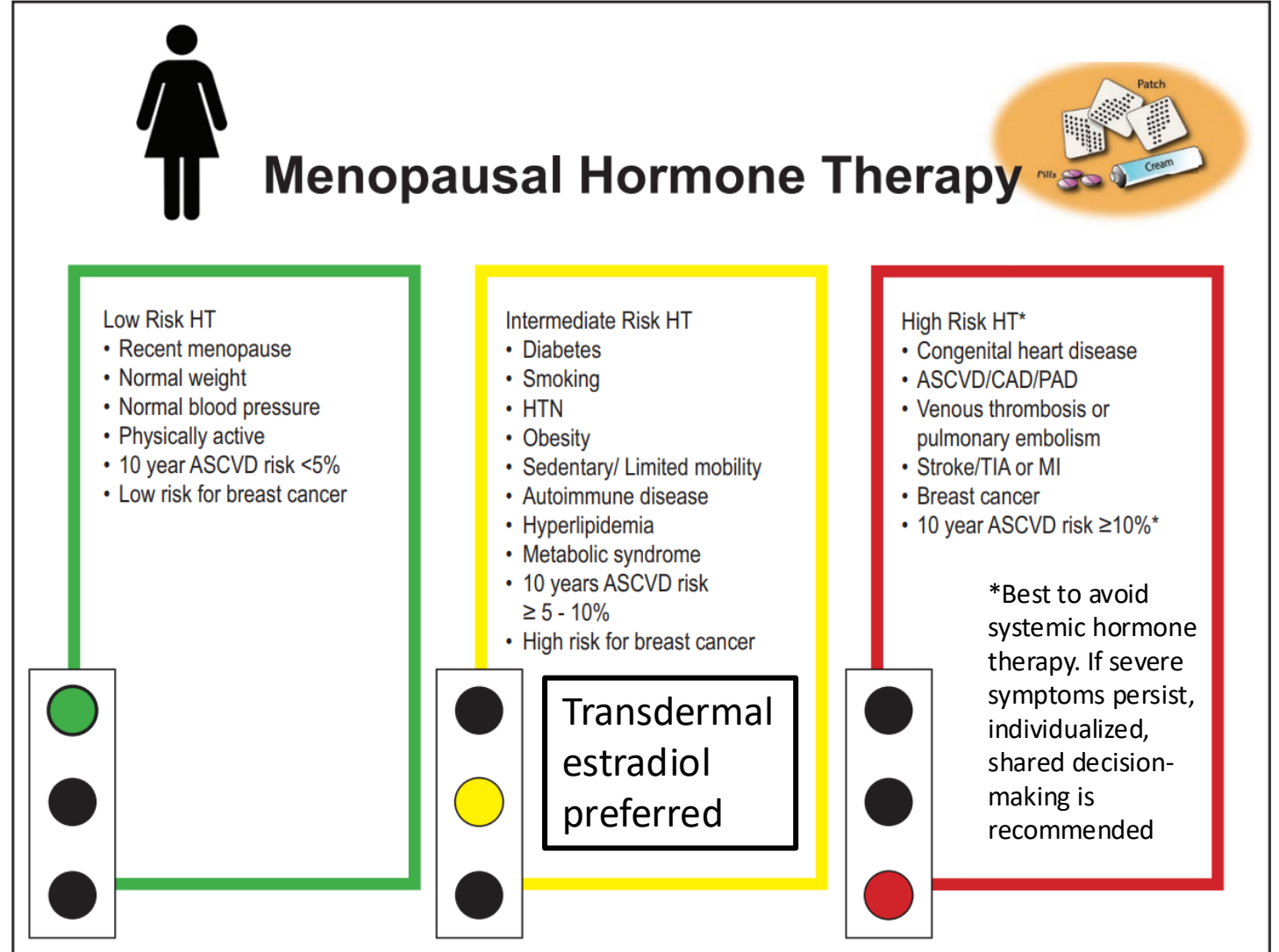
- Removal of Black Box warnings for:
 - CVD risk, breast cancer, and probable dementia
 - Endometrial cancer except for estrogen-alone products
- In labeling:
 - Add consideration for starting hormone therapy for moderate to severe VMS in women <60 years old or <10 years since menopause
 - Add WHI data in women 50-59 years old
 - Retain Boxed Warning for endometrial cancer in systemic estrogen-alone products
 - Retain information about CVD and breast cancer warnings

What does the change in labeling for menopause hormone therapy (MHT) mean?

- The black box warning previously included all estrogen-containing products including systemic (oral, transdermal) and topical (intra-vaginal)
- Incorporated updated safety data, particularly for topical estradiol
- Considered newer formulations of estrogen and progestogens that may carry less risk than the older formulations used in WHI trial
- Relied primarily on updated analyses of the WHI trials, not new studies
- Does NOT mean that MHT is safe for everyone
- The decision to take MHT should be individualized

Recommendations for menopausal hormone therapy

- Age <60, within 10 years of last menstrual period
- For vasomotor symptoms
- Lowest dose for the shortest time
- Indicated for premature (<40) and early (40-45) menopause



Menopausal hormone therapy is underutilized in women with HIV

Use of MHT

- Vancouver study: 12% offered, 5.5% uptake¹
- WHS study: 23% reported ever use, 8% reported current use²
- Swiss HIV Cohort Study: 11% use³

Reasons for underuse

- Provider knowledge/comfort
- Concern for drug-drug interactions with ART
- Pill burden
- Concerns about side effects

¹Duff PK et al. *Menopause*. 2018;25(5):531-537

²Peters BA et al. *Clin Infect Dis*. 2023;76(3):e661-e670

³Hachfeld A et al. *HIV Med*. 2022;23(4):417-425

King EM et al. *Lancet HIV*. 2021;8(9):e591-e598

Untreated menopause symptoms are linked to a lack of discussion with HIV care providers

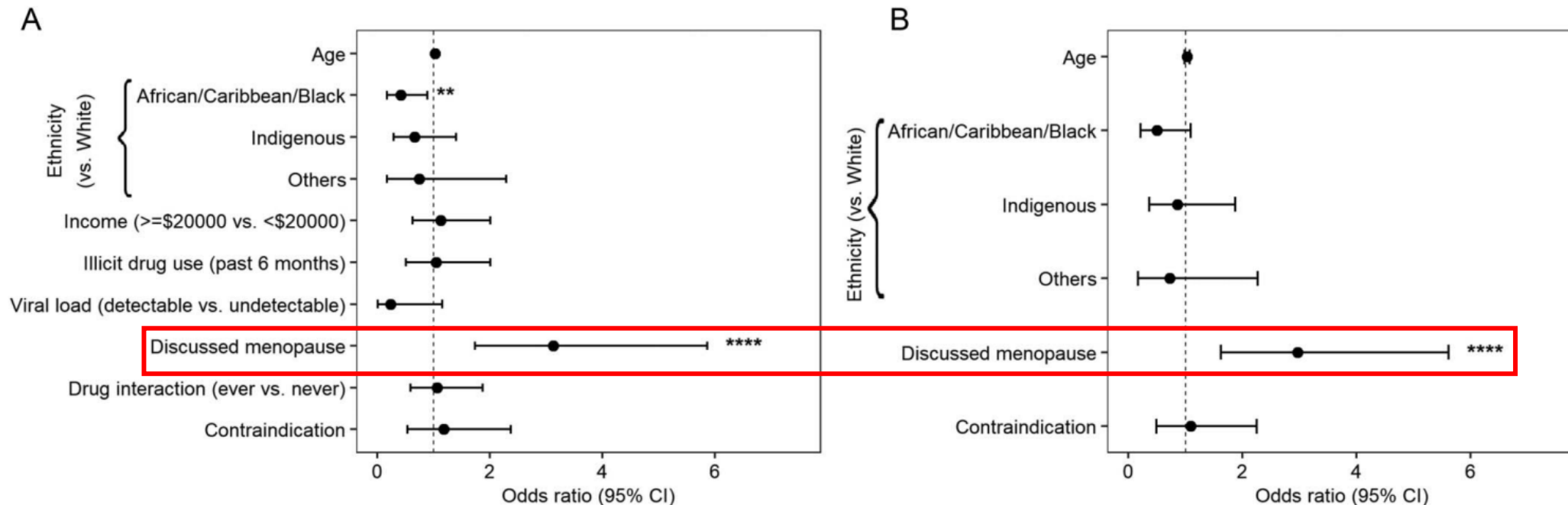
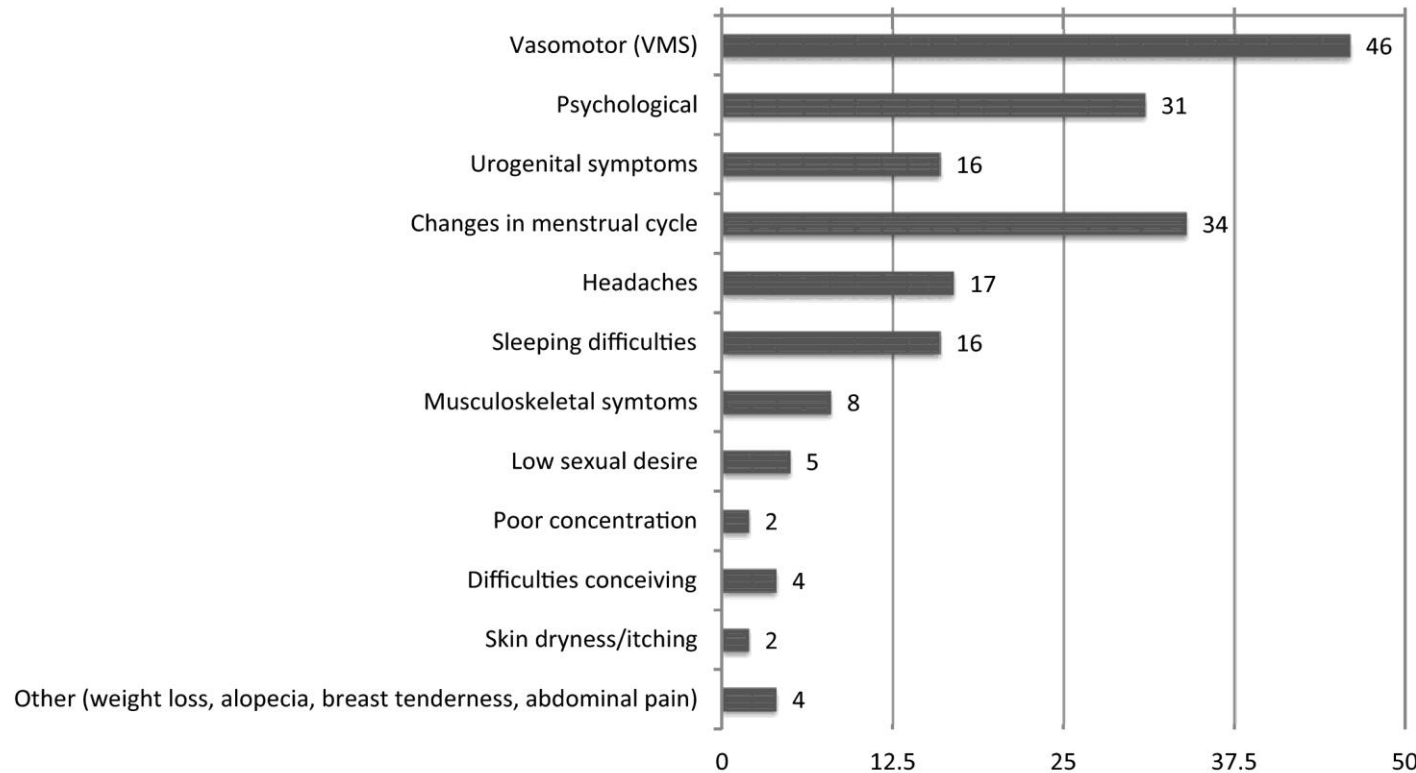


FIGURE 1. Univariable (A) and multivariable (B) analyses of factors associated with ever using menopausal hormone therapy in perimenopausal/menopausal women living with HIV (n = 464). ** $P < 0.05$; **** $P < 0.001$.

97.8% had regular HIV follow-up (71.8% with ID, 17.2% with general practitioner)
44.8% ever discussed menopause (35.9% Black, 37.2% Indigenous vs 50.6% white)
47.8% had a first-line indication for MHT
11.8% ever used MHT (16.5% with early menopause)

Speak up! Women with HIV who are treated with MHT have menopause symptom improvement



Key:

- Vasomotor symptoms: hot flushes, sweats and palpitations
- Psychological symptoms: labile mood, depression, anxiety, irritability and fatigue
- Urogenital symptoms: vaginal dryness, urinary tract symptoms and dyspareunia
- Changes in menstrual cycle: Any change of normal menstrual cycle due to menopause transition
- Musculoskeletal symptoms: joint and/or muscle pains

HIV Menopause Clinic

- 55 women
- Average age: 49 years
- Average symptom duration: 31 months
- 73% prescribed MHT (transdermal patch > oral)
- Median MHT duration: 10 months
- 73% reported symptom improvement

Treatment options for menopause symptoms



Systemic menopause hormone therapy

- Estrogen (no uterus)
- Estrogen + progestin (uterus)



Topical hormone therapy

- Low-dose vaginal estrogen
 - For vaginal dryness
 - Prevents recurrent UTIs



Non-hormonal medication

- Sleep aids
- Antidepressants (citalopram, venlafaxine, paroxetine)
- Gabapentin
- Clonidine
- Oxybutynin
- Neurokinin B receptor antagonists

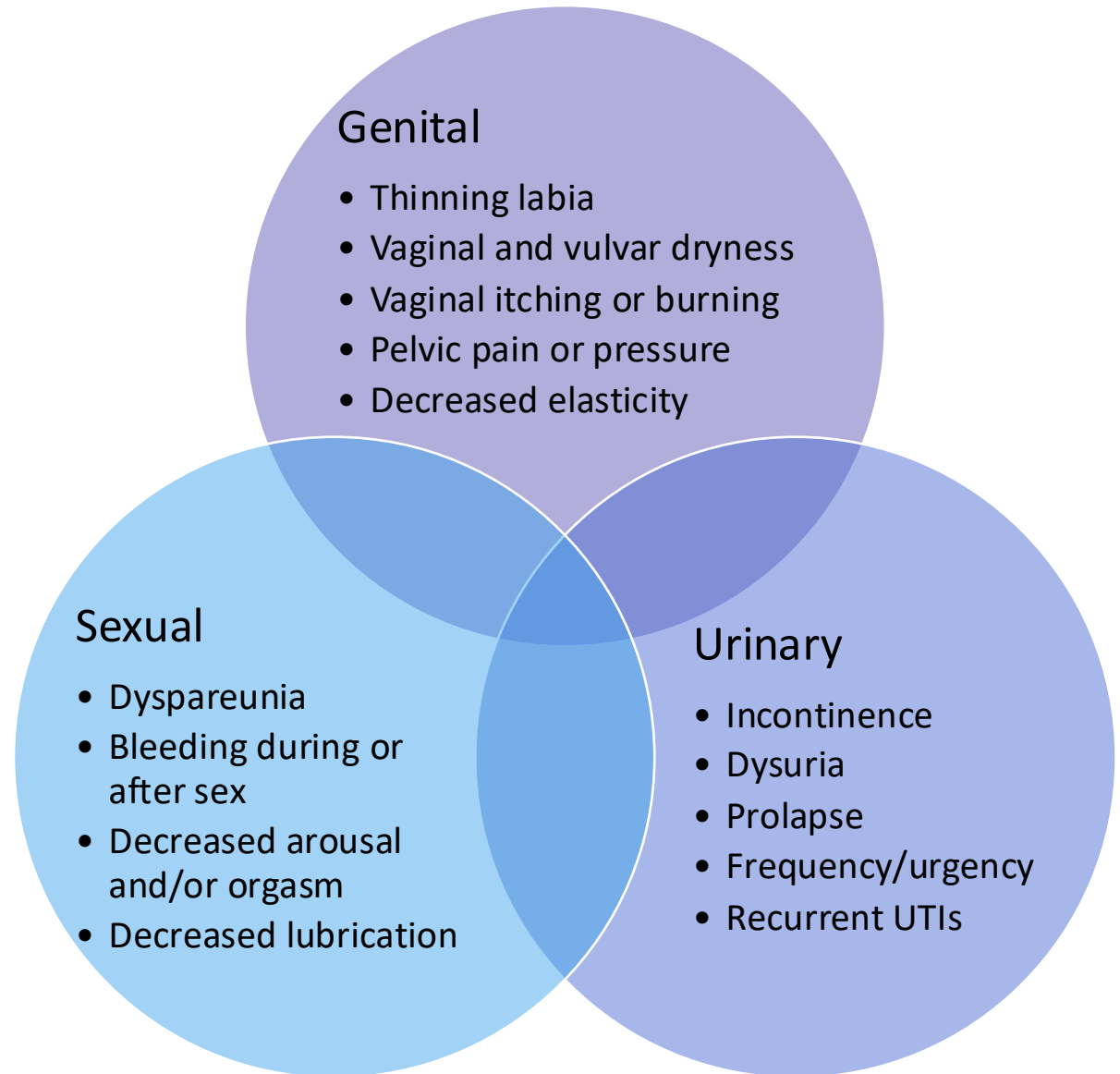


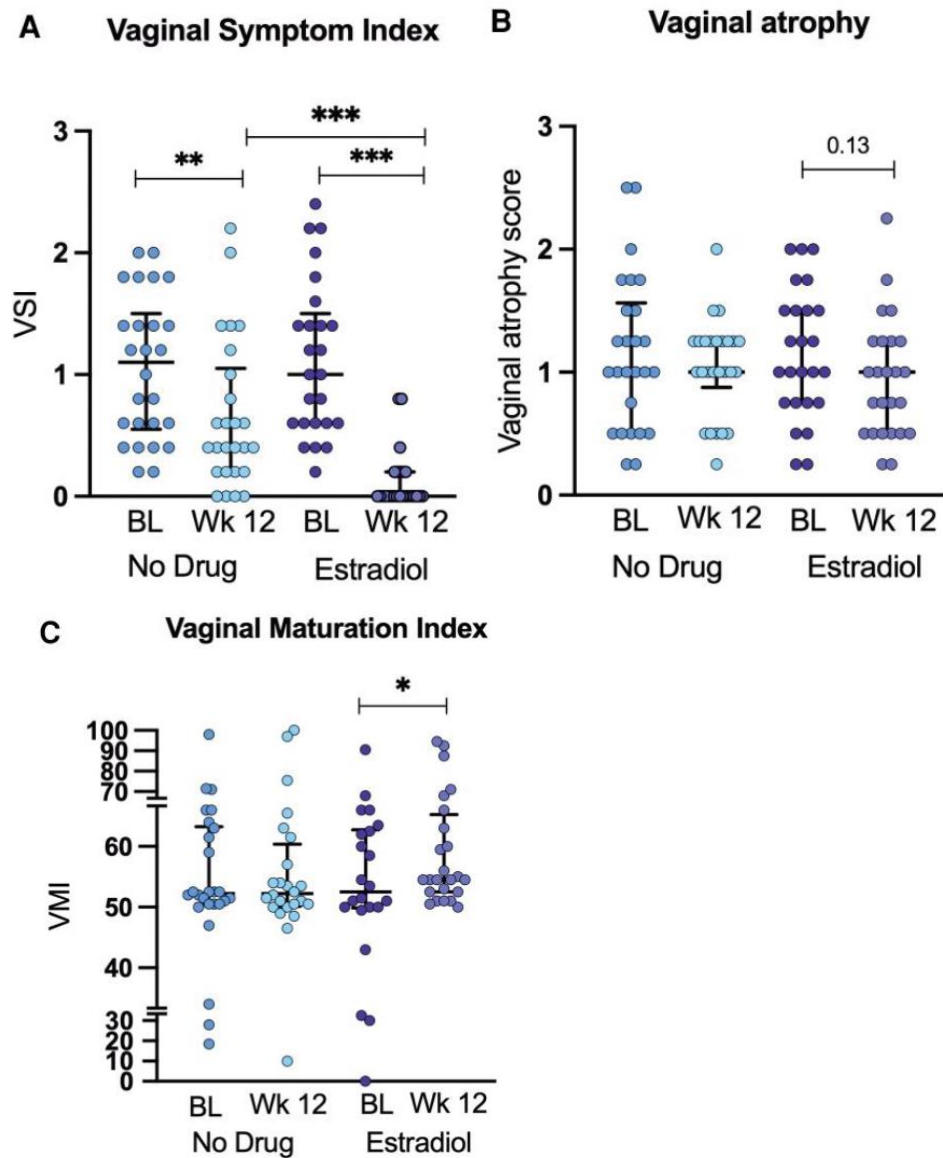
Non-pharmacologic treatments

- Cognitive behavioral therapy
- Hypnotherapy
- Acupuncture

Genitourinary Syndrome of Menopause

- Highly prevalent (up to 84% of women 6 years after menopause)
- Generally progressive (in contrast to vasomotor symptoms)
- Caused by estrogen withdrawal to vagina, vulva, and bladder
- Can be treated with nonhormonal (lubricants) and hormonal (vaginal estrogen) therapies
- Almost all women are candidates for low-dose vaginal estrogen therapy for genitourinary symptoms of menopause regardless of cardiovascular risk





Vaginal estradiol improves vaginal symptoms in menopausal women with HIV

Table 2. Change in Most Bothersome Vulvovaginal Symptom Severity Over 12 Weeks

	No Treatment BL (n = 26)	No Treatment Week 12 (n = 26)	PValue		Estradiol BL (n = 25)	Estradiol Wk 12 (n = 25)	PValue	Difference at 12 Weeks No Treatment Versus Estradiol
Vaginal dryness (n = 14/26)	2 (2, 3)	1 (0.75, 3)	.08	Vaginal dryness (n = 11/25)	2 (1, 2)	0 (0, 1)	.002	0.003
Vaginal itching (n = 7/26)	2 (1, 2)	1 (1, 2)	.38	Vaginal itching (n = 11/25)	2 (2, 3)	0 (0, 0)	.001	.01
Dyspareunia (n = 4/11) ^a	2 (1.3, 2.8)	0 (0, 2.3)	...	Dyspareunia (n = 2/13)	2.5 (2, 3)	0 (0, 0)	...	...
Vaginal soreness	NA	...	...	Vaginal soreness (n = 1/25)	2 (2, 2)	0 (0, 0)	...	...
Vaginal irritation (n = 1/26)	1 (1, 1)	1 (1, 1)	...	Vaginal irritation	NA	...	...	...

Median (IQR) severity of participants' most bothersome symptom identified at baseline and at 12 weeks. Severity scores reported on scale from 0 (none) to 3 (severe) symptoms. P values calculated with Wilcoxon test for difference in median severity of symptoms between baseline and 12 weeks within groups and with Mann Whitney and unpaired t-tests between the no treatment and estradiol treatment groups at the 12-week end point.

^aOne participant reported dyspareunia as their MBS at baseline but had no partners in the prior 3 months. Removal of this participant's data did not change the results.

