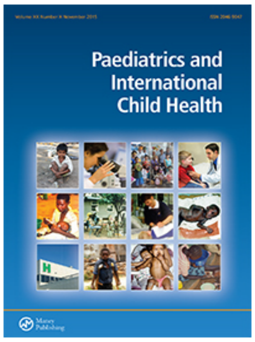

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Association between cardiorespiratory fitness and cardiometabolic risk factors in Brazilianchildren and adolescents: the mediating role of obesity parameters

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ABSTRACT

Background: There is a lack of clarity as to which obesity parameters may be more important in the association between cardiorespiratory fitness (CRF) and cardiometabolic risk factors (CMRF).
Aim: To verify the mediating role of different obesity parameters on the association between CRF and CMRF in normal weight and overweight/obese children and adolescents.
Methods: This cross-sectional study comprised 999 children and adolescents (534 boys) aged 7–14 years from the south of Brazil. Body mass index (BMI), waist circumference (WC), waist-to-height ratio (WHtR) and percentage of body fat were assessed. Participants were classified as normal weight, overweight and obese according to BMI. CRF was evaluated by the 6-minute run/walk test. . A continuous CMRF score was calculated by summing the Z-scores of the following variables: systolic and diastolic blood pressure, glucose, total cholesterol, high-density lipoprotein cholesterol and triglycerides. Data analysis was performed using partial correlation and linear regression models.
Results: BMI, WC, WHtR and percentage of body fat mediated the relationship between CRF and CMRF in overweight/obese boys and girls but not those of normal weight. Additionally, the percentage of the influence of each obesity parameter was 20% for BMI and WC, 16% for percentage of body fat and 18% for WHtR in girls. For boys, the mediation effect was 25% for BMI, 26% for WC, 28% for percentage of body fat and 25% for WHtR.
Conclusion: Adiposity plays a central role in CMRF; therefore, maintaining an adequate weight status should be an important objective of health-promoting programmes in early age.
Abbreviations: CMRF, cardiometabolic risk factors; CRF, cardiorespiratory fitness; BMI. body mass index; HDL-c, high-density lipoprotein cholesterol, PROCESS PROESP-Br, Projeto Esporte Brasil; SPSS, Package for Social Sciences; TC, total cholesterol; TG, triglycerides; WC, waist circumference; WHtR, waist-to-height ratio; %BF, percentage of body fat.

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Metabolic health; body mass index; waist circumference; waist-to-height ratio; percentage of body fat

Introduction

Cardiometabolic risk factors (CMRF) in childhood have been of public health concern as studies consistently report that metabolic abnormalities such as insulin resistance, dyslipidaemia and hypertension begin to develop in early life [1–3]. Beyond the genetic contribution, this scenario is a result of an inappropriate lifestyle characterised by an unhealthy diet alongside increasingly sedentary behaviour and low levels of physical activity [4,5].

Cardiorespiratory fitness (CRF) is recognised as an important health indicator, irrespective of age [6]. In children and adolescents, high CRF levels have been associated with a healthier cardiometabolic profile and are considered to be a predictor of cardiovascular complications in adulthood [7,8]. Importantly, cardiometabolic health is also mainly affected by obesity [9]. In recent years, several studies have been conducted to understand the association between different obesity parameters and CMRF. Systematic review data also identify that body mass index (BMI), waist circumference (WC) and waist-to-height ratio (WHtR) are similarly predictive of CMRF in childhood and adolescence [10]. However, other research has identified different associations between measures of weight status and CMRF. In Colombian adolescents, for example, WC had a stronger association with cardiometabolic risk than WHtR [11], and, in Portuguese children, BMI was more strongly associated with cardiometabolic risk than skinfold thickness [12]. Thus, there is currently no consensus on which obesity parameter is the most appropriate predictor of CRMF.

Beyond the independent associations regarding the aforementioned variables, some researchers have suggested that obesity plays a mediating role in the relationship between CRF and CMRF. Pérez-Bey et al. [13] and Diez-Fernandez et al. [14] indicated that BMI

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mediated the association between CRF and clustered cardiovascular disease risk factors in children and adolescents. Similar findings were reported using WC as an obesity parameter [15]. Percentage of body fat (%BF) is also a mediator of the relationship between CRF and mean arterial pressure in Brazilian children [16]. Although the mediating role of obesity has been established by these studies, there is a lack of clarity as to which obesity parameters including BMI, WC, WHtR and %BF may be more important in the association between CRF and CMRF. Without examining the strength of these obesity measures in the relationship between CRF and CMRF, it is not possible to provide evidence-based public health guidance as to which measure of obesity should be used in monitoring community health. Furthermore, as these measures relate to both central and total adiposity, understanding its role could provide more precise information regarding obesity's influence on the association between CRF and CMRF, allowing more accurate determination of which aspect intervention programmes should focus on. It is also important to note that none of the above-mentioned studies examining this issue has examined whether the mediating role of difference measures of obesity varies according to weight status. The present study therefore aimed to verify the mediating role of different obesity parameters on the association between CRF and CMRF in normal weight and overweight/obese children and adolescents.

