**Protocol Title:** PRECIDENTD: PREvention of CardIovascular and DiabEtic kidNey disease in Type 2 Diabetes

**Principal Investigator:** Brendan M. Everett, Deborah J.Wexler, and Robert J. Glynn

**Site Principal Investigator**:

**Description of Study Population:** Adults with type 2 diabetes and atherosclerotic cardiovascular disease (ASCVD) or high ASCVD risk

**About this Consent Form**

Please read this form carefully. It tells you important information about a research study called PRECIDENTD. A member of our research team will talk to you about taking part in this research study. People who agree to take part in research studies are called “participants.” This term is used throughout this consent form.

You must sign this form to take part in this research study. We will give you a signed copy to keep.

**Key Information**

We are asking you to be in a research study. This form will tell you what you should expect if you agree to be in the study. You will find more information about each of the following points later in this form.

It is your decision whether to join the study. We are asking you to be in this study because you have type 2 diabetes and a history of heart disease or have high risk for heart disease. People with type 2 diabetes have a higher risk for heart disease than people without diabetes. We are doing this research to learn more about which diabetes medications are the best for lowering the risk of heart and kidney disease in people with type 2 diabetes.

If you agree to join the study, you will be randomly assigned by a computer to one of two diabetes medication options. You would be asked to take an FDA-approved diabetes medication that is safe and effective for you. The medications can be taken alone or with other diabetes medications. Medications used in this study will be billed to your insurance. You will have to pay a co-payment or percent of the cost, as you normally do for your medications. Your usual diabetes care provider will continue to manage your diabetes care. You will be in the study for as long as 8 years if you decide to stay for the whole study.

The main risks of being in the study are having side effects of the medications, which are described in detail below.

You might benefit from being in the study because everyone will be asked to take a medication that lowers blood sugar and hemoglobin A1c, helps with weight loss, and prevents heart and kidney problems.

If you decide not to be in the study, some other things that might help your condition are eating a healthy diet, regular exercise, and taking these or other diabetes and heart medications. You do not have to be in the study to take one of these medications.

You will be paid $500 for every year that you take part in this research study up through 2029. Later in this form, there are details about study visits and payment amounts.

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Dr. Brendan Everett is the person in charge of this research study. You can call him at 617-732-8790 M-F 9 am-5 pm. You can also call **[Insert name(s)] at [Insert phone number(s)] [Insert when each person is available M-F 9-5 or 24/7]** with questions about this research study. **[You can add name/contact information for local site investigator]**

If you have questions about the scheduling of appointments or study visits, call **[Insert name(s)] at [Insert phone number(s)].**

If you want to speak with someone **not** directly involved in this research study, please contact [**ADD LOCAL IRB CONTACT INFORMATION**].

You can talk to them about:

* Your rights as a research subject
* Your concerns about the research
* A complaint about the research
* Any pressure to take part in, or to continue in the research study

You can also contact the Mass General Brigham IRB, the group that reviewed the protocol. You can call them at 857-282-1900.

**Detailed Information**

A description of this clinical trial will be 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.

# Why is this research study being done?

We are doing PRECIDENTD to learn more about diabetes medications that also reduce the risk of heart and kidney disease in people with type 2 diabetes. People with type 2 diabetes are twice as likely to have heart disease or a stroke compared to someone who does not have diabetes. They are likely to have heart disease or stroke at a younger age. People with heart disease, stroke, or other vascular (blood vessel) disease or who have high risk for these can participate in the study.

* We are studying 2 classes of medications that reduce the risk of heart and kidney problems in people who qualify for this study. A medication “class” means different medications that work the same way and have the same effects.
* The medication classes in this study are SGLT2 inhibitors and GLP-1 receptor agonists. These medications are approved by the FDA to treat type 2 diabetes. Both classes have been studied in many clinical studies in large groups of patients.
* Medications in this study lower blood sugar and hemoglobin A1c, help with weight loss, and prevent heart and kidney problems. They can be taken alone or with other diabetes medications.
* However, we do not know which class of medication works better. This has not been studied.

The goal of this study is to find out: Is one class of medication (SGLT2 inhibitor OR GLP-1 receptor agonist) better than the other at reducing the risk of heart and kidney problems and death?

PRECIDENTD is a pragmatic trial. This means we are studying these medications in real-world treatment for diabetes. We will try to keep everything the same as usual diabetes care except the study medication.

