PEDIATRIC OBESITY
ORIGINAL RESEARCH
doi:10.1111/ijpo.12285

Waist-to-height ratio as a risk marker for metabolic syndrome in childhood. A meta-analysis

C. Ochoa Sangrador[1] and J. Ochoa-Brezmes[2]

[1]Hospital Virgen de la Concha and School of Nursing, Zamora, Spain; [2]School of Medicine, University of Valladolid, Valladolid, Spain

Address for correspondence: Carlos Ochoa Sangrador, Hospital Virgen de la Concha and School of Nursing, Zamora, Spain.
E-mail: cochoas2@gmail.com

Received 3 January 2018; revised 14 February 2018; accepted 21 February 2018

Summary

Background: Individuals with abdominal obesity have a higher cardiovascular risk, regardless of the degree of global overweight.

Objective: To estimate the accuracy of the Waist/height ratio (WtHR) as a risk marker for metabolic syndrome (MS) in children or adolescents.

Methods: Published cohort or cross-sectional studies (Pubmed, Embase-SCOPUS and CINAHL) were searched, with no limits of time. Studies providing Waist/height ratio and clustered criteria of metabolic syndrome were included.

Results: Thirty-one studies (66,912 subjects) were selected. Overall, a high WtHR (≥0.5) was associated with a four-fold increased risk of clustered criteria of MS (odds ratio [OR] 4.15, 95% confidence interval [95% CI]: 2.69 to 6.42) and two-fold increased risk when adjusted by general obesity (adjusted OR 2.26, 95% CI: 1.29 to 3.98). The WtHR, as a quantitative measure, showed a pooled area under the curve of 0.76 (95% CI: 0.71 to 0.80) and, as a dichotomous measure, with a cut-off point close to 0.5, a sensitivity of 60% (95% CI: 50% to 68.8%) and a specificity of 79% (95% CI: 71.6% to 83.9%).

Conclusions: Measuring WtHR may be considered in regular health checks of children and adolescents, as it can measure cardiovascular risk regardless of the degree of general obesity.

Keywords: cardiovascular risk, metabolic syndrome, obesity, sensitivity and specificity, waist-to-height ratio.

Introduction

Cardiovascular diseases are one of the leading causes of morbidity and mortality and have a significant impact on quality of life and health expenditure. It has been estimated that about 40% of children have overweight or obesity (1). We also know that obesity is associated, since childhood, with cardiovascular risk factors (2,3). In addition, obesity in childhood is associated with obesity and cardiovascular disease in adulthood, whether or not there is obesity in later ages (3,4).

General and abdominal obesity can have different consequences and trends in the paediatric population (5). It is known that, regardless of the degree of global overweight, individuals with abdominal obesity have a higher cardiovascular risk (6–8). In fact, abdominal obesity is more related to these factors than general obesity. Among the diagnostic criteria of Metabolic Syndrome (MS), we usually find an index of abdominal obesity (waist circumference [WC] above the 90th percentile for age and sex) (9) and not the body mass index (BMI). Much of the evidence comes from studies in adults, although there is sufficient evidence that the same happens in childhood (10).

There is still no consensus about which factors and levels of risk should be used to identify MS in childhood. In fact, there have been recommendations to restrict this term to children older than 10 years (9). The most commonly used criteria are those of the International Diabetes Federation (IDF) (9), which require the presence of abdominal obesity (WC at <16 years >90th percentile) and at least two of the following criteria: high blood glucose (≥100 mg/dl), low HDL cholesterol (> 40 mg/dl; <50 mg/dl for women >16 years), high triglycerides (≥150 mg/dl) or high blood pressure (systolic >135 mmHg and/or diastolic >85 mmHg).

Although there are WC reference curves for age and sex, measurement and relative assessment require a

time, which is not always available in clinical practice. In addition, this measurement does not allow us to adjust the waist size to the degree of growth of the evaluated child. For this reason, the use of the waist/height ratio (WtHR), has been extended, with a relatively stable reference risk value, applicable to different ethnic, age and sex groups. Computing a simple ratio is less time consuming than searching for age-sex reference values. For adulthood, the WtHR threshold above 0.5 has been generalized as an alternative risk criterion for WC (6).

There is heterogeneous information that, also in childhood and adolescence, WtHR is associated with cardiovascular risk factors, both separately and clustered (11), but its predictive capacity, or a specific reference threshold, has not been systematically established.

Methods

Systematic review of published studies on the accuracy of WtHR as a marker for clustered criteria of MS in childhood (review registered in PROSPERO 2017: CRD42017054428; available at http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42017054428). The recommendations of the MOOSE guidelines were followed.

Types of studies

Observational cohort studies, prospective or retrospective, and cross-sectional studies.

Types of participants

Children and adolescents under 18 years of age who had simultaneous or serial measurements of WtHR (using standard measurement procedures carried out by trained people) and other MS criteria (blood pressure, fasting blood glucose, insulin, triglycerides, total cholesterol and/or HDL and/or LDL fractions). We excluded studies that did not analyse the simultaneous presence of at least two of the MS criteria and those in which people without obesity were excluded.

Exposure and comparison evaluated

WtHR as a continuous or dichotomous variable.

Outcome measures

Clustered criteria of MS (two or more MS criteria apart from WC); Risk scores of MS (sum of the values of the standardized MS criteria); Prevalences, prevalence ratios, relative risks, odds ratios [OR], and accuracy indicators (sensitivity, specificity, area under the curve [AUC] of the receiver operating characteristic [ROC]). Our primary objective was to estimate the accuracy of a high WtHR (≥ 0.5) as a risk marker of MS. As secondary objectives we aim to compare the accuracy of alternative WtHR thresholds and to estimate the risk of having a high WtHR, adjusting by global obesity, age and sex.

