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Alternative waist-to-height ratios associated with risk biomarkers in youth with diabetes: comparative models in the SEARCH for Diabetes in Youth Study

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Abstract

Background/objectives—The waist-to-height ratio (WHtR) estimates cardiometabolic risk in youth without need for growth charts by sex and age. Questions remain about whether waist circumference measured per protocol of the National Health and Nutrition Examination Survey (W_{NHA}HtR) or World Health Organization (W_{WHO}HtR) can better predict blood pressures and lipid parameters in youth.

Participants/methods—WHtR was measured under both anthropometric protocols among participants in the SEARCH Study, who were recently diagnosed with diabetes (ages 5–19 years; $N = 2\,773$). Biomarkers were documented concurrently with baseline anthropometry and again ~7 years later (ages 10–30 years; $N = 1\,712$). For prediction of continuous biomarker outcomes, baseline W_{NHA}HtR or W_{WHO}HtR entered semiparametric regression models employing restricted cubic splines. To predict binary biomarkers (high-risk group defined as the most adverse

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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quartile) linear W_{NHA}HtR or W_{WHO}HtR terms entered logistic models. Model covariates included demographic characteristics, pertinent medication use, and (for prospective predictions) the follow-up time since baseline. We used measures of model fit, including the adjusted-R^2 and the area under the receiver operator curves (AUC) to compare W_{NHA}HtR and W_{WHO}HtR.

Results—For the concurrent biomarkers, the proportion of variation in each outcome explained by full regression models ranged from 23 to 46%; for the prospective biomarkers, the proportions varied from 11 to 30%. Nonlinear relationships were recognized with the lipid outcomes, both at baseline and at follow-up. In full logistic models, the AUCs ranged from 0.75 (diastolic pressure) to 0.85 (systolic pressure) at baseline, and from 0.69 (triglycerides) to 0.78 (systolic pressure) at the prospective follow-up. To predict baseline elevations of the triglycerides/HDL cholesterol ratio, the AUC was 0.816 for W_{WHO}HtR compared with 0.810 for W_{NHA}HtR ($p = 0.003$), but otherwise comparisons between alternative WHtR protocols were not significantly different.

Conclusions—Among youth with recently diagnosed diabetes, measurements of WHtR by either waist circumference protocol similarly helped estimate current and prospective cardiometabolic risk biomarkers.

Introduction

The ratio of waist circumference-to-height, commonly abbreviated as WHtR, has gained recognition as an easily obtained indicator of abdominal adiposity associated with cardiometabolic risk in adults [1–3]. Among children and adolescents, likewise, WHtR is associated with various cardiometabolic risk markers [4–12]. Because WHtR varies only slightly by sex and age for these younger populations, WHtR values may be interpreted without use of percentiles or z-scores relative to a pediatric, normative growth chart developed from the body mass index (BMI) [5, 9, 13–15]. Normative BMI growth charts are based on healthy youth assessed at a specific place and time, but they might not serve the interpretive needs of clinicians caring for youth with chronic diseases or those from many different ancestries. There is a need, therefore, to confirm the utility of WHtR for identification of cardiometabolic risk factors among diverse youth confronted with adverse medical conditions.

Applications of the WHtR have been questioned because there is no global standardization of the protocol for measuring waist circumference (WC) [16–18]. Height measurements are usually well standardized, but variation in the protocols for measuring WC is likely to create inconsistencies in calculated values for WHtR. We have previously reported discrepancies between WC measurements made simultaneously by either the protocol WC_{NHA} (National Health and Nutrition Examination Survey; NHANES) or WC_{WHO} (World Health Organization; WHO) [17]. Thus, there is a need to compare the utilities of WHtR values (W_{NHA}HtR or W_{WHO}HtR) that are calculated from WCs obtained from these alternative WC-measurement protocols.

The SEARCH for Diabetes in Youth Study (SEARCH) is a population-based, incidence registry network that provides detailed information about young persons with recently diagnosed diabetes. For this report, our first objective was to compare cross-sectional associations in SEARCH between baseline W_{NHA}HtR or W_{WHO}HtR and baseline

cardiometabolic biomarkers. For a subset of SEARCH participants, biomarkers were measured at least once more in subsequent years. Our second objective was to compare the prospective associations between baseline W_{NHA}HtR or W_{WHO}HtR and the participants' future biomarker values. For these cross-sectional and prospective objectives, we sought to demonstrate whether W_{NHA}HtR or W_{WHO}HtR could provide a meaningfully stronger biomarker association than the alternative adiposity indicator.

