Department of Veterans Affairs

Research Consent Form

Participant Name: _____ Date: _____

Title of Study: Improving glycemic control and clinical outcomes in DM2 patients in the ambulatory setting, a pilot study.

Principal Investigator: Ilias Spanakis, MD Facility: VA Maryland Health Care System

"improving Glycemic Control in DM2 Patients in the Ambulatory Setting"

Introduction

PI: Ilias Spanakis

NCT 04800471

Date: 02/26/2023

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IRB Study Number: HP-00095543

INTRODUCTION: You are being asked to participate in a research study that is being done at the VA Maryland Health Care System (VAMHCS). Before you decide to take part, it is important for you to know why the research is being done and what it will involve. This includes any potential risks to you, as well as any potential benefits you might receive.

Read the information below closely, and discuss it with family and friends if you wish. Ask one of the study staff if there is anything that is not clear or if you would like more details. Take your time to decide. If you do decide to take part in this study, your signature on this consent form will show that you received all of the information below, and that you were able to discuss any questions and concerns you had with a member of the study team.

CONCISE SUMMARY

The purpose of this research study is to find out if using Continuous Glucose Monitoring (CGM), smart insulin pens, software applications, counselling for increasing exercise and telemedicine all together (video, secured messaging or phone) can improve glucose control and decrease risk of **hypo**glycemia (low blood sugars), **hyper**glycemia (high blood sugars), hospitalizations or emergency department visits.

You were identified as an individual who has diabetes, are treated with insulin and need help with diabetes management in order to improve your diabetes/glucose (sugars) control. If you participate in this study, you may be managed with a new telemedicine tool, which may help you to improve your glucose (sugars) values, improve your physical activity levels and avoid hospitalizations and emergency department visits. Telemedicine is a way to manage patients remotely. For example, patients with diabetes can be at home and they do not need to come at the clinic frequently, as their doctors or providers can manage their diabetes remotely. They will need to review your glucose (sugars) and insulin numbers (using the internet) and adjust your diabetes medications accordingly by telemedicine (i.e., phone, video, or secured messaging).

Participants will need to wear research related CGM devices either through the entire study or for shorter 10-day periods based on enrollment group assignment (Telemedicine [intervention] vs. control group). There will be a total of 3 or 4 clinic visits for all participants, regardless of group assignment, over 6 months. For some, there will also be a telemedicine communication follow-up

every couple of weeks. Participants will have their diabetes managed by the diabetes specialists at the outpatient diabetes clinic. At clinic visits you may have physical exams, blood and urine samples collected, and complete surveys. You will be asked to wear an acetometer device for 7 days which will help us to evaluate your exercise activity levels and whether these will improve during the duration of the study. This device is easy to use and you will be asked to wear it in your waist , like a belt. This study is voluntary. You will receive advise of how you can exercise more. Benefits of enrolling include having your diabetes managed by diabetes experts and improvement in your blood sugar control. You may have less hypoglycemia or hyperglycemia events. Your physical activity levels may increase. Risks of enrolling are described in this document but may include small discomfort or irritation with CGM sensor placement, technical problems with CGM devices or smart insulin pens or loss of confidentiality risk. You will be paid to participate in this study lasting 6 months.

If you are interested in learning more about this study, please continue reading below.

RESEARCH DETAILS

PURPOSE OF THE STUDY

High blood sugar (**hyper**glycemia) in patients with diabetes is linked to diabetes complications, a higher risk of death and a greater chance of infections.

Very **low blood sugars** (**hypo**glycemia) can also have negative effects, such as brain damage, seizures and cause fatal abnormal heart rhythms (arrhythmias). This is more likely in patients who already have coronary heart disease.

High and low blood sugars have been also associated with frequent hospital stays and/or emergency department visits. Almost all patients with Diabetes Mellitus (DM) check their glucose levels with Point of Care-**Finger Stick** Blood Glucose (POC-FSBG), by using glucometers. Continuous glucose monitoring (CGM) systems have been giving excellent clinical care in patients with Type 2 DM. They have even been approved by Food and Drug Administration (FDA) to replace the glucometers, as a way to measure glucose (sugar) values.

