

THE RELATIONSHIP BETWEEN INSULIN RESISTANCE AND SURROGATES OF
ADIPOSITY IN CHILDREN AND ADOLESCENTS

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ABSTRACT

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The relationship between insulin resistance and surrogates of adiposity in children and adolescents

(Under the direction of Dr. Robert McMurray)

This study investigated the relationship between insulin resistance (HOMA-IR>4.0) and six adiposity surrogates in children and adolescents: body mass index (BMI), BMI percentiles (BMI %), sum of skinfolds (SSF), waist circumference (WC), WC percentiles (WC %), and waist circumference to height ratio (WHtR). Step-wise multiple regression models for HOMA-IR, including age, sex, and ethnicity, found that SSF was the strongest surrogate for predicting insulin resistance ($r^2=0.298$) with little influence from age, sex, and ethnicity. The weakest predictor was BMI % ($r^2=0.148$) and was significantly influenced by age, sex, and ethnicity. Odds ratios were determined for risk of developing insulin resistance. These were highest for SSF compared to the other surrogates, with SSF >28 mm, increasing the risk of insulin resistance 9.2 times (CI=7.0-11.9). Thus, SSF appears to be the most independent surrogate to predict insulin resistance and BMI % the least independent surrogate.

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Chapter 1

Introduction

Obesity has become an epidemic in children, adolescents, and adults (Gielen and Hambrecht, 2004; Kimm and Obarzanek, 2002). In 1991 40% of men and 26% of women were overweight and 20% and 26%, respectively, were obese (Gielen and Hambrecht, 2004). According to Gielen and Hambrecht (2004), by 2015 30% of adults will be obese, and by 2025 more than 40% of adults will be obese. Obesity has been linked to many disease states like cardiovascular disease and Type II diabetes (Kimm and Obarzanek, 2002). When obesity is present in childhood and adolescence the risks of disease states are started earlier (Gielen and Hambrecht, 2004; Kimm and Obarzanek, 2002). Thus, there is a need to quickly and simply quantify adiposity in children and adolescents. In doing so, researchers, teachers, physicians, and parents will be able to identify obesity and intervene early. This section will begin with the examining insulin resistance and transition into examining each of the six adiposity surrogates to be reviewed in this study.

Insulin Resistance

Insulin resistance has been shown to be directly related to the development of Type II diabetes (ADA, 2005; Scott, 2006; Soltész, 2006). The on-set of Type II diabetes is marked by high insulin levels rather than high glucose levels. In individuals that develop insulin resistance the body is unable to respond properly to the insulin that it secretes. Thus, the pancreas's β -cells compensate by producing more insulin creating the state known as hyperinsulinemia, or high blood insulin levels. Eventually, β -cell function fails to keep up

with the insulin demand and glucose levels begin to increase which develops into Type II diabetes. The number of children and adolescents, as well as adults, affected by Type II diabetes is on the rise; thus, there is an increased interest in insulin sensitivity and resistance (Kimm and Obarzanek, 2002). However, very little research has explored insulin resistance in children (Katzmarzyk et al., 2004; Maffei et al., 2002; Roemmich et al., 2002). Maffei et al. (2002) used the Homeostasis Model of Assessment (HOMA), as defined by Matthews et al. (1985), to determine insulin resistance in adults by looking at fasting levels of blood glucose and insulin. It was found that childhood insulin resistance according to the HOMA technique was a good predictor of obesity in women (Maffei et al., 2002). Roemmich et al. (2002) found that insulin resistance in adolescents was related to fat mass ($r=0.59$, $P<0.001$). These studies found insulin resistance to be an accurate predictor of obesity in both children and adolescents (Katzmarzyk et al., 2004; Maffei et al., 2002; Roemmich et al., 2002).

Fortunately, there are more studies examining the various surrogates of adiposity, in children, than those that have examined insulin resistance. Previous researchers have used various means of measuring adiposity in children. These include body mass index (BMI), BMI percentiles, sum of skin folds (SSF), waist circumference (WC), and waist circumference percentiles (Fernández et al., 2004; Freedman et al., 1999; Gallagher et al., 2000; Kahn et al., 2005; Katzmarzyk et al., 2004; Watts et al., 2006). Each method will be discussed individually. However, most of these methods use complex tables and equations that are dependent on age, sex, and ethnicity. An ideal surrogate would estimate obesity independent of age, sex, and ethnicity because children and adolescents are at different pubertal stages of development.

Body Mass Index

Body Mass Index (BMI) is the most common surrogate of adiposity. It appears to be a simple model since it is solely based on mass and height (kg/m^2). Although the model seems simple, it requires the use of charts and tables that are broken down by both age and sex. Also, Gallagher et al. (2000) found that BMI has a tendency to be a curvilinear function. If this is true, then the regression equation used to find BMI may not actually be a good predictor. Gallagher et al. (2000) also concluded that BMI may be somewhat influenced by age. This could be true because as one gets older the body often loses muscle mass and gains fat mass thus rearranging the proportion of free fat mass to fat mass. Moreover, it has been recently shown that BMI is a poor predictor ($r^2 = 0.34$) of fat mass in male children and adolescents (Ellis et al., 1999). Ellis et al. (1999) found that children with similar BMI values, especially males, did not actually have similar body fat percentages as when measured by dual energy x-ray absorptiometry. For example, BMI identified 28.5% to be at risk or overweight, while dual energy x-ray absorptiometry only identified half as many to be at risk or overweight (Ellis et al., 1999).

BMI Percentiles

The Center for Disease Control (CDC) has taken BMI for children and adolescents and calculated into percentiles in order to determine if they were at risk for being overweight ($\geq 85^{\text{th}} - 94.9^{\text{th}}$ percentile) or overweight ($\geq 95^{\text{th}}$ percentiles). These percentiles are broken down by both age and sex. They require the use of complicated charts in order to find the correct percentiles. Previous research has shown BMI percentiles are not very accurate at determining obesity (Demerath et al., 2006, Kahn et al., 2005). Kahn et al. (2005) found that BMI percentiles identified those with high blood pressure, but no other risk factors.

Demerath et al. (2006) found BMI percentiles to overestimate percent body fat in the higher percentiles and underestimate in the lower percentiles.

Sum of Skinfolds

Another common method of predicting adiposity is sum of skinfolds (SSF). SSF requires the proper use of a variety of skills and equipment. These skills include accurate and precise measurements at each body site, the use of calipers, the ability to separate subcutaneous fat from muscle, and the utilization of a variety of equations (Kravitz and Heyward, 2006). To obtain percent body fat from SSF, equations depend on age, sex, and ethnicity. Once again, this is straying away from the ideal surrogate that is independent of age, sex, and ethnicity. Moreover, a recent study in children and adolescents has shown that SSF is a poor predictor of body fat as compared to DXA measurements of body fat, especially in the obese population (Watts et al., 2006).

Waist Circumference

Waist circumference (WC) is associated with predictors of obesity (Savva et al., 2000; Taylor et al., 2000). Taylor et al. (2000) found that WC predicted which children would have a high percentage of trunk fat, as when measured by DXA ($r = 0.92$). Moreover, Savva et al. (2000) found that WC had strong relationships with several predictors of cardiovascular disease ($r = 0.914$). However, they adjusted for age, sex, and pubertal maturation, so once again, this adds to the complexity of the surrogate (Savva et al., 2000). Savva et al. (2000) and Taylor et al. (2000) have shown that WC is independent from ethnicity in youth. From these studies it is obvious that WC is a good surrogate of adiposity to use when trying to predict obesity. Katzmarzyk et al. (2004) found that WC can be used to predict cardiovascular disease risk factors in children and adolescents across age and gender.

