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Associations between cardiorespiratory fitness, physical activity, and clustered cardiometabolic risk in children and adolescents: the HAPPY study.

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Abstract

Clustering of cardiometabolic risk factors can occur during childhood and predisposes individuals to cardiometabolic disease. This study calculated clustered cardiometabolic risk in 100 children and adolescents aged 10-14 years (59 girls) and explored differences according to cardiorespiratory fitness (CRF) levels and time spent at different physical activity (PA) intensities. CRF was determined using a maximal cycle ergometer test and PA was assessed using accelerometry. A cardiometabolic risk score was computed as the sum of the standardised scores for waist circumference, blood pressure, total cholesterol:HDL ratio, triglycerides, and glucose. Differences in clustered cardiometabolic risk between fit and unfit participants, according to previously proposed health-related threshold values, and between tertiles for PA subcomponents, were assessed using ANCOVA. Clustered risk was significantly lower ($p < 0.001$) in the fit group (mean 1.21 ± 3.42) compared to the unfit group (mean -0.74 ± 2.22), while no differences existed between tertiles for any subcomponent of PA. *Conclusion* These findings suggest that CRF may have an important cardioprotective role in children and adolescents, and highlights the importance of promoting CRF in youth.

Keywords

Cardiometabolic risk; metabolic syndrome; cardiorespiratory fitness; physical activity; children; adolescents

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Introduction

The metabolic syndrome is a clustering of risk factors for cardiovascular disease (CVD) and type 2 diabetes (T2DM) [48]. The International Diabetes Federation (IDF) defines the metabolic syndrome as the presence of abdominal obesity plus at least two of the following risk factors: high triglycerides, low HDL, raised blood pressure, and impaired fasting glucose [48]. Although each of these is an independent risk factor for CVD and T2DM in adults [21], clustering of these risk factors may confer additive risk beyond the level predicted by individual components [20]. Clustering of these cardiometabolic risk factors can occur in childhood and adolescence [12] and evidence suggests that clustering can persist into adulthood [11]. Identifying clustered cardiometabolic risk and exploring its correlates in childhood is important given evidence that atherosclerotic processes manifest during childhood [32] and that increased risk factor clustering is associated with the severity of these processes [5].

Increased levels of cardiorespiratory fitness (CRF) and physical activity (PA) have been consistently associated with lower risk of CVD outcomes in adults [6] and these associations may also be evident in children. Indeed, higher levels of CRF have been negatively associated with single cardiometabolic risk factors in youths [15,41,10], although inconsistencies in the evidence exist [43]. The potential importance of CRF in youths is further highlighted by evidence that high CRF during childhood is associated with a healthier cardiovascular profile in adult years [47] and that CRF tracks from childhood into adulthood [46]. In this context, it is of concern that recent evidence suggests CRF levels are declining in youths [7]. Ruiz et al. [41] recently proposed that CRF (VO_{2max}) levels > 37.0 and 42.1 mL/kg/min in 9-10 year-old girls and boys, respectively, identified those with low metabolic risk when determined using a maximal cycle ergometer test. Since these findings were published, no subsequent study has investigated whether these levels are appropriate for use in older youths or those in other European countries.

Current UK PA guidelines suggest that children and adolescents should engage in at least 60 minutes of moderate-to-vigorous PA (MVPA) daily and at least three days per week should include vigorous PA (VPA) [14]. It is also suggested that the amount of time spent in sedentary behaviours should be reduced [14]. Although some data has linked engagement in moderate PA (MPA) and MVPA with individual cardiometabolic risk factors in youths [33,15], numerous investigations have found no such associations [16,42,29]. Recent studies have suggested that youths engaging in larger amounts of VPA are more likely to benefit from improved body composition [23,36]. However, little evidence is yet available concerning other cardiometabolic risk

factors such as lipid profile and blood pressure. Additionally, few data have explored the association between objectively determined PA subcomponents and the clustering of cardiometabolic risk factors.

To date, relatively little is known about the relationship of CRF and PA subcomponents with cardiometabolic risk in children and adolescents, while evidence-based health criteria thresholds for CRF are also lacking in this population. The objectives of this study were therefore to calculate clustered cardiometabolic risk and explore associations with objectively determined CRF and subcomponents of PA.

