Youth Living With Perinatally Acquired HIV Have Lower Physical Activity Levels as They Age Compared With HIV-Exposed Uninfected Youth

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Background: Few studies have evaluated physical activity patterns or their association with vascular inflammation among youth living with perinatally acquired HIV (YPHIV).

Methods: We assessed YPHIV and youth perinatally HIV-exposed but uninfected (YPHEU) in the PHACS Adolescent Master Protocol with at least one Block physical activity questionnaire (PAQ) completed between ages 7–19 years. Physical activity metrics were as follows: (1) daily total energy expenditure (TEE) and (2) physical activity duration (PAD) defined as the minutes of daily moderate and vigorous activities. In a subgroup, we measured serum biomarkers of coagulation (fibrinogen and P-selectin) and endothelial dysfunction (soluble intracellular cell adhesion molecule-1, soluble vascular cell adhesion molecule-1, and E-selectin) obtained within 3 months of a single PAQ. Repeated measures linear regression models were used to compare the trajectories of log-transformed TEE and PAD by HIV status, adjusting for confounders. Spearman correlations were calculated to assess the relationship of TEE and PAD with vascular biomarkers.

Results: Five hundred ninety-six youth (387 YPHIV and 209 YPHEU) completed 1552 PAQs (median PAQs completed = 3). The median age at enrollment (Q1, Q3) was 11 (9, 13) years. TEE and PAD increased with age in both YPHIV and YPHEU. However, even after adjusting for confounders, YPHIV had significantly less increase per year than YPHEU for TEE (5.7% [95% confidence interval (CI): −9.9% to −1.4%, P = 0.010] less) and PAD (5.2% [95% CI: −9.2% to −1.1%, P = 0.016] less). Among 302 youth with biomarker measures (187 YPHIV and 114 YPHEU), we observed little correlation with TEE or PAD.

Conclusions: Both groups had increases in physical activity levels as they aged, but YPHIV had smaller increases throughout adolescence compared with YPHEU, which may impact long-term health.

Key Words: exercise, pediatric, cardiovascular, inflammation

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INTRODUCTION

Physical activity has gained renewed attention as a strategy to minimize the risk of cardiovascular disease (CVD) in adults living with HIV. Several studies have evaluated and reviewed the effects of exercise on health in adults living with HIV and have shown benefits in body composition, lipid profile, inflammatory biomarkers, and vascular disease[1–3]. Low physical activity levels decrease total life expectancy in uninfected adults,[4] and as such physical inactivity is comparable to other modifiable risk factors such as smoking and obesity. There are limited data describing physical activity patterns and barriers to exercise in youth living with perinatally acquired HIV (YPHIV). Several small cross-sectional studies suggest that YPHIV have lower physical activity duration (PAD) and intensity compared with uninfected youth.[5–8] However, few studies have evaluated longitudinal changes in physical activity in the pediatric

HIV population or its relationship with vascular inflammation.[5,6,9] We evaluated participants enrolled in a Pediatric HIV/AIDS Cohort Study (PHACS) network study for the purposes of (1) assessing physical activity patterns across age in YPHIV compared with youth perinatally HIV-exposed but uninfected (YPHEU) and (2) investigating the association between physical activity measures and biomarkers of vascular dysfunction. These data will be useful in obtaining information about general activity levels and patterns in YPHIV and may inform development of targeted strategies designed to promote exercise as a nonpharmacological tool to decrease morbidity related to CVD.

METHODS

The Adolescent Master Protocol (AMP) is a prospective cohort study conducted by the PHACS network at 14 sites across the United States, including Puerto Rico.[10] YPHEU with similar ages and sociodemographic backgrounds were also enrolled at the same research sites. For this analysis, we considered physical activity assessments completed when participants were between 7 and 19 years of age. Our analysis was limited to the first 5 physical activity assessments conducted in YPHIV and the first 3 assessments in YPHEU, to prevent undue influence from participants who may have had more assessments than expected. We excluded participants with congenital cardiovascular malformation, pregnancy, HIV encephalopathy, cerebral palsy, or cognitive limitations, and those taking cholesterol-lowering agents, antidepressants, antipsychotics, or treatment for diabetes. Biomarkers of coagulation and endothelial dysfunction were collected at a single time point. Participants who completed a physical activity questionnaire (PAQ) within 3 months of biomarker measurement were included for the biomarker analysis (see Fig. 1, Supplemental Digital Content, http://links.lww.com/QAI/B604).

