Title: The hypertriglyceridaemic waist phenotype and waist-to-height ratio as simple identification tools for cardiometabolic disorders and low cardiorespiratory fitness in children and adolescents

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Abstract

Objective Hypertriglyceridaemic waist (HW) and waist-to-height ratio (WHTR) are simple clinical tools that identify adults at risk of cardiometabolic disorders and cardiovascular disease. However, whether the same applies in youth is under-researched and this study therefore investigated whether the HW phenotype and WHTR could be used to screen for cardiometabolic disorders in children and adolescents. *Study Design* This was a cross-sectional design study. Anthropometry, biochemical parameters and cardiorespiratory fitness (CRF) were assessed in 234 participants (122 girls) aged 10-19 y from Bedfordshire, UK. The HW phenotype was defined as a waist circumference $\geq 90^{th}$ percentile for age and sex and triglyceride concentrations ≥ 1.24 mmol/L and a high WHTR defined as > 0.5. Analysis of covariance and logistic regressions were used in the analysis. *Result* In participants with the HW phenotype, the odds of having high CRF (mL/kg/min) were lower (0.045; 95% CI 0.01, 0.42), and the odds of having low HDL (4.41; 1.50, 12.91), impaired fasting glucose (3.37; 1.06, 10.72), and ≥ 1 (4.78; 1.32, 17.29) and ≥ 2 risk factors (7.16; 2.38, 21.54) were higher, than those without the phenotype. Those with a high WHTR had higher odds of having low HDL (2.57; 1.11, 5.95), high diastolic blood pressure (3.21; 1.25, 8.25) and ≥ 2 risk factors (5.57; 2.05, 15.17) than those with normal WHTR. *Conclusion* The HW phenotype may be a better simple marker than WHTR for identifying children and adolescents at risk for cardiometabolic disorders.

Introduction

Cardiovascular disease (CVD) is the most common cause of death in Europe, being responsible for nearly half (48%) of all deaths and costing the European Union economy €192 billion per year (1). Type 2 diabetes mellitus (T2DM) is also a major health burden that confers to increased risk of death from cardiovascular causes and an increased likelihood of coronary heart disease (CHD) and macrovascular complications, such as stroke and amputations (2). There are several cardiometabolic risk factors that predispose individuals to CVD and T2DM, including obesity, dyslipidaemia, hypertension, impaired fasting glucose and low cardiorespiratory fitness (CRF) (3-4). These risk factors have been identified in children and adolescents (5) and may be linked to the increasing prevalence of T2DM and manifestation of atherosclerotic processes in young (6).

The metabolic syndrome (MetS) is a clustering of risk factors for CVD and T2DM (7), however, a major limitation is that there is no globally accepted definition for use in paediatric populations and prevalence values ranged between 6 and 39% in overweight youths according to eight different definitions (8). It is hypothesised that insulin resistance may be the underlying cause of MetS (7) and viscerally located fat has a

proatherogenic function due to its metabolic and anatomical characteristics that favour insulin resistance and proinflammatory and procoagulant states (7). Visceral obesity may represent a relative inability of subcutaneous adipose tissue to act as a protective 'metabolic sink' for storage of surplus energy derived from dietary triglycerides, leading to ectopic fat deposition (7). Evidence from imaging studies (using MRI and computed tomography) appears consistent that it is excess visceral adiposity and not the amount of subcutaneous abdominal fat which is the key correlate of metabolic abnormalities observed in overweight adults and youths (9-10).

However, costs and risks to the patient associated with accurate measurement of visceral adiposity and insulin resistance represent major challenges to widespread use in clinical practice. Waist circumference (WC) may be a good indicator of visceral adiposity in youths (11). However, not all individuals with a high WC are viscerally obese and at high risk of T2DM or CVD (7). Thus, abdominal obesity may be characterised by a) the presence of abdominal obesity in isolation, which is likely associated with excess subcutaneous fat or b) the presence of abdominal obesity associated with metabolic abnormalities, which is likely associated with excess visceral adiposity (12). To distinguish viscerally obese from subcutaneously obese individuals, the simultaneous measurement of fasting triglycerides and WC has been proposed as a simple screening tool (13). Hypertriglyceridaemia and an elevated WC (hypertriglyceridaemic waist [HW]) could represent a simple clinical phenotype to identify individuals with excess visceral adipose tissue. Indeed, the presence of HW identifies higher visceral fatness in T2DM (14) and when HW is present, it might thus be expected that low HDL, high blood pressure and increased blood glucose are also present given that these are all features of MetS (7). Waist-to-height ratio (WHTR) may also accurately reflect visceral adipose tissue and cardiometabolic health risk in youths as it takes the height of an individual into consideration (15) and these two measures (HW and WHTR) may thus be alternative concepts to MetS as simple and reliable indicators of cardiometabolic risk associated with visceral obesity, which could improve cost-effective screening of the population in primary care settings (13).

