August 8, 2001

Diabetes Mellitus Interagency Coordinating Committee (DMICC)

Scientific Presentation: Diabetes Prevention Program, 12:30 pm

News Briefing, 2:30 pm

NIH Campus, Lister Hill Auditorium, Bethesda, Maryland

Meeting Summary

Introduction

Dr. Allen Spiegel, Director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and Chairman of the Diabetes Mellitus Interagency Coordinating Committee (DMICC), welcomed all to a meeting that he characterized as a unique event. The DMICC is charged with coordinating Diabetes research, not only throughout NIH but throughout all Department of Health and Human Services (DHHS) agencies, and will be integrally involved in the followup of the Diabetes Prevention Program (DPP). Dr. Spiegel explained that the DPP presentation would include a background overview and reports on the results and implications of the study. He took the opportunity to acknowledge all the people involved in the DPP, including the Principal Investigators, Program Coordinators, and, most importantly, the volunteers who participated, some of whom were in the audience. He then introduced the Chair of the DPP Study Group, Dr. David Nathan of Massachusetts General Hospital.

Dr. Nathan reported that the DPP was initiated in 1994 with a planning phase that lasted about 18 months. Recruitment was initiated in mid-1996 and completed 3 years later, ahead of schedule. The original plan was to conclude the treatment phase in 2002, but this phase was ended about 1 year early based on the recommendation of the independent Data Monitoring Board, which concluded in May 2001 that the DPP had succeeded in answering the major study questions. Dr. Nathan introduced Dr. Richard Hamman to present an overview of the background and goals of the DPP.

Background and Goals

Dr. Hamman stated that based on data from the late 1990s, it has been estimated that more than 16 million Americans have been diagnosed with type 2 diabetes, which accounts for more than 90 percent of diabetes cases, affecting almost 6 percent of the U.S. population. Prevalence increases with age, affecting 13 percent of those over 40 and 19 percent of those over 65. It has also been estimated that at least 30 percent of all cases of diabetes are undiagnosed. The impact of diabetes on racial and ethnic minorities is even greater; African Americans, Hispanic Americans, Asian Americans and Pacific Islanders, and Native Americans have rates of diabetes that are one-and-one-half- to eight-fold greater than similarly aged Caucasians.

Diabetes has important complications. It increases the risk of heart attack and stroke to two- to four-fold and is the leading cause of new cases of blindness, end-stage renal disease, and

amputation of lower limbs. Diabetes is the seventh leading cause of death, resulting in at least 193,000 deaths per year, and costs approximately 98 billion dollars per year in 1997 dollars (including direct treatment costs and indirect costs such as work loss and premature mortality). The prevalence of diabetes has been rising steadily; if current trends continue, cases of type 2 diabetes will double by 2050, while the total population will increase by less than 50 percent.

Dr. Hamman discussed specific risk factors for type 2 diabetes of importance to the DPP. These include increasing age, obesity, central body fat distribution, inactivity, and impaired glucose tolerance (IGT). Additional factors include a family history of diabetes and race/ethnicity other than Caucasian. Among women, previous gestational diabetes is also a risk factor.

Weight gain is associated with increased risk of developing diabetes. Every kilogram of weight gain over 10 years is equal to a risk increase of 4.5 percent. It has been estimated that over 70 percent of diabetes risk in the United States can be attributed to excess weight. Many observational studies have found association between physical inactivity and increased risk of developing diabetes and between increased activity and reduced risk. One of the main questions addressed by the DPP was whether a lifestyle intervention with a physical activity component aimed at weight reduction could lower diabetes risk.

IGT, a condition in which glucose levels are higher than normal, but not high enough to be considered diabetic, is a strong risk factor for developing diabetes later in life. About 20 million Americans are thought to be affected by IGT. IGT is identified by performing an oral glucose tolerance test. A sugar solution is administered after an overnight fast; blood tests for glucose levels are taken before the administration of the solution and after a 2-hour fast following its administration. When glucose levels are detected that are increased but not at diabetic levels, the label IGT is applied. IGT increases diabetes risk five- to eight-fold. It is estimated that every year, 1 to 9 percent of individuals with IGT will develop diabetes. IGT is also a major risk factor for cardiovascular disease. IGT may be an optimal pathological state for interventions to prevent diabetes, because it has a long gestational period preceding development of diabetes, it is a reversible condition, and diabetes-specific symptoms have not yet developed. Therefore, the DPP selected individuals with IGT to participate in the study.

