Tracking of cardiometabolic risk in a Brazilian schoolchildren cohort: a 3-year longitudinal study

Tracking of cardiometabolic risk: a longitudinal study

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Abstract

Background: Clustering of cardiometabolic risk factors is a sign of detrimental health. Tracking is a term used to describe a variable longitudinal stability across time. High tracking

provides the chance to determine which cardiometabolic risk factors should be the target of early treatment and prevention efforts. The present study aims to analyze the tracking of cardiometabolic risk factors and clustered cardiometabolic risk score in children across a 3-year time span; and to verify the odds of staying at risk (measured by the clustered score) from baseline to follow-up. **Methods:** Longitudinal study that included 354 (155 boys) children, aged 7-12 years at baseline. A clustered score was calculated by summing the systolic blood pressure, waist circumference, triglycerides, glucose, and the TC/HDL-C ratio Z-scores divided by five. A second clustered score was calculated including cardiorespiratory fitness (CRF). **Results:** CRF and anthropometric parameters presented high tracking (r≥0.662), whereas the cardiometabolic parameters exhibited low-to-moderate tracking (0.100≤r≤0.571). The clustered scores' tracking was moderate (r≥0.508; r≥0.588 [CRF]). Participants in the higher risk groups at baseline presented 3.81 (95% CI: 2.40; 6.05) and 4.64 (95% CI: 2.85; 7.56), including CRF, times higher chance of remaining at risk three years later. Moreover, participants in the worst profile regarding CRF or anthropometrics at baseline presented at least 4.00 times higher chance of being at risk three years later. **Conclusion:** Participants with worst CRF and adiposity had an increased risk of presenting higher clustered risk after three years.

Key-words: Cardiometabolic risk; Cardiovascular disease; Metabolic syndrome; Pediatric.

Introduction

The clustering of cardiometabolic risk factors in the same individual can be viewed as a sign of detrimental metabolic health[1]. It is from this perspective that studies[1–4] have been using continuous variables to construct a clustered cardiometabolic risk score, which combines the traditional risk factors[5], to provide a better view of cardiometabolic health amongst children

and adolescents[1]. However, much of the work conducted on clustered cardiometabolic risk scores thus far has focused on cross-sectional studies of prevalence.

Tracking is a term used to describe a variable of interest and its longitudinal stability and development across time[6]. High tracking identification provides the chance to determine which cardiometabolic risk factors should be the target of early treatment and prevention efforts. Cardiometabolic risk factors may develop at an early age[1], and their clustering (measured by a clustered score) presents moderate stability from childhood into adolescence (0.38 to 0.56)[7], and moderate to high stability from childhood into adulthood (0.42 to 0.67)[8]. Prior findings showed that prevalence of risk factors is high amongst our sample compared to international reference standards[3], especially related to anthropometric, blood pressure, and cardiorespiratory fitness (CRF) indicators[9]. In addition, the clustering of risk factors is evident in some Brazilian children and adolescents[10].

A type of tracking analysis is to examine if children at risk stay at risk across a defined time span. It could be easily postulated that cardiometabolic risk factors with high tracking would influence the long-term cardiometabolic health status of children and adolescents at risk and may provide important information for the implementation of preventive strategies to improve cardiometabolic profiles and to reduce the development of adverse cardiovascular outcomes[11,12]. However, to the best of our knowledge, there is not a tracking study with this approach evaluating Brazilian children and adolescents thus far. From this perspective, the present study aims to: 1. analyze the tracking of cardiometabolic risk factors and the clustered cardiometabolic risk in Brazilian children and adolescents across a 3-year time span; and 2. verify the odds of staying at risk (measured by a clustered score) from baseline to follow-up.

Patients and methods

This is a longitudinal study, part of the Schoolchildren's Health Study, which began in 2011/12. All children from 25 randomly selected public and private schools of Santa Cruz do Sul (RS, Brazil) were invited to participate in the study. It was approved by the Committee of Ethics in Research with Human Subjects of the University of Santa Cruz do Sul (UNISC), under protocol number 3.644.667, and written informed consent was signed by the parents/guardians of 1,129 children, aged 7-12 years, at baseline (2011/12). Children who did not perform blood collection at the baseline were excluded (n = 111). All participants were recalled, but only 354 participants (155 boys) accepted to be followed-up in 2014/15 (Figure 1). The supplementary table I demonstrates the drop-out analysis.

