Published in final edited form as:
Ann Epidemiol. 2018 September ; 28(9): 583–589.e3. doi:10.1016/j.annepidem.2018.02.007.

The association of cardiorespiratory fitness with cardiometabolic factors, markers of inflammation and endothelial dysfunction in Latino Youth. Findings from HCHS/SOL Youth

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Financial disclosure: No financial disclosures were reported by the authors of this paper

Conflict of Interest: The authors were supported by Grant Number R01HL102130 from the National Heart, Lung, and Blood Institute. Additional support was provided by the Life Course Methodology Core of the New York Regional Center for Diabetes Translation Research (DK111022- 8786) The study sponsors did not have any role in study design; collection, analysis, and interpretation of data; writing the report; and the decision to submit the report for publication.

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Abstract

Purpose—To evaluate the relationship of cardiorespiratory fitness (CRF) with cardiovascular disease (CVD) risk factors and a biomarker of endothelial dysfunction (e-selectin) among Hispanic/Latino youth.

Methods—The study included 1380 Hispanic/Latino youths (8-16 years old) from the Hispanic Children Health Study/Study Of Latino Youth (HCHS/SOL Youth) that enrolled from four cities (Bronx, Chicago, Miami, and San Diego). CRF was assessed by a 3-min step test that uses post-exercise heart rate to estimate maximal oxygen uptake. Regression models assessed differences in cardiometabolic markers across quartiles of CRF, adjusting for potential confounders.

Results—CRF was higher among boys (mean: 57.6 ml/kg/min, 95% CI: 56.8, 58.4) compared to girls (mean: 54.7 ml/kg/min, 95% CI: 53.9, 55.5). Higher levels of CRF were associated with more favorable levels of cardiometabolic, inflammation, and endothelial dysfunction factors (p-values<0.001) and independently of physical activity and sedentary time. Compared to the lowest quartile of CRF, the odds of having ≥2 CVD risk factors was lower at higher quartiles of CRF, after adjustment for potential confounders.

Conclusions—Among Hispanic/Latino youth, CRF appears to be a strong protective factor for endothelial dysfunction and cardiometabolic risk factors. Strategies to improve CRF may be a useful approach for improving cardiovascular health in youth.

INTRODUCTION

The epidemic of obesity has underscored the need to identify modifiable factors that could reduce the metabolic abnormalities linked to excess weight. This is particularly important for Hispanic/Latino youth who have high rates of obesity(1). In adults, higher cardiorespiratory fitness (CRF) is associated with lower risk of CVD and mortality (2–6). Evidence suggests that higher CRF levels in youth may be cardio-protective later in life as these are associated with lower BMI and inflammatory markers (7–10). Furthermore, higher levels of CRF in adolescence C predict lower risk of myocardial infarction and premature death (11, 12). Yet, the role of CRF in subclinical cardiovascular disease during adolescence, such as endothelial dysfunction, has been less studied. Several biomarkers may be used as noninvasive measures of endothelial function (13). Selectins are molecules that assist in attracting white blood cells to the lining of the blood vessel at localized sites of inflammation. In particular, e-selectin is a cellular adhesion molecule that is produced in response to inflammation (signaled by IL-1 and TNF-alpha). In addition, plasminogen activator inhibitor-1 (PAI-1) inhibits the degradation of blood clots and has been associated with endothelial dysfunction (13, 14). In youth, markers of endothelial dysfunction are related to obesity and insulin resistance (15), suggesting that alterations of the endothelial function may represent an early manifestation of the atherosclerotic process.

Since prior studies suggest that exercise may improve markers of endothelial dysfunction in youth (16, 17), in this study we examined the role of CRF levels on cardiometabolic risk factors and endothelial dysfunction in a sample of Hispanic/Latino youth, a population that has been largely understudied and is at high risk for metabolic and cardiovascular disease. Because we have identified sex differences in the distribution of cardiometabolic risk factors (1, 18), we also examined whether effects varied by sex. In addition, as prior studies indicate an inverse association between BMI and CRF levels (19, 20), we also tested for interaction by obesity status.