However, it is important to point out that as children age they are also growing, meaning that their WC is increasing (Malina et al., 2004).

Waist Circumference Percentiles

A recent approach has been to examine waist circumference (WC) percentiles, as a means of identifying obesity in children. Fernández et al. (2004) computed waist circumference of Caucasian children and adolescents and ethnic minority children base on NHANES III results (Fernández et al., 2004). This surrogate has a strong association with predictors of cardiovascular disease; however, it is still dependent on sex and ethnicity (Savva et al., 2000; Taylor et al., 2000; Zannoli and Morgese, 1996). Also, it requires the utilization of charts and/or tables in order to make comparisons to the normal values.

Waist Circumference to Height Ratio

Since children are growing, there needs to be a way to account for growth rate. One possibility is looking at waist circumferences and height in the form of a ratio. The ratio would account for the differences in growth rates between sexes and across ages. Thus, this could possibly make a ratio of waist circumference and height (WHtR) an independent surrogate of adiposity. Only a few studies have examined WHtR as an adiposity surrogate in children (Kahn et al., 2005; Savva et al., 2000). Kahn et al. (2005) and Savva et al. (2000) found that WHtR ($r^2 = 0.035$) was a better predictor of cardiovascular disease risk factors than BMI ($r^2 = 0.016$) and was independent of age and sex.

As evident from above, previous research has shown that several of the surrogates of adiposity can be used to predict certain risk factors in children and adolescents. However, it is important to account for the growth and maturation in children and adolescents; thus, the majority of these surrogates are strongly dependent on age, sex, and ethnicity. Moreover,

there is not as much research in the newer interest area of insulin resistance. Thus, there is a need to investigate if surrogates of adiposity can be used to accurately predict insulin resistance in children and adolescents.

Purpose

No previous studies have compared surrogates of adiposity and insulin resistance in children and adolescents. Thus, the aim of the present investigation is twofold. First, we will determine the relationship between insulin resistance and surrogates of adiposity in children and adolescents. Second, we will establish which surrogate is the best predictor of insulin resistance independent of age, sex, and ethnicity.

Hypotheses

H₁: All surrogates of adiposity (BMI, BMI percentile, SSF, WC, WC percentile, and WHtR) will demonstrate a positive relationship with insulin resistance.

H₂: When predicting insulin resistance in children and adolescents, of all of the adiposity surrogates, WHtR will account for the greatest amount of variance with the least influence of age, sex, and ethnicity.

Significance

Since adiposity is linked to disease states like Type II diabetes (Kimm and Obarzanek, 2002), there is a need for a simple method of quantifying adiposity in children and adolescents. By identifying adiposity early in life, researchers, teachers, physicians, and parents will be able to intervene early. An ideal would be to find a surrogate that is independent of age, sex, and ethnicity because children and adolescents are at different pubertal stages of development based on their age, sex, and ethnicity. The surrogate could

then be used both in the clinic and elsewhere to predict insulin resistance, a precursor to Type II diabetes (ADA, 2005; Scott, 2006; Soltész, 2006).

Limitations

1. Participants self-reported their age, sex, and ethnicity.
2. All surrogate measures were taken by several research assistants, but all assistants were trained to meet similar standards.

Delimitations

1. Participants from rural eastern North Carolina schools.
2. Participants' ages were from eight to seventeen years.
3. Insulin resistance was determined by a HOMA-IR greater than 4.0 (Bonora et al., 2000)

Definitions of terms

Body mass index (BMI): the ratio of the weight of the body in kilograms to the square of its height in meters defined as kg/m^2 (Merriam-Webster's Medical Dictionary, 2005) that has been used as an estimate of body fat

BMI percentiles: multiple regression lines established by the CDC to determine cut-points for obesity; regression lines are based on age and sex

Homeostasis Model Assessment of Insulin Resistance (HOMA-IR): measures insulin resistance based on resting levels of insulin and glucose (Matthews et al., 1985; Maffeis et al., 2002):

$$\text{HOMA IR} = \text{IN} * \text{GL} / 22.5$$

IR is insulin resistance, IN is fasting insulin ($\mu\text{IU/mL}$), and GL is fasting glucose (mmol/L)

Insulin resistance (IR): reduced sensitivity to insulin by the body's insulin dependent processes or $\text{HOMA-IR} \geq 4.0$ (Merriam-Webster's Medical Dictionary, 2005; Bonora et al., 2000)

Sum of skinfolds (SSF): the sum of the average measurement taken at the triceps and subscapular locations for skinfolds, as defined by the NIH guidelines

Waist circumference (WC): circumference (cm) of waist taken at the level of the umbilicus

Waist circumference percentiles: multiple regression lines using waist circumferences based on age and sex (Fernández et al., 2004)

Waist circumference to height ratio (WHtR): the ratio of waist circumference (cm) to height (cm) used as an estimate of body fat

Chapter 2

Review of Literature

There has been a wide variety of research done on obesity. The majority of the research has examined adults, rather than youth, and how obesity is related to disease states, like Type II diabetes (Maffeis et al., 2002 and Roemmich et al., 2002). Type II diabetes is related to insulin resistance (Maffeis et al., 2002 and Roemmich et al., 2002). There is also a variety of research in adiposity surrogates, which are a means to determining obesity. The following is a presentation of current research in fields that are related to insulin resistance and body composition surrogates in children and adolescents.

Obesity in Children and Disease Risks

The number of obese children and adolescents is increasing in the United States. Previous research has shown that childhood obesity ($\text{BMI} \geq 95^{\text{th}}$ percentile) is present in 14% of children (Gielen and Hambrecht, 2004). Childhood obesity has increased 1.6 times more than the increase in adults (Gielen and Hambrecht, 2004). Goran and Gower (1998) observed that not only is obesity related to cardiovascular disease (CVD) and Type II diabetes in adults, but obesity is also related to Type II diabetes in children. The authors also noted that children tend to have more subcutaneous fat than adults which is related to insulin resistance (Goran and Gower, 1998). Goran and Gower (1999) also examined visceral fat and disease risk in children. The authors found that visceral fat was significantly related to both dyslipidemia and glucose intolerance (Goran and Gower, 1999). Other authors found that childhood obesity is causing chronic diseases to begin at younger ages, including CVD

and Type II diabetes (Kimm and ObzaraneK, 2002). Moreover, all cut points for obesity were defined by both age and sex (Kimm and Obarzanek, 2002).

