

HIV and Aging: New Frontier, New Challenges

Pedro Cahn



90-90-90 Targets Workshop

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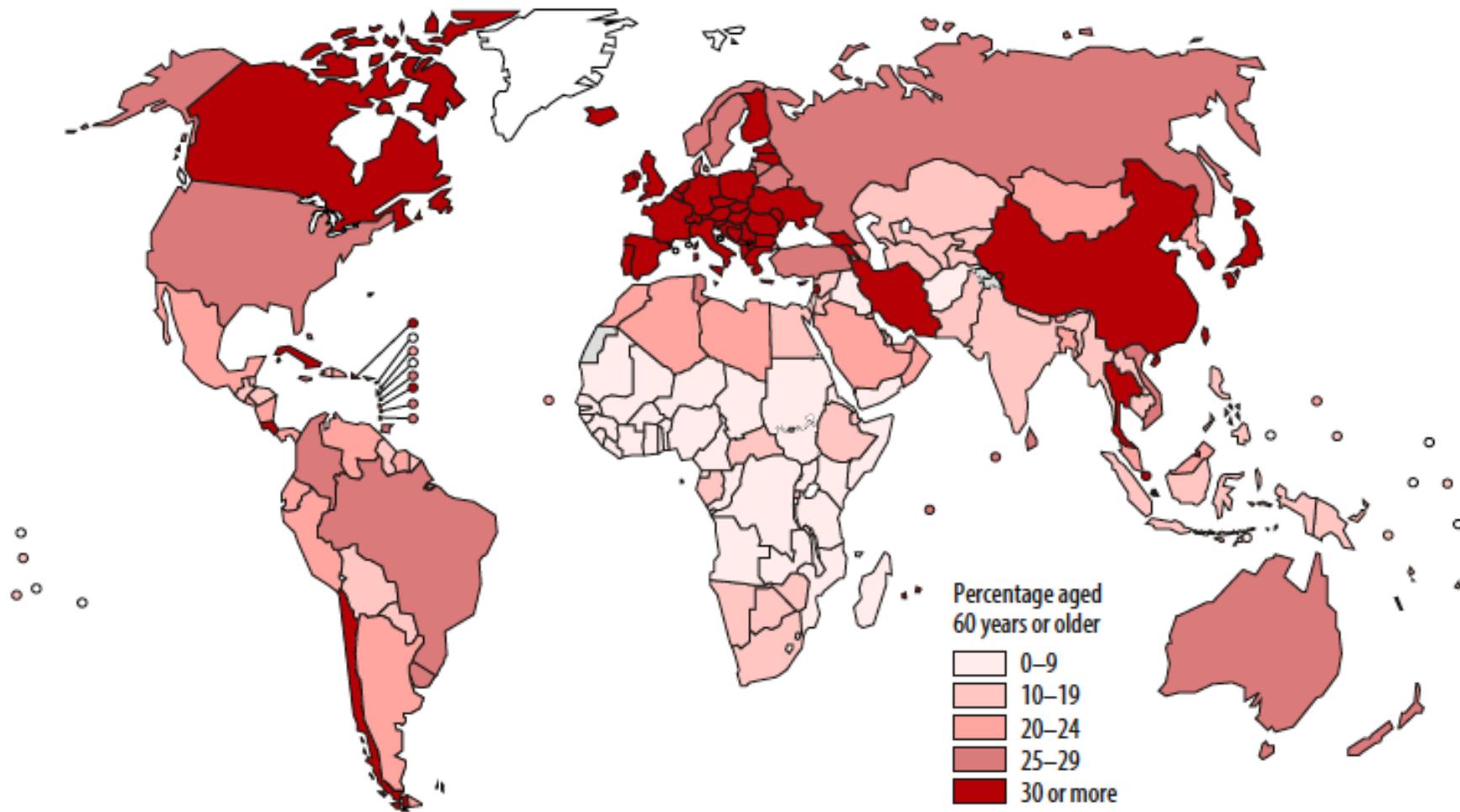
In partnership with



OUTLINE

- Prevalence and forecasts
- Pathogenesis of ageing and HIV
- New challenges for the health care systems
- Some final remarks

Fig. 3.2. Proportion of population aged 60 years or older, by country, 2050 projections