Treatment options for menopause symptoms



Systemic menopause hormone therapy

- Estrogen (no uterus)
- Estrogen + progestin (uterus)



Topical hormone therapy

- Low-dose vaginal estrogen
 - For vaginal dryness
 - Prevents recurrent UTIs



Non-hormonal medication

- Sleep aids
- Antidepressants (citalopram, venlafaxine, paroxetine)
- Gabapentin
- Clonidine
- Oxybutynin
- Neurokinin B receptor antagonists



Non-pharmacologic treatments

- Cognitive behavioral therapy
- Hypnotherapy
- Acupuncture

Nonhormone therapy for vasomotor symptoms

Recommended

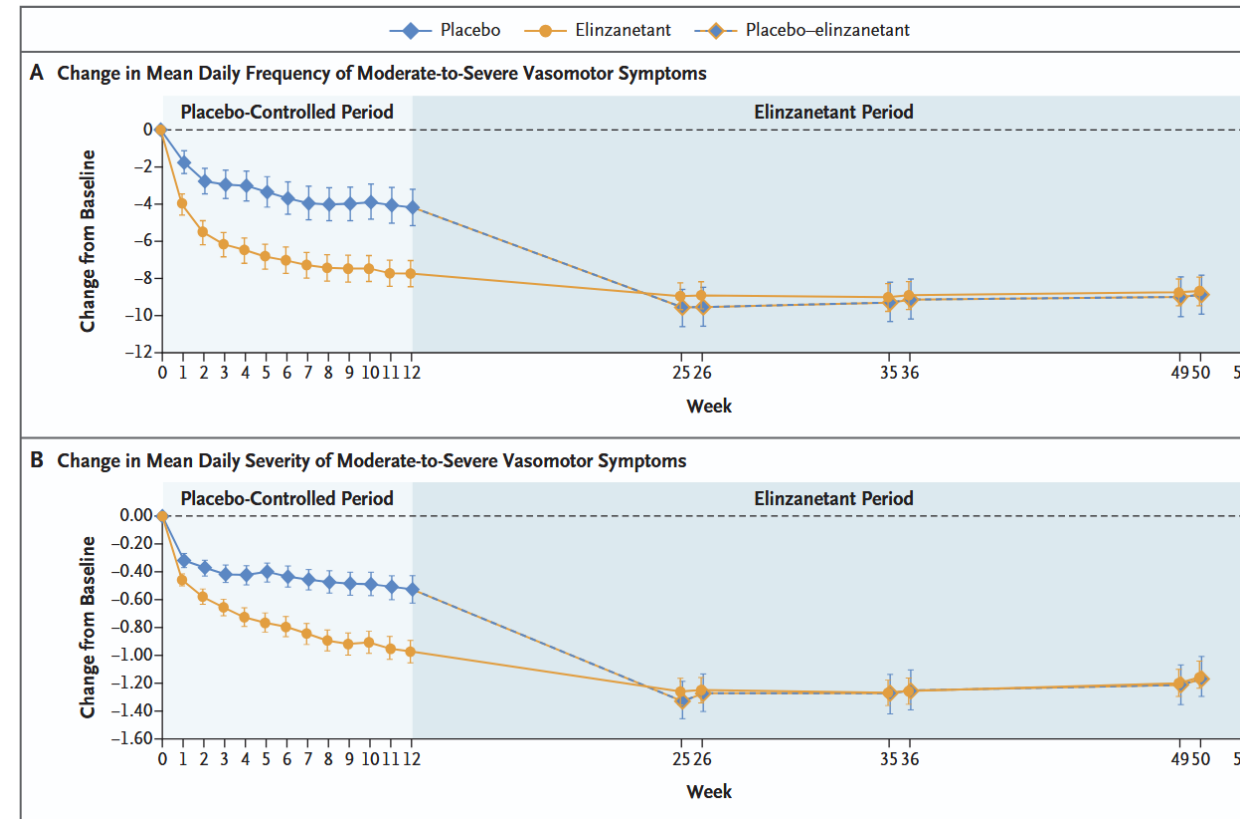
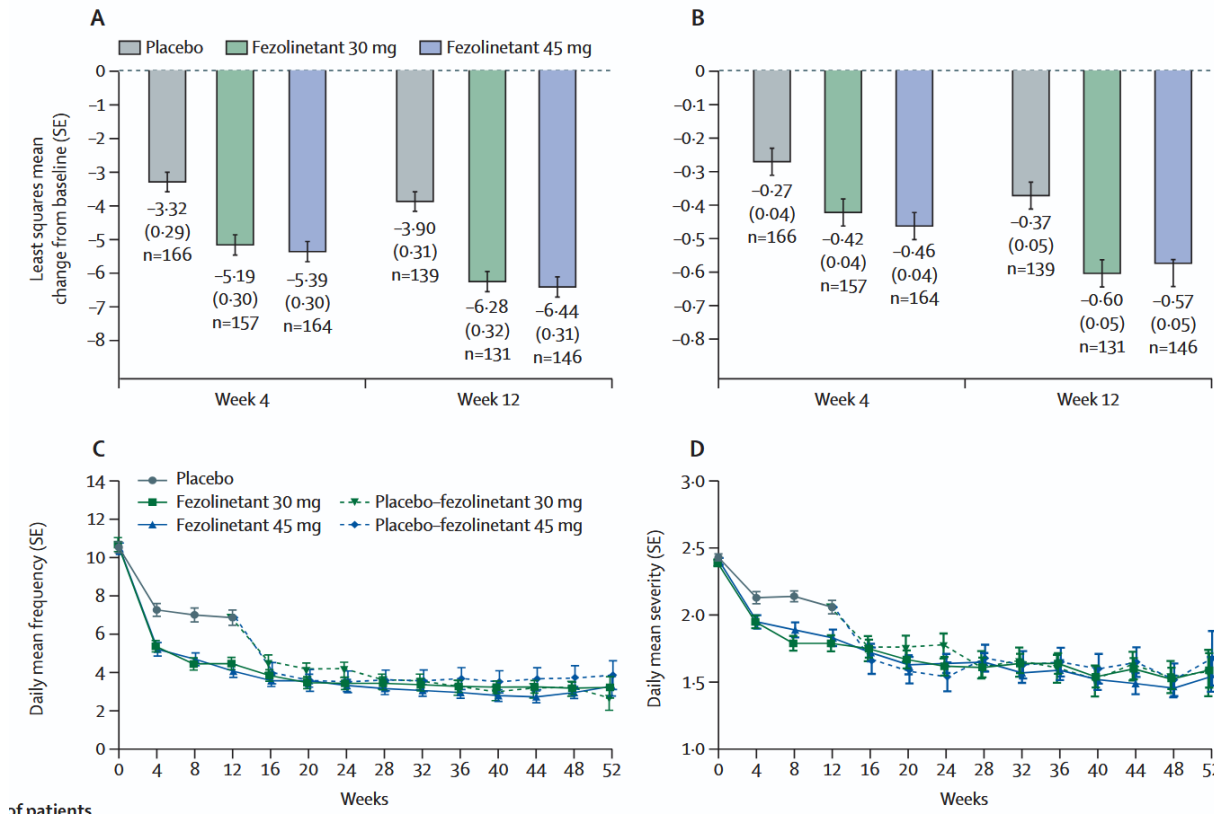
- Cognitive-behavioral therapy
- Clinical hypnosis
- Weight loss
- SSRIs/SNRIs
 - Paroxetine*, escitalopram, citalopram, venlafaxine, desvenlafaxine (large RCTs)
 - Duloxetine (smaller studies)
- Gabapentin
- Oxybutynin
- Neurokinin B receptor antagonists*
 - fezolinetant, elinzanetant
- Stellate ganglion block

*FDA approved indication for VMS

Not recommended

- Cooling techniques
- Avoiding triggers (e.g., alcohol, caffeine, spicy foods, hot beverages)
- Exercise and yoga
- Dietary modifications (e.g., soy, plant-based)
- Mindfulness-based interventions, paced respiration, relaxation
- Pregabalin
- Clonidine
- Suvorexant
- Dietary supplements
- Cannabinoids
- Acupuncture

Neurokinin B antagonists are effective non-hormone therapies for vasomotor symptoms



Lederman S et al. *Lancet*. 2023 Apr 1;401(10382):1091-1102.
Cardoso F et al. *N Engl J Med*. 2025 Aug 21;393(8):753-763.

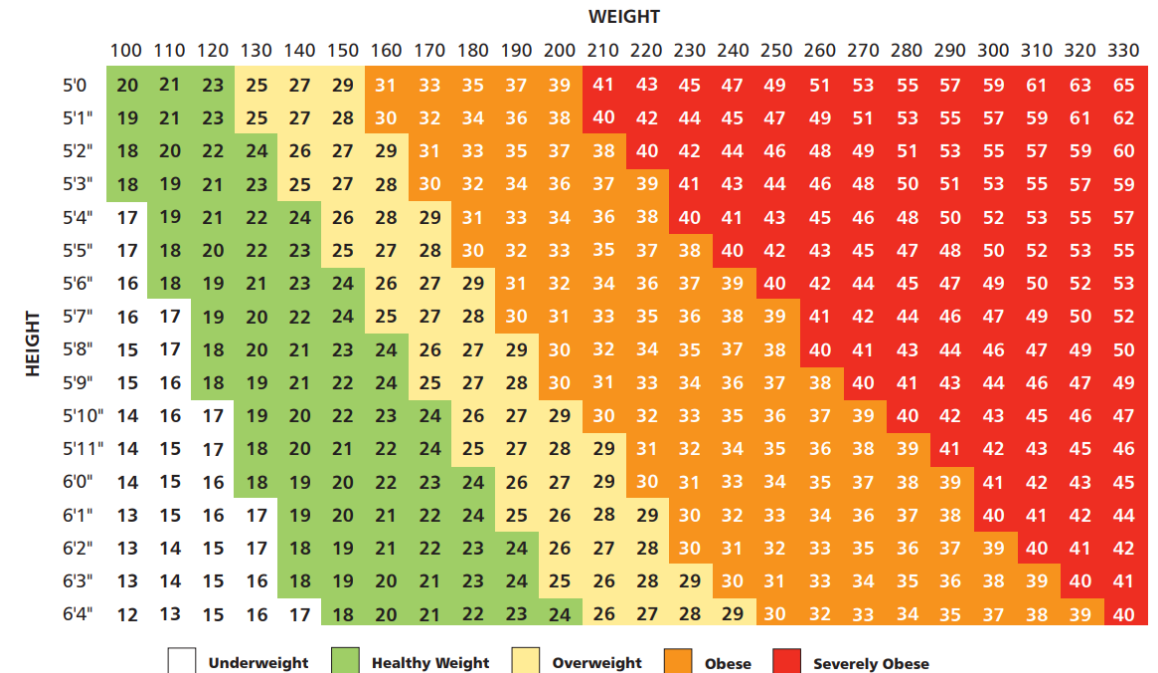
Weight Gain and Obesity in Women with HIV

Effects of antiretroviral therapy

Obesity management options

What is obesity?

- Obesity is:
 - Weight that is higher than what is considered healthy for a given height (BMI ≥ 30 kg/m²)
 - A chronic medical condition
 - Very common (41% of U.S. adults have obesity)
 - Associated with stigma and difficulty accessing medical care
- Obesity is NOT:
 - A sign of laziness, disregard for health, or lack of self-control
- Not all obesity is the same:
 - Sarcopenic obesity (lack of muscle)
 - Abdominal obesity



Many Americans lack healthy, affordable foods and places to be active.

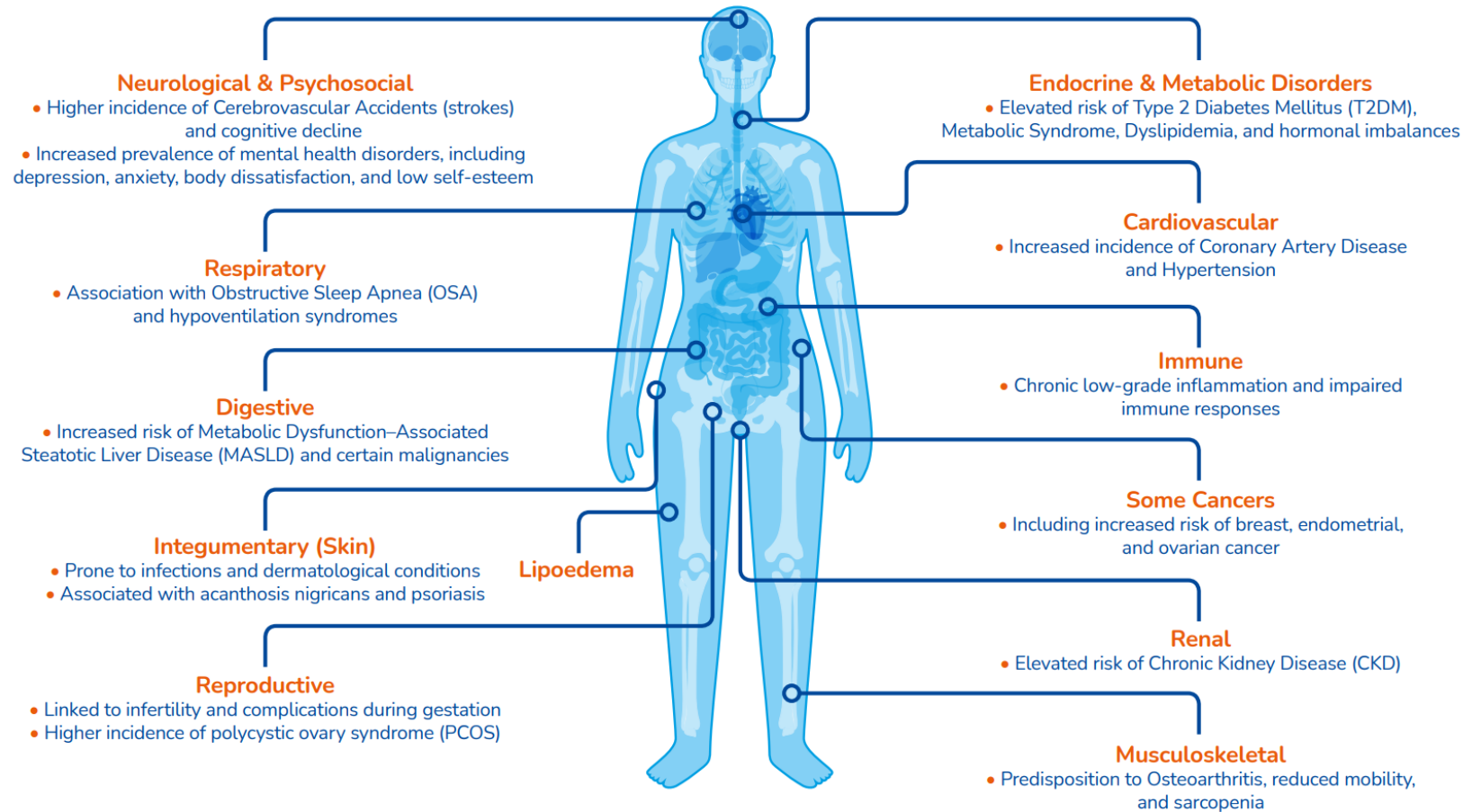


More than **half of Americans** don't live within half a mile of a park.



40% of all US households do not live within 1 mile of healthier food retailers.

Obesity affects most organ systems



FEMALE

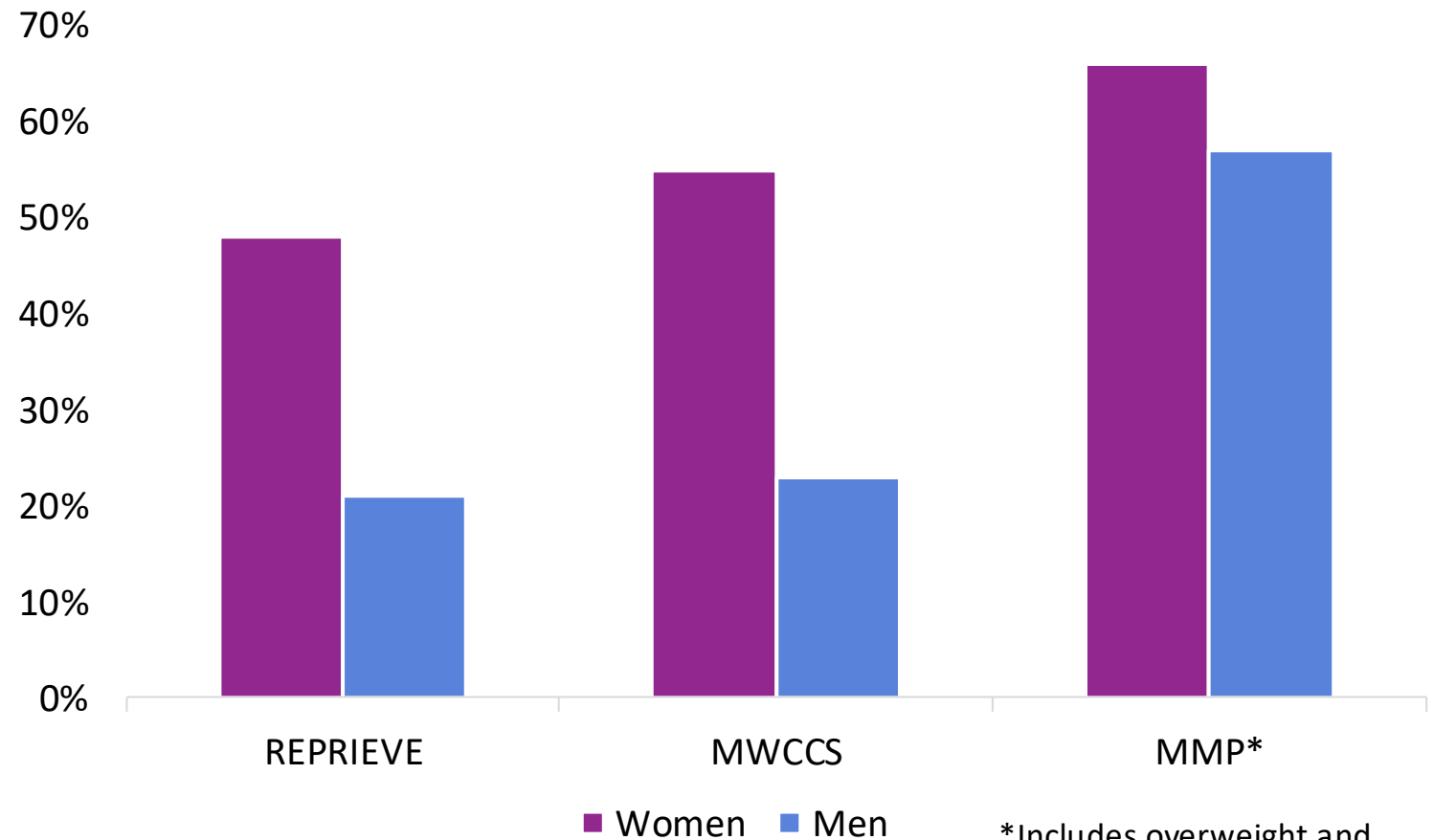
BMI ≥ 30 kg/m² or BMI ≥ 25 kg/m² and Waist to Height Ratio ≥ 0.5 with medical, functional or psychological impairments or complications

Developed by the European Association for the Study of Obesity enquiries@easo.org | www.easo.org
Read the full publication in Nature Medicine: <https://doi.org/10.1038/s41591-024-03095-3>



Obesity is more common in women than men with HIV in the US

Prevalence of Obesity among People with HIV in Three U.S.-based Cohort Studies, Stratified by Sex

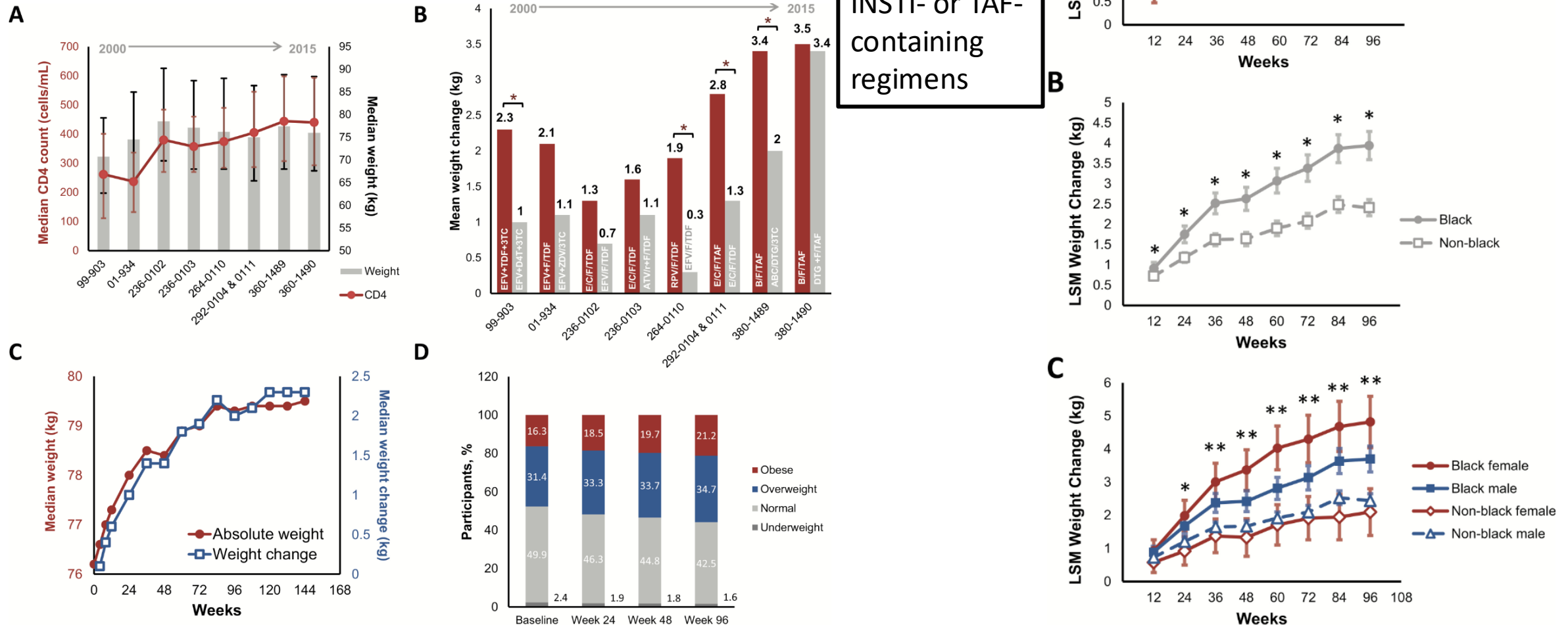


*Includes overweight and obesity

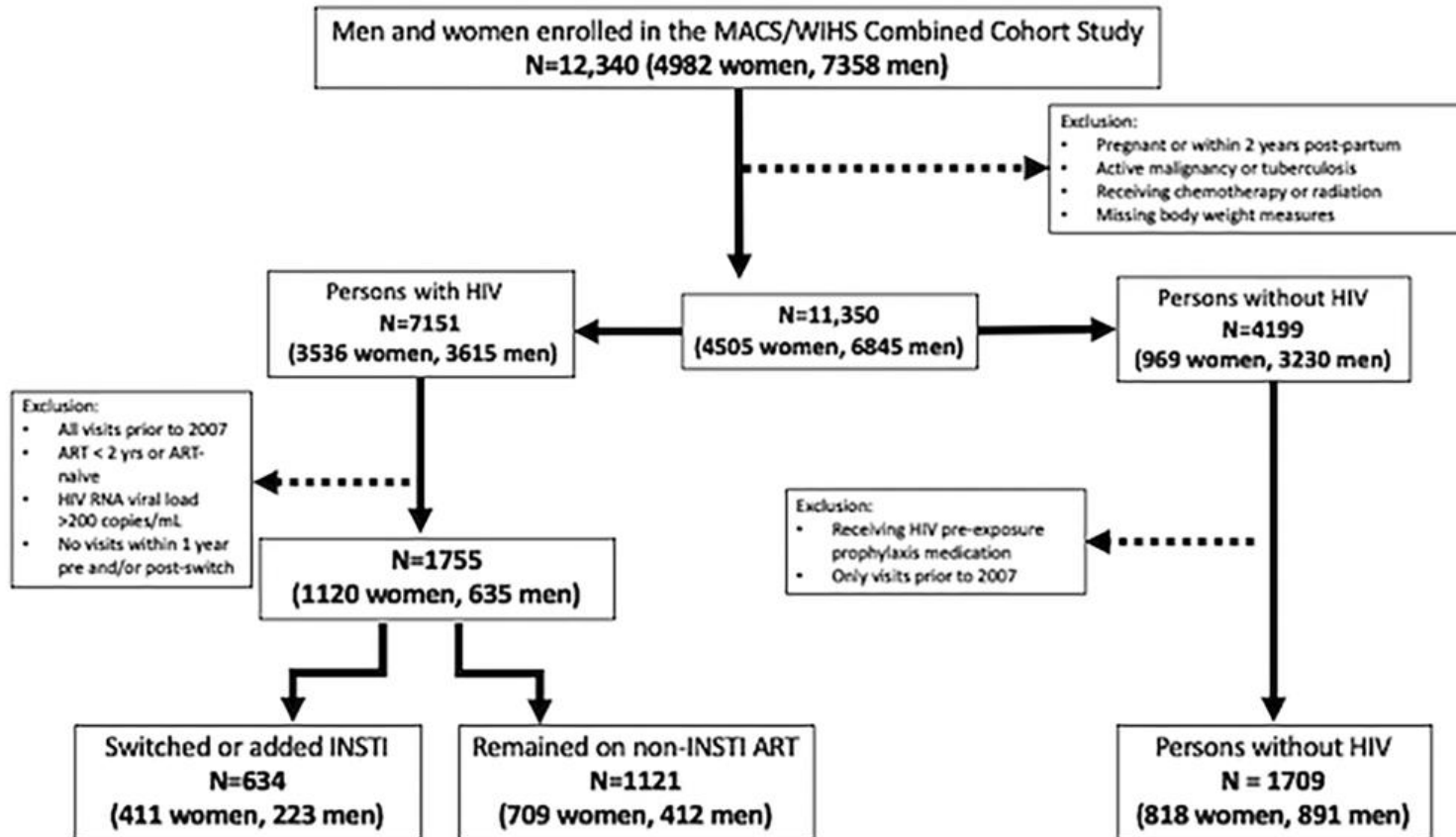
1. Zanni ZM et al. *Clin Infect Dis*, 2023;76(2):323-334
2. D'Souza G et al. *Am J Epi*, 2021;190(8):1457-1475
3. Frazier EL et al. *Clin Infect Dis*, 2019;69(12):2091-2100