All evaluations were carried out in the UNISC campus by trained professionals. CRF was assessed by indirect submaximal exercise tests. The 9-minute running and walking test was used at baseline, described by Projeto Esporte Brasil[13], and the 6-minute running and walking test was used in the follow-up, described by Projeto Esporte Brasil[14]. Both tests were performed on an athletic track and consisted of covering the largest possible distance within the established time, assessed in meters, with subsequent calculation of the peak oxygen uptake (VO_{2peak}) in mL/kg/min. The following equation has used for the 9-minute test: $VO_{2peak} = 47.547 + 0.008 * (Test) – 0.805 * (BMI) + 4.236 * (Sex)$[15]; while the following equation was used for the 6-minute test: $VO_{2peak} = 41.946 + 0.022 * (Test) – 0.875 * (BMI) + 2.107 * (Sex)$[16]. In both tests, the distance performed by the student in meters was used for the value of the '*Test*', and the values of 1 and 0 for males and females, respectively.

Waist circumference (WC) was evaluated using an inextensible anthropometric plastic tape measure, using as reference the narrowest part between the ribs and the iliac crest[17]. The body mass index (BMI) was obtained by calculating the ratio between weight in kilograms and the height squared in meters (*weight/[height]²*) and classified into normal weight, overweight or obesity according to BMI cutoffs to define rates of thinness in children and adolescents[18].

The skinfold thickness was measured with a Lange® caliper (MultiMed, Skinfold Caliper, USA) at calf, triceps, and subscapular sites and summed for the use in analyses. The systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured with the children sitting at rest, using a sphygmomanometer (B-D®, aneroid, Germany) with cuff suitable for the child's arm circumference and stethoscope (Premium, Rappaport, China), in accordance with Brazilian guidelines for blood pressure measurement in children and adolescents[19]. Levels of fasting glucose, triglycerides, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were evaluated through blood collection, after 12-hours-fasting, and carried out through automated equipment Miura 200 (I.S.E., Rome, Italy) using commercial DiaSys (DiaSysDiagnostic Systems, Germany) kits. The serum samples were stored at -80ºC until analysis.

Before analysis, skewed variables (WC, TC/HDL-C ratio, and triglycerides) were transformed by the natural logarithm. The risk factor variables (CRF [VO_{2peak}], WC, SBP, glucose, triglycerides, and TC/HDL-C ratio) were standardized according to sex and age-specific international reference values using the following equation: *Z-score = ($X_{Brazilian}$-$X_{International\ reference}$)/$SD_{International\ reference}$*, suggested by Stavnsbo et al.[3]. A clustered cardiometabolic risk score was calculated by summing the SBP, WC, triglycerides, glucose, and the TC/HDL-C ratio scores and dividing by five. A second clustered cardiometabolic risk score was calculated including CRF (VO_{2peak} inversed), similar to the equation described above, but divided by six. The latter was also examined because CRF plays an important role in cardiometabolic health, and it is strongly related to other cardiometabolic risk factors and poses as a great risk to overall health[1,20]. The clustered cardiometabolic risk score (with or without CRF) values of 0.40 to 0.85 were considered as borderline and above 0.85 were considered as indicating higher cardiometabolic risk, adapted from Andersen et al.[1].

Statistical analysis

The Statistical Package for the Social Sciences (SPSS, version 23.0 IBM, Armonk, NY) software was used for all statistical analysis. Shapiro-Wilk test was used to test data normality. A descriptive analysis was performed to describe the subjects at baseline and at follow-up using means and standard deviations (SD) for continuous variables or absolute and relative frequency for categorical variables. The Student t-test was used to verify differences between sexes. The t-test for paired samples was used to verify differences between baseline and follow-up scores. The descriptive analysis was performed for all participants and stratified by sex. Tracking coefficients for each of the risk factors and the clustered cardiometabolic risk score (with and without CRF) were calculated for all participants and for each age group (7-9→10-12 and 10-12→13-15 years old) and stratified by sex using Spearman correlations. Tracking coefficients below 0.3 were considered low; from 0.3 to 0.6 were considered moderate; and higher than 0.6 were considered high[21]. A proportion was calculated for positive results of participants classified on a respective clustered cardiometabolic risk score classification divided by all participants. Odds ratio and 95% confidence intervals were calculated for how many participants on the respective classification at baseline still were at this or other classification in the follow-up divided by the expected number of participants being at this respective classification in the follow-up. Expected numbers were calculated based on a random distribution of change in risk factors. Additionally, proportions, odds ratio, and confidence intervals were calculated for only those who had a higher risk at baseline according to their levels of adiposity and CRF at baseline to verify whether the higher classification maintenance is stronger. The p-values of $p<0.05$ were considered significant in all analysis.

