HIV, Multimorbidity, and Frailty: what's going on?

(with apologies to Marvin Gaye)

Julian Falutz MD, FRCPC

Director Comprehensive HIV Aging Initiative

Chronic Viral Illness Service

Senior Physician, Division of Geriatrics

McGill University Health Center

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- **Advisory Boards: Merck**

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HIV and Aging: Background

EDITORIAL COMMENT

nearly
A normal life expectancy, despite HIV infection?

Andrew Hill[a] and Anton Pozniak[b]

AIDS 2010, **24**:1583–1584

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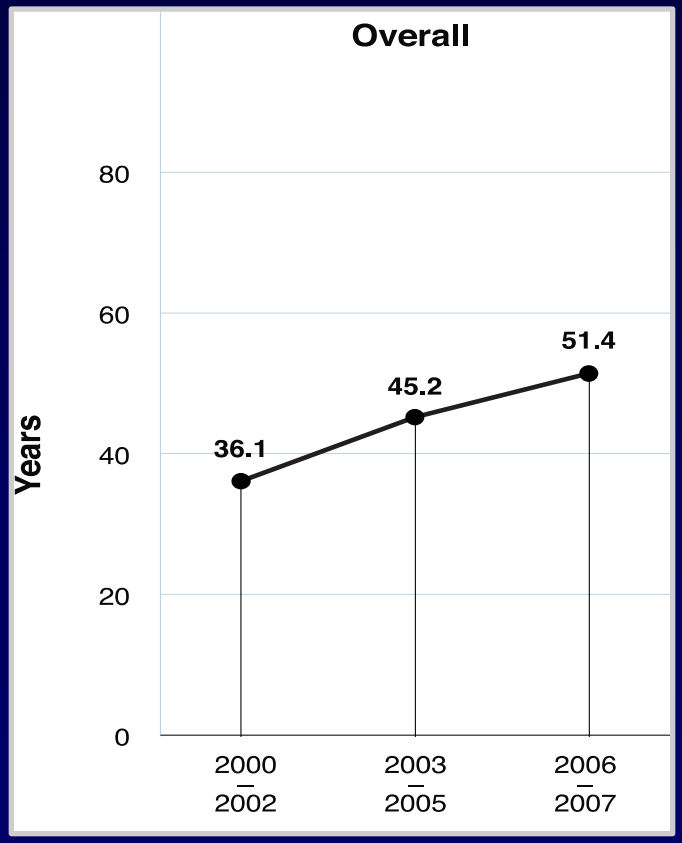
Life expectancy > 70 years (vs ± 80 in controls) for newly Dx HIV pts age 20: gender and risk behaviour affects survival (NA-ACCORD)



Treated patients with CD4 > 500 plus undetectable HIV-VL for
➢5 years likely have normal survival

Samji H et al. PLoS one 2013;8:e81355

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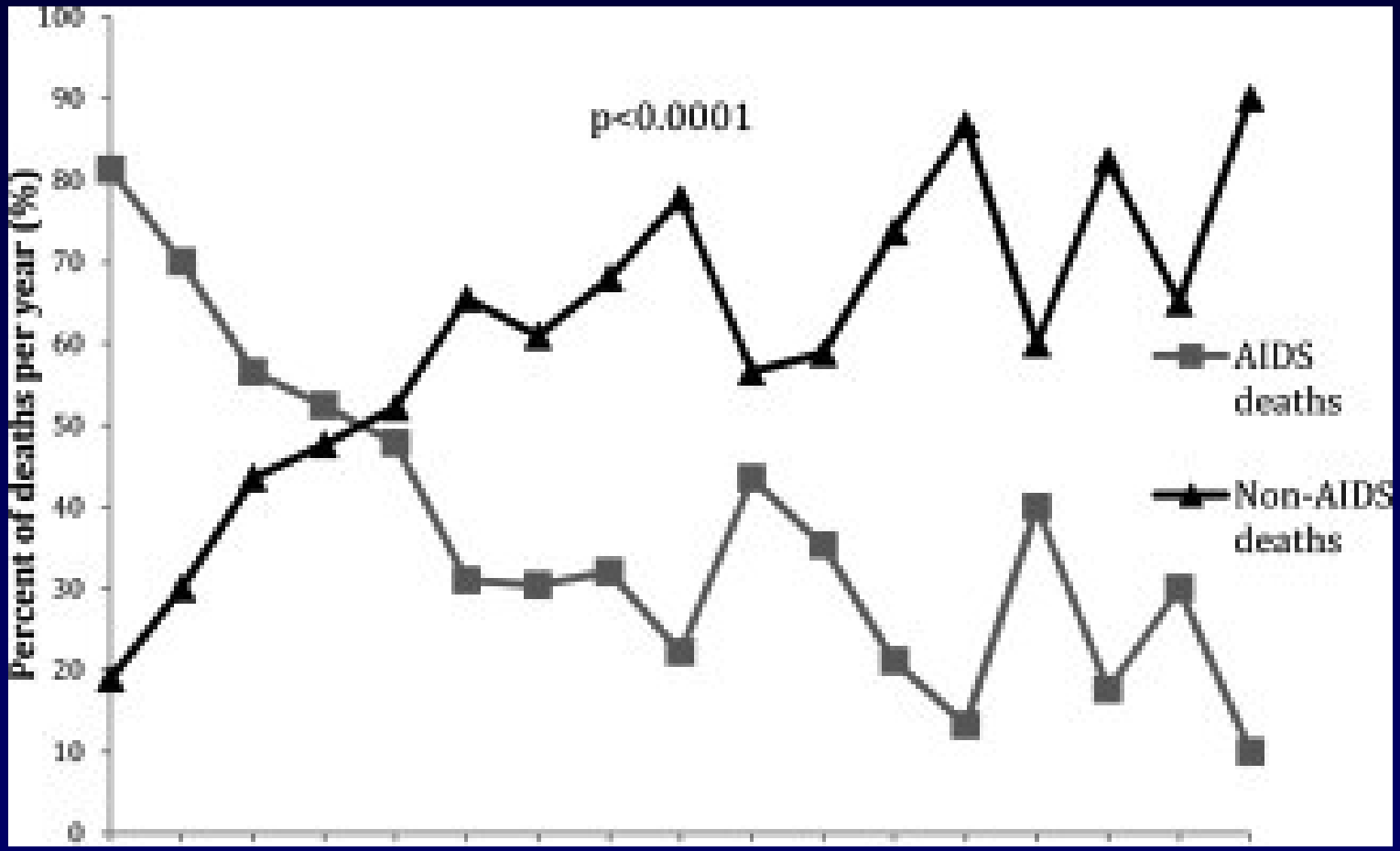
Consequences of improved survival of HIV pts: Impact on AIDS vs non-AIDS related deaths (1995-2011)



