

Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals**Informed Consent A to Participate in Research**H-33130- VITAMIN D AND TYPE 2 DIABETES (D2D STUDY)

Background

You are being invited to take part in a research study to evaluate the effect of taking vitamin D on the prevention of diabetes in persons at high risk for diabetes.

If you decide to take part in this research study, you will be asked to sign this form. You will be given a copy of the signed form. You should keep your copy for your records. The form has information, including important names and phone numbers, to which you may wish to refer in the future.

Please read all the information in this form carefully. Please ask the Principal Investigator, study doctor, or his representative, to explain any words, terms or sections that are unclear to you. You should also ask any other questions that you have about this research study. Do not sign this consent form unless you understand the information in it and have had your questions answered to your satisfaction.

New things might be learned during this study that you should know about. The investigators will tell you about any new information that may affect your willingness to continue in this study.

Diabetes is a serious condition affecting about 1 in 10 people in the United States. Lifestyle changes, such as healthy eating, exercise and weight loss, can decrease the chances of developing diabetes. However, many people still develop diabetes despite trying to change their lifestyle. As a food ingredient or dietary supplement, vitamin D is generally recognized as safe. However, we do not know if vitamin D is effective in preventing diabetes. Taking vitamin D to prevent diabetes is considered experimental. The study takes place at many cities in the United States. There will be a total of 2,382 participants in the D2d study nationwide. There will be 150 participants in this study at Baylor College of Medicine.

The Baylor College of Medicine Institutional Review Board (IRB) is a group of researchers, doctors, nurses and non-medical people who review human research studies for safety and protection of people who take part in the studies. Federal law requires the IRB to review and approve any research study involving humans. This must be done before the study can begin. The study is also reviewed frequently while it is in progress. This research study has been reviewed and approved by the Baylor College of Medicine IRB. Also, an external monitoring committee is watching the study for information on the safety of the participants.

This research study is funded by NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES (NIDDK)

Purpose

The goal of this study is to see whether taking vitamin D can lower the risk of getting diabetes in people with a high risk for diabetes.

Procedures

The research will be conducted at the following location(s): Baylor College of Medicine.

Your participation in the study will last approximately 4 years, depending on when you begin participating. During the study, you will be instructed to take 1 pill every day by mouth in the morning

Version 2.0

Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

Informed Consent A to Participate in Research

H-33130- VITAMIN D AND TYPE 2 DIABETES (D2D STUDY)

with breakfast. The study pill contains either vitamin D (4000 international units) or no vitamin D (placebo, which is a soft-gel pill containing lactose (sugar), cellulose (fiber) and magnesium (mineral) that does not have a medical effect). The two different types of pills will look exactly the same and you will not know whether the pill you are taking has vitamin D or not. The research staff will also not know which pill you are taking. You will be assigned to take the vitamin D or placebo pill by chance (like tossing a coin). There is a 50 percent chance you will receive vitamin D pills. Before starting the study, you will be asked what dietary supplements (minerals and vitamins, including vitamin D and calcium) you are taking. During this study, you will be asked not to take more than a certain amount of vitamin D and calcium on your own and you will be provided with recommendations for sensible sun exposure. During the study, you will also be asked not to start any new supplements (vitamins and minerals), especially vitamin D or calcium, without first discussing it with the investigator, study doctor, or the study's research coordinator because taking additional vitamin D or calcium may lead to side effects.

Participation in the study will require up to 13 scheduled visits to Baylor College of Medicine, as shown below. Additional visits, possibly requiring blood tests, may be needed as determined by the research team. Between visits, you will receive phone calls, emails or texts to see how you are doing, to remind you of your next visit and to share important news about the study.

Your cooperation with all study procedures is essential for your safety and the success of the study.

