Neurodegeneration and Dementia Risk in Older Adults With HIV: Biomarkers and Epidemiology

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CROI 2026

Questions

- Does HIV still effect the brain, and can it lead to early dementia?

- Does the brain age differently in people with HIV from people without HIV?

UK-CAB
HIV TREATMENT ADVOCATES NETWORK

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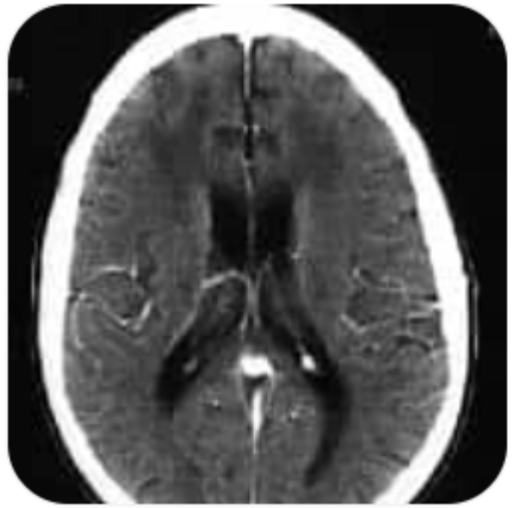
The past – many years ago

Copilot Search

AIDS dementia complex (ADC), also known as HIV-associated dementia, is a neurological disorder caused by HIV infection that leads to cognitive, behavioral, and motor dysfunction.



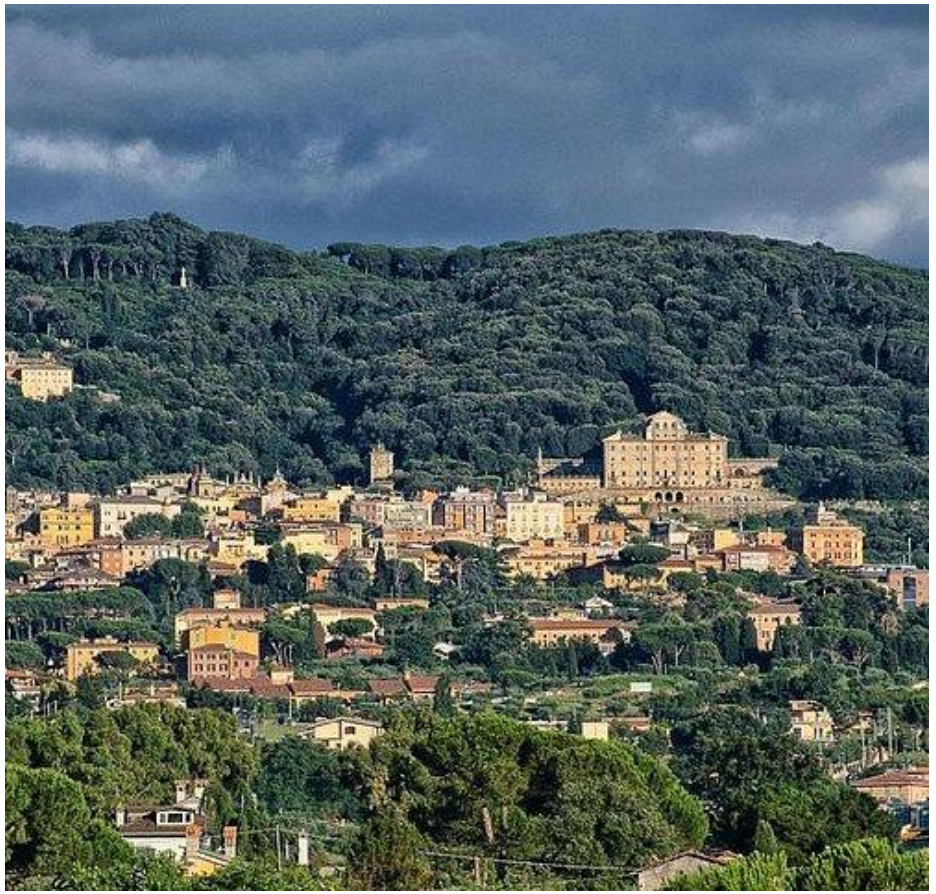
Overview of AIDS Dementia Complex

AIDS dementia complex (ADC) is a condition that occurs in individuals with advanced HIV infection, particularly when the immune system is severely compromised (CD4+ count falls below 200 cells/microliter). It is characterized by a decline in cognitive functions, including memory, reasoning, and judgment, as well as changes in personality and behavior. Symptoms can range from mild cognitive impairment to severe dementia, significantly impacting daily functioning. WebMD +1

The past – more recently

HAND Criteria or Frascati Criteria

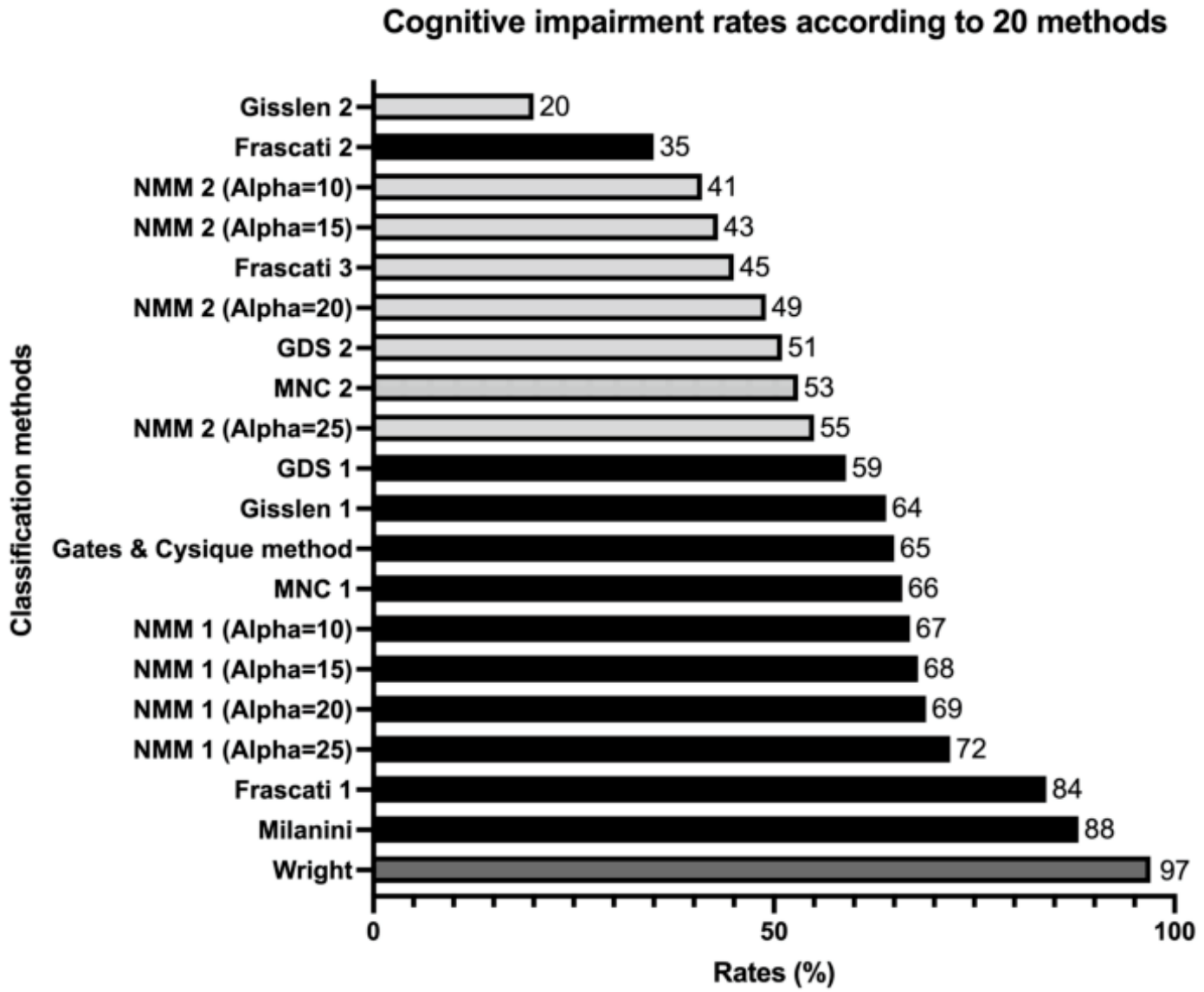
‘HIV-associated neurocognitive disorders’