Physical Activity Measures

Physical Activity attributes were collected using the Block PAQ,[11] relying on self-report or caregiver report. PAQ is designed for school-age children (ages 8–17). This questionnaire asks information over the past 7 days on frequency (times/week) and duration (minutes or h/d) of 9 activities ranging from vigorous physical activity to more sedentary activities, such as watching television and playing video games. Specifically, it asks about walking, inside chores, outside chores, part-time work, sports games with friends, aerobic/weight training, physical education (frequency only), and television/computer use (hours per day only). The possible responses on the questionnaire for frequency and duration of each activity are ordinal categories. Outcomes obtained from PAQ were as follows: (1) daily total energy expenditure (TEE) in kilocalories (kcal) per day; (2) recreational activity excluding chores, part-time work, and walking; and 3) PAD defined as the minutes of daily moderate and vigorous activities. Sufficient daily physical activity was defined as PAD $\geq$ 60 min/d, as recommended by the US Department of Health and Human Services.[12]

Biomarkers of Endothelial Dysfunction

Markers of coagulation (fibrinogen and P-selectin) and endothelial dysfunction [soluble intracellular cell adhesion molecule-1, soluble vascular cell adhesion molecule-1, and E-selectin] were measured as previously described.[13] Fibrinogen was measured by nephelometry (Dade Behring, Deerfield, IL); soluble intracellular cell adhesion molecule-1, soluble vascular cell adhesion molecule-1, P-selectin, and E-selectin were measured by ELISA (R&D Systems, Minneapolis, MN).

Potential Confounders

Variables considered as potential confounders of the relationship between HIV status and physical activity outcomes included sex assigned at birth, race (White or other vs Black/African American), ethnicity (Hispanic/Latino vs non-Hispanic/Latino), geographic region (Midwest, South, West, or Puerto Rico vs Northeast), caregiver education (high school vs less than high school), annual household income ($\leq$vs $>$ $20,000) as reported at study entry, season (spring, summer, or fall vs winter), and body mass index (BMI) z-score at or nearest to each PAQ.

Statistical Methods

Energy expenditure variables were natural log-transformed for analyses. We evaluated each continuous physical activity outcome across age by fitting a repeated measures linear regression model using generalized estimating equations with the robust variance to account for correlation in measurements within participants, adjusting for confounders. From each model, we calculated the predicted mean physical activity outcome for each one-year increase in age and evaluated effect modification of age by HIV status. Among YPHIV alone, we fit similar models to assess the association of nadir CD4% and peak viral load at entry, as well as current viral load and CD4 at each PAQ assessment, with longitudinal patterns of physical activity. For the binary outcome of sufficient daily physical activity, we fit a modified Poisson model using generalized estimating equations to estimate prevalence ratios. We calculated Spearman correlations to assess the relationship between each physical activity measure and each biomarker of coagulation and endothelial dysfunction overall and by HIV status. In YPHIV, the correlations were also computed separately by viral load at the time of the PAQ ($\leq$or $>$400 copies/mL).

RESULTS

Baseline Characteristics

For the longitudinal physical activity analysis, we included 596 participants (n = 387 YPHIV, n = 209 YPHEU) with 1552 completed PAQs. The YPHIV and YPHEU cohorts did not differ substantially with respect to sex, race, or caregiver education. At the time of their first completed PAQ, 78% of YPHIV participants had a CD4 count $>$ 500 cells/mm^3 and 67% had a suppressed viral load ($\leq$400 copies/mL). The most common regimen at the time of the first PAQ was a protease inhibitor (PI)-based regimen (Table 1).

