Study Title: Vitamin D and Type 2 Diabetes (D2d) study

Principal Investigator: Anne L. Peters, M.D.

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

You have been asked to participate as a subject in a medical experiment. Before you decide whether you want to participate in the experimental procedure, you have a right to the following information:

CALIFORNIA LAW REQUIRES THAT YOU MUST BE INFORMED ABOUT:

1. The nature and purpose of the study.
2. The procedures in the study and any drug or device to be used.
3. Discomforts and risks reasonably to be expected from the study.
4. Benefits reasonably to be expected from the study.
5. Alternative procedures, drugs, or devices that might be helpful and their risks and benefits.
6. Availability of medical treatment should complications occur.
7. The opportunity to ask questions about the study or the procedure.
8. The ability to withdraw from the study at any time and discontinue participation without affecting your future care at this institution.
9. Be given a copy of the signed and dated written consent form for the study.
10. The opportunity to consent freely to the study without the use of coercion.

I have carefully read the information contained above and I understand fully my rights as a potential subject in this study.

Date: _____ Time: _____

Signature: _____
(Research Participant)

INFORMED CONSENT

Title:	Vitamin D and Type 2 Diabetes (D2d) study
Principal Investigator:	Anne L. Peters, M.D.
Department:	Medicine
Telephone Number:	310-367-0810 or 800-USC-CARE

We invite you to take part in a research study. Please take as much time as you need to read the consent form. You may want to discuss it with your family, friends, or your personal doctor. You may find some of the language difficult to understand. If so, please ask questions. If you decide to participate, you will be asked to sign this form.

This research study is sponsored by the National Institutes of Health (NIH). They provide funding to cover the costs of conducting this research study.

WHY IS THIS STUDY BEING DONE?

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. Researchers have linked low vitamin D levels to pre-diabetes and diabetes and believe that vitamin D may help the body produce more of the hormone insulin or may increase the body's sensitivity to insulin. 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 (pre-diabetic). However, we do not know if vitamin D is effective in preventing diabetes.

You are invited as a possible participant because you are pre-diabetic and at an increased risk for getting diabetes in the future. About 2,382 participants will take part in the study, with about 160 participants taking part at the Community Diabetes Initiatives of the University of Southern California (USC).

WHAT IS INVOLVED IN THE STUDY?

If you decide to take part, this is what will happen:

Your participation in the study will last about 4 years, depending on when you begin participating.

During the study, you will take 1 study pill every day by mouth in the morning with breakfast. The study pill contains either vitamin D (4000 international units) or no vitamin D (a placebo which is a pill that does not have any active ingredients). You will be randomly assigned (like flipping a coin) to take the vitamin D or placebo pill. There is a 50 percent chance you will receive vitamin D pills. The two different types of pills will look exactly the same so you and the study doctor will not know whether the pill you are taking has vitamin D or not.

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. 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 study doctor or the study's research coordinator because taking additional vitamin D or calcium may lead to side effects.

Study visits will take place at the USC study offices located at the Los Angeles County Roybal Comprehensive Health Center. Participation in the study will require up to 13 scheduled visits 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 text messages 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.

Study Visit	Visit 1 Screen	Visit 2 Baseline	Visit 3 Randomize	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	Visit 10	Visit 11	Visit 12	Visit 13 Study End
Schedule	1-4 weeks before visit 2	1-3 weeks before visit 3	Day 0	Month 3	Month 6	Month 12	Month 18	Month 24	Month 30	Month 36	Month 42	Month 48	Varies
Duration	1- 1.5 hours	3 hours	15-30 min.	30 min.	1 hour	3 hours	1 hour	3 hours	1 hour	3 hours	1 hour	3 hours	1 hours

Visit 1 – Screening: You will have a screening visit to see if you are eligible for the study. To prepare for the visit you must be fasting which means 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 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 have:
   a. A physical exam
   b. Blood collection (about 2 tablespoons of blood), 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 who can become pregnant)
5. A snack will be provided.

Within a few days after the visit, the study doctor will review the results of your lab 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 be fasting 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. You may have a physical examination, if needed.
2. You will have your weight, height, waist, blood pressure and heart rate measured.
3. You will complete questionnaires about your diet and physical activity.
4. You will be provided with information on a healthy lifestyle (eating and exercise) to lower your risk of getting diabetes.

5. 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 collection. To avoid repeated needle 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), for the following tests: glucose (sugar), hemoglobin A1c (a test for diabetes), vitamin D, 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. sugary drink and blood will be collected (about 1 tablespoons of blood), at 30 minutes and then at again two hours after the drink (about 1 tablespoons of blood), to test for glucose and insulin levels.
6. A snack will be provided.