Cowell A et al. J Hosp Med 2015;10:608

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Causes of death 1999-2011(D:A:D): Most deaths are due to non-AIDS conditions

	Number of deaths (%)
Total deaths	3909 (100%)
AIDS-related	1123 (29%)
Liver-related	515 (13%)
Chronic viral hepatitis*	447 (11%)
Liver failure	68 (2%)
CVD-related	436 (11%)
Myocardial infarction, definite or possible	225 (6%)
Stroke	56 (1%)
Other CVD	60 (2%)
Other heart disease	86 (2%)
Complications due to diabetes	9 (<0·5%)
Non-AIDS cancer†	590 (15%)‡
Other or unknown	1245 (32%)
Suicide	150 (4%)
Drug overdose	109 (3%)
Euthanasia	16 (<0·5%)
Homicide	22 (1%)
Accident	74 (2%)
Invasive bacterial infection	259 (7%)
Lactic acidosis	17 (<0·5%)
Pancreatitis	20 (1%)
Renal dysfunction disease	48 (1%)
Other	266 (6%)
Unknown	264 (7%)

Non-AIDS related death (n=2786)

- NADC 590 (21%)
- Liver related 515 (18%)
- CVD related 436 (16%)
- Other 1245 (45%)

Smith CJ et al. Lancet 2014;384:241

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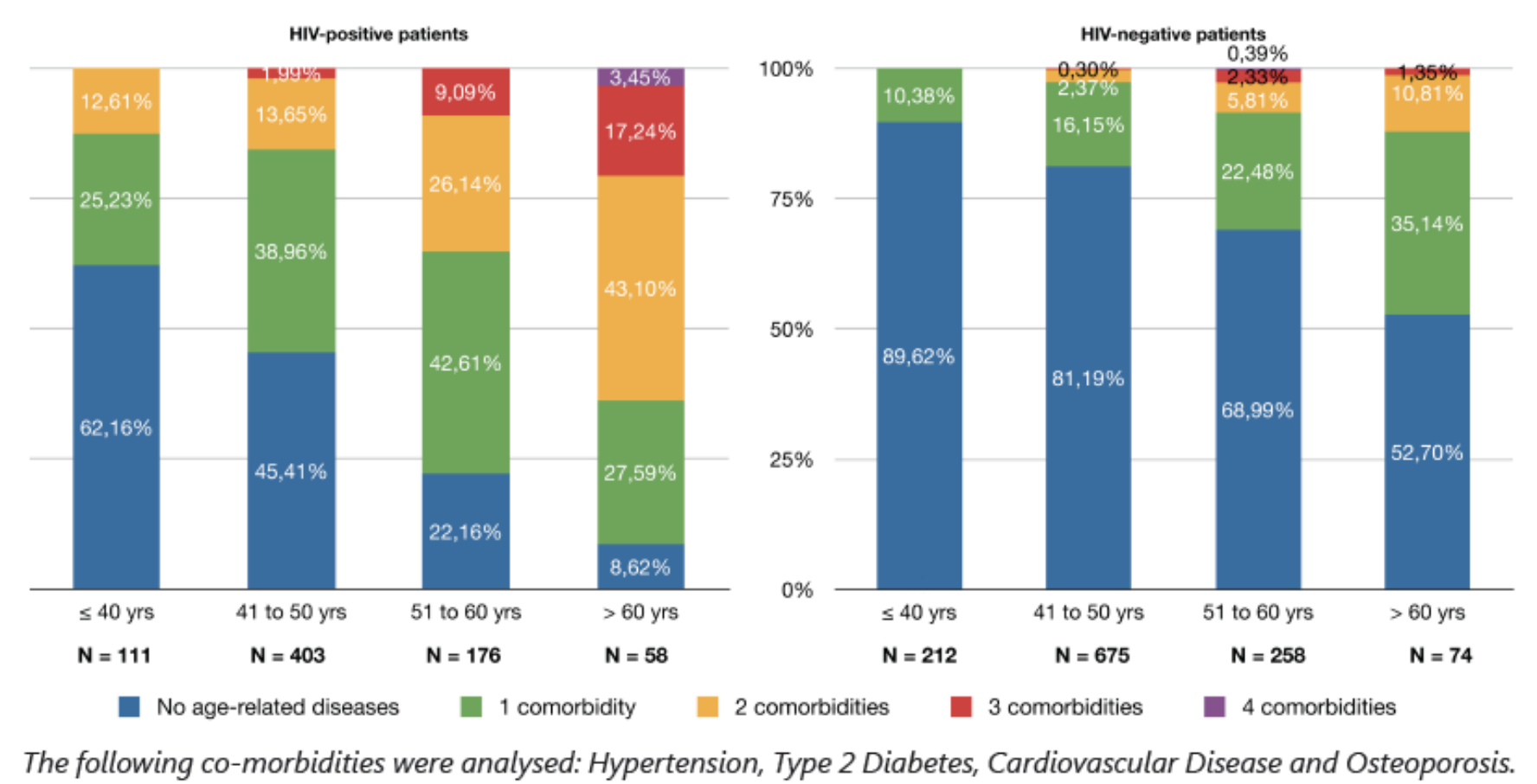
Aging related co-morbidities are increased in all HIV+ c/w HIV-neg pts, especially > 50 yrs



Guaraldi CID 2011

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Common non-AIDS co-morbidities are the same as those occurring in an older population but at a younger age

- Non-AIDS defining cancers
- Liver: viral hepatitis and NAFLD-related
- Cardiovascular
- Bone demineralization
- Renal
- Neurocognitive decline
- Other

