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

Jules Levin

NATAP, National AIDS Treatment Advocacy Project

www.natap.org

NATAP National Treatment Education Project (webinars): 500+ symposiums, 50,000+ participants, 25 cities since 1996

Aging & HIV Policy Program

HCV Policy & Education

The promise of HAART in 1996 has left many elderly PLWH very disappointed. We are back where we began.

There has been no messaging to PLWH patient population that aging & HIV is a problem until recently.

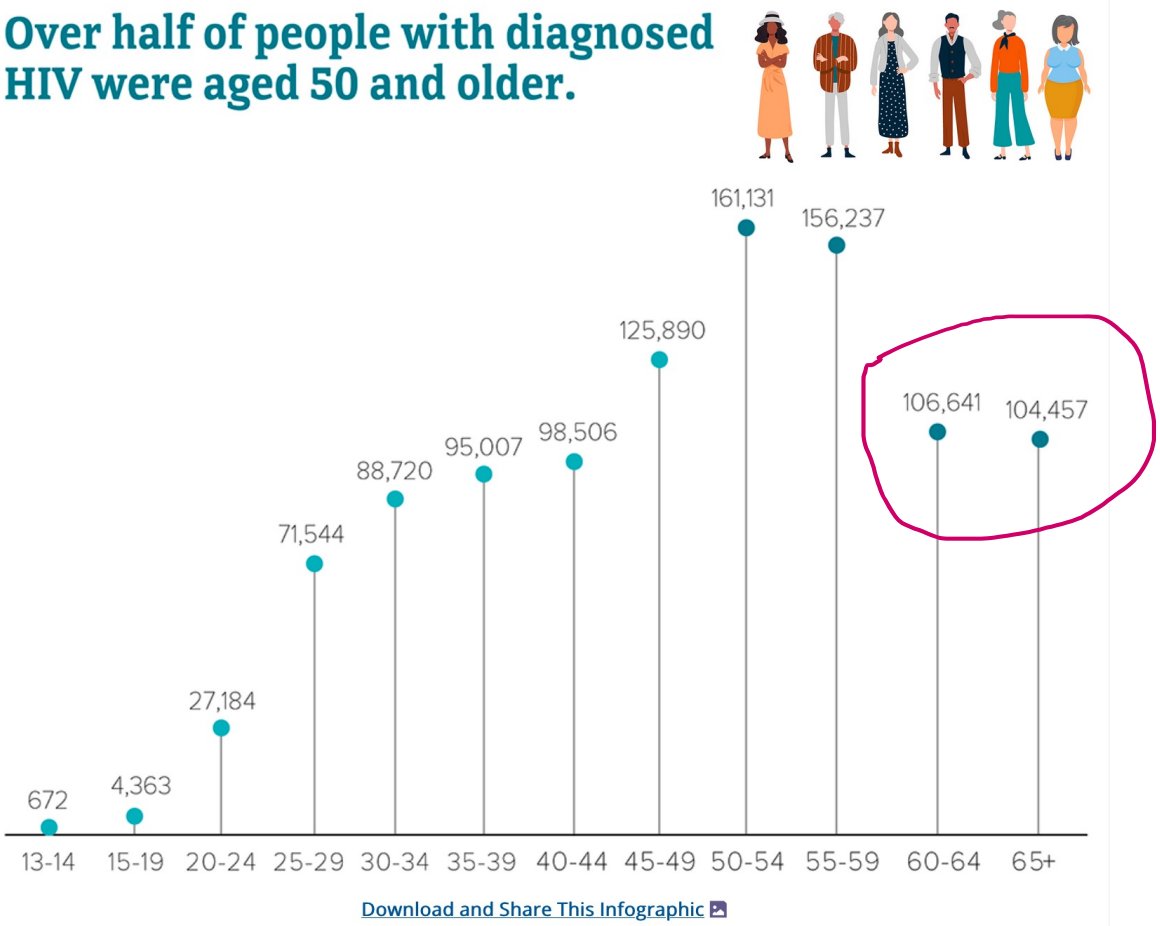
Many PLWH still have no idea this is a problem & don’t understand what is going on.

Some say many marginalized PLWH, if they did not have HIV would not be getting the health-care they in fact do get at RW clinics such as those with a history of drug abuse, so they get better care than those like them who don't have HIV.

- To that I say:

That's not a good excuse for providing less than adequate & poor healthcare & services for PLWH at RW & HIV clinics. We have a dedicated healthcare system called the Ryan White Care Act funded by taxpayer money to provide care to PLWH. We are the only disease with such a dedicated taxpayer funded stream of largescale funding. Yet it does not meet the needs of the majority of the HIV+ population: older, aging & elderly PLWH. Soon its expected 75% of PLWH in the USA will be over 50 & 40% over 60; 200,000 are now over 60, and 400,000 will be over 60 by 2030. the system will have to change. But to not address this problem RIGHT NOW relegates all the elderly PLWH in the USA now to poor care & premature death. The care & services they receive now is horrible, 20-minute visits are wholly inadequate & insulting to PLWH considering taxpayers thought we were getting good care, and are paying for that ! In NYC right now where there are 90,000 PLWH 30% are already over 65 & SF too, soon 50% will be over 65. Do they deserve sub-par care that will result in premature death? Considering that is NOT what taxpayers are paying for.

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

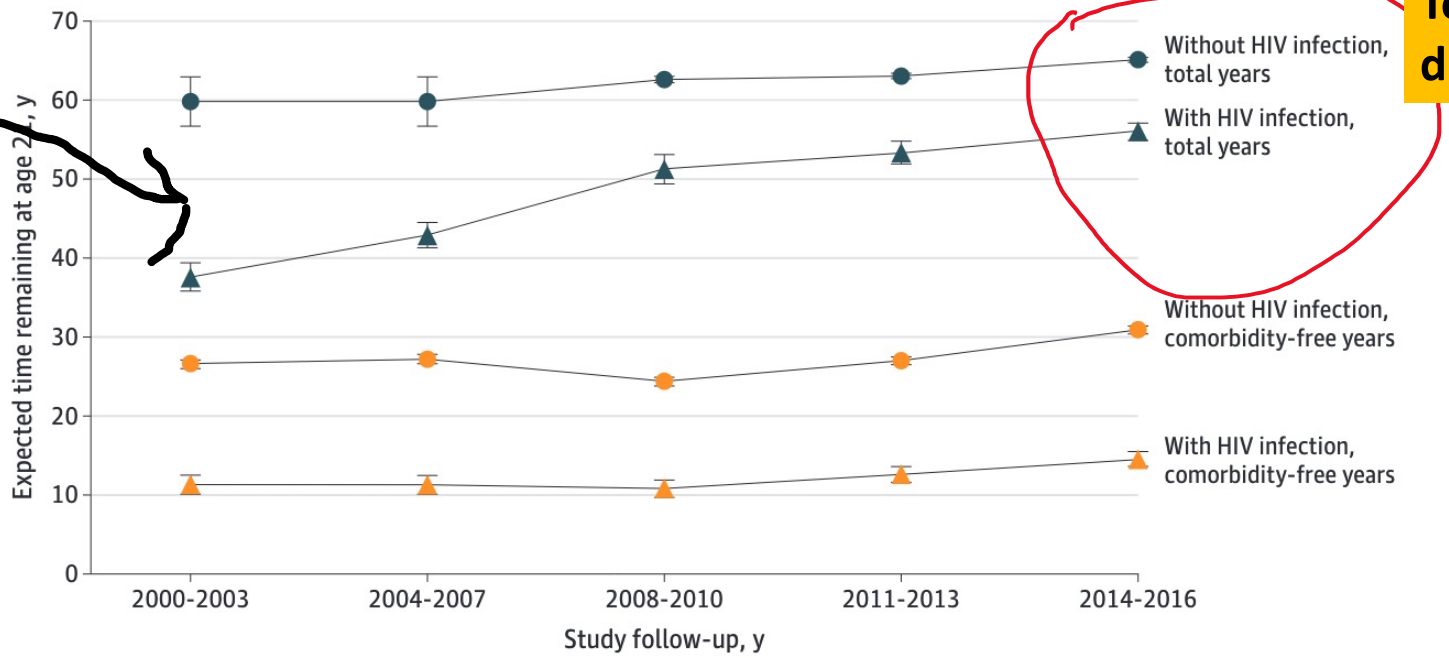


Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2018 (updated). *HIV Surveillance Report* 2020;31.

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

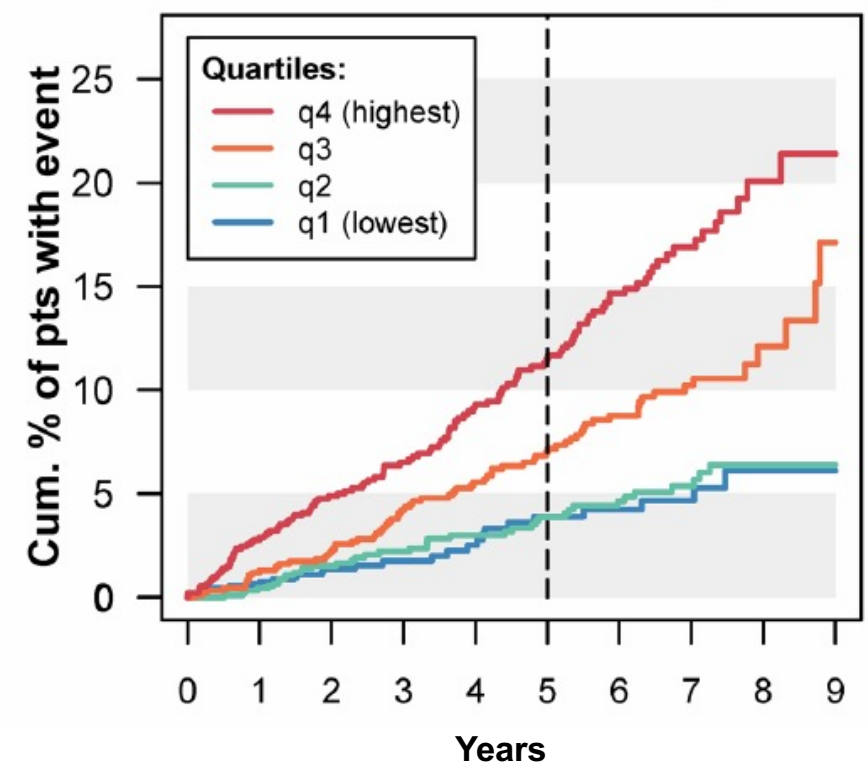
Inflammation Strongly and Durably Predicts Morbidity / Mortality in Treated HIV Infection

