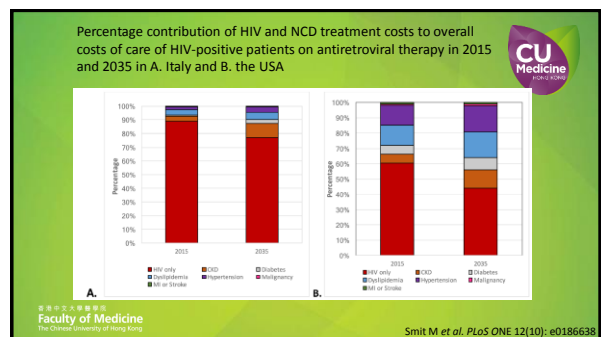
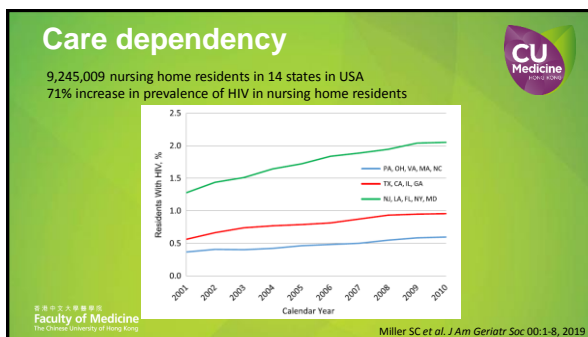
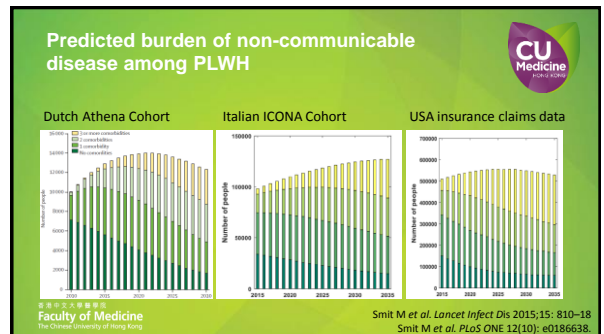
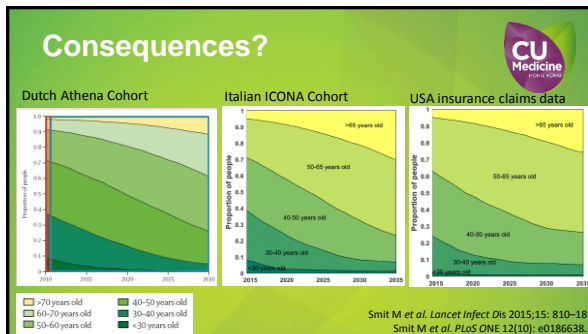
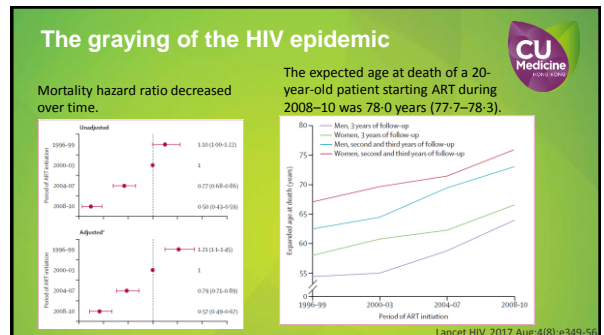


## HIV Infection and Aging

Grace Lui  
Assistant Professor  
Division of Infectious Diseases, Department of Medicine and Therapeutics  
Stanley Ho Centre for Emerging Infectious Diseases

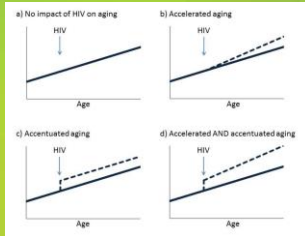
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Faculty of Medicine  
The Chinese University of Hong Kong