Methods

This cross-sectional study comprised 999 children and adolescents of both sexes (534 boys) aged 7–14 years from 19 private and public schools from a municipality in the south of Brazil, selected by conglomerate sampling from a population of 20,540 schoolchildren in all regions of the city and from rural and urban areas. All variables were measured at The University of Santa Cruz do Sul by trained researchers.

The sample size was calculated using the programme G*Power 3.1 (Heinrich Heine Universität, Düsseldorf, Germany). Seven predictors were considered as well as the following criteria: a statistical power of 0.95, an effect size ($F^2 = 0.10$) and $p < 0.05$. Thus, the minimum number of children and adolescents was established as 226 in each age group (normal weight boys and girls and overweight/obese boys and girls).

Cardiorespiratory fitness

CRF was evaluated by the 6-minute run/walk test using the 'Projeto Esporte Brasil' (PROESP-Br) protocol [17]. This test has been used in Brazilian youths as a predictor of peak oxygen uptake and has been internationally validated [18,19]. Children were asked to accomplish the greatest number of laps running or walking they could during 6-minutes. Testing was conducted on a sports track with the perimeter marked with cones and the floor with indications of meters. The number of laps successfully completed plus the additional distance achieved for the ones unable to complete a full lap at the end of the test were calculated. CRF was then determined by multiplying the number of laps by meters covered.

Obesity parameters

Body mass and height were evaluated according to the procedures adopted by PROESP-Br [17]. Then body mass index was calculated by dividing body mass (in kilograms) by height (in square meters). BMI classification used the World Health Organization cut-off points according to age and sex. Subjects <85th percentile were classified as normal weight, ≥85th percentile as overweight and ≥97th percentile as obesity [20]. For the purposes of analysis, the overweight and obese categories were combined. WC was measured at the mid-point between the lower ribs and iliac crest using an inelastic tape with a resolution of 1 mm (Cardiomed®). WHtR was determined by dividing WC by height. Tricipital and subscapular folds were measured and then Slaughter et al.'s equation [21] was used to determine %BF.

Sexual maturity

On the basis of pubic hair, pubertal stage was classified into five categories and subsequently categorised into four classes: stage I (pre-pubertal), stage II (initial development), stages III and IV (ongoing maturation) and stage V (mature) [22]. A survey card with figures was given to the schoolchildren who indicated which one most closely illustrated their stage of development.

Biochemical variables

Blood samples were collected after a 12-hour fast by a professional specialist using disposable materials. Serum samples were used to determine triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c) and glucose. The tests were carried out using Miura One automated equipment (ISE, Rome, Italy).

Blood pressure

Following the recommendations of the VI Brazilian Guidelines on Hypertension, systolic and diastolic blood pressure was measured twice with the students at rest, using a cuff that fitted the arm [23].

Statistical analysis

Descriptive data are presented as means and standard deviations. Independent two-tailed t-tests were used to examine sex differences in all measures. Pearson correlation was used to determine the relationship between obesity parameters and CRF with CMRF, adjusted for age and sexual maturity.

A cardiometabolic risk factor score (composite Z-score) was calculated for each participant using the following variables: cardiometabolic risk factors = z-HDL-C + z-triglycerides + z-total cholesterol + z-glucose + z-systolic blood pressure+ z-diastolic blood pressure. The HDL-C value was multiplied by −1 as it is inversely associated with cardiometabolic risk.

To examine whether the association between CRF and CMRF was mediated by obesity parameters (BMI, WC, %BF and WHtR), linear regression models were fitted using the PROCESS macro for the Statistical Package for Social Sciences (SPSS) version 22.0 (IBM Corp, Armonk NY, USA). The PROCESS macro used bootstrapping methods recommended by Preacher and Hayes [24] to test mediation hypotheses, using a resampling procedure of 10,000 bootstrap samples (used to test the indirect effects, calculating a corrected confidence interval bias).

The aim of this model was to investigate the total (c) and direct effects (a, b, c′), reflected by the unstandardised regression coefficient and significance between the independent and dependent variables in each model. The model also explored the indirect effect obtained from the product of coefficients (a x b) which indicates the change in the dependent variable (CMRF) for every unit change in the CRF mediated by the proposed mediator (BMI, WC, %BF and WHtR). The indirect effect was estimated through point estimates and 95% confidence intervals. When the confidence interval did not contain zero, the point estimate was considered significant. Thus, the following criteria were used to establish mediation: (a) the independent variables (CRF) are significantly related to the mediator (BMI, WC, %BF and WHtR); (b) the independent variables (CRF) are significantly related to the dependent variable (CMRF); (c) the mediator (BMI, WC, %BF and WHtR) is significantly related to the dependent variable (CMRF); and (d) the association between the independent and dependent variables is attenuated when the mediator is included in the regression model. The analyses were adjusted for age and sexual maturity. For all analyses, $p \leq 0.05$ was considered to be statistically significant.