TABLE 1. Characteristics of YPHIV and YPHEU Participants in the PHACS AMP Study

Participants	Perinatal HIV Status		P*
	YPHIV (N=387)	YPHEU (N=209)	
Age at enrollment (yr)			
Median (Q1, Q3)	12 (9, 14)	10 (8, 11)	<0.01
Biological sex at birth			
Male	183 (47%)	110 (53%)	0.21
Female	204 (53%)	99 (47%)	
Race			
Black or African American	274 (71%)	136 (65%)	0.12
White	90 (23%)	65 (31%)	
Other	5 (1%)	4 (2%)	
Hispanic/Latino ethnicity	95 (25%)	70 (33%)	0.01
Geographic region of enrolling clinical site			
Northeast	139 (36%)	56 (27%)	<0.01
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%)	0.21
At least high school	284 (73%)	145 (69%)	
Annual household income ≤ $20,000			
165 (43%)	132 (63%)	<0.01	
BMI z-score at first PAQ			
Median (Q1, Q3)	0.25 (−0.34, 1.23)	0.82 (−0.14, 1.88)	<0.01
TEE (kcal/d) at first PAQ			
Median (Q1, Q3)	257 (114, 550)	242 (130, 546)	0.92
Sum of moderate to vigorous activity (min/d) at first PAQ			
Median (Q1, Q3)	68.4 (26.7, 132.6)	68.4 (32.1, 133.8)	0.83
Sufficient daily physical activity	210 (54%)	115 (55%)	0.859
Nadir CD4 percent ≥15% at study entry	276 (71%)		
Peak viral load at study entry			
<10K copies/mL	23 (6%)		
10K–75K copies/mL	88 (23%)		
>75K copies/mL	275 (71%)		
CD4 cell count (cells/mm$^{3)}$ 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%)		
Type of ARV regimen at last PAQ			
NNRTI-based cART	76 (20%)		
PI-based cART	157 (41%)		
INSTI-based cART	23 (6%)		
More than 2 classes	71 (18%)		
Not on cART	47 (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%)	

P value by the Wilcoxon rank sum test for continuous measures, χ^2 test for categorical measures and Fisher exact test for binary measures.

ARV, antiretroviral; cART, combination antiretroviral therapy; INSTI, integrase strand transfer inhibitor; NNRTI, nonnucleotide reverse transcriptase inhibitor; PI, protease inhibitor; Q1,Q3, first and third interquartile range.

Physical Activity Measures in YPHIV vs YPHEU

Total Energy Expenditure

In adjusted models, log TEE increased with age in both YPHIV and YPHEU. On average, TEE increased by about 5.7% less per year in YPHIV vs YPHEU (95% confidence interval (CI): −9.9% to −1.4%, P = 0.010, Fig. 1A, Supplemental Table 1, Supplemental Digital Content, http://links.lww.com/QAI/B605).

Physical Activity Duration

Overall, log minutes of moderate-to-vigorous activity increased with age; however, the estimated difference per year was approximately 5.2% less for YPHIV compared with YPHEU in adjusted models (95% CI: −9.2%, −1.1% P = 0.016, Fig. 1B, Supplemental Table 1, Supplemental Digital Content, http://links.lww.com/QAI/B605).

Sufficient Physical Activity

There was no overall difference in the proportion meeting sufficient physical activity throughout adolescence by HIV status, nor did the yearly increase in sufficient physical activity differ between YPHIV and YPHEU in adjusted models.

Recreational Activity

Recreational caloric expenditure increased with age; however, the increase per year of age was about 14% less in YPHIV than in YPHEU (95% CI −21% to −5.5%, P = 0.002).