(IL-6 + D-dimer Score)

SMART, ESPRIT, SILCAAT

Median Current CD4: 500

Median Nadir CD4: 181



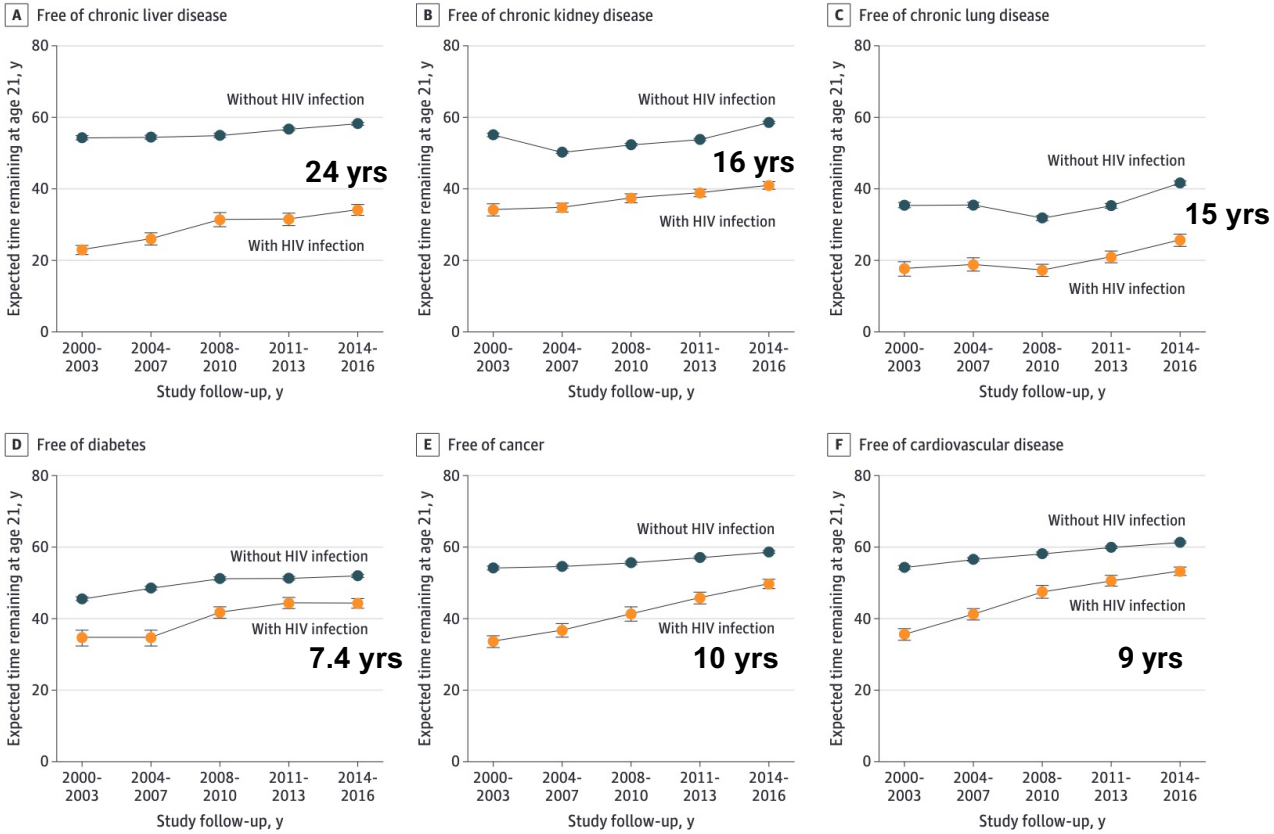
Our Field's Goal: Move people from top two quartiles into the bottom 2 quartiles…

Are there sex differences in inflammation?

Grund et al, PLoS One, 2016

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



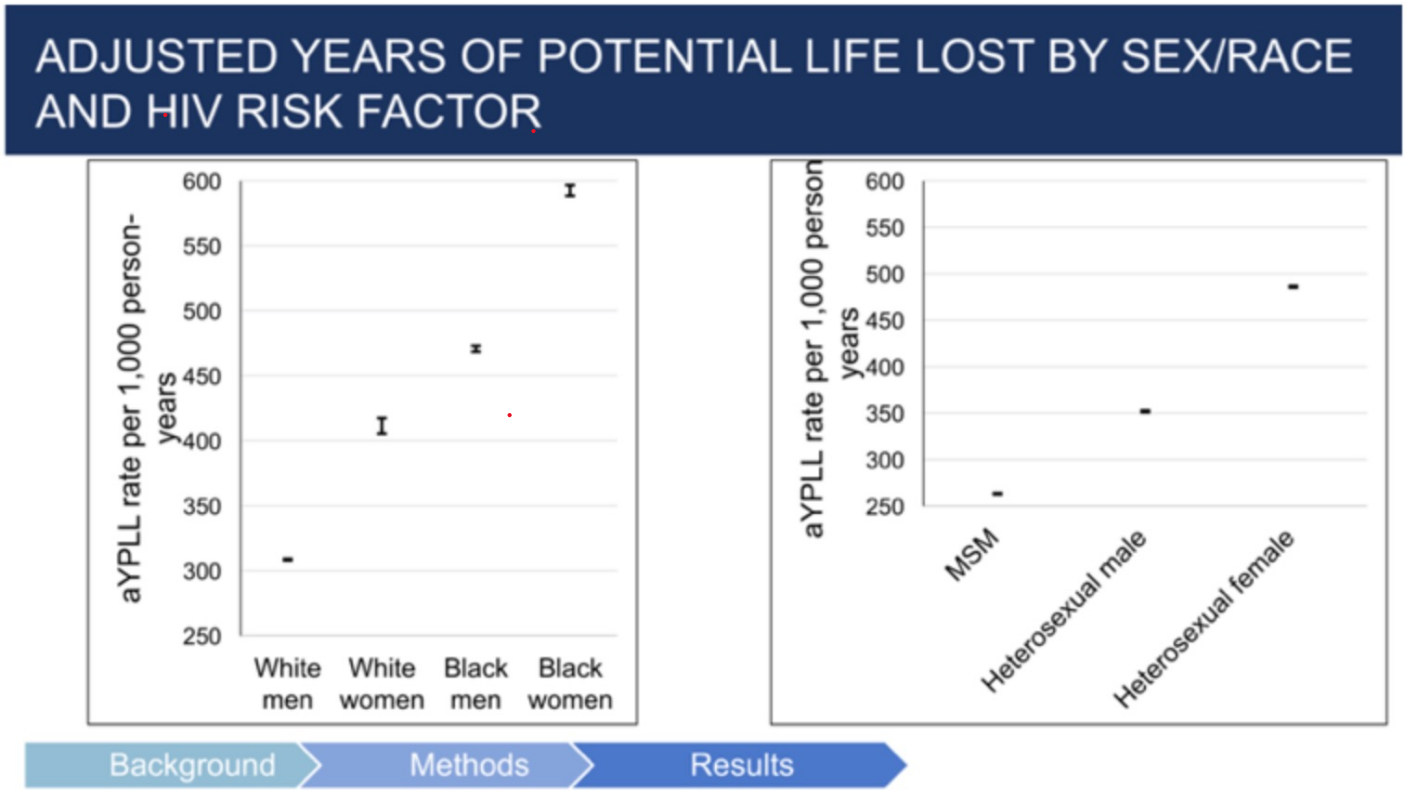
15 Year Gap in Comorbidity-Free Years

10 Years for those with CD4 >500 Nadir: 4.4 CVD to 14 kidney, 15 Liver

Table 3. Overall and Comorbidity-Free Life Expectancy at Age 21 Years for Individuals With and Without HIV Infection and for Individuals With HIV Infection Who Initiated ART at High CD4 Cell Counts, Kaiser Permanente, 2011-2016

	Life expectancy at age 21 y, No. of y (95% CI)			Difference	
Outcome	Individuals with HIV infection	Individuals with HIV infection with CD4 cell count ≥500/μL at ART initiation	Individuals without HIV infection	Individuals with HIV infection vs individuals without HIV infection	Individuals with HIV infection with CD4 cell count ≥500/μL at ART initiation vs Individuals without HIV infection
Overall	54.9 (54.0 to 55.9)	57.4 (55.7 to 59.1)	64.2 (64.0 to 64.4)	9.2 (8.3 to 10.2)	6.8 (5.0 to 8.5)
Comorbidity free[a]	13.7 (13.0 to 14.4)	19.5 (17.8 to 21.2)	29.0 (28.6 to 29.3)	15.3 (14.5 to 16.1)	9.5 (7.7 to 11.2)
Chronic disease					
Liver	33.1 (31.9 to 34.2)	42.5 (39.8 to 45.1)	57.6 (57.3 to 57.9)	24.5 (23.3 to 25.7)	15.1 (12.5 to 17.8)
Kidney	40.2 (39.5 to 41.0)	42.5 (40.8 to 44.2)	56.3 (56.0 to 56.5)	16.1 (15.3 to 16.9)	13.8 (12.0 to 15.5)
Lung	23.4 (22.3 to 24.6)	31.3 (28.5 to 34.1)	38.5 (38.0 to 38.9)	15.0 (13.7 to 16.3)	7.2 (4.3 to 10.0)
Diabetes	44.2 (43.2 to 45.3)	50.2 (47.9 to 52.4)	51.7 (51.3 to 52.0)	7.4 (6.4 to 8.5)	1.5 (−0.8 to 3.8)
Cancer	48.1 (47.0 to 49.1)	52.6 (50.3 to 54.8)	58.0 (57.7 to 58.2)	9.9 (8.8 to 11.0)	5.4 (3.1 to 7.7)
Cardiovascular disease	51.8 (50.9 to 52.7)	56.4 (54.3 to 58.5)	60.8 (60.5 to 61.0)	9.0 (8.0 to 9.9)	4.4 (2.2 to 6.5)

Increased Mortality for Blacks with HIV



Premature Mortality Higher in Women and Blacks in US HIV Group

PLWH Survival Declines with Comorbidities

- **Danish Cohort**

Group 0 (General population comparison cohort): HIV risk factors: –, comorbidity: –, abuse: –.