Search strategy for the identification of studies

We searched in Pubmed, Embase (via SCOPUS) and CINAHL, for articles published in English, Spanish, French, German, Portuguese and Italian, with no limit of time. The search strategy used in Pubmed was: ("W-HtR" or "WC/height" or "WHtR" or "waist:height ratio" or "waist-to-height ratio" or "waist to height ratio" or "wthr" or "Waist-Height Ratio"[Mesh] or "Waist-to-height" or "waist to height" or "waist height" or "waist circumference to height") AND ("Risk"[Mesh] or "Metabolic Syndrome X"[Mesh] or "Cholesterol, HDL"[Mesh] or "Triglycerides"[Mesh] or "Insulin Resistance"[Mesh] or "Hyperlipidemias"[Mesh] or "Hyperglycemia"[Mesh] or "Hypertension"[Mesh] or "Blood Pressure"[Mesh] or "Insulin resistance" or "Dyslipidemia" or "Hyperlipidemia" or "Hypertension" or "hyperglycemia") AND ("infant"[MeSH Terms] or "child"[MeSH Terms] or "adolescent"[MeSH Terms] or infant or child or adolescent). In the other databases, we used adapted searches with filters to exclude Pubmed references. The search was completed by reviewing bibliographic references of articles examined in full text.

Review of papers

Two reviewers (COS and JOB) read the titles and summaries to discard non-related articles and the full text of the related articles in order to select studies. All disagreement was solved by consensus.

Evaluation of the quality of the studies

Newcastle-Ottawa scales for observational studies were used (available at http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp).

Data extraction

Two reviewers (COS and JOB) extracted the data: authors, inclusion/exclusion criteria, sampling method, sample size, WtHR cut-off points, MS criteria, missing data, prevalence of MS, correlation coefficients, accuracy estimators, risk estimates and differences of

means, with their confidence intervals or standard errors.

Statistical analysis

Descriptive summary estimates were made of all outcome measures, common to at least three studies, provided that they were methodologically homogeneous. Meta-analyses were performed using: RevMan 5.3 (OR), Meta-XL (LFK index), MADA package of R (bivariate model for sensitivity and specificity estimation) and MedCalc (AUC ROC). Heterogeneity between studies was estimated using forest plots and the I^2 statistic. Publication bias was assessed using funnel plots and LFK index (Meta-XL). The results were expressed following random effects models. When available data allowed, subgroup analyses were performed by sex, age, cut-off point and risk of bias.

Results:

Thirty-one studies (search flow diagram in Fig. S1 and excluded studies in Table S1 in the Supporting Information) were selected for qualitative synthesis. Table 1 presents their methodological characteristics. The studies were published between 2002 and 2016, with 66,912 patients examined between 1993 and 2014, 12 in Europe, eight in Asia, six in South America, three in North America and two in Africa. Most were cross-sectional studies, only two cohort studies. Sample sizes ranged from 79 to 16,914 subjects (median 1100, interquartile range 2830), aged between 3 and 18 years (14 studies included children younger than 10 years, but only two exclusively). WtHR cut-off points had been *a priori* established in 16 studies, usually above 0.5 (interval 0.45 to 0.55). Other variables of exposure were: BMI, WC, waist/hip index, skin folds, bioimpedanciometry and ergometry.

MS risk scores or scales were elaborated in eight studies, in six of which the sum of standardized values of the risk factors was computed. Scores above 1 standard deviation (SD) or the 90th percentile were considered as high risk in seven studies. The four IDF criteria (9) were evaluated in 14 studies. In ten of them, other risk factors were included (LDL and total cholesterol and insulin). The WC was included as a MS criteria in seven studies and the percentage of overweight in one.

The quality assessment of the selected studies is summarized in Table 1 (detailed data in Table S2 and Table S3 in the Supporting Information), which ranges from 3 to 7 points for cross-sectional studies (maximum 8 points) and between 7 and 8 points for cohort studies (maximum 9 points). Only six cross-sectional studies justified the response rate in the study population. Eighteen studies had a sample size large enough to provide accurate estimates. Adjustments for age and sex were made in all the studies. Adjustments for anthropometric measures (BMI and/or WC) were only made in seven.

The outcome measurement criteria were very heterogeneous. The accuracy of WtHR above the cut-off point to identify the clustering of MS criteria was evaluated in 13 studies, with estimates of sensitivity and specificity (12–24) . The AUC of the progressive increasing measurements of the WtHR to classify MS was estimated in 18 studies (12–20,22–30). The correlation coefficient between the WtHR values and a quantitative MS scale was measured in three studies (20,31,32). The OR of a high WtHR for MS was reported in 12 studies (2,14,15,21,24,29,31,33–37), and the OR adjusted for another measure of obesity in six (2,31,33,35,38,39). Finally, the increase in risk (OR) associated with each unit of increase in WtHR was given in two studies (40,41). The prevalence of clustering MS criteria was around 10%.

Fig. 1 shows the meta-analysis of the risk of MS for a high WtHR, with subgroup analysis by sex. In general, high-level WtHR (≥ 0.5) is associated with a four-fold increased risk of MS (OR 4.15; 95% confidence interval [95% CI] 2.69 to 6.42; 19 subgroups of 12 studies with 24,149 subjects; I^2 94%). Table 2 summarizes the results and analyses by subgroups, which do not show statistically significant differences. In studies where risk was measured simultaneously for other measures (BMI or WC) there were no significant differences (data not shown). Meta-analysis of adjusted risk estimates for other measures (mainly BMI) showed an adjusted OR of 2.26 (95% CI 1.29 to 3.98; 8 subgroups of 6 studies with 13,168 subjects; I^2 85%). The graphical evaluation of publication bias showed a low risk for crude OR (LFK index 1.52, funnel plot not shown) and high risk for adjusted OR (LFK index 3.17).

Fig. S2 in the Supporting Information shows the meta-analysis of the AUC ROC. WtHR showed a pooled AUC of 0.76 (95% CI 0.71 to 0.80; 29 subgroups from 18 studies with 43,753 subjects; I^2 98%).

Fig. S3 in the Supporting Information shows the meta-analysis of the sensitivity and specificity of a high WtHR (≥0.5) for MS. Fig. S4 in the Supporting Information shows the bivariate grouped analysis that allows the estimation of a sensitivity of 60% (IC95% 50% to 68.8%) and a specificity of 79% (95% CI: 71.6% to 83.9%). Table 2 shows the subgroup analyses by sex, age, cut-off point and risk of bias (WC inclusion among MS criteria).