Dr. Hamman summarized the rationale for the DPP. Type 2 diabetes is increasing at epidemic proportions throughout the world, affecting a projected population of 300 million by 2025. Once this disease develops, it is difficult and expensive to treat, and prevention would result in a significant reduction in human and economic costs. The primary goal of the DPP was to determine the feasibility of preventing or slowing the development of type 2 diabetes in individuals with IGT. A secondary goal was to determine whether DPP interventions would reduce cardiovascular disease events, cardiovascular disease risk factors, and atherosclerosis.

DPP Study Design

Dr. Sarah Fowler, Director of the Diabetes Prevention Program Coordinating Center, Department of Biostatistics at the George Washington University, described the DPP as a three-group randomized clinical study conducted at 27 centers throughout the United States. The medication arm was placebo-controlled. Participants were screened to determine eligibility and randomly assigned to one of three groups, receiving an intensive lifestyle intervention, the drug

metformin, or a placebo. A fourth treatment group receiving the drug troglitazone was discontinued in June 1998 due to the potential for liver toxicity. All participants received a standard set of lifestyle recommendations. The primary outcome for the DPP study was time to conversion to diabetes, determined by means of a fasting glucose test. The analytic system used for determining time to convert to diabetes was designed by the American Diabetes Association (ADA). Estimated cumulative incidence curves were calculated for the three treatment groups. A proportional hazard regression model was used to adjust for covariates. The original sample size calculation was based on the following assumptions:

- The protocol specified three pair-wise comparisons between treatment groups on time to conversion over an average followup period of 4.65 years
- The average hazard rate for progression to diabetes in the placebo group was estimated at 6.5 percent per year based on previous studies
- The study was designed to have 90 percent power to detect a 33 percent reduction in the hazard for conversion to diabetes for each pair-wise comparison
- The overall type 1 error was set at 5 percent with a Bonferoni adjustment for three pair-wise comparisons between treatment groups.

With a projected 10 percent per year loss to followup, it was determined that 1,000 participants for each treatment group would be required.

Secondary outcome measures included cardiovascular disease events, atherosclerosis, and risk factors for cardiovascular disease. The incidence of cardiovascular events in the study population to date has been low; thus, the lack of statistical power has prevented the detection of realistic differences between treatment groups. The study, however, has good statistical power to detect differences between groups on other secondary outcome measures; analyses on secondary outcomes are still being performed.

The DPP is funded primarily by the NIDDK through the cooperative agreement mechanism. The design, planning, conduct, and governance of the study was carried out by investigators through a number of committees and working groups. An independent external committee appointed by NIDDK, the Data Monitoring Board, reviewed the study design, performance, and data on an ongoing basis, and was specifically charged with developing stopping rules for the study. Institutions participating in the study include NIDDK, 27 clinical centers, and a data coordinating center. Four of the participating centers are American Indian clinics operated by NIDDK in conjunction with the Indian Health Service.

Eligibility Criteria, Screening and Recruitment Strategy, and Characteristics of the DPP Study Cohort

Dr. Wil Fujimoto from the University of Washington presented the following DPP eligibility criteria:

- Age, at least 25 years

- IGT, defined as a plasma glucose level of between 140 and 199 mg/dL as determined by an oral glucose tolerance test

- Fasting plasma glucose level of between 95 and 125 mg/dL (for Native Americans, a group already considered to be at risk for diabetes, any non-diabetic fasting glucose level was accepted)

- Body mass index (BMI) of at least 24 (derived by dividing weight in kilograms by height in meters squared); lower BMI ratings were accepted for Asians, who are considered to be at risk for diabetes at lower BMI levels than non-Asians.

The DPP also had a goal of recruiting 50 percent of its participants from high-risk racial and ethnic minority populations.