Within a few days after the visit, the study doctor will review the results of your lab 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 any time 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 (vitamin D or placebo) and receive 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 other doctors physicians (for example, you primary care physician, endocrinologist) informing him/her of your participation in the study.

Visit 4 (month 3): To prepare for the visit you must be fasting 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 exam, if needed.
2. You will have your weight, height, blood pressure and heart rate measured.
3. A urine sample and blood sample (about 1 tablespoon of blood) will be collected to measure calcium and 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 be fasting 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 exam, 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 blood collected (about ½ tablespoon of blood) to measure 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 be fasting 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 exam, 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 collection.
    c. Blood collection, (about 2 tablespoon 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) as previously described.
6. A snack will be provided.
8. You will return your bottle with the study pills, whether or not there are any pills left.

9. 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).

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.

Visit 13 (end-of-study): To prepare for this visit, you must be fasting 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 exam.
4. You will have a urine sample collected to measure calcium and creatinine.
5. You will have blood collected (about 1 and 1/2 tablespoons of blood), for the following tests: calcium, creatinine, glucose and hemoglobin A1c.
6. A snack will be provided.
7. You will return your bottle with the study pills, whether or not there are any pills left.

Support and Education Visits: You will be asked to join the study's support and education program. As part of this program, you will attend group meetings, held twice yearly at the Roybal Comprehensive Health Center to discuss specific topics about the prevention of type 2 diabetes.

Additional Visits:
You may need to come for additional visits to evaluate health issues that may be related to the study (such as side effects), which should last about 30-60 minutes.

You may need to come for additional visits to determine whether you meet the criteria for diabetes. To prepare for these visits, you must be fasting 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 ½ 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 at two hours (about 1/3 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.

What if I Develop Diabetes During the Study: 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 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 tests, but will not have the OGTT or insulin.

With your permission, we will provide the results of your lab tests and medical exams 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 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. You will be asked to sign a separate consent form for storage of these samples.

WHAT ABOUT PREGNANCY?

We do not know whether the study procedures might hurt an unborn baby. If you are pregnant or nursing (breastfeeding) a baby or intend to become pregnant during the study, you should not participate in the study and you should notify the study doctor. 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.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

Possible risks and discomforts you could experience during this study include:

Vitamin D: There is a very small risk of developing kidney stones or a high level of calcium in the blood and urine. Symptoms of a high calcium level include 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. If your blood calcium rises above a certain level or if you get a kidney stone, the study pills will be permanently stopped and you will be referred to your primary care provider.

Other side effects: During the study, there is also a very small risk of experiencing a metallic taste, nausea, vomiting, decreased appetite, anemia (low blood count), high level of phosphorus (a mineral) in the blood, fatigue, weakness, difficulty sleeping, frequent urination, headache or kidney damage.

Oral glucose tolerance test (OGTT): there is a very small risk of developing symptoms of low blood sugar level, which include rapid heartbeat, sweating and headache.

Blood draw: Slight discomfort, pain, and some bruising at that site of blood draw may occur. Rarely, dizziness, fainting skin infection and vein inflammation may occur. There is also a very small possibility of anemia from repeated blood collections.

Loss of privacy: There is a small risk that people who are not connected with this study will learn our identity or your personal information. 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.

There may be other risks that the study doctor did not expect. The study doctor will watch you to see if you are experiencing any other side effects.

WILL YOUR INFORMATION BE KEPT PRIVATE?

We will keep your records for this study confidential as far as permitted by law. However, if we are required to do so by law, we will disclose confidential information about you. The University of Southern California's Institutional Review Board (IRB) may review your records. The IRB is a research review board that reviews and monitors research studies to protect the rights and welfare of research participants. We may publish the information from this study in journals or present it at meetings. If we do, we will not use your name.

The study staff and other researchers working on this study will have access to your information. Officials sent by the Food and Drug Administration (FDA), National Institutes of Health (the study sponsor), and study Coordinating Center (Tufts Medical Center) may look at your medical and research records.

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.

WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART IN THIS STUDY? You may or may not receive any direct benefit from being part of the study. However, your participation in this study may help us learn how to take care of individuals with pre-diabetes in the future.

WHAT OTHER OPTIONS ARE THERE?

An alternative would be for you not to be in this study and continue your regular care. You do not have to take part in this study to receive vitamin D.

