

HIV & AGING

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Southeast AETC Webcast
February 10th, 2016

DISCLOSURES

I have no conflicts of interest.

DISCLAIMER

“Older adult” (def in HIV research):
Someone over the age of 50 years.

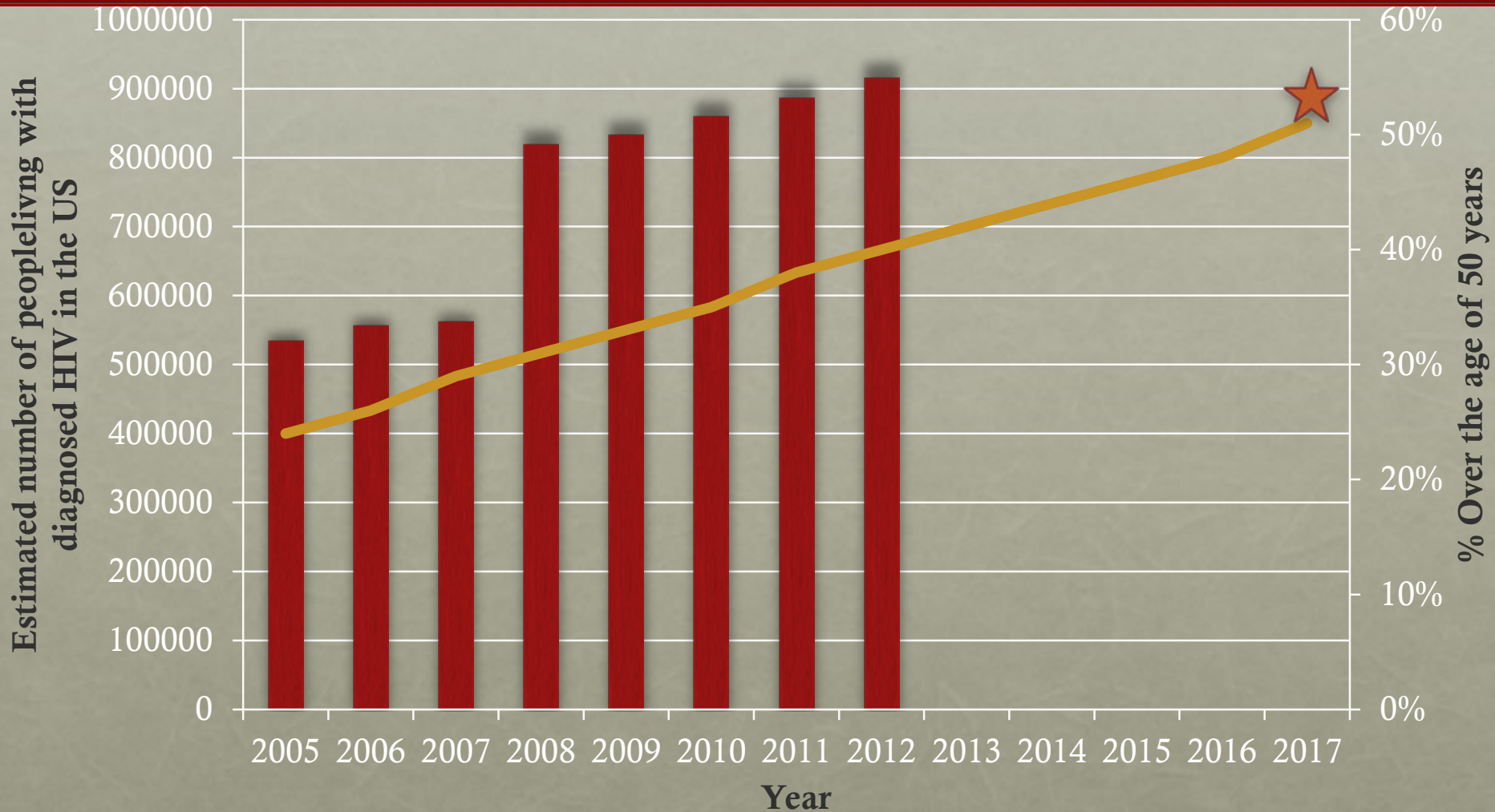
OUTLINE



- Epidemiology
- Clinical challenges: geriatric syndromes
 - Frailty
 - Cognitive decline
 - Polypharmacy
- Complex etiologies: HIV, Aging, & Immunology
- Keys to “successful aging” & resilience in older HIV+ adults

EPIDEMIOLOGY & CLINICAL CHALLENGES

AGING OF HIV+ IN THE US

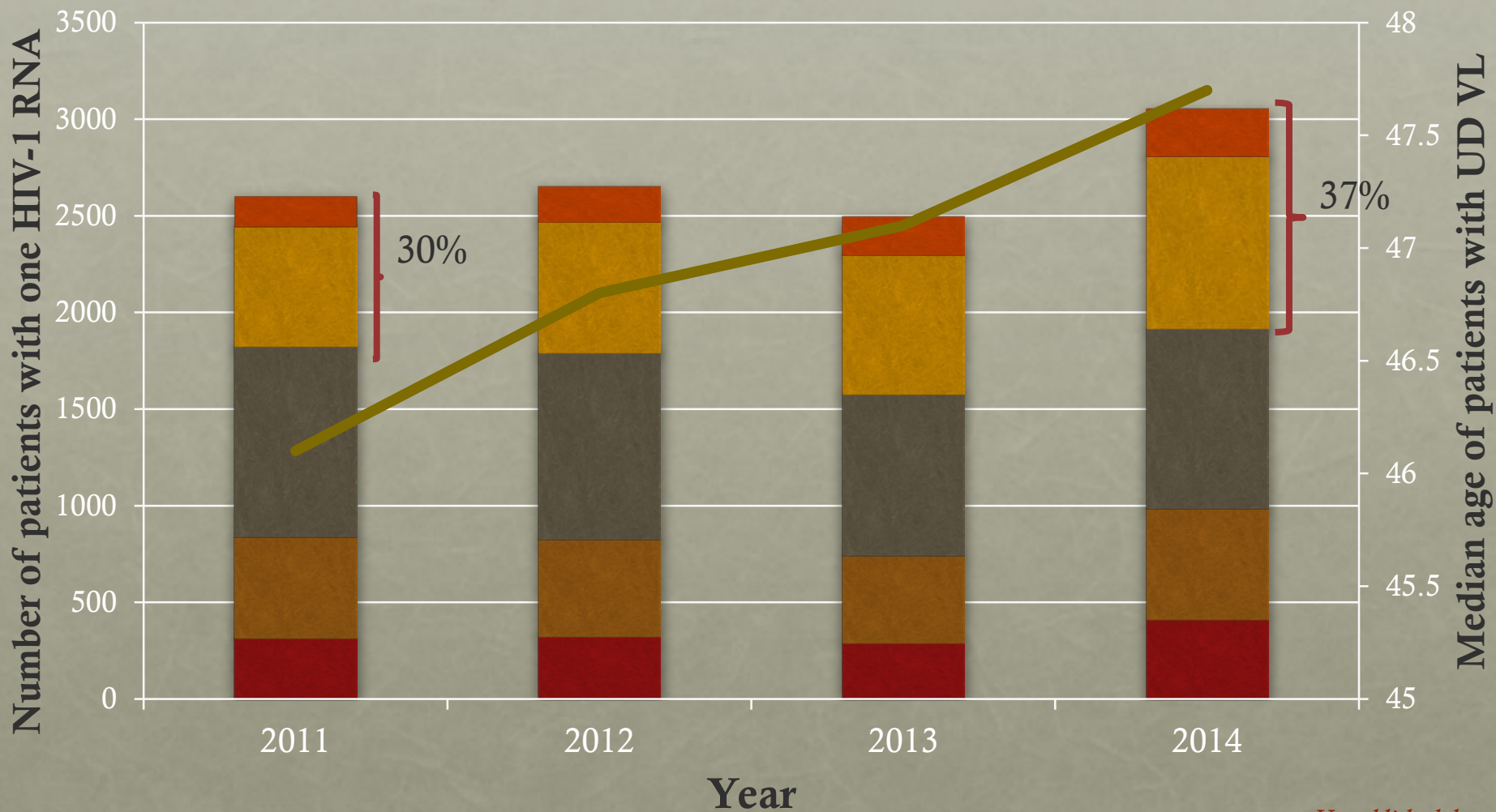


http://www.cdc.gov/hiv/library/reports/surveillance/2013/surveillance_Report_vol_25.html

