



Muscle Fitness Cut Points for Early Assessment of Cardiovascular Risk in Children and Adolescents

José Castro-Piñero, PhD¹, Alejandro Perez-Bey, MS¹, Magdalena Cuenca-Garcia, PhD¹, Verónica Cabanas-Sanchez, PhD², Sonia Gómez-Martínez, PhD³, Oscar L. Veiga, PhD², Ascensión Marcos, PhD³, and Jonatan R. Ruiz, PhD⁴, on behalf of the UP&DOWN Study Group*

Objectives To study the cross-sectional and longitudinal (2-year follow-up) association between muscle fitness and cardiovascular disease (CVD) risk factors in youth; whether there are muscle fitness cut points associated with CVD risk (cross-sectional); and whether the health-related muscle fitness cut points identified at baseline are associated with CVD risk 2 years later.

Study design In total, 237 children (110 girls) aged 6-10 years and 274 adolescents (131 girls) aged 12-16 years with complete data were included in the study (10.3% drop out). The handgrip strength and the standing long jump tests were used to assess muscle fitness. CVD risk score was computed with sum of 2 skinfolds, systolic blood pressure, insulin, glucose, triglycerides, and total cholesterol/high density lipoprotein cholesterol.

Results Muscle fitness at baseline was associated inversely with single CVD risk factors and CVD risk score at baseline and 2-year follow-up (all $P < .05$). Receiver operating characteristics curve analyses showed a significant discriminating accuracy of handgrip strength in identifying CVD risk in children and adolescents (boys: ≥ 0.367 and ≥ 0.473 ; girls: ≥ 0.306 and ≥ 0.423 kg/kg body mass, respectively, all $P < .001$). Similarly, the standing long jump cut points for children and adolescents were ≥ 104.5 and ≥ 140.5 in boys, and ≥ 81.5 and ≥ 120.5 cm in girls, respectively (all $P < .05$). These cut points were associated with CVD risk 2 years later (all $P < .01$).

Conclusions Muscle fitness is associated with present and future cardiovascular health in youth, and is independent of cardiorespiratory fitness. It should be monitored to identify youth at risk who could benefit from intervention programs. (*J Pediatr* 2019;206:134-41).

Physical fitness is considered a marker of cardiovascular health in children and adolescents.^{1,2} Together with cardiorespiratory fitness, upper and lower body muscle fitness has been positively associated with a healthier cardiovascular profile during childhood and adolescence^{1,3} and also later in life.^{2,4-6} The relationships of cardiorespiratory fitness^{7,8} and muscle fitness^{9,10} with cardiovascular risk seem to be mediated by obesity.

A meta-analysis evaluated the relationship between cardiorespiratory fitness and cardiovascular disease (CVD) risk in children and adolescents from multiple countries. This study provided pooled cardiorespiratory fitness cut points in children and adolescents that could serve as standards for international comparisons and to identify the target population for primary CVD prevention.¹¹ Given that cardiorespiratory and muscle fitness are independently associated with CVD risk factors,³ it would be desirable to determine generalized health-related muscle fitness (ie, upper and lower body muscle fitness) cut points associated with a healthier cardiovascular profile in children and adolescents. One cross-sectional study determined health-related handgrip strength cut points for cardiovascular risk in Colombian children and adolescents, with low-middle socioeconomic status.¹² It would be helpful to establish health-related muscle fitness cut points in a sample that includes children and adolescents across socioeconomic status.

Therefore, we studied the cross-sectional association between muscle fitness and CVD risk factors in children (6-10 years old) and adolescents (12-16 years old), as well as the association between muscle fitness in children and adolescents and CVD risk factors 2 years later (longitudinal); whether there are muscle fitness cut

From the ¹Department of Physical Education, Faculty of Education Sciences, University of Cádiz, Puerto Real; ²Department of Physical Education, Sports and Human Movement, Faculty of Teacher Training and Education, Autonomous University of Madrid; ³Immunonutrition Group, Institute of Food Science, Technology and Nutrition (ICTAN), Spanish National Research Council (CSIC), Madrid; and ⁴PROMoting FITness and Health through Physical Activity Research Group (PROFIT), Department of Physical Education and Sports, Faculty of Sport Sciences, University of Granada, Granada, Spain

*List of additional members of the UP&DOWN Study Group is available at www.jpeds.com.

Supported by the DEP 2010-21662-C04-00 (DEP 2010-21662-C04-01; DEP 2010-21662-C04-02; DEP 2010-21662-C04-03; DEP 2010-21662-C04-04) grant from the National Plan for Research, Development and Innovation (R + D + i) MICINN, by the FPU15/05337 grant from the Spanish Ministry of Education, and by Plan Propio de Investigación 2016 of the University of Granada (Spain), Excellence actions: Units of Excellence; Scientific Unit of Excellence on Exercise and Health (UCEES). The authors declare no conflicts of interest.

0022-3476/\$ - see front matter. © 2018 Elsevier Inc. All rights reserved.

<https://doi.org/10.1016/j.jpeds.2018.10.026>

AUC	Area under the curve
CVD	Cardiovascular disease
HDL-C	High-density lipoprotein cholesterol
HOMA-IR	Homeostasis model assessment for insulin resistance
SBP	Systolic blood pressure
TC	Total cholesterol
TG	Triglycerides

points associated with CVD risk in children and adolescents (cross-sectional); and whether the health-related muscle fitness cut points identified at the ages of 6-10 and 12-16 years are associated with CVD risk 2 years later (longitudinal, 8-12 and 14-18 years old, respectively).

Methods

The children and adolescents selected for this study were enrolled in the UP&DOWN study.¹³ Briefly, the UP&DOWN study was a 2-year follow-up study designed to assess the impact of physical activity and sedentary behavior over time on health indicators. It also aimed to identify the psycho-environmental and genetic determinants of physical activity in a sample of Spanish children (Cádiz) and adolescents (Madrid). A total convenience sample of 2225 healthy participants aged 6-18 years participated in the UP&DOWN study, from 23 primary schools (Cádiz) and 22 secondary schools (Madrid). According to the database of the Spanish Institute of National Statistics, our sample size represented 50% ($n = 1188$) and 5% ($n = 1037$) of the total population size of school children and adolescents, respectively; with a 3% error for both sample sizes. Blood sampling was randomly performed in one-fourth of the recruited children and adolescents (514; 244 girls). We collected baseline data from September 2011 to June 2012 on a subsample of 237 children (110 girls) aged 6-10 years and 274 adolescents (131 girls) aged 12-16 years, with complete data on muscle fitness, body composition, systolic blood pressure, and blood sampling. A total of 213 children (98 girls) aged 8-12 years and 245 adolescents (118 girls) aged 14-18 years completed the data in the follow-up study (10.1% and 10.6% drop out, respectively), which was performed from September 2013 to June 2014. The main exclusion criterion was to not to have physical disability or health problems, which might limit levels of physical activity.

The study complies with the Declaration of Helsinki and was approved by the Ethics Committee of the Hospital Puerta de Hierro (Madrid, Spain), the Bioethics Committee of the National Research Council (Madrid, Spain), and the Committee for Research Involving Human Subjects at University of Cádiz (Cádiz, Spain). Parents and school supervisors were informed by letter about the nature and purpose of the study, and written informed consent was provided.

Sexual maturation was self-reported using adapted drawings of the 5 stages according to Tanner and Whitehouse.¹⁴ We used breast development in girls and genital development in boys.