Group 1 (HIV-infected patients): HIV risk factors: –, comorbidity: –, abuse: –.

Group 2 (HIV-infected patients): HIV risk factors: +, comorbidity: –, abuse: –.

Group 3 (HIV-infected patients): HIV risk factors: +/–, comorbidity: +, abuse: –.

Group 4 (HIV-infected patients): HIV risk factors: +/–, comorbidity: +/–, abuse: +..

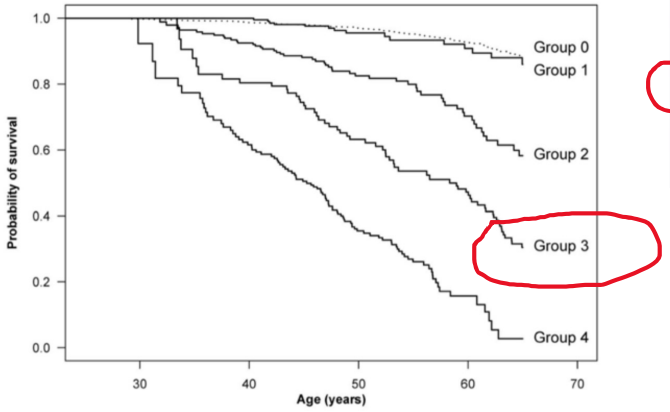


Table 2. Mortality and mortality rate ratios by risk group.

Groups	Probability of survival from age 25 to 65 years	95% CI		Age interval	Deaths	PY**	MR***	95% confidence interval		MRR****	95% confidence interval	
Comparison cohort	0.88	0.86	0.90	25–45	37	29123	1.27	0.92	1.75			
				45–65	101	23899	4.23	3.48	5.14			
HIV overall	0.48	0.42	0.53	25–45	76	6973	10.90	8.70	13.64	8.58	5.79	12.71
				45–65	137	5395	25.39	21.47	30.02	6.00	4.65	7.77
Group 1*	0.86	0.77	0.92	25–45	4	2723	1.47	0.55	3.91	2.02	0.61	6.70
				45–65	11	1891	5.82	3.22	10.50	1.14	0.58	2.23
Group 2*	0.58	0.48	0.67	25–45	21	2525	8.32	5.42	12.76	4.62	2.48	8.60
				45–65	30	1772	16.93	11.84	24.21	4.27	2.57	7.08
Group 3*	0.30	0.21	0.40	25–45	15	826	18.15	10.94	30.11	12.75	4.64	35.09
				45–65	43	1032	41.68	30.91	56.20	10.79	6.29	18.52
Group 4*	0.03	0.003	0.12	25–45	36	898	40.07	28.90	55.55	32.60	12.79	83.08
				45–65	53	701	75.66	57.80	99.03	21.90	11.94	40.17

Medicare USA – *life expectancy* is reduced for those with medium & high comorbidity rates by 2 to 9 years – blacks affected more

Table 3. Estimated Life Expectancy, by Comorbidity Groups*

Age, y	Life Expectancy in Men, y							Life Expectancy in Women, y						
	Average U.S. Population†	Comorbidity						Average U.S. Population†	Comorbidity					
		None	Low/ Medium	High	Diabetes‡	COPD§	CHF‖		None	Low/ Medium	High	Diabetes‡	COPD§	CHF‖
All races														
66	15.4	18.5	15.7	9.9	14.7	12.2	7.4	18.4	22.5	18.4	12.0	16.1	15.4	8.0
70	12.8	16.3	13.5	8.9	13.1	11.0	7.0	15.4	19.3	15.7	10.8	14.7	13.3	8.0
75	9.9	12.7	11.0	7.4	10.3	8.9	5.8	12.0	15.3	12.4	8.5	11.4	10.8	7.1
80	7.4	9.8	8.2	5.8	7.4	7.0	4.8	9.0	11.6	9.4	6.6	8.5	8.0	5.8
85	5.5	7.2	5.8	4.2	5.5	5.1	3.7	6.6	8.7	7.0	5.1	6.2	6.2	4.7
90	3.9	5.1	3.9	3.0	3.7	3.7	3.0	4.7	5.7	4.7	3.5	4.4	4.4	3.5
White persons														
66	15.5	18.6	16.1	9.9	14.8	12.2	7.9	18.5	22.6	18.5	12.0	16.2	14.7	8.5
70	12.9	16.3	13.9	8.9	13.2	11.0	7.0	15.5	19.4	15.8	10.8	14.0	12.7	8.0
75	9.9	12.8	10.7	7.4	10.3	8.9	5.8	12.0	15.3	12.4	8.5	11.4	10.2	7.0
80	7.4	9.9	8.2	5.4	7.4	6.6	4.8	9.0	11.7	9.0	6.6	8.5	8.0	5.8
85	5.4	7.2	5.8	4.2	5.4	4.8	3.6	6.6	8.2	6.6	5.0	6.2	6.2	4.7
90	3.9	5.0	3.9	3.0	3.6	3.6	3.0	4.7	5.7	4.7	3.8	4.3	4.3	3.5
Black persons														
66	13.5	16.3	14.2	9.1	13.5	11.9	7.1	17.0	21.3	17.8	10.9	17.0	17.0	8.1
70	11.4	14.7	12.4	7.9	11.4	9.5	6.4	14.4	18.7	15.3	9.9	14.7	13.8	8.1
75	9.1	11.9	10.0	6.4	9.4	7.9	5.2	11.5	15.3	12.5	8.5	11.5	11.8	7.2
80	7.1	9.8	8.0	5.2	7.7	6.8	4.5	9.0	12.1	10.0	6.9	9.3	9.0	6.1
85	5.5	7.3	6.3	4.5	5.5	5.2	3.8	6.9	9.0	7.5	5.5	6.5	6.9	5.2
90	4.2	5.7	4.7	3.6	4.5	3.1	3.4	5.2	6.7	5.7	4.1	5.2	5.2	4.1

Table 2. Hazard Ratios and Comorbidity Weights Estimated From the Cox Proportional Hazards Model of Medicare Beneficiaries in SEER Areas Without a History of Cancer Diagnosis, 1992–2005*

Variable†	Hazard Ratio (95% CI)	Coefficient‡	SE	*P* Value
Sex and race				
Male	1.45 (1.43–1.46)	0.369	0.006	<0.001
Black	1.04 (1.02–1.06)	0.038	0.010	<0.001
Other	0.90 (0.88–0.93)	−0.101	0.014	<0.001
Comorbid conditions				
Low/medium comorbidity				
History of myocardial infarction	1.11 (1.08–1.15)	0.105	0.016	<0.001
Ulcer	1.13 (1.09–1.17)	0.123	0.018	<0.001
Acute myocardial infarction	1.28 (1.24–1.32)	0.247	0.017	<0.001
Rheumatologic disease	1.31 (1.26–1.35)	0.269	0.018	<0.001
Peripheral vascular disease	1.44 (1.42–1.47)	0.367	0.010	<0.001
Diabetes	1.45 (1.43–1.47)	0.372	0.007	<0.001
Paralysis	1.48 (1.43–1.54)	0.394	0.020	<0.001
Cerebrovascular disease	1.52 (1.50–1.55)	0.420	0.009	<0.001
High comorbidity				
COPD	1.76 (1.74–1.79)	0.567	0.008	<0.001
CHF	2.27 (2.23–2.30)	0.818	0.007	<0.001
Moderate/severe liver disease	2.30 (2.09–2.53)	0.832	0.049	<0.001
Chronic renal failure	2.30 (2.25–2.36)	0.834	0.012	<0.001
Dementia	2.35 (2.31–2.40)	0.855	0.010	<0.001
Cirrhosis and chronic hepatitis	2.82 (2.63–3.01)	1.035	0.035	<0.001
AIDS	3.66 (2.72–4.92)	1.298	0.151	<0.001

Aging & HIV

200,000 PLWH >60 predicted to be 400,000 by 2030

30% >60 in NYC now ↑ to 50%

30% >65 in SF now ↑ to 55%

→ ***NASH, fatty liver, non-viral hepatitis***

PLWH – ***2-5 times more comorbidities*** than HIV-negatives: CVD-heart, cancers, osteoporosis, liver disease, kidney

→ ***Earlier onset by often 10-15 years***

→ ***Doubled rates of falls, fractures, frailty***

- Cognitive impairment & physical disability

- Muscle function, fat metabolism

Functional Impairment - IADLs – Independent Activities of Daily Living

MOST VULNERABLE PLWH:

women

elderly

African-Americans

Latinos

transgender community

more marginalized-less access-social determinants of health

Emerging importance of chronic *comorbidities in patients > 75* in France: doubled rates of CVD/cancers/stroke/bone/hypertension-tripled kidney failure, # with 4 comorbidities

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

Cornell NY HIV Clinic 2016-2017 n=2751

52 YO; 24% female; 29% Latino, 31% African-American; former smokers; MSM 57%;Hetero-UPS 30%' 37 transgender

HIV IS Associated with High-Risk [high impact on mortality] Comorbidities & higher number of functional impairments