http://www.cdc.gov/hiv/pdf/statistics_2011_HIV_Surveillance_Report_vol_23.pdf

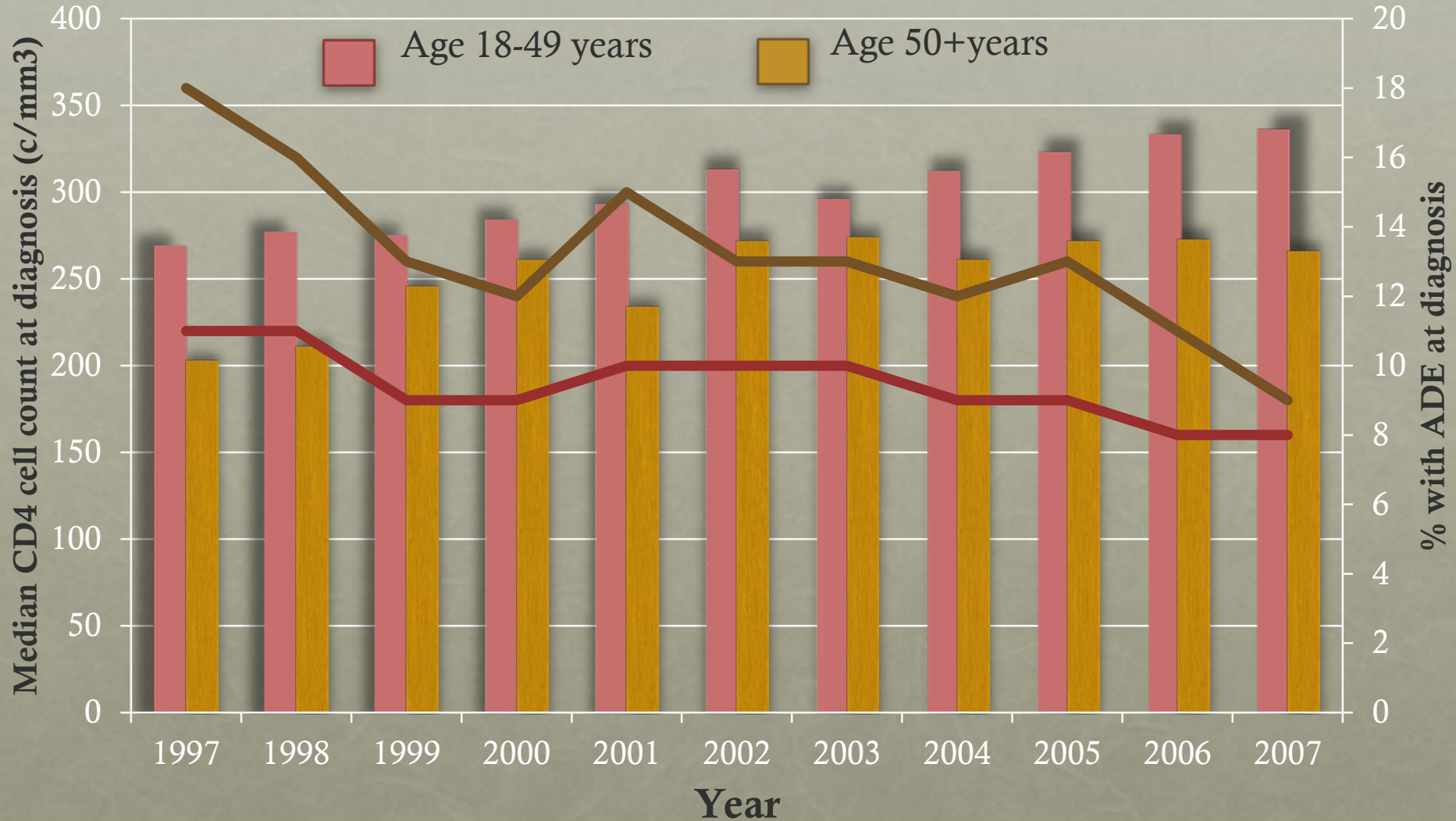
VCCC DATA

■ <30 yrs ■ 30-39 yrs ■ 40-49 yrs ■ 50-59 yrs ■ 60+ yrs



Unpublished data

AGE AT HIV DX



HIV OUTCOMES IN OLDER ADULTS

Once in care, older adults:

- ↓ CD4 cell count recovery with ART
- ↑ Risk of AIDS
- ↑ Risk of death



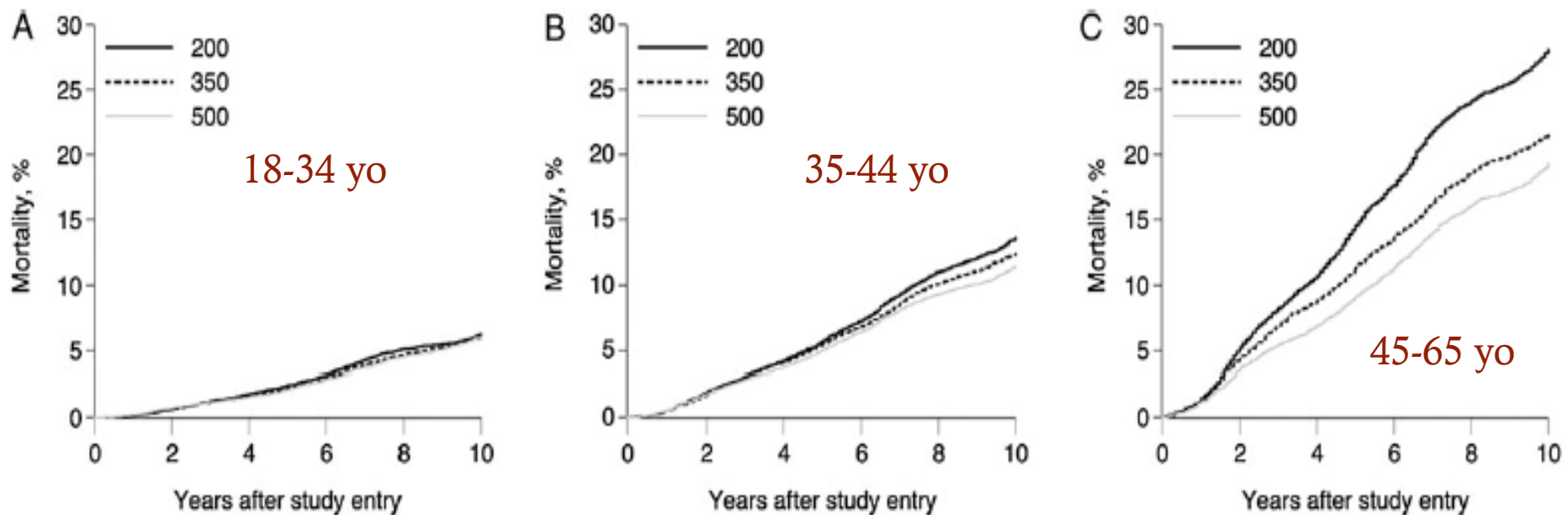
Viard et al. *J Inf Dis.* 2001;183:1290-4.

Balestre et al. *AIDS.* 2012;26:951-7.

Eggar et al. *Lancet.* 2002;360:119-29.

Bakanda et al. *AIDS.* 2011;25:701-5.

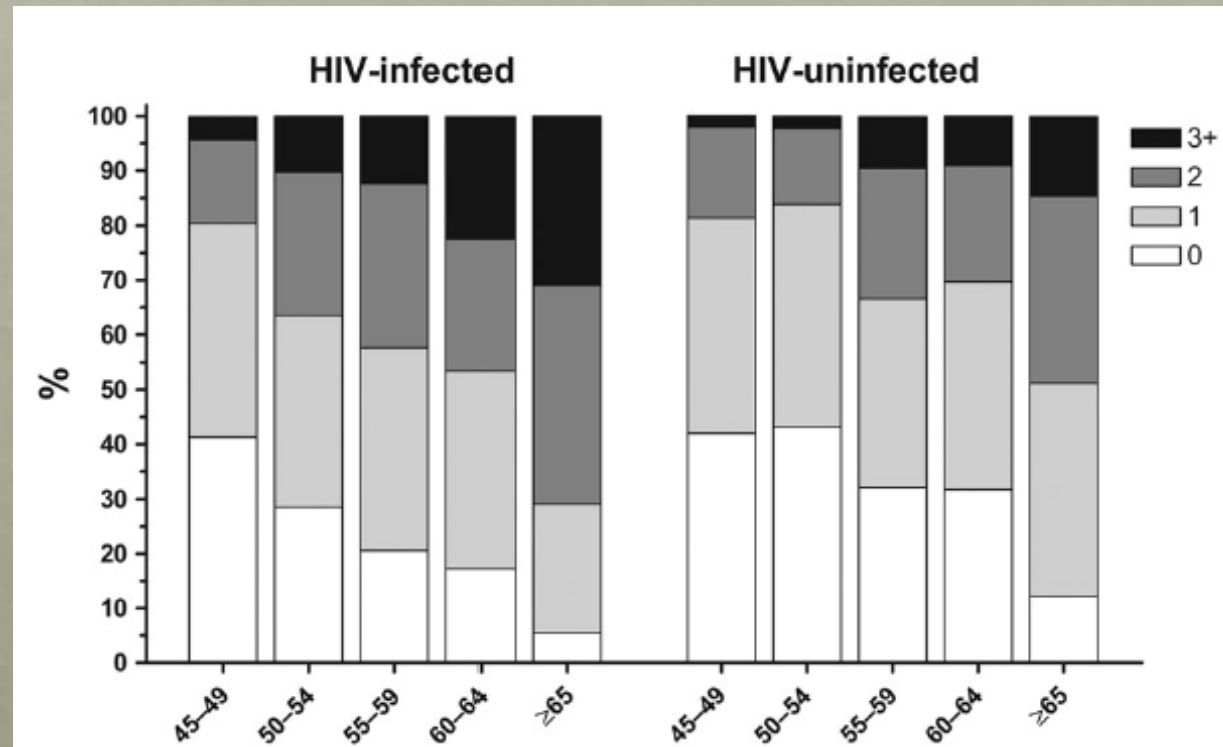
Age at Entry Into Care, Timing of Antiretroviral Therapy Initiation, and 10-Year Mortality Among HIV-Seropositive Adults in the United States



MULTIMORBIDITY

HIV-infected adults at
↑risk of:

- CVD
- Cancers
- Metabolic disorders
- Osteoporosis
- Renal disease
- Liver disease



AGEhIV study: HIV-infected 45+yrs (n=540) & matched, HIV-uninfected controls.

Freiberg et al. *JAMA Int Med.* 2013;173:614-22.

Shiels et al. *JNCI.* 2011;103:753-62.

Lucas et al. *AIDS.* 2007;21:2425-43.

And many more....

Schouten et al. *Clin Inf Dis.* 2014;59:1787-97.