We assessed triceps and subscapular skinfold thickness on the nondominant side of the body with a Holtain calliper (Holtain, Crymych, UK; range, 0-40 mm; precision, 0.2 mm) according to Lohman's anthropometric standardization reference manual.¹⁵ We carried out the measurements twice, but not consecutively, and the mean value of both measurements was used for analyses.

We measured the systolic blood pressure (SBP) with a validated digital automatic blood pressure monitor (Omron M6, Omron Health Care Co, Ltd, Kyoto, Japan) according to the

International Protocol of the European Society of Hypertension.¹⁶ The participants sat quietly on a chair for 5 minutes before the measurements were conducted on the left arm in an extended position. We took 2 measures 1-2 minutes apart. We performed an additional measurement if the first 2 readings differed in >5 mm Hg, and the farthest value was removed. Average values (mm Hg) were calculated.

We obtained a fasting blood sample from the cubital vein at the schools early in the morning.¹³ Ten mL of blood were drawn from each subject (dry gel for serum) and centrifuged; serum removed was frozen at -80°C to be analyzed later. We analyzed serum lipid triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and glucose by enzymatic colorimetric methods (Olympus AU2700 Analyzer; Olympus UK Ltd, Watford, United Kingdom). TC/HDL-C ratio was calculated. We analyzed insulin with the Bio-Plex system and Luminex xMAP technology (Bio-Rad Laboratories, Inc, Hercules, California). Furthermore, we calculated insulin resistance through the homeostasis model assessment for insulin resistance (HOMA-IR) score as $[\text{insulin (mLU/mL)} \times \text{glucose (mmol/L)}] / 22.5$.¹⁷

Muscle fitness was assessed based on the handgrip strength (upper body isometric muscle fitness) and the standing long jump (lower body explosive muscle fitness) tests, according to the Assessing Levels of Physical Activity study health-related fitness test battery protocol.^{18,19} We used a hand dynamometer with an adjustable grip (TKK 5101 Grip D; Takey, Tokyo, Japan) for the handgrip strength test.²⁰ The grip-span of the dynamometer was adjusted according to the hand size for determining the maximum handgrip strength using the equations specifically developed for children²¹ and adolescents.²² We performed the test twice, and we recorded the maximum score for each hand in kilograms. The average of the maximum score achieved by left and right hands was used in the analysis. Because heavier children and adolescents have higher levels of handgrip strength,²³⁻²⁵ we normalized by body mass expressing the handgrip strength score divided by body mass. This allowed us to be more accurate when comparing individuals with different body sizes and to focus on muscle quality rather than muscle quantity.

The standing long jump test was performed from a starting position behind a line, standing with the feet approximately shoulder width apart. We performed the test twice and recorded the best score in centimeters. Trained personnel performed all the tests.

We computed a CVD risk score by sex and age, resulting in 8 different scores (boys and girls, age groups: 6-10, 12-16 years). The variables included in the CVD risk score were sum of 2 skinfolds; SBP, HOMA-IR, TG, and TC/HDL-C ratio.²⁶ These variables were standardized as follows: standardized value = $(\text{value} - \text{mean}) / \text{SD}$. The CVD risk score was calculated as the mean of the 5 standardized scores separately for boys and girls and age groups. Those children with values >1.0 SD in the continuous composite risk score variable were defined as being at risk.^{27,28}

Descriptive data are shown as mean and SD unless otherwise indicated. The Student *t* test was used to test differences

in characteristics of study sample by sex at baseline and follow-up, except for the Tanner stage, which was analyzed by χ^2 test.

We performed multiple linear regression analyses to examine the cross-sectional association between muscle fitness and CVD risk factors in children (6- to 10-year-olds) and adolescents (12- to 16-year-olds), and the association between muscle fitness in children and adolescents and CVD risk factors 2 years later (longitudinal). We entered single CVD risk factors and CVD risk score at baseline (6- to 10-year-olds and 12- to 16-year-olds) and follow-up (8- to 12-year-olds and 14- to 18-year-olds) as dependent variables, handgrip strength test/body mass and standing long jump test at baseline as independent variables, and age as covariate, in separate models. In addition, we controlled longitudinal analyses for the corresponding baseline value.

To determine whether there are muscle fitness cut points associated with CVD risk in children (6- to 10-year-olds) and adolescents (12- to 16-year-olds) (cross-sectional), we established the muscle fitness cut points (ie, handgrip strength test/body mass and standing long jump test) at baseline associated with CVD risk score (CVD risk score >1.0 SD) by using the receiver operating characteristic curve.²⁹ We calculated the area under the curve (AUC), 95% CI, sensitivity, specificity, Youden index, positive and negative predictive value, and likelihood ratio of a positive and negative test results. Binary logistic regression was also used to study the relationship between the muscle fitness cut points (high vs low) and CVD risk score (≤ 1 SD vs >1 SD).

To study whether the health-related muscle fitness cut points identified in 6- to 10-year-olds and 12- to 16-year-olds are associated with CVD risk 2 years later (longitudinal, 8- to 12-year-olds and 14- to 18-year-olds, respectively), we conducted binary logistic regression analysis using muscle fitness cut points (high vs low) at baseline and CVD risk score (≤ 1 SD vs >1 SD) at follow-up, adjusting for age at follow-up. We also assessed differences on CVD risk score at follow-up by muscle fitness levels at baseline (high vs low) by ANCOVA. We entered CVD risk score at follow-up as a dependent variable, muscle fitness tests (high vs low) as an independent variable in separate models, and CVD risk score at baseline, sex, and age at follow-up as a covariate. We also analyzed the association between muscle fitness at baseline and muscle fitness at follow-up by means of linear regression analysis.

The statistical analyses were performed using the IBM SPSS Statistics for Windows v 22.0 (IBM Corp, Armonk, New York), and the level of significance was set at P value of $<.05$.

Results

The characteristics of the study sample are shown in **Table I** (available at www.jpeds.com). Overall, single CVD risk factors values significantly increased from baseline to follow-up in both sexes and age groups (all $P < .05$) except for TG in children, both boys and girls, and TC/HDL-C ratio in children boys and adolescent boys and girls. In contrast, HOMA-IR significantly decreased from baseline to follow-up in adolescent boys and girls. Levels of handgrip strength and standing long jump

significantly increased (all $P \leq .005$), except for the handgrip strength in children boys and the standing long jump in adolescent girls.

Levels of handgrip strength at baseline were inversely associated with single CVD risk factors and CVD risk score at baseline and follow-up (β from -0.002 to -0.753 ; all $P < .05$ and $P < .01$, respectively), except for HOMA-IR at baseline and follow-up, SBP at follow-up in children boys and adolescent boys and girls; and TC/HDL-C ratio at follow-up in adolescent boys (**Table II**). Levels of standing long jump performance were associated inversely with the sum of 2 skinfolds (β from -0.346 to -0.698 ; all $P < .001$) and CVD risk score (β from -0.216 to -0.467 ; all $P < .05$) at baseline and follow-up in children and adolescents in both sexes, with SBP at baseline in children in both sexes ($\beta = -0.118$; $P = .007$ in boys and $\beta = -0.230$; $P = .020$ in girls), TC/HDL-C ratio at baseline in children and adolescents in both sexes (β from -0.221 to -0.239 ; all $P < .05$) and at follow-up in children in both sexes ($\beta = -0.289$; $P = .005$ in boys and $\beta = -0.386$; $P = .001$ in girls), TG at follow-up in children and adolescents in both sexes (β from -0.202 to -0.299 ; all $P < .05$), and HOMA-IR at baseline in children boys ($\beta = -0.279$; $P = .048$) and at follow-up in adolescent boys and girls ($\beta = -0.239$; $P = .040$ in boys and $\beta = -0.271$; $P = .017$ in girls) (**Table III**).