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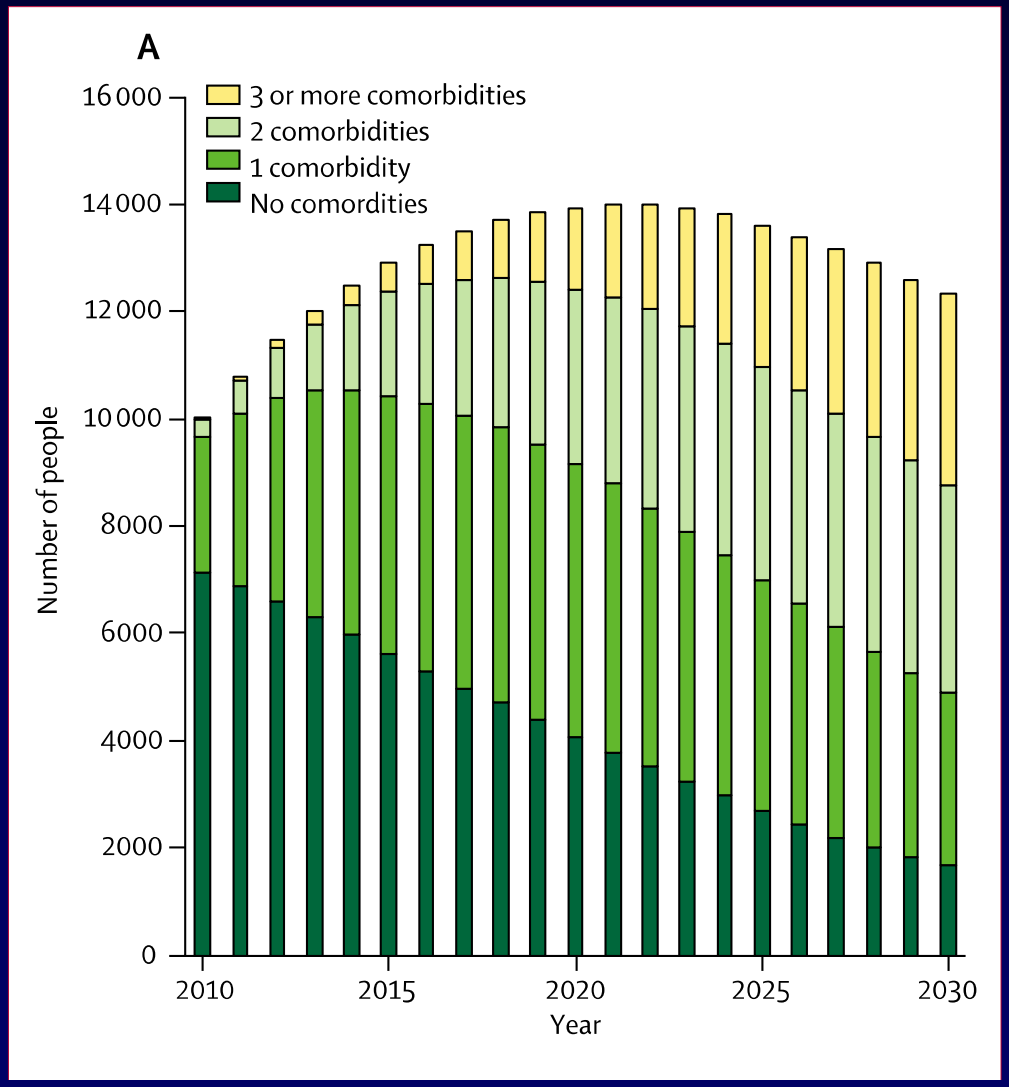
Expected increase in common co-morbidities in HIV pts by 2030



Smit K et al. Lancet Inf Dis 2015;15:810-18

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HIV and Aging: key points

- Mean age of pts in resource rich countries is > 50 (vs 10% in the 1980's): chronically infected pts are living longer: mean age at HIV seroconversion is increasing
- Mean survival of treated patients is 75-85% of age-expected [*pts with undetectable VL plus CD4>500 for > 5 yrs may have normal survival*]
- Co-morbidities in treated pts are generally similar to those occurring in older HIV-neg people: older pts often have low nadir CD4's and 'plateau' CD4< 500 which increases risk
- All currently recommended 1st line HAART regimens are (likely) equipotent, equi-durable and well-tolerated, but adherence and toxicity may vary: are integrase inhibitor based regimens more age-friendly?

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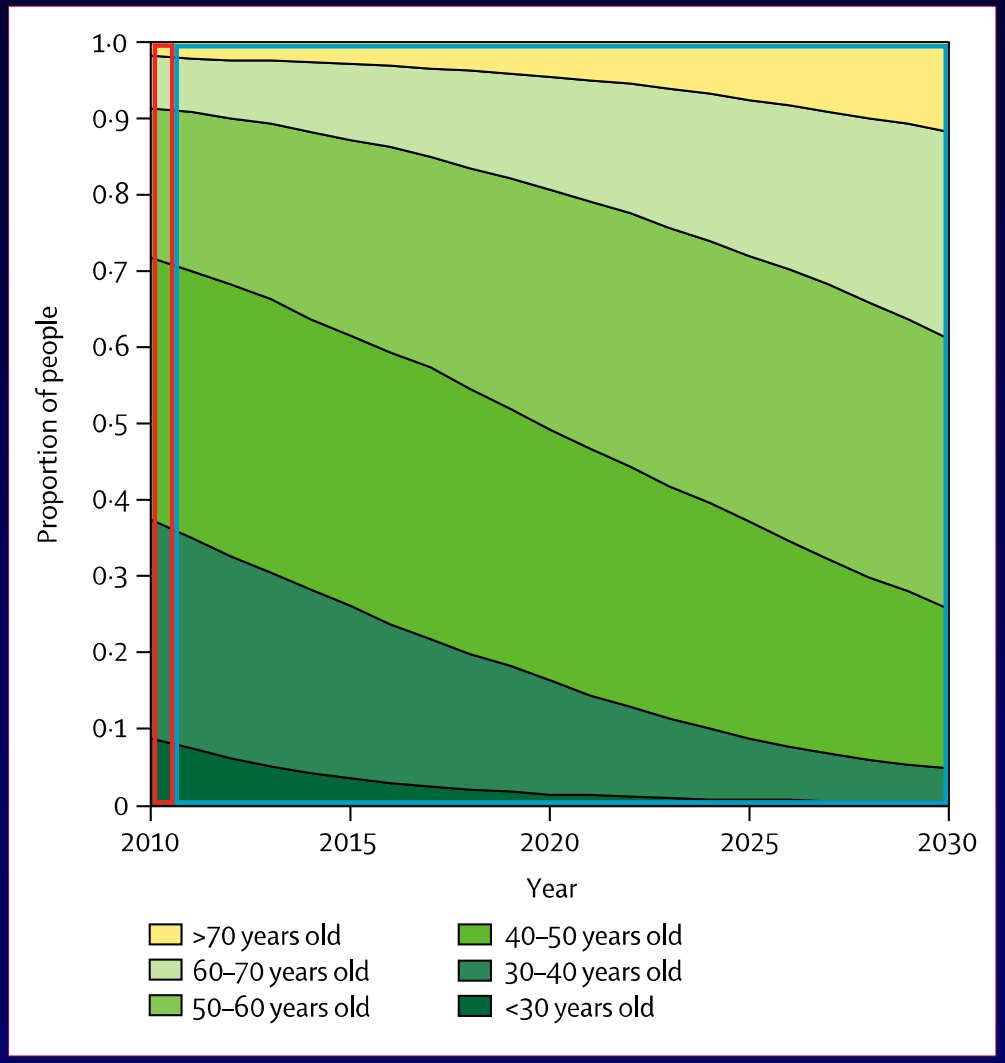
Expected increase in age of HIV pts by 2030: >66% older than 50



Smit K et al. Lancet Inf Dis 2015;15:810-18

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Significance of the changing HIV co-morbidity profile in an aging population: Does this reflect accelerated or accentuated aging?

