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Utility of three anthropometric indices in assessing the cardiometabolic risk profile in children.

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Running Title: Cardiometabolic risk

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

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Abstract

Objectives: To evaluate the ability of BMI, WC and WHtR to identify increased cardiometabolic risk in pre-adolescents.

Methods: This is a cross-sectional study involving 192 children (10.92 ± 0.58 years, 56% female) from the United Kingdom between 2010 and 2013. Receiver operating characteristic curves determined the discriminatory ability of BMI, WC and WHtR to identify individuals with increased cardiometabolic risk (increased clustered triglycerides, HDL-cholesterol, systolic blood pressure, cardiorespiratory fitness and glucose).

Results: A WHtR ≥ 0.5 increased the odds by 5.2 (95% confidence interval 2.6, 10.3) of having increased cardiometabolic risk. Similar associations were observed for BMI and WC. Both BMI-z and WHtR were fair predictors of increased cardiometabolic risk although BMI-z demonstrated the best trade-off between sensitivity and specificity, 76.1% and 63.6%, compared to 68.1% and 65.5% for WHtR. Cross-validation analysis revealed that BMI-z and WHtR correctly classified 84% of individuals (kappa score = 0.671, 95% CI 0.55, 0.79). The sensitivity of the cut-points suggests that 89.3% of individuals were correctly classified as being at risk with only 10.7% misdiagnosed whereas the specificity of the cut-points indicated that 77.8% of individuals were correctly identified as being healthy with 22.2% of individuals incorrectly diagnosed as being at risk.

Conclusions: Findings suggest that WHtR provides similar cardiometabolic risk estimates to age and sex adjusted BMI.

Key Words: Waist-to-height ratio, cardiometabolic risk, youth, screening, adiposity.

Introduction

Body mass index (BMI) is the most commonly used surrogate measure of adiposity in children with its use endorsed by numerous international committees and organizations (Cole and others, 2000; Cornier and others, 2011; Kavey and others, 2011; World Health Organization, 2007). It is an established predictor of a number of adiposity related risk factors but despite its widespread use as a simple and inexpensive screening tool, it is not without its limitations. By its very definition, BMI cannot distinguish between fat and fat-free mass (Khoury and others, 2013) yet obesity is defined as an excess accumulation of body fat with excessive abdominal obesity often cited as a key mediator of cardiometabolic dysfunction.

The measurement of waist circumference (WC) has been used as a simple and inexpensive proxy measure to detect the presence of abdominal obesity with some suggesting that WC may be a more accurate indicator of cardiometabolic risk in youth (Alberti and others, 2009; Savva and others, 2000). Others contend that BMI and WC are comparable indicators (Graves and others, 2014). Since both BMI and WC depend on the use of sex and age specific percentile charts there is interest in alternative anthropometric indices that may be simpler to calculate for practitioners. It has been suggested that a waist-height ratio (WHtR) $\geq$ 0.5 is a valid predictor of cardiometabolic risk irrespective of age, sex or ethnicity and may be superior than BMI to identify increased cardiometabolic risk in youth (Kahn and others, 2014; Khoury and others, 2013). Yet findings are equivocal with some advocating that neither WC nor WHtR are superior than BMI as a screening tool for identifying youth with increased cardiometabolic risk (Bauer and others, 2015; Freedman and others, 2007).

Although variations in methodological approaches and population characteristics may explain the contrasting findings, it is evident that few investigations have examined the predictive utility of different anthropometric indices to discriminate youth for cardiometabolic risk. Moreover, there is a paucity of evidence on the different associations between these anthropometric measures and cardiometabolic risk in samples from different settings within the UK. Therefore, the aim of this study was to examine the utility of BMI, WC and WHtR as screening tools for distinguishing pre-adolescent youth with increased cardiometabolic risk profiles.

Methods:

Data were derived from the collaborative REACH Year 6 study based in Liverpool and Ulster (Boddy and others, 2014) in the summer of 2010 and the baseline data of Scottish children recruited for two unpublished intervention studies between 2011 and 2013. The first of these studies aimed to examine changes in cardiometabolic risk factors following a 10-week school based lifestyle intervention. Ninety-three participants from one school were approached to participate in the study resulting in a convenience sample of 44 pre-adolescent schoolchildren volunteering to participate. The second of these studies aimed to examine changes in cardiometabolic risk factors following an 8-week school based fitness circuit intervention. Eighty-two participants from one school were approached to participate in the study, which resulted in a convenience sample of 55 pre-adolescent schoolchildren volunteering to participate. Only the baseline data of these studies are included in this study.

