Diabetes Prevention Program (DPP)

National Diabetes Information Clearinghouse

U.S. Department of Health and Human Services

NATIONAL INSTITUTES OF HEALTH

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The Diabetes Prevention Program (DPP) was a major multicenter clinical research study aimed at discovering whether modest weight loss through dietary changes and increased physical activity or treatment with the oral diabetes drug metformin (Glucophage) could prevent or delay the onset of type 2 diabetes in study participants. At the beginning of the DPP, participants were all overweight and had blood glucose, also called blood sugar, levels higher than normal but not high enough for a diagnosis of diabetes—a condition called prediabetes.

The DPP found that participants who lost a modest amount of weight through dietary changes and increased physical activity sharply reduced their chances of developing diabetes. Taking metformin also reduced risk, although less dramatically. The DPP resolved its research questions earlier than projected and, following the recommendation of an external monitoring board, the study was halted a year early. The researchers published their findings in the February 7, 2002, issue of the *New England Journal of Medicine*.

DPP Study Design and Goals

In the DPP, participants from 27 clinical centers around the United States were randomly divided into different treatment groups. The first group, called the lifestyle intervention group, received intensive training in diet, physical activity, and behavior modification. By eating less fat and fewer calories and exercising for a total of 150 minutes a week, they aimed to lose 7 percent of their body weight and maintain that loss.

The second group took 850 mg of metformin twice a day. The third group received placebo pills instead of metformin. The metformin and placebo groups also received information about diet and exercise but no intensive motivational counseling. A fourth group was treated with the drug troglitazone (Rezulin), but this part of the study was discontinued after researchers discovered that troglitazone can cause serious liver damage. The participants in this group were followed but not included as one of the intervention groups.

All 3,234 study participants were overweight and had prediabetes, which are well-known risk factors for the development of type 2 diabetes. In addition, 45 percent of the participants were from minority groups—African American, Alaska Native, American Indian, Asian American, Hispanic/Latino, or Pacific Islander—at increased risk of developing diabetes.

Type 2 Diabetes and Prediabetes

Type 2 diabetes is a disorder that affects the way the body uses digested food for growth and energy. Normally, the food one eats is broken down into glucose, a form of sugar. The glucose then passes into the bloodstream, where it is used by the cells for growth and energy. For glucose to reach the cells, however, insulin must be present. Insulin is a hormone produced by the pancreas, a fist-sized gland behind the stomach.

Most people with type 2 diabetes have two problems: insulin resistance—a condition in which muscle, liver, and fat cells do not use insulin properly—and reduced insulin production by the pancreas. As a result, glucose builds up in the blood, overflows into the urine, and passes out of the body, never fulfilling its role as the body's main source of fuel.

About 23.6 million people in the United States have diabetes. Of those, 17.9 million are diagnosed and 5.7 million are undiagnosed. Ninety to 95 percent of people with diabetes have type 2 diabetes. Diabetes

Who should be tested for prediabetes and diabetes?

The American Diabetes Association recommends that testing to detect prediabetes and type 2 diabetes be considered in adults without symptoms who are overweight or obese and have one or more additional risk factors for diabetes. In those without these risk factors, testing should begin at age 45.

Risk factors for prediabetes and diabetes—in addition to being overweight or obese or being age 45 or older—include the following:

- being physically inactive
- having a parent, brother, or sister with diabetes
- having a family background that is African American, Alaska Native, American Indian, Asian American, Hispanic/Latino, or Pacific Islander
- giving birth to a baby weighing more than 9 pounds or being diagnosed with gestational diabetes—diabetes first found during pregnancy
- having high blood pressure—140/90 mmHg or above—or being treated for high blood pressure
- having HDL, or "good," cholesterol below 35 mg/dL, or a triglyceride level above 250 mg/dL
- having polycystic ovary syndrome, also called PCOS
- having impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) on previous testing
- having other conditions associated with insulin resistance, such as severe obesity or a condition called acanthosis nigricans, characterized by a dark, velvety rash around the neck or armpits
- having a history of cardiovascular disease

If results of testing are normal, testing should be repeated at least every 3 years. Doctors may recommend more frequent testing depending on initial results and risk status.

is the main cause of kidney failure, limb amputation, and new-onset blindness in American adults. People with diabetes are more likely than people without diabetes to develop and die from diseases of the heart and blood vessels, called cardiovascular disease. Adults with diabetes have heart disease death rates about two to four times higher than adults without diabetes, and the risk for stroke is two to four times higher among people with diabetes.

Prediabetes is a condition in which blood glucose levels are higher than normal but not high enough for a diagnosis of diabetes. Prediabetes is also called impaired glucose tolerance (IGT) or impaired fasting glucose (IFG), depending on the test used to measure blood glucose levels. Having prediabetes puts one at higher risk for developing type 2 diabetes. People with prediabetes are also at increased risk for developing cardiovascular disease.

Prediabetes is becoming more common in the United States. The U.S. Department of Health and Human Services estimates that about one in four U.S. adults aged 20 years or older—or 57 million people—had prediabetes in 2007. Those with prediabetes are likely to develop type 2 diabetes within 10 years, unless they take steps to prevent or delay diabetes.