Many individuals with diabetes manage blood sugars with multiple insulin injections. They are instructed to measure blood sugars 3-4 times a day in order to take the correct insulin dose. These individuals are at risk for low and high blood sugars and require frequent in-clinic visits to prevent potential health issues. In-person visits may be a problem for individuals with mobility limitations,

transportation issues, or rural residencies. The COVID-19 crisis further complicates the desire to schedule in-person visits. Telemedicine (video, phone, or secured messaging) may provide a tool for health care providers to manage blood sugars without frequent in-patient clinic visits. In this research, we want to evaluate the use of CGM devices combined with smart insulin pens, software applications, and a telemedicine system (video, telephone, and/or secured messaging) in managing blood sugars for individuals with type 2 Diabetes (DM2). Telemedicine refers to a way your doctor can provide health care services to you without needing to come to the clinic in-person. Using Telemedicine, you can, instead, be managed from your home. Telemedicine will enable review your glucose (sugars) and insulin numbers (using the internet), such that the study doctors can adjust your diabetes medications accordingly, simply by contacting you by phone, secured messaging, and/or video.

STUDY PROCEDURES:
You are being asked to take part in this study as a person with Diabetes at high risk for hypoglycemia and/or hyperglycemia.

If enrolled, you would be followed and managed by the VAMHCS outpatient diabetes service for 6 months

You will be randomly assigned to one of 2 groups (like flipping a coin): 1st group (Telemedicine [intervention]) or 2nd group (Control group). You have a 50-50 chance of being enrolled in either group. During the study you will be asked to wear a CGM device. The device is easily placed with the help of a small needle.

If you are in the 1st group (Telemedicine), you will wear the CGM device through the whole study. The CGM device will be used to monitor your blood sugars and results can be seen by you and your diabetes team. You will be trained on how to share the CGM results. You will also be trained on how to use a special insulin pen to share your daily insulin intake with your diabetes team. The glucose and insulin information will be used by the team to manage your blood glucose. You will also be asked to use an additional smart insulin pen cap device that will only be used as an additional method to capture insulin dosing information. We may provide you advise of how you can exercise more and improve your physical activity levels.

If you are in the 2nd group (Control group), you will wear the CGM device 3 times (10 days each time) during the 6-month study period, to collect blood sugar readings. You and your diabetes team will not be able to see the CGM results while you wear the device. You will continue monitoring

your blood sugars with POC-FSBG which will be reviewed by your diabetes team at your clinic visits.

In both groups participants will be asked to wear an accelerometer device. This device is commonly used to evaluate the level of activity-exercise of people. Basic accelerometers are for example utilized in new smartphones. You will wear these for overall 7 days in order to evaluate of how well you exercise.

Clinic visits: The Telemedicine group will have 4 VAMHCS clinic visits and the Control group will have 4 clinic visits during the 6-month study period (see above). At these visits you may have a full physical exam and have a clinical evaluation where we will adjust your diabetes medications based on your blood sugars. You will also give blood and urine samples in the 1st floor lab, this is considered standard and a part usual care for those with diabetes and is not done for research purposes alone. As part of the research, CGM devices may be placed on you during clinic visits and surveys will also be administered during clinic visits. During 3 of these visits you will be asked to fill surveys, which will evaluate whether you had an improvement in your knowledge of diabetes management and your overall health as also to evaluate the overall clinical experience. In addition at the end of the study you will fill a survey which you will evaluate all the devices that you used during this study. If by answering these surveys you develop any depressive or anxiety symptoms , or if you develop any anxiety or depression or any psychiatric symptoms, you will be referred to psychology and psychiatry clinics as clinically indicated.

Telemedicine visits: If you are in the telemedicine group, you will additionally have phone, secure messaging, and/or video follow-ups every couple of weeks in between VAMHCS clinic visits or as your provider deems necessary. During these remote interactions with study personnel, you will share CGM results and insulin dosing data with your diabetes team which will be used to adjust diabetes medications. In 3 of these visit you will be evaluated by an exercise specialist who will give you feedback about how well you exercise and who will try to suggest ways to improve your physical activity.

Blood work and Urine Samples: Blood samples (5mL or 1 teaspoon) will be collected as part of usual care at three clinic visits for a total of 15 mLs or 3 teaspoons to evaluate your A1c, basic metabolic panel, and complete blood count. These lab tests are all considered usual care and are not being collected for research purposes alone. Urine samples (30 mL or 6 teaspoons) will also be collected to measure urine to creatinine ratios, which is as part of usual care for persons with diabetes at 3 clinic visits for a total of 90 mL or 18 tablespoons. Additional or more frequent

laboratory measurements would not be done for research purposes and may be collected if clinically necessary as part of usual care.