The handgrip strength cut points associated with CVD risk were 0.367 and 0.306 kg/kg body mass in children boys and girls, respectively, and 0.473 and 0.423 kg/kg body mass in adolescents boys and girls, respectively (**Figure 1**). The standing long jump cut points associated with CVD risk were 104.5 and 81.5 cm in children boys and girls, respectively, and 140.5 and 120.5 cm in adolescent boys and girls, respectively. Children and adolescents, both boy and girls, with levels of handgrip strength ≥ 0.367 kg/kg body mass, ≥ 0.306 kg/kg body mass, ≥ 0.473 kg/kg body mass, and ≥ 0.423 kg/kg body mass at baseline, respectively, were at greater odds for a favorable CVD risk score at baseline than their peers with lower levels of handgrip strength (**Table IV**; available at www.jpeds.com). Likewise, children and adolescents, both boys and girls, with levels of standing long jump ≥ 104.5 cm, ≥ 81.5 cm, ≥ 140.5 cm, and ≥ 120.5 cm at baseline, respectively, were at greater odds for a favorable CVD risk score at baseline than their peers with lower levels of standing long jump. The AUC, sensitivity, specificity (**Figure 1**), and Youden Index, positive and negative predictive values, and likelihood ratio of a positive and negative test results (**Table V**; available at www.jpeds.com) are the diagnostic variables that have allowed determining the appropriate health-related muscle fitness cut points.

Similarly, logistic regression analysis showed that children and adolescents, both boys and girls, with handgrip strength levels at or above the determined cut points were at greater odds for a favorable CVD risk score at follow-up compared with those with relative handgrip strength levels below the cut points (all $P < .05$) (**Table IV**). Children and adolescents with levels of standing long jump at or above the determined cut points at baseline were at greater odds for a favorable CVD risk score at follow-up compared with those with standing long jump levels below the cut points (all $P < .05$).

Table II. Association of the relative handgrip strength test at baseline in children (6-10 years old) and adolescents (12-16 years old) with CVD risk factors at baseline and at 2-year follow-up (8- to 10-year-olds and 14- to 16-year-olds, respectively)

Dependent variables	Children							
	Boys				Girls			
	B	95% CI	β	P	B	95% CI	β	P
Baseline								
Sum of 2 skinfolds (mm)	-82.396	-92.008;-872,783	-0.565	<.001	-94.443	-104.618;-84.269	-0.585	<.001
SBP (mm Hg)	-12.865	-22.606;-2.230	-0.102	.001	-20.072	-31.113;-9.030	-0.137	.006
HOMA-IR	-2.526	-5.435;0.384	-0.235	.088	-4.243	-9.471;0.985	-0.220	.109
TG (mg/dL)	-59.351	-105.905;-12.798	-0.224	.013	-44.107	-86.465;-1.748	-0.195	.041
TC/HDL-C ratio	-3.708	-5.736;-2.219	-0.396	<.001	-3.515	-5.114;-1.919	-0.384	<.001
CVD risk score	-2.935	-0.4.084;-1.785	-0.424	<.001	-3.810	-5.146;-2.475	-0.484	<.001
2-y follow-up*								
Sum of 2 skinfolds (mm)	-91.180	-103.815;-78.454	-0.525	<.001	-100.740	-115.404;-86.076	-0.516	<.001
SBP (mm Hg)	-5.389	-14.827;4.048	-0.046	.262	-19.647	-32.007;-7.288	-0.123	.002
HOMA-IR	-0.034	-4.286;4.219	-0.002	.987	-1.422	-3.993;1.149	-0.127	.274
TG (mg/dL)	-118.702	-179.357;-58.761	-0.368	<.001	-126.636	-191.628;-61.644	-0.382	<.001
TC/HDL-C ratio	-1.934	-3.581;-2.880	-0.225	.022	-3.922	-5.428;-2.417	-0.471	<.001
CVD risk score	-2.331	-3.830;-0.831	-0.362	.003	-4.087	-5.620;-2.554	-0.540	<.001
Adolescents								
Baseline								
Sum of 2 skinfolds (mm)	-95.935	-103.509;-86.360	-0.753	<.001	-73.638	-84.620;-62.777	-0.515	<.001
SBP (mm Hg)	-16.071	-27.765;-4.376	-0.118	.007	-14.164	-26.097;-0.002	-0.230	.020
HOMA-IR	-0.021	-0.079;0.038	-0.089	.321	-4.483	-10.886;1.921	-0.133	.168
TG (mg/dL)	-50.289	-108.903;-7.844	-0.226	.021	-43.702	-88.241;-0.021	-0.186	.045
TC/HDL-C ratio	-1.039	-2.030;-0.048	-0.210	.040	-1.386	-2.272;-0.051	-0.181	.041
CVD risk score	-2.541	-3.533;-1.549	-0.485	<.001	-1.987	-3.066;-0.914	-0.311	<.001
2-y follow-up*								
Sum of 2 skinfolds (mm)	-71.983	-82.813;-61.154	-0.615	<.001	-85.928	-100.632;-71.225	-0.516	<.001
SBP (mm Hg)	-3.449	-15.414;8.516	-0.029	.571	-14.620	-26.352;-1.113	-0.101	.035
HOMA-IR	-3.702	-7.584;0.181	-0.233	.061	-1.239	-2.766;0.287	-0.181	.110
TG (mg/dL)	-84.042	-135.640;-3.586	-0.218	.032	-62.083	-122.827;-1.339	-0.195	.045
TC/HDL-C ratio	-0.951	-2.159;0.258	-0.161	.122	-2.236	-3.617;-0.856	-0.296	.002
CVD risk score	-2.099	-3.250;-0.948	-0.430	<.001	-3.114	-4.490;-1.738	-0.460	<.001

B, unstandardized coefficient; β , standardized coefficient.

Statistically significant differences are highlighted in bold.

All analyses were controlled for age.

*In addition, for the 2-year follow-up, cardiovascular risk factors and cardiovascular risk scores were adjusted for levels at baseline.

Figure 2 (available at www.jpeds.com) shows a positive association between levels of handgrip strength and standing long jump at baseline and follow-up in both boys and girls and in both age groups (R^2 ranging from 0.49 to 0.63; all $P < .001$). Children and adolescents, both boys and girls, with high levels of handgrip strength or standing long jump at baseline had lower CVD risk score (all $P < .01$ and all $P < .001$, respectively) at follow-up (**Figure 3**). We repeated all analyses after adjusting for pubertal development instead of age, and the results did not change (data not shown). Similarly, we repeated all analyses after further adjusting for cardiorespiratory fitness, assessed by the 20-meter shuttle run test¹⁸ and the results persisted (data not shown).

Discussion

The findings of the present study indicate that poor levels of muscle fitness in children (6-10 years old) and adolescents (12-16 years old) are associated with a higher CVD risk score at

these ages as well as 2 years later. We identified muscle fitness cut points associated with a more favorable cardiovascular health profile in children and adolescents, which seems to be more discriminative for boys than for girls. The health-related muscle fitness cut points identified are associated with CVD risk score 2 years later. The observed consistent cross-sectional and longitudinal associations between muscle fitness and cardiovascular health in children and adolescents are independent of cardiorespiratory fitness, which reinforces the importance of muscle fitness as a marker of health at these ages.

