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Association of Cardiorespiratory Fitness Levels During Youth With Health Risk Later in Life
A Systematic Review and Meta-analysis

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IMPORTANCE Although the associations between cardiorespiratory fitness (CRF) and health in adults are well understood, to date, no systematic review has quantitatively examined the association between CRF during youth and health parameters later in life.

OBJECTIVES To examine the prospective association between CRF in childhood and adolescence and future health status and to assess whether changes in CRF are associated with future health status at least 1 year later.

DATA SOURCES For this systematic review and meta-analysis, MEDLINE, Embase, and SPORTDiscus electronic databases were searched for relevant articles published from database inception to January 30, 2020.

STUDY SELECTION The following inclusion criteria were used: CRF measured using a validated test and assessed at baseline and/or its change from baseline to the end of follow-up, healthy population with a mean age of 3 to 18 years at baseline, and prospective cohort design with a follow-up period of at least 1 year.

DATA EXTRACTION AND SYNTHESIS Data were processed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Random-effects models were used to estimate the pooled effect size.

MAIN OUTCOMES AND MEASURES Anthropometric and adiposity measurements and cardiometabolic health parameters.

RESULTS Fifty-five studies were included with a total of 37 563 youths (46% female). Weak-moderate associations were found between CRF at baseline and body mass index (r = −0.11; 95% CI, −0.18 to −0.04; I^2 = 59.03), waist circumference (r = −0.29; 95% CI, −0.42 to −0.14; I^2 = 69.42), skinfold thickness (r = −0.34; 95% CI, −0.41 to −0.26; I^2 = 83.87), obesity (r = −0.15; 95% CI, −0.23 to −0.06; I^2 = 86.75), total cholesterol level (r = −0.12; 95% CI, −0.19 to −0.05; I^2 = 75.81), high-density lipoprotein cholesterol (HDL-C) level (r = 0.11; 95% CI, 0.05-0.18; I^2 = 69.06), total cholesterol to HDL-C ratio (r = −0.19; 95% CI, −0.26 to −0.13; I^2 = 67.07), triglyceride levels (r = −0.10; 95% CI, −0.18 to −0.02; I^2 = 73.43), homeostasis model assessment for insulin resistance (r = −0.12; 95% CI, −0.18 to −0.06; I^2 = 68.26), fasting insulin level (r = −0.07; 95% CI, −0.11 to −0.03; I^2 = 0), and cardiometabolic risk (r = −0.18; 95% CI, −0.29 to −0.07; I^2 = 90.61) at follow-up. Meta-regression analyses found that early associations in waist circumference (β = 0.014; 95% CI, 0.002-0.026), skinfold thickness (β = 0.006; 95% CI, 0.002-0.011), HDL-C level (β = −0.006; 95% CI, −0.011 to −0.001), triglyceride levels (β = 0.009; 95% CI, 0.004-0.014), and cardiometabolic risk (β = 0.007; 95% CI, 0.003-0.011) from baseline to follow-up dissipated over time. Weak-moderate associations were found between change in CRF and body mass index (r = −0.17; 95% CI, −0.24 to −0.11; I^2 = 39.65), skinfold thickness (r = −0.36; 95% CI, −0.58 to −0.09; I^2 = 96.84), obesity (r = −0.21; 95% CI, −0.35 to −0.06; I^2 = 91.08), HDL-C level (r = 0.05; 95% CI, 0.02-0.08; I^2 = 0), low-density lipoprotein cholesterol level (r = −0.06; 95% CI, −0.11 to −0.01; I^2 = 58.94), and cardiometabolic risk (r = −0.08; 95% CI, −0.15 to −0.02; I^2 = 69.53) later in life.

CONCLUSIONS AND RELEVANCE This study suggests that early intervention and prevention strategies that target youth CRF may be associated with maintaining health parameters in later life.