A MODELING STUDY

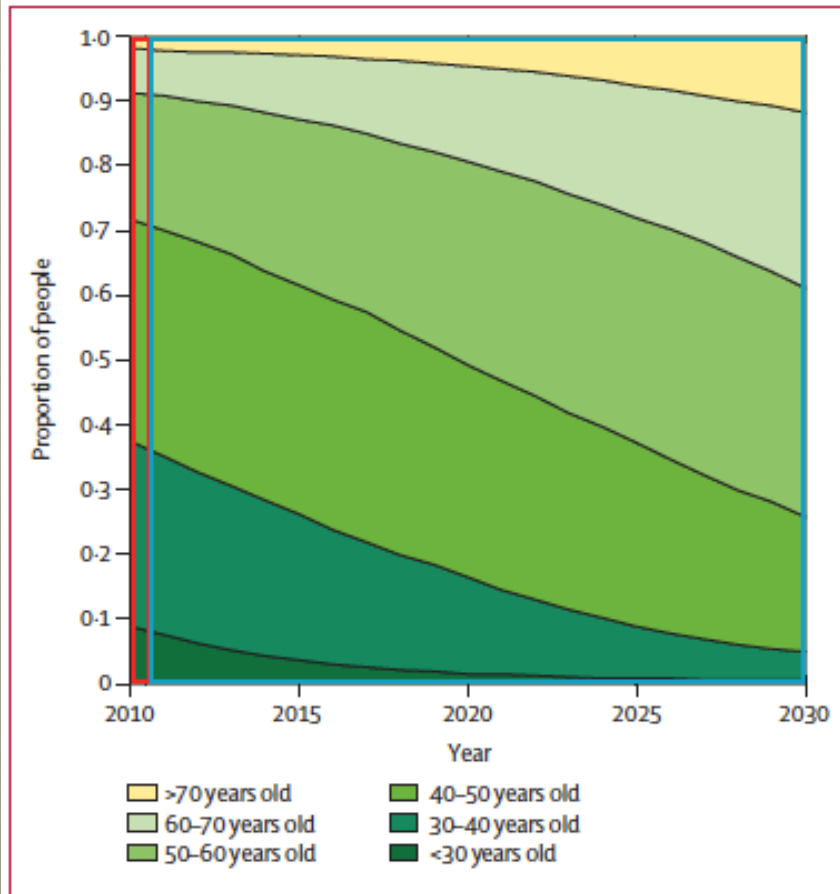


Figure 2: Projected age distribution of HIV-infected patients
The red box shows the age distribution of patients on antiretroviral therapy in clinical care in the Netherlands in 2010, which matches the data exactly, and the blue box shows model output from 2011-30.

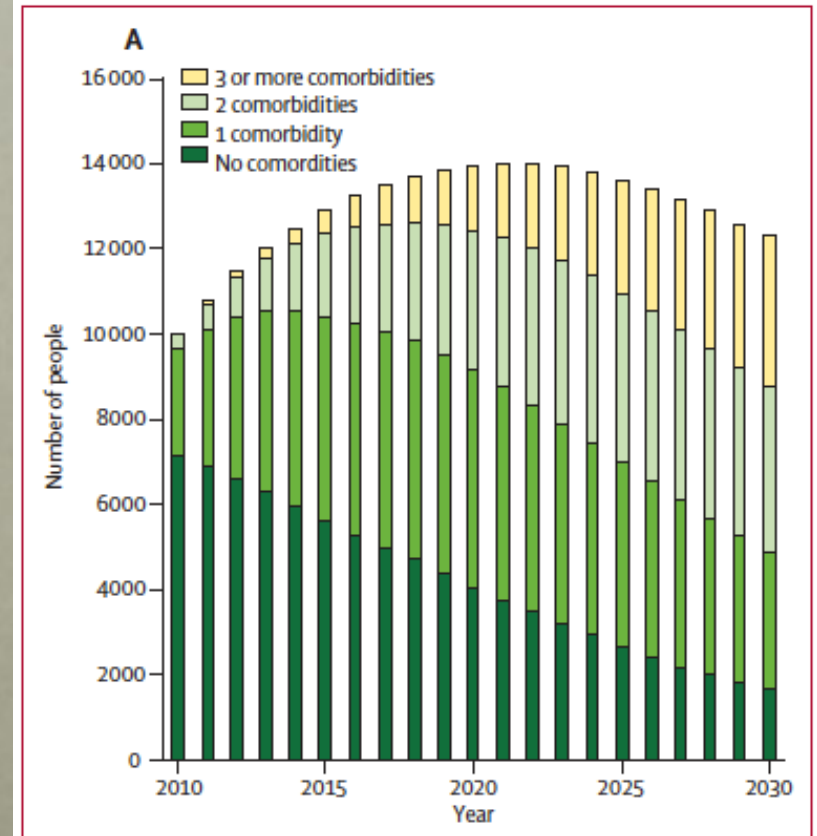


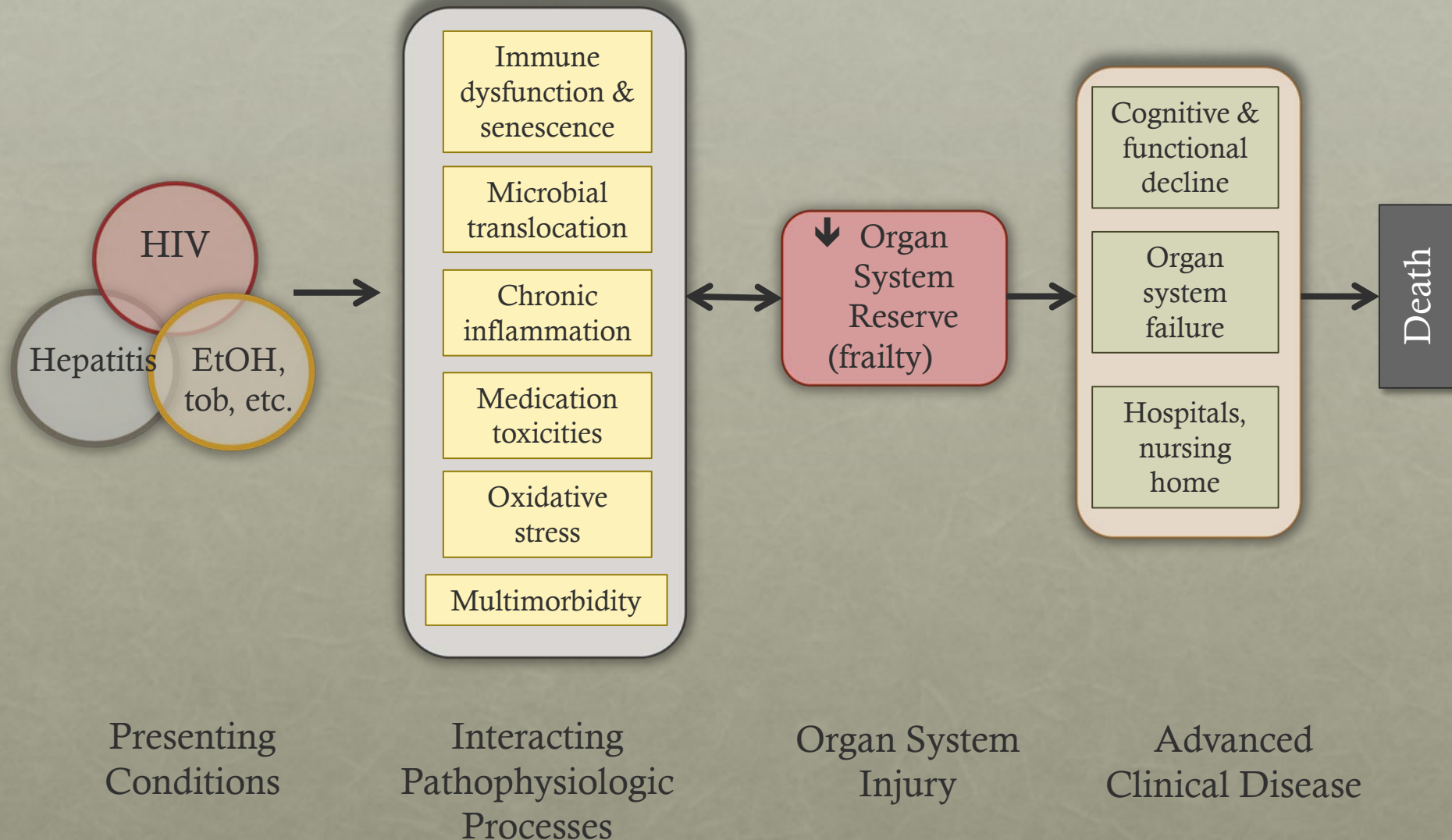
Figure 3: Predicted comorbidities
(A) Predicted burden of NCDs in HIV-infected patients between 2010 and 2030 as simulated by the model. (B) Distribution of the number of NCDs by age group

How can we begin to synthesize all of this into a comprehensive understanding of HIV & Aging?



An Integrated Model of HIV & Aging

AGING →



GERIATRIC SYNDROMES

- **Frailty**
- **Cognitive impairment**
- **Polypharmacy**
- Sarcopenia
- Insulin resistance
- Falls

FRAILTY?