- Does HIV *accelerate* specific pathways and mechanisms common to an aging phenotype(no consensus on definition of aging)?
- Is HIV an additional risk factor for development of chronic conditions *accentuating* prevalence of disease?

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HIV, Aging and Frailty: context

- Age – related co-morbidities that may occur in younger HIV patients:
  - immune-senescence
  - CVD
  - bone demineralization
  - metabolic syndrome
  - hepato-renal
  - certain malignancies
- Clinical conditions in HIV with features similar to common geriatrics “syndromes”:
  - frailty
  - social isolation
  - polypharmacy
  - disability and falls
  - cognitive decline

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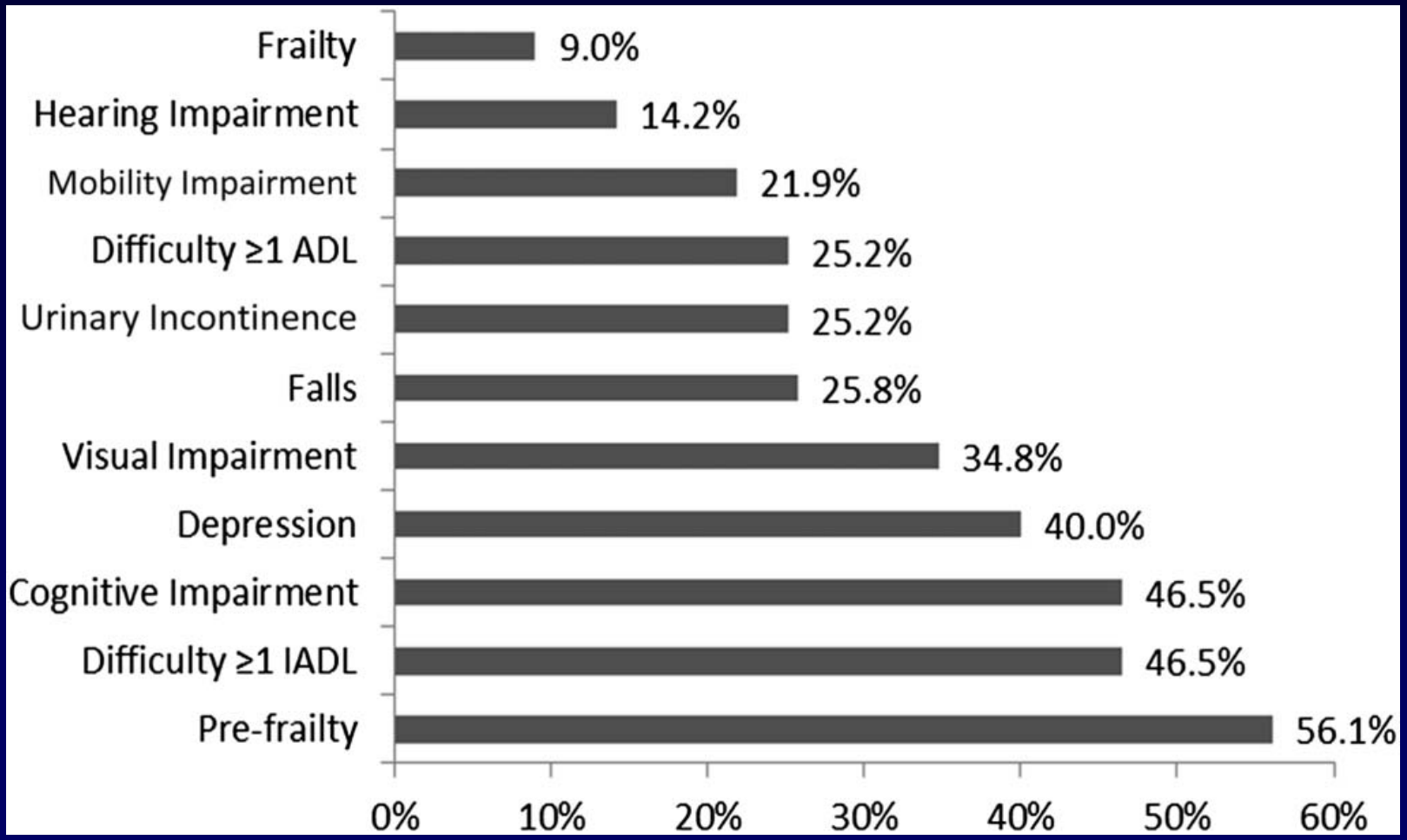
Prevalence of geriatric syndromes in older HIV patients



Greene M et al. JAIDS 2015;69(2):161

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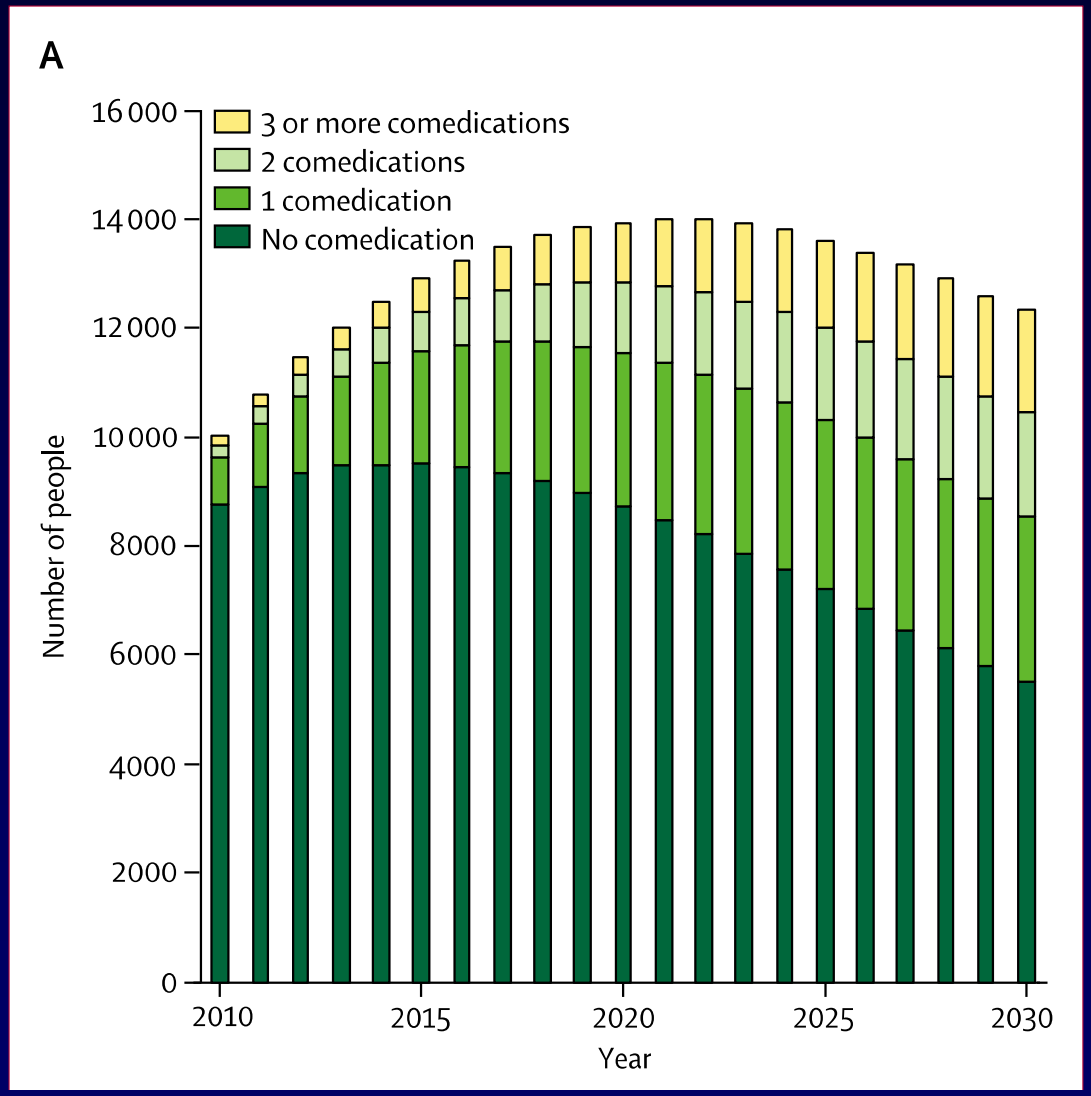
Expected increase in polypharmacy in HIV pts by 2030



