Arc of Aging with HIV 1996-2022: from promise to disappointment & despair

Jules Levin

NATAP, National AIDS Treatment Advocacy Project

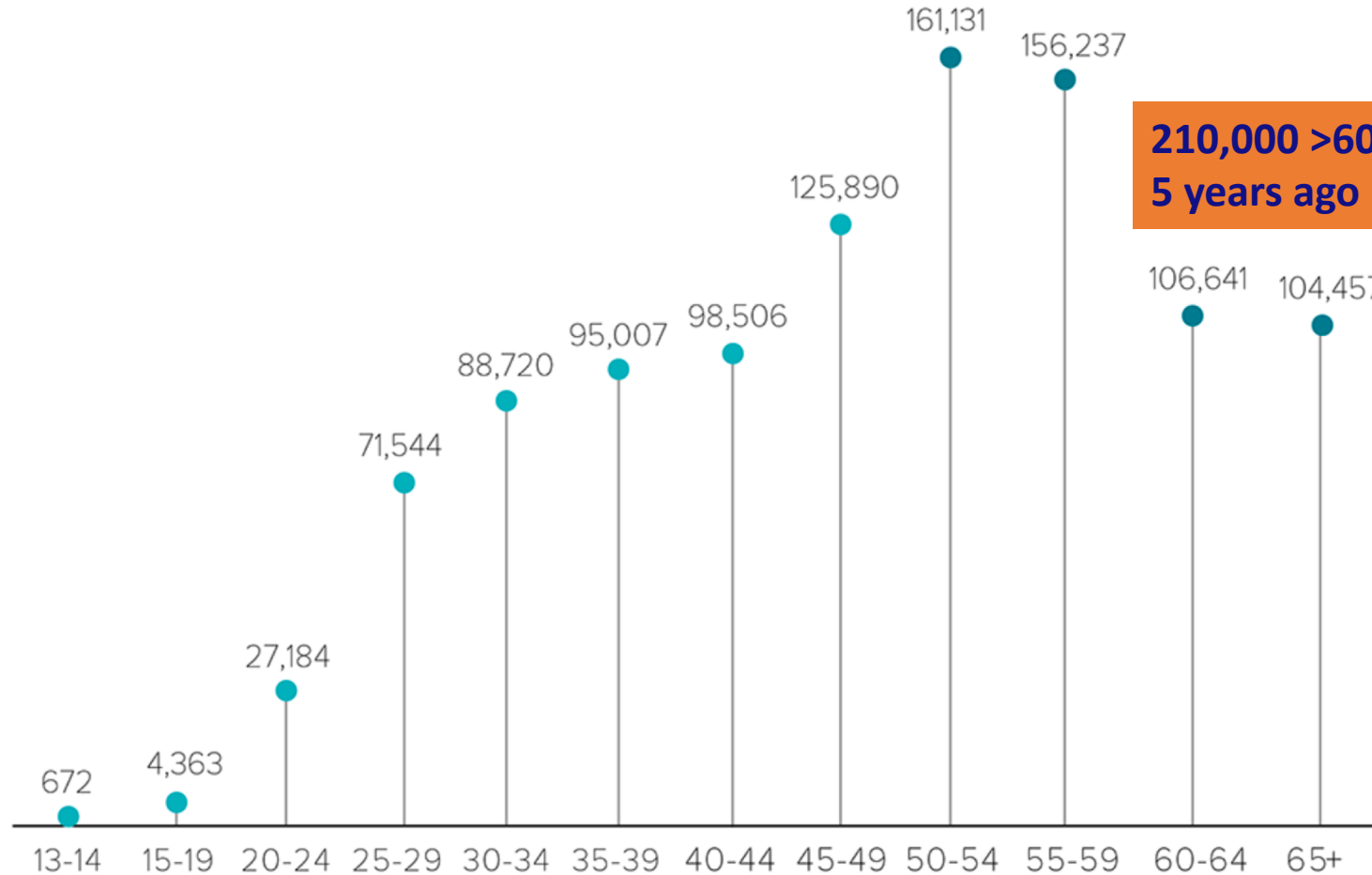www.natap.org

Website

webinar series

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

Over half of people with diagnosed HIV were aged 50 and older.
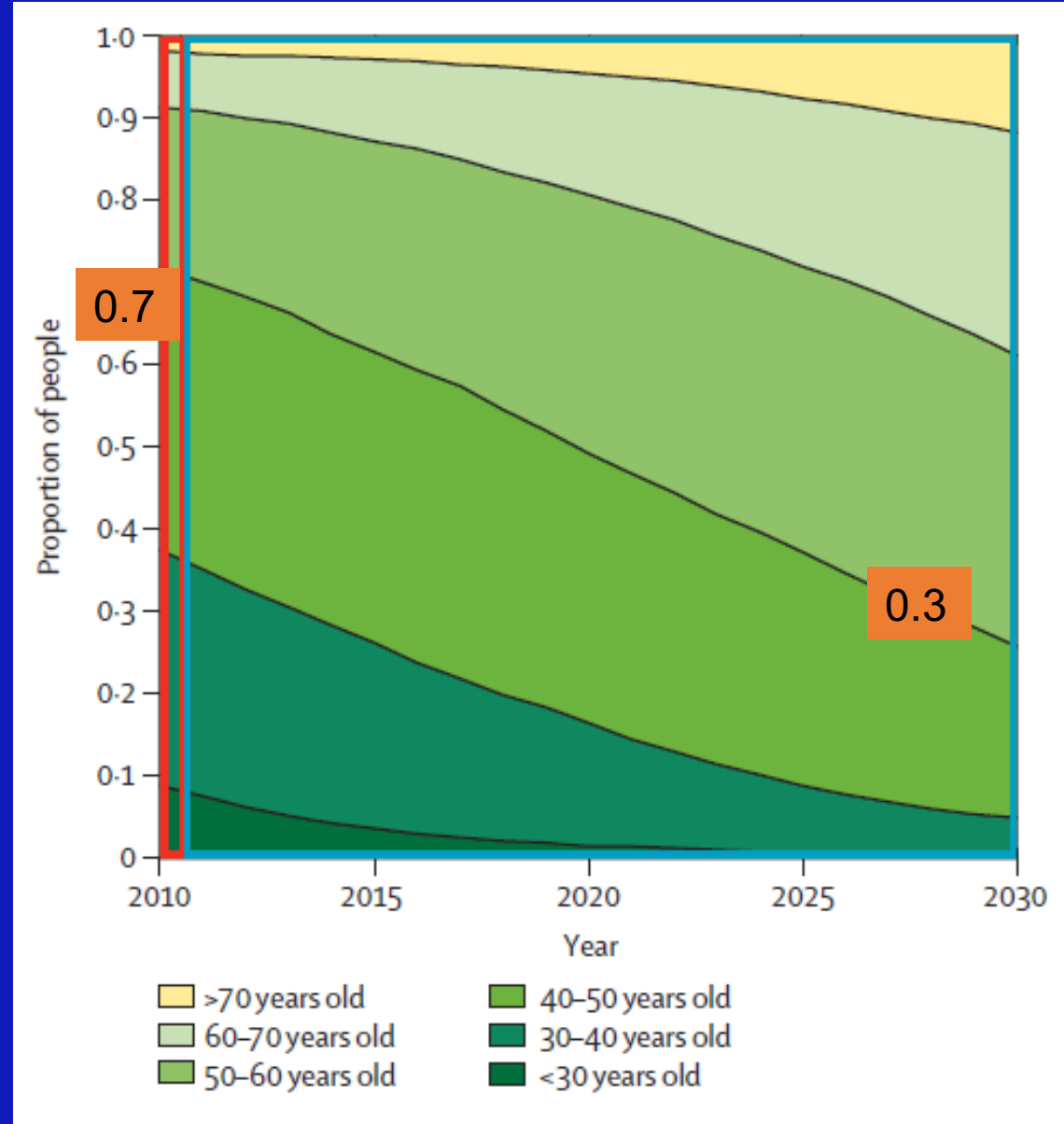
161,131

156,237

**210,000 >60 years old
5 years ago**

125,890

106,641   104,457

98,506

95,007

88,720

71,544

27,184

672   4,363

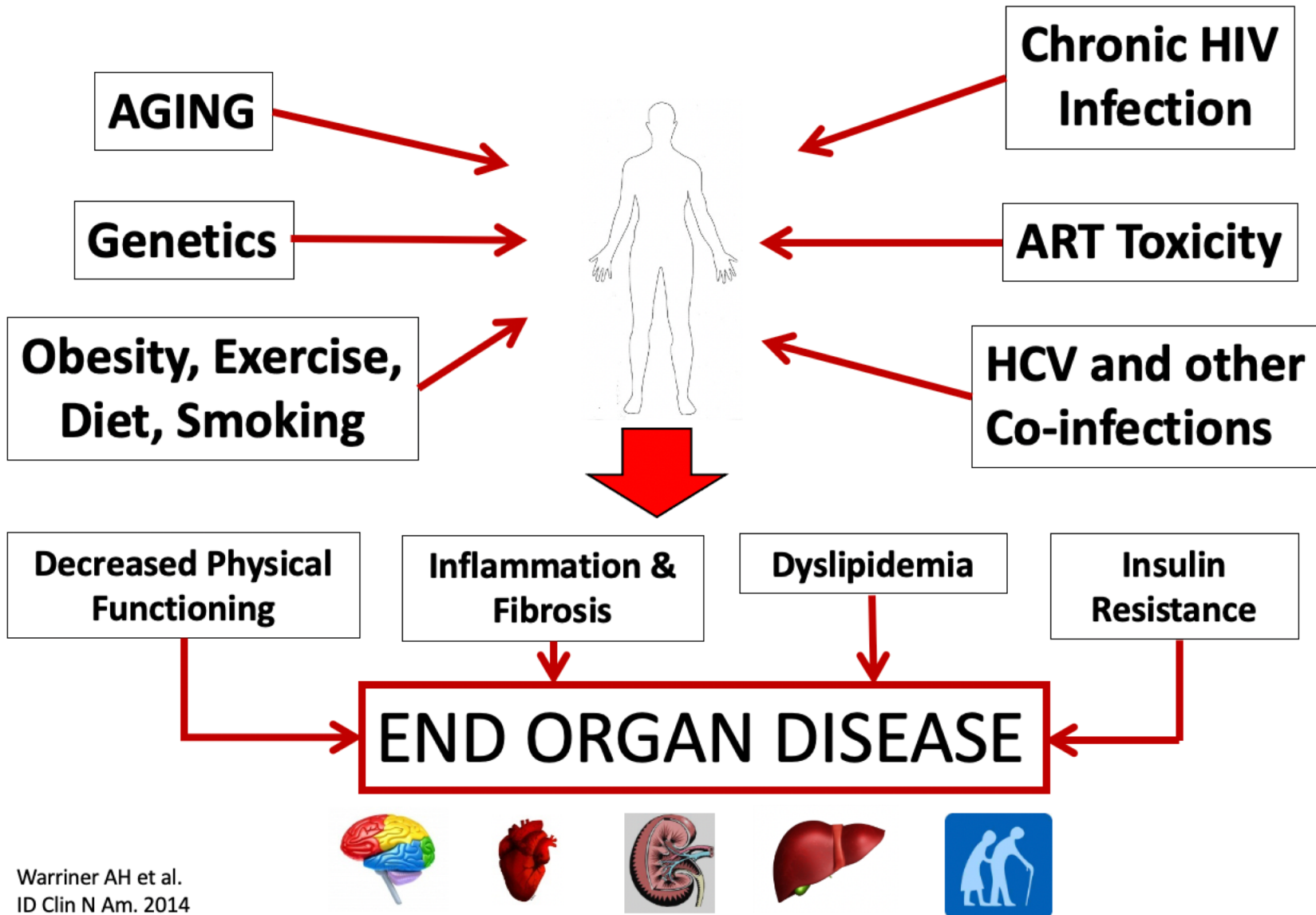| 13-14 | 15-19 | 20-24 | 25-29 | 30-34 | 35-39 | 40-44 | 45-49 | 50-54 | 55-59 | 60-64 | 65+ |

