CDC charts. Other sources of data were also included. There were two important exclusions. Very low birth rate infants were excluded from the infant growth charts and, secondly, all infants excluded from the NHANES III study were also excluded.

The growth charts are not presented here as they are available on the internet (http://www.cdc.gov/growthcharts). They should be very helpful for all physicians and nurses caring for children.

Editor's Comment: *We certainly agree that the new growth charts are an improvement over previous charts available for monitoring growth in children in the United States. The editorial on childhood growth charts written in the same journal as an accompaniment to the publication of the growth charts should be carefully read. Careful measurements of children for both height and weight, and the plotting of the data on an appropriate growth chart MUST BE a routine in all pediatric practices.*

Ogden CL, et al. *Pediatrics* 2002;109:45-60.

Fima Lifshitz, MD
Judith G. Hall, OC, MD

Reduction in the Incidence of Type II Diabetes with Lifestyle Intervention or Metformin

The Diabetes Prevention Research Group, a consortium of 27 clinical centers, conducted a randomized clinical trial involving adults in the U.S. who were at high risk for the development of T2DM. The study was designed to answer three questions: (1) does a lifestyle intervention or treatment with Metformin delay or prevent the onset of diabetes; (2) do the two interventions differ in effectiveness; and (3) does the effectiveness differ according to age, sex, race, or ethnic group. To answer these questions, 3,234 individuals were randomized to one of three treatment groups: (1) standard lifestyle recommendation plus metformin, (850 mg twice daily); (2) standard lifestyle recommendation plus placebo twice daily; or (3) an intensive program of lifestyle modification.

The standard lifestyle recommendation included written information and an annual individual session of 20-30 minutes emphasizing the importance of a healthy lifestyle. The participants in growth 1 and 2 were told to reduce their weight, to increase their physical activity, to follow the Food Pyramid Guide, and to follow a diet the equivalent of a National Cholesterol Diabetes Education Program Step 1. The participants in group 3, the intensive lifestyle intervention group, were to achieve and maintain a weight reduction of at least 7% by following a low fat diet and by performing moderate physical activity such as brisk walking for at least 150 minutes per week. In addition, these subjects participated in a 16-week curriculum promoting dietary education, exercise, and behavior modification.

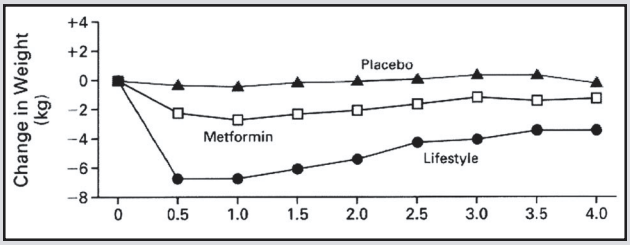
The primary outcome variable was diabetes as diagnosed by an annual oral glucose tolerance test or a semi-annual fasting plasma glucose test. The blinded treatment phase was terminated one year early, because by that time there was evidence of efficacy on the basis of 65% of the planned person-years of observation.

Approximately two-thirds of the subjects in the study were female, 54% were Caucasian, 20% African-American, 16% Hispanic, 5% American-Indian, and 4% Asian. Seventy percent had a positive family history of diabetes. The mean age for the entire group was 50.6, + 10.7 years, the mean weight 94.2 + 20.3 kg; the mean BMI 34 + 6.7, the mean plasma glucose 106.5 + 8.3 mg/dl, and the mean glycated hemoglobin was 5.9%. The mean baseline data were similar in the 3 groups.

In the lifestyle intervention group, 50% achieved the goal of a 7% weight loss by the end of the first 24 weeks and 38% had maintained that weight loss at the last visit. Seventy-five percent participated in 150 minutes of physical activity per week at the end of 24 weeks and 58% maintained that level. Daily caloric intake decreased by a mean of 450 kcal in the lifestyle intervention group, 249 kcal in the placebo group, and 296 kcal in the metformin group. The average fat intake (34.1% of total at baseline) decreased by 6.6 $\pm$ 0.2% in the lifestyle intervention group and by 0.8 $\pm$ 0.2% in the placebo and metformin groups. Participants in the lifestyle intervention group had a much greater weight loss and greater increase in physical activity, than did the subjects in the other groups. The average weight loss was 5.6 kg in the lifestyle intervention group, and 2.1 kg and 0.1 kg in group 2 and 1. (Figure 1)