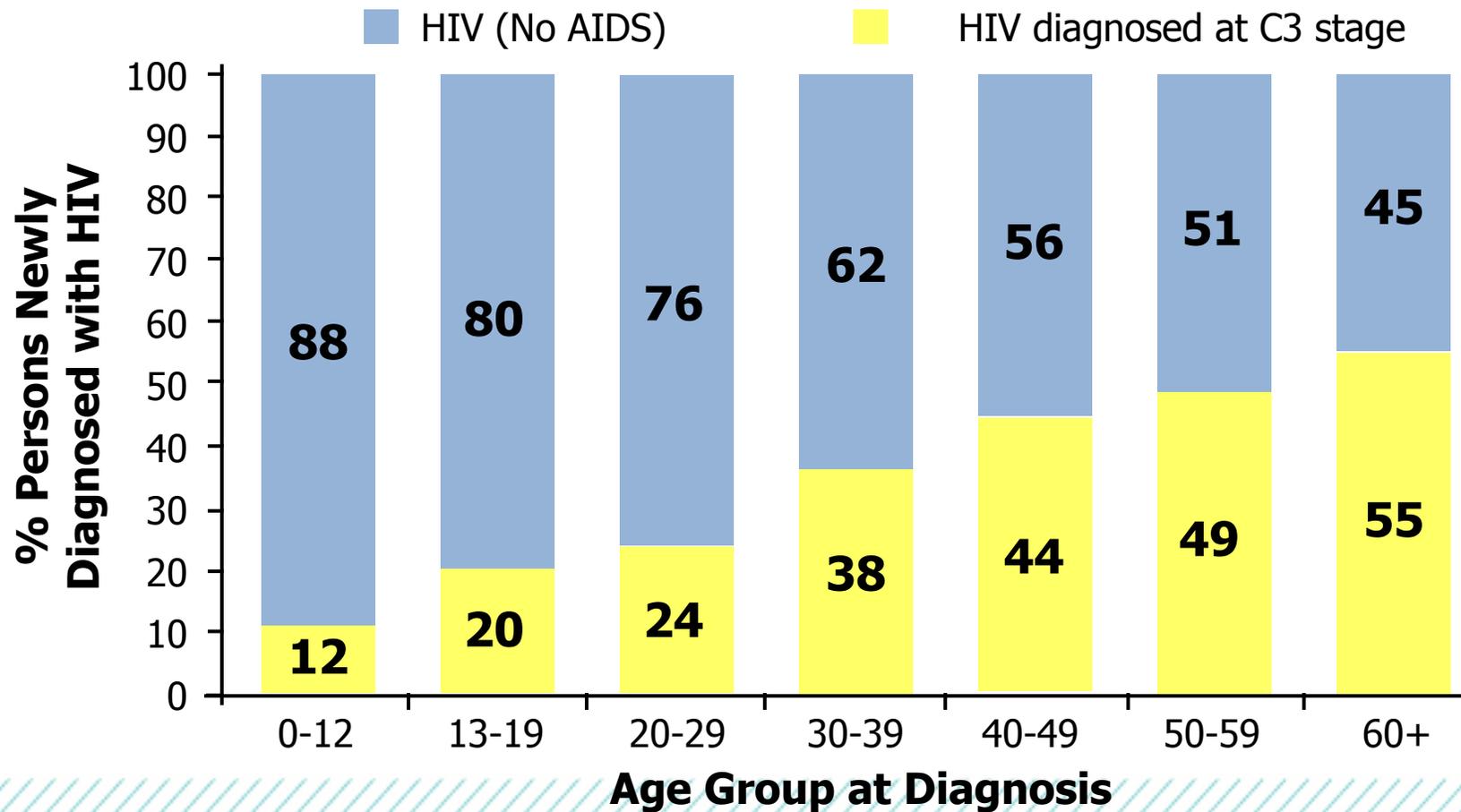


WHO, World report on ageing, 2015

(http://apps.who.int/iris/bitstream/10665/186463/1/9789240694811_eng.pdf)

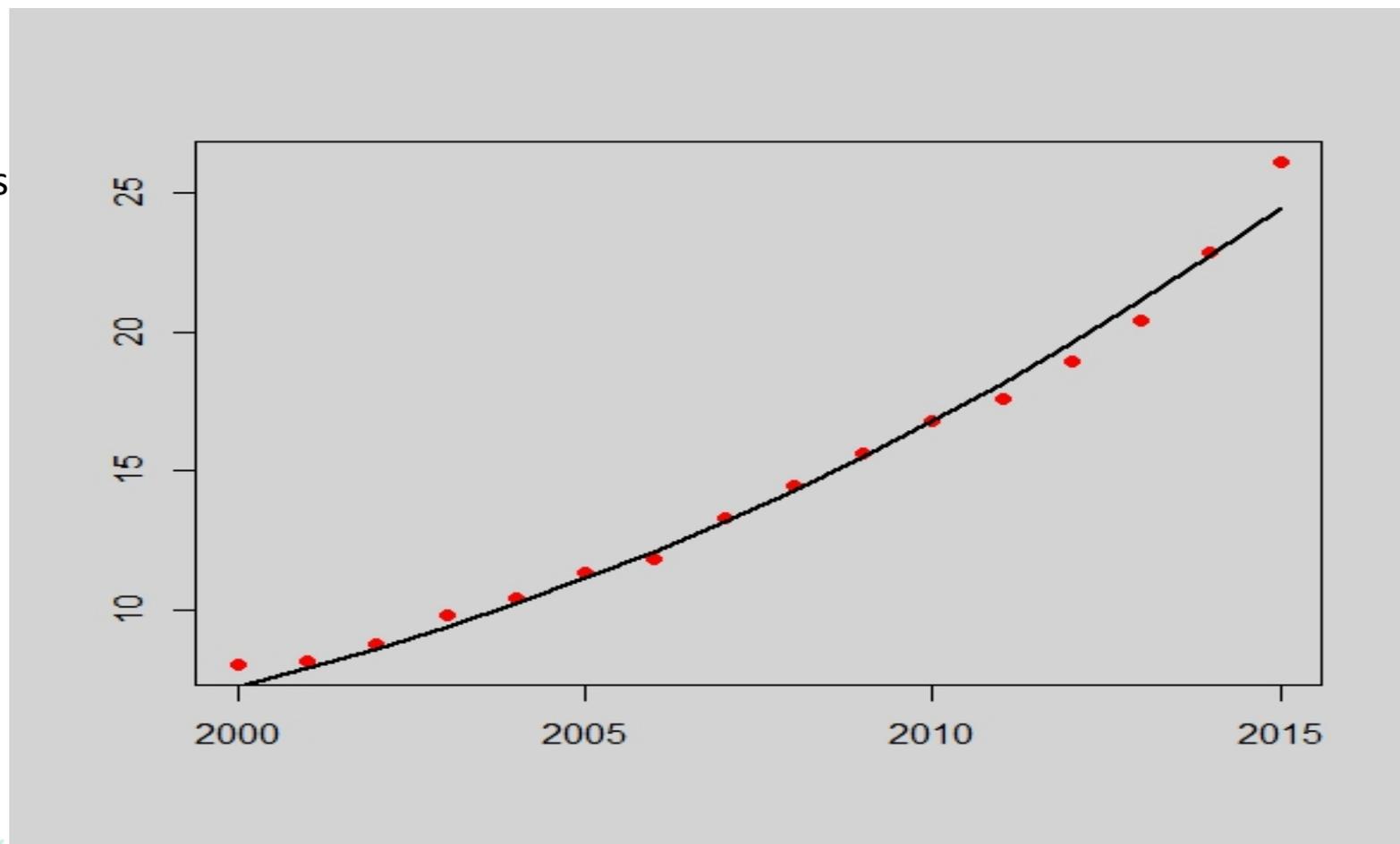
Elderly patients are frequently late presenters

Concurrent HIV/AIDS Among Persons Diagnosed with HIV in US in 2006, by Age Group



Proportion of patients > 50 years in CCASANet*

* Network of 7 cohorts
Involving > 15,000 patients
In 7 countries
in Latin America