Participants and methods

Children and adolescents with diabetes diagnosed at younger than 20 years were identified by the SEARCH Study at five US sites (South Carolina; Cincinnati, Ohio, and surrounding counties; Colorado with southwestern Native American sites; Seattle, Washington, and surrounding counties; and Kaiser Permanente, Southern California) [19]. Patients receiving a new diagnosis of type 1 or type 2 diabetes in 2002–2006 or 2008 came from ongoing surveillance of networks of hospitals and other clinical sites. These incident cases were recruited for a baseline visit (mean of 9.3 months [SD 6.4] from diagnosis) that included the collection of anthropometric data, biomarkers, and medical history. Local institutional review board approval was obtained for each center. Written informed consent was obtained from participants age 18 and older, while assent with parental written informed consent was obtained for participants younger than 18 years.

For this report, we excluded SEARCH participants whose age at baseline anthropometry was less than 5 years, the typical age at which a child's pattern of fat-mass growth velocity (kg/year) changes from declining to increasing [20]. We also excluded 29 participants with one or more implausible WHtR values or an extreme discrepancy between their baseline values of W_{NHA}HtR and W_{WHO}HtR.

Among baseline participants who had at least one additional, in-person assessment, the largest number of repeat examinations occurred at an average follow-up interval of 7 years. For prospective modeling, therefore, we chose follow-up biomarker results for the one return visit that occurred closest to 7 years beyond the baseline exam, but within a follow-up range set arbitrarily at 5–10 years beyond the baseline.

Anthropometry

The SEARCH Study invited participants to in-person visits while metabolically stable, defined as no episode of diabetic ketoacidosis during the previous month. The visits occurred after an overnight fast, and all medication except long-acting insulin was discontinued the night before. Centrally trained staff obtained standardized measures of height and weight. WCs (to the nearest 0.1 cm) were systematically measured by two protocols during each examination. For all measurements, the measuring tape was positioned parallel to the floor with the participant standing, abdomen relaxed, arms at the sides, feet together and facing the observer with the waist exposed. WC_{NHA} assessed the circumference just above the right iliac crest at the mid-axillary line [21]. WC_{WHO} was taken with the tape midway between the lowest rib margin and the right iliac crest at the mid-axillary line [22]. If the rib margin could not be identified, the measurement was made at the point of natural bend (after asking the participant to lean to the side without swaying

backward or forward). The NHANES method was always done first, and the WHO method was done last by study personnel trained and certified centrally on both methods.

For each anthropometric method, two WC measurements were taken; if they differed by more than 1.0 cm, a third measurement was made. For each method, the mean of the two (or mean of the closest two) WC measurements was used for subsequent calculations. We divided the mean WC values by the measured height to generate the W_{NHA}HtR and W_{WHO}HtR.

Biomarker measurements

During in-person visits, fasting blood specimens were processed locally and shipped within 24 h under refrigeration to the SEARCH central laboratory. Measurements of serum triglycerides, total cholesterol, and high-density lipoprotein (HDL) cholesterol were performed on a Hitachi 917 autoanalyzer (Boehringer Mannheim Diagnostics, Indianapolis, IN). Since all participants were under treatment for diabetes, we report no data on circulating glucose or glycated hemoglobin for which values might be unstable. We report no data on circulating insulin, which could include unknown amounts attributable to exogenous insulin therapy. Blood pressure measurements at baseline were performed using a standard mercury sphygmomanometer with one of five cuff sizes chosen based on the circumference of the participant's arm. Follow-up blood pressure measurements used an aneroid manometer (Welch Allyn Tycos 767-Series). Pressures were obtained after at least 5 min of rest, and the average of three measurements was used in the analyses.

Statistical methods

Among the biomarkers evaluated in this cohort, we restricted our analyses to include only the six outcome variables for which the proportion of explained variance (adjusted-R^2 for full multivariable models) at baseline was at least 20%. These outcome variables were the systolic and diastolic blood pressures; plasma concentrations of triglycerides and HDL–cholesterol; and ratios of total cholesterol/ HDL–cholesterol (a predictor of adult risk of cardiovascular disease [23, 24]) and triglycerides/HDL–cholesterol (a proxy variable for insulin resistance [25–27]). Excluded from the presentation are cross-sectional models for biomarker outcomes with substantially smaller adjusted-R^2 at baseline, for example, non-HDL cholesterol (12%), total cholesterol (11%), and LDL–cholesterol (4%).

We initially compared the abilities of W_{NHA}HtR and W_{WHO}HtR to predict biomarker outcomes measured at the baseline visit by fitting linear regression models that were semiparametric. That is, our models include a nonparametric cubic spline component to describe the likely nonlinear effects of the anthropometric measures on the biomarker outcomes along with linear terms included in the models to capture the effects of demographics and other clinical characteristics. For each biomarker outcome considered, the linear component of the semiparametric regression included sex, age, age-squared (centered according to sex-specific mean age), sex-by-age interaction, and mutually exclusive ancestral group (non-Hispanic white, non-Hispanic black, Hispanic, and other). Additional adjustments were made depending on the outcome of interest. Models for the blood pressure outcomes were adjusted for use of any antihypertensive medication (yes/no)

and height obtained at the occasion of pressure measurement. Models for the lipid outcomes were adjusted for use of any hypolipidemic medication (yes/no) at the occasion of lipid measurement. We made no adjustment for diabetes type since this dichotomous variable is strongly correlated with waist circumference in SEARCH [28], and the inclusion of sex, age, and ancestry as covariates in the models removed all remaining residual confounding effects that diabetes type may have on these outcomes.

