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

Daniel P Bailey[1], Lynne M Boddy[2], Louise A Savory[1], Sarah J Denton[1], Catherine J Kerr[1]

Corresponding author: Daniel P Bailey. Email: daniel.bailey@beds.ac.uk. Telephone: +441234 793268

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

[1] Institute for Sport and Physical Activity Research, University of Bedfordshire, Polhill Avenue, Bedford, Bedfordshire, MK41 9EA, UK.

[2] The Research into Exercise, Activity and Children's Health Group (REACH). The Research Institute for Sport and Exercise Sciences, Liverpool John Moores University, Tom Reilly Building, Byrom Street, Liverpool, L3 3AF.

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

144 LPA was positively correlated with waist circumference. VPA was also negatively correlated with body fat % (r
145 = -0.27, $p < 0.05$), and LPA was positively correlated ($r = 0.35$, $p < 0.05$). CRF was negatively correlated with
146 LPA, but was positively associated with time spent in MVPA and VPA (Table 2).
147
148 To further explore the associations of CRF and PA with cardiometabolic risk, participants were divided into
149 high/low CRF [41] and into tertiles for time spent in each PA subcomponent (time spent in each PA tertile can
150 be seen in Table 3. ANCOVA analysis showed that when controlling for age, sex, ethnicity, and SES, those
151 participants classified as fit ($N = 62$) had a significantly lower ($F = 9.79$, $p < 0.001$) clustered risk score than
152 their unfit ($N = 38$) counterparts (Figure 1). No significant differences were found between tertiles in relation to
153 cardiometabolic risk for time spent in sedentary ($F = 1.49$, $p > 0.05$), LPA ($F = 1.39$, $p > 0.05$), MVPA ($F =$
154 2.49, $p > 0.05$), or VPA ($F = 1.42$, $p > 0.05$).
155

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, *$p < 0.05$

163 **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

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

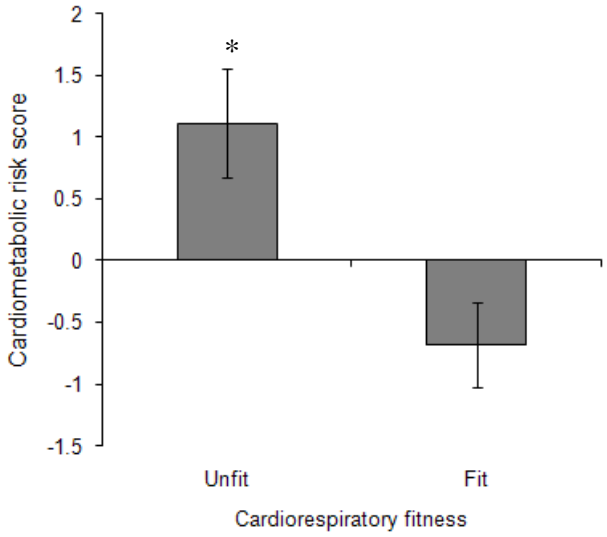

Fig. 1 Association between cardiorespiratory fitness (unfit/fit) and clustered cardiometabolic risk score in children and adolescents. Data shown as mean and SE. Participants in the unfit group had a higher cardiometabolic risk score than in the fit group (* $p < 0.001$)

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.

Acknowledgements

The authors would like to thank the participants who gave their time to the study. We would also like to thank all of the schools who helped facilitate the research. This study was funded by the Bedford Charity.

Conflict of interest

The authors declare that they have no conflict of interest.

253 **References**

254 1. Abbasi F, Brown BW, Jr., Lamendola C, McLaughlin T, Reaven GM (2002) Relationship between obesity,
255 insulin resistance, and coronary heart disease risk. J Am Coll Cardiol 40(5):937-943
256 2. Aires L, Silva P, Silva G, Santos MP, Ribeiro JC, Mota J (2010) Intensity of physical activity,
257 cardiorespiratory fitness, and body mass index in youth. J Phys Act Health 7(1):54-59
258 3. Anderssen SA, Cooper AR, Riddoch C, Sardinha LB, Harro M, Brage S et al. (2007) Low cardiorespiratory
259 fitness is a strong predictor for clustering of cardiovascular disease risk factors in children independent
260 of country, age and sex. Eur Society Cardio 14(4):526-531
261 4. Baquet G, Stratton G, Van Praagh E, Berthoin S (2007) Improving physical activity assessment in prepubertal
262 children with high-frequency accelerometry monitoring: a methodological issue. Prev Med 44(2):143-
263 147
264 5. Berenson GS, Srinivasan SR, Bao W, Newman WP, 3rd, Tracy RE, Wattigney WA (1998) Association
265 between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The
266 Bogalusa Heart Study. N Engl J Med 338(23):1650-1656
267 6. Blair SN, Cheng Y, Holder JS (2001) Is physical activity or physical fitness more important in defining health
268 benefits? Med Sci Sports Exerc 33(Suppl 6):S379-399
269 7. Boddy LM, Hackett AF, Stratton G (2010) Changes in fitness, body mass index and obesity in 9-10 year olds.
270 J Hum Nutr Diet 23(3):254-259
271 8. Boreham C, Twisk J, Murray L, Savage M, Strain JJ, Cran G (2001) Fitness, fatness, and coronary heart
272 disease risk in adolescents: the Northern Ireland Young Hearts Project. Med Sci Sports Exerc
273 33(2):270-274
274 9. Bouchard C, Rankinen T (2001) Individual differences in response to regular physical activity. Med Sci
275 Sports Exerc 33(6 Suppl):S446-451
276 10. Brage S, Wedderkopp N, Ekelund U, Franks PW, Wareham NJ, Andersen LB et al. (2004) Features of the
277 metabolic syndrome are associated with objectively measured physical activity and fitness in Danish
278 children: the European Youth Heart Study (EYHS). Diabetes Care 27(9):2141-2148
279 11. Camhi SM, Katzmarzyk PT (2010) Tracking of cardiometabolic risk factor clustering from childhood to
280 adulthood. Int J Pediatr Obes 5(2):122-129

