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Longitudinal associations between BMI, Waist Circumference and Cardiometabolic Risk in US Youth: Monitoring implications

R. Jago[1], **J. A. Mendoza**[2], **T. Chen**[2], and **T. Baranowski**[2]

[1]Centre for Exercise, Nutrition & Health Sciences, School for Policy Studies, University of Bristol, Tyndall Avenue, Bristol, BS8 1TP, UK

[2]Children's Nutrition Research Center, Baylor College of Medicine, 1100 Bates Street, Houston TX, USA

Abstract

This study examined whether change in Body Mass Index (BMI) or waist circumference (WC) is associated with change in cardiometabolic risk factors and differences between CVD specific and diabetes specific risk factors among adolescents. We also sought to examine any differences by gender or baseline body mass status. The paper is a longitudinal analysis of pre and post data collected in the HEALTHY trial. Participants were 4603 ethnically diverse adolescents who provided complete data at 6th and 8th grade assessments. The main outcome measures were percent change in the following cardiometabolic risk factors: fasting triglycerides, systolic and diastolic blood pressure, HDL-C, and glucose as well as a clustered metabolic risk score. Main exposures were change in BMI or WC z-score. Models were run stratified by gender; secondary models were additionally stratified by baseline body mass index group (normal, overweight or obese). Analysis showed that when cardiometabolic risk factors were treated as continuous variables, there was strong evidence ($p<0.001$) that change in BMI z-score was associated with change in the majority of the cardiovascular risk factors, except fasting glucose and the combined risk factor score for both boys and girls. There was some evidence that change in WC z-score was associated with some cardiovascular risk factors, but change in WC z-score was consistently associated with changes in fasting glucose. In conclusion, routine monitoring of BMI should be continued by health professionals, but additional information on disease risk may be provided by assessing waist circumference.

Keywords

Obesity; risk; monitoring; Pediatric; Prevention

Address for correspondence: Russell Jago PhD, Centre for Exercise, Nutrition & Health Sciences School for Policy Studies, University of Bristol, Tyndall Avenue, Bristol, BS8 1TP, UK Tel: +44 (0) 117 3311141 Fax: +44(0) 117 3311148 Russ.Jago@bris.ac.uk.

INTRODUCTION

Cardiometabolic risk factors (elevated lipids, glucose, and hypertension), have been associated with increased risk of heart disease and type 2 diabetes among adults (1). Risk factors track from childhood to adulthood (2, 3). Childhood cardiometabolic risk factor levels also increase the likelihood of possessing the metabolic syndrome and type 2 diabetes in adulthood (4). Thus, limiting the establishment of cardiometabolic risk factors among youth is important for adult disease prevention. Obesity has been consistently associated with cardiovascular disease and type 2 diabetes among adults (5, 6). Higher body mass has also been associated with dyslipidemia (7, 8), hypertension (8, 9) and decreased insulin sensitivity (10) among youth. Therefore, preventing or ameliorating obesity once it has developed is likely to help prevent the development of cardiometabolic risk factors among youth.

The two most commonly used clinical assessments of obesity status are body mass index (BMI = kg/m^2) and waist circumference (WC) (11). Body mass index provides an overall indication of weight in relation to height while WC provides a measure of central adiposity (11). Studies among adults have suggested that waist circumference is a better predictor of cardiovascular disease and type 2 diabetes than BMI (12–14). Pediatric studies on the relationship with cardiometabolic risk that compared waist circumference and BMI have shown mixed results (15–17). Recent analysis of the prospective Avon Longitudinal Study of Parents and Children (ALSPAC) indicated that waist circumference was no more strongly associated with the cardiometabolic risk factors than BMI (18). The ALSPAC sample was, however, limited to mainly white participants from a single area of the UK and thus comparable patterns may not be obtained with youth from different ethnic and geographic backgrounds. Cross-sectional analysis of US National Health and Nutrition Examination Survey (NHANES) data suggested that WC is more strongly associated with pediatric cardiometabolic risk than BMI z-score (17). It is not clear if associations between change in WC and cardiometabolic risk profile are evident after accounting for the associated change in BMI, or vice versa. Equally it is not clear whether the patterns differ by type of cardiometabolic risk factor such that BMI may be a better predictor of overall risk while WC may be a stronger predictor of insulin and glucose.

This manuscript addresses in a large, ethnically diverse dataset whether change in BMI or WC is associated with change in each of the individual risk factors; whether the associated changes in each risk factor are clinically significant; and whether these relationships vary by gender. A secondary objective was to address whether these relationships vary by baseline body mass group.