[functional: walking, normal daily living activities] of daily living)]:

- cisgender female, transgender FTM, Hispanic, age, more years with HIV, African-American associated with more comorbidities
  - some participants had no comorbidities, the maximum number of comorbidities was 13 inclusive, with 8 in the high risk and 7 in the functional categories

Table 2 HIV parameters and comorbidity types by age category

	Total Median (IQR)	Under 50 Median (IQR)	50–64 Median (IQR)	65–74 Median (IQR)	75+ Median (IQ)	ρ	P value
Years with HIV diagnosis	19 (11–2)	12 (6–19)	22 (17–27)	24 (19–27)	24 (18–29)	0.51	<0.001
Nadir CD4 number	168.5 (50–296)	200 (61.5–338.5)	140 (40–253)	143 (60.5–247)	200 (50–347)	−0.17	<0.001
Most recent CD4 number	578 (392–783)	584 (402–791)	589 (388–805)	556 (393–712)	523 (288–650)	−0.04	0.02
Most recent CD8 number	771 (536–1048)	761 (548–1006)	779 (531–1082)	788 (523–1032)	712 (537–1106)	0.01	0.57
All comorbidity	3 (1–4)	1 (0–3)	3 (2–5)	5 (3–6)	5 (4–7)	0.54	<0.001
High-risk comorbidity	1 (1–3)	1 (0–3)	2 (1–3)	3 (2–3)	3 (2–4)	0.49	<0.001
Functional comorbidity	1 (0–2)	1 (0–1)	1 (1–2)	3 (1–3)	3 (2–4)	0.45	<0.001

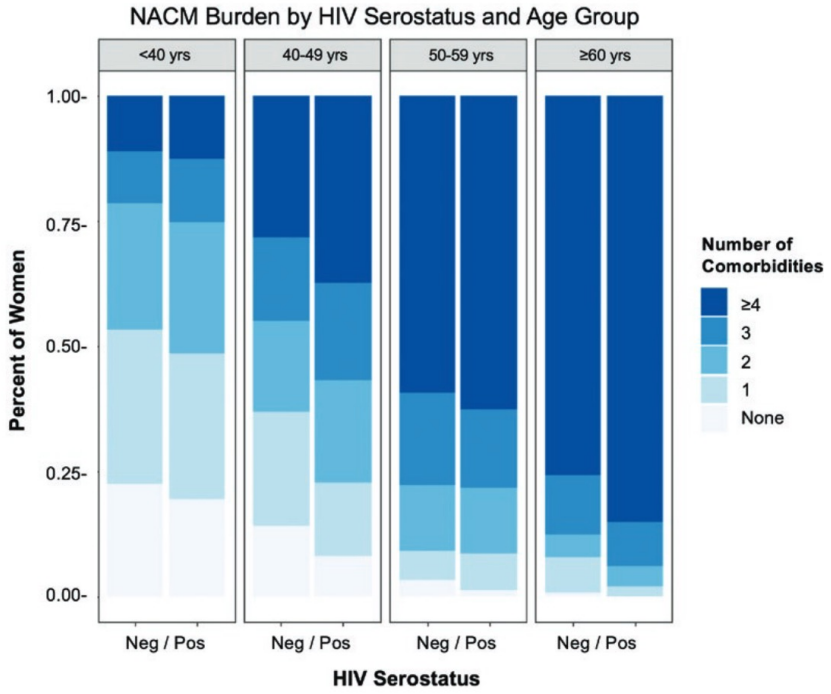
HIGH RISK Comorbidities (83% multimorbidity >50 YO [74%-100%])(Table 1): cardiovascular, hypertension, kidney disease, cerebrovascular, lipohypertrophy/lipoatrophy, non-HIV cancer, bone/joint, neurological, gastrointestinal, COPD, emphysema.

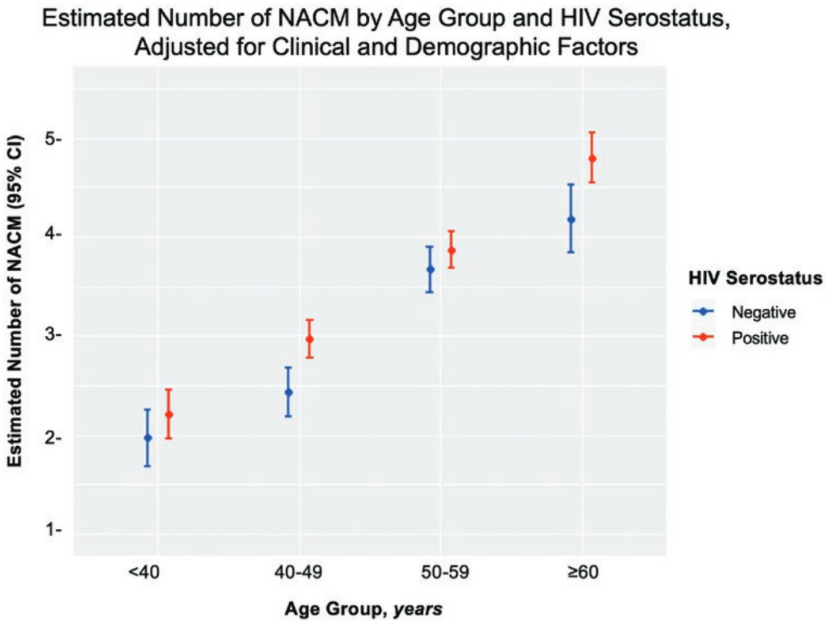
- **NEUROLOGIC DISEASE:** 3.5% <50 had this; 14% of 50-64; 24% of 65-74; **43% of >75**.
- **KIDNEY DISEASE:** from 7% to **32% of 65-74**.
- ***MENTAL HEALTH:*** *34% <50;* ***44% 65-74***.
- **HIGH-RISK Comorbidity:** 59% <50; ***94% 65-74***
- ***Functional comorbidity: 55% <50 had this; 81% of 50-64; 89% of 65-74; 100% of >75 years old.***
- **Cancers: 7-9%** - **Bone/joint:** from 5% increase to 31% -**COPD** increased from 2% to 17% - **Anemia** 21% to 40%
- **Hypertension** from 15% to 65% - ***CVD 78%*** from 23% - **Cerebrovascular** from 2% to 29%

Table 1 Frequency of sample characteristics by age group

	Under 50		50–64		65–74		Over 75		p	P value
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

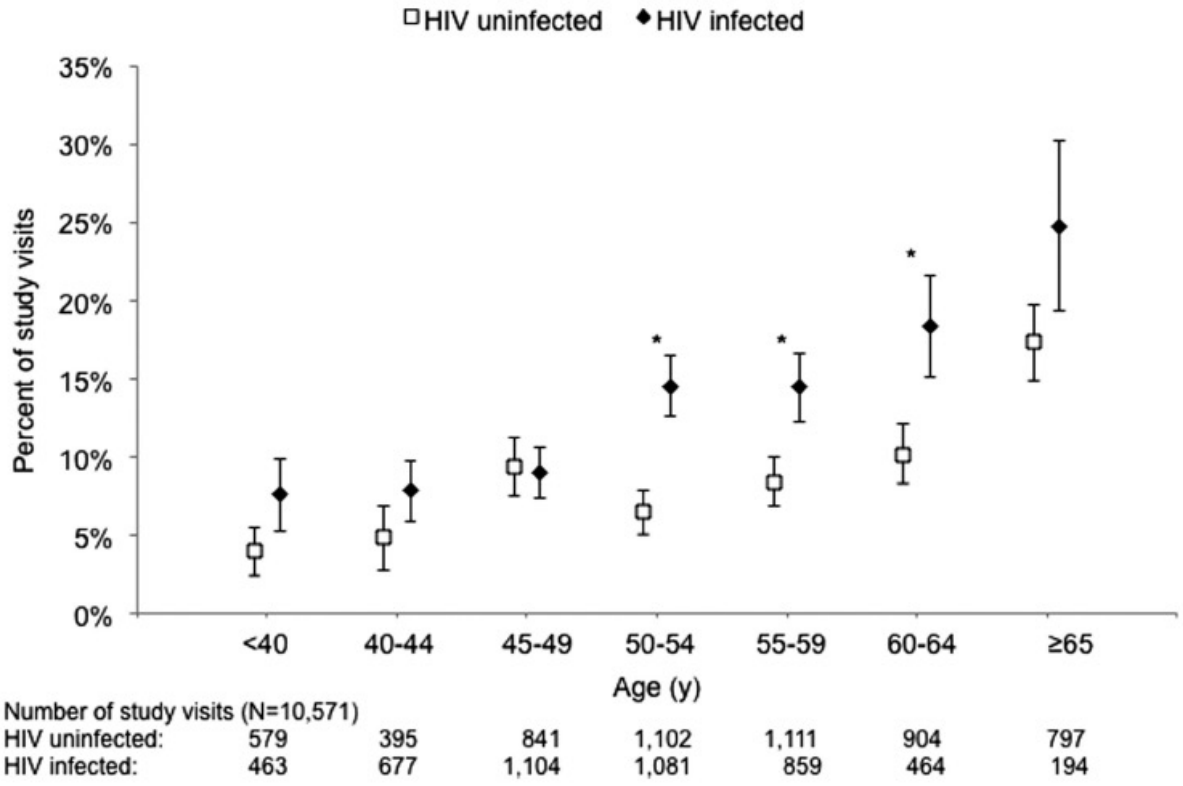
HIV+ Women Increasing with Age & Greater NACM Burden vs HIV- women





