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The Relationship Between Physical Activity and Cardiorespiratory Fitness Among People Living with HIV Throughout the Lifespan

Allison R. Webel, RN, PhD, FAAN [Assistant Professor],
Frances Payne Bolton School of Nursing, Case Western Reserve University Cleveland, Ohio,

International Nursing Network for HIV Research

Joseph Perazzo, RN, PhD, ACRN [Assistant Professor],
International Nursing Network for HIV Research,

University of Cincinnati

J. Craig Phillips, LLM, PhD, RN, APRN, ACRN, FAAN [Vice-Dean Governance and Secretary and Associate Professor],
Faculty of Health Sciences, School of Nursing, University of Ottawa, Ottawa, CA,

International Nursing Network for HIV Research

Kathleen M. Nokes, RN, PhD, FAAN [Honorary Research Professor],
Durban University of Technology, Durban, South Africa

International Nursing Network for HIV Research

Cynthia Rentrope, MPH, MSSA [Research Assistant],
Frances Payne Bolton School of Nursing, Case Western Reserve University Cleveland, Ohio

Rebecca Schnall, RN, PhD,
Columbia University School of Nursing

International Nursing Network for HIV Research

Rita Musanti, RN, PhD,
Rutgers University,

International Nursing Network for HIV Research

Kimberly Adams Tufts, ND, WHNP-BC, FAAN [Professor, School of Nursing],
Old Dominion University, Norfolk, Virginia,

International Nursing Network for HIV Research

Elizabeth Sefcik, RN, PhD,
Texas A &M University, Corpus Christi, Texas,

International Nursing Network for HIV Research

Corresponding Author: Allison R. Webel, RN, PhD, FAAN; Assistant Professor, Frances Payne Bolton School of Nursing, Case Western Reserve University 10900 Euclid Avenue, Cleveland, Ohio 44106-4904, USA.

Mary Jane Hamilton, RN, PhD,
Texas A &M University, Corpus Christi, Texas,

International Nursing Network for HIV Research

Carmen Portillo, RN, PhD [Executive Deputy Dean & Professor],
Yale School of Nursing,

International Nursing Network for HIV Research

Puangtip Chaiphibalsarisdi, RN, PhD [Associate Professor],
Faculty of Nursing, Saint Louis College, Bangkok, Thailand,

International Nursing Network for HIV Research

Penelope Orton, PhD [Senior Lecturer],
Durban University of Technology, Durban, South Africa

International Nursing Network for HIV Research

Liana Davis, PhD [Assistant Professor],
Department of Kinesiology, Texas A &M University, Corpus Christi, Texas,

Carol Dawson Rose, RN, PhD [Professor]
University of California, San Francisco;

International Nursing Network for HIV Research

Abstract

Background: People living with HIV (PLHIV) are at increased risk for developing cardiovascular disease (CVD). Physical activity and cardiorespiratory fitness in PLHIV are poorly understood.

Objective: To describe physical activity and cardiorespiratory fitness by sex and age and to examine the association between physical activity and cardiorespiratory fitness in PLHIV, controlling for covariates.

Methods: Seven-hundred and two PLHIV participated in a cross-sectional study and completed validated measures of self-reported physical activity (7-day physical activity recall) and cardiorespiratory fitness (6-minute walk test [6MWT]). Participants were recruited from seven diverse sites in the United States and Thailand and data were analyzed using descriptive statistics and multiple regression to examine the relationship between physical activity and cardiorespiratory fitness.

Results: On average participants self-reported engaging in in 115 minutes of, mostly light (75%), physical activity. Men reported twice the amount of physical activity as women (155 vs 73 minutes, p=0.01). Participants' ability to achieve their predicted 6MWT distances was similar between men (68%) and women (69%) (p>0.01). For women, vigorous physical activity was associated with a 6.6% increase in cardiorespiratory fitness and being temporarily unemployed was associated with an 18% decline in cardiorespiratory fitness. Cardiorespiratory fitness increased with age (p<0.01).

