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Buchan, Duncan S.; Baker, Julien S.

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Utility of Body Mass Index, Waist-to-Height-Ratio and cardiorespiratory fitness thresholds for identifying cardiometabolic risk in 10.4 – 17.6-year-old children.

*Duncan S. Buchan[1] and Julien S. Baker[1]

[1]Institute of Clinical Exercise and Health Science, University of the West of Scotland, Hamilton, Lanarkshire, ML3 0JB, UK.

* Address correspondence to Dr Duncan Buchan, Institute of Clinical Exercise and Health Science, University of the West of Scotland, Hamilton, Lanarkshire, ML3 0JB, UK.
duncan.buchan@uws.ac.uk. Tel: 01698 283100

Abbreviations: BMI – Body Mass Index; WHtR – Waist-to-height ratio, CRF - Cardiorespiratory fitness; HDL-c - High density lipoprotein cholesterol; ROC - Receiver operator characteristics; AUC - Area under the curve.

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Abstract:

Objective: To examine the utility of body mass index (BMI), waist-to-height-ratio (WHtR) and cardiorespiratory fitness thresholds to identify cardiometabolic risk in youth.

Methods:

Cross-sectional cardiometabolic risk factor variables on 534 children aged 10.4 – 17.6 years of age (52% boys) from the United Kingdom were used. Binary logistic regression and receiver operating characteristic curves were used to examine the utility of established age and gender specific thresholds for BMI, WHtR and cardiorespiratory fitness to identify individuals with increased cardiometabolic risk (increased clustered triglycerides, HDL-cholesterol, systolic blood pressure and glucose).

Results:

A WHtR ≥ 0.5 increased the odds by 11.4 (95% confidence interval 4.7, 27.4, *P* <0.001) of having increased cardiometabolic risk in boys and by 2.5 (1.2, 5.3, *P* = 0.020) for girls. Similar associations were observed for BMI and cardiorespiratory fitness in both boys and girls with increased cardiometabolic risk. BMI-z, WHtR and cardiorespiratory fitness all showed a significant ability in identifying individuals for increased cardiometabolic risk in boys and girls (*P* < 0.05) despite poor area under the curve (AUC) values (<0.70). Combining anthropometrical variables did improve the diagnostic accuracy for identifying cardiometabolic risk in boys, evidenced by an increased AUC of 0.74 (0.64, 0.85, *P* < 0.001), but not in girls.

Conclusion:

The magnitude of associations was broadly similar for BMI, WHtR and cardiorespiratory fitness in identifying individuals at increased cardiometabolic risk. Yet, combining BMI with WHtR in boys may provide a more accurate method for identifying those at increased cardiometabolic risk.

Key Words: Cardiometabolic risk; Waist-to-Height-Ratio; Body Mass Index; Cardiorespiratory fitness; Children.

1. Introduction

Body Mass Index (BMI) is commonly used to define overweight and obesity yet, relying upon this measure as an indicator of excess adiposity and cardiometabolic risk in youth has limitations. Its interpretation relies upon growth charts and the subsequent need for values to be expressed as z-scores or percentiles relative to age and sex and is unable to distinguish between fat and fat-free mass [1]. The waist to height ratio (WHtR) is an alternative anthropometric measure which may be a superior screening method for cardiometabolic risk given its ability to assess central adiposity [1]. An additional benefit of measuring WHtR is the inclusion of height within the calculation which can remove any potential confounding of cardiometabolic risk by height. This may be important in children given recent findings which have shown that the risk of the metabolic syndrome within a given waist circumference stratification is higher amongst shorter adults [2].

Findings from the limited available evidence which has examined the predictive utility of BMI and WHtR for identifying cardiometabolic risk in youth is unclear. Despite some suggesting that a waist-height ratio (WHtR) ≥ 0.5 is a valid predictor of cardiometabolic risk irrespective of age, sex or ethnicity [1, 3, 4], others have reported no differences in the abilities of WHtR and BMI for risk prediction [5-7]. Whilst anthropometric measures are commonly used to identify adolescents of increased cardiometabolic risk, low cardiorespiratory fitness levels are also inversely associated with obesity and poor risk profiles [8]. Yet, there is a paucity of evidence which has examined the different associations between anthropometric measures, cardiorespiratory fitness and cardiometabolic risk in children. Also, most of the evidence has utilized data from the National Health and Nutrition Examination Survey (NHANES) [1, 4-6, 8].

