

PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Improvement in Risk Factors for Metabolic Syndrome and Insulin Resistance in Overweight Youth Who Are Treated With Lifestyle Intervention

Roshanak Monzavi, Daina Dreimane, Mitchell E. Geffner, Sharon Braun, Barry Conrad, Mary Klier and Francine R. Kaufman

Pediatrics 2006;117;1111-1118; originally published online May 8, 2006;
DOI: 10.1542/peds.2005-1532

This information is current as of June 16, 2006

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://www.pediatrics.org/cgi/content/full/117/6/e1111>

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2006 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™



Improvement in Risk Factors for Metabolic Syndrome and Insulin Resistance in Overweight Youth Who Are Treated With Lifestyle Intervention

Roshanak Monzavi, MD^a, Daina Dreimane, MD^a, Mitchell E. Geffner, MD^{a,b}, Sharon Braun, MS, RD, CDE^a, Barry Conrad, MPH, RD, CDE^a, Mary Klier, RD^a, Francine R. Kaufman, MD^{a,b}

^aCenter for Diabetes, Endocrinology, and Metabolism, Los Angeles, California; ^bThe Saban Research Institute, Childrens Hospital Los Angeles, Los Angeles, California

The authors have indicated they have no financial relationships relevant to this article to disclose.

ABSTRACT

OBJECTIVE. To evaluate the prevalence of risk factors that are associated with the metabolic syndrome and insulin resistance in overweight youth and to determine the effect of a short-term, family-centered, lifestyle intervention on various associated anthropometric and metabolic measures.

METHODS. Overweight youth who were between 8 and 16 years of age participated in a 12-week, family-centered, lifestyle intervention program. Anthropometric and metabolic measures were assessed before the program in all participants ($n = 109$) and after the program in a subset of the participants ($n = 43$).

RESULTS. At baseline, 49.5% of youth had multiple risk factors associated with the metabolic syndrome, based on a modified definition of the National Cholesterol Education Program, and 10% had impaired fasting glucose and/or impaired glucose tolerance. Measures of insulin resistance correlated significantly with the risk factors of the metabolic syndrome. Forty-three youth had pre- and postintervention evaluations that showed statistically significant improvements in body mass index, systolic blood pressure, lipids (total, low-density lipoprotein cholesterol, and triglycerides), postprandial glucose, and leptin levels.

CONCLUSION. Overweight youth have multiple risk factors associated with the metabolic syndrome. A 12-week lifestyle program may have a positive effect on reducing risk factors for the metabolic syndrome and insulin resistance in overweight youth.

www.pediatrics.org/cgi/doi/10.1542/peds.2005-1532

doi:10.1542/peds.2005-1532

Key Words

overweight, obesity, BMI, lipid, glucose, type 2 diabetes, physical activity, nutrition

Abbreviations

IGT—impaired glucose tolerance
NCEP—National Cholesterol Education Program
NHANES III—Third National Health and Nutrition Examination Survey
BP—blood pressure
TG—triglycerides
HDL—high-density lipoprotein
IR—insulin resistance
KNF—Kids N Fitness
SDS—SD score
FPG—fasting plasma glucose
LDL—low-density lipoprotein
CV—coefficient of variation
IFG—impaired fasting glucose
HOMA—homeostasis model assessment
QUICKI—quantitative insulin sensitivity check index

Accepted for publication Dec 14, 2005

Address correspondence to Roshanak Monzavi, MD, Childrens Hospital Los Angeles, 4650 Sunset Blvd, Mailstop #61, Los Angeles, CA 90027. E-mail: rmonzavi@chla.usc.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275). Copyright © 2006 by the American Academy of Pediatrics

THE PREVALENCE OF obesity and type 2 diabetes has increased dramatically in both adults and youth in the past 25 years. The number of youth who are overweight, defined as a BMI >95th percentile for age and gender, tripled between 1975 and 2000 to a prevalence of 15%.¹ Sinha et al² documented impaired glucose tolerance (IGT) in 25% of prepubertal and 21% of postpubertal overweight youth. Although they found that 4% of their cohort had silent diabetes, reports from other pediatric diabetes centers indicate that type 2 diabetes now accounts for between 8% and 45% of new-onset cases of diabetes in youth.³

In addition to this increase in incidence of IGT and type 2 diabetes, there has been an increase in the number of youth who have multiple risk factors for the metabolic syndrome. Using criteria similar to those proposed for adults by the National Cholesterol Education Program (NCEP) or Adult Treatment Panel III,⁴ Cook et al⁵ determined the prevalence of the metabolic syndrome in pediatric subjects from the Third National Health and Nutrition Examination Survey (NHANES III) using the following criteria: abnormalities of waist circumference, blood pressure (BP), triglycerides (TG), and high density lipoprotein (HDL) on the basis of age-adjusted normative data, along with the presence of IGT. NHANES III (1988–1994), which evaluated 2430 adolescents from 12 to 19 years of age, found an overall prevalence of the metabolic syndrome of 4.2%; this increased to 28% in the overweight (BMI >95th percentile) cohort.⁵ More recent data from NHANES (1999–2000), which evaluated 991 adolescents, showed an increase in the prevalence of the metabolic syndrome in overweight youth to 32.1%.⁶ This high prevalence of the metabolic syndrome in overweight youth has been confirmed by others. Cruz et al⁷ found that 30% of overweight Hispanic youth who had a family history of type 2 diabetes had the metabolic syndrome, and Weiss et al⁸ reported an even higher percentage in 50% of their overweight young subjects. Both obesity and insulin resistance (IR) are independently associated with the metabolic syndrome in youth.^{9,10} Although the impact of the metabolic syndrome on disease outcomes in children has not yet been investigated directly, its clear relationship to obesity and IR increases the risk for diabetes, as well as other comorbidities, such as early atherosclerosis, hypercoagulation, polycystic ovarian syndrome, and fatty liver.¹¹