The ALPHA study developed a valid, reliable, feasible, and safe health-related fitness test battery for children and adolescents.^{18,19} This study included, besides the handgrip strength test, the standing long jump test to assess skeletal muscle fitness. Pate et al suggested that a US survey of health-related physical fitness in youth should include both, upper and lower body muscle fitness.³⁰ Furthermore, they recommended determining health-related muscle fitness cut points for children and adolescents.

Table III. Association of the standing long jump test at baseline in children (6-10 years old) and adolescents (12-16 years old) with CVD risk factors at baseline and at 2-year follow-up (8- to 10-year-olds and 14- to 16-year-olds, respectively)

Dependent variables	Children							
	Boys				Girls			
	B	95% CI	β	P	B	95% CI	β	P
Baseline								
Sum of 2 skinfolds (mm)	-0.258	-0.398;-0.207	-0.437	<.001	-0.279	-0.328;-0.229	-0.461	<.001
SBP (mm Hg)	-16.071	-27.765;-4.376	-0.118	.007	-14.164	-26.097;-0.002	-0.230	.020
HOMA-IR	-0.019	-0.039;-0.003	-0.279	.048	-0.003	-0.021;0.016	-0.045	.773
TG (mg/dL)	-0.155	-0.341;0.031	-0.60	.101	-0.130	-0.300;0.046	-0.167	.133
TC/HDL-C ratio	-0.015	-0.028;-0.002	-0.235	.037	0.008	-0.015;-0.001	-0.239	.032
CVD risk score	-0.010	-0.014;-0.005	-0.380	<.001	-0.007	-0.013;-0.001	-0.268	.017
2-y follow-up*								
Sum of 2 skinfolds (mm)	-0.280	-0.346;-0.214	-0.394	<.001	-0.324	-0.391;-0.257	-0.444	<.001
Systolic blood pressure (mmHg)	0.020	-0.024;0.063	0.042	.372	-0.012	-0.063;0.041	-0.020	.656
HOMA-IR	-0.001	-0.016;0.015	-0.006	.963	-0.008	-0.018;0.002	-0.211	.094
TG (mg/dL)	-0.145	-0.321;-0.030	-0.219	.029	-0.353	-0.631;-0.075	-0.299	.013
TC/HDL-C ratio	-0.009	-0.015;-0.003	-0.289	.005	-0.011	-0.018;-0.005	-0.386	.001
CVD risk score	-0.008	-0.014;-0.002	-0.359	.006	-0.012	-0.019;-0.006	-0.467	<.001
Adolescents								
Dependent variables	Boys				Girls			
	B	95% CI	β	P	B	95% CI	β	P
Baseline								
Sum of 2 skinfolds (mm)	-0.285	-0.325;-0.245	-0.698	<.001	-0.188	-0.231;-0.144	-0.363	<.001
SBP (mm Hg)	-0.008	-0.036;0.051	-0.018	.724	-0.013	-0.056;0.051	-0.027	.561
HOMA-IR	-0.007	-0.026;0.013	-0.094	.513	-0.017	-0.041;0.007	-0.138	.159
TG (mg/dL)	-0.009	-0.272;0.291	-0.008	.950	-0.173	-0.421;0.075	-0.124	.171
TC/HDL-C ratio	-0.009	-0.014;-0.001	-0.221	.046	-0.011	-0.019;-0.002	-0.230	.039
CVD risk score	-0.007	-0.011;-0.003	-0.397	.002	-0.005	-0.009;-0.001	-0.216	.017
2-y follow-up*								
Sum of 2 skinfolds (mm)	-0.230	-0.272;-0.188	-0.631	<.001	-0.203	-0.260;-0.145	-0.346	<.001
SBP (mm Hg)	0.005	-0.039;0.049	-0.013	.822	-0.045	-0.091;-0.002	-0.202	.047
HOMA-IR	-0.012	-0.027;-0.002	-0.239	.040	-0.007	-0.012;-0.001	-0.271	.017
TG (mg/dL)	-0.140	-0.289;-0.023	-0.202	.038	-0.258	-0.478;-0.039	-0.228	.022
TC/HDL-C ratio	0.001	-0.004;0.005	0.042	.750	-0.003	-0.008;0.003	-0.101	.305
CVD risk score	-0.006	-0.011;-0.002	-0.426	.004	-0.006	-0.011;-0.001	-0.243	.028

Statistically significant differences are highlighted in bold.

All analyses were controlled for age.

*In addition, for the 2-year follow-up, cardiovascular risk factors and cardiovascular risk scores were adjusted for levels at baseline.

Our findings confirm the observed strong evidence of an inverse association between muscle fitness and CVD risk.³ The results of the present study also concur with those from prospective studies showing that children and adolescents with higher levels of muscle fitness have a more favorable cardiovascular profile later in life.^{2,3} Longitudinal studies also showed that muscle fitness was associated with risk of CVD mortality.^{6,31} It is important to highlight that muscle fitness is associated with CVD risk regardless of cardiorespiratory fitness and other confounders^{32,33} in children and adolescents. Our results confirmed the findings reported in previous prospective studies,^{5,6} suggesting that there is both a combined and additive effect of muscle fitness on CVD risk. On the other hand, we observed that children and adolescents with low muscle fitness levels are very likely to have low muscle fitness levels 2 years later. It seems reasonable to include muscle fitness tests in monitoring to identify children and adolescents with poor cardiovascular health levels. Educational and public health policies are needed to promote healthy lifestyles to increase muscle fitness to prevent CVD risk. In this sense, global physical ac-

tivity guidelines for children and adolescents should emphasize participation in high-intensity physical activities and include a recommendation to perform muscle physical activities at least 3 days per week.³⁴

The present study shows that handgrip strength cut points associated with a reduced CVD risk in children and adolescents, both boys and girls, were 0.367 kg/kg body mass, 0.306 kg/kg body mass, 0.473 kg/kg body mass, and 0.423 kg/kg body mass, respectively.³⁵ These results are similar to those reported by Ramirez-Velez et al in Colombian children and adolescents aged 9-17 years.¹² We also identified standing long jump cut points associated with a healthier cardiovascular profile in children (104.5 cm in boys and 81.5 cm in girls) and adolescents (140.5 cm in boys and 120.5 cm in girls). These health-related muscle fitness cut points presented high accuracy (AUC >0.7), except in the standing long jump for adolescent boys and girls which were moderate (0.665 and 0.676).