METHODS

Sample

The current analysis is a secondary examination of data from the HEALTHY Study, a US National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) cluster randomized controlled trial, that aimed to reduce the prevalence of risk factors for type 2 diabetes mellitus among middle school children (6^{th} – 8^{th} grade) (19, 20). The study design

and the analysis of primary outcomes have been reported elsewhere (19, 20). Briefly, participants were recruited from 42 middle schools with six schools recruited from each of seven field centers from across the USA. Participants were recruited from schools that had at least 50% of students eligible for free or reduced-price lunch or belonging to an ethnic minority group and an annual student attrition rate from all causes ≤ 25%. All 6th grade students were invited to participate in a `health screening'. At baseline students were given a $50 incentive for data collection with as many students as possible followed through 8$^{th}$ grade when a second `health screening' was conducted with a $60 incentive given for this data collection. This study was approved by the Institutional Review Boards at each field centre, and written informed parental consent and child assent were obtained.

Procedures

Height and body mass were measured without shoes using the Prospective Enterprises PE-AIM-101 stadiometer and the SECA Corporation Alpha 882 electronic scale. Body mass index (kg/m^2) was calculated and converted to an age and gender specific BMI percentile using CDC 2000 criteria (21). Waist circumference was taken using a Gulick tape measure (G-tape) on bare skin measured just above the iliac crest. An age and gender specific waist circumference z-score was calculated by subtracting its sub-group mean from the raw score and dividing by standard deviation. Blood pressure was recorded three times using an automated blood pressure monitor (Omron HEM-907XL, Vernon Hills IL). The initial value was recorded after the participant had been seated quietly for five minutes with each subsequent value recorded one minute after the preceding recording. The mean of the second and third recordings were used in analyses.

Participants were called the night before data collection to remind them not to eat or drink anything but water after midnight. Participants who reported eating after midnight were considered non-fasting and asked to return another day. Phlebotomists obtained fasting blood samples which were processed. Vacutainers containing Na-fluoride and Na-heparin were used to collect blood for glucose and insulin samples, respectively. Cholesterol samples were collected in EDTA tubes. Blood was spun and separated into serum and plasma, frozen, packed in dry ice, and shipped to the Northwest Lipid Metabolism and Diabetes Research Laboratory at the University of Washington (WA). Analyses of glucose were performed on a Roche P module auto-analyzer by the hexokinase method using reagent from Roche Diagnostics. The measurement of HbA1c level was performed using an automated non-porous ion exchange high-performance liquid chromatography system (G-7 Tosoh Biosciences Inc.). Measurements of total plasma cholesterol, cholesterol in the lipoprotein fractions, and triglycerides were performed enzymatically on the Roche Modular-P autoanalyzer using methods standardized to the Centers for Disease Control and Prevention Reference Methods (22). Determination of high density lipoprotein (HDL-C) cholesterol was performed after precipitation of apolipoprotein B-containing particles by dextran sulfate Mg^{+2}. Low density lipoprotein (LDL-C) cholesterol was calculated using the Friedewald equation (23). This approach for calculating LDL is clinically reliable if the measurements of total and HDL cholesterol are performed with a high level of accuracy and triglycerides are < 400 mg/dL (24). In the case of elevated triglycerides, a complete lipoprotein separation by ultracentrifugation which allows quantification of the individual

lipoprotein classes was performed using the Lipid Research Clinics Beta Quantification procedure (25). Insulin was determined using a double-antibody radioimmunoassay (16). The inter-assay coefficients of variation are consistently < 1.5% for total cholesterol and triglycerides and < 2% for HDL cholesterol. The between assay coefficients of variation (CVs) of the two low- and high- insulin quality control samples were 6.9 and 4.6%, respectively.

Pubertal status was individually self-reported in private using the Pubertal Development Scale (26) and converted to pubertal stage groups consistent with the five pubertal stages outlined by Tanner (27). Ethnicity and household education were obtained via parental report.

Data processing

As the analysis focused on the effect of change in BMI z-score or WC z-score from 6th grade to 8th grade on the change in cardiometabolic risk factors, the sample was limited to the 4603 participants (2,175 males and 2,428 females) who provided some data at both time points. There were a maximum of 6358 participants who provided some data at the 6th Grade health screening and as such the analysis sample is comprised of 72.4% of the potential participants. Since the focus of the analysis was on change in cardiometabolic risk and the association with change in BMI and WC and not the possible contribution of the intervention to facilitating the change, the models included both intervention and control group participants and controlled for group assignment.

Body mass index (kg/m^2) was calculated and converted to an age and gender specific BMI percentile using CDC 2000 criteria (21). Youth with BMI ≥ 85th but < 95th percentile were classified as overweight, those ≥ 95th percentile as obese and those <85th percentile were healthy weight (28). To protect participant confidentiality, very high or low BMI z-score and WC values were recoded in the publicly available dataset. Those values that fall under/above a low/high cut point were recoded as the corresponding cut point itself. The cut-off points for BMI z-score and WC in 6th grade, WC in 8th grade are ≤ −0.50, ≥ 2.10 for BMI SDS and ≤57cm, ≥97cm for WC at 6th grade or ≤64cm, ≥99cm for WC at 8th grade. The age and gender specific WC z-scores were computed from this dataset and as such this score only applied to the current population

To provide an indication of overall risk, a composite metabolic risk factor z-score (MSRS_z) was created based on methods of Andersen and colleagues (29). This approach was used because we have previously reported that less than 10% of the participants were classified as having the metabolic syndrome using the International Diabetes Federation (IDF) criteria (30). Using the Andersen approach, z-scores were obtained for triglycerides, HDL-C (reverse scored), systolic blood pressure, diastolic blood pressure, glucose and waist circumference. The mean of the scores was then derived and labeled as MSRS_z.