Ethics

This study is part of a broader research called School Health—phase III, approved by the Committee of Ethics in Research with Human Subjects of the University of Santa Cruz do Sul (number 714.216/2014). The study subjects' parents or guardians authorised their participation on a free and informed consent form.

Results

Table 1 presents the descriptive characteristics of the sample. Overweight/obese boys were heavier and had higher BMI, WC, HDL-C, WHtR, %BF, total cholesterol, triglycerides, systolic blood pressure, diastolic blood pressure and CMRF scores than their peers of normal weight. Overweight/obese girls were heavier and had higher BMI, WC, WHtR, %BF, triglycerides, systolic blood pressure, diastolic blood pressure and CMRF scores than their normal-weight counterparts.

Partial correlation between obesity parameters (BMI, WC, %BF, WHtR) and CRF and CMRF according to obesity status and sex are presented in Table 2. All obesity parameters and CRF showed correlation with CMRF in overweight/obese boys and girls. CMRF was not associated with CRF in boys of normal weight, nor was WHtR with CRF in girls of normal weight. Considering that one of the criteria for mediation analysis is that all variables in the model show a correlation between each other, the mediator role of obesity was tested only for overweight/obese boys and girls.

Figures 1 and 2 show the models used to test the mediating role of BMI (A), WC (B), %BF (C) and WHtR (D) in the relationship between CRF and CMRF for overweight/obese girls and boys. Overall, when the mediator role of obesity parameters in the relationship between CRF and CMRF was tested, in the first regression equation (a), CRF was negatively associated with obesity parameters ($p < 0.001$) for all. In the second equation (c), CRF was negatively associated with CMRF ($p < 0.001$). In the third equation (b), the relationship between obesity parameters and CMRF was positive ($p < 0.001$). Finally, in the fourth equation (c′), when CRF and obesity parameters were included simultaneously in the model, obesity parameters were associated with CMRF. Additionally, the relationship between CRF and CMRF was attenuated when obesity parameters were included in the models, indicating that the different obesity parameters considered were mediators in the relationship between CRF and CMRF in boys and girls. Also, it was estimated that the percentage of the influence of obesity parameters was similar, once 20%, 20%, 16% and 18% of the total effect of CRF on CMRF was mediated by BMI, WC, %BF and WHtR, respectively, for overweight/obese girls. In overweight/obese boys, BMI mediated 25%, WC 26%, %BF 28% and WHtR 25%.

Discussion

As far as we are aware, this is the first study to examine the mediating role of different obesity parameters on

Table 1. Characteristics of children and adolescents by nutritional profile and sex.

Characteristics	Boys, $n = 534$ Mean (SD) Normal weight $n = 330$	Boys Overweight/obese $n = 204$	Girls, $n = 465$ Mean (SD) Normal weight $n = 283$	Girls Overweight/obese $n = 182$
Age, yrs	9.77 (1.95)	9.33 (1.75)[a]	8.79 (1.14)	8.71 (1.17)
Height, m	1.40 (0.13	1.41 (0.11)	1.35 (0.09)	1.38 (0.09)[a]
Weight, kg	34.10 (9.33)	45.35 (12.33)[a]	30.65 (5.93)	43.76 (10.73)[a]
BMI, kg/m2	16.92 (1.67)	22.07 (3.10)[a]	16.52 (1.47)	22.64 (3.25)[a]
CRF, m	967.16 (165.41)	829.32 (161.79)[a]	825.42 (117.68)	737.02 (115.85)[a]
WC, cm	59.46 (5.71)	70.22 (10.07)[a]	56.89 (4.58)	70.02 (9.75)[a]
WHtR, cm	0.42 (0.03)	0.49 (0.05)[a]	0.42(0.02)	0.50 (0.05)[a]
%BF	14.50 (4.40)	24.48 (7.55)[a]	17.94 (4.24)	26.75 (5.72)[a]
TC, mg/dL	155.64 (30.29)	162.43 (35.43)[a]	163.85 (30.53)	166.32 (32.85)
HDL-C, mg/dL	63.96 (12.55)	61.36 (11.71)[a]	63.17 (11.60)	58.13 (12.83)[a]
TG, mg/dL	58.72 (29.75)	67.61 (34.65)[a]	62.16 (25.96)	77.85 (37.18)[a]
Glucose, mg/dL	88.40 (9.43)	89.94 (12.53)	86.73 (11.30)	87.90 (9.81)
SBP, mmHg	99.81 (12.12)	105.79 (13.61)[a]	97.60 (12.42)	103.70 (13.04)[a]
DBP, mmHg	59.99 (9.18)	63.98 (10.34)[a]	59.83 (9.83)	63.64 (9.22)[a]
CMRF, Z-score	−0.12 (0.45)	0.16 (0.56)[a]	−0.10 (0.46)	0.21 (0.48)[a]
Maturity				
Pre-pubertal	152 (46.1)	80 (39.2)	151 (53.4)	82 (45.1)
Initial development	95 (28.8)	71 (34.8)	86 (30.4)	66 (36.3)
Ongoing maturation (stages III and IV)	76 (23.0)	50 (24.5)	40 (14.1)	29 (15.9)
Mature	7 (2.1)	3 (1.5)	6 (2.1)	2 (2.7)