Finally, we observed that children and adolescents who met the health-related handgrip strength or standing long jump

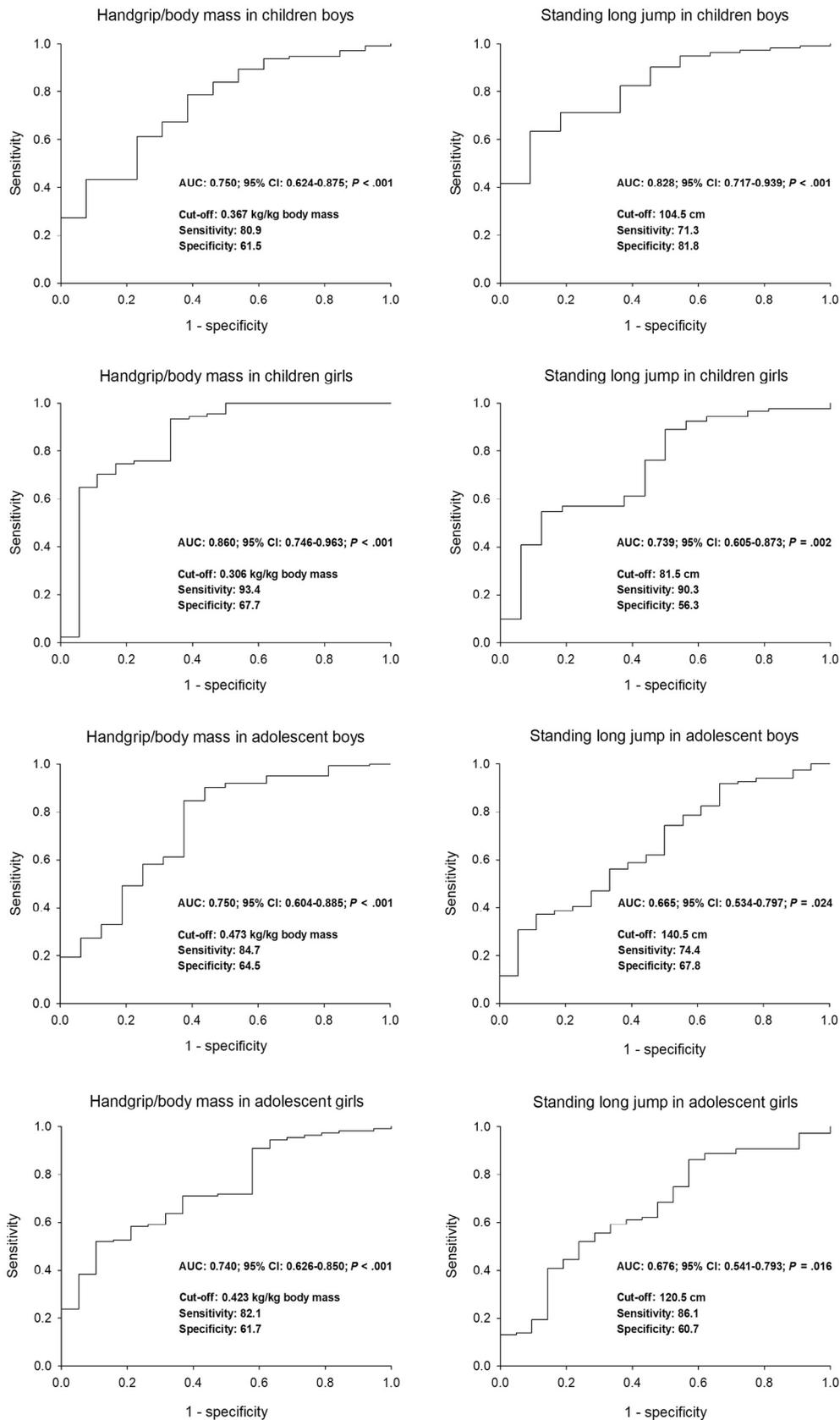


Figure 1. Receiver operating characteristic curve summarizing the potential of muscle fitness to identify cardiovascular health status in children and adolescents, both boys and girls.

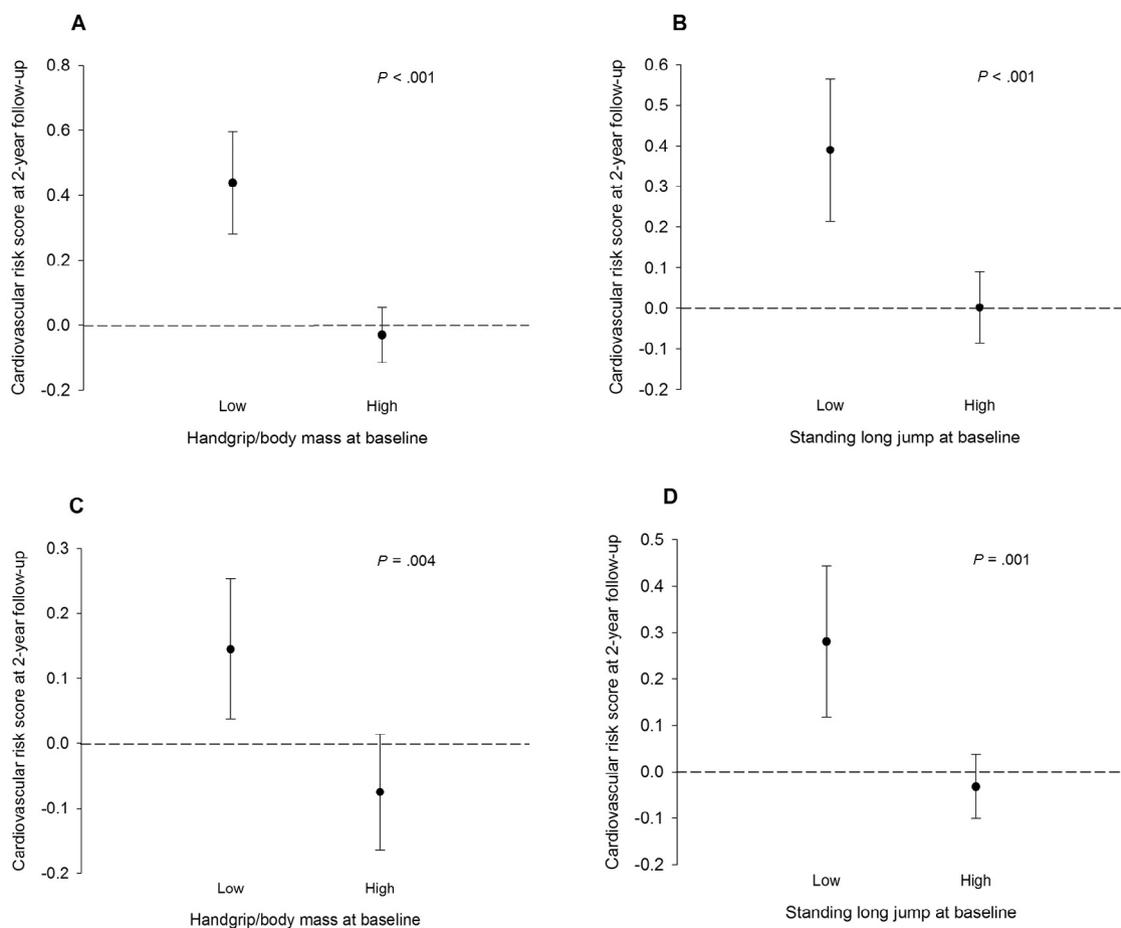


Figure 3. Association between muscle fitness levels at baseline (6- to 10-year-olds and 12- to 16-year-olds) with cardiovascular risk score at 2-year follow-up (8- to 12-year-olds and 14- to 16-year-olds, respectively) for children (**A** and **B**, for the relative handgrip strength and the standing long jump tests, respectively) and adolescents (**C** and **D**, for the relative handgrip strength and the standing long jump tests, respectively), both boys and girls. Analysis adjusted for CVD risk score at baselines, sex, and age at 2-year follow-up.

levels had lower values of CVD risk two years later, which supports the idea that the development of high levels of muscle fitness should start in early childhood.