Download and Share This Infographic

70% by 2030 projected to be over 50 years old, _40-50% over 60_

Older PWH are the majority of PWH but the issue is not treated that way

Smit, Lancet Inf Diseases, 2015
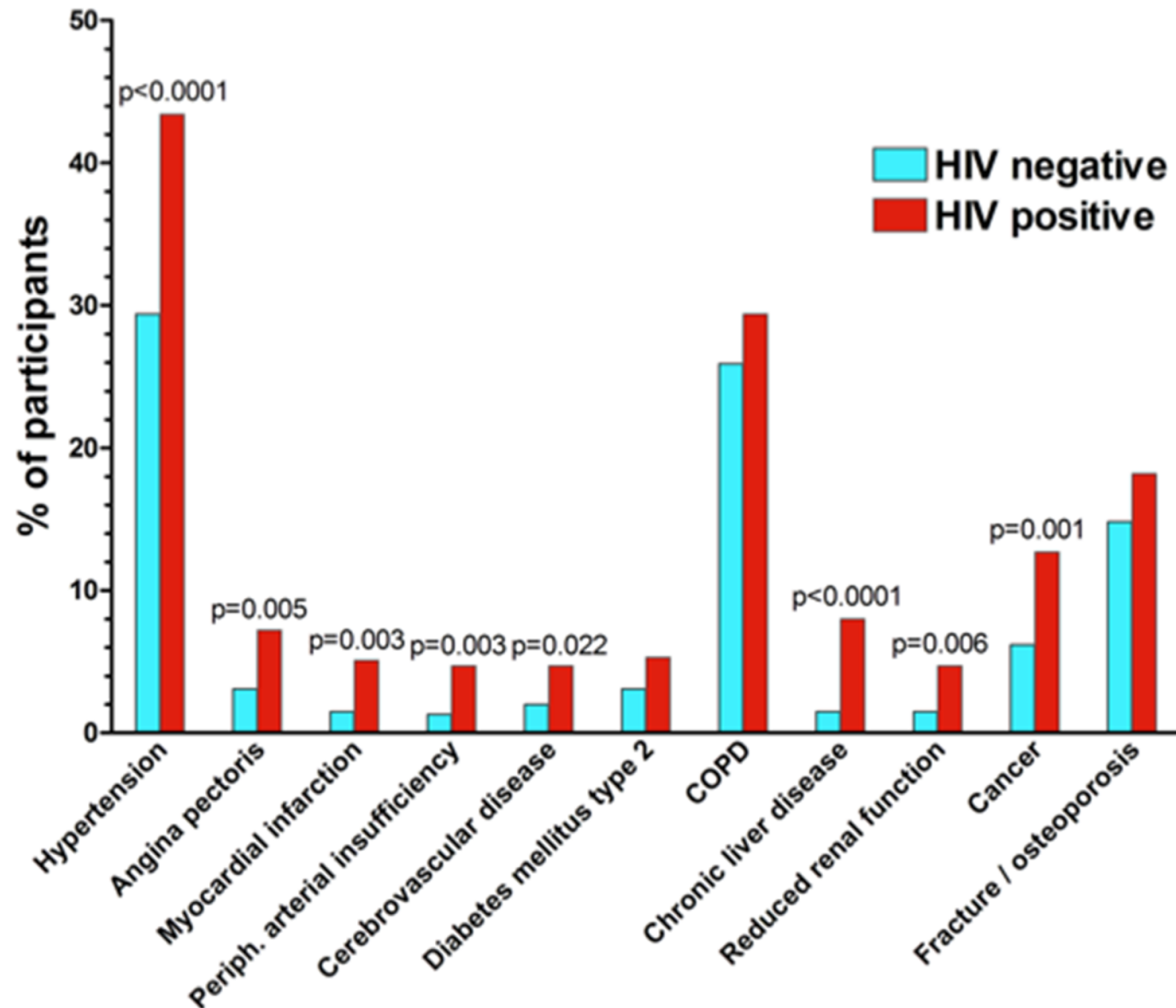
Factors -Impact on Non-AIDS Comorbidities

- Immune Dysfunction & depletion
- Low CD4 nadir
- Genetics
- lifetime trauma
- Discrimination
- Stigma
- mitochondrial damage
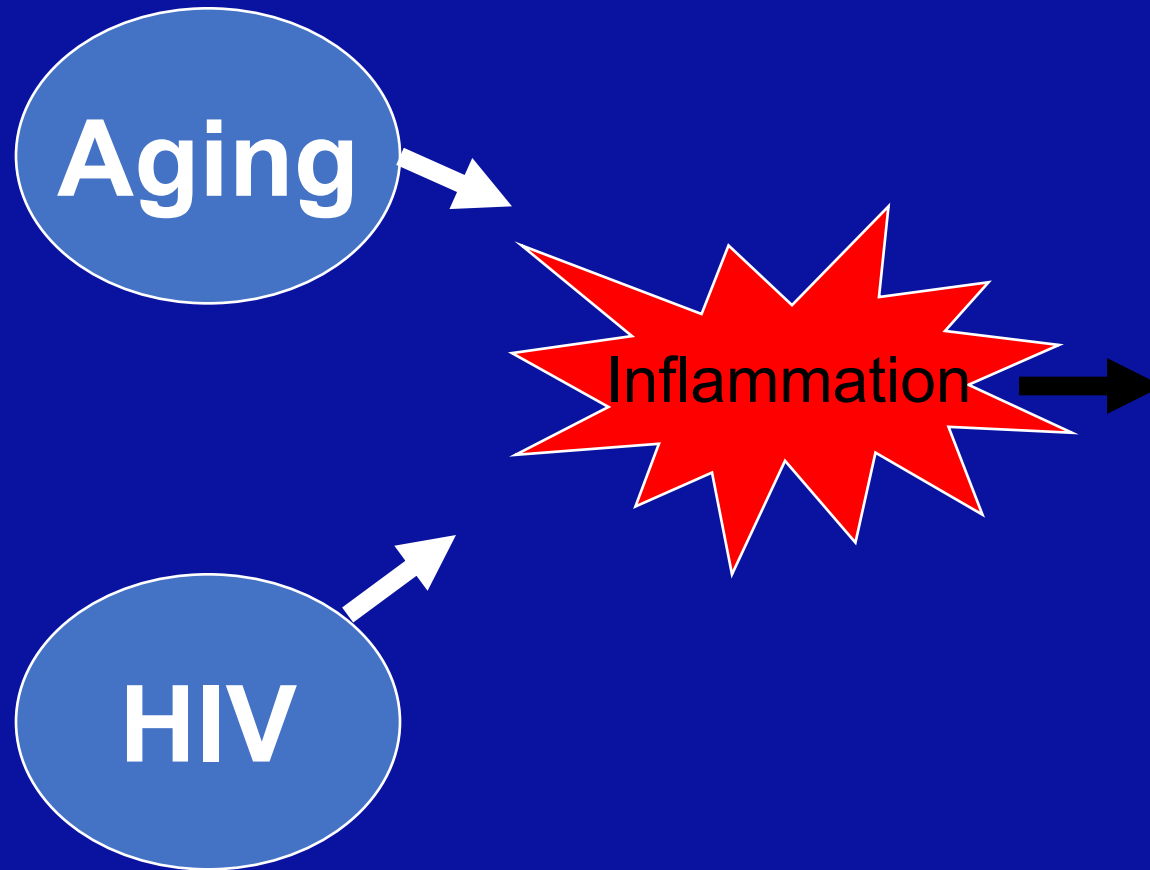- history of IDU, heroin/cocaine use

PWH have more comorbidities than people without HIV
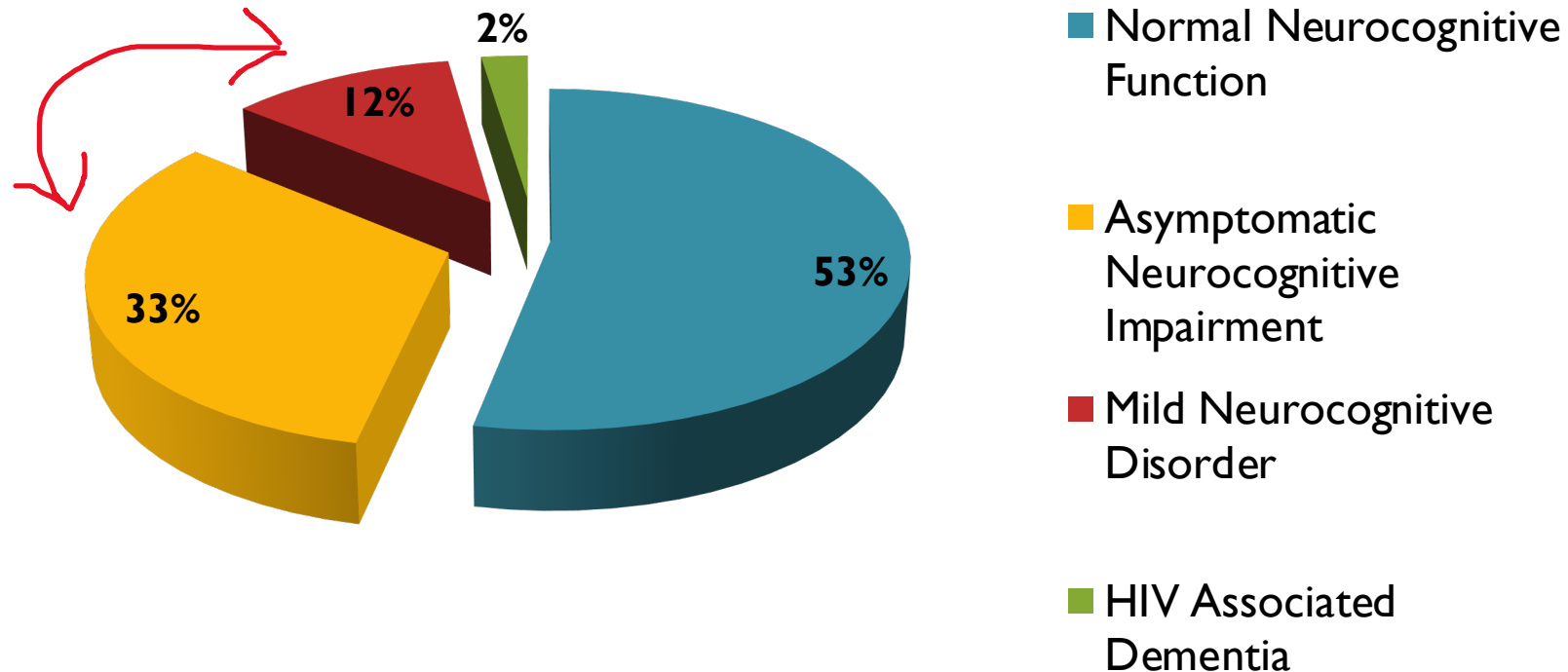