The changing spectrum of HIV care

1996

2005

2010

Pre-
HAART

Early-
HAART

Late-
HAART



Opportunistic infections
AIDS cancers

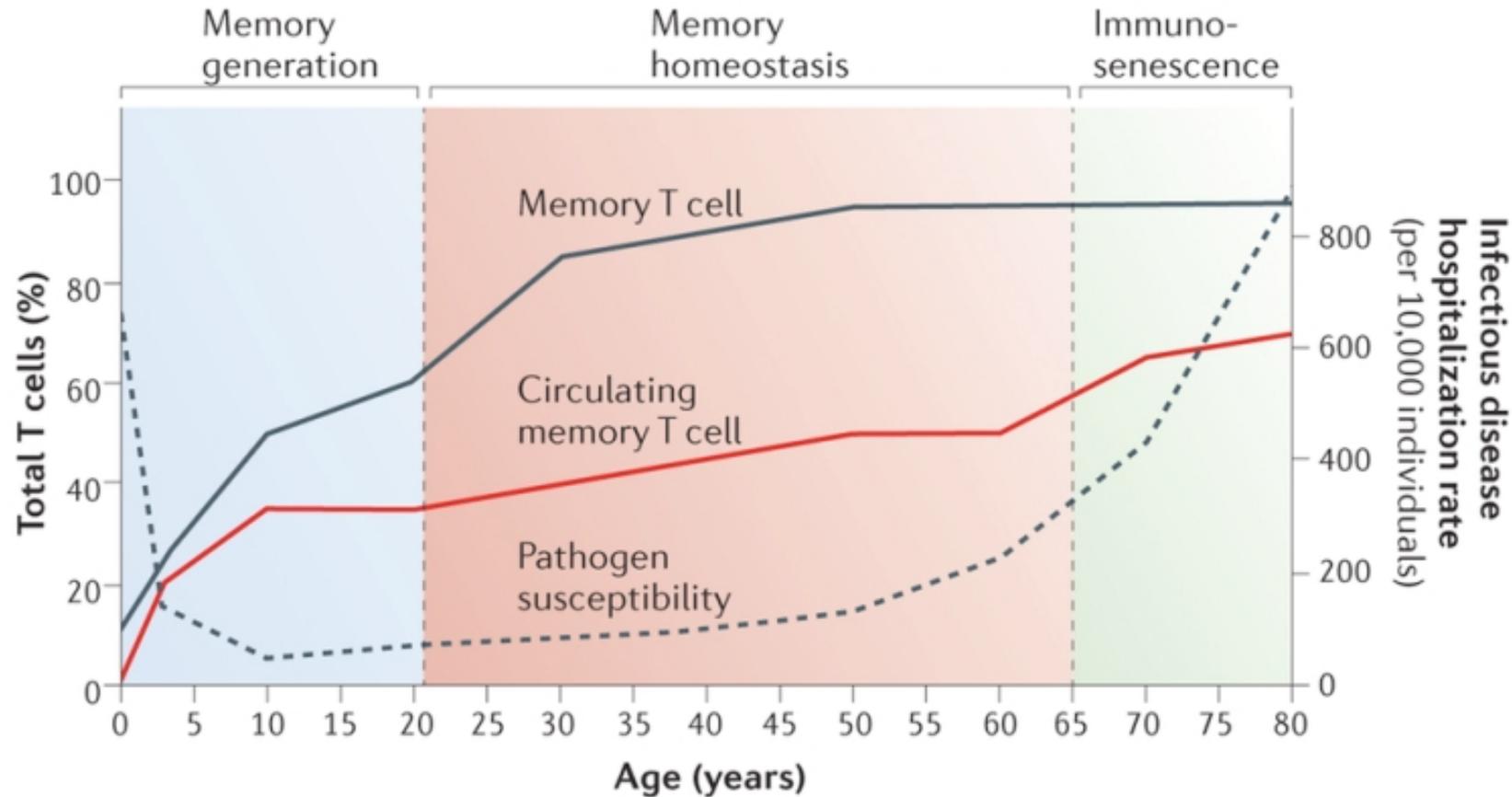


Lipodystrophy
Co-morbidities



Multimorbidity
Frailty & Disability

Immunosenescence. A natural process



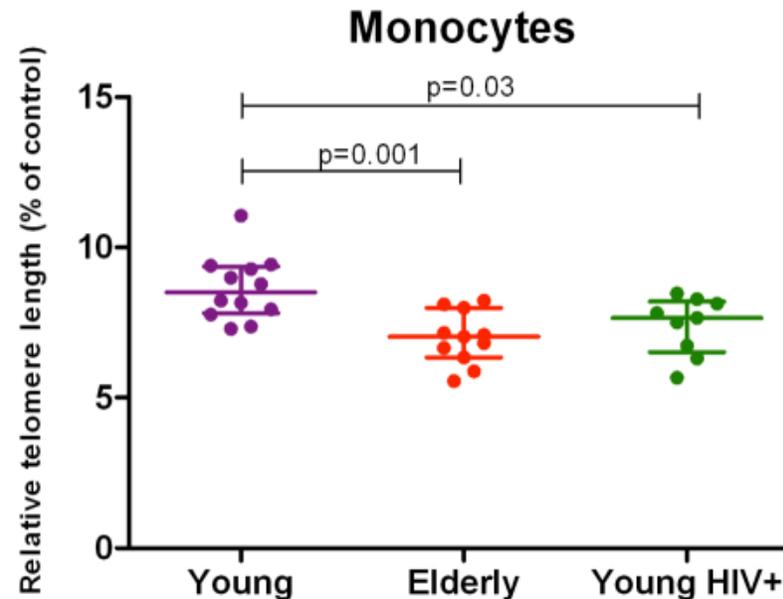
Pathogenesis of HIV and aging share similarities, common link may be inflammation