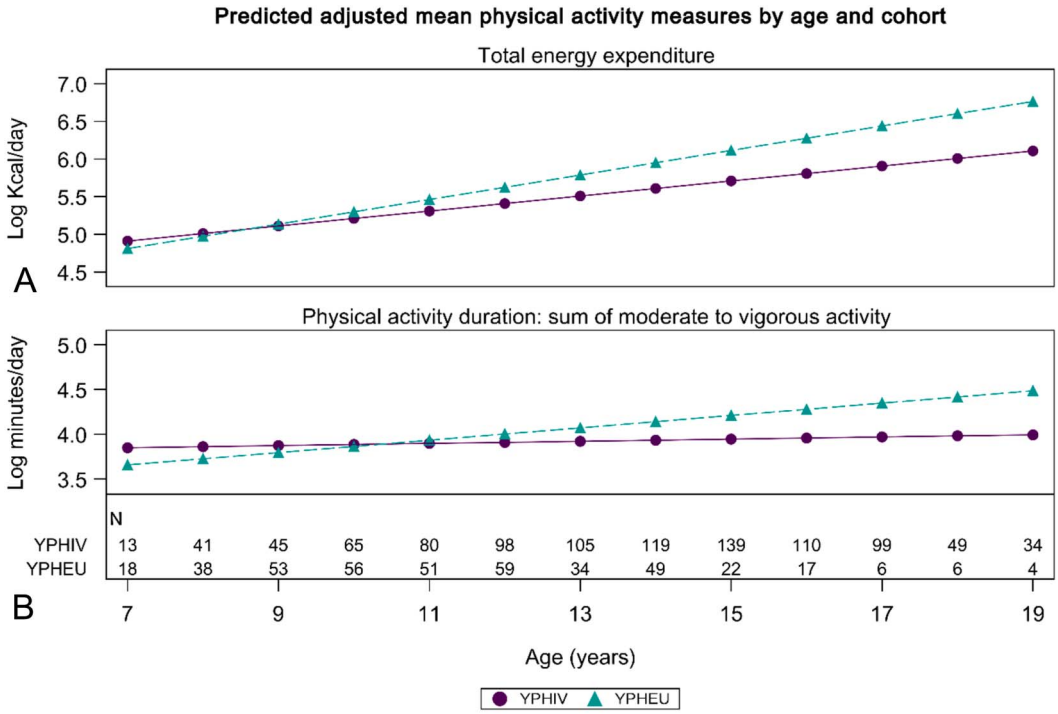

FIGURE 1. Predicted means from repeated measures linear regression adjusted for sex, race and ethnicity, caregiver's education, annual household income and geographic region as reported at enrollment, as well as BMI z-score obtained within 6 months of each PAQ and season at the time of each PAQ. full color online

In multivariable models for each energy expenditure measure, female sex was associated with lower physical activity measures and geographic region differences were also noted (Supplemental Table 1, Supplemental Digital Content, http://links.lww.com/QAI/B605). BMI z-score, race, ethnicity, household income, caregiver education, and season were not associated with physical activity outcomes.

Physical Activity Measures and Associations With HIV Variables

Among YPHIV, in adjusted models, nadir CD4% ≤15% at entry was associated with a lower increase in TEE as youth aged (percent difference: −7.4%, 95% CI −14% to −0.6%, $P = 0.038$). CD4 count and viral load measured at each PAQ and peak viral load at entry were not associated with physical activity.

Physical Activity Measures and Biomarkers

In the subgroup cross-sectional analysis of 301 participants, vascular biomarkers showed no correlations with any of the physical activity measures, overall or within any subgroups (YPHEU, YPHIV, and YPHIV with viral load ≤ or >400 copies/mL), with correlations ranging from −0.11 to 0.17.

DISCUSSION

In this large US cohort, we observed increases in physical activity levels through adolescence in both YPHIV and YPHEU, but these increases were smaller in YPHIV compared with YPHEU. By late adolescence, YPHIV had significantly lower physical activity levels than YPHEU.

Systematic reviews of longitudinal studies have found a decline in physical activity levels during adolescence in youth without HIV.[14,15] There are, however, limited data describing physical activity patterns in YPHIV. Cross-sectional studies suggest that YPHIV have lower PAD and intensity compared with youth without HIV.[5–8]