MATERIALS AND METHODS

Study population

The Hispanic Community Health Study/ Study of Latinos (HCHS/SOL) is a population-based cohort study of 16,415 Hispanic/Latino adults (ages 18–74 years) who were selected using a two-stage probability sampling design from four US communities (Chicago, IL; Miami, FL; Bronx, NY; San Diego, CA). SOL Youth is an ancillary study to HCHS/SOL that enrolled a subset of the offspring of HCHS/SOL participants from the same four field centers. HCHS/SOL enrolled participants form 9,872 households. From these, we identified about 7,350 households that likely had at least one child potentially eligible for SOL Youth. Between 2012 and 2014, 6,741 households were screened (92%) by phone using a standardized script; the screening identified 1,777 eligible youth between the ages of 8-16 years, of whom 1,466 were enrolled (participation rate of 82%). Of these 1,466 youths, we excluded participants who did not provide a fasting blood sample or for whom fasting status was unknown (n=24, 1.8%), and an additional n=55 (3.8%) who did not complete the cardiorespiratory fitness test. Lastly, we excluded seven participants whose BMI or waist circumference were extreme outliers, yielding an analytic sample of n=1,380. Details about the methodology and protocols of HCHS/SOL and SOL Youth are published elsewhere (21, 22). The study was conducted with approval from the institutional review boards of each of the institutions involved. Written informed consent and assent were obtained from parent/ caregivers and their children, respectively.

Measures

Examinations took place at each of the field center research clinics. Staff was centrally trained on each of the study procedures and followed a standardized protocol. Study questionnaires were interviewer-administered.

Cardiorespiratory fitness (CRF)—A submaximal test was used to assess CRF in the study. Youths were asked to perform a 3-minute step test using a height-appropriate bench. Resting and post-exercise heart rates were obtained assessing the heart beats over 15 seconds. This method has been validated for children 6-18 years old (23). VO2max was estimated using published methods [VO2_MAX = 105.3959 – (1.643756 × 15-seconds Post Exercise Heart Rate)] (23–25).

Adiposity Measures—Weight and percentage body fat were obtained using a Tanita Body Composition Analyzer TBF-300A, which applied a bioelectrical impedance method. Height and waist circumference were measured three times per participant and rounded to the nearest centimeter according to a standard protocol. An average of three measurements was used in the study for each participant (26). BMI was calculated as weight (kg) divided by height squared (m^2) and BMI z-scores were derived following CDC guidelines (27). Obesity was defined as BMI≥95th percentile of the sex-specific age-standardized BMI using CDC Growth Charts (28).

Blood pressure—Blood pressure was measured after 5 minutes of sitting rest using an OMRON HEM −907XL sphygmomanometer (Omron Healthcare Co. Ltd., Kyoto, Japan). The mean of the second and third measurements was used for analysis. National Heart, Lung, and Blood Institute blood pressure level tables were used to calculate age-, sex-, and height-specific diastolic and systolic blood pressure percentiles (29).

Laboratory measurements—All blood specimens were drawn in the morning under fasting conditions (at least 10 hours), processed on site, and stored at −70°C. The University of Minnesota's Advanced Research and Diagnostic Laboratory performed all laboratory assays using standard methods. Measures of cardiometabolic factors included fasting glucose, HbA1c, insulin, lipid panel (total cholesterol, LDL-C, HDL-c, and triglycerides). Markers of inflammation included High-sensitivity **C-reactive protein** (hs-CRP),PAI-1, and adiponectin. Endothelial dysfunction was assessed by e-selectin.

Number of cardiovascular disease risk (CVD) factors—An index of overall cardiovascular health was calculated by summing the presence of the following eight risk factors: obesity (BMI ≥95th percentile); SBP or DBP ≥90th percentile, fasting glucose ≥100 mg/dL, HbA1c ≥5.7%; total cholesterol ≥200 mg/dL, LDL-c ≥130 mg/dL, triglycerides ≥100 mg/dL for 8-9 year-olds and ≥130 mg/dL for 10-16 year-olds or HDL-c <40 mg/dL. Meeting one of each of these thresholds added to the count of numbers of CVD risk factors (1). The correlation coefficients between factors ranged from 0.01 to 0.92. The Cronbach alpha coefficient was moderate/low (0.49).

Self-reported and measured covariates—Age, sex, place of birth, and Hispanic/ Latino background were self-reported by the participant. The participant's parent or legal guardian reported annual household income and highest level of educational attainment. Time spent in sedentary behavior and moderate-to-vigorous physical activity (MVPA) was assessed using accelerometers (Actical model 198-0200-03; Respironics Co. Inc., Bend, Oregon) worn for 7 days =. Non-wear time was defined as consecutive zero counts for at least 90 minutes, allowing for short time intervals with nonzero counts lasting up to 2 minutes if no counts were detected during both the 30 minutes upstream and downstream from that interval (30). Data were summarized as the average time spent sedentary and in MVPA on adherent days (at least 8 hours of wear time) for youth with at least three adherent days according to the following cut points: sedentary (<18 counts/15-second epoch) and moderate or vigorous (>440 counts/15 seconds) (31).

