

Study title: Diabetes Prevention Program Outcomes Study (DPPOS)
NCT Number: NCT00038727
Date: November 27, 2017

**CONSENT FORM FOR THE DIABETES PREVENTION
PROGRAM OUTCOMES STUDY PHASE 3**

IRB Template.

NAME OF INSTITUTION

INFORMATION AND CONSENT FOR THE DIABETES
PREVENTION PROGRAM OUTCOMES STUDY (DPPOS) PHASE 3

INVESTIGATORS

Name of Principal Investigator
Title, Affiliation, Phone Number

Name of Co-Investigator(s)
Title, Affiliation, Phone Number

Name of Program Coordinator
Title, Affiliation, Phone Number

Name of Other Staff (optional as per IRB)
Title, Affiliation, Phone Number

24-Hour Emergency Telephone Number
(List phone number(s) here)

INVESTIGATOR'S STATEMENT:

PURPOSE AND BACKGROUND

This research study is called the Diabetes Prevention Program Outcomes Study and is an extension of the Diabetes Prevention Program (DPP), of which you were a participant. The purpose of Phase 3 of the DPPOS is to look at the effects of the study interventions on the development of type 2 diabetes as well as diabetes related health problems and cancer diagnosis over a longer period of time (up to five additional years). In this type of research, health information is combined from many volunteers.

Diabetes is a disease in which there is too much glucose (sugar) in the blood. Diabetes causes damage to blood vessels, heart, kidneys, eyes, and nerves. Diabetes affects at least 24 million Americans. Ninety to ninety-five percent of those affected have type 2 diabetes.

The interventions that were studied during the DPP were intensive lifestyle modification and metformin. The results of the DPP showed that the risk of type 2 diabetes was reduced by 58% in the intensive lifestyle group and 31% in the metformin group. The DPPOS is examining the continued effects of these study interventions over a longer period of time. You will take part in the DPPOS for up to five additional years. All participants who were in the original DPP study groups randomized to intensive lifestyle modification, metformin or placebo (approximately 3,200) are being asked to continue to take part in the DPPOS.

DPPOS is currently funded through January 2021. This document obtains your consent to continue in DPPOS through January 2021 (Phase 3).

PROCEDURES

If you choose to take part in Phase 3 of the DPPOS you will continue in your original randomly assigned intervention group. Although many of the features of DPPOS Phase 3 are the same as for DPPOS, there are some differences:

- Participants in all treatment groups will be invited to take part in an annual Healthy Lifestyle Program (HELP) class. HELP sessions will focus on diabetes-related topics. The original exercise and diet goals of the intensive lifestyle intervention, walking (or similar activity) 2 ½ hours (150 minutes) per week and using healthy eating habits to lose and maintain a 7% weight loss, may be discussed. You may be weighed. A trained professional will lead the group sessions. Each class will last about 1 hour. If you choose not to attend the HELP classes, you may still take part in the DPPOS.

- For participants in the original metformin intervention group: you may be asked to continue taking metformin depending on your laboratory tests or medical conditions. If you are unable or choose not to take metformin, you may still take part in the DPPOS.
- For participants in the original intensive lifestyle intervention group: healthy lifestyle messages will be reinforced at the annual visit as part of your “lifestyle check-up”.

Clinic Visits: As a participant in the DPPOS, you will be asked to attend a clinic visit once or twice a year. In some cases, you may be asked to attend an additional interim visit. If you are not able to come to the clinic, the clinical center staff may offer to visit you for data collection. If neither a clinic nor home visit is possible, you may be asked to provide information by telephone. These visits and procedures to be completed are described below:

Mid-year visit:

- At mid-year visits, no measurements will be taken. Mid-year visits will be completed by phone, or occasionally in clinic. You will be asked to answer questions about your health. For those taking study metformin, pills will be provided in person or mailed if the mid-year visit is completed by phone.

Annual Visit:

For annual visits (approximately 1-4 hours), you will be asked not to eat or drink anything, except water, for 12 hours before your appointment.