Insulin Resistance

Insulin resistance is defined, by Merriam-Webster's Medical Dictionary (2005), as reduced sensitivity to insulin by the body's insulin dependent processes. The current study used the homeostasis model assessment for insulin resistance (HOMA-IR) as first defined by Matthews et al. in 1985. Matthews et al. (1985) measured insulin resistance, via HOMA-IR, using fasting measures of insulin and glucose, and compared the results to the hyperglycemic clamp and intravenous glucose tolerance test already in use. The results showed that the HOMA-IR model yielded strong correlations with the hyperglycemic clamp and intravenous glucose tolerance test ($r = 0.88$, $p < 0.0001$), which allow for it to be used to predict levels of insulin resistance (Matthews et al., 1985). Bonora et al. (2000) supports these claims as they compared the HOMA-IR model to the hyperglycemic clamp. The authors noted that HOMA-IR was not as accurate as the hyperglycemic clamp, but it still produced strong correlations ($r = 0.801$, $p < 0.0001$) with insulin resistance (Bonora et al., 2000). Based on these studies, fasting levels of insulin and glucose can predict insulin resistance (Bonora et al., 2000; Matthews et al., 1985).

Insulin Resistance in Children. Adiposity in children and adolescents has been shown to be related to insulin resistance. Maffeis et al. (2002) investigated the relationship between childhood obesity and insulin resistance using the HOMA-IR method. The authors found that insulin resistance in childhood is a predictive factor of obesity in adulthood (Maffeis et al., 2002). Roemmich et al. (2002) found that insulin resistance was the greatest in late-

pubertal groups. Roemmich and colleagues (2002) determined that insulin resistance at puberty was related to fat mass ($r=0.59$, $P<0.001$).

Body Composition Surrogates as Predictors of Insulin Resistance. Previous studies have examined adiposity surrogates and their relationship to insulin resistance. Maffeis et al. (2003) did a study looking at insulin resistance as cardiovascular risk factors in girls while using waist circumference (WC). Maffeis and colleagues (2003) found that WC was correlated with insulin ($r = 0.43$) and insulin resistance ($r = 0.40$) independent of age and puberty levels. Moreover, Lee et al. (2006) has shown that WC could be used as a predictor of insulin resistance in children and adolescents. The authors explain that WC, as an adiposity surrogate, accounts for a greater amount of variance in insulin resistance ($r^2=0.875$) as compared to BMI percentile ($r^2=0.555$). Both of these studies show surrogates of adiposity can be successful in predicting insulin resistance (Lee et al., 2006; Maffeis et al., 2003).

Body Composition in Children and Adolescents

Since it has been shown that body composition is related to insulin resistance, it is important to examine the research completed in children and adolescents. Malina et al. (2004) proposed a need to modify some surrogate measurements because children and adolescents are growing and changing at different rates based on their age and sex. Malina and colleagues (2004) point out that the changes in fat-free mass occur throughout childhood and adolescence, but that the greatest increase in fat mass occurs just after birth and then almost levels out. However, relative fatness increases earlier in girls than boys, such that by adolescence girls have a higher percentage of body fat than boys, partly due to the growth spurt that boys exhibit just before adolescence (Malina et al., 2004). Overall, Malina et al.

(2004) aimed to show that children are growing and maturing at different rates, so not all body composition surrogates are going to be accurate measurements. Rodríguez et al. (2004) supported this idea by noting that body composition changes during adolescence is different based on sex and pubertal development. They also observed that higher levels of visceral fat were related to health issues such as dyslipidemia, hypertension, insulin resistance and impaired glucose tolerance (Rodríguez et al., 2004). Wells and Victoria (2005) investigated various ratios of quantifying body fat, such as fat mass to weight, fat mass to fat-free mass, triceps skinfold to subscapular skinfold, and its inverse. They found these ratios of estimating body fat were strongly influenced by the size of the subject (Wells and Victoria, 2005). The following will explore research from each of the six adiposity surrogates used in the current investigation.

Body Mass Index of Children and Adolescents

Body mass index (BMI) is one of the most common body composition surrogates. However, research has found that BMI may not be the best predictor of obesity or cardiovascular disease (CVD) risk factors. Ellis et al. (1999) found that BMI and percent body fat (%BF) had significant correlations with each other in both females and males ($r = 0.79$, $p < 0.0005$ and $r = 0.34$, $p < 0.001$, respectively). In addition, the authors pointed out that BMI had an error rate of 4.6-7.3% for percent body fat (Ellis et al., 1999). Mei et al. (2002) completed a study on the validation of age and sex-specific BMI in children 2-19y. Mei and colleagues (2002) found that BMI was able to predict body fat percentages in underweight and overweight children, but not in children within the normal range. Research has shown that BMI is dependent on age, sex, and ethnicity, thus it may not be the best “independent” predictor of insulin resistance (Ellis et al., 1999; Mei et al., 2002).

BMI Percentiles

BMI percentiles (BMI %) were derived by the Center for Disease Control by ranking BMI values and placing them into percentiles as related to body fatness (CDC). Katzmarzyk et al. (2004) did a study to determine BMI % for children and adolescents to predict risk factors for CVD. The authors examined age-adjusted percentiles and identified the BMI % thresholds for overweight and at risk for overweight: males at the 53rd and 50th percentiles and females at the 57th and 51st percentiles, respectively (Katzmarzyk et al., 2004). These thresholds had little interaction between ethnicity (Katzmarzyk et al., 2004). However, Karasalıhoğlu et al. (2003) completed a study using adolescent girls in Edirne, Turkey. The authors found that BMI percentiles were useful in determining those that were obese, 95th percentile (Karasalıhoğlu et al., 2003). Despite only looking at one sex, Karasalıhoğlu et al. (2003) found that BMI percentiles still depended on ethnicity. Demerath et al. (2006) completed a study to see if changes in BMI percentiles changed with the same degree as changes in body composition in children. Demerath and colleagues examined BMI as it related to total body fat, fat free mass, and %BF (Demerath et al., 2006). The authors found that fat free mass had a linear relationship with BMI percentile (Demerath et al., 2006). They also found fat mass and %BF increased dramatically at the higher BMI percentiles (Demerath et al., 2006). These results showed that changes in BMI percentile were able to reflect similar changes in body composition of children.

Sum of Skinfolds

Various studies have been done using skinfolds to predict adiposity in children and adolescents. Bedogni et al. (2003) completed a study on the sensitivity and specificity of skinfolds in children. They found skinfolds had high sensitivity and specificity allowing

them to be used to quantify adiposity of children age 8-12 years (Bedogni et al., 2003). Freedman et al. (1999) found skinfolds could be used to determine adverse risk factor concentration of lipids and insulin in children, but were dependent on age and sex. Watts et al. (2006) examined the ability of skinfolds to assess changes in body compositions in children and adolescents. They found that there was a strong relationship ($r = 0.69$) in the sum of skinfolds and %BF; however, the sum of skinfolds are poorly predictive of abdominal and total fat as measured by dual energy x-ray absorptiometry (Watts et al., 2006). In addition, to achieve accuracy there are standardized testing procedures that must be met (Kravitz and Heyward, 2006). Furthermore, skinfolds require a skilled technician to get an accurate measurement (Kravitz and Heyward, 2006).

Waist Circumferences

Adults. There are a number of studies that used waist circumferences (WC) to determine central adiposity in adults. Arden et al. (2004) tried to find WC thresholds within BMI categories for adults. The authors found that WC thresholds increased with increasing BMI categories (Arden et al., 2004). Arden and colleagues (2004) determined the following cut-off points to identify those at normal weight, overweight, and obese: 90cm, 100cm, and 110cm in men and 80cm, 90cm, and 105cm in women, respectively. Janssen et al. (2002) completed a study with adults to determine whether BMI and WC contribute to non-abdominal, abdominal subcutaneous and visceral fat. Janssen et al. (2002) found the combination of BMI and WC accounted for a greater amount of variance in each of the previously stated variables separately. This study also found that BMI and WC both contribute to the variable independently, thus both should be used in clinical practices (Janssen et al., 2002).

