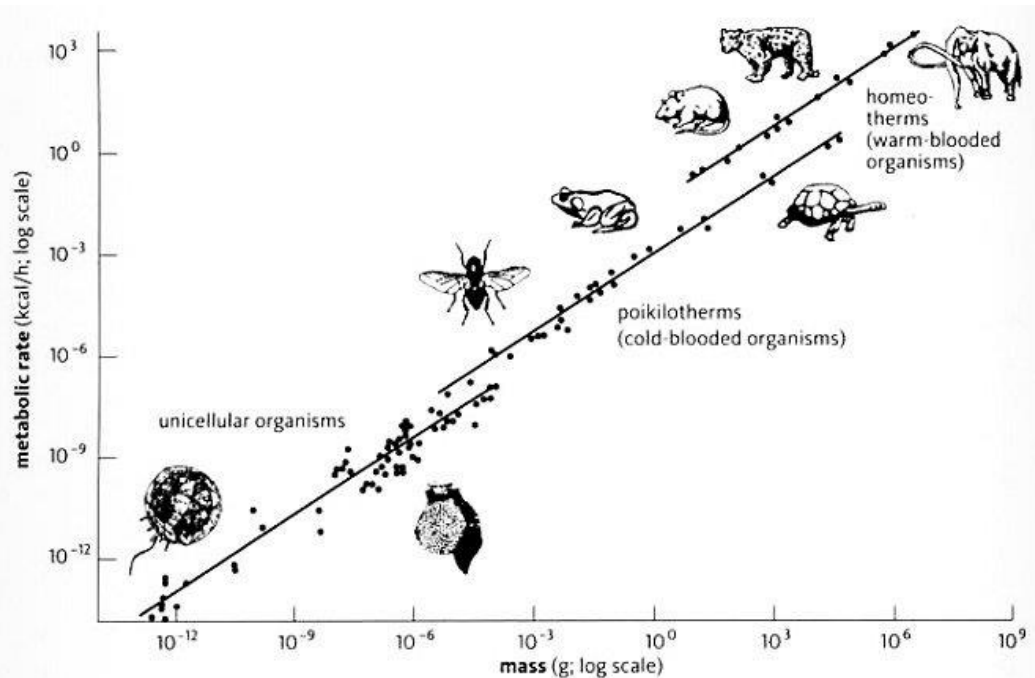


HIV-Infection Attenuates the Age Associated Decline in Resting Metabolic Rate

Jennifer Schrack, PhD

Rate-of-Living Theory:

(Max Rubner, 1908)



1 kcal/h = 1.162 watts

- Slower rate of metabolism associated with greater longevity
 - Smaller animals have greater rate of metabolism per body mass & have shorter life span
- (Harris & Benedict, 1938)

Higher Energy Expenditure in Humans Predicts Natural Mortality

Reiner Jumpertz, Robert L. Hanson, Maurice L. Sievers, Peter H. Bennett, Robert G. Nelson, and Jonathan Krakoff