1. An electrocardiogram (ECG) will be performed every other year. This will take about one-half hour.
2. Blood pressure will be measured in your arm. This will take about 10 minutes.
3. Body measurements: Your weight will be measured yearly and waist size will be measured every other year. This will take about 10 minutes. You may have your height measured. This will take about 5 minutes.
4. You will receive a test for neuropathy (problems with nerves in the feet). This will involve an examination of the sensation in your feet. This test will take about 5 minutes.
5. Oral glucose tolerance test every other year: This test will take about 2 and ½ hours. A blood sample will be taken from your arm. You will then be asked to drink a glassful of flavored sugar water over 5 minutes. Another blood sample will be taken from your arm again at 120 minutes. The total amount of blood drawn for this test is approximately 1 tablespoon. All participants will have a fasting blood glucose drawn at each annual visit. A repeat blood draw or an oral glucose tolerance test may be necessary.
6. People with diabetes will not be asked to complete the oral glucose test, but will have a fasting blood glucose drawn (approximately one teaspoon) following the same 12 hour fasting instructions as stated above.

7. Additional blood samples may be taken from your arm at the same time that you are having blood drawn for the oral glucose test or fasting sample, for lipids (blood fats), hemoglobin A1c (HbA1c, a measure of the average blood glucose level control over three months time), serum creatinine (a measure of kidney function), and other blood tests related to diabetes and heart disease (total amount of blood drawn equals approximately 4 to 5 tablespoons). Some of this blood will be stored for future studies described below if you agree. If you were assigned to the metformin group and are taking metformin provided by the study, an additional sample might be drawn for a vitamin B12 test (about 10ml or two teaspoons). A repeat blood sample might be necessary for some persons.
8. You will be asked to provide a urine sample for measurement of urine albumin and creatinine (measures of kidney function). A repeat urine sample may be necessary for some persons.
9. You may be asked to complete several questionnaires. You may be asked questions about your health, medications, physical activity, diet and feelings. Some of the questionnaires will be completed by interview and others you will complete yourself. These will take about 30 minutes to 2 hours to complete.
10. You may be given questionnaires regarding your cognitive status such as memory and verbal learning .
11. Your physical function may be measured by grip strength, balance, chair rises, and walking speed.
12. You may be asked to walk for 6 minutes down a corridor at a normal pace. The distance you walk and how fast you walk will be measured.
13. Your lung function may be measured using a portable spirometer. . A spirometer is a hand-held device that you blow into as hard and as fast as you can. You will be asked to do this several times. A new, clean mouthpiece will be used for each participant. Spirometry takes about 20 minutes.
14. If you are a woman assigned to and taking metformin provided by the DPPOS and there is a chance that you could become pregnant, you will be asked whether you are willing to use medically effective birth control methods for the duration of the study. If you decide to become pregnant during the study, you must notify the clinic staff immediately. If there is a chance that you could be pregnant, a pregnancy test will be done. If you suspect that you are pregnant you should stop your metformin immediately and notify clinic staff.
15. We have previously asked you to give us personal information such as address, phone numbers, and social security number, to help us to reach you if we lose touch. We will ask you to update this information each year and as necessary.
16. Some people enrolled in DPPOS have developed serious illness or disability that prevent them from participating in study data collection on their own. You will be asked to name a health informant (proxy) to DPPOS in the event you cannot participate in study data collection on your own. If you choose not to name a health informant (proxy) you may still participate in DPPOS to the extent that you are able.

17. Some people enrolled in DPPOS have moved far away or have physical limitations that may prevent them from visiting their DPPOS clinic. If you cannot have specimens collected at a DPPOS clinic and DPPOS staff cannot come to you for a home visit, we may arrange to have a health technician visit you at home to collect annual blood and urine sample and measures your weight and blood pressure. The DPPOS will provide the health technician with your name, address and/or location of home, phone number and DPPOS study number. This will allow the health technician to schedule the sample collection with you at your convenience. Your samples will be sent to the DPPOS laboratory identified only by your study number but not your name. Your measurements will be given to your DPPOS clinic staff. Your contact information will be destroyed by the health technician after the data collection. You will receive clear instructions from your clinic about what to expect and how to get the tests completed, if needed. These tests are completed at no cost to you. If you are taking study metformin and cannot have specimens collected at a DPPOS Clinic, DPPOS needs to check your kidney function once a year and vitamin B12 every other year with a blood test to be sure it is safe for you to continue taking study metformin. If you cannot come to a DPPOS clinic for this blood test, DPPOS may arrange for you to have the blood tests done as described above. If you agree, DPPOS may also contact your doctor to check if you had this safety test in the last year. If the kidney blood test cannot be done once a year, we will ask you to stop taking study metformin.

