Study Consent

Official Title: Remission through Early Monitored Insulin Therapy - Duration Month (REMIT-DM)

ClinicalTrials.gov ID (NCT number): NCT03670641

Consent Date: 06 July 2021

Division of Endocrinology and Metabolism
Consent to Act as a Participant in a Research Study

Study Title:
Remission through Early Monitored Insulin Therapy Duration-Month (REMIT-DM)

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What is the purpose of this study?
The purpose of this study is to see if use of continuous glucose monitoring data from people diagnosed with type 2 diabetes within the past 4 years and started on insulin temporarily can guide an insulin dosing system, called an algorithm, with the hopes of achieving diabetes remission after the short-term use of insulin. We also want to find out about experiences of patients using a CGM device in this way.

Why is this research being done?
Type 2 diabetes is a disease where the pancreas does not make enough insulin and/or the insulin doesn't work as it should. Many people with type 2 diabetes will use insulin to control their blood sugars, often after they have had the disease for a while.

However, there have been studies showing that giving insulin early on for a very short period can rest the insulin-making cells in the body. In many cases, it can make it so that people who recently found out that they have type 2 diabetes can have normal blood sugars without needing medication for a year or more. This is called diabetes *remission*.

Studies about this, so far, have taken place with people admitted to the hospital for several weeks. While in the hospital, blood sugar finger stick tests are done so that doctors can adjust insulin doses. This study will use this method by giving insulin within 4 years of a diabetes diagnosis, to cause a remission without having the person stay in

the hospital and without frequent finger sticks. This study will be done in the outpatient setting.

This study will use newer blood sugar testing technology that is available to people with diabetes. It can give blood sugar readings every few minutes with minimal finger pricks. (You may have to prick your finger if there is inconsistency between your blood sugar reading and your symptoms.) This technology is called Continuous Glucose Monitoring, or CGM for short. CGM is already tested and available. The CGM device has 3 parts: a catheter, a small sensor that is placed on your stomach and a pager-like device that gives you your blood sugar readings.

Many of our patients are already using CGM to measure their blood sugars instead of doing finger pricks. Instead of admitting people to the hospital to achieve a “remission” with frequent finger pricks to gauge insulin doses, we want to use CGM to measure blood sugars as an outpatient. This allows for less finger pricks and many more blood sugar values to help guide better insulin adjusting. We will show you how to use your CGM and we will give you a lot of education and support to ensure your safety and well-being during this study.

Who is being asked to take part in this research study?
You are invited to be part of this study as you have been diagnosed with type 2 diabetes in the last 4 years as diagnosed by your endocrinologist or primary care provider. We plan to invite 10 people with type 2 diabetes to participate. You are a good fit for this study because you have type 2 diabetes, a hemoglobin A1C level >7.0% (a measure of blood sugars over a 3-month period), are over the age of 18 years old, and have access to a home computer (desktop or laptop for downloading CGM records).

What procedures will be performed for research purposes?
If you decide to take part in this research study, you will have the following procedures that are not part of your standard medical care:

1. You will be asked to sign a consent form agreeing to participate in this study

2. You will be prescribed insulin therapy from the beginning for up to 4 weeks to try and achieve diabetes remission. If you are already on metformin therapy, you may continue this medication but will be asked to hold it for 2 days twice during the study to perform standard blood tests, which includes an oral glucose tolerance test (OGTT) performed at the first and third study visit.

3. You will be asked to use the readings from a CGM so that your insulin doses can be adjusted daily to achieve diabetes remission. You will have access to a team of experienced diabetes educators who will guide you during this process under the direction of our endocrinologists Dr. Sobel and Dr. Rometo.

4. You will be asked to complete surveys about:
    a. your satisfaction with the study
    b. your experience now living with diabetes

    The surveys will be done when you are having your initial, 3 month and at the final study visit.

5. Your Private Health Information in your Electronic Medical Record will be accessed by our team. Members of the research team including the diabetes educators, physicians, statistician and/or study coordinator will access your record for up to 24 months after the study is complete to obtain lab values, data, and changes in condition or medical care.

6. After you have returned the CGM at one month, we will collect all of your CGM data from the Dexcom CLARITY software as well as medical record data from your routine diabetes care team visits. There are no procedures you will be asked to do. We will collect all the data from all of the participants and analyze it to see if the use of CGM and algorithm were effective in getting patients to normal blood sugars.