Methods

Sample

The 100 participants (59 girls) included were part of the HAPPY (Health And Physical activity Promotion in Youth) study. This school-based study explored the effects of three interventions on PA levels and health outcomes in 249 children and adolescents (10-14 years). Participants were recruited on a voluntary basis in 11 schools across Bedfordshire, UK and baseline data from 40% of the total sample was used for analyses in the present study. Participants were excluded if they had any contraindications to taking part in physical exercise. The study was approved by the University of Bedfordshire ethics review board. Written informed consent was obtained from participants' parents and verbal assent from the participants before any testing procedures. Parents were provided with their child's physiological results at the end of the HAPPY study.

Measurements

Age, ethnicity, and socioeconomic status

Age was recorded as a decimal value for each participant using date of birth. Ethnicity was recorded as white or non-white. A score for socioeconomic status (SES) was attributed to each participant using home postcode and the 2007 Indices of Multiple Deprivation (IMD) [17,1]. Postcodes were converted into IMD scores using the GeoConvert application [1]. These scores were categorised into tertiles with the lowest tertile indicating the most deprived.

Anthropometry

Stature and waist circumference (at the umbilicus) were recorded to the nearest 0.5 cm using the portable Leicester Height Measure (Seca, Birmingham) and an adjustable tape measure (Hoechstmass, Germany), respectively. Body mass was recorded to the nearest 0.1 kg using the Tanita BC-418® (Tanita Corp., Tokyo).

Body mass index (BMI) was calculated using the equation: BMI = body mass (kg) ÷ stature^2 (m^2). UK 1990 reference values were used to calculate *z*-scores for height, weight, and BMI [18,13]. Body fat % was measured to the nearest 0.1% via bioelectrical impedance analysis (BIA) using the Tanita BC-418® (Tanita Corp., Tokyo). Participants were required to have fasted from 9 pm the night before the measurement was taken between 8-10 am and were instructed to bring a snack with them to eat for breakfast after testing.

Cardiometabolic risk factors

Sitting blood pressure (BP) was measured (Omron M5-I automated oscillatory device, Omron Matsusaka Co. Ltd., Matsusaka, Japan) after the participant had rested for 5 min. Three BP readings were obtained, and the average for the lowest two readings recorded. Fasting blood samples were obtained using a finger prick method and were transferred into a cassette sample well and placed in the drawer of a Cholestech LDX analyser (Cholestech Corp., Hayward, CA.) to provide a valid measure of total cholesterol (TC), HDL, triglycerides, and blood glucose levels (r = 0.77-0.91 with core laboratory values) [35,44].

Cardiorespiratory fitness

To determine CRF, participants completed an age- and sex-specific all-out progressive cycle ergometer test to exhaustion using a previously validated protocol [37]. Workloads increased every 3 min until the participant was no longer able to continue. A maximal effort was deemed as a final heart rate ≥ 185 beats per min (bpm) and subjective observation from the researcher that the child could not continue. Power output (watts) was calculated as being equal to $W_1 + (W_2 \cdot t/180)$, where W_1 is work rate at fully completed stage, W_2 is the work rate increment at final incomplete stage, and t is time in seconds at final incomplete stage. VO_{2max} was calculated using previously described formulae [37] and expressed as mL per kilogram body mass per min (mL/kg/min). Values > 37.0 mL/kg/min for girls and > 42.1 mL/kg/min for boys represented a high level of CRF, while values below these levels represented low CRF [41].

Physical activity

RT3® triaxial accelerometers (Stayhealthy, Inc., Monrovia, CA.) were used to measure seven consecutive days of minute-by-minute habitual PA and to determine time spent being sedentary (< 288 counts per min [cpm]) and time spent engaged in light PA (LPA; 288-969 cpm), MVPA (970-2332 cpm), and VPA (≥ 2333 cpm). The activity intensity cut-off points were based on previously published literature in which the RT3® triaxial

accelerometer was validated against oxygen consumption (r = 0.87) in children [40]. Time spent in each PA subcomponent was calculated and presented as the average time per day during the monitoring period.

Participants were only included for data analysis if they had worn the accelerometer for a minimum of three days [30] and acquired a minimum daily wear time of nine hours for weekdays [30] and eight hours for weekend days [39]. Sustained 10 min periods of zero counts were removed during the recoding process.

Clustered cardiometabolic risk score

Waist circumference, TC:HDL ratio and triglycerides were non-normally distributed and were subsequently log-transformed. A continuous clustered cardiometabolic risk variable was then constructed by standardising (to the mean by sex) and then summing the *z*-scores of the following continuously distributed metabolic syndrome variables: waist circumference, diastolic BP, fasting blood glucose, TC:HDL ratio, and fasting triglycerides.