The nonparametric component of the semiparametric models were fitted using cubic splines [29]. We estimated the number of knots separately for W_{NHA}HtR and W_{WHO}HtR using generalized cross-validation. The maximum (k) of the two numbers was used in the models. Knots were placed between the 5th and 95th at every (95/k)th percentile. Measures of model fit, including the adjusted-R^2 criteria and the area under the receiver operator curves (AUC) were used to compare W_{NHA}HtR and W_{WHO}HtR. Diagnostic tests were performed for each fitted model, and observations that had high studentized residual (abs(residuals) > 3) and/or high Cook's distance (> (4/sample size)) when W_{NHA}HtR or W_{WHO}HtR served as the main predictor were removed from the analyses. The observations excluded from the analyses were no more than 25 (baseline models) or 15 (prospective models).

For comparison of logistic regression models, we dichotomized each of the same biomarkers using its 75th percentile as the high-risk cut point (or the 25th percentile as the cutoff value for HDL cholesterol). These logistic regression models included covariates similar to those fitted with the continuous outcomes, except that W_{NHA}HtR and W_{WHO}HtR were included as linear terms instead of nonparametric functions. We summarized the predictive values of the logistic regression models using the AUC. Comparisons between AUC W_{NHA}HtR and AUC W_{WHO}HtR were made using a bootstrapping procedure, which also produced 95% bootstrap percentiles confidence intervals. Because we made comparisons for six different outcome variables, we modified the conventional threshold for alpha significance to p = 0.0083 (0.05/6, Bonferroni correction).

In addition to cross-sectional modeling, we also fitted semiparametric and logistic models in which the baseline anthropometry was employed for prospective prediction of biomarkers obtained at the designated follow-up visit. For these prospective models, we included an additional covariate describing the time between the baseline assessment and collection of the prospective biomarker outcome values.

For all linear and logistic regression models, we attempted to isolate the contribution of WHtR by distinguishing between the "basic" models that included independent variables exclusive of WHtR (that is, only demographic descriptors and medication use or height or time since baseline where appropriate) and the "full" models that included WHtR in addition to those covariates. We performed data quality control measures in SAS 9.4. Statistical analyses were performed in SAS and R. Models were fitted primarily in R using *splines* (now under MASS) [30]. The area under the ROC curves was estimated using *pROC*; confidence intervals were generated with *boot* under R and *proc surveyselect* under SAS [31, 32].

Results

Baseline, cross-sectional associations with biomarkers

Our baseline analytic sample included 1382 girls and 1391 boys (described in Table 1), whose first in-person assessment occurred 3–30 months after their diabetes diagnosis. Overall, the participants' W_{NHA}HtR was slightly greater than W_{WHO}HtR (median 0.48 vs. 0.45). With sex and age stratification, the relatively larger values of W_{NHA}HtR were most evident among the older girls (median 0.52 for ages 12 + vs. 0.47 for ages < 12). The girls at ages 12–19 years included 30% with a physician diagnosis of type 2 diabetes, whereas younger girls and all boys had fewer than 19% with a type 2 diagnosis. Among participants 12–19 years old, girls had lower blood pressures than boys and lower use of antihypertensive drugs. The older girls, compared with older boys, had relatively higher triglycerides and triglycerides/HDL cholesterol, but relatively lower use of hypolipidemic drugs.

Figure S1 (Supplementary material) includes scatterplots (red circles for W_{NHA}HtR, blue triangles for W_{WHO}HtR) for each baseline outcome biomarker along with the values predicted for each model. For these cross-sectional analyses, full regression models predicted blood pressures with a nearly linear relation to WHtR, irrespective of the WC-measurement protocol, but there were nonlinear relations to triglycerides, HDL cholesterol, and both lipid ratios.

For each outcome biomarker, the competing adiposity indicators provided roughly similar results. The proportion of explained variation in outcomes (adjusted-R^2 values) of these full models ranged from ~23% (for diastolic blood pressure) to 46% (for systolic blood pressure) (Table 2A). The R^2 incremental improvements attributable to WHtR ranged from ~3% (diastolic blood pressure) to 19% (for total cholesterol/HDL cholesterol or triglycerides/HDL cholesterol). The R^2 incremental improvements associated specifically with W_{WHO}HtR tended (with exception of diastolic blood pressure) to be greater than those associated with W_{NHA}HtR, but these anthropometric improvements were very small. The estimated incremental benefit of using W_{WHO}HtR reached 1% only for cross-sectional models of triglycerides and triglycerides/HDL cholesterol.