Outcome variables

Three types of outcome variables were analyzed: 1) change in individual cardiometabolic risk factors; 2) change in composite metabolic risk score; and 3) change in whether the participant had values above the risk factors level in the 8th grade. The first analyses focused

on whether there was a percentage change e.g., increase (or decrease), from 6th to 8th grade in the variable of interest. The second analyses included the MSRS_z composite variable as the outcome. The third analysis examined whether the participant exceeded the IDF values for each of the cardiometabolic risk factors (i.e. did the participant have an elevated level of risk for that variable) at 8th grade. The following values were therefore used to indicate the presence of an elevated level of risk: triglycerides >=150 mg/dl, HDL-C <40 mg/dl, LDL-C ≥ 130 mg/dl, glucose >=100 mg/dl, systolic blood pressure >=130 mm Hg, diastolic blood pressure>=85 mm Hg.

Statistical Analyses

Descriptive statistics were calculated for all metabolic risk factors and demographic characteristics as appropriate in 6th and 8th grades. To ensure data involving missing values did not result in biased estimates, Little's chi-square test for Missing Completely at Random was performed (31). To examine if the truncated BMI and WC values were similarly chosen, we compared the z-scores for low and high WC, weight and height with participants from the U.S. National Health and Nutrition Survey (NHANES 2007 to 2008) database. These analyses indicated that the high and low cut-points applied to our data were broadly similar across weight, height and WC to the NHANES thresholds. The z-scores of low and high cut-points were at the ranges of −1.30 to 0.43 and 1.36 to 2.50, respectively.

Linear mixed models (LMM) and generalized linear mixed models (GLMM) were used to investigate the effect of BMI z-score change and WC z-score change on the change of risk factors and at risk or not in 8th grade, respectively. Analyses were run for each risk factor to identify the percent change in the outcome variable that was associated with a 1-unit change in BMI or WC z-score change. The main models controlled for potential confounding variables (e.g., ethnicity, 6th grade pubertal development and parental education) and were stratified by gender alone. Secondary analyses, which were stratified by both gender and weight status (healthy weight, overweight and obese) were also run. We tested the main effect of change of BMI z-score or change of WC z-score when all the covariates listed above were included along with the other z-score. As this paper was focused on how change in BMI or WC z-score was associated with change in risk, the sample for the third analyses was limited to only those participants with values below the risk factor threshold during 6th grade. The process was then repeated using a logistic regression approach with binary outcome (above the threshold or not) for each risk factor. For all models, students were modelled as nested within schools with school treated as a random effect. As previous research has reported that a ½ standard deviation reduction in BMI z-score has been associated with improvement in the risk profile of obese youth (10, 32) we also calculated the odds ratios associated with a ½ unit change. This was achieved by multiplying the log odds estimates by 0.5 and interpreting the exponential transformation of this value as the odds ratio associated with ½ standard deviation change. All the analyses were completed using the PROC MIXED and PROC GLIMMIX procedures in Statistical Analysis Systems (version 9.2, 2009, SAS Institute Inc., Cary, NC).

RESULTS

The sample was 54% Hispanic, 18% Black and 19.3% White. At 6th grade 50.2% of the sample were healthy weight, 19.5% were overweight and 30.2% were obese. The study participants consisted of 47.3% boys and 52.8% girls. The percentage of the educational level was 52.4% and 47.7% for high school graduate or less and some college or above, respectively. (Little's chi-square test for whether participants were missing data completely at random (MCAR) indicated that there was no evidence of systematic missing data (χ^2 = 639.9, df = 605, p = 0.16). Under MCAR, the failure to observe a certain data point is assumed independent of the unobserved (missing) value (31).

Descriptive statistics (means and standard deviations) are presented stratified by grade and gender in Table 1. Table 1 also includes the percent of participants classified as at risk for each of the risk factors by grade and gender. There was evidence of a gender difference in 8th grade for all risk factors, but there was only evidence for a gender difference in LDL-C, SBP and glucose in 6th grade ($p<0.01$). It is also noticeable that fasting insulin levels were higher among males than females during 6th grade (12.2 vs. 10.76 μU/dL, $p<0.01$), while HBA1C(%)* was higher among males than females at 8th grade (5.2 vs. 5.1%, $p<0.01$). In terms of prevalence of risk factors above threshold values, there was some evidence of gender differences for triglycerides, HDL-C, SBP and glucose in 8th grade and glucose in 6th grade ($p<0.01$).

