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## Childhood Wrist Circumference is Not a Predictor of Insulin Resistance in Adulthood

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### Abstract

We sought to determine if childhood wrist circumference predicts insulin resistance in adulthood. Measures were taken in pre-pubertal children and then approximately 30 years later in the same subjects as adults. Our findings suggest that wrist circumference in childhood is not a predictor of insulin resistance in adulthood.

### Keywords

Obesity; Children; Adults; Insulin; Insulin resistance; Wrist

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The gold standard measurement of insulin resistance (IR), the euglycemic, hyperinsulinemic clamp ( $M_{Ibm}$ ),<sup>1,2</sup> is technically challenging, invasive, and expensive, limiting its clinical usefulness. Surrogate measures of IR including fasting insulin and the homeostasis model assessment of IR (HOMA-IR)<sup>3</sup> require a blood sample, show only moderate correlation with direct measures of IR in children,<sup>2</sup> and vary greatly among laboratories.<sup>4</sup> A non-invasive

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screening tool easy to perform in the office that provides an acceptable estimate of IR risk is needed.

It has been proposed that wrist circumference (WrC) may be a good surrogate in children as a simple, non-invasive marker of IR.<sup>5</sup> A close cross-sectional relationship between pediatric WrC and HOMA-IR has been reported in overweight youth,<sup>5</sup> and supported by recent findings that wrist breadth was associated with HOMA-IR in normal-weight children.<sup>6</sup>

We hypothesized that childhood WrC would positively predict adult IR as measured by euglycemic hyperinsulinemic clamp. We also assessed HOMA-IR to provide a direct comparison to the previous cross-sectional studies.

## Methods

The University of Minnesota Institutional Review Board approved the research. All parents and subjects provided informed consent and assent, respectively. A previously-established cohort was used.<sup>7</sup> Subjects were excluded if: body mass index (BMI) and WrC measurements in childhood were obtained greater than six months apart ( $n=75$ ), age data discrepant ( $n=5$ ), or IR data not available ( $n=41$ ). The final cohort included 275 individuals.

Height and weight were measured, and BMI ( $\text{kg}/\text{m}^2$ ) and BMI-percentile were calculated.<sup>8</sup> WrC was measured on the right wrist immediately proximal to the ulnar and radial epicondyles to the nearest 0.5 cm by trained technicians.<sup>7</sup>

Adult testing was conducted at the University of Minnesota Clinical Research Center after a 10-hour fast. Height and weight were measured, and BMI was calculated. Waist circumference was measured to the nearest 0.5 cm. Body fat percent, fat mass, lean mass, and bone mineral density were determined by dual energy X-ray absorptiometry (Lunar Prodigy, General Electric Medical Systems, Madison, WI, USA). All scans were analyzed using General Electric Medical Systems enCore™ software platform version 10.5. IR was measured by euglycemic hyperinsulinemic clamp as previously described.<sup>9</sup> IR was expressed as the glucose infusion rate ( $\text{mg}/\text{kg}/\text{min}$  of glucose), adjusting for lean mass ( $M_{\text{lbm}}$ ). A lower  $M_{\text{lbm}}$  indicates greater IR. Glucose and insulin were measured using standard procedures. HOMA-IR was calculated as previously described.<sup>3</sup>

## Statistical Analyses

Stata/SE 12.0 (StataCorp, College Station, TX, USA) was used for statistical analyses. Results are expressed as mean±standard error of the mean. An independent t-test was used to compare demographic characteristics. Stepwise multivariate linear regression (backward elimination,  $P=0.05$ ) was used to identify the best predictor of  $M_{\text{lbm}}$  and HOMA-IR from childhood WrC, sex, BMI-percentile, and height. Weight and BMI were not included due to concerns about multicollinearity. HOMA-IR data were logarithmically transformed. Spearman correlation was used to evaluate relationships between WrC and adulthood height, weight, BMI, percent fat mass, fat mass, lean mass, bone mineral density, waist circumference, fasting glucose, fasting insulin, log HOMA-IR, and  $M_{\text{lbm}}$ . Statistical significance was determined at the 0.05 level.