At baseline, the full logistic models adequately identified high-risk status for all six biomarkers (Figure S2). The competing adiposity indicators provided roughly similar results with AUCs ranging from about 0.75 (diastolic blood pressure) to 0.85 (systolic blood pressure) (Table 4A). The AUC incremental improvements attributable to WHtR, irrespective of WC-measurement protocol, ranged from ~0.02 (for diastolic blood pressure) to 0.11 (for total cholesterol/HDL cholesterol). For blood pressure outcomes, there were no significant differences between AUC incremental improvements associated with W_{WHO}HtR or W_{NHA}HtR. Among the lipid outcomes, the use of W_{WHO}HtR rather than W_{NHA}HtR was associated with a significant improvement in the model's power to predict only the triglycerides/HDL cholesterol ratio (ΔAUC = 0.006, 95% CI [0.002–0.010]; $p = 0.003$) (Table 3A). For the other lipid outcomes, the improvements associated with use of W_{WHO}HtR (ΔAUC = 0.004–0.006; all $p < 0.02$) were not significant after consideration of multiple comparisons (Bonferroni corrections).

Thus, our cross-sectional models comparing W_{NHA}HtR and W_{WHO}HtR, found no difference for blood pressures between these anthropometric predictors. Slightly stronger associations (about 1%) were found for W_{WHO}HtR in the cross-sectional prediction of triglycerides and triglycerides/HDL cholesterol. In the logistic models, however, only for the triglycerides/HDL cholesterol ratio did this advantage reach statistical significance.

Prospective associations with follow-up biomarkers

We obtained follow-up biomarkers on 892 girls and 820 boys, ~62% of the baseline sample (Table 3). The median time interval between baseline and the selected follow-up exam was 6.4 years. At these follow-up encounters, a majority of participants were 18 + years old. The girls (women) continued to have slightly lower blood pressures than the boys (men), but they now had a slightly higher use of antihypertensive drugs. They also had a slightly higher use of hypolipidemic drugs.

For follow-up blood pressures, the prospective associations with baseline WHtR, irrespective of WC-measurement protocol, became slightly non-linear. We found an inflection point (nadir) for WHtR values at about 0.42 (Figure S3). Baseline WHtR predicted non-linear follow-up values for lipid outcomes.

Competing adiposity indicators again provided roughly similar results. The explained variation of these prospective models ranged from ~12% (triglycerides) to 30% (for systolic blood pressure) (Table 3B). In these prospective, full regression models, the R^2 incremental improvements attributable to baseline WHtR, irrespective of WC-measurement protocol, ranged from ~4% (diastolic blood pressure) to 13% (total cholesterol/HDL cholesterol). We observed slight improvements in the predictive ability (R^2) of the models with W_{WHO}HtR compared with W_{NHA}HtR for all six outcome variables. The estimated incremental benefit of using W_{WHO}HtR reached 2% only for predictive models of HDL cholesterol and the two lipid ratios.

At the follow-up visit, the full logistic models with baseline WHtR, irrespective of WC-measurement protocol, provided AUCs that ranged from ~0.69 (triglycerides) to 0.78 (systolic blood pressure) (Table 4B; Supplementary data Figure S4). The AUC incremental improvements attributable to WHtR ranged from ~0.03 (for diastolic blood pressure) to 0.09 (for HDL cholesterol and the lipid ratios). The prospective AUC incremental improvements associated with W_{WHO}HtR tended to be greater than those associated with W_{NHA}HtR, but these small differences were not significant for blood pressure or triglycerides outcomes ($\Delta AUC \leq 0.006$; $p > 0.05$). For HDL cholesterol and the lipid ratios, there were larger AUC incremental benefits of using W_{WHO}HtR rather than W_{NHA}HtR ($\Delta AUC = 0.007–0.010$; $p < 0.05$) (Table 4B), but these differences in AUC's did not remain statistically significant after adjustment for multiple comparisons.

Thus, our prospective models comparing W_{NHA}HtR and W_{WHO}HtR, found no difference in the ability to predict prospective blood pressures between these anthropometric predictors. For the prospective prediction of HDL cholesterol and lipid ratios W_{WHO}HtR may have been slightly more predictive than W_{NHA}HtR (by ~2% of explained variation in the regression models), but in the logistic models these benefits were not significant.

Among both cross-sectional and prospective analyses, inclusion of a covariate for diabetes type did not materially change our full models. Tests for effect modification of the associations between two WHtRs and six outcomes by diabetes type were largely non-significant; out of 24 tests we found two interaction effects with a p-value of 0.04.

Discussion

In our SEARCH sample of diverse youth with diabetes, we have demonstrated that either W_{NHA}HtR or W_{WHO}HtR can contribute to the cross-sectional estimation of blood pressures and at least four lipid-related risk variables. These alternative adiposity indicators had similar strengths of association with biomarker outcomes.