Since the associations between anthropometric indices, cardiorespiratory fitness and cardiometabolic risk may differ in children from different cultural settings [9], it is important to determine whether the magnitude of association with cardiometabolic risk in children varies between geographical settings. Moreover, studies that have assessed the predictive abilities of combining adiposity measures or combining adiposity measures with fitness measures as screening tools for cardiometabolic risk among youth are particularly scarce. Furthermore, and to the best of our knowledge, no study has examined these associations using cohorts from Scotland and Wales. Thus, the objective of this study was to examine the predictive abilities of BMI, WHtR and cardiorespiratory fitness for identifying individuals of increased cardiometabolic risk.

2. Methods

Data were derived from studies evaluating the health status of Scottish and Welsh youth. Details of the measurement protocols have been described previously [10, 11]. The study sample consisted of a Welsh cohort of white schoolchildren (N = 100 boys and 108 girls, 12.9 ± 0.3 years of age) who were recruited from two secondary schools. The Scottish cohort of white schoolchildren (N = 226 boys and 178 girls, 13.8 ± 2.9 years of age) were recruited from three secondary schools and one primary school between 2010 and 2014. Studies were approved by the University of the West of Scotland and the University of South Wales institutional research ethics committees in accordance with the Declaration of Helsinki. After excluding those participants who were absent from data collection, withdrawal of blood sampling consent or having identified themselves as being non-fasted, 547 children aged 10.4 – 17.6 years (52% boys) with complete data were included within the study. We decided to only include participants with complete data on cardiorespiratory fitness and cardiometabolic risk factors to avoid imputation of biological variables and improve the stability of our results, as undertaken elsewhere [8].

2.1 Measures

Stature without shoes was measured to the nearest 1 mm using a portable stadiometer (Seca Stadiometer, Seca Ltd, Birmingham, UK and Holtain Ltd, Crymych, Pembrokeshire, UK). Mass without shoes, was measured to the nearest 0.1 kg using calibrated electronic weighing scales (Seca 880, Digital Scales, Seca Ltd, Birmingham, UK or Holtain Ltd, Crymych, Pembrokeshire, UK). WC was measured at the narrowest point between the lower ribs and iliac crest (natural waist) using an anthropometric tape in accordance with established guidelines [12]. From measured stature and body mass, participants were classified as obese/overweight or a healthy weight using BMI-z scores relative to the UK 1990 BMI population reference data [13]. Using software provided by the Child Growth Foundation [14] the following definitions were applied for healthy weight (BMI z-score <1.04, below the 85th percentile) and overweight / obese (BMI z-score ≥1.04, above the 85th percentile) individuals. WHtR was determined by dividing WC by height with values ≥ 0.5 considered high [5, 7]. Systolic and diastolic BP (mmHg) was determined using automated monitors (Omron M10-IT Blood Pressure Monitor HEM-7080IT-E, Omron Healthcare UK Ltd, Milton Keynes, UK and a Dinamap XL automatic BP monitor, Critikron, Inc., Tampa, FL) after participants had sat quietly for a minimum of 5 minutes. The average of the second and third measures was used as the criterion value. Free school meal eligibility was used as a measure of socio-economic status (SES) whereas cardiorespiratory fitness (CRF) was measured using the 20m multi stage fitness test (20-MSFT) as described previously [15] and estimated the maximum oxygen consumption (VO_{2max}, mL/kg/min) from the 20 m shuttle run test scores using validated equations [16].

2.2 Metabolic Measures

Venous blood samples were collected between 8am and 12pm following an overnight fast and 30 min seated rest. Blood was sampled from the antecubital vein and collected in a BD Vacutainer plasma tube (Becton, Dickinson and Company, Franklin Lakes, USA). Blood samples were allowed to clot and then centrifuged at 4000 rpm for 10 minutes. In Scotland, samples were transferred to aliquots and frozen at -80oC within two hours of collection. Samples were then analysed within 3 months using standard procedures. Triglycerides were measured by enzymatic methods (Randox, Antrim, UK) and a Camspec M107 spectrophotometer (Camspec, Leeds, UK). Concentration of high density lipoprotein cholesterol (HDL-c) was determined after precipitation of very low density and low-density lipoproteins by the addition of phosphotungstic acid in the presence of magnesium ions. Whereas glucose was measured with the glucose oxidase method (Randox, Antrim, UK) and analyzed using a Camspec M107 spectrophotometer (Camspec, Leeds, UK).

In Wales, Blood samples were allowed to clot and then centrifuged at 3,500 rpm for 10 min and analysed immediately. Triglycerides and glucose were measured by routine enzymatic techniques using the Vitros 950 System (Ortho-Clinical Diagnostics, Amersham, Bucks). The concentration of HDL-C was determined after precipitation of very low-density and low-density lipoproteins with dextran sulphate and magnesium chloride using the ILAB™ 600 System (Instrumentation Laboratory Company, Lexington, MA, USA). Metabolic measurements were taken on a separate day to all other measurements.