* Medications used in this study will be billed to your insurance. The study team will find out which specific medications are covered or “preferred” by your insurance company. Then you will be prescribed the specific medication within the class of medication you were assigned.
* You will have to pay a co-payment or percentage of the cost, as you normally do for your medications. These are brand-name medications. For most insurance plans, these medications will have a higher co-payment than a generic medication.
* Your usual diabetes care provider will continue to manage your diabetes. We will work with them to safely add the study medication to your current medications.
* We ask you try to take the study medication as long as you can or until the study ends. We ask that you stay in the study even if you stop taking the study medication.

The parts of the study that are different from usual care are:

* The medication assignment will be randomly chosen by a computer. (Because of your conditions, you could benefit from any of the medications being studied.)
* We will ask you to complete study visits and questionnaires.
* We ask you to share your health information with the research team so that we may answer the study questions.

Because it takes a long time for heart and kidney problems to develop, this is a long-term study. We will ask people who join the study to stay in the study for up to 8 years, even if they stop taking the study medications.

**Who will take part in this research?**

We are asking you to take part in this study because you have type 2 diabetes and have a history of heart or blood vessel disease or are at high risk for heart disease based on your other health conditions. Because of these conditions, you could benefit from the medications being studied.

About 6,000 people in the United States will take part in the research study. Up to 250 people at **[Name of Hospital]** will take part.

The Patient-Centered Outcomes Research Institute, an organization responsible for evaluating different treatment options, is paying for this research to be done.

**What will happen in this research study?**

First, you will have an in-person or videoconference visit to meet the study provider and study team. This will take up to 1 hour. During this visit, the study provider will look at your medical history and your other medications to make sure it is safe for you to take these medications. Then the study team will make sure you can afford these medications with your insurance. You will not be in the study if it is not safe for you to take these medications or if you would have a hard time paying for these medications.

Joining the study/first visit:

* We will ask you to complete study questionnaires. We will ask you about your medical history, your other medications, and your current health.
* If you have not had recent routine diabetes tests, the study provider will order blood and urine tests that are recommended for diabetes care. These tests measure hemoglobin A1c, kidney function, and cholesterol. The lab tests will be drawn in your usual clinical laboratory and billed to your insurance. If you have completed recent diabetes tests, we will use the results from those tests.
* At the end of this first visit, you will be randomly assigned by a computer to one of two medication treatment options. Any medication you will be prescribed has shown benefits in prior studies.
	+ 1. If you are assigned to take an SGLT2 inhibitor, the provider will prescribe Invokana (canagliflozin), Jardiance (empagliflozin), or Farxiga (dapagliflozin), or other medications that are FDA-approved in the same class. These medications are pills.
		2. If you are assigned to take a GLP-1 receptor agonist, the provider will prescribe Victoza (liraglutide), Trulicity (dulaglutide), or Ozempic (semaglutide) given by injection or Rybelsus (semaglutide) tablets, or other medications that are FDA-approved in the same class.
* The study provider will prescribe a one-year supply of the medication.
* We will ask you to get the medication through your usual pharmacy covered by your health insurance.
* We will ask you to refill the medication through your insurance monthly or every three months, depending on how you usually get your prescriptions.
* The study provider and team will teach you about the medication you are prescribed, including how to take it and what side effects may come with it.
* If you are on other diabetes medications, the study provider will tell you if you need to adjust the other medications for safety.
* The study team will work with your usual diabetes care provider to make sure this medication is working well for you.
* Your usual diabetes care provider will know you joined the study and what medication you have been assigned. Your usual diabetes care provider will continue to manage your overall diabetes care.
	+ We will ask you to keep taking the assigned medications for the rest of the study as long as they keep working and you do not have side effects.

Follow up after first visit:

* We will ask you to have a brief (less than 30 minutes) in-person or videoconference visit 2 months after the first visit. You will be asked to answer questions. The study team will work with your usual diabetes care provider to adjust medications if needed.
* If your insurance coverage for study medication changes, we will change the prescription to provide the medication covered by your insurance.

Follow up visits and questionnaires:

* We will ask you to come for an in-person or videoconference visit once per year after you join the study. At the yearly visit, we will take the same measurements as we do at the first visit. We will also ask you about study outcomes (heart and kidney events) and side effects. This will take up to 1 hour.
* We will prescribe the study medication every year, or your own diabetes care provider may prescribe the medication.
* If your insurance coverage for study medication changes, we will change the prescription to the medication covered by your insurance within each medication class.
* If you have not had routine diabetes blood and urine tests, we will ask you to do these on your own at your usual clinical lab. This will take up to 30 minutes.
* We will call you 6 months after each yearly visit to ask about the study outcomes and side effects. This will take up to 30 minutes.
* After every annual visit and 6 months call, we will ask you to complete questionnaires about your health online or with study staff over the phone. This will take up to 30 minutes.
* We ask you to stay in the study for up to 8 years, but you will have fewer visits if you join later in the project.

