

# NIH Public Access

Author Manuscript

Obesity (Silver Spring). Author manuscript; available in PMC 2009 November 20

Published in final edited form as:

Obesity (Silver Spring). 2008 May ; 16(5): 1072–1077. doi:10.1038/oby.2008.16.

# Cardiorespiratory fitness predicts changes in adiposity in overweight Hispanic boys

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# Abstract

We have previously shown that cardiorespiratory fitness predicts increasing fat mass during growth in white and African-American youth, but limited data are available examining this issue in Hispanic youth. Study participants were 160 (53% boys) overweight (BMI ≥ 85<sup>th</sup> percentile for age and gender) Hispanic children (mean  $\pm$  SD age at baseline =11.2  $\pm$  1.7 yrs). Cardiorespiratory fitness, or VO<sub>2max</sub>, was measured via a maximal effort treadmill test at baseline. Body composition by dualenergy x-ray absorptiometry and Tanner stage by clinical exam were measured at baseline and annually thereafter for up to four years. Linear mixed models were used to examine the gender specific relationship between VO<sub>2max</sub> and increases in adiposity (change in fat mass independent of change in lean tissue mass) over four years. The analysis was adjusted for changes in Tanner stage, age, and lean tissue mass. In boys, higher  $VO_{2max}$  at baseline was inversely associated with the rate of increase in adiposity ( $\beta$ = -0.001, p=0.03); this effect translates to a 15% higher VO<sub>2max</sub> at baseline resulting in a 1.38kg lower fat mass gain over four years. However, VO<sub>2max</sub> was not significantly associated with changes in fat mass in girls ( $\beta$ =0.0002, p=0.31). In overweight Hispanic boys, greater cardiorespiratory fitness at baseline was protective against increasing adiposity. In girls however, initial cardiorespiratory fitness was not significantly associated with longitudinal changes in adiposity. These results suggest that fitness may be an important determinant of changes in adiposity in overweight Hispanic boys but not in girls.

#### Keywords

Children; Youth; Longitudinal; Gender

# Introduction

The prevalence of overweight in youth is increasing at an alarming rate, and this epidemic is disproportionately affecting ethnic minorities, particularly Hispanic youth (1). The most recent data indicate approximately 43% of Mexican American youth are either at risk for overweight or are overweight (2). Of particular public health concern are the negative health consequences

None of the authors had any financial or personal conflicts of interest.

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associated with adiposity during adolescence, such as risk factors for cardiovascular disease and type 2 diabetes (3). Furthermore, overweight and obesity track into adulthood where negative health consequences extend to include other chronic diseases, including pancreatic and liver cancers (4,5).

There are a myriad of factors that contribute to the trend of increasing adiposity; one of these hypothesized factors is a lack of cardiorespiratory fitness (6,7). Cardiorespiratory fitness is an independent determinant of health across the lifespan (8). In adults, higher cardiorespiratory fitness is protective against cardiovascular disease and all-cause mortality (9). In adolescents, cardiorespiratory fitness has been inversely associated with blood pressure (10), total cholesterol, and pro-inflammatory markers (11). These adverse associations between fitness and disease risk factors may be a direct function of the relationship between cardiorespiratory fitness and adiposity.

Overweight adolescents exhibit lower cardiorespiratory fitness than their normal weight peers (12). African American (6) and white youth (6,7) with lower levels of cardiorespiratory fitness experience significantly greater increases in fat mass during growth compared to their more fit counterparts. To our knowledge, the longitudinal association between cardiorespiratory fitness and fat mass has not been examined in Hispanics adolescents.

Arriving at a better understanding of the associations between cardiorespiratory fitness and adiposity among Hispanic youth is of particular interest due to the high rates of obesity and increased risk of metabolic disease in this population. Therefore, the purpose of the present investigation was to examine whether cardiorespiratory fitness affected the rate of increase in adiposity over time during adolescent growth, and whether this was moderated by gender.

