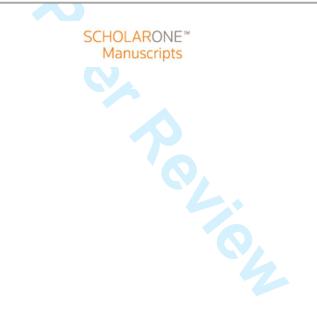
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RELATIONSHIP BETWEEN METABOLIC SYNDROME AND MODERATE-TO-VIGOROUS PHYSICAL ACTIVITY IN YOUTH

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Metabolic and behavioral risk factors in youth

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ABSTRACT

Background: Associations of metabolic syndrome (MetS) with lifestyle behaviours in youth is potentially important for identifying subgroups at risk and encourage interventions. This study evaluates the associations among the clustering of metabolic risk factors and moderate-to-vigorous physical activity (MVPA) in youth. Methods: The sample comprised 924 youth (522 girls) aged 11-17 years. Height, weight, waist circumference (WC), fasting glucose, HDL-cholesterol, triglycerides, and blood pressures were measured. Cardiorespiratory fitness (CRF) was assessed using the 20-m shuttle run test. MVPA was estimated with a 3-day diary. Outcome variables were statistically normalized and expressed as Z scores. A clustered metabolic risk score was computed as the mean of Z scores. Multiple linear regression was used to test associations between metabolic risk and MVPA by sex, adjusted for age, WC and CRF. **Results:** After adjustment for potential confounders, MVPA was inversely associated with the clustering of metabolic risk factors in girls, but not in boys; in addition, after adjusting for WC, the statistical model of that relationship was substantially improved in female youth. *Conclusion:* MVPA was independently associated with increased risk of MetS in girls. Additional efforts are needed to encourage research with different analytical approach and standardization of criteria for MetS in youth.

22 Keywords: Metabolism, Moderate-to-Vigorous Physical Activity, Inactivity, Youth

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INTRODUCTION

The Metabolic Syndrome (MetS) is often defined as the clustering of three or more risk factors including adiposity, hypertension, hyperglycemia, low high-density lipoproteincholesterol (HDL-C), and high triglycerides ¹. The prevalence of MetS has increased among youth and is an increasingly important health challenge worldwide². Based on modified ATPIII criteria³, prevalence estimates of MetS among obese adolescents range from 18% in Spain⁴ to 42% in the US⁵. The most common metabolic abnormalities among youth with MetS were elevated waist circumference (WC, 96.2%), low HDL-C (96.2%) and hypertriglyceridemia (73.1%); insulin resistance was also identified in youth having MetS⁶. Relatively recent environmental and behavioural changes associated with increased sedentary behaviour and reduced physical activity (PA) may have contributed to this phenomenon.

Health authorities in most countries have recognized the potentially negative effects of inactive lifestyles for health and have compiled guidelines to enhance the level of PA among children and adolescents ⁷. Recent reviews confirm the importance of improving habitual PA in youth and suggest that higher levels of moderate tovigorous physical activity (MVPA) are inversely associated with adiposity ⁸ and an adverse cardiometabolic risk profile ⁹⁻¹¹. However, with an increase in MVPA, the risk of an unfavourable risk profile is reduced ^{2,10}.

Adolescence is a period during which involvement in PA may contribute to a physically active lifestyle that persists into adulthood ¹². Young people, particularly during adolescence, tend to show lower levels of PA and should be a target for prevention strategies aimed at healthy lifestyles. For example, 80% or more of adolescent girls in 100 of 105 countries (95%) and of adolescent boys in 56 (53%) of 105 countries did not achieve the objective of 60 minutes MVPA per day ¹³. As such,

better understanding of interactions among MVPA and metabolic health of youth,
 particularly in under studied populations of children and adolescents, can be helpful in
 designing effective and targeted strategies to reduce metabolic disease risk.

In context of the preceding trends, the objective of this study is to evaluate the relationships between the clustering of metabolic risk factors and MVPA among adolescents aged 11-17 years after adjusting for several potential confounders. It was hypothesized that adolescents classified as less active would be more likely to have higher metabolic risk than more active peers.