In our analysis, YPHIV showed a more blunted increase in physical activity measures as they aged through adolescence compared with YPHEU. Although the difference over time between the groups is small, it may have clinical significance as children who are active but become less active as they age have a higher risk of becoming obese in young adulthood when compared with individuals who are consistently active throughout childhood and adolescence.[16] Among YPHIV, those with a less severe history of HIV disease (eg, higher nadir CD4%) had steeper increases in PAD and intensity, suggesting, not surprisingly, that better childhood HIV health status and potentially overall health status contribute to improved physical activity even later in adolescence. YPHIV have a dampened increase in vigorous physical activity as they age compared with YPHEU,

but this did not translate to a difference in the proportion meeting sufficient physical activity. This lack of difference between groups may be because HIV status does not influence an underlying phenomenon to fall short of meeting national guidelines when one already has little activity. The design of our study did not allow us to investigate the reasons why lower levels of activities have been found in the context of HIV. We can hypothesize these are likely multifactorial and may include fewer opportunities for physical activity that require space and are costly (gymnasiums, membership, and clubs), social support from parents and friends, social isolation and stigma, physical activities included as part of their activities of daily living (public transportation and occupation related)[17] that may not be captured adequately by self-reporting are all possible explanations. Data from studies in adults living with HIV suggest that some of the barriers to engaging in physical activity participation that could be extrapolated to YPHIV include bodily pain and depression. Potential facilitators include higher cardiorespiratory fitness and motivation,[18] as well as sustained self-efficacy, the belief in one's capability to participate in physical activity and to choose activity over existing barriers.[19]

Interventions designed to increase aerobic exercise in adults living with HIV have proven to be safe and beneficial[20]; however, interventions using self-determination, the internet or gaming platforms, and school-based programs to promote self-efficacy and social support may be more appropriate and sustainable for YPHIV.[21–23]

Physical activity achieves its benefits through several hypothesized mechanisms.[24,25] Pathways that are of particular interest in HIV and CVD include physical activity's anti-inflammatory effects.[25] In this analysis, we did not identify a relationship between physical activity and plasma biomarkers of coagulation or endothelial dysfunction. These findings could be secondary to our cross-sectional study design, or the fact that the relationship between physical activity and cardiometabolic benefits at a young age may be independent of vascular inflammation and is different than what has been observed in adults. More research is needed in this area.

Our study has several strengths including the detailed analysis of the physical activity patterns in YPHIV. This study is limited by the self-report nature of the physical activity, subject to recall bias. However, questionnaires such as ours have wide applicability, low participant burden, and the capability to broadly assess different physical activity intensities. The design of the AMP study, which only enrolls YPHIV and YPHEU, precluded inclusion of a comparator group of youth who were HIV-unexposed uninfected. However, our large sample size among YPHIV with a comparison group of YPHEU provide one of the first published data on longitudinal changes in physical activity in this important population. Finally, we were not able to directly measure subclinical vascular changes in our study.

CONCLUSIONS

YPHIV have lower increases in physical activity as they age compared with YPHEU, and this results in lower activity levels by their late teens. Early interventions to attenuate this decline could be beneficial for long-term cardiometabolic health. Further research is warranted to understand this change and how other social determinants can modify the biological tendency of activity to decline with age in this population.

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REFERENCES

1. Guariglia DA, Pedro RE, Deminice R, et al. Effect of combined training on body composition and metabolic variables in people living with HIV: a randomized clinical trial. *Cytokine* 2018;111:505–510.
2. Marzel A, Kouyos RD, Reinschmidt S, et al. Dietary patterns and physical activity correlate with total cholesterol independently of lipid-lowering drugs and antiretroviral therapy in aging people living with human immunodeficiency virus. *Open Forum Infect Dis.* 2018;5:ofy067.
3. Dirajlal-Fargo S, Webel AR, Longenecker CT, et al. The effect of physical activity on cardiometabolic health and inflammation in treated HIV infection. *Antivir Ther.* 2016;21:237–245.
4. Franco OH, de Laet C, Peeters A, et al. Effects of physical activity on life expectancy with cardiovascular disease. *Arch Intern Med.* 2005;165:2355–2360.
5. de Lima LRA, Silva DAS, da Silva KS, et al. Aerobic fitness and moderate to vigorous physical activity in children and adolescents living with HIV. *Pediatr Exerc Sci.* 2017;29:377–387.
6. Martins PC, Lima LRA, Teixeira DM, et al. Physical activity and body fat IN adolescents living with HIV: a comparative study. *Rev Paul Pediatr.* 2017;35:69–77.