Children and Adolescents. Waist circumference has also been used to look at health risk in children and adolescents. Based on regression models for both BMI and WC, for predicting coronary artery disease risk factors, Janssen et al. (2005) concluded that the combination of both should be used to determine health risk in children and adolescents. Maffeis et al. (2001) completed a study to determine if WC could predict high lipid concentrations and hypertension in children. The authors also revealed that WC was easy to measure, and identified that 19% of children with a WC in the 90th percentile had two or more risk factors for cardiovascular disease (Maffeis et al., 2001). Taylor et al. (2000) tried to validate the measurement of waist circumference when looking at trunk fat in 508 children and adolescents. They found that 80th percentile identifies 89% of girls and 87% of boys with high trunk fat mass, and is therefore dependent on sex and age (Taylor et al., 2000). However, Savva et al. (2000) completed a study looking at cardiovascular disease risk factors in children. They found WC was the most significant predictor of cardiovascular disease risk factors for both sexes and BMI had the lowest (Savva et al., 2000). Maffeis et al. (2003) also did a study looking at cardiovascular risk factors in girls while using WC. They found that WC was correlated with insulin ($r = 0.43$, $p < 0.001$) and insulin resistance ($r = 0.40$, $p < 0.001$) independent of age and puberty levels (Maffeis et al., 2003). Moreover, Lee et al. (2006) has shown that WC could be used as a predictor of insulin resistance in children and adolescents. They explain that WC accounts for a greater amount of the partial variance in abdominal fat and insulin resistance ($r^2 = 0.875$), compared to BMI percentile ($r^2 = 0.555$) (Lee et al., 2006).

Waist Circumference Percentiles

Some research has shown that waist circumference percentiles (WC %) aided in identifying obese children, but it was found that because children were maturing, the

percentiles were based on age and sex (Eisenmann, 2005; Fernández et al., 2004; Katzmarzyk, 2004; McCarthy et al., 2001; Zannoli and Morgese, 1996). Zannoli and Morgese (1996) found that WC %, based on age and sex, were a simple way to determine obesity in children. The authors also found that WC % could help predict risk of CVD (Zannoli and Morgese, 1996). Researchers found WC increased with age in both sexes; however girls reached a plateau after the age of 13, but they were able to develop WC %curves for British children (McCarthy et al., 2001). Eisenmann (2005) completed a study to find reference values for WC in Australian children and adolescents. He found that percentile groups could be used for international cut-off points similar to BMI percentiles, but were still dependent on age and sex (Eisenmann, 2005). Fernández et al. (2004) aimed to create estimates for multi-ethnic children in WC percentiles. The authors found that WC increased with age, but all percentiles were based on age, sex, and ethnicity (Fernández, 2004). Katzmarzyk (2004) examined WC percentiles in Canadians between 11-18 years of age; and also found that WC increased with age in both sexes. He also found that although no optimal WC percentiles threshold existed, WC percentiles could be used to determine those with elevated risks for obesity-related diseases (Katzmarzyk, 2004).

Waist Circumference to Height Ratio

Adults. Waist circumference to height ratio (WHtR) is a newer body composition surrogate. Thus, there have been a few studies completed on WHtR in adults. Bosy-Westphal et al. (2006) recently completed a study looking at BMI, WC, and WHtR and various metabolic risk factors, including insulin resistance. They found that WHtR was the primary predictor (27% of variance) of risk factors in both sexes combined (Bosy-Westphal et al., 2006). Hsieh and Muto (2005) examined WHtR in 4,668 and 1,853 Japanese men and women,

respectively, and its relationship with coronary risk factors. They found that the sum of the coronary artery disease risk factors had a positive correlation ($r = 0.312$, $p < 0.0001$ and $r = 0.343$, $p < 0.0001$) with WHtR in men and women, respectively (Hsieh and Muto, 2005). Hsieh and Muto (2005) also observed that a WHtR of 0.5 predicted those with more than one coronary artery disease risk factor. Ashwell and Hsieh (2005) believe that WHtR should be used as a health risk screening tool in adults. They point out that WHtR was a better predictor of health risk than BMI, as well as easier to measure and calculate (Ashwell and Hsieh, 2005). Ashwell and Hsieh (2005) also indicated that WHtR was independent of age, sex, and ethnicity, and thus, it could be used in children and adolescents.

Children and Adolescents. There has been little research done on children and adolescents using a WHtR as predictors of obesity or cardiovascular risk factors. Kahn et al. (2005) completed a study to determine if WHtR or BMI percentiles were better predictors of CVD risk factors. They found that WHtR was a simpler method and a good predictor of cardiovascular risk factors (Kahn et al., 2005). Savva et al. (2000) yielded similar results, finding that WHtR and WC were better predictors of CVD risk factors in children than BMI. For example, WC (14.2 %) and WHtR (3.5%) accounted for a higher percentage of the total variance of systolic blood pressure as compared to BMI (1.8 %) (Savva et al., 2000).

As evident from previous research, there are several body composition surrogates that can be used to determine if a child is at risk for certain disease risk factors. The current investigation is examining insulin resistance, a risk factor to Type II diabetes. Little research has compared the abilities of the various childhood adiposity surrogates with insulin resistance. Thus, the current investigation aims to find the simplest body composition

surrogate, independent of age, sex, and ethnicity, that is best able to predict insulin resistance in children and adolescents. The study aims to find a surrogate that will have clinical significance by defining cut-points to predict insulin resistance levels.

Chapter 3

Methodology

Sample

The participants were recruited from different school sites in rural eastern North Carolina. All were part of the Cardiovascular Health in Children and Youth Study (CHIC III). The children and adolescents were limited to the ages of eight to seventeen years, but included both sexes. Informed consent was obtained from all participants and their parents, as they were all minors.

Procedures

Data were obtained from participants at their schools. On the day of testing, the subjects arrived after an overnight fast, verified by the research assistants. The participants rested in the seated position for five minutes before blood was drawn via venipuncture. A 10 ml blood draw was taken using sterile techniques by a phlebotomist. Following the blood draw or on a separate day, subjects then self-reported their age, sex, and ethnicity. All of the physical measurements were taken by trained research assistants. Height was measured, to the closest 0.1 cm, using a stadiometer (Perspective Enterprises, Kalamazoo, MI, USA). Body mass was measured, to the closest 0.1 kg, with an electronic Pro Plus metric scale (Healthometer Medical, Bridgeview, IL, USA), which had been calibrated with standardized weights. Both height and body mass were measured with subjects clothed and shoeless. Then the participants were assessed for body composition using waist circumference and sum of skinfolds.

Insulin and Glucose. The fasting blood samples were immediately placed on ice. The samples were centrifuged on site to separate plasma for analysis for glucose and insulin concentrations. Glucose was analyzed using the Johnson & Johnson (J&J) vitros dry slide method (glucose oxidase/peroxidase) on a J&J 950 automated chemistry system (UNC Hospital Core Chemistry Lab). Insulin was analyzed using the radio-immunoassay technique (RIA, Penn Medical Laboratory, Medstar Research Institute, Washington, DC, USA). Each was done in triplicate and averaged.