Conclusions: PLHIV's weekly physical activity averaged 85 minutes of mostly light activity, well below the recommended 150 minutes of moderate activity. Vigorous physical activity was associated with improved cardiorespiratory fitness in women, but not men. While PLHIV would benefit from interventions to increase physical activity, our data suggest a need to develop sex-specific physical activity strategies.

BACKROUND

People living with HIV (PLHIV) are living longer due to increased access to effective medications that slow disease progression. As PLHIV age, they are at increased risk for developing cardiovascular disease (CVD) and over the past 20 years [1], the global burden of HIV-associated CVD has tripled. Cardiorespiratory fitness is one of the best indicators of CVD-related morbidity and mortality among PLHIV, yet cardiorespiratory fitness is low. A recent systematic review and meta-analysis of 24 studies reported that PLHIV have among the lowest levels of cardiorespiratory fitness (26.4 ml/min/kg) of any population living with a chronic illness [2].

Increasing amount and intensity of physical activity is one of the best strategies to improve cardiorespiratory fitness. Data from recent clinical trials suggests that physical activity can also improve cardiorespiratory fitness in PLHIV [3 4], but physical activity among PLHIV in the community remains low [5]. Further, physical activity varies by sex and age in both PLHIV [5], and general populations, yet how the relationship between physical activity and cardiorespiratory fitness in PLHIV is moderated by sex and age is not well described. Cardiorespiratory fitness (CRF) reflects one's ability to transport inhaled oxygen to the muscles, enabling him or her to perform physical work. Untangling these relationships in a large, multi-site, heterogeneous population can help to better identify potential intervention strategies to improve physical activity in PLHIV globally. Our study purposes were to describe physical activity and cardiorespiratory fitness by sex and age and examine the association between physical activity and cardiorespiratory fitness in a diverse sample of PLHIV.

METHODS

Study Design

Researchers from the International Nursing Network for HIV Research conducted a multi-site cross-sectional study to describe physical activity and cardiorespiratory fitness by sex and age as well as the association between physical activity and cardiorespiratory fitness in PLHIV [6]. As a skilled research network, each site contained significant infrastructure to facilitate participant recruitment. This infrastructure included local Institutional Review Board (IRB)-approved research registries maintained by the sites, and collaborative relationships with local clinical providers, community centers, and AIDS Service Organizations. [6]. Consistent with this network's procedural framework, the coordinating site finalized the study protocol, developed the standardized training modules, and obtained the primary IRB approval from University Hospital's Cleveland Medical Center. All site Principal Investigators provided input to enhance the final study design, were trained and certified in all study procedures, and obtained local IRB approval prior to data collection.

Sample and Recruitment

To be eligible for study participation, individuals had to be ≥18 years of age and have a confirmed positive HIV laboratory test (HIV+ ELISA with confirmatory PCR or Western blot). Those who had a medical contraindication for exercise as determined by the American Heart Association criteria [7], were not able to be physically active without an assistive device (i.e. cane, walker, wheelchair), or were not able to communicated in English or Spanish were excluded.

Participants were recruited either via telephone or in person using locally approved IRB procedures, responding to study advertisements in relevant venues (e.g., clinic waiting rooms, AIDS service organizations). If interested, a research assistant screened potential participants with an IRB-approved script to describe the study purpose and determine whether candidates met eligibility criteria. All sites completed a common screening form that tracked recruitment method, number of potential participants contacted, and the number of and reason for those who screened out of the study. Those who were eligible for the study were given informed-consent documents to review, including a consent for the study team to access to his or her medical records, and scheduled for a data collection visit.

Due to the cross sectional nature of the study, and to help account for the potential confounding effects of weather-related changes in different seasons [8], we planned to recruit and enroll an evenly distributed number of participants across seasons. Each site attempted to enroll approximately 25% of the total anticipated sample in each quarter of the calendar year.