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Supplemental content

CME Quiz at jamacmelookup.com and CME Questions page 1011

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Cardiorespiratory fitness (CRF) reflects the integrated ability to transport oxygen from the atmosphere to the mitochondria to perform physical work and thus reflects the overall capacity of the cardiovascular and respiratory systems and the ability to perform prolonged exercise.[1] An increasing body of epidemiological and clinical evidence demonstrates that low levels of CRF are associated with a high risk of cardiovascular disease, all-cause mortality, and various cancers.[2]

Although the associations between CRF and health in adults are well understood,[1] few studies have examined how CRF affects health during youth. Overall, higher CRF during youth is associated with a healthier cardiometabolic profile at this time.[3] However, some studies[4,5] have found limited associations between CRF and health parameters later in life. The recent systematic review by Mintjens et al[4] reported that there was no convincing evidence of an association of a high level of CRF in childhood and adolescence with better blood pressure, lipid profile, or glucose homeostasis in adulthood. Furthermore, Hamer et al[5] suggest that associations between estimated CRF and risk factors are stronger in adulthood than from childhood to adulthood. Therefore, whether physical fitness accrued through adulthood can counteract poor fitness during youth should be examined.

Several reviews on the benefits associated with CRF in youths have been published,[4,6] but to our knowledge, no previous systematic review and meta-analysis has assessed the association between CRF during childhood and adolescence and health parameters later in life. Therefore, our aim was to perform a systematic review and meta-analysis on the prospective association between CRF in childhood and adolescence and future health status and to examine whether changes in CRF are associated with future health status at least 1 year later.

Key Points

Question Is cardiorespiratory fitness associated with future health benefits in children and adolescents?

Findings This systematic review and meta-analysis of 55 studies that included 37 563 youths revealed that cardiorespiratory fitness levels and change over approximately 1 year during youth were associated with lower risk of developing obesity and cardiometabolic disease later in life. These early associations detected from baseline to follow-up dissipated over time.

Meaning The study suggests that prevention strategies that target youth cardiorespiratory fitness may be associated with improved health parameters in later life.

Methods

The methods applied in this systematic review and meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guideline, and the study was registered in the PROSPERO database (CRD42020166432). The study also followed the Meta-analysis of Observational Studies in Epidemiology (MOOSE) reporting guideline. The entire process from literature selection to data extraction was performed independently by 2 of us (A.G.-H. and R.R.-V.). Any disagreements were resolved through consultation with 1 of us (M.I.).

Search Strategy and Selection Criteria

The MEDLINE, Embase, and SPORTDiscus electronic databases were searched for articles published from database inception to January 30, 2020 (eMethods in the Supplement). To be eligible for inclusion in the meta-analysis, studies needed to meet the following criteria: (1) CRF measured using a validated test (ie, field or laboratory tests) and assessed at baseline and/or its change from baseline to the last point of follow-up, (2) generally healthy population with a mean age of 3 to 18 years at baseline, and (3) prospective cohort design with a follow-up period of at least 1 year. Articles not published in the English language were excluded.

Data Collection Process

Two of us (A.G.-H. and R.R.-V.) independently extracted the following data from the identified studies: study characteristics (first author, sample size, sex and age of participants, country, duration of follow-up, and publication year), exposure details (method of CRF assessment), and analysis and results (adjusted variables, outcome of interest, and main results). The end points included were classified as anthropometric and adiposity parameters (body mass index [BMI; calculated as weight in kilograms divided by height in meters squared], waist circumference [WC], skinfold thickness, and body fat percentage) and cardiometabolic parameters (total cholesterol level, high-density lipoprotein cholesterol [HDL-C] level, total cholesterol to HDL-C ratio, low-density lipoprotein cholesterol [LDL-C] level, triglyceride [TG] levels, fasting glucose level, fasting insulin level, homeostatic model assessment for insulin resistance [HOMA-IR], blood pressure [systolic and diastolic], and cardiometabolic risk or metabolic syndrome) (**Table 1**). We also assessed the risk of bias of studies according to the Newcastle-Ottawa Scale, assigning up to 9 points for selection, comparability and exposure.[7]

Statistical Analysis

A meta-analysis was performed when at least 3 studies provided data for a given health parameter.[8] The effect sizes reported by studies were given as standardized and unstandardized regression coefficients (β) and odds ratios (ORs). All these estimates were converted to correlations coefficients (r) according to their corresponding formulas.[9-11] All analyses were conducted using random-effects models[12] and performed using Comprehensive Meta-analysis, version 2.2 (Biostat). According to McGrath and Meyer classification,[13] r values of 0.10 or less are considered weak effects, r values of 0.10 to 0.36 are considered moderate effects, and r values of 0.37 are considered large effects. A 2-sided $P < .05$ was considered to be statistically significant.