## Results

Data from childhood and adulthood are shown in the Table. Childhood WrC correlated with childhood age ( $\rho=0.175$ ,  $P=0.004$ ), height ( $\rho=0.557$ ,  $P<0.001$ ), weight ( $\rho=0.812$ ,  $P<0.001$ ), BMI ( $\rho=0.778$ ,  $P<0.001$ ), BMI-percentile ( $\rho=0.752$ ,  $P<0.001$ ), and BMI category ( $\rho=0.606$ ,  $P<0.001$ ).

Childhood weight ( $\rho=0.125$ ,  $P=0.039$ ) and BMI-percentile ( $\rho=0.120$ ,  $P=0.048$ ) correlated with adult HOMA-IR, whereas other childhood variables did not (race:  $P=0.093$ ; height:  $P=0.088$ ; BMI:  $P=0.078$ ; WrC:  $P=0.177$ ). No childhood measures correlated with adult  $M_{I_{bm}}$  (race:  $P=0.513$ ; height:  $P=0.700$ ; weight:  $P=0.270$ ; BMI:  $P=0.257$ ; BMI-percentile:  $P=0.229$ ; WrC:  $P=0.051$ ).

Childhood BMI-percentile predicted adult HOMA-IR ( $\beta=0.004$ ,  $P=0.033$ ), but not  $M_{I_{bm}}$  ( $P=0.653$ ). When analyzed by sex, childhood BMI-percentile no longer predicted HOMA-IR. Childhood WrC correlated with adult height ( $\rho=0.274$ ,  $P<0.001$ ), weight ( $\rho=0.436$ ,  $P<0.001$ ), BMI ( $\rho=-0.444$ ,  $P<0.001$ ), bone mineral density ( $\rho=0.393$ ,  $P<0.001$ ), waist circumference ( $\rho=0.336$ ,  $P<0.001$ ), fat mass ( $\rho=0.306$ ,  $P<0.001$ ), lean mass ( $\rho=0.414$ ,  $P<0.001$ ), and fasting glucose ( $\rho=0.163$ ,  $P=0.007$ ), but not percent fat mass ( $P=0.083$ ) or fasting insulin ( $P=0.259$ ).

Childhood WrC did not predict adult IR as measured by  $M_{I_{bm}}$  ( $P=0.575$ ) or HOMA-IR ( $P=0.426$ ). The correlations of childhood WrC with adult log HOMA-IR and  $M_{I_{bm}}$  are shown in the Figure. No sex differences were observed for the relations between WrC and  $M_{I_{bm}}$  or HOMA-IR. WrC did not predict  $M_{I_{bm}}$  or HOMA-IR for any child BMI category; however, the P-value for WrC and  $M_{I_{bm}}$  in the overweight category was marginal but not significant ( $P=0.068$ ).

## Discussion

In a previous study<sup>5</sup> reporting a positive correlation between WrC and HOMA-IR in childhood, the authors explained this relationship by hypothesizing that bone diameter might increase with increasing IR. A compensatory increase in insulin secretion is typical with IR.<sup>10</sup> Insulin overproduction has been linked with increased bone formation,<sup>11,12</sup> likely mediated by insulin-like growth factor 1 (IGF-1).<sup>13-15</sup> IGF-1 levels have been linked with bone cross-sectional area,<sup>17</sup> and WrC provides a view of bone formation<sup>18,19</sup> that is minimally affected by fat deposition.<sup>20</sup> Adult WrC has been shown to predict diabetes, even after controlling for BMI and waist circumference,<sup>21</sup> indicating that a larger WrC may become a predictor of IR later in life. In the current study, childhood WrC was related to childhood age, height, weight, BMI, BMI-percentile, and BMI category, but did not predict adult IR.

