INVESTIGATOR STUDY PLAN - REQUIRED

Title: Continuous Glucose Monitoring in the Intensive Care Unit

NCT Number: NCT06190808

Unique Protocol Id STUDY00001138

Document Date: December 1, 2023

INSTRUCTIONS:

- **Provide information once.** It's better to refer to earlier items (e.g., "See #...") than to repeat.
- **If an item does not apply, type "NA."**
- **If the information is available in a sponsor protocol, grant, investigator brochure, or proposal – for any item marked with an asterisk (*) – simply reference the title and page numbers of that reference document and upload a copy of the document to eIRB.**
- **Delete instructions as you answer each item.**
- **Use a version number or date in the file name. When you upload the document to eIRB, leave the optional fields blank so that eIRB uses the file name to label the document.**

1. TITLE
Continuous Glucose Monitoring in the Intensive Care Unit: Validation and Implementation

2. EXTERNAL IRB REVIEW HISTORY*
NA

3. PRIOR APPROVALS:
UMMMC Intensive Care Unit (ICU) Committee approvals

- Director of UMMMC 6-ICU and 7-ICU, Nicholas Smyrnios, MD
  - See updated letter in Local Site Documents/#3
- 6-ICU Nurse Manager, Fred Osterberg, RN, and 6-ICU and 7-ICU Nurse Education Safety Specialists, Tarryn Long, RN and Kelly Joyce, RN
  - See letter in Local Site Documents/#3
- 7-ICU Nurse Manager, Justina Devries. RN
  - See letter in Local Site Documents #3

Conflict of Interest (COI):
NA

Clinical Engineering Department:
The Clinical Engineering Department has been contacted at 508-334-1111. They have agreed to inspect the G7 continuous glucose sensor (Fig. 1), cell phone, cell phone charger, iPad, and iPad charger before their initial use in the study. Earlier versions of the Dexcom continuous glucose monitor (CGM) have received emergency authorization for use in hospital settings, and some are in use in non-ICU settings at UMMHC.

Biohazardous Agents:
NA

***Radiation**:*
NA

***Students as Subjects**:*
NA

Research Informatics Core:
The Research Informatics Core has been informed of the design and requirements of the study and quoted a budget. All data extraction from the UMMMC Electronic Medical Record be performed by the Research Informatics Core. The Research Informatics Core will construct a de-identified database with 1) time-stamped glucose concentration data obtained in the course of usual care in 6-ICU and 2) time-stamped glucose concentration data obtained from Dexcom G7 continuous glucose sensors. The Research Informatics Core will also perform the two key statistical analyses comparing usual care data with CGM data, the 'Mean absolute relative difference' (MARD, expressed as a percentage) and the Clarke Error Grid.
These procedures have been reviewed by

Yurima Guilarte-Walker, MS, Director, Research Informatics Operations
Adrian Zai, MD, PhD, MPH, Chief Research Informatics Officer
Bruce Barton, PhD, Biostatistician, Research Informatics Core

UMCCTS Protocol Review Committee (PRC)
This protocol was submitted to the PRC and their recommendations were incorporated into the prior version of this ISP. See letter in Local Site Documents/#3
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4. OBJECTIVES*

The aim of the proposed clinical trial is to study the use of the Dexcom G7 continuous glucose monitor (CGM) within the intensive care unit (ICU) environment. The overall goal is to validate the accuracy and practicality of the Dexcom G7 when used to assess glycemia in critically ill patients. The specific goals are 1) to work with ICU staff, in a respiratory ICU setting, to determine how best to place and maintain sensors on patients and how to place recording devices and chargers in that environment, 2) download CGM readings to the Dexcom Dashboard in an analyzable format, and 3) to compare simultaneous CGM readings with glucose measurements obtained in the course of routine care as recorded in the electronic medical record. The primary analytical goal is the correlation of CGM glucose measurements with those obtained in the course of routine care. A secondary goal is to determine the frequency of device malfunctions that occur



Fig. 1. The Dexcom G7 Sensor

either as a result of device failure (*e.g*. it falls off) or adverse events (*e.g*. removal due to skin irritation).