Lifestyle programs that are designed to modify nutrition and physical activity patterns have been developed to reduce obesity and its associated comorbidities, including the metabolic syndrome, in youth. The rationale for these programs includes the Diabetes Prevention Program,¹² as well as pediatric studies such as that reported by Brage et al,¹³ who showed an association between decreased physical activity and criteria for the metabolic syndrome, including IR and dyslipidemia, in overweight

youth. In the current study, we evaluated the prevalence of risk factors for the metabolic syndrome, as well as IR, in an overweight pediatric population and the effects of a clinic-based, 12-week family-centered lifestyle intervention program on these measures.

METHODS

Lifestyle Intervention Program

The lifestyle intervention program, Kids N Fitness (KNF), that was used in this study was developed at Childrens Hospital Los Angeles in 2000. The initial objective was to alter eating and exercise patterns in youth for the purpose of weight management. After pilot testing showed a significant decrease in weight gain velocity in participants of KNF,¹⁴ the program was offered to children who were 8 to 16 years of age and were accompanied by a parent or a guardian. The program consisted of 12 consecutive weekly sessions, each of 90 minutes' duration, and was offered to the youth free of charge. The personnel who were involved in the program included 2 physicians, 4 dietitians, and 1 social worker. The initial 45-minute period of each session involved a concurrent exercise program for the youth and a standardized education session for parents, led by physicians, dietitians, and social workers. During the exercise sessions, children participated in dodge ball, volleyball, jumping rope, and running to promote moderate to vigorous cardiovascular physical activity. This was simultaneous with an education session for parents that covered topics regarding comorbidities of obesity, such as type 2 diabetes and hyperlipidemia. The second 45-minute period was devoted to a family-centered nutrition education session for both the youth and the parent/guardian that was conducted by a registered dietitian. Topics included the food pyramid, how to reduce total and saturated fat and cholesterol intake, how to determine and limit carbohydrate intake, portion control, improving the quality of snacks, strategies for eating out of the home, understanding food labeling, and healthful food shopping.

Study Population

Youth who were referred for weight management by the endocrinology or general pediatrics clinics in our institution or by community physicians were invited to participate in KNF. Youth were recruited between June 2002 and August 2004. Inclusion criteria were (1) age between 8 and 16 years, (2) BMI ≥ 25 kg/m² according to the revised Centers for Disease Control and Prevention growth charts¹⁵ or height to weight ratio >85th percentile, and (3) previous physician approval. Exclusion criteria were (1) disinterest in the program; (2) a known diagnosis of diabetes; (3) inability to ambulate; (4) preexisting medical conditions or administration of medications such as glucocorticoids, insulin sensitizers,

or psychotropics, which may affect appetite regulation; and (5) lack of approval by a physician to do physical activity. The protocol was approved by our institutional review board, and written informed consent and assent were obtained from all parents and youth, respectively.

Protocol

At enrollment, anthropometric and laboratory measures were obtained. Participants' height measurements were measured in 0.1-cm increments using a Harpenden Stadiometer (Cambridge, MD), weight measurements were obtained to the nearest 0.1 kg using a Detecto electronic weight scale (Webbcity, MO), and BP was measured with a Criticon Dinamap Monitor (Tampa, FL); each was measured once. BMI and BMI SD score (SDS) was calculated on the basis of Centers for Disease Control and Prevention growth charts. The following laboratory samples were obtained after at least an 8-hr overnight fast: plasma glucose (FPG) and serum insulin, c-peptide, total cholesterol, HDL cholesterol, LDL cholesterol, TG, leptin, and hemoglobin A1c. Repeat sampling for FPG and serum insulin was performed 2 hours after ingestion of 1.75 g/kg (maximum dose 75 g) of Glucola (Fisherbrand, Fisher Health Care, Houston, TX), an oral glucose solution. FPG, total cholesterol, HDL cholesterol, and TG were measured via Vitros 960 colorimetric assay, and LDL cholesterol was calculated. Hemoglobin A1c was measured using a DCA 2000 (Bayer Corporation, Elkhart, IN). Insulin and c-peptide levels were measured by immunochemiluminescent assay (Esoterix Laboratories, Calabasas Hills, CA), with an interassay coefficient of variation (CV) of 9.8% and an intra-assay CV of 6.8% for insulin, and interassay CV of 11.8% and intra-assay CV of 6.8% for c-peptide. Leptin levels were measured via double-antibody radioimmunoassay (Esoterix Laboratories), with interassay CV of 9.6% and intra-assay CV of 12%. Outcome measures were obtained within 3 weeks before the start of the program and were repeated at or within 3 weeks after the end of the final session. Weight, height, and BP measurements were obtained on a weekly basis, but these data were not analyzed, because not all patients attended the same sessions. Outcome measures after completion of the program were offered to youth who had attended at least 50% of the sessions. Informal telephone surveys were done by calling families who did not complete the program. A total of 39 families were called, and 8 questions were asked regarding reasons for dropping out of the program.