This is a useful confirmation since W_{NHA}HtR values reported in SEARCH at baseline are substantially larger than W_{NHA}HtR values reported at ages 5–19 years in an earlier community-based sample of US youth [8]. Similarly, values of W_{WHO}HtR reported here are larger than W_{WHO}HtR reported at similar ages in community-based youth samples from England [33, 34] or continental Europe [35]. On the other hand, we noted that the W_{WHO}HtR values in our SEARCH sample were similar to the values found in a large sample of black and white youth from the Bogalusa Heart Study (Louisiana, USA) [5].

Among the cross-sectional associations in SEARCH, we found no significant differences between the alternative WHtR measurements in the strengths of association with blood pressures, triglycerides, HDL cholesterol, or total cholesterol/HDL cholesterol. The triglycerides/HDL cholesterol ratio, however, was more strongly associated with W_{WHO}HtR than with W_{NHA}HtR, a difference that was nominally significant in our logistic, cross-sectional analyses. This lipid ratio is an indirect, proxy indicator of homeostatic insulin resistance in healthy adults [27] and in adults with newly diagnosed diabetes [26]. Among Asian youth without diabetes, the triglycerides/HDL cholesterol ratio is strongly associated with prevalent metabolic syndrome [9, 36]. For these reasons, even small improvements in the anthropometric approaches to the clinical estimation of triglycerides/HDL cholesterol may merit consideration for the evaluation of high-risk youth.

Our finding of some small, albeit non-significant, advantages for W_{WHO}HtR over W_{NHA}HtR for identifying metabolic risk is consistent, in some respects, with previous reports that compared alternative protocols for WC measurement (but without calculating WHtR). A study of overweight Canadian youth without diabetes found that waist WC_{WHO} had a stronger association than WC_{NHA} with the metabolic syndrome [37]. The benefit of the WHO protocol appears to have been driven by its slightly stronger associations with triglycerides, insulin, and homeostatic assessment of insulin resistance. However, none of these differences alone was statistically significant. Among healthy adult volunteers (BMI range 16.8–40.2 kg/m^2) in Germany [16] the WC_{WHO} tended toward modestly stronger associations than WC_{NHA} with blood pressures, HOMA-IR, HDL cholesterol (but not with triglycerides), and with visceral fat volume. The large Taiwan Lifestyle Study of healthy adults [18] (mean BMI 24.2 kg/m^2) reported that WC_{WHO} had stronger associations than WC_{NHA} with systolic blood pressure, triglycerides, HDL cholesterol, and with single-slice, visceral fat area.

Two cross-sectional studies of US adult volunteers have compared how well different anatomic locations of visceral fat areas were associated with a variety of cardiometabolic risk factors [38, 39]. Their reports found generally that the level of several risk factors was not estimated optimally by visceral fat located at the level of the lumbar interspace L4–L5, but rather by visceral fat areas located several centimeters more in the cephalad direction. The level of L4–L5 is consistent with the iliac crest landmark [40], which defines the WC_{NHA}. Since the WC_{WHO} location relates also to the lowest rib margin, it is necessarily more cephalad than the L4–L5 level. These adult studies lend further support to our youth findings that W_{WHO}HtR (relatively cephalad) might correlate more strongly than W_{NHA}HtR with metabolic risk, although not with hypertensive risk.

A review of pediatric CT scans from Ireland reported for ages 6–16 years old that single-slice images having the strongest associations with visceral fat volume were best located at levels L2–L3 or L1–L2 for girls and at L1–L2 for boys [41]. These anatomic locations are more cephalad than L4–L5 level, but this study presented no correlation with any cardiometabolic risk factors. If it is true that visceral fat in childhood and adolescence is related to cardiometabolic risks, then these anatomic findings are also consistent with the marginal advantages we found for using W_{WHO}HtR. However, the pathogenicity of visceral relative to subcutaneous abdominal fat depots may not be consistent at all ages [42, 43].

In the current analyses, we expanded upon a prior SEARCH publication that compared how W_{NHA}HtR and W_{WHO}HtR were associated with blood pressures and levels of circulating lipids [44]. The earlier study found that W_{WHO}HtR was more strongly associated than W_{NHA}HtR with fasting triglycerides, but not with other outcome biomarkers. The models analyzed in that earlier report did not include lipid ratios as outcomes. Its analyses included 3615 participants at ages 10–19 years, many of whom had prevalent, long-standing diagnoses of diabetes. Its models included adjustment for diabetes type, but neither did evaluate nonlinear associations between W_{NHA}HtR or W_{WHO}HtR and cardiometabolic risk, nor did the earlier report present any prospective associations. By contrast, the current report includes as baseline participants only those with a relatively recent diabetes diagnosis. It includes also younger participants (ages 5–9 years), and presents models that acknowledge non-linear associations with cardiometabolic risk.