5. BACKGROUND*

Dysglycemia (both hypo- and hyperglycemia) is associated with increased morbidity and mortality in hospitalized patients, including inpatients not known to have diabetes prior to hospitalization. Point-of-care "fingerstick" glucose measurements and plasma glucose testing have been the gold standard in the hospital setting, but these methods have significant limitations in that they capture only intermittent single-point-in-time data. CGM technology offers significant advantages in capturing blood glucose trends over time that would allow for earlier and more timely therapeutic interventions. CGM permits determination of time in range (TIR), glycemic variability (GV), and glycemic risk index (GRI), all of which also reportedly influence morbidity and mortality in the outpatient setting. CGM devices have only recently been approved under emergency use in the inpatient setting, and research is necessary if CGM is to become a standard of ICU care. A 2022 meta-analysis of 16 studies of CGM use in the ICU concluded that the quality of existing studies is only "low to moderate" and that additional controlled trials are needed. We hope to build on previous preliminary studies and show that CGM is accurate in the ICU and has the potential to be integrated with insulin infusion algorithms.

6. INCLUSION AND EXCLUSION CRITERIA*

Inclusion:

- Patients admitted to either the 6-ICU or 7-ICU UMass Memorial Medical Center (UMMMC) University Campus medical intensive care unit for any reason who have known diabetes or who are hyperglycemic (blood glucose concentration ≥200 mg/dL) with diabetes that was previously undiagnosed or unrecognized.
- Persons with either type 1 or type 2 diabetes.
- Persons of either sex.
- Persons of any age over 18.
- Persons able to give informed consent or cognitively impaired adults whose legally authorized representative (LAR) can give informed consent.
- English or Spanish speaking adults.

Exclusion:

- Persons unable to provide informed consent.
- Cognitively impaired persons whose LAR declines to provide informed consent.
- Patients receiving hydroxyurea, which interferes with sensor function.
- Patients receiving high dose acetaminophen (> 4 gm/day), which interferes with sensor function.
- Anasarca affecting preferred areas for device placement (arm, upper buttocks, or thigh), which may interfere with sensor accuracy.
- Severe cachexia with absence of subcutaneous fat at preferred sensor placement sites, which might interfere with sensor accuracy.
- Persons who are pregnant.
- Prisoners.

7. STUDY-WIDE NUMBER OF SUBJECTS*
NA

8. STUDY-WIDE RECRUITMENT METHODS*
NA

9. STUDY TIMELINES*

- *The duration of an individual subject's participation in the study*
  10 days (the maximum lifetime of G7 sensors) or time to discharge from the ICU (average of 4.5 days)
- *The duration anticipated to enroll all study subjects.*
  3 to 6 months
- *The estimated date for the investigators to complete this study (complete primary analyses)*
  12/30/2024

10. STUDY ENDPOINTS*
Describe:

- Comparison of glucose concentration in hyperglycemic ICU patients as determined in the course of routine care and recorded in EPIC, with glucose concentrations as measured by the Dexcom G7 CGM. Comparisons will use two standard analytic tools for comparing glucose measurement devices, the Clarke Error Grid, and the calculation of Mean Absolute Relative Difference (MARD).
- The principal safety measures to be recorded are: 1) the frequency of skin irritation, 2) the frequency of insertion site infection, and 3) any interference with other telemetry signals present in the ICU.



Fig. 2, the Dexcom G7 sensor and applicator

11. PROCEDURES INVOLVED*

- Volunteers who meet the inclusion/exclusion criteria will have a G7 glucose sensor/transmitter (Fig 1.) applied to the skin of an arm or leg using the Dexcom Application device following manufacturer's instructions (Fig. 2).
- ICU nurses will be trained to apply the device by the 6- and 7-ICU Nurse Education Safety Specialists (NESS, either Tarryn Long, RN or Kelly Joyce, RN) on the ICU floor during the nurses' shifts in the 2-4 weeks prior to the start of patient enrollment. The 6- and 7-ICU NESS and/or Nurse Managers, Fred Osterberg, RN or Justina DeVries will report to the Study Coordinator that this training has taken place before any patients are enrolled.