Smit K et al. Lancet Inf Dis 2015;15:810-18

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Frailty

- State of increased vulnerability to stressors occurring in the elderly
- Decreased physiologic reserve: increases risk of negative outcomes including loss of independence, requirement for supervised housing, increased morbidity and mortality, dementia
- Validated, easily obtained and uniformly accepted diagnostic criteria remain under investigation

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Consequences of frailty in the general elderly population

- Hospitalization
- Multimorbidity and disability
- Malnutrition
- Loss of independence
- Dementia
- Increased mortality

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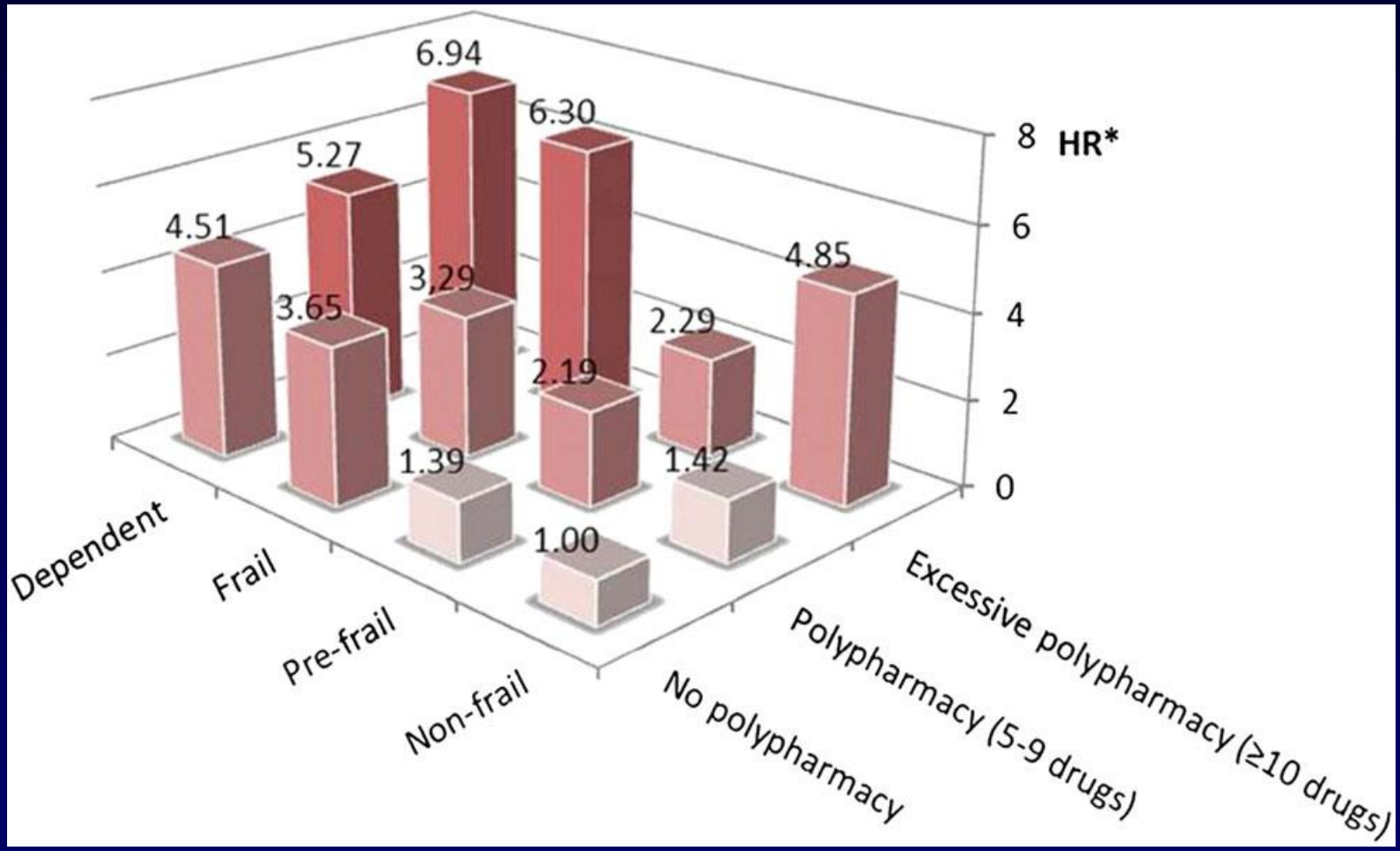
Frailty and polypharmacy increase mortality: impact in HIV pts ?



Herr M et al. Pharmacoepid & Drug Safety 2015

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Operationalization of frailty: general population

- **Frailty Phenotype** (Fried): *syndrome of poor nutrition, sarcopenia, weakness and impaired exercise tolerance*
- **Frailty Index** (Rockwood): *state representing the cumulative effects of multiple non-specific health deficits arising from aging process*
- Others (eg VACS-Index)

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Objective definition of frailty* as proposed by Fried et al

FP features of slowness, weakness and weight loss are associated with sarcopenia

	Parameter	Frailty Indicator
1.	Weight loss	> 10 lbs weight loss in one year
2.	Grip strength	Lowest 20% of population
3.	Exhaustion	Self report
4.	Walking speed	Lowest 20% of population
5.	Low activity	Males < 383 Kcals/week Females < 270 Kcals/week

*Frailty is defined as having three or more of the above criteria.