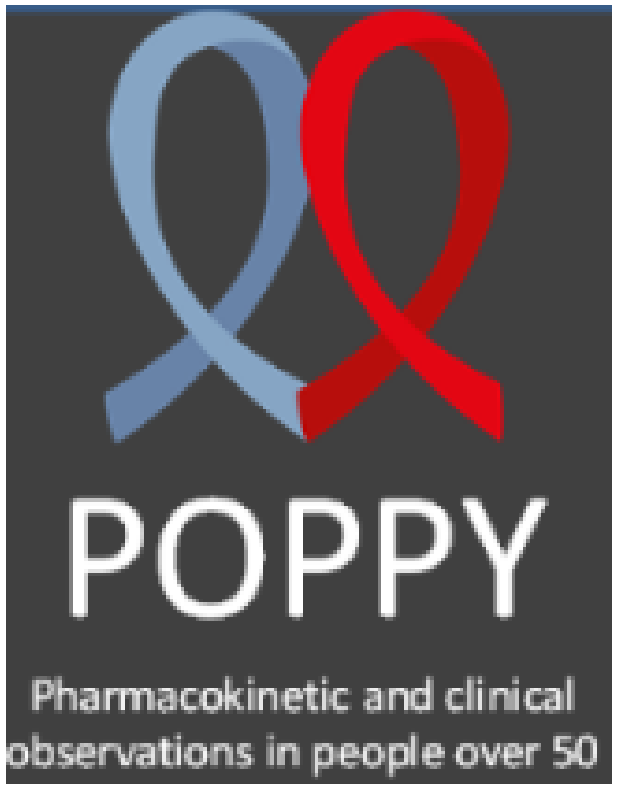
Cognitive impairment in Cape Town

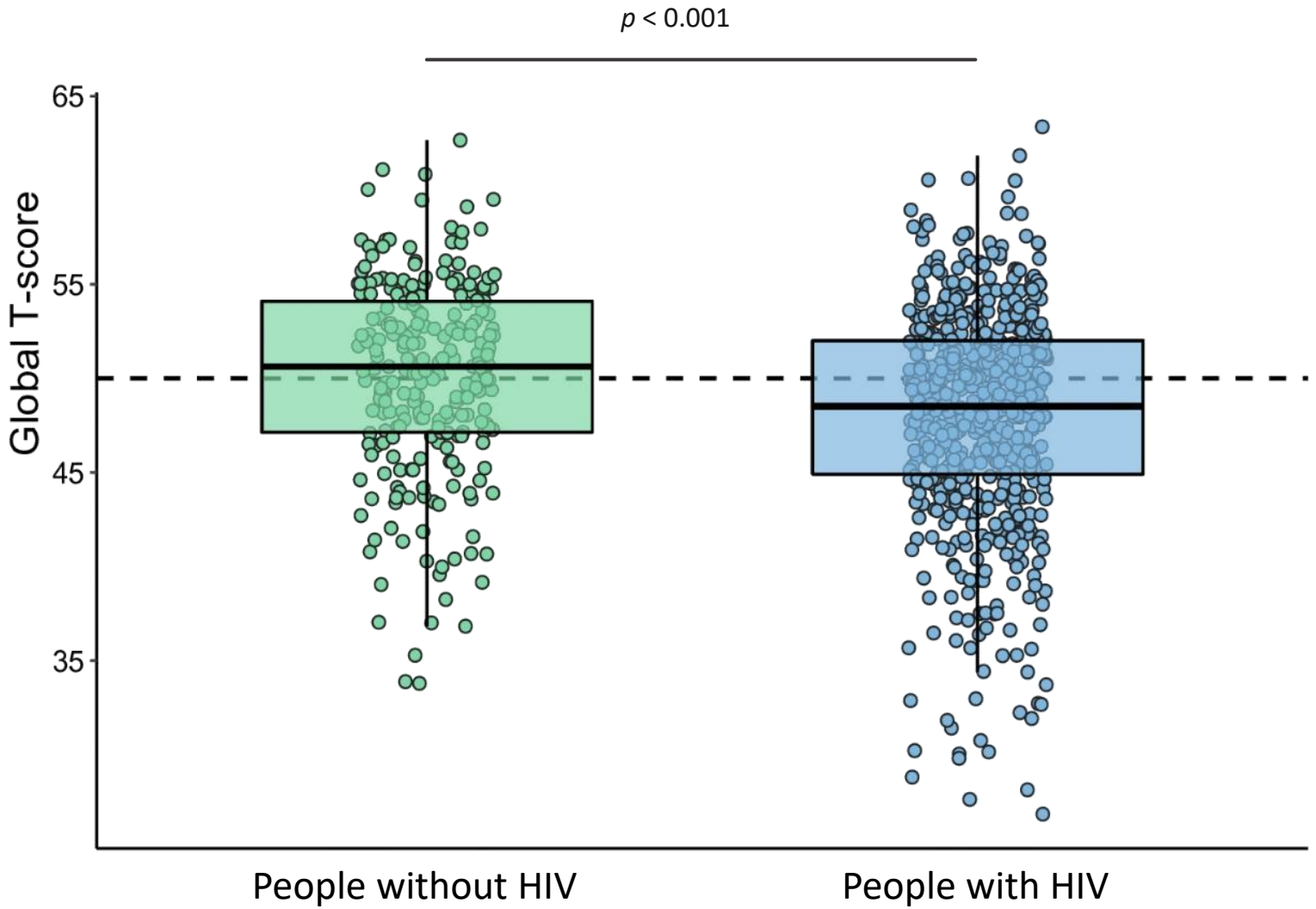
Rates of cognitive impairment in a South African cohort of people with HIV: variation by definitional criteria and lack of association with neuroimaging

Journal of NeuroVirology ***27****, 579-594 (2021)*



Cognitive function in the POPPY cohort





median (IQR): 50.6 (47.1, 54.1) 48.5 (44.9, 52.1)

BMC Infect Dis. 2016 Oct 28;16(1):617

Unintended consequences

CLINICAL SCIENCE

Impact of HIV on Cognitive Performance in Professional Drivers

CONCLUSION

Drivers with HIV may be at risk of poorer long-term health and employment outcomes. Programs that monitor and support their long-term cognitive health are needed

J Acquir Immune Defic Syndr. 2022 Apr 15;89(5):527-536

NEWS | UK

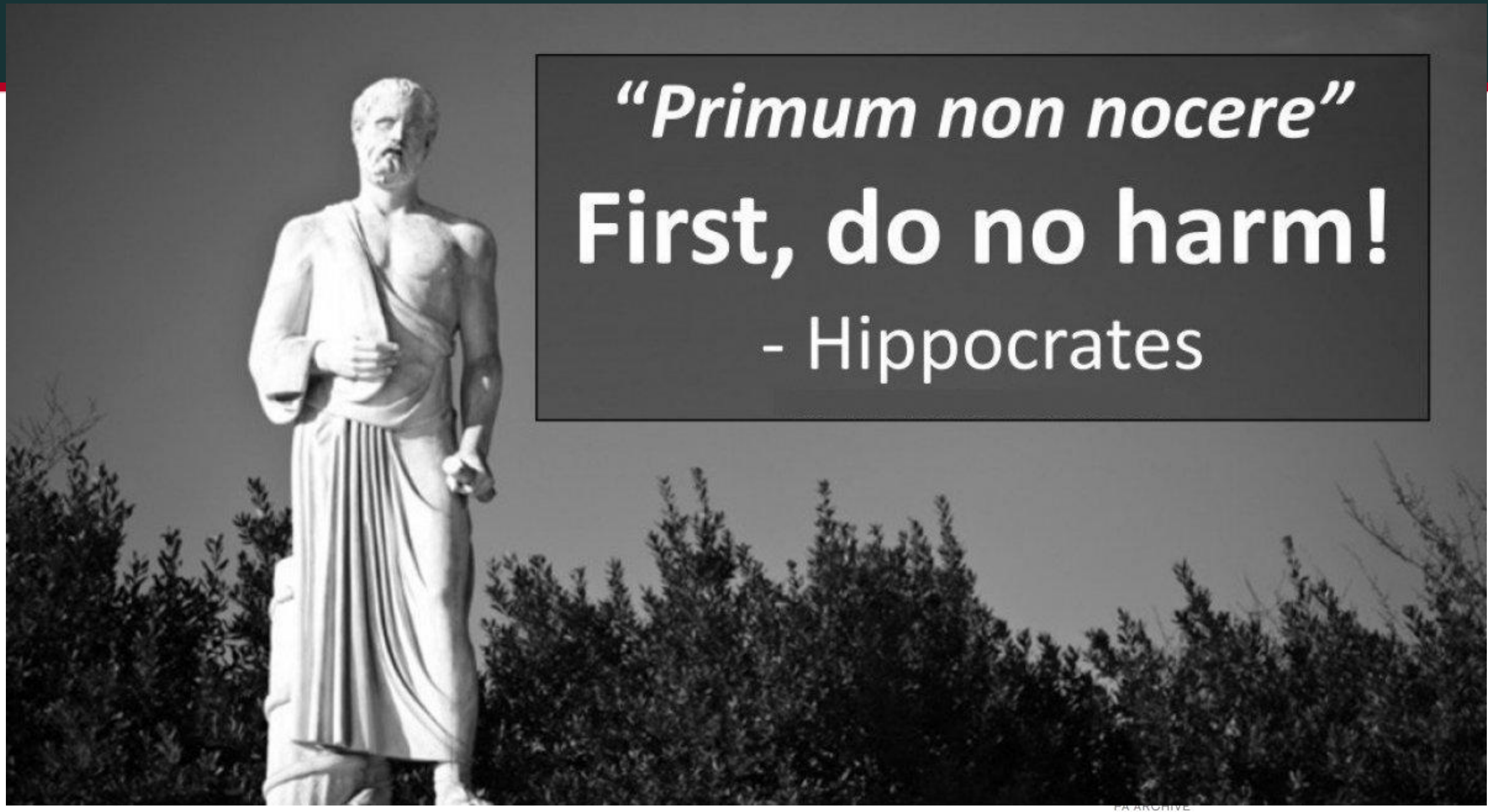
20 JUNE 2022

UK pilots with HIV able to work unrestricted after 'landmark changes'

New guidelines for how people with HIV can have full careers as commercial pilots has been issued.

THE MEASURES ARE BELIEVED TO BE A WORLD-FIRST FOR AVIATION WORKERS (STEVE PARSONS/PA)

PA ARCHIVE

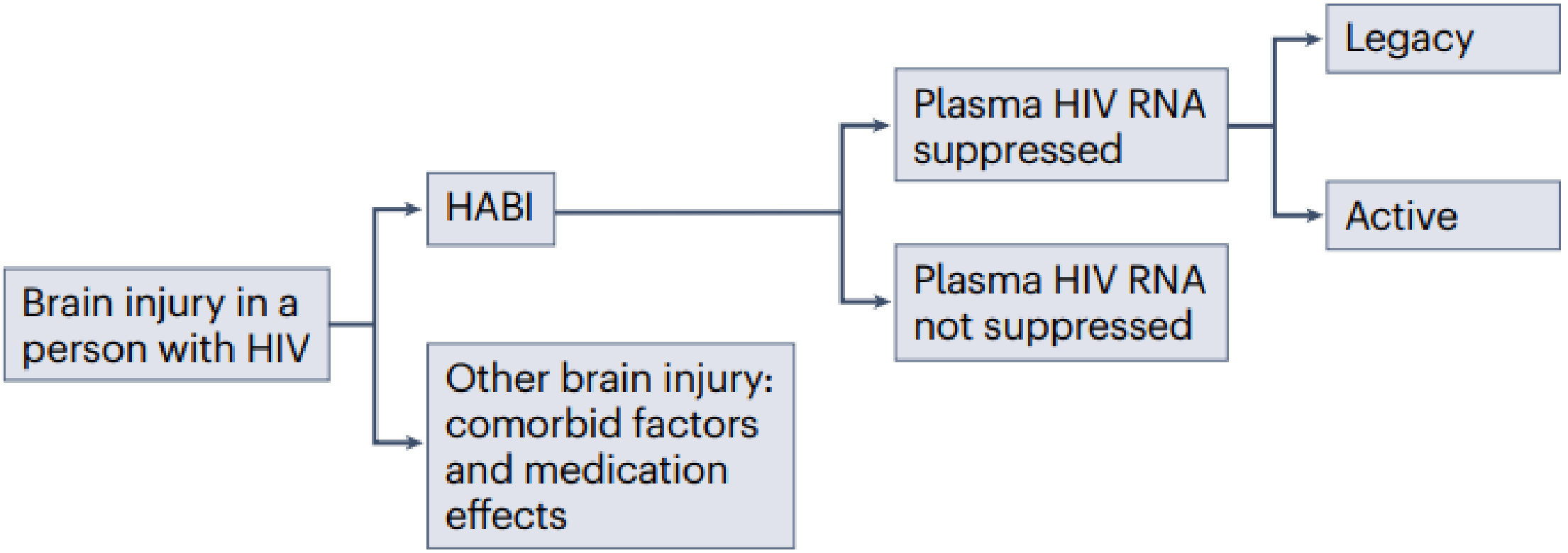

"Primum non nocere"
First, do no harm!
- Hippocrates

Consensus recommendations

nature reviews neurology

Cognitive impairment in people living with HIV: consensus recommendations for a new approach

Nature Reviews Neurology: 19, 424-433 (2023)