7. Wong M, Shiau S, Yin MT, et al. Decreased vigorous physical activity in school-aged children with human immunodeficiency virus in johannesburg, South Africa. *J Pediatr.* 2016;172:103–109.
8. Tanaka LF, Latorre Mdo R, Silva AM, et al. [High prevalence of physical inactivity among adolescents living with HIV/Aids]. *Rev Paul Pediatr.* 2015;33:327–332.
9. de Lima LRA, Back IC, Nunes EA, et al. Aerobic fitness and physical activity are inversely associated with body fat, dyslipidemia and inflammatory mediators in children and adolescents living with HIV. *J Sports Sci.* 2019;37:50–58.
10. Siberry GK, Patel K, Van Dyke RB, et al. CD4+ lymphocyte-based immunologic outcomes of perinatally HIV-infected children during antiretroviral therapy interruption. *J Acquir Immune Defic Syndr.* 2011;57:223–229.
11. Quest N. *Assessment and Analysis Services*; 2020 Nutrition Quest, Berkeley, CA.
12. U.S. Department of Health and Human Services. *Physical Activity Guidelines for Americans, 2nd edition*: Washington, DC: U.S. Department of Health and Human Services; 2018.
13. Miller TI, Borkowsky W, DiMeglio LA, et al. Metabolic abnormalities and viral replication are associated with biomarkers of vascular dysfunction in HIV-infected children. *HIV Med.* 2012;13:264–275.
14. Dumith SC, Gigante DP, Domingues MR, et al. Physical activity change during adolescence: a systematic review and a pooled analysis. *Int J Epidemiol.* 2011; 40:685–698.
15. Farooq A, Martin A, Janssen X, et al. Longitudinal changes in moderate-to-vigorous-intensity physical activity in children and adolescents: a systematic review and meta-analysis. *Obes Rev.* 2020;21:e12953.
16. Kwon S, Janz KF, Letuchy EM, et al. Active lifestyle in childhood and adolescence prevents obesity development in young adulthood. *Obesity (Silver Spring, MD).* 2015;23:2462–2469.
17. Mabweazara SZ, Leach LL, Ley C. Development of a context-sensitive physical activity intervention for persons living with HIV and AIDS of low socioeconomic status using the behaviour change wheel. *BMC Public Health.* 2019;19:774.
18. Vancampfort D, Mugisha J, Richards J, et al. Physical activity correlates in people living with HIV/AIDS: a systematic review of 45 studies. *Disabil Rehabil.* 2018; 40:1618–1629.
19. Voskuil VR, Pierce SJ, Robbins LB. Comparing the psychometric properties of two physical activity self-efficacy instruments in urban, adolescent girls: validity, measurement invariance, and reliability. *Front Psychol.* 2017;8:1301.
20. O'Brien K, Nixon S, Tynan AM, et al. Aerobic exercise interventions for adults living with HIV/AIDS. *Cochrane database Syst Rev.* 2010; 2010: Cd001796.
21. Corder K, Werneck AO, Jong ST, et al. Pathways to increasing adolescent physical activity and wellbeing: a mediation analysis of intervention components designed using a participatory approach. *Int J Environ Res Public Health* 2020;17:390.
22. Smedegaard S, Christiansen LB, Lund-Cramer P, et al. Improving the well-being of children and youths: a randomized multicomponent, school-based, physical activity intervention. *BMC Public Health.* 2016;16:1127.
23. Miragall M, Domínguez-Rodríguez A, Navarro J, et al. Increasing physical activity through an Internet-based motivational intervention supported by pedometers in a sample of sedentary students: a randomised controlled trial. *Psychol Health.* 2018; 33:465–482.
24. Warburton DER, Bredin SSD. Health benefits of physical activity: a systematic review of current systematic reviews. *Curr Opin Cardiol.* 2017;32:541–556.
25. Fiuza-Luces C, Garatachea N, Berger NA, et al. Exercise is the real polypill. *Physiology (Bethesda, MD).* 2013;28:330–358.