For each meta-analysis, heterogeneity across studies was calculated using the total variance, the degrees of freedom, and the inconsistency index (I^2),[14] considering I^2 values less than

Table 1. Associations Between Cardiorespiratory Fitness at Baseline and Anthropometric, Adiposity, and Cardiometabolic Parameters at Follow-up

Parameter	No. of studies (No. of patients)	*r* (95% CI)	*P* value	I^2	Egger test *P* value
Anthropometric and adiposity parameters					
Body mass index					
Overall	7 (2747)	−0.11 (−0.18 to −0.04)	.002	59.03	.60
Field tests	5 (1983)	−0.10 (−0.18 to −0.01)	.02	66.06	.91
Waist circumference	4 (653)	−0.29 (−0.42 to −0.14)	<.001	69.42	.12
Skinfolds thickness					
Overall	11 (4190)	−0.34 (−0.41 to −0.26)	<.001	83.87	.07
Male	5 (744)	−0.41 (−0.51 to −0.31)	<.001	69.77	.93
Female	5 (771)	−0.39 (−0.45 to −0.32)	<.001	31.55	.59
Field tests	5 (1866)	−0.37 (−0.48 to −0.25)	<.001	89.57	.12
Laboratory tests	7 (2324)	−0.30 (−0.37 to −0.22)	<.001	60.11	.06
Body fat percentage					
Overall	4 (518)	−0.13 (−0.26 to 0.02)	.08	63.01	.61
Laboratory tests	3 (376)	−0.07 (−0.20 to 0.06)	.31	42.38	.10
Obesity					
Overall	8 (13 289)	−0.15 (−0.23 to −0.06)	.001	86.75	.053
Male	3 (5486)	−0.05 (−0.26 to 0.17)	.66	92.12	.56
Female	3 (5870)	−0.10 (−0.22 to 0.02)	.10	57.77	.01
Field tests	6 (12 235)	−0.15 (−0.27 to −0.03)	.01	86.83	.02
Cardiometabolic parameters					
Total cholesterol level					
Overall	7 (3823)	−0.12 (−0.19 to −0.05)	.001	75.81	.11
Laboratory tests	5 (3211)	−0.20 (−0.32 to −0.08)	.001	84.82	.04
HDL-C level					
Overall	8 (3923)	0.11 (0.05 to 0.18)	.001	69.06	.78
Male	4 (610)	0.16 (0.07 to 0.25)	.001	44.74	.56
Female	4 (646)	0.15 (0.01 to 0.27)	.03	73.91	.83
Laboratory tests	6 (2445)	0.07 (−0.03 to 0.16)	.19	67.06	.95
Total cholesterol to HDL-C ratio					
Overall	8 (2616)	−0.19 (−0.26 to −0.13)	<.001	67.07	.15
Male	3 (464)	−0.27 (−0.37 to −0.15)	<.001	59.80	.07
Field tests	4 (2046)	−0.19 (−0.27 to −0.10)	<.001	74.10	.03
Laboratory tests	4 (570)	−0.21 (−0.32 to −0.10)	<.001	36.41	.53
LDL-C level	3 (1670)	−0.08 (−0.16 to 0.01)	.06	55.90	.11
Triglyceride levels					
Overall	8 (3210)	−0.10 (−0.18 to −0.02)	.02	73.43	.28
Male	4 (553)	−0.15 (−0.32 to 0.02)	.08	75.35	.81
Female	3 (452)	−0.20 (−0.28 to −0.10)	<.001	0	.04
Field tests	3 (1047)	−0.15 (−0.25 to −0.06)	.002	59.92	.001
Laboratory tests	5 (2163)	−0.04 (−0.17 to 0.09)	.50	77.10	.86
Fasting glucose level					
Overall	4 (2178)	−0.02 (−0.07 to 0.02)	.27	0	.20
Laboratory tests	3 (1414)	−0.02 (−0.07 to 0.04)	.56	0	.32
Fasting insulin level	3 (2130)	−0.07 (−0.11 to −0.03)	.001	0	.98
HOMA-IR					
Overall	9 (4188)	−0.12 (−0.18 to −0.06)	<.001	68.26	.15
Field tests	5 (2045)	−0.08 (−0.14 to -0.04)	<.001	29.90	.67
Laboratory tests	4 (2143)	−0.18 (−0.29 to −0.05)	.005	85.10	.06

(continued)

Table 1. Associations Between Cardiorespiratory Fitness at Baseline and Anthropometric, Adiposity, and Cardiometabolic Parameters at Follow-up (continued)