Morley JE et al. The Aging Male 2005;8(3/4):135-40

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Criteria for Dx of Frail Phenotype: metrics for HIV pts

Criteria	*Definition*			
Unintentional weight loss[a]	>10 pound weight loss documented in the last year or ≥5% of the previous body weight			
Physical inactivity	Subjects answering 3 when asked whether their health limits vigorous activities such as running, lifting heavy objects, participating in strenuous sports: 1=not at all, 2=yes, limited a little, or 3=yes, limited a lot			
Exhaustion	Subjects answering 2 or 3 to either one of two statements: How often have you felt that: (a) everything you did was an effort or (b) I could not ''get going'' 0=rarely (<1 day), 1=some of the time (1–2 days), 2=occasionally (3–4 days), or 3=most of the time (5–7 days)			
Weak grip strength	*Male*		*Female*	
	BMI kg/m²	*kg*	*BMI kg/m²*	*kg*
	≤24	≤29	≤23	≤17
	24.1–26.0	≤30	23.1–26.0	≤17.3
	26.1–28.0	≤30	26.1–29.0	≤18
	>28	≤32	>29	≤21
Slow walking time	*Male*		*Female*	
	Height (cm)	*Seconds*[b]	*Height (cm)*	*Seconds*
	≤173	≥7	≤159	≥7
	>173	≥6	>159	≥6

Escota GV et al. AIDS Res and Human Retroviruses 2015;31:313

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FRP and MACS Cohort: Results

- Low nadir CD4's increase risk of frailty (*Desquilbet AIDS 2009)*
- Prevalence of FP+ in untreated HIV+ males 55 yr old (3.9%) was similar to that of HIV-neg males >65 yrs old *(Desquilbet J Gerontol 2007)*
- Frailty is increased in HIV+ vs neg males > 50 yrs old *(Althoff J Gerontol 2014)*
- Asymptomatic HIV+ males with frailty pre-HAART are more likely to develop AIDS or die after Rx initiation c/w non-frail pts *(Desquilbet J Gerontol 2011)*
- Frailty is a dynamic process: HIV+ males who are frail are more likely than HIV-neg males to remain frail at followup *(Desquilbet J Gerontol 2011)*

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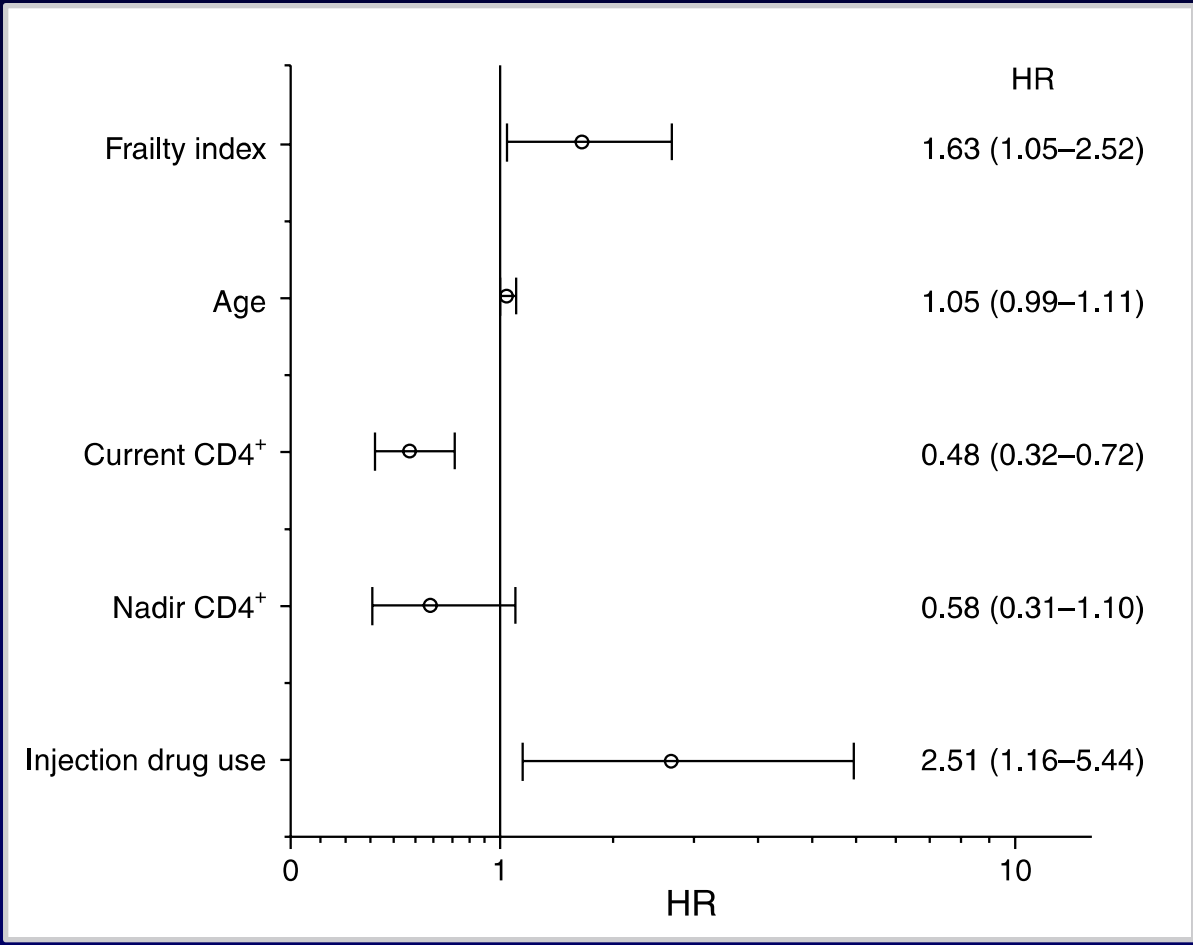
Cumulative deficit model of frailty : FI

- Frailty is related to the cumulative effects of general health deficits
- Frailty severity is described by the Frailty Index (FI) which refers to the proportion of deficits an individual has from a group of at least 30 commonly available health variables which *can vary* across clinical sites
- FI accurately and reliably predicts morbidity and mortality in the elderly
- Utility of using the FI to predict various clinical states in HIV disease is under evaluation