# **Subjects and Methods**

#### Subjects

Study participants in the current investigation consisted of a sub-group of children who are participating in the SOLAR (Study of Latino Adolescents at Risk) Diabetes Project, an ongoing longitudinal study to explore risk factors for the development of type 2 diabetes among Hispanic adolescents. Beginning in 2001, participants between the ages of 8 and 13 were recruited for the study through medical referrals, advertisements, and word of mouth in and around the greater Los Angeles County area. The procedures for the SOLAR Project have been detailed elsewhere (13-15). The current analysis included 160 participants (84 boys and 76 girls) who had completed a baseline measure of VO2max and had complete data for relevant variables during at least two annual visits. Of the participants excluded from the analysis, 42 were excluded because they failed to reach the criteria for VO<sub>2max</sub>, and 39 were excluded because they did not have complete data on all variables used in the current analysis during at least two visits. The participants who were included were not significantly different in percent male, mean age, mean Tanner stage, mean VO2max, mean total fat mass, or mean total lean tissue mass from the participants who were excluded (all p>0.10). The analysis included a total of 597 observations consisting of 23 students completing two visits, 34 students completing three visits, 66 completing four visits, and 37 students completing five visits. Participants had fewer than five visits for two reasons: participants missed at least one annual visit and the open enrollment design of the study. Participants missing one or more visits were not statistically significantly different than those with complete data in percent male, mean age, Tanner stage, VO<sub>2max</sub>, total fat mass, or total lean tissue mass (all p>0.20). Informed consents and assents were obtained from parents and children prior to any testing procedures. The study was approved by the Institutional Review Board of the University of Southern California.

#### Methods

**Outpatient screening visit**—On an annual basis, each participant arrived at the University of Southern California (USC) General Clinical Research Center (GCRC) at the Los Angeles County Hospital at approximately 0800 h following an overnight fast. At the screening visit, a physical examination including the assessment of maturation according to established criteria, Tanner stage (16), was performed by a licensed pediatric health care provider. A detailed medical history was conducted, including parental interview detailing family history of diabetes, ethnicity and demographics of the participants. Height using wall mounted stadiometer and weight using a medical balance beam were measured to the nearest 0.1 cm and 0.1 kg, respectively.

Children who met the following screening criteria were invited back for further testing during an inpatient GCRC visit: 1) aged 8-13 years at baseline assessment, 2) BMI  $\geq 85^{\text{th}}$  percentile for age and gender (at risk for overweight and overweight) defined by the CDC standards (17) calculated from the height and weight measurements completed at the GCRC outpatient screening, 3) absence of type 1 and type 2 diabetes defined by the guidelines provided by the American Diabetes Association, 4) positive family history for type 2 diabetes (sibling, parent or grandparent), 5) Hispanic ethnicity (all four grandparents of Hispanic descent), 6) not currently taking medication or diagnosed with a condition known to affect body composition or total energy expenditure or physical activity. For the sake of brevity, the participants will be referred to as overweight instead of at risk for overweight and overweight.

**Inpatient visit**—Participants who met inclusion criteria were admitted to the GCRC within two weeks after their initial outpatient screening where they completed measurements for cardiorespiratory fitness and body composition. Assessment of cardiorespiratory fitness was collected at baseline assessment only. All other measures were assessed annually for up to four years.

