Youth living with perinatally-acquired HIV have lower physical activity levels as they age compared to HIV-exposed uninfected youth

•Sahera Dirajlal-Fargo[1], Paige L. Williams[2,3], Carly Broadwell[3], Elizabeth J. McFarland[4], Kathleen M. Powis[5], Denise Jacobson[3], Jennifer Jao[6],
for the Pediatric HIV/AIDS Cohort Study (PHACS)

•1.Rainbow Babies and Children's Hospital, Cleveland, OH, 2.Department of Biostatistics, Harvard T.H. Chan School of Public Health, Boston, MA, 3.Center for Biostatistics in AIDS Research, Harvard T.H. Chan School of Public Health, Boston, MA, 4.Children's Hospital Colorado Anschutz Medical Campus, Aurora, CO, 5.Massachusetts General Hospital, Departments of Medicine and Pediatrics, Boston, MA, 6.Northwestern University Feinberg School of Medicine, Chicago, IL

Sahera Dirajlal-Fargo, MS, DO
Assistant Professor of Pediatrics
Division of Pediatric Infectious Diseases
11100 Euclid Avenue
Cleveland, OH 44106
Phone: (216)844-3644
Sahera.dirajlal-fargo @uhhospitals.org

BACKGROUND

❖ Physical activity has gained renewed attention as a strategy to minimize the risk of developing cardiovascular disease in adults living with HIV. However, few studies have evaluated the longitudinal changes of physical activity in the pediatric HIV population or the relationship of physical activity with vascular inflammation[1-3].

❖ Prior studies have shown that:
- Regular physical activity can improve body composition, lipid profile and vascular disease in adults living with HIV
- Cross sectional studies suggest that youth living with perinatally acquired HIV have lower physical activity duration and intensity compared to uninfected youth [1-3]

OBJECTIVES

1) To compare the level and type of physical activity in youth living with perinatally acquired HIV (YPHIV) to youth perinatally HIV exposed but uninfected (YPHEU).
2) To evaluate the association between physical activity and biomarkers of endothelial dysfunction stratified by perinatal HIV status.

METHODS

❖ **Study Population:**
- Maybe, "YPHIV and YPHEU enrolled in the Adolescent Master Protocol (AMP) study within the Pediatric HIV/AIDS Cohort Study (PHACS), with 14 U.S. based AMP study sites.

❖ **Inclusion criteria:**
- 7-19 years of age

❖ **Exclusion criteria:**
- Congenital cardiovascular malformation
- Pregnancy
- HIV encephalopathy, cerebral palsy or cognitive limitations
- Cholesterol-lowering agents, anti-depressants, anti-psychotics or treatment for diabetes

❖ **Outcomes:**
1) **PAQ**
- Our analysis was limited to the first 5 PAQs in YPHIV and the first 3 PAQs in YPHEU, to prevent undue influence from participants who may have had more assessments than expected during the study.
- Daily total energy expenditure (TEE) in kilocalories per day (kcal)
- Physical activity duration (PAD): minutes of daily moderate and vigorous activity
- Sufficient daily physical activity: having ≥ 60 minutes/day of physical activity, as recommended by the US Department of Health and Human Services [4].

2) **Biomarkers**
- Markers of coagulation: Fibrinogen, P selectin
- Markers of endothelial dysfunction: soluble intracellular cell adhesion molecule 1 (sICAM), soluble vascular cell adhesion molecule-1 (sVCAM), E-selectin

❖ **Statistical analyses:**
- TEE and PAD were natural log-transformed for analyses.
- Repeated measures linear regression models were fit for TEE and PAD using generalized estimating equations (GEEs) to account for within-subject correlation
- Among YPHIV, similar models were fit to assess associations of nadir CD4%, current CD4 and VL, and peak viral load on longitudinal patterns of physical activity.
- A Poisson GEE model was fit to estimate prevalence ratios (PRs) for sufficient physical activity.
- Spearman correlations were calculated between each physical activity measure and each biomarker of endothelial dysfunction, overall and by HIV status.