10 METHODS

11 Sample

The cross-sectional study was carried out in Curitiba (about 1,678,965 inhabitants), Paraná, Brazil. Curitiba has nine administrative districts with 293 schools. The proportion of students in each of the nine administrative areas was as follows: Santa Felicidade 6.6%; Matriz, 12.3%; Boa Vista, 14.7%; Cajuru, 12%; Portão, 10.6%; Boqueirão, 13.1%; Bairro Novo, 9.6%; Pinheirinho, 9.5%; and CIC, 11.6%. Schools were randomly selected among the districts and all students in the respective schools were invited to participate in the study. The final sample represents the students who returned written informed consent appropriately signed by parents or guardians. The survey was conducted in 2009. Accordingly, 924 youth (522 girls) 11 to 17 years of age had complete data for metabolic variables of interest and were retained for the present analysis. The project was approved by the Scientific Committee of the Federal University of Paraná which requires anonymity and non-transmissibility of data.

25 Anthropometry

Measurements were taken by trained research assistants at each school. Participants wore t-shirts and shorts and shoes were removed. Body height was measured to the nearest 0.1 cm with a portable stadiometer (Ottoboni HM-210D; RJ, Brazil) and body weight was measured to the nearest 0.1 kg with a calibrated beam balance scale (Toledo 2096 PP; SP, Brazil). The mean of the two measurements was used for analysis. Waist circumference (WC) was measured at the end of a normal expiration midway between the lower rib margin and iliac crest. Replicate measurements of WC were taken on 89 students within the same day. Technical errors of measurement (σ_e) and reliability (R)¹⁴ were 2.09 cm and 0.97, respectively.

11 Blood sampling

Blood samples were collected by trained nurses from the antecubital vein between 8:00 and 10:00 am with subjects in a fasted state (10 hours) and seated position. The blood samples were drawn in vacuum tubes gel (Sarstedt). After resting at room temperature for about 30 minutes, samples were centrifuged for 10 minutes at 3000 rpm to obtain serum. Samples were divided into aliquots, separated within 30 minutes and stored at -80°C until analysis. HDL-C, TG, and glucose levels were measured by colorimetric assay on a random access Spectrum CCX analyzer (Abbott Diagnostics, Abbott Park, IL, USA). A single certified laboratory was used for all analyses.

21 Blood pressure (BP)

BP was measured according to the method described in *The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents* ¹⁵. Both systolic blood (SBP) and diastolic blood (DBP) pressures were measured in the right arm using a sphygmomanometer. Two measurements were taken

by trained technicians before blood samples were drawn and after 5 and 10 minutes rest
in a seated position. The mean of the two measurements was used for analysis. If the
two measurements differed by > 2 mmHg, a third measure was obtained, and the mean
of the two closest measurements was retained for analysis.

Within day technical errors of measurement (σ_e) and reliability (R) ¹⁴ based on
replicated measurements of 89 students were as follows: SBP, 2.43 mmHg; DBP, 2.52
mmHg, while reliability coefficients were as follows: SBP, 0.96; DBP, 0.92.

MetS risk score

The definition of the syndrome and cutoff points for specific components vary among studies ¹⁶, but none apply specifically to children and adolescents. Since the primary objective was to investigate the clustering of risk factors relative to MVPA, a continuous metabolic syndrome risk score^{1,17} was used. Each indicator (insulin, triglycerides, blood glucose, HDL-C, BP) was converted to a Z score, where Z = ([value]- mean]/SD). Z scores were multiplied by -1 if necessary to indicate higher metabolic risk with increasing value. Z scores of systolic and diastolic BP were averaged and treated as a single indicator. Z scores for the five MetS criteria were summed and divided by five to derive an average of clustered metabolic risk score as in other epidemiological studies of youth 9,17.

21 Daily physical activity

Each participant completed a dairy protocol ¹⁸ over three complete days (Thursday, Friday and Saturday). The protocol divided each day into 96 periods of 15 minutes. Participants were required to record all activities and to rate the intensity of the primary activity performed in each 15-minute period using a numeric code ranging from one to

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nine. Energy expenditure (EE) was estimated from equivalents for each category: [1] sleeping or resting in bed: 0.26 Kcal/kg/15min; [2] sitting: 0.38 Kcal/kg/15min; [3] light activity standing: 0.57 Kcal/kg/15min); [4] slow walking ~ 4 km/hr: 0.69 Kcal/kg/15min; [5] light manual tasks: 0.84 Kcal/kg/15min; [6] leisure and recreational sports: 1.2 Kcal/kg/15min; [7] manual tasks at a moderate pace: 1.4 Kcal/kg/15min; [8] leisure and sport activities of higher intensity – not competitive: 1.5 Kcal/kg/15min; [9] very intensive activities – competitive sports: 2.0 Kcal/kg/15min. Total daily energy expenditure (TDEE) was estimated for each of the three days. Intensity categories 6-9 (4.8-7.8 METs) represented MVPA¹⁸.