12. Chen W, Srinivasan SR, Elkasabany A, Berenson GS (1999) Cardiovascular risk factors clustering features of insulin resistance syndrome (Syndrome X) in a biracial (Black-White) population of children, adolescents, and young adults: the Bogalusa Heart Study. Am J Epidemiol 150(7):667-674

13. Cole TJ, Freeman JV, Preece MA (1995) Body mass index reference curves for the UK, 1990. Arch Dis Child 73(1):25-29

14. Department of Health (2011). Start Active, Stay Active: a report on physical activity for health from the four home countries' Chief Medical Officers. http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_128210.pdf . Accessed 14 July 2011

15. Ekelund U, Anderssen SA, Froberg K, Sardinha LB, Andersen LB, Brage S (2007) Independent associations of physical activity and cardiorespiratory fitness with metabolic risk factors in children: the European Youth Heart Study. Diabetologia 50(9):1832-1840

16. Ekelund U, Sardinha LB, Anderssen SA, Harro M, Franks PW, Brage S et al. (2004) Associations between objectively assessed physical activity and indicators of body fatness in 9- to 10-y-old European children: a population-based study from 4 distinct regions in Europe (the European Youth Heart Study). Am J Clin Nutr 80(3):584-590

17. Fairclough SJ, Boddy LM, Hackett AF, Stratton G (2009) Associations between children's socioeconomic status, weight status, and sex, with screen-based sedentary behaviours and sport participation. Int J Pediatr Obes 4(4):299-305

18. Freeman JV, Cole TJ, Chinn S, Jones PR, White EM, Preece MA (1995) Cross sectional stature and weight reference curves for the UK, 1990. Arch Dis Child 73(1):17-24

19. Gami AS, Witt BJ, Howard DE, Erwin PJ, Gami LA, Somers VK et al. (2007) Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. J Am Coll Cardiol 49(4):403-414

20. Golden SH, Folsom AR, Coresh J, Sharrett AR, Szklo M, Brancati F (2002) Risk factor groupings related to insulin resistance and their synergistic effects on subclinical atherosclerosis: the atherosclerosis risk in communities study. Diabetes 51(10):3069-3076

21. Graham I, Atar D, Borch-Johnsen K, Boysen G, Burell G, Cifkova R et al. (2007) European guidelines on cardiovascular disease prevention in clinical practice: executive summary: Fourth Joint Task Force of

the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice. Eur Heart J 28(19):2375-2414

22. Gutin B, Barbeau P, Owens S, Lemmon CR, Bauman M, Allison J et al. (2002) Effects of exercise intensity on cardiovascular fitness, total body composition, and visceral adiposity of obese adolescents. Am J Clin Nutr 75(5):818-826

23. Gutin B, Yin Z, Humphries MC, Barbeau P (2005) Relations of moderate and vigorous physical activity to fitness and fatness in adolescents. Am J Clin Nutr 81(4):746-750

24. Hannon TS, Janosky J, Arslanian SA (2006) Longitudinal study of physiologic insulin resistance and metabolic changes of puberty. Pediatr Res 60(6):759-763

25. Hawley JA (2002) Adaptations of skeletal muscle to prolonged, intense endurance training. Clin Exp Pharmacol Physiol 29(3):218-222

26. Holten MK, Zacho M, Gaster M, Juel C, Wojtaszewski JF, Dela F (2004) Strength training increases insulin-mediated glucose uptake, GLUT4 content, and insulin signaling in skeletal muscle in patients with type 2 diabetes. Diabetes 53(2):294-305

27. Kelly AS, Wetzsteon RJ, Kaiser DR, Steinberger J, Bank AJ, Dengel DR (2004) Inflammation, insulin, and endothelial function in overweight children and adolescents: the role of exercise. J Pediatr 145(6):731-736

28. Lee IM, Paffenbarger RS, Jr. (2000) Associations of light, moderate, and vigorous intensity physical activity with longevity. The Harvard Alumni Health Study. Am J Epidemiol 151(3):293-299