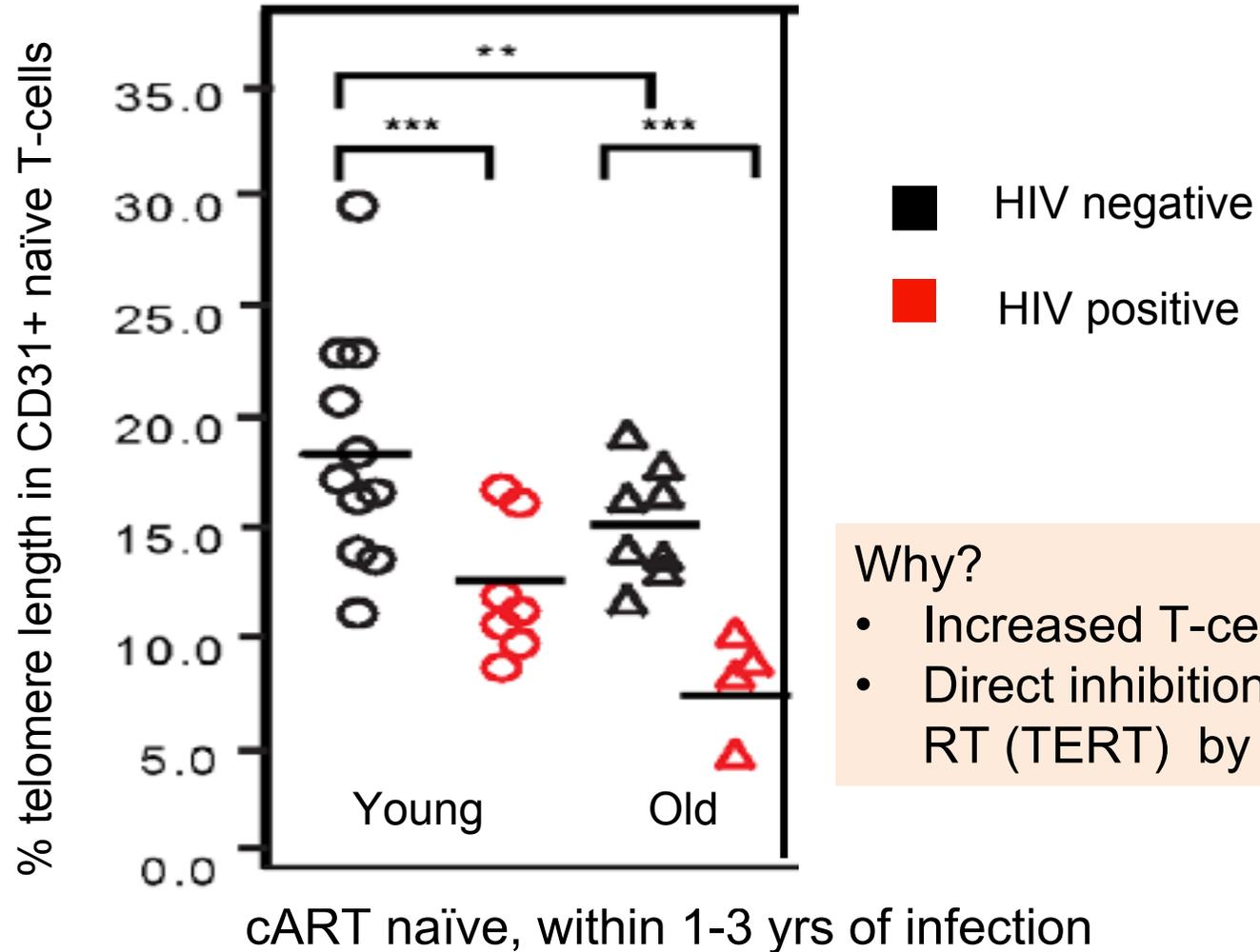
Shortened telomeres in young HIV+ and in healthy elderly

- Short hexonucleotide repeats at ends of chromosomes
- Protect the DNA
- Telomeres are shortened during each cell division
- If telomeres shorten, cells age
- Classical marker of immune ageing

Telomere length is shorter in healthy elderly and young HIV+



Telomere length is significantly reduced in cART naïve HIV+ individuals



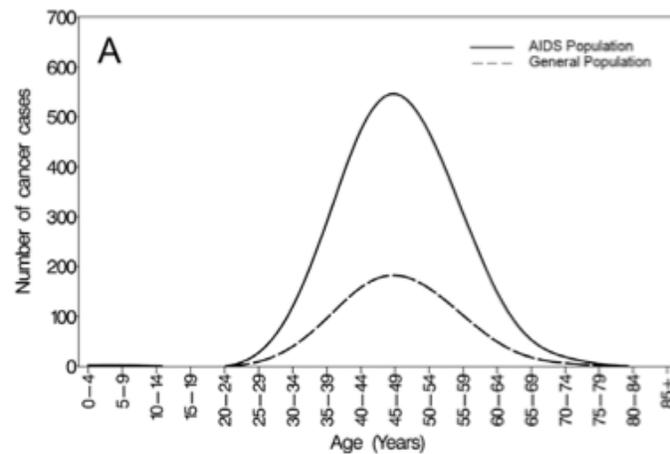
Why?

- Increased T-cell turnover
- Direct inhibition of telomerase RT (TERT) by HIV

Review Article

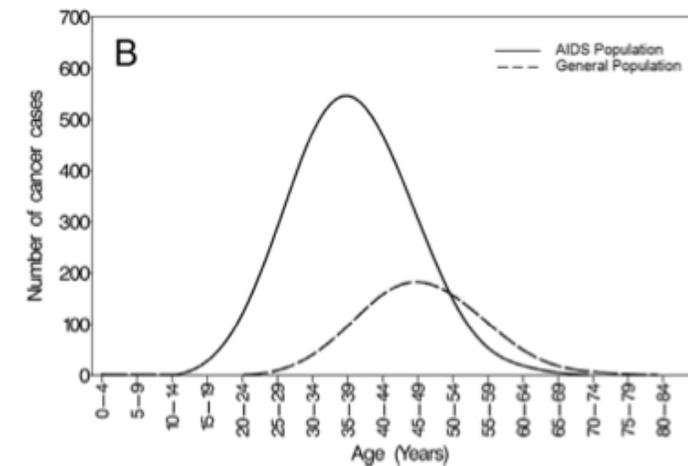
Is HIV a Model of Accelerated or Accentuated Aging?

Sophia Pathai,^{1,*} Hendren Bajillan,^{2,*} Alan L. Landay,^{3,4} and Kevin P. High⁵



Accentuated Aging: cancer (and **geriatric syndroms**) occurs at the same ages but more often among HIV-infected participants than among HIV-uninfected comparators.