Weight gain is common after starting ART

Most weight gain with INSTI- or TAF-containing regimens



Effects of switching or adding INSTIs on weight in virally suppressed people with HIV

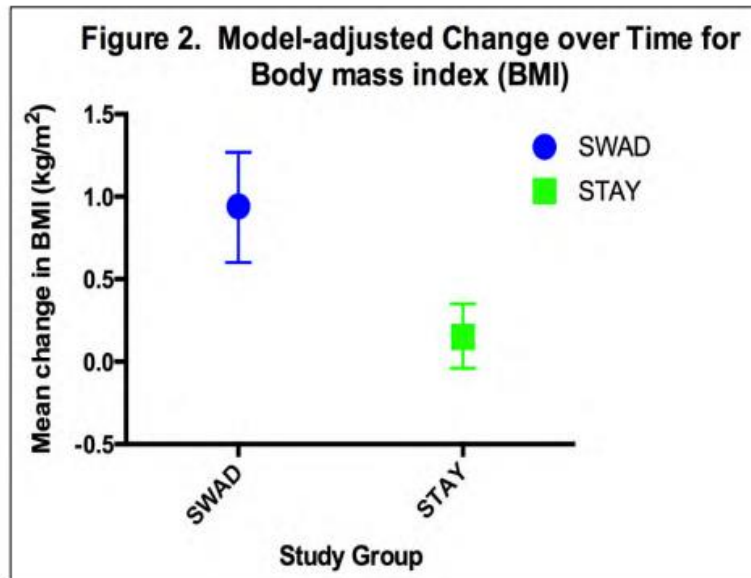
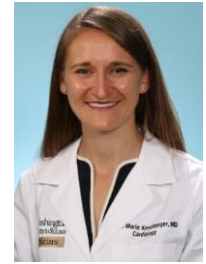


Cecile Lahiri, MD, MSc

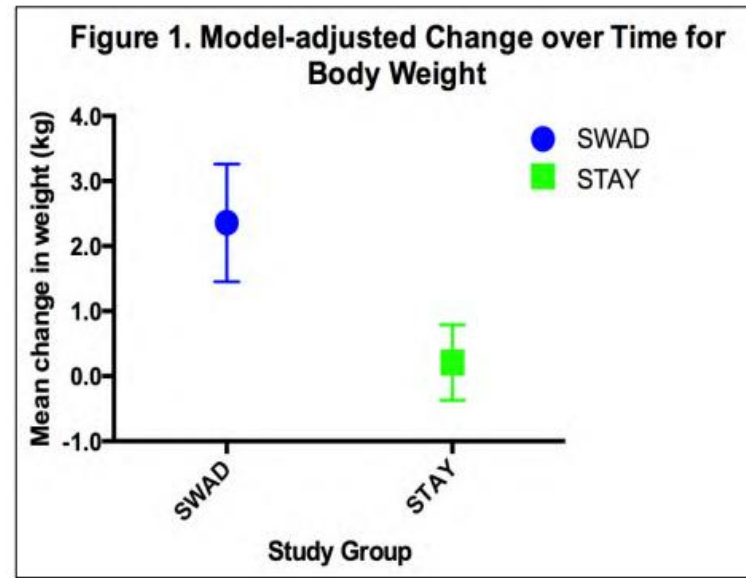


Jessica Alvarez, PhD, RD

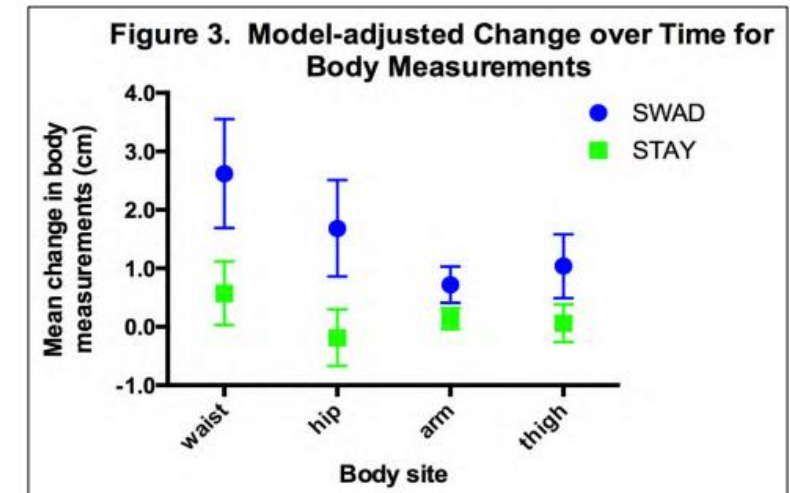
Weight gain is associated with switching to INSTIs in virally-suppressed women with HIV



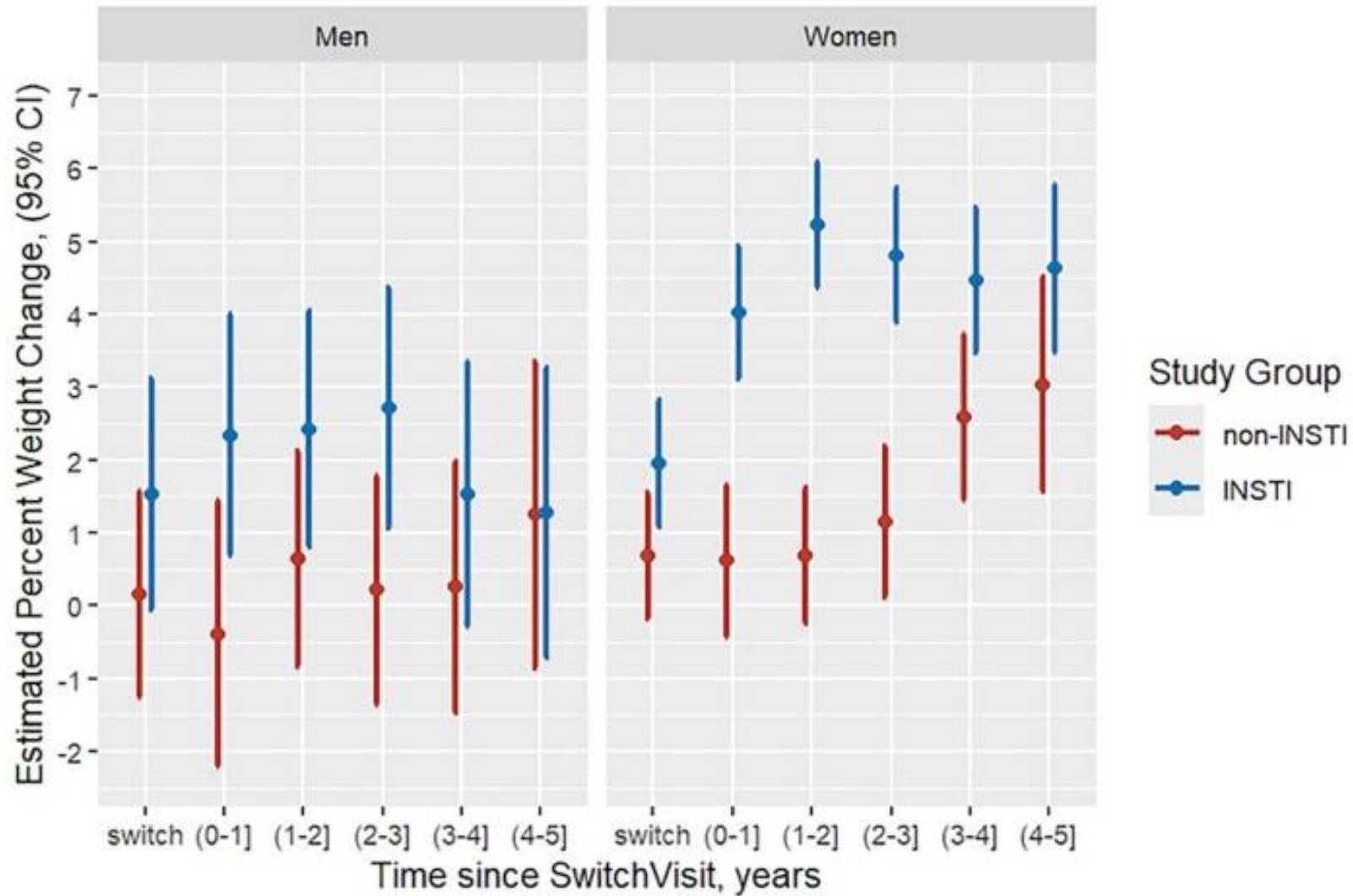
SWAD group had larger gains in BMI compared to STAY: 0.94 (CI 0.60, 1.27) kg/m² vs. 0.15 (CI -0.04, 0.35) kg/m².



SWAD group had larger gains in body weight compared to STAY: 2.36 (CI 1.45, 3.26) kg vs. 0.21 (CI -0.37, 0.79) kg.



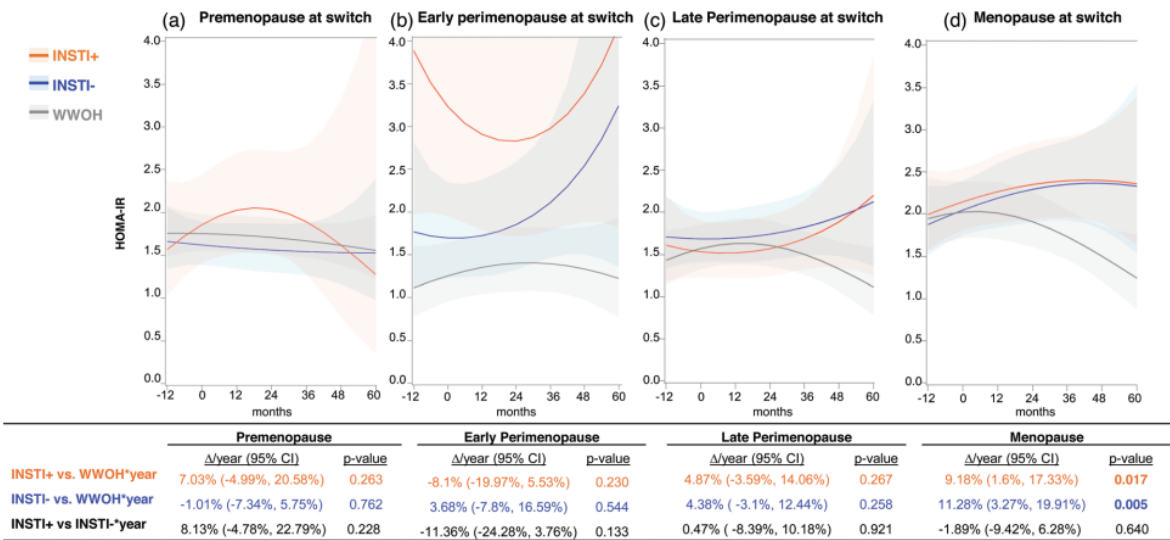
SWAD group had larger gains in BCM compared to STAY: Waist Circumference 2.62 (CI 1.69, 3.55) cm vs. 0.57 (CI 0.03, 1.12) cm.



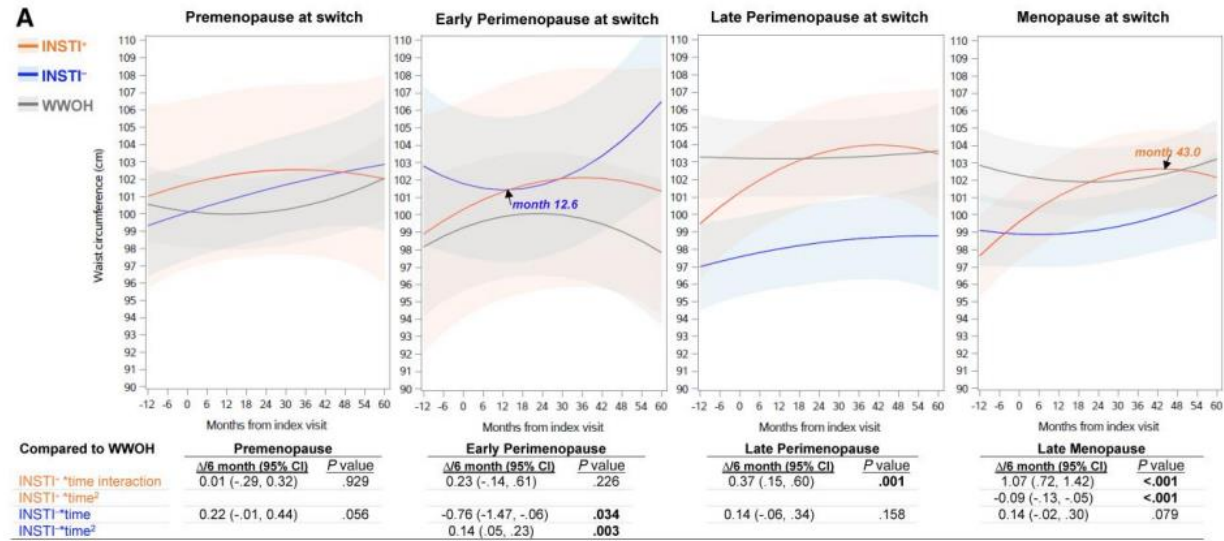
Virally suppressed women with HIV gain more weight than virally suppressed men with HIV after switching to INSTIs

Switching to INSTIs during the menopausal transition is associated with accelerated body composition changes and insulin resistance

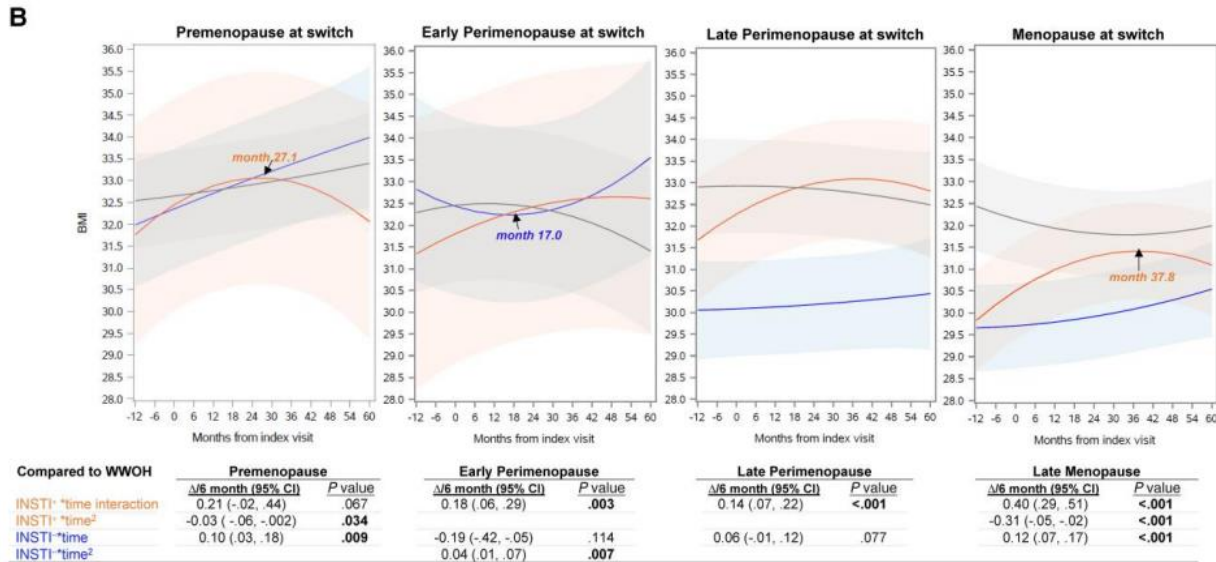
HOMA-IR



Waist circumference



BMI



A5391: Doravirine for Obese Persons on Integrase Inhibitors and Tenofovir Alafenamide



INSTI + TAF/FTC for ≥ 48 weeks
Stable viral suppression
BMI ≥ 30 kg/m²

DOR + TAF/FTC
N=47

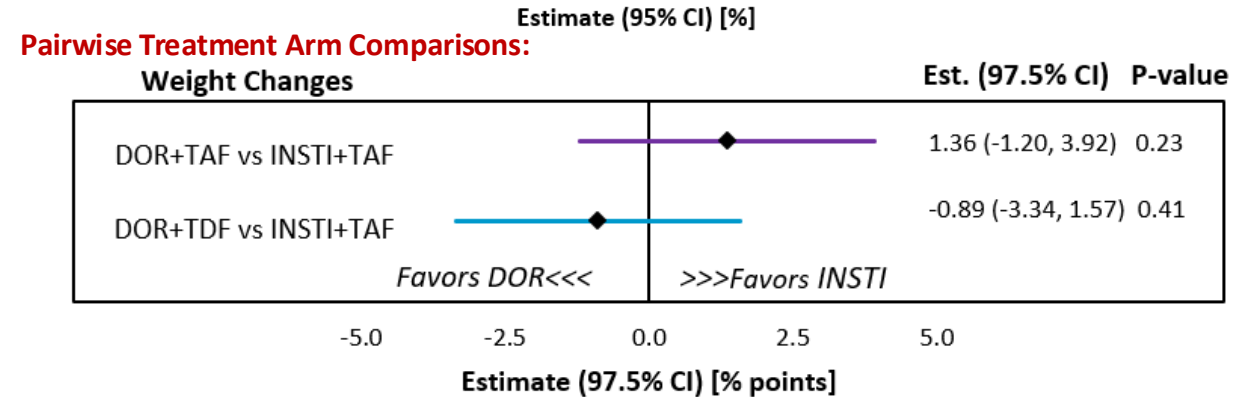
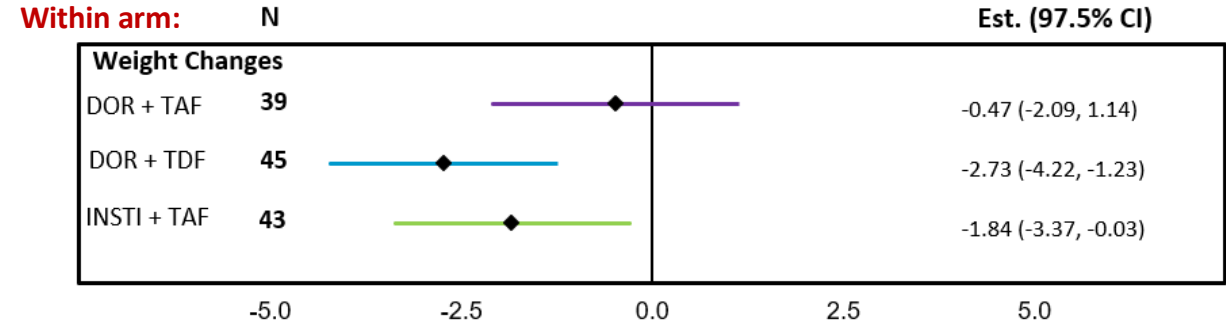
DOR + TDF/FTC
N=49

INSTI + TAF/FTC
N=49

Primary endpoint: $\geq 5\%$ point between-group difference in body weight change

Baseline characteristics:

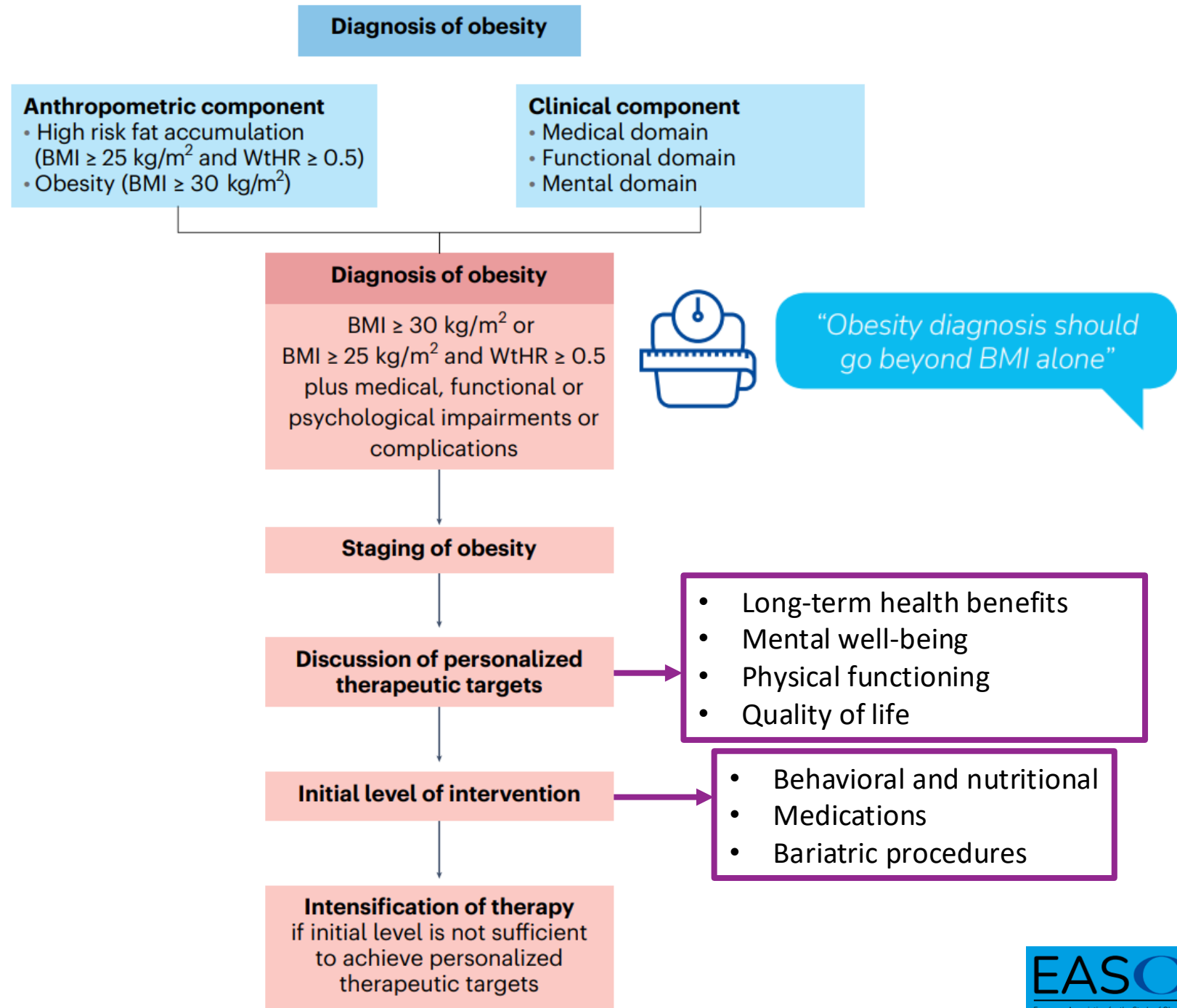
- 49% women
- 53% Black race
- Median age: 49 years
- Median BMI: 34.5
- >10% weight gain in 1-3 years: 65%
- Median duration on INSTI: 3.4 years
- 86% BIC-based ART



Switching to DOR with or without switching TAF to TDF did not result in more weight loss than maintaining TAF/INSTI-based ART

Subgroups: no significant benefit in women, Black race, or people with >10% weight gain in first 3 years on INSTI

A new framework for obesity as a chronic disease with holistic management goals



Treatments for obesity includes lifestyle, medical, and surgical interventions



Goal: to prevent, treat, or reverse complications of obesity and improve quality of life



Lifestyle measures:
everyone

Low calorie diet, 150 minutes
of exercise/week
5-7% weight loss



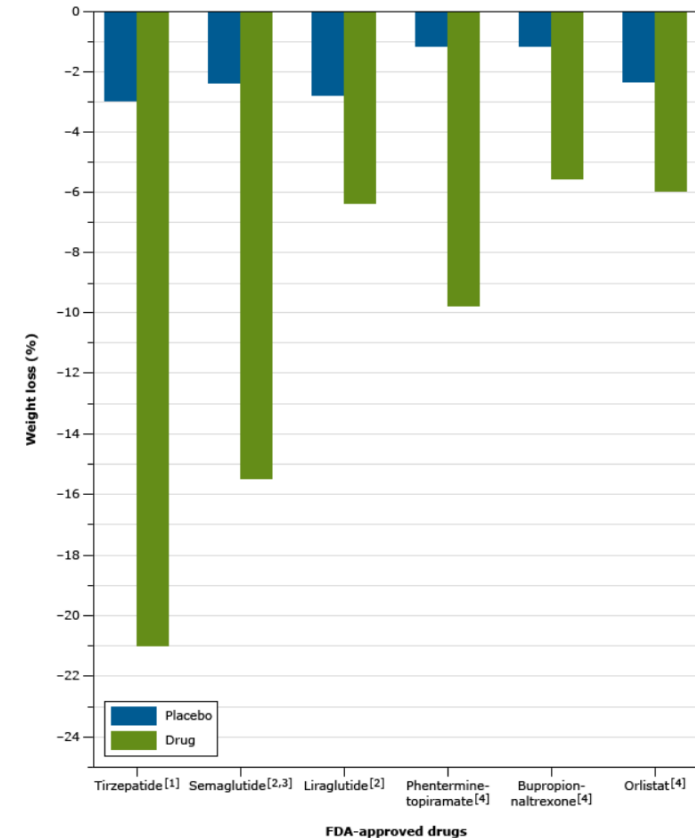
Medical: BMI ≥ 30 or 27-29
with certain medical
conditions

GLP-1 Receptor Agonists
(semaglutide, liraglutide)
5-15% weight loss
Side effects, availability



Surgical: BMI ≥ 40 or 35-39
with certain medical
conditions

Gastric banding, gastric
bypass
Up to 40% weight loss



Weight loss reflects results at 72 weeks (tirzepatide), 68 weeks (semaglutide, liraglutide), or 52 weeks (other medications).

Perreault L. *UpToDate*. 2025

McCarty TR et al. *Bariatr Surg Pract Patient Care*. 2020;15(3):116-123

In summary

Obesity is a chronic medical condition that affects multiple organ systems

ART-associated weight gain is complex and is not reversed by switching off of INSTIs

Management of obesity should focus on a holistic approach to health and well-being

Managing Cardiovascular Disease Risk

Cardiovascular risk factors

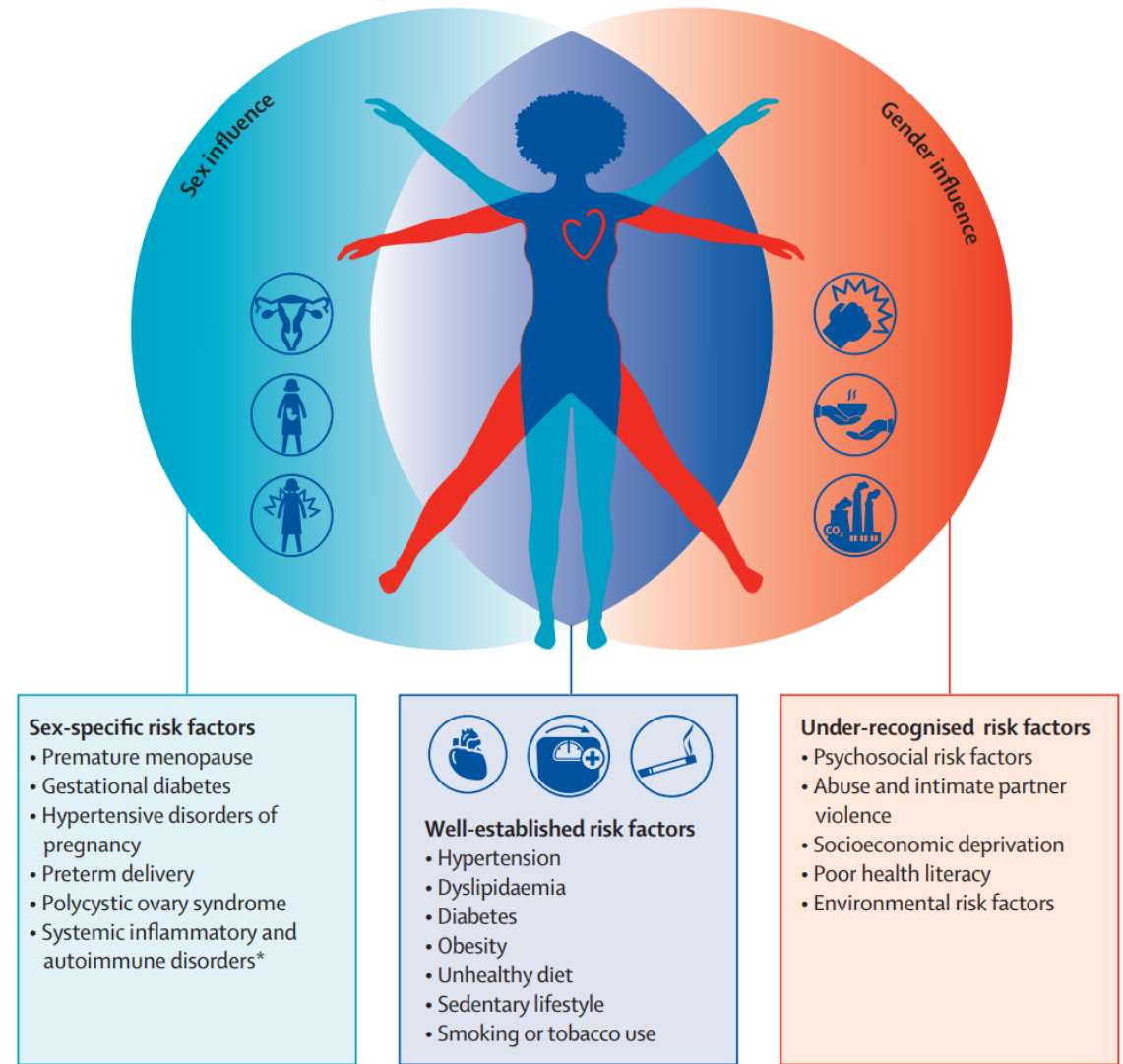
Lifestyle interventions

Medications

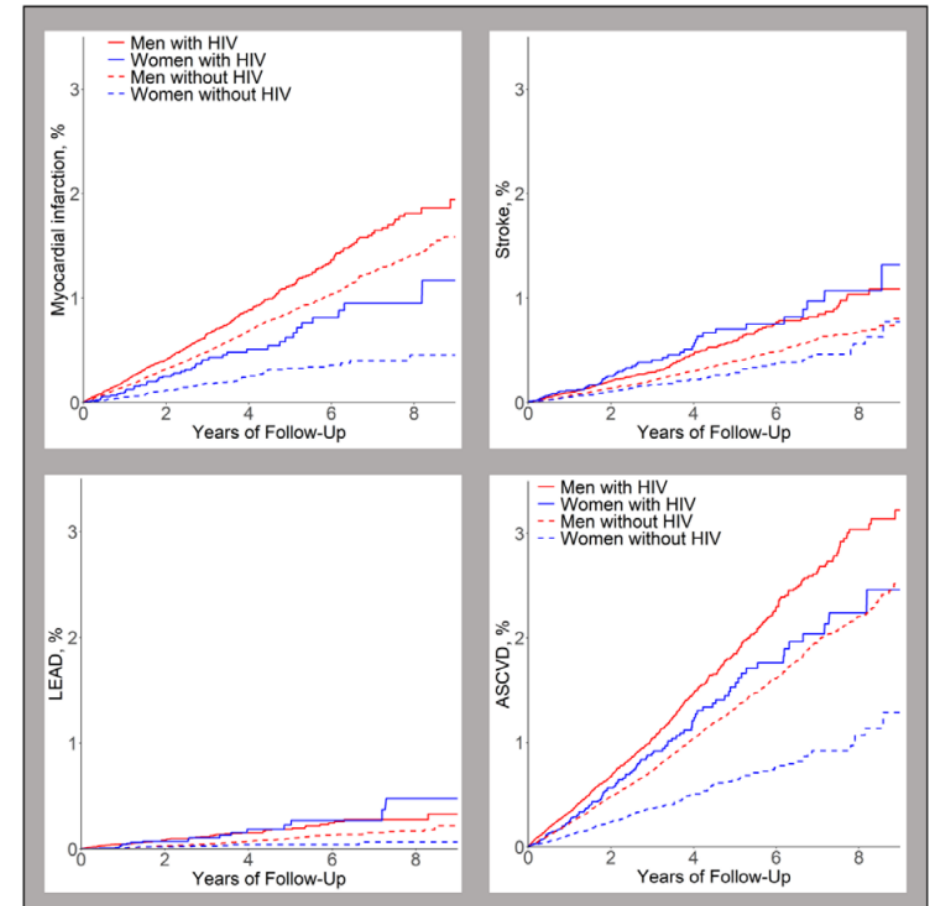
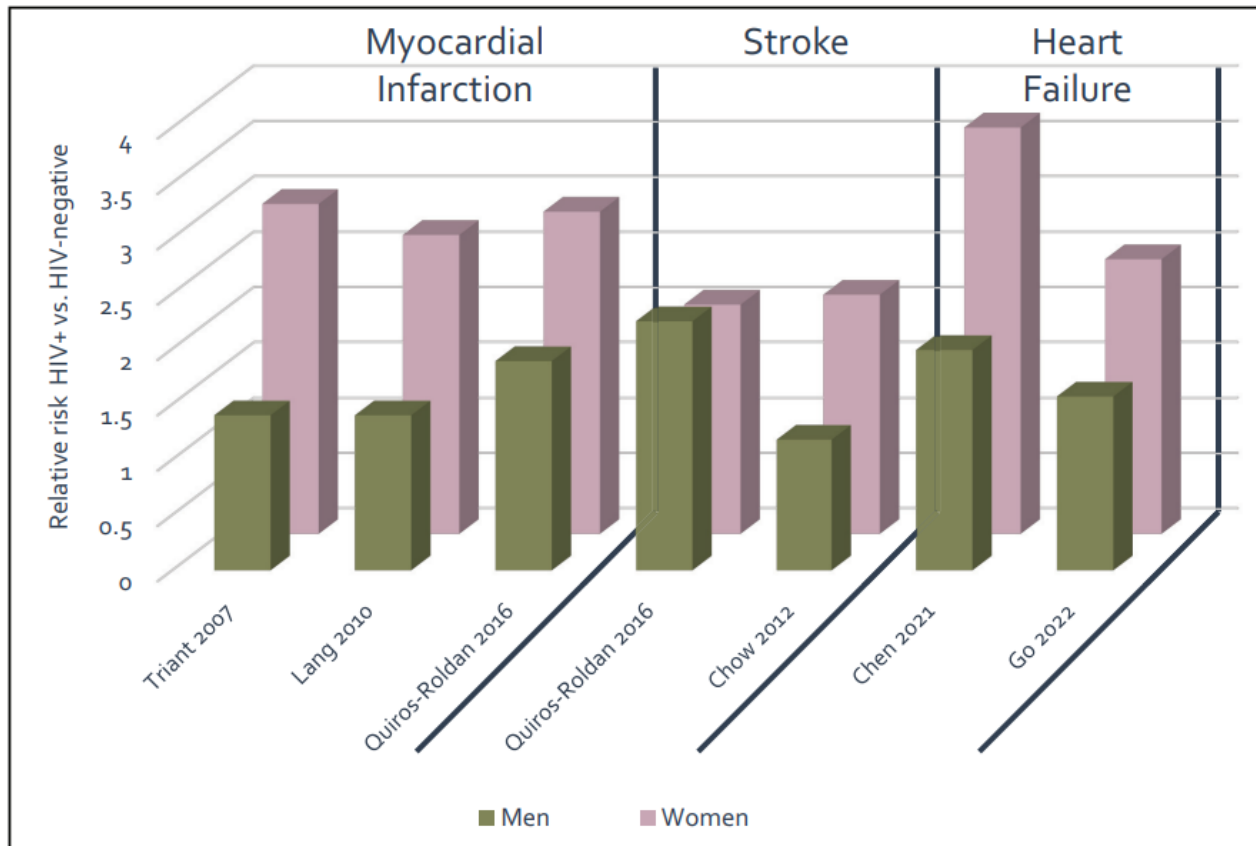
Heart disease in women



- Leading cause of death in women worldwide
- Improvements in prevalence and mortality have slowed over the past decade
- Rates are increasing among younger women
- Risk in women is often underestimated by both patients and healthcare providers



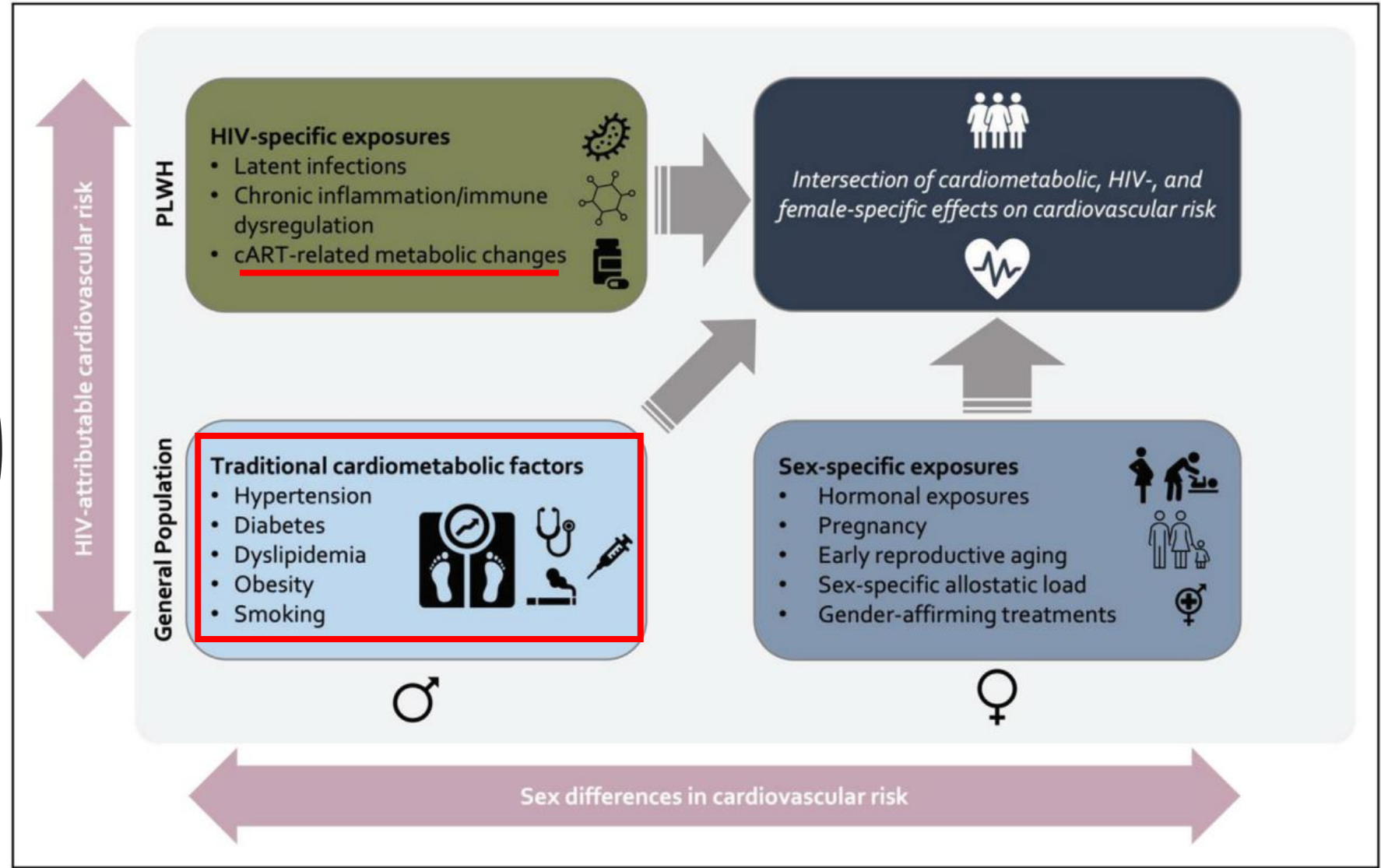
The relative risk of CVD in people with HIV is greater in women than in men



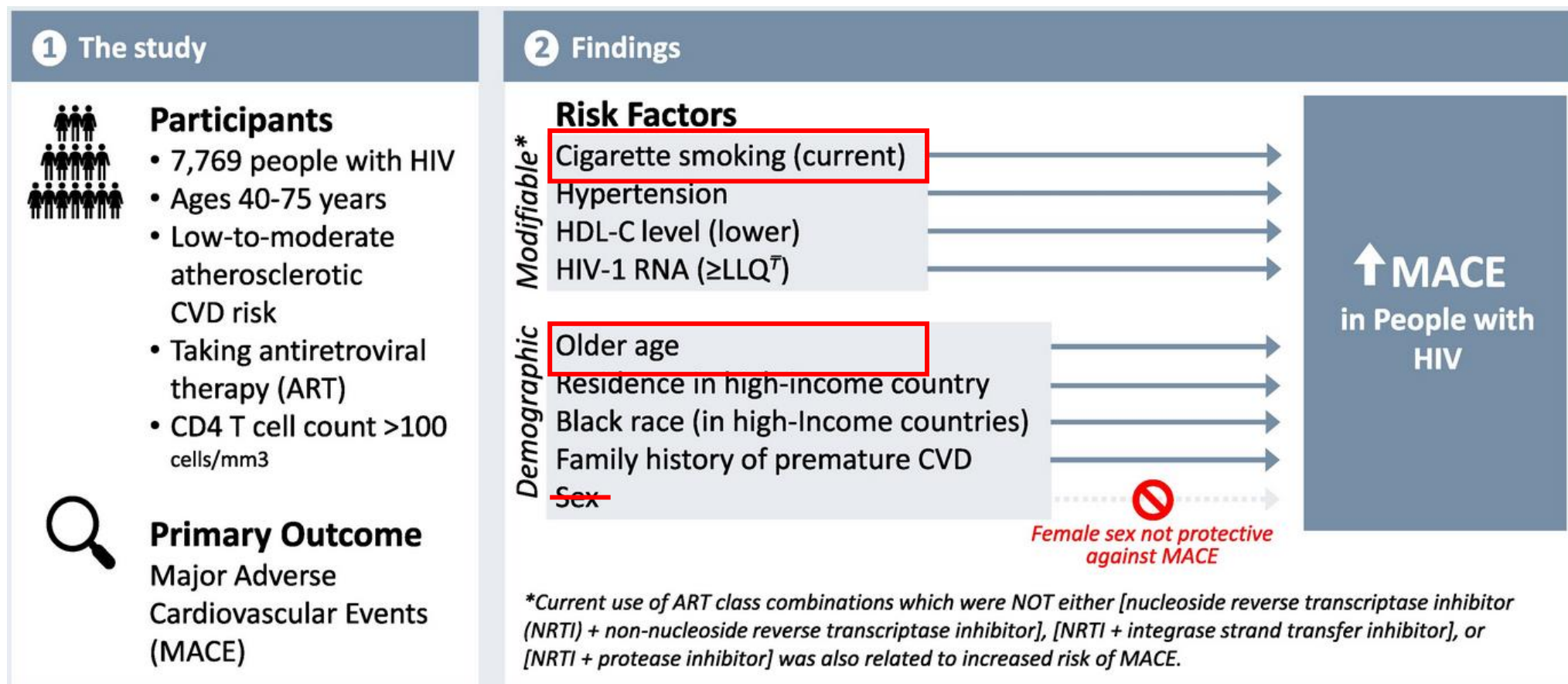
Kentoffio K et al. *Curr Opin HIV AIDS* 2022;17(5):270-278

Wise J et al. *AIDS* 2023;May.[Epub ahead of print]