**CU Medicine**  
HONG KONG





## Is HIV associated with accelerated or accentuated aging?

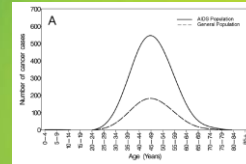


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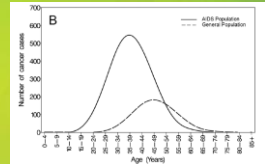
Sabin CA & Reiss P. *AIDS* 2017, 31 (Suppl 2):S121–S128

## Is HIV associated with accelerated or accentuated aging?

Accentuated aging



Accelerated and accentuated aging



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Pathai S et al. *J Gerontol A Biol Sci Med Sci* 2014 July;69(7):833–842

## Do PLWH develop age-related diseases at an earlier age?

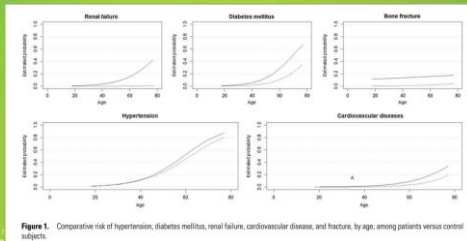
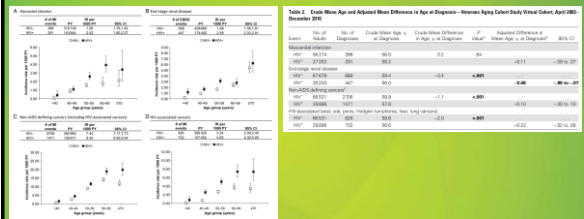


Figure 1. Comparative risk of hypertension, diabetes mellitus, renal failure, cardiovascular disease, and fracture, by age, among patients versus control subjects.

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Clinical Infectious Diseases 2011;53(11):1120–6

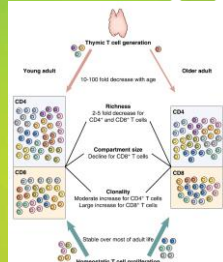
## Do PLWH develop age-related diseases at an earlier age?



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Althoff KN et al. *Clin Infect Dis*. 2015;60(4):627–38

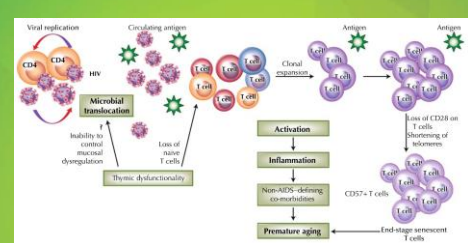
## Immunosenescence in aging



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Goronzy JJ et al. *The Journal of Immunology* 2015, 194: 4073–4080