The HW phenotype effectively identifies adults characterised by cardiometabolic disorders (13, 16), while the internationally proposed WHTR boundary value of 0.5 predicts diabetes and CVD in men and women (17). However, to the authors' knowledge, only data from Iranian youths has been published concerning the use of HW to identify cardiometabolic disorders in youths (18-20). In Iranian adolescents, those with the HW phenotype were more likely to have high LDL, low HDL, hypercholesterolaemia and ≥ 1 and ≥ 2 cardiometabolic risk factors than those without the phenotype (19). However, there appears to be no similar

evidence that explores the association of the HW phenotype to individual cardiometabolic risk factor levels, a clustering of risk factors or level of CRF in youths. Furthermore, the suitability of the HW phenotype as a screening tool for cardiometabolic disorders in youths is under-researched and has not been explored in a sample of European youths. Concerning WHTR, overweight classified children are more likely to have higher systolic BP and triglyceride levels and lower HDL compared to non-overweight (21). However, there appears to be no evidence that explores the association of WHTR to clustering of risk factors or level of CRF in youths, while the suitability of the internationally proposed 0.5 boundary value is unexplored.

The purpose of this study was therefore to investigate the association of the HW phenotype and WHTR with cardiometabolic risk factors and CRF in a sample of children and adolescents from Bedfordshire, UK, and their potential as screening tools for the presence of cardiometabolic disorders.

Methodology

Sample

The 234 participants (122 girls) aged 10-19 y that took part in this study were recruited on a voluntary basis from local schools and via advertisement in local press in Bedfordshire, UK. 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. For participants aged 16 y or less, written informed consent was obtained from parents and verbal assent from the participants before any testing procedures. For participants over 16 y of age, written informed consent was obtained from the participant only.

Measurements

Age (y) was recorded as a decimal value for each participant. Information on sexual maturity was not collected and associated limitations are alluded to in the discussion section. Ethnicity was recorded as white or non-white. Stature and WC (at the umbilicus) were recorded to the nearest 0.1 cm using the portable Leicester Height Measure (Seca, Birmingham) and an adjustable tape measure (Hoechstmass, Germany), respectively. WHTR was calculated as WC (cm) ÷ stature (cm). Body mass was recorded to the nearest 0.1 kg using the Tanita BC-418® (Tanita Corp., Tokyo). 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 and weight (22). Body fat% (BF%) and fat free mass (FFM) were measured to the nearest 0.1% and 0.1 kg, respectively, via bioelectrical impedance analysis using the Tanita BC-418® (Tanita Corp., Tokyo). Participants were required to have fasted from 9 pm the night

before the measurement. Measurements were taken between 8-10 am and participants were instructed to bring a snack with them to eat for breakfast after testing.

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 then 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) (23).

To determine CRF, participants completed an age- and sex-specific all-out progressive cycle ergometer test to exhaustion using a previously validated protocol (24). 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 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 (25) and expressed as litres per min (L/min) and mL per kilogram body mass per min (mL/kg/min).

A continuous clustered cardiometabolic risk variable was constructed by standardising and summing the *z*-scores of the following continuously normally distributed cardiometabolic variables: TC, HDL, diastolic BP and fasting blood glucose. A second clustered risk score was constructed that also included the *z*-score of CRF (mL/kg/min; inverted). The second risk score was constructed only for the 147 participants that provided valid CRF data.