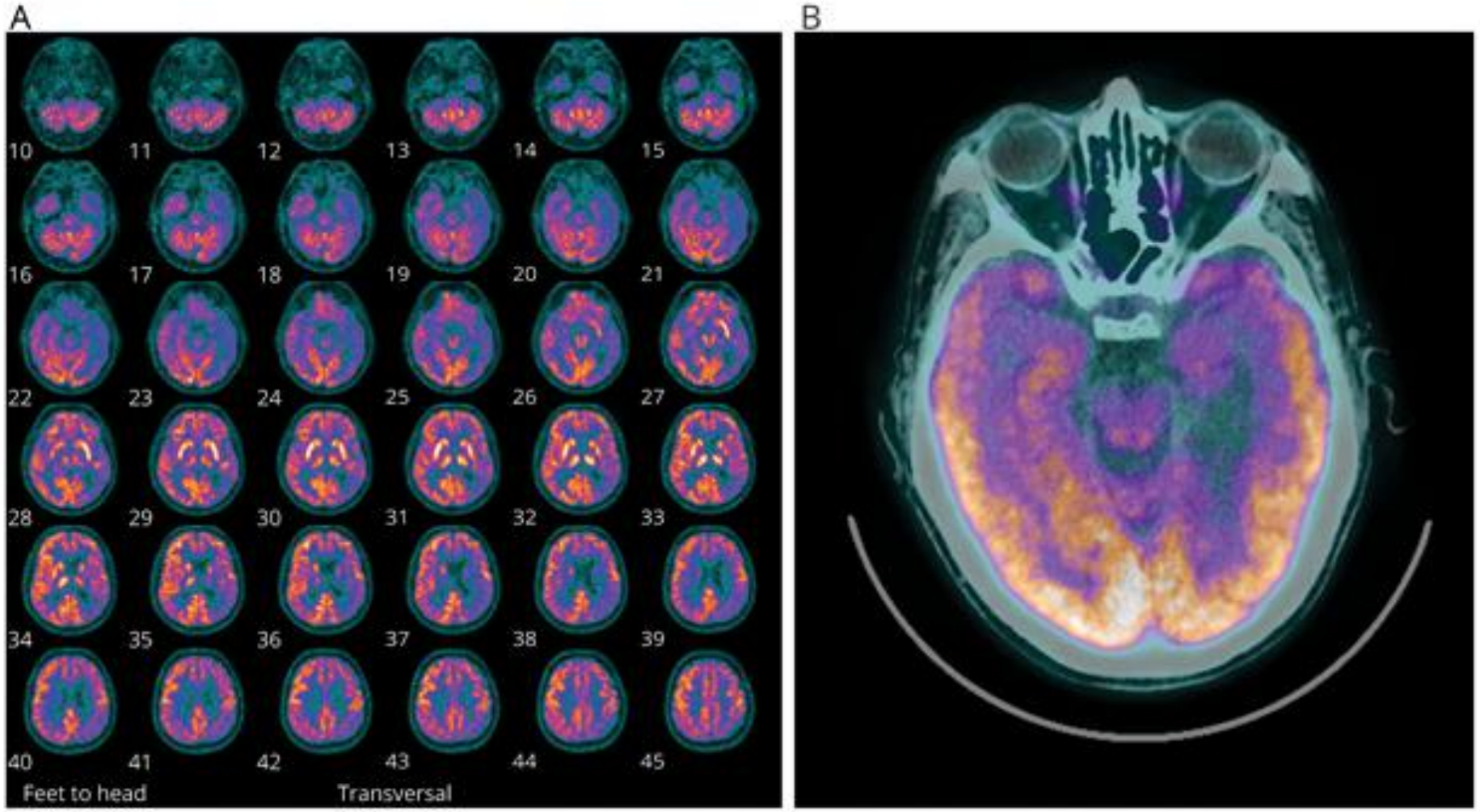


Neurodegenerative conditions

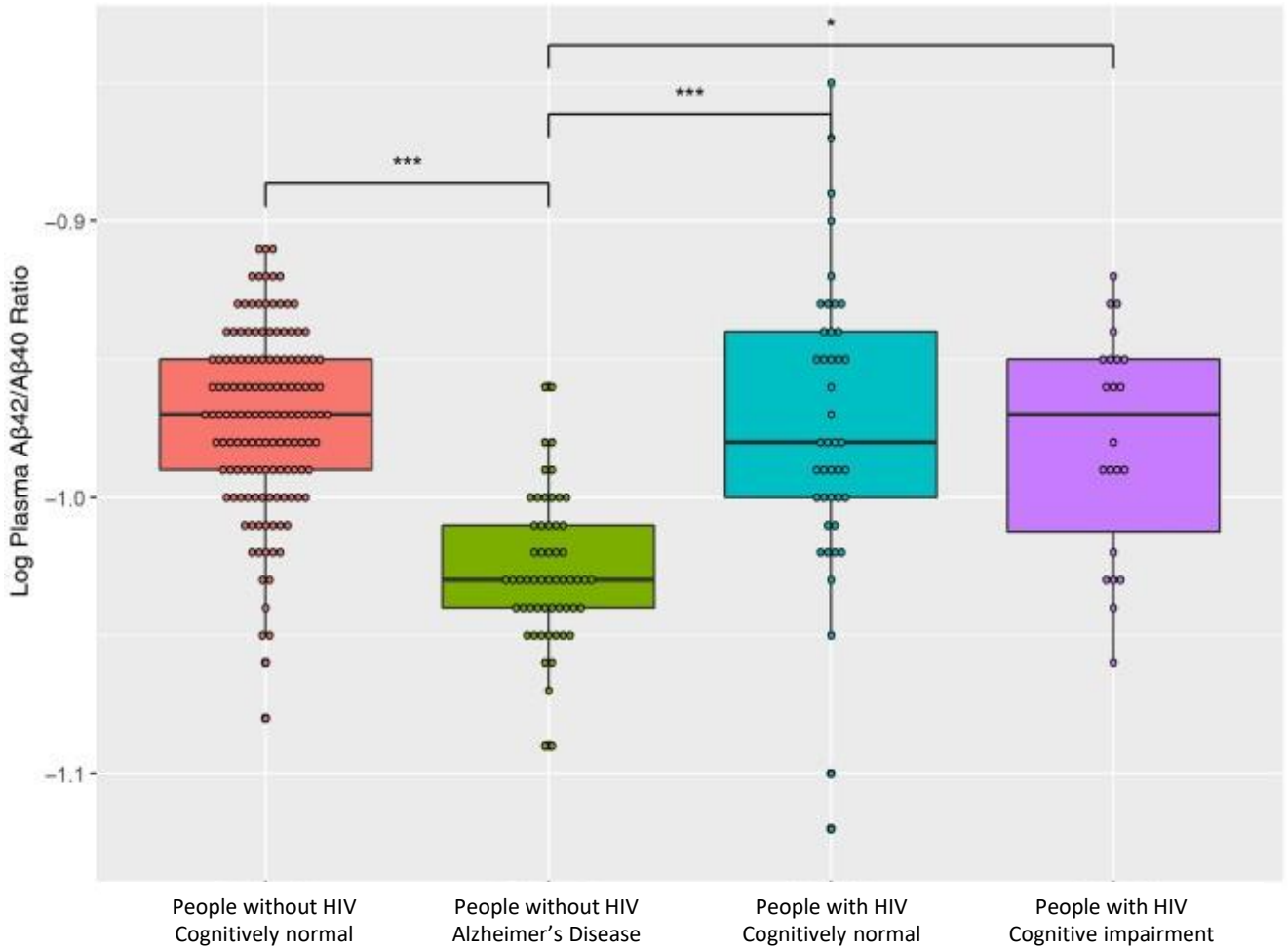
Neurology® Clinical Practice | American Academy of Neurology

Alzheimer Dementia in People Living With HIV

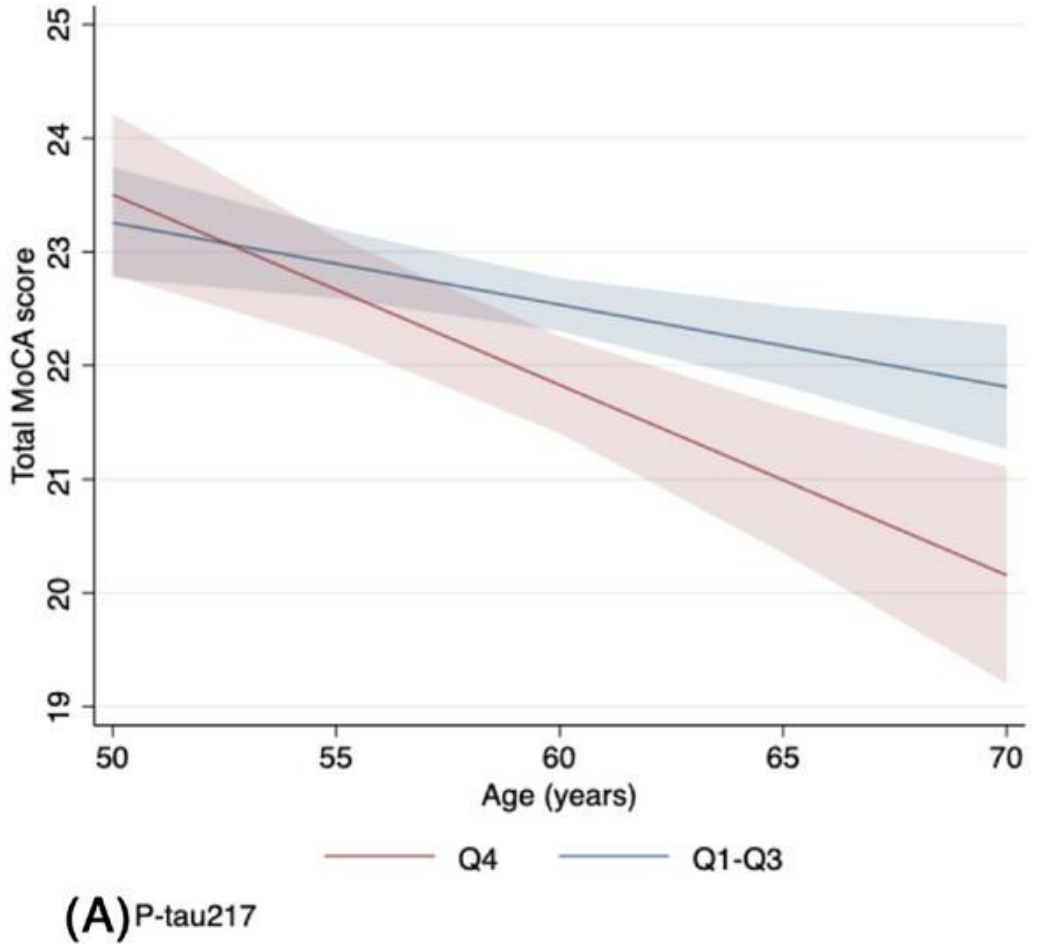
Neurol Clin Pract 2021 Oct 11(5): e627-e633