Statistical analysis—All reported values are weighted to the sampling frame and account for clustering within sampling units and households. Sampling weights were also non-response adjusted, trimmed and calibrated by age and sex distributions of Hispanic/Latinos in the target areas according to the 2010 U.S. Population Census. P-values corresponding to Wald F-statistics and 95% confidence intervals were computed using variance estimates derived from Taylor series linearization methods using SUDAAN release 11.0.1 (RTI International, Research Triangle Park, NC). All tests of significance were two-sided using a threshold of 5%.

Missing values of accelerometer measures (n=338), parent education (n=3), household income (n=44), and place of birth (n=11) were imputed using 10 imputed data sets. Imputation models included all variables in analytical models, as well survey design variables, hours of accelerometer wear time, and inclusion of a weekend day in accelerometer measurement. Primary analyses were performed on the 10 imputed data sets and carried out using SUDAAN survey procedures with proper variance estimation. Results were combined using Rubin's rule accounting for uncertainty of the imputation in SAS.

Multiple linear regression models were used to estimate the association of CRF with cardiometabolic risk factors and makers of endothelial function, with CRF as a continuous variable and also in quartiles. Mean (95% CI) levels of cardiometabolic risk factors, markers of endothelial function, and accelerometer variables were estimated within quartiles of fitness as predicted marginal means, derived from linear regression models adjusted for age and sex. Regression coefficients for differences in cardiometabolic risk factors and markers of endothelial function were estimated from models that were further adjusted for a series of additional potential confounders. Initial models adjusted for sociodemographic variables determined *a priori* as potential confounders including age, sex, field center, Hispanic/Latino background, place of birth, annual household income, parent educational attainment, time per day spent in physical activity and sedentary behavior, which are closely linked with fitness. Then, in order to examine the effect of fitness levels beyond adiposity, final models further adjusted for z-score of waist circumference, which was previously reported as a stronger correlate of cardiovascular disease risk factors than BMI in Hispanic youth (32). Similarly, prevalence ratios for a 3-level CVD risk factors (1, 2+, relative to 0) were derived from multinomial logistic regression models. Heterogeneity in the associations was examined across levels of age, sex, and obesity status using two-way interaction terms.

RESULTS

The study included 699 girls and 681 boys between the ages of 8 and 16 (mean age 12.2 years). Fifty-four percent were 8-12 years old, 23% were between 13-14 years and 24% were 15-16 years old. The majority (78%) of youth were born within the US 50 states. Youth of Mexican heritage comprised 47.6% of the sample. The sample was predominantly of low socioeconomic status; 51% of youth were living in families reporting an annual household income ≤\$20,000 and 38% of their caregivers did not graduate from high school. Boys had higher levels of CRF than girls (57.6 vs. 54.7, p-value <0.0001). CRF levels also varied by Hispanic background. (Table 1). Time spent at MVPA was higher at higher quartiles of CRF

(Figure 1). Conversely, youth at lower quartiles of CRF spent more time in sedentary behaviors.

Cardiorespiratory fitness, adiposity, and cardiometabolic risk factors

CRF was inversely associated with measures of adiposity in multivariate models (all p-values<0.0001) (Table 2). Compared to the lowest quartile of CRF, each increasing quartile of CRF was associated with lower BMI-z score, waist circumference, and percent body fat. These associations were independent of time spent in MVPA and sedentary behaviors.

We also observed strong inverse associations between CRF and cardiometabolic risk factors (p-values <0.05 for all markers except fasting plasma glucose)(Table 2), even after the adjustment for MVPA and sedentary behaviors. These associations were attenuated when models were further adjusted for waist circumference, but remained statistically significant for systolic and diastolic blood pressure, HOMA-IR, total cholesterol, and triglycerides. As expected, there was a positive association between CRF and HDL-c, and an inverse association between CRF and LDL-c independent of MVPA and sedentary behaviors. However, after the adjustment for waist circumference, the association between CRF and HDL was no longer statistically significant. When examining the association of cardiometabolic risk factors across quartiles of CRF, we observed protective associations even at moderate levels of CRF (quartiles 2 and 3) but associations appeared to be stronger at highest levels of fitness (quartile 4). Furthermore, the number of cardiovascular disease risk factors, an index of cardiovascular health, was also inversely related to CRF (Figure 2). The odds of having one, or ≥2 cardiovascular risk factors decreased across higher quartiles of CRF. This trend was independent of MVPA, sedentary behavior and waist circumference.