Rockwood, K et al BMC Geriatrics 2008

Frailty Index predicts survival in HIV patients



Guaraldi G et al. AIDS 2015;29:1633

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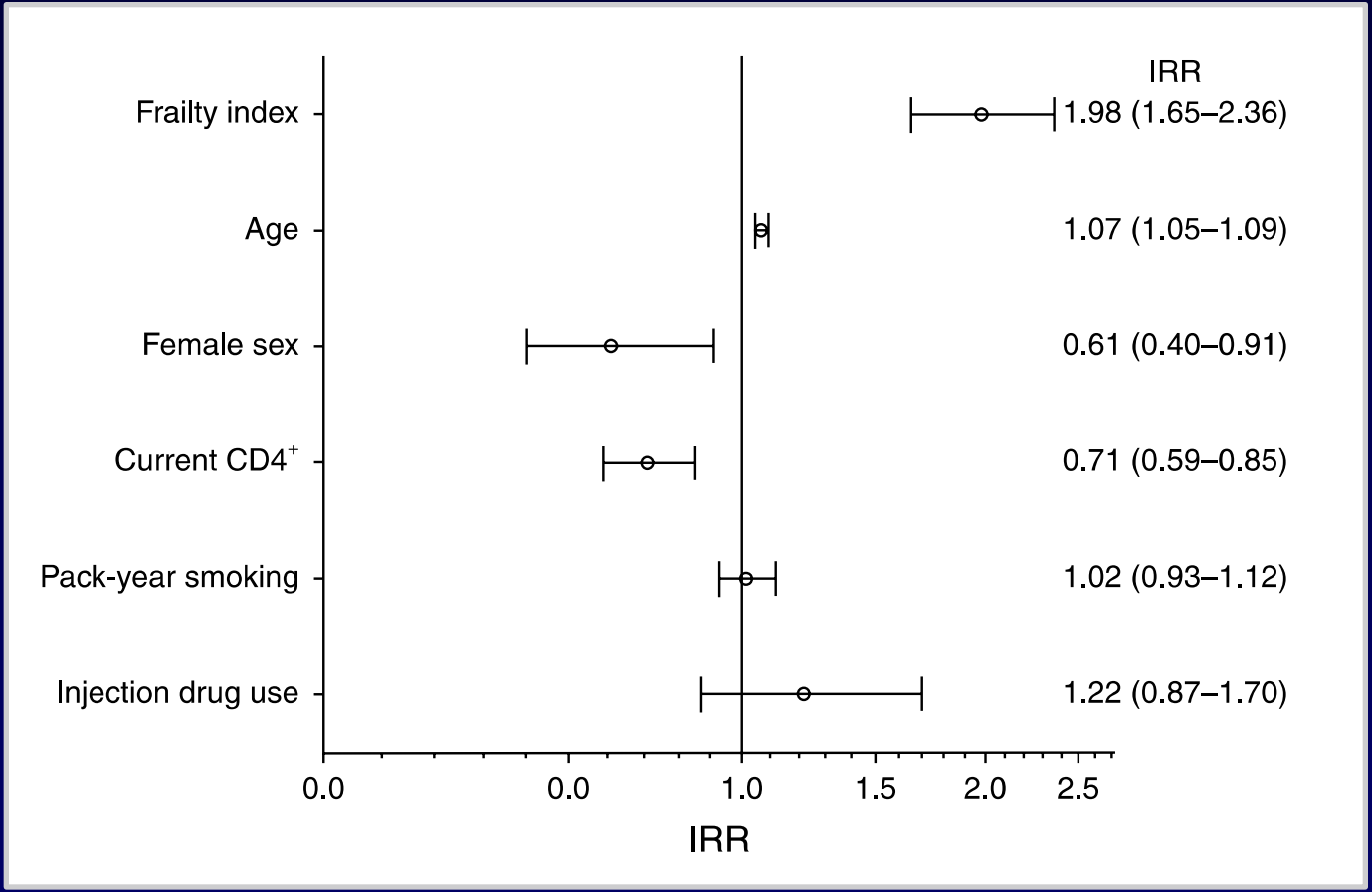
Frailty Index predicts development of multi-morbidity in HIV patients



Guaraldi G et al. AIDS 2015;29:1633

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VACS Index

Variables	*Value*	*Points*
Age (years)	< 50	0
	50–64	12
	≥ 65	27
CD4 (cells/mm^3)	≥ 500	0
	350–499	6
	200–349	6
	100–199	10
	50–99	28
	< 50	29
HIV-1 RNA (copies/ml)	< 500	0
	500–1×10^5	7
	≥ 1×10^5	14
Hemoglobin (g/dl)	≥ 14	0
	12–13.9	10
	10–11.9	22
	< 10	38
FIB-4[a]	< 1.45	0
	1.45–3.25	6
	> 3.25	25
eGFR (ml/min)[b]	≥ 60	0
	45–59.9	6
	30–44.9	8
	< 30	26
HCV infection[c]		5

Escota GV et al. AIDS Res and Human Retroviruses 2015;31:313

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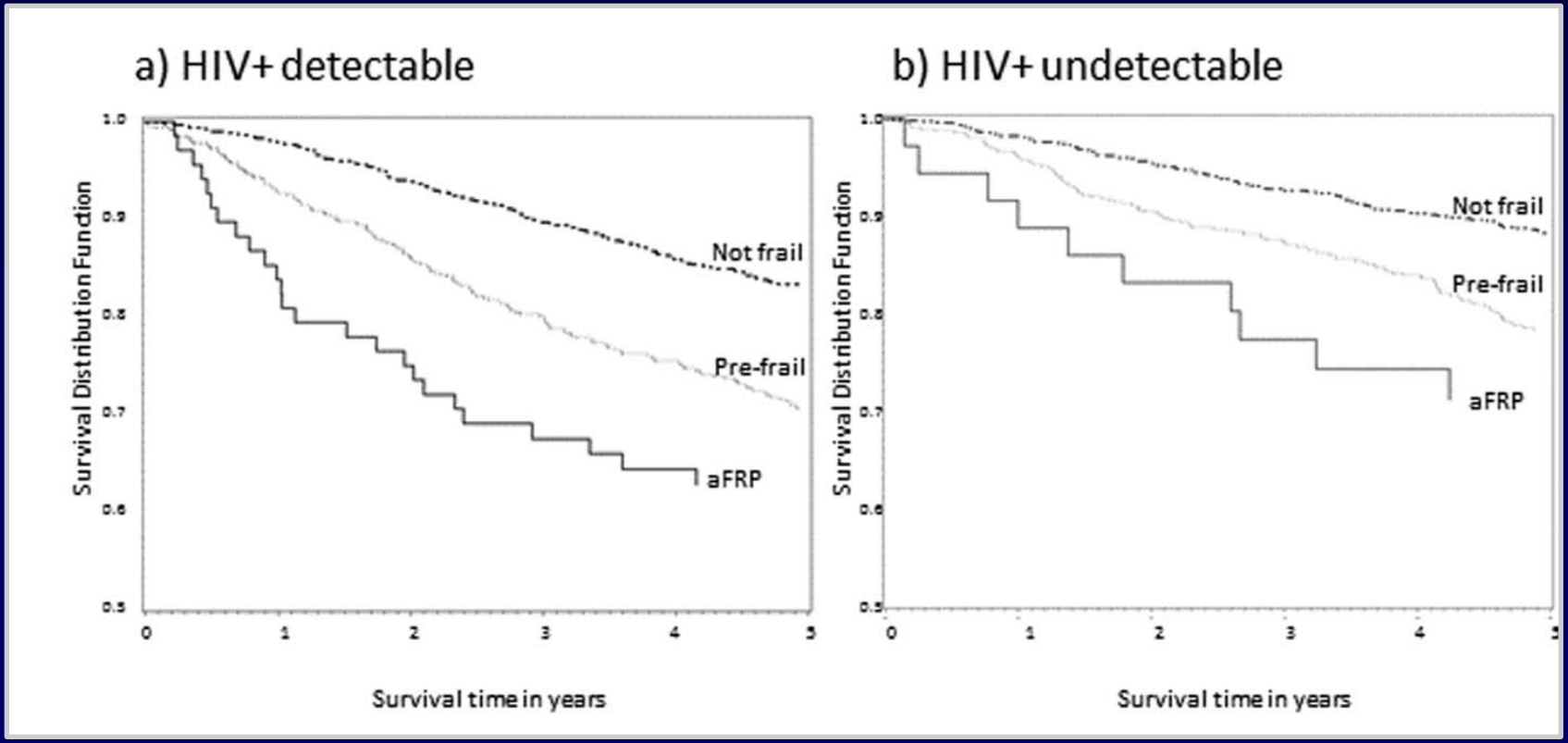
VACSI is associated with health problems often associated with frailty