Alzheimer’s biomarkers



Clin Infect Dis. 2023 Jan 5;76(10):1776–1783

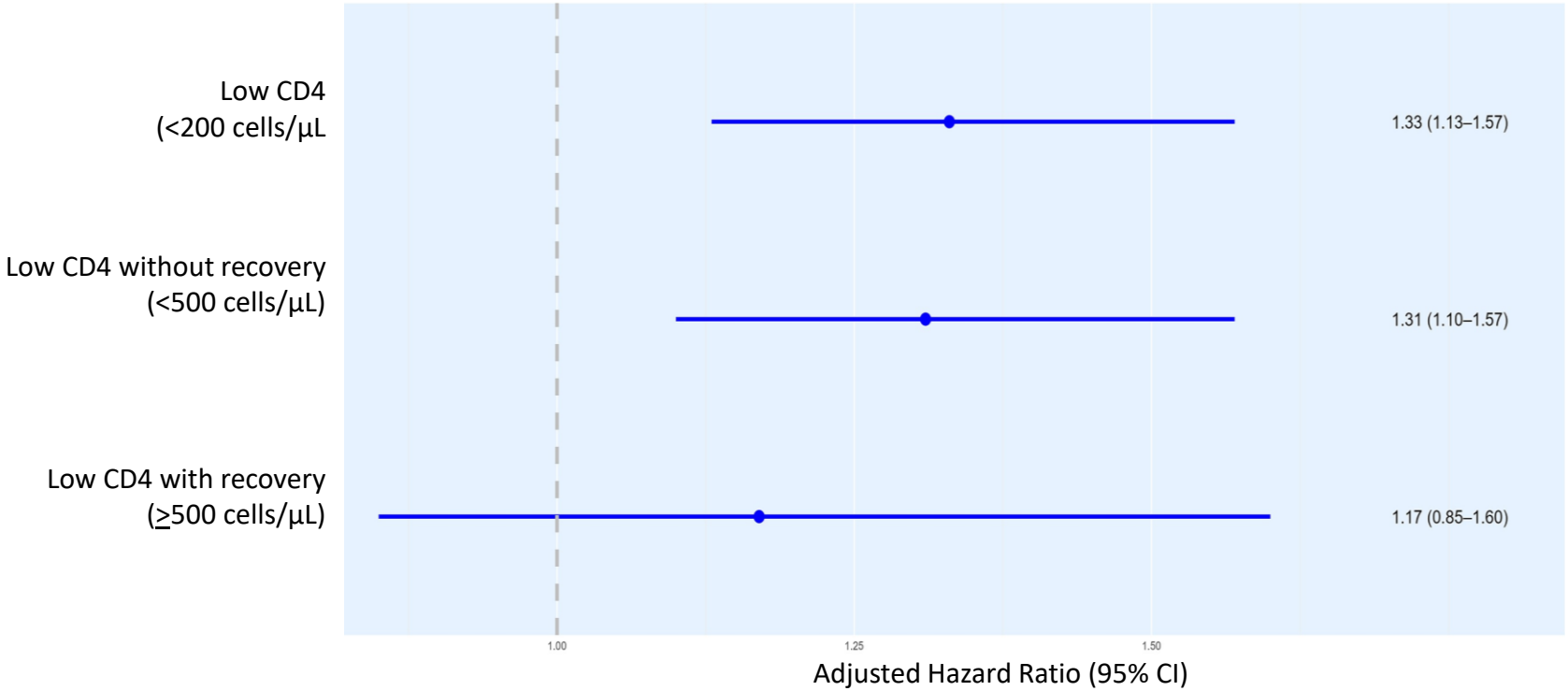


Alzheimers Dement. 2026 Jan;22(1):e71101

Dementia risk and delayed HIV diagnosis

Impact of Delayed HIV Diagnosis and Treatment on Dementia Risk in Later Life

Open Form Infectious Diseases, Volume 13, Issue 1, January 2026



Characteristic	N = 21 354
	n (%)
Age, mean years (SD)	53.8 (5.6)
Male	18 584 (87.0)
CD4 cell count, cells/µL[c]	…
≥500	11 363 (53.2)
200–499	6887 (32.3)
<200	2351 (11.0)
Unknown	753 (3.5)

Questions

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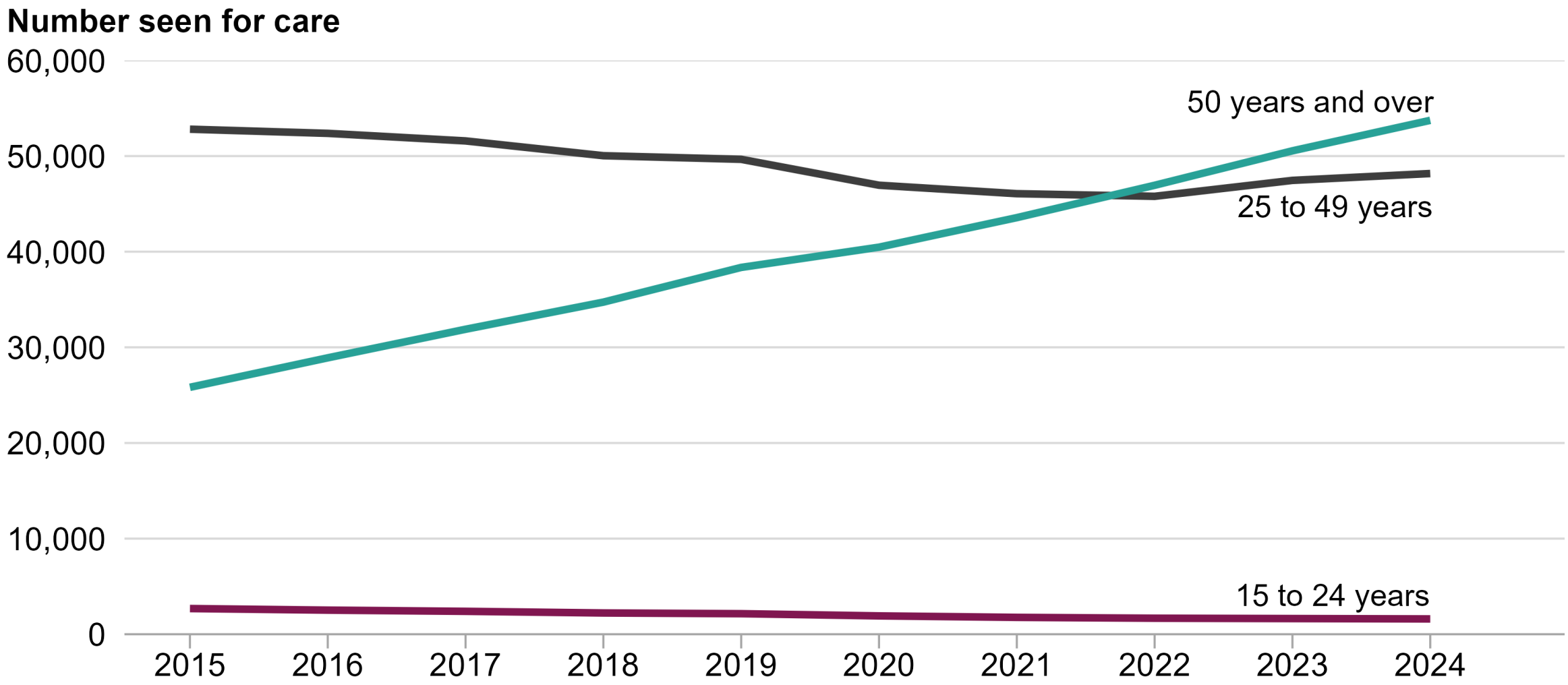
UK-CAB
HIV TREATMENT ADVOCATES NETWORK

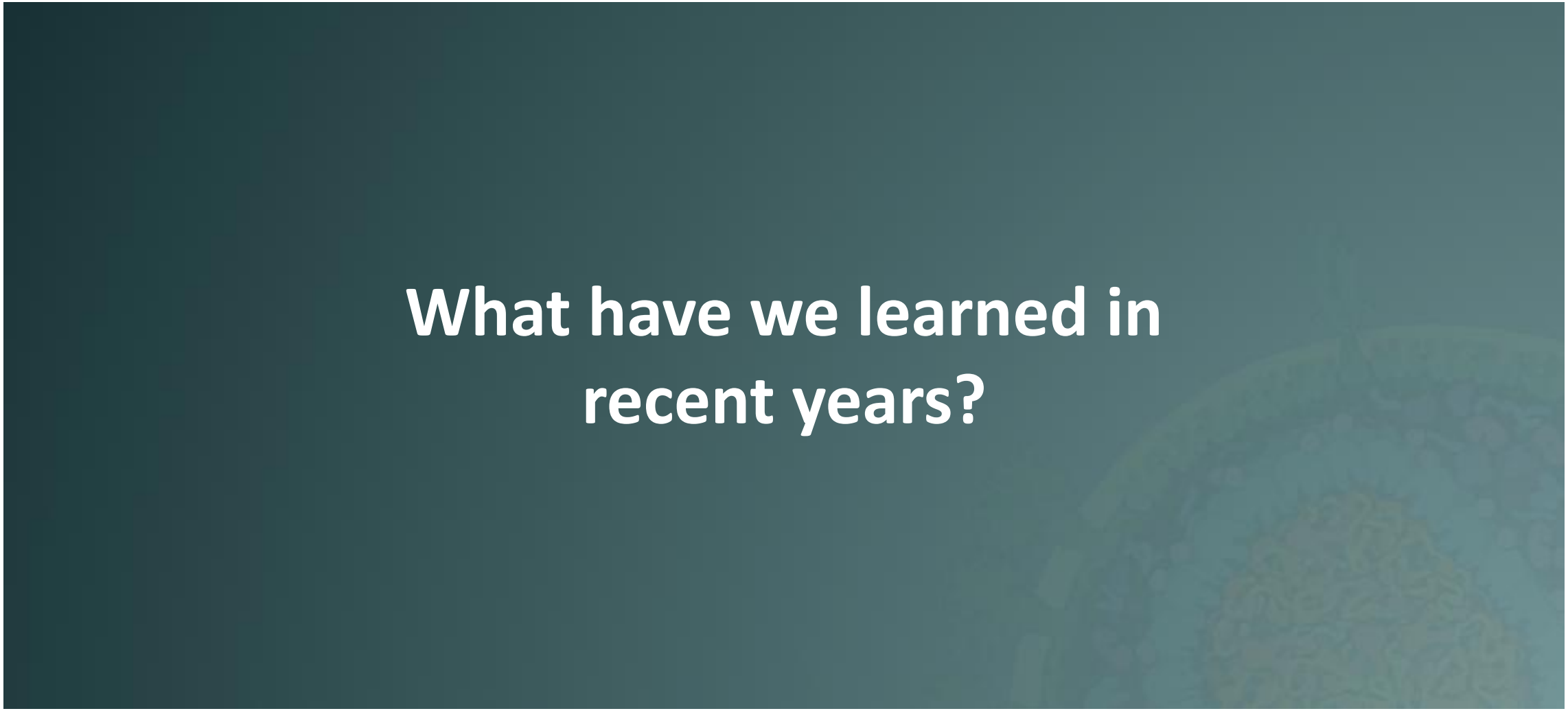
Number of people aged 15 years and over accessing HIV care by age group: England, 2015 to 2024