DPP Results

The DPP's results indicate that millions of high-risk people can delay or avoid developing type 2 diabetes by losing weight through regular physical activity and a diet low in fat and calories. Weight loss and physical activity lower the risk of diabetes by improving the body's ability to use insulin and process glucose. The DPP also suggests that metformin can help delay the onset of diabetes.

Participants in the lifestyle intervention group—those receiving intensive individual counseling and motivational support on effective diet, exercise, and behavior modification—reduced their risk of developing diabetes by 58 percent. This finding was true across all participating ethnic groups and for both men and women. Lifestyle changes worked particularly well for participants aged 60 and older, reducing their risk by 71 percent. About 5 percent of the lifestyle intervention group developed diabetes each year during the study period, compared with 11 percent of those in the placebo group.

Participants taking metformin reduced their risk of developing diabetes by 31 percent. Metformin was effective for both men and women, but it was least effective in people aged 45 and older. Metformin was most effective in people 25 to 44 years old and in those with a body mass index of 35 or higher, meaning they were at least 60 pounds overweight. About 7.8 percent of the metformin group developed diabetes each year during the study, compared with 11 percent of the group receiving the placebo.

Further Analyses of DPP Data

In the years since the DPP was completed, further analyses of DPP data continue to yield important insights into the value of lifestyle changes in helping people prevent type 2 diabetes and associated conditions. For example, one analysis confirmed that DPP participants carrying two copies of a gene variant, or mutation, that significantly increased their risk of developing diabetes benefited from lifestyle changes as much as or more than those without the gene variant. Another analysis found that weight loss was the main predictor of reduced risk for developing diabetes in

DPP lifestyle intervention group participants. The authors concluded that diabetes risk reduction efforts should focus on weight loss, which is helped by increased exercise.

Analyses of DPP data have added to the evidence that changes in diet and physical activity leading to weight loss are especially effective in helping reduce risk factors associated with both diabetes and cardiovascular disease, including high blood pressure and metabolic syndrome. A person with metabolic syndrome has several of a specific group of risk factors for developing diabetes and heart disease, such as having excess fat deposited around the waist, high triglyceride levels, and high fasting blood glucose levels. One analysis found that DPP participants in the lifestyle intervention group who did not have metabolic syndrome at the beginning of the study—about half of the participants—were less likely to develop it than those in the other groups. Another analysis of DPP data found that the presence of high blood pressure in DPP participants decreased in the lifestyle intervention group but increased in the metformin and placebo groups over time. Measures of triglyceride and HDL cholesterol levels also improved in the lifestyle intervention group. A third analysis found that levels of C-reactive protein and fibrinogen—risk factors for heart disease—were lower in the metformin and lifestyle intervention groups, with a larger reduction in the lifestyle group.

In addition, one study focused on urinary incontinence in women who participated in the DPP. Women in the lifestyle intervention group who lost 5 to 7 percent of their body weight through dietary changes and exercise had fewer problems with urinary incontinence than women in the other study groups.

Points to Remember

- The DPP showed that people at risk for developing diabetes can prevent or delay the onset of diabetes by losing a modest amount of weight through diet and exercise. DPP participants in the lifestyle intervention group reduced their risk of developing diabetes by 58 percent during the study.
- DPP participants who took the oral diabetes medication metformin also reduced their risk of developing diabetes, but not as much as those in the lifestyle intervention group.
- The DPP's impact continues as new research builds on the study's results to find the best ways to delay, prevent, and treat diabetes.

Hope through Research

The DPP contributed to a better understanding of how diabetes develops in people at risk and how they can prevent or delay the development of diabetes by making behavioral changes leading to weight loss. These findings are reflected in recommendations from the American Diabetes Association for the prevention or delay of type 2 diabetes, which stress the importance of lifestyle changes and weight loss. The DPP's impact continues as new research, building on the study's results, seeks the most effective ways to prevent, delay, or even reverse diabetes.

DPP researchers continue to examine the roles of lifestyle and metformin and other diabetes medications in preventing type 2 diabetes. They also continue to monitor participants to learn more about the study's long-term effects through the Diabetes Prevention Program Outcomes Study (DPPOS), a follow-up to the DPP. DPPOS is examining the impact of long-term risk reduction on diabetes-related health problems, such as nerve damage and heart, kidney, and eye disease.

The National Institute of Diabetes and Digestive and Kidney Diseases supports a wide range of research related to the DPP, such as studies that assess cost-effective methods of delivering lifestyle modifications in group settings and over the Internet, as well as methods to sustain behavior change and weight loss. Other researchers are testing interventions similar to those used in the DPP to help prevent the development of or treat existing type 2 diabetes in children and youth.

Participants in clinical trials can play a more active role in their own health care, gain access to new research treatments before they are widely available, and help others by contributing to medical research. For information about current studies, visit *www.ClinicalTrials.gov*.

For More Information

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Publications produced by the Clearinghouse are carefully reviewed by both NIDDK scientists and outside experts. This publication was originally reviewed by David M. Nathan, M.D., Massachusetts General Hospital.

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