Data Analysis and Statistics

Modified criteria for metabolic syndrome were defined as the presence of 3 or more of the following (modified from the NCEP criteria above): age-adjusted BMI \geq 95th percentile, age-adjusted systolic or diastolic BP \geq 90th percentile,¹⁶ age-adjusted TG \geq 90th percentile, age-adjusted HDL \leq 10th percentile,¹⁷ and impaired fasting glu-

cose (IFG) or IGT. IFG was defined as a FPG \geq 100 mg/dL, and IGT was defined as a FPG \geq 140 and $<$ 200 mg/dL 2 hr after a standard glucose load. IR was calculated on the basis of 2 indices to evaluate change in degree of IR. These indices included homeostasis model assessment of IR [HOMA-R = $(I_F \times G_F)/22.5$],¹⁸ where I_F is fasting insulin (mU/L) and G_F is fasting glucose (mmol/L), and quantitative insulin sensitivity check index {QUICKI = $1/[\log(I_F) + \log(G_F \text{ in mg/dL})]$ }.¹⁹ Note that with increasing IR, the HOMA-R index increases and the QUICKI index decreases. Although there are conflicting data regarding the reliability of HOMA and QUICKI in assessing IR in youth, recent data have shown reliable sensitivity and specificity of these indices to evaluate IR in this population.^{20,21} We used both calculations to assess a trend in change of IR, rather than define IR cutoffs.

The prevalence of each of the risk factors of the metabolic syndrome was calculated. Logistic regression was used to evaluate the difference in the prevalence of metabolic syndrome on the basis of gender and ethnicity. The difference in IR among youth with and without the metabolic syndrome was assessed using Student's *t* test; the difference in IR among youth with different numbers of risk factors for the metabolic syndrome was evaluated using linear regression. Paired *t* tests were used to compare different outcome measures before and after completion of the KNF program. Nonparametric Spearman rank correlation was used to evaluate the correlation between the change in BMI and that of the other metabolic measures.

The study initially was powered on the basis of an assumption that \sim 50 youth would be enrolled into and complete the study, yielding a power of 80% for detecting differences of approximately one third of an SD based on a 1-sided paired *t* test at a 5% significance level. The resulting study actually had a smaller power, allowing detection of one third of an SD (\sim 65%), as a result of the failure of all youth to provide follow-up data.

RESULTS

Baseline measures were obtained in 109 youth with demographic data, as indicated in Table 1. Although this program was open to children and youth from all ethnic groups, on the basis of the demography of our center, most of the youth who enrolled were self-identified as Hispanic in origin. The overall prevalence of risk factors for the metabolic syndrome, on the basis of our modified criteria, was 49.5% in this population, with the prevalence of each individual criterion indicated in Table 1. The prevalence of IFG/IGT was 10%. The prevalence of the risk factors for the metabolic syndrome was 55% in Hispanic and 27% in black participants, a statistically significant difference even when adjusted for the gender difference between the 2 groups, although this was not adjusted for BMI (Table 2). However, the difference in

TABLE 1 Prevalence of the Metabolic Syndrome and Its Various Components

Criteria	All N = 109	Male N = 60	Female N = 49	Hispanic N = 85	AA N = 15
Gender, %					
Male	55			60	25
Female	45			40	75
Ethnicity, % of total					
Hispanic	78	85	69.5		
Black	14	5	24.4		
White	5	8.3	2		
Other	3	1.7	4.1		
Mean age, y	11.5 ± 1.9	11.4 ± 1.9	11.9 ± 1.8	11.6 ± 1.9	11.9 ± 1.8
Mean BMI SDS	+2.35 ± 0.32	+2.41 ± 0.30	+2.27 ± 0.33	+2.35 ± 0.38	+2.29 ± 0.38
Mean BMI percentile	98.1	98.3	98.0	98.8	93.3
Metabolic syndrome, % of total	49.5	58.3	42.9	56.5	20.0
BMI, % >95th percentile	98.2	98.3	98.0	98.8	93.3
BP, % ≥90th percentile	30.2	30	30.6	30.6	33.3
TG, % ≥90th percentile	61.4	71.7	49.0	69.4	20.0
HDL, % ≥90th percentile	40.4	43.3	36.7	44.7	26.7
IFG/IGT, % of total with either	10	8.3	12.2	10.6	6.7

TABLE 2 Prevalence of the Metabolic Syndrome on the Basis of Ethnicity and Gender

	Hispanic	Black
Male, %	56.9 (n = 51)	33.3 (n = 3)
Female, %	52.9 (n = 34)	16.7 (n = 9)

When adjusted for gender, Hispanic youth had 4.5 times the odds ratio of having metabolic syndrome versus black youth ($P < .05$). When adjusted for ethnicity, male youth had 1.2 times the odds ratio of having the metabolic syndrome versus female youth ($P = .6$).

the prevalence of the risk factors for the metabolic syndrome between boys and girls was not statistically significant. Youth with the risk factors for the metabolic syndrome had significantly higher HOMA-IR and lower QUICKI indices, suggesting a higher degree of IR than in those without the metabolic syndrome (Table 3). Assessment of IR by both measures correlated significantly with the number of risk factors for the metabolic syndrome that were present (Fig 1).