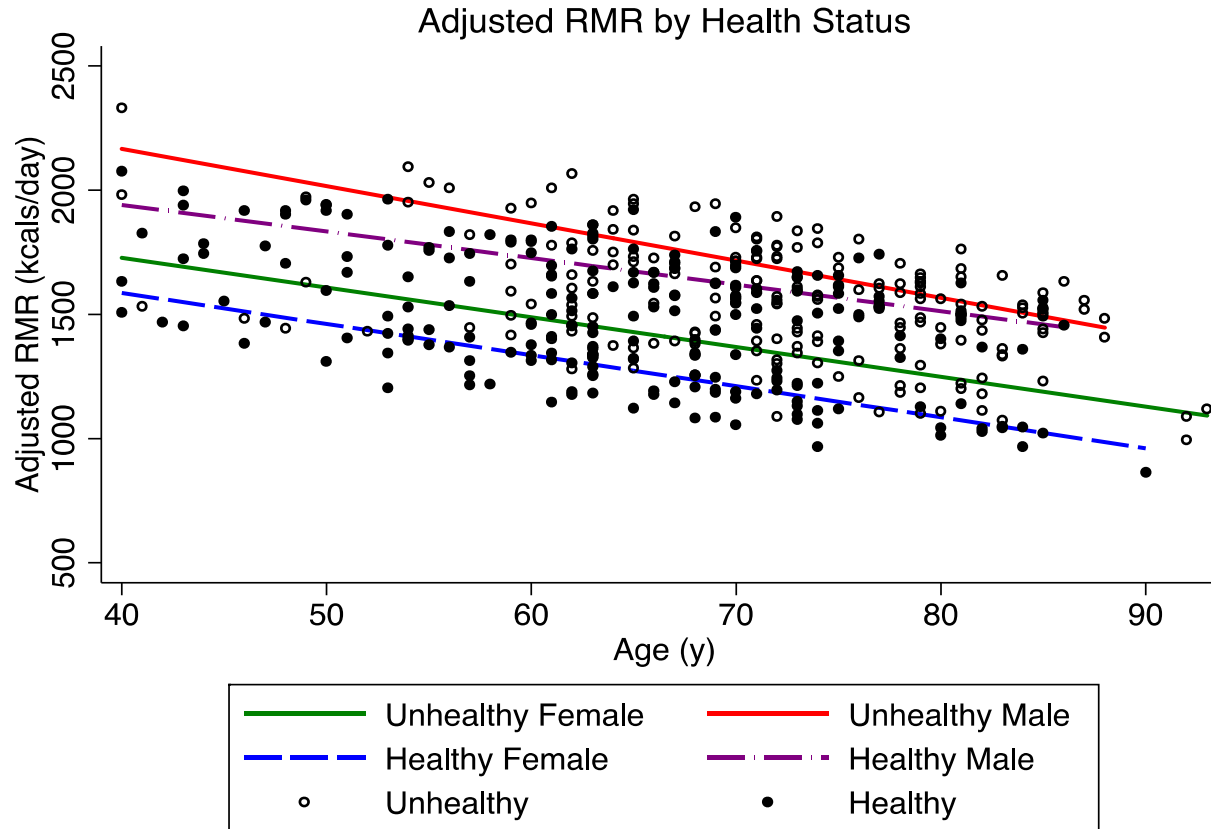
Design: Nondiabetic healthy Pima Indian volunteers ($n = 652$) were admitted to an inpatient unit for approximately 7 d as part of a longitudinal study of obesity and diabetes risk factors. Vital status of study participants was determined through December 31, 2006. Twenty-four-hour energy expenditure (24EE) was measured in 508 individuals, resting metabolic rate (RMR) was measured in 384 individuals, and 240 underwent both measurements on separate days. Data for 24EE were collected in a respiratory chamber between 1985 and 2006 with a mean (SD) follow-up time of 11.1 (6.5) yr and for RMR using an open-circuit respiratory hood system between 1982 and 2006 with a mean follow-up time of 15.4 (6.3) yr. Cox regression models were used to test the effect of EE on natural mortality, controlled for age, sex, and body weight.

Results: In both groups, 27 natural deaths occurred during the study period. For each 100-kcal/24 h increase in EE, the risk of natural mortality increased by 1.29 (95% confidence interval = 1.00–1.66; $P < 0.05$) in the 24EE group and by 1.25 (95% confidence interval = 1.01–1.55; $P < 0.05$) in the RMR group, after adjustment for age, sex, and body weight in proportional hazard analyses.

Conclusions: Higher metabolic rates as reflected by 24EE or RMR predict early natural mortality, indicating that higher energy turnover may accelerate aging in humans. (*J Clin Endocrinol Metab* 96: E972–E976, 2011)

“IDEAL” Aging Is Associated with Lower Resting Metabolic Rate: The Baltimore Longitudinal Study of Aging