FRAIL



NOT FRAIL



“**frailty**” (def): a state of increased vulnerability to poor resolution of homeostasis after a stressor event

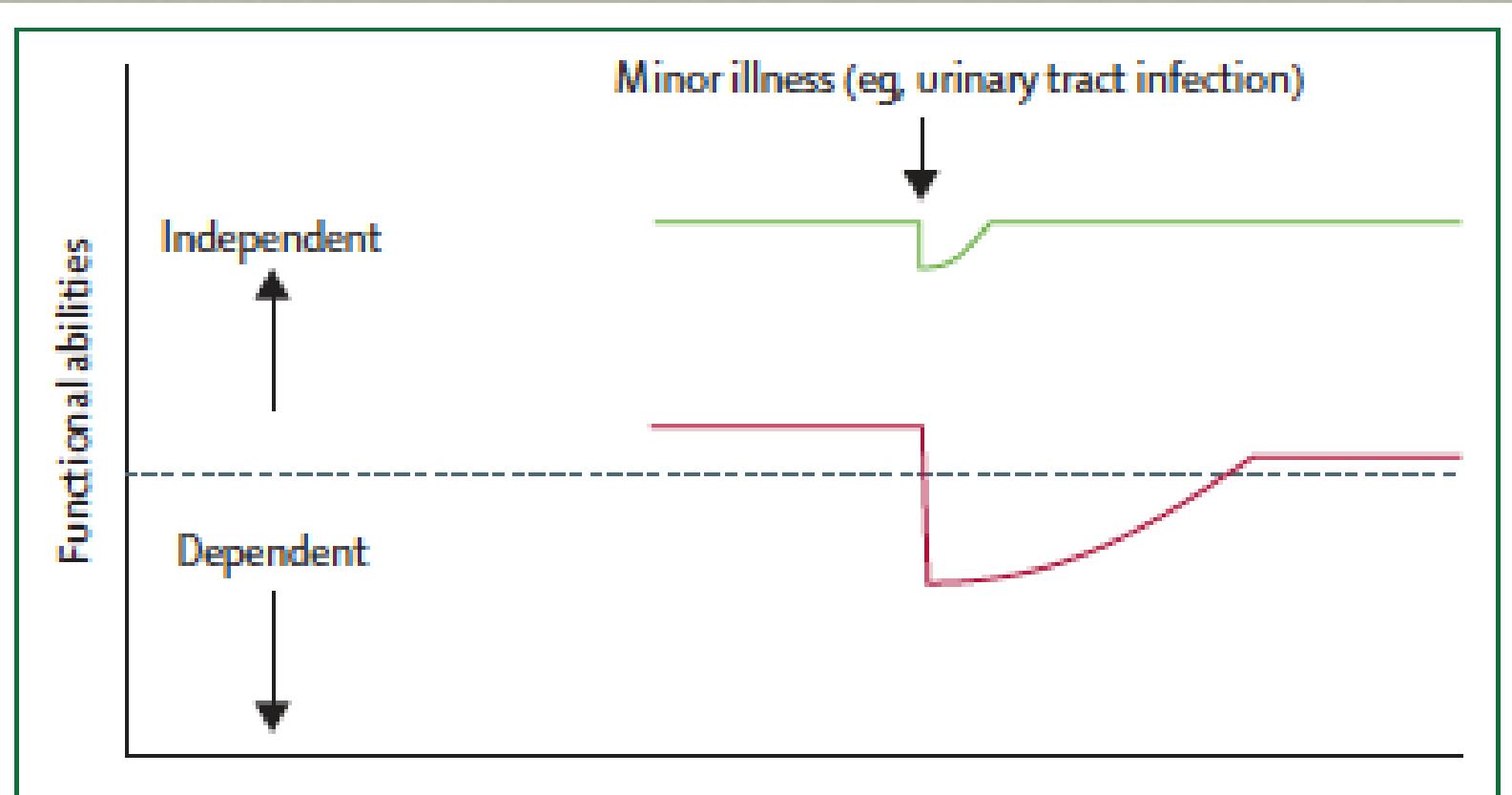
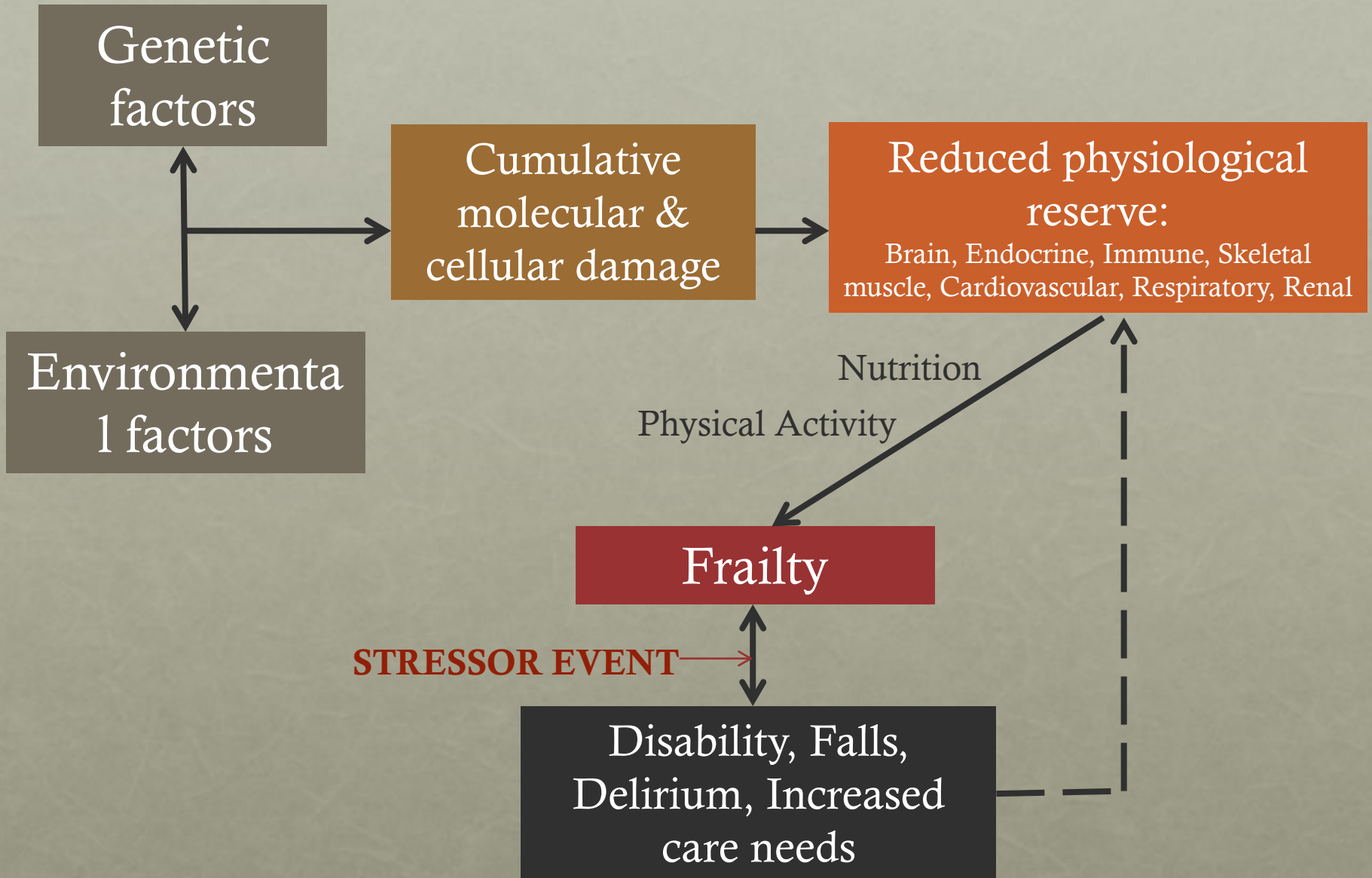
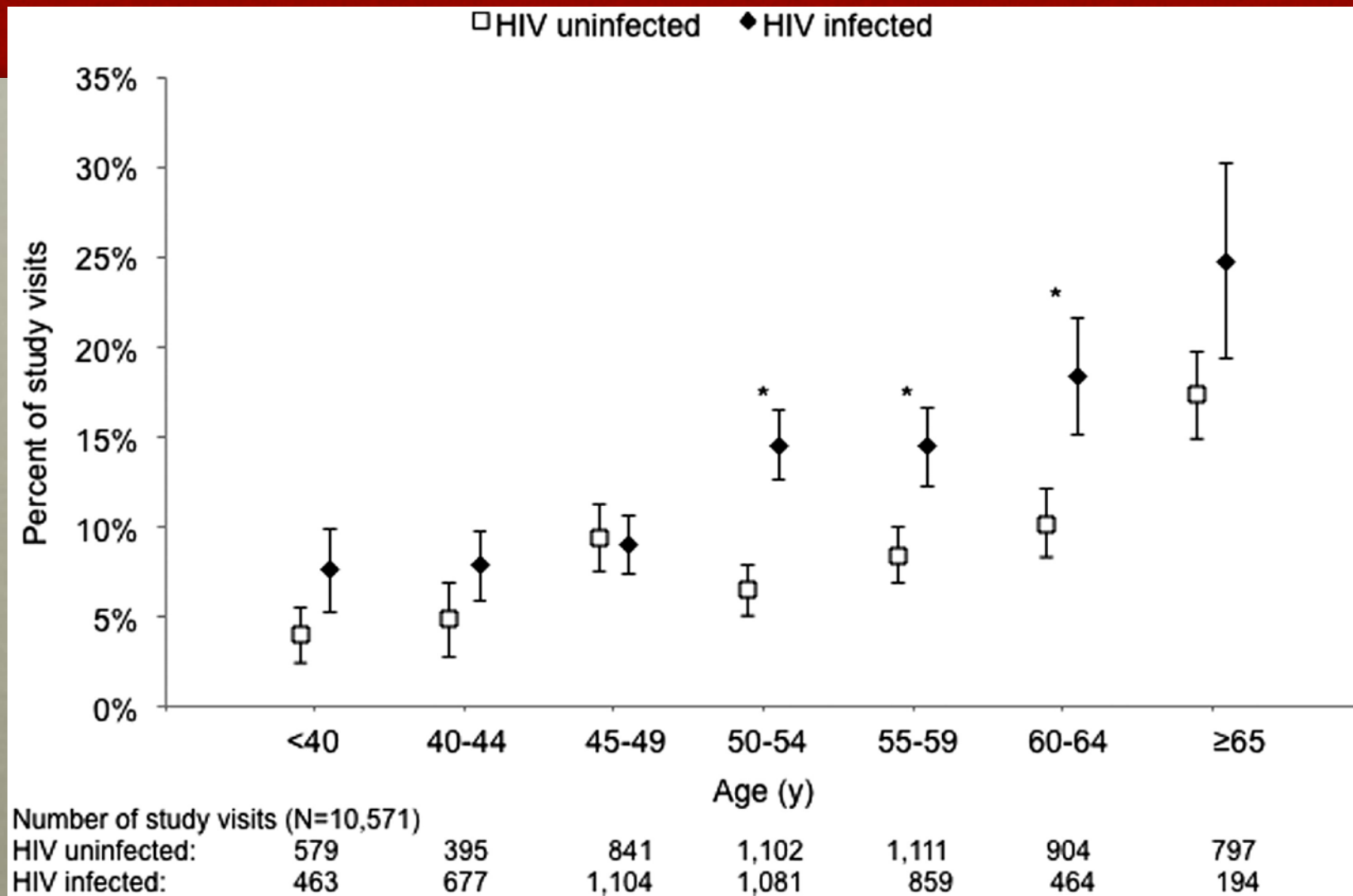