Statistical analysis

All analyses were completed using SPSS version 17.0 (SPSS Inc., Chicago, IL.). Descriptive data are presented as mean±SD. Associations between variables were explored using tests of simple correlation analysis. ANCOVA was used to investigate differences in clustered risk score between high and low CRF groups according to Ruiz et al's [41] previously proposed health-related thresholds, and between tertiles for each PA subcomponent (lowest tertile representing the least time spent in each subcomponent). Covariates entered into the model were age, sex, ethnicity, and SES.

Results

Table 1 shows the descriptive characteristics of the participants. One-way ANOVA revealed that body fat % and time spent in LPA were both significantly greater in girls versus boys. CRF and time spent in MVPA and VPA were significantly greater in boys versus girls. According to McCarthy et al's body fat reference curves for children [31], 85% of the sample was non-overweight, while 9% were overweight and 6% obese.

Table 2 shows correlations between CRF, PA subcomponents, and cardiometabolic risk factors. Simple correlation analysis revealed that CRF was negatively associated with waist circumference, triglycerides, diastolic BP, and clustered cardiometabolic risk score. VPA was negatively correlated with diastolic BP, while

LPA was positively correlated with waist circumference. VPA was also negatively correlated with body fat % (r = -0.27, $p < 0.05$), and LPA was positively correlated ($r = 0.35$, $p < 0.05$). CRF was negatively correlated with LPA, but was positively associated with time spent in MVPA and VPA (Table 2).

To further explore the associations of CRF and PA with cardiometabolic risk, participants were divided into high/low CRF [41] and into tertiles for time spent in each PA subcomponent (time spent in each PA tertile can be seen in Table 3. ANCOVA analysis showed that when controlling for age, sex, ethnicity, and SES, those participants classified as fit (N = 62) had a significantly lower ($F = 9.79$, $p < 0.001$) clustered risk score than their unfit (N = 38) counterparts (Figure 1). No significant differences were found between tertiles in relation to cardiometabolic risk for time spent in sedentary ($F = 1.49$, $p > 0.05$), LPA ($F = 1.39$, $p > 0.05$), MVPA (F = 2.49, $p > 0.05$), or VPA ($F = 1.42$, $p > 0.05$).

Table I Descriptive characteristics of participants

	All (*N* = 100)	Boys (*N* = 41)	Girls (*N* = 59)
Age (y)	11.76 (1.33)	11.76 (1.32)	11.76 (1.34)
z-height	0.42 (1.03)	0.34 (1.11)	0.47 (0.97)
z-weight	0.11 (1.15)	-0.04 (1.22)	0.22 (1.10)
z-BMI	-0.19 (1.29)	-0.34 (1.21)	-0.09 (1.35)
Body fat %	20.8 (6.6)	16.7 (5.8)*	23.5 (5.7)
Waist (cm)	62.3 (8.3)	61.5 (7.1)	62.8 (9.1)
Systolic BP (mm Hg)	105.6 (10.7)	106.6 (10.5)	104.9 (10.9)
Diastolic BP (mm Hg)	65.3 (7.2)	64.5 (7.9)	65.8 (6.6)
TC (mmol/L)	3.98 (0.72)	3.82 (0.71)	4.09 (0.71)
HDL (mmol/L)	1.48 (0.41)	1.50 (0.45)	1.46 (0.38)
TC:HDL ratio	2.88 (0.97)	2.70 (0.71)	3.01 (1.10)
Triglycerides (mmol/L)	0.85 (0.60)	0.73 (0.33)	0.93 (0.72)
Blood glucose (mmol/L)	5.06 (0.50)	5.07 (0.47)	5.05 (0.52)
CRF (mL/kg/min)	41.58 (9.38)	45.96 (8.21)*	38.54 (8.98)
Time sedentary (min/d)	451.91 (79.74)	439.75 (73.09)	460.37 (83.61)
Time in LPA (min/d)	179.81 (42.66)	165.62 (31.32)*	189.67 (46.78)
Time in MVPA (min/d)	109.24 (37.31)	119.10 (37.13)*	102.40 (36.18)
Time in VPA (min/d)	23.33 (16.77)	30.09 (18.12)*	18.64 (14.10)

BMI, body mass index; BP, blood pressure; TC, total cholesterol; CRF, cardiorespiratory fitness; LPA, light physical activity; MVPA, moderate-to-vigorous physical activity; VPA, vigorous physical activity. Data reported as mean (SD). *$p < 0.05$ between sexes

160 **Table II** Bivariate correlations between cardiorespiratory fitness, physical activity subcomponents, and cardiometabolic risk factors