**<u>Cardiorespiratory Fitness:</u>** To assess cardiorespiratory fitness, participants completed an allout, progressive, continuous treadmill protocol, which has been previously described (13,14) and is summarized here. The participants walked for four minutes at 0% grade and four km/h, after which the treadmill grade was raised to 10%. Each ensuing work level lasted two minutes, during which the grade was increased 2.5%. The speed remained constant until a 22.5% grade was reached at which time the speed was increase by 0.6 km/h until the subject reached exhaustion. Respiratory gases were collected and measured using open circuit spirometry and analyzed on a Med Graphics CardiO<sub>2</sub>/CP Combined Exercise System (St. Paul, MN). Heart rate was measured continuously using a Polar Vantage XL heart rate monitor (Port Washington, NY). Absolute VO<sub>2max</sub> (mL of O<sub>2</sub> per minute) was used as a measure of cardiorespiratory fitness. Criteria for VO<sub>2 max</sub> included participants meeting two of three criteria during a maximal effort treadmill test: 1) respiratory exchange ratio (RER) > 1.0, 2) heart rate  $\geq$  195 bpm, and 3) a leveling of VO<sub>2</sub> (defined as an increase of O<sub>2</sub> uptake < 2 mL/kg/min with a simultaneously increasing workload). VO<sub>2 max</sub> was defined as the highest oxygen uptake obtained over the final 1.5 min of the protocol.

**<u>Body Composition:</u>** A whole-body dual-energy x-ray absorptiometry (DEXA) scan was performed to assess total body composition, including fat mass, soft lean tissue mass, and percentage body fat, using a Hologic QDR 4500W (Hologic, Bedford, MA).

#### **Statistical Analysis**

Descriptive statistics were generated for variables of interest and demographic variables. Students *t*-tests were conducted to determine if there were statistically significant gender differences in baseline characteristics.

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For longitudinal analyses, linear mixed effects models were then used to examine whether baseline  $VO_{2max}$  was associated with total fat mass at age 11 and whether baseline  $VO_{2max}$  was associated with the change in total fat mass as the youth age after adjusting for the changes in total lean tissue mass, Tanner stage, gender, and age. Additionally, an interaction term was included in the mixed effects regression models to investigate whether gender was an effect modifier of the relationship between cardiorespiratory fitness at baseline and changes in adiposity. Because the interaction term was found to be statistically significant, the data were stratified by gender, and the relationship was re-examined in boys and girls separately. All statistical analyses were performed using Statistical Analysis Software (v9.1, SAS Institute Inc., Cary, NC). The linear mixed effect analyses were performed using the Mixed Procedure.

Although  $VO_{2max}$  is generally expressed relative to total body mass or fat free mass (FFM), we chose to express  $VO_{2max}$  in absolute terms (mL/min). There is currently no consensus on the appropriate units of expression when comparing participants with differing body composition, gender, and age. It has previously been shown that the ratio method, which adjusts for body composition by dividing  $VO_{2max}$  values by body mass or FFM, may create spurious results, because it fails to take into account the nonzero intercept (18). It has also been shown that using a regression-based method is a more appropriate approach to normalizing  $VO_{2max}$  data (18), and as a result lean tissue mass was used as a covariate in the model in the current study. Even though the ratio methods were not used in the regression analysis, to facilitate comparison among studies, we reported baseline mean  $VO_{2max}$  relative to fat free mass (mL/kg FFM/min) and total body mass (mL/kg/min).

# Results

Baseline characteristics for the 160 participants (84 boys and 76 girls) are shown in Table 1. At baseline, there were statistically significant gender differences in absolute  $VO_{2max}$  (mL/min),  $VO_{2max}$  divided by body mass (mL/kg/min),  $VO_{2max}$  divided by fat free mass (mL/kg FFM/min), Tanner stage, and total body fat (kg; all p<0.05). The number of boys and girls completing two, three, four, and five annual visits is shown in Table 2.