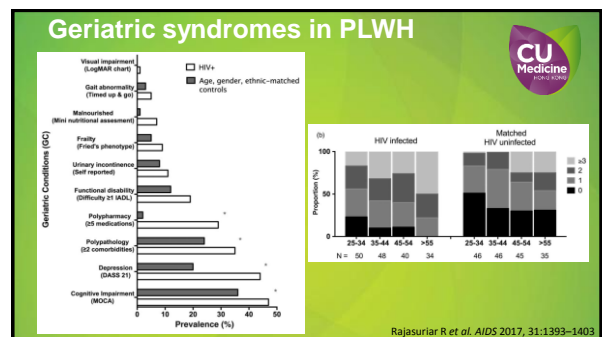
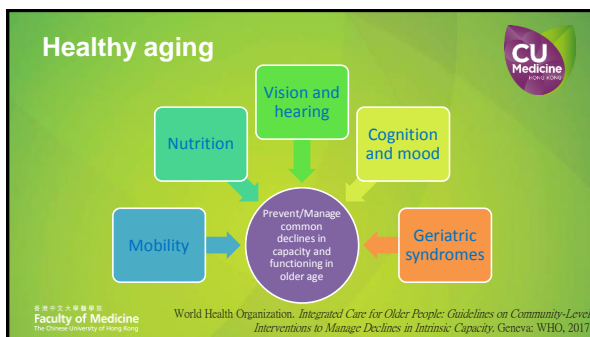
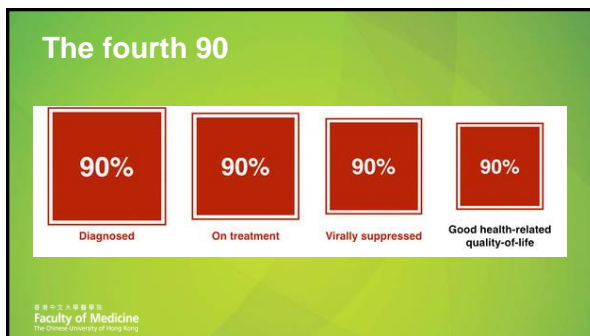
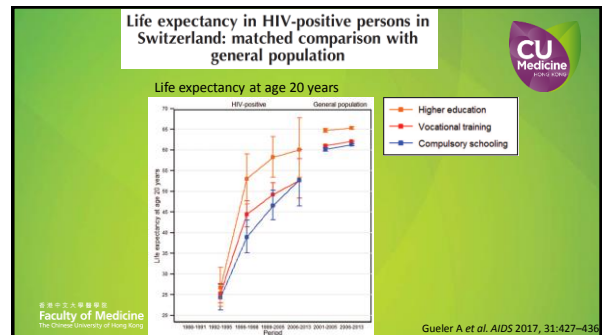
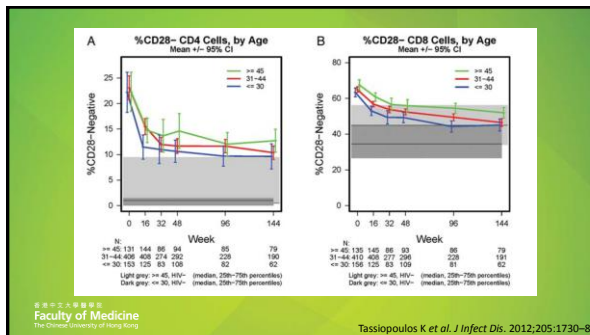
## Immunosenescence in HIV



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Desai S et al. *Curr HIV/AIDS Rep* (2010) 7:4–10







## Multimorbidity

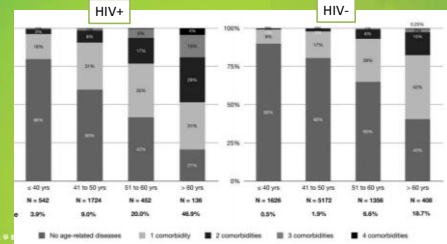
Presence of two or more comorbidities

Cardiovascular disease  
Diabetes mellitus  
Hypertension  
Chronic obstructive pulmonary disease  
Cirrhosis  
Anemia  
Obesity  
Chronic kidney disease  
Osteopenia/Osteoporosis

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Guaraldi G et al. *Curr Opin HIV AIDS* 2014;9(4):386-97

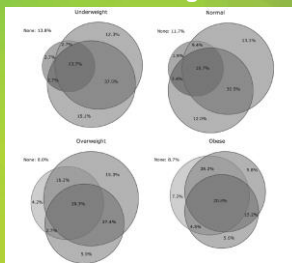
## Age-related comorbidities



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Clinical Infectious Diseases 2011;53(11):1120-6

## Chronic disease clustering in PLWH

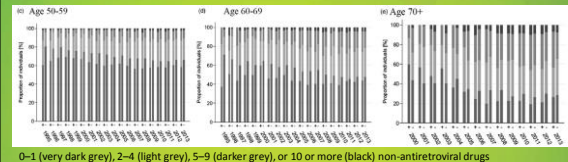


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The Chinese University of Hong Kong