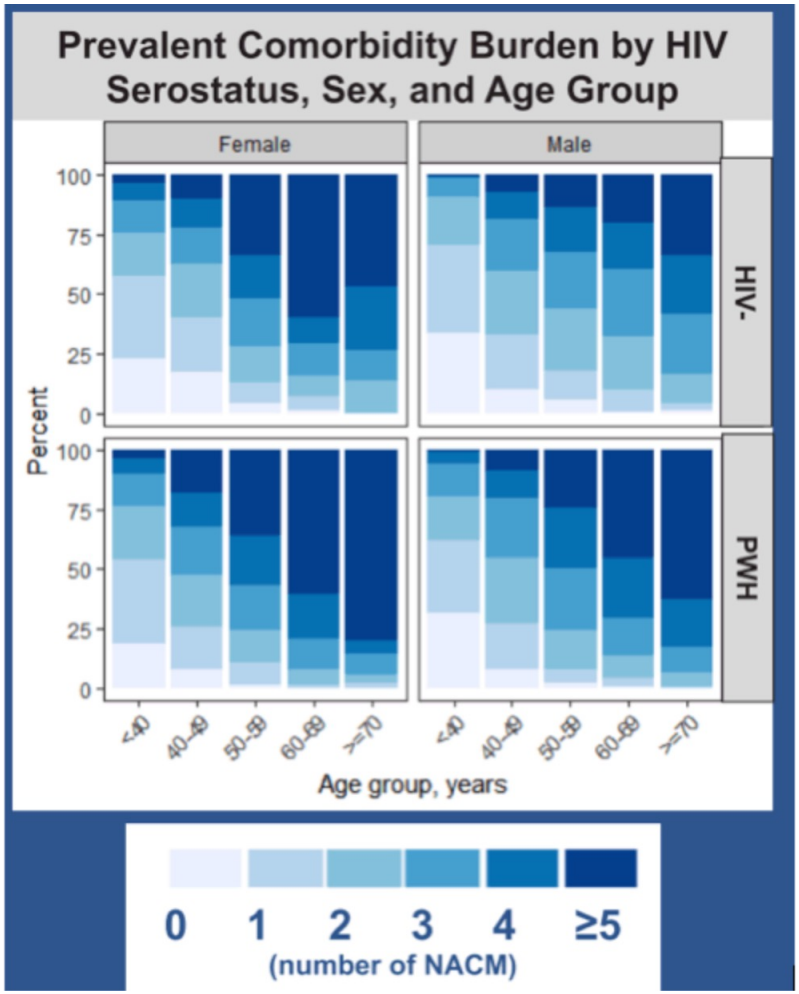
	Estimated Number of NACM (95% CI)			
	<40 years	40-49 years	50-59 years	≥60 years
HIV+ women	2.21 (1.96-2.46)	2.97 (2.78-3.15)	3.87 (3.69-4.05)	4.80 (4.55-5.05)
HIV- women	1.97 (1.68-2.26)	2.44 (2.19-2.68)	3.67 (3.44-3.90)	4.19 (3.85-4.52)
P value (HIV+ vs HIV-)	0.1420	<0.0001	0.0888	0.0009

Frailty Phenotype in MACS – doubled rates of frailty for >65



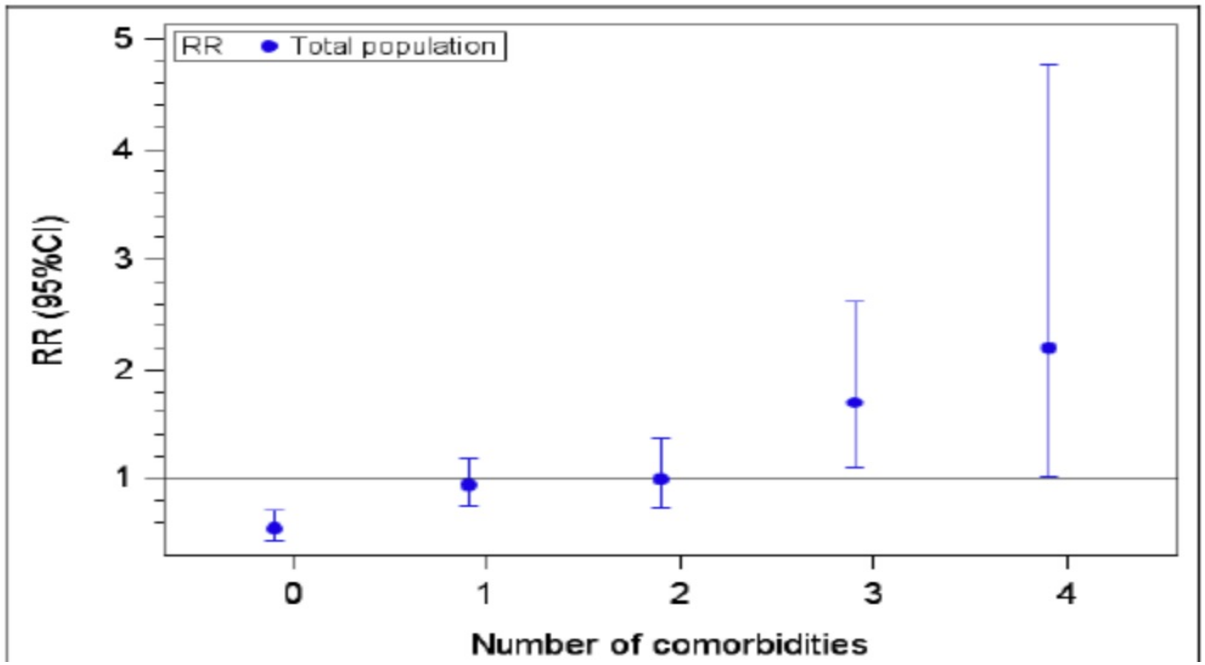
Althoff, J of Gerontology, 2013

Older Women Have More Comorbidities & Worse Physical Function Than Men



Women Have More Multimorbidity & mortality

Multimorbidity and mortality: women relative to men



	Total population
0	0.55 (0.43-0.70)
1	0.94 (0.76-1.18)
2	1.00 (0.73-1.36)
3	1.69 (1.09-2.61)
4	2.21 (1.02-4.77)

Multimorbiditv Increases Death Rates – ATHENA Cohort Glasgow 2018

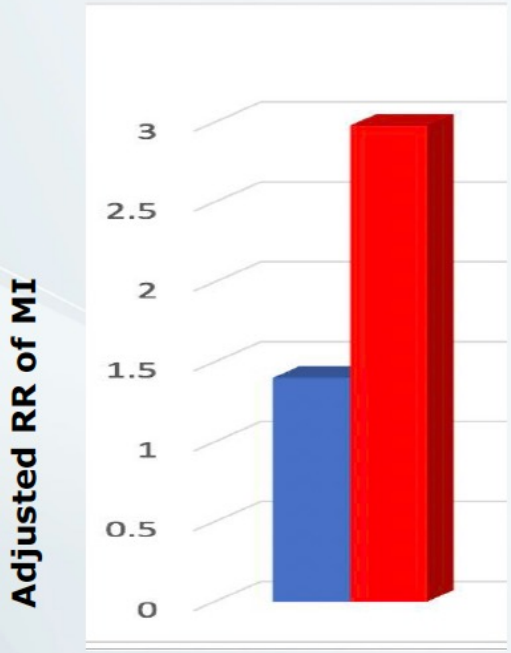
Multimorbidity and mortality

- 30% >70 have 3-4+ comorbidities.
- HIV+ Women have higher multi-comorbidity rates at younger ages than men. Death rates higher in women. Menopause?

Crude mortality rates

Multimorbidity	PYFU	Deaths	Rate /1000 PYFU
0	152,088	899	5.9 (5.5-6.3)
1	38,361	805	21.0 (19.6-22.5)
2	11,476	404	35.2 (31.9-38.8)
3	2,025	164	81.0 (69.1-94.4)
4+	306	53	173 (130-226)

Sex-Differences in HIV-Attributable Myocardial Infarction Risk in US



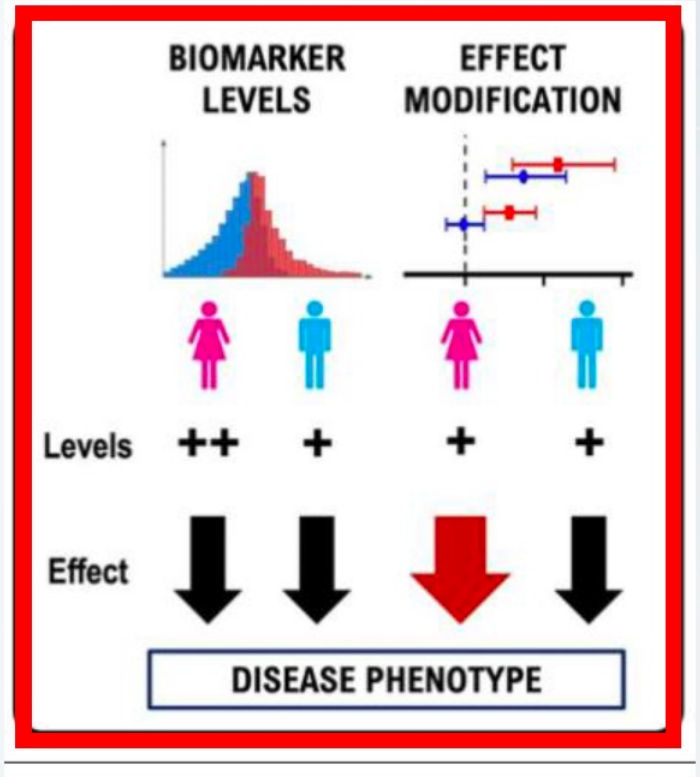
- Males with vs. without HIV
- Females with vs. without HIV

Triant / Grinspoon JCEM 2007

Implications of Key Findings:

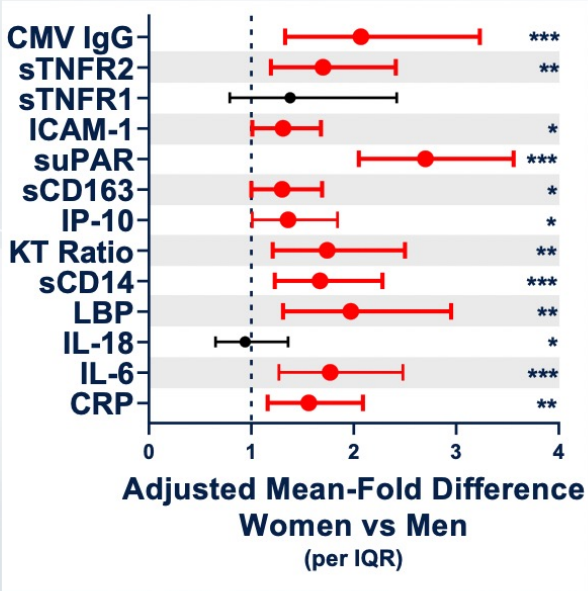
- Females vs. males showed higher levels of IL-6, hsCRP, and D-dimer and lower levels of LpPLA-2.