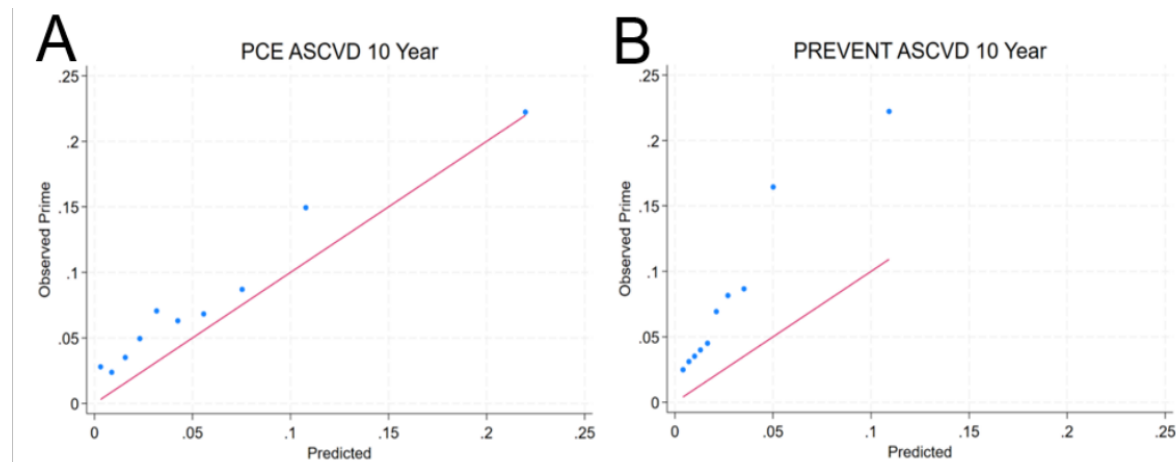
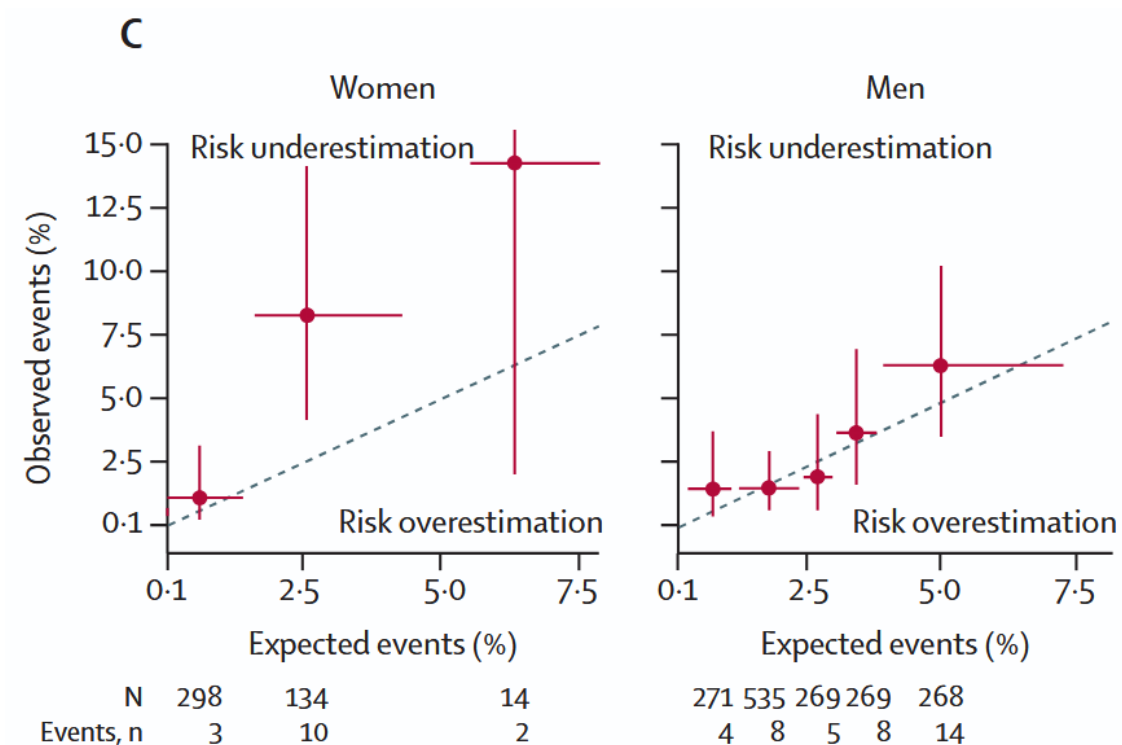
Mechanisms of CVD in Women with HIV



Smoking is the most impactful modifiable CVD risk factor in PWH



Commonly-used CVD risk equations underestimate risk in people with HIV, particularly women





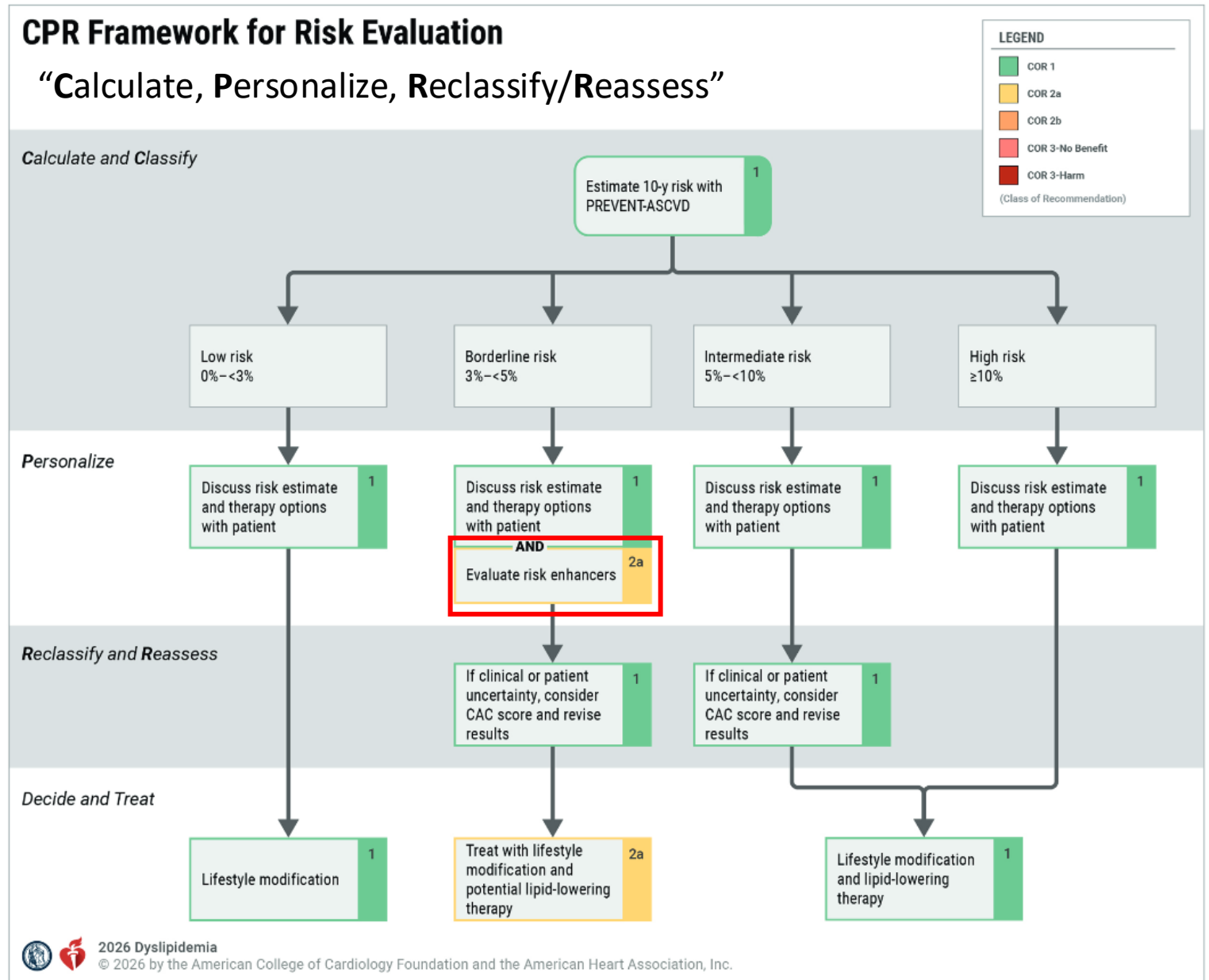
Cardiovascular disease prevention strategies

Lifestyle modifications (diet,
physical activity, quitting smoking)

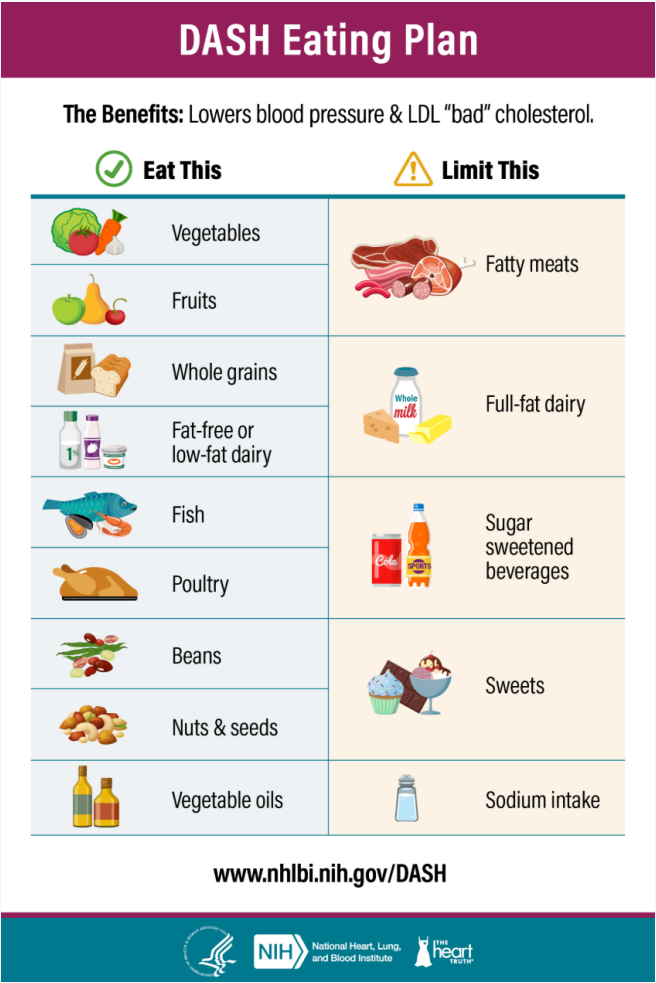
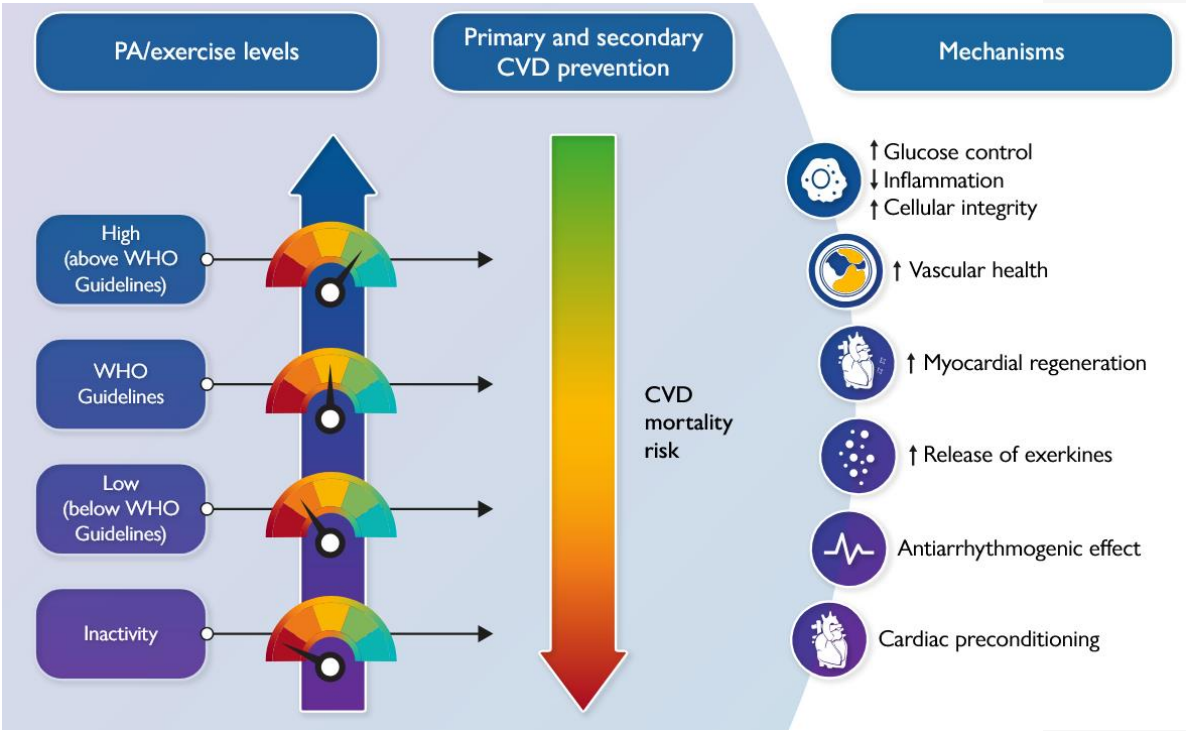
Medications



Standard Recommendations for Lipid Management in the General Population (updated 2026)

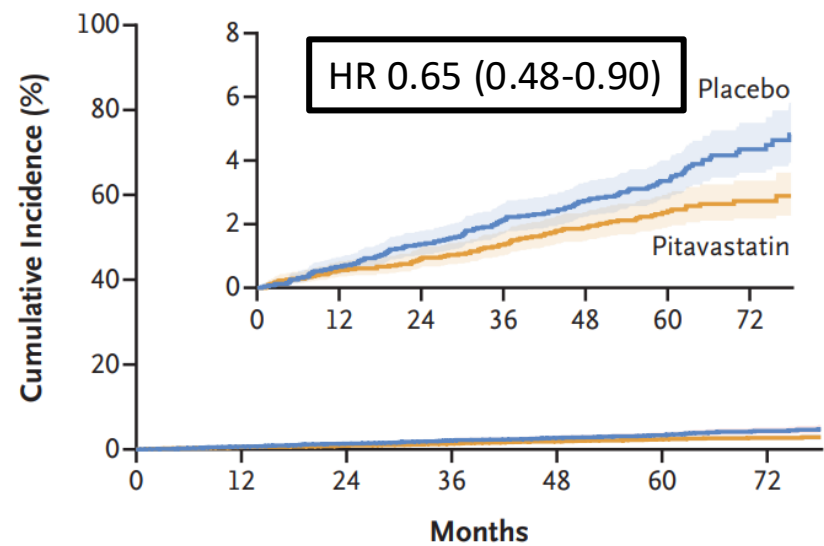


Lifestyle modifications include diet and physical activity



The REPRIEVE trial: Statins reduce risk of cardiovascular disease in people living with HIV

B First MACE



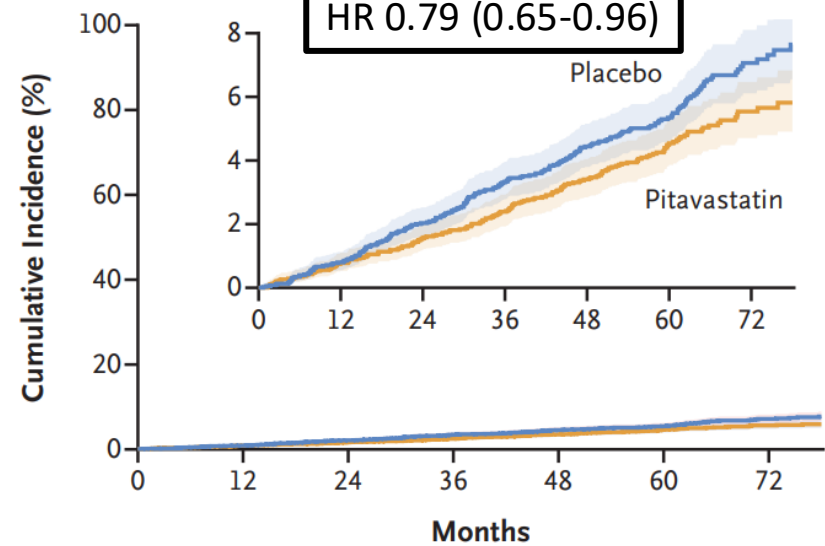
Cumulative Incidence of Event (%)

Placebo	0.00	0.66	1.38	2.14	2.74	3.36	4.36
Pitavastatin	0.00	0.56	0.95	1.35	1.89	2.41	2.73

No. at Risk

Placebo	3881	3693	3506	3356	2997	2182	959
Pitavastatin	3888	3647	3475	3364	2997	1947	1052

C First MACE or Death



Cumulative Incidence of Event (%)

Placebo	0.00	0.80	2.03	3.34	4.44	5.35	7.06
Pitavastatin	0.00	0.77	1.58	2.39	3.40	4.54	5.54

No. at Risk

Placebo	3881	3693	3506	3356	2997	1975	919
Pitavastatin	3888	3647	3475	3364	2998	1948	1027

Statin Recommendations for People Living with HIV

Recommendations for the Use of Statin Therapy as Primary Prevention of Atherosclerotic Cardiovascular Disease (ASCVD) in People with HIV

For people with HIV who have **low-to-intermediate (<20%) 10-year ASCVD risk** estimates

- Age 40-75 years
 - When 10-year ASCVD risk estimates are **5% to <20%**, initiate at least moderate-intensity statin therapy (A1)
 - When 10-year ASCVD risk estimates are **<5%**, initiate at least moderate-intensity statin therapy (C1). The absolute benefit from statin therapy is modest in this population; therefore, the decision to initiate a statin should take into account the presence or absence of HIV-related factors that can increase ASCVD risk.
- Age <40 years
 - Data are insufficient to recommend for or against statin therapy



In summary

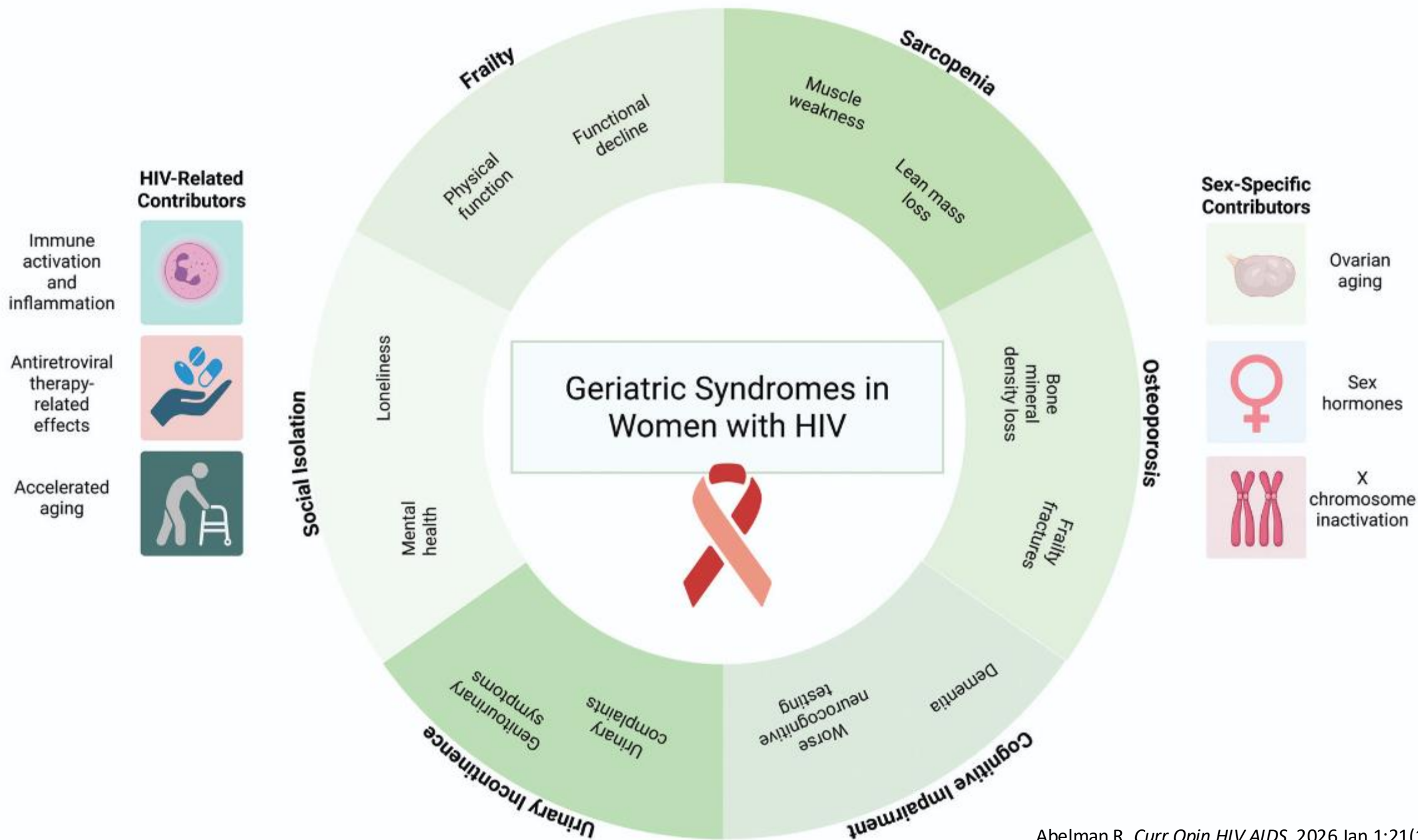
CVD risk is often underestimated in women living with HIV

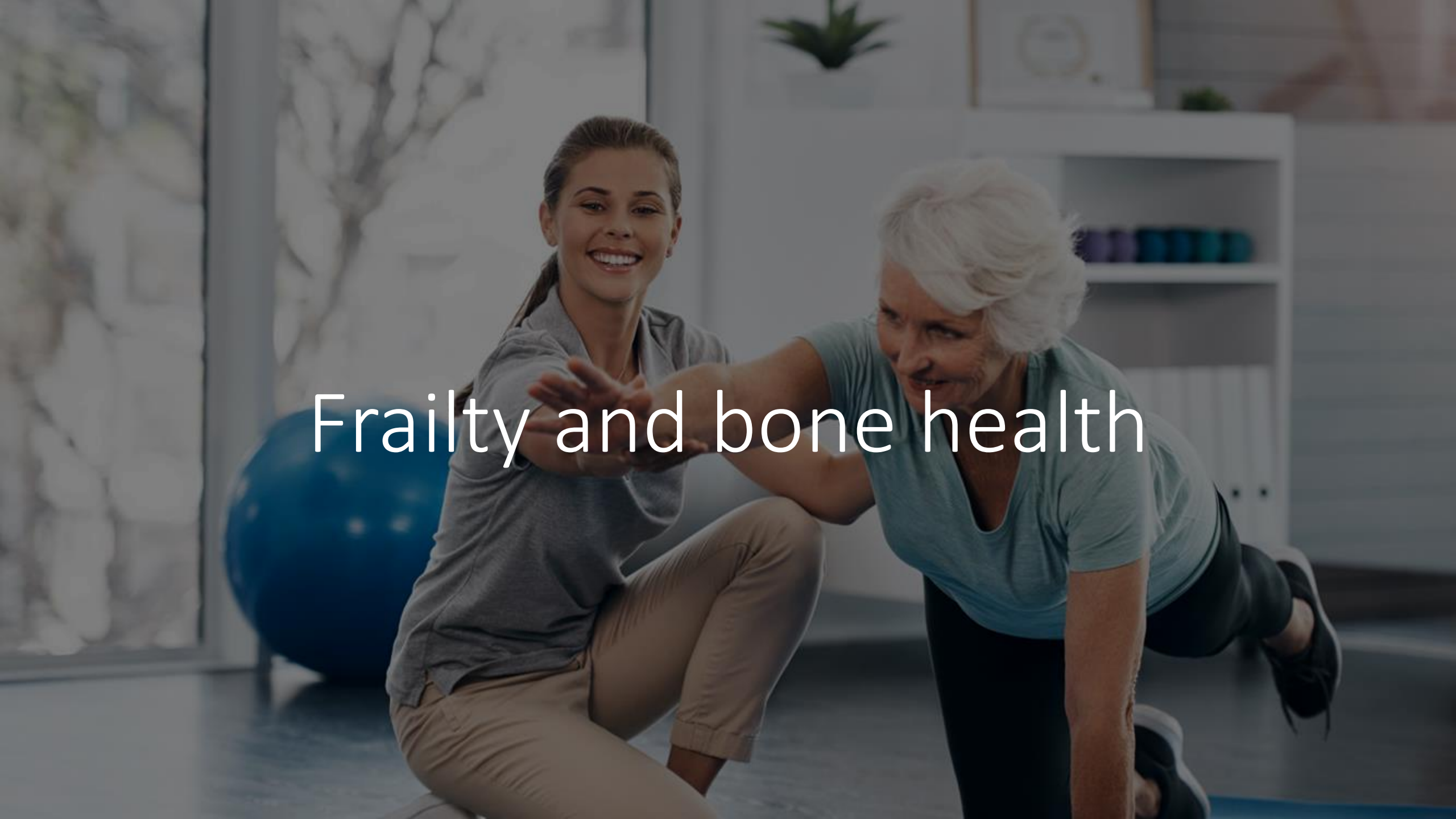
Smoking is the most impactful modifiable CVD risk factor in PWH