Visit 1 - Screening: 1-4 weeks before visit 2, 1-1.5 hours, parking costs will be paid

Visit 2 - Baseline: 1-3 weeks before visit 3, 3 hours, parking costs will be paid

Visit 3 - Randomize: Day 0, 15-30 minutes, compensation of \$55 plus parking

Visit 4: Month 3, 30 minutes, compensation of \$55 plus parking

Visit 5: Month 6, 1 hour, compensation of \$55 plus parking

Visit 6: Month 12, 3 hours, compensation of \$50 plus parking

Visit 7: Month 18, 1 hour, compensation of \$50 plus parking

Visit 8: Month 24, 3 hours, compensation of \$50 plus parking

Visit 9: Month 30, 1 hour, compensation of \$50 plus parking

Visit 10: Month 36, 3 hours, compensation of \$50 plus parking

Visit 11: Month 42, 1 hour, compensation of \$50 plus parking

Visit 12: Month 48, 3 hours, compensation of \$50 plus parking

Visit 13: End-of-Study: Month varies, 1 hour, compensation of \$50 plus parking

Visit 1 – Screening: To prepare for the visit you must not have anything to eat or drink (other than water) for the 8 hours before arriving for your morning visit. You also must not participate in vigorous physical activity for 24 hours before the visit. Please take any medications you normally take in the morning. During this visit, we will find out if you meet the study requirements and are eligible to participate. During the visit:

1. You will first review this Informed Consent Forms and discuss them with research staff. If you decide that you want to participate, you will be asked to sign the forms.
2. You will be asked questions about your health, medications, dietary supplements or other pills you may be taking.
3. You will have your weight, height, blood pressure and heart rate measured.
4. If your medical history, weight, blood pressure are within the study requirements, then you will

Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

Informed Consent A to Participate in Research

H-33130- VITAMIN D AND TYPE 2 DIABETES (D2D STUDY)

have:

- a. Blood collection (about 2 tablespoons of blood), while fasting, for the following tests: complete blood cell count, liver tests, calcium, creatinine (kidney test), glucose (sugar), hemoglobin A1c (a test for diabetes) and pregnancy test (for women of reproductive potential).
- 5. A snack will be provided.

Within a few days after the visit, the investigator will review the results of your laboratory tests. If the results are within the study requirements, you will be asked to return within four weeks for the baseline visit, as described below.

Visit 2 – Baseline: To prepare for the visit you must not have anything to eat or drink (other than water) for the 8 hours before arriving for your morning visit. You also must not participate in vigorous physical activity for 24 hours before the visit. Please take any medications you normally take in the morning. During the visit:

- 1. You will be asked if you have had any changes, since the last visit, in your health or medications, dietary supplements or other pills you may be taking.
- 2. You will have your weight, height, waist, blood pressure and heart rate measured.
- 3. You will have a physical examination.
- 4. You will complete questionnaires about your diet and physical activity.
- 5. You will be provided with information on a healthy lifestyle (eating and exercise) to lower your risk of getting diabetes.
- 6. You will have:
 - a. Urine sample collected to measure calcium and creatinine (kidney test).
 - b. A small tube inserted in a vein in your arm for blood draw. To avoid repeated sticks, the small tube will stay in your vein for the entire test and all blood samples will be drawn from the same tube.
 - c. Blood collection (about 2 tablespoons of blood), while fasting, for the following tests: glucose (sugar), hemoglobin A1c (a test for diabetes), 25-hydroxyvitamin D (a test for vitamin D level), and insulin (test for pancreas function).
 - d. After fasting blood collection is done, you will have an oral glucose tolerance test (OGTT), which measures how your body uses glucose. You will drink a 10 oz. glucose drink and blood will be collected at 30 minutes (about 1 tablespoon of blood) and two hours (about 1 tablespoon of blood) after the glucose drink, to test for glucose and insulin.
- 7. A snack will be provided.

Within a few days after the visit, the investigator will review the results of your laboratory tests. If the results are within the study requirements, you will be asked to continue in the study and return within three weeks for the next visit, as described below.

Visit 3 – Randomization: This visit can occur at anytime of the day. There is no special preparation for this visit. During this visit:

- 1. You will get a 6-month supply of the study pills and receive verbal and written instructions on how to take them (one pill daily in the morning with breakfast).
- 2. With your permission, a letter will be sent to your physicians (primary care physician, endocrinologist) informing him/her of your participation in the study.