2.3 Cardiometabolic risk score

A continuous cardiometabolic risk score was constructed using the following variables: Triglycerides, HDL-c (inverted), glucose and systolic BP. The rationale of including triglycerides, HDL-c (inverted), glucose and systolic BP was to calculate a continuous score that is reflective of glucose metabolism, lipid metabolism and resting systolic blood pressure. Since these variables are used in the adult definition of the metabolic syndrome, our clustered cardiometabolic risk score follows previous recommendations which support the inclusion of key metabolic syndrome variables within continuous cardiometabolic risk scores [17]. Each variable was standardized as follows: standardized value = value-mean/SD, separately for boys and girls and by 1 yr. age groups. The z-scores were subsequently summed to construct a cardiometabolic risk score for each individual with a lower score being indicative of a healthier risk profile. Individuals with a cardiometabolic risk score +1SD above the grand mean were identified as having increased cardiometabolic risk, as previously suggested [6].

2.4 Adverse levels of cardiometabolic risk factors

Reference values from the National Cholesterol Education Program's (NCEP) Pediatric Panel Report [18] define a borderline high range for triglyceride concentrations as 90-129 mg/dL (1.02-1.46 mmol/L). Thus, 1.24 mmol/L was used as the midpoint with values ≥ 1.24 mmol/L considered elevated. For borderline low HDL-c the NCEP Pediatric Panel Report propose a range of between 0.91 - 1.16 mmol/L regardless of gender or age [18]. As with triglycerides, the midpoint of this range (1.03 mmol/L) was used to define low HDL-c levels. Impaired fasting glucose was defined as ≥ 5.6

mmol/L according to the International Diabetes Federation recommendation for youth [19]. Blood pressure was converted to standardized z-scores using software provided by the Child Growth Foundation [14] with values greater than the 91st percentile considered elevated as recommended [20]. Participants were classified as ‘fit’ or ‘unfit’ using recommended thresholds (41.8 and 39.5 mL/kg/min for boys and girls, respectively) [21].

2.5 Statistical analysis

Independent associations between the two anthropometric indices (BMI and WHtR) and cardiometabolic risk were examined using separate multivariable binary logistic regression analysis models controlled for age and SES. The presence or absence of at risk levels of the two anthropometric indices and cardiorespiratory fitness (yes/no) was used as the dependent variable with the calculated odds ratios (OR) presented with their 95% confidence intervals (CIs). Receiver operating characteristic (ROC) curve analyses demonstrated the discriminatory ability of the anthropometric indices and cardiorespiratory fitness for predicting increased cardiometabolic risk quantified by the area under the curve (AUC). At each value the sensitivity (true-positive rate), specificity (true-negative rate) and positive and negative predictive values (PPV and NPV) for predicting increased cardiometabolic risk was calculated. The most sensitive cut-off value for the detection of increased cardiometabolic risk was obtained from the Youden index with greater accuracy reflected in a higher score. ROC AUC values of ≥0.90 were considered excellent, 0.80–0.89 good, 0.70–0.79 fair, and <0.70 poor [22]. The statistical significance of the difference between AUC’s was tested using the method by DeLong and colleagues [23]. Analyses were conducted for boys and girls separately. AUC’s were compared using MedCalc 12.5 (MedCalc software, Mariakerkem Belgium) whereas all other data were analyzed using IBM SPSS Statistics 22 (IBM, Chicago, IL, USA) with $P < 0.05$ considered statistically significant.

3 Results

Participant characteristics and mean levels of cardiometabolic risk factors are presented in Table 1. For boys, analysis indicated that 30% of participants were overweight/obese from their BMI, 11% had a high WHtR and 10% had low cardiorespiratory fitness levels. For the individual components of the continuous cardiometabolic risk score (triglycerides, HDL-cholesterol, systolic blood pressure and glucose), 23% had hypertriglyceridemia; 16% had low levels of HDL-c; 21% had elevated systolic BP and 18% had impaired fasting glucose. Supplementary Figure 1 displays the proportion (%) of boys who presented with a clustering of individual cardiometabolic risk factors and revealed that 35% presented with no adverse risk factors, 31% presented with one, 26% presented with two and 8% presented with three.