Limitations of the present study include the lack of consensus in children and adolescents regarding the definition of cardiovascular health. We included a clustered CVD risk score (z score) because this type of outcome may be a better indicator of health in apparently healthy children and adolescents compared with individual risk factors. Moreover, adiposity was assessed by anthropometry (skinfolts). The major drawback with the skinfold technique lies in the extensive expertise one must have in taking readings accurately and with consistency. However, trained professionals measured skinfolts using standard methods of data collection, and the skinfold assessment has been suggested to be a valid tool to evaluate adiposity in children.³⁶ Finally, muscle fitness was assessed by the handgrip strength and the standing long jump test, which may not represent overall muscle strength. Nevertheless, the standing long jump test is strongly associated with both lower and upper body muscle fitness, and has been considered a good marker of overall muscle fitness.³⁷

Muscle fitness should be considered in monitoring children at high risk of poor cardiovascular health. Public health as well as school-based strategies, and intervention programs to increase physical activity levels to meet health-related muscle fitness levels could be helpful. ■

We thank the children and adolescents who participated in the study and their parents and teachers for their collaboration. We also acknowledge the members involved in fieldwork for their efforts.

Submitted for publication Jul 24, 2018; last revision received Oct 10, 2018; accepted Oct 12, 2018

Reprint requests: José Castro-Piñero, PhD, Department of Physical Education, School of Education, University of Cádiz, Puerto Real 11519, Spain. E-mail: jose.castro@uca.es

References

- Ortega FB, Ruiz JR, Castillo MJ, Sjostrom M. Physical fitness in childhood and adolescence: a powerful marker of health. *Int J Obes (Lond)* 2008;32:1-11.
- Ruiz JR, Castro-Piñero J, Artero EG, Ortega FB, Sjostrom M, Suni J, et al. Predictive validity of health-related fitness in youth: a systematic review. *Br J Sports Med* 2009;43:909-23.

3. Smith JJ, Eather N, Morgan PJ, Plotnikoff RC, Faigenbaum AD, Lubans DR. The health benefits of muscular fitness for children and adolescents: a systematic review and meta-analysis. *Sports Med* 2014;44:1209-23.
4. Kvaavik E, Klepp KI, Tell GS, Meyer HE, Batty GD. Physical fitness and physical activity at age 13 years as predictors of cardiovascular disease risk factors at ages 15, 25, 33, and 40 years: extended follow-up of the Oslo Youth Study. *Pediatrics* 2009;123:e80-6.
5. Grontved A, Ried-Larsen M, Moller NC, Kristensen PL, Froberg K, Brage S, et al. Muscle strength in youth and cardiovascular risk in young adulthood (the European Youth Heart Study). *Br J Sports Med* 2015;49:90-4.
6. Timpka S, Petersson IF, Zhou C, Englund M. Muscle strength in adolescent men and risk of cardiovascular disease events and mortality in middle age: a prospective cohort study. *BMC Med* 2014;12:62.
7. Diez-Fernandez A, Martinez-Vizcaino V, Torres-Costoso A, Canete Garcia-Prieto J, Franquelo-Morales P, Sanchez-Lopez M. Strength and cardiometabolic risk in young adults: the mediator role of aerobic fitness and waist circumference. *Scand J Med Sci Sports* 2018;28:1801-7.
8. Diez-Fernandez A, Sanchez-Lopez M, Mora-Rodriguez R, Notario-Pacheco B, Torrijos-Nino C, Martinez-Vizcaino V. Obesity as a mediator of the influence of cardiorespiratory fitness on cardiometabolic risk: a mediation analysis. *Diabetes Care* 2014;37:855-62.
9. Diez-Fernandez A, Sanchez-Lopez M, Gullias-Gonzalez R, Notario-Pacheco B, Canete Garcia-Prieto J, Arias-Palencia N, et al. BMI as a mediator of the relationship between muscular fitness and cardiometabolic risk in children: a mediation analysis. *PLoS ONE* 2015;10:e0116506.
10. Perez-Bey A, Segura-Jimenez V, Fernandez-Santos JDR, Esteban-Cornejo I, Gomez-Martinez S, Veiga OL, et al. The role of adiposity in the association between muscular fitness and cardiovascular disease. *J Pediatr* 2018;199:178.e4-85.e4.
11. Ruiz JR, Caverio-Redondo I, Ortega FB, Welk GJ, Andersen LB, Martinez-Vizcaino V. Cardiorespiratory fitness cut points to avoid cardiovascular disease risk in children and adolescents; what level of fitness should raise a red flag? A systematic review and meta-analysis. *Br J Sports Med* 2016;50:1451-8.
12. Ramirez-Velez R, Pena-Ibagon JC, Martinez-Torres J, Tordecilla-Sanders A, Correa-Bautista JE, Lobelo F, et al. Handgrip strength cutoff for cardiometabolic risk index among Colombian children and adolescents: the FUPRECOL Study. *Sci Rep* 2017;7:42622.
13. Castro-Pinero J, Carbonell-Baeza A, Martinez-Gomez D, Gomez-Martinez S, Cabanas-Sanchez V, Santiago C, et al. Follow-up in healthy schoolchildren and in adolescents with Down syndrome: psychosocial and genetic determinants of physical activity and its impact on fitness, cardiovascular diseases, inflammatory biomarkers and mental health; the UP&DOWN study. *BMC Public Health* 2014;14:400.
14. Tanner J. Growth at adolescence. Oxford (United Kingdom): Blackwell; 1962.
15. Lohman TG, Roche AF, Matorell R. Anthropometric standardization reference manual. Champaign (IL): Human Kinetics; 1991.
16. Topouchian JA, El Assaad MA, Orobinskaia LV, El Feghali RN, Asmar RG. Validation of two automatic devices for self-measurement of blood pressure according to the International Protocol of the European Society of Hypertension: the Omron M6 (HEM-7001-E) and the Omron R7 (HEM 637-IT). *Blood Press Monit* 2006;11:165-71.
17. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985;28:412-9.
18. Ruiz JR, Castro-Pinero J, Espana-Romero V, Artero EG, Ortega FB, Cuenca MM, et al. Field-based fitness assessment in young people: the ALPHA health-related fitness test battery for children and adolescents. *Br J Sports Med* 2011;45:518-24.
19. Ruiz JR, Espana Romero V, Castro Pinero J, Artero EG, Ortega FB, Cuenca Garcia M, et al. [ALPHA-fitness test battery: health-related field-based fitness tests assessment in children and adolescents]. *Nutr Hosp* 2011;26:1210-4.
20. Espana-Romero V, Ortega FB, Vicente-Rodriguez G, Artero EG, Rey JP, Ruiz JR. Elbow position affects handgrip strength in adolescents: validity and reliability of Jamar, DynEx, and TKK dynamometers. *J Strength Cond Res* 2010;24:272-7.
21. Espana-Romero V, Artero EG, Santaliesra-Pasias AM, Gutierrez A, Castillo MJ, Ruiz JR. Hand span influences optimal grip span in boys and girls aged 6 to 12 years. *J Hand Surg Am* 2008;33:378-84.
22. Ruiz JR, Espana-Romero V, Ortega FB, Sjostrom M, Castillo MJ, Gutierrez A. Hand span influences optimal grip span in male and female teenagers. *J Hand Surg Am* 2006;31:1367-72.
23. Milliken LA, Faigenbaum AD, Loud RL, Westcott WL. Correlates of upper and lower body muscular strength in children. *J Strength Cond Res* 2008;22:1339-46.
24. Artero EG, Espana-Romero V, Castro-Pinero J, Ruiz J, Jimenez-Pavon D, Aparicio V, et al. Criterion-related validity of field-based muscular fitness tests in youth. *J Sports Med Phys Fitness* 2012;52:263-72.
25. Fernandez Santos JR, Ruiz JR, Gonzalez-Montesinos JL, Castro-Pinero J. Reliability and validity of field-based tests to assess upper-body muscular strength in children aged 6-12 years. *Pediatr Exerc Sci* 2016;28:331-40.
26. Lobelo F, Pate RR, Dowda M, Liese AD, Ruiz JR. Validity of cardiorespiratory fitness criterion-referenced standards for adolescents. *Med Sci Sports Exerc* 2009;41:1222-9.
27. Andersen LB, Harro M, Sardinha LB, Froberg K, Ekelund U, Brage S, et al. Physical activity and clustered cardiovascular risk in children: a cross-sectional study (The European Youth Heart Study). *Lancet* 2006;368:299-304.
28. Andersen LB, Bugge A, Dencker M, Eiberg S, El-Naaman B. The association between physical activity, physical fitness and development of metabolic disorders. *Int J Pediatr Obes* 2011;6:29-34.
29. Zweig MH, Campbell G. Receiver-operating characteristic (ROC) plots: a fundamental evaluation tool in clinical medicine. *Clin Chem* 1993;39:561-77.
30. Institute of Medicine (IOM). Fitness measures and health outcomes in youth. Washington (DC): The National Academies Press; 2012.
31. Ortega FB, Silventoinen K, Tynelius P, Rasmussen F. Muscular strength in male adolescents and premature death: cohort study of one million participants. *BMJ* 2012;345:e7279.
32. Artero EG, Ruiz JR, Ortega FB, Espana-Romero V, Vicente-Rodriguez G, Molnar D, et al. Muscular and cardiorespiratory fitness are independently associated with metabolic risk in adolescents: the HELENA study. *Pediatr Diabetes* 2011;12:704-12.
33. Steene-Johannessen J, Anderssen SA, Kolle E, Andersen LB. Low muscle fitness is associated with metabolic risk in youth. *Med Sci Sports Exerc* 2009;41:1361-7.
34. WHO. Global recommendations on physical activity for health. Geneva: World Health Organization; 2010.
35. Artero EG, Lee DC, Lavie CJ, Espana-Romero V, Sui X, Church TS, et al. Effects of muscular strength on cardiovascular risk factors and prognosis. *J Cardiopulm Rehabil Prev* 2012;32:351-8.
36. Castro-Pinero J, Artero EG, Espana-Romero V, Ortega FB, Sjostrom M, Suni J, et al. Criterion-related validity of field-based fitness tests in youth: a systematic review. *Br J Sports Med* 2009;44:934-43.
37. Castro-Pinero J, Ortega FB, Artero EG, Girela-Rejon MJ, Mora J, Sjostrom M, et al. Assessing muscular strength in youth: usefulness of standing long jump as a general index of muscular fitness. *J Strength Cond Res* 2010;24:1810-7.