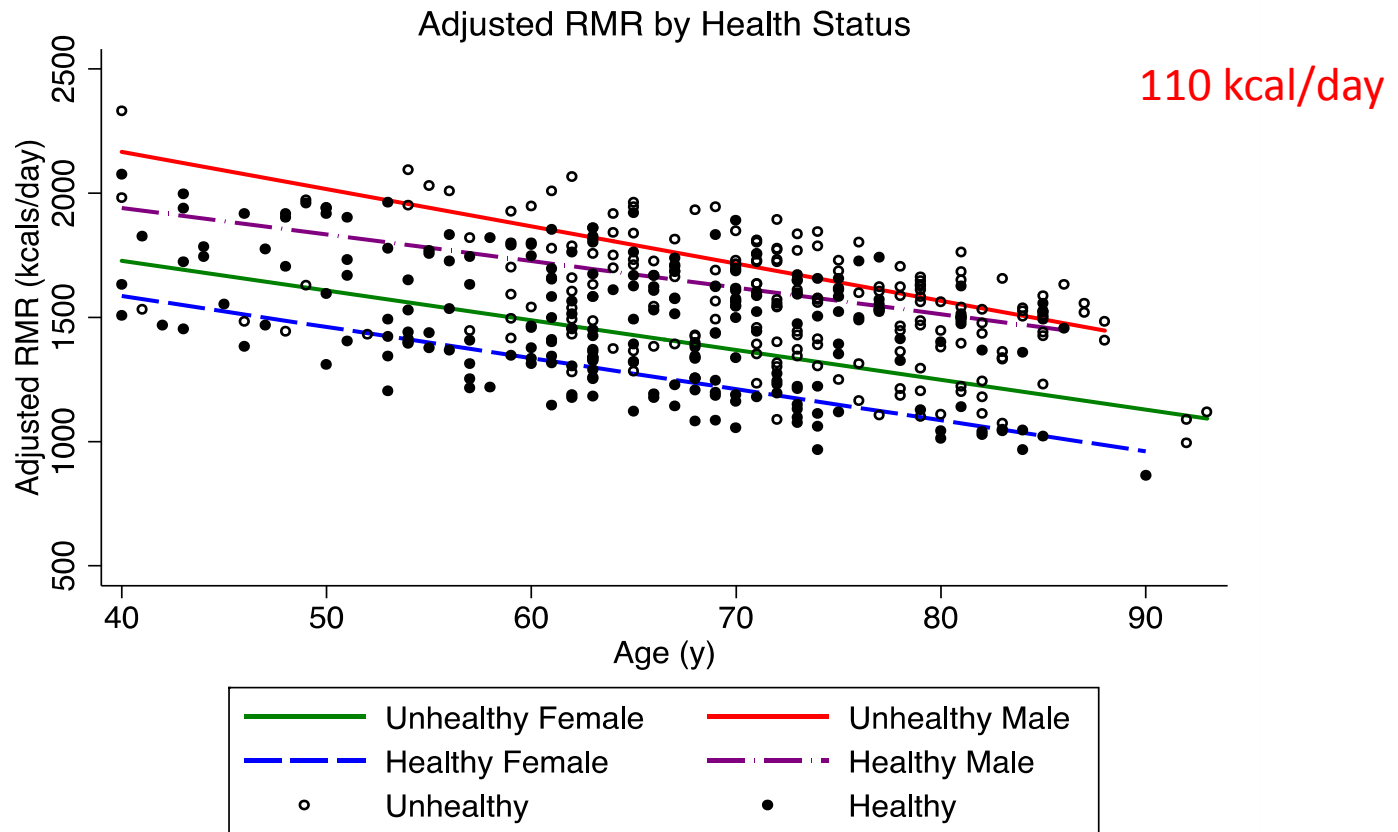
Jennifer A. Schrack, PhD,^{*†} Nicolas D. Knuth, PhD,[‡] Eleanor M. Simonsick, PhD,[†] and Luigi Ferrucci, MD, PhD[†]



Data from the Baltimore Longitudinal Study of Aging showing Resting Metabolic Rate (kcal per day) stratified by sex and health status, adjusted for lean and fat mass (N = 420)

“IDEAL” Aging Is Associated with Lower Resting Metabolic Rate: The Baltimore Longitudinal Study of Aging

Jennifer A. Schrack, PhD,^{*†} Nicolas D. Knuth, PhD,[‡] Eleanor M. Simonsick, PhD,[†] and Luigi Ferrucci, MD, PhD[†]