This configure a **Premature aging process.**



Accelerated Aging and accentuated aging: cancer (and **geriatric syndroms**) occurs earlier among HIV-infected participants compared with HIV-uninfected comparators and there are more cancer events.

Potential covariates and Confounders

Demographics

Age, gender, ethnicity, yrs education, socio-economic, un/employment, etc.

NeuroPsych

HAND, dementia, depression, disposition/mood, substance ab/use, etc

Medical-Physion

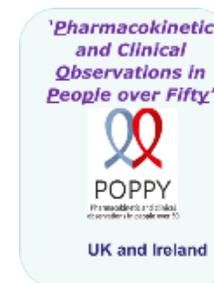
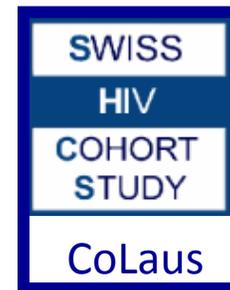
Other meds, cardiometabolic risk, hepatorenal status, cancer BMD, lat/lean, endocrine and inflammatory markers, lifestyle, tobacco, rec. drugs, diet, physical inactivity, ADL, IADL, etc

HIV Related

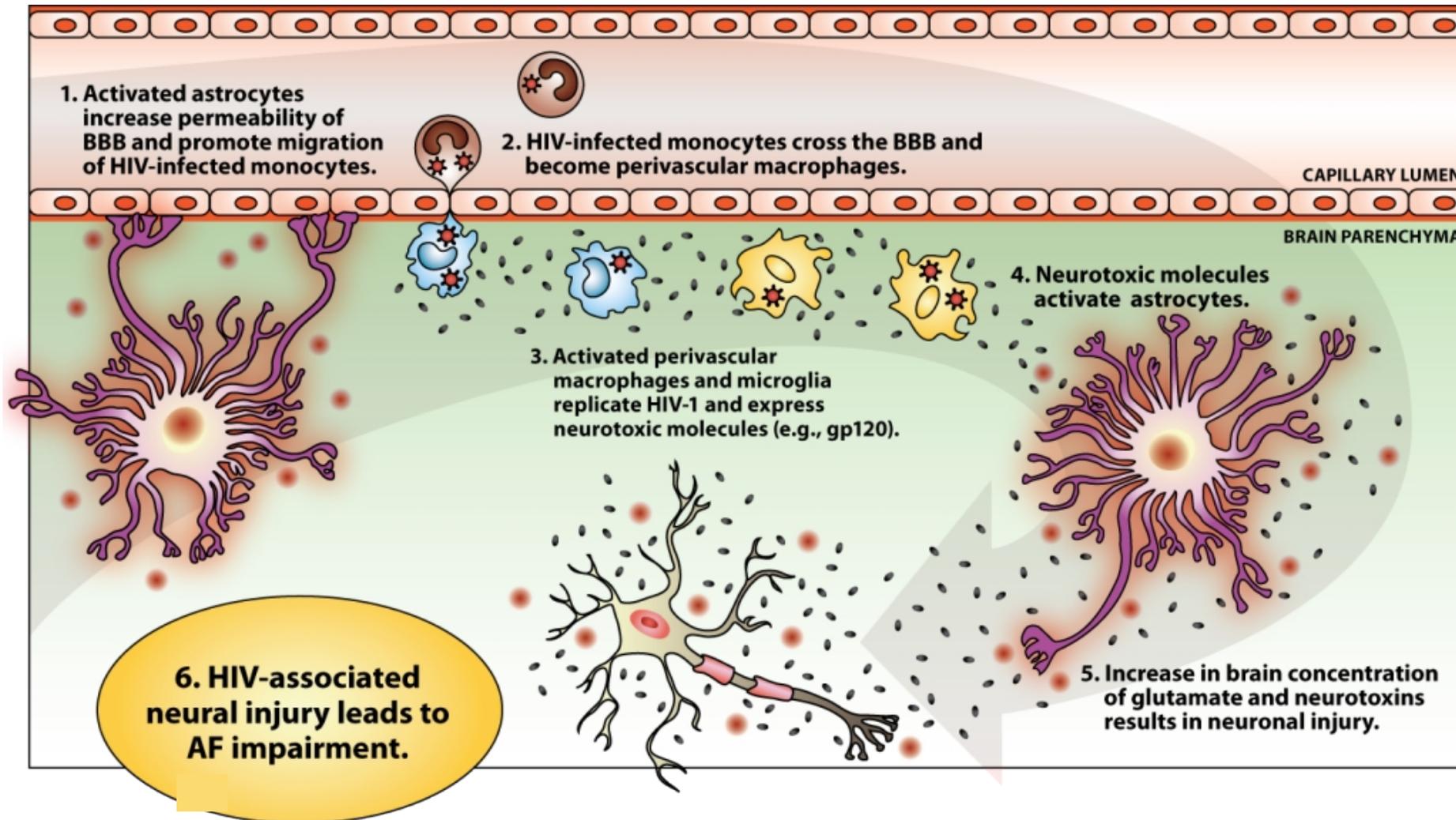
Yrs HIV, AIDS dx, HIV med compliance-complication, CD4, plasma and CSF viremia, immune activation, co-infections, chronic inflammation, etc

Social Vulnerability aspects

Poverty, food security, Access to care, social justice, etc.