Definition of terms

A high WC was defined as ≥ 90th percentile for age and sex according to McCarthy et al (26) reference curves for children aged 10-16.9 y. For participants aged 17-19 y, high WC was defined as ≥ 94 cm and 80 cm, respectively, for males and females according to the International Diabetes Federation (IDF) adult definition for MetS (27). In children aged 10-19 y, reference values from the National Cholesterol Education Program's (NCEP) Pediatric Panel Report (28) define a borderline high range for triglyceride concentrations as 90-129 mg/dL (1.02-1.46 mmol/L). Thus, the midpoint value for triglyceride concentrations (≥ 110 mg/dL = 1.24 mmol/L) was taken as the 90th percentile value for age. HW was defined as having a high WC (≥ 90th percentile

for age and sex) and elevated triglyceride concentrations (≥ 1.24 mmol/L). An elevated WHTR was defined as > 0.5; a boundary value that may be suitable across all ages, sex and ethnicities (29).

Hypercholesterolaemia was defined as TC ≥ 200 mg/dL (5.17 mmol/L) (28). The NCEP Pediatric Panel Report (28) gives a range of 35-45 mg/dL (0.91-1.16 mmol/L) for borderline low HDL levels for all sexes and ages. Therefore, the midpoint of this range (≤ 40 mg/dL = 1.03 mmol/L) was used as the 10^{th} percentile value to define low HDL. Impaired fasting glucose was defined as ≥ 5.6 mmol/L according to the IDF recommendation for children and adolescents (27). High systolic and diastolic BP were defined as ≥ 90^{th} percentile for age, sex, and height based on published reference values (30). The Updated Task Force on High Blood Pressure in Children and Adolescents only applies to individuals up to the age of 18 y, therefore cutoffs of ≥ 130 and ≥ 85 mmHg for systolic and diastolic BP, respectively, were used for participants above this age on the basis of recommendations of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (31).

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 (25). A median split was also used to define high CRF in absolute terms (i.e. L/min) and participants with values ≥ 1.67 L/min were categorised into the high fit group. Level of adiposity was defined using BF% ≥ 85^{th} and 95^{th} percentiles, respectively, for overweight and obesity according to McCarthy et al (32) body fat reference curves for children. MetS was defined as ≥ 3 of the following cardiometabolic risk factors: high WC, low HDL, elevated triglycerides, elevated systolic or diastolic BP, and impaired fasting glucose.

Statistical analyses

All analyses were completed using SPSS version 19.0 (SPSS Inc., Chicago, IL.). Sex differences in baseline characteristics were explored using one-way ANOVA. Associations between *z*WC, triglycerides and WHTR with cardiometabolic risk factors were explored using partial correlation analysis controlling for age, sex and ethnicity. For correlations between adiposity markers (*z*WC and WHTR) and CRF expressed in L/min, FFM was additionally controlled for as this variable is known to influence VO_{2max}. MANCOVA was used to compare cardiometabolic risk factor levels (TC, HDL, blood glucose, systolic BP, diastolic BP, CRF and clustered risk scores) between participants with and without the HW phenotype and between WHTR overweight and non-overweight. Covariates entered into the models were age, sex and ethnicity. Separate ANCOVA was conducted for CRF expressed in L/min where FFM was included as a further covariate. Odds ratios (ORs) and 95%

confidence intervals (CI) for having hypercholesterolaemia, low HDL, impaired fasting glucose, elevated systolic BP, elevated diastolic BP and high CRF were explored using logistic regression. Participants without the HW phenotype (i.e. normal WC and normal triglyceride levels) and WHTR non-overweight were considered as the reference groups. Logistic regression was also employed to determine the likelihood (OR, 95% CI) of having ≥ 1 and ≥ 2 of the following risk factors: hypercholesterolaemia, low HDL, impaired fasting glucose and elevated systolic or diastolic BP. All regression models were controlled for age, sex and ethnicity with FFM additionally controlled for in the model where CRF was expressed in L/min. The prevalence of MetS according to HW and WHTR category was also calculated and differences explored using X^2. The level of significance was set at $p < 0.05$.

Results

Table 1 shows the descriptive characteristics of the participants. One-way ANOVA revealed that girls had significantly higher scores than boys for *z*-weight, *z*BMI, BF%, WHTR, TC, and triglycerides**.** Boys had significantly higher scores for systolic BP, diastolic BP, and CRF compared to girls. 73.8% of the sample were non-overweight, 11.8% overweight and 14.3% obese according to BF% (32).