In total, 101 healthy participants (n = 45 boys, n = 56 girls), from approximately 300 participants invited, were recruited for the REACH Year 6 study that examined the relationships between cardiometabolic risk, adiposity, cardiorespiratory fitness and objectively measured physical activity levels in 9-12-year-old children (Boddy and others,

2014). The study was conducted in Liverpool UK and Belfast UK and a convenience sample of participants were recruited via primary schools (n= 6 Liverpool Schools, n= 1 Belfast school) across both areas. The University of the West of Scotland, Liverpool John Moores University and Ulster University ethics committees approved each study. After gaining informed consent and participant assent from 200 participants for baseline measures, eight were excluded because they were either absent from data collection, withdrew consent or identified themselves as being non-fasted. This left 192 children (10.92 ± 0.58 years, ranging from 9.5 – 11.9 years, 56% female) as the final sample for this cross-sectional study.

Measures

Stature was measured to the nearest 1 mm using a portable stadiometer (Seca Stadiometer, Seca Ltd, Birmingham, UK). Body mass was measured to the nearest 0.1 kg using calibrated electronic weighing scales (Seca Digital Scales, Seca Ltd, Birmingham, UK).Waist circumference was measured at the mid-point between the lower ribs and iliac crest using an anthropometric tape as recommended (Ledoux and others, 1997). 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 (Cole and others, 1995). Using software provided by the Child Growth Foundation (Pan and Cole, 2010) 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. Waist circumference-z scores were calculated relative to the UK 1988 reference data (McCarthy and others, 2001) using software provided by the Child Growth Foundation (Pan and Cole, 2010) with a high WC defined as ≥ the 85th percentile (z-score ≥1.04). WHtR was determined by dividing WC by height with values ≥ 0.5 considered high (Bauer and others, 2015; Graves and others, 2014).

Blood pressure (mmHg) was measured once on the participants left arm using automated monitors (Omron M10-IT Blood Pressure Monitor HEM-7080IT-E, Omron Healthcare UK Ltd, Milton Keynes, UK and a GEDINAMAP ProCare 100–400 Series, UK) after participants sat quietly for 10 mins. Cardiorespiratory fitness (CRF) was measured using the 20m multi stage fitness test (20-MSFT) as described previously (Buchan and others, 2013) or through an individually calibrated, continuous incremental treadmill (HP Cosmos, Traunstein, Germany) test to volitional exhaustion using breath-by-breath gas analysis (Liverpool: Jaeger Oxycon Pro, Viasys Health Care, Warwick, UK, Belfast: COSMED, Quark, Italy). Peak VO_2 was defined as the highest 15-s average oxygen uptake achieved during the test when participants reached volitional exhaustion, and the subjective endpoints were met (respiratory exchange ratio>1.05 and/or HR>199 beats/min) or was calculated from the 20MSFT score using previously validated equations (Leger and others, 1988).

In both of the studies from Scotland, venous samples were obtained from children in a fasted state (12 hour fast) by trained phlebotomists. Prior to sampling, participants confirmed that they were fasted. Blood samples were taken between 9am - 11am with breakfast provided thereafter. Venous samples were collected in a lithium heparin BD Vacutainer Plasma Tube. Plasma was isolated through centrifugation at 3500 rpm for 10 minutes, transferred to aliquots and stored at – 80° C within 2 hours of collection. Samples were subsequently analysed within three months using a RX Monza Clinical Chemistry Analyser (Randox Laboratories Limited, Antrim, United Kingdom) for triglyceride (TG), high density lipoprotein cholesterol (HDL-C), and glucose. TG content was measured through colorimetry and determined through enzymatic hydrolysis (TR 210, Randox, Antrium, UK) with lipases. HDL-C was directly measured by precipitating low-density lipoprotein cholesterol (LDL-C) and very low-density lipoprotein cholesterol (VLDL-C) through adding phosphotungstic acid in the presence of magnesium ions and then centrifuged. Glucose was measured through the

glucose oxidase method (GL 364, Randox, Antrium, UK). All physiological and metabolic measurements were taken on consecutive days beginning with the metabolic measurements.

Venous samples from the collaborative REACH Year 6 study were collected by paediatric phlebotomists between 8.30am and 10.30am on school sites after confirmation of overnight fast. Samples were collected using vacutainers (Gold 5ml Clot Activator, Purple 4ml K2EDTA, Grey 4ml Sodium Fluoride/Potassium Oxalate) and were then transported to the pathology laboratories at Alder Hey Children's Foundation NHS Trust, or the Ulster Hospital for analysis. All analysis assays used in the Reach Year 6 study were standardized between the two sites. Samples were measured using the Architect Aeroset System™ for fasting plasma glucose [REF 3L82-30], HDL-c [REF 3k33-20] and triglycerides [REF 7D74]. All physiological and metabolic measurements were taken on separate days no more than 1 week apart.