Figure 1: Vulnerability of frail elderly people to a sudden change in health status after a minor illness

Pathophysiology of Frailty

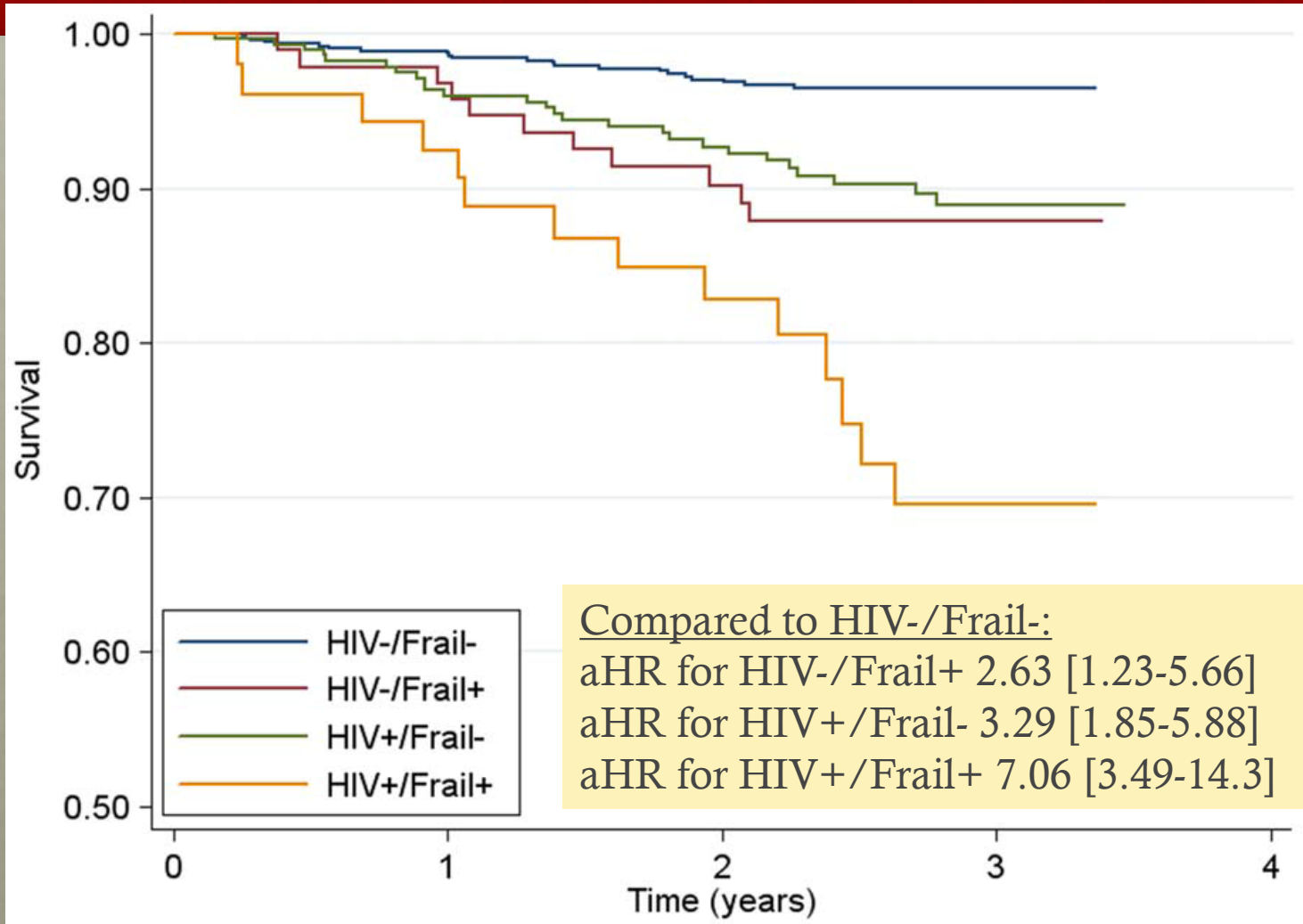


FRAILTY & HIV



Fried frailty phenotype present at any study visit in MACS cohort

FRAILTY & MORTALITY



ALIVE Cohort (2005-2008)

HAND

- Prevalence of HIV-associated neurocognitive disorder (HAND): 50% of HIV+ adults



HIV-Associated
Dementia
($<5\%$)

HAD: severe impairment in at least 2 cognitive domains + severe functional impairment

Mild Neurocognitive
Disorder
(17%)

MND: mild to mod impairment in at least 2 cognitive domains + mild to mod functional impairment

Asymptomatic Neurocognitive
Impairment
(28%)

ANI: any impairment in at least 2 cognitive domains + no functional impairment

COGNITIVE DEFICITS

- Cognitive domains:
 - Not just memory but also...
 - Concentration
 - Attention
 - Working memory
 - Comprehension
 - Motor effects (ex: changes in gait or poor coordination)
- Predicted by:
 - Low CD4+ lymphocyte count
 - High HIV RNA

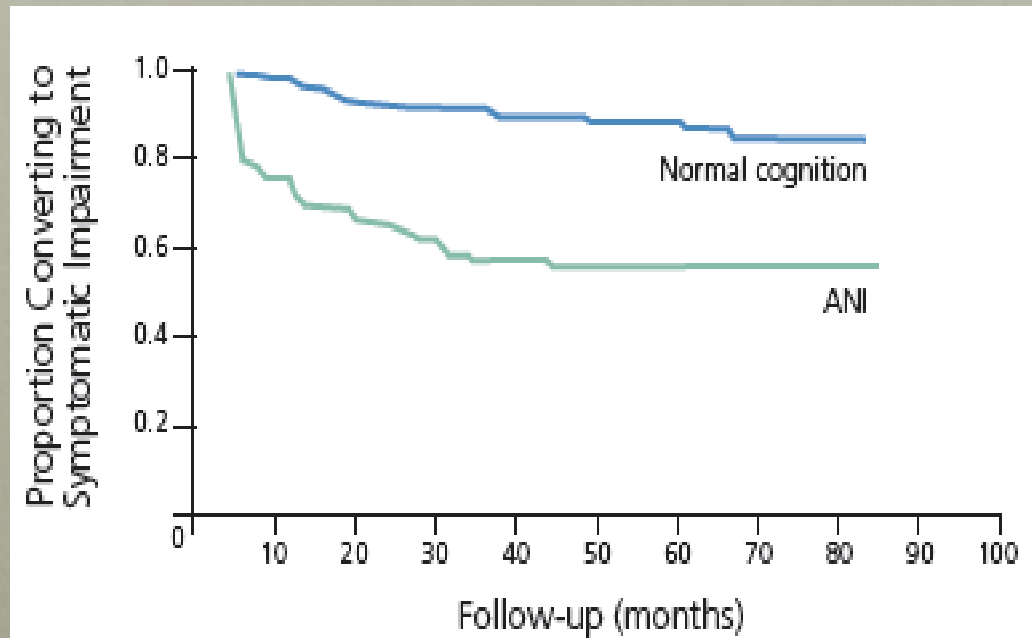


Figure 3. Conversion to symptomatic impairment over time in 347 patients with asymptomatic neurocognitive impairment (ANI) or normal findings on neuropsychologic testing in the CHARTER (Central Nervous System HIV Antiretroviral Therapy Effects Research) cohort. Adapted with permission from Grant et al.¹²

AGING & COGNITION

- Does HIV and/or HAND increase the risk of aging-associated cognitive decline or dementia?
- **Mild cognitive impairment (MCI):** transitional state between typical cognitive aging and dementia (defined for HIV-uninfected populations, prevalence of 5-20%)
- Study of HIV+ and HIV- adults in San Diego. Excluded HIV+ with MND.
- HIV+ were 7.4x more likely to have MCI (95% CI: 1.6-34), particularly older adults
- MCI was not *not* associated with ANI in older populations