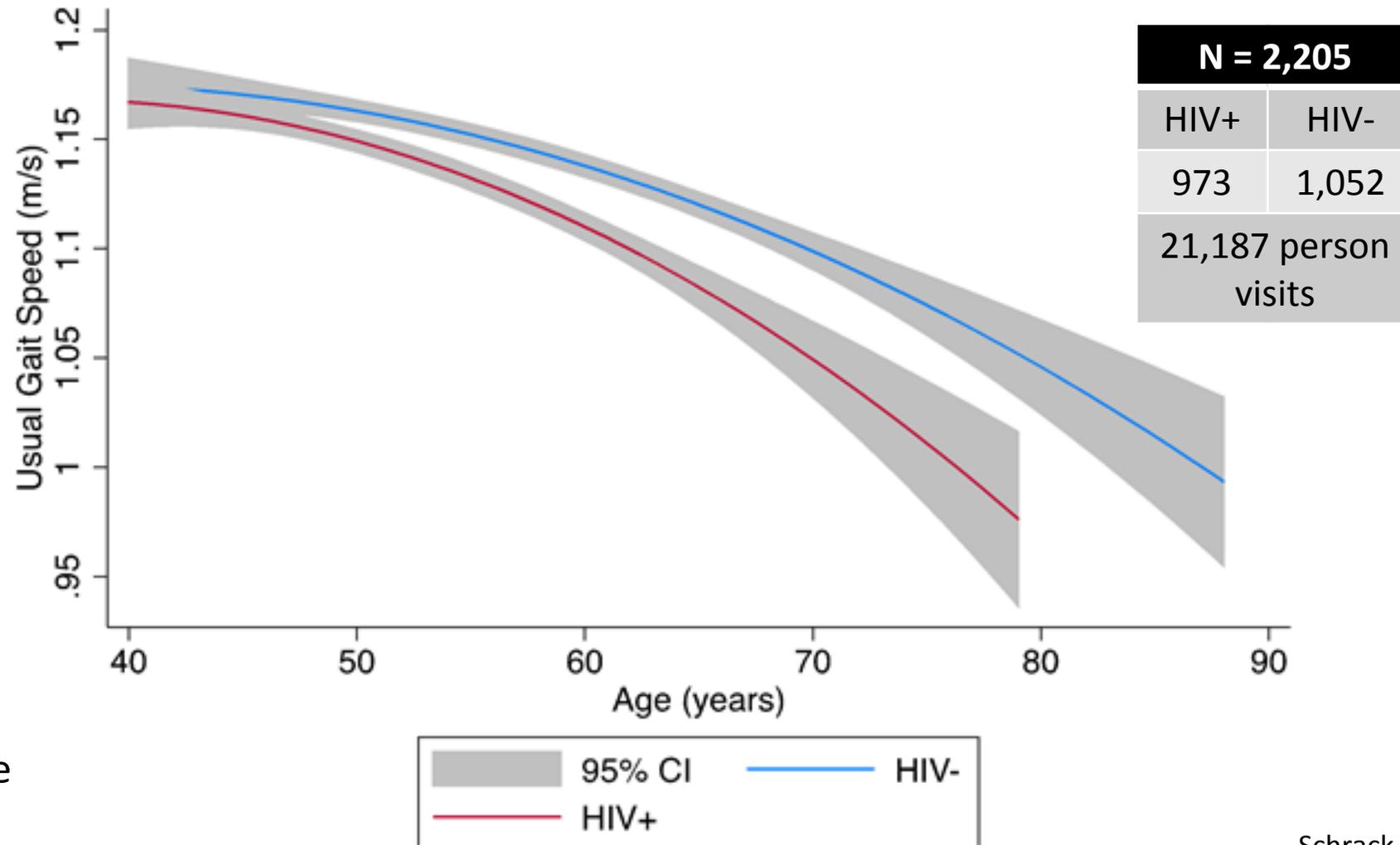
HIV infects microglia and promotes neuronal injury



CNS and HIV Infection

- Like metabolic and vascular disease, neurocognitive disease also appears to be more common in aging adults living with HIV
- Starting ART that fully suppresses HIV early in disease is critically important
- As HIV+ adults age, we must consider other diseases like Alzheimer's dementia

Frailty: Gait speed declines faster in HIV+ men

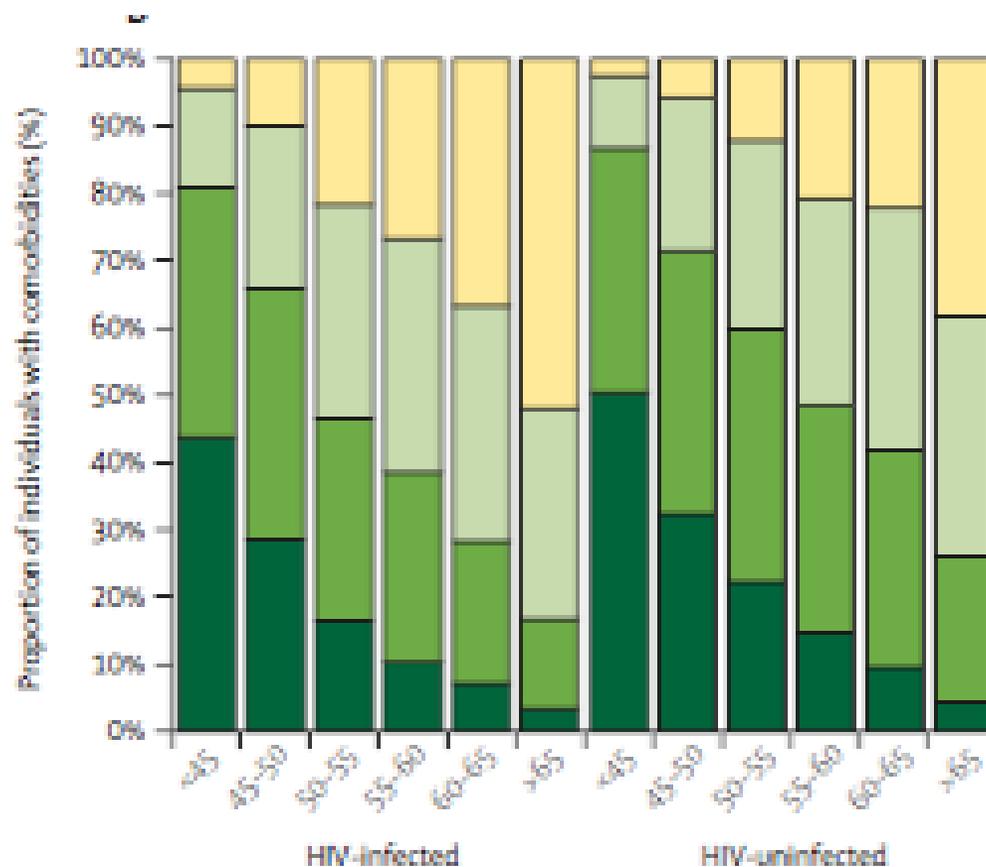


Frailty phenotype defined by Fried (slowness, weakness, weight loss, low activity, fatigue) may induce **disability**

Future challenges for clinical care of an ageing population infected with HIV: a modelling study