Kim D et al. *J Acquir Immune Defic Syndr* 2012;61:600-605

## Polypharmacy

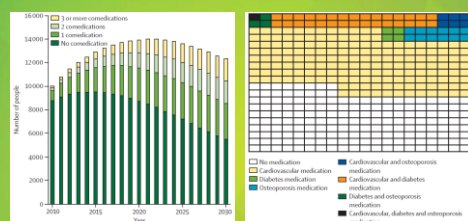
- Use of  $\geq 5$  concomitant (non-ARV) medications
- More common in PLWH



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The Chinese University of Hong Kong

Rasmussen LD et al. *Infectious Diseases* 2017;49(1): 42-54

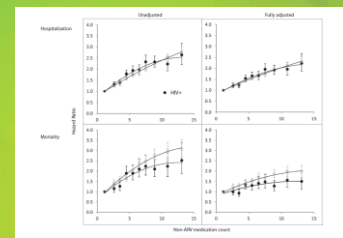
## Co-medications in PLWH



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The Chinese University of Hong Kong

Smit M et al. *Lancet Infect Dis* 2015;15: 810-18

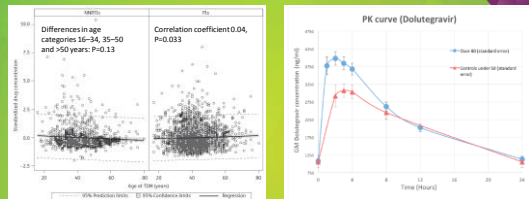
## Polypharmacy and adverse outcomes



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Justice AC et al. *AIDS* 2018; 32:739-740





Elliot ER et al. Clin Infect Dis. 2019;68(1):87–95



Drug class	Pharmacodynamic issues	Recommendations
Anti-hypertensives	Orthostatic hypotension	Start with lower dose and titrate
Beta-blockers	Beta-receptor function	May require higher dose
Diuretics	Sensitivity to drug effect	Monitor BP / electrolytes
Benzodiazepines	Sensitivity (sedation at lower doses and lower concentrations, postural sway)	Use at lowest dose and for a short duration
Opioids	Sensitivity (risk of respiratory depression)	Use with caution at the lowest efficient dose
Anticholinergic drugs	Sensitivity (anticholinergic adverse reactions: constipation, dry mouth, urinary incontinence, delirium)	Avoid
Vitamin K antagonists	Effect (inhibition of synthesis of vitamin K dependent clotting factors)	Start with lower dose and adjust dose based on INR

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Marzolini C et al. *Expert Rev Clin Pharmacol*. 2019 Jun 3

Initial treatment	Adverse drug reaction	Subsequent treatment
Nitrofur	Rise in blood pressure	Antihypertensive
ATC antibiotic	Cough	Cough suppressant, antibiotic
Thiazide diuretic	Hypertension, gout	Allopurinol, cefixime
Antacid	Edema	Diuretic
Rota blocker	Depression	Antidepressant
Antiparkinsonian	Dizziness	Prochlorperazine
Erythromycin	Acetylenia	Antacids/analgesic
Quinine	Delirium	Antipsychotic
Contraceptive inhibitor	Incontinence	Anticholinergic
Contraceptive inhibitor	Vertigo	Anticholinergic
Contraceptive inhibitor	Diarrhea	Antidiarrheal
SNI/SNI	Bones	Bonecalciferol
Tetracycline antidepressant	Decreased cognition	Contraceptive inhibitor
Tetracycline	Constipation	Laxative
Meprobamate	Delirium	Antipsychotic
Lithium	Finger	Preparations
Meclofenamate	Unpleasant effect	Antiparkinsonian agent
Antipsychotic	Unpleasant effect	Antiparkinsonian agent

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Marzolini C *et al. Expert Rev Clin Pharmacol*. 2019 Jun 3;