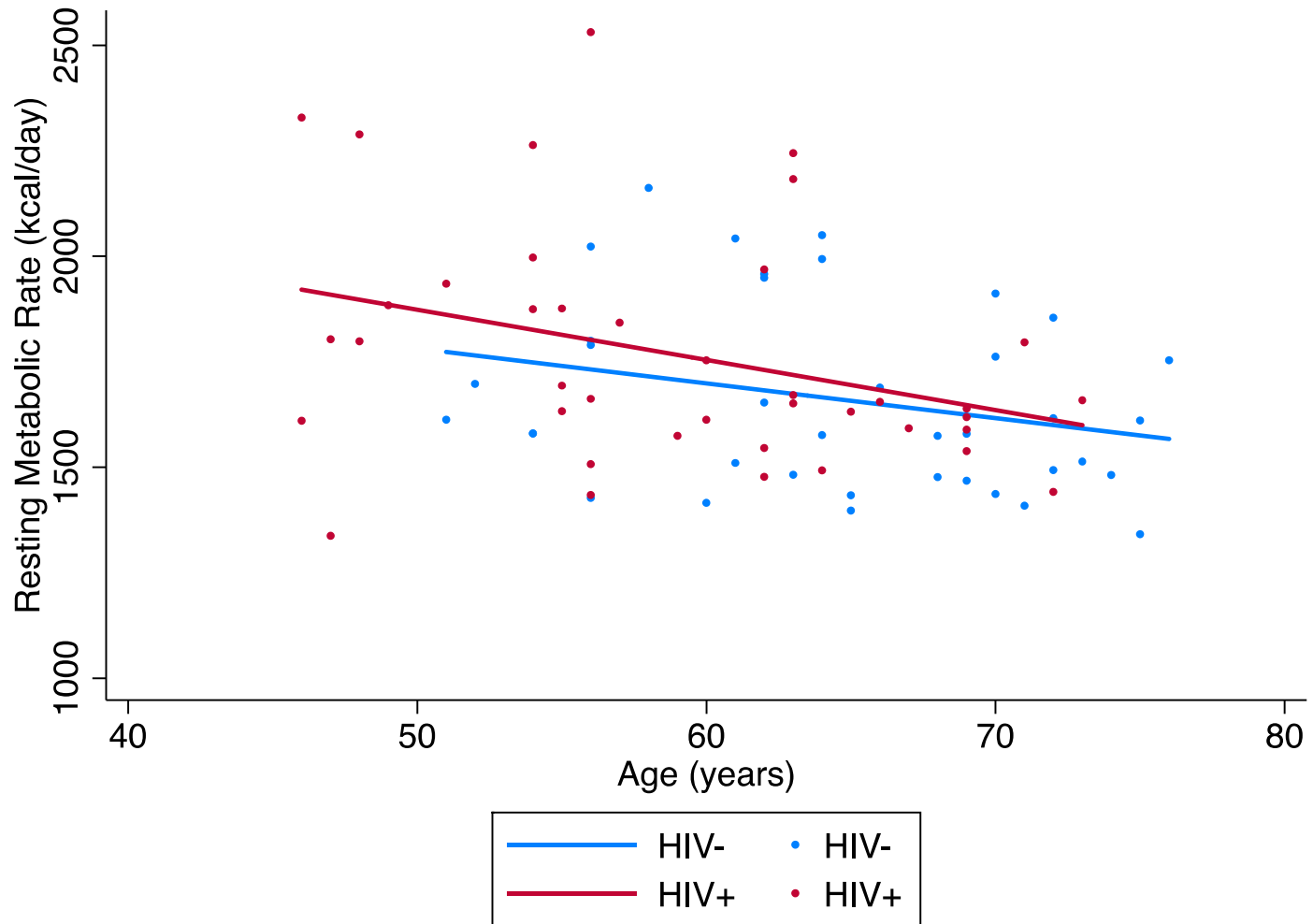
Data from the Baltimore Longitudinal Study of Aging showing Resting Metabolic Rate (kcal per day) stratified by sex and health status, adjusted for lean and fat mass (N = 420)