Procedures

Trained study staff met with eligible participants and reviewed an informed consent document that described the study's purpose, procedures, risks and potential benefits. After confirming understanding, the staff member obtained written informed consent and was available to assist participants to complete the measures. Study staff collected anthropometric assessments and the 6-minute walk test (6MWT) to measure cardiorespiratory fitness. All data were entered in a central Research Electronic Data Capture (RedCAP) database housed at the coordinating site, where it was cleaned and checked for quality regularly. Upon completion of the procedures, participants received an incentive amount consistent with local standards (USD $5 -$50). All study procedures for this analysis occurred between January 2016 and September 2017.

Measures

Our primary predictor variables were age, sex and physical activity. Our primary outcome was cardiorespiratory fitness as measured by the 6MWT. Demographic, clinical, and anthropomorphic variables were collected either to describe the sample or to examine as potential effect modifiers.

Demographic, Clinical, and Anthropometric Characteristics—All participants completed self-reported sociodemographic items; medical chart abstraction identified the number of years a participant had been living with HIV, current CD4+ T- cell count, current

HIV viral load, and current and past comorbid conditions. Participants' standardized height, weight, and waist and hip circumference measures (in triplicate, to the nearest cm) were measured by the study staff.

Physical Activity—Participants' physical activity in the past week was assessed using the *7-day Physical Activity Recall* (PAR). The *7-day PAR* is a semi-structured interview that estimates an individual's time spent in light, moderate, and vigorous physical activity for the 7 days prior to the interview (Table 1).[9] Its validity and reliability have been repeatedly evaluated in diverse samples over the past 20 years and its psychometric properties are sound [10]. It has been correlated with the gold standard, objective measure of accelerometer (rho=0.50–0.54, p<0.001) [11]. The standardized interview format was as follows: An interviewer explains (e.g. defines) light, moderate, and vigorous physical activity to the participant and asks the participant to recall activities over the past 7 days. The interviewer guided each participant through the recall process, day-by-day, to determine duration and intensity of the physical activities. We used REDCap's calculation feature to total the time spent doing light, moderate, and vigorous physical activities in the past 7 days.

Cardiorespiratory Fitness—Cardiorespiratory fitness was measured with the widely used and validated 6MWT [12 13]. We conducted the 6MWT according to American Thoracic Society guidelines[14]. Prior to each test, participants remained seated for 10 minutes. After this rest period, we obtained the participant's blood pressure, heart rate, dyspnea and overall fatigue using the Borg scale. After that, participants were instructed to walk as far as possible for six minutes, back and forth in a 30-meter long pre-measured course on a flat surface, with the distance marked using cones. Participants were instructed to not run or jog during the walk test. Standard phrases of encouragement were given during the test. After each test, heart rate, Borg dyspnea and fatigue levels as well as guides marking the distance covered were recorded by the research assistant. The total distance walked was rounded to the nearest meter. We recently validated this submaximal measure against maximal cardiorespiratory fitness tests in PLHIV, and found it was associated with VO_2 Peak [15]. We calculated sex and age predicted distance using the Ross et al. (2010) validated equation to estimate VO_2Peak from total distance achieved on the 6MWT (VO_2 Peak [ml/kg/min] = 4.948 + 0.023 × 6 MWD [meters])[16]. We used REDCap's calculation feature to ensure accurate conversion of participant weights (kg) and 6MWT distances (meters) collected across sites. The calculation yielded a value which can be interpreted as participants' VO_2 Peak [16].

Analysis

Data were cleaned before any analyses and distributional assumptions for the outcome variables were checked before studying relationships among our variables of interest. We checked all variable distributions (Table 1), by running frequency analyses, univariate statistics, and inspecting graphs. Categorical variables were summarized using frequencies and percentages. Continuous variables, depending on their distribution, were summarized using either mean values and standard deviations or medians and interquartile ranges.

We used analysis of covariance to examine the physical activity and cardiorespiratory fitness patterns by sex and age. Consistent with previous work describing cardiorespiratory fitness in large samples [17 18], we categorized age by decade to examine these patterns over time. To assess the association between physical activity and sex, we conducted two multiple linear regressions. In addition to this primary relationship, we examined the independent effects of age, employment status, HIV viral load, and season enrolled by adding these covariates to the models. All statistical analyses were performed using Stata version 14.0 (College Station, TX) and *p*-values <0.05 were considered statistically significant.