Direct comparisons with the prior report in children<sup>5</sup> were not possible due to three important differences. The prior study was cross-sectional, a high proportion of children were overweight/obese (in the current study they were normal weight), and used HOMA-IR (the current study used a direct measure of IR [ $M_{I_{bm}}$ ]).

In the current study, none of the childhood anthropometric variables (BMI-percentile, height, weight, or WrC) correlated with adult IR measured by  $M_{I_{bm}}$ . Although childhood BMI-percentile was a predictor of HOMA-IR, when analyzed by sex, BMI-percentile was no longer significant.

Limitations of the current study include the single time point for WrC assessment in childhood and for IR in adulthood, precluding analyses of these correlations in the two age groups, as well as of their tracking into adulthood. It is conceivable that WrC might be associated with child lean body mass, however, in the absence of body composition measurements in children, this could not be assessed. Finally, although separating by sex or BMI-percentile did not yield significant results, this may be related to power limitations of each category size.

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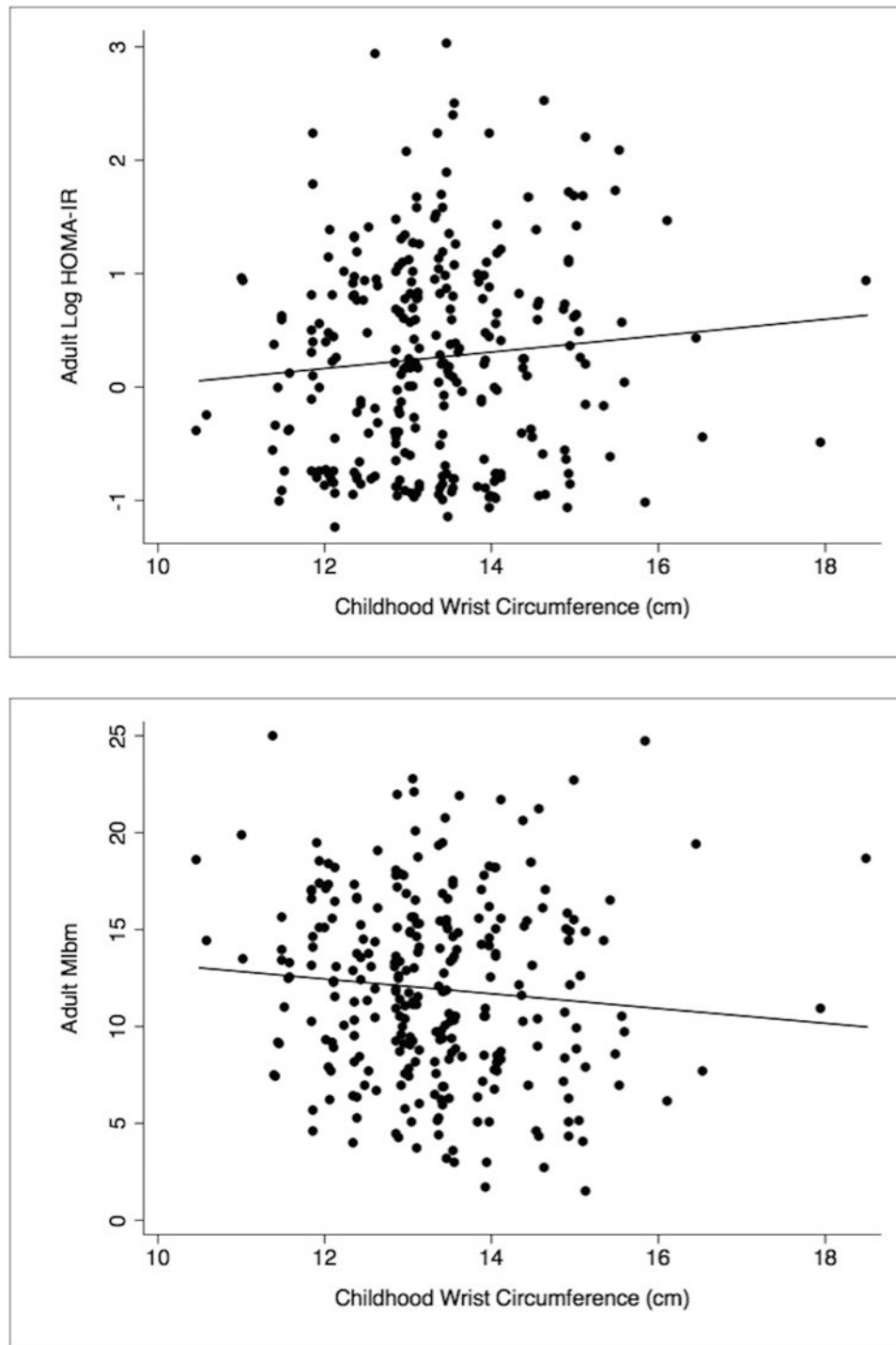
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## Abbreviations