Waist Circumference. Waist circumferences (WC) were measured using a Figure Finder tape (Novel Products Inc., Rockton, IL, USA). The measurements were taken directly against the skin in the horizontal plane on the umbilicus level in both males and females. In order to assure an accurate measurement, two assistants were used: one to take the measurement from the front, and one to keep the tape flat and horizontal in the back. Three measurements were taken and averaged for one value.

Sum of Skinfolts. Skinfolts were measured at the triceps and subscapular sites using Lange skinfold calipers following NIH guidelines. The calipers provided 10 g/mm² of pressure on the skinfold which was checked prior to use at each school. The triceps skinfold measurement was a vertical pinch at the midpoint between the acromion and the olecranon process of the elbow. The location of the subscapular skinfold measurement was a diagonal pinch 1 cm below the inferior angle of the scapula. All measurements were performed on the right side of the body. The measurements were taken in triplicate and averaged for one value at each site.

Data Reduction

Height (m) and body mass (kg) were combined into body mass index ($BMI = kg/m^2$). BMI and WC were converted to percentiles and added as adiposity surrogates. BMI percentiles (BMI %) were based on CDC/NHANES norms (NHANES). WC percentiles (WC %) were based on previous work by Fernández et al. (2004) with percentiles categorized as $<10^{th}$, 10^{th} - 25^{th} , 26^{th} - 50^{th} , 51^{st} - 75^{th} , 76^{th} - 90^{th} , and $>90^{th}$ percentiles. The skinfolds were summed to form one surrogate. WC and height were combined in a ratio of waist to height (cm/cm).

Insulin Resistance. Insulin resistance was determined using the HOMA-IR technique (Matthews et al., 1985): $IR = IN * GL/22.5$ where IR was insulin resistance, IN was fasting insulin ($\mu IU/mL$), and GL was fasting glucose (mmol/L).

Data Analysis

Adiposity surrogates included in this analysis were BMI, BMI %, sum of skinfolds (SSF), WC, WC %, and waist circumference to height ratio (WHtR). Data analysis was completed using SAS 13.0 for Windows (Cary, NC).

Means and standard deviations (SD) were computed for each variable. These means were computed both overall and by gender. Hypothesis 1 stated: All surrogates of adiposity (BMI, BMI %, SSF, WC, WC %, and WHtR) will demonstrate a positive relationship with insulin resistance. This was statistically evaluated by calculating correlations with each of the six surrogates and insulin resistance.

Hypothesis 2 stated: When predicting IR in children and adolescents, of all of the adiposity surrogates, WHtR ratio will account for the greatest amount of variance with the least influence of age, sex, and ethnicity. This was statistically evaluated using multiple

regression models. Step-wise multiple regressions were run to determine the surrogate with the least dependence on age, sex, and ethnicity. In addition, box plots were used to visually determine a cut-point for each surrogate at which there were the fewest false negatives and false positives for insulin resistance. Then, logistical regression was used to determine clinical significance, based on the cut-points, in the form of an odds ratio. The odds ratio was used to determine which surrogate is the best predictor of insulin resistance in children and adolescents based on the increase in risk for developing insulin resistance in those that lie at or above the cut-point.

Chapter 4

Results

There were 1511 total participants, 752 females and 759 males, ranging in age from 8 to 17 years. There was a disproportionately small sample in both sexes for 13 year olds. The characteristics of the subjects are presented in Tables 1 and 2. In general, height and body mass increased with age. The BMI % for the sample suggests that there was a large proportion of high-normal and above normal weight children. However, the WC % for the sample was within the normal range. Also, WHtR did not appear to change with age for both sexes.

Table 1. The physical characteristics (means \pm SD) of the female subjects.

Age (yr)	8	9	10	11	12	13	14	15	16	17
N	78	142	187	93	10	5	43	83	73	38
Height (cm)	133.8 \pm 7.3	137.6 \pm 7.2	144.7 \pm 7.9	151.0 \pm 7.2	155.5 \pm 5.6	159.3 \pm 5.8	159.4 \pm 6.3	161.2 \pm 6.6	163.0 \pm 7.8	161.8 \pm 5.6
Mass (kg)	35.33 \pm 10.28	37.80 \pm 11.63	46.03 \pm 14.91	52.12 \pm 18.90	52.12 \pm 7.84	71.56 \pm 31.91	64.15 \pm 19.62	64.29 \pm 16.46	67.65 \pm 17.69	66.42 \pm 20.39
BMI (kg/m ²)	19.52 \pm 4.76	19.76 \pm 4.44	21.68 \pm 5.69	22.51 \pm 6.64	21.50 \pm 2.75	27.74 \pm 10.41	25.12 \pm 6.89	24.74 \pm 6.11	25.41 \pm 6.17	25.39 \pm 7.82
BMI %	73.1 \pm 27.3	73.6 \pm 23.5	75.3 \pm 27.6	73.6 \pm 29.3	76.7 \pm 21.5	77.5 \pm 35.7	75.6 \pm 23.5	72.2 \pm 25.8	73.1 \pm 24.7	63.3 \pm 28.2
SSF (mm)	25.6 \pm 14.6	25.5 \pm 13.8	29.8 \pm 15.2	29.8 \pm 15.0	25.2 \pm 5.3	40.7 \pm 26.0	36.5 \pm 20.8	34.3 \pm 15.8	39.0 \pm 17.8	37.2 \pm 19.0
WC (cm)	63.1 \pm 10.8	65.4 \pm 11.2	70.2 \pm 13.0	73.7 \pm 14.7	70.1 \pm 6.9	82.2 \pm 24.8	79.5 \pm 16.6	79.3 \pm 13.2	80.7 \pm 16.5	81.0 \pm 16.6
WC %	55.7 \pm 32.5	56.8 \pm 29.1	60.5 \pm 30.3	64.4 \pm 29.1	60.5 \pm 30.6	64.0 \pm 34.9	60.7 \pm 28.3	59.1 \pm 26.9	59.5 \pm 27.2	49.7 \pm 30.9
WHtR	0.47 \pm 0.07	0.47 \pm 0.07	0.48 \pm 0.08	0.49 \pm 0.08	0.45 \pm 0.04	0.51 \pm 0.14	0.50 \pm 0.10	0.49 \pm 0.08	0.50 \pm 0.08	0.50 \pm 0.10

N = number of subjects; BMI = body mass index; BMI % = body mass index percentile; SSF = sum of skinfolds; WC = waist circumference, WC % = waist circumference percentile; WHtR = waist circumference to height ratio

Table 2. The physical characteristics (means \pm SD) of the male subjects.