In the linear mixed effects regression model with the total sample, initial  $VO_{2max}$  was not associated with changes in total fat mass over age after adjusting for changes in Tanner stage, gender, and lean tissue mass (data not shown;  $\beta$ =-0.0005, p=0.18). Table 3 shows the effect of the predictor of interest, baseline cardiorespiratory fitness, on total fat mass at age 11 after adjusting for covariates; at baseline when the mean age of the participants was 11 years, each one mL/min change in VO2max was marginally associated with a 0.002 kg change in total fat mass after adjusting for covariates (p < 0.10). Table 3 also shows the effect of baseline cardiorespiratory fitness on total fat mass over age after adjusting for covariates; each year, a one mL/min change in VO2max was significantly and inversely associated with a 0.001 kg change in total fat mass independent of covariates (p < 0.01). When gender was investigated as a potential effect modifier (Table 3), it was found to be a significant effect modifier in the relationship between VO2max and change in total fat mass after adjusting for changes in Tanner stage and lean tissue mass (β=0.002, p=0.0007). Figure 1 is a graphical representation of Table 3 in which the estimated marginal means of the regression equations were plotted. While holding the covariates constant (intercept = 23.9 kg, Tanner stage = 2, lean tissue mass = 37kg), the values of gender and VO<sub>2max</sub> were manipulated to illustrate the gender- and fitness level-specific trajectories of total fat mass as the youth age. The value used to represent high fitness was the 95<sup>th</sup> percentile of VO<sub>2max</sub>, and the value used to represent low fitness was the 5<sup>th</sup> percentile of VO<sub>2max</sub>.

Subsequent analyses were stratified by gender, as shown in Table 4. Among boys,  $VO_{2max}$  was a significant predictor of change in total fat mass adjusting for changes in lean tissue mass,

Tanner stage, and age ( $\beta$ = -0.001, p=0.03). On the other hand, as also shown in Table 4, VO<sub>2max</sub> was not a significant predictor of change in total fat mass in girls after controlling for changes in Tanner stage, lean tissue mass, and age ( $\beta$ =0.0005, p=0.37).

# Discussion

The primary finding of this investigation was that the longitudinal relationship between initial cardiorespiratory fitness and changes in adiposity in children is different in overweight Hispanic boys and girls. In boys, higher initial cardiorespiratory fitness was associated with less subsequent gain in body fat. However, initial cardiorespiratory fitness was not significantly associated with subsequent fat mass gain in overweight Hispanic girls. These results suggest that the longitudinal association between cardiorespiratory fitness and obesity in Hispanic youth may be gender specific.

In adolescents, cardiorespiratory fitness, defined as the ability of the cardiovascular and respiratory systems to supply oxygen to skeletal muscles during sustained physical activity, correlates to habitual physical activity, which is defined as the amount a person moves around during the day (12,19,20). Importantly, cardiorespiratory fitness is more strongly associated with moderate to vigorous physical activity than total physical activity (12,19). Thus, one potential explanation for our findings is that cardiorespiratory fitness may be acting as a proxy indicator of moderate to vigorous physical activity. Whereby, Hispanic boys who engage in greater amounts of moderate to vigorous physical activity (as indicated by higher initial cardiorespiratory fitness) may have a more balanced energy equation than non-active boys resulting in less adiposity in the active boys. In support of this hypothesis, our group previously reported (21) cross-sectionally that Hispanic overweight boys engaged in significantly less moderate to vigorous physical activity than non-overweight boys  $(3.2 \pm 2.1\% \text{ vs}, 4.8 \pm 2.9\% \text{ vs})$ of day spent in moderate to vigorous activity, respectively; p=0.01), but we did not find a significant difference in moderate to vigorous physical activity between overweight and normal weight Hispanic girls in that study  $(2.9 \pm 1.5\% \text{ vs}, 2.5 \pm 1.6\%; p=0.33)$ . Although those youth were not followed longitudinally, our previous cross-sectional results coupled with our current longitudinal findings suggest that physical activity / cardiorespiratory fitness and obesity are differentially influenced by gender in Hispanic youth.

There is no clear consensus on whether cardiorespiratory fitness in youth is indicative of habitual moderate to vigorous physical activity. According to a review that included over 25 studies, which used a myriad of methods to assess cardiorespiratory capacity, there is a only a small to moderate relationship between physical activity and cardiorespiratory fitness in adolescents (22). While it is acknowledged that other factors, such as genetics (23), contribute to individual levels of cardiorespiratory fitness, studies examining fitness and physical activity make reasonable arguments for the use of cardiorespiratory fitness as a proxy measure for habitual moderate to vigorous physical activity at the group level. Regionally and nationally representative studies in Spain (24) and the US (12) have reported that adolescents who engaged in more moderate to vigorous physical activity had higher values of VO<sub>2max</sub>. Nonetheless, we cannot exclude the possibility that undetermined physiologic or behavioral gender differences in our sample were operational in the observed longitudinal associations between cardiorespiratory fitness and adiposity.