Of the 234 participants, 22.2% had a high WC and 14.5% had hypertriglyceridaemia. 7.3% were defined as having the HW phenotype; 6.3% in boys and 8.2% in girls (difference not significant, $p = 0.57$). The prevalence of overweight according to WHTR was 16.7%; 9.8% in boys and 23% in girls ($p = < 0.01$). Of the remaining cardiometabolic risk factors, 5.6% had hypercholesterolaemia (28), 19.7% had low levels of HDL (28), 12.8% had impaired fasting glucose (27), 15% had high systolic BP (31), 15.8% high diastolic BP (31), and 17.5% had low CRF (mL/kg/min) (25).

Partial correlation analysis showed that *z*WC was associated with triglycerides ($r = 0.23$, $p = 0.01$), HDL ($r = -0.16$, $p = 0.05$), blood glucose ($r = 0.17$, $p = 0.05$), diastolic BP ($r = 0.25$, $p = < 0.01$) and CRF when expressed in mL/kg/min ($r = -0.58$, $p = < 0.01$) and L/min ($r = -0.24$, $p = < 0.01$). However, *z*WC was not associated with TC ($r = 0.05$, $p = 0.53$) or systolic BP ($r = 0.15$, $p = 0.08$). In addition to being associated with *z*WC, triglyceride levels were also associated with TC ($r = 0.17$, $p = 0.04$), blood glucose ($r = 0.18$, $p = 0.03$) and diastolic BP ($r = 0.16$, $p = 0.05$), but not associated with HDL ($r = -0.13$, $p = 0.12$), systolic BP ($r = 0.10$, $p = 0.22$) or CRF when expressed in mL/kg/min ($r = -0.12$, $p = 0.17$) or L/min ($r = -0.02$, $p = 0.78$). WHTR was associated with triglycerides ($r = 0.20$, $p = 0.02$) and CRF when expressed in mL/kg/min ($r = -0.52$, $p = < 0.01$)

and L/min (r = -0.28, p < 0.01), but was not associated with TC (r = 0.11, p = 0.21), HDL (r = -0.14, p = 0.09), blood glucose (r = 0.12, p = 0.17), systolic BP (r = 0.01, p = 0.87) or diastolic BP (r = 0.15, p = 0.08).

Comparisons were made between participants with and without the HW phenotype and between those non-overweight and overweight according to WHTR for levels of cardiometabolic risk factors (see Table 2). MANCOVA revealed that when controlling for age, sex, and ethnicity, participants with the HW phenotype had significantly higher levels of TC, blood glucose and diastolic BP compared to those without the phenotype. Boys and girls with the HW phenotype also had significantly lower levels of HDL and CRF (only when expressed in mL/kg/min). The HW group also had significantly higher average scores for both clustered cardiometabolic risk scores compared to the non-HW group. For WHTR, overweight participants had significantly lower levels of HDL and CRF and significantly higher diastolic BP compared to non-overweight participants. Overweight participants also had increased clustered cardiometabolic risk but only when CRF was included in the score.

Multivariate adjusted ORs (and 95% CIs) for having adverse levels for cardiometabolic risk factors across HW phenotypes and WHTR categories are presented in Table 3. Children and adolescents with the HW phenotype were significantly more likely to have low HDL and impaired fasting glucose and less likely to have high CRF (when expressed in mL/kg/min only) compared to those without the HW phenotype. Those overweight according to WHTR were significantly more likely to have low HDL and elevated diastolic BP and less likely to have high CRF (only when expressed in L/min) compared to non-overweight participants. Children and adolescents with the HW phenotype were 4.78 (95% CI 1.32, 17.29, p = 0.02) and 7.16 (2.38, 21.54, p = < 0.01) times more likely to have ≥ 1 and ≥ 2 of the following risk factors, respectively, than those without the HW phenotype (hypercholesterolaemia, low HDL, high systolic or diastolic BP, and impaired fasting glucose). For WHTR, overweight participants were not significantly more likely to have ≥ 1 risk factor (1.98; 95% CI 0.91, 4.29, p = 0.08) than non-overweight participants, but were significantly more likely to have ≥ 2 risk factors (5.57; 2.05, 15.17, p = < 0.01). 82.4% (N = 14) of participants with the HW phenotype had MetS compared to only 1.8% (N = 4) of participants who did not have the phenotype (p = < 0.001). 25.6% (N = 10) of overweight WHTR participants had MetS compared to 4.1% (N = 8) of participants who were non-overweight (p = < 0.001).