Individuals were recruited predominantly through mailings, the media, and screening events. Potentially eligible individuals were given an oral glucose tolerance test. Those who met all study criteria were invited to participate in a 3-week run-in period during which their ability to adhere to the protocol was evaluated. Those who were still considered eligible were invited to join the study and their consent was obtained. More than 158,000 people were screened nationwide. Of these, 30,985 received an oral glucose tolerance test; 4,719 entered the run-in period; 4,080 completed the run-in; and 3,819 were randomly assigned to one of the original four therapies. The number of participants in the full three-group study was 3,234.

Forty-five percent of the study participants were recruited from among racial and ethnic minority groups; 20 percent were African American, 16 percent Hispanic, 4 percent Asian or Pacific Islander, and 5 percent Native American. Twenty percent of the DPP study participants were 60 years of age or older; 49 percent were 45 to 59; and 31 percent were 25 to 44. Sixty-eight percent were women, and 32 percent men. Sixty-nine percent had a family member with type 2 diabetes. The mean BMI was 34 kg/m^2.

The randomization process was very effective at creating similar groups at baseline. There were no significant differences between the three treatment groups in terms of mean age (51), sex, or other characteristics. BMI, fasting glucose levels, and blood pressure were almost identical for the three groups. About three-quarters were employed full- or part-time, and a similar number were educated beyond high school.

The DPP was successful in recruiting a study population that met all study criteria; and special efforts were made to ensure that individuals who entered the study would be able to adhere to a long-term, complicated protocol. These efforts were rewarded with a high level of retention and adherence.

Interventions

Intensive Lifestyle Intervention

Dr. Rena Wing from the University of Pittsburgh described the DPP's intensive lifestyle intervention. Participants were encouraged to lose at least 7 percent of their initial body weight

and to maintain this loss throughout the trial. They were also encouraged to achieve and maintain at least 150 minutes per week of physical activity, using activities similar in intensity to brisk walking. Participants were assigned to case managers who worked with them throughout the trial to help them meet these goals. The intervention began with a 16-session core curriculum delivered over the first 24 weeks. All lifestyle participants received the same core curriculum to standardize the intervention. Following the core curriculum, participants had at least 1 monthly contact with their case managers, and an in-person contact at least every 2 months. The intervention also included periodical refresher courses and motivational campaigns. Participants were given recommended dietary fat intake levels, expressed in grams of fat per day and designed to produce a 25-percent-fat diet. Their recommended caloric intake was 1,200 to 1,800 per day. Fat and calorie intake was self-monitored. A toolbox of strategies that could be individualized to help achieve the weight loss goal was provided (e.g., some participants enrolled in cooking classes).

Physical activity was a separate goal from the weight loss goal, although it was useful in achieving maintenance of weight loss. Participants gradually increased their activity levels in order to reach the goal of 150 minutes per week, or approximately 30 minutes on each of 5 days during a week. Participants were able to choose any type of activity that they enjoyed. While most acted on their own, the study provided supervised activity sessions and used behavioral strategies for those who were having difficulty in achieving the goal.

At the end of the core curriculum, participants in the lifestyle intervention had an average weight loss of 6.6 kilograms, or 14.5 pounds. This represented a 7 percent decrease in initial body weight. One half of the participants achieved or exceeded this goal. Some participants reported 224 minutes per week of physical activity, and 74.4 percent met the physical activity goal. Data from participants' most recent visit show some weight regain, but minutes of activity have remained high. At the most recent visit, the average weight loss was 4.7 kilograms, or 10.3 pounds, which represents a 5 percent decrease. Thirty-eight percent continued to meet or exceed the 7 percent weight loss goal. Physical activity at the most recent visit averaged 189 minutes per week, and 58 percent still met or exceeded the physical activity goal.

The average weight loss over the entire study for the lifestyle group was 5.6 kilograms, which was significantly higher than for the placebo group, for whom the average weight loss was 0.1 kilograms, and the metformin group, which had an average weight loss of 2.1 kilograms. Reduction in calories was significantly greater in the lifestyle group than in the other two groups. Similarly, the lifestyle group had greater reductions in the percentage of calories from fat.