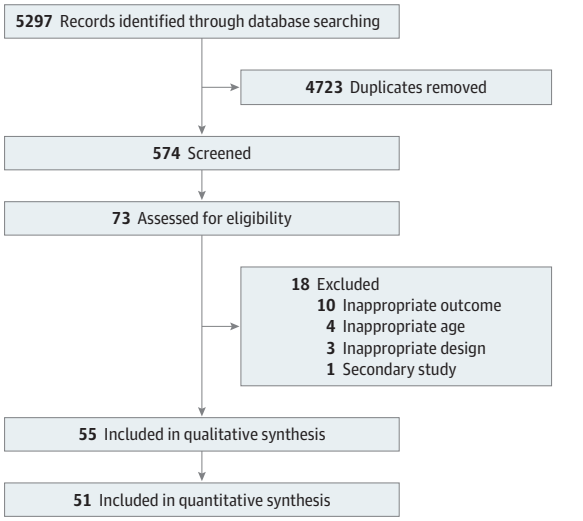
Parameter	No. of studies (No. of patients)	r (95% CI)	P value	I^2	Egger test P value
Systolic blood pressure					
Overall	12 (5843)	−0.02 (−0.08 to 0.04)	.44	75.10	.28
Male	3 (432)	0.04 (−0.04 to 0.11)	.31	0	.86
Female	3 (443)	−0.02 (−0.10 to 0.05)	.54	0	.10
Field tests	4 (2109)	−0.02 (−0.13 to 0.08)	.64	80.31	.04
Laboratory tests	8 (3734)	−0.02 (−0.10 to 0.06)	.66	74.63	.73
Diastolic blood pressure					
Overall	10 (5231)	−0.05 (−0.10 to 0.01)	.07	63.91	.63
Field tests	3 (1346)	−0.05 (−0.16 to 0.06)	.38	82.13	.052
Laboratory tests	7 (3895)	−0.03 (−0.07 to 0.01)	.08	0	.42
Cardiometabolic risk or metabolic syndrome					
Overall	8 (4495)	−0.18 (−0.29 to −0.07)	.001	90.61	.41
Field tests	3 (2370)	−0.25 (−0.45 to −0.03)	.02	93.75	.44
Laboratory tests	5 (2125)	−0.14 (−0.28 to 0.02)	.08	89.52	.92

Abbreviations: HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment for insulin resistance; LDL-C, low-density lipoprotein cholesterol.

25% as low heterogeneity, 25% to 75% as moderate heterogeneity, and greater than 75% as high heterogeneity.[15] Sensitivity analysis was performed to determine whether any single study with extreme findings had an undue influence on the overall results. The presence of potential small-study effects was conducted using the Egger regression test.[16]

We identified potential moderator variables a priori. The variables were sex and CRF test used (laboratory or field test), and meta-analyses were stratified by each of these factors. Random-effects meta-regression analyses were conducted to examine whether length of follow-up (in years) was a factor in these associations.

Figure. PRISMA Flow Diagram



Results

Study Selection and Characteristics

In total, 55 studies[17-71] met the inclusion criteria and were included in the systematic review. The flow diagram is shown in the **Figure**. Details of the study end points are given in eTable 1 in the Supplement. The final analysis included a total of 37 563 youths (46% female). All studies included male and female participants with the exception of 2 studies that included only female participants[19,61] and 2 that included only male participants.[42,49] Sample sizes across studies ranged from 48[24] to 6297.[39] The length of follow-up ranged from 1 year[34,39,47,53,55] to 27 years[65] (mean [SD], 8.6 [7.5] years).

CRF Measurement

Cardiorespiratory fitness was most often assessed with laboratory tests (eg, maximal or submaximal test on a cycloergometer or treadmill with spirometry to determine oxygen consumption and the physical work capacity at a heart rate of 170/min cycle test) or field tests (eg, 20-m shuttle run test,[17,18,20,22,34,39,46,47,53-56,59,60,62,67-69] 1.6-km run,[29,57,58] 9- or 12-minute run/walk test,[19,30,51,64] 2000-m run test,[49] and Andersen test[40]) (eTable 1 in the Supplement). Most studies expressed oxygen consumption as a function of body mass, with the exception of 3 studies[33,42,48] that included oxygen consumption as a function of fat-free mass and 2 as absolute terms.[61,63] The quality of included studies per the Newcastle-Ottawa Scale ranged from 4 to 8 (eTable 2 in the Supplement).