- Among females, but not among males, D-dimer was associated with an increased prevalence of nc/v-plaque.



Lau Circ Res 2022

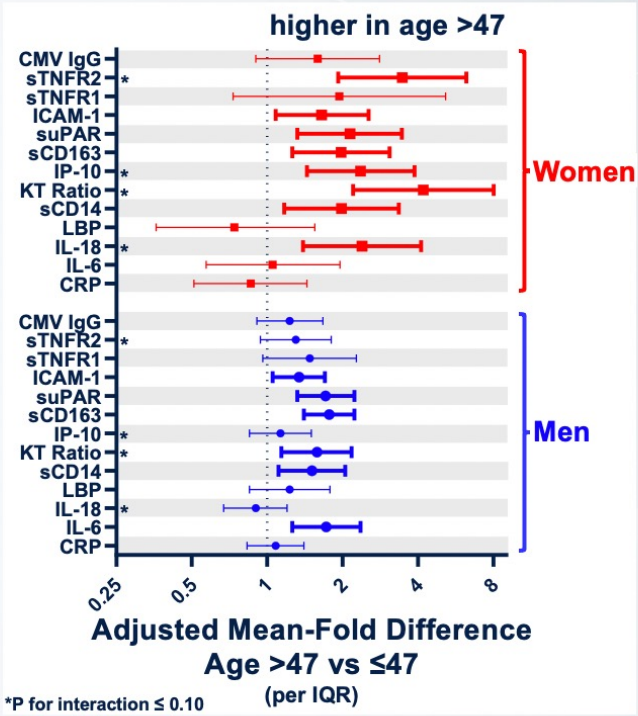
Women have higher levels of inflammation than men during suppressive ART



Is there a menopause effect?

Median age in cohort: 47

Models adjusted for: age, race/ethnicity, smoking, HCV, IDU history, ASCVD score, nadir CD4, CNICS site



Schnittman et al, CROI 2021, #98 (see also: Peters, JID, 2022)

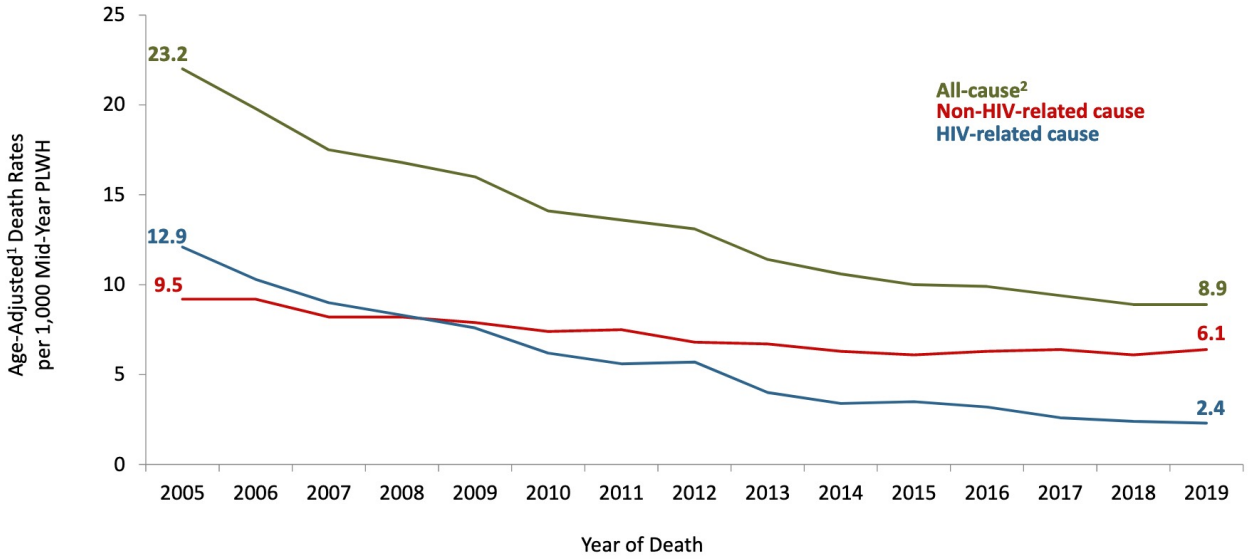
Almost Doubled Death Rate PLWH

The all-cause death rate (8.9 per 1,000 in 2019) among people with HIV decreased by 60% from 2005 to 2019 but remained higher than the death rate for the overall NYC population (5.5 in 2017)

- slope of curve (Non-HIV cause) increasing since 2018 suggesting further increases in deaths due to comorbidities

Mortality Among People With HIV

Figure 18.1: Age-adjusted death rates among people with HIV by HIV-related and non-HIV-related cause of death, NYC 2005-2019



The all-cause death rate (8.9 per 1,000 in 2019) among people with HIV decreased by 60% from 2005 to 2019 but remained higher than the death rate for the overall NYC population (5.5 in 2017). Although the rates of both HIV-related and non-HIV-related causes of death decreased during this time, the decrease in the all-cause death rate was driven by fewer deaths attributed to HIV (Figure 18.1). During this time, the median age at death from all causes among PWH increased from 49 years in 2005 to 59 years in 2019 but was lower than the median age at death for NYC overall (77 years in 2017). Age at death increased by a similar amount for people with an HIV-related cause of death (by 8.4 years) and a non-HIV-related cause of death (by 8.8 years) from 2005 to 2019.

End of 2019, the majority (73%) of deaths were due to non-HIV-related causes. Since 2005, substantial increases (**Doubled**) in the proportions of deaths due to cardiovascular diseases (19% of all deaths in 2019) & non-HIV-related cancers (18% of all deaths in 2019) among PWH = **Cancer + CVD 37% vs 25% HIV-Related**

Mortality Among People With HIV

Table 18.1: Trends in proportions of major causes of death among people with HIV, NYC 2005-2019

	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Total Deaths (N)	(2,701)	(2,481)	(2,372)	(2,377)	(2,269)	(2,097)	(2,094)	(1,943)	(1,919)	(1,865)	(1,815)	(1,841)	(1,810)	(1,770)	(1807)
CAUSE OF DEATH[1]															
HIV-RELATED (%)	59	55	53	52	48	47	42	38	35	33	34	30	27	26	25
NON-HIV-RELATED (%)	39	43	45	46	50	50	52	57	58	60	61	65	69	70	73
CVD	9	10	11	12	13	13	13	14	14	15	16	19	22	17	19
CANCER[2]	10	11	12	13	14	13	14	16	16	15	17	16	17	18	18
ACCIDENTAL OD	0	1	5	3	4	3	3	5	3	4	5	7	8	5	0
INFECTIOUS DISEASES	4	4	5	3	4	5	4	5	5	6	5	5	3	5	3
EXTERNAL CAUSES	3	4	3	4	3	5	3	5	4	4	4	4	4	4	9
OTHER	13	13	9	11	12	11	15	12	16	16	14	14	15	21	24

Trend within a cause of death over time

Lowest — Middle — Highest

In 2005, the leading cause of death among people with HIV (PWH) was HIV, representing 59% of all deaths. At the end of 2019, although HIV was still the single leading cause of death among PWH, the majority (73%) of deaths were due to non-HIV-related causes. Since 2005, there have been substantial increases in the proportions of deaths due to cardiovascular diseases (19% of all deaths in 2019) and non-HIV-related cancers (18% of all deaths in 2019) among PWH (Table 18.1).

ACTG HAILO Study - IADL disability occurs frequently among middle-aged and older HIV-infected adults on effective antiretroviral therapy

(37% pre-frail, 6% frail). More comorbidities increased IADL risk – 94% <200 c/ml, 67% >500cd4 – 6% had 2 or more comorbidities

Higher Than Expected: 2 to 3 times higher rate of IADL impairment observed across cohorts compared to the general population

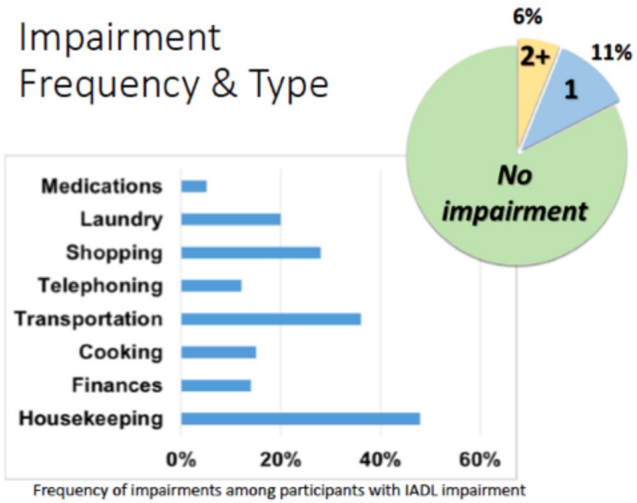
Unable to Perform Normal Daily Activities of Living

ACTG N=1015, median age=51; 15% >60 - strong association between **disability & neurocognitive impairment** (comorbidity most strongly associated with IADL risk), , **socioeconomic** (education, health insurance)/ **socioeconomic disadvantages** & lifestyle factors (**smoking**, **low physical activity**): proxy for financial resources/employment/housing access - inability to mobilize resources, stigma, ageism, gender identity, no family-alone, no social support, temporary disability

Table 2. Type of Impairment Present Among Participants with at Least One IADL Impairment

		IADL impairment at baseline	
Type of Impairment	Total (N=178)	1 impaired category (N=115)	≥2 impaired categories (N=63)
Housekeeping difficulty	48%	39%	63%
Transportation difficulty	36%	25%	56%
Shopping difficulty	28%	10%	59%
Laundry difficulty	20%	4%	48%
Finance management difficulty	14%	10%	21%
Cooking difficulty	15%	7%	29%
Difficulty in using the phone	12%	2%	30%
Difficulty with medications	5%	2%	11%

ACTG HAILO Study CID Johs et al 2017.