We also explored potential effect modification by sex, age group, and obesity status. There was an interaction by sex in the association of CRF with percent body fat, which suggested a stronger effect among boys (supplemental eTable 1). However, no interactions by sex were observed for the association between CRF and cardiometabolic risk factors (supplemental Table e1). Age and obesity status did not modify the associations of CRF with adiposity or cardiometabolic risk factors (supplemental eTables 2 and 3).

Cardiorespiratory fitness, inflammatory makers, and endothelial function biomarkers

CRF was inversely related to C-reactive protein and PAI-1, in models adjusted for sociodemographic characteristics, sedentary behavior and MVPA (Table 3). Furthermore, these inverse associations were observed at moderate (quartile 3) and high (quartile 4) levels of CRF. Associations were attenuated but remained significant after adjusting for waist circumference. The association of CRF with PAI-1 was stronger in boys compared to girls (p-value for interaction=0.016; supplemental eTable 1). On average, each 10 mL/kg/min increase in CRF was associated with a 0.39 (95% CI −0.49, −0.28) decrease in log-transformed PAI-1 in boys and 0.24 (95% CI −0.34, −0.13) decrease in log-transformed PAI-1 in girls. These associations were consistent by age group or obesity status (supplemental eTables 2–3). Adiponectin levels were significantly higher at higher levels of fitness (p-value = 0.0019), but the association did not remain significant after adjustment for waist circumference (P=0.67).

We also observed evidence for an association of CRF with endothelial dysfunction. (Table 3),. Each 10 mL/kg/min increase in CRF was associated with a 0.8 (95% CI −0.12, −0.04) reduction in log-transformed e-selectin, independent of physical activity and sedentary behavior (P<0.0001). Similar to other cardiometabolic risk factors, lower levels of e-selectin were observed at moderate levels of CRF, with effects stronger at the highest quartile of fitness. After adjusting for waist circumference the association of CRF with e-selectin was no longer significant. Lastly, the association of CRF with e-selectin was stronger in younger children (8–12 years old) compared to adolescents (13–16 years old) (Supplemental eTable2). No other interactions were observed (Supplemental eTables 1 and 3).

DISCUSSION

As we hypothesized, the study showed protective associations of CRF for cardiometabolic risk factors and biomarkers of endothelial dysfunction, independently of time spent in moderate-to-vigorous physical activity and sedentary behaviors. These results showed graded associations with all but one (fasting glucose) of studied biomarkers. Importantly, the inverse associations of CRF with measures of cardiovascular health were also observed at moderate levels of CRF, albeit associations were stronger among the fittest youth. Furthermore, the protective associations of CRF were observed in youth with and without obesity. Despite differences in CRF between boys and girls, associations were consistent across sex, except for PAI-1. The study results are consistent with other studies (33). The European Heart study, which included youths of similar age, showed inverse associations of CRF with cardiometabolic risk factors in boys and girls (34, 35), but the study did not include measures of endothelial function. A study of South Korean school children reported inverse associations of CRF with adiposity and lipids, but no associations with glycemic traits or blood pressure.(9) Similarly, other studies in youth have reported inverse associations of cardiorespiratory fitness and low-grade inflammation (7, 8, 36). Few studies examined the role of CRF on early markers of atherosclerosis. One such study, showed an association of CRF with left ventricular mass, but endothelial function was not assessed (37).

Taken together, these studies and ours, indicate that there is an independent association of CRF on cardiometabolic risk factors in youth. However, the mechanisms linking CRF to cardiovascular health remains to be elucidated. In our study, relationships were attenuated after adjusting for waist circumference, suggesting that central adiposity may mediate this association but the cross-sectional design prevented us from formally testing for mediation. In addition, as CRF is related to muscles' ability to utilize oxygen and nutrients, improvements in muscle metabolism may be another explanation for the association of CRF with cardiovascular health. In fact, a small study of children showed that fat-free mass is associated with higher CRF (38). CRF is influenced by aerobic exercise levels, but it is also hypothesized to have a substantial genetic component.(39, 40) However, genetic studies offering insights about the biological mechanisms behind CRF are still limited. Available studies identified genes that regulate the aerobic response to exercise training (41, 42). Yet functional studies are needed to understand the common pathways that may regulate aerobic fitness and cardiometabolic traits (43, 44).