Resting Metabolic Rate in the Baltimore/Washington MACS

	HIV +	HIV -	P-value
N	40	35	
Age (years)	58.5	64.5	< 0.01
Age range	43 – 73	51 - 76	
Race (% black)	57.5%	22.9%	< 0.01
BMI (kg/m²)	27.0	27.7	0.60
Extremity fat mass (kg)	11.6	13.3	0.18
Trunk fat mass (kg)	16.1	16.1	0.70
Lean mass (kg)	53.2	51.8	0.40
Diabetes (%)	22.5%	14.3%	0.36
EGFR (ml/min/1.73m²)	79.7	90.3	0.04
RMR (kcal)	1748	1668	0.20
Nadir CD4 (cells/ul)	308.2		
Peak viral load (copies/ml)	159,829	(93% suppressed)	

Unadjusted Resting Metabolic Rate (kcal/day) in MACS Participants by HIV-Serostatus



Combined Regression Model of the Association between HIV and RMR

Dependent variable: Resting Metabolic Rate (kcal/day)

N = 75 (40 HIV+, 35 HIV-)

Independent variables:	Coefficient	S.E.	p-value
HIV	66.1	47.2	0.17
Age	-3.7	2.8	0.20
Lean mass (kg)	15.9	4.5	< 0.01
Fat mass (kg)	6.2	2.8	0.03
Diabetes (y/n)	105.3	58.7	0.08
EGFR (ml/min/1.73m ²)	2.1	1.0	0.04
Intercept	674.1	328.8	0.04

Combined Regression Model of the Association between HIV and RMR

Dependent variable: Resting Metabolic Rate (kcal/day)

N = 75 (40 HIV+, 35 HIV-)

Independent variables:	Coefficient	S.E.	p-value
HIV	86.7	44.7	0.05
Lean mass (kg)	17.1	4.4	< 0.01
Fat mass (kg)	5.9	2.8	0.04
Diabetes (y/n)	117.7	58.3	0.04
EGFR (ml/min/1.73m ²)	2.4	1.0	0.02
Intercept	361.8	225.6	0.11

Stratified Regression Model of the Association between HIV and RMR

Dependent variable: Resting Metabolic Rate (kcal/day)

	HIV+ n = 40			HIV- n = 35		
Independent variables:	Coefficient	S.E.	p-value	Coefficient	S.E.	p-value
Age	- 2.1	3.9	0.59	-9.8	3.4	< 0.01
Lean mass (kg)	21.5	5.4	< 0.01	- 0.9	6.9	0.90
Fat mass (kg)	2.6	3.6	0.48	18.0	3.7	< 0.01
Diabetes (y/n)	225.4	76.1	< 0.01	-171.8	75.4	0.03
EGFR (ml/min/1.73m ²)	4.5	1.6	< 0.01	-0.84	1.1	0.44
Intercept	240.1	428.4	0.58	1880.8	417.8	< 0.01

Difference in RMR driven by metabolic complications?

HIV+

- 60 y.o. man
- 60 kg lean mass
- 30 kg fat mass (33%)
- Diabetic
- EGFR = 90 ml/min/1.73m²
- RMR = 2114 kcal/day

HIV-

- 60 y.o. man
- 60 kg lean mass
- 30 kg fat mass (33%)
- Diabetic
- EGFR = 90 ml/min/1.73m²
- RMR = 1530 kcal/day

Difference = 584 kcal/day

Difference in RMR driven by metabolic complications?

HIV+

- 60 y.o. man
- 60 kg lean mass
- 30 kg fat mass (33%)
- Non-Diabetic
- EGFR = 90 ml/min/1.73m²
- RMR = 1889 kcal/day

HIV-

- 60 y.o. man
- 60 kg lean mass
- 30 kg fat mass (33%)
- Non-Diabetic
- EGFR = 90 ml/min/1.73m²
- RMR = 1702 kcal/day

Difference = 187 kcal/day

Residuals Analysis

(measured vs. predicted)

- Possible link to viral control?
- Non-suppressed were on average 76 kcals/day higher than suppressed
- Among HIV+, those with higher than expected RMR:
 - Tended to have lower nadir CD4 (253 cells/ul vs. 344 cells/ul, $p = 0.24$)
 - No effect of viral load, either concurrent or cumulative