29. Martinez-Gomez D, Eisenmann JC, Warnberg J, Gomez-Martinez S, Veses A, Veiga OL et al. (2010) Associations of physical activity, cardiorespiratory fitness and fatness with low-grade inflammation in adolescents: the AFINOS Study. Int J Obes (Lond) 34(10):1501-1507

30. Mattocks C, Ness A, Leary S, Tilling K, Blair SN, Shield J et al. (2008) Use of accelerometers in a large field-based study of children: protocols, design issues, and effects on precision. J Phys Act Health 5(Suppl 1):S98-111

31. McCarthy HD, Cole TJ, Fry T, Jebb SA, Prentice AM (2006) Body fat reference curves for children. Int J Obes (Lond) 30(4):598-602

32. McGill HC, Jr., McMahan CA, Zieske AW, Tracy RE, Malcom GT, Herderick EE et al. (2000) Association of coronary heart disease risk factors with microscopic qualities of coronary atherosclerosis in youth. Circulation 102(4):374-379

340 33. Mitchell MS, Gaul CA, Naylor PJ, Panagiotopoulos C (2010) Habitual moderate-to-vigorous physical
341 activity is inversely associated with insulin resistance in Canadian first nations youth. Pediatr Exerc Sci
342 22(2):254-265
343 34. Moran A, Jacobs DR, Jr., Steinberger J, Steffen LM, Pankow JS, Hong CP et al. (2008) Changes in insulin
344 resistance and cardiovascular risk during adolescence: establishment of differential risk in males and
345 females. Circulation 117(18):2361-2368
346 35. Parikh P, Mochari H, Mosca L (2009) Clinical utility of a fingerstick technology to identify individuals with
347 abnormal blood lipids and high-sensitivity C-reactive protein levels. Am J Health Promot 23(4):279-
348 282
349 36. Patrick K, Norman GJ, Calfas KJ, Sallis JF, Zabinski MF, Rupp J et al. (2004) Diet, physical activity, and
350 sedentary behaviors as risk factors for overweight in adolescence. Arch Pediatr Adolesc Med
351 158(4):385-390
352 37. Riddoch C, Edwards D, Page A, Froberg K, Anderssen SA, Wedderkopp N et al. (2005) The European
353 Youth Heart Study - cardiovascular disease risk factors in children: rationale, aims, study design, and
354 validation of methods. J Phys Act Health 2(1):115-129
355 38. Ridgers ND, Fairclough SJ (2011) Assessing free-living physical activity using accelerometry: Practical
356 issues for researchers and practitioners. Eur J Sport Sci 11(3):205-213
357 39. Rowlands AV, Pilgrim EL, Eston RG (2008) Patterns of habitual activity across weekdays and weekend
358 days in 9-11-year-old children. Prev Med 46(4):317-324
359 40. Rowlands AV, Thomas PW, Eston RG, Topping R (2004) Validation of the RT3 triaxial accelerometer for
360 the assessment of physical activity. Med Sci Sports Exerc 36(3):518-524
361 41. Ruiz JR, Ortega FB, Rizzo NS, Villa I, Hurtig-Wennlof A, Oja L et al. (2007) High cardiovascular fitness is
362 associated with low metabolic risk score in children: the European Youth Heart Study. Pediatr Res
363 61(3):350-355
364 42. Ruiz JR, Rizzo NS, Hurtig-Wennlof A, Ortega FB, Warnberg J, Sjostrom M (2006) Relations of total
365 physical activity and intensity to fitness and fatness in children: the European Youth Heart Study. Am J
366 Clin Nutr 84(2):299-303
367 43. Shaibi GQ, Cruz ML, Ball GD, Weigensberg MJ, Kobaissi HA, Salem GJ et al. (2005) Cardiovascular
368 fitness and the metabolic syndrome in overweight Latino youths. Med Sci Sports Exerc 37(6):922-928

44. Shemesh T, Rowley KG, Shephard M, Piers LS, O'Dea K (2006) Agreement between laboratory results and on-site pathology testing using Bayer DCA2000+ and Cholestech LDX point-of-care methods in remote Australian Aboriginal communities. Clin Chim Acta 367(1-2):69-76

45. Stratton G, Canoy D, Boddy LM, Taylor SR, Hackett AF, Buchan IE (2007) Cardiorespiratory fitness and body mass index of 9-11-year-old English children: a serial cross-sectional study from 1998 to 2004. Int J Obes (Lond) 31(7):1172-1178

46. Twisk JW, Kemper HC, van Mechelen W (2000) Tracking of activity and fitness and the relationship with cardiovascular disease risk factors. Med Sci Sports Exerc 32(8):1455-1461

47. Twisk JW, Kemper HC, van Mechelen W (2002) The relationship between physical fitness and physical activity during adolescence and cardiovascular disease risk factors at adult age. The Amsterdam Growth and Health Longitudinal Study. Int J Sports Med 23(Suppl 1):S8-14

48. Zimmet P, Alberti KG, Kaufman F, Tajima N, Silink M, Arslanian S et al. (2007) The metabolic syndrome in children and adolescents - an IDF consensus report. Pediatr Diabetes 8(5):299-306