Data availability

The data associated with the paper are not publicly available but are available from the corresponding author on reasonable request.

Results

Table I presents the descriptive characteristics at each evaluation period (baseline and follow-up). Regarding the clustered cardiometabolic risk score (with and without CRF) profile based on the standardized sex and age-specific international reference values[3], the clustered cardiometabolic risk scores for boys and girls were significantly more favorable in the follow-up ($p < 0.05$). Furthermore, the frequency of followed children and adolescents defined with overweight and obesity was 33.6% at baseline and 33.3% in the follow-up.

Table I. Descriptive sample characteristics.

	Boys	Girls	Total
	n = 155	n = 199	n = 354
	Mean (SD)		
Age (years, baseline)	9.45 (1.57)	9.37 (1.54)	9.40 (1.55)
Age (years, follow-up)	12.20 (1.54)	12.05 (1.55)	12.11 (1.54)
Cardiorespiratory fitness (mL/kg/min, baseline)	47.12 (4.19)	41.87 (3.48)	44.17 (4.61) †
Cardiorespiratory fitness (mL/kg/min, follow-up)	47.81 (6.91)	**42.65 (5.36)**	**44.91 (6.60)** †
Waist circumference (cm, baseline)	64.54 (10.88)	61.83 (8.86)	63.02 (9.87) †
Waist circumference (cm, follow-up)	**71.01 (12.04)**	**67.55 (9.72)**	**69.06 (10.92)** †
Body mass index (kg/m^2, baseline)	18.92 (3.84)	18.49 (3.64)	18.68 (3.73)
Body mass index (kg/m^2, follow-up)	**20.98 (4.68)**	**20.76 (4.33)**	**20.86 (4.48)**
Sum of 3 Skinfolds (mm, baseline)	25.37 (11.92)	26.99 (9.74)	26.28 (10.76)
Sum of 3 Skinfolds (mm, follow-up)	**22.68 (9.73)**	26.30 (9.42)	**24.72 (9.71)** †
Systolic blood pressure (mmHg, baseline)	98.50 (10.48)	96.65 (10.37)	97.46 (10.44)
Systolic blood pressure (mmHg, follow-up)	**108.27 (14.04)**	**107.97 (12.71)**	**108.10 (13.29)**
Diastolic blood pressure (mmHg, baseline)	59.29 (10.24)	58.27 (10.22)	58.72 (10.22)
Diastolic blood pressure (mmHg, follow-up)	**65.66 (11.88)**	**65.73 (10.24)**	**65.70 (10.97)**
Total cholesterol (mmol/L, baseline)	4.75 (1.06)	4.90 (0.92)	4.83 (0.98)
Total cholesterol (mmol/L, follow-up)	**4.10 (0.85)**	**4.18 (0.78)**	**4.14 (0.81)**
HDL-C (mmol/L, baseline)	1.53 (0.31)	1.47 (0.30)	1.50 (0.31)
HDL-C (mmol/L, follow-up)	**1.65 (0.33)**	**1.56 (0.33)**	**1.60 (0.33)** †
LDL-C (mmol/L, baseline)	2.91 (0.93)	3.08 (0.82)	3.00 (0.88)
LDL-C (mmol/L, follow-up)	**2.11 (0.71)**	**2.25 (0.69)**	**2.19 (0.70)**
Glucose (mmol/L, baseline)	5.03 (0.54)	4.98 (0.53)	5.00 (0.54)
Glucose (mmol/L, follow-up)	5.11 (0.49)	4.96 (0.56)	5.03 (0.54) †
TC/HDL-C (mmol/L, baseline)	3.18 (0.80)	3.43 (0.80)	3.32 (0.81) †
TC/HDL-C (mmol/L, follow-up)	**2.56 (0.68)**	**2.77 (0.77)**	**2.68 (0.74)** †
Triglycerides (mmol/L, baseline)	0.68 (0.31)	0.77 (0.32)	0.73 (0.32) †