BMI, body mass index; CMRF, cardiometabolic risk factors; CRF, cardiorespiratory fitness; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; %BF, percentage of body fat; SBP, systolic blood pressure; SD, standard deviation; TC, total cholesterol; TG, triglycerides; WC, waist circumference; WHtR, waist-to-height ratio. [a]Independent *t*-test for differences between normal weight and overweight/obese boys and girls ($p \leq 0.05$).

Table 2. Partial correlation between obesity indicators and cardiorespiratory fitness with cardiometabolic risk factors for overweight and overweight/obese girls and boys.

	BMI		WC		%BF		WHtR		CRF	
	r	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*
Girls										
Normal weight										
CMRF	0.17	**0.003**	0.20	**0.001**	0.17	**0.003**	0.03	0.60	−0.03	0.57
CRF	−0.03	0.54	−0.06	0.27	−0.09	0.12	0.03	0.58	-	-
Overweight/obese										
CMRF	0.36	**<0.001**	0.35	**<0.001**	0.28	**<0.001**	0.32	**<0.001**	−0.20	**0.007**
CRF	−0.35	**<0.001**	−0.30	**<0.001**	−0.36	**<0.001**	−0.31	**<0.001**	-	-
Boys										
Normal weight										
CMRF	0.21	**<0.001**	0.14	**0.008**	0.14	**0.01**	0.11	**0.03**	−0.50	0.36
CRF	0.03	0.57	0.02	0.70	−0.15	**0.005**	−0.01	0.75	-	-
Overweight/obese										
CMRF	0.35	**<0.001**	0.39	**<0.001**	0.41	**<0.001**	0.37	**0.001**	−0.21	**0.003**
CRF	−0.21	**0.002**	−036	**<0.001**	−0.36	**<0.001**	−0.37	**<0.001**	-	-

BMI, body mass index; %BF, percentage of body fat; CMRF, cardiometabolic risk factors; CRF, cardiorespiratory fitness; *r*, correlation value; WHtR, waist-to-height ratio. All analyses were adjusted for age and sexual maturity. Statistically significant *p*-values are in bold type.

the relationship between CRF and CMRF in children and adolescents. The main findings of the present study indicate that (i) BMI, WC, WHtR and %BF are mediators in the association between CRF and CMRF but only in the overweight/obese, regardless of gender, and (ii) the mediation effect is similar among obesity parameters since in girls BMI and WC mediated 20%, percentage of body fat 16% and WHtR 18%, and in boys BMI and WHtR mediated 25%, WC 26% and percentage of body fat 28%.

There was no association between CMRF and CRF in boys and girls of normal weight, and therefore mediation analysis was not applied for these groups. One of the possible explanations for this lack of association is that, in general, children are healthy, especially those with normal weight, which leaves little room for a positive effect of CRF on CRMF. These results are supported by Nyström et al. [25] who showed that CRF attenuated the CMRF score in obese children, indicating no effect in normal-weight children. In the present study, most of the CMRF evaluated were greater in the overweight/obese group than in the normal-weight group.

Previous evidence has demonstrated that obesity is a mediator in the relationship between CRF and CMRF, although all prior studies have examined only one obesity parameter rather than comparing the strength of multiple parameters, as is the case in the current study. Secondly, no study has examined the possibility that the mediating effects of obesity differ according to weight status. For instance, BMI mediated the association between CRF and CMRF in 81.2% of boys and 55.7% of adolescent girls [13]. The same results were reported in Spanish children, with smaller percentages