The findings from the current study could help to inform future interventions with overweight Hispanic children. Although cardiorespiratory training intervention studies conducted in healthy, non-obese, normotensive youth tend to have negligible effects on body composition, blood lipids, and blood pressure (25,26), cardiorespiratory training interventions in overweight and obese samples have reported more successes (27,28). Training interventions designed for overweight adolescents may result in a reduction of total body weight, though sometimes

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inconsistently. Additionally, these intervention studies have reported beneficial changes in insulin sensitivity (27), muscular strength, endothelial function, and cardiorespiratory fitness (27). For example, Rowland et al. reported a walking training intervention with sedentary overweight adolescents that resulted in an increase in cardiorespiratory fitness of 9.9% (28). The findings from the current study suggest that if interventions were able to improve the cardiorespiratory fitness of overweight Hispanic boys by as little as 15%, this may result in a lesser accumulation of 1.38 kg of fat mass over four years than otherwise would have been observed. Additional studies should be conducted with overweight Hispanic adolescents to examine whether increased cardiorespiratory fitness has beneficial effects on body composition and other chronic disease risk factors.

As observed in other studies (29,30), the baseline values of  $VO_{2max}$  for girls in the current study were significantly lower than the values for boys. Regardless of how  $VO_{2max}$  was expressed, the cardiorespiratory fitness of girls was at least 11% lower than boys, and this difference in cardiorespiratory fitness will increase as the boys and girls mature (29). When cardiorespiratory fitness levels of the girls from the current study are compared to a nationally representative sample (12), girls in the current study would fall below the lower 40th percentile for age and gender adjusted fitness levels.

The null finding that initial cardiorespiratory fitness at 11years is not predictive of changes in adiposity may indicate that energy intake in overweight Hispanic girls rather than energy expenditure may be a more important determinant of increases in adiposity. The poor cardiorespiratory fitness levels may be an indication of insufficient levels of physical activity necessary to counterbalance higher levels of energy intake in order to prevent increases in adiposity over time. Even more troubling is that low levels of physical activity are likely to decline even more as the girls progress through adolescence and into adulthood (31) at which point low cardiorespiratory fitness levels and a sedentary lifestyle may result in the development of adiposity-related comorbidities such as type 2 diabetes and cardiovascular disease. Thus, targeting overweight Hispanic girls for physical activity interventions coupled with dietary interventions at a young age may help to improve their body composition and energy balance equations resulting in less adiposity increases over time.

The strengths of this study include a precise measure of body composition using DEXA (32), a direct measure of  $VO_{2max}$ , the repeated measures design, and the use mixed effects regression modeling. The repeated measures design allowed us to follow the same individuals over time to observe changes in adiposity. The use of linear mixed effects regression models was a distinct benefit, because it accounts for the violation of the assumption of independence across repeated measures and is able to include cases with missing waves of data allowing for a larger sample size to be included in the analysis.

Notwithstanding these strengths, we acknowledge several limitations of the study that may impede the generalizability of the findings. The current study consisted only of overweight Hispanic adolescents with a family history of diabetes. The possibility of gender moderating the relationship between initial cardiorespiratory fitness and changes in adiposity in youths of other ethnicities has not been addressed in this investigation, and as a result, no conclusions should be drawn about the moderating effects of gender in other ethnicities. Also, due to the homogeneity of the sample, it may not be appropriate to generalize these findings to Hispanic adolescents with a different overweight status or a different family history of disease. Despite the potential limitations of the homogenous sample, we believe the investigation of increasing adiposity in these already overweight adolescents has scientific merit, because the overweight status and ethnicity of these youth increase their risk for chronic diseases, such as type 2 diabetes and cardiovascular disease.