ARE THERE ANY PAYMENTS TO YOU FOR TAKING PART IN THE STUDY?

You will receive payments for taking part in this study. The payments for each study visit have a combined maximum value of $395. After completing of each visit you will receive a gift card to compensate you for your time and travel costs. The payment schedule is shown below.

Study Visit	Visit 1 Screen	Visit 2 Baseline	Visit 3 Randomize	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	Visit 10	Visit 11	Visit 12	Visit 13 Study End
Stipend	$25	$50	$10	$10	$20	$50	$20	$50	$20	$50	$20	$50	$20

WHAT ARE THE COSTS?

All research tests and procedures provided to you for this study are being paid for by the sponsor. Neither you and/or your health plan/insurance company will be charged for the cost of any research tests or procedures that are being done for this study. If you require any routine tests or procedures to treat your illness that are not related to this study (meaning you would normally receive them if you were not participating in this study), you and/or your health plan/insurance company will be billed for the costs of the routine tests and procedures in the same way as if you were not in a study. You will also be responsible for any co-payments and deductibles that are standard for your health plan/insurance coverage. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. If you have any questions about which tests or procedures will be billed to you and/or your health plan/insurance company, ask the study doctor.

WHAT HAPPENS IF YOU GET INJURED OR NEED EMERGENCY CARE?

It is important that you tell the study doctor, Anne Peters MD, if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call her at (310) 367-0810.

If you require medical care/treatment for an injury you experience while participating in this study, medical care/treatment will be provided. You will be billed for the cost of treatment for all injuries you may experience during your participation in the study. The costs for this medical care/treatment will not be paid for by the study sponsor or will not be billed to your health plan/insurance company.

However, by signing this form you have not given up any of your legal rights.

WILL YOU RECEIVE NEW INFORMATION ABOUT THIS STUDY?

During the study, we may learn new things about the risks or benefits of being in the study. If we do, we will share this information with you. You might change your mind about being in the study based on this information.

WHAT ARE YOUR RIGHTS AS A PARTICIPANT, AND WHAT WILL HAPPEN IF YOU DECIDE NOT TO PARTICIPATE?

Your participation in this study is voluntary. Your decision whether or not to take part will not affect your current or future care at this institution. You are not giving up any legal claims or rights. If you do decide to take part in this study, you are free to change your mind and stop being in the study at any time. If you decide to leave the study, an end of study visit is recommended and will be available to you.

CAN YOU BE REMOVED FROM THE STUDY?

You may be removed from this study without your consent for any of the possible reasons:

- You do not follow the study doctor's instructions
- At the discretion of the study doctor or the sponsor
- It is determined that you were not eligible for the study.
- The study is stopped.
- There are unanticipated circumstances.

If you leave the study early for any reason, the information that has already been collected will remain in the study database, but no further information will be collected for the study.

WHOM DO YOU CALL IF YOU HAVE QUESTIONS OR CONCERNS?

You may contact Anne L. Peters, MD at 310-367-0810 with any questions or concerns about your participation in this study. If you feel you have been hurt by taking part in this study, please contact Anne L. Peters, MD at 310-367-0810 or 800-USC-CARE. If you have questions, concerns, or complaints about the research and are unable to contact the research team, contact the Institutional Review Board (IRB) Office at 323-223-2340 between the hours of 8:00 AM and 4:00 PM. (Fax: 323-224-8389 or email at irb@usc.edu).

If you have any questions about your rights as a research participant, or want to talk to someone independent of the research team, you may contact the University of Southern California Institutional Review Board Office at the numbers above or write to the Institutional Review Board at the LAC+USC Medical Center, General Hospital, 1200 North State Street, Suite 4700, Los Angeles, CA 90033.

You will get a signed copy of this consent form.

AGREEMENT:

I have read (or someone has read to me) the information provided above. I have been given a chance to ask questions. All my questions have been answered. By signing this form, I am agreeing to take part in this study.

Name of Research Participant	Signature	Date Signed (and Time)

I have personally explained the research to the research participant and answered all questions. I believe that he/she understands the information described in this informed consent and freely consents to participate.

Name of Person Obtaining Informed Consent	Signature	Date Signed (and Time)

If informed consent is obtained using the Short Form method (oral translation of this document in a language understood by the participant combined with the written Short Form in the participant's language), the witness must sign and date the informed consent below. A witness signature is required ONLY when the Short Form method is used. If you are not using the Short Form method to obtain consent, no witness is needed and you may leave this signature line blank.

Name of Witness	Signature	Date Signed