CGM and smart insulin pen devices are not research devices (investigational). They are already approved for use and can be used as part of usual care for individuals with diabetes. The smart insulin pen cap is not part of usual care for management of diabetes and is only being used as an additional tool to capture insulin dosing data. Software applications allow data sharing (glucose and insulin) between patients and health care providers which is also used as part of usual care for persons who use these devices. Telemedicine services is a VA approved way to deliver usual care within the VA system. The combination of all these parts (CGM + smart insulin pens + software applications to share data + telemedicine) is what is a new model of care.

A total of 30 patients with diabetes will be recruited for this pilot research study. The research study will not affect any care you are receiving already from VAMHCS primary care or other specialty services. Your participation in this clinical trial will end after 6 months.

After the study ends, it is recommended that you have a follow up appointment with your VAMHCS Primary Care Physician (PCP) and/or your diabetes care team provider.

WILL I BE TOLD NEW INFORMATION ABOUT THIS STUDY?
You will be told if any new information is discovered during the course of the research study that might affect your willingness to continue taking part in the research.

FUTURE USE OF DATA AND RE-CONTACT
Data collected from this research project may be used for future research. Subjects will not be re-contacted in the future, after the completion of the study, unless we discover missing information pertaining to your participation. In that case, you would be contacted and asked if you are willing to provide the missing information.

WHAT ARE MY RESPONSIBILITIES IF I TAKE PART IN THIS RESEARCH?
If you take part in this research, you will be responsible for:

- Complying with the study design
- Completing the study related procedures as described in this informed consent document

By taking part in this study, you agree to use the CGM, accelerometer device and smart insulin pens based on the instructions given to your group assignment. You agree to return study devices to study investigators when no longer in use. Devices that are lost or stolen will not be replaced.

POTENTIAL RISKS/DISCOMFORTS:

We often use CGM devises and have not had any skin or other types of infections or side effects. Acelerometer devices have been extensive studied and there is no known risks related to their use. However, potential risks of participation include the following:

1. Continuous Glucose Monitor: You may experience a small amount of pain or discomfort at the CGM, smart pen, or blood draw site. Sometimes it can cause a bruise. Rarely, some people get an infection or redness at the site. If this happens, you will be given antibiotics and medicine to decrease the pain. To decrease the risk infection, we will clean the site before each procedure. You will be trained on how to use the CGM, smart insulin pen devices, and the smart insulin pen cap. We will also check for signs of irritation or infection at your clinic visits. The CGM adhesive may irritate your skin. A barrier film will be used to provide protection to your skin, if necessary.

2. Privacy and Confidentiality: Your data will be kept confidential to the fullest extent possible. There is a small chance that your research data (CGM and smart pen) could be lost or accidently released when using the software applications and telemedicine systems. To ensure confidentiality and secrecy, you will be assigned a study number. Your data will be labeled with this study number. Therefore, your transmitted glucose and insulin data by internet will contain only values and subject identification number with no references to your personally identifiable information. The study software applications (Glooko/Clarity) and telemedicine systems (secure messaging, telephone, and VA Video Connect) are already approved for use in the VA clinical setting. Your research documents will be stored at the Baltimore VA. Paper documents will be filed in cabinets in the PI's and/or study coordinator's offices. The access to this information is limited to research team members. The offices and file cabinets will be locked when not in use by the research team. Electronic data will be stored on VA password protected computers behind the VA firewall.

3. Technical Problems: It is possible, but not likely, that the CGM, smart insulin pen, smart insulin pen cap will have a technical problem. We are familiar with troubleshooting any problems it may have. For example, your glucose value may not be displayed by the CGM receiver (loss signal). This technical issue is fixed by making sure you are within 20 feet of the receiver. Your CGM device may need to be replaced if this solution does not resolve the problem. CGM adhesion is

another potential technical problem. Adhesion issues may be caused by lotion usage near the CGM location. You will be asked to refrain from using lotion at the CGM site. We may apply adhesive spray or tape to your CGM site to resolve the adhesion problem.

4. During clinic visits your doctors/providers and team members may ask you questions or you may fill surveys that may increase your anxiety or cause depression. If this happens you will be referred to psychology and psychiatry clinics as clinically indicated.

5. Unknown Risks: There may be other risks in this study which are not yet known. You will be notified if any new risks are discovered during your study participation.

POTENTIAL BENEFITS

A direct benefit cannot be guaranteed for taking part in this study. A potential benefit of taking part may be improved blood sugar levels. You will have a diabetes expert manage your diabetes care while you take part. You may have fewer hypoglycemic and/or hyperglycemic events which are can result in improved health. By encouraging you to exercise more you may become more physically active.