The main regression models which predict percent change in risk factors for participants are presented by gender in Table 2. Among boys, these was strong evidence ($p<0.001$) that change in BMI z-score was associated with change in all of the risk variables except glucose. For example, a one standard deviation change in BMI z-score from 6th to 8th grade was associated with an 18.6% increase in triglycerides. There was also strong evidence ($p<0.001$) that change in BMI z-score was associated with change in triglycerides, HDL-C, LDL-C and the combined risk factor score, and some evidence ($p=0.02$) that BMI z-score was associated with change in diastolic pressure among girls. There was strong evidence ($p<0.001$) that WC z-score was associated with change in triglycerides, HDL-C, LDL-C and the combined risk factor score among boys, and some evidence ($p=0.04$) that WC z-score was associated with change in glucose. There was also strong evidence ($p<0.001$) that change in WC z-score was associated with change in HDL-C, glucose and the combined risk factor score among girls.

The secondary analyses, which present percent change in risk factors for participants stratified by gender and 6th grade body mass group are presented in Table 3. For healthy weight boys, there was some evidence that change in BMI z-score was associated with a change in triglycerides ($p =0.01$) and HDL-C ($p =0.01$), and likewise strong evidence ($p<0.001$) of an association with change in systolic blood pressure and the combined risk factor score. There was some evidence that change in WC z-score was associated with change in HDL-C ($p=0.01$) and LDL-C ($p=0.02$). For girls who were healthy weight in 6th grade there was some evidence that change in BMI z-score was associated changes in triglycerides ($p=0.01$), LDL-C ($p=0.01$) and the combined risk factor score ($p = 0.01$), and likewise strong evidence of an association with change in HDL-C ($p<0.001$). There was

some evidence that change in WC z-score was associated with changes in girls' HDL-C ($p = 0.01$) and strong evidence of an association with glucose ($p<0.001$) and the combined risk factor score ($p<0.001$).

For boys who were overweight in 6th grade, there was some evidence that change in BMI z-score was associated with change in triglycerides ($p=0.01$), LDL-C ($p = 0.03$), and systolic blood pressure ($p = 0.01$), and strong evidence for an association with the combined risk factor ($p<0.001$). There was some evidence that change in WC z-score was associated with change in glucose ($p = 0.04$) and the combined risk factor score ($p = 0.02$).

For girls who were overweight in 6th grade, there was strong evidence that change in BMI z-score was associated with change in triglycerides, HDL-C, LDL-C, systolic blood pressure and the combined risk factor score and some evidence of an association with change in diastolic blood pressure ($p=0.01$). There was no evidence that change in WC z-score was associated with change in any of the cardiometabolic risk factors among girls who were overweight at 6th grade.

For boys who were obese in 6th grade, there was strong evidence ($p<0.001$) that change in BMI z-score was associated with change in HDL-C and the combined risk factor score with some evidence of an association with change in triglycerides ($p = 0.04$), LDL-C ($p = 0.01$) and glucose ($p = 0.04$). Among girls who were obese at 6th grade there was strong evidence ($p<0.001$) that change in BMI z-score was associated with change in triglycerides, HDL-C, LDL-C and the combined risk factor score with some evidence of an association with change in diastolic blood pressure ($p = 0.03$) and glucose ($p =0.01$). There was strong evidence ($p<0.001$) that change in WC z-score was associated with change in triglycerides and some evidence of an association with change in HDL-C ($p=0.01$), LDL-C ($p = 0.03$) and the combined risk factor score among boys who were obese at 6th grade but no evidence of an association between WC change and risk factor change among girls.

Logistic regression models predicting the presence of each of the cardiometabolic risk were run stratified by gender and are presented in Table 4. There was some evidence that change in BMI z-score was associated with an increased risk of elevated systolic blood pressure ($p = 0.02$) with a ½ BMI SDS unit change associated with a 56% increase in the likelihood of elevated systolic blood pressure. There was also some evidence that change in WC z-score was associated with an increased likelihood of possessing elevated triglycerides ($p=0.02$) among boys. These findings suggest that a ½ unit change in WC z-score was associated with 56% increase in the likelihood that the participants had high triglycerides. Among girls there was some evidence ($p = 0.01$) that change in WC z-score was associated with an increased risk of high triglycerides with a ½ unit change in WC z-score associated with a 61% increase in the likelihood that the girl had a triglyceride level that exceeded the threshold of 150 mg/dl in 8th grade. Change in WC Z-score was also associated with lower HDL-C, with a ½ standard deviation change associated with a 38% increase in the likelihood of having HDL-C < 40 mg/dl in 8th grade. Because of the small number of participants in some cells it was not possible to get the logistic regression model that examined the how change in BMI and WC z-score was associated with change in risk factor prevalence, which was stratified by gender and 6th BMI group to converge.