For girls, analysis indicated that 33% of participants were overweight/obese from their BMI, 11% had a high WHtR and 12% had low cardiorespiratory fitness levels. For the individual components of the continuous cardiometabolic risk score (triglycerides, HDL-cholesterol, systolic blood pressure and glucose), 23% had hypertriglyceridemia; 9% had low levels of HDL-c; 12% had elevated systolic BP and 14% had impaired fasting glucose. Supplementary Figure 1 displays the proportion (%) of girls who presented with a clustering of individual cardiometabolic risk factors and revealed that 35% presented with no adverse risk factors, 37% presented with one, 21% presented with two and 7% presented with three.

The results of the multivariable binary logistic regression analysis are presented in Tables 2 and 3. For boys (Table 2), those classified as overweight/obese according to their BMI were significantly more likely to have elevated triglycerides, lower HDL-c and elevated systolic BP when compared to those of a healthy BMI. Moreover, these individuals were also significantly more likely to present with 2 cardiometabolic risk factors and have increased cardiometabolic risk scores. Boys with a high WHtR were also significantly more likely to have elevated triglycerides, low HDL-c and elevated systolic BP as well as increased cardiometabolic risk scores when compared to those of a healthy WHtR. Finally, boys with low CRF were significantly more likely to have elevated triglycerides, low HDL-c and to present with 2 cardiometabolic risk factors as well as increased cardiometabolic risk scores when compared to those of a healthy CRF.

For girls (Table 3), those classified as overweight/obese according to their BMI were significantly more likely to have elevated glucose and systolic BP as well as presenting with 2 cardiometabolic risk factors and increased cardiometabolic risk scores than those of a healthy BMI. Girls with an elevated WHtR were significantly more likely to have elevated triglycerides and systolic BP as well as presenting with 2 cardiometabolic risk factors and increased cardiometabolic risk scores than those of a healthy WHtR. Finally, girls with low CRF were significantly more likely to have elevated triglycerides, present with 2 cardiometabolic risk factors and have increased cardiometabolic risk scores than those of a healthy CRF.

The AUC's of BMI-z, WHtR and cardiorespiratory fitness for the prediction of increased cardiometabolic risk are presented in Table 4. For boys, BMI-z, WHtR and cardiorespiratory fitness demonstrated similar discriminatory abilities for identifying individuals with increased cardiometabolic risk. Further analysis revealed that adding WHtR to the BMI-z model yielded a higher AUC compared to the model with BMI-z alone yet the inclusion of cardiorespiratory fitness to the BMI-z model yielded a lower AUC. The PPV of the BMI-z + WHtR model also yielded an improvement with 64.6% of individuals who screened positive for increased cardiometabolic risk having increased risk.

For girls as with boys, BMI-z, WHtR and cardiorespiratory fitness demonstrated similar discriminatory abilities for identifying individuals with increased cardiometabolic risk. Unlike boys, further analysis revealed that adding WHtR to the BMI-z model did not yield a higher AUC compared to the model with BMI-z alone despite an improvement in the PPV. As with boys, including cardiorespiratory fitness to the BMI-z model yielded a lower AUC. Finally, comparisons between the BMI-z + WHtR and BMI-z + cardiorespiratory fitness models revealed significant differences in the AUC's for both boys ($P = 0.032$) and for girls ($P = 0.017$).

4 Discussion

The purpose of this study was to examine the predictive abilities of BMI, WHtR and cardiorespiratory fitness for identifying individuals of increased cardiometabolic risk. We found that individuals categorized as having an increased WHtR, BMI or low cardiorespiratory fitness were between 2.4 and 11.4 times more likely to have increased cardiometabolic risk than individuals categorized as having a healthy WHtR, BMI and high cardiorespiratory fitness. When examining the individual risk factors of cardiometabolic risk in boys it was evident that BMI, WHtR and cardiorespiratory fitness demonstrated a broadly similar ability in identifying individuals with increased risk of hypertriglyceridemia, low-HDL-c, elevated systolic BP and the clustering of 2 risk factors. Similarly in girls, strong and significant associations with increased cardiometabolic risk were also evident as was the ability of BMI, WHtR and cardiorespiratory fitness to identify those with the clustering of 2 risk factors.

Previous studies have demonstrated that individuals presenting with an elevated BMI or WHtR perform similarly in identifying individuals with increased cardiometabolic risk [6, 24] albeit using different BMI growth standards. Our observations using UK population reference data extend these findings. Our findings relating to cardiorespiratory fitness are also in agreement with others that suggest that low cardiorespiratory fitness is a prominent correlate of increased cardiometabolic risk in children [8, 21, 25] and indicated that the association appears stronger for clustered rather than for individual risk factors.