Interim Visit (approximately 30 minutes to 2.5 hours):

Some participants may be asked at times to attend an interim visit. At this visit the following tests/procedures may occur:

1. You may be asked to attend an interim visit for a repeat urine sample, repeat blood sample or oral glucose tolerance test when necessary as indicated above. If you are taking metformin, an additional blood test (1 teaspoon) for kidney function, or if female a pregnancy test, may be required.
2. You may have your weight measured.
3. You may have your blood pressure measured.
4. You may be asked questions concerning your health, given information about your health and health education, or provided with information about the study.

Diabetes diagnosed during study: We ask that you report any symptoms of diabetes to the clinic for further evaluation. Symptoms of diabetes include:

Extreme thirst
Frequent urination
Blurry vision
Unusual tiredness or drowsiness

Unexplained weight loss
Frequent or recurring skin, gum or bladder infections

If you develop diabetes during the study, you will no longer be asked to have the oral glucose tolerance test; however, you will continue to be asked to provide blood for a fasting glucose and hemoglobin A1c test, as well as the other blood samples and tests listed above. In addition, you will be given a general overview of diabetes care. You will be referred to your primary care provider (PCP) for additional diabetes education and follow-up. If you do not have a PCP, we can help you find one. The DPPOS cannot provide individual diabetes counseling and it will be your responsibility to follow-up with your physician for your diabetes care. If you wish, the DPPOS may assist you in locating diabetes care.

If your hemoglobin A1c test reaches 7% or higher and you are taking metformin provided by DPPOS, we will refer you to your physician for evaluation and further treatment, and will no longer provide metformin.

Retinal photographs and Ocular Tomography (1-2 hours):

Retinal photos including ocular tomography will be completed during the middle of DPPOS Phase 3. At this visit the following tests/procedures may occur:

1. You will make one visit to a retinal photograph center [local address if available] which will last about one (1) to two (2) hours.
2. You will answer some questions about your eyes, including any allergies to eye drops used to open (dilate) the pupil. These drops are [XXX – replace with clinic-specific language]. A brief examination of your eye will be done to see if this will be safe for you. [Replace with clinic-specific language if necessary] This will not be a complete eye examination by an eye specialist (Ophthalmologist) but only for safety and research purposes.
3. Drops will be put in both eyes to dilate your pupils, and you will wait about 30 minutes for the drops to work.
4. You will have pictures taken with a camera of the back of your eyes (retina) using a bright flash. There will be about 20 pictures taken of each eye.
5. Another test to examine the back of your eye is the Ocular Tomography test. This test provides a detailed image of the retina (back of your eye). It is painless and requires about 10 additional minutes.
6. The photographs will be sent to the Reading Center in Wisconsin identified only with a study number. Your name will not be sent.
7. You may be asked to return for additional photos if the first ones were not of acceptable quality for grading, or for other reasons.

ALTERNATIVE TREATMENTS FOR IMPAIRED GLUCOSE TOLERANCE

The DPP showed that metformin or the DPP intensive lifestyle program is effective in preventing or delaying the development of diabetes. At the end of DPP all participants were offered the DPP lifestyle training in group sessions. During DPPOS, continued lifestyle lessons were offered to all participants on a quarterly basis. During Phase 3 of DPPOS these sessions will be offered once annually. If you wish to participate in an additional lifestyle modification program outside the study, you are free to do so. Although the DPP proved its effectiveness, metformin is currently not an approved drug for prevention of diabetes. If you are not in the metformin treatment group and you want to take metformin, you should discuss this with your primary healthcare provider.