DISCUSSION

This paper longitudinally compared changes in BMI and WC with changes in cardiometabolic risk factors among an ethnically diverse sample of US youths. When cardiometabolic risk factors were treated as continuous variables, change in BMI z-score, while controlling for WC z-score, was associated with change in the majority of the cardiovascular risk factors and the combined risk factor score for both boys and girls in all three 6th grade BMI groups after accounting for waist circumference. In contrast, we are the first to report that change in WC z-score was associated with fewer cardiovascular risk factors, but was consistently associated with changes in serum fasting glucose. Collectively, these findings imply that limiting increases in BMI is likely to provide the greater overall protection against the potential development of cardiometabolic risk factors but specifically limiting increases in central adiposity may be beneficial for controlling glucose levels which is critical for the prevention of type 2 diabetes. Our findings are consistent with current guidance in the UK (33) and US (34) which recommends the routine assessment of BMI among youth. However, the data presented here indicate that change in WC contributed independent information and it may be of value for health care providers to routinely measure WC.

The findings reported here are similar to a recent report from the Bristol (UK) based ALSPAC study which concluded that BMI can identify children who are at adverse risk of cardiovascular disease and that no additional benefit is obtained by using a measure of central adiposity (18). The data presented here extended those findings by showing that among a more ethnically diverse sample of US adolescents change in BMI was more strongly associated with cardiometabolic risk factors than change in WC but change in WC may be an important indicator for high fasting glucose. The increased ethnic variability of this sample was important as levels of central adiposity, as indicated by a high waist circumference have been shown to differ by ethnicity. For example, data from the 2001–2006 NHANES survey indicated that 22.7% of 12 to 19 year old Hispanics had a waist circumference ≥90th percentile but only 18.5% of white and 17.5% of black adolescents (35). Thus, by showing that within an ethnically diverse sample that BMI is more closely associated with adverse cardiovascular profiles than WC we have extended the previous UK findings. Present findings stand in contrast to analyses of the US NHANES database, which reported that WC had stronger associations with cardiometabolic risk compared to BMI z-score (17). However, that study was nationally representative for 6–19 year olds, considered accelerometer-determined moderate-to-vigorous physical activity in analyses, and was cross-sectional in design, which makes direct comparisons difficult. Regardless, altogether both studies indicated that WC is an important predictor of paediatric cardiometabolic risk.

As noted in the introduction to this paper, the presence of high levels of cardiometabolic risk factors in youth increases the risk of adult coronary heart disease and type 2 diabetes. At the 6th grade assessment 9% of our participants had high triglycerides, approximately 13% had low HDL-C and 19% of boys and 13% of girls had high glucose levels. Thus, at the start of secondary school (middle school in the US), a number of children have levels of cardiometabolic risk factors that are concerning. Due to the relatively small proportion of participants who had risk factor levels that would be classified as at risk in 8th grade it was

not possible to stratify the analyses to examine how change in BMI or WC z-score was associated with risk factor classification in gender and 6th grade BMI sub-groups. When these findings are viewed in conjunction with the continuous analyses discussed above, the analyses suggest that although increases in BMI are associated with an increase in cardiometabolic risk factors during adolescence, the change in BMI may not be sufficient to yield a change in the classification of youth as possessing risk factor levels that could be classified as at risk. The lack of evidence to indicate an effect of change on classified risk does not however indicate the absence of an association, but rather that there is a change which over the 3 year time period might not be detected by a simple classification process. As such, it might be important for clinicians to monitor the risk factor levels of children whose BMI is increasing to identify worsening trends in cardiometabolic values that could act as early warning signs of future health problems. Identification of these trends may in turn facilitate early intervention.

The current study does not provide information on why change in BMI is more closely associated with adverse cardiovascular risk factors than change in WC among adolescents. Data from the Diabetes Prevention Program indicated that models which included baseline waist circumference accounted for more of the variance when predicting the likelihood of developing type 2 diabetes than baseline BMI suggesting that waist circumference in adults is a better predictor of adult type 2 diabetes than BMI. Similarly, an analysis of the third NHANES survey indicated that waist circumference was a stronger predictor of metabolic syndrome than BMI (36). It has been suggested that central adiposity, for which waist circumference is a proxy measure (11), may reflect higher amounts of subcutaneous abdominal and/or visceral fat which impairs insulin control (37, 38). A key component in the establishment of cardiometabolic risk factors, MRI determined visceral fat, has also been associated with higher levels of triglycerides among obese adolescent girls (39). The weaker associations between change in waist circumference and adverse cardiometabolic risk factors in our study may suggest that the effects on insulin regulation occur over sustained periods of time. It may also be the case that the importance of WC and BMI in predicting clinically classified cardiovascular risk factors differs by baseline adiposity status, gender, or physical activity, but we were unable to test these associations and as such this could be a focus for future research.

Strengths and limitations

The major strength of this study is the relatively large dataset which includes a high proportion of Hispanic and African-American participants recruited from across the US. The available data were, however, only collected at two time points, 2.6 years apart, which means that it was not possible to assess the impact of BMI or WC change in between assessments or if associations continued into adulthood. We also used a clustered risk factor score for the continuous measures as we have previously reported that less than 10% of the participants would be classified as possessing the metabolic syndrome when using the International Diabetes Federation criteria (40). Sample size may have been inadequate for analyses stratified by gender and weight status.