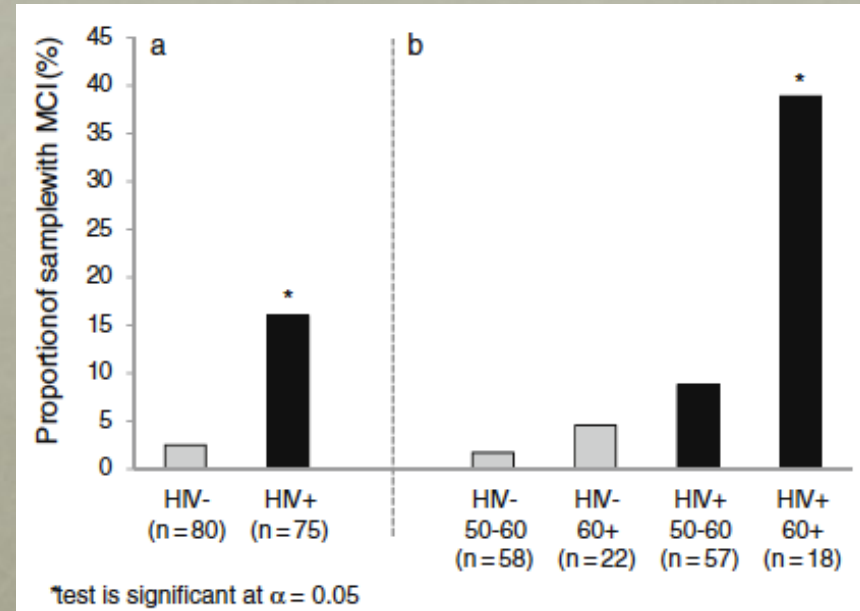
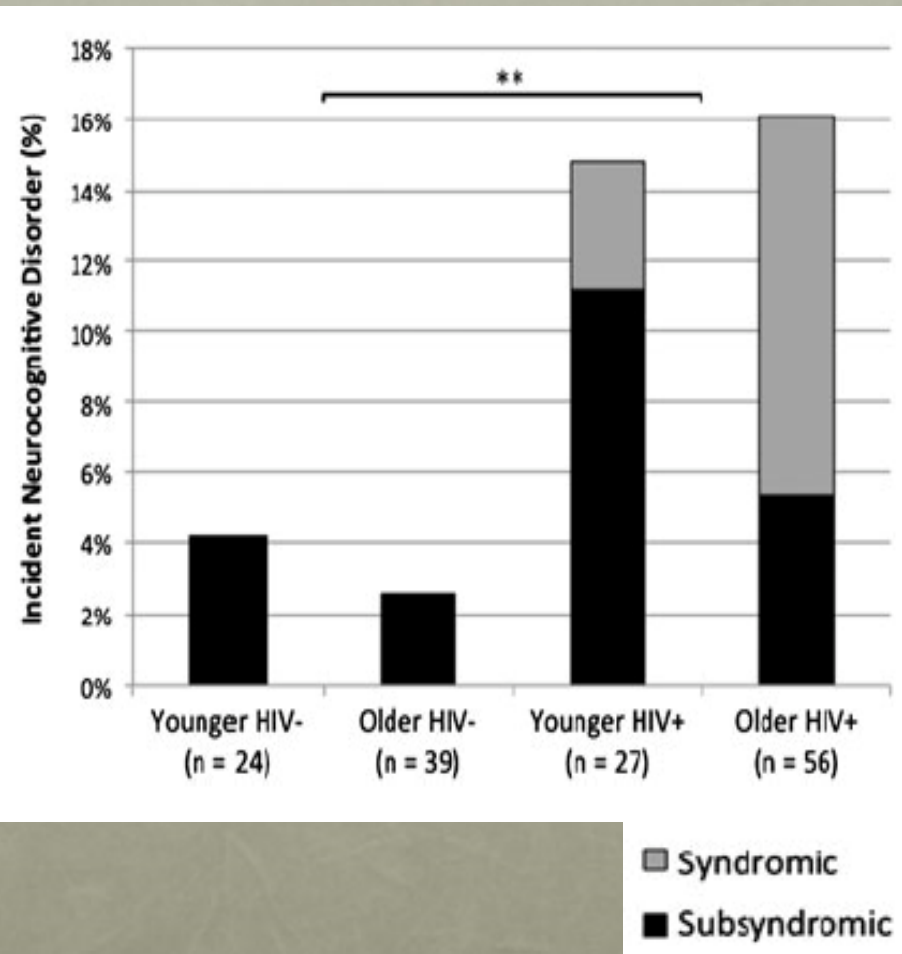


Table 2 MCI and asymptomatic neurocognitive impairment (ANI) designations for the HIV+ group

		ANI		Totals
		Present	Absent	
MCI	Present	5	7	12
	Absent	15	48	63
	Totals	20	55	75

AGING & COGNITION

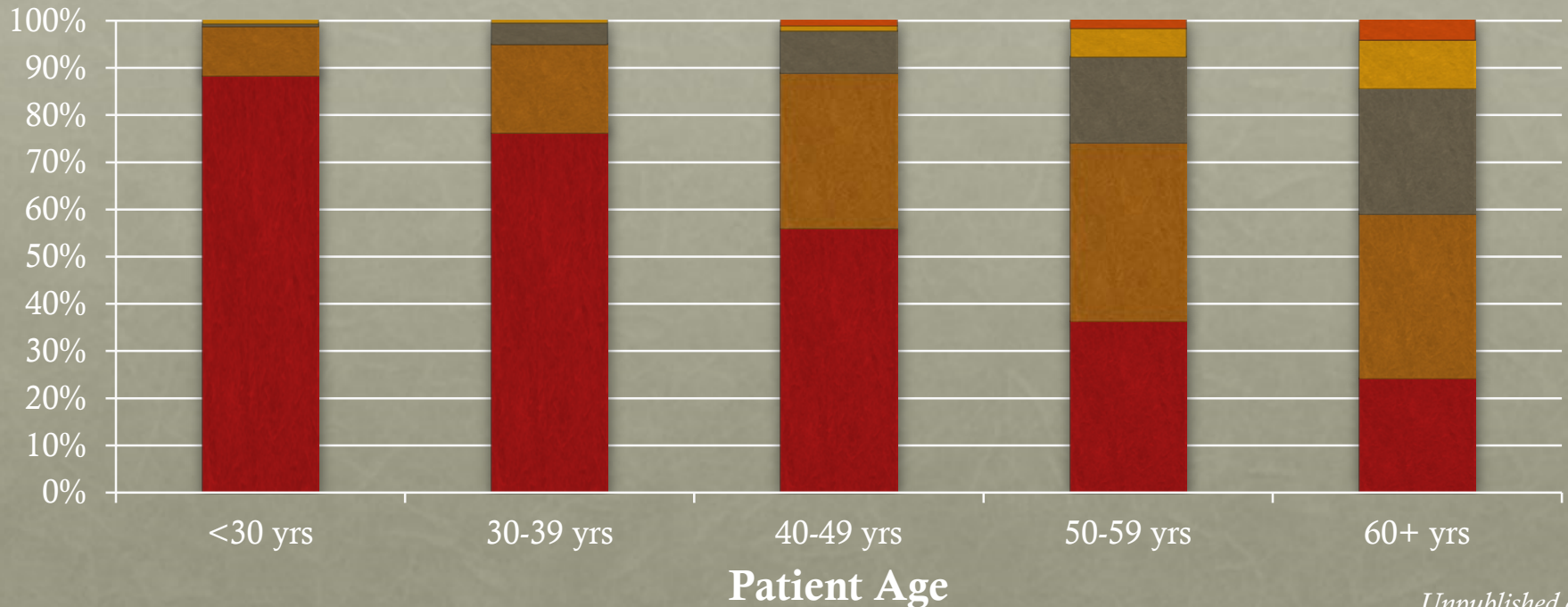
- Does older age increase the risk of HAND (symptomatic or asymptomatic) in aging HIV+ adults?
- Study of HIV+ and HIV- adults in San Diego. Ages ≤ 40 and ≥ 50 yrs
- Underwent battery of neuropsych tests at baseline and 1 year
- HIV seropositivity associated with 5-fold increased incidence in neurocognitive disorders but there was no statistical modification by age



POLYPHARMACY

Definition: daily use of 5 or more medications

Polypharmacy @ VCCC (excludes ART)