Findings from the ROC analysis indicated that the AUC's for both BMI-z and WHtR did not differ, consistent with the findings of others [5-7]. Moreover, the ROC analysis also demonstrated a significant discriminatory accuracy of cardiorespiratory fitness to identify the presence of cardiometabolic risk both in boys and in girls. Our findings are in agreement with those of Moreira and colleagues who found that Matsuzaka equation showed a significant discriminatory accuracy for cardiorespiratory fitness for identifying both boys and girls with increased cardiometabolic risk [21].

More recently Ruiz and colleagues [25] also demonstrated similar findings albeit using a marginally lower threshold for girls and a higher threshold for boys.

In this study, boys with cardiorespiratory fitness levels below 41.8 mL/kg/min were 5.3 times more likely to have increased cardiometabolic risk whereas girls with cardiorespiratory fitness levels below 39.5 mL/kg/min were 3.3 times more likely to have increased cardiometabolic risk. Collectively one could suggest that our findings support the need for high levels of cardiorespiratory fitness to reduce the likelihood of increased cardiometabolic risk. Whilst our findings appear to suggest that a high BMI, a high WHtR and a low cardiorespiratory fitness is associated with increased cardiometabolic risk it is prudent to note that the AUC's from the ROC analysis were far from excellent. Yet, the reported AUC's are similar to previous studies that have examined the predictive utility of BMI and WHtR [6, 26] and cardiorespiratory fitness [21, 27] for identifying increased cardiometabolic risk using apparently healthy participants. It may be that the magnitude of associations and accuracy of the thresholds may have increased in a population with underlying cardiovascular conditions.

Unlike previous studies [6] we did observe an improvement in the AUC when combining anthropometric variables with a greater accuracy evident for boys when compared to girls. The greater sensitivity reported for boys in comparison to girls is similar to the findings reported by Khoury and colleagues [1] which they explain may be a result of the number of post-pubertal female subjects used in their sample. As in this study, the age of participants ranged from 10.4 – 17.6 years and since post-pubertal females have a predisposition for gluteofemoral fat deposition which is known to have a protective role in the development of cardiometabolic risk [28], the lower AUC for girls may be the result of the inclusion of post-pubertal females. Nonetheless, the improved sensitivity of the combined anthropometric models is unsurprising and supports the findings of others which advocate the use of an index of body fat distribution in addition to BMI to improve the sensitivity of detecting youth with increased cardiometabolic risk [1, 3]. Certainly the findings reported here support that assertion yet it is difficult to ascertain the independent effects of WHtR within BMI categories since both measures are strongly correlated. Further longitudinal work would be needed to ascertain the relationship of BMI and WHtR combined as a useful indicator of cardiometabolic risk into adulthood.

The reduced diagnostic accuracy of combining cardiorespiratory fitness with BMI for both genders was surprising. Higher cardiorespiratory fitness levels in youth are associated with reduced cardiometabolic risk [8, 25] and with a reduced risk of myocardial infarction in adulthood [29] yet it is unclear how the interplay between fitness and fatness is related to increased cardiometabolic risk. So despite BMI and cardiorespiratory fitness demonstrating similar predictive abilities in identifying increased cardiometabolic risk, our findings suggest that the effects of cardiorespiratory fitness in this cohort was mediated by body weight. Body fatness influences both cardiometabolic risk and cardiorespiratory fitness and this interplay may have confounded the associations when BMI was combined with cardiorespiratory fitness to identify those at increased cardiometabolic risk. Although weight loss appears more relevant to cardiometabolic health in this cohort of participants who are overweight/obese from their BMI, improving cardiorespiratory fitness early in one's life is also warranted given the body of evidence supporting its protective role both in youth and in adulthood [29].

The findings of this study are limited due to its cross-sectional nature and our inability to draw definitive casual attributions. The lack of objectively measured physical activity, dietary habits and maturation status, which are well-established confounders of a number of indicators measured, are also acknowledged. We would also like to highlight that the present study is based on a convenience sample of children who were white which limits the generalizability of our findings. We therefore suggest caution in the extrapolation of our findings and advise that further population based studies involving other geographical locations, ethnicities and socio-economic groups are undertaken. Finally, the z-score approach is common in the paediatric literature but it's not without its limitations. Each selected variable is equally weighted within the score as well as being specific only to the sample used [30]. Strengths of this study include the use of data from a sample of UK children with complete data on cardiorespiratory fitness and cardiometabolic risk factors. An additional strength of this study is the use of UK recommended thresholds. Since previous studies have tended to focus on North American cohorts, our findings add to the paucity of evidence examining the associations between anthropometric indices, cardiorespiratory fitness and cardiometabolic risk in children living in different cultural settings.