Triglycerides (mmol/L, follow-up)	0.75 (0.36)	0.81 (0.35)	**0.78 (0.36)**
Clustered cardiometabolic risk score (baseline)	0.094 (0.604)	0.124 (0.645)	0.111 (0.627)
Clustered cardiometabolic risk score (follow-up)	**-0.032 (0.648)**	**0.016 (0.690)**	**-0.005 (0.671)**
Clustered cardiometabolic risk score with CRF (baseline)	0.089 (0.565)	0.123 (0.597)	0.108 (0.583)
Clustered cardiometabolic risk score with CRF (follow-up)	**-0.004 (0.637)**	**-0.008 (0.654)**	**-0.006 (0.646)**
	n (%)		
Body mass index (baseline)			
Normal	102 (65.8)	133 (66.8)	235 (66.4)
Overweight	34 (21.9)	42 (21.1)	76 (21.5)
Obesity	19 (12.3)	24 (12.1)	43 (12.1)
Body mass index (follow-up)			
Normal	102 (65.8)	134 (67.3)	236 (66.7)
Overweight	33 (21.3)	44 (22.1)	77 (21.7)
Obesity	20 (12.9)	21 (10.6)	41 (11.6)

Note: Data are expressed as mean and standard deviation (SD) for continuous variables or as absolute and relative frequency for categorical variables; † denotes difference between sexes calculated using the Student t-test (p<0.05); Bold denotes statistical differences between baseline and follow-up scores using the t-test for paired samples (p<0.05); CRF: Cardiorespiratory fitness; mL/kg/min: Milliliters per kilogram per minute; cm: centimeters; kg: Kilograms; m: Meters; Sum of 3 Skinfolds: Sum of calf, triceps, and subscapular skinfolds; mm: Millimeter; mmHg: Millimeters of mercury; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; TC/HDL-C: Total cholesterol/HDL-C ratio; mmol/L: Millimole per liter; Clustered cardiometabolic risk score: sum of glucose, systolic blood pressure, TC/HDL-C ratio, triglycerides, and waist circumference Z-scores divided by five; Clustered cardiometabolic risk score with CRF: sum of glucose, systolic blood pressure, TC/HDL-C ratio, triglycerides, waist circumference, and VO_{2peak} (inversed) Z-scores divided by six; VO_{2peak}: Peak oxygen uptake.

Table II presents the tracking coefficients of each risk factor and the clustered cardiometabolic risk scores (with and without CRF) for all participants included in the tracking analysis stratified by sex. Additionally, it presents the tracking coefficients stratified by sex and age groups. All coefficients showed a positive correlation between baseline and follow-up. Amongst boys, CRF, WC, BMI, and the sum of skinfolds showed high tracking coefficients, whereas, except for DBP, glucose, and TG, the other risk factors and the cluster cardiometabolic risk scores (with and without CRF) presented moderate tracking coefficients. Amongst girls, CRF, WC, BMI, and the sum of skinfolds also showed high tracking coefficients, whereas, except for glucose, the other risk factors and the cluster cardiometabolic risk scores (with and without CRF) presented moderate tracking coefficients. Also, Table II shows that the inclusion of CRF in the clustered cardiometabolic risk score strengthened the correlations independent of sex and age group at baseline.

Table II. Tracking coefficients of the clustered cardiometabolic risk score and the risk factors for all participants stratified by sex and by sex and age groups.