Discussion

This study, conducted on a sample of UK based children and adolescents, revealed that the presence of the HW phenotype and a high WHTR conferred to increased likelihood of cardiometabolic abnormalities. This is one of the first studies to explore the suitability of HW as a screening tool for the presence of cardiometabolic abnormalities in children and adolescents and is the first of its kind in a sample based in a European constituent.

The HW phenotype and WHTR were used in this study as an alternative, or stand in, for the metabolic syndrome as rationalised above, and it was revealed that WHTR-overweight children had higher diastolic BP and lower HDL and CRF levels compared to non-overweight participants, with these differences also being evident between those with the HW phenotype compared to those without. However, participants with the HW phenotype also had higher levels of TC and blood glucose compared to their non-HW counterparts. Although this type of evidence is lacking in youths, these are important findings as CRF and risk factor levels track from childhood and adolescence into adulthood (33-34) and the development of CRF during youth is linked to improved CVD profile in adult years (34). Similarly, in Iranian adult males, systolic and diastolic BP and TC were higher and HDL lower in those with HW phenotype (16), although blood glucose did not differ between group combinations of triglyceride and WC levels (16). These are important findings as CHD and stroke mortality increase progressively and linearly from BP levels as low as 115 mmHg systolic and 75 mmHg diastolic upward in adults (35) and there is equivocal evidence that dyslipidaemia causes atherosclerotic vascular disease (3). A progressive relationship between glucose levels and cardiovascular events was also reported in a meta-regression analysis study in 95,783 adults (36).

A clustering of cardiometabolic risk factors may confer additive risk beyond the level predicted by individual components (37) and as risk factor clustering tracks from childhood into adulthood (33), this study explored whether a clustered risk score differed between children and adolescents with and without the HW phenotype and central obesity defined by WHTR. Two clustered risk scores were constructed (with and without the inclusion of CRF) and participants with the HW phenotype had increased clustered risk compared to those without the phenotype regardless of whether CRF was included or not. For WHTR, clustered risk was only higher in the overweight group when CRF was included in the score. Previous evidence demonstrated increased severity of asymptomatic coronary and aortic atherosclerosis in young people with increasing number of cardiometabolic risk factors present (38) and the HW phenotype may thus identify individuals at high risk of cardiometabolic illness to a greater degree than WHTR.

The HW phenotype and proposed 0.5 WHTR boundary value have received very limited attention in paediatric populations. In Tehranian adolescents, those with the HW phenotype were more likely to have high

LDL (OR 1.8; 95% CI 1.3, 2.7), low HDL (1.6; 1.3, 2.0), hypercholesterolaemia (2.9; 2.0, 4.2), elevated BP (2.1; 1.7, 2.7), and ≥ 1 (1.4; 1.1, 1.7) and ≥ 2 (2.2; 1.6, 3.0) metabolic risk factors than those without the phenotype (19). Similarly, youths with the HW phenotype in the current research were more likely to have low levels of HDL and ≥ 1 and ≥ 2 risk factors. However, the likelihood of having hypercholesterolaemia or elevated systolic or diastolic BP was not higher, although the odds ratio for hypercholesterolaemia was close to statistical significance ($p = 0.07$). Unlike Esmaillzadeh et al's (19) study, participants with the HW phenotype in the current research were more likely to have impaired fasting glucose. However, it is not possible to account for any impact of differences in ethnic background or dietary intake on glucose levels between the studies, which may be influencing factors. In the present study, the odds of having high CRF (mL/kg/min) were lower in participants with the HW phenotype compared to those without and this was not explored by Esmaillzadeh et al (19) and thus represents a novel finding.