Some important study limitations have to be noted. First, the cross-sectional design limits any causal inference. Second, the study sample is not representative of the overall Hispanic/ Latino youth population in the US, but only of the communities from which the study enrolled; although these four urban communities are among the 15 metropolitan areas with the largest concentration of Hispanic/Latinos (45). The sample size does not allow us to test differences by Hispanic/Latino national background. However, we previously reported similar prevalence of cardiometabolic risk factors in youth of Mexican background and youth of other backgrounds were similar (1). The potential for measurement error is present; for example, using bioelectrical impedance method may underestimate percentage body fat in children (46, 47). In addition, our index of overall cardiovascular health had modest reliability. Furthermore, the study was limited to a measure of aerobic fitness, and other dimensions of fitness that may be relevant to cardiovascular health, such as strength and endurance (48), were not included. Despite these limitations, the study contributes to the growing literature about the importance of CRF for cardiovascular health. Unique contributions of this research are an understudied population, young age group, and measures of endothelial function, a marker of early atherosclerosis. The study also has important implications related to youths' future health once they reach adulthood given that high levels of fitness during adolescence predict lower risk of metabolic syndrome (10), CVD, and lower mortality in adulthood (11, 12, 49). Furthermore, low aerobic capacity in adolescence is associated with higher risk of hypertension and stroke later in life (50, 51).

CONCLUSION

The protective associations of fitness were observed in youth with and without obesity; suggesting that programs that aim to improve CRF could be useful to improve cardiovascular health among at-risk youth. Other than increases in vigorous activity, there is little information of other modifiable factors that may lead to improvements in CRF. Since our findings were independent of physical activity, studies exploring the biological pathways are needed to identify other strategies than increases in aerobic exercise that may lead to improvements of CRF.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The SOL Youth Study was supported by Grant Number R01HL102130 from the National Heart, Lung, and Blood Institute. The children in SOL Youth are drawn from the study of adults: The Hispanic Community Health Study/ Study of Latinos, which was supported by contracts from the National Heart, Lung, and Blood Institute (NHLBI) to the University of North Carolina (N01-HC65233), University of Miami (N01-HC65234), Albert Einstein College of Medicine (N01-HC65235), Northwestern University (N01-HC65236), and San Diego State University (N01-HC65237). The following Institutes/Centers/Offices contribute to the HCHS/SOL through a transfer of funds to NHLBI: National Center on Minority Health and Health Disparities, the National Institute of Deafness and Other Communications Disorders, the National Institute of Dental and Craniofacial Research, the National Institute of Diabetes and Digestive and Kidney Diseases, the National Institute of Neurological Disorders and Stroke, and the Office of Dietary Supplements. Additional support was provided by the Life Course Methodology Core of the New York Regional Center for Diabetes Translation Research (DK111022- 8786). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Heart, Lung, and Blood Institute or the National Institutes of Health. No financial disclosures were reported by the authors of this paper

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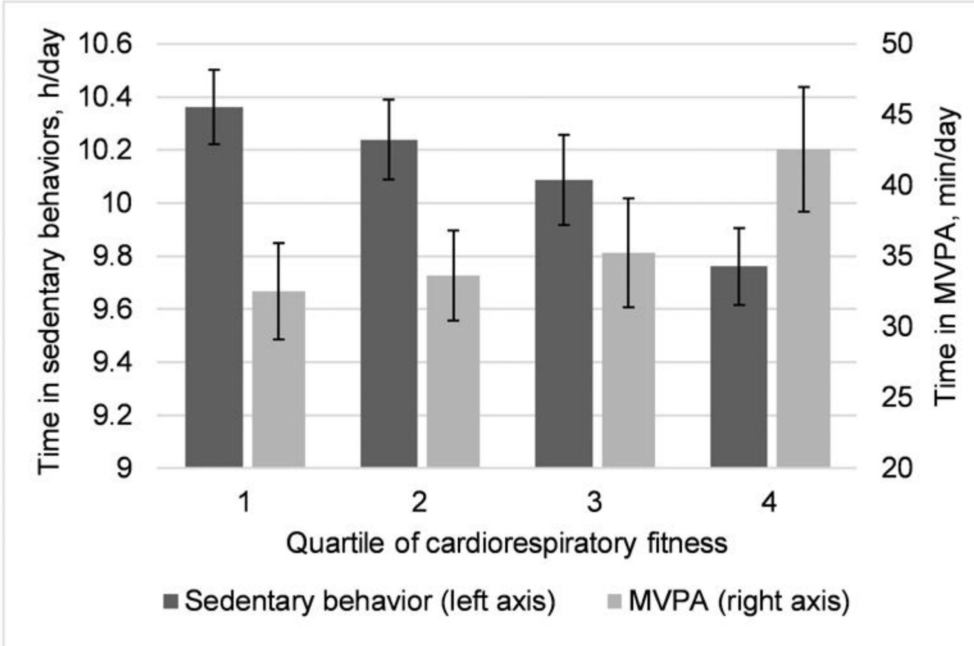

CRF (ml/kg/min)	Weighted Median (Range)
Quartile 1	45.8 (33.1 – 49.5)
Quartile 2	52.9 (51.2 – 56.1)
Quartile 3	58.6 (57.7 – 61.0)
Quartile 4	63.9 (62.7 – 75.8)

Figure 1.