Rates of retention versus attrition of youth are indicated in Fig 2. Of the 109 youth, 50 (46%) dropped out of the program, with almost half of them never even attending a single session after enrollment. Our informal questionnaires indicated that transportation, language barrier (although interpreters were used during the class), and the time requirement were found to be the main reasons for dropping out of the program. Of the 59 youth who completed the program with at least 50% of the sessions attended, 43 completed postprogram outcome measures, and data were available on 35 to 43 youth, depending on the measure; the other 19 youth did not return for the final outcome assessment.

The subset of youth with final outcome measures showed a significant decrease in BMI and leptin levels; systolic BP; and total cholesterol, LDL cholesterol, and TG; and 2-hour postprandial glucose levels (Table 4). Although youth did not show a significant decrease in

TABLE 3 Assessment of IR in Youth With and Without the Metabolic Syndrome

	With Metabolic Syndrome	Without Metabolic Syndrome	P
Fasting insulin, $\mu\text{U/mL}$	28.6 ± 4.0	16.8 ± 1.6	<.005
2-hour insulin, $\mu\text{U/mL}$	128 ± 17.4	76.8 ± 7.0	<.005
HOMA-R	6.49 ± 1.0	3.69 ± 0.4	<.01
QUICKI	0.308 ± 0.004	0.325 ± 0.004	<.005
C-peptide, ng/mL	3.90 ± 0.32	3.56 ± 0.30	NS

Data are mean ± SE. NS indicates not significant.

absolute weight, they showed a significant increase in their height gain during the study period; therefore, they had a statistically significant improvement in BMI and BMI SDS. A trend of improvement in IR also was noted; however, this improvement was not statistically significant (Table 5). The improvement in none of the other metabolic measures correlated with the presence and/or the magnitude of the improvement of BMI.

DISCUSSION

On the basis of criteria that were adapted from the NCEP, we found that approximately half of our overweight pediatric population had multiple risk factors for the metabolic syndrome, a prevalence that is consistent with the findings of Weiss et al⁸ but higher than that found in other studies of overweight youth.^{5,6} This may be explained by a recruitment bias, because most of our participants were referred by their primary care providers. It is likely that the presence of acanthosis nigricans, a known abnormal lipid profile, a positive family history, or a greater weight/BMI prompted referral. Because we used a BMI ≥95th percentile as a criterion for the metabolic syndrome, as opposed to a waist circumference ≥90th percentile, we may have increased falsely the