Conclusions

- HIV appears to attenuate the age-related decline in resting metabolic rate
- Metabolic comorbidities exacerbate this effect (diabetes, kidney function)
- Potential for a link with viral control
- Greater sample size is needed for more in-depth analyses

Acknowledgements

CFAR/K01 Mentors

Joseph Margolick, MD PhD

Todd Brown, MD PhD



NIA/K01 Mentor

Luigi Ferrucci, MD PhD



JHU CRU/SHARE Staff

Bobbie Barron, RD, LDN

Robin Lincoln

Jacquett Johnson

Lisette Johnson-Hill, MS



Funding: JHU CFAR 1P30AI094189 - 01A1 (Chaisson), NIA K01AG048765

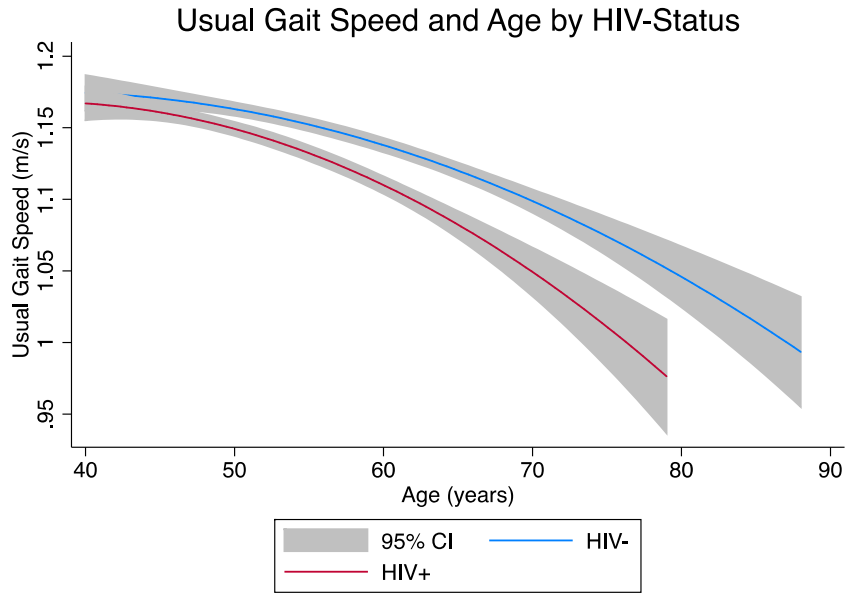
Combined Regression Model of the Association between HIV and RMR

Dependent variable: Resting Metabolic Rate (kcal/day)

N = 75 (40 HIV+, 35 HIV-)

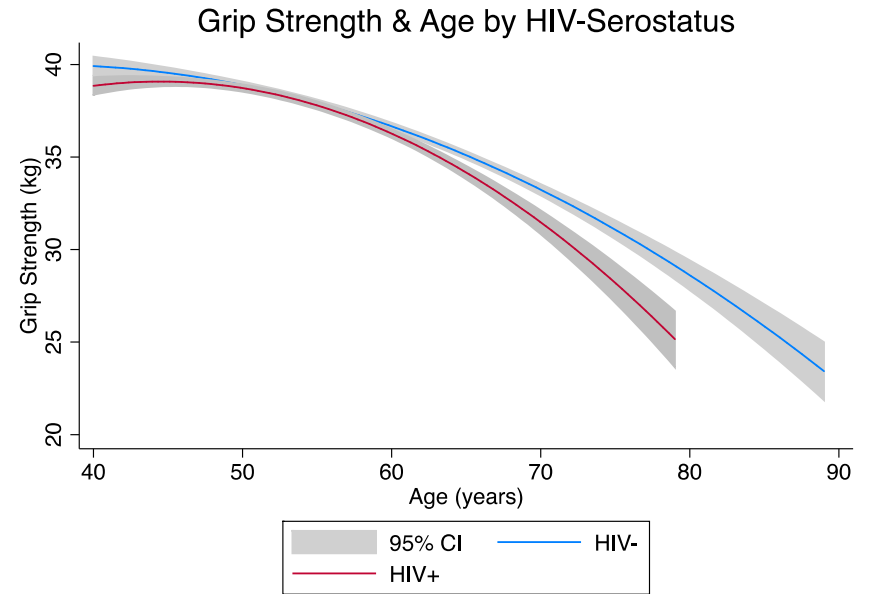
Independent variables:	Coefficient	S.E.	p-value
Age	-5.0	2.7	0.06
Lean mass (kg)	16.6	4.5	< 0.01
Fat mass (kg)	5.4	2.7	0.05
Diabetes (y/n)	109.7	59.1	0.07
EGFR (ml/min/1.73m ²)	1.8	1.0	0.08
Intercept	806.5	317.1	0.01

