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Understanding the Nature of Metabolic Syndrome Components in Children and What They Can and Cannot Do to Predict Adult Disease

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To better understand the stability of metabolic syndrome components and their predictive characteristics of adult metabolic syndrome and type 2 diabetes, the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), with co-sponsorship from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the National Heart, Lung, and Blood Institute (NHLBI), organized a second meeting of the Pediatric Metabolic Syndrome Working Group (PMSWG) in February 2008. The PMSWG had met previously in July 2006, and both a history of the PMSWG and the collection of seminal papers resulting from that first meeting were published in the February 2008 issue of *The Journal*.[1] The PMSWG was not designed to generate consensus guidelines; rather, members of the PMSWG were invited to assist the sponsoring organizations in conducting, reviewing, and discussing new secondary data analyses of existing longitudinal or national databases to improve our understanding of the nature of the metabolic syndrome and its components in youth and their utility for predicting adult disease outcomes.

For this second round of analyses, there were 3 primary objectives: (1) to test the stability of the metabolic syndrome and its components over time in serial childhood data; (2) to estimate the predictive utility of metabolic syndrome components in childhood for metabolic syndrome and type 2 diabetes in adulthood, combining long-term data from the Fels

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Longitudinal Study, Princeton-Lipid Research Clinic Cohort Study, and the Muscatine Study; and (3) to generate growth curves of waist circumference and lipids using historic and recent data from the National Health and Nutrition Examination Surveys (NHANES).

The current supplement in *The Journal* includes a collection of 8 papers that were discussed at the February 2008 meeting. Contents of this group submission include a review of the physiology and epidemiology of metabolic risk factors in white versus African American children (article by Sumner et al). This review is followed by 2 papers showing that even though the metabolic syndrome as a whole appears to be quite unstable across different stages of sexual maturation (article by Goodman et al), individual components are relatively stable over time on a population level (article by Li et al). Because data from the Muscatine Study had not been included in prior PMSWG work, the article by Burns et al examined the predictive utility of select metabolic risk components in childhood in relation to adult outcomes using this data set.

Combining data from 3 longitudinal cohorts (The Fels Longitudinal Study, The Muscatine Study, and the Princeton-Lipid Research Clinic Cohort Study), the article by Schubert et al estimated the predictive statistics of childhood metabolic components in relation to both adult metabolic syndrome and type 2 diabetes. This study confirms prior findings that childhood components are highly specific but not sensitive when used to screen for children at risk for adult disease, suggesting that metabolic markers in childhood are better characterized as screening tools for individuals at no risk to low risk rather than individuals at high risk. Consistent with prior research, this paper also shows that the combination of metabolic risk factors can increase the probability that those with a positive test are truly diseased in adulthood, even though only a fraction of the diseased adult population is being identified by these childhood biomarkers. Because of lower rates in adult cases of type 2 diabetes compared to the metabolic syndrome, prediction estimates for childhood parameters in relation to the adult metabolic syndrome may be more robust; however, trends are similar using both outcomes.

Because of the ongoing debate on the role of body mass index (BMI) versus waist circumference in risk screening among children, a second paper by Schubert et al examined the predictive probability of adding waist circumference as well as family history of type 2 diabetes or cardiovascular disease to BMI in relation to the adult metabolic syndrome. This analysis found that the combination of a positive family history and overweight status (BMI between the 85th and 94th percentiles) in childhood yielded a >50% probability of having the metabolic syndrome in adulthood, an 80% increase in risk from relying on child overweight status alone. The combination of family history and BMI was more predictive than the combination of waist circumference and BMI, and the use of all 3 variables did not appear to improve the prediction overall. Given the recent recommendation from the American Medical Association Expert Committee to perform detailed blood screening in all youth between the 85th and 94th percentiles for BMI, these findings coupled with considerations for the relative ease of assessing family history versus waist circumference may have important clinical implications.

Furthermore, the paper by Cook et al fitted growth curves to waist circumference and lipids by fixing the risk thresholds at age 18 years on the Adult Treatment Panel III criteria. This is the first paper to conduct these analyses, using both NHANES data as well as data from existing longitudinal cohorts, in children age 6 years and older, providing a population-based reference for US youth. Finally, using extensive serial data from the Fels Longitudinal Study, Sun et al showed that an accelerated versus a retarded tempo of growth during childhood and adolescence, as assessed by the timing of peak height velocity, predicted

adult metabolic outcomes. This paper provides a preview of additional biomarkers that can be potentially used to discover childhood origins of adult disease.

This supplement contains summaries of the current state of knowledge of factors related to the metabolic syndrome in youth. Although this collection of articles was meant to disseminate the work of some members of the PMSWG to date to the larger scientific community, each paper was evaluated independently in *The Journal* review process and should not be construed as representing the consensus view of the PMSWG. There were many data set limitations that constrained our analyses. For instance, there was insufficient longitudinal data on minority populations for stratified analyses, despite some ethnic differences as shown in the review paper by Sumner. Findings from these papers may be limited to white children. The working group considered incorporating cohorts from the Bogalusa Heart Study and the NHLBI Growth and Health Study, but the former was a much younger cohort (with lower disease prevalence in adulthood) and the latter did not have data beyond age 19 years. Thus, longitudinal data sets, such as the Fels Longitudinal Study, in different ethnic groups are clearly needed.

In summary, individual metabolic components appear to be more stable than the structure of the metabolic syndrome as a whole during childhood and adolescence. In addition, childhood components of the metabolic syndrome are specific but not sensitive for the prediction of adult metabolic syndrome or type 2 diabetes. These childhood biomarkers are better at capturing no-risk to low-risk than high-risk individuals. Adding family history to BMI in childhood improves the prediction of adult metabolic syndrome significantly, compared with BMI alone or the combination of BMI and waist circumference. The combination of family history and BMI may be a useful tool for identifying overweight but not yet obese children who require additional blood tests or other detailed screening of disease risk.

References

1. Cook S, Auinger P, Li C, Ford ES. Metabolic Syndrome Rates in United States Adolescents from the National Health and Nutrition Examination Survey, 1999–2002. J Pediatr. 2009; 152:165–70. [PubMed: 18206683]

Glossary

BMI	Body mass index
NICHD	Eunice Kennedy Shriver National Institute of Child Health and Development
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NHLBI	National Heart, Lung, and Blood Institute
PMSWG	Pediatric Metabolic Syndrome Working Group