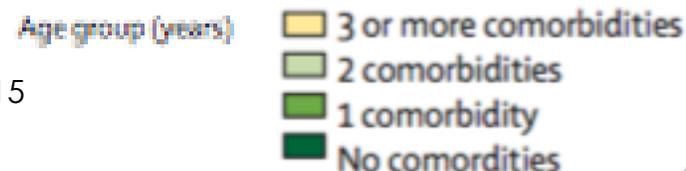


Mikaela Smit, Kees Brinkman, Suzanne Geerlings, Colette Smit, Kalyani Thyagarajan, Ard van Sighem, Frank de Wolf, Timothy B Hallett, on behalf of the ATHENA observational cohort

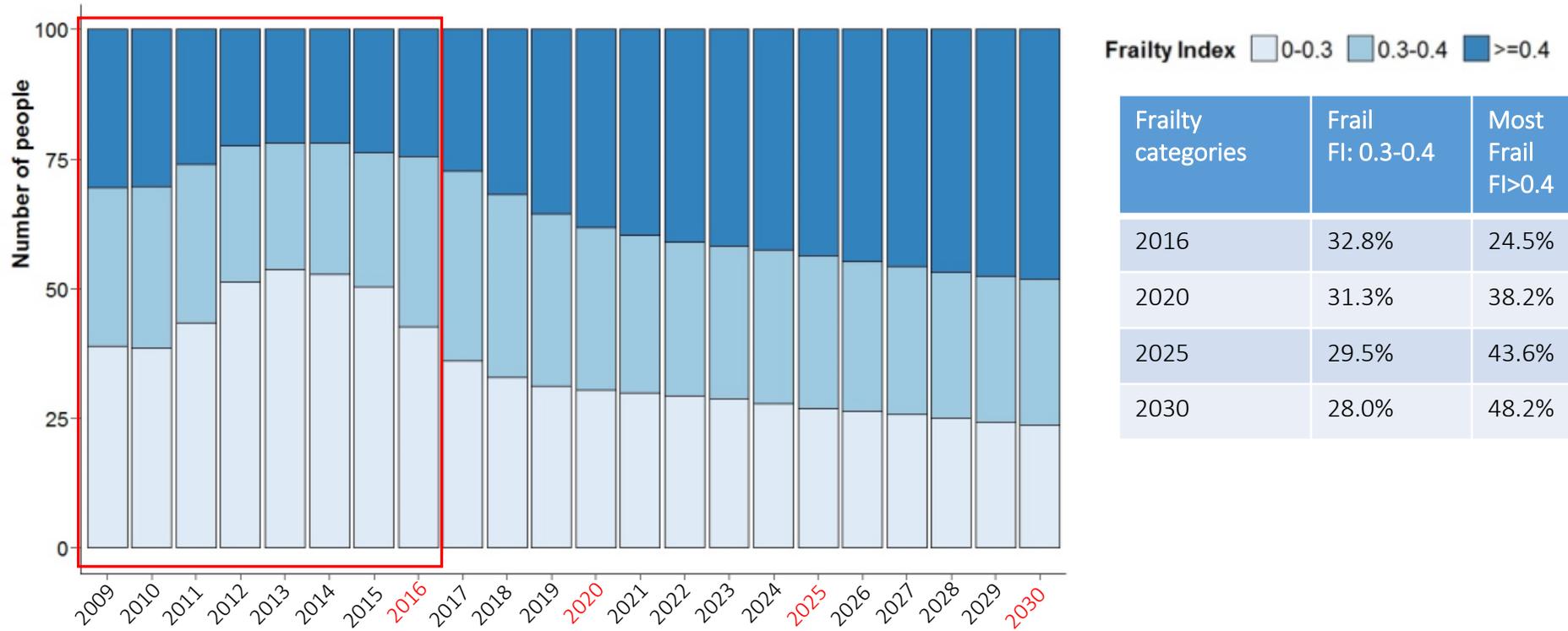


- In the ATHENA cohort, proportion of patients on ART aged ≥ 50 years old will increase from 28% to 73% between 2010 and 2030
- Burden of NCDs mostly driven by larger increases in cardiovascular disease compared with increases in other comorbidities