ALTERNATIVES TO PARTICIPATION

Your alternative is to not take part. If you choose not to take part, your healthcare at the VA Maryland Health Care System (VAMHCS) will not change. If you decide not to take part, you will still get the same standard of care and your diabetes will be managed by your primary care team. Our diabetes team can assist with the management of diabetes if that is requested by the primary team.

COSTS TO PARTICIPANTS

You will not be charged for any treatments or procedures that are performed for research purposes in this study. If you usually pay co-payments for VA care and medications, you will still pay these co-payments for VA care and medications that are not part of this study. It will not cost you anything to take part in this study.

PAYMENT/REIMBURSEMENT TO PARTICIPANTS
You will be paid 50$ in three different time periods which time periods will be approximately after enrollment as also 3 months and 6 months following enrollment. Overall, you will be compensated with $150 for taking part in the study.

MEDICAL TREATMENT AND COMPENSATION FOR INJURY
The VA will provide treatment for research related injury in accordance with applicable federal regulations (38 CFR 17.85). Every reasonable safety measure will be used to protect your well-being. If you are injured as a result of taking part in this study, the VAMHCS will provide necessary medical treatment at no cost to you unless the injury was due to your not following the study procedures. This care may be limited by local or federal law.

If you have a medical concern or get hurt or sick from taking part in this study, call: Dr. Ilias Spanakis MD at 410-605-7394, during the day or after hours.

The VA does not normally give any other form of compensation for injury. However, by signing this form, you have not waived any legal rights or released the VAMHCS, or its agents from liability for negligence.

CONFIDENTIALITY AND ACCESS TO RECORDS
Information from this research study will be kept confidential as required by law. The results of this study may be published for scientific purposes. Your records or identity will not be revealed unless required by law.

Only approved research team members and the company that is providing the CGM devices will see your information. On all study forms and papers, you will be known only by a code number. Any papers linking your name to the research information (including this consent form) will be kept in a locked file cabinet in a locked office. All electronic research data will be kept on password protected computers at the Baltimore VA Medical Center, behind the protective VA firewall. All data taken from your medical record will be tagged by a code number so that your name or any other identifying information will not show on that data. When the research data is studied and the results are published, they will be shown as a group with no personally identifiable information.

The Veterans Health Administration (VHA) and its Offices may review your research records. Your research records will be stored at the VA Maryland Health Care System (VAMHCS). Your research records and/or identifiers will be kept according to the VA records control schedule. The "records control schedule" is a set of rules set by the federal government that states when federal agencies are allowed to dispose of records. The VA and VHA must follow these rules.

During the study period, the study team will review data from your medical record. We will look at:

- lab tests (HbA1c, BMP, urine albumin to creatinine ratios),
- Weight, height, vitals,
- medication use,
- medical care during the study period,
- and past medical history.

The data from the study may be published. However, you will not be identified by name. People designated from the institutions where the study is being conducted and people from the sponsor will be allowed to inspect sections of your medical and research records related to the study. Everyone using study information at the VAMHCS will work to keep your personal information confidential. Your personal information will not be given out unless required by law or authorized by you. However, if your information is disclosed to other entities, the VAMHCS no longer has control of that information. Please see the "Health Information Portability and Accountability Act" section below for further details.

If you are a patient in the VAMHCS, the results of your medical tests for this study may be included in your medical record. Your medical and research records will be kept strictly confidential to the fullest extent permitted by law.

Efforts will be made to limit your personal information, including research study and medical records, to people who have a need to see it. We cannot promise complete secrecy. Organizations that may look at and copy your information include:

- the University of Maryland IRB,
- the VA Office of Research and Development,
- VA Office of Research Oversight (ORO),
- Office for Human Research Protections (OHRP),
- VA Office of Inspector General (OIG),

- VAMHCS Office of Research Compliance,
- and other representatives of this organization.

The monitors, auditors, the IRB, and regulatory authorities will be given direct access to your medical records to verify the research procedures. By signing this document, you are approving this access.

Health Information Portability and Accountability Act (HIPAA)

There are rules to protect your private health information. Federal and state laws and the federal medical law, known as the HIPAA Privacy Rule, also protect your privacy. By signing this form, you provide your permission called your 'authorization,' for the use and disclosure of information protected by the HIPAA Privacy Rule.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical records such as medical history, medication history, age, gender, race.