General information about the study:

* This study does not have a placebo, or sugar pill. This study is not blinded. You, your usual diabetes care provider, and the study team will know which medication you are assigned.
* If you are currently taking an SGLT2 inhibitor or a GLP-1 receptor agonist medication, you must be willing to stop it order to join the study.
	+ You may be assigned to the medication class you are already taking. If so, you can keep taking it.
	+ You may be assigned to the other medication class. If so, you would need to stop taking the medication you are currently taking and switch to a different medication.
* You will continue your other diabetes medications if they are still needed. The study provider will work with your usual diabetes care provider to recommend any changes to your medication.
* If you do not want to take the study medication, you may stop it. We will ask you why you stopped the medication.
* Even if you do not keep taking study medication, we would like you to stay in the study for up to 8 years, depending on when you join This is important so that researchers can compare what happened to people assigned to each study treatment.
* Staying in the study means that you would keep attending annual in-person or videoconference visits, completing study questionnaires, and contributing your health information to the study.
* We will also collect information from your health record twice per year. . To be sure that we collect all important health events, we may continue to review your health information for up to 3 years after the study visits are complete.
* As part of the study, we will send you text messages to see how you are doing with the study medication. Some text messages will contain your name and the study medication you are taking. If you share or lose your phone, others could find out that you have diabetes and take diabetes medication. The text messages are not encrypted or secure. If you want to stop receiving text messages at any point during the study, you can tell a study team member or text STOP.
* We will share your health information with research collaborators outside **[NAME OF INSTITUTION]**.

**Study Information Included in Your Electronic Medical Record**

* A note that you are taking part in this research study will be made in your electronic medical record.
* The study team will tell your usual diabetes care provider (primary care provider or endocrinologist) that you joined the study. Your usual diabetes care provider will continue to manage your diabetes medications, including the study medication.
* Your answers to study questionnaires will not be included in the electronic medical record.

**Study compensation**

Everyone who takes part in the study will receive a $500 participant payment on a study gift card or a check at randomization and after each yearly visit completed through 2029.

Study payments are provided through an approved, outside vendor (Advarra). Payments are made to you via a reloadable credit card-based system, called Advarra Participant Payments. This secure system is similar to a gift card or credit card.

To be paid by this system, you will be given an Advarra Participant Payments Visa card when you enroll in the study. Once the card is activated, the study team will add a payment after each paid visit you complete. The payment should be available to you within a day. You may use the card anywhere Visa cards are accepted, such as at a grocery store.

We will need to collect your Social Security number, address, and date of birth to make these payments. This information will be shared securely with Advarra, the company that runs the payment card system. Payments like this are considered taxable income. If you receive more than $600 in one year, the payment will be reported to the IRS as income by the hospital. If you prefer NOT to disclose your social security number, you may still join the study, but you will not be eligible to receive a gift card or a check.

**How may we use and share your health information for other research?**

The information we collect in this study may help advance other research. If you join this study, we may remove all information that identifies you (for example your name, medical record number, and date of birth) and use these de-identified data in other research. It won’t be possible to link the information back to you. Information may be shared with investigators at our hospitals, at other academic institutions or at for-profit, commercial entities. You will not be asked to provide additional informed consent for these uses.

At the completion of this research study, we would like to store and be able to use and share your identifiable health information with researchers at Mass General Brigham for other research related to diabetes, heart, or kidney disease. If we share your health information with other researchers outside of Mass General Brigham, we will label the information with a code instead of your name or other directly identifying information. The key to the code connects your name or other identifiers to your information. We will keep the code in a **[password protected computer].**

Because the health information is identifiable, we are asking your permission to store, use, and share it for other research. You can still take part in the research study whether or not you give permission for the storage, use, and sharing of the health information for other research.

Do you agree to let us store and use your health information for other research related to diabetes, heart, or kidney disease?

 YES NO Initial \_\_\_\_\_\_\_\_\_\_\_\_\_\_

In addition, we would like your permission to obtain your medical records from other hospitals. We will use these records to confirm the details of medical events that you report to us. This will help us make sure that we can get the information we need to answer the study questions. You can take part in the research study whether or not you give permission for the study to obtain your medical records from other hospitals.

Do you agree to let us obtain your medical records from other hospitals?