Age and sex adjusted means of accelerometer-based physical activity and sedentary behavior across quartiles of cardiorespiratory fitness,* HCHS/SOL Youth (n=1,380)

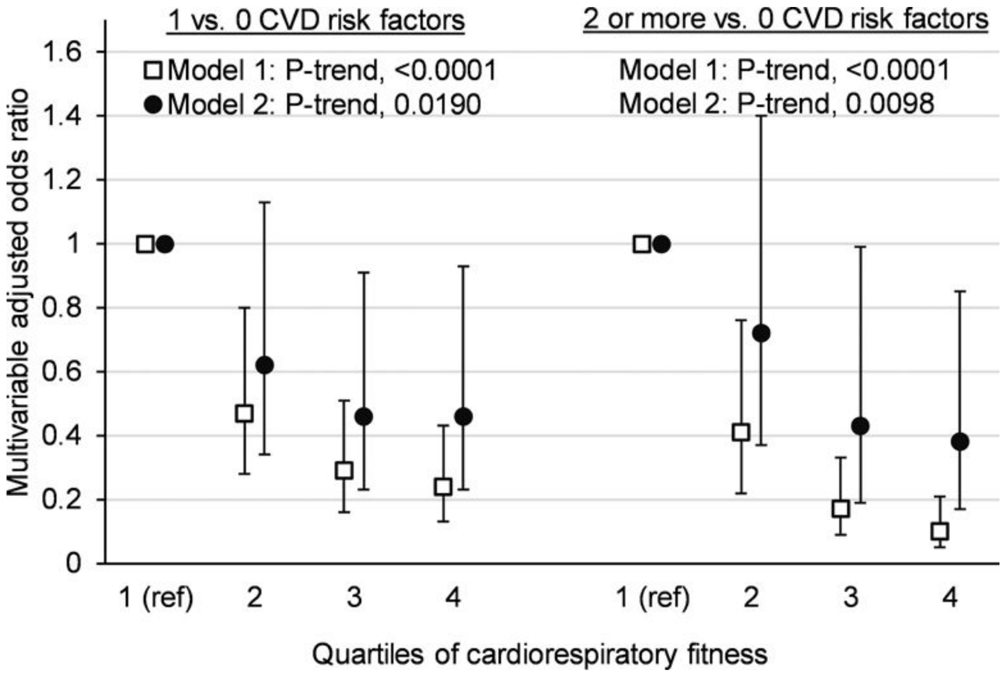

Figure 2. Odds ratios (95% Confidence Interval) for the association of CRF (quartiles) with number of CVD risk factors. HCHS/SOL Youth (n=1380)

*CVD risk factors include obesity (BMI ≥95th percentile), high blood pressure, high fasting plasma glucose, high HbA1c, high total cholesterol, high LDL-cholesterol, high triglycerides, and low HDL-cholesterol

**Derived from proportional odds model for ordinal dependent variable

***Odds ratios for each level of the dependent variable relative to zero cardiovascular risk factors, derived from multivariable adjusted generalized logit models

****Tests for a trend for increasing odds of 1 and ≥2 CVD risk factors, relative to 0 CVD risk factors, across higher quartiles of cardiorespiratory fitness

Model 1 adjusted for age, sex, field center, Hispanic/Latino background, place of birth, annual household income, and parent education level, physical activity and sedentary behavior

Model 2 is further adjusted for waist circumference

Table 1

Mean cardiorespiratory fitness of Hispanic/Latino youth by socio-demographic characteristics. HCHS/SOL Youth (n=1,380)