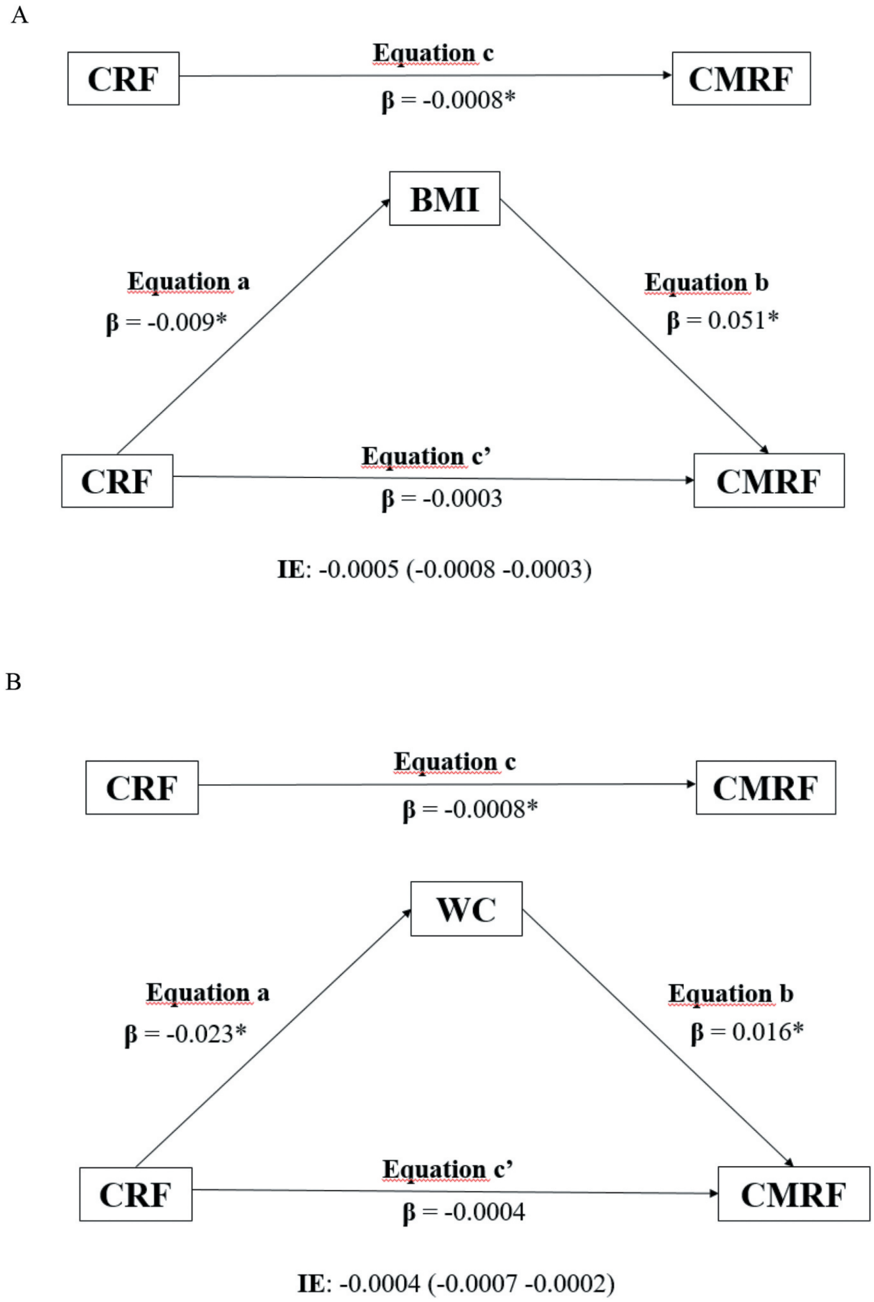

Figure 1. The role of body mass index (a), waist circumference (b), percentage of body fat (c), and waist-to-height ratio as mediators in the relationship between cardiorespiratory fitness and cardiometabolic risk factors in overweight/obese girls. The analyses were adjusted for age and sexual maturity. BMI, Body mass index; %BF, Percentage of body fat; CMRF, Cardiometabolic risk factors; CRF, Cardiorespiratory fitness; WC, waist circumference; WHtR, waist-to-height ratio. *Statistically significative association ($p < 0.05$).

of mediation (38% for boys and 39.8% for girls) [14]. WC was also considered a mediator of the relationship between CRF and CMRF, although the percentage of the total effect was not determined [11]. Another study investigated the mediating role of %BF in children but against an outcome variable of arterial pressure [16].

This study extends these previous findings by investigating the role of different obesity parameters in normal weight and overweight/obese children and adolescents. This is justified since obesity indicators used in the present study have different characteristics that should be taken into consideration. In epidemiological studies, BMI is widely used as an anthropometric index to assess metabolic risk relative to total body composition; however, it cannot distinguish between fat and lean mass [26,27]. %BF fat allows the determination of subcutaneous fat accumulation [26], while WC is a well accepted indicator of central adiposity [28]. WHtR has been proposed as a simple and rapid screening tool for the identification of height-based abdominal fat [29]. All these obesity parameters are suggested as CMRF predictors in childhood and adolescence [10,11,12], which agrees with the present study. In this study, WHtR was the obesity parameter most strongly associated with CMRF in boys and girls (Figures 1(d) and 2(d)). Indeed, some