- A distinct clinical syndrome
- Characterized by diminished strength, endurance, and physiologic function
- Increases an individual's vulnerability for developing increased dependency and death

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Table 1. Operationalizing a Phenotype of Frailty

A. Characteristics of Frailty	B. Cardiovascular Health Study Measure <sup>a</sup>
Shrinking: Weight loss (intermediate or Severe)	Baldwin: >10 lbs lost unintentionally in prior year
Sarcopenia (loss of muscle mass)	
Weakness	Grip strength: lowest 20% (by gender, body mass index)
Poor endurance; Exhaustion	"Exhausted" (self-report)
Slowness	Walking 100 ft: slowest 20% (by gender, height)
Low activity	Kcal/week: lowest 20% males: <383 Kcal/week females: <270 Kcal/week
	C. Presence of Frailty
	Positive for frailty phenotype: $\geq 3$ criteria present
	Intermediate or prefrail: 1 or 2 criteria present

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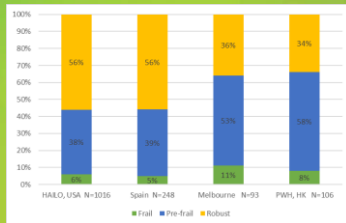
Fried LP et al. *J Gerontol* 2001[illegible]

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The Chinese University of Hong Kong

Rockwood K et al. J Gerontol 2007  
Yeoh HL et al. Antiviral Therapy 2018



## Prevalence of frailty and pre-frailty



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Kelly SG et al. Clin Infect Dis. 2019  
Yeoh HL et al. Antiviral Therapy 2018  
Blanco JR et al. PLoS ONE 2019;14(5):e0215764

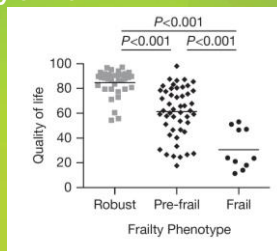
## Factors associated with frailty

Demographics	Age
	Female (menopause)
Comorbidities	Diabetes
	Depression
	Cognitive impairment
HIV-related	History of AIDS
	Pre-1996 ART
Inflammation	C reactive protein

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Morgello S et al. AIDS 2019  
Yeoh HL et al. Antiviral Therapy 2018  
Blanco JR et al. PLoS ONE 2019;14(5):e0215764

## Frailty associated with poorer outcomes and quality of life

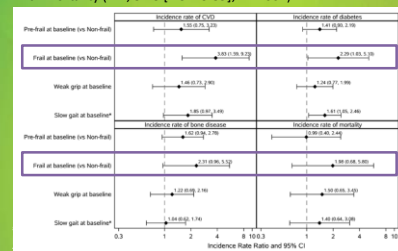


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Yeoh HL et al. Antiviral Therapy 2018

## Clinical implications of frailty

An increase in frailty from baseline to week 48 was significantly associated with mortality (IRR, 3.78 [1.52–9.39];  $P = .004$ )



Kelly SG et al. Clin Infect Dis. 2019

## Sarcopenia

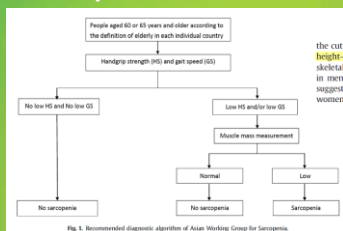


Fig. 1. Recommended diagnostic algorithm of Asian Working Group for Sarcopenia.