	Cardiorespiratory fitness,* ml/kg/min	
Sociodemographic characteristics	**Mean (95% CI)***	**P**
Age group		0.8023
8 – 12 years	56.2 (55.4, 56.9)	
13 – 14 years	56.5 (55.3, 57.7)	
15 – 16 years	55.9 (54.3, 57.4)	
Sex		<0.0001
Girls	54.7 (53.9, 55.5)	
Boys	57.6 (56.8, 58.4)	
Nativity		0.1763
Foreign born (includes Puerto Rico)	55.3 (53.8, 56.8)	
Born in US 50 states	56.4 (55.7, 57.1)	
Hispanic/Latino background		0.0497
Mexican	57.0 (56.1, 57.9)	
Central American	56.6 (54.6, 58.7)	
Cuban	56.7 (54.9, 58.5)	
Dominican	54.1 (52.4, 55.7)	
Puerto Rican	54.5 (52.3, 56.7)	
South American	55.7 (53.4, 58.0)	
Other/>1	55.9 (54.2, 57.6)	
Annual household income		0.2136
≤$20,000	55.7 (54.8, 56.6)	
$20,001 - $40,000	56.9 (55.7, 58.1)	
>$40,000	56.9 (55.2, 58.5)	
Parent educational attainment		0.3383
No H.S. Diploma/GED	56.3 (55.3, 57.3)	
High school diploma/GED	55.5 (54.6, 56.5)	
> H.S. diploma/GED	56.6 (55.4, 57.8)	

* Values are non-response adjusted and weighted to the age and sex distribution of the target population.

Table 2

Multiple linear regression (β; 95% Confidence Interval) for the association of cardiorespiratory fitness (CRF) with adiposity and cardiometabolic risk factors, HCHS/SOL Youth (n=1380)*

	CRF		Quartiles of CRF		
	Each 10mL/kg/min	p-value	Quartile 2	Quartile 3	Quartile 4
Adiposity					
BMI, z-score	−0.48 (−0.60, −0.36)	<0.0001	−0.38 (−0.60, −0.16)	−0.66 (−0.88, −0.44)	−0.97 (−1.21, −0.73)
WC, z-score	−0.48 (−0.57, −0.39)	<0.0001	−0.45 (−0.65, −0.25)	−0.71 (−0.91, −0.52)	−0.92 (−1.11, −0.73)
BF, %	−5.35 (−6.34, −4.35)	<0.0001	−5.1 (−7.1, −3.0)	−8.4 (−10.3, −6.4)	−10.8 (−12.8, −8.8)
Blood Pressure					
SBP, percentile					
Model 1	−3.78 (−5.96, −1.60)	0.0007	−0.1 (−4.6, 4.3)	−2.6 (−7.6, 2.4)	−9.5 (−13.9, −5.2)
Model 2†	−3.36 (−5.84, −0.88)	0.0081	0.3 (−4.2, 4.8)	−2.0 (−7.3, 3.2)	−8.8 (−13.7, −3.8)
DBP, percentile					
Model 1	−5.93 (−7.97, −3.88)	<0.0001	−3.6 (−7.8, 0.6)	−8.6 (−12.7, −4.4)	−12.0 (−16.1, −8.0)
Model 2†	−4.45 (−6.57, −2.32)	<0.0001	−2.2 (−6.4, 2.0)	−6.3 (−10.5, −2.1)	−9.1 (−13.3, −4.8)
Glycemic markers					
FPG, mg/dL					
Model 1	−0.60 (−1.22, 0.02)	0.0596	−0.7 (−1.9, 0.4)	−1.1 (−2.3, 0.1)	−1.3 (−2.7, 0.0)
Model 2†	−0.37 (−0.99, 0.26)	0.2516	−0.5 (−1.6, 0.6)	−0.8 (−1.9, 0.4)	−0.9 (−2.2, 0.4)
HbA1c, %					
Model 1	−0.04 (−0.06, −0.01)	0.0094	−0.08 (−0.13, −0.02)	−0.08 (−0.14, −0.02)	−0.06 (−0.12, 0.01)
Model 2†	−0.01 (−0.04, 0.02)	0.3878	−0.05 (−0.11, 0.00)	−0.05 (−0.10, 0.01)	−0.01 (−0.07, 0.05)
log(HOMA-IR)					
Model 1	−0.27 (−0.33, −0.21)	<0.0001	−0.30 (−0.44, −0.17)	−0.36 (−0.49, −0.22)	−0.54 (−0.67, −0.42)
Model 2†	−0.10 (−0.16, −0.05)	0.0003	−0.14 (−0.26, −0.03)	−0.10 (−0.21, 0.01)	−0.22 (−0.34, −0.10)
Lipids					