Table 1 Characteristics of included studies

Author / Countries/ Years	Design[1]	N (age)[2]	Exposure[3]	Effect
Adegboye 2010 Estonia, Denmark, Portugal 1997–2000	CS (6/8)	2837 (GA: 1451, 8,2–11,3 y.; GB: 1384, 14–17.3 y.)	WtHR (GA 0.43 {0.04}; GB 0.41 {0.04}); BMI, WC	≥3 risk factors (TC ≥ 4.4 mmol/l; HDL-C < 1.03 mmol/l (boys) y 1.29 mmol/l (girls); TG ≥ 1.1 (<10 y.) y 1.5 mmol/l (≥10 y.); SBP and/or DBP ≥ P90; glucose ≥5.6 mmol/l; insulin >55 (pre-puberty) >97 pmol/l (puberty); low aerobic physical fitness) >1 SD of sum of Z scores.
Agirbasli 2011 Turkey 2007–2008	CS (6/8)	1194 (9 y.)	WtHR (>0.5: 13.5%); BMI, WC, Waist/Hip ratio, skin folds	≥2 IDF criteria (apart from WC)
Agredo-Zuñiga 2015 Colombia	CS (7/8)	1672 (10–18 y.); M 831; F 841	WtHR (>percentil 75: 0.44; median M 0.42; F 0.41); WC; BMI; skin folds	≥2 risk factors (TG ≥110 mg/dl, HDL-C ≤ 40 mg/dl; SBP and/or DBP ≥ Per90; glucose ≥100 mg/dl; LDL-C ≥ 130 mg/dl)
Arnaiz 2010 Chile 2005–2006	CS (4/8)	209 (6–16 y.); M 105; F 104; includes selected people with obesity	WtHR (>0.55; 0.53 {0.08})	≥1, 2 or 3 Cook criteria (WC ≥ Per90, HDL-C ≤ 40 mg/dl, TG ≥110 mg/dl, glucose ≥100 mg/dl and SBP and/or DBP ≥ Per90); Risks estimated by including and excluding WC
Bailey 2013 United Kingdom	CS (5/8)	234 (10–19 y.); M 112; F 122	WtHR (>0.5; 16.7% {M 9.8%; F 23%}; WC, Ergometry, BMI	≥2 criteria (Criteria: TC ≥200 mg/dl, HDL-C ≤ 40 mg/dl, TG ≥110 mg/dl, glucose ≥5.6 mmol/L y SBP and/or DBP ≥ Per90);
Barzin 2013 Iran 1999–2001	CE (8/9)	1100 (GA 11–14 y.: 531 [F/M: 281/259]; GB 15–18 y.: 569 [F/M: 336/236])	WtHR (GA F/M 0.43/0.42 {0.05}; GB F/M 0.44/0.41 {0.05/0.04}); BMI, WC	Follow-up 10.2 years ≥3 Cook criteria (WC included ≥91/89 {F/M}, HDL-C < 50/40 {F/M} mg/dl or treatment, TG ≥150 mg/dl, glucose ≥100 mg/dl y SBP ≥130 and/or DBP ≥80 or treatment)
Bauer 2015	CS (7/8)	6097 (10–13 y.; F 3195; M 2902)		

(*continues*)

Table 1 (Continued)

Author / Countries/ Years	Design[1]	N (age)[2]	Exposure[3]	Effect
USA			WtHR (0.50 {F/M 0.08/0.10}); BMI, WC	≥1, 2 or 3 criteria (TC ≥ 200 mg/dL, HDL-C ≤ 40 mg/dl, TG ≥130 mg/dl, glucose ≥100 mg/dl, insulin ≥30 uU/ml and SBP and/or DBP ≥ Per95);
Benmohammed 2015 Algeria 2007	CS (5/8)	1100 (12–18 y.; F 563; M 537)	WtHR (>0.50; F 0.47 {0.07}; M 0.45 {0.06}); BMI, WC	≥3 Cook criteria (WC included>Per90; HDL-C ≤ 40 mg/dl, TG ≥110 mg/dl, glucose ≥110 mg/dl and SBP and/or DBP ≥ Per90); IDF criteria (WC > 80 + ≥ other 2 criteria: HDL-C < 40 mg/dl {<50 F ≥ 16 y.}, TG ≥150 mg/dl, glucose ≥100 mg/dl and SBP ≥130 and/or DBP ≥ 85)
Buchan 2017 United Kingdom 2010–2014	CS (6/8)	547 (10,4–17,6 y.; M 52%)	WtHR (≥0.50; 11%); BMI, Ergometry	>1 SD sum of Z scores (TG; glucose, SBP, HDL-C reversed); ≥2 criteria: TG ≥1.24 mmol/L; HDL-C ≥ 1.03 mmol/L; glucose ≥5.6 mmol/L; SBP > Per91
Buchan 2016 United Kingdom	CS (5/8)	223 (5,4–12,3 y.;M 55,2%)	WtHR (≥0.50; 0.46 {0.04}); BMI, WC	>1 SD sum of Z scores (TG; glucose, SBP, HDL-C reversed); ≥2 criteria: TG ≥1.24 mmol/L; HDL-C ≤ 1.03 mmol/L; glucose ≥5.6 mmol/L; SBP > Per91
Campagnolo 2011 Brazil 2001–2002	CS (6/8)	315 (3–4 y.; 0,49 [0,03])	WtHR (>F/M 0.49/0.51; 0.49 {0.03}); BMI, WC	2 Criteria: HDL-C < 35 mg/dl, LDL-C ≥ 110 mg/dl, TG ≥150 mg/dl and SBP ≥130 and/or DBP ≥ 85
Chung 2016 Korea 1998–2008	CS (5/8)	4068 (10–19 y.; F/M 1929/2139)	WtHR (≥0.50; F/M 7.7%/8.1%); BMI, WC	≥2 IDF criteria: HDL-C < 40 mg/dl {<50 F ≥ 16 y.}, TG ≥150 mg/dl, glucose ≥100 mg/dl and SBP ≥130 and/or DBP ≥ 85
Faria 2014 Brazil 2006–2007	CS (3/8)	100 F (14–17 y.)	WtHR (no descriptive data); BMI, WC, BIM	Adapted IDF criteria (WC included>Per90 + ≥ other 2 Criteria:

(*continues*)

Table 1 (Continued)

Author / Countries/ Years	Design[1]	N (age)[2]	Exposure[3]	Effect
				HDL-C < 45 mg/dl, TG ≥100 mg/dl, glucose ≥100 mg/dl and SBP and/or DBP ≥ Per90)
Elizondo-Montemayor 2011 Mexico 2010	CS (3/8)	261 (6–12 y.): 214 with overweight or obesity	WtHR (no descriptive data); BMI, WC, BIM	≥3 Cook Criteria (WC included>Per90; HDL-C ≤ 40 mg/dl, TG ≥110 mg/dl, glucose ≥110 mg/dl and SBP and/or DBP ≥ Per90);
Freedman 2007 USA 1993–1994	CS (7/8)	315 (5–17 y.)	WtHR (F/M 0.45/0.46 {0.06/0.06}); BMI, WC	≥ Per90 of the sum of Z scores (TG; insulin, (SBP + DBP)/2, LDL-C, HDL-C reversed);
Garnett 2008 Australia 2004–2005	CS (5/8)	164 (14–15 y.; F/M 78/86)	WtHR (≥0.50; 18.9%); BMI, WC	≥3 criteria: TG ≥ Per80; HDL-C ≤ Per20; insulin ≥Per80; glucose ≥6.1 mmol/L; SBP ≥ Per90
Gonçalves 2015 Brazil	CS (5/8)	290 (6–10 y.; F/M 132/158)	WtHR (F/M 0.45/0.46 {0.06/0.06}); BMI, WC, Ergometry	≥3 criteria (LDL-C > 100 mg/dl, HDL-C < 50 mg/dl, TG > 100 mg/dl, glucose >100 mg/dl, insulin ≥Per80, SBP and/or DBP ≥ Per80)
Gracia-Marco 2016 Europe 2006–2007	CS (6/8)	748 (12,5–17,49 y.; F/M 383/365)	WtHR (0.4 {0.1}); BMI, WC, skin folds	≥ 1 SD of the sum of Z scores (TG; TC/HDL-C, HOMA-IR, SBP, reactive C protein, maximum oxygen consume)
Graves 2014 United Kingdom 2001–2006	CE (7/9) CS (7/8)	2706 children (7–9 y.) 2858 adolescents (15 y.)	WtHR (≥0.50; F/M 7.4%/6.2%) at 7–9 y. and at 15 y.; BMI	≥3 criteria at 15 year old: TG ≥1.7 mmol/L, LDL-C ≥ 2.79 mmol/L, HDL-C < 1.03 mmol/L, glucose ≥5.6 mmol/L, insulin ≥16.95 IU/L, SBP ≥130 or DBP ≥85
Haas 2011 Germany 2000–2007	CS (5/8)	3850 (3–11 y.; F/M 1869/1981)	WtHR (≥Per90; F/M 9.2/9.8%; 0.44/0.45 {0.04/0.04}); BMI, WC, skin folds	≥3 criteria (LDL-C > 130 mg/dl, HDL-C < 40 mg/dl, TG > 150 mg/dl No HDL-C > 123 mg/dl, TG/HDL-C ratio > 1.5, glucose >100 mg/dl, Hypertension)
Hara 2002	CS (4/8)			

(*continues*)

Table 1 (Continued)

Author / Countries/ Years	Design[1]	N (age)[2]	Exposure[3]	Effect
Japan		GA: 374 (9–10 y.) GB: 506 (12–13 y.)	WtHR (GA 0.43 {0.05}); GB: F/M 0.41 {0.05}); BMI, WC, Waist/Hip ratio, skin folds	Score: TC mg/dl (≥280 6; ≥240 3; ≥200 and ≤119 1; ≤99 2); TG mg/dl (≥200 3; ≥160 1); DBP (≥90 3); SBP/DBP (GA ≥135/80 GB ≥140/80 2); Overweight percentage (≥50% 3; ≥30% 2; ≥20% 1)
Jung 2010 Germany	CS (4/8)	79 (M; 13–17 y.)	WtHR (median 0.46 {IQR 0.15}); BMI, WC, Waist/Hip ratio	Adapted IDF criteria (WC included; TG ≥1.69 mmol/L, LDL-C ≥ 2.6 mmol/L, HDL-C < 1.03 mmol/L, SBP and/or DBP ≥ Per90)
Khashayar 2013 Iran 2009–2010	CS (6/8)	5738 (10–18 y.; F/M 2875/ 2863)	WtHR (>0.5; F/M 17.8%/15%); BMI, WC	≥1, 2 or 3 criteria: 1) dyslipidemia: HDL-C < 40 mg/dl or TC >200 mg/dl; y.}, TG ≥150 mg/dl, 2) glucose ≥100 mg/dl; 3) SBP and/or DBP ≥ Per90
Lu 2010 China 2006	CS (6/8)	1665 (13–15 y.; F/M 819/846)	WtHR (≥0.46; F/M 15.7%/23.1%); BMI	2 criteria: 1) dyslipidemia TG ≥1.70 mmol/L and/or HDL-C < 1.03 mmol/L; 2) glucose ≥100 mg/dl
Maffeis 2008 Italy 2003–2004	CS (6/8)	1479 (5–15 y.; F/M 739/740; 1/3 with overweight or obesity)	WtHR (>0.5; 25.4%); BMI, WC	≥2 Criteria: HDL-C < Per5, TG ≥ Per95, glucose ≥100 mg/dl and SBP and/or DBP > Per95
Matsha 2013 South Africa 2007–2008	CS (6/8)	1272 (10–16 y.; F/M 776/496)	WtHR (F/M 0.45/0.42); BMI, WC, Waist/Hip ratio	≥2 IDF criteria: HDL-C < 40 mg/dl, TG ≥150 mg/dl, glucose ≥100 mg/dl and SBP ≥130 and/or DBP ≥ 85
Mirmiran 2014 Iran 2007	CS (4/8)	134 (10–18 y.; F/M 68/66)	WtHR (F/M 0.46/0.49 {0.05/0.06}); BMI, WC, BIM	≥3 Adapted Cook Criteria (WC included>Per90; HDL-C ≤ 40 mg/dl, TG ≥110 mg/dl, glucose ≥100 mg/dl and SBP and/or DBP ≥ Per90);
Mokha 2010 USA	CS (7/8)	3091 (4–18 y.; F/M 1619/1619)	WtHR(≥0.50; 20.9%); BMI	≥3 Cook Criteria (probably WC included)