RISKS, STRESS, AND DISCOMFORT

Oral Glucose Tolerance and Blood Tests: The risks of drawing blood include temporary discomfort from the needle stick, possible bruising or redness of the skin, lightheadedness, and on rare occasion, infection. It is possible that some may get nausea or an upset stomach with the glucose (sugar) drink that is given during the oral glucose test. Rarely some people may experience a mild low blood sugar reaction (symptoms like nervousness or sweating) at the end of the test. You will be given a snack to guard against this.

Electrocardiogram (ECG): The risks associated with the use of the ECG electrodes include possible skin irritation, redness and/or chaffing at the application site.

Metformin: The risks of taking metformin were described to you previously in the DPP and have not changed. This medicine has been used for many years to treat patients with diabetes. Side effects include: loss of appetite, upset stomach, vomiting, stomach pain, diarrhea, bloating or gas, or a funny taste (like metal). These are usually mild and lessen with continued use of the medicine. Mild side effects might happen in one out of five persons. Only one or two persons out of fifty are expected to have to stop metformin because of side effects. Anemia (insufficient Vitamin B12) might also happen very rarely in some persons. Very few persons (3 in 100,000 and usually persons with poor kidney function or with severe liver disease) have serious problems (a condition known as lactic acidosis) with metformin that might result in death. Lactic acidosis has also occurred in people who are heavy or binge alcohol drinkers. Persons with poor kidney function or severe liver disease, women planning to become pregnant, or persons who are heavy or binge alcohol drinkers should not take metformin. You cannot take the study medication, metformin, if you have poor kidney function or severe liver disease or you plan to become pregnant. For those assigned to and taking metformin provided by the DPPOS, tests will be done to check on kidney function and vitamin B12 levels. It is always possible that you could have an unexpected serious reaction to metformin or any other medicine.

Persons with congestive heart failure (CHF) should not take metformin. You should report the symptoms of CHF, shortness of breath or swelling in the ankles, to your healthcare provider immediately, and stop taking metformin until you are instructed to use it again.

If you are a woman assigned to the Metformin group and taking metformin provided by the DPPOS and there is a chance that you could become pregnant, you will be asked whether you are willing to use medically effective birth control methods for the duration of the study. If you decide to become pregnant during the study, you must notify the clinic staff immediately. If there is a chance that you are pregnant, you should stop the metformin, inform us, and a pregnancy test will be done.

Metformin has not been approved for use in pregnancy. Metformin has not resulted in any increased risk during pregnancy. Some medicines might, however, cause birth defects to an unborn baby. It is important that you tell us if you suspect at all that you might be pregnant. Study medicines will be stopped if you get pregnant. You will continue in the DPPOS if you are pregnant, and will be asked to re-start your study medicine after pregnancy and breast feeding.

There are some other circumstances for which metformin should be discontinued temporarily. These include overnight hospitalization, some surgical procedures and tests using a contrast dye. It is requested that you notify the clinic if any of these situations occur so that you may be instructed concerning stopping the study metformin.

Physical function: You may experience some imbalance or lightheadedness when the walking tests, chair rises, and the balance tests are performed. You may also experience some muscle strain or muscle soreness while the grip strength or other measurements are being performed. There is a rare risk of injury, muscle fatigue, and joint discomfort with some of the tests. This risk is lowered by not doing the test if you have had any new symptoms of heart disease, recent injury, soreness, or any joint procedure in the past 3 months. After the demonstration by the staff, if you feel that any of the motor movements, such as walking, hand gripping a measuring device, rising up from a chair several times, or any of these movements maybe unsafe, do not attempt them. There is a risk that you may find the walking test tiring or too hard to finish. Trained personnel will be there to monitor you to see how you are doing during these tests. You may stop the test if you need to rest. You may also stop to rest if you become tired because of the number of tests.

Lung function (spirometry): You may become short of breath, start coughing or experience chest tightness or dizziness while doing the spirometry. You will be asked some questions prior to the spirometry to assure that it is safe for you to do the test.