Cardiometabolic risk score

A continuous cardiometabolic risk score was constructed using the following variables: Triglycerides, HDL-c (inverted), glucose, systolic BP and cardiorespiratory fitness (VO_2peak (inverted)). 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 (Eisenmann, 2008). The inclusion of cardiorespiratory fitness within the continuous cardiometabolic risk score was based on findings which suggests that high cardiorespiratory fitness confers significant protection from the clustering of cardiometabolic risk factors (Anderssen and others, 2007). 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.

Adverse levels of cardiometabolic risk factors

Reference values from the National Cholesterol Education Program's (NCEP) Pediatric Panel Report (National Cholesterol Education Program, 1992) 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 (National Cholesterol Education Program, 1992). 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 (Zimmet and others, 2007). Elevated Systolic BP was defined as ≥ 90^{th} percentile for age, sex and height in accordance with published guidelines (National High Blood Pressure Education Program, 2004). Participants were classified as 'fit' or 'unfit' using recommended thresholds (46.6 and 41.9 mL/kg/min for boys and girls, respectively) (Boddy and others, 2012).

Statistical analysis

Data were checked for normality of distribution and analysed using the Students t-test or the Mann Whitney test where appropriate. Categorical variables were compared using the chi-squared test. Independent associations between the three anthropometric indices (BMI, WC, and WHtR) and cardiometabolic risk were examined using separate multivariable logistic regression analysis models. Analyses examined the potential effect modifiers of gender and

age with effect modification considered present when the interaction term *P*-value was <0.05. Models then controlled for gender and/or age where necessary. The presence or absence of at risk levels of the three anthropometric indices (yes/no) was used as the dependant variable with the calculated odds ratios (OR) presented with their 95% confidence intervals (CIs).

Receiver operating characteristics (ROC) curve analyses demonstrated the discriminatory ability of the anthropometric indices 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 (Bauer and others, 2015). ROC AUC values of ≥0.90 were considered excellent, 0.80–0.89 good, 0.70–0.79 fair, and <0.70 poor (Metz, 1978). Once we identified which adiposity measure was the single best predictor for increased cardiometabolic risk, we analysed whether adding more adiposity measures would lead to a better prediction of increased cardiometabolic risk. The statistical significance of the difference between AUCs was tested using the method by DeLong and colleagues (DeLong and others, 1988). The goodness of fit of the models was summarised using the Hosmer-Lemeshow chi-square statistic with a corresponding *P*-value <0.05 indicating poor fit. For each model, the Akaike and Bayesian information criteria (AIC and BIC) are presented as descriptive indicators of the relative quality of competing statistical models with smaller AICs and BICs indicating preferred models.

Finally, cross-validation analysis evaluated the accuracy of the established thresholds to classify individuals at increased cardiometabolic risk with the classification agreement, sensitivity, specificity and kappa coefficients presented. Kappa coefficients were interpreted as follows: <0 less than chance agreement; 0.01–0.20 slight agreement; 0.21–0.40 fair; 0.41–

0.60 moderate; 0.61–0.80 substantial; 0.81–1.00 almost perfect agreement (Cohen, 1960). McNemars χ^2 statistic was used to determine whether significant differences were present between the anthropometrical indices in terms of accuracy in classifying individuals according to the presence/absence of increased cardiometabolic risk. AUC's were compared using MedCalc 12.5 (MedCalc software, Mariakerkem Belgium) whereas all other data were analysed using IBM SPSS Statistics 22 (IBM, Chicago, IL, USA) with $P < 0.05$ considered statistically significant.

Results

As shown in Table 1, the overweight/obese group presented with a significantly higher BMI, WHtR, WC, triglycerides, systolic and diastolic blood pressure, but significantly lower cardiorespiratory fitness levels than healthy weight individuals. The overweight/obese group also presented with a significantly higher cardiometabolic risk score than healthy weight individuals. Analysis indicated that 29% of participants were overweight/obese from their BMI; 34% had a high WC and 14% had a high WHtR. For the individual components of the continuous cardiometabolic risk score (triglycerides, HDL-cholesterol, cardiorespiratory fitness, systolic blood pressure and glucose), 8% had hypertriglyceridemia; 16% had low levels of HDL-c; 49% were unfit; 21% had elevated systolic BP and 8% had impaired fasting glucose. Supplementary Figure 1 displays the proportion (%) of individuals who presented with a clustering of individual cardiometabolic risk factors and revealed that 32% presented with no adverse risk factors, 46% presented with one, 13% presented with two and 9% presented with three.