(*continues*)

Table 1 (Continued)

Author / Countries/ Years	Design[1]	N (age)[2]	Exposure[3]	Effect
Moreira 2011 Portugal	CS (6/8)	517 (15–18 y.; F/M 297/220)	WtHR (F/M 0.48/0.47); BMI, WC	>1 SD sum of Z scores (TC/HDL-C ratio, TG; HOMA, SBP)
Sardinha 2016 Estonia, Denmark, Portugal 1998–2009	CS (7/8)	4255 (8–17 y.; F/M 2191/2064)	WtHR (F/M 0.44/0.44); BMI, WC	>1 SD sum of Z scores (HDL-C reversed, TG; {SBP + DBPx2}/3; HOMA)
Zhou 2014 China 2010	CS (5/8)	16914 (7–17 y.; F/M 8071/8843)	WtHR (0.43 {0.05}); BMI, WC	≥3 Cook Criteria (WC included>Per90; HDL-C ≤ 40 mg/dl, TG ≥110 mg/dl, glucose ≥100 mg/dl and SBP and/or DBP ≥ Per90)

[1]Design and quality score (Newcastle-Otawa scale); points/maximum.
[2]N global simple size global and by subgroups (i.e.: **M**ale/**F**emale).
[3]Means or medians {standard deviation (SD) or interquartile range (IQR)} o cut-off point (>) and percentage (%)
BIM, bioimpedanciometry; BMI, body mass index; CE, cohort study; CS, cross-sectional study; DBP, diastolic blood pressure; F, female; G, group; HDL-C, HDL cholesterol; HOMA, homeostatic model assessment (glucose x insulin/22.5); IDF, International Diabetes Federation; M, male; SBP, systolic blood pressure; SD, standard deviation; Per, percentile; TC, total cholesterol; TG, triglycerides; y, years; WC, waist circumference; WtHR, waist to height ratio

Discussion:

This systematic review shows that WtHR is associated with an increased risk of clustering of MS criteria (two or more MS criteria apart from WC). A high level of WtHR represents a risk that is at least four times greater, when only WtHR is considered, and two-fold increased, when the risk was adjusted by general obesity (BMI). The diagnostic utility of the WtHR is satisfactory considering its quantitative value (AUC 0.76); as the WtHR rises progressively the risk increases.

However, neither in the results of the individual studies, nor in the pooled analyses of this review, has it been possible to find a WtHR cut-off value that optimizes MS detection. The ROC curves of the individual studies show a progressive slope with no inflection points that maximize sensitivity without loss of specificity or *vice versa*. In the analysis of diagnostic accuracy for cut-off points near WtHR ≥0.5, we found moderate value of sensitivity (60%) and good value of specificity (79%). The use of lower cut-off points presents a slight improvement in sensitivity, which does not compensate for the loss of specificity. In any case, the differences are not statistically significant. Therefore, whatever the cut-off point we choose, high to maximize specificity (avoid false positives) or low to maximize sensitivity (avoid false negatives), will lead to misclassification.

If we use WtHR as a risk marker, we can assume that children or adolescents with high WtHR (greater than or equal to 0.5) are likely to have a clustering of other MS criteria of approximately 25% (for a prevalence of 10%), while in those with normal-low WtHR that probability would be approximately 5%. In addition, the higher the WtHR, the higher the risk. Depending on the prevalence in the population group where we are going to explore cardiovascular risk, it is advisable to use alternative cut-off points, although always accepting that none will be optimal. Therefore, it should be a public health decision to use one or another cut-off point, depending on the cost and acceptance of the studies and preventive interventions to be implemented.

A recent systematic review has evaluated the predictive capacity of anthropometric measures, BMI, WtHR and WC, in childhood and adolescence, for the different cardiovascular risk factors, separately and grouped (11). This review concluded that WtHR can be used as a marker of cardiovascular risk, with no differences with other anthropometric measures. However, this review only analysed AUC data, not other accuracy (sensitivity or specificity) or risk (OR) estimates, nor did it detail the results by sex or age groups. In addition, only ten studies analysed MS risk,