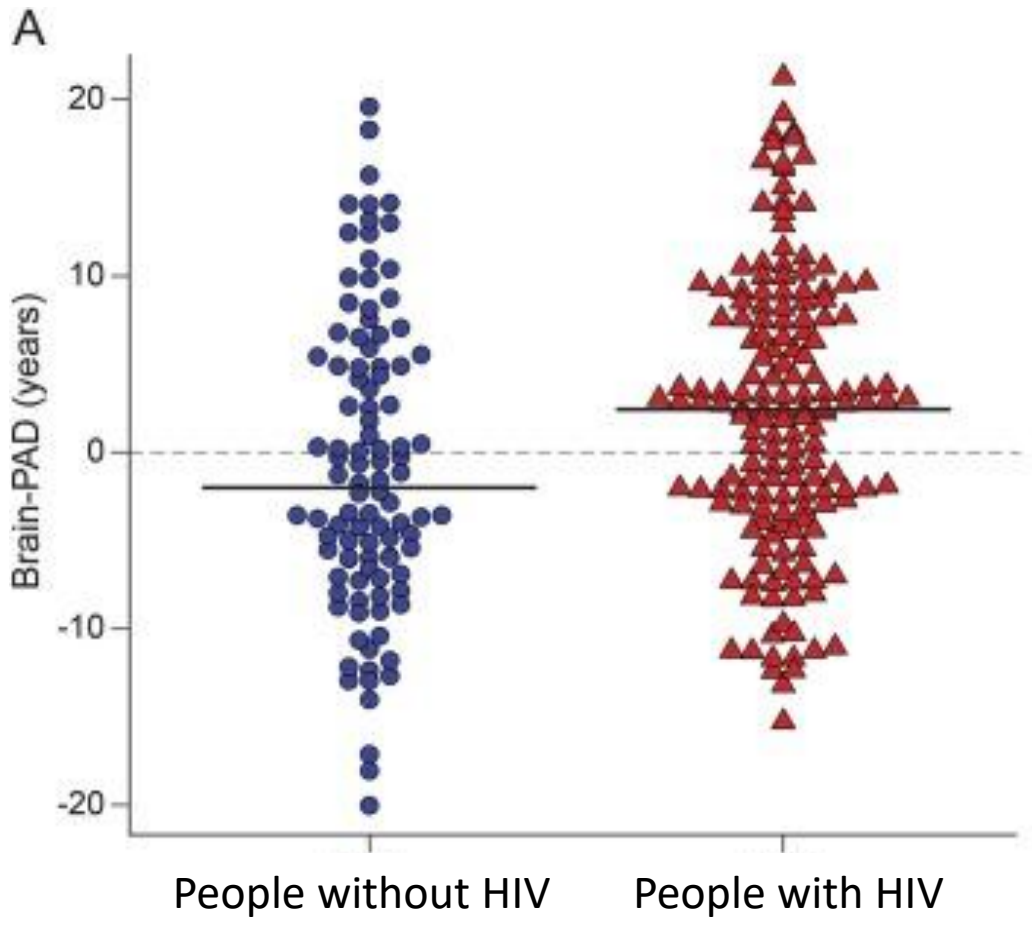
HIV in England: 2025 slide set (version 1.0, published 7 October 2025)