Meta-analysis

There was a weak-moderate association between CRF at baseline and BMI (r = -0.11; 95% CI, -0.18 to -0.04; I^2 = 59.03), WC (r = -0.29; 95% CI, -0.42 to -0.14; I^2 = 69.42), and skinfold thickness (r = -0.34; 95% CI, -0.41 to -0.26; I^2 = 83.87). Cardiorespiratory fitness was also associated with a lower risk of being overweight or obese at follow-up (r = -0.15; 95% CI, -0.23 to -0.06; I^2 = 86.75).

Table 2. Associations Between Change in Cardiorespiratory Fitness and Anthropometric, Adiposity, and Cardiometabolic Parameters

Parameter	No. of studies (No. of patients)	*r* (95% CI)	*P* value	I^2	Egger test *P* value
Anthropometric and adiposity parameters					
Body mass index	4 (1902)	−0.17 (−0.24 to −0.11)	<.001	39.65	.28
Skinfolds thickness					
Overall	6 (1641)	−0.36 (−0.58 to −0.09)	.01	96.84	.48
Male	4 (484)	−0.36 (−0.72 to 0.17)	.18	96.92	.60
Female	4 (1157)	−0.45 (−0.79 to 0.10)	.11	97.96	.91
Field tests	3 (1260)	−0.48 (−0.76 to −0.03)	.04	98.58	.22
Laboratory tests	3 (381)	−0.23 (−0.33 to −0.13)	<.001	0	.63
Obesity					
Overall	5 (4805)	−0.21 (−0.35 to −0.06)	.006	91.08	.055
Field tests	4 (4047)	−0.25 (−0.38 to −0.12)	<.001	76.56	.72
Cardiometabolic parameters					
Total cholesterol level					
Overall	6 (5431)	−0.07 (−0.14 to 0.01)	.052	77.74	.39
Laboratory tests	4 (1457)	−0.18 (−0.33 to −0.02)	.02	78.36	.21
HDL-C level					
Overall	5 (4355)	0.05 (0.02 to 0.08)	.001	0	.58
Laboratory tests	3 (381)	0.01 (−0.09 to 0.11)	.81	0	.20
Total cholesterol to HDL-C ratio	3 (632)	−0.01 (−0.18 to 0.17)	.97	79.21	.58
LDL-C level	3 (4716)	−0.06 (−0.11 to −0.01)	.01	58.94	.10
Fasting glucose level	3 (4639)	−0.02 (−0.05 to 0.01)	.08	0	.02
Systolic blood pressure					
Overall	6 (4480)	0.03 (−0.04 to 0.09)	.40	63.26	.05
Laboratory tests	4 (391)	0.11 (−0.01 to 0.08)	.11	3.57	.97
Diastolic blood pressure					
Overall	6 (4480)	−0.03 (−0.10 to 0.04)	.41	67.38	.75
Laboratory tests	4 (391)	−0.05 (−0.14 to 0.04)	.28	7.66	.69
Cardiometabolic risk or metabolic syndrome					
Overall	6 (5337)	−0.08 (−0.15 to −0.02)	.009	69.53	.55
Laboratory tests	4 (1457)	−0.09 (−0.14 to −0.04)	<.001	62.28	.81

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

With regard to cardiometabolic parameters, total cholesterol level (*r* = -0.12; 95% CI, -0.19 to -0.05; I^2 = 75.81), total cholesterol to HDL-C ratio (*r* = -0.19; 95% CI, -0.26 to -0.13; I^2 = 67.07), TG levels (*r* = -0.10; 95% CI, -0.18 to -0.02; I^2 = 73.43), HOMA-IR (*r* = -0.12; 95% CI, -0.18 to -0.06; I^2 = 68.26), fasting insulin level (*r* = -0.07; 95% CI, -0.11 to -0.03; I^2 = 0), cardiometabolic risk (*r* = -0.18; 95% CI, -0.29 to -0.07; I^2 = 90.61), and HDL-C level (*r* = 0.11; 95% CI, 0.05-0.18; I^2 = 69.06) at follow-up had weak-moderate relationships with CRF at baseline.

The overall results remained significant independently of sex and type of test used (field or laboratory). However, the effect sizes were higher when analyzing laboratory tests for total cholesterol level (*r* = -0.20; 95% CI, -0.32 to -0.08; I^2 = 84.82), total cholesterol to HDL-C ratio (*r* = -0.21; 95% CI, -0.32 to -0.10; I^2 = 36.41), and HOMA-IR (*r* = -0.18; 95% CI, -0.29 to -0.05; I^2 = 85.10) (Table 1 and eFigures 1-17 in the Supplement).