For inclusion, all (96) 15-min episodes per day had to be completed with a categorical value from 1 to 9 for the three days. Records of participants who did not complete the diary for 3 days were excluded from analysis. Data for 924 youth (94% of the initial sample) met the criteria for inclusion and were used for subsequent analyses. There were no significant differences in the distributions of included and excluded participants by sex $[\chi_{(1)}^2=0.72; p=0.39]$, age $[\chi_{(1)}^2=6.13 p=0.41]$, and weight status $[\chi_{(1)}^2 = 0.20 \text{ p} = 0.91]$. Data processing and inclusion criteria were the same as in European^{19,20}, U.S.²¹ or Asian²² studies. Reproducibility of this instrument was r=0.91 in subjects ≥ 10 years of age ¹⁸ and was validated in adolescents against objective measures of PA²³.

21 Cardiorespiratory fitness (CRF)

22 CRF was measured with the 20-meter multistage shuttle run endurance test ²⁴. The test 23 was scored as the number of "laps" completed at volitional exhaustion. Participants ran 24 between 2 lines, 20-m apart, following the cadence dictated by a CD emitting audible

signals at prescribed intervals. Initial speed was set at 8.5 km/h for the first minute and then was increased 0.5 km/h each subsequent minute. When participants could no longer keep up with the pace by reaching the line at the time of the tone, the test was terminated at the second fault and the number of laps completed was recorded. The test provides a valid and reliable field measure of VO_{2max} in adolescents ²⁴. The protocol was explained in full before the test. All testing was done during physical education classes under dry weather conditions, and carried out and managed by the same researcher who provided the essential instructions for the participants. In addition, two master's level students monitored each line 20-m apart to verify the correct execution of the protocol and also to help encourage and motivate participants to give a maximal effort. At the end of the test, all participants showed signs of intense effort (e.g., hyperphoea, facial flushing and grimacing, unsteady gait, sweating).

14 Statistical procedures

Sex-specific descriptive statistics were calculated for age, height, weight, WC, MVPA, CRF, and all metabolic variables. One-way analysis of covariance (ANCOVA) was used to test the effect of gender on the above mentioned variables, controlling for chronological age. All ANCOVAs were followed with Bonferroni-corrected *post hoc* tests.

20 Prior to analysis, distributions of the clustering of metabolic risk factors, MVPA 21 and CRF scores were tested for normality and normalized if necessary. Insulin, glucose, 22 triglycerides, CRF and MVPA were logarithmically transformed. Log transformation of 23 the variables improved normality for these variables, and as such, they were used as 24 transformed variables in the several analyses.

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1	Adiposity is often indicated as factors affecting habitual PA ^{12,25,26} and to a lesser
2	extent metabolic health ² . Associations between the clustered metabolic risk factors and
3	MVPA, controlling for the potentially confounding effects of chronological age, WC,
4	and CRF were estimated using multiple linear regression analysis. In the minimally
5	adjusted model (Model 1), MVPA was the sole predictor of clustered metabolic risk.
6	WC and chronological age were subsequently added as potential confounders (Model 2).
7	Finally, CRF was then added as a potential confounder (Model 3). Significance was set
8	at 5%. SPSS 17.0 (SPSS Inc., Chicago, Illinois, USA) was used.
9	
10	RESULTS
11	Characteristics of the sample are summarized in Table 1. About 79% of boys were
12	categorized as normal weight, 17% as overweight, and 4% as obese; corresponding
13	percentages for girls for were 76%, 18%, and 6%, respectively. Males and females did
14	not differ in triglycerides, glucose, HDL cholesterol, and diastolic BP. Height, body
15	mass, WC, systolic BP, PA and CRF were, on average, significantly higher in males,
16	whereas insulin level was higher in females. HDL level tended to be higher in females
17	and the difference was marginally significant (p=0.056).
18	
19	[Table 1]
20	
21	Bivariate associations
22	In girls, clustered metabolic risk score was inversely correlated with MVPA (r=-0.09,
23	$p\leq0.05$) and positively related with weight (r=0.36, $p\leq0.01$), height (r=0.16, $p\leq0.01$),
24	and WC (r=0.31, p \leq 0.01). MVPA was also positively related to HDL-C (r=0.04,
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p≤0.05) and PA (r=0.49, p≤0.01), and inversely related to blood pressure (r=-0.09,
 p<0.05). The magnitude of those relationships was weak to moderate.