	CRF		Quartiles of CRF		
	Each 10mL/kg/min	p-value	Quartile 2	Quartile 3	Quartile 4
Cholesterol, mg/dL					
Model 1	−4.94 (−7.43, −2.46)	0.0001	−3.1 (−8.2, 2.0)	−5.4 (−11.2, 0.5)	−10.1 (−15.2, −5.0)
Model 2[†]	−4.03 (−6.62, −1.43)	0.0025	−2.2 (−7.4, 3.0)	−3.9 (−9.9, 2.2)	−8.2 (−13.4, −2.9)
HDL, mg/dL					
Model 1	1.74 (0.79, 2.70)	0.0004	2.4 (0.4, 4.3)	2.4 (0.4, 4.4)	3.8 (1.8, 5.8)
Model 2[†]	−0.37 (−1.29, 0.54)	0.4217	0.4 (−1.3, 2.2)	−0.7 (−2.6, 1.2)	−0.2 (−2.1, 1.8)
LDL, mg/dL					
Model 1	−3.71 (−5.85, −1.56)	0.0008	−2.9 (−7.4, 1.6)	−4.2 (−9.2, 0.9)	−8.0 (−12.5, −3.5)
Model 2[†]	−2.19 (−4.39, 0.01)	0.0511	−1.5 (−5.9, 2.9)	−1.9 (−7.1, 3.2)	−5.1 (−9.6, −0.5)
log(TG, mg/dL)					
Model 1	−0.18 (−0.23, −0.13)	<0.0001	−0.14 (−0.25, −0.03)	−0.22 (−0.33, −0.10)	−0.36 (−0.46, −0.25)
Model 2[†]	−0.09 (−0.15, −0.04)	0.0007	−0.06 (−0.16, 0.04)	−0.09 (−0.20, 0.02)	−0.19 (−0.30, −0.09)

[*] Lowest quartile of CRF is the reference category for quartile analysis; values are betas (95% confidence intervals) derived from survey linear regression models adjusted for age, sex, field center, Hispanic/Latino background, place of birth, annual household income, and parent education level, MVPA, and sedentary behavior.

[†] Model 2 is further adjusted for waist circumference z-score.

BF, body fat; BMI, body mass index; CRF, cardiorespiratory fitness; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL, high density lipoprotein; HOMA-IR, homeostasis model assessment – insulin resistance; LDL, low density lipoprotein; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; WC, waist circumference.

Table 3

Multiple linear regression (β; 95% Confidence interval) for the association of cardiorespiratory fitness (CRF) with adiponectin, inflammatory markers, and e-selectin. HCHS/SOL Youth (n=1380)[*]

	CRF		Quartiles of CRF		
	Each 10mL/kg/min	**p-value**	**Quartile 2**	**Quartile 3**	**Quartile 4**
log(CRP, mg/dL)					
Model 1	−0.44 (−0.55, −0.33)	<0.0001	−0.46 (−0.69, −0.24)	−0.70 (−0.94, −0.46)	−0.88 (−1.13, −0.63)
Model 2[†]	−0.14 (−0.24, −0.04)	0.0088	−0.18 (−0.36, 0.00)	−0.25 (−0.46, −0.04)	−0.31 (−0.54, −0.07)
log(PAI-1, ng/mL)					
Model 1	−0.29 (−0.37, −0.20)	<0.0001	−0.28 (−0.43, −0.13)	−0.36 (−0.52, −0.20)	−0.59 (−0.78, −0.40)
Model 2[†]	−0.09 (−0.17, −0.01)	0.0300	−0.10 (−0.24, 0.04)	−0.07 (−0.22, 0.08)	−0.22 (−0.39, −0.04)
Adiponectin, ug/mL					
Model 1	0.59 (0.22, 0.96)	0.0019	0.72 (−0.08, 1.52)	0.82 (0.02, 1.61)	1.31 (0.54, 2.08)
Model 2[†]	−0.08 (−0.47, 0.31)	0.6783	0.11 (−0.61, 0.84)	−0.16 (−0.98, 0.65)	0.06 (−0.73, 0.85)
log(e-selectin, ng/mL)					
Model 1	−0.08 (−0.12, −0.04)	<0.0001	−0.07 (−0.14, 0.01)	−0.08 (−0.15, −0.01)	−0.18 (−0.26, −0.10)
Model 2[†]	−0.03 (−0.07, 0.01)	0.1206	−0.02 (−0.09, 0.05)	0.00 (−0.07, 0.07)	−0.08 (−0.16, 0.00)

[*] Lowest quartile of CRF is the reference category for quartile analysis; values are betas (95% confidence intervals) derived from survey linear regression models adjusted for age, sex, field center, national background, place of birth, annual household income, and parent education level, physical activity, and sedentary behavior.

[†] Model 2 is additionally adjusted for waist circumference z-score.

CRF, cardiorespiratory fitness; CRP, C-reactive protein; PAI-1, plasminogen activator inhibitor-1.