RESULTS

Table 1: Demographic characteristics of YPHIV and YPHEU in AMP Study

Participants		YPHIV (N=387)	YPHEU (N=209)
Age at enrollment (years)	Median (Q1, Q3)	12 (9, 14)	10 (8, 11)
Biological sex at birth	Male	183 (47%)	110 (53%)
	Female	204 (53%)	99 (47%)
Race	Black/African American	274 (71%)	136 (65%)
	White	90 (23%)	65 (31%)
	Other	5 (1%)	4 (2%)
BMI z-score across PAQs	Median (Q1, Q3)	0.32 (-0.38, 1.24)	0.83 (-0.17, 1.85)
Hispanic/Latino Ethnicity		95 (25%)	70 (33%)
Geographic region of clinical site	Northeast	139 (36%)	56 (27%)
	Midwest	60 (16%)	21 (10%)
	South	132 (34%)	76 (36%)
	West	35 (9%)	33 (16%)
	Puerto Rico	21 (5%)	23 (11%)
Caregiver education	Less than High School	99 (26%)	64 (31%)
	At least High School	284 (73%)	145 (69%)
Annual household income ≤ $20,000		165 (43%)	132 (63%)
Nadir CD4% ≥15% at study entry		276 (71%)	
Peak viral load at study entry	<10K copies/mL	23 (6%)	
	10K-75K copies/mL	88 (23%)	
	>75K copies/mL	275 (71%)	
CD4 cell count (cells/mm3) at first PAQ	< 200	10 (3%)	
	200-350	26 (7%)	
	350<-500	48 (12%)	
	> 500	302 (78%)	
Viral load ≤ 400 copies/mL at first PAQ		258 (67%)	
Type of ARV regimen at first PAQ	NNRTI-based cART	59 (15%)	
	PI-based cART	228 (59%)	
	INSTI-based cART	4 (1%)	
	More than 2 classes	44 (11%)	
	Not on cART	45 (12%)	
Percent of lifetime on cART at first PAQ	Median (Q1, Q3)	69.0 (51.0, 86.0)	

PAQs		YPHIV (N=1116)	YPHEU (N=436)
Season when PAQ administered	Winter	156 (14%)	111 (25%)
	Spring	303 (27%)	118 (27%)
	Summer	441 (40%)	152 (35%)
	Fall	216 (19%)	55 (13%)

cART: combination antiretroviral therapy; INSTI: integrase strand transfer inhibitor; NNRTI: non-nucleoside reverse transcriptase inhibitor; PI: protease inhibitor; PAQ: physical activity questionnaire; Q1/Q3: first and third quartile, respectively