The random-effects meta-regression model showed that the above-mentioned associations of WC (β = 0.014; 95% CI, 0.002-0.026), skinfold thickness (β = 0.006; 95% CI, 0.002-0.011), HDL-C level (β = −0.006; 95% CI, −0.011 to −0.001), LDL-C level (β = 0.008; 95% CI, 0.002-0.015), TG levels (β = 0.009; 95% CI, 0.004-0.014), and cardiometabolic risk (β = 0.007; 95% CI, 0.003-0.011) were associated with the length of follow-up (eTable 3 in the Supplement).

There was an association between change in CRF and BMI (*r* = -0.17; 95% CI, -0.24 to -0.11; I^2 = 39.65), skinfold thickness (*r* = -0.36; 95% CI, -0.58 to -0.09; I^2 = 96.84), obesity (*r* = -0.21; 95% CI, -0.35 to -0.06; I^2 = 91.08), HDL-C level (*r* = 0.05; 95% CI, 0.02 to 0.08; I^2 = 0), LDL-C level (*r* = -0.06; 95% CI, -0.11 to -0.01; I^2 = 58.94), and cardiometabolic risk (*r* = -0.08; 95% CI, -0.15 to -0.02; I^2 = 69.53) (**Table 2** and eFigures 18-28 in the Supplement).

The Egger linear regression tests indicated no study bias among evaluated parameters. Sensitivity analysis confirmed

that associations remained significant when each of the studies was excluded.

Discussion

This systematic review and meta-analysis supports an inverse prospective association between CRF at baseline and anthropometric, serum lipid, insulin sensitivity, and cardiometabolic risk parameters later in life. However, these early associations detected from baseline to follow-up dissipated over time. In addition, change in CRF was associated with anthropometric, serum lipid, and cardiometabolic risk parameters at follow-up. These data suggest that prevention strategies that target youth physical fitness[8] may be associated with improved health parameters in later life. However, because each unit of CRF is not equally valuable, future research should focus on determining the minimum level of CRF during childhood and adolescence that is associated with a healthy long-term profile.

Anthropometric and Body Composition Variables

This study found inverse moderate associations between CRF and BMI, WC, and skinfold thickness later in life, with a stronger association with laboratory test results. The present findings support results of a previous systematic review[4] that suggested that higher CRF in childhood and adolescence is associated with lower BMI and body fat at least 2 years later. Gutin[72] proposed a possible mechanism for the association between the development of CRF and the individual trajectories of adiposity growth; he suggested that vigorous exercise during the growing years, the type of physical activity that is associated with CRF improvement,[73] may promote the differentiation of stem cells into bone and muscle rather than into fat cells.

The present study revealed that change in CRF negatively correlated with BMI, skinfold thickness, and obesity later in life. The results remained significant when analyzing field tests only, which showed lower heterogeneity. These associations suggest that youths whose CRF increased during the years of the study ended the study with more favorable adiposity levels. Change in fitness in an individual is correlated with a change in daily energy expenditure and physical activity undertaken during leisure time,[74] which seems to have a positive association with weight status over time. For example, Johnson et al[37] reported that even after accounting for baseline adiposity, increasing CRF by only 8% would be associated with a reduced rate of increasing adiposity and a decrease of 1.3% body fat during a 3- to 5-year study period. Similarly, Hruby et al[66] investigated the association of 1 to 4 years of changes in CRF with the maintenance or achievement of healthy weight among 2793 youths and concluded that positive changes in CRF would be associated with an increased likelihood of developing or maintaining a healthy weight.

Therefore, the present data may be important for obesity prevention because they suggest that being physically fit and/or improving fitness levels may be associated with healthy weight maintenance. Nevertheless, because obesity is a multifaceted disorder with complex interactions over time, these findings should be interpreted with caution.