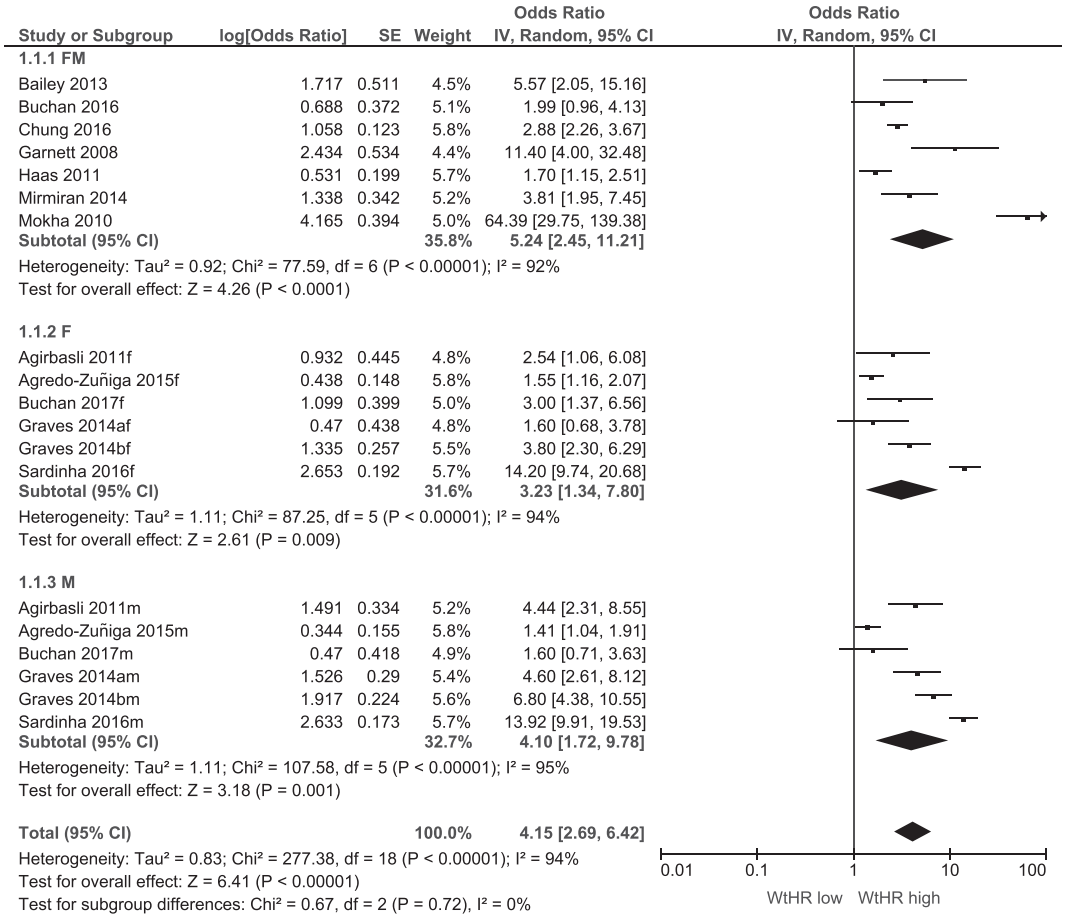

Figure 1 Meta-analysis of the risk (OR) of clustered criteria of MS for a high WtHR. Subgroup analysis (F female; M male; FM grouped).

some of which excluded people without obesity or did not take into account the inclusion of WC as a reference criterion, which could bias the results.

We know that there is a good correlation between abdominal perimeter and other methods of estimation of body fat, such as the measurement of skin folds, dual photon x-ray absorptiometry, air displacement plethysmography or bioelectrical impedance, much more laborious or inaccessible (42).

The use of WtHR has advantages over WC use, a measure included among the most accepted criteria of MS (9). WtHR is easy to measure and its value is relatively stable in different ethnic, age and sex groups. Consultation of reference values by age and sex requires a time (43), not always available, and the available reference values are not adjusted to the individual degree of pubertal development and growth, a factor that is reflected in the height.

Here it is important to point out that all our estimations are referred to clustering of MS criteria (at least two), not MS itself. There is no consensus about its meaning for children under the age of ten, and we know little about its predictive utility for those above this age (9). Therefore, the attributable risk of having MS in childhood can only be established by performing wide and long cohort studies, with cardiovascular events as clinical outcomes.

This systematic review has some limitations that are, mainly, related to the heterogeneity of the samples studied and to differences in the criteria of measurement of exposure and effect between studies. It is therefore not surprising to find significant statistical heterogeneity in all pooled estimates. We analysed the possible factors involved in this heterogeneity, making estimates of subgroups and excluding studies, without correcting it. One of the factors controlled in our analyses was the inclusion of WC as a MS risk criteria; when we excluded studies with this criterion, accuracy decreased slightly, but non-significantly. On the other hand, the existence of publication biases does not seem to be expected due to the nature of

Table 2 Summary of meta-analyses of risk and diagnostic accuracy of MS for a high WtHR, with subgroup analyses

Subgroups	Studies (subgroups)	N	Estimator	95% CI	
MS risk			**OR**		**I^2**
Global	12(19)	24149	4.15	(2.69 to 6.42)	94%
Excluding WC	10(17)	20924	3.58	(2.34 to 5.48)	93%
Female sex	5(6)	6877	3.23	(1.34 to 7.80)	94%
Male sex	5(6)	6503	4.10	(1.72 to 9.78)	95%
< 10 years	6(9)	14475	3.14	(2.12 to 4.63)	85%
≥ 10 years	7(10)	9674	5.41	(2.53 to 11.54)	94%
MS adjusted risk			**aOR**		**I^2**
Global adjusted	6(8)	13168	2.26	(1.29 to 3.98)	85%
Excluding WC	5(7)	10077	1.62	(1.05 to 2.52)	74%
MS diagnostic accuracy					
Continuous value			**AUC**		**I^2**
Global	18(29)	43753	0.76	(0.71 to 0.80)	98%
Excluding WC	13(22)	25784	0.71	(0.66 to 0.75)	97%
Female sex	12(12)	17185	0.75	(0.68 to 0.83)	98%
Male sex	12(12)	17385	0.74	(0.67 to 0.82)	97%
< 10 years	8(13)	27562	0.74	(0.67 to 0.80)	97%
≥ 10 years	10(16)	16191	0.78	(0.71 to 0.84)	98%
Dichotomous value of cut-off point close to 0.5			**Se**		**AUC**
			Sp		
Global	13(24)	23665	60.0%	(50.5 to 68.8%)	0.755
			78.4%	(71.6 to 83.9%)	
Excluding WC	11(21)	22470	56.7%	(47.7 to 65.2%)	0.754
			80.3%	(74.5 to 85.1%)	
Cut-off point 0.5	7(13)	11208	60.0%	(41.2 to 76.9%)	0.793
			80.9%	(70.8 to 88.1%)	
Cut-off point <0.5	5(9)	6063	62.9%	(51.5 to 73.1%)	0.733
			73.5%	(63.2 to 81.7%)	
Female sex	9(10)	7659	55.8%	(43.3 to 67.6%)	0.741
			78.0%	(70.6 to 84.0%)	
Male sex	9(10)	6957	58.5%	(41.7 to 73.5%)	0.822
			84.5%	(77.9 to 89.4%)	
< 10 years	7(11)	10669	57.0%	(40.3 to 72.2%)	0.719
			76.3%	(61.6 to 86.6%)	
≥ 10 years	7(13)	12996	53.4%	(52.1 to 73.4%)	0.794
			80.0%	(73.9 to 85.0%)	

aOR, adjusted OR; AUC, area under the ROC curve; OR, odds ratio; Se, sensitivity; Sp, specificity

the phenomenon studied. Therefore, we believe that our results are sufficiently valid.