	All participants				Boys				Girls			
	Boys		Girls		7-9→10-12 y/a		10-12→13-15 y/a		7-9→10-12 y/a		10-12→13-15 y/a	
	n = 155		n = 199		n = 76		n = 79		n = 104		n = 95	
	r	p	r	p	r	p	r	p	r	p	r	p
CRF (mL/kg/min)	0.700	<0.001	0.742	<0.001	0.760	<0.001	0.636	<0.001	0.803	<0.001	0.691	<0.001
WC (cm)	0.866	<0.001	0.842	<0.001	0.834	<0.001	0.836	<0.001	0.893	<0.001	0.758	<0.001
BMI (kg/m^2)	0.832	<0.001	0.849	<0.001	0.822	<0.001	0.821	<0.001	0.876	<0.001	0.812	<0.001
S3SF (mm)	0.687	<0.001	0.662	<0.001	0.776	<0.001	0.593	<0.001	0.707	<0.001	0.618	<0.001
SBP (mmHg)	0.397	<0.001	0.464	<0.001	0.373	0.001	0.207	0.068	0.534	<0.001	0.339	0.001
DBP (mmHg)	0.275	0.001	0.396	<0.001	0.245	0.033	0.191	0.092	0.388	<0.001	0.295	0.004
TC (mmol/L)	0.473	<0.001	0.475	<0.001	0.321	0.005	0.633	<0.001	0.517	<0.001	0.426	<0.001
HDL-C (mmol/L)	0.387	<0.001	0.448	<0.001	0.299	0.009	0.478	<0.001	0.482	<0.001	0.408	<0.001
LDL-C (mmol/L)	0.567	<0.001	0.539	<0.001	0.484	<0.001	0.650	<0.001	0.562	<0.001	0.520	<0.001
Glucose (mmol/L)	0.257	0.001	0.129	0.069	0.443	<0.001	0.037	0.744	0.158	0.109	0.082	0.431
TC/HDL-C (mmol/L)	0.569	<0.001	0.571	<0.001	0.503	<0.001	0.647	<0.001	0.547	<0.001	0.589	<0.001
TG (mmol/L)	0.100	0.218	0.325	<0.001	0.073	0.531	0.146	0.201	0.273	0.005	0.372	<0.001
Clustered cardiometabolic risk score	0.516	<0.001	0.508	<0.001	0.493	<0.001	0.571	<0.001	0.491	<0.001	0.505	<0.001
Clustered cardiometabolic risk score (CRF)	0.592	<0.001	0.588	<0.001	0.618	<0.001	0.594	<0.001	0.573	<0.001	0.567	<0.001

Note: Spearman correlations between the variable at baseline and in the follow-up. y/a: years of age; r: Tracking coefficient; CRF: Cardiorespiratory fitness; WC: Waist circumference; BMI: Body mass index; S3SF: Sum of calf, triceps, and subscapular skinfolds; mm: Millimeter; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; TC: Total cholesterol; mmol/L: Millimole per liter; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TC/HDL-C: Total cholesterol/HDL-C ratio; TG: Triglycerides; Clustered cardiometabolic risk score: sum of SBP, WC, TG, glucose and TC/HDL-C ratio divided by five; Clustered cardiometabolic risk score (with CRF): sum of SBP, WC, TG, glucose, TC/HDL-C ratio and VO$_{2peak}$ (inversed) divided by six; VO$_{2peak}$: Peak oxygen uptake.

Figure 2 shows the prevalence classification at baseline and in the follow-up for all participants (Figure 2A for the clustered cardiometabolic risk score without CRF and Figure 2B for the clustered cardiometabolic risk score with CRF). Overall, 11.9% and 10.2% of the cohort was at a higher risk at baseline for the clustered cardiometabolic risk score without and with CRF, respectively. For those participants in the highest risk group at baseline, 47.2% (score with CRF) and 45.2% (score without CRF) continued in the highest risk group in the follow-up.

Table IIIA presents odds ratios and confidence intervals for the number of participants on a classification at baseline who continued at the same or changed to another classification in the follow-up, divided by the expected number of participants at this respective classification in the follow-up if risk factors changed randomly. For those who were at risk at baseline, the odds of staying at higher risk were 3.81 (CI: 2.40 to 6.05) and 4.64 (CI: 2.85 to 7.56) times more than expected for the classification without and with CRF, respectively.

Additional analyses estimated the odds of being in the higher clustered score in the follow-up according to the levels of adiposity and CRF at baseline to verify whether the higher classification maintenance was stronger (Table IIIB). It showed that those who were classified as overweight at baseline had 4.92 (CI: 2.18 to 11.07) and 5.46 (CI: 2.12 to 14.05) times higher chance of staying in the highest risk classification without and with CRF, respectively. For children who were obese at baseline, the odds of being classified in the higher clustered score was 4.60 (CI: 2.35 to 8.98) and 5.36 (CI: 2.68 to 10.73) not including and including CRF in the score, respectively. None of the participants classified as normal BMI at baseline had a higher clustered score in the follow-up. With respect to the participants with less favorable classification of the sum of skinfolds and WC at baseline, the odds of staying at higher risk in the follow-up for those with less favorable sum of skinfolds classification were 4.21 (CI: 2.29 to 7.56) and 4.21 (CI: 2.18 to 8.13) higher than expected for the clustered score without and