Visit 4 (month 3): To prepare for the visit you must not have anything to eat or drink (other than

Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

Informed Consent A to Participate in Research

H-33130- VITAMIN D AND TYPE 2 DIABETES (D2D STUDY)

water) for the 8 hours before arriving for your morning visit. You also must not participate in vigorous physical activity for 24 hours before the visit. Please take any medications you normally take in the morning, including the study pill. During the visit:

1. You will be asked if you have had any changes, since the last visit, in your health or medications, dietary supplements or other pills you may be taking. You may have a physical examination, if needed.
2. You will have your weight, height, blood pressure and heart rate measured.
3. You will have:
 - a. Urine sample collected to measure calcium and creatinine.
 - b. Blood collection (about 1 tablespoon of blood), while fasting, for the following tests: calcium, creatinine.
4. A snack will be provided.

Visit 5 (month 6), visit 7 (month 18) and visit 9 (month 30), visit 11 (month 42): To prepare for these visits, you must not have anything to eat or drink (other than water) for the 8 hours before arriving for your morning visit. You also must not participate in vigorous physical activity for 24 hours before the visits. Please take any medications you normally take in the morning, including the study pill.

During these visits:

1. You will be asked if you have had any changes, since the last visit, in your health or medications, dietary supplements or other pills you may be taking. You may have a physical examination, if needed.
2. You will have your weight, height, blood pressure and heart rate measured.
3. You will complete a questionnaire about your physical activity.
4. You will have:
 - a. Blood collection (about 1/2 a tablespoon of blood), while fasting, for the following tests: glucose and hemoglobin A1c.
5. A snack will be provided.
6. You will return your bottle with the study pills, whether or not there are any pills left.
7. You will get a new 6-month supply of the study pills and receive verbal and written instructions on how to take them (one pill daily in the morning with breakfast).

Visit 6 (month 12), visit 8 (month 24) and visit 10 (month 36), visit 12 (month 48): To prepare for these visits, you must not have anything to eat or drink (other than water) for the 8 hours before arriving for your morning visit. You also must not participate in vigorous physical activity for 24 hours before the visits. Please take any medications you normally take in the morning, including the study pill. During these visits:

1. You will be asked if you have had any changes, since the last visit, in your health or medications, dietary supplements or other pills you may be taking. You may have a physical examination, if needed.
2. You will have your weight, height, blood pressure and heart rate measured.
3. You will complete a questionnaire about your physical activity.
4. You will complete a questionnaire about your diet (at the month 12 and 36 visits only).
5. You will have:
 - a. Urine sample collected to measure calcium and creatinine.
 - b. A small tube inserted in a vein in your arm for blood draw. To avoid repeated sticks, the small tube will stay in your vein for the entire test and all blood samples will be drawn from the same tube

Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

Informed Consent A to Participate in Research

H-33130- VITAMIN D AND TYPE 2 DIABETES (D2D STUDY)

- c. Blood collection, (about 2 tablespoons of blood), while fasting, for the following tests: calcium, creatinine, glucose, hemoglobin A1c, Vitamin D, and insulin.
- d. After fasting blood collection is done, you will have an oral glucose tolerance test (OGTT), which measures how your body uses glucose. You will drink a 10 oz. glucose drink and blood will be collected at 30 minutes (about 1 tablespoon of blood) and two hours (about 1 tablespoon of blood) after the glucose drink, to test for glucose and insulin.
- 6. A snack will be provided.
- 7. You will return your bottles with the study pills, whether or not there are any pills left.
- 8. At the month 12, month 24 and month 36 visit, you will get a 6-month supply of the study pills and receive verbal and written instructions on how to take them (one pill daily in the morning with breakfast).