Another limitation is that the current study did not provide repeated measures of dietary data or cardiorespiratory fitness. Dietary data would have allowed for the influence of energy intake on adiposity to be examined. Additionally, because cardiorespiratory fitness was only assessed at baseline, the change in  $VO_{2max}$  and its effect on change in fat mass could not be examined. Future longitudinal studies that include repeated measures of  $VO_{2max}$ , dietary intake and adiposity are warranted. Investigating the association between the change in  $VO_{2max}$  and changes in fat mass independent of energy intake would provide further information on how cardiorespiratory fitness may influence adiposity.

In summary, these findings suggest the relationship between cardiorespiratory fitness and subsequent adiposity may differ by gender suggesting that gender-specific interventions targeting changes in adiposity may be more effective. To further explain this relationship, additional intervention studies that manipulate cardiorespiratory fitness to examine the effects on adiposity in overweight Hispanic youth are needed, as are longitudinal studies that include direct measures of cardiorespiratory fitness, objective measures of physical activity, and measures of dietary intake.

#### Acknowledgments

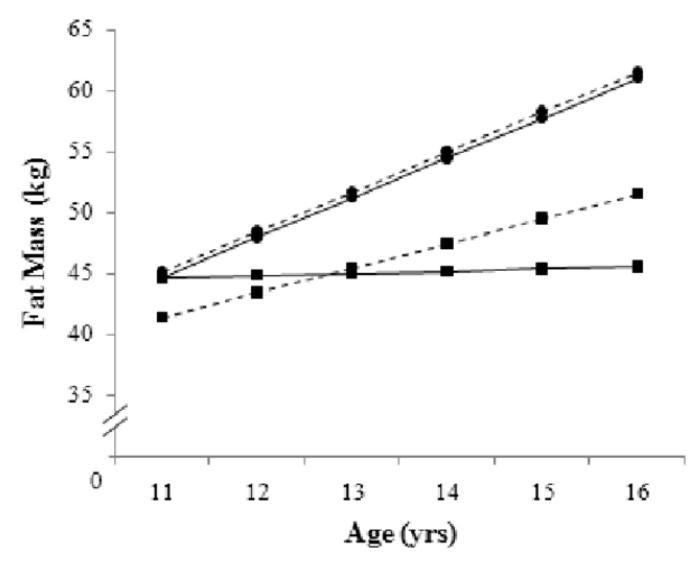
We would like to thank study coordinators, Christina Ayala, and the nursing staff at the USC-GCRC. Additionally, we are grateful to our study participants and their families for their involvement. This study was supported by the National Institutes of Health (R01 DK 59211) and National Cancer Institute (Cancer Control and Epidemiology Research Training Grant, T32 CA 09492 and the USC Center for Transdisciplinary Research on Energetics and Cancer, U54 CA 116848).

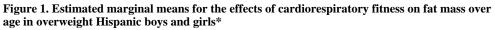
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\*Model is adjusted for Tanner stage and lean tissue mass. Value used to represent high fitness was 95<sup>th</sup> percentile of VO<sub>2max</sub>, and value used to represent low fitness was 5<sup>th</sup> percentile of VO<sub>2max</sub>.