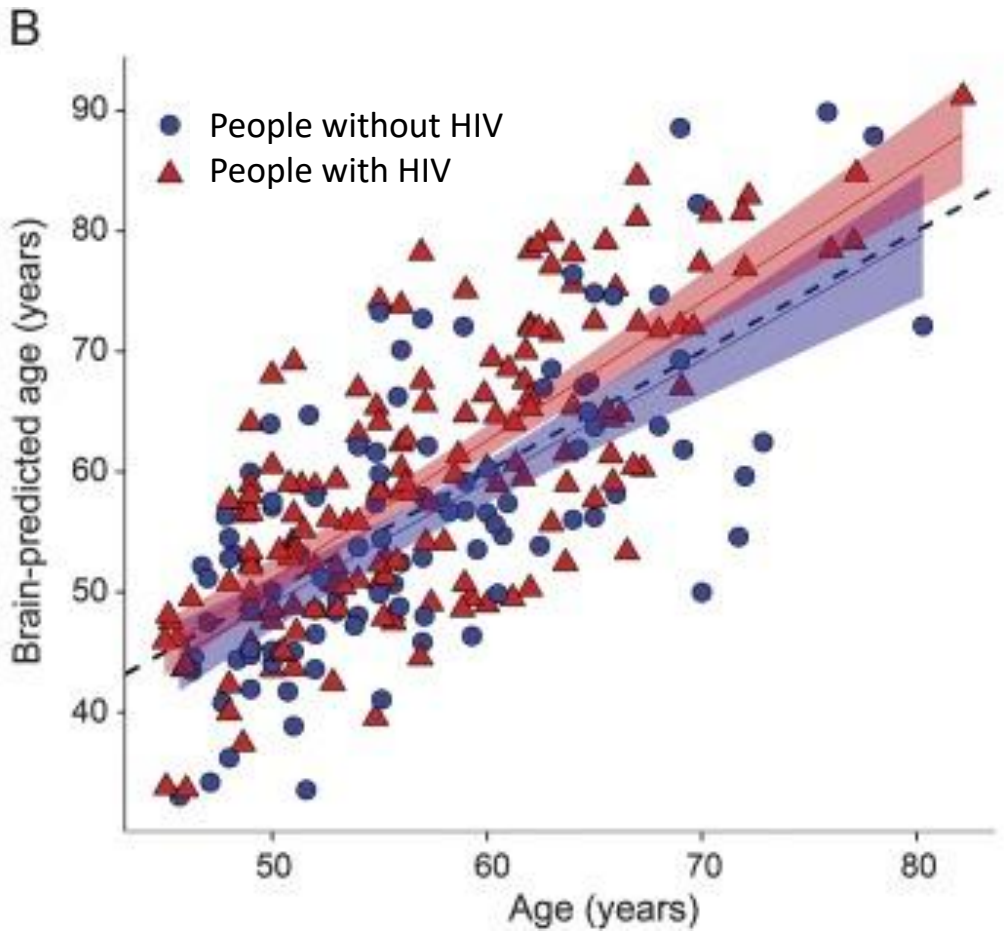
We don’t all age the same

Recent years



Brain Predicted Age



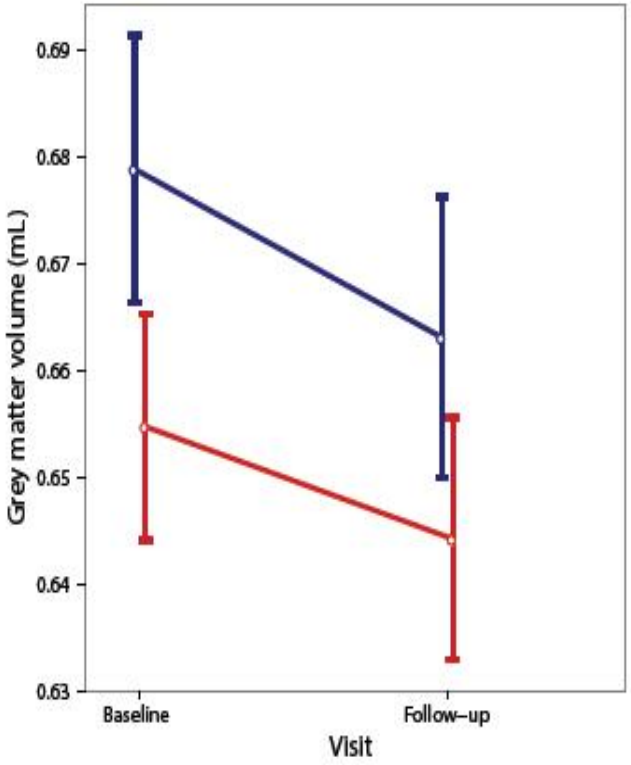


Neurology 2017 Apr 4;88(14):1349-1357

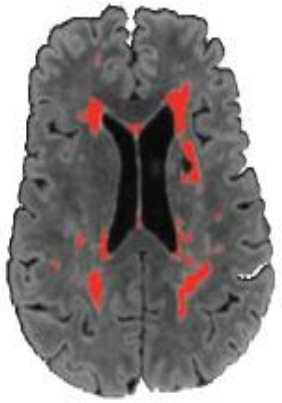
Longitudinal observations

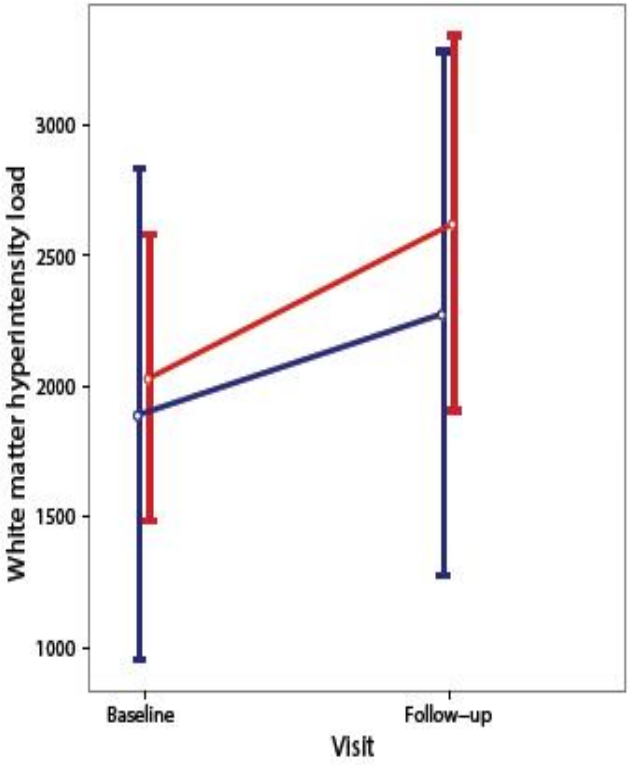
COBRA
CO-MORBIDITY IN RELATION TO AIDS

A) T1 - Grey matter volume



B) FLAIR - White Matter Hyperintensities





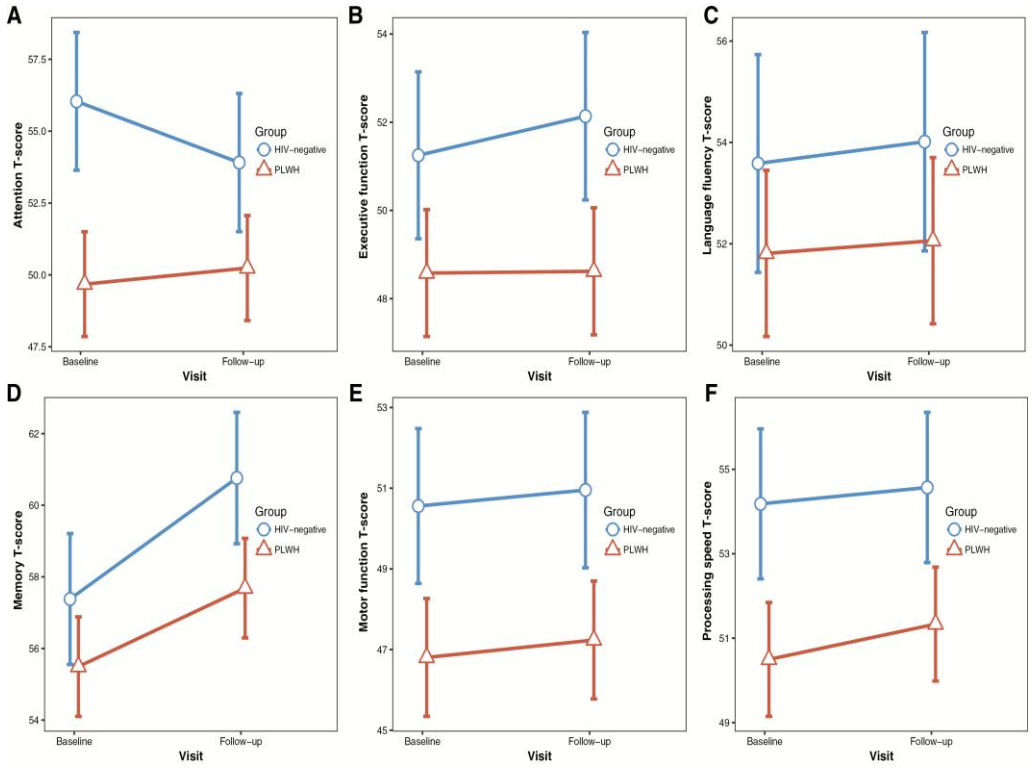
People without HIV

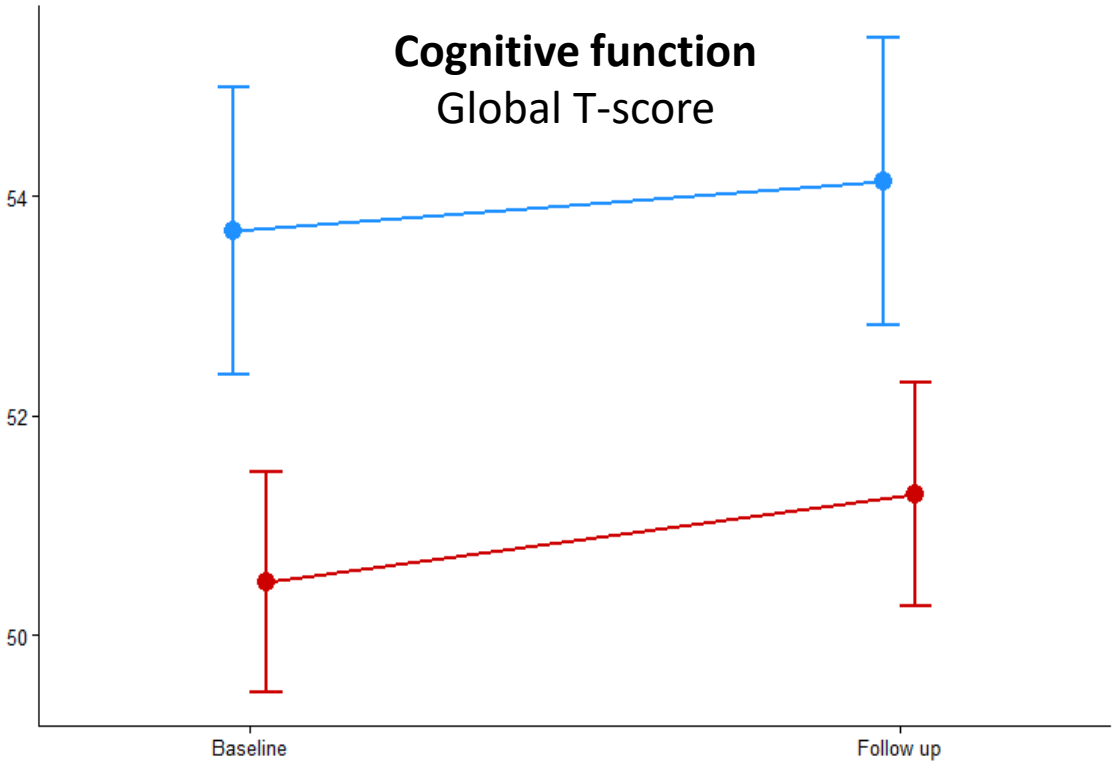
People with HIV

Clin Infect Dis. 2018 Jun 1;66(12):1899-1909

Longitudinal observations

COBRA
CO-MORBIDITY IN RELATION TO AIDS



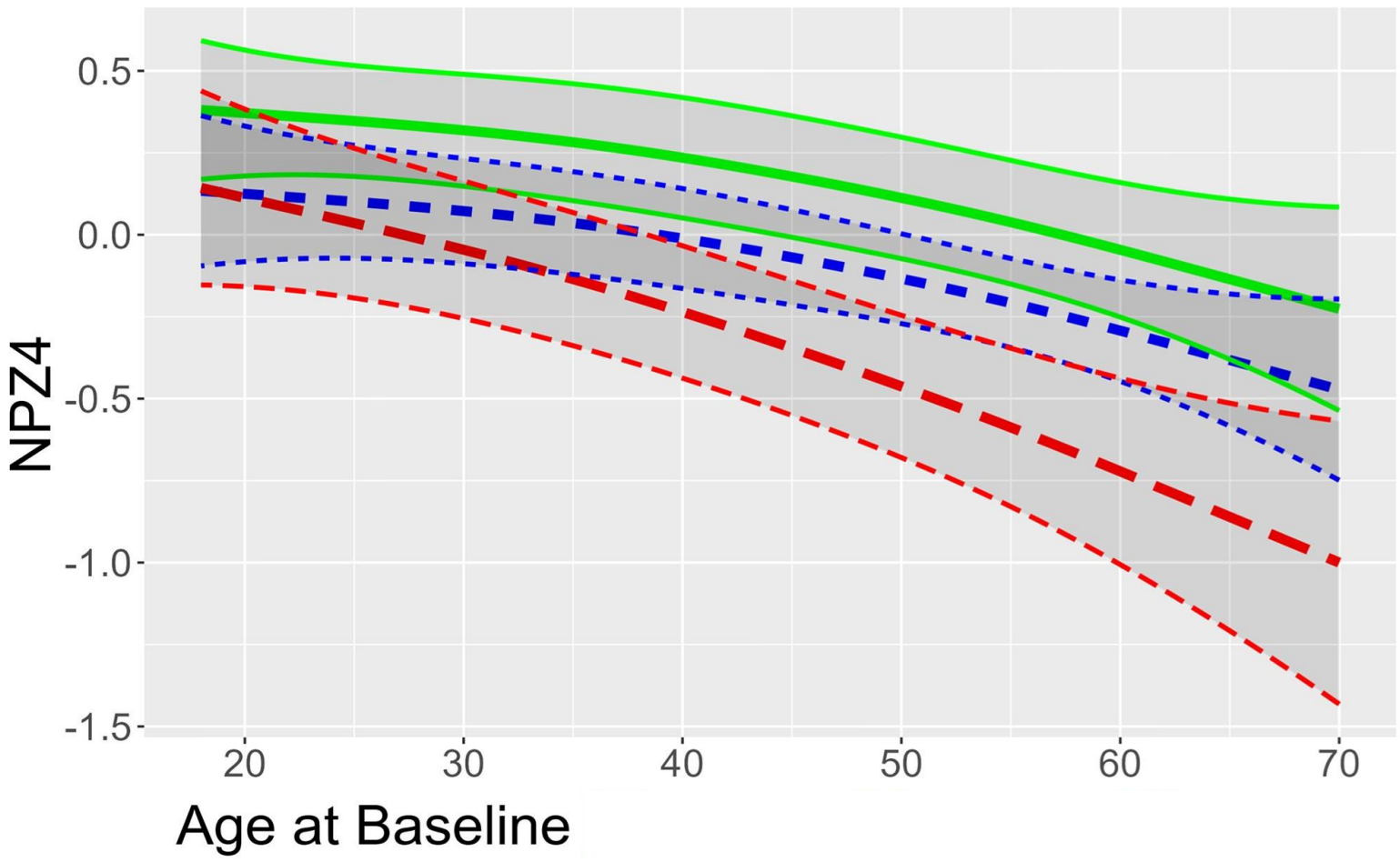


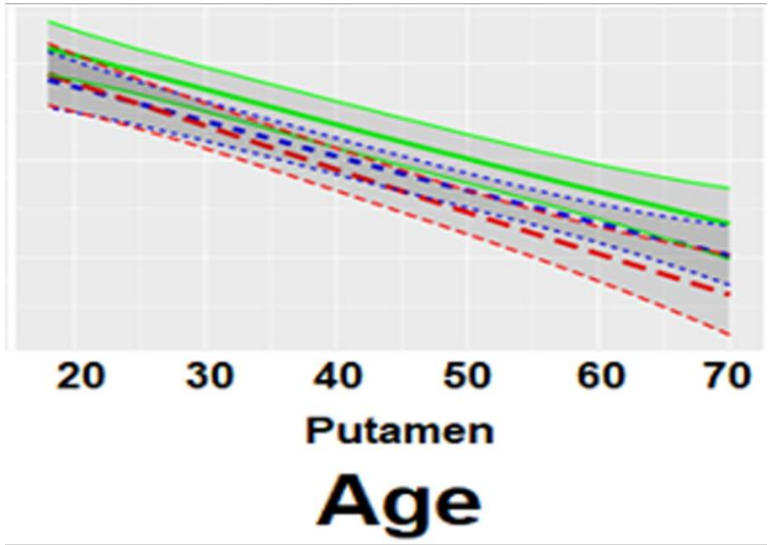
People without HIV

People with HIV

Clin Infect Dis. 2018 Jun 1;66(12):1899-1909

Longitudinal Trajectories





People without HIV

People with HIV
with undetectable HIV RNA

People with HIV
with **detectable** HIV RNA

J Infect Dis. 2026 Jan 16: Online ahead of print.

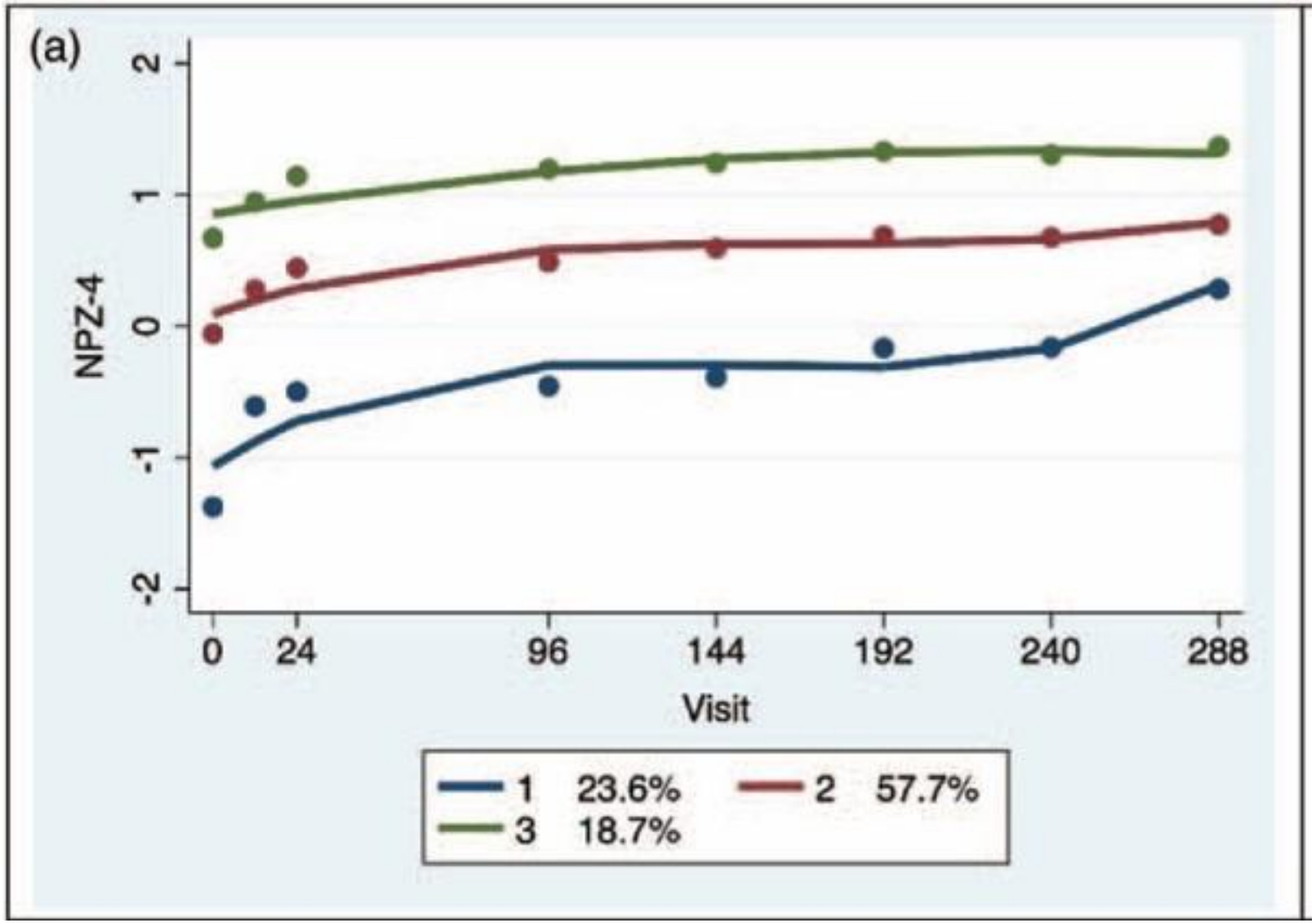
Going forward

What does this mean going forward?