CONCLUSIONS

Change in BMI z-score was associated with change in the majority of cardiovascular risk factors across body mass index groups. Change in WC z-score was associated with fewer cardiovascular risk factors, but was consistently associated with changes in serum fasting glucose. Data suggest that routine monitoring of BMI should be continued by general practitioners, primary care physicians and pediatricians but some additional information on future disease risk may also be provided by also assessing waist circumference and as such health professionals should also consider assessing waist circumference.

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Table 1

Descriptive statistics and prevalence of risk factors stratified by grade and gender

	6th Grade				8th Grade			
	Male		Female		Male		Female	
Descriptive Statistics	**Mean**	**Std Dev**	**Mean**	**Std Dev**	**Mean**	**Std Dev**	**Mean**	**Std Dev**
BMI Z-score[#]	0.99	0.93	0.86	0.90	0.89	0.91	0.87	0.84
WC Z-score	0.00	1.00	0.00	1.00	0.00	1.00	0.00	1.00
WC (cm)[$]	61.42	28.73	64.60	25.45	59.24	32.89	66.23	28.70
Triglycerides (mg/dl)[*]	87.71	51.95	90.15	53.28	85.15	54.12	80.89	38.33
HDL-C (mg/dl)[*]	52.92	12.34	52.19	12.06	49.39	11.83	53.31	12.49
LDL-C (mg/dl)[$]	88.76	23.72	85.73	22.68	79.07	22.83	81.59	22.22
Systolic Blood Pressure (mm.Hg)[$]	108.00	10.29	106.77	9.98	114.36	10.47	108.03	9.57
Diastolic Blood Pressure (mm.Hg)[*]	63.74	8.82	63.82	8.62	64.03	8.05	65.22	7.82
Glucose (mg/dl)[$]	94.43	6.60	92.69	6.63	95.88	7.84	92.13	8.22
Insulin (μU/dL)[#]	12.22	12.23	14.18	10.76	16.72	15.93	17.58	12.73
HBA1C(%)[*]	5.15	0.31	5.13	0.29	5.17	0.35	5.11	0.32

	6th Grade		8th Grade	
	% At Risk (n)		% At Risk (n)	
Prevalence (% At Risk, n)	**Male**	**Female**	**Male**	**Female**
Triglycerides >=150 mg/dl[*]	9.66 (204)	9.55 (225)	8.62 (183)	5.38 (128)
HDL-C <40 mg/dl[*]	12.84 (271)	13.41 (316)	19.59 (416)	12.37 (294)
LDL-C ≥ 130 mg/dL	5.16 (109)	3.65 (86)	2.45 (52)	2.61 (62)
Systolic Blood Pressure >=130 mm.Hg[*]	2.30 (50)	1.86 (45)	6.81 (148)	1.57 (38)
Diastolic Blood Pressure>=85 mm.Hg	1.89 (41)	1.86 (45)	1.38 (30)	1.20 (29)
Glucose >= 100 mg/dl[$]	19.28 (407)	13.11 (309)	29.96 (636)	14.89 354)

[#]Gender difference at 6th Grade (p<.01)

* Gender difference at 8th Grade ($p<0.01$)

$ Gender difference at 6th Grade and 8th Grade ($p<0.01$)

Table 2

Linear regression with change in BMI and WC z-score predicting percent change in risk factors*

	Change of BMI Z-score			Change of WC Z-score		
	Estimate	**95% CI**	***p*-value**	**Estimate**	**95% CI**	***p*-value**
Male (n=2175)						
Triglycerides (mg/dl)	18.64	(9.64, 27.65)	<0.001	17.88	(9.69, 26.08)	<0.001
HDL-C (mg/dl)	−6.07	(−8.77, −3.37)	<0.001	−6.53	(−8.99, −4.08)	<0.001
LDL-C (mg/dl)	5.13	(1.89, 8.36)	<0.001	7.51	(4.57, 10.46)	<0.001
Systolic Blood Pressure (mm.Hg)	2.35	(0.6, 4.11)	<0.001	0.23	(−1.37, 1.83)	0.78
Diastolic Blood Pressure (mm.Hg)	3.15	(0.71, 5.58)	<0.001	1.98	(−0.23, 4.19)	0.08
Glucose (mg/dl)	1.31	(−0.17, 2.79)	0.08	1.42	(0.07, 2.77)	0.04
MSRS_Z#	0.24	(0.15, 0.32)	<0.001	0.21	(0.13, 0.29)	<0.001
Female (n=2428)						
Triglycerides (mg/dl)	22.91	(16.55, 29.28)	<0.001	4.32	(−0.64, 9.27)	0.09
HDL-C (mg/dl)	−10.96	(−13.55, −8.37)	<0.001	−3.59	(−5.62, −1.56)	<0.001
LDL-C (mg/dl)	6.65	(3.53, 9.78)	<0.001	2.28	(−0.16, 4.72)	0.07
Systolic Blood Pressure (mm.Hg)	1.57	(0.02, 3.13)	0.05	0.97	(−0.25, 2.19)	0.12
Diastolic Blood Pressure (mm.Hg)	2.63	(0.37, 4.88)	0.02	1.64	(−0.13, 3.41)	0.07
Glucose (mg/dl)	0.21	(−1.18, 1.59)	0.77	1.79	(0.7, 2.87)	<0.001
MSRS_Z#	0.29	(0.21, 0.38)	<0.001	0.13	(0.07, 0.2)	<0.001