WHTR-overweight participants were more likely to have low HDL, elevated diastolic BP and ≥ 2 risk factors compared to their non-overweight counterparts. In Australian youths, those with WHTR ≥ 0.48 had significantly higher values for triglycerides (boys only), systolic BP (girls only) and lower levels of HDL compared to those with ratios < 0.46 (21), but there appears to be no study that has investigated the 0.5 boundary value specifically in youths. Regarding CRF, the odds of having high CRF were lower in WHTR-overweight participants but only when expressed in absolute terms (L/min). To the author's knowledge, this is the first study to investigate the association of WHTR to CRF. CRF was associated with HW only when expressed relative to body mass (mL/kg/min). As FFM was adjusted for in correlation analysis for CRF expressed in absolute terms (L/min) but not when expressed relative to body mass (mL/kg/min), it seems that the relationship between CRF and the phenotypes described in this study (HW and WHTR) may be mediated through body composition. It would have been statistically inappropriate to adjust for FFM in partial analysis for adiposity markers and CRF when expressed relative to body mass (mL/kg/min) as body mass is used to determine the dependent variable and is also strongly related to the controlling variable (FFM) ($r = 0.94$ in our dataset). However, for arguments sake, when this analysis was conducted, significant ($p < 0.01$) negative associations between zWC and WHTR with CRF (mL/kg/min) remained evident ($r = -0.31$ and -0.35, respectively). Shaibi et al (39) reported similar findings in overweight Latino youths. Simple correlation analysis showed that WC was significantly related to CRF when expressed in mL/kg/min ($r = -0.53$, $p < 0.001$), however, when analysed using partial correlation analysis with models adjusted for age, sex, fat mass and FFM and CRF expressed in absolute terms (L/min), there was no significant relationship ($r = 0.05$, $p = 0.58$). Further

298 research including longitudinal and intervention studies are thus needed to determine whether changes in HW
299 and WHTR status over time are linked to improved levels of CRF.

300 As stated, abdominal obesity may be characterised by a) the presence of abdominal obesity in isolation,
301 or b) the presence of abdominal obesity associated with metabolic abnormalities, which is likely associated with
302 excess visceral adiposity (12). Accumulation of visceral fat is strongly associated with and may be the cause of
303 cardiometabolic disorders (40) and in children, visceral adiposity is associated with cardiometabolic risk factors
304 (11). Hypertrophied visceral adipocytes are characterised by a hyperlipolytic state that is resistant to the
305 antilipolytic effect of insulin (7). The resulting flux of free fatty acids to the liver stimulates increased secretion
306 of triglyceride-rich lipoproteins, reduced hepatic degradation of apolipoprotein B and insulin leading to
307 hyperapolipoprotein B and hyperinsulinaemia, and to increased hepatic glucose production contributing to
308 glucose intolerance and risk of developing T2DM (7). Previous evidence suggests that WC may be a good
309 indicator of visceral adiposity in youths (41). However, not all individuals with a high WC are viscerally obese
310 or at high risk of CVD and T2DM (12) and WC may be a better predictor of subcutaneous abdominal adipose
311 tissue as opposed to visceral (41). It is proposed that subcutaneous fat may not be detrimental to health and
312 instead acts as a 'metabolic sink' that stores with great efficiency the excess energy derived from dietary
313 triglycerides (12) and data shows that WC by itself is not enough to identify men with the atherogenic metabolic
314 triad (13). Instead, raised triglyceride levels in the presence of an elevated WC may distinguish viscerally obese
315 from subcutaneously obese individuals (13) and, as tested in the present study, may identify individuals with
316 associated cardiometabolic disorders.

317 The data from this present study and past investigations indicates that the HW phenotype and WHTR
318 may be simple, inexpensive tools to identify high-risk youths (19, 21). A limited number of studies, however,
319 have explored the prevalence of HW and high WHTR in this population (18, 20, 42). In 1998, the prevalence of
320 HW in Tehranian 10-19 y-old adolescents was 7.3% for males and 5.6% for females (overall prevalence =
321 6.4%) (18). In the CASPIAN study based in Northern Iran, the HW phenotype was prevalent in 8.5% of boys
322 and girls (mean age 12.07 ± 3.2 y) in 2003-04 (20). In the current study, HW was prevalent in 6.3% of boys and
323 8.2% of girls with an overall prevalence of 7.3%. In 1997, prevalence of a high WHTR ranged from 10.8-19.3%
324 in boys and 7.9-14.5% in girls from the UK (42). The prevalence of a high WHTR was 9.8% in boys and 23%
325 in girls with an overall prevalence of 16.7%. However, the small and heterogeneous sample assessed in this
326 study is unlikely to be representative of a larger regional population and future research should be conducted
327 that incorporates larger representative samples in the UK.