In summary, we found that BMI-z, WHtR and cardiorespiratory fitness have similar associations and discriminatory abilities in identifying youth at increased cardiometabolic risk. Yet, the findings of this present study emphasize the utility of WHtR in further specifying increased cardiometabolic risk in overweight and obese boys and girls.

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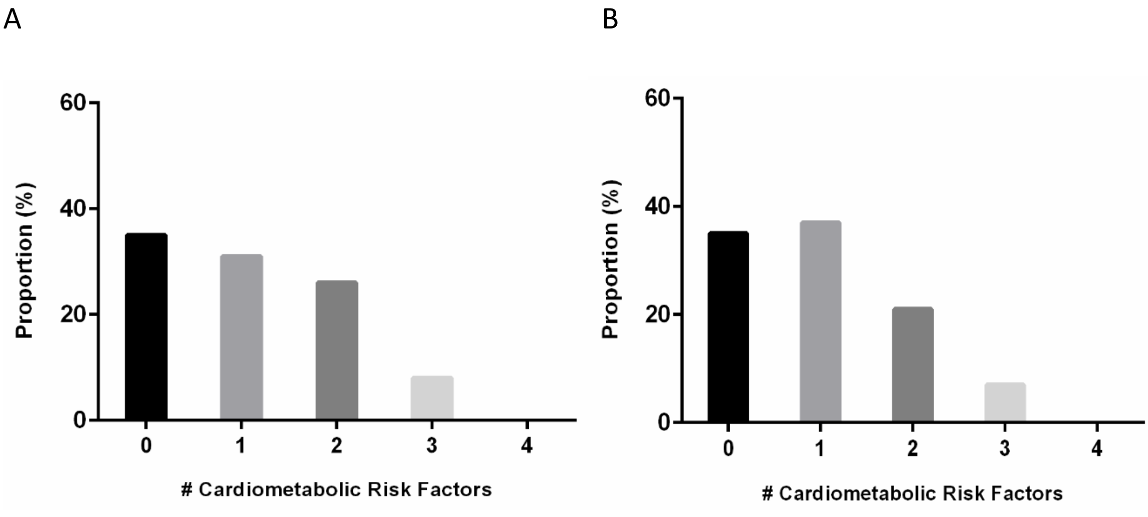

Supplementary Figure 1. Proportion of boys and girls with cardiometabolic risk factors.

The proportion of individuals with adverse levels for the following cardiometabolic risk factors (triglycerides, HDL-c, glucose and systolic BP) were examined. Values ≥ 1.24 mmol/L were considered elevated for triglycerides; values ≤ 1.03 mmol/L were used to define low HDL-c levels; Values ≥ 5.6 mmol/L for fasting glucose were considered elevated (Zimmet and others, 2007). Systolic BP was converted to standardized z-scores using software provided by the Child Growth Foundation (Pan and Cole, 2010) with values greater than the 91st percentile considered elevated as recommended (Jackson et al., 2007). (A) Boys; (B) girls. Data are presented as proportions (%).

Table 1 – Descriptive characteristics of study participants

	Boys N = 286 (52%)	Girls N = 261 (48%)
Variable		
Age (years)	13.6 (2.5)	13.6 (2.4)
BMI (kg/m^2)	20.5 (4.0)	21.1 (4.1)
Waist-to-height ratio	0.44 (0.05)	0.43 (0.05)
Systolic BP (mmHg)	118 (14)	116 (11)
Diastolic BP (mmHg)	67 (10)	70 (10)
Glucose (mmol/L)	5.0 (0.8)	4.9 (0.9)
Triglycerides (mmol/L)	0.9 (0.5)	0.8 (0.4)
HDL-c (mmol/L)	1.6 (0.8)	1.7 (0.8)
CRF (ml/kg/min)	51.1 (5.4)	45.8 (5.5)
Cardiometabolic risk-z score	0.1 (2.3)	-0.1 (2.3)

Values presented as mean (SD). BMI = Body mass index; HDL-c = high-density lipoprotein cholesterol; CRF = cardiorespiratory fitness. BP = Blood Pressure.