Implications of early ART

Cognitive trajectories after treatment in acute HIV infection

AIDS 35(6):p 883-888, May 1, 2021



Switching ART

Cognitive performance, neuropsychiatric symptoms, and cerebrospinal fluid viral control following programmatic switch from efavirenz-based to dolutegravir-based antiretroviral therapy in South Africa (CONNECT): a prospective cohort study

Lancet HIV 2024; 11: e680–89

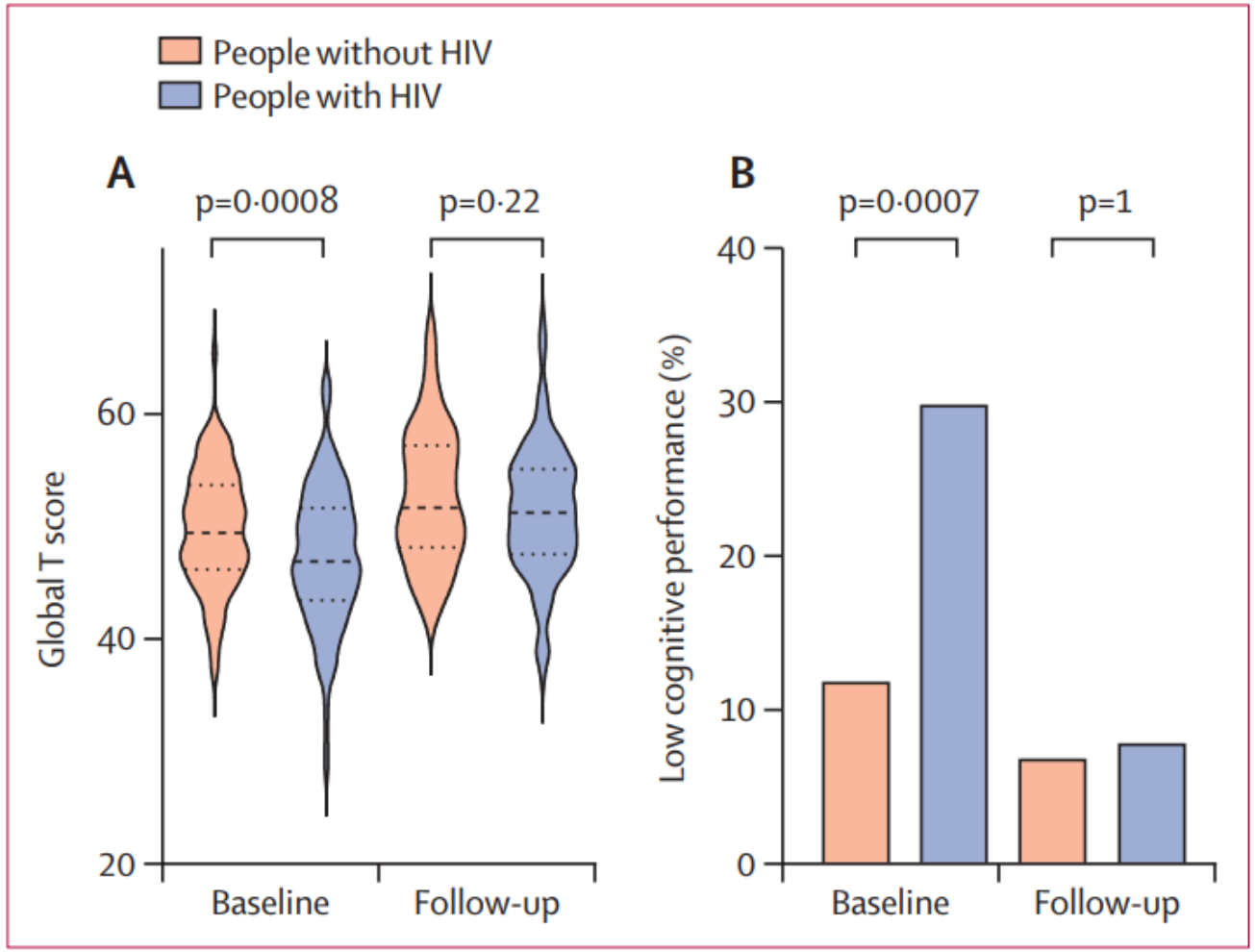
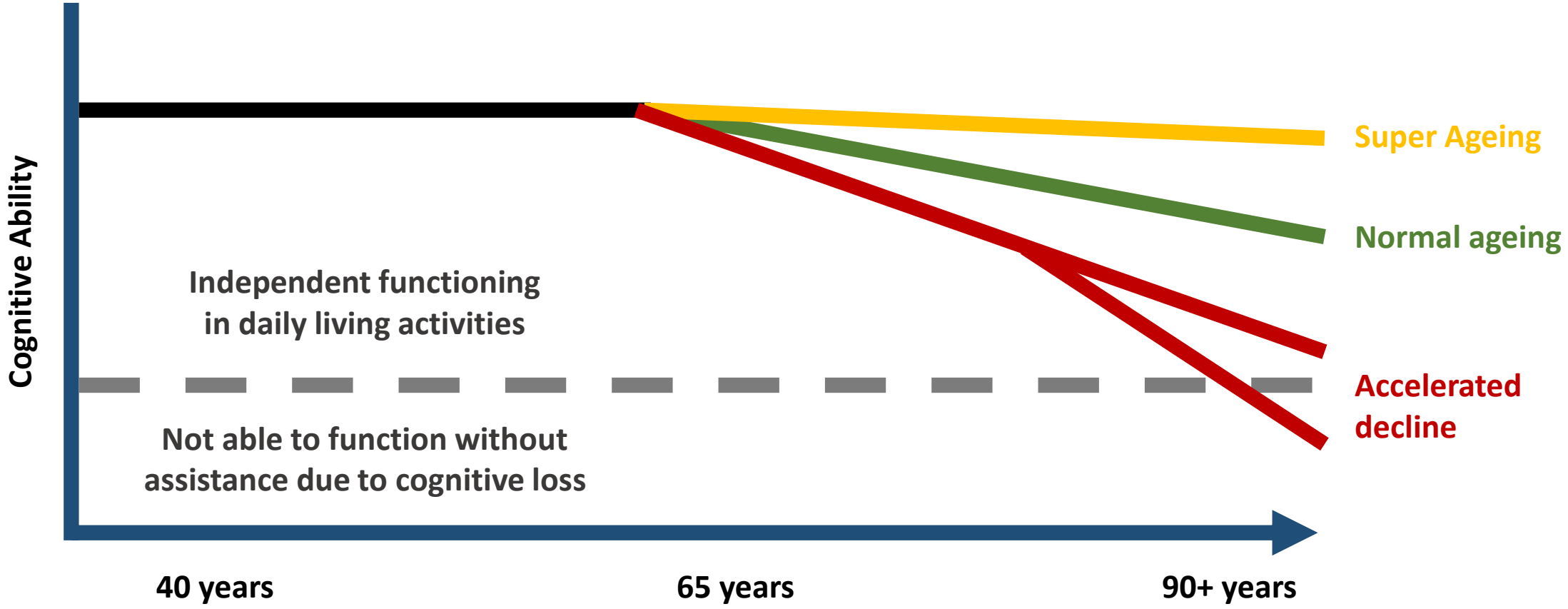
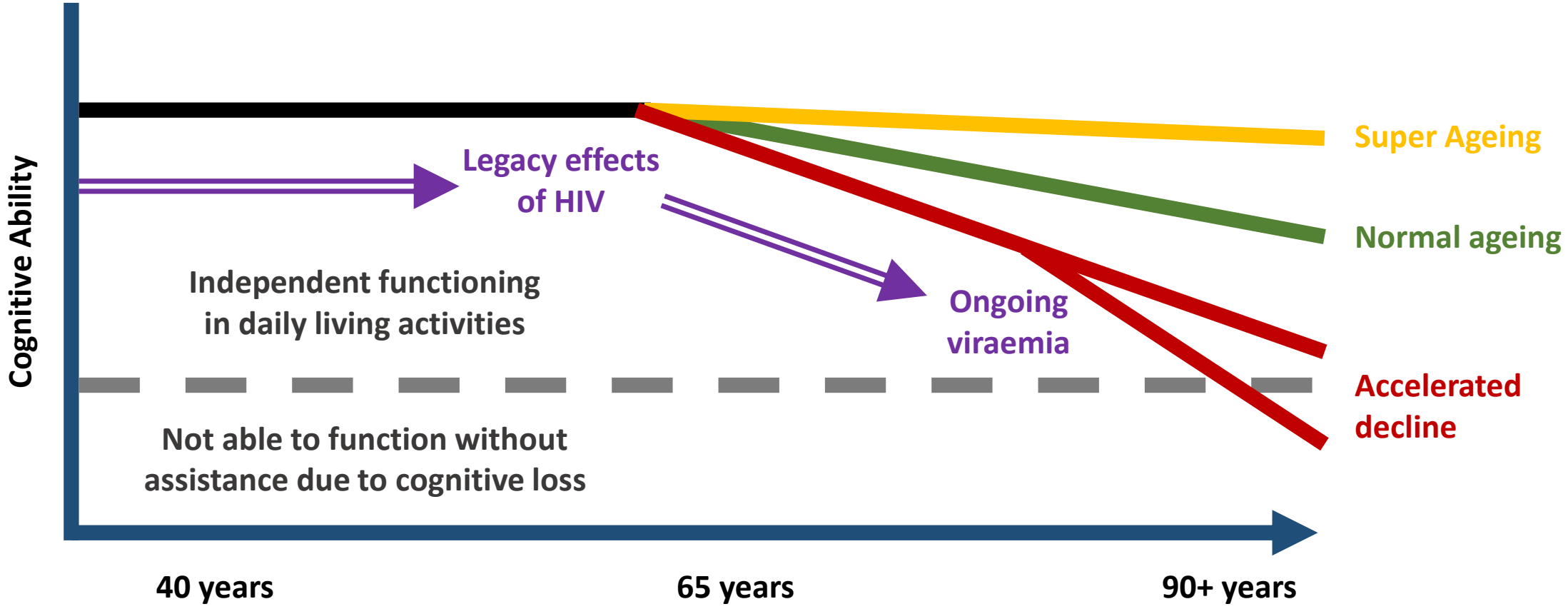


Figure 2: **Cognitive performance at baseline (on efavirenz) and follow-up (on dolutegravir)**
(A) Global T score. (B) Global deficit score.

Considerations of Trajectories of Cognitive Change



Considerations of Trajectories of Cognitive Change



In addition….