Other important limitations should be considered when interpreting the current study's results. A major limitation is how the HW phenotype was defined. For 10-16 y-olds, an elevated WC was defined as ≥ 90th percentile for age and sex (26) and > 94 cm and 80 cm, respectively, for 17-19 y-old males and females (27). These were selected as individuals with a WC above these thresholds are more likely to have multiple risk factors for CVD and T2DM (43). However, fat distribution is affected by puberty (44) and although an attempt was made to control for this by using age- and sex-specific WC percentiles, data on pubertal development was not collected and it was therefore not possible to present data on HW phenotype prevalence according to pubertal stage. Hypertriglyceridaemia was defined as the midpoint value (≥ 110 mg/dL = 1.24 mmol/L) of the borderline high range for triglycerides provided by the NCEP Pediatric Panel Report (28). However, there have been alternative thresholds proposed to define hypertriglyceridaemia in youths (27) but it is unknown which of these thresholds is most closely linked to adverse health outcomes. There is a need to develop age-, sex- and puberty-specific thresholds since triglyceride levels are also influenced by puberty (45). Another limitation is the cross-sectional design of the study meaning that casual inferences cannot be made. In addition, other factors that may confound the association between HW and WHTR with cardiometabolic risk, such as dietary intake, physical activity levels, pregnancy, presence of Type 1 or Type 2 diabetes, smoking status, or use of oral contraceptives, lipid lowering drugs, or corticosteroids were not accounted for and should be considered in future research.

In conclusion, this study suggests that the HW phenotype may be a better simple marker than WHTR for identifying children and adolescents at risk for cardiometabolic disorders. Because measurement of WC and triglycerides is relatively inexpensive and readily available in clinical settings, use of the HW phenotype may improve the ability of healthcare professionals to identify high-risk youths who may benefit from lifestyle intervention. Future research should evaluate HW and WHTR in larger populations and their potential as universally acceptable tools in primary care settings. In addition, whether decreases in WC and triglycerides confer beneficial effects on cardiometabolic risk factors should be explored.

List of abbreviations:

HW, hypertriglyceridaemic waist; WC, waist circumference; WHTR, waist-to-height ratio; MetS, metabolic syndrome; CRF, cardiorespiratory fitness; TC, total cholesterol; HDL, high-density lipoprotein cholesterol; T2DM, Type 2 diabetes mellitus; CVD, cardiovascular disease; BMI, body mass index; BP, blood pressure; CHD, coronary heart disease; NCEP, National Cholesterol Education Programme.

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Table 1 Descriptive characteristics of participants by sex

	All (*N* = 234)	Boys (*N* = 112)	Girls (*N* = 122)	*p* value[a]
Age (y)	13.38 (2.58)	13.47 (2.50)	13.30 (2.65)	0.62
z-height	0.35 (1.01)	0.33 (1.10)	0.37 (0.92)	0.73
z-weight	0.36 (1.37)	0.12 (1.31)	0.60 (1.38)	0.01
*z*BMI	0.15 (1.47)	-0.13 (1.34)	0.40 (1.54)	0.01
Body fat%	22.18 (8.66)	17.41 (6.40)	26.60 (8.13)	< 0.01
Waist (cm)	70.25 (12.93)	69.11 (12.37)	71.31 (13.40)	0.19
WHTR	0.45 (0.07)	0.43 (0.06)	0.46 (0.08)	< 0.01
TC (mmol/L)	3.91 (0.73)	3.73 (0.71)	4.08 (0.72)	< 0.01
HDL (mmol/L)	1.35 (0.39)	1.34 (0.40)	1.35 (0.38)	0.82
Triglycerides (mmol/L)	0.86 (0.56)	0.77 (0.41)	0.94 (0.67)	0.02
Blood glucose (mmol/L)	4.97 (0.52)	5.03 (0.49)	4.91 (0.54)	0.08
Systolic BP (mm Hg)	111.6 (12.8)	113.8 (15.4)	109.5 (9.4)	0.01
Diastolic BP (mm Hg)	70.2 (7.6)	69.1 (7.6)	71.1 (7.5)	0.04
CRF (mL/kg/min)[b]	42.58 (9.78)	46.58 (8.86)	38.63 (9.05)	< 0.01
CRF (L/min)[b]	1.71 (0.42)	1.85 (0.42)	1.58 (0.36)	< 0.01

BMI, body mass index; WHTR, waist-to-height ratio; TC, total cholesterol; HDL, high-density lipoprotein; BP, blood pressure; CRF, cardiorespiratory fitness; [a] between sexes; [b] *N* = 147 (74 girls). Data reported as mean (SD).