<b>BMI</b>	body mass index
<b>HOMA-IR</b>	homeostasis model assessment of insulin resistance
<b>IGF-1</b>	insulin-like growth factor 1
<b>IR</b>	insulin resistance
<b>M<sub>Ibm</sub></b>	insulin-stimulated glucose uptake = insulin sensitivity/resistance (clamp method)
<b>WrC</b>	wrist circumference



**Figure 1.** Correlation of child WrC and adult insulin resistance as measured by A, log HOMA-IR ( $\rho=0.082$ ,  $P=0.177$ ; higher log HOMA-IR indicates greater insulin resistance), and B,  $M_{1bm}$  ( $\rho=-0.118$ ,  $P=0.051$ ; lower  $M_{1bm}$  indicates greater insulin resistance). A jitter of 4 was applied to avoid point overlap.

**Table 1**  
**Demographic and Clinical Characteristics**

	Mean( $\pm$ SEM)
Sex (% Male)	54.9% (151 male)
Race: n (%)	
1 – White	196 (71.3%)
2 – African American	49 (17.8%)
3 – Other	30 (10.9%)
In Childhood	
Age (yrs)	8.4 $\pm$ 0.05
Height (cm)	129.3 $\pm$ 0.4
Weight (kg)	27.4 $\pm$ 0.3
BMI (kg/m <sup>2</sup> )	16.2 $\pm$ 0.1
BMI Percentile	48.9 $\pm$ 1.7
Underweight (%)	6.5
Normal (%)	80
Overweight (%)	10.2
Obese (%)	3.3
Wrist Circumference (cm)	13.3 $\pm$ 0.1
In Adulthood	
Age (yrs)	39.0 $\pm$ 0.1
Height (cm)	172.4 $\pm$ 0.7
Weight (kg)	85.4 $\pm$ 1.2
BMI (kg/m <sup>2</sup> )	25.5 $\pm$ 0.4
Underweight (%)	3.3
Normal (%)	49.8
Overweight (%)	25.1
Obese (%)	21.8
Fat Mass (%)	34.6 $\pm$ 0.6
Fat Mass (kg)	29.2 $\pm$ 0.8
Lean Mass (kg)	52.5 $\pm$ 0.7
Waist Circumference (cm)	97.5 $\pm$ 1.0
Bone Mineral Density (z-score)	1.3 $\pm$ 0.01
Fasting Glucose (mmol/L)	5.0 $\pm$ 0.04
Fasting Insulin (mU/L)	8.7 $\pm$ 0.6
HOMA-IR	2.0 $\pm$ 0.2
M <sub>IBM</sub> (mg/kg/minute)	11.9 $\pm$ 0.3

BMI, body mass index; BMI percentile determined using the 2000 CDC Growth Charts<sup>9</sup>; HOMA-IR, Homeostasis Model for Assessment–Insulin Resistance; M<sub>IBM</sub>, insulin resistance adjusted for lean body mass.