*All models are mutually adjusted for BMI and WC z-score as well as thence group, pubertal development and parental education

#MSRS_Z = Combined multiple risk factor score

Table 3

Change in BMI and WC z-score predicting percent change in risk factors – stratified analyses

	Change of BMI Z-score			Change of WC Z-score		
Healthy Weight (n=2311)	**Estimate**	**95% CI**	***p*-value**	**Estimate**	**95% CI**	***p*-value**
Male (n=1019)						
Triglycerides (mg/dl)	17.70	(4.31, 31.09)	0.01	15.63	(−0.84, 32.1)	0.06
HDL-C (mg/dl)	−5.35	(−9.09, −1.6)	0.01	−5.86	(−10.47, −1.25)	0.01
LDL-C (mg/dl)	2.89	(−1.31, 7.08)	0.18	6.22	(1.06, 11.39)	0.02
Systolic Blood Pressure (mm.Hg)	4.41	(2.02, 6.8)	0.001	−1.84	(−4.78, 1.1)	0.22
Diastolic Blood Pressure (mm.Hg)	3.68	(0.01, 7.35)	0.05	0.15	(−4.37, 4.67)	0.95
Glucose (mg/dl)	1.08	(−1.16, 3.33)	0.34	−0.02	(−2.78, 2.75)	0.99
MSRS_Z[#]	0.26	(0.14, 0.38)	<0.001	0.06	(−0.09, 0.2)	0.45
Female (n=1292)						
Triglycerides (mg/dl)	11.75	(2.89, 20.6)	0.01	7.76	(−0.61, 16.13)	0.07
HDL-C (mg/dl)	−5.54	(−8.84, −2.24)	<0.001	−4.00	(−7.15, −0.85)	0.01
LDL-C (mg/dl)	5.54	(1.57, 9.52)	0.01	2.42	(−1.34, 6.18)	0.21
Systolic Blood Pressure (mm.Hg)	0.78	(−1.35, 2.91)	0.47	0.82	(−1.21, 2.84)	0.43
Diastolic Blood Pressure (mm.Hg)	0.82	(−2.29, 3.93)	0.61	0.27	(−2.68, 3.22)	0.86
Glucose (mg/dl)	−1.20	(−3.19, 0.79)	0.24	2.88	(0.99, 4.78)	<0.001
MSRS_Z[#]	0.14	(0.03, 0.24)	0.01	0.15	(0.05, 0.25)	<0.001

	Change of BMI Z-score			Change of WC Z-score		
Overweight (n=899)	**Estimate**	**95% CI**	***p*-value**	**Estimate**	**95% CI**	***p*-value**
Male (n=409)						
Triglycerides (mg/dl)	33.00	(9.13, 56.88)	0.01	4.40	(−17.88, 26.69)	0.70
HDL-C (mg/dl)	−6.38	(−13.4, 0.65)	0.08	−4.99	(−11.58, 1.6)	0.14
LDL-C (mg/dl)	9.49	(1.08, 17.9)	0.03	5.47	(−2.39, 13.32)	0.17
Systolic Blood Pressure (mm.Hg)	6.23	(1.79, 10.67)	0.01	−1.48	(−5.62, 2.65)	0.48
Diastolic Blood Pressure (mm.Hg)	5.11	(−0.66, 10.89)	0.08	0.32	(−5.07, 5.7)	0.91
Glucose (mg/dl)	0.45	(−3.25, 4.15)	0.81	3.66	(0.21, 7.12)	0.04
MSRS_Z[#]	0.30	(0.1, 0.51)	<0.001	0.22	(0.03, 0.41)	0.02

	Change of BMI Z-score			Change of WC Z-score		
Overweight (n=899)	**Estimate**	**95% CI**	***p*-value**	**Estimate**	**95% CI**	***p*-value**
Female (n=490)						
Triglycerides (mg/dl)	24.50	(8.88, 40.12)	<0.001	1.33	(−9.13, 11.78)	0.80
HDL-C (mg/dl)	−19.36	(−26.56, −12.17)	<0.001	0.05	(−4.77, 4.88)	0.98
LDL-C (mg/dl)	13.85	(5.13, 22.57)	<0.001	−3.07	(−8.89, 2.75)	0.30
Systolic Blood Pressure (mm.Hg)	6.68	(2.94, 10.43)	<0.001	−0.44	(−2.96, 2.09)	0.73
Diastolic Blood Pressure (mm.Hg)	7.09	(1.45, 12.73)	0.01	−0.49	(−4.3, 3.32)	0.80
Glucose (mg/dl)	2.71	(−0.67, 6.09)	0.12	0.20	(−2.06, 2.45)	0.87
MSRS_Z[#]	0.59	(0.36, 0.81)	<0.001	0.02	(−0.13, 0.17)	0.77