The results of the multivariable logistic regression analysis are presented in Table 2. Participants who were classified as overweight/obese according to their BMI were 4.8 (95%CI 2.3, 10.1, P <0.001) times more likely to be unfit, 1.8 (0.9, 3.4) times more likely to

present with 2 risk factors and 3.1 (1.6, 6.3, P <0.001) times more likely to have increased cardiometabolic risk. Participants with a high WC were 4.6 (1.5, 8.3, P = 0.06) times more likely to have elevated triglycerides, 3.2 (1.4, 7.3, P = 0.07) times more likely to have low HDL-c, 3.5 (1.7, 7.3, P <0.001) times more likely to be unfit and 2.1 (0.9, 4.9, P = 0.003) times more likely to have increased cardiometabolic risk. Participants with an elevated WHtR were 5.3 (2.6, 14.6, P <0.001) times more likely to be unfit, 2.3 (1.0, 5.5, P = 0.042) times more likely to present with 2 cardiometabolic risk factors and 5.2 (2.6, 10.3, P <0.001) times more likely to have increased cardiometabolic risk than those of a healthy WHtR.

The AUCs of the three anthropometric indices for the prediction of cardiometabolic risk are provided in Table 3. Both BMI-z and WHtR demonstrated similar discriminatory abilities for the prediction of cardiometabolic risk suggested by BMI-z cut-off values ≥0.94 and by WHtR cut-off values ≥ 0.43. There was no evidence of poor calibration for any models, with all Hosmer-Lemeshow P-values > 0.05. The BMI-z model demonstrated the best fit when compared to the other adiposity measures since it presented with the lowest AIC and BIC values. BMI-z demonstrated the best trade-off between sensitivity and specificity for detecting increased cardiometabolic risk, 76.1% and 63.6% compared to 68.1% and 65.5% for WHtR. Using a BMI-z threshold cut-point of ≥1.04, the NPV was high, 82.7%, suggesting that the risk of individuals with increased cardiometabolic risk is low for those of a healthy weight. Nonetheless, the PPV was low indicating a high proportion of false positive findings with only 56.5% of individuals who screened positive having increased cardiometabolic risk. For WC-z and WHtR, both the observed PPV and NPV were lower than those observed for BMI-z (Table 3). Comparison between the two models that demonstrated the greatest AUC's, BMI-z and WHtR, revealed no significant differences (P = 0.46). 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 (data not shown).

Comparisons between the anthropometric indices and their ability to predict the presence/absence of increased cardiometabolic risk is shown in Table 4. Only the level of agreement between the two models demonstrating the highest AUC (BMI-z and WHtR) for the prediction of cardiometabolic risk was examined. Cross-validation analysis revealed that BMI-z and WHtR correctly classified 84% of individuals (kappa score = 0.671, 95% CI 0.55, 0.79). The sensitivity of the cut-points suggests that 89.3% of individuals were correctly classified as being at risk with only 10.7% misdiagnosed whereas the specificity of the cut-points suggests that 77.8% of individuals were correctly identified as being healthy with 22.2% of individuals incorrectly diagnosed as being at risk. McNemars χ^2 test revealed no significant differences ($P = 0.79$) between the percentage of individuals whose risk status was correctly predicted by WHtR and BMI-z.

Discussion

Findings from this cross-sectional study suggest that the UK 1990 BMI definition of overweight and obesity performed well in identifying those with increased cardiometabolic risk profiles. Comparisons between healthy weight and overweight/obese individuals stratified by BMI revealed significant differences in measures of adiposity, blood pressure, triglycerides, cardiorespiratory fitness and cardiometabolic risk which is indicative of the well-established link between BMI and health-related disorders (Cornier and others, 2011; Kavey and others, 2011). Despite this well-established link, some argue that adiposity measures that incorporate visceral adiposity may be more accurate in distinguishing individuals at increased cardiometabolic risk since excessive visceral adiposity is a key mediator of cardiometabolic dysfunction (Lemieux and others, 2000). Yet, findings form this study suggests that neither WC-z nor WHtR affords superior discriminatory ability over BMI-z in identifying those at increased cardiometabolic risk.