--- Boys low fitness

—∎-— Boys high fitness

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—•— Girls high fitness

Table 1

#### Participant characteristics at baseline, mean $\pm$ SD

Characteristics	Boys (n=84)	Girls (n=76)
Age (years)	$11.2 \pm 1.6$	$11.2 \pm 1.8$
Weight (kg)	$62.5 \pm 16.8$	$65.6 \pm 20.1$
Height (M)	$150.7 \pm 10.9$	$149.4 \pm 11.2$
BMI $(kg/m^2)$	$27.3 \pm 4.6$	$28.8 \pm 5.4$
BMI Z-score	$2.0 \pm 0.4$	$2.1 \pm 0.4$
BMI percentile	$96.8 \pm 3.3$	$97.2 \pm 2.9$
Total body fat (kg)	$23.1 \pm 9.0$	$26.2 \pm 10.3^*$
Total lean tissue mass (kg)	$37.0 \pm 9.2$	$36.9 \pm 9.9$
Tanner stage (1-5)	$1.7 \pm 1.0$	$2.97 \pm 1.4$
VO <sub>2max</sub> (mL/min)	$2292.6 \pm 574.1$	$2043.6 \pm 475.0^{**}$
VO <sub>2max</sub> (mL/kg/min)	$37.5 \pm 6.9$	$32.1 \pm 5.1^{***}$
VO <sub>2max</sub> (mL/kg FFM/min)	$58.4 \pm 5.8$	$52.6 \pm 5.5^{***}$

For gender:

p<0.05,

\*\* p<0.01,

\*\*\* p<0.001

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#### Table 3

#### Effects of Predictors on Total Fat Mass (kg) from Linear Mixed Effects Regression (n=160)

#### Effect of predictors on total fat at age 11

Predictors	Estimate (SE)	
Intercept	23.95 (0.72)****	
Gender (male=0, female=1)	2.78 (1.11)****	
Lean tissue mass (kg)	0.48 (0.5)***	
Tanner stage (1-5)	$-0.46(0.26)^+$	
Age (yrs)	-0.28 (0.29)	
Baseline cardiorespiratory fitness (VO <sub>2max</sub> )	$0.002 (0.001)^+$	
Effect of predictors on total fat mass over age	Estimato (CE)	
Predictors	Estimate (SE)	
Predictors Gender (male=0, female=1)	1.66 (0.31)****	
Predictors	$\begin{array}{c} 1.66\ (0.31)^{***}\\ -0.0002\ (0.01)\\ -0.27\ (0.10)^{**}\end{array}$	
Predictors Gender (male=0, female=1) Lean tissue mass (kg)	1.66 (0.31)****	

<sup>+</sup>p<0.10,

\* p<0.05,

\*\* p<0.01,

\*\*\* p<0.001

Effects of Linear Mixed Effects Regressions on Total Fat Mass (kg) by Gender	sions on Total Fat Mass (kg) by Ge	nder	
Boys (n=84)		Girls (n=76)	
Effect of predictors on total fat at age 11 <u>Predictors</u> Intercept Lean tissue mass (kg) Tanner stage (1-5) Age (yr) Baseline cardiorespiratory fitness (VO <sub>2max</sub> )	$\frac{\text{Estimate (SE)}}{24.31(0.78)^{\text{#F}}_{\text{#}}}$ $2.37(0.06)$ $-0.26(0.43)$ $0.35(0.36)$ $0.001(0.002)$	Effect of predictors on total fat at age 11 Predictors Intercept Lean tissue mass (kg) Tanner stage (1-5) Age (yr) Baseline cardiorespiratory fitness (VO <sub>2max</sub> )	Estimate (SE) 25.76 (0.63) *** 0.77 (0.07) **** -0.61 (0.31) <sup>+</sup> 0.02 (0.28) 0.002 (0.002)
Effect of predictors on total fat mass over age <u>Predictors</u> Lean tissue mass (kg) Tanner stage Baseline cardiorespiratory fitness (VO <sub>2max</sub> )	Estimate (SE) 0.01 (0.02) -0.44 (0.17) -0.001 (0.0004)*	Effect of predictors on total fat mass over age <u>Predictors</u> Lean tissue mass (kg) Tanner stage Baseline cardiorespiratory fitness (VO <sub>2max</sub> )	Estimate (SE) -0.01 (0.02) -0.01 (0.02) 0.0005 (0.0005)
+ p<0.10, * p<0.05,			

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\*\* p<0.01, \*\*\* p<0.001