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Chen LK et al. JAMDA 15 (2014) 95e101

## Measurement of muscle mass

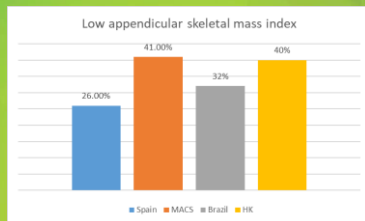


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Chen LK et al. JAMDA 15 (2014) 95e101



## Prevalence of sarcopenia in PLWH

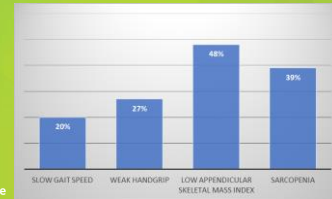


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Echeverria P et al. BioMed Research International 2018:5074923  
Hawkins KL et al. AIDS. 2018 Jun 19;32(10):1257-1266  
Mialch MS et al. J Clin Densitom. 2017 Jan - Mar;20(1):73-81

## Muscle mass and strength in PLWH in Hong Kong

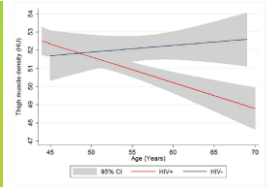
136 PLWH aged 50 years or above



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## HIV Infection Is Associated with Increased Fatty Infiltration of the Thigh Muscle with Aging Independent of Fat Distribution

Javzandulam Natsag<sup>1\*</sup>, Kristine M. Erlandson<sup>2\*</sup>, Deborah E. Selimeyer<sup>3</sup>, Sabina A. Haberlen<sup>4</sup>, Joseph Margolick<sup>5</sup>, Lisa P. Jacobson<sup>6</sup>, Frank J. Palella, Jr<sup>6</sup>, Susan L. Koletar<sup>7</sup>, Jordan E. Lake<sup>8</sup>, Wendy S. Post<sup>1</sup>, Todd T. Brown<sup>1\*</sup>

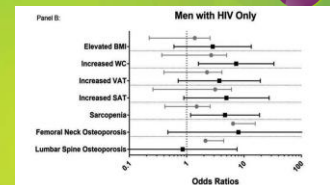


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PLoS ONE 2017; 12(1): e0169184.

## Sarcopenia in PLWH is associated with:

- Age
- Female
- Obesity
- Osteoporosis
- Lipodystrophy
- Duration on D-drugs
- Nadir CD4
- Frailty



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Echeverria P et al. BioMed Research International 2018:5074923  
Hawkins KL et al. AIDS. 2018 Jun 19;32(10):1257-1266  
Mialch MS et al. J Clin Densitom. 2017 Jan - Mar;20(1):73-81  
Abdul Aziz et al. AIDS 2018. 32:1025-1034

## Poor health outcomes associated with sarcopenia

Health outcomes	Multiple linear regression <sup>a</sup>	
	Coefficient (95% CI)	P value
Mortality risk <sup>b</sup>	5.42 (1.46–9.37)	<b>0.007</b>
Quality of life <sup>c</sup>	–1.83 (–4.19 to 0.52)	0.126
Healthcare utilization <sup>d</sup>	–0.81 (–2.84 to 1.23)	0.435
Functional disability <sup>e</sup>	3.95 (1.57–9.97)	<b>0.004</b>
Falls <sup>f</sup>	1.22 (0.35–3.62)	0.842

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Abdul Aziz et al. AIDS 2018. 32:1025–1034

## Impact of HIV and aging on functioning / disability

**Table 1.** Comparison of Katz ADLs and Lawton IADLs

Activities of Daily Living (ADLs)	Instrumental Activities of Daily Living (IADLs)
Feeding	Using the telephone
Continence	Shopping
Transferring	Preparing food
Toileting	Housekeeping
Dressing	Doing laundry
Bathing	Using transportation
	Handling medications
	Handling finances

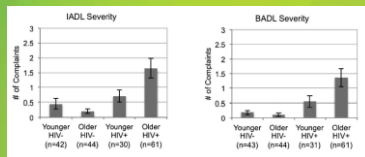
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Graf C. AJN April 2008 Vol. 108, No. 4



### Synergistic Effects of HIV Infection and Older Age on Daily Functioning

Erin E. Morgan, PhD,\* Jennifer E. Indicello, PhD,\* Erica Weber, MS,† Nichole A. Duarte, PhD,\* P. Katie Riggs, BS,‡ Lisa Delano-Wood, PhD,\*§ Ronald Ellis, MD, PhD,‡ Igor Grant, MD,\* and Steven P. Woods, PhD,\* For The HIV Neurobehavioral Research Program (HNRP) Group