Eye drops: Some people feel slight burning or tearing when the eye drops are put in. Your vision may be blurred while the eyes are dilated, and you should not drive for 2-3 hours after the test. There is a less than 1% chance that the drops could cause closed-angle glaucoma, a rapid increase in the pressure inside the eye. Symptoms could include pain in your eye, decreased vision, headache and/or nausea. If any of these symptoms occur after your visit, you should call the eye center immediately [phone number] and follow their instructions.

Photographs: There is no risk to your eyes from the photos. Some people feel discomfort from the flash; however, this lasts only a few seconds.

This eye photography study is for research purposes only and should not replace regular eye examinations and follow-up. [As with any investigational study, there may be adverse events or side effects that are currently unknown and it is possible that certain of these unknown risks could be permanent, serious or life threatening. insert only if required by local IRB]

Other: Some people may feel uncomfortable about some of the questions we ask. You may decide not to answer any question.

There is also the risk that a breach of confidentiality could occur, however, every effort is made to prevent this from happening.

As with any investigational study, there may be adverse events or side effects that are currently unknown and it is possible that certain of these unknown risks could be permanent, serious or life threatening.

BENEFITS

You may not receive any benefit from taking part in this study.

During your participation in the DPPOS, you will receive medical testing. We will tell you if we find any problem. This information may be given to your doctor if you agree. Problems such as diabetes and diabetes related health conditions might be found and treated sooner than if you were not in the study. This might improve your health.

Your participation in this study may benefit society by helping researchers learn more about the onset of type 2 diabetes and the relationships between blood sugar levels and complications.

After detailed central grading of the retinal photographs, you will receive a summary report of the photography that you can share with your health care provider.

PROXY

- Add information about proxy/health informant if approved by your IRB

CONFIDENTIALITY

To help us further protect your privacy, the investigators have obtained a Confidentiality Certificate from the Department of Health and Human Services (DHHS).

With this Certificate, the investigators cannot be forced (for example by court subpoena) to disclose research information that may identify you in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings. Disclosure will be necessary, however, upon request of DHHS for audit or program evaluation purposes.

You should understand that a Confidentiality Certificate does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. Note however, that if an insurer or employer learns about your participation, and obtains your consent to receive research information, then the investigator may not use the Certificate of Confidentiality to withhold this information. This means that you and your family must also actively protect your own privacy.

Finally, you should understand that the investigator is not prevented from taking steps, including reporting to authorities, to prevent serious harm to yourself or others.

Information that we receive from you will be kept confidential to the extent allowed by law. Information we collect about you will be put into a research record that will be sent to a central data site at The George Washington University for statistical analysis, and samples will be sent to a central laboratory at the University of Washington. Your central research record and samples will not be directly identified with your name. A code number and/or letters will identify your records. The link between the code and your name is stored in a secure location at the (insert your institution name.) Only authorized personnel at (insert institution name) will have access to the key to the code. Anonymous coded information may be released to a DPP investigator (or other investigator authorized by the DPP) only after determination of the scientific usefulness of a proposed study. [Insert appropriate language as determined by your IRB].

A description of this clinical trial is available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

OTHER INFORMATION

[Your IRB may require that some or all of these sections be inserted in other parts of the consent]

Some of the test results will not be made known to you or the clinic staff or your own doctor. This is known as “masking”. The only blood tests that will

be masked in some cases will be the results of the oral glucose tolerance test or fasting glucose test. When the test is confirmed to be normal or shows that diabetes has developed, the results will be unmasked.

You will be given results from the glucose, lipid, blood pressure, ECG, kidney function and neuropathy tests. If you wish these results to be sent to your physician, we will ask you to sign a permission form indicating to whom you would like the results sent. The other tests and procedures performed are for research purposes only and for these you will not receive individual results. Some of the samples collected at your annual visits will be stored for future use for studies related to diabetes development, cancer, and other health related conditions. If you do not want your samples to be stored and utilized for future studies of diabetes and related health conditions such as heart disease, please indicate below. No samples for this purpose will be drawn or stored.