Cardiometabolic Parameters

We found that CRF during youth was modestly but beneficially associated with serum lipid levels, insulin sensitivity, and cardiometabolic risk at least 1 year later, with lower heterogeneity between results from only laboratory tests. This finding suggests that CRF during youth may be associated with cardiometabolic health status later in life and is in line with the cross-sectional association between fitness and cardiometabolic health status in childhood and adolescence.[3] In accordance with the present analysis, previous prospective studies from a large cohort of Swedish men examined at 18 years of age suggested that low CRF, estimated by a maximal cycling test, was associated with an increased risk of type 2 diabetes,[75] myocardial infarction,[76] and early death[77] later in life. The pathways through which youth CRF may be associated with adult cardiometabolic risk factors have been addressed previously.[78] A possible explanation for these findings is that the CRF of youths continues later in life,[79] and it is well known that the CRF levels in adults are associated with their cardiometabolic health.[1] However, meta-regression findings in this study indicate that early associations in HDL-C level, TG levels, and cardiometabolic risk from baseline to follow-up dissipated over time.

This study found that correlation coefficients narrowed as follow-up time increased. These results are in agreement with those reported by Hamer et al,[5] who suggested that associations between estimated CRF (based on an established algorithm comprising sex, age, BMI, resting heart rate, and self-reported physical activity at 10 years of age) and cardiometabolic risk factors are stronger in adulthood than from childhood to adulthood.

As with anthropometric parameters, CRF change was associated with serum lipid levels and cardiometabolic risk parameters at follow-up. Recently, Mäestu et al[45] suggested that increasing CRF from adolescence to adulthood is associated with reduced risk of metabolic syndrome later in adulthood. Similarly, Hasselstrøm et al[32] found that change in CRF was associated with the absolute levels of cardiometabolic risk factors in young adulthood, especially in men. Therefore, our findings suggest that it is important to improve CRF throughout life because it is associated with reduced cardiometabolic risk. As suggested previously,[80] improvements in CRF are associated with increases in use of muscle glycogen, improvements in the body's ability to oxidize intramuscular fatty acids, and decreases in blood insulin concentration (an important inhibiting factor to lipid mobilization).

Nevertheless, some studies[31,40] report that CRF is not independently associated with cardiometabolic risk factors after adjustment for adiposity because body fat is known to be associated with CRF.[1] According to Jago et al,[69] the association with CRF was negligible once change in body mass was considered; therefore, increasing youths' CRF level may attenuate, but not eliminate, the adverse risk of adiposity.[40] By contrast, Mäestu et al[45] reported that for some factors, the cor-

relation with CRF was lost after adjusting for body fat (glucose level, LDL-C level, total cholesterol level, and systolic blood pressure), whereas for others, the correlation was stronger (insulin level, HOMA-IR, HDL-C level, and diastolic blood pressure). Dissonance between findings could be attributable to (1) heterogeneity in CRF and body composition assessments used by studies; (2) a combination of genetic aspects, physical activity, and functional health of several organ systems[81]; (3) interindividual, environment-controlled variability in the response to CRF[82]; and (4) factors such as diet, inflammation, oxidative stress, immune dysfunction, and genetic parameters that may be underlying causes of cardiometabolic risk. [83]

Strengths and Limitations

To our knowledge, this was the first systematic review and meta-analysis to provide a quantitative and comprehensive evaluation of the range of future health parameters associated with CRF during youth and its change.

There are some limitations in this study that should be considered. First, most studies that directly determined oxygen consumption only reported this measure in the ratio to body mass and not fat-free mass, which has the greatest morphologic influence on oxygen consumption. [84] In this regard, 3 studies[33,42,48] expressed oxygen consumption in terms of fat-free mass, showing a negative association with insulin secretion,[33] but results were inconsistent regarding metabolic syndrome.[42,48] In addition, CRF should be reported in absolute (only 2 studies[61,63] gave the association of peak oxygen consumption expressed in absolute values with health parameters, with inconsistent results) and relative values, which would aid comparisons of the studies. Second, only a few studies adjusted the outcome variable of interest for baseline values of adiposity, age, and maturation,[84] a key issue for the interpretation of the temporal sequence and thus causality. Fourth, the included studies were diverse with respect to methods, measurement of CRF, outcomes, length of follow-up, race/ethnicity, and potential confounders, which might explain the heterogeneity in results.

Conclusions

These findings suggest that CRF levels during youth and their improvement may be associated with a lower risk of developing obesity and cardiometabolic disease later in life. However, early associations from baseline to follow-up dissipated over time. Therefore, because the origins of cardiometabolic disease begin early in childhood and cardiometabolic disease risk factors continued from early childhood to adulthood,[85] the results suggest that early intervention and supporting prevention strategies (eg, at school[86]) that promote CRF may help children maintain or achieve a healthy status and thus help circumvent many future health problems.

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