Statins reduce the risk of CVD by 35% in PWH with low-moderate CVD risk

Aging in Women with HIV

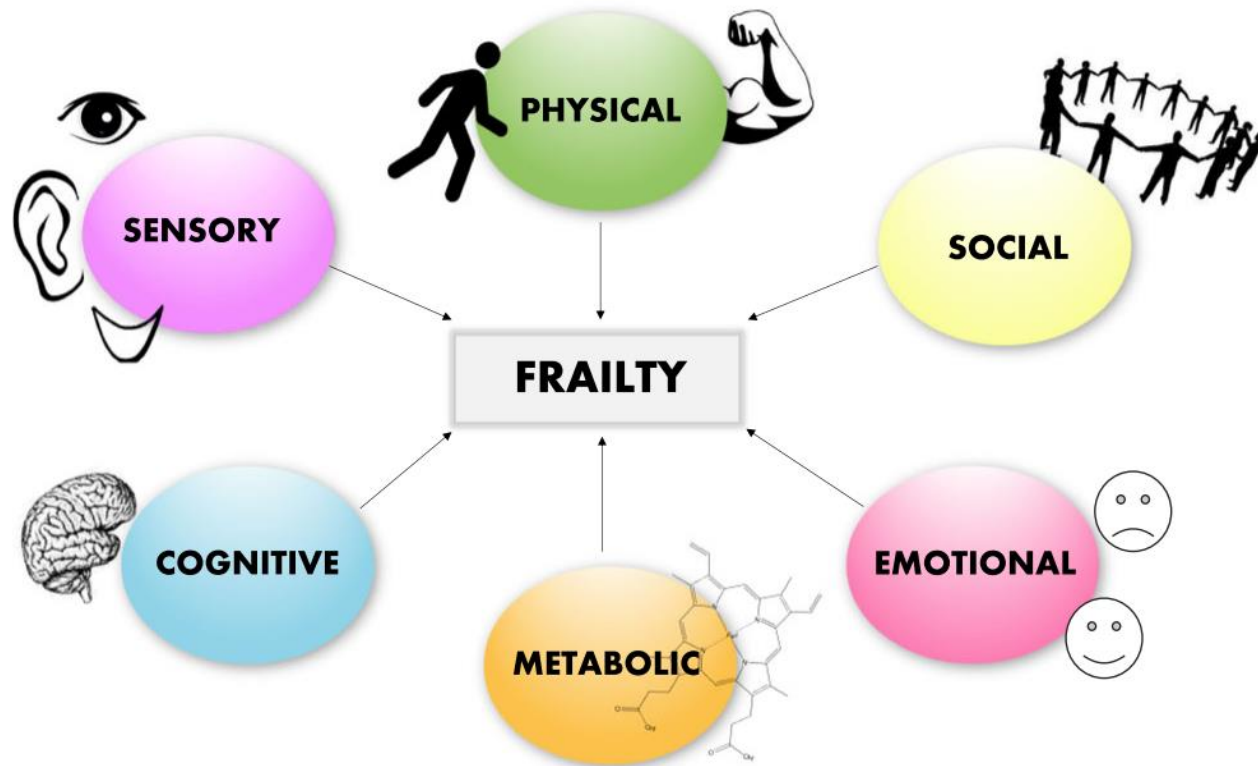
Frailty
Bone and joint health
Mental health
Cognition



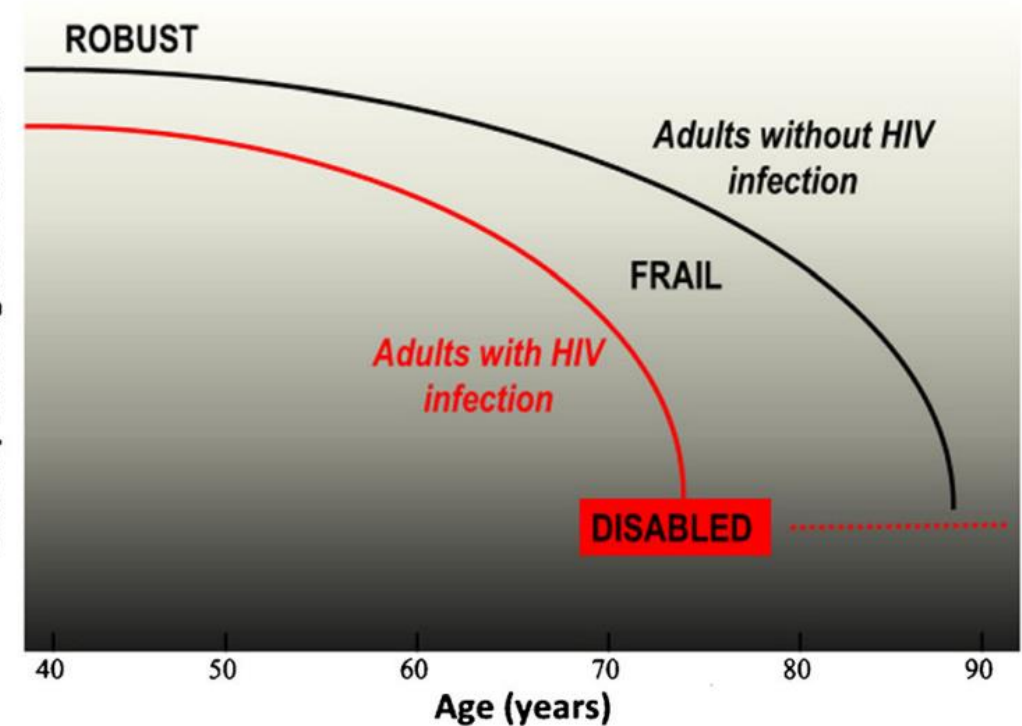
A young woman with dark hair tied back, wearing a grey long-sleeved shirt and tan pants, is smiling and assisting an elderly woman with a squat exercise. The elderly woman has short white hair, is wearing a light blue t-shirt and black leggings, and is in a low squat position with her hands on the floor. The young woman is crouching behind her, with her hands extended to assist. In the background, there is a large blue exercise ball, a white shelving unit with various items, and a window with a view of trees. The text "Frailty and bone health" is overlaid in white in the center of the image.

Frailty and bone health

Frailty is a vulnerability state characterized by impairments and limitations that might lead to disability



Physical, social, emotional, metabolic, sensory and cognitive health



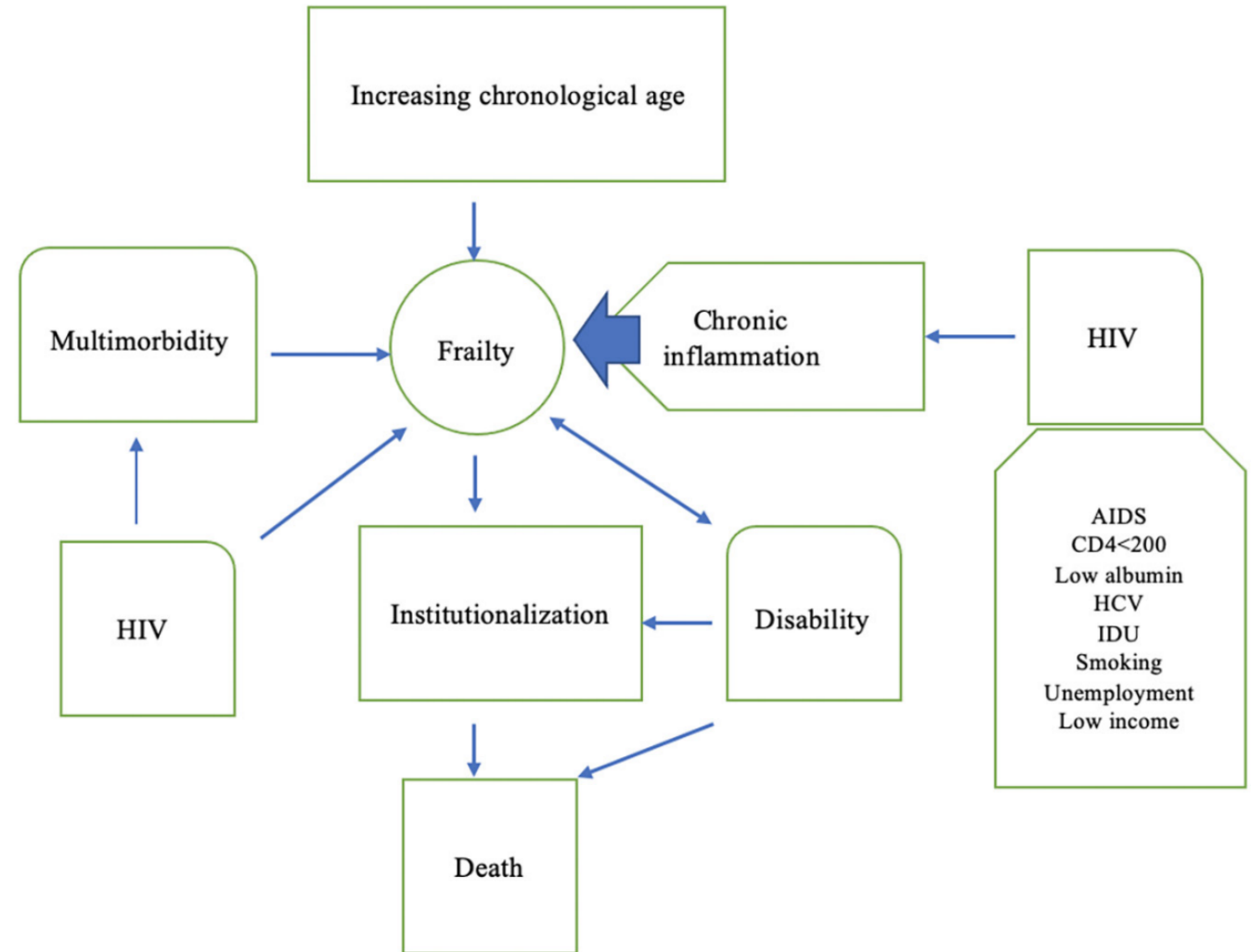
Fried Frailty Phenotype (at least 3):

- Unintentional weight loss (at least 4.5 kg or $\geq 5\%$ of body weight in 1 year)
 - Self-reported exhaustion (effort required for activity)
 - Weakness (grip strength)
 - Slow walking speed (distance covered over 4 minutes)
 - Low physical activity
-
- Prefrailty: 1 or 2

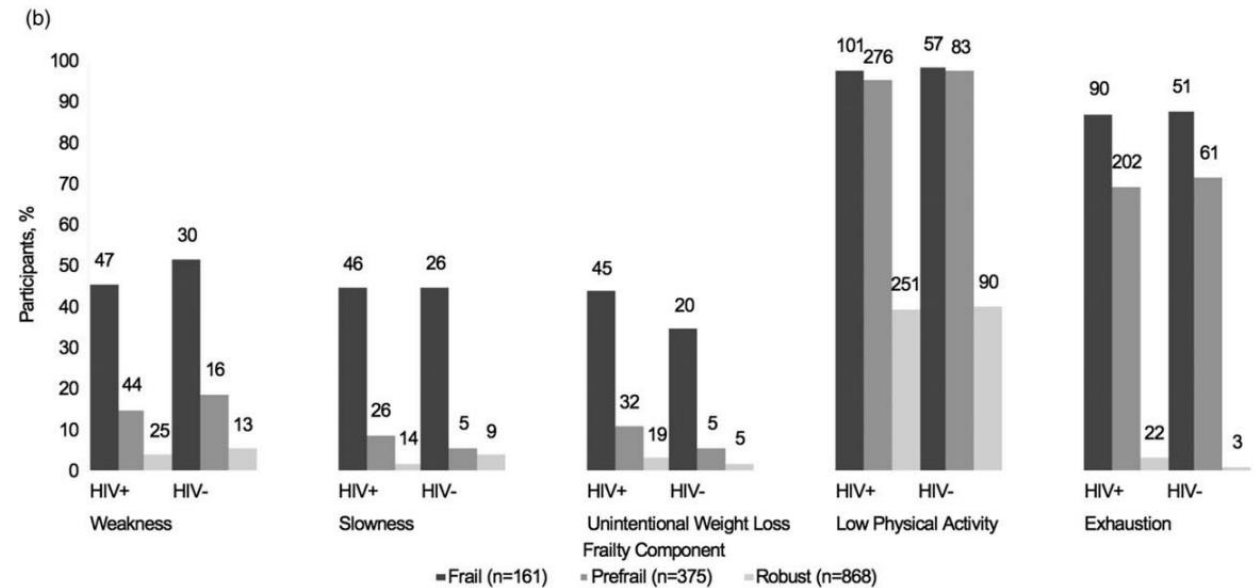
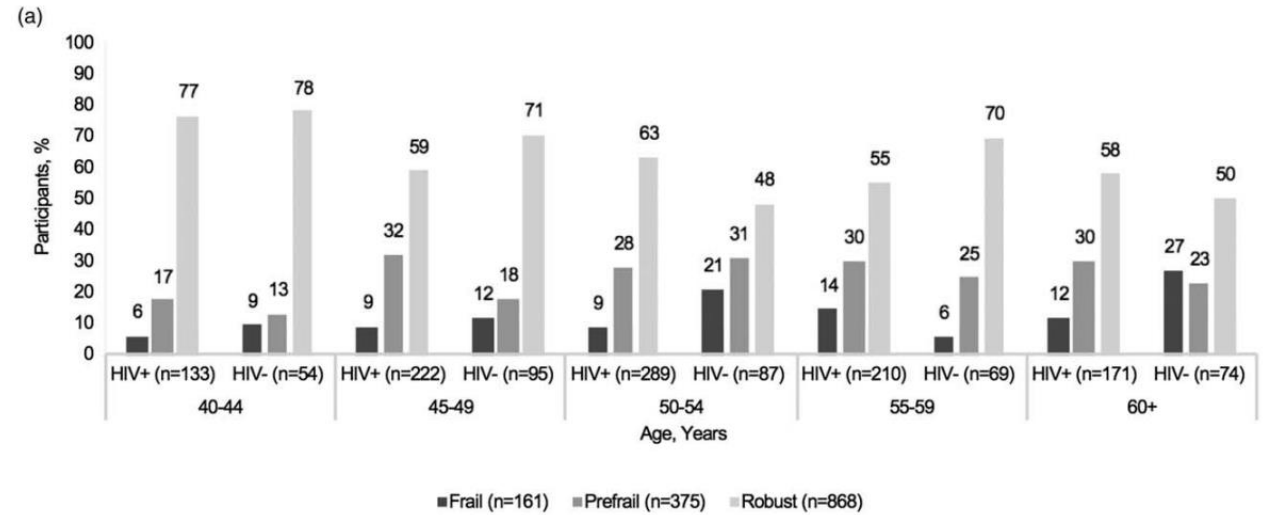
Frailty in people with HIV is multifactorial

Risk factors:

- Comorbidities
 - Cardiovascular disease
 - Diabetes
 - Depression
 - Obesity
- Polypharmacy
- Detectable HIV viral load
- ART side effects (bone mineral density loss)

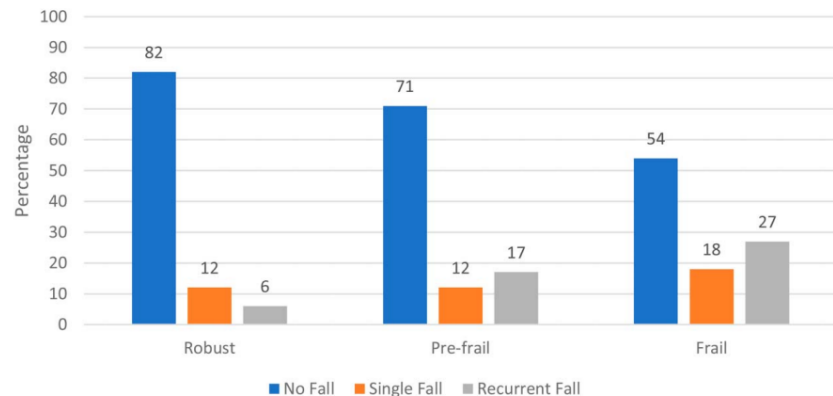


Frailty is common in middle-aged women with and without HIV in the WIHS

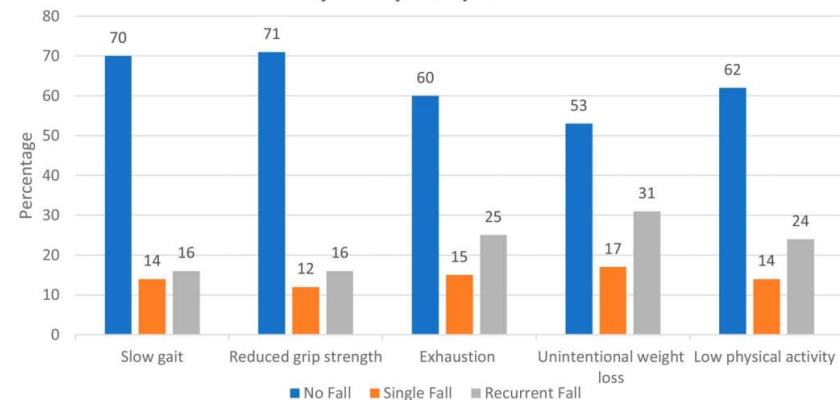


Frailty is associated with frequent falls and mortality

Proportion of WIHS Participants with Single and Recurrent Falls by Frailty Status

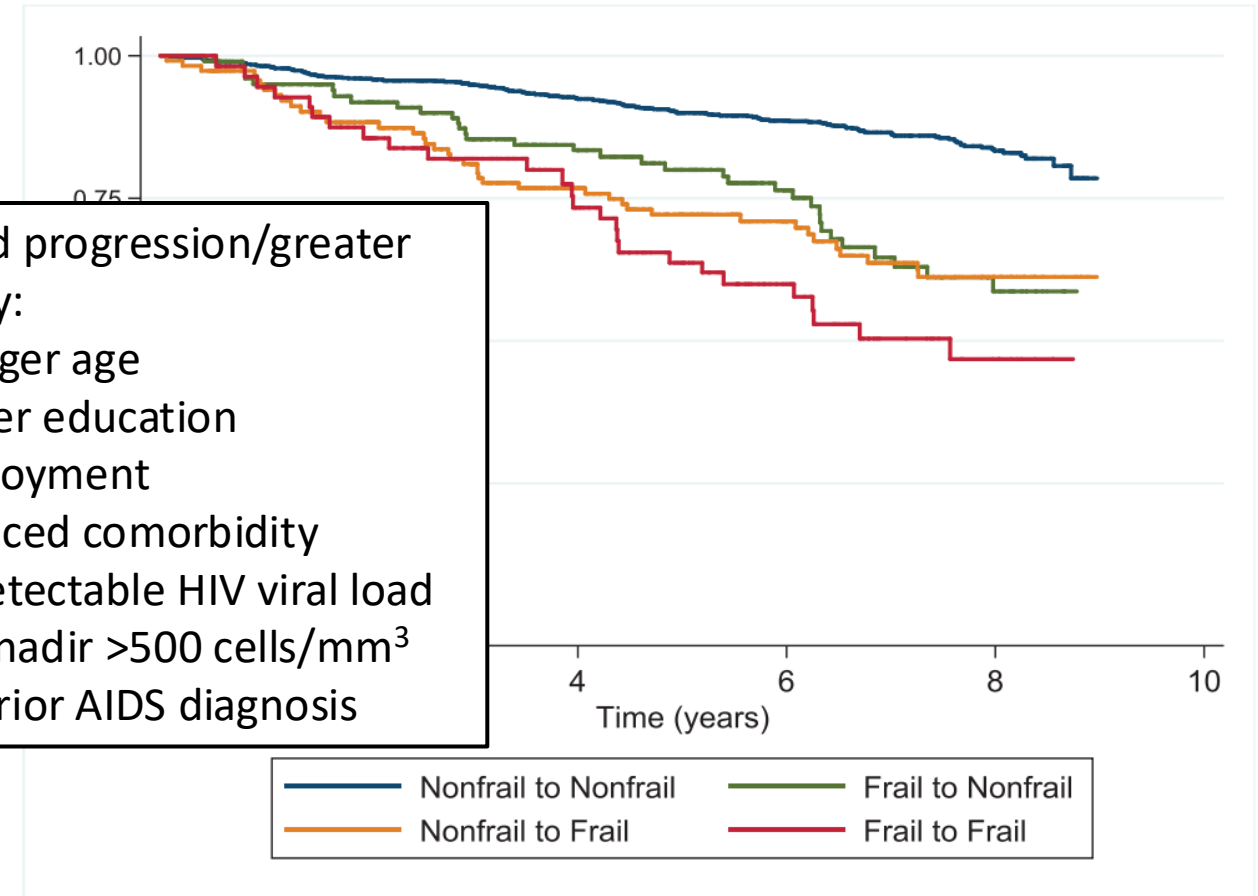


Proportion of WIHS Participants with Single and Recurrent Falls by Frailty Component Status



Reduced progression/greater recovery:

- Younger age
- Higher education
- Employment
- Reduced comorbidity
- Undetectable HIV viral load
- CD4 nadir >500 cells/mm³
- No prior AIDS diagnosis