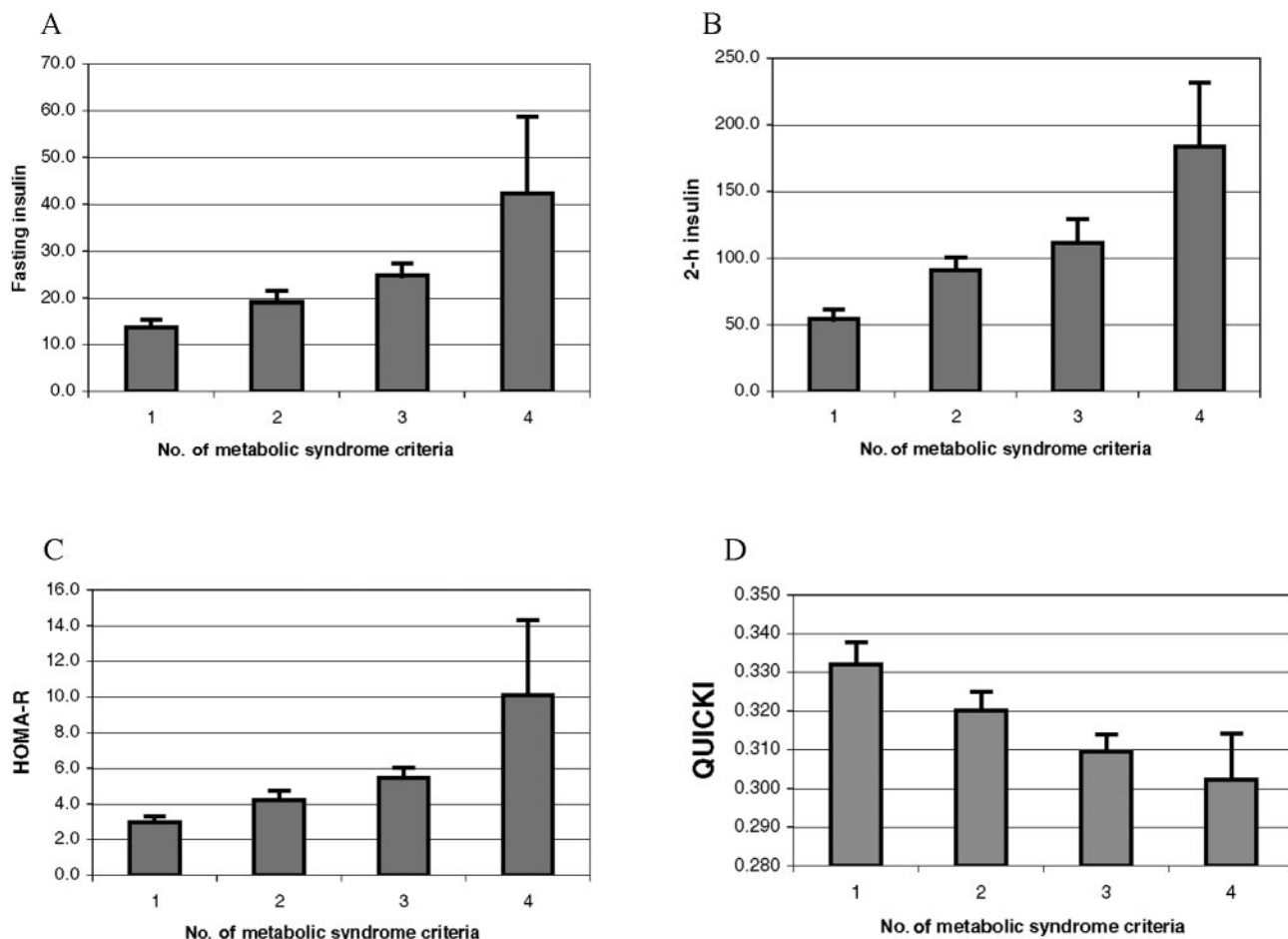


FIGURE 1 IR and the metabolic syndrome. Number of metabolic syndrome criteria versus measures of IR as assessed by fasting insulin (A), 2-hour insulin (B), HOMA-R (C), and QUICKI (D). $P < .05$ for all.

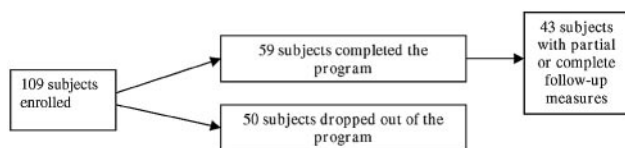


FIGURE 2 Participant retention versus attrition.

number of youth with multiple risk factors for the metabolic syndrome. However, this was similar to criteria used by Weiss et al⁸ in their study of overweight youth, and we chose BMI because of the lack of normative data on waist circumference in youth when we began our study. Because normative waist circumference data since have been published for the adolescent population,²² measuring waist circumference in future studies should be promoted so that more standardized definitions of metabolic syndrome can be used. We used IGT, in addition to IFG, as a criterion for the metabolic syndrome because previous studies showed a higher prevalence of IGT than of IFG in an obese pediatric popula-

tion.² In addition, we used age-adjusted percentile cutoffs for TG and HDL, rather than absolute values, to provide a more comprehensive assessment, because normal ranges for TG and HDL levels in youth are age dependent.¹⁷

The severity of obesity in our population may explain the high prevalence of the metabolic syndrome. Our youth were very overweight, with an average BMI SDS of 2.35 ± 0.32 above the mean, and >95% of our youth had a BMI ≥ 97 th percentile for age and gender. Comparable results were found by Weiss et al, who, using a similar definition for the metabolic syndrome, found a prevalence of 38.7% in moderately obese youth (BMI SDS +2.0–2.5) and 49.7% in severely obese youth (BMI SDS $> +2.5$).⁸ These investigators also found, as we did, a lower prevalence of risk factors for the metabolic syndrome, as well as lower lipid levels, in black youth than in those of other ethnicities. A more favorable lipid profile has been noted in the black population, both in adults and in youth.^{23,24}

Similar to previous reports,^{7,8} our data suggest that there is a direct relationship between IR and the risk

TABLE 4 Changes in Anthropometric and Metabolic Outcomes Before and After Completion of KNF Program