[Institutional language as suggested by your IRB should be substituted for the following sections.]

Participation in this study is completely voluntary. You are free to take back your consent and stop taking part in this study at any time. You may ask any questions about the study at any time. Your current or future care will not be affected by your stopping the study

[Each center should incorporate a statement to address medical liability.]

If a test result shows that you should get medical care, you will be referred to your doctor. If you do not have a doctor, we will help you to see a doctor for medical care.

This study can be stopped or modified at any time.

If you have any questions about your rights as a research subject, you may call (IRB contact name) at (IRB phone number.)

COSTS AND PAYMENTS: All study procedures for the DPPOS will be free of charge. You will receive money (up to \$125 a year) for your time and effort for participating in the study.

PARTICIPANT'S STATEMENT:

The study described above has been explained to me. I understand that I am consenting to participate in the DPPOS. If I have any questions, I know that I can contact one of the investigators listed on the first page.

In addition, I agree to the following:

I give permission for my blood and urine to be stored in a central bank (currently at the University of Washington) for future use by the DPPOS investigators in studies of diabetes, related complications, and heart disease:

_____ YES _____ NO _____ INITIALS

When I die, the specimens I have donated may still be used for the research purposes agreed to above.

_____ YES

_____ NO (my specimens MUST be destroyed once you have been notified of my death).

_____ INITIALS

We are also asking you to allow samples of your blood and your research data to be sent to the NIDDK Central Repositories, a research resource supported by the National Institutes of Health. The Repository collects, stores, and distributes biological samples and associated data from people with many kinds of disorders, from unaffected family members, and from other healthy people. The purpose of this collection is to make samples available for use in research for the study of diabetes, related complications and heart disease after the current study is completed. Sending samples to the Repository may give scientists valuable research material that can help them to develop new diagnostic tests, new treatments, and new ways to prevent diseases.

The Repository will take measures to protect your privacy, although no guarantee of confidentiality can be absolute. Before the DPPOS researchers send samples to the Repository, each sample will be given a code number. Your name and all personal identifying information, such as address, social security number, date of birth, and clinic location will not be included. Therefore, the Repository will not be able to give out your name, or other information that identifies you to the scientists who receive the samples. However, the Repository and scientists will also have some research data about you, such as age, sex, diagnosis, treatment group, race, and outcomes of the study.

You will not receive any direct benefit or payment for participating, but your sample may benefit the future health of the community at large or some particular group. Because other researchers will not have access to your identity, neither you nor your physician will get the eventual results of studies that might be performed using your sample. It is possible that data resulting from use of your sample may eventually be used in a research publication. In that event, your name or other identifying information will not be included, as this information will not be available to the researchers.

It is important for you to understand that there is a small chance that some research may yield results that may indirectly have a negative impact on insurability, employability, and/or family relationships of some individuals or groups of people.

Sometimes, research results in findings or inventions that have value if they are made or sold. These findings or inventions may be patented or licensed, which could give a company the sole right to make and sell products or offer

testing based on the discovery. Some of the profits from this may be paid back to the researchers and the organizations doing this study, but you will not receive any financial benefits.

Your donation is voluntary, and if you choose not to participate there will be no penalty or loss of benefits to which you are entitled.

If you agree to have your sample stored in the Repository, you can change your mind up until the end of the DPPOS. When we receive written instructions from you, we will destroy your sample and all information that identifies you. After the DPPOS ends, you will not be able to withdraw your samples because the Repository will not know which one is yours. The samples will stay in the Repository indefinitely or until they are used up.

1) Data

I give permission for my research data to be sent to the NIDDK Central Repository for future use by NIH approved investigators in studies of diabetes, related complications and heart disease.

_____ YES _____ NO _____ INITIALS

2) Blood

I give permission for my blood to be sent to the NIDDK Central Repository after the end of DPPOS for future use by NIH approved investigators in studies of diabetes, related complications and heart disease.

_____ YES _____ NO _____ INITIALS

Participant's Printed Name

Participant's Signature Time Date

Investigator's Signature
Date

Person obtaining consent Date

cc: Investigator
 Participant