The research team may also need to disclose your health information and the information it collects to others as part of the study progress. Others may include the VA Cooperative Studies Program (CSPCC); CSP Clinical Research Pharmacy Coordinating Center (CSPCRPCC); CSP Site Monitoring; Auditing and Review Team (SMART); CSPCC's Human Research Committee (HRC)]; DEXCOM (San Diego, California) who provided some of the CGM supplies, Institutional Review Board, Food and Drug Administration, Office (FDA), Office of Human Research Protections (OHRP), the VA Office of Research Oversight (ORO), and the Government Accountability (GAO).

Your health information disclosed pursuant to this authorization may no longer be protected by Federal laws or regulations and may be subject to re-disclosure by the recipient.

You can revoke this authorization, in writing, at any time. To revoke your authorization, you must write to the Release of Information Office at this facility or you can ask a member of the research team to give you a form to revoke the authorization. Your request will be valid when the Release of Information Office receives it. If you revoke this authorization, you will not be able to continue to

participate in the study. This will not affect your rights as a VHA patient to treatment or benefit outside of the study.

If you revoke this authorization, Dr. Ilias Spanakis and his research team can continue to use information about you that was collected before receipt of the revocation. The research team will not collect information about you after you revoke the authorization.

Treatment, payment or enrollment/eligibility for benefits cannot be conditioned on you signing this authorization. This authorization will expire at the end of the research study unless revoked prior to that time.

WILL MY INFORMATION BE USED FOR RESEARCH IN THE FUTURE?
Information collected from you for this research may be used for future research studies or shared with other researchers for future research. If this happens, information which could identify you will be removed before any information or specimens are shared. Since identifying information will be removed, we cannot ask for your additional consent.

RIGHT TO WITHDRAW
Your participation in this study is voluntary. You do not have to take part in this research. You are free to withdraw your consent at any time. Refusal to take part or to stop taking part in the study will involve no penalty or loss of benefits to which you are otherwise entitled. Your participation will not affect the way you now pay for medical care at the VAMHCS.

If you decide to stop taking part, if you have questions, concerns, or complaints, or if you need to report a medical injury related to the research, please contact the investigator Dr. Ilias Spanakis [PI] at 410-605-7394.

There are no negative consequences (physical, social, economic, legal, or psychological) of a participant's decision to withdraw from the research.

If you withdraw from this study, already collected data may not be removed from the study database. You will be asked whether the investigator can collect data from your routine medical care. If you agree, this data will be handled the same as research data.

You will be told of any significant new findings which develop during the study which may affect your willingness to participate in the study.

CAN I BE REMOVED FROM THE RESEARCH?
The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include failure to follow instructions of the research staff, if the person in charge decides that the research study is no longer in your best interest. The sponsor can also end the research study early. The study doctor will tell you about this and you will have the chance to ask questions if this were to happen.

The VA Maryland Health Care System (VAMHCS) has designated the University of Maryland Baltimore (UMB) Institutional Review Board (IRB) to review this research study.

If you wish to confirm that this study is in fact IRB approved and is being conducted at the VAMHCS, or if you have any questions, concerns, complaints, you may contact:

University of Maryland Baltimore
Human Research Protections Office
620 W. Lexington Street, Second Floor
Baltimore, MD 21201
410-706-5037

You may also contact the VAMHCS Research Protections Officer (RPO)**.**

VAMHCS Research Protections Officer
Baltimore VA Medical Center
10 North Greene Street, Mail Stop 151
Baltimore, MD 21201
410-605-7000, extension 56510

The VAMHCS Research Protections Officer may contact you in the future to ask you about your experiences with this research study.

Participant Name: _____ Date: _____

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Principal Investigator: Ilias Spanakis, MD Facility: VA Maryland Health Care System

AGREEMENT TO PARTICIPATE IN THE RESEARCH STUDY

Your signature indicates that the research team member obtaining consent has explained the research study to you. You have been told of the risks or discomforts and possible benefits of the study. You have been told of other choices of treatment available to you. You have been given the chance to ask questions and obtain answers.

By signing this document below, you voluntarily consent to participate in this study and authorize the use and disclosure of your health information for this study. You also confirm that you have read this consent or it has been read to you. You will receive a copy of this consent after you sign it.

I agree to participate in this research study as has been explained in this document.		
_____ Participant's Name (Print)	_____ Participant's Signature	_____ Date

_____ Person Obtaining Consent (Print)	_____ Consenter's Signature	_____ Date