Comorbidity distribution

% of participants

HIV negative
HIV positive

p<0.0001 (Hypertension)
p=0.005 (Angina pectoris)
p=0.003 (Myocardial infarction)
p=0.003 (Periph. arterial insufficiency)
p=0.022 (Cerebrovascular disease)
p<0.0001 (Chronic liver disease)
p=0.006 (Reduced renal function)
p=0.001 (Cancer)

Hypertension, Angina pectoris, Myocardial infarction, Periph. arterial insufficiency, Cerebrovascular disease, Diabetes mellitus type 2, COPD, Chronic liver disease, Reduced renal function, Cancer, Fracture / osteoporosis

Current puzzle (2020): persistent mild forms of neurocognitive impairment in treated HIV

- 1555 person USA urban CHARTER cohort - 71% on antiretroviral therapy (excluding most 'confounded' participants):


Legend:
- Normal Neurocognitive Function
- Asymptomatic Neurocognitive Impairment
- Mild Neurocognitive Disorder
- HIV Associated Dementia

Pie chart values: 2%, 12%, 33%, 53%

Many individuals with 'co-morbidities' in this cohort.

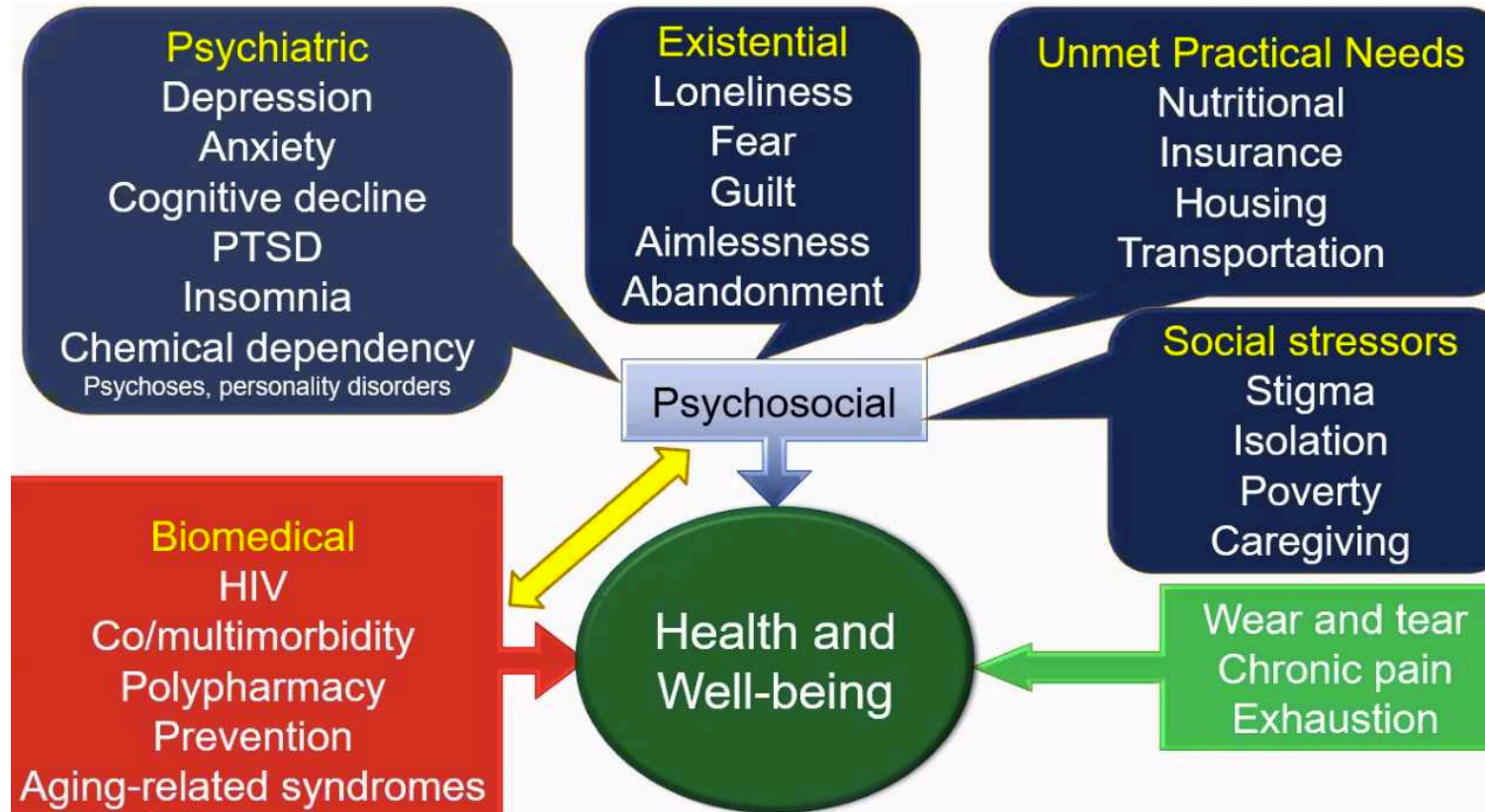Adapted from: Heaton, et al. *Neurology.* 2010;75; 2087.
Also: Robertson, et al. *AIDS* 2007, 21:1915; Simioni, et al. *AIDS* 2010, 24: 1243.

Brain-age gap greater in PWH vs Pw/oH

- Brain-age gap related to:
  - CVD risk
  - HCV
  - Detectable VL
  - Early life stress
  - Socioeconomic challenges

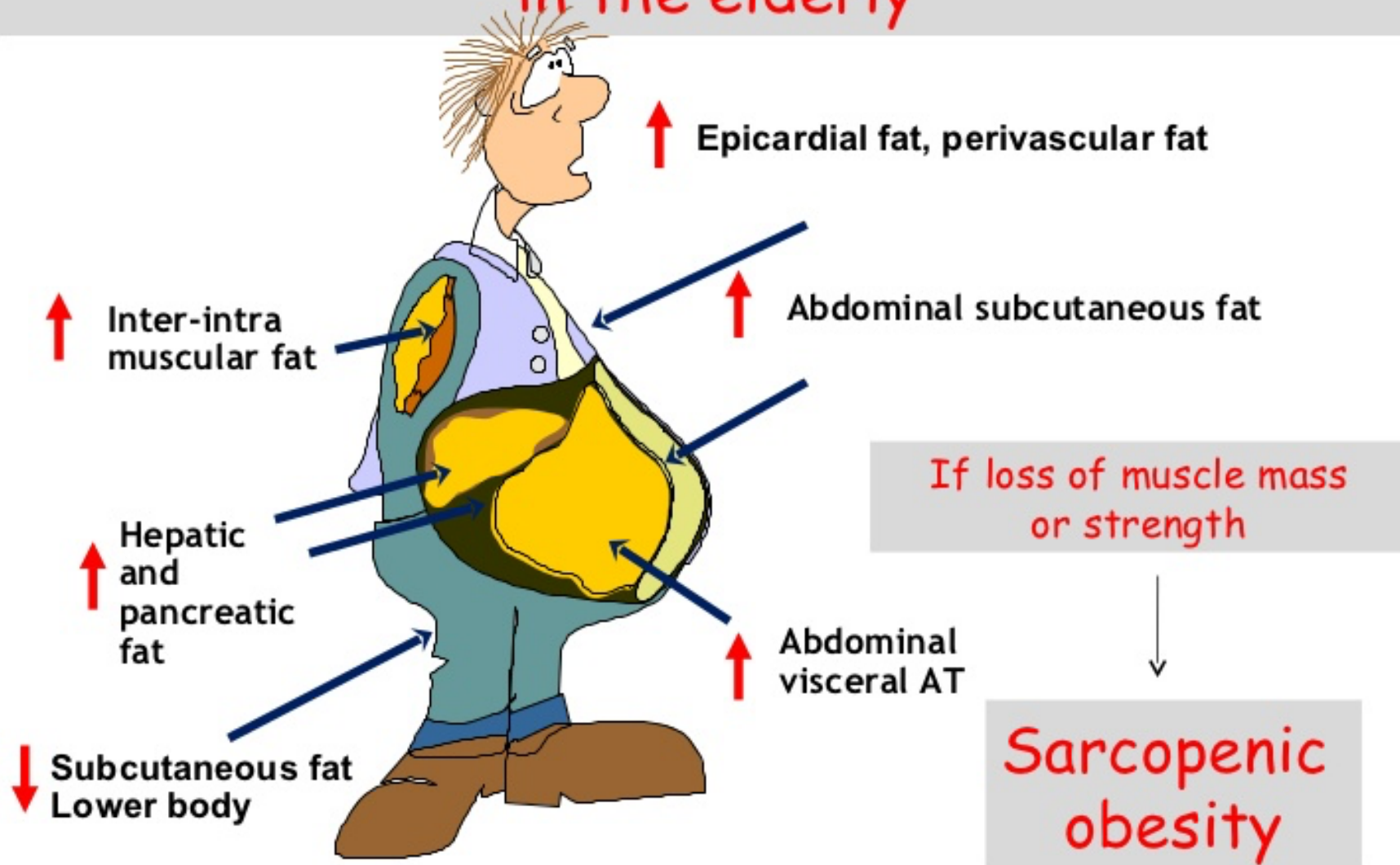- Brain regions were affected differently in those with and without HIV
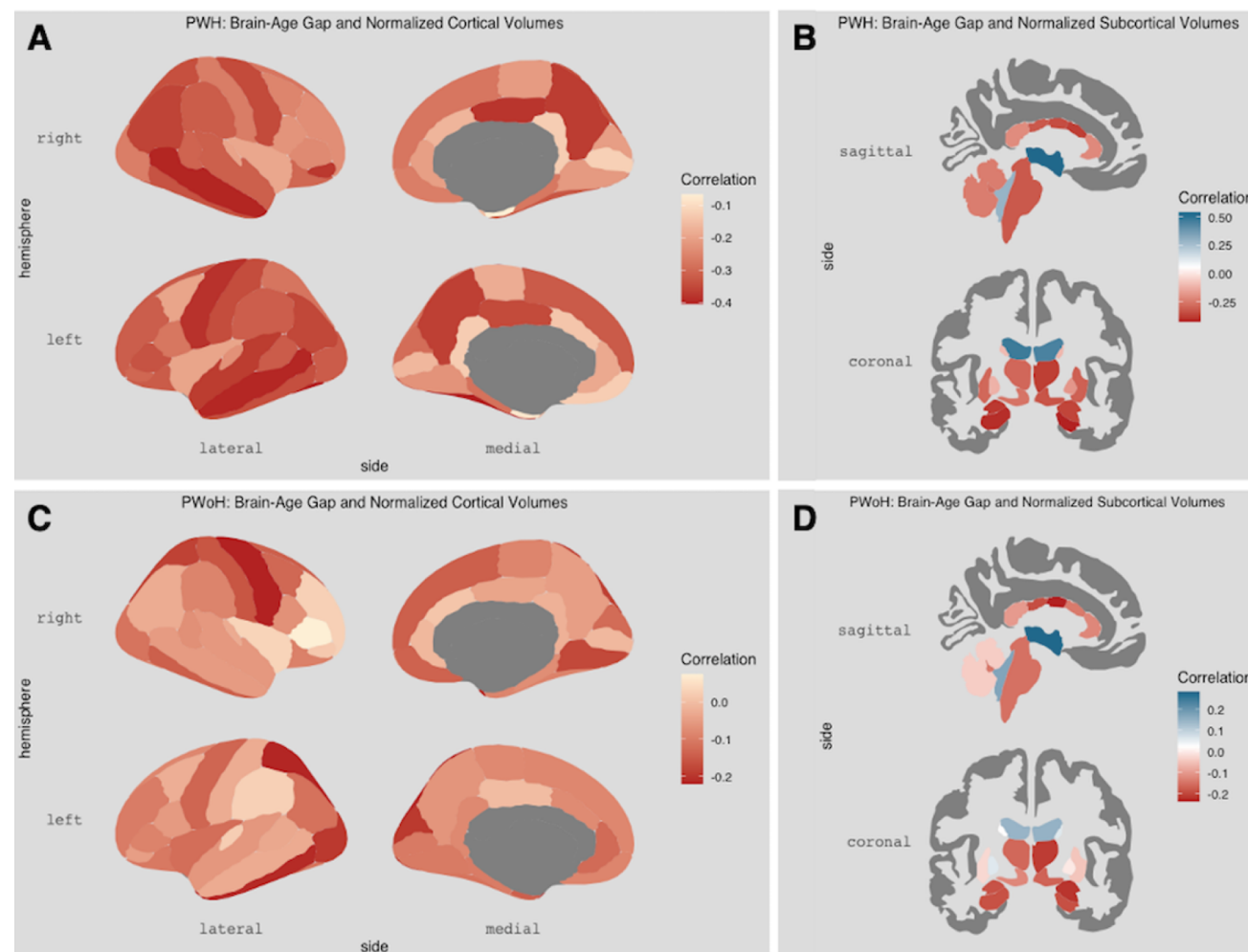
"Aging & HIV Syndrome"