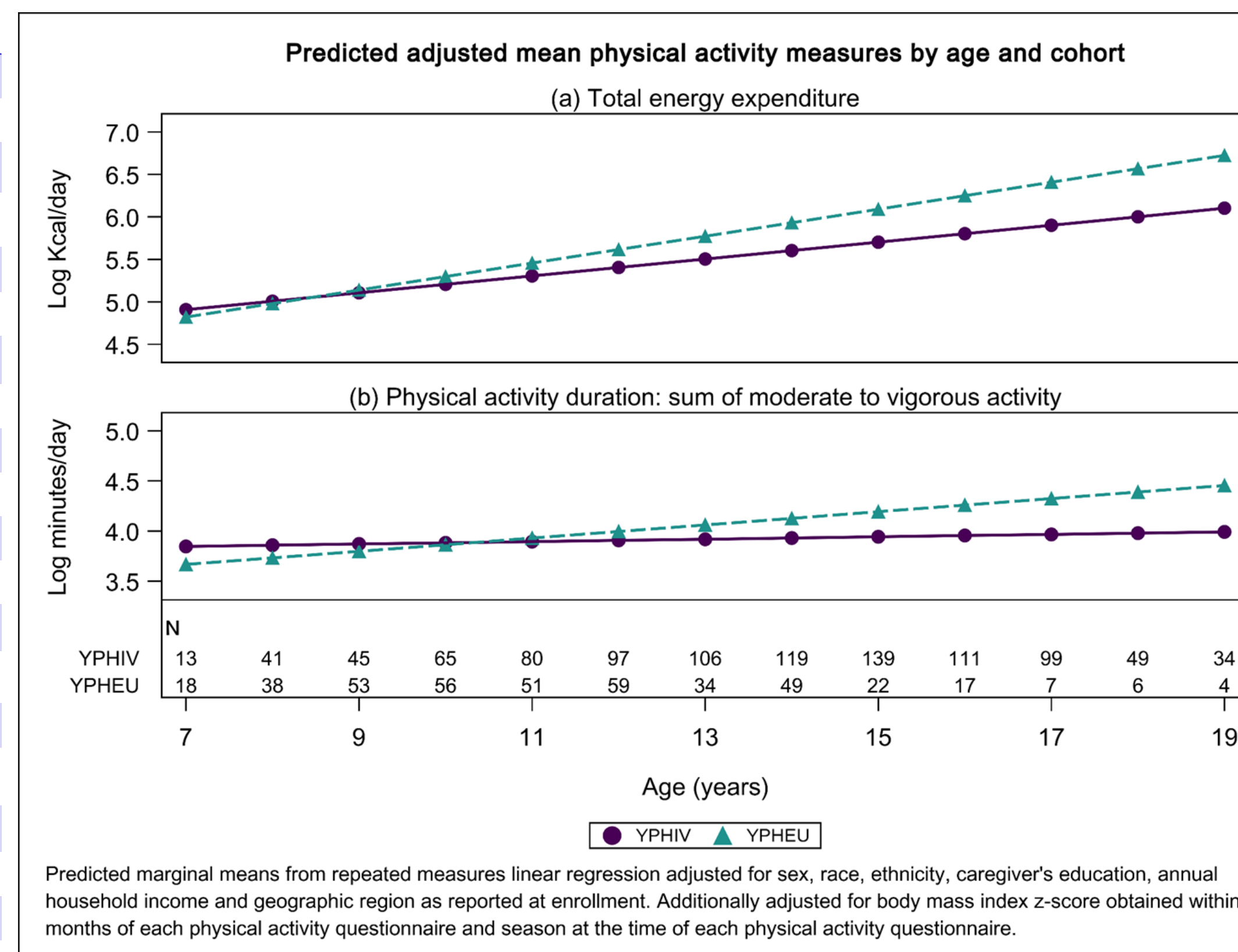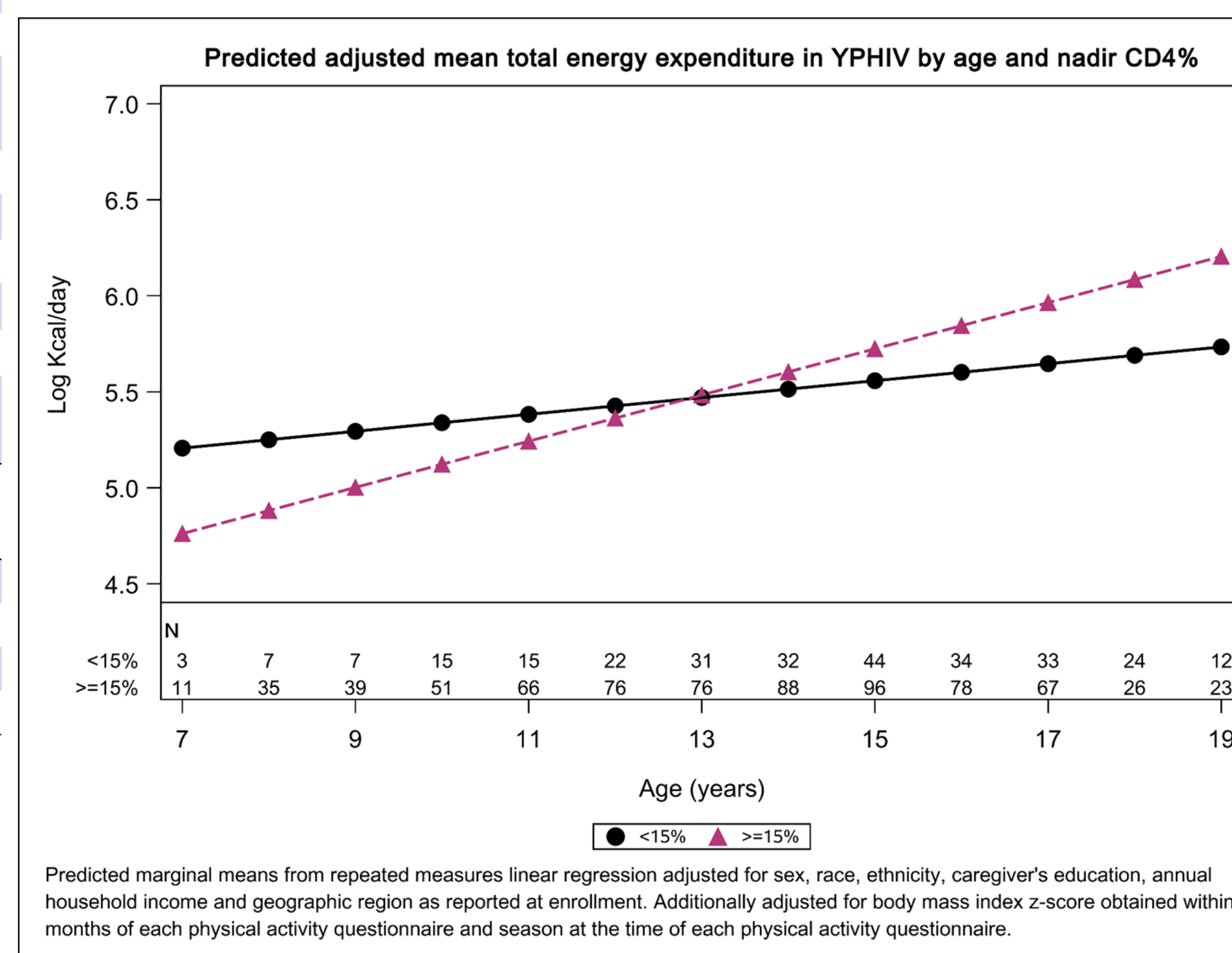### Figure 1: Predicted adjusted mean physical activity measures by age and cohort