Unpublished data

COMPLICATIONS OF POLYPHARMACY IN ELDERLY

Medication Complications

- Adverse drug reactions
- Drug-drug interactions
- Non-adherence

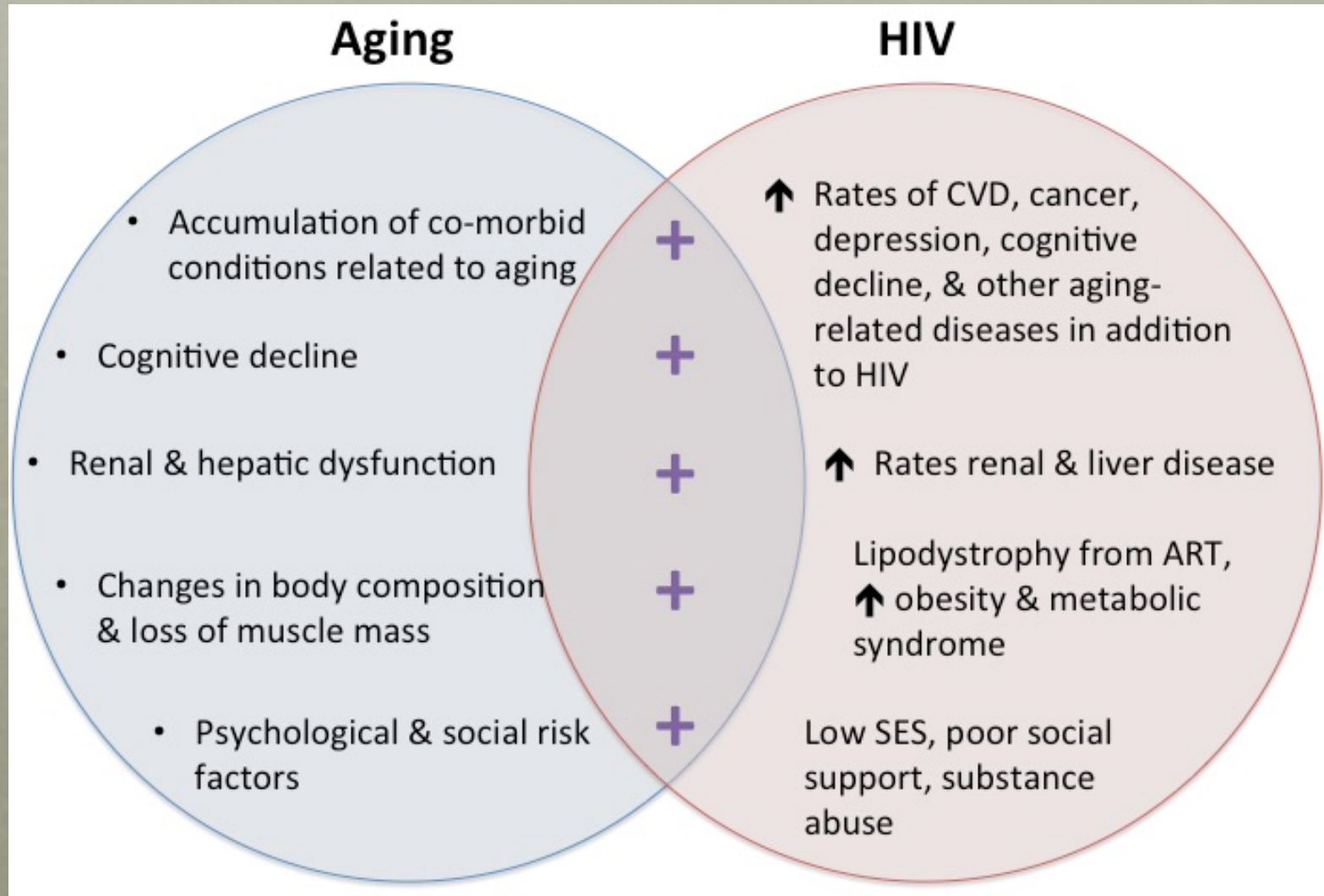
Mortality

Cognitive Decline

Falls & Frailty



RISK FACTORS FOR POLYPHARMACY COMPLICATIONS

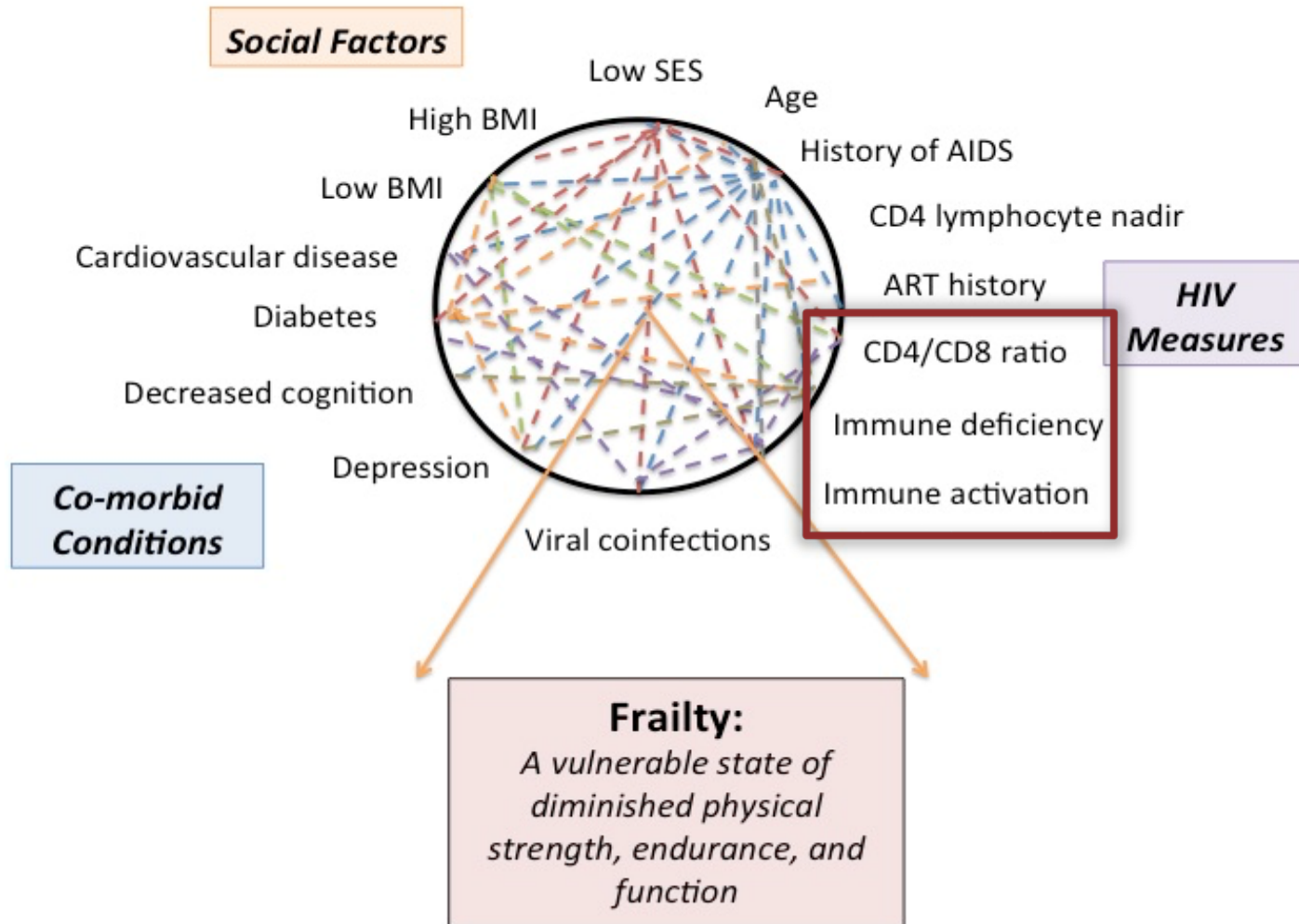


EPIDEMIOLOGY & CLINICAL CONCLUSIONS

- Increasing number and proportion of older HIV+ adults in care
- High burden for co-morbid conditions
- High rates of geriatric syndromes and need for holistic perspective in approach to care
- Particular attention to frailty, cognition, and polypharmacy is needed for the care of older HIV+

HIV, AGING, & IMMUNOLOGY

CAUSES OF FRAILITY IN HIV



ADDITIVE IMMUNE SENESCENCE

Aging

Shift naïve → memory T cells

↓ Thymus volume & function

↑ T cell activation

↓ T cell co-stimulatory molecule expression

↑ T cell terminal differentiation & clonal expansion

↑ Systemic inflammation

HIV infection

Shift naïve → memory T cells

↓ Thymus volume & function

↑ T cell activation

↓ T cell co-stimulatory molecule expression

↑ T cell terminal differentiation & clonal expansion

↑ Systemic inflammation

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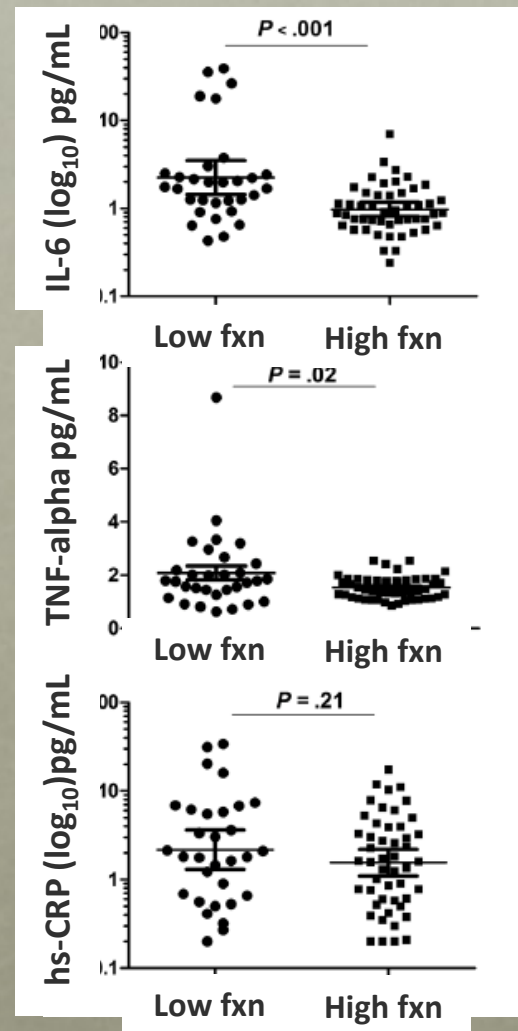
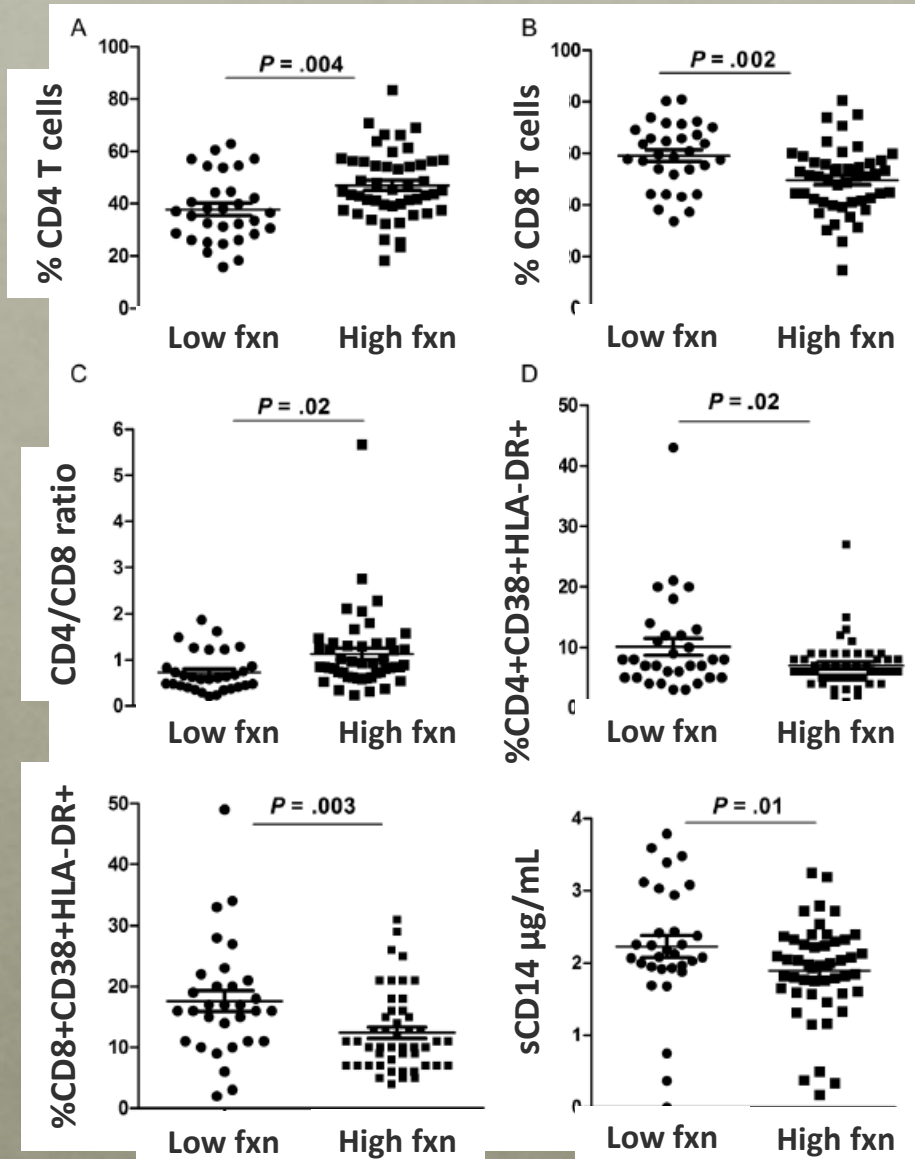
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Association of Functional Impairment with Inflammation and Immune Activation in HIV Type 1-Infected Adults Receiving Effective Antiretroviral Therapy