with CRF, respectively, whereas, the odds of staying at higher risk in the follow-up for those with less favorable WC classification were 4.10 (CI: 2.23 to 7.56) and 4.09 (2.12 to 7.89) higher than expected for the clustered score without and with CRF, respectively. Those with the lowest levels of CRF had 4.58 (CI: 2.46 to 8.40) and 5.22 (CI: 2.72 to 10.05) higher odds than expected of staying in the highest risk cluster for the clustered score without and with CRF, respectively. Lastly, it is also interesting to highlight that in the upper half of CRF (more favorable) none of the participants had a higher clustered score in the follow-up.

Table III. Odds ratio of the clustered cardiometabolic risk score classification (without and with CRF) from baseline to follow-up for all participants (Table IIIA), and for those who had a higher risk at baseline specifically according to their levels of adiposity and CRF at baseline (Table IIIB).

	Clustered cardiometabolic risk score classification				Clustered cardiometabolic risk score (with CRF) classification			
	Baseline	Follow-up			Baseline	Follow-up		
		Lower	Borderline	Higher		Lower	Borderline	Higher
	n (P; 95% CI)	OR_1 (95% CI)	OR_1 (95% CI)	OR_1 (95% CI)	n (P; 95% CI)	OR_1 (95% CI)	OR_1 (95% CI)	OR_1 (95% CI)
Table IIIA*								
All participants								
Lower	261 (0.74; 0.69 to 0.78)	1.14 (0.92 to 1.42)	0.80 (0.55 to 1.16)	0.36 (0.19 to 0.65)	261 (0.74; 0.69 to 0.78)	1.18 (0.95 to 1.47)	0.57 (0.38 to 0.86)	0.34 (0.17 to 0.66)
Borderline	51 (0.14; 0.11 to 0.19)	0.66 (0.44 to 0.99)	2.18 (1.32 to 3.60)	1.65 (0.88 to 3.10)	57 (0.16; 0.12 to 0.20)	0.67 (0.45 to 0.98)	1.85 (1.14 to 3.02)	2.07 (1.16 to 3.68)
Higher	42 (0.12; 0.09 to 0.16)	0.55 (0.34 to 0.89)	0.99 (0.44 to 2.22)	3.81 (2.40 to 6.05)	36 (0.10; 0.07 to 0.14)	0.41 (0.23 to 0.76)	1.38 (0.68 to 2.78)	4.64 (2.85 to 7.56)
Table IIIB**	n	OR_2 (95% CI)	OR_2 (95% CI)	OR_2 (95% CI)	n	OR_2 (95% CI)	OR_2 (95% CI)	OR_2 (95% CI)
Body mass index								
Normal	8	1.19 (0.53 to 2.67)	0.87 (0.12 to 6.31)	-	5	1.09 (0.38 to 3.07)	1.24 (0.17 to 9.07)	-
Overweight	12	0.45 (0.16 to 1.27)	0.58 (0.08 to 4.21)	4.92 (2.18 to 11.07)	9	0.45 (0.14 to 1.47)	0.69 (0.09 to 5.04)	5.46 (2.12 to 14.05)
Obese	22	0.37 (0.16 to 0.88)	1.26 (0.45 to 3.54)	4.60 (2.35 to 8.98)	22	0.25 (0.09 to 0.70)	1.69 (0.70 to 4.07)	5.36 (2.68 to 10.73)
Sum of three skinfolds								
Lower 50th Percentile	6	0.90 (0.32 to 2.53)	1.16 (0.16 to 8.41)	1.40 (0.19 to 10.21)	4	0.68 (0.16 to 2.82)	1.74 (0.24 to 12.67)	2.11 (0.29 to 15.38)
Higher 50th Percentile	36	0.49 (0.25 to 0.94)	0.96 (0.38 to 2.45)	4.21 (2.29 to 7.76)	32	0.38 (0.18 to 0.81)	1.52 (0.67 to 3.47)	4.21 (2.18 to 8.13)
Waist circumference								
Lower 50th percentile	5	1.09 (0.39 to 3.04)	-	1.69 (0.23 to 12.26)	3	0.90 (0.22 to 3.76)	-	2.81 (0.38 to 20.51)
Higher 50th percentile	37	0.48 (0.25 to 0.95)	1.13 (0.47 to 2.67)	4.10 (2.23 to 7.56)	33	0.37 (0.17 to 0.79)	1.68 (0.77 to 3.69)	4.09 (2.12 to 7.89)
Cardiorespiratory fitness								
Lower 50th percentile	35	0.39 (0.19 to 0.79)	1.19 (0.50 to 2.82)	4.58 (2.49 to 8.40)	32	0.30 (0.13 to 0.68)	1.55 (0.71 to 3.41)	5.22 (2.72 to 10.05)
Higher 50th percentile	7	1.36 (0.60 to 3.05)	-	-	4	1.36 (0.48 to 3.84)	-	-