RESULTS

We screened 741 adult PLHIV, of which four did not meet eligibility criteria. Of the 737 who did meet criteria, 35 were lost to follow-up. We enrolled 702 adult PLHIV at six diverse sites across the United States (Cleveland, Ohio; Newark, New Jersey; New York City, New York; Norfolk, Virginia; Corpus Christi, Texas, San Francisco, California) and in Bangkok, Thailand. Participant's average age was 50.5 years (±11.1), most were male (61%), disabled or unemployed (54%), and permanently housed (77%). On average, participants had been living with HIV for approximately 14 (±9.35) years, were prescribed HIV medications (92%), virally suppressed (78%), and had at least one physical comorbidity (61%).

Participants reported engaging in a median of 85 minutes of light physical activity and 30 minutes of moderate physical activity in the past seven days. However, men reported engaging in more light and moderate physical activity compared to women (all $p<0.05$). Participants walked an average of 402 (±104) meters on the 6-minute walk test, with expected differences by sex. However, both men and women achieved similar rates (68 vs 69%; $p=0.96$) of their sex and age predicted distance on the 6MWT. Additional demographic and medical characteristics of the sample can be found in Table 2.

Table 3 displays the physical activity and cardiorespiratory fitness characteristics of our sample by sex and age. The amount of physical activity participants engaged in did not vary significantly by decade, nor did the number of participants engaging in any physical activity (all $p>0.05$). However, the ability to achieve the age- and sex- predicted distance on the 6MWT improved as ages increased among both men and women ($p<0.001$). This relationship persisted even after controlling for employment status, season, and physical activity (Table 4).

Finally, in examining the association of physical activity to cardiorespiratory fitness, we observed that for women engaging in any vigorous physical activity in the past week, there was a 7.31% increase in achieving their age- and sex-predicted distanced on the 6MWT ($p<0.001$). After controlling for known covariates, we did not observe a similar relationship in men ($p>0.05$). Full multiple regression models can be found in Table 4.

DISCUSSION

This large, multi-site study confirmed that among PLHIV engaged in HIV care, self-reported physical activity is markedly low. Similar findings have been reported in other clinic-based cohorts-- CNICS (n=5,370) and the Women's Interagency HIV Study (n=178) research cohorts [5 19]. Internationally, the Dutch AGEhIV cohort also found that PLHIV engaged in less physical activity compared with HIV negative participants (44.3 vs 53%, p=0.005) [20], as did the Swiss HIV Cohort Study [21]. Taken together, these studies suggest that PLHIV across settings engage in low levels of physical activity and interventions to improve the amount of physical activity in PLHIV are needed. However, these data conflict with VanCampfort et al.'s, (2016) meta-analysis of physical activity among PLHIV, which that found on average, PLHIV engaged in 92.4 minutes of physical activity per day [22]. This discrepancy may be explained by the small number (n=144) of pooled participants in that meta-analysis.

In addition to low amounts of physical activity reported, PLHIV in our study engaged in very little vigorous physical activity. Yet among women living with HIV, engaging in any vigorous physical activity was the only physical activity intensity associated with improved cardiorespiratory fitness. Moderate to vigorous physical activity has been shown to reduce mortality among adults 50–79 years old in the National Health and Nutrition Examination Survey (NHANES) observational cohort [23]. However, an additional NHANES analysis suggested that this relationship was dose dependent, and varied based on participant's baseline physical activity level [24]. In other words, sedentary adults may benefit from light or moderate physical activity, compared to highly active adults who only experience a mortality benefit from vigorous activity. These data highlight how little is known about how physical activity duration, frequency and intensity impact cardiorespiratory fitness, and cardiovascular health in PLHIV, specifically in women who have increased rates of cardiovascular disease compared with women not living with HIV [25]. Yet they also suggest that there is a clear need to evaluate baseline activity levels in PLHIV and that physical activity interventions targeted to this population should carefully consider how to assist this population to engage in higher-intensity physical activity. Furthermore, these data demonstrate that age and gender are potential tailoring factors. Our finding that women derive the most cardiorespiratory benefits from higher intensity physical activity is novel and if replicated, could help us understand how to address their elevated cardiovascular risk [26]. A potential explanation for this finding is that women with HIV, particularly those who are postmenopausal [26], may have too many cardiovascular risk factors for traditional exercise strategies to work and they may need boosted strategies such as high intensity interval training to help overcome this heightened risk.