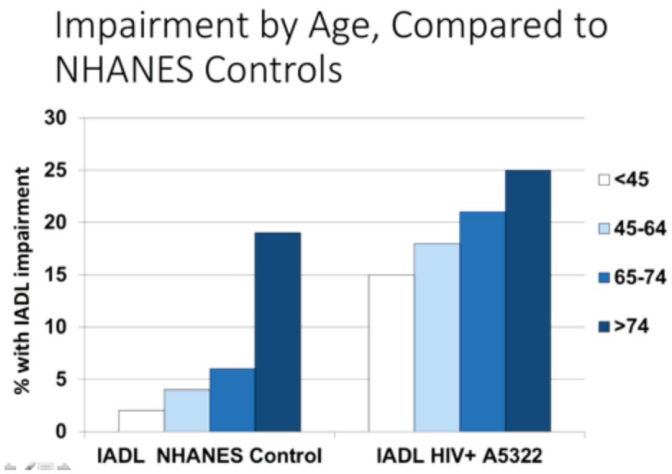
Public Insurance coverage may limit access to services

Why Might Middle-Aged or Older HIV-infected Adults be Particularly Vulnerable to Reporting Disability?

- May have difficulty accessing usual resources for older adults (churches, senior centers), etc due to HIV or gender/sexual identity stigma
- Fractured family relationships; few have adult children that take on the caregiver role
- Economic challenges from long-term disability (limited financial reserves, retirement plans, long-term care insurance, etc)

It Gets Worse with age:

HAILO ACTG:
Factors Associated with Limitations in Daily Activity Among Older HIV+ Adults....
2-4x rates worse daily functioning.
N=1000
Age 51(46-56).
15%>60



Summary of Key Findings

- Middle-aged and older HIV-infected participants had 2-3 x higher rate of IADL disability compared to the general population (NHANES).
- Neurocognitive impairment was the only comorbidity associated with IADL impairment.
- Strong associations between IADL impairment and socioeconomic & lifestyle factors were seen.
- Notably, HIV-related factors were not associated with IADL impairment.

CID 2017. Erlandson et al.

SF Gen SCOPE Study Cohort. 2015 N=155 age 57 (54-62) 94% men; 80% MSM; 21 yrs HIV-infected median 4 comorbidities; 9 non-HIV medications; cd4 nadir 57 (51-327); undetectable VL. - multidisciplinary team of physicians, nurses, pharmacists, and social workers: **"takes a team of people to take good care of an older person with HIV"**

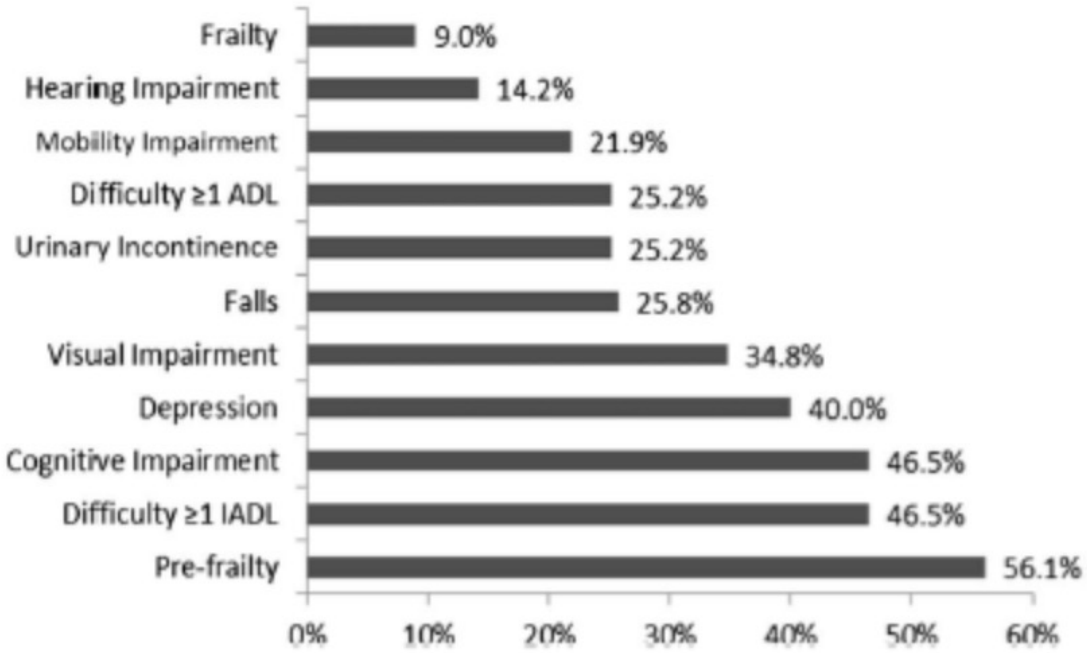


FIGURE 1. Frequencies of geriatric syndromes. Each bar reflects the percentage of participants with each geriatric syndrome. Actual percentages are shown at the end of each bar. Horizontal axis only shown to 60%.

A combination of risk factors for geriatric syndromes including psychosocial factors, such as social isolation and substance use, multimorbidity and polypharmacy, and chronic inflammation, is common among older HIV-infected adults

We identified a frequent occurrence of geriatric syndromes, with prefrailty, difficulty with IADLs, and cognitive impairment particularly common even among participants with well-controlled HIV. A combination of both HIV-related factors (CD4 nadir) and non–HIV-related factors (comorbidities, non-white race) was associated with increased risk of having more geriatric syndromes.

JAIDS 2015. Meredith Greene et al.

SF Silver Project 2012-2014: UCSF Positive Care Clinic, SF General Pos Health program (Ward 86)-publicly insured n=359; med. Age 56 (50-80)85% male; 66% homosexual; 60% white; highly educated; low income

TABLE 2. (*Continued*) Participant Characteristics, Overall and by Age Group, Silver Project, San Francisco

	Age Group			
Characteristic	**Overall N (%), 359 (100)**	**50–59 yrs N (%), 244 (68)**	**60–80 yrs N (%), 115 (32)**	***P****
Current cigarette smoker†	109 (30.6)	79 (32.3)	30 (26.0)	0.20
Current alcohol use‡	212 (59.4)	145 (59.7)	67 (58.8)	0.87
Binge drinking§	96 (27.8)	72 (31.0)	24 (21.2)	0.06
Cocaine use‖	42 (11.8)	27 (11.1)	15 (13.3)	0.56
Crack use‖	37 (10.9)	28 (11.5)	11 (9.7)	0.62
Methamphetamine use‖	48 (13.5)	38 (15.6)	10 (8.9)	0.08
>10 yrs HIV-infected	262 (85.1)	179 (84.8)	83 (85.6)	0.87

a trend existed toward lower **binge drinking rates** in the older age group (21% 60–80 years vs 31% 50–59 years

a trend toward less **methamphetamine use** was seen in the older age group (9% vs 16%)

older age group were more likely to have CD4 counts below 500 than those age 50–59 years

41% reporting a fall in the past year

60% endorsing at least mild symptoms of loneliness

50% reporting low social support

34% meeting criteria for possible mild cognitive impairment

60+ had higher frequencies of problems with balance *(47% vs 33%* in the 50–59 year group

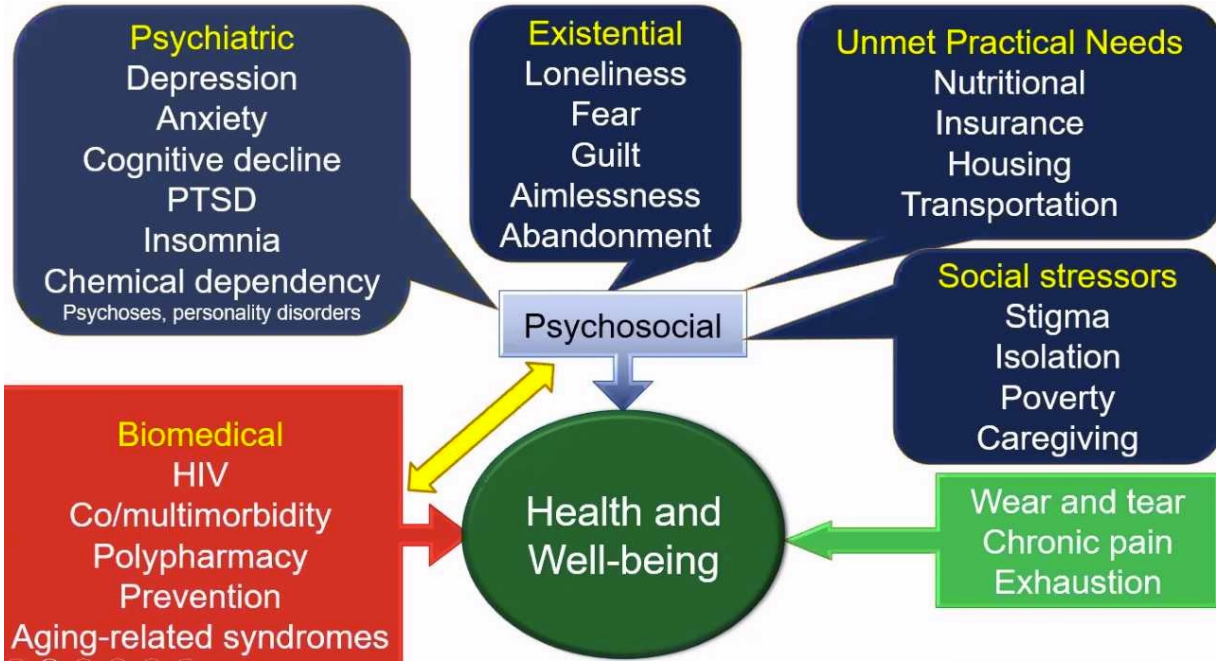
60+ or older had *slower gait speed* compared with those aged 50–59