In this study, it was demonstrated that being overweight/obese according to participants BMI was associated with a more than threefold-increased odds of having increased cardiometabolic risk compared to the healthy weight participants. Strong and significant associations with increased cardiometabolic risk were also apparent in those individuals presenting with an elevated WC and WHtR. Previous investigations have also shown that BMI, WC and WHtR perform similarly when identifying individuals with increased cardiometabolic risk scores (Kahn and others, 2014; Sardinha and others, 2016). Our observations using UK population reference data extend these findings. Another important observation was the predictive ability of both BMI and WC. Despite the external reference data proposed for WC and BMI coming from two different UK samples, it is encouraging to note that both anthropometrical indices are able to identify those individuals at increased cardiometabolic risk.

Findings from the ROC analysis indicated that the AUC's for both BMI-z and WHtR did not differ demonstrating similar abilities in distinguishing those individuals with increased cardiometabolic risk profiles, consistent with the findings of others (Bauer and others, 2015; Graves and others, 2014; Sardinha and others, 2016). Although the AUC values were far from excellent, they are very similar to recent observations (Sardinha and others, 2016) and greater than those noted by Magnussen and colleagues (Magnussen and others, 2010) (AUC = 0.65) who used childhood BMI values to diagnose adult metabolic syndrome. The optimal cut-off points suggested by the ROC analysis for BMI-z (0.94) is below the 85th percentile for BMI (Cole and others, 1995) yet, when examining the UK 1990 BMI population reference data the z score for BMI lies just below the 83rd percentile. The optimal cut-off point suggested by the ROC analysis for WHtR (0.43) appears to be considerably lower than the proposed international cut-off point of 0.5 to identify those at increased cardiometabolic risk. Nonetheless, a WHtR of 0.50 has yet to be established as the optimal threshold for all ages

and ethnicities. Future studies that can determine population specific WHtR thresholds for accurate identification of a number of cardiometabolic disorders may indicate that a WHtR close to 0.43 may be an appropriate cut-off point in this population.

When comparing the classification agreement between the thresholds for BMI-z and WHtR a high level of agreement was noted in addition to a greater sensitivity compared to specificity. We believe that these observations are important since the well-established thresholds appear to be able to identify a greater number of those with increased cardiometabolic risk (i.e. true positives). Given the stigma of being incorrectly identified as being at risk it could be suggested that a higher, and more specific, cut-point is used for identifying individuals with increased cardiometabolic risk. There is certainly merit to this suggestion but if the consequence is a more focused behaviour and lifestyle intervention being accorded to healthy individuals who may be exhibiting some level of risk, our findings support the continued use of the well-established thresholds. As long as resources are available, lifestyle interventions are likely to benefit healthy individuals as well as those identified as being at risk.

Overall, our findings are in agreement with others who have demonstrated that BMI-z and WHtR have similar associations with cardiometabolic risk in youth and that neither WC-z nor WHtR provide superior identification of increased cardiometabolic risk when compared to BMI (Freedman and others, 2007; Graves and others, 2014; Kahn and others, 2014; Sardinha and others, 2016). Yet, the WHtR is a more simplistic index to apply within both the clinical and public setting since its measurement does not require conversion to standardized z-scores or percentiles. If the intention is to communicate simple messages about health risk, certainly the proposal of ‘Keeping your waist circumference to less than half your height’ may be much easier for parents and families to remember and understand.

Nonetheless, a WHtR of 0.50 has yet to be established as the optimal threshold to identify increased cardiometabolic risk for all age groups and ethnicities. Future work needs to determine whether a lower or higher threshold than 0.5 may be more accurate in identifying cardiometabolic risk in different populations. Advocates of the WHtR must also address the numerous protocols available for WC measurement if practitioners are to be advised to capture this measure as part of routine risk assessments (Kahn and others, 2014). Certainly, the standardization of a single protocol would likely enhance the adoption of WC as an indicator of cardiometabolic risk, which could then be used as part of the WHtR index.

Limitations of this study should be considered. This cross-sectional design does not allow us to confer causality whilst the lack of objectively measured physical activity and dietary habits, which are well-established confounders of a number of indicators measured, are acknowledged. Another limitation relates to the different protocols used between studies to measure cardiorespiratory fitness. Direct assessments of VO_{2peak} require specialised equipment and are time-consuming to participants. In the absence of this specialised equipment within Scotland, cardiorespiratory fitness was measured using the 20-m multistage fitness test with $VO2_{peak}$ estimated using validated equations (Leger and others, 1988). Whilst we accept that the determination of VO_{2peak} isn't likely to be equal between different protocols, the equations used to calculate VO_{2peak} from 20mSRT scores have been widely used and are validated for use in this age group of children (Leger and others, 1988).