Metformin

Dr. Elizabeth Walker from the Albert Einstein College of Medicine discussed the metformin treatment arm of the DPP. Criteria for choosing the pharmacological agent for this part of the study included efficacy in lowering glycemia, evidence of safety and tolerability with minimal side effects, an acceptable dosing regimen, potential for translation with regard to availability and cost, the ability to mask with a placebo, and potential for clinical application across the diverse populations participating in the DPP. Metformin is an anti-hyperglycemic agent approved in 1995 for use in treating diabetes. It is an investigational drug for the treatment of

IGT to prevent or delay the onset of type 2 diabetes. Its most prominent effect is a decrease in hepatic glucose production.

Metformin and its corresponding placebo were started at a dose of 850 milligrams per day and adjusted after 4 weeks to 850 milligrams twice a day. To reduce potential gastrointestinal side effects, an alternative adjustment option allowed initiation of one half of an 850-milligram tablet, still attempting to reach the protocol dose of 850 milligrams twice per day by the third month.

Adherence was promoted through a quarterly structured interview. Trained medication case managers helped participants overcome barriers to taking the metformin, using a variety of individualized strategies. Adherence to both metformin and the placebo were stable throughout the trial. Adherence to the metformin over the entire length of the study was 72 percent, and adherence to the placebo was slightly higher.

Major Results

Dr. William Knowler of the NIDDK presented the results of the DPP. Overall participation study was very high, with 93 percent completing the study and a similarly high level of annual visits completed. The average followup was 2.8 years (ranging from 1.8 to 4.6 years). The calculated incidence of diabetes after 3 years of treatment was 29 percent for the placebo group, 22 percent for the metformin group, and 14 percent for the group that received the intensive lifestyle intervention. These differences were highly statistically significant for all measures of comparison. Over the course of the study, 11 percent per year of the placebo developed diabetes, compared with 7.8 percent of the metformin group and 4.8 percent of the lifestyle group. The reduction in development of diabetes compared with the placebo was 58 percent for the lifestyle group and 31 percent for the metformin group. The intensive lifestyle intervention reduced the development of diabetes by 39 percent when compared with metformin.

The interventions were similarly effective for men and women, and there were no statistically significant differences in the effects of the treatment among the racial and ethnic populations that participated in the study. Risk reduction was greatest in the lifestyle group, and there were no significant variations in efficacy among racial and ethnic groups.

Age had a statistically significant effect on the relative benefits of the interventions. In the 25-44 age group, metformin and lifestyle were both more effective than the placebo and their reduction in risk was similar. In the intermediate age group, metformin and lifestyle were both more effective than the placebo, and lifestyle was more effective than metformin. Among those age 60 and older, lifestyle was more effective than placebo, but metformin was not effective.

To examine the relationship between initial body weight and intervention effectiveness, the study population was divided into three subgroups. For the least overweight participants, with a BMI of less than 30, lifestyle was effective, but metformin was not. In the middle third of the distribution, metformin was effective, but less so than lifestyle; for the third of the population that was heaviest at study entry, with a BMI of 36 or higher, metformin and lifestyle were similarly effective. The interaction between BMI and treatment effectiveness was statistically significant.

In addition to diabetes incidence, the study investigated whether the interventions restored normal glucose levels. At 3-year followup, 30 percent of lifestyle participants had normal glucose tolerance; 21 percent of the metformin group and 19 percent of the placebo group had normal glucose tolerance.

Dr. Knowler presented data on cumulative incidence of an outcome representing more pronounced hyperglycemia than the ADA criteria, and hence more advanced disease, based on a fasting plasma glucose level of at least 140. At this level, drugs are often added to the treatment regimen for diabetes. Lifestyle and metformin reduced the incidence of this outcome by 61 percent and 51 percent, respectively.

There were few deaths during the DPP study, and death rates did not vary significantly between groups. There were also no differences in the rates of serious adverse events. Both interventions were well accepted, as evidenced by high levels of adherence.

DPP Conclusions

Dr. David Nathan stated that the DPP was conducted to determine whether the ever increasing health and economic burdens of type 2 diabetes could be curtailed through prevention. This disease is an appropriate target for prevention: more than 16 million Americans are affected, and there are 800,000 new cases per year. Diabetes is a major cause of new onset blindness, kidney failure, amputations, heart disease, and stroke. Individuals at risk for diabetes can be identified using the glucose tolerance test. The critical question in the study was whether safe and acceptable interventions could effectively prevent the development of diabetes in a susceptible population. Prevention interventions would need to be effective across a broad spectrum of the population. The DPP recruited participants with the highest risk of developing type 2 diabetes, including individuals with IGT, those over the age of 60, women with a history of gestational diabetes, and people with diabetes in their families. Those ethnic and racial minorities who are at highest risk for diabetes were also included.