Predicted adjusted mean physical activity measures by age and cohort
(a) Total energy expenditure
(b) Physical activity duration: sum of moderate to vigorous activity

Predicted marginal means from repeated measures linear regression adjusted for sex, race, ethnicity, caregiver's education, annual household income and geographic region as reported at enrollment. Additionally adjusted for body mass index z-score obtained within 6 months of each physical activity questionnaire and season at the time of each physical activity questionnaire.

Figure 2: Predicted adjust mean total energy expenditure in YPHIV by age and nadir CD4%

Predicted adjusted mean total energy expenditure in YPHIV by age and nadir CD4%

Predicted marginal means from repeated measures linear regression adjusted for sex, race, ethnicity, caregiver's education, annual household income and geographic region as reported at enrollment. Additionally adjusted for body mass index z-score obtained within 6 months of each physical activity questionnaire and season at the time of each physical activity questionnaire.

RESULTS

❖ Physical activity measures
- In adjusted models, log TEE increased with age in both groups but was approximately 6% less in YPHIV (coefficient for age-cohort interaction: -0.06, 95% confidence interval (CI): -0.10, -0.02, p=0.010, Figure 1).
- The estimated rate of change per year for log of moderate to vigorous activity was approximately 5% less for YPHIV compared to YPHEU in adjusted models (coefficient for age-cohort interaction: -0.05, 95% CI: -0.10, -0.01, p=0.016, Figure 1b).
- There was no overall difference in the percent meeting sufficient physical activity throughout adolescence by HIV status.

❖ Physical activity and HIV-related characteristics:
- Among YPHIV, in adjusted models, nadir CD4% ≤15% at entry was associated with lower increase in TEE as youth aged (interaction coefficient: -0.076, 95% CI -0.15, -0.01, p=0.038, Figure 2).

❖ Physical activity and biomarkers:
- In the sub-group cross-sectional analysis of 301 participants, vascular biomarkers showed no correlation with any of the physical activity measures, overall or within YPHIV or YPHEU, with correlations ranging from -0.11 to 0.17.
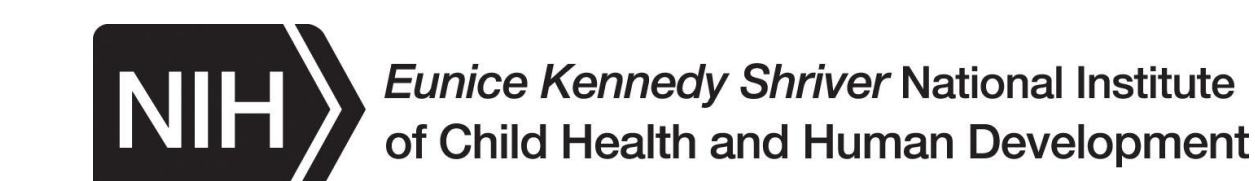
CONCLUSIONS

We found that YPHIV had lower physical activity when compared to YPHEU throughout adolescence, and that this difference became more striking as youth reached their late teens. Early interventions to attempt to attenuate this decline could be beneficial.

REFERENCES

- 1. Martins PC, Lima LRA, Teixeira DM, Carvalho AP, Petroski EL. **Physical activity and body fat in adolescents living with HIV: a comparative study.** Revista paulista de pediatria : orgao oficial da Sociedade de Pediatria de Sao Paulo 2017; 35(1):69-77.
- 2. de Lima LRA, Back IC, Nunes EA, Silva DAS, Petroski EL. **Aerobic fitness and physical activity are inversely associated with body fat, dyslipidemia and inflammatory mediators in children and adolescents living with HIV.** Journal of sports sciences 2018:1-9.
- 3. de Lima LRA, Silva DAS, da Silva KS, Pelegrini A, de Carlos Back I, Petroski EL. **Aerobic Fitness and Moderate to Vigorous Physical Activity in Children and Adolescents Living with HIV.** Pediatric exercise science 2017; 29(3):377-387.
- 4. Promotion OoDPaH. **Physical Activity Guidelines for Americans.** In. Edited by Services HaH; 2018.

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