Assessing for frailty is recommended at age ≥ 50 by EACS

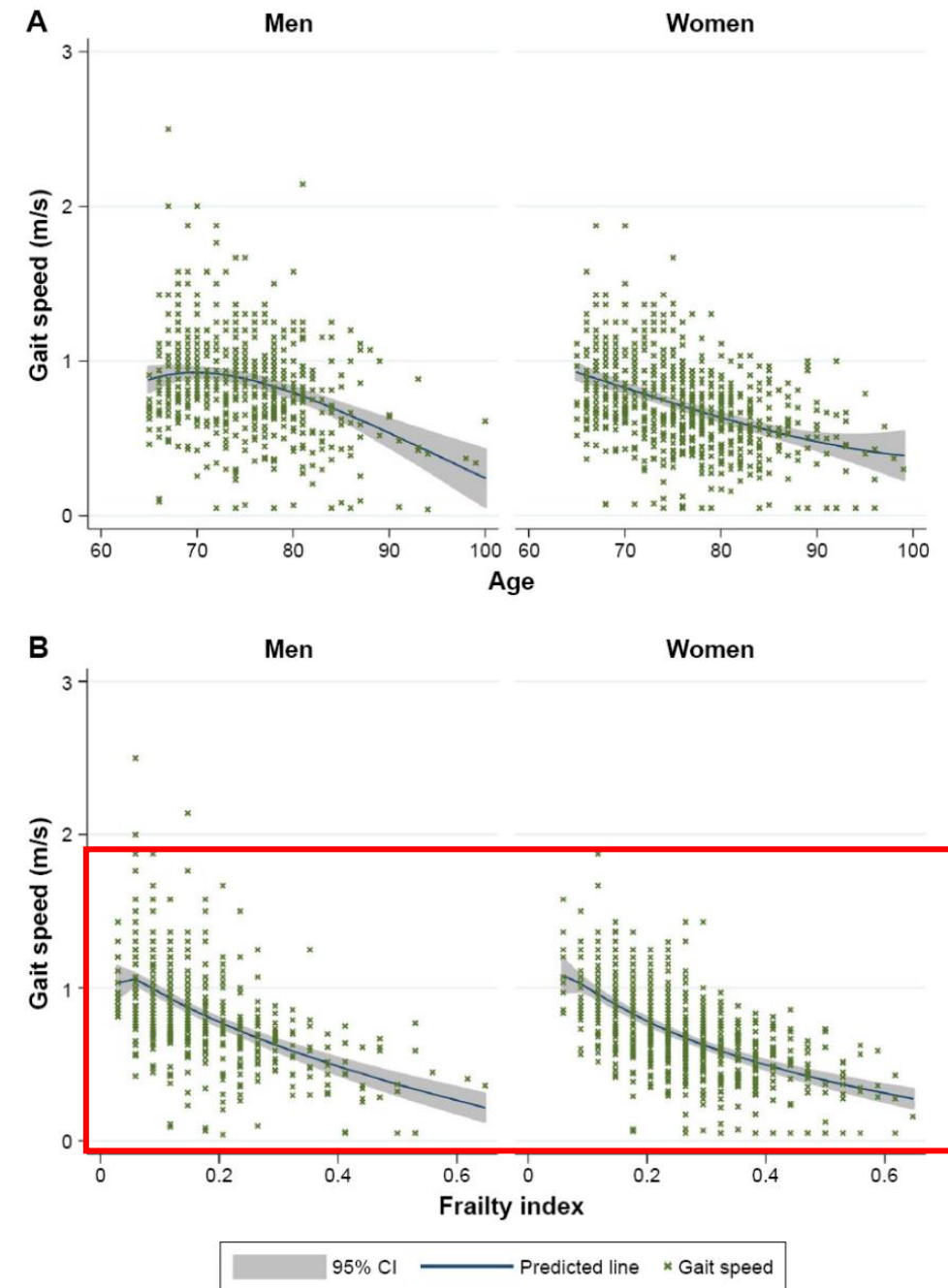
- FRAIL Scale
- Clinical Frailty Scale
- Gait Speed

FRAIL Scale
F__atigue
R__esistance (ability to climb one flight of stairs)
A__mbulation (ability to walk one block)
I__llnesses (Greater than 5)
L__oss of Weight ($\geq 5\%$ over 1 year)
$\geq 3 = \text{frail} / 1 - 2 = \text{pre-frail} / 0 = \text{robust}$

Reference: Woo, Jean, Jason Leung, and John E. Morley. "Comparison of frailty indicators based on clinical phenotype and the multiple deficit approach in predicting mortality and physical limitation." *Journal of the American Geriatrics Society* 60.8 (2012): 1478-1486.

Barber TJ et al. *AIDS Care*. 2023;35(8):1149-1153.

Jung HW et al. *Clin Interv Aging*. 2018;13:1079-1089

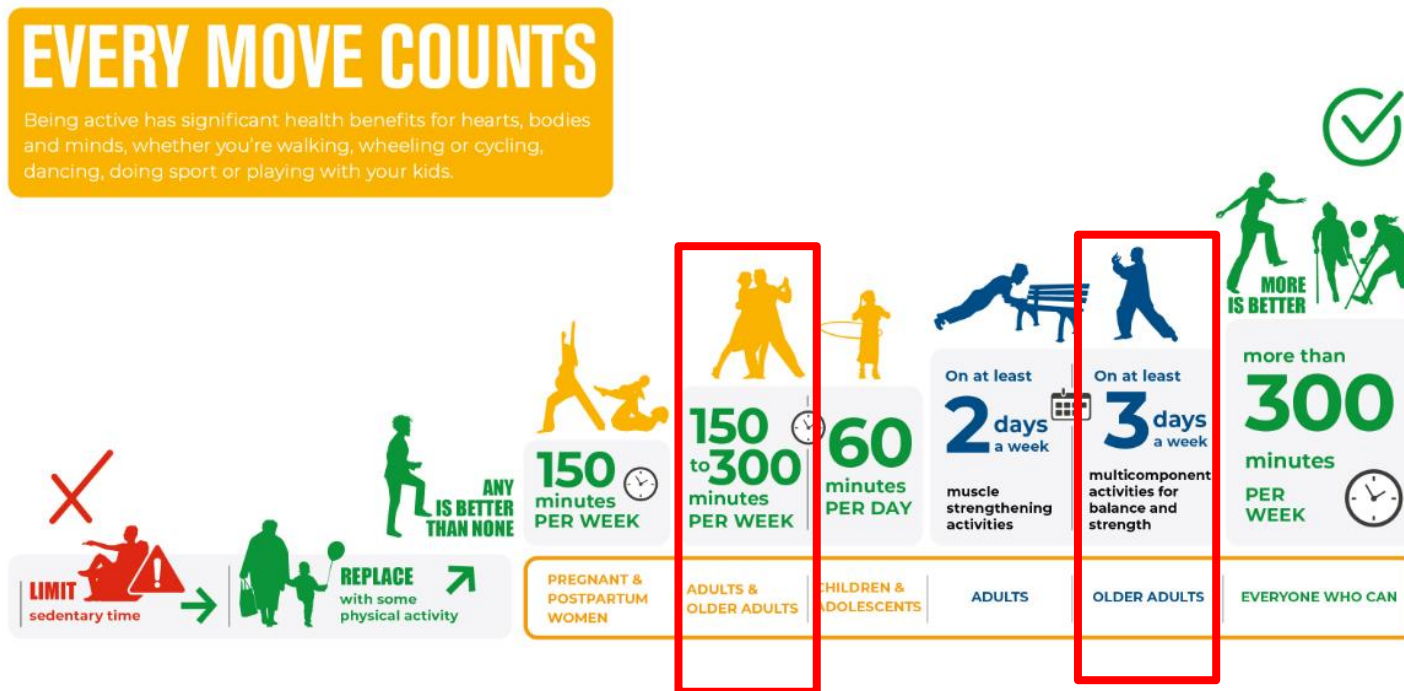




Tips for preventing/limiting frailty

- Physical exercise
- Good nutrition
- Social engagement
- Keep your mind active
- ART and management of co-infections
- Management of comorbidities
- Management of polypharmacy

A mix of aerobic, balance, and strengthening activities in older adults is associated with a reduced risk of falls, more independent years, and improved brain health



Examples of strengthening exercises:

- Lift weights
- Dig in a garden
- Body resistance exercises (push ups, sit ups, etc.)

Examples of balance exercises:

- Walk heel-to-toe
- Stand from a seated position
- Stand on one leg

Multicomponent exercises:

- Tai chi
- Yoga
- Gardening
- Many sports

WHO Guidelines on Physical Activity and Sedentary Behavior. 2020. World Health Organization. Available at <https://www.who.int/health-topics/physical-activity> Accessed 7 September 2025

What Counts as Physical Activity for Older Adults. 2023. Centers for Disease Control and Prevention. Available at <https://www.cdc.gov/physical-activity-basics/adding-older-adults/what-counts.html> Accessed 8 September 2025

Bone disease is common in people with HIV, especially postmenopausal women

Types of bone disease

- Osteoarthritis/avascular necrosis – younger age for joint replacements
- Osteoporosis/fracture (2-4x risk)

Risk factors for osteoporosis

- ART
 - loss of 2-6% bone mineral density with ART start
 - Ongoing loss with TDF, some PIs
- BMI
- Vitamin D deficiency
- Female sex
- Alcohol use

Screening for osteoporosis

- FRAX
 - Women: all premenopausal ≥ 40
 - Men: age 40-49
- DEXA
 - Women: all postmenopausal women
 - Men: all men ≥ 50 years

General osteoporosis risk factors

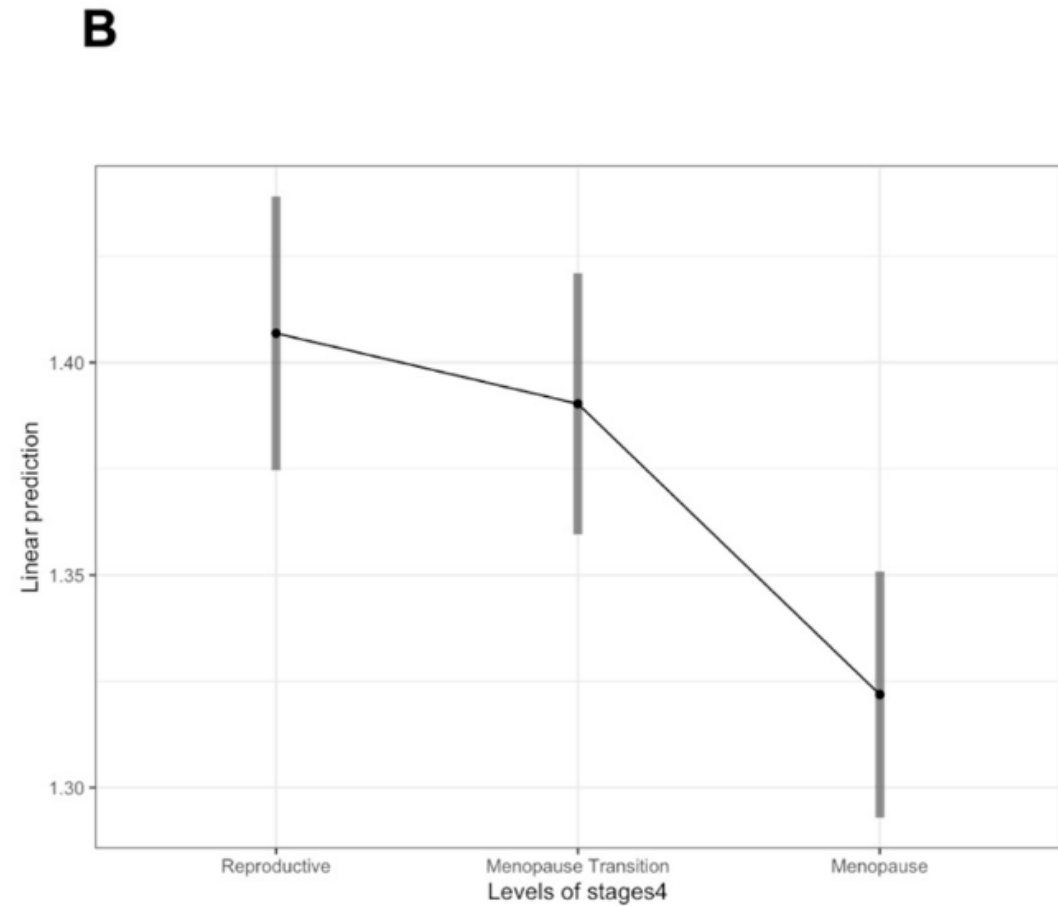
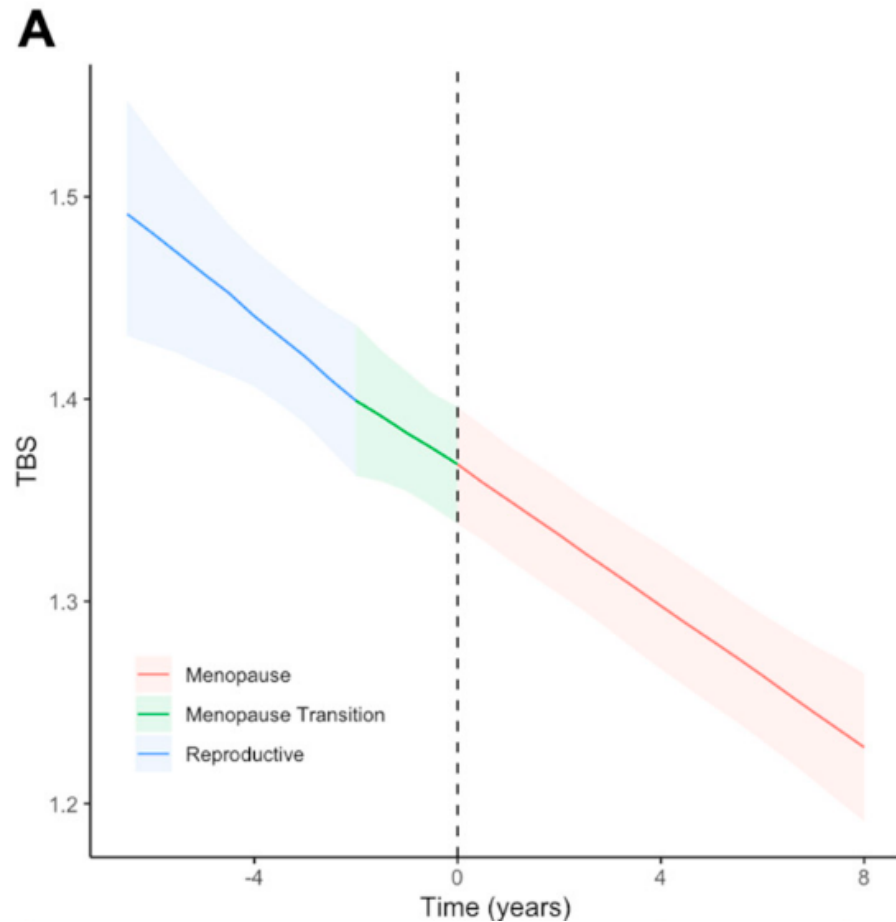
Non-modifiable

- Age (peak bone mass at age 30, decline starts ~age 40)
- Female sex
- Ethnicity (Asian, Northern European)
- Genetics
- Body frame
- Early menopause (age <45)*
 - Removal of both ovaries
 - Chemotherapy

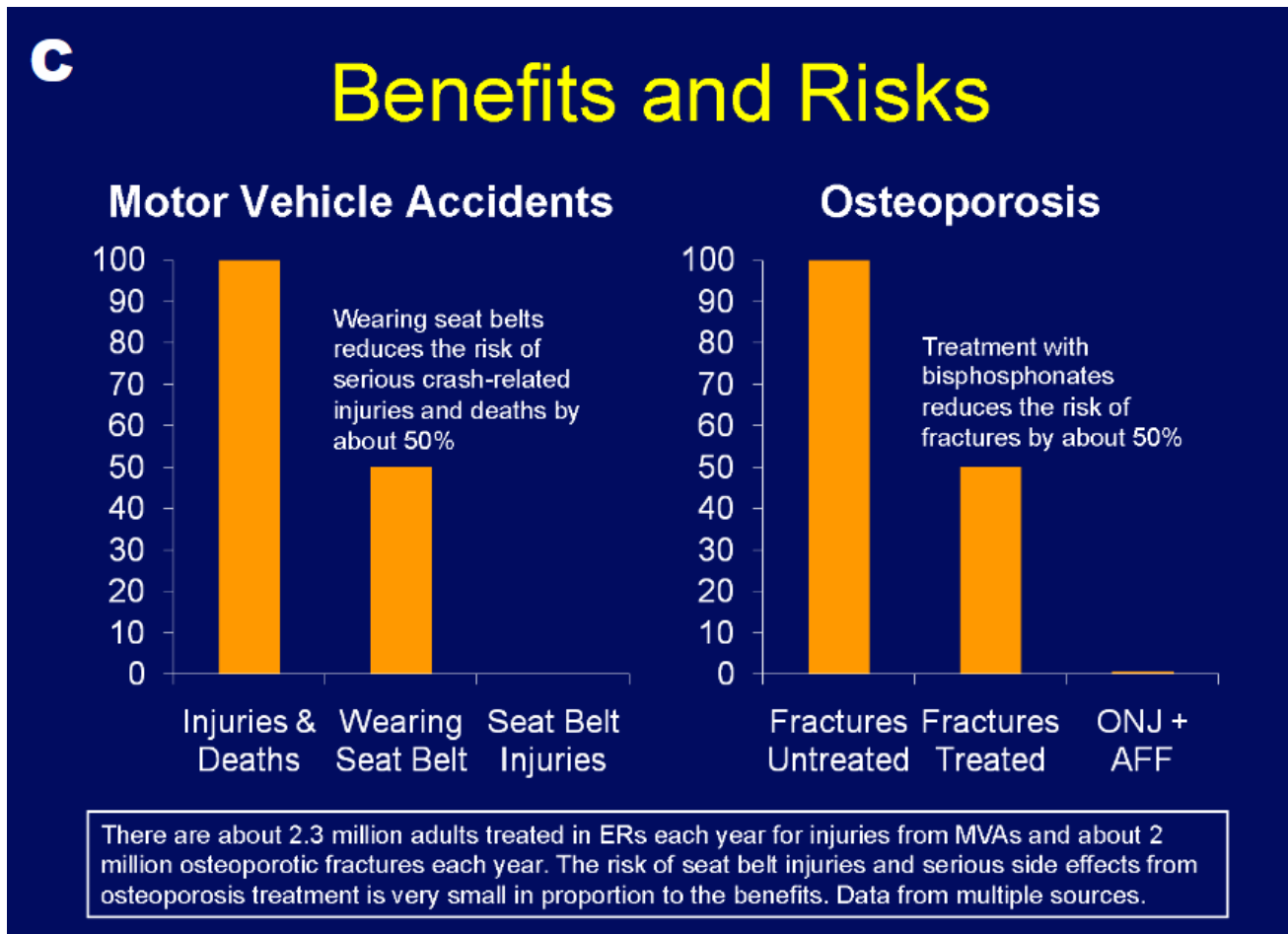
Modifiable

- Underweight
- Diet (low calcium and/or vitamin D intake)
- Low sun exposure
- Smoking
- Heavy alcohol use
- No weight-bearing exercises
- Emotional stress
- Medications (glucocorticoids, PPIs, some ART (TDF))

Bone loss accelerates at the time of the menopausal transition in women with HIV: an important time for screening



Osteoporosis treatment benefits far outweigh the risks



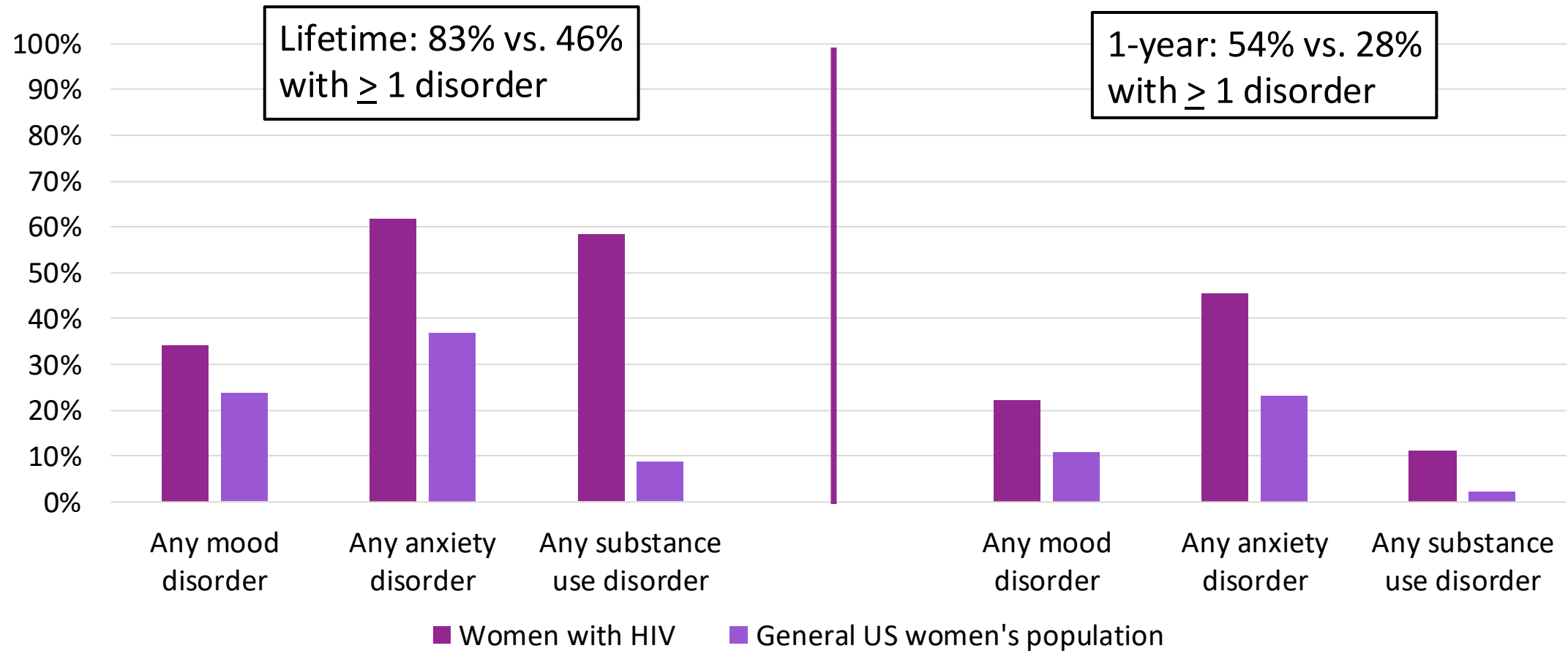
Treatment options:

- Antiresorptives (high risk/no prior fracture)
 - Bisphosphonates (first line)
 - Denosumab
 - Raloxifene
- Anabolics (very high risk/prior fracture)
 - PTH analogues (teriparatide, abaloparatide)
 - Romosozumab

A chalk drawing of a human brain on asphalt, with several pieces of colored chalk scattered around it. The brain is drawn with pink chalk for the outline and internal structures, yellow for the cerebral cortex, green for the cerebellum, and purple for the brainstem. The text "Mental Health and Cognition" is written in white across the center of the brain drawing.