Obese (n=1393)	**Change of BMI Z-score**			**Change of WC Z-score**		
	Estimate	**95% CI**	***p*-value**	**Estimate**	**95% CI**	***p*-value**
Male (n=747)						
Triglycerides (mg/dl)	18.85	(0.85, 36.85)	0.04	18.26	(6.83, 29.69)	<0.001
HDL-C (mg/dl)	−9.51	(−15.74, −3.27)	<0.001	−5.11	(−9.07, −1.15)	0.01
LDL-C (mg/dl)	11.27	(3.31, 19.23)	0.01	5.68	(0.64, 10.73)	0.03
Systolic Blood Pressure (mm.Hg)	2.18	(−1.83, 6.19)	0.29	0.72	(−1.83, 3.27)	0.58
Diastolic Blood Pressure (mm.Hg)	4.62	(−0.67, 9.9)	0.09	1.53	(−1.83, 4.89)	0.37
Glucose (mg/dl)	3.19	(0.22, 6.17)	0.04	0.78	(−1.11, 2.67)	0.42
MSRS Z[#]	0.35	(0.14, 0.55)	<0.001	0.18	(0.05, 0.31)	0.01
Female (n=646)						
Triglycerides (mg/dl)	32.14	(16.76, 47.52)	<0.001	2.35	(−5.58, 10.29)	0.56
HDL-C (mg/dl)	−19.01	(−26.44, −11.58)	<0.001	−3.08	(−6.91, 0.76)	0.12
LDL-C (mg/dl)	15.23	(6.53, 23.94)	<0.001	2.07	(−2.42, 6.55)	0.37
Systolic Blood Pressure (mm.Hg)	3.01	(−1.27, 7.29)	0.17	0.04	(−2.16, 2.24)	0.97
Diastolic Blood Pressure (mm.Hg)	6.58	(0.69, 12.47)	0.03	1.94	(−1.09, 4.96)	0.21
Glucose (mg/dl)	4.81	(1.42, 8.19)	0.01	0.03	(−1.72, 1.77)	0.98
MSRS_Z[#]	0.64	(0.42, 0.86)	<0.001	0.04	(−0.07, 0.16)	0.47

[*] All models are mutually adjusted for BMI and WC z-score as well as ethnic group, pubertal development and parental education

[#] MSRS_Z = Combined multiple risk factor score

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Table 4

Logistic regression with change in BMI and WC z-score predicting IDF threshold values by gender*

	Change of BMI Z-score				Change of WC Z-score			
	OR (1 SD)	**95% CI**	***p*-value**	**OR (1/2 SD)**	**OR (1 SD)**	**95% CI**	***p*-value**	**OR (1/2 SD)**
Male (n=2175)								
Triglycerides >=150 mg/dl	1.96	(0.86, 4.48)	0.11	1.40	2.42	(1.15, 5.1)	0.02	1.56
HDL-C <40 mg/dl	1.28	(0.72, 2.26)	0.40	1.13	1.72	(1.01, 2.93)	0.05	1.31
LDL-C ≥ 130 mg/dL	2.23	(0.37, 13.44)	0.38	1.49	1.46	(0.3, 7.11)	0.64	1.21
Systolic Blood Pressure >=130 mm.Hg	2.42	(1.14, 5.15)	0.02	1.56	0.72	(0.37, 1.42)	0.35	0.85
Diastolic Blood Pressure>=85 mm.Hg	2.91	(0.52, 16.35)	0.22	1.71	0.54	(0.12, 2.51)	0.44	0.74
Glucose >=100 mg/dl	1.33	(0.82, 2.16)	0.24	1.15	1.30	(0.84, 2)	0.23	1.14
Female (n=2428)								
Triglycerides >=150 mg/dl	1.33	(0.51, 3.46)	0.56	1.15	2.58	(1.22, 5.46)	0.01	1.61
HDL-C <40 mg/dl	1.30	(0.67, 2.52)	0.44	1.14	1.90	(1.13, 3.18)	0.02	1.38
LDL-C ≥ 130 mg/dL	1.87	(0.51, 6.84)	0.34	1.37	0.78	(0.28, 2.19)	0.64	0.88
Systolic Blood Pressure >=130 mm.Hg	0.39	(0.11, 1.47)	0.17	0.63	1.66	(0.61, 4.49)	0.32	1.29
Diastolic Blood Pressure>=85 mm.Hg	0.59	(0.12, 2.95)	0.52	0.77	2.26	(0.69, 7.37)	0.18	1.50
Glucose >=100 mg/dl	1.28	(0.74, 2.22)	0.37	1.13	1.20	(0.78, 1.85)	0.40	1.10

The sample only included participants with values below the risk factor threshold during 6th grade.

*All models are mutually adjusted for BMI and WC z-score as well as thence group, pubertal development and parental education OR=odds ratio.