Eugenia Siegler, Cornell.

Body fat changes and ectopic fat deposition in the elderly

↑ Epicardial fat, perivascular fat

↑ Inter-intra muscular fat

↑ Abdominal subcutaneous fat

↑ Hepatic and pancreatic fat

↑ Abdominal visceral AT

↓ Subcutaneous fat Lower body

If loss of muscle mass or strength

↓

Sarcopenic obesity

HIV damages fat Causes fat depots around the heart & in muscles - Fatty liver

What is Ectopic Fat?

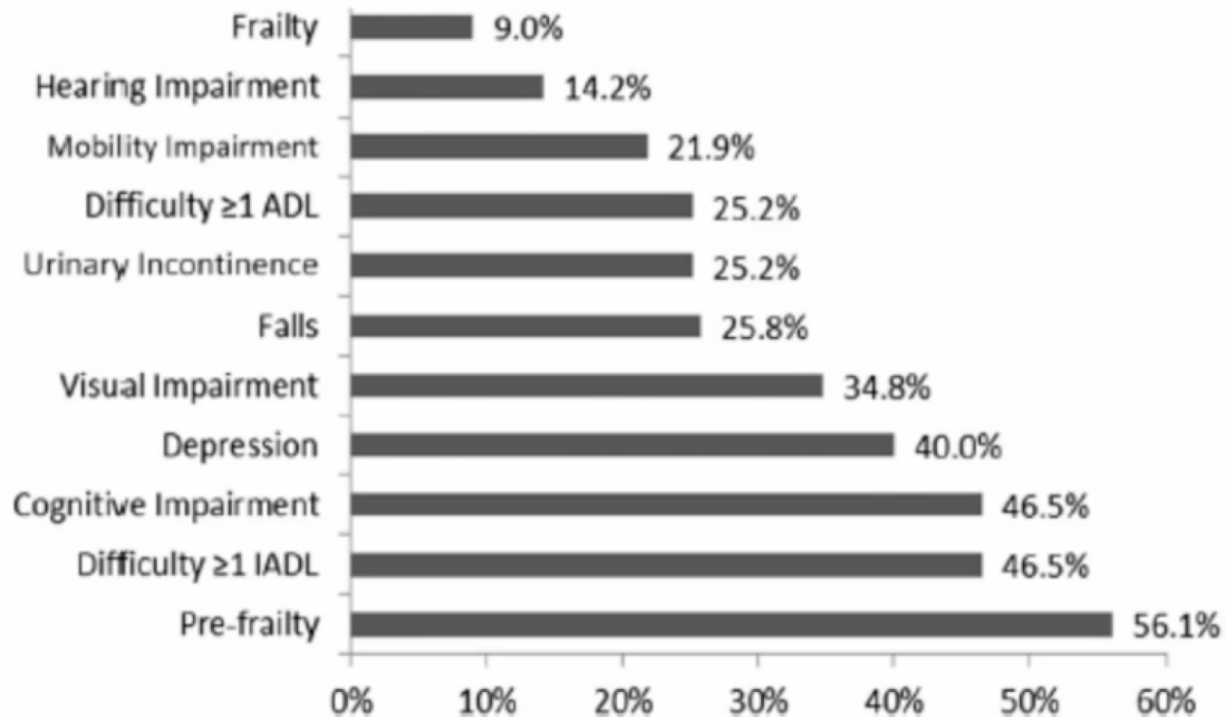Gaggini M, et al. Horm Mol Biol Clin Investig 2015;22:7–18
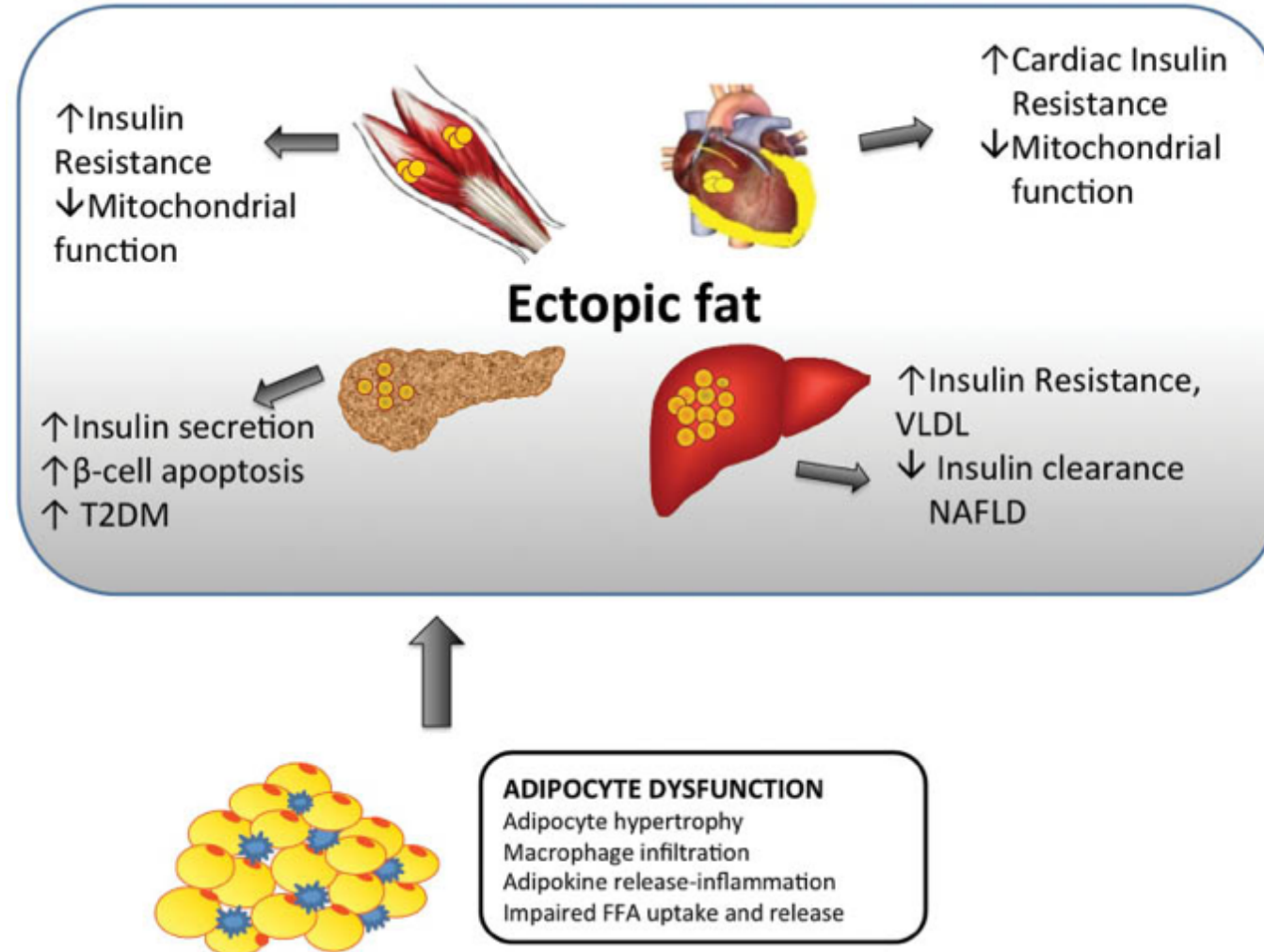
'20 years Difference between HIV + vs HIV-'

"These things are Happening A lot Earlier for PWH than they should be. These syndromes in this chart happen to 80 year olds without HIV but in PWH at 60 or younger"
George Kuchel at CROI 2023