Among boys, clustered metabolic risk score was positively correlated with weight (r=0.36, p \leq 0.01), height (r=0.17, p \leq 0.01), and WC (r=0.42, p \leq 0.01). MVPA was also positively related to PA (r=0.43, p \leq 0.01) and inversely related to blood pressure (r=-0.10, p \leq 0.05). The magnitude of the aforementioned relationships was weak to moderate.

[Table 2]

11 Association between CRF and the clustered metabolic risk score

12 Results of the regression analyses are summarized in Tables 2 and 3 for females and 13 males, respectively. MVPA was inversely associated with clustered metabolic risk Z-14 score after adjustment for several potential confounders in girls (β =-0.08; 95% CI, -0.91 15 to -0.08). In the final model, the additional significant predictors of the clustered 16 metabolic risk were WC (β =0.55; 95% CI, 0.16 to 0.22), age (β =0.53; 95% CI, 0.08 to 17 0.30) and CRF (β =-0.06; 95% CI, -0.04 to 0.00).

In contrast, there was no significantly association between MVPA and the clustered metabolic risk Z-score in boys neither in model 1 (β =-0.02; 95% CI, -0.83 to 0.53) nor after adjustment for potential confounding factors (model 3). In the final model, WC (β =0.61; 95% CI, 0.19 to 0.24), age (β =0.16; 95% CI, 0.12 to 0.41), and CRF (β =-0.14; 95% CI, -0.03 to -0.01) were the sole significant predictors of clustered metabolic risk in boys.

[Table 3]

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DISCUSSION

Research on the MetS and associations with lifestyle behaviours in adolescents is potentially important for identifying subgroups of youth at whom interventions should be targeted. Systematic evaluation of the independent contributions of MVPA to clustered metabolic risk factors in Brazilian youth is lacking. This cross-sectional analysis indicated a negative relationship between the clustering of metabolic risk factors and MVPA in girls 11-17 years, but not in boys. The association in girls was not altered with adjustment for the potential confounding factors included in the regression model. The results for Brazilian adolescent girls were consistent with other studies in showing that overall PA and time spent in MVPA was associated with a healthy cardiometabolic profile in youth ^{2,9,27,28}.

The observed association between MVPA and clustered metabolic risk factors in girls was independent of adiposity and other biological confounding factors such as CRF and chronological age. By inference, it is reasonable to assume that MVPA can improve the metabolic-risk profile of adolescent girls, possibly with the exception of adiposity. Regular PA improves insulin action and glucose transport²⁹, and also increases blood flow and oxygen supply through increased capillarization and vasodilatation by nitric oxide, which improves fat metabolism ³⁰. Regular PA may also affect sympathetic tone with an associated reduction in blood pressure through a more efficient recruitment of the motor units in the muscle³¹.

The lack of regular PA was associated with the development of cardiovascular disease risk factors in youth, including lipid disorders, high BP, insulin resistance, and others ^{2,32}. Data for a representative sample of U.S. adolescents 12-19 years indicated that only about 8% attained the recommendation of 60 min/day of PA of moderate or

greater intensity. Similar low rates were also noted in European youth using both objective ³³ and subjective ³⁴ measures of PA. More recently, only 36% of Portuguese youth 10–11 years (boys=51.6%, girls=22.5%) and 4% of youth 16–17 years (boys=7.9%, girls=1.2%) were considered sufficiently active by achieving 60 minutes of MVPA daily³⁵. The majority (58%) of Brazilian adolescent girls in the present study did not achieve 60 minutes of MVPA daily; corresponding data for boys was 30%. Overall, evidence from many parts of the world suggests significant metabolic health risk among youth which has implication for public health as metabolic risk and PA tend to track from adolescence into adulthood 36 .