Additional Members of the UP&DOWN Study Group

Coordinator: Ascension Marcos.

Principal Investigators: Ascension Marcos, Jose Castro-Piñero, Oscar L. Veiga, and Fernando Bandres.

Scientific Coordinators: David Martinez-Gomez (chair), Jonatan R. Ruiz (co-chair), Ana Carbonell-Baeza, Sonia Gomez-Martinez, and Catalina Santiago.

Spanish National Research Council: Ascension Marcos, Sonia Gomez-Martinez, Esther Nova, Ligia-Esperanza Diaz, Belen Zapatera, Ana M. Veses, Aurora Hernandez, and Alina Gheorghie.

University of Cadiz: José Castro-Piñero, Jesus Mora-Vicente, Jose L. Gonzalez-Montesinos, Julio Conde-Caveda, Jonatan R.

Ruiz (University of Granada [UGR]), Francisco B. Ortega (UGR), Carmen Padilla Moledo, Ana Carbonell Baeza, Palma Chillon (UGR), Jorge del Rosario Fernandez, Ana Gonzalez Galo, Gonzalo Bellvis Guerra, Alvaro Delgado Alfonso, Fernando Parrilla, Roque Gomez, and Juan Gavalá.

Autonomous University of Madrid: Oscar L. Veiga, H. Ariel Villagra, Juan del-Campo, Carlos Cordente (UPM), Mario Diaz, Carlos M. Tejero, Aitor Acha, Jose M. Moya, Alberto Sanz, David Martinez-Gomez, Veronica Cabanas-Sanchez, Gabriel RodriguezRomo (UPM), Rocio Izquierdo, Laura Garcia-Cervantes, and Irene Esteban-Cornejo.

Complutense University of Madrid: Fernando Bandres, Alejandro Lucia (European University of Madrid [UEM]), Catalina Santiago (UEM), and Felix Gomez-Gallego (UEM).