Visit 13 (end-of-study): To prepare for this visit, you must not have anything to eat or drink (other than water) for the 8 hours before arriving for your morning visit. You also must not participate in vigorous physical activity for 24 hours before the visits. Please take any medications you normally take in the morning, including the study pill. During the visit:

- 1. You will be asked if you have had any changes, since the last visit, in your health or medications, dietary supplements or other pills you may be taking.
- 2. You will have your weight, height, blood pressure and heart rate measured.
- 3. You will have a physical examination.
- 4. You will have:
 - a. Urine sample collected to measure calcium and creatinine.
 - b. Blood collection (about 1 and 1/2 tablespoons of blood), while fasting, for the following tests: calcium, creatinine, glucose and hemoglobin A1c.
- 5. A snack will be provided.
- 6. You will return your bottle with the study pills, whether or not there are any pills left.

Additional Visits: You may need to come for additional visits to determine whether you meet the criteria for diabetes. To prepare for these visits, you must not have anything to eat or drink (other than water) for the 8 hours before arriving for your morning visit. You must also not participate in vigorous physical activity for 24 hours before the visits. Please take any medications you normally take in the morning, including the study pill. During these visits, which will last 30 minutes or 3 hours, depending on whether an OGTT is done:

- 1. You will be asked if you have had any changes, since the last visit, in your health or medications, dietary supplements or other pills you may be taking. You may have a physical examination, if needed.
- 2. You will have your weight, height, blood pressure and heart rate measured.
- 3. You will have:
 - a. Blood collection, (about 1/2 a tablespoon of blood), while fasting, for the following tests: glucose and/or Hemoglobin A1c.
 - b. After fasting blood collection, you may have an oral glucose tolerance test (OGTT), which measures how your body uses glucose. You will drink a 10 oz. glucose drink and blood will be collected (one teaspoon) at two hours (about 1/3 a tablespoon of blood) after the glucose drink, to test for glucose. The research team will tell you, before the visit, if an OGTT needs to be done so you can plan your time.
- 4. A snack will be provided.

Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals**Informed Consent A to Participate in Research**H-33130- VITAMIN D AND TYPE 2 DIABETES (D2D STUDY)

You will be asked to join the D2d support and Education program. As part of this program, you will attend group meetings, held twice yearly at our site Behavioral Medicine Research Center (located at 6655 Travis St., Suite 320, Houston, Texas 77030), to discuss specific topics about prevention of diabetes.

You may need to come for additional visits to evaluate health issues that may be related to the study, which should last about 30-60 minutes.

If the results of your blood tests meet the study criteria for diabetes, we will refer you to your health care provider for additional testing and treatment. You will remain in the D2d study, continue taking the study pills and return for all scheduled visits. Your continued participation is important to the study. At the annual visits (at 12, 24, 36, and 48 months) you will have blood drawn fasting, but will not have the oral glucose tolerance test, or blood collection for insulin.

With your permission, we will provide the results of your laboratory tests and medical examinations to your health care provider. We will also ask you to give your provider(s) permission to share medical information related to the diagnosis of diabetes with the D2d study doctor.

Blood and urine samples that remain after all planned tests have been completed will be destroyed, unless you agree to have your samples stored in the research repository.

PRIVACY AND CONFIDENTIALITY

As a participant in the D2d study, your identity, medical records, and data relating to this research will be kept confidential, except as required by law. If you agree to take part in this research study, your personal information will not be given to anyone unless we get your permission in writing. Your personal information will also only be given for regular hospital treatment, payment, and hospital management activities. We will make every effort to keep your information private, but it cannot be completely guaranteed. Certain government agencies (the Office for Human Research Protections, U.S. Food and Drug Administration), the National Institutes of Health (the study sponsor), the Baylor College of Medicine Institutional Review Board and Baylor College of Medicine, or representatives of the D2d study Coordinating Center at Tufts Medical Center may check records that identify you. This might include your medical or research records and the informed consent form you signed. The records of this study might also be reviewed to make sure all rules and regulations were followed.

A description of this study will be available on 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 for all participants. You can search this web site at any time.

Your research doctor may never be able to provide you with your research related health information.