Reports describing prospective associations between youth BMI and later risk biomarkers are relatively common [45], but publications evaluating how well the use of WHtR in youth predicts future levels of cardiometabolic risk have been rare. An Australian study of healthy youth ages 7–15 years reported correlations between childhood WHtR (WC measured at umbilical level) and cardiometabolic risk factors in adulthood 20 years later [46]. The authors reported, among other outcomes, a highly significant prospective prediction by WHtR of fasting plasma insulin and the metabolic syndrome. A study of healthy English children ages 7–9 reported that their childhood W_{WHO}HtR was significantly correlated with levels of systolic blood pressure, HDL cholesterol (inversely), LDL cholesterol, and insulin measured in adolescence about 7 years later [33]. In prospective analyses based on a diverse sample of London schoolchildren, significant associations were reported between W_{WHO}HtR at ages 11–13 years and their level of allostatic load a decade later [34].

From our current sample of young patients, recently diagnosed with diabetes, we developed models that evaluated prospective associations between the baseline WHtR (by alternative WC-measurement protocols) and subsequent biomarker outcomes obtained ~7 years later. For our prospective models predicting HDL cholesterol and two lipid ratios, we demonstrated that WHtR obtained at baseline could contribute incrementally ~9–13% to the explanation of biomarker variation measured several years in the future (Table 3B). Baseline WHtR also added ~0.09 to the AUC of these same future biomarkers (Table 4B; Figure S4), implying perhaps that HDL cholesterol and the lipid ratios represent features of cardiometabolic risk that are relatively stable from childhood through early adulthood. For the prospective models predicting blood pressures and triglycerides, however, baseline anthropometry was less useful. The baseline WHtRs contributed no more than 8% to their explanation of biomarker variation, and they added <0.07 to the AUC. For none of the future outcomes did we find a significant difference between the alternative WHtR protocols.

Our SEARCH Study is strengthened by its large sample size, well-defined anthropometric protocols, and standardized laboratory methods. The sample is limited; however, by its restriction to youth who are under treatment for diabetes. Their measurements of glycemia or insulin are often unstable or far outside the normal ranges. Therefore, in contrast to studies of youth without diabetes, SEARCH cannot report useful associations between adiposity indicators and biomarkers of glycemia or insulin. Our study of alternative anthropometric protocols is also limited by consideration only of the WC-measurement methods recommended by the WHO and NHANES. Additional WC sites, such as the umbilical level and minimal waist, have been employed in various reports, but none is in wide current usage. Nevertheless, for participants of any age the WC measurement values will differ according to the anthropometric method in use. If the WC values differ, then the values calculated for WHtR will not be equivalent. Thus, WHtR values obtained in settings that employed different WC-measurement protocols cannot be simply substituted for one another for purposes of descriptive epidemiology.

It may be the case, as was concluded a decade ago from studies of adults [47, 48], that the choice of WC-measurement protocol has only modest influence on associations with mortality, major clinical outcomes, or cardiometabolic risk factors. Clinical anthropometry will benefit eventually from standardization of its methods. In pursuit of standardized, and improved indicators of abdominal adiposity, future researchers might investigate the use of the supine sagittal abdominal diameter (SAD, sometimescalled “abdominal height”) [49–52] or the SAD-to-height ratio [53].

Our current analysis of two alternative WHtR protocols in a large sample of high-risk youth has identified only small potential advantages for the W_{WHO}HtR method in relation to some lipid biomarkers. Our overall conclusion, however, is that there were no substantial or meaningful predictive benefits related to use of one WHtR protocol over the other.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Baseline anthropometry and other characteristics by sex and age group

Variable	All		Girls		Boys	
	N	Median (p25, p75) or %	*N*	Median (p25, p75) or %	*N*	Median (p25, p75) or %
Age, y	2773	12.3 (9.3, 15.0)	1382	12.1 (9.1, 14.5)	1391	12.5 (9.5, 15.3)
W_{NHA}HtR	2773	0.48 (0.44, 0.55)	1382	0.49(0.45, 0.56)	1391	0.47(0.44, 0.53)
W_{WHO}HtR	2773	0.45 (0.42, 0.51)	1382	0.46 (0.42, 0.52)	1391	0.45 (0.42, 0.50)
BMI, kg/m^2	2766	20.3 (17.3, 24.9)	1380	20.4 (17.2, 26.1)	1386	20.1 (17.4, 24.1)
Systolic BP, mmHg	2726	102.7 (94.7, 111.3)	1360	101.3 (93.8, 110.0)	1366	103.3 (95.3, 112.7)
Diastolic BP, mmHg	2724	64.7 (58.7, 71.3)	1358	64.7 (58.8, 71.0)	1366	64.7 (58.7, 71.3)
Using antihypertensive drug, %	2739	0.5%	1359	0.4%	1380	0.7%
Triglycerides, mmol/l	2696	0.68 (0.51, 0.97)	1334	0.72 (0.54, 1.03)	1362	0.64 (0.47, 0.90)
HDL cholesterol, mmol/l	2696	1.35 (1.11, 1.58)	1334	1.35 (1.11, 1.58)	1362	1.32 (1.11, 1.58)
Total cholesterol, mmol/l	2696	4.09 (3.65, 4.64)	1334	4.20 (3.70, 4.71)	1362	4.01 (3.57, 4.53)
Total cholesterol/HDL cholesterol	2696	3.04 (2.57, 3.61)	1334	3.06 (2.61, 3.64)	1362	3.00 (2.53, 3.58)
Triglycerides/HDL cholesterol	2696	1.16 (0.78, 1.85)	1334	1.21 (0.83, 1.95)	1362	1.08 (0.74, 1.78)
Using hypolipidemic drug, %	2739	3.0%	1359	2.3%	1380	3.6%
Ancestry, %						
White		68.0%		63.8%		72.2%
Black		14.2%		18.0%		10.5%
Hispanic		14.1%		14.5%		13.7%
Other		3.7%		3.7%		3.7%
Physician diagnosis, %						
Type 1		85.4%		82.4%		88.4%
Type 2		14.6%		17.6%		11.6%