Finally, whilst the use of clustered cardiometabolic risk scores is common within paediatric research it does have its limitations. The z-score approach is based on the premise that each selected variable is equally important in defining cardiometabolic risk, but at present, this has yet to be confirmed. Despite this limitation, no published weightings for risk components are currently available which is why this method of calculating cardiometabolic risk is commonly

used in paediatric research which can also compensate, to an extent, for the day-to-day fluctuation in single risk factors.

A strength of this study relates to the additional analysis examining the discriminatory ability of established UK thresholds. To the best of our knowledge, only one previous study (Graves and others, 2014) has examined the associations between BMI and WHtR with cardiometabolic risk using 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 and cardiometabolic risk in children living in different cultural settings. Finally, the inclusion of CRF within the cardiometabolic risk score is an additional strength of this study. Individuals with high fitness typically have highly functional cardiorespiratory systems that can attenuate cardiometabolic risk, even in the presence of excess adiposity. To the best of our knowledge, this is the first study to examine the utility of BMI-z, WC-z and WHtR as screening tools to identify cardiometabolic risk that has incorporated CRF.

In conclusion, we have demonstrated that BMI-z and WHtR have similar discriminatory abilities in identifying those at cardiometabolic risk. Yet, despite WHtR being a simple calculation that may offer a greater understanding from families and children its use by practitioners will be limited until a single standardized waist measurement is proposed and widely accepted.

Conflicts of Interest: The authors have no conflicts of interest relevant to this article to disclose.

Author Contributions:

DSB analysed the data and wrote this manuscript. DSB and JSB designed and conceived the study in Scotland. DSB, FMG, NS and EB collected and analysed the data from Scotland.

LMB and GS designed and conceived the study in England. LMB, LF, RD, LEFG, and NDH collected and analysed the data from England. MHM and CC collected and analysed the data from Ireland.

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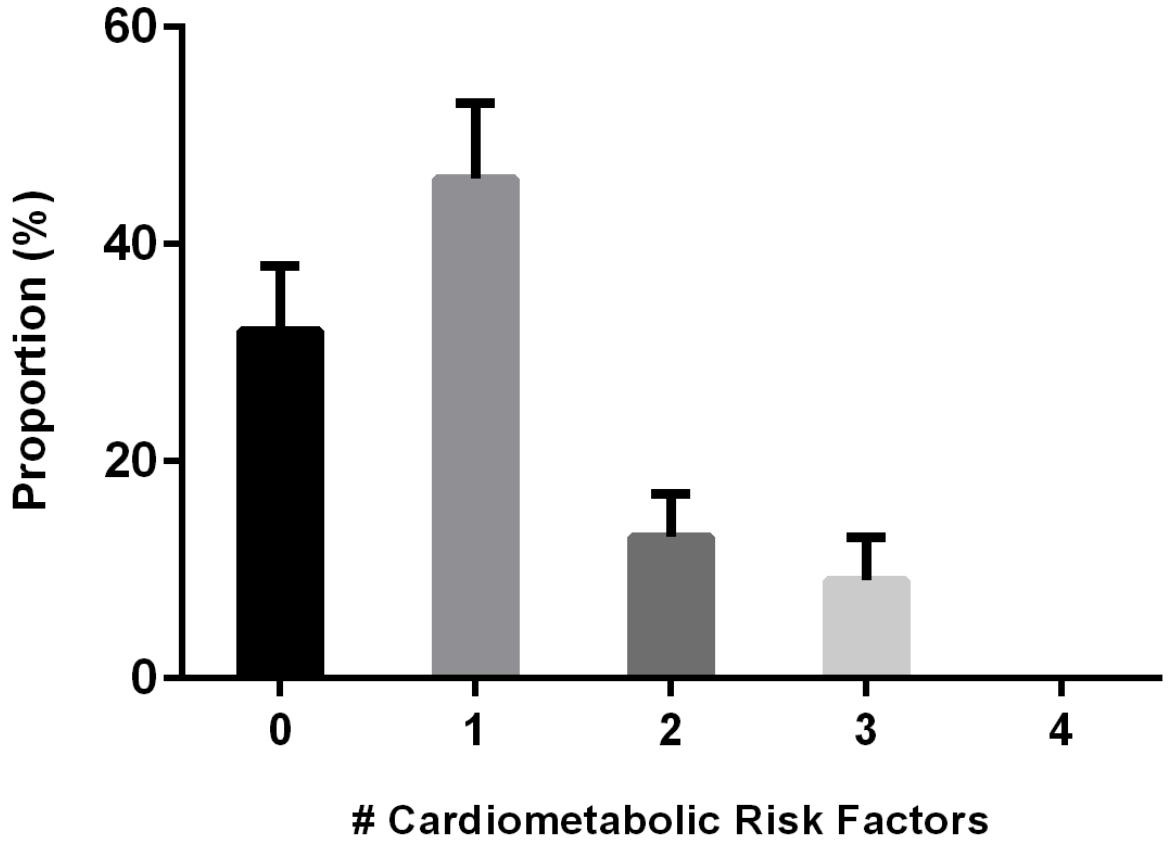