Age (yr)	8	9	10	11	12	13	14	15	16	17
N	88	141	202	98	30	7	41	83	57	31
Height (cm)	132.9 \pm 5.3	136.9 \pm 6.8	143.8 \pm 7.3	146.3 \pm 7.5	149.9 \pm 6.8	157.2 \pm 6.7	169.3 \pm 8.0	161.2 \pm 6.6	174.0 \pm 6.6	175.1 \pm 5.4
Mass (kg)	32.86 \pm 7.74	36.73 \pm 10.56	44.37 \pm 13.73	45.09 \pm 13.69	48.04 \pm 13.08	52.83 \pm 12.33	64.15 \pm 19.62	64.30 \pm 16.46	75.63 \pm 17.23	77.01 \pm 13.11
BMI (kg/m ²)	18.49 \pm 3.67	19.39 \pm 4.31	21.16 \pm 5.05	20.81 \pm 4.91	21.17 \pm 4.62	21.42 \pm 5.16	25.12 \pm 6.89	24.74 \pm 6.11	25.03 \pm 5.74	25.08 \pm 3.81
BMI %	72.7 \pm 24.9	73.1 \pm 25.6	76.5 \pm 25.7	71.7 \pm 27.8	70.4 \pm 28.8	62.9 \pm 38.4	67.8 \pm 29.1	72.2 \pm 25.8	73.2 \pm 27.6	76.3 \pm 23.3
SSF (mm)	19.1 \pm 11.3	21.0 \pm 11.8	26.7 \pm 16.3	24.5 \pm 14.4	23.6 \pm 13.6	21.4 \pm 12.0	36.5 \pm 20.8	34.3 \pm 15.8	23.0 \pm 10.4	21.7 \pm 9.9
WC (cm)	61.5 \pm 9.6	64.1 \pm 10.8	70.4 \pm 13.8	70.3 \pm 13.6	71.8 \pm 12.1	74.0 \pm 13.2	79.5 \pm 16.6	79.3 \pm 13.2	84.3 \pm 13.8	81.6 \pm 8.6
WC %	46.3 \pm 32.9	51.2 \pm 32.2	58.4 \pm 33.0	57.7 \pm 30.7	57.2 \pm 31.3	56.4 \pm 39.6	60.7 \pm 28.3	59.1 \pm 26.9	68.7 \pm 22.3	57.7 \pm 22.7
WHtR	0.46 \pm 0.07	0.47 \pm 0.07	0.49 \pm 0.08	0.48 \pm 0.08	0.48 \pm 0.08	0.47 \pm 0.09	0.50 \pm 0.10	0.49 \pm 0.08	0.48 \pm 0.08	0.47 \pm 0.05

N = number of subjects; BMI = body mass index; BMI % = body mass index percentile; SSF = sum of skinfolds; WC = waist circumference, WC % = waist circumference percentile; WHtR = waist circumference to height ratio

Table 3 presents the glycemic status results by age group for both sexes. The nine to thirteen year old females appear more insulin resistant than their male counterparts. The females who were insulin resistant had a HOMA-IR range from 4.03 to 21.52, while the males ranged from 4.03 to 28.37.

Table 3. Glycemic variables (mean \pm SD) presented by sex

Age	Females			Males		
	Insulin (μ IU/mL)	Glucose (mmol/L)	HOMA-IR	Insulin (μ IU/mL)	Glucose (mmol/L)	HOMA-IR
8	13.40 \pm 7.38	88.6 \pm 6.6	2.96 \pm 1.71	9.66 \pm 4.48	89.0 \pm 8.3	2.14 \pm 1.06
9	14.66 \pm 9.03	89.2 \pm 10.4	3.28 \pm 2.28	11.17 \pm 7.12	90.8 \pm 6.0	2.49 \pm 1.62
10	18.10 \pm 10.78	90.8 \pm 10.1	4.06 \pm 2.44	14.12 \pm 8.70	91.9 \pm 10.2	3.22 \pm 2.01
11	21.12 \pm 14.21	90.4 \pm 8.9	4.75 \pm 3.32	15.14 \pm 12.49	92.0 \pm 9.0	3.52 \pm 3.39
12	19.60 \pm 8.85	88.3 \pm 11.9	4.36 \pm 2.48	16.27 \pm 11.40	92.2 \pm 6.4	3.41 \pm 2.07
13	24.60 \pm 20.62	93.6 \pm 6.4	5.61 \pm 4.65	13.43 \pm 5.29	86.4 \pm 7.7	2.91 \pm 1.29
14	18.79 \pm 13.34	86.0 \pm 8.5	3.99 \pm 2.70	18.79 \pm 13.34	90.8 \pm 8.2	3.99 \pm 2.70
15	15.82 \pm 7.11	85.3 \pm 9.0	3.40 \pm 1.80	15.82 \pm 7.11	85.3 \pm 9.0	3.40 \pm 1.80
16	17.55 \pm 12.58	84.9 \pm 6.9	3.75 \pm 2.87	14.30 \pm 5.82	87.8 \pm 8.1	3.14 \pm 1.41
17	14.50 \pm 5.88	86.3 \pm 9.4	3.13 \pm 1.43	14.39 \pm 7.59	88.8 \pm 7.6	3.22 \pm 1.85

The relationship of the surrogates with each other and the HOMA-IR values were determined using Pearson product correlations (Table 4). All the surrogates were significantly correlated with each other ($p < 0.05$), with the strongest relationship between BMI and WC ($r = 0.923$). Significant ($p < 0.05$) and positive relationships existed between all the surrogates and the HOMA-IR values. The strongest relationship of a surrogate with HOMA-IR was with BMI ($r = 0.560$). This was closely followed by SSF, WC, and WHtR, with r values of 0.546, 0.538, and 0.523, respectively.

Table 4. Correlations between the six surrogates and HOMA-IR values.

	BMI %	SSF	WC	WC %	WHtR	Insulin	Glucose	HOMA-IR
BMI (kg/m ²)	0.70	0.86	0.92	0.72	0.87	0.60	0.05*	0.56
BMI %		0.63	0.59	0.79	0.68	0.38	0.14	0.37
SSF (mm)			0.80	0.71	0.85	0.59	0.03*	0.55
WC (cm)				0.78	0.88	0.58	0.02*	0.54
WC %					0.80	0.46	0.10	0.47
WHtR						0.56	0.07	0.52
Insulin (μIU/mL)							0.16	0.98
Glucose (mmol/L)								0.31

*p > 0.05

Figure 1. The total and partial variances within each multiple regression for HOMA-IR related to the surrogate, age, sex, and ethnicity.