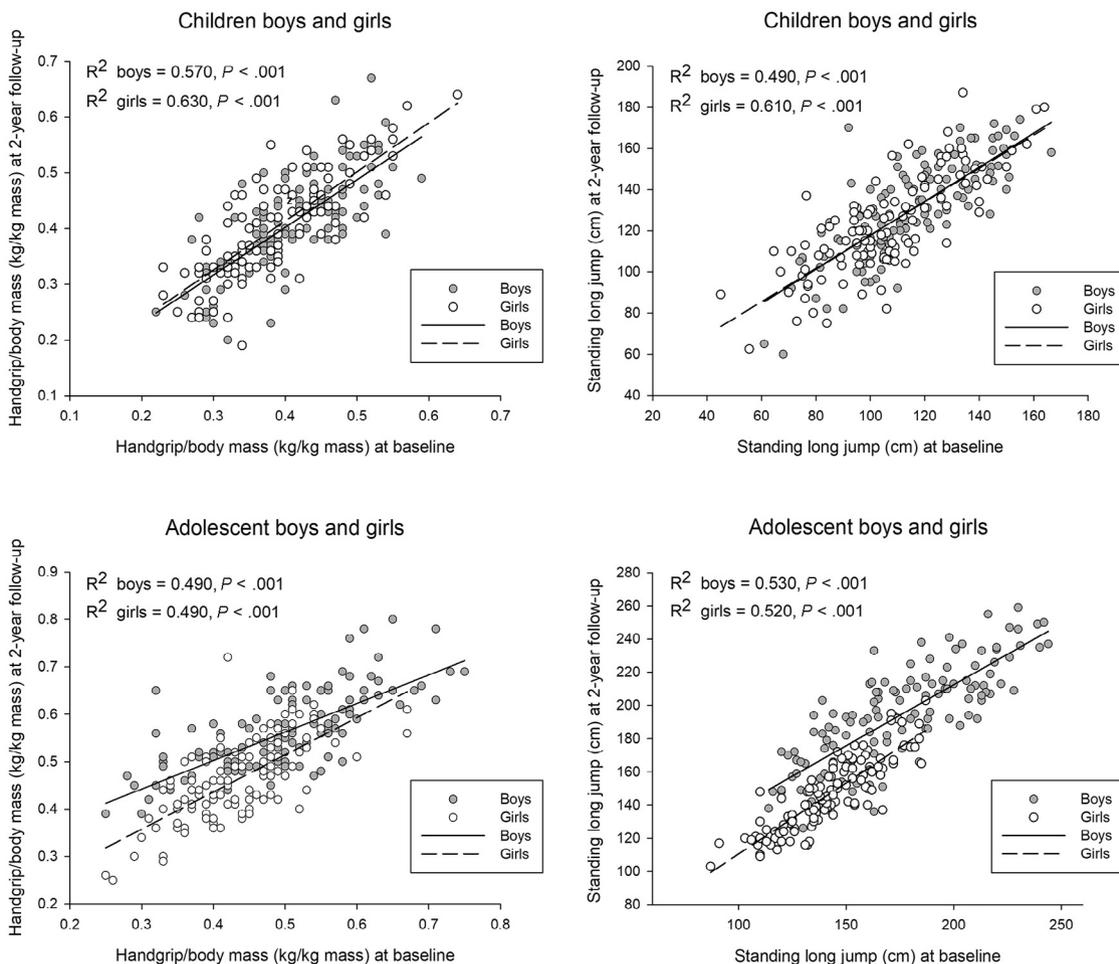


Figure 2. Scatterplot of muscle fitness levels at baseline (6- to 10-year-olds and 12- to 16-year olds) and at 2-year follow-up (8- to 12-year-olds and 14- to 16-year-olds, respectively) in children and adolescents, both boys and girls.

Table I. Baseline and 2-year follow-up characteristics of study sample by sex

Variables	Children						Adolescents					
	Boys			Girls			Boys			Girls		
	Baseline (n = 127)	2-y follow-up (n = 115)	<i>P</i> *	Baseline (n = 110)	2-y follow-up (n = 98)	<i>P</i> *	Baseline (n = 143)	2-y follow-up (n = 127)	<i>P</i> *	Baseline (n = 131)	2-y follow-up (n = 118)	<i>P</i> *
Pubertal development, n (%)			<.001			<.001			<.001			<.001
1	62 (48.8)	6 (5.2)		72 (65.2)	34 (33.3)		—	—		1 (0.8)	—	
2	56 (44.1)	73 (63.5)		28 (27.7)	27 (26.5)		16 (11.2)	—		11 (8.4)	—	
3	9 (7.1)	33 (28.7)		8 (7.3)	30 (29.4)		46 (32.2)	7 (5.5)		61 (46.6)	26 (20.0)	
4	—	3 (2.6)		2 (1.8)	11 (10.8)		49 (34.3)	53 (41.7)		46 (35.1)	70 (59.3)	
5	—	—		—	—		32 (22.4)	67 (52.8)		12 (9.2)	22 (18.6)	
Age (y)	7.6 (1.5)	10.1 (1.5)	<.001	7.5 (1.6)	10.1 (1.6)	<.001	13.6 (1.7)	16.0 (1.6)	<.001	13.5 (1.6)	15.9 (1.5)	<.001
Sum of 2 skinfolds (mm)	21.7 (9.7)	26.7 (13.6)	<.001	25.0 (12.8)	28.1 (14.9)	<.001	23.7 (13.7)	25.3 (10.5)	<.001	30.3 (11.9)	30.5 (13.4)	.457
SBP (mm Hg)	101.8 (11.0)	105.0 (9.3)	.001	99.4 (11.6)	104.8 (10.8)	<.001	112.9 (15.6)	114.7 (13.2)	.071	106.8 (10.5)	104.6 (10.8)	.002
HOMA-IR	0.8 (0.8)	1.1 (1.3)	.021	1.2 (1.4)	1.1 (0.9)	.630	2.8 (2.2)	0.9 (1.6)	<.001	3.2 (2.7)	0.6 (0.5)	<.001
TG (mg/dL)	41.1 (20.5)	40.8 (19.1)	.906	46.3 (17.9)	48.3 (27.4)	.248	54.38 (36.4)	67.8 (31.1)	<.001	57.8 (29.6)	63.7 (24.2)	<.001
TC/HDL-C ratio	3.0 (0.6)	3.1 (0.6)	.223	3.2 (0.7)	3.0 (0.7)	.022	2.8 (0.5)	2.9 (0.6)	.245	2.8 (0.6)	2.7 (0.6)	.162
Handgrip strength/body mass	0.41 (0.1)	0.41 (0.1)	.921	0.39 (0.1)	0.40 (0.1)	.005	0.50 (0.1)	0.56 (0.1)	<.001	0.43 (0.1)	0.46 (0.1)	<.001
Standing long jump (cm)	114.8 (21.1)	129.8 (25.3)	<.001	106.5 (22.9)	122.9 (24.1)	<.001	175.3 (33.2)	190.2 (38.9)	<.001	141.1 (21.2)	143.8 (28.3)	.196

*VO*_{2max}, maximum oxygen consumption.

Values represent mean (SD) unless otherwise indicated.

**P*: significant differences between baseline and 2-year follow-up are highlighted in bold.

Table IV. Binary logistic regression statistics testing the predictive capacity of the muscle fitness testing thresholds derived from the receiver operating characteristic curve analysis for having higher CVD risk score at the baseline and 2-year follow-up

Predictive variables	Children								
	Boys				Girls				
	β	95% CI	OR	P	β	95% CI	OR	P	
Baseline									
Handgrip/body mass	1.833	1.859;21.036	6.254	.003	3.799	9.455;211.125	44.68	<.001	
Standing long jump	2.579	2.497;69.629	13.184	.002	2.520	2.706;57.034	12.424	.001	
2-year follow-up*									
Handgrip/body mass	1.739	1.373;23.582	5.691	.017	2.083	2.023;31.867	8.029	.003	
Standing long jump	1.857	1.478;27.739	6.403	.013	2.491	2.696;54.052	12.072	.001	
Predictive variables	Adolescents								
	Boys				Girls				
	β	95% CI	OR	P	β	95% CI	OR	P	
Baseline									
Handgrip/body mass	3.043	4.538;96.867	20.970	<.001	2.179	1.931;40.440	8.837	.005	
Standing long jump	2.131	1.735;40.397	8.427	.008	1.832	2.060;18.943	6.246	.001	
2-year follow-up*									
Handgrip/body mass	1.989	1.701;27.434	6.421	.010	1.644	1.235;23.146	4.666	.029	
Standing long jump	1.918	1.260;36.787	6.809	.026	1.661	1.629;16.995	5.262	.006	

β indicates standardized coefficient.
 Statistically significant differences are highlighted in bold.
 All analyses were controlled for age.
 *In addition, for the 2-year follow-up, cardiovascular risk scores were adjusted for levels at baseline.

Table V. Diagnostic variables for muscle fitness tests to determine elevated CVD riskscore

Muscle fitness test	Children									
	Boys					Girls				
	Youden index	PPV	NPV	LR+	LR-	Youden index	PPV	NPV	LR+	LR-
Handgrip strength/body mass	0.42	5.0	75.0	2.10	0.31	0.61	3.4	75.7	2.90	0.10
Standing long jump	0.53	37.5	97.6	3.92	0.35	0.47	43.8	90.3	2.07	0.17
Muscle fitness test	Adolescents									
	Boys					Girls				
	Youden index	PPV	NPV	LR+	LR-	Youden index	PPV	NPV	LR+	LR-
Handgrip strength/body mass	0.49	5.4	65.5	2.39	0.24	0.44	3.4	75.7	2.14	0.29
Standing long jump	0.42	37.5	90.2	2.31	0.38	0.47	38.0	88.1	2.19	0.23

PPV, positive predictive value; NPV, negative predictive value; LR+, likelihood ratio of a positive test results; LR-, likelihood ratio of a negative test results,.