Supplementary Figure 1. Proportion of individuals with cardiometabolic risk factors.

The proportion of individuals with adverse levels for the following cardiometabolic risk factors (triglycerides, HDL-c, glucose, systolic BP and cardiorespiratory fitness) 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). Elevated Systolic BP was defined as ≥ 90th percentile for age, sex and height in accordance with published guidelines (National High Blood Pressure Education Program, 2004). Values ≤ 46.6 and 41.9 mL/kg/min for boys and girls were used to identify low cardiorespiratory fitness (Boddy and others, 2012). Data are presented as mean proportion with 95% CI.

Table 1 – Descriptive characteristics of participants by weight status

Variable	Healthy Weight ǂ N = 137 (72%)	Overweight/obese ǂ N = 55 (28%)	*P* value
Gender % (Girls/Boys)	56/44	58/42	0.73
Age (years)	10.9 (0.6)	11.0 (0.6)	0.41
BMI (kg/m^2)	16.9 (1.5)	23.0 (2.7)	<0.001
Waist-to-height ratio	0.41 (0.04)	0.48 (0.05)	<0.001
Waist Circumference (cm)	59.6 (5.3)	72.2 (7.8)	<0.001
Systolic BP (mmHg)	110 (13)	113 (14)	0.039
Diastolic BP (mmHg)	64 (7)	67 (8)	0.037
Glucose (mmol/L)	4.9 (0.6)	4.8 (8)	0.98
Triglycerides (mmol/L)	0.7 (0.3)	0.8 (0.3)	0.021
HDL-c (mmol/L)	1.6 (0.7)	1.5 (0.6)	0.11
CRF (ml/kg/min)	46.1 (7.3)	40.4 (6.1)	<0.001
Cardiometabolic risk-z score	-0.56 (2.9)	1.05 (2.1)	<0.001

Values presented as mean (SD). BMI = Body mass index; HDL-c = high-density lipoprotein cholesterol; CRF = cardiorespiratory fitness. BP = Blood Pressure. ǂ Participants were classified as obese/overweight, or a healthy weight using BMI-z scores relative to the UK 1990 BMI population reference data (Cole and others, 1995). 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.

Table 2. Multivariable adjusted OR (95% CI) for cardiometabolic risk indicators across 3 anthropometric indices

	Body Mass Index [a]		Waist Circumference [b]		Waist-to-Height Ratio [c]	
Variable	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Hypertriglyceridemia [d]	1.2 (0.4, 3.5)	0.81	4.6 (1.5, 8.3)	0.06≠	1.9 (0.3, 6.4)	0.21
Low HDL-c [e]	0.7 (3.0, 1.5)	0.35	3.2 (1.4, 7.3)	0.07	1.6 (0.6, 4.5)	0.35
Impaired fasting Glucose [f]	1.1 (0.3, 3.8)	0.83	1.4 (0.5, 4.2)	0.55≠	0.9 (0.2, 4.3)	0.91
Elevated systolic BP [g]	0.7 (0.3, 1.4)	0.32	1.2 (0.6, 2.4)	0.68	0.3 (0.6, 1.2)	0.08
Low CRF [h]	4.8 (2.3, 10.1)	<0.001	3.5 (1.7, 7.3)	<0.001	5.3 (2.6, 14.6)	<0.001¶
1 risk factor [i]	1.3 (0.5, 3.2)	0.57	1.5 (0.8, 2.8)	0.19ǂ	0.5 (0.1, 2.4)	0.40ǂ
2 risk factors [j]	1.8 (0.9, 3.4)	0.09ǂ	1.2 (0.5, 2.8)	0.75	2.3 (1.0, 5.5)	0.042
Cardiometabolic risk * [k]	3.1 (1.6, 6.3)	<0.001	2.1 (0.9, 4.9)	0.003	5.2 (2.6, 10.3)	<0.001

The presence or absence of at risk levels of the three anthropometric indices (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). ǂ Model was adjusted for age. ≠ Model was adjusted for gender. ¶ Model was adjusted for age and gender. HDL-c = high-density lipoprotein cholesterol; BP = Blood Pressure. CRF = cardiorespiratory fitness. * Cardiometabolic risk score (Top tertile vs. rest was used). [a] Healthy *N* = 137, overweight/obese *N* = 55. [b] Healthy *N* = 125, High *N* = 66. [c] Healthy *N* = 164, High = 28.

