DPP Metadata

General
• IND # 49,782
• Institution conducting study – Multiple centers
• Data Coordinating Center, PI – George Washington University Biostatistics Center; Sarah Fowler, PhD
• Study Website – See http://www.bsc.gwu.edu/dpp
• Publications – See http://www.bsc.gwu.edu/dpp/pps/registry.cgi
• Disease – Type 2 diabetes mellitus (Non-insulin-dependent diabetes mellitus) Principal

Period of Performance/Timeline
Phase I July 1994 - June 1996 Protocol Development and Implementation
Phase II July 1996 - June 2002 Randomization, Recruitment, Follow-up
Phase III July 2002 - June 2003 Study Close-out and Data Analysis

Objective
The principal objective was to prevent or delay the development of non-insulin-dependent diabetes mellitus (NIDDM) in people having impaired glucose tolerance (IGT)which placed them at high risk for NIDDM. IGT represents a less severe stage of blood glucose abnormalities that often precedes NIDDM

Primary Research Questions
o Does a lifestyle intervention or treatment with metformin prevent or delay the onset of diabetes?
o Do these two interventions differ in effectiveness?
o Does their effectiveness differ according to age, sex, or race or ethnic group?

Hypothesis
Some risk factors for type 2 diabetes such as elevated blood glucose and impaired glucose tolerance (IGT),, obesity, and a sedentary lifestyle are potentially reversible. The study hypothesized that modifying these factors with a lifestyle intervention program or the administration of metformin would prevent or delay the development of diabetes.

Study Design
The study was a randomized clinical trial to test the safety and efficacy of each of two interventions designed to prevent NIDDM. Participants with IGT and fasting plasma glucose (FPG) values of 95 - 125 mg/dL [5.3 - 6.9 mmol/L] were recruited, and the recuitment of individuals with additional risk factors was emphasized. Individuals with particularly high risk of development of NIDDM included those with obesity, the elderly, women with a history of gestational diabetes, and members of minority groups such as African Americans, Hispanic Americans, Asian and Pacific Island Americans, and Native Americans.

Eligible volunteers were stratified according to center and assigned to one of the two intervention or control groups during a two and two-thirds year recruitment period.

The interventions included an intensive lifestyle intervention and two pharmacological interventions. The intensive lifestyle intervention focused on a healthy diet to achieve and maintain at least a 7% loss of body weight and to maintain at least 150 min/week of moderate intensity exercise. Standard lifestyle recommendations, which included conventional instructions regarding diet and exercise, were provided to all participants, including a placebo treated group which served as the control group for the study. The pharmacological interventions included the biguanide metformin and the thiazolidinedione troglitazone. Randomization to the troglitazone pharmacological intervention was suspended on May 27, 1998, and discontinued by the NIDDK on June 3, 1998 due to liver toxicity.

The pharmacological intervention was double blind and placebo controlled. Masking intensive lifestyle intervention assignment to the participants was not possible. After randomization, participants had quarterly clinical evaluations with FPG at semi-annual visits and a 75 gram oral glucose tolerance test (OGT) at annual visits. All participants were followed for a minimum of three and one-third years after the close of recruitment resulting in 3 1/3 to 6 years of participant follow-up.

Three thousand participants (one thousand per group) provide 90% power to detect a 33% reduction in the progression to diabetes, assuming an annual rate of progression to diabetes in the control group of at least 6.5%.

Enrollment

- At least 25 years of age
- Body-mass index (the weight in kilograms divided by the square of the height in meters) of 24 or higher (22 or higher in Asians)
- Plasma glucose concentration of 95 to 125 mg per deciliter (5.3 to 6.9 mmol per liter) in the fasting state (125 mg per deciliter in the American Indian clinics) and 140 to 199 mg per deciliter (7.8 to 11.0 mmol per liter) two hours after a 75-g oral glucose load.
- Recruitment was designed to enroll approximately half the participants from racial or ethnic minority groups.
- Eligible persons were excluded if they were taking medicines known to alter glucose olerance or if they had illnesses that could seriously reduce their life expectancy or their ability to participate in the trial.

Cohort

- Sex - Women 68%, Men 32%
- Age distribution - 25-44 31%, 45-59 49%, 60 and over 20%
- Ethnicity - white (58%), African American (19%), Hispanic (17%), Asian American (5%), Native American (1%)

Recruitment and Randomization

A total of 3,819 study subjects were randomized to 4 study arms:

- Troglitazone arm n=585 (discontinued)
- Intensive lifestyle n=1079
- Metformin -n=1073
- Placebo n=1082

Samples

Samples of plasma and blood were stored for possible future analyses, including genetic typing and other analyses related to NIDDM.

Outcomes

Principal Outcome

The primary outcome was diabetes, diagnosed on the basis of an annual oral glucose-tolerance test or a semiannual fasting plasma glucose test, according to the 1997 criteria of the American Diabetes Association [a value for plasma glucose of 126 mg per deciliter (7.0 mmol per liter) or higher in the fasting state or 200 mg per deciliter (11.1 mmol per liter) or higher two hours after a 75-g oral glucose load].

Secondary Outcomes

Secondary outcomes focused on cardiovascular disease and its risk factors and changes in
glycemia, insulin secretion and sensitivity, obesity, physical activity and nutrient intake, quality of life, and the occurrence of adverse events. Levels of leisure physical activity were assessed annually as self-reported on the Modifiable Activity Questionnaire. Usual daily caloric intake during the previous year was assessed at base line and at one year using a modified version of the Block food-frequency questionnaire.

Follow-Up

Follow-up visits were scheduled at 3 month intervals throughout the duration of the study. Participants assigned to the intensive lifestyle intervention had more frequent scheduled follow-up visits to implement the program of weight reduction and increased calorie expenditure. Participants assigned to the two pharmacological treatments (metformin or placebo) were scheduled for one visit one month after randomization for dose titration. All randomized participants continued their scheduled follow-up
visits for the duration of the study regardless of their level of compliance with the assigned treatment.

Results

- The study was completed by 93% of the cohort
- Average follow-up was 2.8 years (range 1.8-4.6)
- Lifestyle was more effective than metformin
- The lifestyle intervention resulted in a 58% reduction in the incidence of diabetes compared with the placebo
- Metformin reduced the development of diabetes by 31%
- Lifestyle intervention was beneficial regardless of ethnicity, age, BMI, or sex.
- The efficacy of lifestyle relative to metformin was greater in older persons and in those with lower BMI
- The efficacy of metformin relative to placebo was greater in those with higher baseline fasting glucose and BMI

Clinical Centers

Principal Investigator	**Institute**	**City, State**
George A Bray, MD	Pennington Biomedical Research Center	Baton Rouge LA
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