Table 2. Multivariable adjusted OR (95% CI) for cardiometabolic risk factor variables in overweight and unfit boys

	Body Mass Index [a]		Waist-to-Height Ratio [b]		Cardiorespiratory Fitness [c]	
Variable	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Hypertriglyceridemia [d]	3.6 (2.0, 6.5)	<0.001	10.1 (1.5, 23.1)	<0.001	3.1 (1.3, 7.1)	0.010
Low HDL-c [e]	2.8 (1.5, 5.2)	0.002	2.3 (1.3, 6.4)	0.011	3.2 (1.4, 7.0)	0.005
Impaired fasting Glucose [f]	0.8 (0.4, 1.5)	0.40	0.8 (0.3, 2.2)	0.68	1.4 (0.6, 3.7)	0.444
Elevated systolic BP [g]	2.1 (1.3, 3.5)	0.003	3.4 (1.6, 7.1)	0.001	1.2 (0.5, 2.8)	0.60
1 risk factor [h]	0.9 (0.5, 1.5)	0.57	0.61 (0.3, 1.5)	0.61	0.6 (0.3, 1.6)	0.32
2 risk factors [i]	2.1 (1.2, 3.6)	0.009	1.6 (0.7, 3.6)	0.22	2.6 (1.2, 5.7)	0.017
Cardiometabolic risk * [j]	3.1 (1.8, 5.4)	<0.001	11.4 (4.7, 27.4)	<0.001	5.3 (2.4, 11.6)	<0.001

The presence or absence of at risk levels of the two anthropometric indices and cardiorespiratory fitness (yes/no) were used as the dependant variable with the healthy weight group for each anthropometric used as the reference group (OR = 1.0). Calculated odds ratios (OR) are presented with their 95% confidence intervals (CIs). Models were adjusted for age. HDL-c = high-density lipoprotein cholesterol; BP = Blood Pressure. CRF = cardiorespiratory fitness. *Cardiometabolic risk was constructed using the following variables: Triglycerides, HDL-c (inverted) glucose and systolic BP. [a] Healthy *N* = 194, overweight/obese *N* = 92. [b] Healthy *N* = 254, High *N* = 32. [c] Healthy CRF *N* = 254, Low CRF *N* = 32.

[d] Healthy BMI-z *N* = 35, overweight/obese from BMI-z *N* = 36; Healthy WHtR *N* = 51, High WHtR *N* = 20. Healthy CRF *N* = 57, Low CRF *N* = 14

[e] Healthy BMI-z *N* = 25, overweight/obese from BMI-z *N* = 27; Healthy WHtR N = 40, High WHtR *N* = 12. Healthy CRF *N* = 34, Low CRF *N* = 16

[f] Healthy BMI-z *N* = 41, overweight/obese from BMI-z *N* = 15; Healthy WHtR N = 51, High WHtR *N* = 10. Healthy CRF *N* = 48, Low CRF *N* = 18

[g] Healthy BMI-z *N* = 37, overweight/obese from BMI-z *N* = 28; Healthy WHtR N = 53, High WHtR *N* = 11. Healthy CRF *N* = 53, Low CRF *N* = 15

[h] Healthy BMI-z *N* = 63, overweight/obese from BMI-z *N* = 29; Healthy WHtR N = 82, High WHtR *N* = 13 . Healthy CRF *N* = 81, Low CRF *N* = 17

[i] Healthy BMI-z *N* = 10, overweight/obese from BMI-z *N* = 43; Healthy WHtR N = 64, High WHtR *N* = 11. Healthy CRF *N* = 61, Low CRF *N* = 14

[j] Healthy BMI-z *N* = 47, overweight/obese from BMI-z *N* = 43; Healthy WHtR N = 65, High WHtR *N* = 24. Healthy CRF *N* = 71, Low CRF *N* = 18

Table 3. Multivariable adjusted OR (95% CI) for cardiometabolic risk factor variables in overweight and unfit girls

	Body Mass Index [a]		Waist-to-Height Ratio [b]		Cardiorespiratory Fitness [c]	
Variable	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Hypertriglyceridemia [d]	1.4 (0.8, 2.6)	0.24	2.3 (1.0, 5.2)	0.038	2.3 (1.1, 5.1)	0.034
Low HDL-c [e]	0.7 (0.3, 1.7)	0.42	0.8 (0.2, 3.7)	0.79	1.7 (0.4, 6.4)	0.45
Impaired fasting Glucose [f]	3.3 (1.6, 6.7)	0.001	1.5 (0.6, 4.0)	0.37	0.8 (0.3, 2.3)	0.74
Elevated systolic BP [g]	2.7 (1.3, 5.4)	0.006	5.0 (2.2, 11.5)	<0.001	1.5 (0.5, 4.0)	0.44
1 risk factor [h]	1.2 (0.7, 2.0)	0.50	0.7 (3.0, 1.5)	0.33	0.6 (0.3, 1.4)	0.25
2 risk factors [i]	1.8 (0.9, 3.2)	0.07	3.0 (1.4, 6.7)	0.006	2.4 (1.2, 5.0)	0.017
Cardiometabolic risk * [j]	2.6 (1.5, 4.5)	<0.001	2.5 (1.2, 5.3)	0.020	3.3 (1.5, 7.3)	0.002