One of the most intriguing findings from this study was that as PLHIV aged, there was a significant increase in their ability to achieve their sex- and age- predicted 6MWT distance. Specifically, we observed that starting in their 5th decade ~70% of PLHIV achieved their age-and sex- predicted 6MWT distance, compared to 63% of those in 3rd or 4th decade. If replicated, there are several possible explanations for this finding. The care of PLHIV across the lifespan and around the world requires frequent contact with the health care team to obtain routine lab values, prescribe and dispense HIV anti-retroviral medications, and follow up for side effects [27]. Through various mechanisms (e.g., increased diagnosis and treatment), this increased contact may improve their cardiorespiratory fitness reducing other comorbidities such as respiratory and cardiovascular disease. An important implication of this finding is that as this older group of PLHIV has survived a once-fatal disease and have become more engaged in their health care, they may be more amendable to interventions to improve higher intensity physical activity interventions compared to younger PLHIV. Messages conveyed to PLHIV at routine health care appointments should emphasize how all physical activity can lead to healthy aging with HIV, and highlight the potential importance and safety of high intensity or vigorous physical activity [28]. However, more research is needed to understand the effect of various physical activity intensities on physical functioning, symptom experience, and cardiovascular health in order to design precise, effective physical activity interventions for PLHIV across the lifespan [3 29].

Our study yielded additional data reinforcing the low levels and intensities of physical activity of PLHIV in the U.S. and in Thailand and novel data describing unique relationships between physical activity and sex and cardiorespiratory fitness by age. These findings are bolstered by our large, diverse, multi-site cohort of PLHIV and purposive sampling by season, yet there are limitations that must be considered. Most importantly, our measure of physical activity was self-reported. While the *7-day physical activity recall* was validated against objective measures of physical activity (i.e. accelerometer) [11], it still relies on individual participant recall and may over- or under-estimate activity. Similarly, we used the 6MWT, not maximal cardiorespiratory stress testing, to estimate VO_2 Peak. These measures were chosen because some of our sites had limited resources and would not have been able to use more robust testing measures. By selecting assessments that are less resource intensive, we were able to describe important relationships for this growing population. Future work should carefully consider how to include these gold standard measures in large, diverse, global HIV cohorts. Additionally, our sample predominately includes PLHIV who are in routine HIV care, and our findings, particularly the relationship between age and ability to achieve sex- and age-predicted 6MWT distance, may not be generalizable to those who are not engaged in HIV care.

CONCLUSION

A large, diverse sample of PLHIV engages in low amounts of physical activity, yet among women living with HIV, engaging in vigorous physical activity was associated with improved cardiorespiratory fitness. This study suggests that while we clearly need more effective interventions to improve physical activity amount and intensity, we also need more evidence on how to tailor those interventions, the clinical and mechanistic effects of various types of physical activity on the cardiovascular health of PLHIV, and the role of sex and age in modifying these relationships. Future work should consider these important factors in order to develop effective, sustainable and cost-effective physical activity interventions.

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Table 1:

Physical Activity Levels Defined

Physical Activity Level	Definition	Examples
Sedentary/Sleep	<1.0 MET [*a]	No Activity
Light	1.0-<3.0 METs	Slow walking Light work (cooking, washing dishes, sitting), instrument playing
Moderate	3.0–6.0 METs	Brisk walking, heavy cleaning (vacuuming, mopping), light bicycling
Vigorous	>6.0 METs	Hiking, jogging, shoveling, heavy lifting, fast bicycling, basketball, soccer, tennis

Adapted from data from Sallis's et al. 2006 Physical Activity Recall, [30] the Harvard Obesity Prevention Source, [31] and the Centers for Disease Control and Prevention's Guidelines for Defining Physical Activity by Intensity [32]