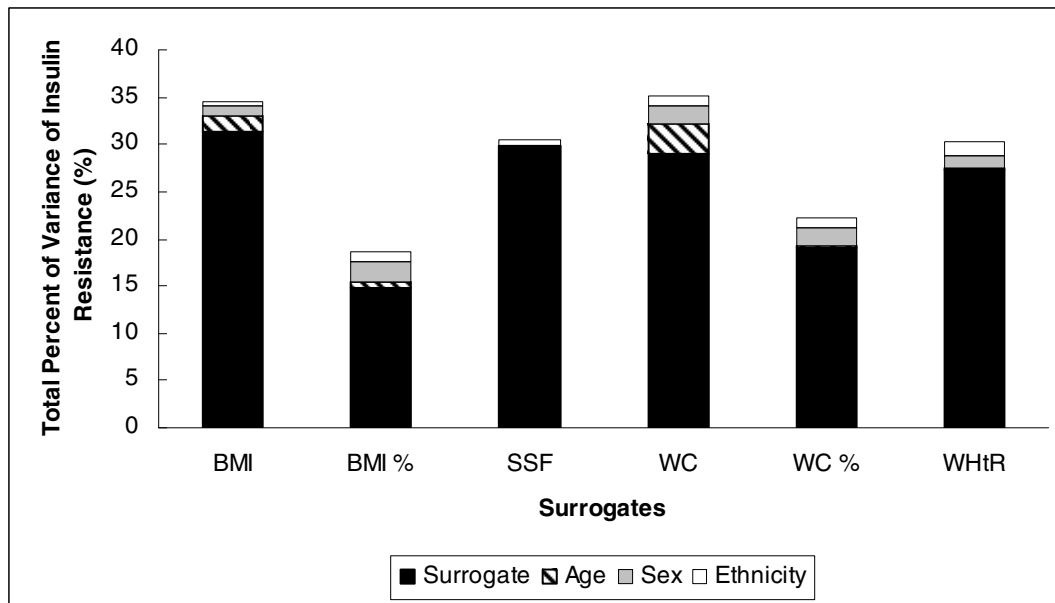


Figure 1 illustrates the results of the multiple regression models for the relationship between the HOMA-IR and each of the surrogates for obesity and the partial correlations for age, sex, and ethnicity. Table 5 presents the exact percentages of the variance for each of the independent variables. WC has greatest total amount of variance, but it included greater proportions of the variance for age, sex, and ethnicity, particularly when compared to SSF.

BMI yielded results similar to WC. However, according to the multiple regression models, SSF is the least influenced by age, sex, and ethnicity, of which only ethnicity makes a significant impact ($p < 0.05$), adding 0.7% of the variance.

Table 5. Partial and total variances for the multiple regression models for each surrogate and the effects of age, sex and ethnicity.

Model	Surrogate	Age	Sex	Ethnicity	Total
BMI (kg/m^2)	0.314	0.017	0.009	0.006	0.346
BMI %	0.148	0.007	0.021	0.010	0.186
SSF (mm)	0.298	0.000*	0.000*	0.007	0.305
WC (cm)	0.289	0.033	0.018	0.011	0.351
WC %	0.191	0.002*	0.018	0.012	0.221
WHtR	0.274	0.002*	0.013	0.014	0.301

* $p > 0.05$

The logistic regression analyses, for the presence of insulin resistance ($\text{HOMA} > 4.0$) when each of the surrogates were considered “at risk”, are presented in Table 6. The “at risk” cut-points for the surrogates were: BMI = 23.0 kg/m^2 , BMI% = 89.6, SSF = 28 mm, WC = 72.5 cm, WC% = 75, and WHtR = 0.48. These were chosen from the box plots of each surrogate, as the point with the fewest false negative and false positive cases of insulin resistance ($\text{HOMA} > 4.0$). SSF had the highest odds ratio for predicting the HOMA-IR, while BMI % had the lowest odds ratio. When SSF were greater than 28 mm, the risk of developing insulin resistance was 9.2 times greater than for those with SSF below 28 mm.

Table 6. Odds ratios and confidence intervals for the presence of insulin resistance based on the cut-points for each of the six surrogates.

Surrogate (Cut-Point)	Odds Ratio	95% Confidence Interval
BMI (23)	8.0	6.2-10.3
BMI % (89.6 th %tile)	5.0	6.5-11.0
SSF (28 mm)	9.2	7.0-11.9
WC (52.5 cm)	6.1	4.8-7.8
WC % (75 th %tile)	8.1	6.3-10.5
WHtR (0.48)	7.6	5.8-9.8

Chapter 5

Discussion

The present study was designed with two aims: first, to determine the relationships between adiposity surrogates and insulin resistance in children and adolescents, and second, to establish which surrogate is the best predictor of insulin resistance, independent of age, sex, and ethnicity. Six different surrogates were investigated: body mass index (BMI), BMI percentile (BMI %), sum of skinfolds (SSF), waist circumference (WC), WC percentile (WC %), and waist circumference to height ratio (WHtR). In general, sum of skinfolds was the best predictor of insulin resistance and was independent of age, sex, or ethnicity (Tables 5 and 6). The following discussion examines the results for each of the surrogates and is followed by a review of the strengths, limitations, conclusions, and future recommendations.

Body Mass Index

Table 4 shows that BMI, alone, was strongly correlated with HOMA-IR. In the multiple regression models, BMI accounted for 31% of the variance, but was significantly influenced by age, sex, and ethnicity (Figure 1 and Table 5). The results of the present study are reinforced by two previous studies in children and adolescents. First, Katzmarzyk et al. (2004) found that BMI was a predictor of high insulin and glucose levels; moreover, their results were influenced by age, sex, and ethnicity. Second, Ellis et al. (1999) found that BMI was influenced by sex and ethnicity; especially since they found ethnic differences in the females, but not the males.

The current investigation determined that youth with a BMI greater than 23.0 kg/m² had a high odds ratio for developing insulin resistance, 8.0 (CI: 6.2-10.3), meaning that those above 23.0 kg/m² are 8.0 times more likely to develop insulin resistance than those with a BMI below 23.0 kg/m². However, BMI had a tendency to overestimate insulin resistance in adolescents. For example, HOMA-IR determined that 25% of the adolescents in this study had insulin resistance, but BMI predicted 51% to have insulin resistance. BMI is the most common adiposity surrogate used in field settings and with clinicians because it only requires height and body mass. However, based on the results of this study, BMI may not be the best choice to predict insulin resistance independent of age, sex, and ethnicity.

BMI Percentile

BMI % had a moderate bivariate correlation with HOMA-IR (Table 4). When using the multiple regression models, BMI % accounted for the least amount of variance of all the surrogates (Figure 1 and Table 5). BMI % requires the use of tables that are based on age and sex, and in this study despite using age- and sex-specific percentiles, BMI % was still significantly influenced by age, sex, and ethnicity. Similar to the current study, Lee et al. (2006) and Demerath et al. (2006) found sex and ethnicity differences for BMI %. BMI % also had the lowest odds ratio (5.0, CI: 6.5-11.0) among the surrogates. Thus, BMI % may not be the best predictor of insulin resistance in youth.

Sum of Skinfolds

SSF were strongly correlated with HOMA-IR in the bivariate analysis (Table 4). The multiple regression models determined that SSF accounted for the most variance (29.8%), independent of age and sex (Figure 1 and Table 5). However, SSF were slightly influenced by ethnicity ($r^2 = 0.07$). The results of the present study were emphasized by several other

perspectives. Roemmich et al. (2002) found SSF and HOMA-IR were significantly correlated ($r = 0.55$) in children. Freedman et al. (1999) observed when children's skinfolds were separated into triceps and subscapular skinfolds, the subscapular skinfold was able to predict "adverse" concentrations of insulin. Subscapular skinfold is believed to represent central adiposity which is more strongly related to IR than peripheral adiposity (Malina et al., 2004). Slinger et al. (2007) concluded that although SSF was higher in females than males, SSF was an adequate predictor of HOMA values (females $r^2 = 0.276$ and males $r^2 = 0.359$). According to the results of the current study, SSF had the highest odds ratio (9.2) and the highest confidence interval (7.0-11.9). This means that those above 28 mm are at the greatest risk for developing insulin resistance, as compared to the other surrogates. SSF, however, had a tendency to overestimate insulin resistance at all ages, but provided fewer false negatives in the adolescents, as compared to BMI and WC. For example, HOMA-IR determined that 25% of both children and adolescents were insulin resistant, while the cut-point of 28 mm for SSF predicted 33% of children (ages 8-12 years) and 43% of adolescents (ages 13-17 years) to be insulin resistant. Despite the false negatives, SSF may be the best predictor of insulin resistance since it was not influenced by age or sex. Furthermore, because of the lower rate of false negatives, SSF may be more suited to predict insulin resistance than BMI, BMI%, WC, or WC%.