We can conclude by saying that measuring WtHR may be considered in regular health checks of children and adolescents, as it measures cardiovascular risk regardless of the degree of general obesity. We must consider that a child with a WtHR ≥0.5 has a fourfold higher risk of clustered criteria for MS and that this risk justifies the initiation of preventive interventions. There is no optimal WtHR threshold that maximizes diagnostic performance, so alternative cut-off points can be chosen, taking into account the cost and social acceptance of the interventions to be taken.

We consider that there is enough evidence about the cardiovascular risk of having a high WtHR to implement its estimation into our clinical practice. Children, adolescents and their families have to be informed of this risk and become familiar with its measurement. We must spread this message to involve society in the common goal of reducing cardiovascular disease, from childhood.

Conflict of interest statement

There are no conflicts of interest to declare.

Acknowledgements

This article has no funding source.

The two authors have contributed to study design, literature search, data collection, data analysis, data interpretation, generation of tables and figures, and writing of the manuscript.

References

1. Estudio ALADINO 2013. Estudio de Vigilancia del Crecimiento, Alimentación, Actividad Física, Desarrollo Infantil y Obesidad en España 2013. Agencia Española de Consumo, Seguridad Alimentaria y Nutrición. Ministerio de Sanidad, Servicios Sociales e Igualdad. Madrid, 2014.
2. Mokha JS, Srinivasan SR, Dasmahapatra P, *et al*. Utility of waist-to-height ratio in assessing the status of central obesity and related cardiometabolic risk profile among normal weight and overweight/obese children: the Bogalusa Heart Study. *BMC Pediatr* 2010; 10: 73.
3. Freedman DS, Dietz WH, Srinivasan SR, Berenson GS. Risk factors and adult body mass index among overweight children: the Bogalusa Heart Study. *Pediatrics* 2009; 123: 750–757.
4. Venn AJ, Thomson RJ, Schmidt MD, *et al*. Overweight and obesity from childhood to adulthood: a follow-up of participants in the 1985 Australian Schools Health and Fitness Survey. *Med J Aust* 2007; 186: 458–460.
5. Fernandez JR, Bohan Brown M, Lopez-Alarcon M, *et al*. Changes in pediatric waist circumference percentiles despite reported pediatric weight stabilization in the United States. *Pediatr Obes* 2017; 12: 347–355.
6. Browning LM, Hsieh SD, Ashwell M. A systematic review of waist-to-height ratio as a screening tool for the prediction of cardiovascular disease and diabetes: 0·5 could be a suitable global boundary value. *Nutr Res Rev* 2010; 23: 247–269.
7. Buchan DS, Boddy LM, Despres JP, *et al*. Utility of the hypertriglyceridemic waist phenotype in the cardiometabolic risk assessment of youth stratified by body mass index. *Pediatr Obes* 2016; 11: 292–298.
8. Heinzle S, Ball GD, Kuk JL. Variations in the prevalence and predictors of prevalent metabolically healthy obesity in adolescents. *Pediatr Obes* 2016; 11: 425–433.
9. Zimmet P, Alberti KG, Kaufman F, *et al*. The metabolic syndrome in children and adolescents - an IDF consensus report. *Pediatr Diabetes* 2007; 8: 299–306.
10. Kelishadi R, Mirmoghtadaee P, Najafi H, Keikha M. Systematic review on the association of abdominal obesity in children and adolescents with cardio-metabolic risk factors. *J Res Med Sci* 2015; 20: 294–307.
11. Lo K, Wong M, Khalechelvam P, Tam W. Waist-to-height ratio, body mass index and waist circumference for screening paediatric cardio-metabolic risk factors: a meta-analysis. *Obes Rev* 2016; 17: 1258–1275.
12. Bauer KW, Marcus MD, El ghormli L, Ogden CL, Foster GD. Cardio-metabolic risk screening among adolescents: understanding the utility of body mass index, waist circumference and waist to height ratio. *Pediatr Obes* 2015; 10: 329–337.
13. Benmohammed K, Valensi P, Benlatreche M, *et al*. Anthropometric markers for detection of the metabolic syndrome in adolescents. *Diabetes Metab* 2015; 41: 138–144.
14. Buchan DS, Baker JS. 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. *Obes Res Clin Pract* 2017; 11: 567–575.
15. Buchan DS, McLellan G, Donnelly S, Arthur R. Diagnostic performance of Body Mass Index, Waist Circumference and the Waist-to-Height Ratio for identifying cardiometabolic risk in Scottish pre-adolescents. *Ann Hum Biol* 2016: 1–6.
16. Campagnolo PD, Hoffman DJ, Vitolo MR. Waist-to-height ratio as a screening tool for children with risk factors for cardiovascular disease. *Ann Hum Biol* 2011; 38: 265–270.
17. Elizondo-Montemayor L, Serrano-Gonzalez M, Ugalde-Casas PA, Bustamante-Careaga H, Cuello-Garcia C. Waist-to-height: cutoff matters in predicting metabolic syndrome in Mexican children. *Metab Syndr Relat Disord* 2011; 9: 183–190.
18. Freedman DS, Kahn HS, Mei Z, *et al*. Relation of body mass index and waist-to-height ratio to cardiovascular disease risk factors in children and adolescents: the Bogalusa Heart Study. *Am J Clin Nutr* 2007; 86: 33–40.
19. Goncalves R, Szmuchrowski LA, Prado LS, *et al*. Selected anthropometric variables and aerobic fitness as predictors of cardiovascular disease risk in children. *Biol Sport* 2015; 32: 255–260.
20. Gracia-Marco L, Moreno LA, Ruiz JR, *et al*. Body Composition Indices and Single and Clustered Cardiovascular Disease Risk Factors in Adolescents: Providing Clinical-Based Cut-Points. *Prog Cardiovasc Dis* 2016; 58: 555–564.
21. Graves L, Garnett SP, Cowell CT, *et al*. Waist-to-height ratio and cardiometabolic risk factors in adolescence: findings from a prospective birth cohort. *Pediatr Obes* 2014; 9: 327–338.
22. Matsha TE, Kengne AP, Yako YY, Hon GM, Hassan MS, Erasmus RT. Optimal waist-to-height ratio values for cardiometabolic risk screening in an ethnically diverse sample of South African urban and rural school boys and girls. *PLoS One* 2013; 8: e71133.
23. Moreira C, Santos R, Vale S, *et al*. Ability of different measures of adiposity to identify high metabolic risk in adolescents. *J Obes* 2011; 2011: 578106.
24. Sardinha LB, Santos DA, Silva AM, Grontved A, Andersen LB, Ekelund U. A Comparison between BMI, Waist Circumference, and Waist-To-Height Ratio for Identifying Cardio-Metabolic Risk in Children and Adolescents. *PLoS One* 2016; 11: e0149351.
25. Adegboye ARA, Andersen LB, Froberg K, Sardinha LB, Heitmann BL. Linking definition of childhood and adolescent obesity to current health outcomes. *Int J Pediatr Obes* 2010; 5: 130–142.