The VACS-I betters predicts hospitalization and mortality than an adapted FRP :
Veterans Aging Cohort Study



Akgun KM et al. JAIDS 2014;67:397

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Is frailty in HIV patients, regardless of how it is diagnosed, the same clinical entity with the same biologic determinants as that described in the elderly?

Possibly

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Take home message regarding HIV and frailty

- Best tool to diagnose frailty- in evolution
- Are reliable biomarkers available- no
- Can HAART help avoid frailty- likely, but to be determined: treat early, treat safely, improve chronic inflammation
- *Interdisciplinary approach has always been most effective model of care* for complicated “AIDS” pts; the makeup of the team must evolve as the HIV pandemic matures and must include social workers, pharmacists, occupational and physical therapists, and access to geriatric support in addition to traditional medical care model

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HIV and Aging

Are the “50’s” the new “70’s”?

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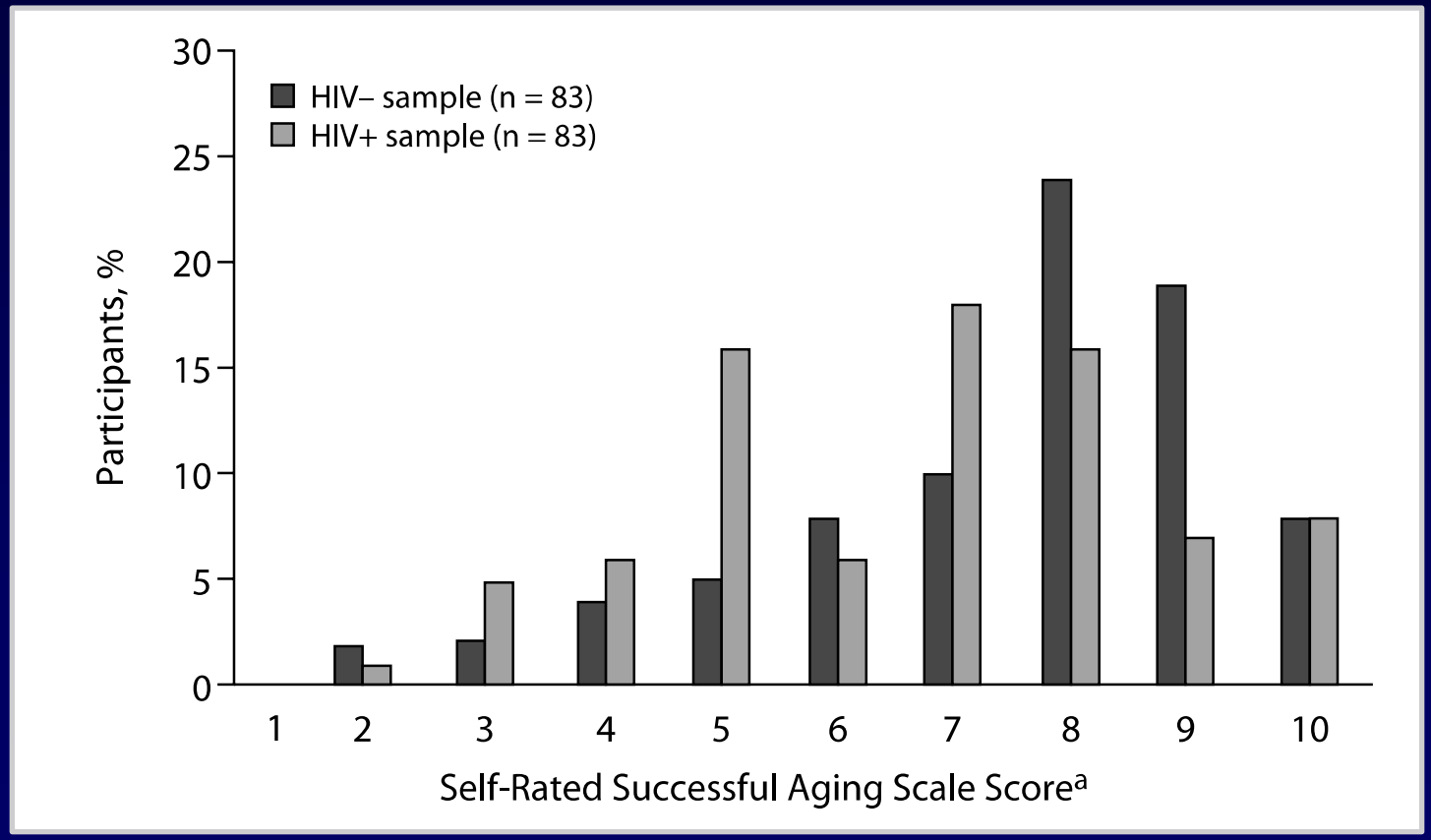
Self-rated successful aging scale in HIV+ vs HIV-neg older adults: 66% self-rated in upper portion of scale



Moore RC et al. J Clin Psychiatry 2013;74:e417

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Thank you