Table 2 Associations between the hypertriglyceridaemic waist phenotype and waist-to-height ratio with cardiometabolic risk factors in children and adolescents (*N* = 234). Covariates entered into the model were age, sex and ethnicity

	Hypertriglyceridaemic waist[a]				Waist-to-height ratio[b]			
	Non-HW	HW	*F*-value	*p* value	Non-overweight	Overweight	*F*-value	*p* value
TC	3.88 (0.72)	4.31 (0.76)	5.74	0.02	3.88 (0.70)	4.06 (0.88)	0.98	0.32
HDL	1.36 (0.37)	1.13 (0.51)	4.84	0.03	1.39 (0.39)	1.13 (0.31)	7.26	0.01
Blood glucose	4.95 (0.51)	5.20 (0.60)	4.07	0.05	4.97 (0.51)	5.00 (0.55)	2.49	0.12
Systolic BP	111.3 (12.9)	115.6 (10.4)	1.65	0.20	111.1 (13.1)	114.1 (10.3)	0.25	0.62
Diastolic BP	69.7 (7.4)	76.5 (6.8)	10.81	< 0.01	69.0 (7.3)	76.2 (5.8)	18.26	< 0.01
Body fat%	21.48 (8.34)	31.69 (6.90)	26.38	< 0.01	19.34 (5.57)	36.68 (6.58)	30.32	< 0.01
CRF (mL/kg/min)[c]	43.15 (9.51)	32.66 (5.57)	10.98	< 0.01	43.88 (8.70)	26.54 (4.33)	43.63	< 0.01
CRF (L/min)[c]	1.71 (0.42)	1.78 (0.37)	1.51	0.22	1.72 (0.42)	1.67 (0.40)	18.57	< 0.01
Clustered risk[d]	-0.09 (2.24)	1.27 (2.42)	5.51	0.02	-0.09 (2.33)	0.50 (1.93)	2.99	0.09
Clustered risk[e]	0.09 (2.43)	2.57 (2.94)	9.14	< 0.01	0.04 (2.49)	2.71 (1.81)	10.12	< 0.01

HDL, high-density lipoprotein cholesterol; BP, blood pressure; CRF, cardiorespiratory fitness; HW, hypertriglyceridaemic waist; [a] non-hypertriglyceridaemic waist *N* = 217, hypertriglyceridaemic waist *N* = 17; [b] non-overweight *N* = 195, overweight *N* = 39; [c] non-hypertriglyceridaemic waist *N* = 136, hypertriglyceridaemic waist *N* = 10, non-overweight *N* = 133, overweight *N* = 13; [d] clustered risk excluding CRF; [e] clustered risk including CRF. Data presented as mean (SD).

Table 3 Multivariate-adjusted odds ratios (and 95% CIs) for cardiometabolic risk factors across hypertriglyceridaemic waist phenotypes (non-hypertriglyceridaemic waist = reference group) and waist-to-height ratio categories (non-overweight = reference group)

	Hypertriglyceridaemic waist		Waist-to-height ratio	
	Odds ratio (95% CI)	*p* value	Odds ratio (95% CI)	*p* value
Hypercholesterolaemia[1]	4.04 (0.88, 18.49)	0.07	1.85 (0.47, 7.29)	0.38
Low HDL[2]	4.41 (1.50, 12.91)	< 0.01	2.57 (1.11, 5.95)	0.03
Impaired fasting glucose[3]	3.37 (1.06, 10.72)	0.04	1.69 (0.58, 4.88)	0.34
Elevated systolic BP[4]	1.21 (0.32, 4.54)	0.78	1.64 (0.60, 4.46)	0.34
Elevated diastolic BP[4]	2.22 (0.69, 7.21)	0.18	3.21 (1.25, 8.25)	0.02
High CRF (mL/kg/min)[5]	0.05 (0.01, 0.42)	0.01	0.00 (0.00, 0.00)	0.99
High CRF (L/min)[6]	0.33 (0.03, 3.19)	0.34	0.08 (0.01, 0.71)	0.02

All models adjusted for age, sex and ethnicity. HDL, high-density lipoprotein cholesterol; BP, blood pressure; CRF, cardiorespiratory fitness; [1] $\geq$ 5.17 mmol/L; [2] $\leq$ 1.03 mmol/L; [3] $\geq$ 5.6 mmol/L; [4] $\geq$ 90th percentile for age, sex and height; [5] > 42.1 and 37.0 mL/kg/min for boys and girls, respectively; [6] $\geq$ 1.67 L/min.