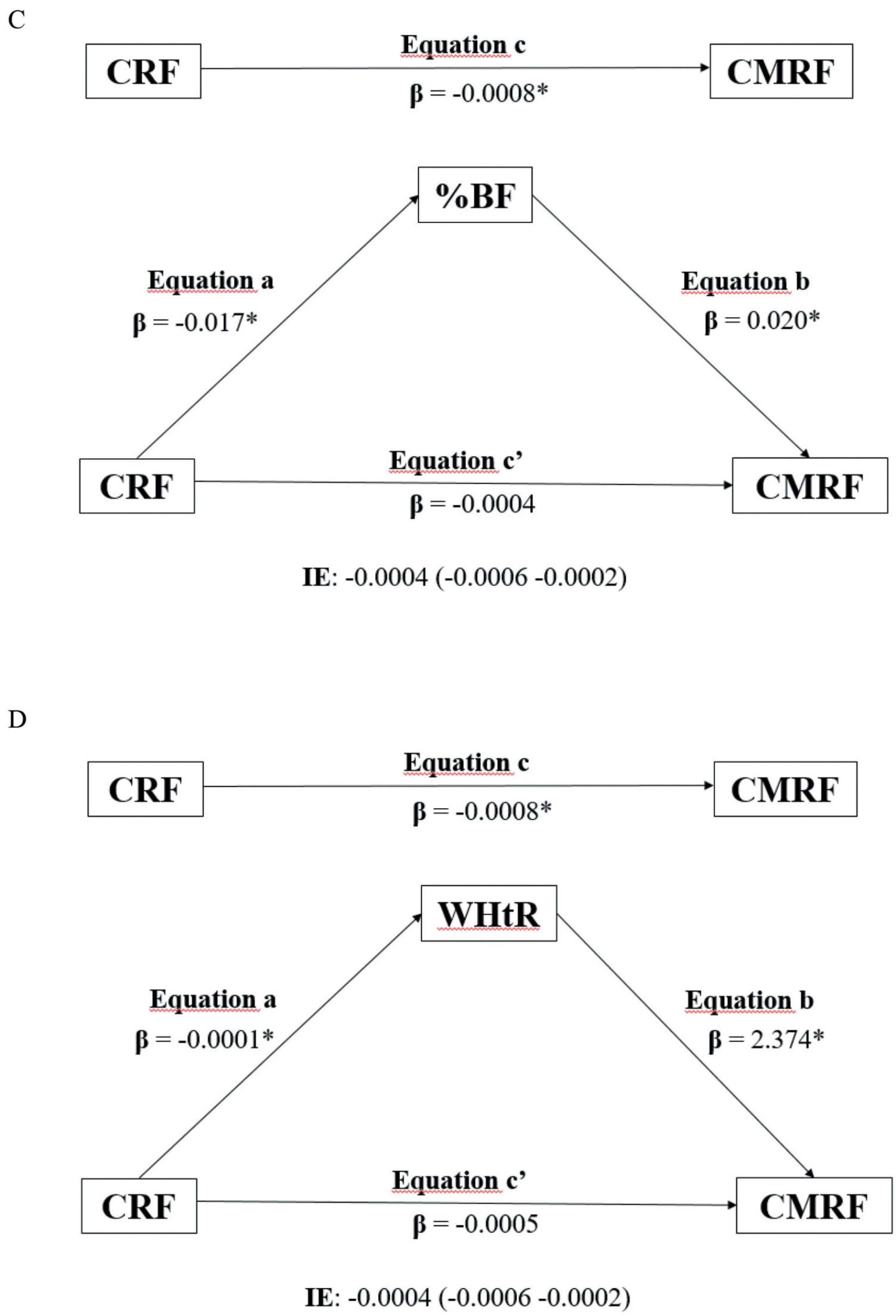

Figure 1. (Continued).

investigators have suggested that it could be a better predictor of metabolic risk than BMI and WC [30,31], although its role as a mediator is similar to those of the other obesity parameters.

Taking these aspects into consideration, adiposity, determined by BMI, WC, %BF and WHtR, was a mediator in the relationship between CRF and CMRF in both boys and girls. Therefore, regardless of the parameter adopted, obesity may be an intermediate step in the causal pathway between CRF and CMRF in children and adolescents, independent of age and sexual maturity. In addition, it was observed that the mediation effect is similar for obesity parameters, since in girls BMI and WC mediated 20%, %BF 16% and WHtR 18%, while in boys BMI and WHtR mediated 25%, WC 23% and the %BF fat 24%. Therefore, all obesity parameters influence the relationship between CRF and CMRF in a similar way, although the values are slightly greater in boys, suggesting a greater effect of obesity on this relationship in boys than in girls.