We will provide you with standard diabetes clinical procedures and education that are considered usual care. <u>These are not research procedures.</u> If you are a patient in our clinic not in a study, your care includes:

- Visits with your endocrinologist which include an initial visit and follow-up visits at 3 months, 6 months, 9 months, and 12 months.

- The visit with the endocrinologist will include a full assessment that includes a physical exam and review. Your endocrinologist will also order routine diabetes labs for these visits.

- You will also be asked to wear a Continuous Glucose Monitor (CGM) to determine the right insulin doses for you.

- You will also visit with a diabetes educator and dietitian who will provide instruction on healthy eating, activity, care of high and low blood sugars, CGM use and information on who and when to call the Diabetes Team.

As part of your standard medical care, you will be asked to come in 4-6 weeks after you start the insulin for a visit with the endocrinologist who will review your test results and see if you have rested your insulin-making cells for diabetes remission. If further medicines should be needed to help control your blood sugars after the short-term use of insulin, then the endocrinologist will follow the current standard of diabetes management according to the American Diabetes Association guidelines in prescribing your therapy. After that, the follow-up portion of the study will last 12 months and most data collection will take place as part of the routine visits with the endocrinologist. You will have a visit with the diabetes educator and endocrinologist at 12 months.

Your participation in this study will not change your standard medical care nor eliminate the need for medical visits as per your doctor's order.

What are the possible risks, side effects, and discomforts of this research study?

1. There is a risk of a breach of confidentiality if your medical information or your identity are obtained by someone other than the investigators, but precautions will be taken to prevent this from happening.

2. We also cannot guarantee that your diabetes responds to the use of insulin and achieves remission.

3. Risks of insulin use include low blood sugar, weight gain, allergic reactions and infections, and drug interactions. Symptoms of low blood sugar include headache, hunger, weakness, sweating, tremors, irritability, trouble concentrating, rapid breathing, fast heartbeat, fainting, or seizure (severe hypoglycemia can be fatal).

4. Risks of CGM use include mild pain at time of insertion of subcutaneous catheter, minor bleeding or bruising at insertion site, skin irritation around insertion site, infection or lipohypertrophy.

Are there any possible benefits from taking part in this study?
There is no guarantee that you will benefit from being in this research, however this study may contribute to diabetes care knowledge for all.

What treatments or procedures are available if I decide not to take part in this research study?
If you choose not to participate you will still see your endocrinologist as usual and you can still see the diabetes educator and registered dietitian. You can also utilize a professional continuous glucose monitor for 2 weeks as part of routine care.

If I agree to take part in this research study, will I be told of any new risks that may be found during the study?
You will be promptly notified if any new information either good or bad about type 2 diabetes intensive insulin therapy for remission develops during this study and which may cause you to change your mind about continuing to participate.

Will my insurance provider or I be charged for the costs of any procedures performed as part of this research study?
Neither you nor your insurance provider will be charged for the costs of any of the procedures performed for this research study. You will be charged in the usual manner for your standard medical care (care you would receive even if you were not participating in this research study).

Will I be paid if I take part in this study?
Yes, you will be paid $250 for participating. You will receive this stipend at clinic visits 1, 3, 4, 6 and 7 where we obtain information for use in our study. You will receive $50 at each of these visits. You will be paid on a reloadable debit card. We are also paying for your parking.

Since you are being compensated for your participation in this study, your name, address, and social security number will be released to the Accounting Office. If the total reimbursement for your participation in research is greater than $600 in a year, this will be reported to the Internal Revenue Service (IRS) as income.

The insulin and CGM are being paid for through a $25,000 PINCH award and the blood glucose testing supplies are being donated by the UPMC Center for Diabetes and Endocrinology.

Who will pay if I am injured because of taking part in this study?
You waive no legal rights from signing this consent form. Emergency medical treatment for injuries directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance company may be billed for the costs of this emergency treatment, but none of these costs will be charged directly to you. If your

research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation.

If you believe that the research procedures have resulted in an injury to you:
Immediately contact the Principal Investigator Sandra Sobel, MD. She is listed on the first page of this form.