p25 25th percentile, *p75* 75th percentile, $W_{NHA}HtR$ ratio of waist circumference-to-height using WC measurement per protocol of NHANES, $W_{WHO}HtR$ ratio of waist circumference-to-height using WC measurement per protocol of World Health Organization

SEARCH Study sample of youth recently diagnosed with diabetes (ages 5–19 years)

Table 2

Variations explained at baseline (A) or at follow-up (B) after adding $W_{NHA}HtR$ and $W_{WHO}HtR$, respectively, to a basic model Outcome Degrees of freedom (DF) and adjusted R-squares of baseline models

Outcome	Degrees of freedom (DF) and adjusted R-squares of baseline models								
	N	DF_{basic}	R_2 basic model	DF_{Full}	R_2 $W_{NHA}HtR$		R_2 $W_{WHO}HtR$		Δ($W_{NHA}HtR$, $W_{WHO}HtR$)
					R_2	ΔR_2	R_2	ΔR_2	Compare ΔR_2
A: Baseline data									
Systolic BP	2680	10	0.396	13	0.459	0.063	0.465	0.069	0.006
Diastolic BP	2674	10	0.205	15	0.237	0.032	0.233	0.028	−0.004
Log(triglycerides)	2669	8	0.156	13	0.306	0.150	0.317	0.161	0.011
HDL cholesterol	2673	8	0.138	13	0.271	0.133	0.274	0.136	0.002
Log(total cholesterol/HDL cholesterol)	2646	9	0.110	14	0.300	0.190	0.309	0.199	0.009
Log(triglycerides/HDL cholesterol)	2646	9	0.189	14	0.374	0.184	0.388	0.199	0.015
B: Follow-up data									
Systolic BP	1677	11	0.220	16	0.302	0.082	0.306	0.086	0.004
Diastolic BP	1680	11	0.145	16	0.185	0.040	0.187	0.042	0.002
Log(triglycerides)	1664	9	0.038	14	0.112	0.074	0.122	0.084	0.010
HDL cholesterol	1664	9	0.053	14	0.145	0.092	0.165	0.112	0.020
Log(total cholesterol/HDL cholesterol)	1647	10	0.031	15	0.146	0.115	0.169	0.138	0.023
Log(triglycerides/HDL cholesterol)	1648	10	0.049	15	0.155	0.106	0.180	0.131	0.025

Basic models include all the model covariates EXCEPT for those describing the WHtR

$W_{NHA}HtR$ ratio of waist circumference-to-height using WC measurement per protocol of NHANES, $W_{WHO}HtR$ ratio of waist circumference-to-height using WC measurement per protocol of World Health Organization, ΔR^2 change in the proportion of variation explained, relative to the basic model

Int J Obes (Lond). Author manuscript; available in PMC 2022 August 30.

Table 3

Changes in AUC at baseline (A) or at follow-up (B) after adding W_{NHA}HtR and W_{WHO}HtR, respectively, to a basic model