Two studies investigating the mediator role of BMI in the relationship between CRF and CMRF have demonstrated that the percentage of mediation was higher than that in the present study, *viz* 81.2% in boys and 55.7% in adolescent girls [13] and 38% in boys and 39.8% in girls [14]. The discordance between these

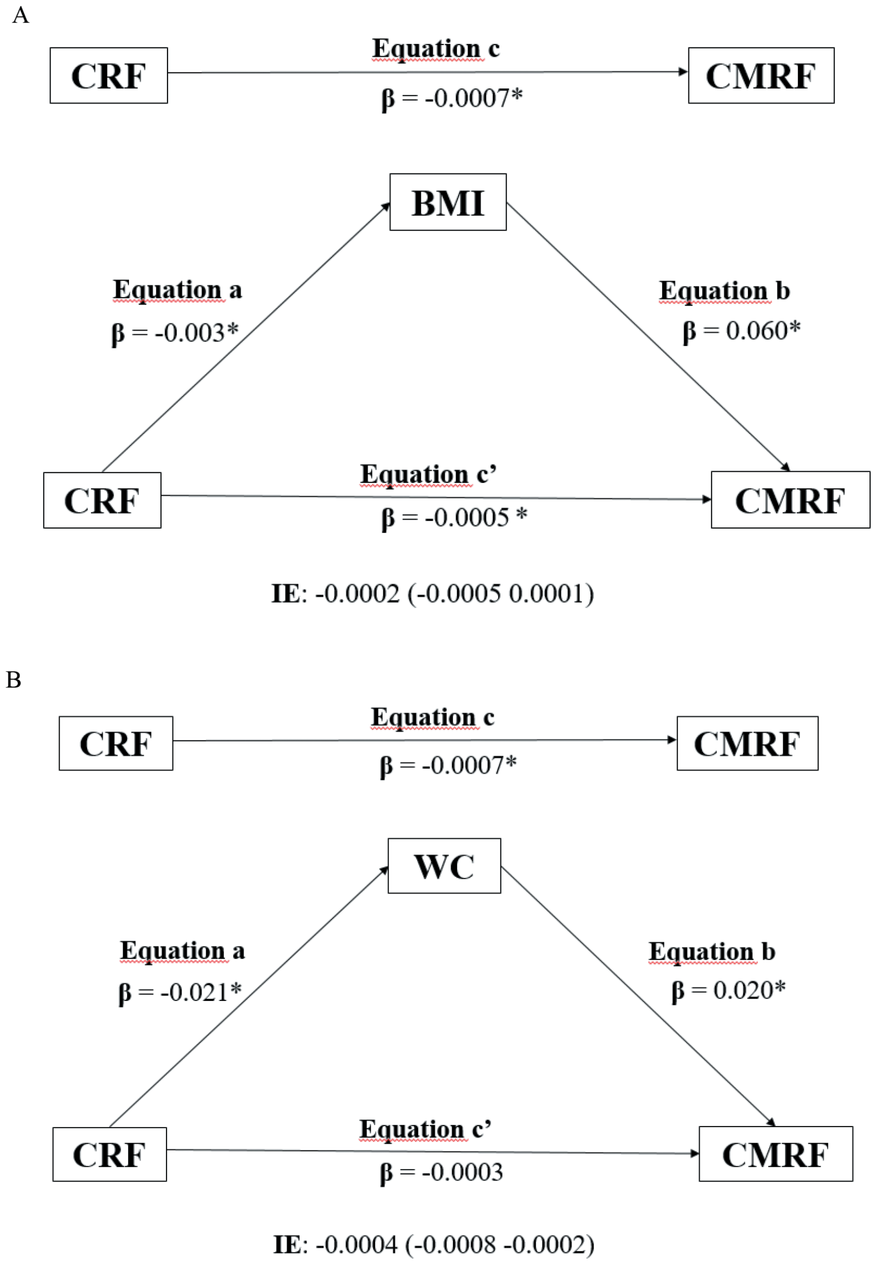

Figure 2. The role of body mass index (a), waist circumference (b), percentage of body fat (c), and waist-to-height ratio (d) as mediators in the relationship between cardiorespiratory fitness and cardiometabolic risk factors in overweight/obese boys. The analyses were adjusted for age and sexual maturity. BMI, Body mass index; %BF, Percentage of body fat; CMRF, Cardiometabolic risk factors; CRF, Cardiorespiratory fitness; WC, waist circumference; WHtR, waist-to-height ratio. *Statistically significative association ($p < 0.05$).

values could be partly owing to methodological variation. For instance, while the 6-minute walk/run test was used in our study, Pérez-Bey et al. [13] assessed CRF by the 20-minute shuttle run test. Using different variables to compose the CMRF score could also affect the results.

The results of this study indicate that physical exercise interventions should be developed to promote improved CRF in order to reduce obesity and CMRF. Considering that CMRF and obesity tend to track into adulthood [32], it is essential to implement public health policies to promote child and adolescent cardiometabolic health. Previous reviews investigating the effect of lifestyle interventions have investigated mainly BMI, WC and percentage body fat as obesity parameters, along with various CMRF such as HDL-C, triglycerides, fasting insulin and blood pressure. It has been suggested that lifestyle interventions can improve reduce weight and cardiometabolic outcomes [33,34]. This study demonstrates that adiposity (independently of the parameter) is an intermediate step in the association between CRF and CMRF and so all these adiposity parameters could be evaluated to determine nutritional status. Also, better CRF should improve cardiometabolic health.