[d] Healthy BMI-z *N* = 11, overweight/obese from BMI-z *N* = 5; Healthy WC-z *N* = 8, High WC-z *N* = 11; Healthy WHtR N = 12, High WHtR *N* = 4.

[e] Healthy BMI-z *N* = 19, overweight/obese from BMI-z *N* = 11; Healthy WC-z *N* = 6, High WC-z *N* = 18; Healthy WHtR N = 24, High WHtR *N* = 6.

[f] Healthy BMI-z *N* = 11, overweight/obese from BMI-z *N* = 4; Healthy WC-z *N* = 1, High WC-z *N* = 7; Healthy WHtR N = 13, High WHtR *N* = 2.

[g] Healthy BMI-z *N* = 26, overweight/obese from BMI-z *N* = 14; Healthy WC-z *N* = 48, High WC-z *N* = 15; Healthy WHtR N = 38, High WHtR *N* = 2.

[h] Healthy BMI-z *N* = 55, overweight/obese from BMI-z *N* = 41; Healthy WC-z *N* = 51, High WC-z *N* = 42; Healthy WHtR N = 73, High WHtR *N* = 22.

[i] Healthy BMI-z *N* = 57, overweight/obese from BMI-z *N* = 29; Healthy WC-z *N* = 51, High WC-z *N* = 34; Healthy WHtR N = 69, High WHtR *N* = 16.

[j] Healthy BMI-z *N* = 16, overweight/obese from BMI-z *N* = 18; Healthy WC-z *N* = 15, High WC-z *N* = 19; Healthy WHtR N = 22, High WHtR *N* = 11.

[k] Healthy BMI-z *N* = 31, overweight/obese from BMI-z *N* = 25; Healthy WC-z *N* = 21, High WC-z *N* = 34; Healthy WHtR N = 43, High WHtR *N* = 18.

Table 3. Results of the ROC analysis to identify optimal BMI-z, WC-z and WHtR cut-offs to predict increased cardiometabolic risk.

Variable		BMI-z	Waist Circumference-z	Waist-to-Height Ratio
Cardiometabolic risk*	AUC	0.72	0.67	0.71
	(95% CI)	(0.65, 0.79)	(0.59, 0.73)	(0.63, 0.77)
	PPV (%)	56.5	39.6	45.6
	NPV (%)	82.7	76.5	80.6
	P Value	<0.001	<0.001	<0.001
	Sensitivity (%)	76.1	64.6	68.1
	Specificity (%)	63.6	55.4	65.5
	Hosmer-Lemeshow *P* value	0.36	0.93	0.77
	AIC	195.6	213.4	205.6
	BIC	198.7	302.1	216.2
	Cut-points**	0.94 / 82.7	0.50 / 69	0.43

The AUC was computed over the entire range of specificity and sensitivity values. Results represent the optimal BMI-z, WC-z and WHtR cut-points of these continuous measures as identified by the Youden index. *Cardiometabolic risk was calculated from the standardized values (z-scores calculated separately for gender and by 1 yr. age groups) of the following variables: Triglycerides, HDL-c (inverted), glucose, systolic BP and cardiorespiratory fitness (VO_2peak (inverted)) with the top tertile vs. rest used to indicate increased risk. ** Optimal cut-points are presented as z-score / percentile for BMI-z and WC-z only to aid interpretations. AUC = Area under the curve. PPV = positive predictive value; NPV = Negative predictive value; AIC = Akaike information criteria; BIC = Bayesian information criteria.

Table 4 Comparison of classification agreement, sensitivity, specificity and kappa coefficients between selected anthropometric indices for identfying individuals at increased cardiometabolic risk.

	Agreement %	Kappa (95% CI)	Sensitivity %	Specificity %	P value for McNemar's χ^2 statistic
WHtR vs. BMI-z for cardiometabolic risk*	84	0.671 (0.55, 0.79)	89.3	77.8	0.79

* Established thresholds for BMI-z and WHtR (BMI-z score ≥1.04; WHtR ≥0.5) were used to compare classification agreements.