HIV as accelerated (accentuated) aging

Geriatric Syndromes in Older HIV-Infected Adults

| Syndrome	Percentage
Frailty	9.0%
Hearing Impairment	14.2%
Mobility Impairment	21.9%
Difficulty ≥1 ADL	25.2%
Urinary Incontinence	25.2%
Falls	25.8%
Visual Impairment	34.8%
Depression	40.0%
Cognitive Impairment	46.5%
Difficulty ≥1 IADL	46.5%
Pre-frailty	56.1%

Nearly two-thirds of these individuals were still 60 years or younger

Greene *et al.*, JAIDS 2015

UConn Pepper

Accelerated or Premature aging: 15 (7-15) Years Earlier Onset of Comorbidities

Figure 2. Comorbidity-Free Life Expectancy at Age 21 Years for Individuals With and Without HIV Infection Stratified by Comorbidity, Kaiser Permanente, 2000-2016
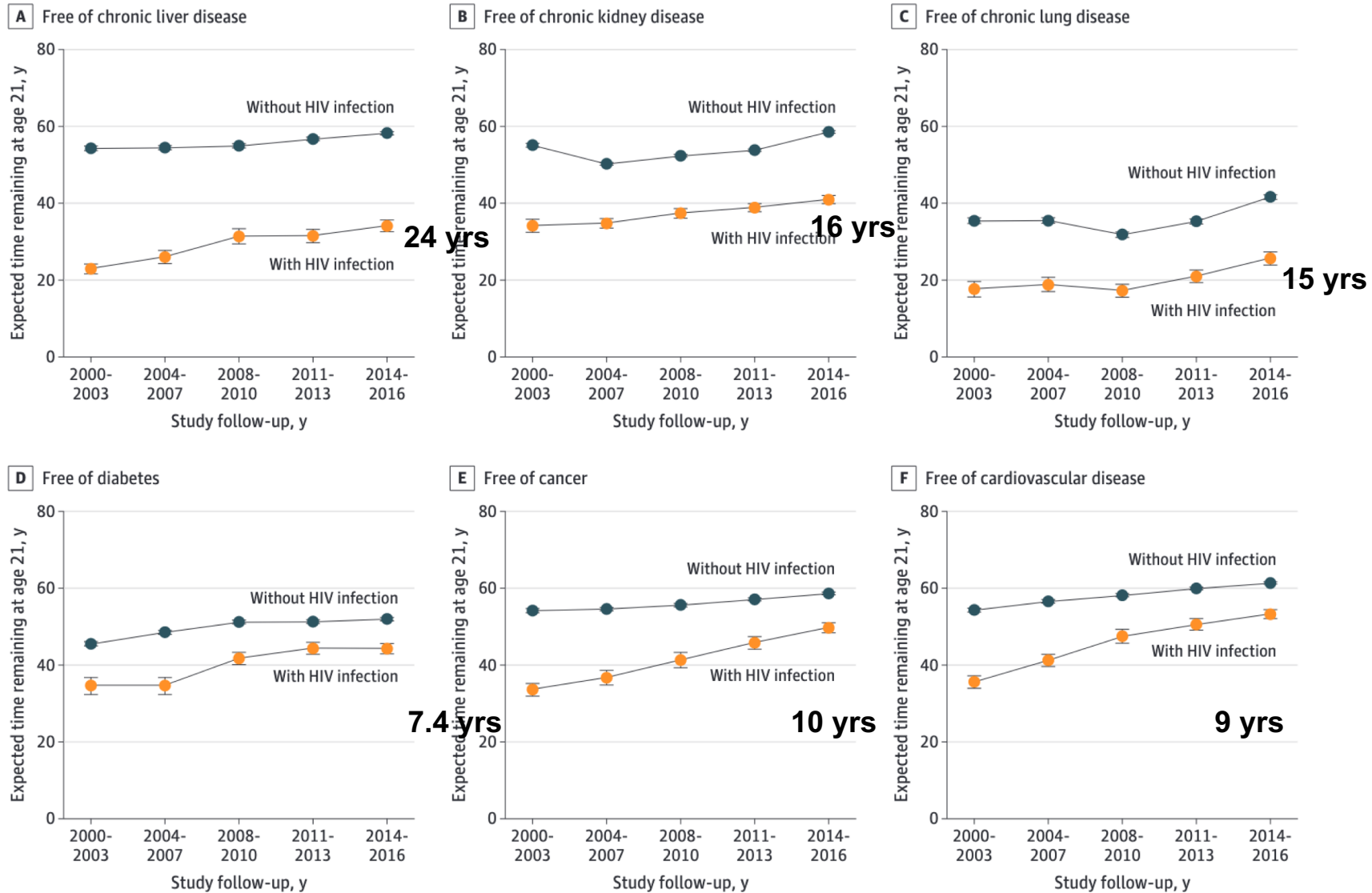
Women with HIV Have More Comorbidities than Men & Women Without HIV, More Inflammation, Worse Physical Function - MACS/WIHS
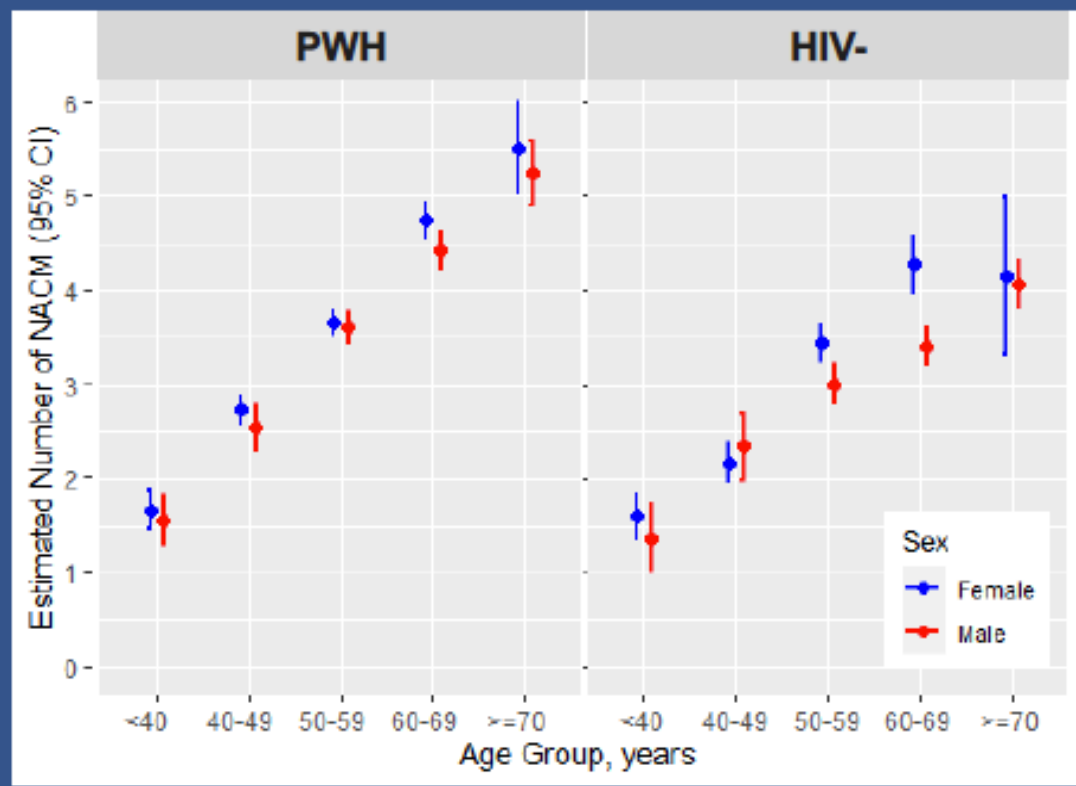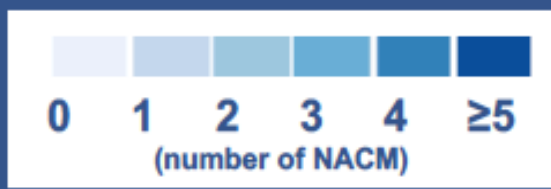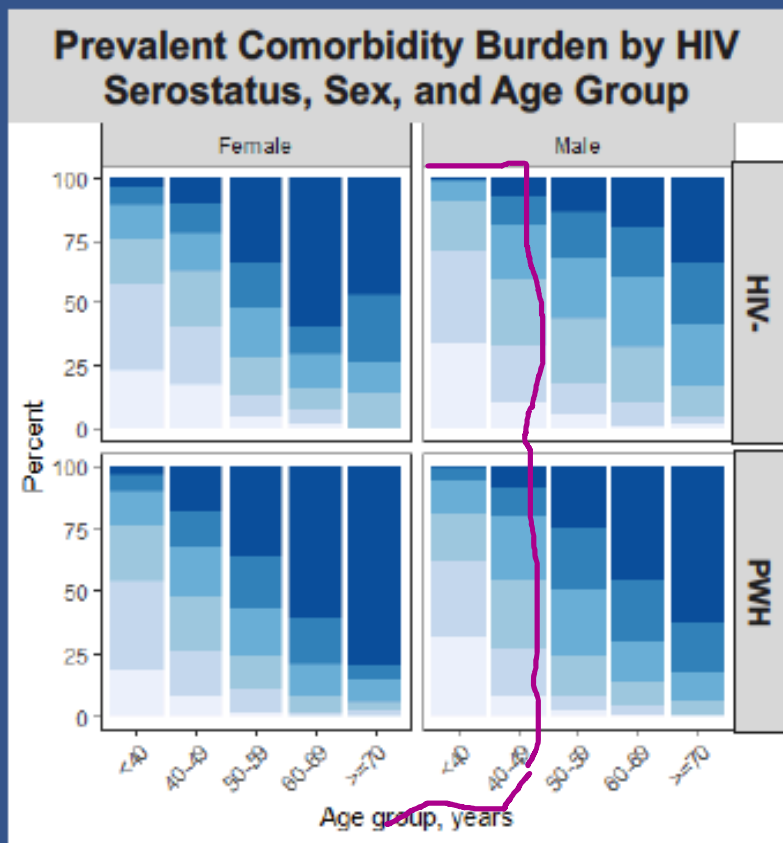
In the adjusted model[†], findings were attenuated but HIV and age still significantly modified the estimated mean NACM burden by sex (HIV*age*sex, *p*=0.038)

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

Collins, CROI 2021

Doubling After 75 Years Old

Emerging importance of chronic _comorbidities in patients > 75_ in France:

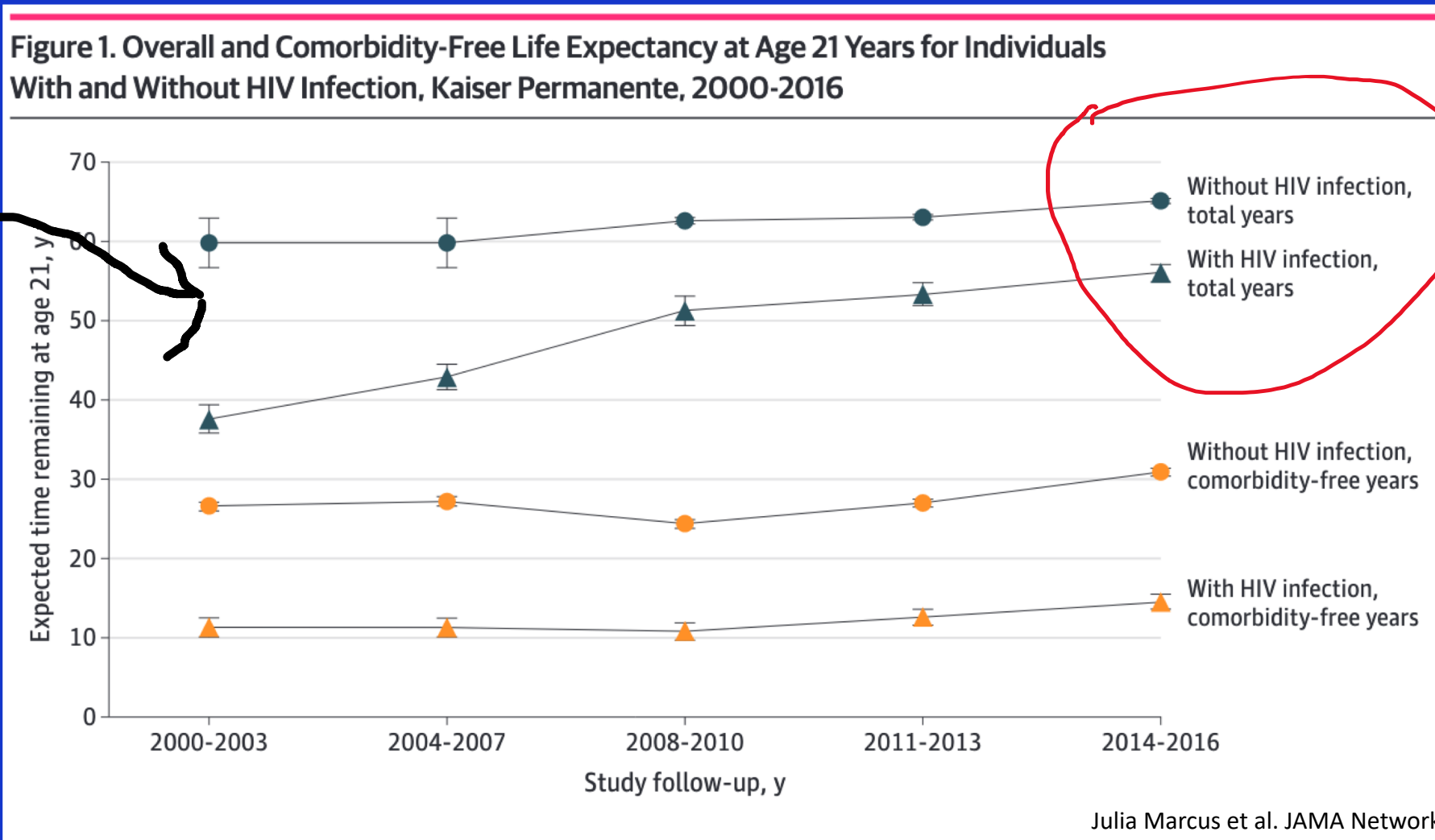## Table 5 : Age-associated non communicable comorbidities (AANC)

N(%)	Elderly [50-75[n=12748	Geriatric ≥75 n=430	P. value
Diabetes	1195 (9.4)	96 (22.3)	< 0.001
Hypertension	2685 (21.1)	182 (42.3)	< 0.001
Hyperlipidemia	2700 (21.2)	120 (27.9)	0.001
Cardio-vascular disease	1081 (8.5)	89 (20.7)	< 0.001
Stroke	319 (2.5)	27 (6.3)	< 0.001
Osteoporosis	626 (4.9)	36 (8.4)	0.002
Neoplasia	1526 (12)	97 (22.6)	< 0.001
Renal failure*	594 (4.7)	60 (14)	< 0.001
Depression	2114 (16.6)	65 (15.1)	NS
Liver fibrosis	620 (4.9)	10 (2.3)	0.021
Number of AANC			< 0.001
- 0-1	9058 (71.1)	197 (45.8)	
- 2-3	3147 (24.7)	173 (40.2)	
- ≥4	543 (4.3)	60 (14)	

*eGFR <60 ml/mn/1,73m^2

C. Allavena. France. CROI 2026

9 Years Less Life Expectancy – 77 for PLWH vs 86

mean age 41 (10.8), 87% male; 25.1%) were non-Hispanic black and 87 191 (24.3%) were Hispanic; HIV+ more poor; drug use disorders, ever smoked, lower rate of obesity or overweight, 70% MSM

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

Improved from 22 yrs diff.

To 9 yrs diff.

CD4 nadir >500: 6-year gap

Julia Marcus et al. JAMA Network Open 2020

Increased Mortality for Blacks with HIV

ADJUSTED YEARS OF POTENTIAL LIFE LOST BY SEX/RACE AND HIV RISK FACTOR

Premature Mortality Higher in Women and Blacks in US HIV Group
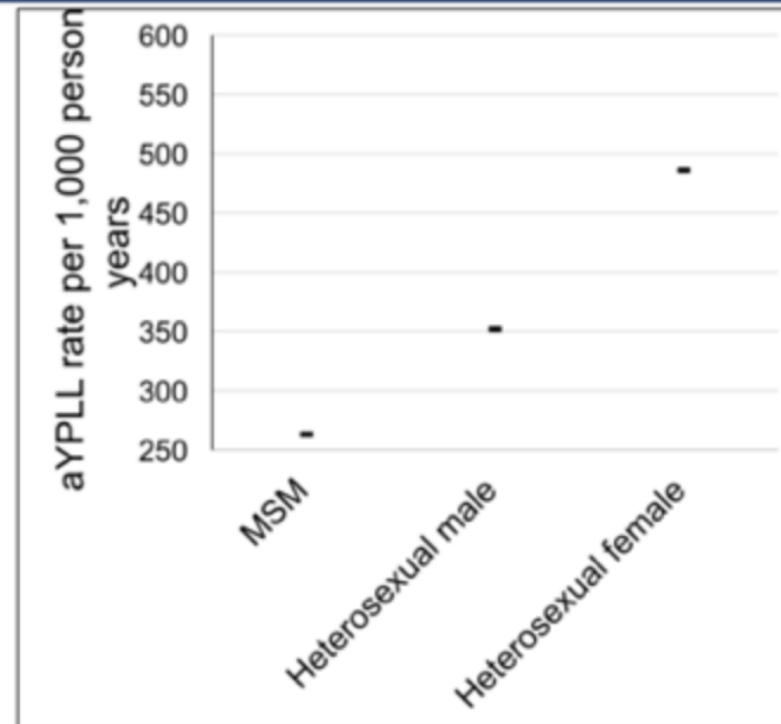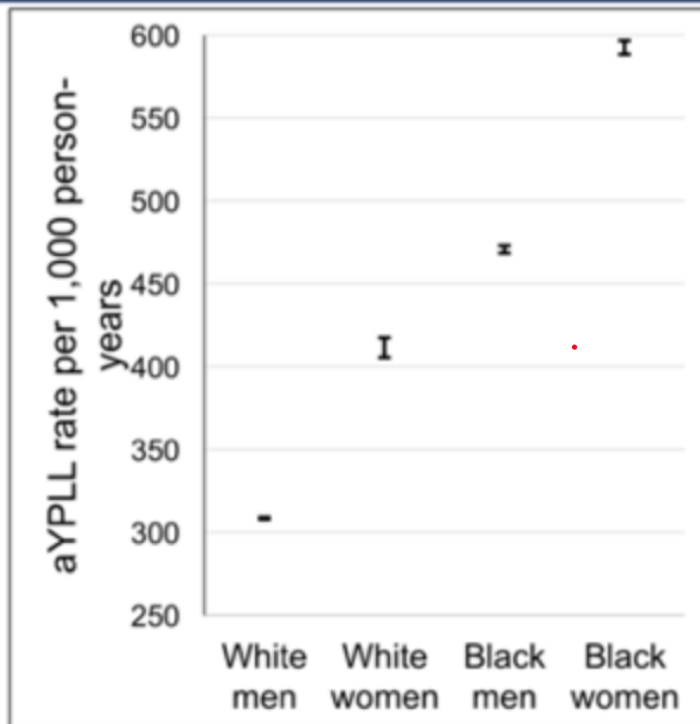
https://www.natap.org/2021/IDWeek/IDWeek_36.htm

Pellegrino et al. Vanderbilt U. Sex and race disparities in premature mortality among people with HIV: a 21-year observational cohort study. IDWeek, 2021. Abstract 53