There are some limitations to the study. Owing to the cross-sectional design, it was not possible to make cause–effect inferences which does not allow

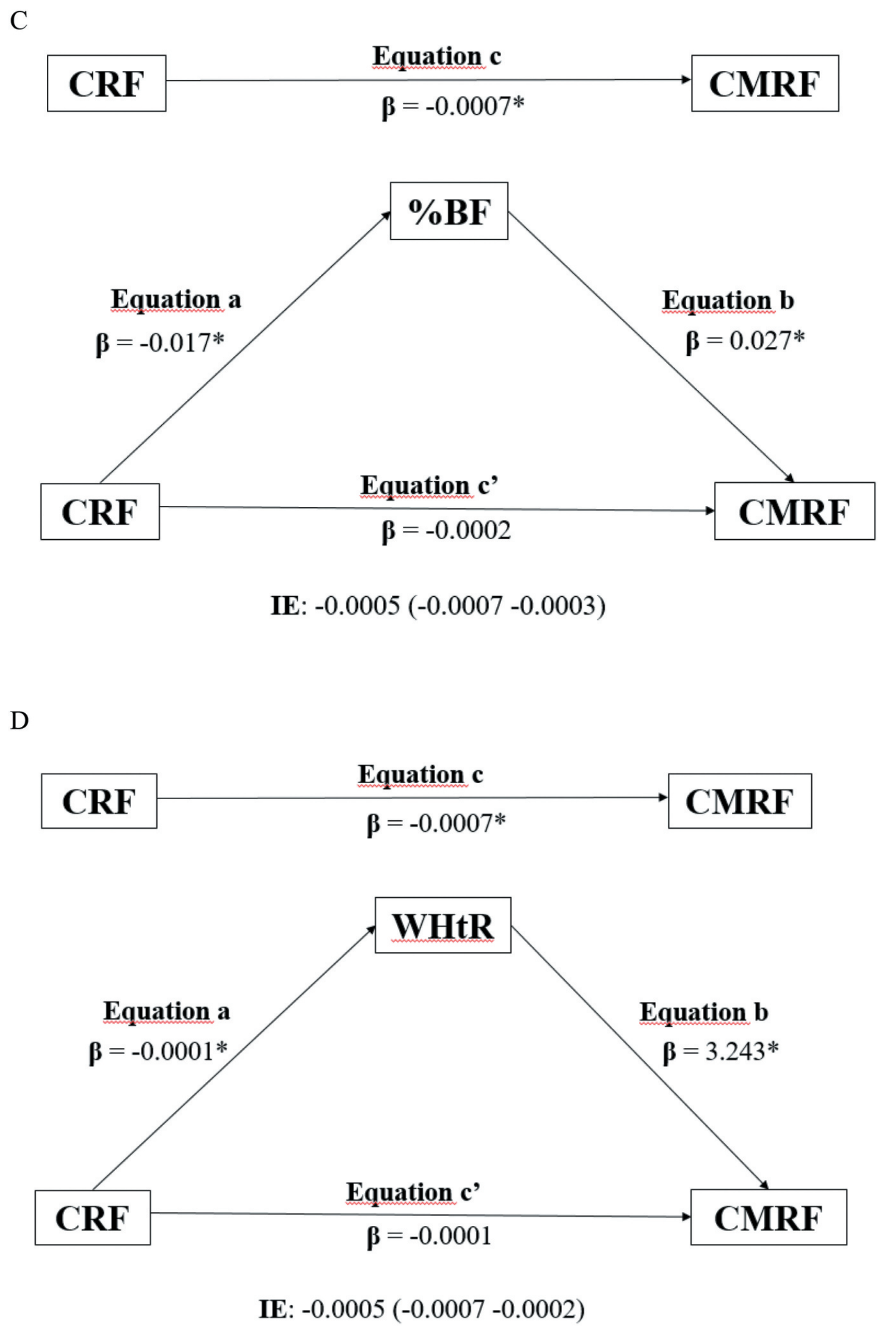

Figure 2. (Continued).

firm conclusions about the direction of the association. Also, the results might be influenced by confounding variables which were not considered such as diet, socio-economic status and physical activity. These variables could affect adiposity, CRF and CMRF and therefore the results. Nevertheless, this assessment of the role of four obesity parameters adds to the literature as most prior studies have investigated only one parameter, usually BMI. Moreover, the statistical analyses undertaken allow estimation of the percentage of the total effect of the mediator variable.

In conclusion, in overweight/obese children and adolescents of both sexes, BMI, WC, WHtR and %BF fat mediated the association between CRF and CRMF. These results extend current knowledge as the mediation analysis allowed determination of the extent to which the association between CRF and CMRF is affected by various obesity parameters. Indeed, the findings indicate that they exert a similar influence, suggesting that all parameters can be considered in future studies. Therefore, maintaining an adequate weight status along with high CRF levels should be an important objective of health promotion in children and adolescents.

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