**RESILIENCE &
“SUCCESSFUL AGING”
IN HIV**

RESILIENCE

Generally involves two components:

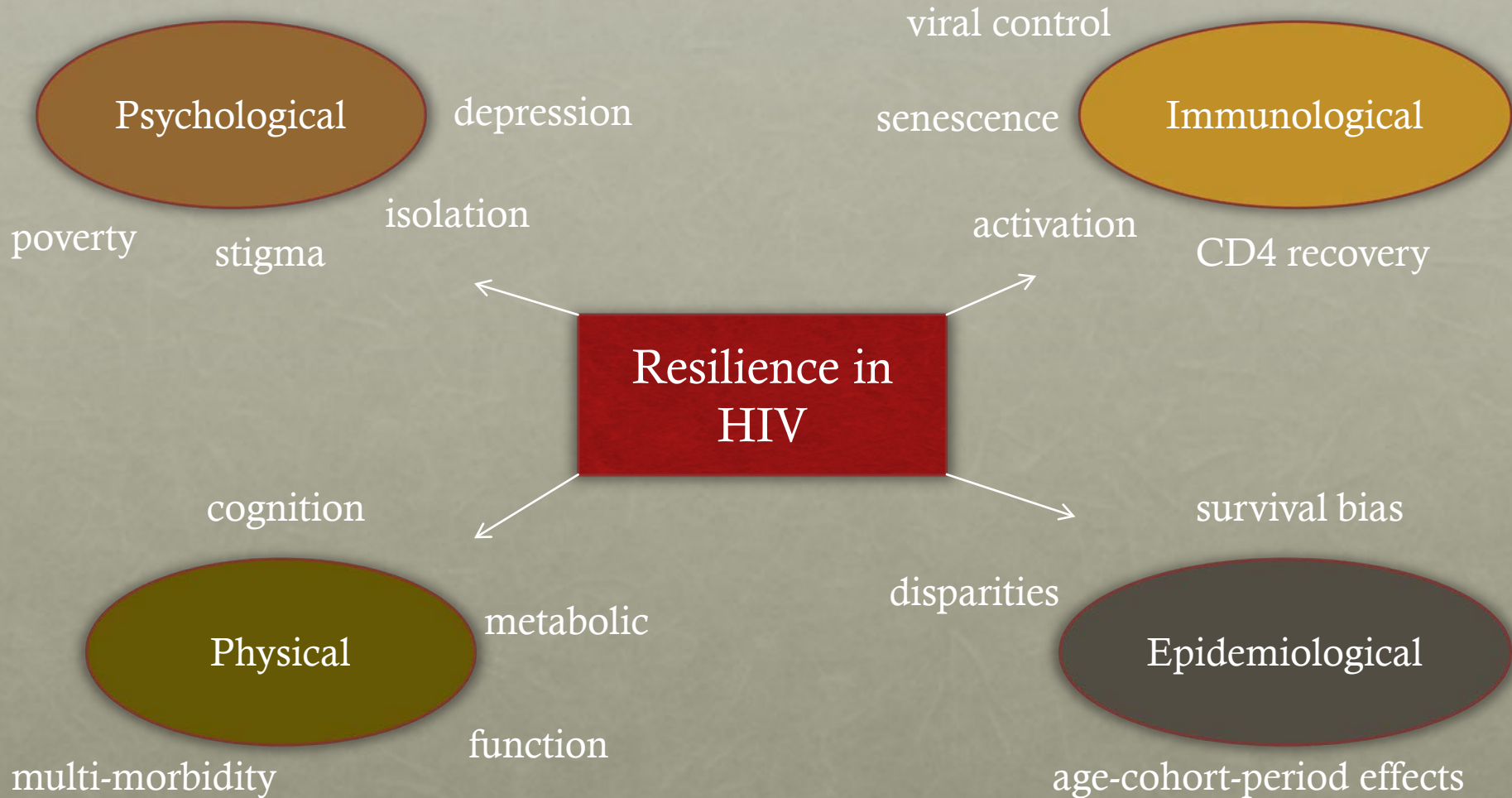
1. Exposure to significant adversity
2. Positive adaptation despite the adversity

(Inverse of frailty)



RESILIENCE:

THE ABILITY TO BECOME STRONG, HEALTHY, OR SUCCESSFUL AGAIN AFTER SOMETHING BAD HAPPENS



PSYCHOLOGICAL RESILIENCE

Older HIV+ adults

Life Stressors:

- General
- HIV-related

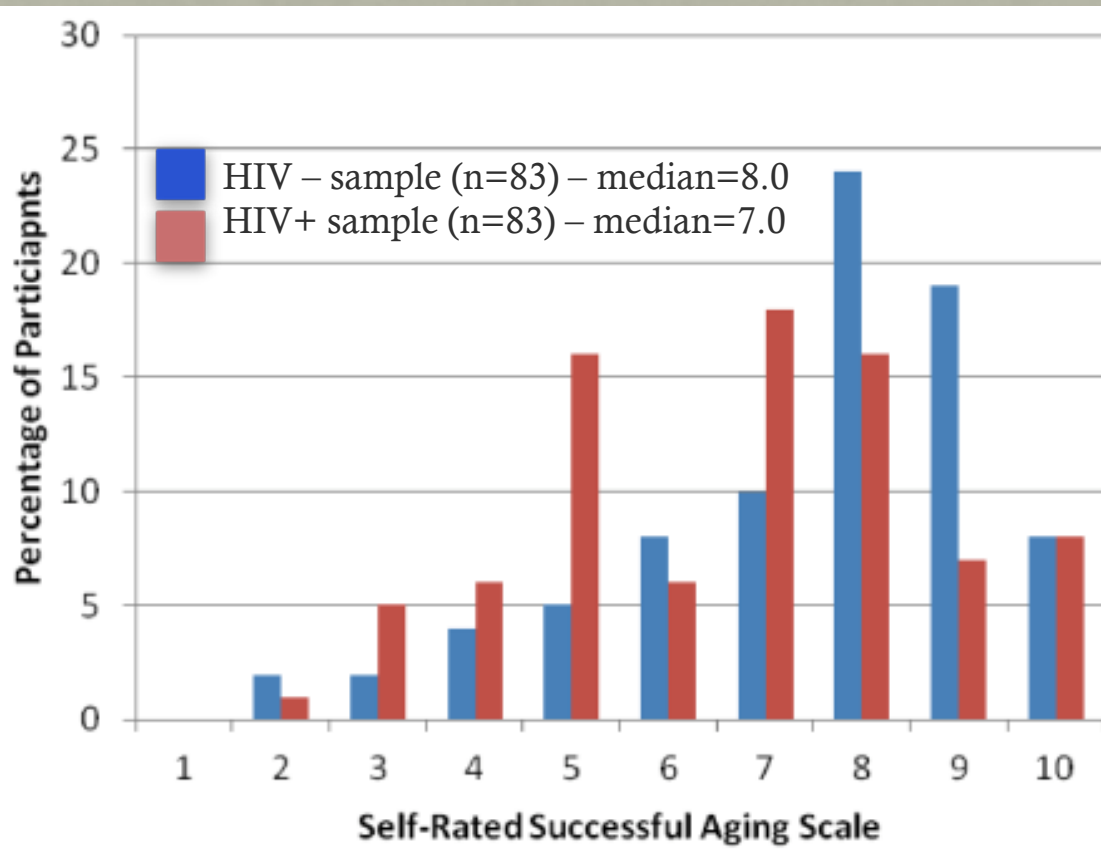
Resilience = coping, self-efficacy,
hope/optimism, and social support

Physical
Well-being

Function &
Global Well-
being

Emotional
Well-being

“SUCCESSFUL AGING”



Higher Self-Reported Successful Aging scores correlated with:

- Improved physical and mental functioning
- Lower depression scores
- Increased happiness
- Resilience
- Optimism
- Personal mastery
- Lower perceived stress

CONCLUSIONS

- Older HIV+ adults are a growing and complex patient population.
- Holistic approach to their medical care and awareness of geriatric syndromes are needed.
- Causes of their health conditions are complex, including immunologic changes that mimic those of aging.
- Building resilience through therapeutic relationships is one way to promote “successful aging” in this population.

ACKNOWLEDGEMENTS

Vanderbilt Mentors

Tim Sterling (ID)

Cathy McGowan (ID)

Spyros Kalams (ID)

David Haas (ID)

Keipp Talbot (ID)

Matt Freiberg (Cardiology)

Laura Dugan (Geriatrics)

Jack Schnelle (Geriatrics)

VCCC

Steve Raffanti

Todd Hulgán

Staff & Providers

Funding

K12 HD043483

P30 AI110527

U01 AI069923

UL1 TR000445

My patients

QUESTIONS?