The success in reaching recruitment goals and the high levels of retention and adherence allowed the DPP to answer the study questions definitively and ahead of schedule. Interventions were generally accepted, well tolerated, and safe. The majority of participants assigned to the lifestyle intervention achieved the goals of a 7 percent weight loss and at least 150 minutes of moderately intensive physical activity per week, and these changes were maintained throughout the study. The DPP was able to demonstrate that at 3-year followup, the lifestyle intervention reduced the development of diabetes by 58 percent and metformin reduced diabetes development by 41 percent. Both therapies were effective in the diverse groups recruited for the study. The effectiveness of the lifestyle intervention with people over the age of 60 is particularly important because this population has a prevalence of diabetes that approaches 20 percent.

The implication of the DPP results are that diabetes can be prevented over an average period of at least 3 years in persons at high risk. Identification of similar at-risk populations in the United States, estimated to total more than 10 million, might require widespread oral glucose tolerance testing. The results of the DPP, in which prevention interventions were accepted by a diverse population, suggest that such interventions could be widely implemented.

Several remaining questions need to be addressed. First, the long-term impact of the DPP must be determined, and the investigators hope to continue to follow the DPP population. Second, further analyses are needed to examine the effectiveness of DPP interventions in reducing cardiovascular disease, atherosclerosis, and risk factors for cardiovascular disease. Third, the cost-effectiveness of DPP interventions and the ability to translate its results economically into practice will be examined. Finally, further research is needed to determine whether and how the results of this clinical trial can be translated to the general population.

The results of the DPP strongly support the hypothesis that diabetes can at least be delayed. This means that the development of complications can also be delayed or prevented, thereby reducing the health and economic burden of diabetes in the United States.

Dr. Nathan acknowledged the contributions of more than 400 investigators who formed the DPP research group, the NIDDK and other Federal agencies and groups that participated in the DPP, and industrial sponsors of the study, and the 3,834 volunteers without whom the DPP study could not have been conducted.

Questions and Comments

Q. Are variations in BMI- and age-related outcomes associated with differences in implementation or adherence?

A. Adherence does not appear to be associated with such differences. However, secondary analyses have not yet been performed to look at correlations of particular behaviors with particular outcomes.

Q. Did the DPP find that different lifestyle strategies are required by specific ethnic groups?

A. This is the type of question the DPP would like to examine in the future. So far, lifestyle interventions have been studied together as one arm of the DPP. To date, no analyses have been done on specific strategies.

Q. A key question concerns how to package physical activity as an intervention across all populations. Would the DPP consider recommending legislation to make exercise equipment or health club membership reimbursable?

A. The study did not examine exercise in isolation from weight loss. The lifestyle intervention as a whole was found to be effective. Further analysis will consider whether there were selective responses to specific aspects of the intervention. The DPP will refrain from making policy recommendations on how to apply DPP findings to diabetes prevention and education programs.

Q. Are any data available on weight loss and activity levels in the metformin and placebo groups?

A. The placebo group lost about 0.1 kilograms over the entire study, while the metformin group lost about 2 kilograms. Comparative measures of physical activity remain to be examined.

Q. How does glucose tolerance testing fit into public health recommendations for the general population? Study findings seem to suggest that at-risk individuals should initiate behavioral therapy without glucose testing, which is not generally performed.

A. It is likely that high-risk individuals similar to those who participated in the study would have similar benefits; methods to identify high-risk individuals other than the glucose test are available. Those at lower risk might also benefit, but it would be difficult to measure the risk reduction in those at lower risk.

Q. Will the study results be able to show what elements of the lifestyle intervention, such as weight loss, physical activity, and dietary modification, were responsible for risk reduction, and how much change in any of these factors is sufficient to reduce risk?

A. These are questions that will be addressed in secondary analyses. Sufficient data are available to address some of these questions.