The Faces of Frailty

Thurn & Gustafson, *Current HIV/AIDS Reports*, 2017.
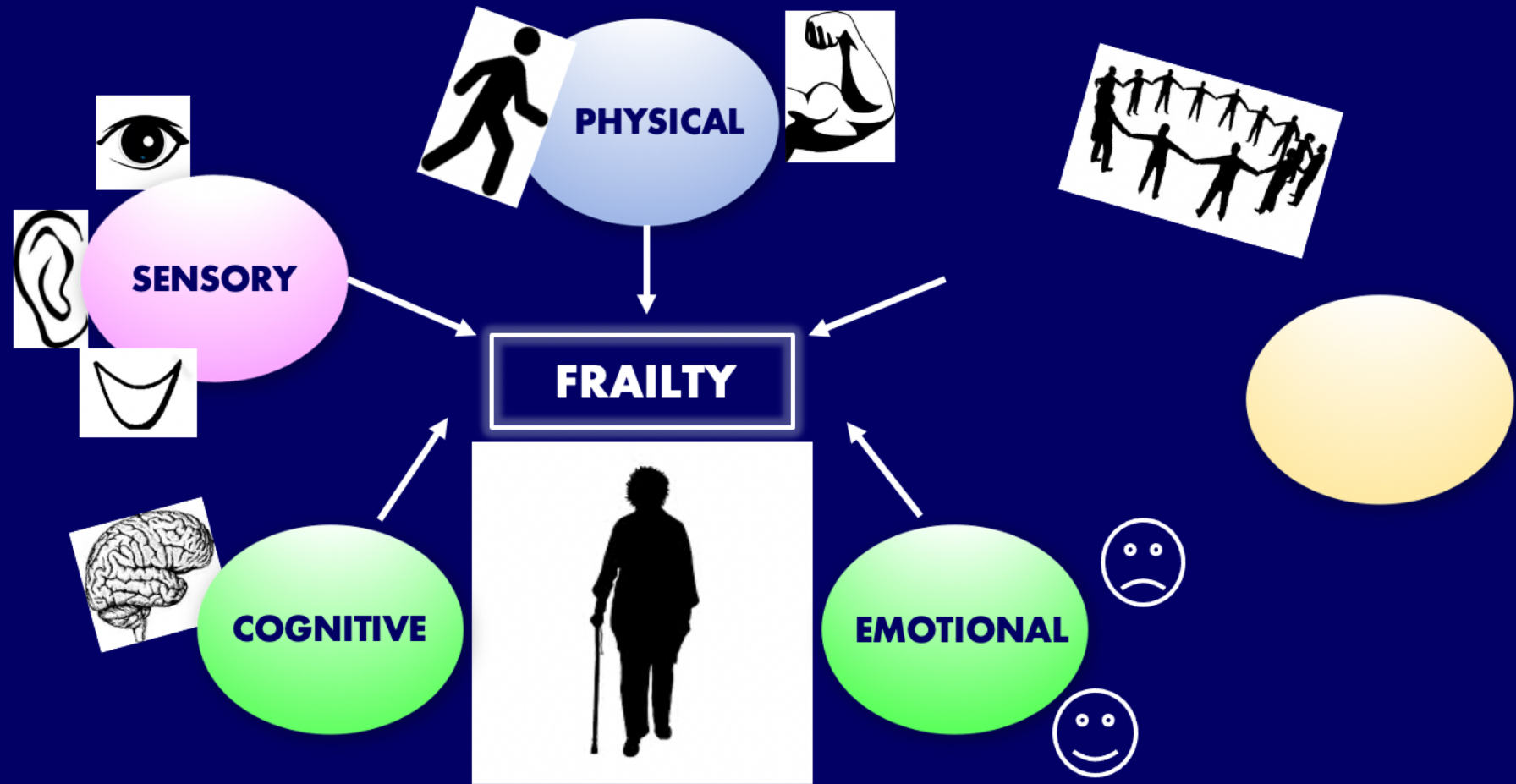
HIV+ Men are More Frail at a Younger Age vs HIV-, Slope increases for PWH
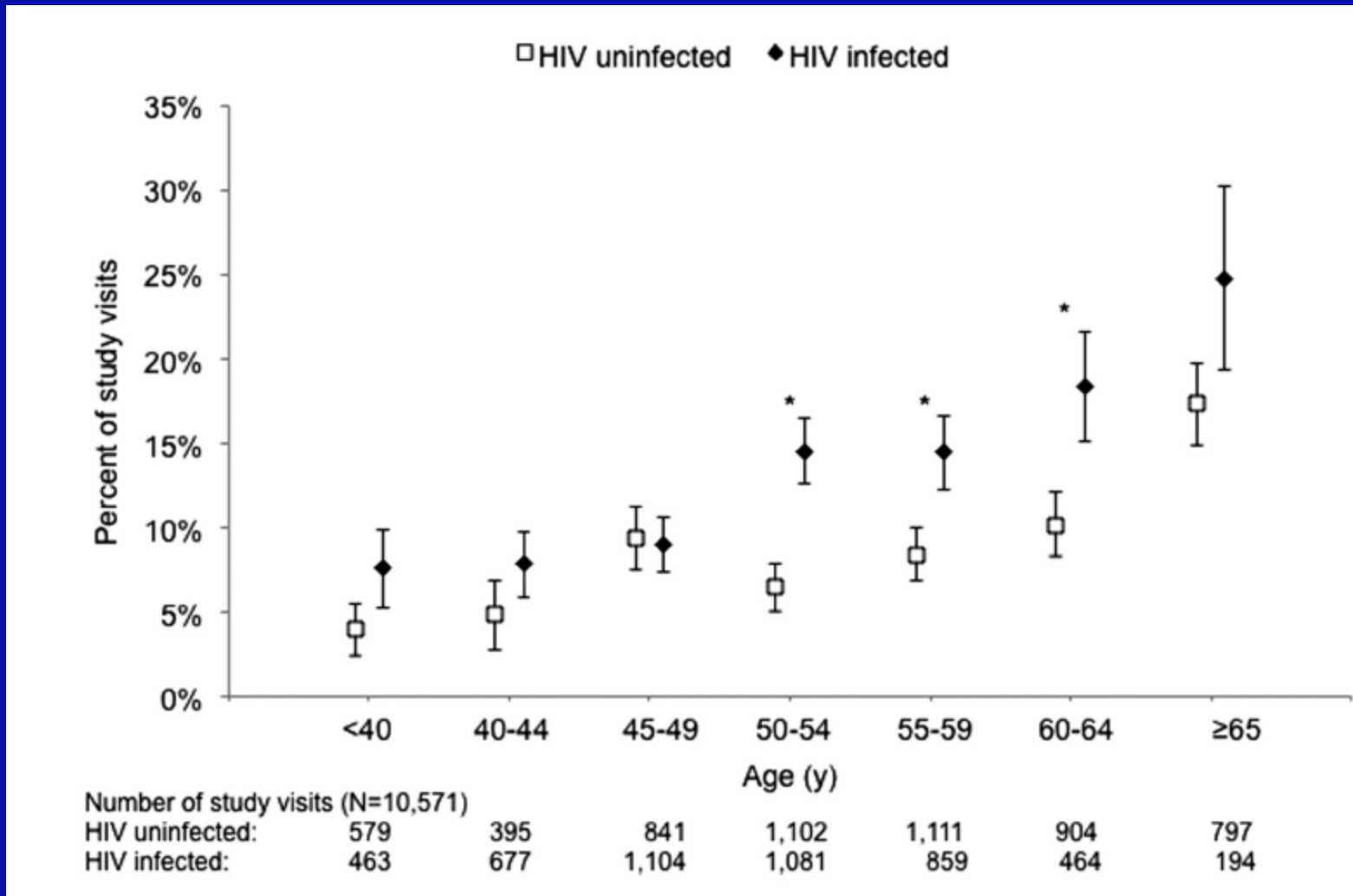
Double the Fracture Rates, Slope Sharply Increases with Age for PWH

Fracture prevalence is higher in HIV+ patients

The Mediterranean Diet

Source: Oldways Preservation & Exchange Trust and The Harvard School.

Exercise Reduces Inflammation

Adjusted for age, sex, ethnicity, education, work status, smoking status, HTN, BMI, HDL, ASA