	CRF (mL/kg/min)	Sedentary (min/d)	LPA (min/d)	MVPA (min/d)	VPA (min/d)
Waist circumference (cm)[a]	-0.43*	-0.10	0.23*	0.00	-0.08
Systolic BP (mm Hg)	0.00	-0.03	-0.10	-0.01	-0.10
Diastolic BP (mm Hg)	-0.26*	-0.01	0.09	-0.12	-0.27*
TC:HDL ratio[a]	-0.07	0.06	0.13	-0.08	-0.12
Triglycerides (mmol/L)[a]	-0.20*	-0.04	0.15	0.17	0.05
Blood glucose (mmol/L)	-0.09	0.00	-0.12	0.06	0.09
Clustered risk score	-0.31*	-0.04	0.12	0.04	-0.07
Sedentary (min/d)	0.02				
LPA (min/d)	-0.35*	-0.36*			
MVPA (min/d)	0.22*	-0.49*	0.24*		
VPA (min/d)	0.39*	-0.28*	-0.08		

161 CRF, cardiorespiratory fitness; LPA, light physical activity; MVPA, moderate-to-vigorous physical activity; VPA, vigorous physical activity; BP, blood pressure; TC, total

162 cholesterol; HDL, high-density lipoprotein; [a] log transformed, *$p < 0.05$

Table III Time spent in each physical activity tertile

Tertile	Sedentary (min)	Light PA (min)	MVPA (min)	Vigorous PA (min)
1	229.63 – 411.38	68.58 – 158.38	25.25 – 87.75	0.17 – 13.88
2	412.50 – 481.63	161.50 – 193.88	90.75 – 124.63	14.00 – 26.88
3	482.13 – 729.50	194.88 – 330.38	126.67 – 206.25	27.00 – 83.17

PA, physical activity; MVPA, moderate-to-vigorous physical activity

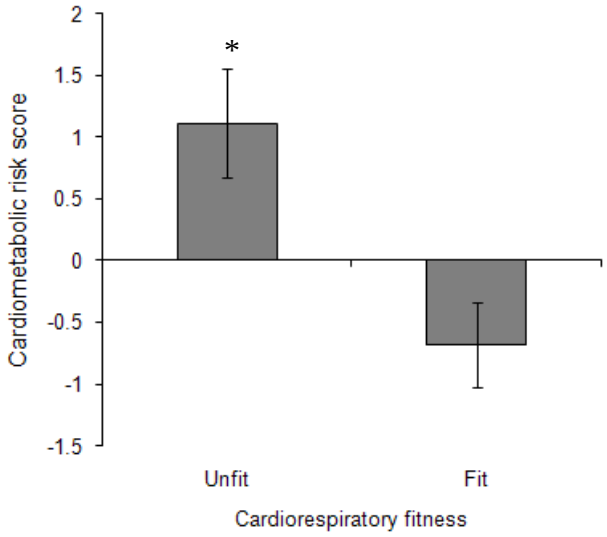

Fig. 1 Association between cardiorespiratory fitness (unfit/fit) and clustered cardiometabolic risk score in children and adolescents. Data shown as mean and SE. Participants in the unfit group had a higher cardiometabolic risk score than in the fit group (* $p < 0.001$)

Discussion

The primary finding of this study was that children and adolescents with higher levels of cardiorespiratory fitness (CRF) had reduced clustered cardiometabolic risk scores, whereas objectively measured PA was not associated with clustered risk. This is an important finding given the literature that has reported decreases in childhood CRF in recent years [7,45] and that CRF during youth is related to cardiometabolic risk profile in adulthood [47].

Previous studies have reported weak correlations between CRF and individual risk factors in youths [29,8], while another investigation found no associations between CRF and features of the metabolic syndrome in 8-14 year-old overweight Latino adolescents [43]. The current findings suggest that higher levels of CRF are associated with reduced abdominal adiposity, diastolic BP, and triglycerides in children and adolescents. However, exploring associations with clustered cardiometabolic risk may be preferable as differences in individual risk markers between participants may be too subtle to investigate in isolation, and a clustered score can compensate for daily fluctuations in individual markers [3]. Furthermore, cardiometabolic diseases are characterised by a constellation of risk markers, and a clustered risk score may detect an array of cardiometabolic disturbances rather than focussing on one or two particular markers, whilst individuals with multiple risk factors also have a poorer health status than if a single risk factor was present [19].