[*] MET= Metabolic Equivalents [30–32]

[a] MET defined by baseline energy expenditure at rest (approximately 3.5ml of oxygen uptake per kg of body weight per minute; e.g. 2 MET activity= 2x energy expenditure of sitting at rest)[32]

Table 2:

Demographic and Medical Characteristics of Participants

	Overall (*n*=702)	Men[1] (*n*=428)	Women (*n*=274)	Difference[2]
	***n* (%)**[3]	***n* (%)**	***n* (%)**	
Mean Age (years)[4]	50.5 (±11.1)	49.4 (±11.8)	52.1 (±9.7)	0.002
Current Gender				**<0.001**[5]
Male	397 (57)	396	1	
Female	274 (39)	2	272	
Transgender Male	5 (0.7)	4	1	
Transgender Female	14 (2)	1	0	
Genderqueer or other	12 (2)	12	0	
Employment Status				**0.001**[5]
Working now	194 (28)	123 (29)	62 (23)	
Temporarily not working	11 (2)	6 (1)	5 (2)	
Looking for work, unemployed	102 (15)	66 (15)	36 (13)	
Retired	55 (8)	37 (9)	18 (7)	
Disabled	271 (39)	159 (37)	112 (41)	
Keeping House	41 (6)	12 (3)	29 (11)	
Student	16 (2)	9 (2)	7 (3)	
Permanent Housing	541(77)	321 (75)	220 (80)	0.104[5]
Time Since HIV diagnosis (years)[4]	13.94 (±9.35)	13.93 (±9.81)	13.95 (±8.61)	0.220
Current CD4+ T Cell count[4]	647.36 (±372)	605.0 (±339)	710.0 (±414)	**0.001**
Currently taking HIV Medication[4,6]	621 (92)	375	356	0.955
Undetectable HIV Viral Load	544 (78)	316 (74)	228 (83)	0.004[5]
Self-reported 30 day HIV Medication Adherence[4]	89.9 (±18.0)	89.6 (±19.0)	90.4 (±16.6)	0.572
Currently have comorbidity (%)	430 (61)	258 (60)	172 (63)	0.90[5]
Body Mass Index[4]	27.2 (±7.85)	26.3 (±5.8)	28.7 (±10.0)	**<0.001**
Waist Circumference (inches)[4]	24.89 (±4.45)	24.75 (±4.16)	25.10 (±4.84)	0.360
Waist-to-Hip Ratio[4]	0.911 (±0.09)	0.924 (±0.08)	0.892 (±0.09)	<**0.001**
Median minutes of light physical activity in the past week (Q1, Q3)	85 (3, 240)	105 (4, 300)	60 (1.75, 210)	0.002[7]
Median minutes of moderate physical activity in the past week (Q1, Q3)	30 (0, 165)	50 (0, 200)	13 (0, 125)	0.017[7]
Median minutes of vigorous physical activity in the past week (Q1, Q3)	0 (0, 45)	0 (0, 60)	0 (0,30)	0.287[7]

	Overall (*n*=702)	**Men[1] (*n*=428)**	**Women (*n*=274)**	**Difference[2]**
	***n* (%)[3]**	***n* (%)**	***n* (%)**	
Distance on the Six Minute Walk Test (meters)[4]	401.71 (±104.0)	422.41 (±98.8)	369.5 (±103.8)	<0.001
Age and Gender predicted distance[4]	n/a	625.4 (±82.2)	537.7 (±75.0)	<0.001
% achieved of predicted Six Minute Walk Test[4]	n/a	68.2 (±18.1)	69.2 (±21.3)	0.963
Mean Estimated VO_2 peak (ml/kg/min)[4]	14.2	14.7 (±2.3)	13.4 (±2.4)	**<0.001**

1: Sex assigned at birth;

2: Differences between men and women were tested using t-tests, unless otherwise noted;

3: Data are presented as frequency and percent, unless otherwise noted;

4: Data presented as means standard deviations;

5: Differences between men and women were tested using a chi-square test;

6: ART medication data were available for 676 of participants; 676 was used as the denominator in calculating percent;