How will my data be protected?
Any data produced from this study will be stored in your electronic health record and available to physicians and medical professionals that you see for care. Data from surveys or from the Dexcom CGM will be de-identified and assigned a subject ID if moved from a secure server. The research team will have access to your electronic health record. Every member of the research team is under a confidentiality agreement. Just as with the use of your information for health care purposes, we cannot guarantee its privacy. Your data, if printed and/or published, will be de-identified. Hard copies of research data will be de-identified and stored in locked file cabinets in the Division of Endocrinology and Metabolism for a minimum of 7 years. Any information related to adverse events you may suffer during the study period will be disclosed to your physician in your electronic medical record.

Who will have access to identifiable information related to my participation in this research study?
The investigators listed on the first page of this consent form and their clinical staff (who help to provide your diabetes care, like the dietitian) may have access to identifiable information (which may include your identifiable medical information) related to your participation in this research study:

Authorized representatives of the University of Pittsburgh Research Conduct and Compliance Office. Their office is responsible for monitoring appropriate conduct of research studies on campus.

Authorized representatives of the sponsor of this research study, the Clinical and Translational Science Institute (CTSI) on behalf of the Pitt Innovation Challenge (PInCh 2017) award.

In unusual cases, the investigators may be required to release identifiable information (which may include your identifiable health information) related to your participation in this research study in response to an order from a court of law. If the investigators learn that you or someone with whom you are involved with is in danger or potential harm, they will need to inform, as required by Pennsylvania law, the appropriate agencies.

Authorized representatives of the UPMC Health system hospitals or other affiliated health care providers may have access to identifiable information (which may include your identifiable medical information). The fact that you are participating in a research study and that you are undergoing certain research procedures (but not the results of these procedures) may also be made known to individuals involved in insurance billing and/or other administrative activities associated with conduct of the study.

Your data from your blood sugar monitoring and medical record used in this research may contribute to a new discovery or treatment. In some instances, these discoveries or treatments may be of commercial value and may be sold, patented, or licensed by the investigators and the University of Pittsburgh for use in other research or the development of new products. You will not retain any property rights nor will you share in any money that the investigators, the University of Pittsburgh, or their agents may receive.

Is my participation in this study voluntary?
Your participation in this research study, to include the use and disclosure of your identifiable information for the purposes described above, is completely voluntary. (Note, however, that if you do not provide your consent for the use and disclosure of your identifiable health information for the purposes described above, you will not be allowed, in general, to participate in the research study.) Whether you provide your consent for participation in this research study will have no effect on your current or future medical care at a UPMC Health systems hospital or affiliated health care provider or your current or future relationship with a health insurance provider.

May I withdraw, at a future date, my consent for participation in this research study?
At any time, you may withdraw your participation from REMIT DM: Remission through Early Monitored Insulin Therapy Duration-Month. You may withdraw by telling the team in writing that you are no longer interested in participating in the research study. You may do this by using the MyUPMC communication platform or by sending a letter in the mail. This letter must be signed and dated and should be sent to:

Sandra Indacochea Sobel, MD
Clinical Assistant Professor of Medicine, Division of Endocrinology and Metabolism
Clinical Chief of Endocrinology, UPMC Mercy
1400 Locust Street Suite 5120 Pittsburgh, PA 15217

If you withdraw from the study, your de-identified research data, up until the time you withdrew, may still be published. Your participation is completely voluntary and your decision to participate, or to later withdraw from it, will not affect your current or future medical care at UPMC or your participation in the current research protocol. If you would like additional information, you may contact the study coordinator, Shari Reynolds

at 412-383-0570. Questions about your rights as a research participant may be answered by the Human Subjects Protection Advocate at the University of Pittsburgh IRB Office 866-212-2668.

It is possible that you may be removed from the research study by the researchers if, for example, you are not able to keep up with the visits, calls, dosing instructions or if, for any reason you have to be admitted to the hospital during the one month of insulin therapy.

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VOLUNTARY CONSENT
All the above has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of this research study during this study, and that such future questions will be answered by the researchers listed on the first page of this form.

Any questions that I have about my rights as a research participant will be answered by the Human Subject Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668)

By signing this form, I agree to participate in this research study. A copy of this consent form will be given to me.

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Participant's Signature Date and time

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Participant's Printed Name

CERTIFICATION of INFORMED CONSENT
I certify that I have explained the nature and purpose of this research study to the above-named individual(s), and I have discussed the potential health benefits and possible risks of study participation. Any questions the individual(s) have about the study have been answered, and we will always be available to address future questions as they arise.

_____

Printed Name of Person Obtaining Consent Role in Research Study

_____

Signature of Person Obtaining Consent Date and time