JAIDS 2016 John et al

TABLE 3. Geriatric Assessment Results Overall and by Age Group, Silver Project, San Francisco

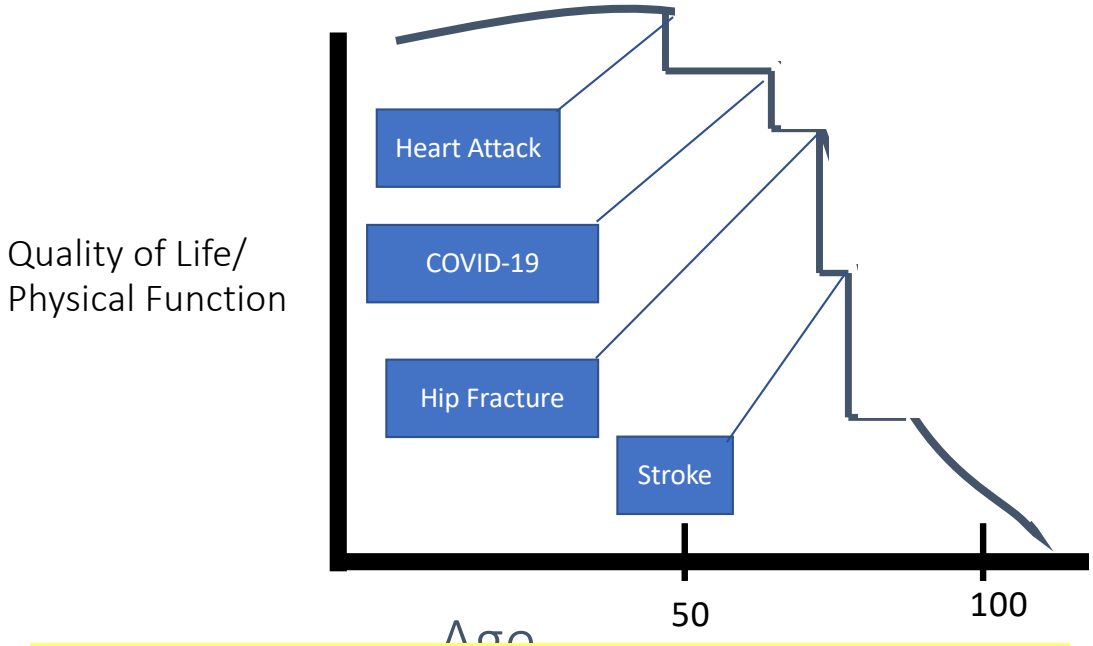
	Age Group			
Geriatric Assessment*	**Overall N (%), 359 (100)**	**50–59 yrs N (%), 244 (68)**	**60–80 yrs N (%), 115 (32)**	***P*†**
Physical domain				
Fall in the past year	145 (40.7)	94 (38.5)	51 (45.5)	0.21
Problems with balance	134 (37.6)	81 (33.3)	53 (46.9)	**0.01**
Dependent in ≥1 activity of daily living (ADL)	43 (12.2)	29 (12.0)	14 (12.5)	0.90
Dependent in ≥1 IADL	136 (38.9)	100 (42.4)	36 (31.6)	0.05
Gait speed 4-meter walk (sec)				**0.03**
0.01–4.81	247 (70.0)	174 (72.5)	73 (64.6)	
4.82–6.20	75 (21.3)	51 (21.3)	24 (21.2)	
6.21–8.70	23 (6.5)	13 (5.4)	10 (8.9)	
8.71–18.99	8 (2.3)	2 (0.8)	6 (5.3)	
Social domain				
Loneliness				0.35
None (<17)	150 (42.1)	95 (39.3)	55 (48.3)	
Mild (17–20)	85 (23.9)	59 (24.4)	26 (22.8)	
Moderate (21–24)	78 (22.0)	55 (22.7)	23 (20.2)	
Severe (25–32)	43 (12.1)	33 (13.6)	10 (8.8)	
Perceived social support				0.49
Normal (<36)	174 (50.0)	122 (51.7)	52 (46.4)	
Mild (36–47)	147 (42.2)	98 (41.5)	49 (43.8)	
Moderate (48–53)	27 (7.8)	16 (6.8)	11 (9.8)	
Low physical social support	180 (50.1)	120 (49.2)	59 (51.3)	0.71
Cognitive and mental health domain				
Cognitive impairment	121 (33.7)	84 (34.4)	37 (32.2)	0.67
Depressive symptoms				0.72
None (<5)	161 (45.4)	105 (43.6)	56 (49.1)	
Mild (5–9)	99 (27.9)	69 (28.6)	30 (26.3)	
Moderate (10–14)	52 (14.7)	38 (15.8)	14 (12.3)	
Severe (15–27)	43 (12.1)	29 (12.0)	14 (12.3)	
Anxiety				**0.02**
Normal (<5)	179 (50.6)	110 (45.3)	69 (62.2)	
Mild (5–9)	108 (30.5)	84 (34.6)	24 (21.6)	
Moderate (10–14)	44 (12.4)	31 (12.8)	13 (11.7)	
Severe (15–21)	23 (6.5)	18 (7.4)	5 (4.5)	
PTSD symptoms	44 (12.5)	34 (14.2)	10 (9.0)	0.17

“Aging & HIV Syndrome”



Eugenia Siegler, Cornell.

Decline in Function May Not Be Gradual



A major goal of the treatment of acute illness is to regain function → Use physical and occupational therapy

$64,000 Question ?

Will PLWH who started ART earlier suffer the same outcomes ?

We don't know !

- CD4 nadir
- Immune derangement, immune exhaustion accumulated for years
- Immune activation, inflammation
- Immuno-senescence (premature aging of the immune system (by 3-15 years)
- Family genes
- 40% of PLWH in USA not in care, detectable viral load
- Discrimination (sex, race), lifetime trauma, marginalization, poverty

Daily Problems, Barriers Elderly Face

Viral Suppression is NOT the only care concern !!! For aging & elderly its less concern

Stigma is Big

- ***internal***: feel bad, self-blame, ignored, abandoned; worried about sickness & health; worried about having to go in nursing facility; worried who will take care of them; isolated (no family)
- ***Functionally impaired***: debilitating fatigue; QOL, cant shop, prepare food, cant pay bills – co-pays; cant engage on telephone, "brain fog"; walk with cane (mobility, homebound) – fractures/falls- transportation; no exercise/diet(healthy food access) programs which they do NOT understand; dental; Cure & PrEP & young HIV+ is all they see & hear
- ***Cognitive decline underappreciated***: memory, motor function, alzheimers
- ***Mental health: anxiety about future***, lifetime trauma, discrimination (sex, race, age) PTSD, depression, apathy, abandonment, polypharmacy, adherence, iritabitability/agitation; language problems expressing themselves & communicating
- **Death sentence, Suicide ideation**
- ***HIV healthcare system*** **left them** high & dry
- **External stigma: ageism** – other advocates; doctors don't pay attention; HHS-ACTG;
- These elderly fought for what you all have now – an open system allowing you to participate in
- **Pain**, opioid prescriptions

HIV Healthcare System is Broken

We are Unprepared for Now & the Future "Silver Tsunami"

- PLWH Do not understand "aging phenomena"; never received federal education
- **Mortality**, lied to about that
- ***20-minute doctor visits BIGGEST BARRIER***
- *Inadequate/**No care coordination*** between specialist & primary HIV doctor
- **Physical therapy, mental health care services inaccessible**
- **Many have Returned to substance abuse**
- Don't get Bone Dexas, CVD evaluation & treatment, diabetes mgt.
- State & Federal officials oblivious
- **Home Care** – Housing for elderly, Impaired – Nursing homes doubled for PLWH Use - How will we deliver care for disabled elderly ? **Poverty**

Research Needs – Implementation Studies

- Exercise & Diet studies
- Frailty, cognitive assessments
- Flexible time medical visits
- Health foods education & access programs
- Care Coordination & coordinators for Aging population: between doctor-specialist-PLWH
- ***PREVENTION*** - Cardiovascular, heart nursing education support
- Diabetes management programs
- Bone education
- Physical therapy access unfettered
- Mental health care support & services unfettered access
- Social engagement, isolation, loneliness
- HIV-focused community services programs

Research needs (2) – Fast track Research Mechanisms

- Senolytics Anti-Aging drugs
- Jak Inhibitor
- GLP-2 Agonists reduced inflammation (CROI 2022)

Ryan White Care Act – ***HIV Healthcare System is Broken***, is Sub-Optimal

- It needs to be reconfigured, rebooted to meet needs of the elderly & aging population.
- For people without HIV in the USA their primary care dictors issue referrals & provide care for all conditions & comorbidities without barriers as the RWCA is full of barriers preventing normal care.

New Models of Care Needed **- NY Example**

- 3 new HIV Geriatric Clinics
- 2 standing HIV Geriatric Clinics: Mt Sinai
- 2 more expected next year
- Integration of Geriatric Care elements into Ryan White & HIV Clinics next year ????
- CFAR Women's Study

Thanks to Peter Hunt, Todd Brown, others