#### Disability in PLWH:

- older age
- low CD4 cell count
- Depression
- low physical activity
- neurocognitive decline

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Morgan EE et al. J Acquir Immune Defic Syndr 2012;61:341-348  
Hawkins KL et al. AIDS. 2017 June 01; 31(Suppl 2): S137-S146

### Frailty index predicts quality of life in Chinese people living with HIV

Lui G<sup>1</sup>, Kwok T<sup>1</sup>, Wong A<sup>1</sup>, Cheung CSK<sup>1</sup>, Wong RYK<sup>1</sup>, Chan WL<sup>1</sup>, Yung I<sup>1</sup>, Guaraldi G<sup>2</sup>

<sup>1</sup>Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong SAR.

<sup>2</sup>Department of Medical and Surgical Sciences for Adults and Children, Clinic of Infectious Diseases, University of Modena and Reggio Emilia, Modena, Italy

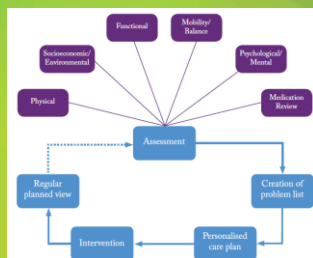
Variables	Results
Number	52
Male	46 (88.5%)
Age, years (median, IQR)	61.5 (56 - 65)
Chinese	52 (100%)
Multi-morbidity (presence of ≥2 comorbidities)	23 (45.1%)
Polypharmacy (≥5 medications)	21 (40.4%)
Depression (CESD ≥16)	18 (36.0%)
Fried phenotype	
Robust	6 (11.8%)
Pre-frail	39 (76.5%)
Frail	6 (11.8%)
Frailty index	0.31 ± 0.088

Multivariable linear regression model showing variables associated with QOL

Variables	$\beta$	p
Frailty index	-61.91	0.005
Diabetes	-8.00	0.036
Depression	-8.66	0.030

HIV and Aging Workshop, NY 2018

### Comprehensive geriatric assessment



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British Geriatrics Society

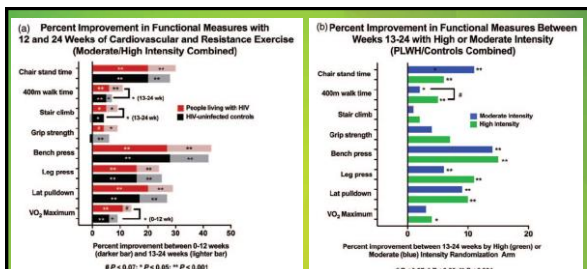
### Physical function improvements with moderate or high-intensity exercise among older adults with or without HIV infection

Kristine M. Erlandson<sup>a,b</sup>, Samantha MaWhinney<sup>c</sup>, Melissa Wilson<sup>c</sup>, Lilyana Gross<sup>c</sup>, Sean A. McCandless<sup>a,b</sup>, Thomas B. Campbell<sup>a</sup>, Wendy M. Kohrt<sup>b,d</sup>, Robert Schwartz<sup>b,d</sup>, Todd T. Brown<sup>e</sup> and Catherine M. Jankowski<sup>f</sup>



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AIDS. 2018 Oct 23;32(16):2317-2326



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The Chinese University of Hong Kong

AIDS. 2018 Oct 23;32(16):2317-2326

### Research gaps

- The burden and impact on health in the aging PLWH started on contemporary regimens
- Pathogenesis of accelerated / accentuated aging in PLWH
  - Implications on monitoring and therapeutics
- Most effective/efficient strategies to monitor the aging process in the clinic
- Interventions to prevent and manage geriatric syndromes and prevent disability

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