The finding that children and adolescents with higher levels of CRF have reduced clustered cardiometabolic risk is in agreement with other recent evidence [41,3]. In a study by Anderssen and colleagues [3] in 9-15 year-olds, the odds of having clustered risk increased across decreasing quartiles of CRF ($p < 0.001$ for trend). Ruiz et al. [41] found that boys (9-10 years) with a CRF level above 42.1 mL/kg/min were 3.09 times more likely to have a low metabolic risk score compared to those with levels below that value. In girls, a CRF level of 37.0 mL/kg/min equated to a 2.42 times increased likelihood of having a low metabolic risk score compared to those with lower values. Using these same thresholds, the current research shows that high levels of CRF are also important in cardiometabolic risk protection in later childhood and adolescence (10-14 years). Furthermore, favourable associations of CRF with clustered risk have been shown to exist in spite of using alternative health markers when constructing clustered risk scores. Ruiz et al. [41], for example, included insulin, glucose, HDL, and skinfold thickness in their clustered risk score, but excluded waist circumference and TC:HDL ratio in comparison to the risk score calculated in this report and others [3].

CRF is mainly influenced by two components: 1) the genetic constitution of the person [9] and 2) the physical activities an individual takes part in [9]. It is known that physical exercise results in skeletal muscle cell

adaptations in adults [25] and some of these adaptations, such as increased capillary density and limb blood flow [26], increased mitochondrial electron transport chain enzyme activity [25], and increased mitochondrial volume and density [25], may be mediating factors in improved cardiometabolic health in adults and children, although further investigations are needed to confirm these hypotheses. The strongest correlation between CRF and PA variables was between CRF and VPA (r = 0.39), which might suggest that engaging in more vigorous physical exercise promotes cardioprotective adaptations within skeletal muscle.

The present study found that time spent in VPA was not statistically associated with clustered cardiometabolic risk in 10-14 year-old children and adolescents. Although little data exists exploring such associations, other evidence in differently aged youths (9-10 and 15-16 year-olds) has shown a negative relationship between PA subcomponents (sedentary, LPA, MPA, and VPA) and clustered metabolic risk [15]. Engagement in VPA was negatively associated with body fat % and diastolic BP, though, and previous studies have reported similar findings in children [14] and adolescents [23] in addition to favourable relationships with glucose and insulin levels [15]. Engagement in LPA was positively correlated with waist circumference and body fat %. Although LPA would heighten energy expenditure above sedentary levels, this type of activity has limited health benefits [28] and is insufficient to stimulate improvements in CRF [2]. Indeed, LPA was negatively correlated with CRF in the current study, whereas MPA and VPA were positively correlated with CRF. Although time spent in MVPA and VPA were not negatively associated with cardiometabolic risk, they may have had an indirect beneficial influence via increases in CRF. Indeed, longitudinal development of PA and CRF are linked to a healthier CVD risk profile [46], while training studies that engage youths in MVPA may also be effective for increasing CRF [22] and improving cardiometabolic health [27].

This study used an objective method of PA monitoring by employing triaxial accelerometry, although it should be noted that the device and its associated cut-points used to define PA intensities may differ slightly compared to other studies, including Ekelund et al. [15]. There remains controversy regarding which set of cut-points for PA intensity thresholds is most representative of ‘moderate’ and ‘vigorous’ levels of physical exertion in youths [38]. Furthermore, given the sporadic nature of children’s PA [4], the use of one minute measurement time frames (epochs) may lead to under-estimations of time spent in higher intensity activities. Although the use of five second epochs were beyond the scope of the equipment used here, technological advances mean five second epochs are now possible for more detailed PA analysis and should be used in similar studies in the future. Accelerometry is also limited since many devices cannot be used during water-based

activities and also fail to accurately reflect energy expenditure associated with cycling, upper body movements, and walking up-hill.

Other limitations include the cross-sectional design of the study and hence the direction of causality cannot be determined, although subsequent post intervention analyses will assess the effects of interventions on cardiometabolic risk. Secondly, the effects of maturation on cardiometabolic risk were not controlled for and since it has been previously reported that transient changes in cardiometabolic risk factors occur during puberty [24,34], their associations with CRF and PA may have been confounded. Lastly, because CRF was normalised for body mass and fatness influences body mass, the relationship between CRF and waist circumference and clustered risk may have been overestimated. However, waist circumference is a key component of the metabolic syndrome [48] and should thus be included when examining global cardiometabolic risk.

In conclusion, the present study shows that higher levels of CRF, but not time spent in various PA subcomponents, were associated with reduced clustered cardiometabolic risk in children and adolescents. Since the clustering of risk factors persists into adulthood, these data suggest that interventions to reduce the likelihood of developing cardiometabolic illness should target increases in higher intensity PA engagement and improvements in CRF as standard.

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Conflict of interest

The authors declare that they have no conflict of interest.

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