Outcome Measure	Before KNF	After KNF	P (Paired t Test)	CI
Weight, kg (n = 43)	78.23 ± 3.69	78.31 ± 3.64	NS	-0.72 to 0.54
Height, cm (n = 43)	151.1 ± 1.6	152.2 ± 1.6	<.005	-1.4 to -0.9
BMI, kg/m ² (n = 43)	33.65 ± 1.15	33.19 ± 1.12	<.005	0.2 to 0.7
BMI SDS (n = 43)	2.39 ± 0.05	2.34 ± 0.06	<.005	0.016 to 0.076
SBP, mm Hg (n = 40)	118.3 ± 2.8	113.3 ± 2.8	<.05	0.45 to 9.4
DBP, mm Hg (n = 40)	65.9 ± 1.5	62.3 ± 1.4	NS	-0.05 to 7.4
FPG, mg/dL (n = 39)	89.2 ± 1.1	87.9 ± 1.1	NS	-1.1 to 3.4
2-hour glucose, mg/dL (n = 35)	111.5 ± 4.2	102.5 ± 2.5	<.05	1.3 to 16.8
Cholesterol, mg/dL (n = 40)	183.0 ± 5.9	171.8 ± 5.3	<.005	5.03 to 17.5
HDL, mg/dL (n = 41)	42.5 ± 1.7	41.7 ± 1.6	NS	-1.5 to 3.09
LDL, mg/dL (n = 40)	109.9 ± 4.7	103.3 ± 4.9	<.05	1.4 to 12.0
TG, mg/dL (n = 39)	148.1 ± 11.5	120.8 ± 8.7	<.05	8.7 to 45.9
Leptin (n = 35)	32.0 ± 3.8	26.3 ± 3.0	<.05	1.1 to 10.4

Data are mean ± SE. CI indicates confidence interval; SBP, systolic BP; DBP, diastolic BP.

TABLE 5 Measures of IR Before and After Completion of the KNF Program

Measure	Before KNF	After KNF	P (Paired t Test)	CI
Fasting insulin, μ U/mL (n = 35)	24.2 ± 5.5	16.8 ± 1.7	NS (.1)	-1.6 to 16.4
2-hour insulin, μ U/mL (n = 35)	100.7 ± 18.0	72.9 ± 9.1	NS (.058)	-1.1 to 56.6
C-peptide, ng/mL (n = 35)	4.15 ± 0.46	3.54 ± 0.30	NS (.19)	-0.31 to 1.51
HOMA-R (n = 35)	5.52 ± 1.40	3.72 ± 0.41	NS (.12)	-0.53 to 4.1
QUICKI (n = 35)	0.318 ± 0.005	0.326 ± 0.005	NS (.1)	-0.05 to 0.003

Data are mean ± SE.

factors for the metabolic syndrome. The association between IR and serum lipids, including TG, has been attributed to altered action of insulin on lipoprotein metabolism. IR is associated with decreased lipoprotein lipase activity, resulting in decreased clearance of TG, as well as increased lipolysis in adipose tissue and increased synthesis of very-low-density lipoprotein particles in the liver.²⁵

In contrast to Sinha et al,² who reported IGT in 23% of children and adolescents with a BMI \geq 95th percentile, and Goran et al,²⁵ who reported IGT in 28% of overweight Latino children with a family history of type 2 diabetes, we found IGT or IFG in only 10% of our youth. Our study cohort may be different from that of these other studies^{2,8} in that it largely was Hispanic and our youth had a greater derangement in lipid than in glucose metabolism. Although the ethnicity on our study population was similar to that of Goran et al,²⁵ we did not use family history of type 2 diabetes as an inclusion criterion. Therefore, we may have included some youth who had a negative family history and may have had more effective compensatory β -cell function and, thus, could tolerate more IR without the development of diabetes. Indeed, elevated fasting insulin levels were found in the majority of our patients, suggesting intact compensation by the β cells to prevent disturbed glucose metabolism. A recent study by Rosenbaum et al²⁶ that evaluated insulin secretion and IR in 72 Latino youth found that children with a family history of type 2

diabetes were more likely to be in the lowest quartile for insulin secretory capacity, for glucose disposal, and for insulin sensitivity, leading to more insulin deficiency and dysregulation of glucose control.

Programs that attempt to modify lifestyle have been the mainstay of therapy for obesity and have proved to be effective in reducing the incidence of type 2 diabetes in adults, as reported by the DPP Research Group.¹² In adults, lifestyle modification also has proved to be beneficial in improving dyslipidemia, especially when high-intensity exercise is integrated into the program.²⁷ Early studies by Epstein et al²⁸ showed long-term benefits of a family-based lifestyle intervention in achieving weight loss in obese youth. However, studies that examined the effect of lifestyle intervention on metabolic derangements in youth have been limited. Kang et al²⁹ found an improvement in triacylglycerol, cholesterol/HDL, diastolic BP, and improvement in measures of IR in 80 obese youth who were between 13 and 16 years of age and involved in 8 months of lifestyle education and intense physical activity compared with those who underwent lifestyle education alone. A 3-year study of Zuni Pueblo American Indian high school students showed that diet education and increased physical activity reduced fasting and 30-minute insulin levels.³⁰ A recent study by Balagopal et al³¹ showed a decrease in weight gain and improvement of inflammatory markers in obese youth who participated in a 3-month exercise program. Our study suggests that an intensive lifestyle

intervention that combines nutrition education and exercise may improve metabolic outcomes in as little as 12 weeks, with a more significant effect in ameliorating lipid abnormalities than in improving IR.