The incidence of diabetes was 4.8, 7.8, and 11.0 cases/hundred patient years for groups 3, 2, and 1 respectively. The incidence of diabetes was 58% lower in the lifestyle intervention group (group 3) than in the placebo group (group 2) and 31% lower in the metformin group than in the placebo group. (Figure 2) These results were statistically significant and the estimated cumulative incidence of diabetes at 3 years was 28.9%, 21.7%, and 14.4% in groups one, two, and three, respectively. Unfortunately, the study had inadequate power to access the significance of the effects within ethnic groups, but effects did not differ significantly according to sex, race, or ethnic group.

Figure 1



Changes in body weight according to study group. Each data point represents the mean value for all participants examined at that time. The number of participants decreased over time because of the variable length of time that persons were in the study. For example, data on weight were available for 3085 persons at 0.5 year, 3064 at 1 year, 2887 at 2 years, and 1510 at 3 years. Changes in weight and leisure physical activity over time differed significantly among the treatment groups (P<0.001 for each comparison).

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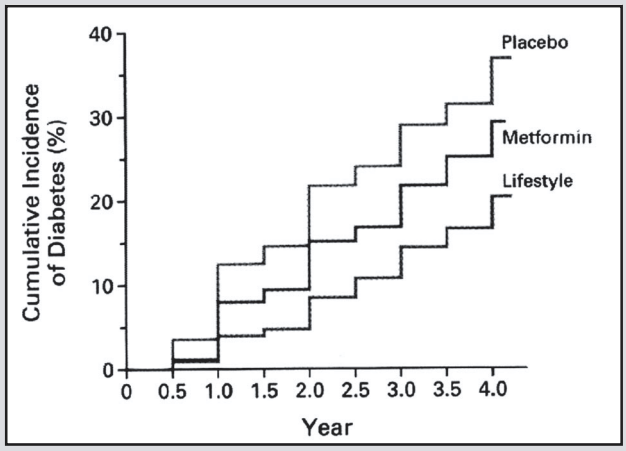
Figure 2



Cumulative incidence of diabetes according to study group. The diagnosis of diabetes was based on the criteria of the American Diabetes Association. The incidence of diabetes differed significantly among the three groups (P< 0.001 for each comparison).

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The authors state the hypothesis that Type II diabetes can be prevented or delayed in persons at high risk for diabetes was proven, and the effects were similar in men and women and in all racial and ethnic groups, regardless of age. The authors point out that their results show a risk reduction associated with lifestyle intervention that is similar to a previous test study conducted in Finland. The current study however, was not designed to test the relative contribution of dietary changes, increase in physical activity and/or weight loss. This is the first study, however, to demonstrate the efficacy of drug therapy in reducing the risk of developing Type II diabetes in high risk individuals.

Diabetes Prevention Group *N Engl Med* 2002;346:393-403.

***Editor's Comment**: This is an exceedingly important publication, as was another significant paper published last year in the New England Journal of Medicine on the prevention of Type II diabetes mellitus by making alterations in lifestyle among subjects with impaired glucose tolerance (N Engl J Med 2001;344:1343-1350). The current study conducted in an older group of subjects has similar implications for children at high risk of developing Type II diabetes. In addition, the current study suggests that metformin, at a relatively modest dose (850 mg bid), can reduce the risk by 31%.*

Most pediatric endocrinologists are faced with increasing numbers of overweight children coming to their clinics for evaluation. Many of these children are at very high risk for the development of Type II diabetes. The clinical armamentarium remains limited. Clearly, studies are needed to confirm the effectiveness of metformin in preventing the onset of Type II diabetes in the pediatric age group. However, previous experiences amongst pharmaceutical companies attempting to recruit and retain children with Type II diabetes for clinical trials suggest that this will be a very difficult task. Such a clinical trial may require nearly as much effort as the clinical treatment of Type II diabetes. Although, most physicians would recommend a change in lifestyle modification for overweight children, the execution of changes in dietary intake and physical activity within the context of a family with varying degrees of motivation remains extremely difficult.

William L. Clarke, MD

***Second Editor's Comment**: This editor must conclude that we may succeed in changing the lifestyle of some obese adults but only in a few obese children, but we should keep trying. With children and adolescents, gentle persuasion will be more effective than parental demand.*

Robert M. Blizzard, MD