 YES  NO Initial \_\_\_\_\_\_\_\_\_\_\_\_\_\_

Finally, we would like your permission to obtain your insurance claims from Medicare or other insurance claims data sources. We will use the insurance claims to make sure that we can keep track of health care services you receive, such as whether you are admitted to a hospital and the reason for being admitted to the hospital. This will help us make sure that we can get the information we need to answer the study questions. You can still take part in the research study whether or not you give permission for the study to obtain your insurance claims for research.

Do you agree to let us contact Medicare or other insurance claims data sources to obtain your insurance claims for research?

 YES  NO Initial \_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Will you get the results of this research study?**

You will get all your results from taking part in this study through usual care. They will be available through the usual methods (such as a letter from a provider or the health portal).

During the study, we will send you a newsletter that will tell you about the research study overall. This newsletter will not report anyone’s individual results. It will tell you some information about what we are learning about heart and kidney risk reduction in type 2 diabetes. We will also publish what we learn in medical journals.

We will share the overall results of the study with all people who take part and with the diabetes community (patients, providers, professional organizations, health insurers) more broadly.

**What are the risks and possible discomforts from being in this research study?**

The medications being used in this study are approved by the FDA for the treatment of type 2 diabetes. Each medication has known common and rare side effects. The most common and serious side effects are:

SGLT2 inhibitors

* Common side effects (> 5% of people taking the medication) include genital yeast infections and urinary tract infections.
* Other, less common, side effects include dehydration and low blood pressure.
* Rarely, a serious complication called diabetic ketoacidosis may occur. This is when there is acid build up in the blood along with severe dehydration. This risk can be reduced by stopping the medication when you are sick, not eating, or when you are preparing for or having a procedure, such as a colonoscopy, or surgery.

GLP-1 receptor agonists

* Common side effects (> 5% of people taking the medication) include nausea, vomiting, diarrhea, abdominal pain, and constipation, which often improve with time.
* Very rare possible side effects include pancreatitis and worsening of proliferative diabetic retinopathy.

All medications used in this study can cause low blood sugar when combined with other diabetes medications such as insulin or sulfonylureas. Each medication class has additional side effects that occur more rarely. Although these medications have been studied, there may be other risks that are currently unknown.

You may pay more for medications than you would if you were not in this study. Generics may become available over the course of the study.

We will ask you to contribute up to 3 hours per year to this study.

**What are the possible benefits from being in this research study?**

People who take part in this study may benefit by having improved blood sugar and hemoglobin A1c, weight loss, and lower risk of future heart and kidney problems, based on prior studies of these medications.

Future patients with type 2 diabetes and their health care providers will benefit from being more informed about the best diabetes medication treatment approach to reduce heart and kidney problems.

**What other treatments or procedures are available for your condition?**

You do not have to take part in this study to be treated for type 2 diabetes. Other treatments or procedures that are available to treat type 2 diabetes include the following medications or combinations of these medications:

* Metformin
* Sulfonylureas such as glipizide, glimepiride, or glyburide
* DPP-4 inhibitors such as sitagliptin or linagliptin
* Insulin
* Many other diabetes medications alone or in combination with each other

**Can you still get medical care within [Relying Institution] if you don’t take part in this research study, or if you stop taking part?**

Yes. Your decision won’t change the medical care you get within [institution] now or in the future. There will be no penalty, and you won’t lose any benefits you receive now or have a right to receive.

We will tell you if we learn new information that could make you change your mind about taking part in this research study.

**What should you do if you want to stop taking part in the study?**

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

Also, it is possible that we will have to ask you to drop out of the study before you finish. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

**Will you be paid to take part in this research study?**

Everyone who takes part in the study will receive a $500 gift card after each yearly visit up through 2029 To receive the payment, you must share your name, address, and email address with the central study team and the gift card payment processing system.

**What will you have to pay for if you take part in this research study?**

All the lab tests done and medication you will take while in this study are approved by the FDA and considered best practice for care of patients with diabetes. The costs of lab tests and medication will be billed to your insurer in the usual way. You will be responsible for the out-of-pocket costs like you are when you get any clinical care for diabetes. We know these costs can be a burden. We will do our best to keep these costs as low as possible. For example, we will prescribe the specific medication included in the list of medications covered by your insurance.

Costs thatwill be billed to your insurer include:

* Any blood tests that are ordered by the study team.
* The medication you are prescribed. Your insurer will be billed for the medication, and you will pay for any deductibles and co-payments required by your insurer.
* If you are on Medicare, paying for medications for this study could increase the chance that you will be in the Medicare coverage gap or “donut hole” part of the way through the year. Once you and your insurance plan have spent a certain amount of money on prescription medications, you will be in the coverage gap. You will need to pay 25% of the cost for brand-name prescription medications like the ones in this study. The amount Medicare asks you to pay may change over the course of this study.