Q. How many of the participants completed the 16-session curriculum and monthly visits?

A. Data will be available. The vast majority did complete the 16-session curriculum and met with their case managers on a regular basis.

Q. Is there any information on physiological aspects of the differential effect of metformin by age?

A. This will be studied. As people age, their 2-hour glucose levels disproportionately compare with their fasting glucose levels. A partial explanation of this differential effect may be the fact that metformin has an effect on fasting glucose levels.

Q. Are there any predictive thoughts on the additive effect? Should both lifestyle change and metformin be recommended for high-risk individuals?

A. This is an interesting issue that the DPP will be considering during long-term followup.

Q. How was the weight loss goal set? Would greater weight loss have greater effect?

A. The first step was to look at other studies, and it was found that an average of 5 percent was used in those studies. The DPP team decided to place the target at 7 percent to see whether pushing for a higher goal produced greater benefits. A new NIDDK trial to study the long-term effect of weight loss on individuals with diabetes will use a 10 percent goal.

Q. What was the range of weight loss?

A. Some lost more than average, some gained weight. The distribution of weight change is a normal distribution, but shifted toward weight loss in the lifestyle group. Data on the range of weight loss will be included in secondary analyses.

Q. What are the prospects for testing other drugs in diabetes prevention?

A. There is one study that is testing glitazone (a sulfonylurea); this study is halfway through. Another study that will conclude in about 3 months is testing acarbose, a glucosidase inhibitor. Another trial that is under development will test second-generation glucosone inhibitors.

Comment. The comment needs to be made that the diabetes education community faces a significant challenge in the next couple of decades. This study is important not only because it shows that prevention works, but also because it shows that it can be done.

News Briefing

Dr. Allen Spiegel welcomed the media and members of the public in attendance. He stated that the DPP is important because the Nation is in the midst of a surging epidemic of type 2 diabetes. Launched by the NIDDK in 1996, the DPP study focused on 3,234 men and women with impaired glucose tolerance, or IGT, which is a precursor for type 2 diabetes. Almost half of the study's subjects were members of minority groups. Findings from the DPP were so clear cut that the study has been ended a year early.

Dr. Spiegel introduced the Honorable Tommy Thompson, Secretary, of Health and Human Services.

Secretary Thompson thanked everyone involved in the DPP. He extended particular appreciation to the representatives of the Native American community in the audience, noting that diabetes hits minority groups the hardest.

He stressed that this study brings to the attention of the American people the importance of caring for yourself and becoming involved in disease prevention. He stressed the significance of the DPP's findings that modest adjustments in lifestyle can save billions of dollars in health care costs in the United States. The exciting news from this study, he announced, is that prevention works. The DPP shows that there are two ways to prevent the development of type 2 diabetes. Reasonable changes in physical activity and diet reduced the risk of developing diabetes by 58 percent among men and women in all racial and ethnic groups. In another arm of the study, the use of the drug metformin, currently used to treat diabetes, but not previously used in prevention, reduced that risk by 31 percent.

Secretary Thompson stressed the urgency of spreading the word about the effectiveness of diabetes prevention. He announced that he is directing the National Diabetes Education Program, a joint effort of the National Institutes of Health and the Centers for Disease Control and Prevention, to develop a new all-out public health campaign. As researchers develop interventions based on DPP findings, information about those interventions will be disseminated through this campaign. As those researchers develop prevention-specific educational materials, this campaign will make sure they are distributed to doctors' offices and find their way into people's lives. He also announced that he has established an agencywide task force within the DHHS to identify steps that can be taken to put this new knowledge into action. He has asked for these recommendations by the end of this year.

Dr. David Nathan provided an overview of the DPP study design, eligibility criteria, interventions, outcomes, and questions for further study. This was an abbreviated version of the scientific presentations made earlier in the afternoon by Dr. Nathan and other DPP investigators.

Dr. Christopher Saudek, President of the ADA, observed that the announcement of the results of the DPP is truly a landmark moment in the history of diabetes research. The ADA has always been interested in prevention, believing that type 2 diabetes is not inevitable. The solution may be as simple as exercise and dietary modification. This gives physicians solid evidence to use in helping their patients. The DPP demonstrates the value of the health care team approach. Just as it takes a team of health professionals to treat diabetes, it also takes a team of doctors, dieticians, educators, and others working together to implement disease prevention.