Note: CRF: Cardiorespiratory fitness; P: The proportion of positive results for the participants classified on the respective clustered cardiometabolic risk score classification divided by all participants (354); 95% CI: 95% confidence interval; OR_1: Odds ratio of how many participants were at a lower, a borderline or a higher risk classification in the follow-up divided by the expected number of being at this classification in the follow-up if risk factors changed randomly; *Classification based on the cutoff points to define children and adolescents at cardiometabolic risk (score values < 0.4 = lower; score values from 0.4 to 0.85 = borderline; score values > 0.85 = higher), adapted from Andersen et al.[1]; **Analysis for only those who had a higher risk at baseline; OR_2: Odds ratio of how many participants were at a lower, a borderline or a higher risk classification in the follow-up divided by the expected number of children at a higher risk at baseline changing to a lower, a borderline or a higher risk classification in the follow-up if risk factors changed randomly.

Discussion

This study evaluated the tracking of cardiometabolic risk factors in Brazilian children and adolescents across a three-year time span. In summary, the CRF and anthropometric parameters presented high tracking, whereas the others cardiometabolic parameters exhibited low-to-moderate tracking. Regarding the clustered cardiometabolic score, the tracking was moderate. Importantly, participants in the higher clustered cardiometabolic score group at baseline presented 3.81 and 4.64 (not including and including CRF in the score) times higher chance of remaining in the higher risk of clustered cardiometabolic score group three years later. Moreover, participants in the worst profile regarding anthropometrics or CRF at baseline presented at least 4.00 times higher chance of being in the higher clustered cardiometabolic risk group three years later. Previous studies reported similar associations of CRF[22–25] and adiposity[22,26,27] with clustered cardiometabolic risk scores. Additionally, Bugge et al.[7] verified clustered cardiometabolic risk scores' tracking coefficients stratified by CRF (directly measured VO_{2peak}) and adiposity (sum of four skinfolds) tertiles at baseline. Their results demonstrated more stability of cardiometabolic health within the less favorable tertiles of CRF as compared with the most fit group. However, the same has not been found for analysis with adiposity tertiles; this does not mean that adiposity is not important for cardiometabolic health. Less favorable adiposity levels increase the risk of suffering from a cardiovascular event across the life[28]. Furthermore, weight excess tracks from childhood to adolescence[7] and from childhood to adulthood[29,30]. It is important to recognize that some risk factors like adiposity and CRF track differently from others.

Our findings clearly support the importance of CRF and adiposity on predicting later clustered cardiometabolic risk in children and adolescents. However, systematic reviews indicate that it remains unclear whether childhood CRF is an independent risk factor for

adulthood cardiometabolic risk, whereas, childhood obesity may be a great risk factor for adult cardiometabolic risk factors[31,32]. Mintjens et al.[32] demonstrated that higher CRF levels were associated with more favorable anthropometric measurements (BMI, percentage body fat, and WC) and with a lower metabolic syndrome prevalence later in life. However, the evidence regarding the association between CRF levels and blood pressure, lipid profile, and glucose homeostasis was inconclusive. Moreover, authors indicated that improvements on cardiometabolic health could be achieved by reducing adiposity.

On the other hand, there is also evidence indicating that improving CRF levels may be more important to overall health than adiposity levels, or at least as important as preventing excess weight[20,33,34]. Some findings demonstrate that CRF seems to attenuate the adverse consequences of adiposity excess to overall health[34]. DuBose et al.[35] examined the combined influence of CRF and BMI in the clustered cardiometabolic risk scores. Highly fit children had lower clustered scores amongst normal weight, at risk for overweight, and overweight children compared to unfit peers. Similar cross-sectional analysis demonstrated that CRF may confer a protective effect against the cardiometabolic risk factors associated with adiposity excess[36]. Interestingly, individuals classified as normal-weight and presenting lower CRF levels could be at a higher risk compared to those individuals classified as obese and presenting higher CRF levels[34].