There is no cost for study visits or speaking with the study team.

**What happens if you are injured as a result of taking part in this research study?**

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the beginning of this consent form.

**If you take part in this research study, how will we protect your privacy?**

Federal law requires Mass General Brigham and [RELYING INSTITUTION] to protect the privacy of health information and related information that identifies you. We refer to this information as “identifiable information.”

In this study, we may collect identifiable information about you from:

* Past, present, and future medical records
* Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable information and why:

* [RELYING INSTITUTION] researchers and staff involved in this study
* The sponsor(s) of the study, and people or groups it hires to help perform this research or to audit the research
* Other researchers and medical centers that are part of this study
* The Mass General Brigham ethics board and [RELYING INSTITUTION] ethics board that oversee the research
* A group that oversees the data (study information) and safety of this study
* Non-research staff within [RELYING INSTITUTION] who need identifiable information to do their jobs, such as for treatment, payment (billing), or hospital operations (such as assessing the quality of care or research)
* Federal agencies (such as the U.S. Department of Health and Human Services (DHHS) and agencies within DHHS like the Food and Drug Administration (FDA), the National Institutes of Health (NIH), and the Office for Human Research Protections(OHRP)), state agencies, and foreign government bodies that oversee, evaluate, and audit research, which may include inspection of your records
* Public health and safety authorities, if we learn information that could mean harm to you or others (such as to make required reports about communicable diseases or about child or elder abuse)

**Certificate of Confidentiality:**

A federal Certificate of Confidentiality (Certificate) has been issued for this research to add special protection for information and specimens that may identify you. With a Certificate, unless you give permission (such as in this form) and except as described above, the researchers are not allowed to share your identifiable information or identifiable specimens, including for a court order or subpoena.

Certain information from the research will be put into your medical record and will not be covered by the Certificate. This includes records of medical tests or procedures done at the hospitals and clinics, and information that treating health care providers may need to care for you.Please ask your study doctor if you have any questions about what information will be included in your medical record. Other researchers receiving your identifiable information or specimens are expected to comply with the privacy protections of the Certificate. The Certificate does not stop you from voluntarily releasing information about yourself or your participation in this study.

Even with these measures to protect your privacy, once your identifiable information is shared outside Mass General Brigham, and [RELYING INSTITUTION] we cannot control all the ways that others use or share it and cannot promise that it will remain completely private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your identifiable information. Your permission to use and share your identifiable information does not expire.

The results of this research may be published in a medical book or journal or used to teach others. However, your name or other identifiable information will not be used for these purposes without your specific permission.

**Your Privacy Rights**

You have the right **not** to sign this form that allows us to use and share your identifiable information for research; however, if you don’t sign it, you can’t take part in this research study.

You have the right to withdraw your permission for us to use or share your identifiable information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others, and such information may continue to be used for certain purposes, such as to comply with the law or maintain the reliability of the study.

You have the right to see and get a copy of your identifiable information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

**Informed Consent and Authorization**

**Statement of Person Giving Informed Consent and Authorization**

* I have read this consent form.
* This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
* I have had the opportunity to ask questions.
* I understand the information given to me.

# Signature of Subject:

I give my consent to take part in this research study and agree to allow my identifiable information to be used and shared as described above.

Subject Date Time (optional)

### Statement of Study Doctor or Person Obtaining Consent

* I have explained the research to the study subject.
* I have answered all questions about this research study to the best of my ability.

Study Doctor or Person Obtaining Consent Date Time (optional)

### Statement of Study Research Staff assisting with Informed Consent

* I have explained the research to the study subject.
* I have answered all questions about this research study to the best of my ability.

Study Research Staff assisting with Informed Date Time (optional)

Consent

## Consent of Non-English Speaking Subjects Using the “Short Form” in the Subject’s Spoken Language

### Statement of Hospital Medical Interpreter

As someone who understands both English and the language spoken by the subject, I interpreted, in the subject's language, the researcher's presentation of the English consent form. The subject was given the opportunity to ask questions.

Hospital Medical Interpreter Date Time (optional)

**OR**

### Statement of Other Individual (Non-Interpreter)

As someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject’s own language, and that the subject was given the opportunity to ask questions.

Name Date Time (optional)

## Consent of Subjects Who Cannot Read or Write or are Physically Unable to Talk or Write

The consent form was presented orally to the subject in the subject’s own language, the subject was given the opportunity to ask questions, and the subject has indicated his/her consent and authorization for participation by (check one box as applicable):

[ ]  Making his/her mark above

[ ]  Other means \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

(fill in above)

Consent Form Version Date: // 02/16/2024