The improvement in BMI SDS as the result of our lifestyle program, although small, was statistically significant. BMI and BMI SDS rather than absolute change in weight were analyzed because our youth still were growing in height. Although the youth did not have significant weight loss, they had statistically significant improvements in their BMI and BMI SDS because they also grew in height during the 12-week intervention. It is likely that without lifestyle modification, this population would have continued to gain weight and increased their BMI and BMI SDS. This decrease in BMI paralleled an improvement in the concentration of serum leptin. This is consistent with previous studies that found a correlation between weight loss and a decrease in leptin levels in youth.^{32,33}

In our study, we did not find an association between the degree of improvement in metabolic measures and the presence and the degree of improvement in BMI in individual patients. This may be secondary to our small study sample size and the modest degree of change in BMI. However, it also may suggest that lifestyle intervention has beneficial effects on metabolic derangements, regardless of change in BMI. In addition, because we did not evaluate total body or visceral fat, it is possible that the improvement in metabolic derangements in our population was secondary to a decrease in global or compartmental fat, without a major change in total BMI.

The attrition rate in our program was ~46%, which is consistent with the rates seen in other pediatric weight management programs.^{34,35} Previous studies in similar programs found a higher dropout rate in black participants, which may be caused by other confounding factors, such as socioeconomic status.³⁵ We saw a trend of higher attrition rate in male and black patients, but our population was too small to analyze this. In addition, we did not evaluate either socioeconomic status or health insurance status because the program was offered without charge to the family. Through our telephone surveys from families who dropped out of the program, we found the attrition rate to be related, at least in part, to transportation, distance from the program center, and language limitations, despite attempts to use translators and bilingual material. We were able to obtain outcome measures in only 43 of 59 youth who completed the program. It is possible that youth who did not complete the outcome measures were those who were less successful. As a result, our findings might be biased by the fact that more successful youth might have completed the final assessments.

CONCLUSION

A 12-week family-based lifestyle intervention program for overweight youth may have beneficial effects on anthropometric and metabolic measures related to obesity, the metabolic syndrome, and IR. In addition, improvements in abnormal lipid levels, such as total cholesterol, LDL, and TG levels, showed a greater degree of improvement than did measures of IR during a 12-week period. Longer term studies with greater duration of a postintervention observation period and larger sized study cohorts are necessary to evaluate whether the observed improvements are sustainable and clinically relevant.

ACKNOWLEDGMENTS

This research was supported partly by funding from Teammates for Kids Foundation (Littleton, CO), KTLA Charities Fund (Los Angeles, CA), Citigroup Foundation (New York, NY), and Million Dollar Round Table (Park Ridge, IL).

We thank Dr Fred Dorey, MD, for assistance with the statistical analyses of the data.

REFERENCES

1. Ogden CL, Flegal KM, Carroll MD, Johnson CL. Prevalence and trends in overweight among US children and adolescents, 1999–2000. *JAMA*. 2002;288:1728–1732
2. Sinha R, Fisch G, Teague B, et al. Prevalence of impaired glucose tolerance among children and adolescents with marked obesity. *N Engl J Med*. 2002;346:802–810
3. Kaufman FR. Type 2 diabetes mellitus in children and youth: a new epidemic. *J Pediatr Endocrinol Metab*. 2002;15:737–744
4. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP). Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA*. 2001;285:2486–2497
5. Cook S, Weitzman M, Auinger P, Nguyen M, Dietz W. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988–1994. *Arch Pediatr Adolesc Med*. 2003;157:821–827
6. Duncan GE, Li SM, Zhou XH. Prevalence and trends of a metabolic syndrome phenotype among U.S. adolescents, 1999–2000. *Diabetes Care*. 2004;27:2438–2443
7. Cruz ML, Weigensberg MJ, Huang TTK, Ball G, Shaibi GQ, Goran MI. The metabolic syndrome in overweight Hispanic youth and the role of insulin sensitivity. *J Clin Endocrinol Metab*. 2004;89:108–113
8. Weiss F, Dziura J, Burgert T, et al. Obesity and the metabolic syndrome in children and adolescents. *N Engl J Med*. 2004;350:2362–2374
9. Raitakari OT, Porkka KV, Ronnema T, et al. The role of insulin in clustering of serum lipids and blood pressure in children and adolescents. The Cardiovascular Risk in Young Finns Study. *Diabetologia*. 1995;38:1042–1050
10. Srinivasan SR, Myers I, Berenson GS. Predictability of childhood obesity and insulin for developing insulin resistance syndrome (syndrome X) in young adulthood: the Bogalusa Heart Study. *Diabetes*. 2002;51:204–209
11. Ten S, Maclaren N. Insulin resistance syndrome in children. *J Clin Endocrinol Metab*. 2004;89:2526–2539
12. Diabetes Prevention Program Research Group. Reduction in