The presence or absence of at risk levels of the two anthropometric indices and cardiorespiratory fitness (yes/no) was used as the dependant variable with the healthy weight group for each anthropometric used as the reference group (OR = 1.0). Calculated odds ratios (OR) are presented with their 95% confidence intervals (CIs). Models were adjusted for age. HDL-c = high-density lipoprotein cholesterol; BP = Blood Pressure. CRF = cardiorespiratory fitness. *Cardiometabolic risk was constructed using the following variables: Triglycerides, HDL-c (inverted) glucose and systolic BP . [a] Healthy *N* = 171, overweight/obese *N* = 90. [b] Healthy *N* = 230, High *N* = 31. Healthy CRF *N* = 226, Low CRF *N* = 35.

[d] Healthy BMI-z *N* = 70, overweight/obese from BMI-z *N* = 60; Healthy WHtR *N* = 47, High WHtR *N* = 12. Healthy CRF *N* = 44, Low CRF *N* = 14

[e] Healthy BMI-z *N* = 44, overweight/obese from BMI-z *N* = 34; Healthy WHtR N = 24, High WHtR *N* = 9. Healthy CRF *N* = 20, Low CRF *N* = 13

[f] Healthy BMI-z *N* = 58, overweight/obese from BMI-z *N* = 38; Healthy WHtR N = 33, High WHtR *N* = 10. Healthy CRF *N* = 33, Low CRF *N* = 16

[g] Healthy BMI-z *N* = 53, overweight/obese from BMI-z *N* = 49; Healthy WHtR N = 25, High WHtR *N* = 12. Healthy CRF *N* = 27, Low CRF *N* = 16

[h] Healthy BMI-z *N* = 123, overweight/obese from BMI-z *N* = 61; Healthy WHtR N = 86, High WHtR *N* = 11. Healthy CRF *N* = 85, Low CRF *N* = 16

[i] Healthy BMI-z *N* = 74, overweight/obese from BMI-z *N* = 58; Healthy WHtR N = 43, High WHtR *N* = 13. Healthy CRF *N* = 41, Low CRF *N* = 15

[j] Healthy BMI-z *N* = 93, overweight/obese from BMI-z *N* = 87; Healthy WHtR N = 73, High WHtR *N* = 17. Healthy CRF *N* = 76, Low CRF *N* = 14

Table 4. Results of the ROC analysis to identify optimal BMI-z, WHtR and cardiorespiratory fitness cut-offs to predict increased cardiometabolic risk in boys and girls

Boys	BMI-z	Waist-to-Height Ratio	Cardiorespiratory fitness	BMI-z + Waist-to-Height Ratio	BMI-z + Cardiorespiratory fitness
AUC (95% CI)	0.62 (0.56, 0.67)	0.61 (0.55, 0.67)	0.58 (0.51, 0.64)	0.74 (0.64, 0.85)	0.39 (0.27, 0.50)
PPV (%)	35.1	34.6	28.6	64.6	53.5
NPV (%)	79.7	78.9	73.5	72.7	58.7
P Value	0.002	0.004	0.042	< 0.001	0.064
Sensitivity (%)	62.7	60.1	53.3	71.4	48.5
Specificity (%)	55.8	56.9	49.2	62.5	42.2
Cut-points	0.52 / 70**	0.43	46.2	0.48	46.9
Girls					
AUC (95% CI)	0.67 (0.61, 0.73)	0.64 (0.57, 0.69)	0.59 (0.53, 0.65)	0.67 (0.57, 0.79)	0.49 (0.37, 0.61)
PPV (%)	43.2	44.7	42.5	66.1	50.0
NPV (%)	73.5	74.6	73.1	69.8	51.4
P Value	<0.001	<0.001	0.01	0.004	0.89
Sensitivity (%)	60.1	61.1	60.2	71.2	55.7
Specificity (%)	58.5	60.2	57.3	61.8	45.3
Cut-points	0.63 / 74**	0.42	42.3	0.46	41.9

The AUC was computed over the entire range of specificity and sensitivity values. Results represent the optimal BMI-z, WHtR and cardiorespiratory fitness cut-points of these continuous measures as identified by the Youden index. *Cardiometabolic risk was calculated from the following variables: Triglycerides, HDL-c (inverted) glucose and systolic BP. ** Optimal cut-points are presented as z-score / percentile for BMI-z only to aid interpretations. AUC = Area under the curve. PPV = positive predictive value; NPV = Negative predictive value.