The ADA, Dr. Saudek reported, is pleased to be taking a leadership role in deciding how to apply DPP results. The ADA will use these findings to develop and disseminate recommendations and guidelines for office practice and public health policy, and will incorporate DPP findings into the Association's programs.

Questions and Comments

Q. Can the NIDDK tell the public, based on DPP findings, who should be screened for IGT and how much this will cost? Should everyone in all risk groups be tested? What is known about the effectiveness of prevention for age groups other than those over 60?

A. All age groups benefited during the DPP trial. The oral glucose tolerance test was used in the study to identify risk. The question of how to cost-effectively identify similar individuals in the general population needs to be addressed. Those who feel that they may be at risk should consult their physicians, who may recommend testing.

Q. Are there benefits from lifestyle modification for those already diagnosed with diabetes?

A. People who have diabetes are at risk for the many complications of the disease. Many people with impaired glucose tolerance have returned to normal glucose tolerance through lifestyle modification. Both DPP therapies have been shown to be effective in preventing individuals with early-stage diabetes from moving to higher stages of the disease.

Q. Should recommendations related to diabetes prevention include advising people to consult with their doctors or undergo screening before starting a program of physical activity?

A. Fitness testing was performed during the trial prior to initiating physical activities. As programs are being developed to implement DPP findings, consideration should be given to recommending fitness testing prior to starting similar activity programs.

Q. In the face of the diabetes epidemic, will the research design and structure exemplified by the DPP be used to examine other drugs that are under development? Will the DPP continue?

A. Secretary Thompson stated that the research will continue to move forward. This study demonstrates that savings will be made possible through prevention, since prevention costs

less than treating disease. Dr. Spiegel added that strong consideration is being given to continued followup of DPP participants to examine additional questions such as those listed by Dr. Nathan, particularly about the durability of the prevention achieved.

Q. Will Secretary Thompson be looking for addition money in the U.S. Government's budget for prevention?

A. The Secretary stated that he is passionate about prevention. Prevention will be a key element in most decisions made throughout the Department of Health and Human Services.

1: N Engl J Med 2002 Feb 7;346(6):393-403

Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin.

Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM; Diabetes Prevention Program Research Group.

Diabetes Prevention Program Coordinating Center, Biostatistics Center, George Washington University, 6110 Executive Blvd., Suite 750, Rockville, MD 20852, USA.

BACKGROUND: Type 2 diabetes affects approximately 8 percent of adults in the United States. Some risk factors--elevated plasma glucose concentrations in the fasting state and after an oral glucose load, overweight, and a sedentary lifestyle--are potentially reversible. We hypothesized that modifying these factors with a lifestyle-intervention program or the administration of metformin would prevent or delay the development of diabetes. METHODS: We randomly assigned 3234 nondiabetic persons with elevated fasting and post-load plasma glucose concentrations to placebo, metformin (850 mg twice daily), or a lifestyle-modification program with the goals of at least a 7 percent weight loss and at least 150 minutes of physical activity per week. The mean age of the participants was 51 years, and the mean body-mass index (the weight in kilograms divided by the square of the height in meters) was 34.0; 68 percent were women, and 45 percent were members of minority groups. RESULTS: The average follow-up was 2.8 years. The incidence of diabetes was 11.0, 7.8, and 4.8 cases per 100 person-years in the placebo, metformin, and lifestyle groups, respectively. The lifestyle intervention reduced the incidence by 58 percent (95 percent confidence interval, 48 to 66 percent) and metformin by 31 percent (95 percent confidence interval, 17 to 43 percent), as compared with placebo; the lifestyle intervention was significantly more effective than metformin. To prevent one case of diabetes during a period of three years, 6.9 persons would have to participate in the lifestyle-intervention program, and 13.9 would have to receive metformin. CONCLUSIONS: Lifestyle changes and treatment with metformin both reduced the incidence of diabetes in persons at high risk. The lifestyle intervention was more effective than metformin.

Publication Types:

- Clinical Trial
- Multicenter Study
- Randomized Controlled Trial

PMID: 11832527 [PubMed - indexed for MEDLINE