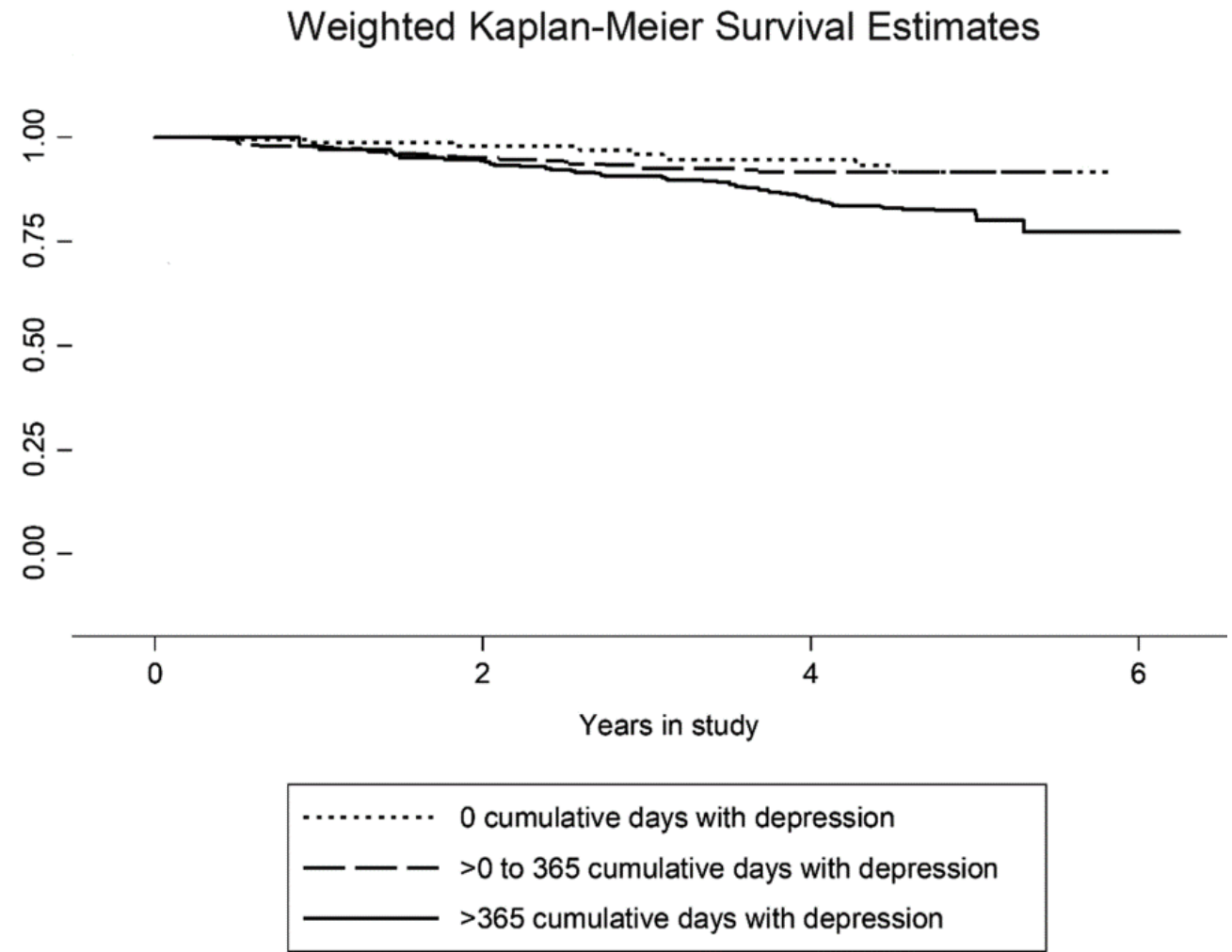
Mental Health and Cognition

Lifetime and 1-year prevalence of mental health disorders in women with HIV compared to the general U.S. women's population, 2010-2013



Depression is very common and associated with mortality in women with HIV

- 52% of women reported depressive symptoms at study entry
- Each additional 365 days of depressive symptoms was associated with a 72% increase in mortality

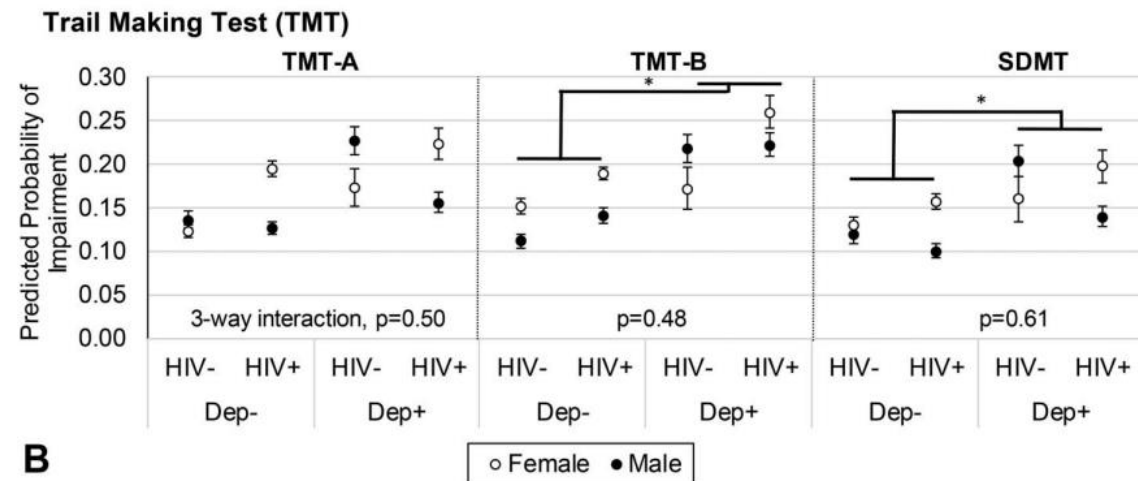
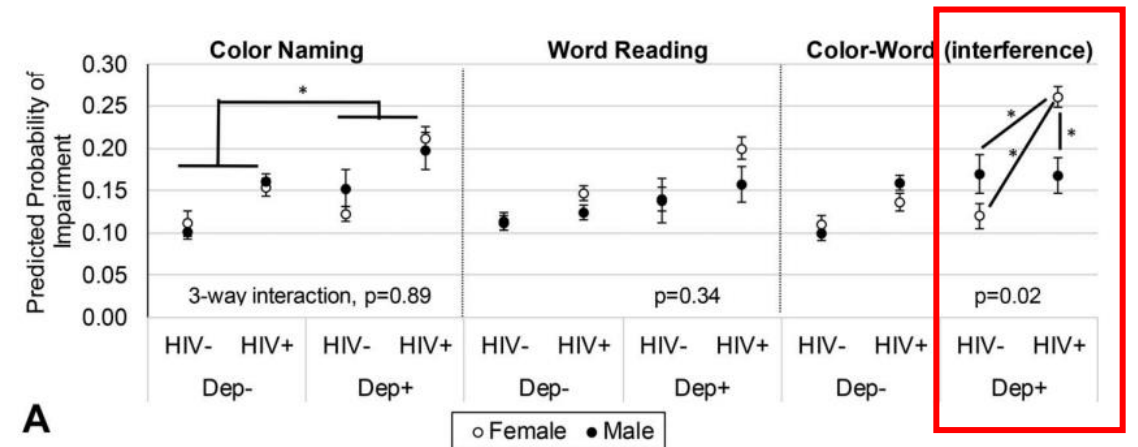
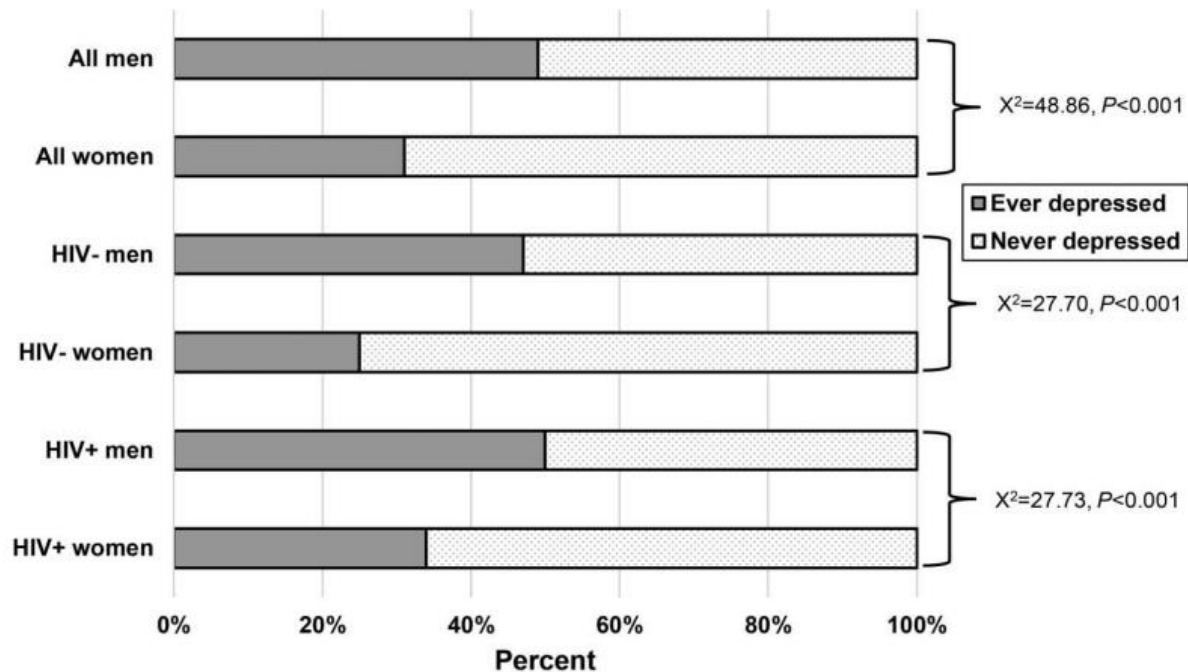


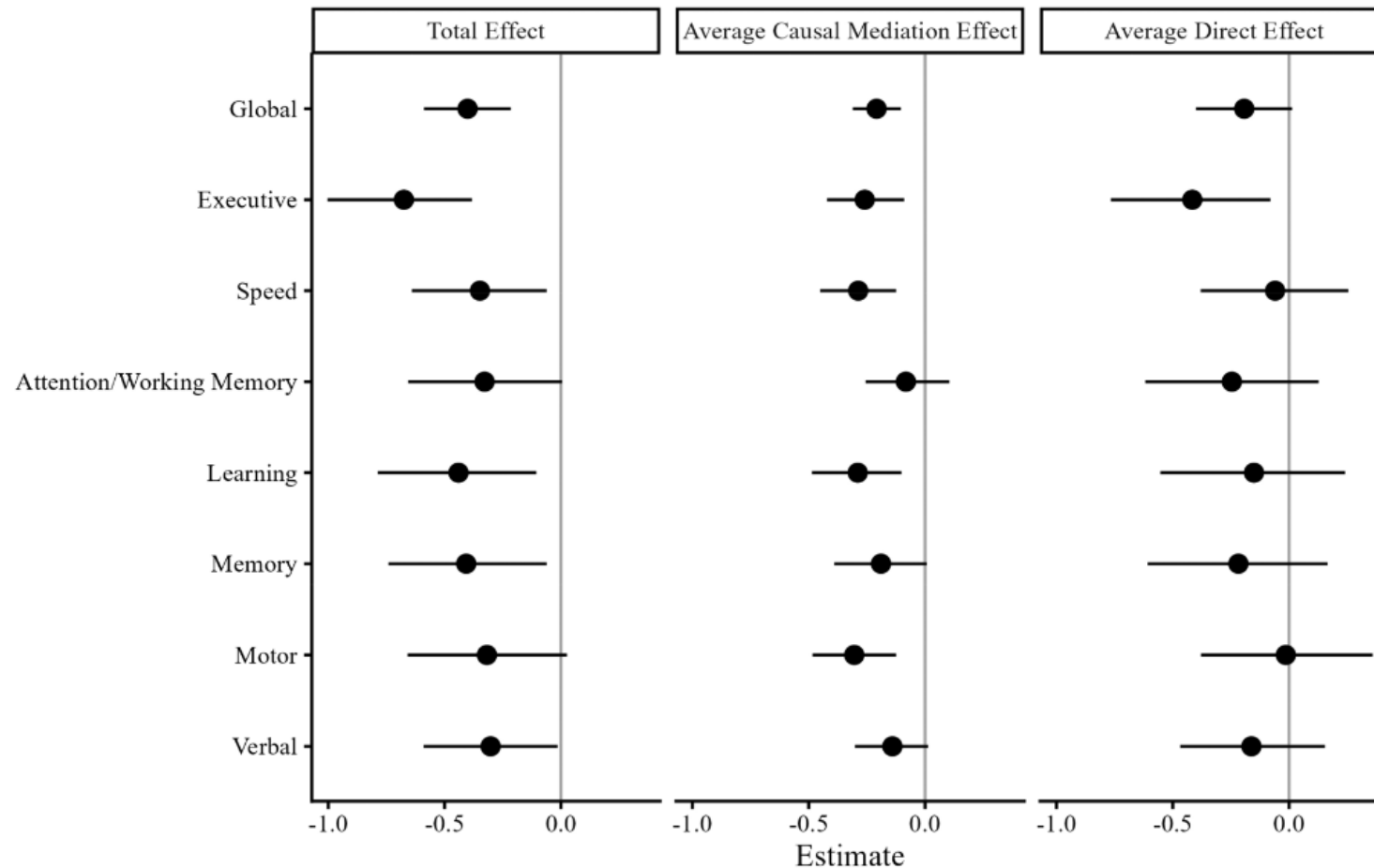


Cognitive impairment is common in older people with HIV

- HIV-associated neurocognitive disorders (HAND)
 - More common in prior eras, ~45% prevalence
 - More stable, less degenerative than AD
- Alzheimer's Disease (AD)
 - Will likely become more common as the population ages
 - Little research in AD in people with HIV- cohorts may be too young
 - May be misdiagnosed as HAND
 - Risk factors: older age, vascular disorders, depression, genetics
- Vascular dementia
 - Cardiometabolic risk factors
 - Vascular risk factors are an important driver of cognitive decline in PWH

Depressive symptoms are associated with executive dysfunction in women with HIV more than in men with HIV





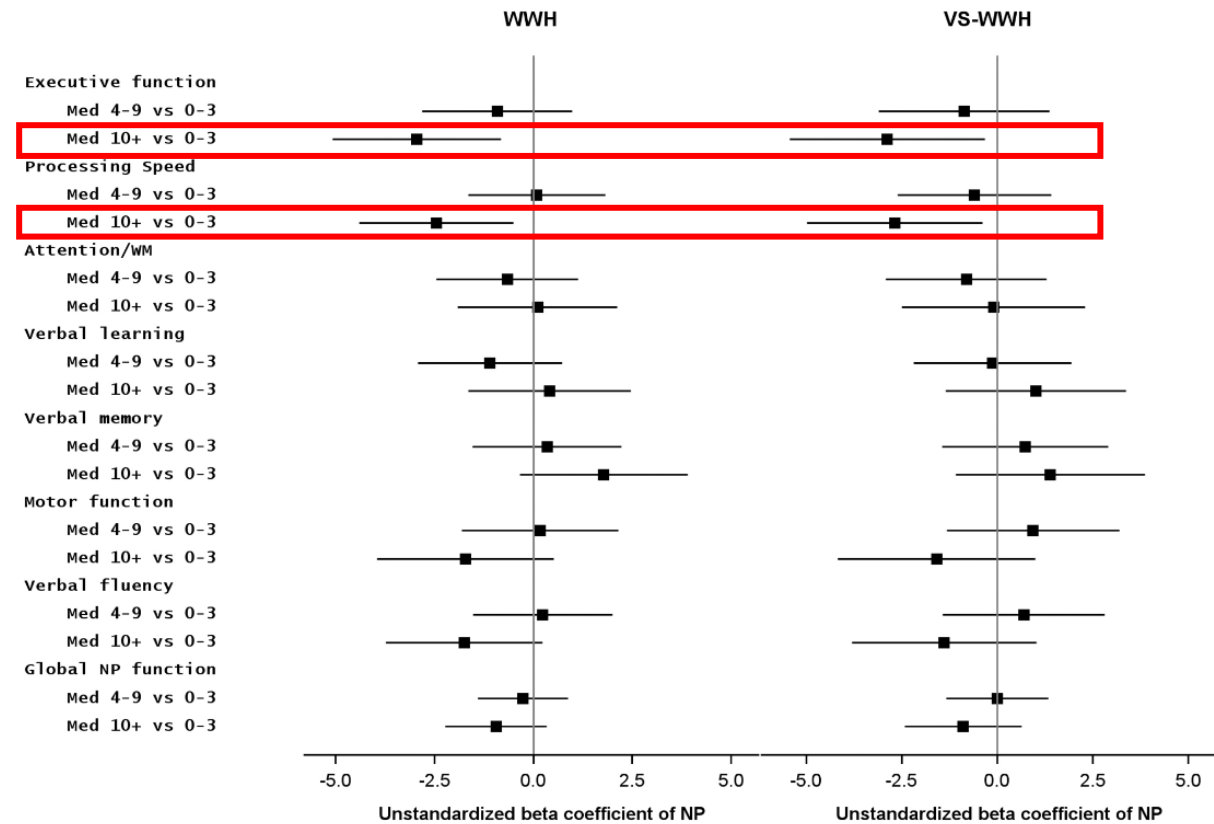
Depressive symptoms mediate the association between loneliness and cognitive performance in women with HIV

Figure 1. Forest plot of associations between loneliness and cognitive domains, mediated by depressive symptoms.

Medication use may impact neurocognitive impairment in women with HIV

- Women with HIV are on almost twice as many medications than age-matched women without HIV (7.5-8 vs. 3.5)
- Common non-antiretroviral medication classes can impact the central nervous system
 - Anticonvulsant
 - Antianxiety*
 - Anticholinergic
 - Antipsychotic
 - Amphetamine
 - Opioid*
 - Beta-blocker
 - Gastrointestinal*
 - Antihistamine*
 - Muscle relaxant
 - Antidepressant*

*More common in women with HIV



34.5% with moderate (5-9 meds) polypharmacy
24% with severe (≥ 10 meds) polypharmacy

Spence AB et al. *AIDS Res Hum Retroviruses*. 2022;38(7):561-570.
Radtke KK et al. *J Acquir Immune Defic Syndr*. 2018;78(2):202-208
Rubin LH et al. *AIDS Res Hum Retrovirus*. 2022;38(7):571-5790

Many dementia risk factors are modifiable

- Less education/cognitive stimulation
- Vision loss
- Hearing loss
- Head injury
- Smoking
- Excessive alcohol consumption
- Physical inactivity
- Infrequent social contact
- Air pollution
- High LDL cholesterol
- Hypertension
- Obesity
- Diabetes
- Depression

Livingston, Gill et al. Dementia prevention, intervention, and care: 2024 report of the *Lancet* standing Commission. *The Lancet*, Volume 404, Issue 10452, 572 - 628

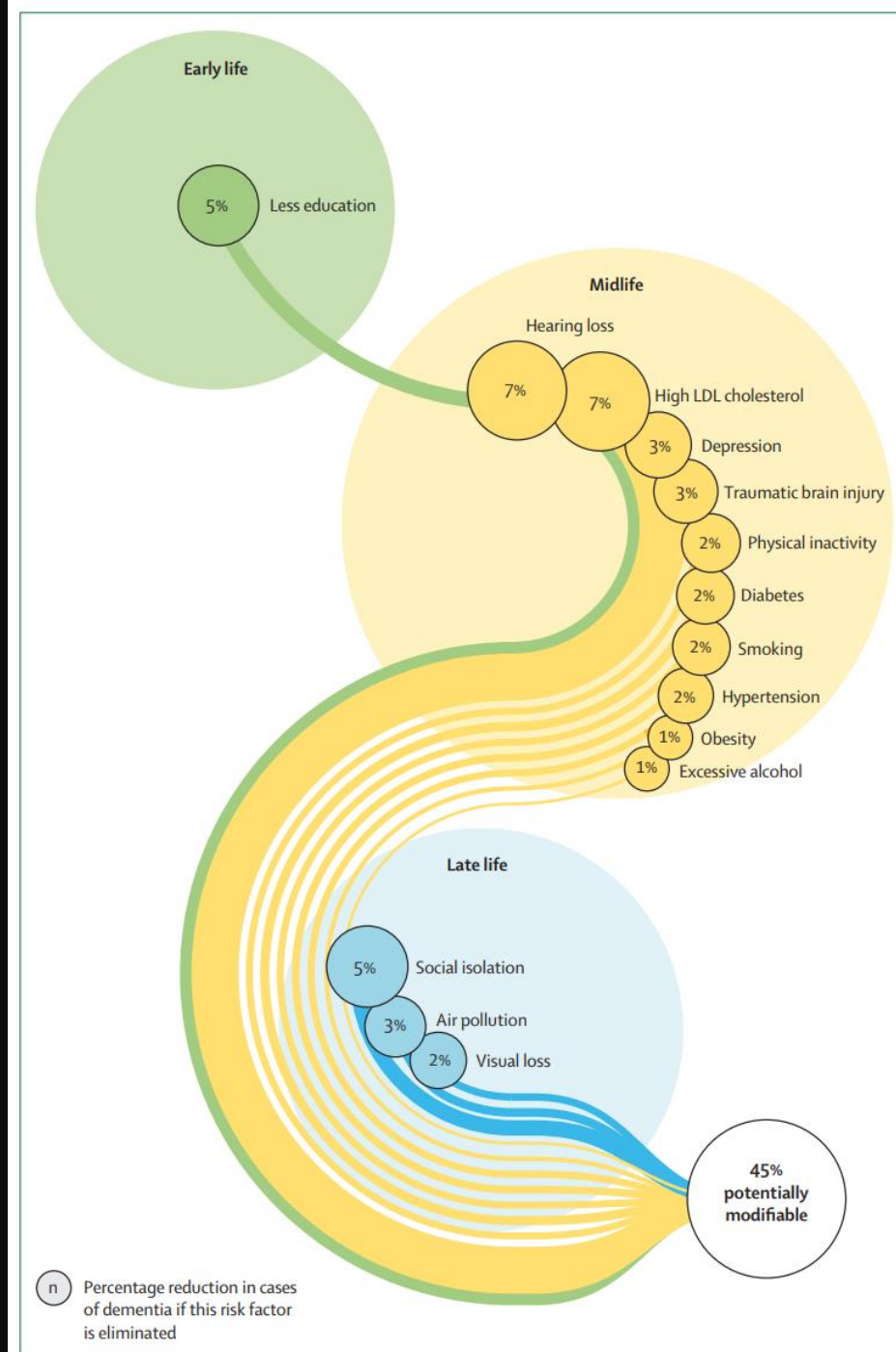


Figure 9: Population attributable fraction of potentially modifiable risk factors for dementia



In summary

Frailty and prefrailty
are common in people
living with HIV

Physical activity that
includes aerobic and
strengthening exercises
is important to
preserve health

Many risk factors for
cognitive decline are
modifiable

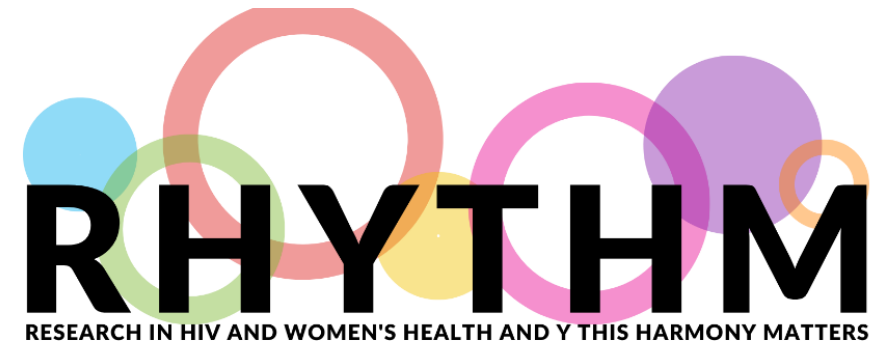
Consider screening for
frailty and cognitive
decline starting at age
50

Thank you!!

- Study participants
- Funding sources
- Colleagues and mentors



SPECIALIZED CENTER OF RESEARCH
EXCELLENCE ON SEX DIFFERENCES





Questions?