Our results from boys contradict findings of girls suggesting that MVPA is not significantly associated with the clustered of metabolic outcomes. Those sex-differences can be explained, in part, by the between-individual variability of PA which vary between boys and girls; this variability impacts the ability to measure MVPA and consequently influences their relationship with metabolic outcomes. When interpreting those sex-related differences, the significant difference in the prevalence of some outcomes of MetS between boys and girls should be also considered, such as insulin and systolic BP of the present study; this may be related to hormonal differences, such as testosterone and sex-hormone binding globulin between genders ³⁷. Those notable differences between genders, for which probably we do not have an adequate explanation, could possibly be explained by more focus of public educational programs on girls compared to boys or even by some specific cultural and lifestyle differences, leading to discrepant trend on the association between the clustered of metabolic risk factors and PA in boys and girls.

24 Some observational studies ^{10,28,38} examined large and heterogeneous samples of 25 children and adolescents, suggesting that the findings are quite generalizable to the

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1	general population. However, in some cross-sectional studies that were employed self-
2	reported measures of PA, the reported associations with the MetS were either weak or
3	modest in strength, and were non-significant ^{39,40} . In contrast, studies that used objective
4	measures (e.g. accelerometers) to assess PA ¹⁰ , it was reported strong and significant
5	relations with the MetS. Thus, variation in results among studies may be related to the
6	assessment of PA and its multidimensional nature per see; PA protocols may be affected
7	by the nature of behavior recalled. Most daily activities are intermittent and may involve
8	substantial rest periods, which may lead to significant overestimation of time spent on
9	daily activities ⁴¹ . Such intermittent activities are probably more difficult to define or
10	quantify than occupational activities or structured exercises ⁴² . Therefore, it is plausible
11	that the lack of observed associations between MVPA and clustered metabolic risk in
12	boys were likely to be due, in part, to measurement accuracy since self-report
13	instrument are often viewed as having less precision for high intensity levels of PA ^{42,43} .
14	However, despite of some studies have revealed clear associations, the nature (e.g.,
15	linear or curvilinear) of the dose-response relation is still unclear claiming for further
16	research with different analytical approach and design.
17	Additional sources of variation among studies, in the association of MVPA and

the clustering of metabolic risk factors, may be related to the cut-off criteria used to define MetS and in turn the metabolic risk factors in the present study. Results for the Brazilian adolescents showed considerable variation in prevalence of MetS. For example, only 1.5% of the female adolescents from the Vitoria region of Brazil were classified as having ≥ 3 MRF ⁴⁴ compared to 6.5% of girls from Curitiba in the present study. On the other hand, 13.7% and 15% of adolescents from the São Paulo region ⁴⁵ were classified as having MetS according to different criteria ⁴⁷. Results of the different surveys of Brazilian youth should thus be evaluated and interpreted with care. Further efforts are needed to encourage standardization of criteria for MetS in children and
 adolescents.

In summary, generalization of the observed association between MVPA and the clustered metabolic risk factors in Brazilian youth to other populations of adolescents should be done with care. The study has several limitations that should be noted. First, causal relationship between low MVPA and increased risk for MetS cannot be inferred from a cross-sectional design. Second, an indicator of biological maturity status was not included in the study protocol. Although chronological age was adjusted for the analyses, this may not be sufficient because biological maturity different may impact in insulin levels of youth and therefore should be considered in future research. Third, the results are based on a relatively small sample of Brazilian girls 11 to 17 years living in the urban center of the Paraná region. Further, the use of PA self-report instruments is challenging and, as aforementioned, requires several cautions and standardizing procedures to decrease potential measurement errors. Although different models of association had been tested, experimental and longitudinal investigations are needed to draw conclusions about the etiologic influence of PA, WC and fitness on cardiometabolic risk.

19 CONCLUSION

MVPA was independently associated with an increased risk of MetS in Brazilian
adolescent girls, but not in boys. Findings highlight the importance of preventive
actions against metabolic risk in female youth which may need to target active lifestyle.
Additional efforts are needed to encourage research with different analytical approach
and standardization of criteria for MetS in children and adolescents.