Potential Risks and Discomforts

While taking the study pill, which may be vitamin D, there is a very small risk of developing kidney stones or a high level of calcium in your blood and urine. A high calcium level may give you

Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

Informed Consent A to Participate in Research

H-33130- VITAMIN D AND TYPE 2 DIABETES (D2D STUDY)

symptoms of stomach pain, nausea, vomiting, headache, and fatigue. Persons who are at risk for high calcium levels or kidney stones will not be allowed to participate in the study. Blood and urine tests will be done during the study to monitor for high calcium level. We will permanently stop the study pills and refer you to your primary care provider if your blood calcium rises above a certain level or if you get a kidney stone. During the study, there is also a very small risk of developing a metallic taste in your mouth, nausea, vomiting, decreased appetite, anemia (low blood count), high level of phosphorus (a mineral) in your blood, fatigue, weakness, difficulty sleeping, frequent urination, headache or kidney damage. During the oral glucose tolerance test, there is a very small risk of developing symptoms of low blood sugar level, which include rapid heartbeat, sweating and headache. If you stop taking the pills because of a medical condition, you will not re-start the pills. However, you will be asked to stay in the study and complete the scheduled visits and all procedures.

There may be slight discomfort during the blood draw and there is the possibility of a small bruise at that skin area of the blood draw. There is a small risk of skin infection at the area of the blood draw. There is also a very small possibility of vein inflammation. There is also a very small possibility of anemia from repeated blood collections.

There is potential loss of privacy. We will protect your information by labeling your research records with a code, and keeping the key to the code in a password protected database.

For women, if you are pregnant or nursing a baby or intend to become pregnant during the study, you should not participate in the study and you should notify the investigator, if you become pregnant or you miss a period during the study, you should notify the research team. A pregnancy test will be performed if you report missing two periods in a row. Prior to the start of the study, women who can get pregnant will be instructed to use a birth control method of their choice. Stable regimen of oral contraceptives or any other hormonal method of contraception (implantable) is allowed. If you have started using oral contraceptives within 3 months of baseline you cannot participate in this study.

Study staff will update you in a timely way on any new information that may affect your decision to stay in the study.

Potential Benefits

The benefits of participating in this study may be: we do not know whether you will receive any benefit from participating in this study. However, during the study, you will have the opportunity to learn how healthy eating and exercise can lower your risk of getting diabetes. During the screening, we will provide you with the results of your medical examination and laboratory results. You will be advised to contact your personal physician if any unexpected medical condition or problem is identified. During the study, you will receive testing for diabetes. The information we learn from this study may help people in the future who are at high risk for getting diabetes.. However, you may receive no benefit from participating.

Alternatives

You may choose to not participate in this study.

Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals**Informed Consent A to Participate in Research**H-33130- VITAMIN D AND TYPE 2 DIABETES (D2D STUDY)

Subject Withdrawal from a Study

There will be no physical, social, economic, legal, or psychological consequences if you decide to withdraw from the study. Also, there are no consequences or possible side effects for suddenly discontinuing the study medication.

You can withdraw from the study and withdraw your consent, if you no longer wish to participate in all aspects of the trial. Unless you permanently withdraw from the study, you will be asked to return for all scheduled follow-up evaluations to collect data. It is important to complete all planned assessments.

You may also, for safety reasons, personal choice or any other reason, stop the treatment but continue with all other aspects of the study, such as visits and data collection as planned.

Investigator Withdrawal of Subject from a Study

The investigator may withdraw you from the study for a safety reason.

The investigator or sponsor may decide to stop you from taking part in this study at any time. You could be removed from the study for reasons related only to you (for example, if you move to another city, if you do not take your study medication, or if you have a serious reaction to your study medication) or because the entire study is stopped. The sponsor, investigator, or Institutional Review Board may stop the study at any time.

Subject Costs and Payments

You will not be asked to pay any costs related to this research.

