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## Determination of body size measures and blood pressure levels among children\*,,\*\*

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Vague observed in 1956 that women with android (central) obesity had a high prevalence of diabetes and atherosclerosis,<sup>1</sup> and a review by Stern and Haffner in 1986<sup>2</sup> greatly stimulated interest in the health effects of body fat distribution. Numerous studies have since documented the importance of visceral adipose tissue in the development of coronary heart disease (CHD) and type 2 diabetes.<sup>3</sup> Moser et al.<sup>4</sup> are to be congratulated for their efforts in obtaining and analyzing data on the relation of various measures of body size to levels of SBP and DBP among 1,441 10-to 16-year-olds. Their main finding, that body mass index (BMI, kg/m<sup>2</sup>) appears to be a more important predictor of high blood pressure levels among children than waist circumference (WC), waist-to-height ratio, or triceps skinfold thickness, is in general agreement with the results of other studies.<sup>5</sup>

There are, however, several points that should be considered in the interpretation of these findings. It is exceedingly difficult to disentangle the effects of body size measures that are highly intercorrelated (r=0.80 to 0.90, Table 2), and as the authors note, this multicollinearity makes it difficult to draw valid conclusions. Although the overall predictive power of a statistical model may not be greatly affected by this multicollinearity, it is difficult or impossible to interpret the independent influence of individual coefficients in a regression model that incorporates several measure of body size. If predictors are highly intercorrelated, it is likely that few children, for example, will have significantly different levels of WC but similar levels of BMI and triceps skinfold thickness. This leads to very imprecise estimates of the individual regression coefficients, and it is even possible that the sign of the coefficients will be reversed. The independent effect of WC, at constant levels of BMI and triceps skinfold thickness that the sign of the coefficients will be reversed. The independent effect of WC, at constant levels of BMI and triceps skinfold thickness, cannot be assessed in a regression model because the levels of these three variables almost always vary together.

It appears, however, that the authors may have attempted to interpret individual regression coefficients from a model with high multicollinearity. The text accompanying Table 3 states that BMI and triceps skinfold thickness were each associated with high blood pressure

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 $<sup>\</sup>stackrel{\text{th}}{\rightarrowtail} \stackrel{\text{th}}{\Longrightarrow}$  See paper by Moser DC et al. in pages 243–9.

"independently of abdominal obesity," and the Methods state that the models were adjusted "for all measures of adiposity". Although it's not certain how the authors derived the estimates in Table 3, it appears that the coefficients are from a single regression model that included BMI, WC, and triceps skinfold thickness (along with sexual maturation and economic status). Although the levels of BMI, WC, and triceps skinfold thickness were treated as dichotomous variables in the regression analyses, they would still be strongly intercorrelated. This is likely the reason why the odds ratio for WC, which shows a correlation of r = 0.89 with BMI and a correlation of about r = 0.25 with blood pressure levels (Table 2), is less than 1.0 (but not statistically significant) in Table 3. It is also known that the effects of multicollinearity are particularly problematic when the intercorrelation among the predictor variables is stronger than the relation of the predictors to the outcome. This is the case in the study of Moser et al.<sup>4</sup> the intercorrelations among the body size measure are much stronger (r > 0.8) than their associations with blood pressure levels (r  $\approx$ 0.25). It should also be noted that all analyses of the relation of body size measures to CHD risk factors should almost certainly control for gender and age. This is not specified in the Methods, Results, or in the table, and it's not certain how the authors controlled for these covariates.

In the presence of multicollinearity, how should one compare the importance of different body size measures? The simplest solution may be to compare the overall fit of various models, each of which contain only one body size measure. The fit or agreement of the model with the observed data could be assessed using the multiple R<sup>2</sup> for continuous outcomes or the kappa statistic<sup>6</sup> for dichotomous outcomes. The statistical significance of the differences in the multiple R<sup>2</sup> values could then be assessed using formulas for correlated correlations<sup>7</sup> or for the kappa statistic, through bootstrapping.<sup>8</sup> Another possibility for a dichotomous outcome, such as high blood pressure (Table 3), would be to compare areas under the receiver operator characteristic (ROC) curve.<sup>9</sup> ROC curves assess the sensitivity and specificity (expressed as the false positive rate) of an association over all possible cut-points of the predictor, and they have been used to examine the relation of several measures of body size (including BMI, WC, and triceps skinfold thickness) to CHD risk factors among children from three large cities in Brazil.<sup>10</sup>

The areas under the ROC curve of the various measures of body size could then be compared.<sup>9</sup> It would also be possible to examine whether a model with two of the body size measures accounts for more of the variability in blood pressure levels than does a model with only a single measure. For example, if the  $R^2$  (or kappa) of a model with both BMI and WC is similar to that of a model containing only WC, but is substantially higher than that of a model containing only BMI, it would indicate that WC is the more important characteristic.

Moser et al.<sup>4</sup> examined blood pressure levels among 10-to 16-year-olds, but it should be realized that the relative importance of body size measure may depend upon the examined risk factor. In general, studies of children and adolescents have found that levels of blood pressure and insulin are more strongly correlated with BMI than with WC or skinfold thickness, but lipid levels tend to show slightly stronger associations with WC. This is somewhat similar to the results of studies in adults that have indicated that while visceral fat

may be the more important predictor of diabetes mellitus, general adiposity may be more important for cardiovascular disease.<sup>11</sup> It is even possible that differences in the relative importance of the various measures of body size vary by age. Rimm et al., for example, found that the best predictor of CHD before age 65 years was BMI, whereas the waist-to-hip ratio was a stronger predictor of CHD incidence among older men.<sup>12</sup> The possibility that the relative importance of BMI, WC, and triceps skinfold thickness differs across risk factors, age, and possibly, gender and race, could make the identification of the 'best' measure exceedingly difficult.