Outcome	*N* used	AUC for basic model	W_{NHA}HtR		W_{WHO}HtR		Δ(W_{NHA}HtR, W_{WHO}HtR)			
			AUC	ΔAUC	W_{WHO}HtR	ΔAUC	Compare ΔAUC	95% CI		*P*-value
								LB	UB	
A: Baseline data										
Systolic BP	2693	0.829	0.853	0.024	0.855	0.026	0.002	−0.0002	0.0036	0.07
Diastolic BP	2692	0.727	0.747	0.020	0.747	0.020	0.000	−0.0028	0.0022	0.80
Triglycerides	2663	0.731	0.800	0.069	0.804	0.073	0.004	0.0008	0.0081	0.018
HDL cholesterol	2663	0.720	0.778	0.058	0.783	0.063	0.005	0.0009	0.0082	0.016
Total chol/HDL cholesterol	2663	0.675	0.775	0.100	0.781	0.106	0.006	0.0014	0.0108	0.012
Triglycerides/HDL cholesterol	2663	0.730	0.810	0.080	0.816	0.086	0.006	0.0021	0.0099	0.003
B: Follow-up data										
Systolic BP	1688	0.730	0.775	0.046	0.778	0.048	0.002	−0.0027	0.0076	0.35
Diastolic BP	1688	0.682	0.707	0.024	0.710	0.028	0.003	−0.0011	0.0077	0.14
Triglycerides	1661	0.627	0.687	0.060	0.693	0.066	0.006	−0.0006	0.0125	0.07
HDL cholesterol	1660	0.630	0.715	0.085	0.724	0.094	0.010	0.0020	0.0173	0.013
Total chol/HDL cholesterol	1660	0.635	0.724	0.089	0.732	0.097	0.008	0.0001	0.0167	0.046
Triglycerides/HDL cholesterol	1660	0.627	0.715	0.088	0.723	0.095	0.007	0.0004	0.0144	0.040

AUC area under the receiver operator curve (ROC), *NHAHtR* ratio of waist circumference-to-height using WC measurement per protocol of NHANES, *WWHOHtR* ratio of waist circumference-to-height using WC measurement per protocol of World Health Organization, *ΔAUC* change in the area under the ROC curve, relative to the basic model

Basic models include all the model covariates EXCEPT for those describing the WHtR

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Table 4

Follow-up characteristics by sex and baseline age group

Variable	All		Girls		Boys	
	N	Median (p25, p75) or %	*N*	Median (p25, p75) or %	*N*	Median (p25, p75) or %
Age at follow-up exam, y	1712	18.3 (15.4, 21.0)	892	18.3 (15.6, 20.9)	820	18.2 (15.3, 21.3)
Time between measurements, y	1712	6.4 (5.5, 7.7)	892	6.5 (5.6, 7.8)	820	6.4 (5.5, 7.7)
W_{NHA}HtR at *baseline*	1712	0.50 (0.46, 0.57)	892	0.53 (0.48, 0.61)	820	0.47 (0.44, 0.53)
W_{WHO}HtR at *baseline*	1712	0.46 (0.43, 0.52)	892	0.48 (0.43, 0.54)	820	0.45 (0.42, 0.50)
Baseline BMI, kg/m^2	1709	19.8 (17.0, 24.1)	891	20.2 (17.2, 25.4)	818	19.5 (16.9, 22.9)
BMI, kg/m^2	1709	24.2 (21.3, 28.5)	890	25.1 (22.1, 29.9)	819	23.3 (20.7, 27.1)
Systolic BP, mmHg	1708	108.0 (100.7, 115.3)	890	106.0 (99.3, 112.7)	818	109.7 (102.0, 118.5)
Diastolic BP, mmHg	1708	70.0 (63.3, 76.0)	890	69.3 (62.8, 76.0)	818	70.0 (64.0, 76.7)
Using antihypertensive drug, %	1691	8.1%	884	8.6%	807	7.6%
Triglycerides, mmol/l	1682	0.89 (0.66, 1.31)	871	0.93 (0.69, 1.33)	811	0.86 (0.62, 1.28)
HDL cholesterol, mmol/l	1681	1.35 (1.14, 1.61)	871	1.40 (1.14, 1.68)	810	1.27 (1.09, 1.53)
Total cholesterol, mmol/l	1682	4.31 (3.78, 4.97)	871	4.48 (3.91, 5.10)	811	4.12 (3.68, 4.78)
Total cholesterol/HDL cholesterol	1681	3.16 (2.62, 3.96)	871	3.16 (2.57, 3.95)	810	3.16 (2.66, 3.96)
Triglycerides /HDL cholesterol	1681	1.51 (1.00, 2.47)	871	1.49 (1.00, 2.44)	810	1.52 (1.00, 2.49)
Using hypolipidemic drug, %	1691	3.3%	884	3.8%	807	2.7%
Ancestry, %						
White		3.4%		3.3%		3.7%
Black		14.5%		19.7%		8.8%
Hispanic		12.3%		12.2%		12.3%
Other		69.8%		64.8%		75.2%
Physician diagnosis, %						
Type 1		86.4%		83.9%		89.3%
Type 2		13.6%		16.1%		10.7%

p25 25th percentile, *p75* 75th percentile, *W_{NHA}HtR* ratio of waist circumference-to-height using WC measurement per protocol of NHANES, *W_{WHO}HtR* ratio of waist circumference-to-height using WC measurement per protocol of World Health Organization

SEARCH Study participants examined on one occasion 5–10 years after baseline. At baseline exam all participants were between 5 and 19 years old

Data in Table 2 were obtained at the follow-up visit with the exception of three anthropometric variables designated as "*baseline*"

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