In order to reimburse you for your time, travel, and efforts while participating in this research study, monetary compensation as well as parking vouchers will be provided to you according to the following schedule. At the first 2 visits, you will receive only a parking voucher. For the completed visits 3, 4, and 5 you will receive \$55.00 plus a voucher for your parking for each visit. For the completed visits 6-12 you will receive \$50.00 plus a voucher for your parking for each visit. Vouchers for parking will be provided to you at the end of all completed visits. The monetary payment will be mailed to you in the form of a check. You will receive the first monetary payment (check) for visit 3, after you complete visit 3 (\$55). You will receive one check for both visits 4 and 5 after you complete visit 5 (a total of \$110 for both visits). You will then receive the monetary payment (check) for visits 6-12 after you complete each visit (\$50 for each visit).

Research Related Injury

Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals**Informed Consent A to Participate in Research**

H-33130- VITAMIN D AND TYPE 2 DIABETES (D2D STUDY)

Emergency medical treatment will be given to you if you are hurt or get sick as a direct result of taking part in this research study. Any needed medical care is available at the usual cost. All needed facilities, emergency treatment, and professional services are available to you, just as they are to the general public. You or your medical insurance company will pay for any such medical care.

There are no plans to pay for your treatment if you get hurt or sick as part of this study. The institution where this research is being conducted has not set aside any money to pay for a research-related injury or illness.

Research personnel will try to reduce, control, and treat any complications from this research. If you are injured because of this study, you will receive medical care that you or your insurance will have to pay for just like any other medical care.

Subject's Rights

Your signature on this consent form means that you have received the information about this study and that you agree to volunteer for this research study.

You will be given a copy of this signed form to keep. You are not giving up any of your rights by signing this form. Even after you have signed this form, you may change your mind at any time. Please contact the study staff if you decide to stop taking part in this study.

If you choose not to take part in the research or if you decide to stop taking part later, your benefits and services will stay the same as before this study was discussed with you. You will not lose these benefits, services, or rights.

Your Health Information

We may be collecting health information that could be linked to you (protected health information). This protected health information might have your name, address, social security number or something else that identifies you attached to it. Federal law wants us to get your permission to use your protected health information for this study. Your signature on this form means that you give us permission to use your protected health information for this research study.

If you decide to take part in the study, your protected health information will not be given out except as allowed by law or as described in this form. Everyone working with your protected health information will work to keep this information private. The results of the data from the study may be published. However, you will not be identified by name.

People who give medical care and ensure quality from the institutions where the research is being done, the sponsor(s) listed in the sections above, representatives of the sponsor, agents of the Food and Drug Administration, and regulatory agencies such as the U.S. Department of Health and Human Services will be allowed to look at sections of your medical and research records related to this study. Because of the need for the investigator and study staff to release information to these parties, complete privacy cannot be guaranteed.

The people listed above will be able to access your information for as long as they need to, even

Version 2.0

Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals**Informed Consent A to Participate in Research**

H-33130- VITAMIN D AND TYPE 2 DIABETES (D2D STUDY)

after the study is completed.

If you decide to stop taking part in the study or if you are removed from the study, you may decide that you no longer allow protected health information that identifies you to be used in this research study. Contact the study staff to tell them of this decision, and they will give you an address so that you can inform the investigator in writing. The investigator will honor your decision unless not being able to use your identifiable health information would affect the safety or quality of the research study.

The investigator, JOHN P FOREYT, and/or someone he/she appoints in his/her place will try to answer all of your questions. If you have questions or concerns at any time, or if you need to report an injury related to the research, you may speak with a member of the study staff: JOHN P FOREYT at 713-798-3839 during the day and SHARON GRIGGS at 713-798-5757 after hours.

Members of the Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals (IRB) can also answer your questions and concerns about your rights as a research subject. The IRB office number is (713) 798-6970. Call the IRB office if you would like to speak to a person independent of the investigator and research staff for complaints about the research, if you cannot reach the research staff, or if you wish to talk to someone other than the research staff.

CONSENT FORM

HIPAA Compliant

Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

Informed Consent A to Participate in Research

H-33130- VITAMIN D AND TYPE 2 DIABETES (D2D STUDY)

Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

Subject Date

Investigator or Designee Obtaining Consent Date

Witness (if applicable) Date

Translator (if applicable) Date