Ford, Epidemiology, 2002
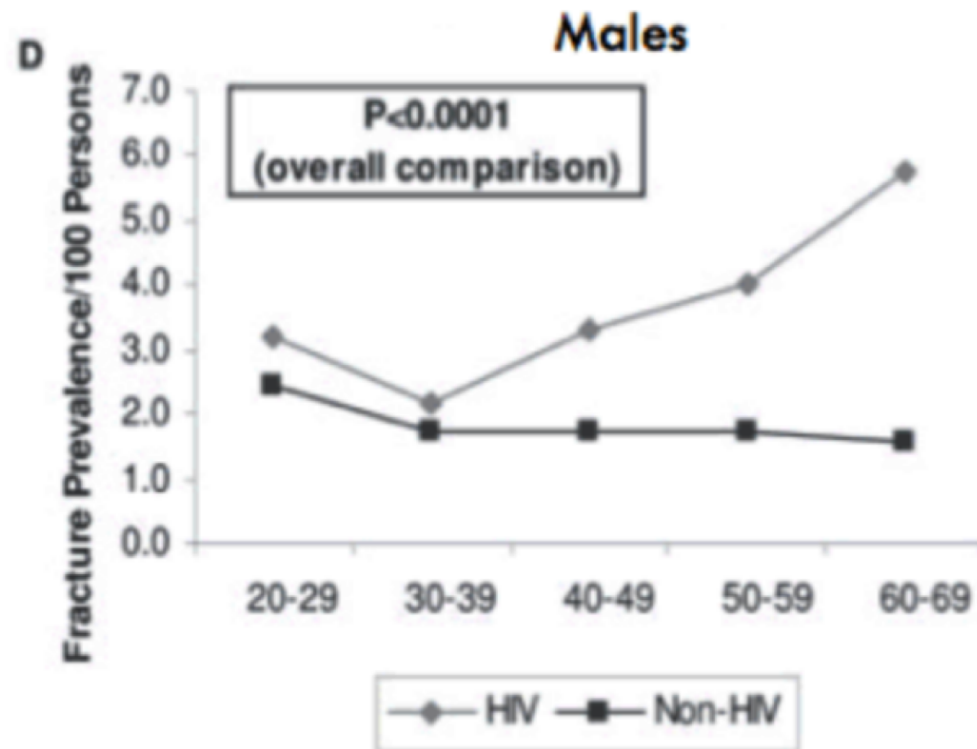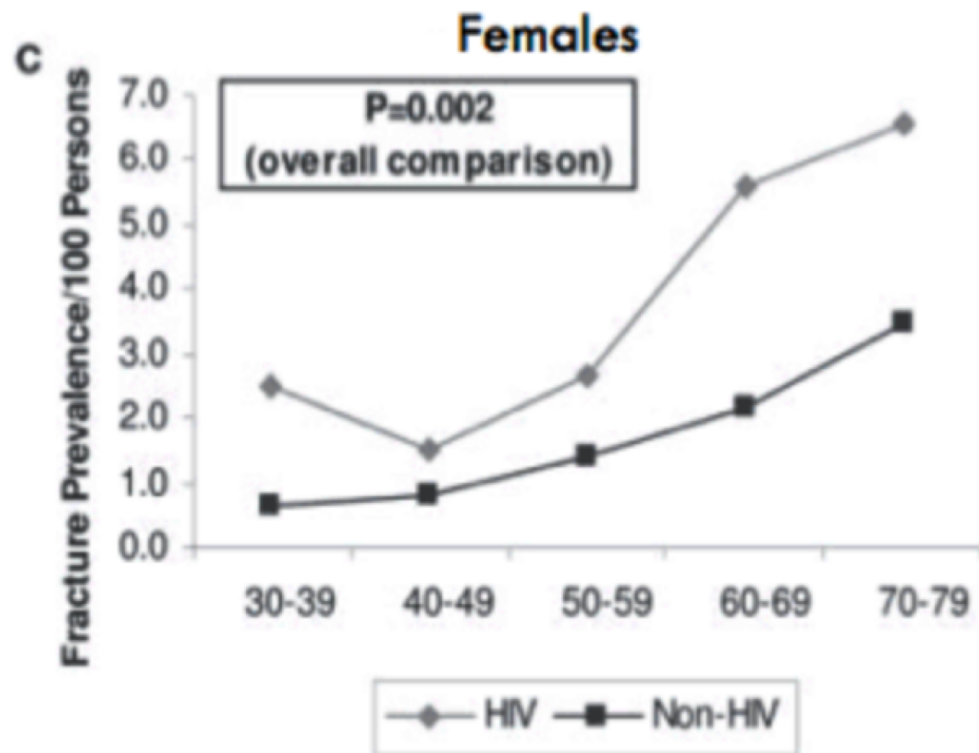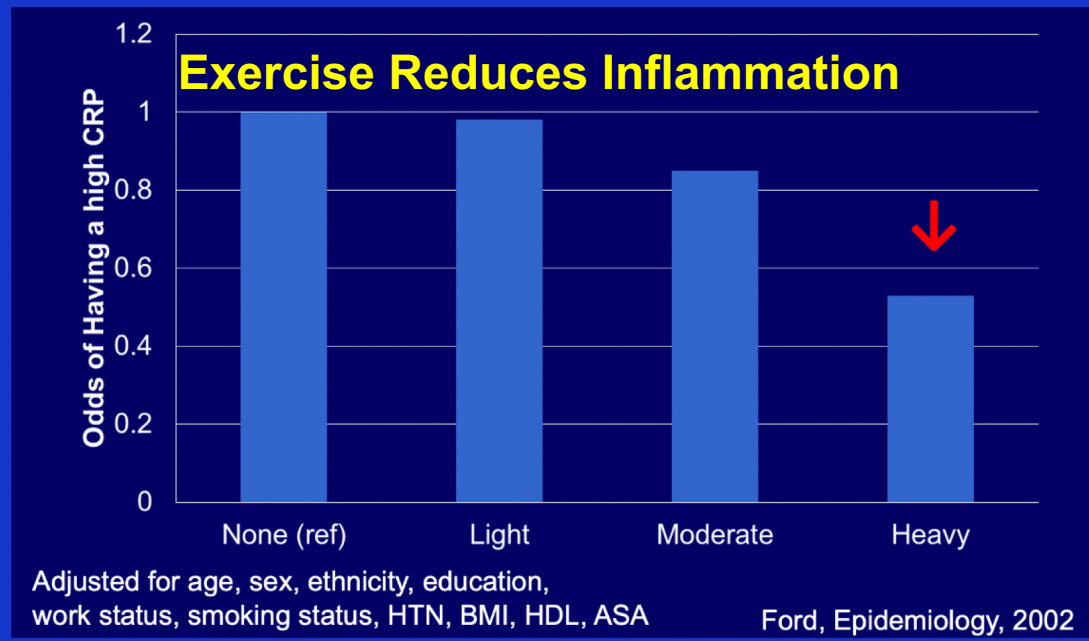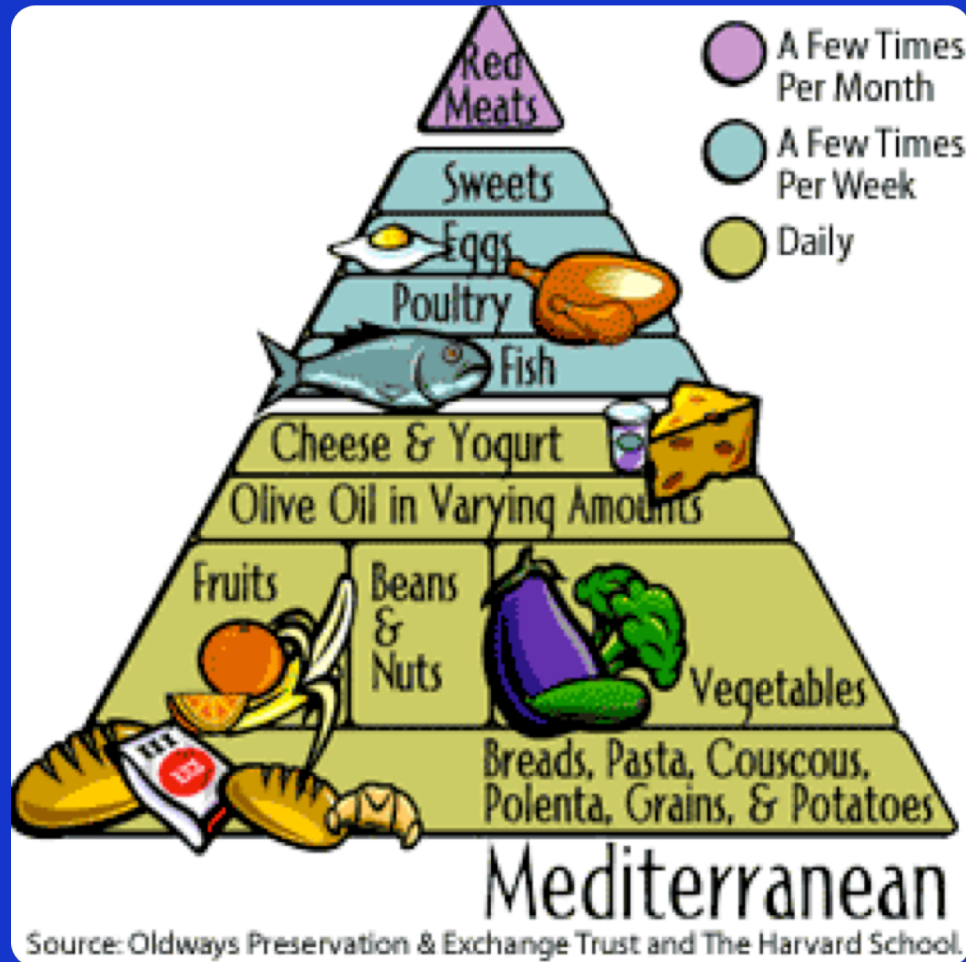
High rates of functional and high- risk multimorbidity in New York City - (Cornell HIV Clinic) 2751 PWH

- *"we found significant burdens of functional multimorbidity in addition to high- risk comorbidities (impact on mortality)."*

    functional impairment (eg, walking or carrying out tasks of daily living), termed 'functional'

- **Geriatric assessment, which evaluates the impact of medical and psychosocial factors on individual's function, has been proposed as a way to help optimise care of people with HIV as they age.**

- Avg age 52;
- 24% cisgender women;
- 31% AA;
- 29% Hispanic;
- 57% MSM
- 33 TG

Factors

- Aging: **Functional and high- risk comorbidities were common** in all age groups, but risk ***increased with age***.

- ***Mental health problems* were highly prevalent** in all age groups, slightly more so in older patients.

- more years with an HIV diagnosis

- being an African- American

- Hispanic-American

- being a cisgender female, being a transgender FTM

Table 1 Frequency of sample characteristics by age group

	Under 50		50–64		65–74		Over 75		ρ	P value
	n	%	n	%	n	%	n	%		
Viral load >200	163	14.6	113	8.4	12	4.7	1	2.4	−0.13	<0.001
Comorbidity										
Multimorbidity	557	49.8	1124	83.9	236	93.3	40	97.6	0.45	<0.001
Any comorbidity	834	74.7	1282	95.7	249	98.4	41	100	0.35	<0.001
Functional comorbidity	620	55.5	1084	81.0	225	88.9	41	100	0.34	<0.001
High-risk comorbidity	670	59.9	1166	87.1	239	94.5	37	90.2	0.37	<0.001
Cardiovascular (H)	267	23.9	725	54.1	170	67.2	32	78.0	0.37	<0.001
Diabetes (H)	46	4.1	254	19.0	70	27.7	11	26.8	0.26	<0.001
Hypertension (H)	168	15.0	567	42.4	161	63.6	27	65.8	0.37	<0.001
Kidney disease (H)	80	7.2	207	15.5	83	32.8	13	31.7	0.22	<0.001
Cerebrovascular (H,F)	17	1.5	90	6.7	36	14.2	12	29.3	0.19	<0.001
Obesity (H,F)	234	23.5	357	26.7	54	22.3	8	19.5	0.03	0.15
Lipohypertrophy/ lipoatrophy (H,F)	252	22.5	416	31.1	73	28.8	9	22.0	0.09	<0.001
Mental health (F)	390	34.9	581	43.4	113	44.7	18	43.9	0.10	<0.001
Non-HIV cancer (H)	4	0.4	31	2.3	5	2.0	3	7.3	0.09	<0.001
HIV cancer (H)	54	4.8	121	9.0	23	9.1	3	7.3	0.09	<0.001
Bone/joint (F)	33	3.0	186	13.9	83	32.8	13	31.7	0.30	<0.001
Eye/ear (F)	127	11.4	498	37.2	131	51.8	28	68.3	0.37	<0.001
Neurological (F)	39	3.5	193	14.4	62	24.5	18	43.9	0.24	<0.001
Anaemia (H)	235	21.8	312	23.7	89	35.6	16	40.0	0.08	<0.001
Gastrointestinal (F)	79	7.1	117	8.7	26	10.3	5	12.2	0.04	<0.001
Genitourinary (F)	19	1.7	174	13.0	68	26.9	17	41.5	0.28	<0.001
COPD/emphysema (H)	24	2.2	198	8.1	39	15.4	7	17.1	0.17	<0.001

Multimorbidities: 49% <50 v 83% >50. 93% 65-74

Functional comorbidity: 55% <50 v 88% 65-74 YO

High-Risk Comorbiities: 90% >50 YO vs 59% <50

Kidney disease (31% >75), hypertension (65% >65)

Neurologic: 3.5% <50 v 24% 65-74

IAS USA Treatment Guidelines Dec 2022 in JAMA

Box 4. Recommendations for Older People With HIV

- Screening for HIV is recommended in older individuals to prevent late diagnosis with advanced disease (evidence rating: AIIa)
- Initiation of ART is recommended as soon as possible after diagnosis, either the same day of diagnosis, first clinic visit, or within 7 days. Assessment of comorbidities, kidney function, and medications will influence the choice of ART (evidence rating: AIa)
- Assessment of polypharmacy and simplification of complex regimens, both ART and comorbidity treatments, is recommended to improve adherence, prevent adverse drug-drug interactions, reduce falls risk, and reduce costs (evidence rating: AIIb)
- Screening for comorbidities, impaired cognitive and function, poor mobility, frailty, and falls risk is recommended for older people with HIV, using validated tools. The frequency of assessment is determined by the baseline assessment (evidence rating: BIII)[1]
- Consideration of integrated care models and Antiretroviral Stewardship models is recommended to improve outcomes and quality of life for people aging with HIV (evidence rating: BIII)

New Models of Care Needed - NY Example

- 3 new HIV Geriatric Clinics in **NYC**

- 2 standing HIV Geriatric Clinics: New Mt Sinai, Cornell

- 2 more expected next year

- 'Integration' of Geriatric Care elements, 'personalized care' into Ryan White & HIV Clinics next year – not being done????

- **HRSA $10 Mill Grant for 10 HIV Geriatric Clinics** – 3-yr grants - awards just announced.

- **NYS 10 Aging HIV Clinics** $20 mill, 5 years

- BUT there are >220,000 PWH over 60 in USA, 95% are getting zero.

Updated Care Infrastructure Needed

- RWCA failing us - many are NOT getting needs met.

- Federal & State Local authorities are not meeting our needs.

- HRSA: "Personalized Care & integrated care" needed.

- We need to structure Care in the clinic and community in the USA to meet the changing & modern needs of the HIV patient population in care who are aging, since the HIV/aged population IS the majority Now & more so in future.