In 15 years time the most frail HIV population will increase from 24% to 48%

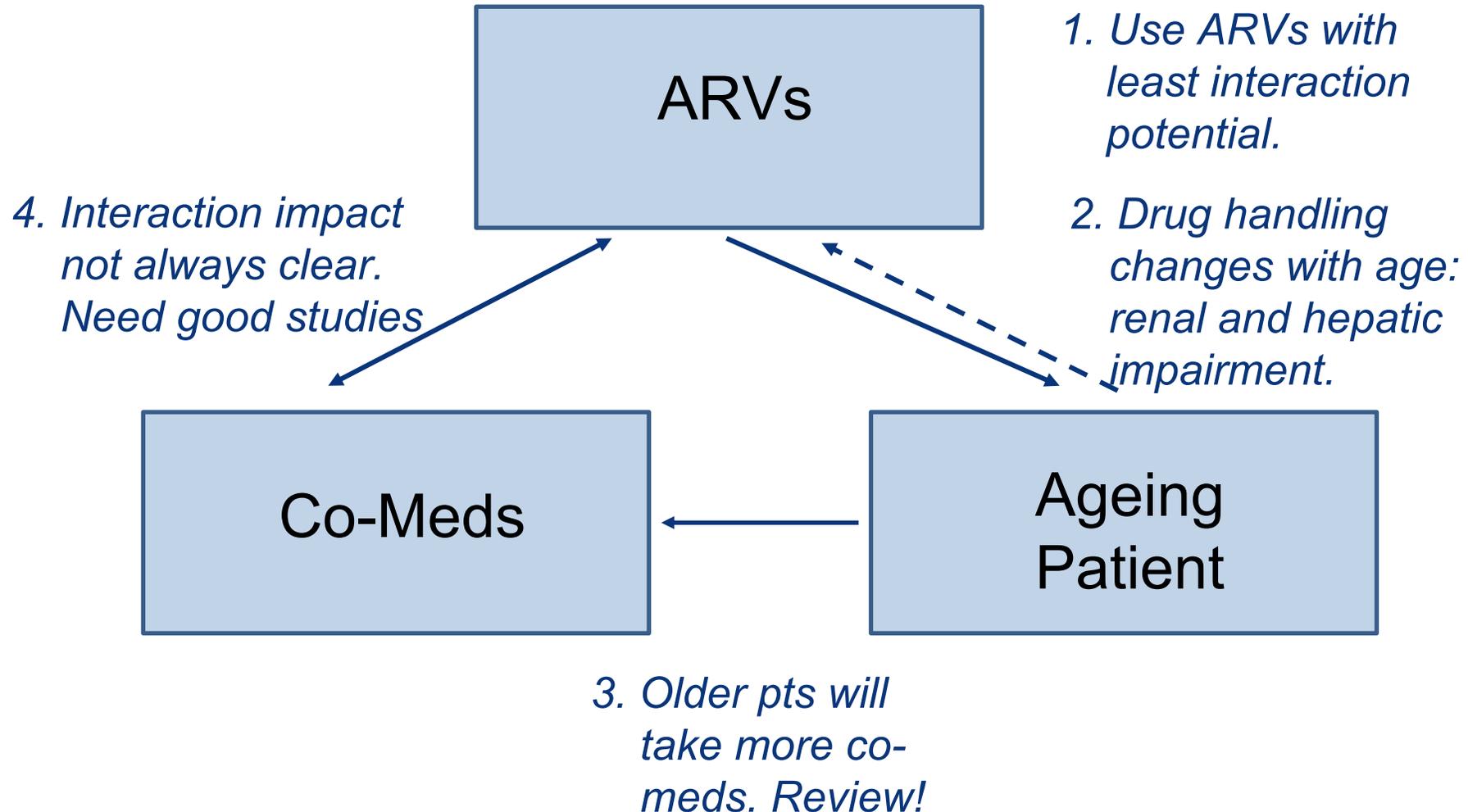


Observed (red area) and predicted burden of Frailty in HIV-infected patients between 2009 and 2030 as simulated by the model



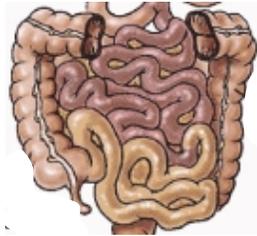
In 15 years time the most frail HIV population will increase from 24% to 48%

ARVs, Ageing Patients and Co-meds



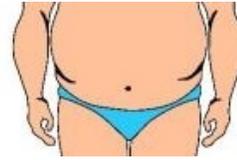
Why should we be concerned about age and drug pharmacokinetics?

Absorption



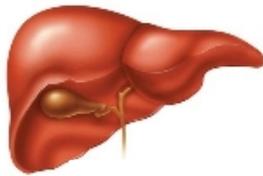
Increased gastric pH and decreased small bowel surface area may lead to a **higher inter individual variability in drug exposure.**
[1]

Distribution



Increase in body fat with older age increases V_d of some drugs and may increase the $t_{1/2}$. **Greater drug accumulation and increased risk of toxicity** are possible.

Metabolism



Reduced liver volume and blood flow with reduced enzyme activity can give **decreased drug clearance.** Also altered transporters.
Hepatic Impairment.

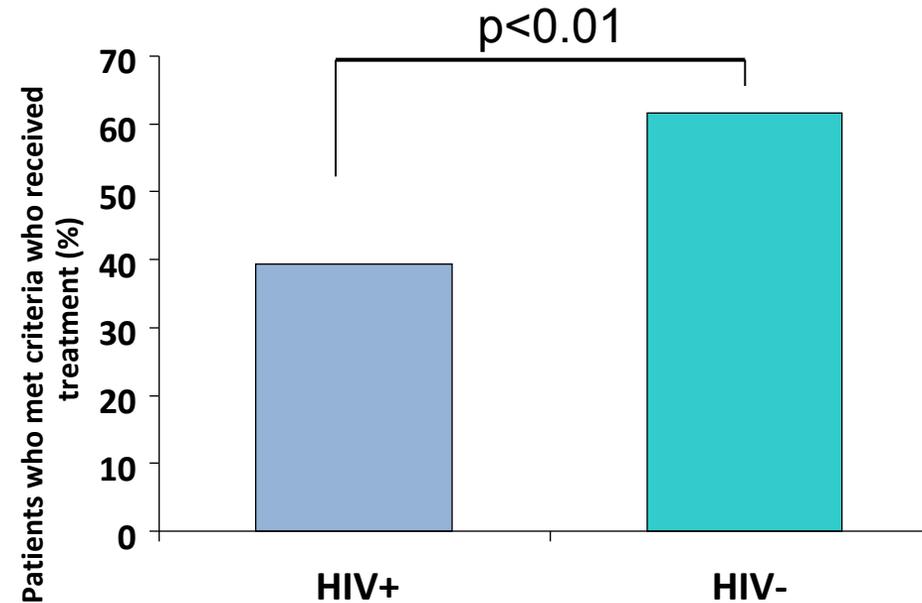
Renal elimination



GFR may decrease as much as 50% with increasing age, which can affect renal elimination of some drugs. Clinical consequence (**toxicity**) depends on the extent of renal elimination.

Are HIV Specialists treating Co-Morbidities?

- US study explored use of lipid-lowering therapy in HIV+ or HIV- veterans:
 - HIV+, n=926; HIV-, n=651
 - NCEP/ATP III factor criteria guidelines used to assess need for lipid-lowering therapy



Receipt of therapy lower in HIV+ vs. HIV- patients
(39% vs. 61%)

Aging and HIV: Some final considerations

- Sexual activity has no age limits
- The “grey generation” goes for a 2nd round
- Older patients don’t feel at risk
- Elderly patients show up later
- HCW are less prone to discuss sexual activity with older patients.
- HIV testing is not part of regular screening in elderly
- Symptoms are initially attributed to other diseases, both by patients and HCW



As time goes by....

- **HIV is the major driver of M&M, but other bugs are also involved**
- **Immunosenescence strongly correlated with inflammation**
- **Frailty is the pathway to disability, and is correlated with mortality**
- **HIV may accelerate and/or accentuate aging**
- **Being old is bad**
- **Having HIV infection is bad**
- **Being old and HIV+ is certainly worst !!!**
- **Exercise, diet, lifestyle changes should be reinforced at each visit**
- **As we succeed with 90/90/90, millions of PLWHA will become older, challenging our already weak healthcare systems.**