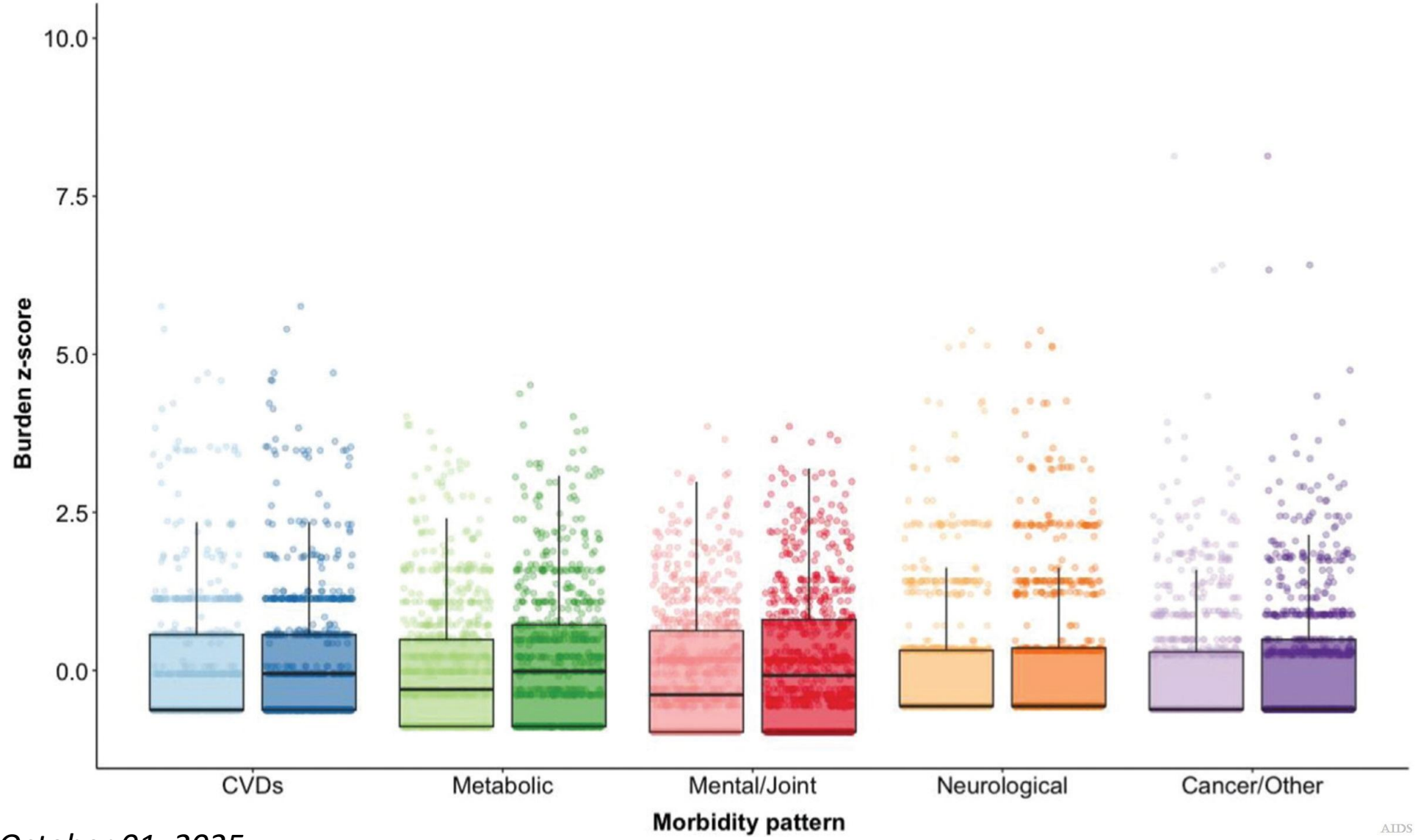
Some crucial aspects which have not always had the attention they may deserve

Clusters of comorbidities

POPPY
Pharmacokinetic and clinical observations in people over 50

Short Form Health Survey (SF-36) questionnaire:

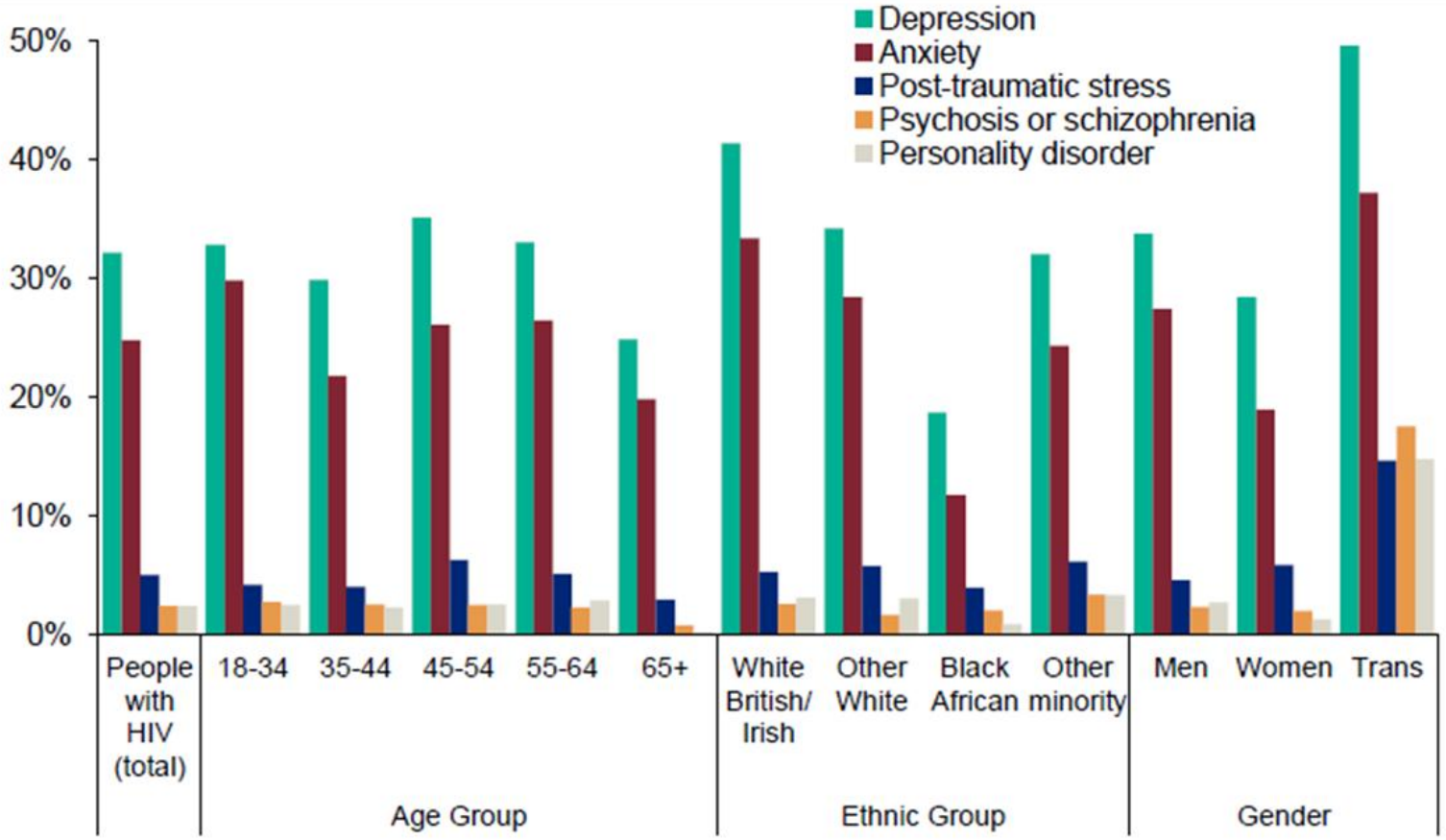
physical and mental health summary scores (z-score)



AIDS 39(12):1784-1793, October 01, 2025

Mental Health

Self-reported prevalence of mental health conditions diagnosed in 4,422 people with HIV by age, ethnicity and gender



[Positive Voices 222: survey report - GOV.UK]

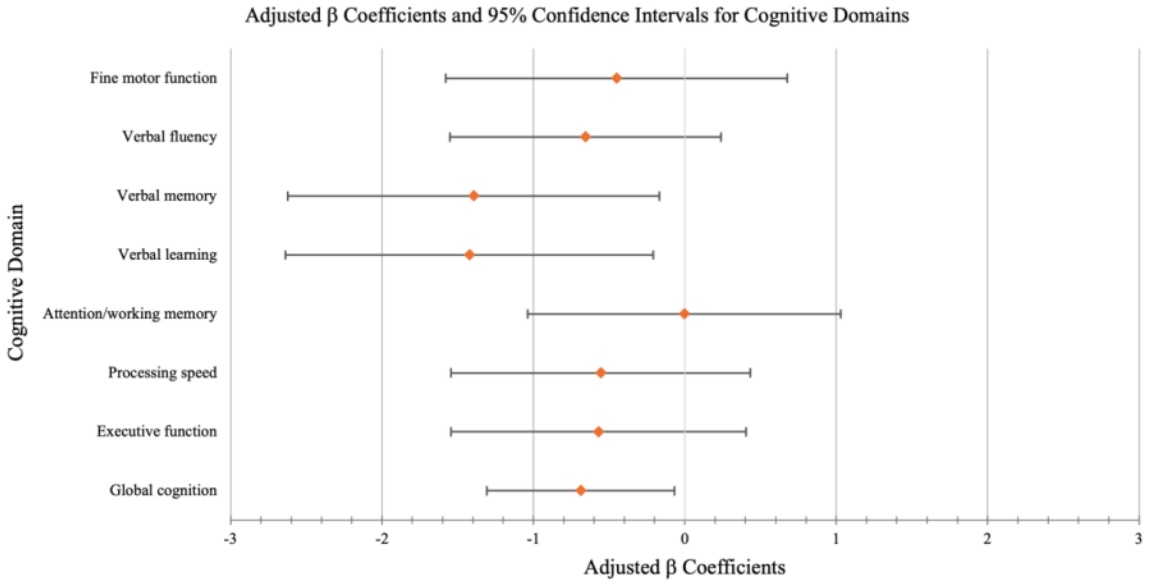
Stigma

MACS/WIHS Women's Interagency HIV Study
MULTICENTER AIDS COHORT STUDY

Associations Between Internalized HIV Stigma and Cognitive Function Among Older Women With HIV

Conclusions: Higher internalized HIV stigma at baseline was associated with worse global cognitive function

Figure 1



J Gerontol B Psychol Sci Soc Sci. 2025 May 8;80(6)

Psychosocial factors account for a proportion of the difference in cognitive performance between persons with and without HIV

Conclusions: Persons with HIV in this setting have lower psychosocial indices, both current and in childhood, which are associated with lower cognitive test performance as an adult.

Variables	Beta estimate	95% CI	*P*
Childhood Psychosocial Variables component	1.78	1.07–2.49	<0.001
Current Psychosocial Variables component	0.51	−0.23–1.25	0.174
Experience of Childhood Trauma component	−0.25	−0.99–0.49	0.505

95% CI, 95% confidence interval.

AIDS. 2025 Mar 15;39(4):393-402.

Summary

Does HIV still effect the brain, and can it lead to early dementia?

- Measures of cognitive function are often very similar in people with and without HIV
- Definitions used have hampered the field
- Delayed HIV diagnosis remains a significant risk factor for poor brain health

Does the brain age differently in people with HIV from people without HIV?

- Trajectories of ageing are similar in people with and without HIV
- Legacy effects of HIV, comorbidities, mental health, stigma and social determinants of health impact brain health

Thank you

POPPY

Pharmacokinetic and clinical observations in people over 50

Imperial College London

COBRA

CO-MORBIDITY IN RELATION TO AIDS