Evidence of Accelerated Decline



Schrack et al, JAIDS, 2015

57% greater risk of slowed gait (< 1.0 m/s)



Schrack et al, AIDS, 2016

70% greater risk of clinical weakness (< 26 kg)



Energy Metabolism and the Burden of Multimorbidity in Older Adults: Results From the Baltimore Longitudinal Study of Aging

Elisa Fabbri,^{1,2} Yang An,¹ Jennifer A. Schrack,^{1,3} Marta Gonzalez-Freire,¹ Marco Zoli,² Eleanor M. Simonsick,¹ Jack M. Guralnik,⁴ Cynthia M. Boyd,⁵ Stephanie A. Studenski,¹ and Luigi Ferrucci¹

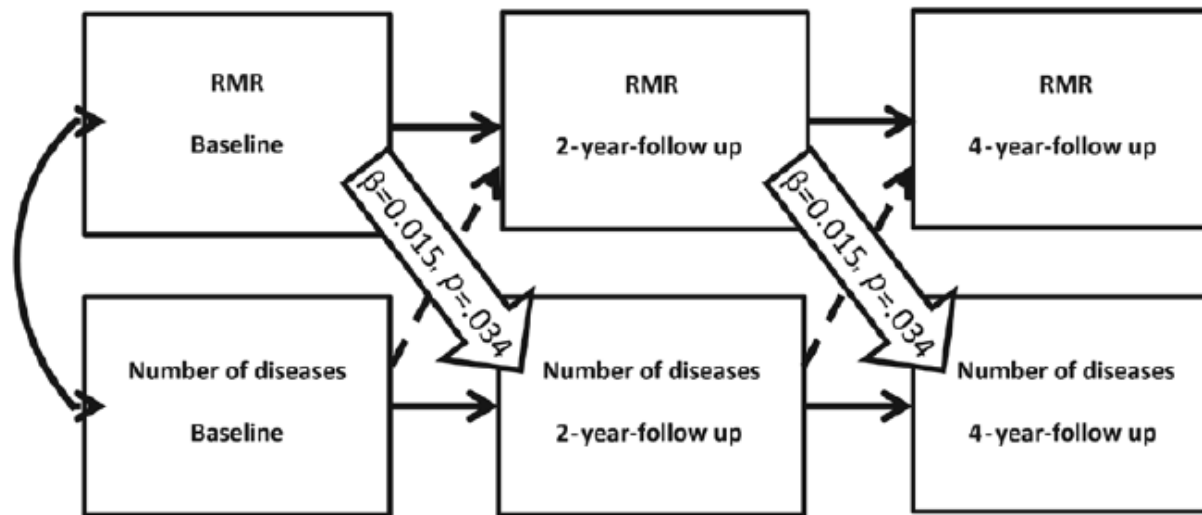


Figure 1. Three-wave bivariate autoregressive cross-legged model testing the longitudinal association between resting metabolic rate (RMR; kcal/d) and number of diseases. The model includes three time points: baseline visit ($N = 695$), 2-year follow-up visit ($N = 248$), and 4-year follow-up visit ($N = 109$). At each time point, the cross-lagged associations between RMR and number of diseases were simultaneously tested, adjusting for the autoregressive ones and baseline correlation. Baseline age, sex, and baseline dual-energy x-ray absorptiometry-measured total body fat mass and lean mass were also included in the model as covariates (not shown in the figure). Significant associations ($p < .05$) are represented using solid arrows, whereas not significant ones are represented using dashed arrows.

Aging Phenotypes and the Genesis of Geriatric Syndromes