Based on this knowledge, children and adolescents at risk of being in the less favorable clustered cardiometabolic profile should be the focus of early health interventions because of the higher risk for long-term cardiovascular disease morbidity and mortality[28,37]. A reasonable number of studies have implemented physical activity school-based interventions targeting adiposity and cardiometabolic parameters. However, most of these studies failed at improving adiposity and cardiometabolic parameters in children and adolescents[38]. The relatively high tracking of CRF and anthropometric measurements reported in our study and the absence of a

successful intervention implementation might partly explain this failed attempt in targeting adiposity and cardiometabolic parameters in youth. Nevertheless, there are successful interventions that effectively targeted adiposity and cardiometabolic parameters in youth. Kriemler et al.[39] reported decreased adiposity, clustered cardiometabolic risk score, triglycerides, HDL-C, and glucose levels and increased CRF by increasing the number of physical education lessons and improving the content of the lessons in schools in two provinces in Switzerland. Another intervention protocol that increased the number of physical education lessons for four and a half years observed 50% lower chance of children remaining overweight or obese[40].Thus, it is possible to positively affect adiposity and CRF via interventions, despite high tracking.

Our findings are particularly salient for children and adolescents who do not meet healthy levels for both risk factors, especially in Brazil, which has an estimation of only one-third of children and adolescents meeting health criteria for CRF[41], and a quarter presenting weight excess[42]. Fitness and fatness are biological traits strongly related to cardiometabolic health. One should consider both parameters when looking at cardiometabolic health. Therefore, reducing adiposity and increasing physical activity and exercise training, such that CRF levels are improved[33], may play a crucial role to improve children's and adolescents' cardiometabolic health[43].

Our study has some worthwhile strengths. First, the use of a randomly selected sample of children and adolescents from Southern Brazil was a strength. Secondly, the use of a standardized and internationally accepted method for defining children' and adolescents' cardiometabolic health is better than previous methods of creating scores relative to the study sample. Lastly, our study presents additional tracking coefficients within sex and age groups (7-9→10-12 and 10-12→13-15 years old), which is important to consider given known sex differences exist for several cardiometabolic risk variables. However, our study also has some

limitations. Firstly, caution should be exerted with interpretation of tracking coefficients because an extremely high tracking is both good and bad news. On one hand, participants with healthy measurements tend to keep their good levels, but on the other hand it also means that the few who are not healthy tend to stay within unhealthy risk groups. In other words, it may be very difficult to change risk factors with high tracking. Additionally, a tracking coefficient can never be better than the reproducibility of a measure. Secondly, the use of a field test with subsequent VO_{2peak} prediction instead of a maximum protocol as a measure of CRF was a limitation. Lastly, the use of fasting glucose measure as a marker of glycemic metabolism was not as accurate as use of fasting insulin or HOMA score, which can regulate glucose levels, even in children with severe insulin resistance[44].

Conclusions

High tracking coefficients were found for CRF and adiposity measurements (BMI, WC, and the sum of skinfolds) for both boys and girls, whereas, moderate tracking coefficients were found for the clustered cardiometabolic risk score across the three-year time span. Furthermore, participants classified with less favorable CRF and adiposity measurements at baseline had an increased risk of presenting clustered cardiometabolic risk after three years of follow-up. Based on these findings, CRF and adiposity measurements should be considered in future intervention studies targeting children's and adolescents' cardiometabolic health.

Authors' contribution: João Francisco de Castro Silveira, Cézane Priscila Reuter, Letícia Welser, Hildegard Hedwig Pohl, and Rodrigo Antunes Lima developed the idea and design of the work. João Francisco de Castro Silveira, Cézane Priscila Reuter, and Letícia Welser collected data. João Francisco de Castro Silveira, Cézane Priscila Reuter, Lars Bo Andersen, and Rodrigo Antunes Lima analyzed and interpreted data. Cézane Priscila Reuter, Karin Allor Pfeiffer, Lars Bo Andersen, and Rodrigo Antunes Lima were helpful with statistical guidance when needed. All authors have contributed to critical revisions, writing, and editing the manuscript. All authors read and approved the final version of the manuscript.

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