SSF had the least influence from age, sex, and ethnicity, but it requires specific skills to get accurate measurement, making it complicated to perform. Measurements require the technician to use the calipers correctly and to be able to separate the layer of subcutaneous fat from the muscle tissue (Kravitz and Heyward, 2006). Most importantly, there must be correct identification of the skinfold site (Kravitz and Heyward, 2006). Thus, SSF requires a

skilled technician, someone that has performed the skills many times, making SSF a more complex surrogate as compared to BMI, WC, or WHtR.

Waist Circumference

In this study as with previous studies, WC was a moderate predictor of insulin resistance (Lee et al., 2006; Maffeis et al., 2003). In the bivariate analysis, WC had one of the strongest relationships with HOMA-IR (Table 4). Similar to BMI, in the multiple regression models, WC accounted for over 35% of the variance, but was significantly influenced by age, sex, and ethnicity (Figure 1 and Table 5). Lee et al. (2006) found that WC accounted for 55% of the variance when predicting insulin resistance in children. However, Maffeis et al. (2003) found that WC accounted for only 23% of the variance, while in a separate analysis pubertal development accounted for 28%. In the current investigation, WC, like BMI%, had a low odds ratio (6.1, CI: 4.8-7.8) when compared to the SSF, WC %, and BMI (O.R. ~ 8.0-9.2). It also overestimated those with insulin resistance, especially between the ages of 14 and 17, as compared to those with insulin resistance based on the HOMA-IR values. Thus, WC may not be the best predictor of insulin resistance.

Although, WC seems like a simple measurement, it is difficult to get an accurate measurement. Two people are needed to measure WC: one in the front to take the measure and one in the back to ensure the tape remains level across the back. It is also important to make sure the client does not hold their breath during the measurement, as this will impede the accuracy of the measurement.

Waist Circumference Percentile

WC% had a moderate bivariate correlation with HOMA-IR (Table 4). WC% was the second weakest predictor of insulin resistance, and was significantly influenced by sex and

ethnicity. Overall, WC%, age, sex, and ethnicity only accounted for 22% of the variance (Figure 1 and Table 5). WC% tables are based on age, sex and ethnicity (Fernández et al., 2004). The results of the present study suggest that WC% accounts for age, but sex and ethnicity added approximately 3% to the total variance. Eisenmann (2005) and Katzmarzyk (2004) found that males had higher WC % than the females at every age-specific percentile. Fernández et al. (2004) found significant differences in age, sex, and ethnicity when using WC % in children and adolescents. Although, in the current study, WC % had a high odds ratio (8.1) and high confidence interval (6.3-10.5), it was not the best predictor of insulin resistance.

Waist Circumference to Height Ratio

Initially, WHtR was predicted to be the most independent surrogate because it seemed to account for the change in body mass and stature as children grow. In addition, WHtR requires two measurements (waist circumference and height), similar to BMI. The current investigation, as well as previous research by Kahn et al. (2005), and Savva et al. (2000), found that WHtR was a better predictor of adverse concentrations within lipid profiles than BMI. WHtR had a strong bivariate correlation with HOMA-IR (Table 4). In the multiple regression models, WHtR accounted for 27.4% of the variance when predicting insulin resistance (Figure 1 and Table 5). Although WHtR was not significantly influenced by age, it was significantly influenced by both sex and ethnicity ($r^2 = 0.013$ and $r^2 = 0.014$, respectively). However, this amount of variance, <3%, could be considered of little significance. The influence from sex may have occurred because males and females develop at different rates throughout childhood and puberty (Malina et al., 2004). Malina et al. (2004) indicated that males' and females' body densities change differently over the course

of adolescence. For example, males tend to gain more fat-free mass during adolescents while females tend to gain more fat mass during adolescence (Malina et al., 2004). According to Malina et al. (2004), females, in general, have more body fat than males. As for the influence from ethnicity, Goran et al. (1999) has shown ethnic differences in body fat distribution, such that African-American children have less “intra-abdominal adipose tissue” than Caucasian children. In the current investigation, WHtR had a relatively low odds ratio (7.6, CI: 5.8-9.8) as compared to SSF (9.2). However, WHtR was able to account for 27.4% of the variance and was not significantly influenced by age; so based on these results, WHtR could be a useable predictor of insulin resistance.

Strengths and Limitations

This was the first study to include a very large sample of youth of many ages, as well as African Americans and Caucasians. However, there may have been some confounding variables, such as pubertal development stages, that were not included in the analyses because the study sought to find a surrogate independent of age, sex, and ethnicity. The study also lacked a sufficient sample of thirteen year old males and females; a possible critical developmental age. All of these things may have influenced some of the results.

Conclusions

This study sought to define the relationship between adiposity surrogates and insulin resistance in children and adolescents. It also aimed to determine which surrogate is the best predictor of insulin resistance. Based on the results of the current investigation, H_1 is accepted. All of the surrogates had positive bivariate correlations with insulin resistance; the strongest being BMI and SSF. H_2 failed to be accepted, since WHtR only accounted for 27.4% of the variance in insulin resistance, while SSF accounted for 29.8% of the variance in

insulin resistance and had the least influence from age, sex, and ethnicity. In addition, SSF also had the highest odds ratio, meaning that those youth with sum of triceps and subscapular skinfolds above 28 mm were at the greatest risk for developing insulin resistance. However, WHtR was minimally influenced by age, sex, and ethnicity (~3%), but requires two measurements. Thus, for clinical use, WHtR may be a better predictor than SSF for defining those “at risk” for developing insulin resistance.

Future Recommendations

In this study only ~ 30% of the total variance was accounted for by one surrogate, suggesting that more research needs to be completed in order to determine which method is truly the best predictor. Future research may attempt to define the other 70% of the variance when predicting for insulin resistance. Several recommendations could be used to improve this study in the future. It would be important to explore the influence of pubertal development on insulin resistance, especially since Maffeis et al. (2003) found that it accounted for 28% of the variance in insulin resistance. In addition, the sample of 13 year olds should be increased because this could be a transition time for puberty. Another recommendation is to simply use insulin levels, since they can predict insulin resistance as well as HOMA-IR, and most youth do not have fully developed Type 2 Diabetes, but some are developing insulin resistance or pre-diabetes (Conwell et al., 2004). It could also be beneficial to expand to area from which participants are drawn outside of eastern North Carolina to see if there is a regional effect. Another suggestion may be to examine the growing population of Hispanics/Latinos. Finally, in another analysis, ROC curves could be used to better predict the cut-points for the surrogates.

The aim of the study was to find an adiposity surrogate, independent of age, sex, and ethnicity, which could be used to predict insulin resistance in children and adolescents. Based on the results of this study, WHtR would be the best surrogate. WHtR accounted for similar amounts of variances as compared to SSF when predicting insulin resistance (Table 5). It is a simpler measurement as compared to SSF, which is ideal for a field or clinic setting. Therefore, WHtR should be used to determine those that are “at risk” for developing insulin resistance in children and adolescents.

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