- the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. 2002;346:393–403
13. Brage S, Wedderkopp N, Ekelund U, et al. Features of the metabolic syndrome are associated with objectively measured physical activity and fitness in Danish children: the European Youth Heart Study (EYHS). *Diabetes Care*. 2004;27:2141–2148
 14. Mackenzie M, Halvorson M, Kaufman F, Braun S, Conrad B. Effect of a Kids N Fitness weight management program on obesity and other pediatric health factors [Abstract]. Presented at the American Diabetes Association 61st Scientific Session; June 22–26, 2001; Philadelphia, PA
 15. Kuczmarski RJ, Ogden CL, Guo SS, et al. *CDC Growth Charts, United States*. Hyattsville, MD: National Center for Health Statistics in collaboration with National Center for Chronic Disease Prevention and Health Promotion; 2000
 16. Horan MJ, Sinaiko AR. Synopsis of the report of the second task force on blood pressure control in children. *Hypertension*. 1987;10:115–121
 17. Williams OD, Stinnett S, Chambless LE, et al. Populations and methods for assessing dyslipoproteinemia and its correlates. The Lipid Research Clinic Program Prevalence Study. *Circulation*. 1986;73(pt 2):I4–I11
 18. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Teacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta cell function from fasting plasma glucose and insulin concentration in man. *Diabetologia*. 1985;28:412–419
 19. Katz A, Nambi SS, Mather K, et al. Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. *J Clin Endocrinol Metab*. 2000;85:2402–2410
 20. Conwell LS, Trost SG, Brown WJ, Batch JA. Indexes of insulin resistance and secretion in obese children and adolescents: a validation study. *Diabetes Care*. 2004;27:314–319
 21. Keskin M, Kurtoglu S, Kendirci M, Atabek ME, Yazici C. Homeostasis model assessment is more reliable than the fasting glucose/insulin ratio and quantitative insulin sensitivity check index for assessing insulin resistance among obese children and adolescents. *Pediatrics*. 2005;115(4). Available at: www.pediatrics.org/cgi/content/full/115/4/e500
 22. Fernandez JR, Redden DT, Pietrobelli A, Allison DB. Waist circumference percentiles in nationally representative samples of African-American, European-American, and Mexican-American children and adolescents. *J Pediatr*. 2004;145:439–444
 23. Ford ES, Wayne HG, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third national health and nutrition examination survey. *JAMA*. 2002;287:356–359
 24. William CL, Strobino B, Bollella M, Brotanok J. Body size and cardiovascular risk factor in preschool population. *Prev Cardiol*. 2004;7:116–121
 25. Goran MI, Bergman RN, Avila Q, et al. Impaired glucose tolerance and reduced beta-cell function in overweight Latino children with a positive family history for type 2 diabetes. *J Clin Endocrinol Metab*. 2004;89:207–212
 26. Rosenbaum M, Nonas C, Horlick M, et al. Beta-cell function and insulin sensitivity in early adolescence: association with body fatness and family history of type 2 diabetes mellitus. *J Clin Endocrinol Metab*. 2004;89:5469–5476
 27. Kraus WE, Houmard JA, Duscha BD, et al. Effects of the amount and intensity of exercise on plasma lipoproteins. *N Engl J Med*. 2002;347:1483–1492
 28. Epstein LH, Valoski A, Wing RR, McCurley J. Ten-year outcomes of behavioral family-based treatment for childhood obesity. *Health Psychol*. 1994;13:373–383
 29. Kang HS, Gutin B, Barbeau P, et al. Physical training improves insulin resistance syndrome markers in obese adolescents. *Med Sci Sports Exerc*. 2002;34:1920–1927
 30. Ritenbaugh C, Teufel-Shone NI, Aickin MG, et al. A lifestyle intervention improves plasma insulin levels among Native American high school youth. *Prev Med*. 2003;36:309–319
 31. Balagopal P, George D, Yarandi H, Funanage V, Bayne E. Reversal of obesity-related hypoadiponectinemia by lifestyle intervention: a controlled, randomized study in obese adolescents. *J Clin Endocrinol Metab*. 2005;90:6192–6197
 32. Pilcova R, Sulcova J, Hill M, Blaha P, Lisa L. Leptin levels in obese children: effects of gender, weight reduction and androgens. *Physiol Res*. 2003;52:53–60
 33. Sudi KM, Gallistl S, Borkenstein MH, et al. Effects of weight loss on leptin, sex hormones, and measures of adiposity in obese children. *Endocrine*. 2001;14:429–435
 34. Tershakovec AM, Kuppler K. Ethnicity, insurance type, and follow-up in a pediatric weight management program. *Obes Res*. 2003;11:17–20
 35. Zeller M, Shelly K, Randal C, et al. Predictors of attrition from a pediatric weight management program. *J Pediatr*. 2004;144:466–470

Improvement in Risk Factors for Metabolic Syndrome and Insulin Resistance in Overweight Youth Who Are Treated With Lifestyle Intervention

Roshanak Monzavi, Daina Dreimane, Mitchell E. Geffner, Sharon Braun, Barry Conrad, Mary Klier and Francine R. Kaufman

Pediatrics 2006;117;1111-1118; originally published online May 8, 2006;

DOI: 10.1542/peds.2005-1532

This information is current as of June 16, 2006

Updated Information & Services	including high-resolution figures, can be found at: http://www.pediatrics.org/cgi/content/full/117/6/e1111
References	This article cites 31 articles, 20 of which you can access for free at: http://www.pediatrics.org/cgi/content/full/117/6/e1111#BIBL
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): Nutrition & Metabolism http://www.pediatrics.org/cgi/collection/nutrition_and_metabolism
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://www.pediatrics.org/misc/Permissions.shtml
Reprints	Information about ordering reprints can be found online: http://www.pediatrics.org/misc/reprints.shtml

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