26. de Faria ER, Gontijo CA, Franceschini Sdo C, Peluzio Mdo C, Priore SE. Body composition and risk for metabolic alterations in female adolescents. *Rev Paul Pediatr* 2014; 32: 207–215.
27. Jung C, Fischer N, Fritzenwanger M, Figulla HR. Anthropometric indices as predictors of the metabolic syndrome and its components in adolescents. *Pediatr Int* 2010; 52: 402–409.
28. Khashayar P, Heshmat R, Qorbani M, *et al*. Metabolic syndrome and cardiovascular risk factors in a national sample of adolescent population in the middle east and north africa: The CASPIAN III study. *Intl J Endocrinol* 2013; 2013.
29. Mirmiran P, Rezaei M, Asghari G, Mehrabi Y, Azizi F. Association of metabolic syndrome with body fat percent, anthropometric indices in 10 to 18 year old adolescents. *Iran J Public Health* 2014; 43: 193–201.
30. Zhou D, Yang M, Yuan ZP, *et al*. Waist-to-Height Ratio: a simple, effective and practical screening tool for childhood obesity and metabolic syndrome. *Prev Med* 2014; 67: 35–40.
31. Agirbasli M, Agaoglu NB, Ergonul O, *et al*. Comparison of anthropometric indices in predicting metabolic syndrome components in children. *Metab Syndr Relat Disord* 2011; 9: 453–459.
32. Hara M, Saitou E, Iwata F, Okada T, Harada K. Waist-to-height ratio is the best predictor of cardiovascular disease risk factors in Japanese schoolchildren. *J Atheroscler Thromb* 2002; 9: 127–132.
33. Agredo-Zuniga RA, Aguilar-de Plata C, Suarez-Ortegon MF. Waist:height ratio, waist circumference and metabolic syndrome abnormalities in Colombian schooled adolescents: a multivariate analysis considering located adiposity. *Br J Nutr* 2015; 114: 700–705.
34. Bailey DP, Savory LA, Denton SJ, Davies BR, Kerr CJ. The hypertriglyceridemic waist, waist-to-height ratio, and cardiometabolic risk. *J Pediatr* 2013; 162: 746–752.
35. Chung IH, Park S, Park MJ, Yoo EG. Waist-to-Height Ratio as an Index for Cardiometabolic Risk in Adolescents: Results from the 1998-2008 KNHANES. *Yonsei Med J* 2016; 57: 658–663.
36. Garnett SP, Baur LA, Cowell CT. Waist-to-height ratio: a simple option for determining excess central adiposity in young people. *Int J Obes (Lond)* 2008; 32: 1028–1030.
37. Haas GM, Liepold E, Schwandt P. Predicting cardiovascular risk factors by different body fat patterns in 3850 german children: The PEP family heart study. *Int J Prev Med* 2011; 2: 15–19.
38. Lu Q, Iseli TJ, Yin FZ, *et al*. The relationship between the waist-to-height ratio and glucose and lipid metabolism in Han adolescents. *Indian J Pediatr* 2010; 77: 547–550.
39. Maffeis C, Banzato C, Talamini G. Waist-to-height ratio, a useful index to identify high metabolic risk in overweight children. *J Pediatr* 2008; 152: 207–213.
40. Arnaiz P, Marin A, Pino F, *et al*. Waist height ratio, ultrasensitive c reactive protein and metabolic syndrome in children. *Rev Med Chil* 2010; 138: 1378–1385.
41. Barzin M, Asghari G, Hosseinpanah F, Mirmiran P, Azizi F. The association of anthropometric indices in adolescence with the occurrence of the metabolic syndrome in early adulthood: Tehran Lipid and Glucose Study (TLGS). *Pediatr Obes* 2013; 8: 170–177.
42. Jensen NS, Camargo TF, Bergamaschi DP. Comparison of methods to measure body fat in 7-to-10-year-old children: a systematic review. *Public Health* 2016; 133: 3–13.
43. Moreno LA, Fleta J, Mur L, Rodriquez G, Sarria A, Bueno M. Waist circumference values in Spanish children - Gender related differences. *Eur J Clin Nutr* 1999; 53: 429–433.

Supporting information

Additional Supporting Information may be found online in the supporting information tab for this article.

Table S1.- Excluded studies.
Table S2.- Newcastle-Ottawa Quality Assessment Scale for cross-sectional studies.[a]
Table S3.- Newcastle-Ottawa Quality Assessment Scale for cohort studies.[a]
Fig. S1. Search flow diagram.
Fig. S2. Forest-plot of sensitivity and specificity and confidence intervals of the risk of clustered MS criteria for a high WtHR. TP (true positive), FP (false positive), FN (false negative) and TN (true negative) counts. Sex subgroups (F female; M male; FM grouped).
Fig. S3.- Forest-plot of areas under the ROC curve of continuous value of WtHR.
Fig. S4.- Bivariant analysis of sensitivity and specificity of the risk of clustered MS criteria for a high WtHR.