The biological interpretation of BMI and WC can also be problematic. Although WC is correlated with the amount of intra-abdominal visceral fat, which may be the most detrimental fat depot,<sup>13</sup> it is also associated with subcutaneous abdominal fat and with total body fat.<sup>11,14</sup> In addition, the waist-to-hip ratio and BMI are more strongly associated with each other ( $r \approx 0.90$ ) than with percent body fat ( $r \approx 0.70$ ) as determined by air-displacement plethysmography.<sup>15</sup> Therefore, it should not be assumed that BMI and WC are indices of generalized and abdominal adiposity, respectively. Another complication is that studies have consistently found that levels of various risk factors are related to BMI as least as strongly as they are to more accurate estimates of body fatness based on air-displacement plethysmography,<sup>15</sup> dual-energy x-ray absorptiometry (DXA),<sup>16</sup> or underwater weighing.<sup>17</sup> This seems contradictory if it is assumed that some measure of adiposity (or a specific fat depot) is the body size characteristic of primary interest.

The use of skinfold thicknesses should also be approached with caution. Skinfold thickness measurements have long been considered to be an attractive alternative to BMI, and they have been found to be stronger correlates of body fat (as determined by more accurate methods) among children than the BMI.<sup>18,19</sup> However, there can be large errors in the measurement of skinfolds,<sup>20</sup> there is little agreement on the optimal sites for these measurements, and, as the authors note, these measurements are more intrusive than are those for weight and height. It is also possible that the stronger relation of skinfold thickness to body fat is largely due to the improved prediction of adiposity among children with low to normal levels of fat. Although BMI is a good surrogate for body adiposity among fatter children, it is "almost useless" in assessing the body fat of normal-weight children.<sup>18</sup> Based on national (NHANES) data in the U.S., we have found that BMI is nearly as good as skinfold (subscapular plus triceps) thicknesses in identifying children who have elevated levels of DXA-calculated body fat.<sup>21</sup> It is likely that it is these children with high levels of body fat who have adverse levels of various risk factors.

Another concern is with the statistical methods that were used in the study<sup>4</sup>. The estimation of standard deviations, correlation coefficients, and regression coefficients are appropriate for a simple random sample, but as described in the Methods, the sample was selected by first choosing one school in each of the five regions. All children within the five selected schools were then invited to participate. This is a clustered design, with children clustered within schools, and it is likely that children from the same school are more alike than children from different schools. This is referred to as intra-cluster (or intra-class) correlation, and the observations are not independent. In general, the treatment of clustered data as a random sample results in standard errors that are too small. Since children within a school

do not provide completely independent information, the 'effective' sample size is less than the total number of children in the study. Although there are several methods that can be used to correctly analyze clustered data,<sup>22</sup> including open-source statistical software<sup>23</sup> and the 'Complex Samples' add-on for the Statistical Package for Social Sciences (SPSS), it's not clear whether clustering was taken into account. It is also possible to use multilevel or hierarchical regression models to account for clustering, but regardless of the statistical technique used, it is important for the analyses to account for the structure of the data.

It can also be difficult to disentangle the importance of the various measures of body size from the cut-points that were used to form the dichotomous categories for the logistic regression analyses (Table 3). The BMI levels of the children were categorized as 'adequate' or 'overweight' based on extrapolating a BMI of 25kg/m<sup>2</sup> at age 20 years to younger ages in 1989 data from Brazil.<sup>24</sup> In contrast, WC was categorized using the 75<sup>th</sup> percentile from U.S. data collected from 1988–1984, and the triceps skin-fold thickness was categorized using the 90<sup>th</sup> percentile of U.S. data collected from 1971–1974. The classification of high blood pressure was also based on levels among U.S. children and adolescents, and accounted for gender, height, and age. Because associations between dichotomous variables can be strongly influenced by the prevalence of each characteristic, with more extreme cutpoints typically resulting in higher odds ratios, it would have been helpful to be informed of the prevalences of high levels of BMI, WC, triceps skinfold thickness, and blood pressure.

The desire to use cut-points that facilitate comparisons with the results of other studies is commendable, but in many cases, it may be best to use cut-points that result in roughly equivalent proportions of children being classified as 'high' for each exposure characteristic. Comparisons between the results of the current study with others in the literature would also have been facilitated if the authors presented the prevalence of overweight or obesity as assessed by the BMI cut-points in the widely used 2000 CDC growth charts or in the International Obesity Task Force (IOTF) cut-points. Based on the presented results, it is not possible to determine whether the higher odds ratio for BMI than for triceps skinfold thickness (2.9 *vs.* 1.9) in Table 3 is due to the superiority of BMI itself or to the use of more extreme cut-points for BMI than for triceps skinfold thickness.

In summary, although the study of Moser et al.<sup>4</sup> provides some useful information, further study is needed to determine the relative importance of various measure of body size. The intercorrelations among these measures, along with the possibility that the best measure may differ according the outcome examined and age, may make the determination of the best measure exceedingly difficult. In the presence of highly correlated measures of body size, it may not be possible for a single measure to be optimal for all situations.

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