7: Differences tested using a two-sample Wilcoxon Rank-Sum Test

Table 3:

Physical Activity and Physical Fitness Characteristics by Sex and Age

	20–29 years		30–39 years		40–49 years		50–59 years		60–69 years		70–82 years		Difference by Decade[1]	
	Women *n*=9	**Men** *n=36*	**Women** *n*=23	**Men** *n=56*	**Women** *n=49*	**Men** *n=88*	**Women** *n=139*	**Men** *n=171*	**Women** *n=46*	**Men** *n*=60	**Women** *n=4*	**Men** *n*=11	**Women**	**Men**
Median Light Activity (mins/week)	140	120	60	90	85	140	30	77	90	111.5	395	70	0.24	0.81
Median Moderate Activity	60	60	90	90	60	70	1.5	7.8	1.8	1.4	0	76	0.73	0.99
Number engaging in vigorous physical activity	3 (56%)	18 (61%)	10 (54%)	28 (45%)	26 (40)	38 (57%)	37 (24%)	49 (40%)	11 (19%)	21 (40)	0 (0%)	2 (0)	0.45	0.31
Median Distance on the 6MWT (meters)	360	411	338	420	361	413	361	420	330	405	300	345	0.61	0.17
Mean estimated VO_2 peak (ml/kg/min)	13.5	14.6	13.3	14.8	13.3	14.6	13.7	14.9	13.2	14.6	11.9	12.9	0.63	0.15
Age and Gender predicted distance	671	738	645	695	591	644	522	597	482	560	418	453	<0.001	<0.001
% achieved of predicted 6MWT	54%	55%	52%	61%	62%	62%	72%	68%	71%	74%	73%	73%	**<0.001**	**<0.001**

[1]: We used ANOVA to examine differences by decade between women and men

Table 4:

Multiple regression of the effect of physical activity on cardiorespiratory fitness by sex, adjusting for age, employment, HIV Viral suppression, season enrolled, and VO2Peak

	β	SE(β)	p-value	95% Confidence Interval	
Women: Predicted distance achieved on the 6-Minute Walk Test (%)					
Age (10 years)	4.52	1.20	**<0.001***	2.23	6.80
Employment Status					
Temporarily unemployed (sick/maternity leave)	13.05	7.42	0.08	−1.57	27.66
Unemployed but looking for work	4.17	3.62	0.25	−2.97	11.31
Retired	8.58	4.64	0.07	−0.55	17.71
Disabled	4.17	2.83	0.142	−1.41	9.76
Keeping House	−3.04	3.66	0.41	−10.24	4.16
Student	14.88	6.90	0.03*	1.29	28.48
Intermittent Employment	3.41	8.29	0.68	−12.93	19.74
Detectable HIV Viral Load	−2.73	2.84	0.34	−8.33	2.86
Season Enrolled	−0.87	0.95	0.36	−2.75	1.00
Engaged in any Vigorous Physical Activity	7.31	2.25	**0.001***	2.88	11.74
Constant	1.82	0.377	<0.000*	1.07	2.56
Men: Predicted distance achieved on the 6-Minute Walk Test (%)					
Age (years)	4.22	0.75	**<0.001***	2.74	5.70
Employment Status					
Temporarily unemployed	9.53	6.03	0.12	−2.33	21.40
Unemployed but looking for work	1.67	2.27	0.46	−2.80	6.13
Retired	−0.94	3.18	0.78	−7.20	5.31
Disabled	−.82	1.92	0.67	−4.60	2.97
Keeping House	.50	4.76	0.92	−8.86	9.86
Student	−1.05	5.28	0.84	−11.43	9.33
Intermittent Employment	7.98	6.54	0.22	−4.88	20.84
Detectable HIV Viral Load	−0.15	1.78	0.93	−3.66	3.36
Season Enrolled	−0.44	0.71	0.54	−1.82	0.95
Engaged in any Vigorous Physical Activity	−0.44	1.52	0.77	−3.43	2.55
Constant	1.80	0.28	<0.001*	1.25	2.36