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Metabolic and behavioral risk factors in youth

Table 1. Descriptive characteristics of participants.

Variable	All	Boys	Girls	
		(n=402)	(n=522)	
Chronological age, years	13.7±1.9	13.9±1.9	13.6±1.9	
Weight (kg)	52.2±13.0	54.5±14.5	50.5±11.3 **	
Height (m)	159.0±11.2	162.8±13.4	156.0±8.1 **	
WC (cm)	68.2±8.8	70.3±9.1	66.5±8.2 **	
Insulin ^a (pmol/l)	6.03±3.78	5.02±4.18	6.80±3.25 **	
Glucose ^a (mmol/l)	94.64±12.08	94.98±10.69	94.38±13.05	
Triglycerides ^a (mmol/l)	84.98±35.10	84.17±39.74	85.61±31.08	
HDL cholesterol (mmol/l)	44.79±10.00	44.00±9.26	45.39±10.51	
Systolic BP (mmHg)	102.33±12.41	104.32±12.50	100.80±12.13 *	
Diastolic BP (mmHg)	67.97±9.94	68.76±10.03	67.36±9.84	
Metabolic syndrome (Z score)	0.00±3.02	-0.1±3.17	0.09±2.90	
CRF ^{a, b} (#)	40.9±21.0	56.2±21.6	29.0±10.0 **	
MVPA ^a (minutes)	77.2±80.2	102.8±80.9	57.6±74.0 **	

5 * *P*<0.05; ** *P*<0.01; ^a Log-transformed values were used in the analysis; ^b Adjusted for age and gender;

6 WC (waist circumference); BP (Blood Pressure); MVPA (Moderate to Vigorous Physical Activity).

Metabolic and behavioral risk factors in youth

Table 2. Prediction of the metabolic syndrome Z score in females aged 11-17 years.

		Metabolic Syndrome Z score							
				Unstandardized					Standardized
	Model	\mathbf{R}^2 A	Adjusted R ²	Predictor	coefficients		95% CI for Beta		Beta coefficient
Model					Beta	St. error	Lower	Upper	
	F _(1,520) =9.990 (p<.01)	1.9%	1.7%	MVPA	-0.81	0.26	-1.31	-0.31	-0.14
FEMALES	F _(2,518) =132.192 (p<.01)	35.0%	34.7%	МУРА	-0.51	0.21	-0.30	-0.03	-0.09
				Age WC	0.17 0.20	0.06 0.01	0.06 0.17	0.28 0.22	0.11 0.55
	F _(1,517) =3.043 (p<.05)	35.4%	34.9%	MVPA	-0.49	0.21	-0.91	-0.08	-0.08
				Age	0.19	0.06	0.08	0.30	0.53
				WC	0.19	0.01	0.16	0.22	0.55
				CRF	-0.02	0.01	-0.04	0.00	-0.06

Model 1 = unadjusted; Model 2 = adjusted for chronological age, and waist circumference; Model 3 = model 2 + adjusted for CRF (cardiorespiratory fitness).

WC (waist circumference); MVPA (Moderate to Vigorous Physical Activity).

Table 3. Prediction of the metabolic syndrome Z score in males aged 11-17 years.

		Metabolic Syndrome Z score							
					Unstan	dardized			Standardized
	Model	R ² Adjusted R ²	Predictor _	coefficients		95% CI for Beta		Beta coefficient	
	Widdel			Beta	St. error	Lower	Upper		
MALES	F _(1,400) =0.183 (n.s)	0.00%	0.00%	МУРА	-0.15	0.35	-0.83	0.53	-0.02
	F _(2,398) =146.002 (p<.01)	42.3%	41.9%	Age Waist circumference	0.17 0.21	0.07 0.01	0.03 0.19	0.30 0.24	0.10 0.62
	F _(1,397) =10.806 (p<.01)	43.9%	43.3%	Age Waist circumference CRF	0.27 0.21 -0.02	0.07 0.01 0.01	0.12 0.19 -0.03	0.41 0.24 -0.01	0.16 0.61 -0.14

Model 1 = unadjusted; Model 2 = adjusted for chronological age, and waist circumference; Model 3 = model 2 + adjusted for CRF (cardiorespiratory fitness).

WC (waist circumference); MVPA (Moderate to Vigorous Physical Activity).