- The training material consists of the manufacturer's instructions at https://www.dexcom.com/en-us/dexcom-g7-setting-up-your-system. A copy of the link to this video will be kept in the PI's Regulatory Binder.
- The sensor is held in place by an adhesive patch visible in Fig 1. An overcover is applied after the CGM is in place to protect the device and insertion site from contamination. A video showing the procedure for applying and setting up a G7 sensor is available at https://www.dexcom.com/en-us/dexcom-g7-setting-up-your-system.
    - ICU nursing staff in consultation with ICU medical staff will identify a suitable placement site on an arm, thigh, or upper buttock that is not edematous and has subcutaneous fat present and that will not interfere with routine ICU care. Sensors will be applied as far as possible from intravenous lines or sites of injections. The manufacturer specifies at least 3 inches.
    - The practitioner identified to place the sensor will inspect and open the box with the device to confirm that it contains an undamaged, unopened Dexcom G7.
    - The site of application will be cleansed with an alcohol wipe.
    - The box will be opened, and the applicator removed and opened by unscrewing the cover on the bottom.
    - The sensor will be applied by pushing the button on the applicator using sterile technique (*i.e*. not touching the sensor wire)
    - The sensor will be inspected for correct placement.
    - The protective film on the overcover will be removed and the overcover layer will be applied over the sensor to increase adherence and prevent contamination.
    - The device will be paired using the Bluetooth communication protocol to an Apple smartphone that has been supplied by UMMMC Information Technology, is accessible only to study and ICU nursing staff, and is connected only to the encrypted UMMHC internal internet Wi-Fi.
    - The G7 requires a 30-minute stabilization period before readings become accurate.
- For safety monitoring, the sensor placement site will be inspected visually for signs of infection or dermatitis on every nursing shift. Patients able to communicate with nursing staff will be asked if the sensor is causing pain or discomfort. Any safety issues will be communicated to the ICU attending physician, Study Coordinator, and PI. All adverse events will be recorded in EPIC on a flow sheet created for use in this study (see below) by the patient's caregivers. The data will be entered in EPIC as described in the next bullet, and these records will be available to the study staff and the Research Informatics Core as part of the study.
- As shown in Figures 3 and 4 (below), nursing documentation tabs in EPIC will be used to record the qualitative event and pain and safety data checklists. The nursing staff will record these data as needed on the basis of clinical judgment. The staff of the Research Informatics Core will have access to these data and incorporate them into their statistical analyses.
- ICU nurses will be trained in the use of the new fields (Figures 3 and 4, below) in EPIC by the 6- and 7-ICU Nurse Education Safety Specialists (NESS, either Tarryn Long, RN or Kelly Joyce, RN) on the ICU floor during the nurses' shifts in the 2-4 weeks prior to the start of patient enrollment. The ICU NESSs and/or Nurse Managers, Fred Osterberg, RN and Justina DeVries, RN will report to the Study Coordinator that this training has

taken place before any patients are enrolled. We will document the training of nurses to apply the Dexcom G7, to pair the G7 with the Dexcom app, and to access and use the study-specific tabs and fields in EPIC training in a training log that includes an attendance list, dates of training, and copies of materials used for training. Copies of the training log will be kept in the PI's Regulatory Binder. These fields will be filled out up to twice per shift but only when an adverse reaction occurs.

- Specifically in regard to pain as a possible adverse event, patients in both ICUs are routinely asked at least once per shift if they have pain. If there is pain reported, the next step will be to determine whether or not it localizes to the study device, as pain is not uncommon in ICU patients. If pain associated with the device is noted, it and its severity will be recorded in the study-specific EPIC (See Figure 3). Larger images of Figures 3 and 4 have been uploaded to: Local Site Documents/#3
- This electronic checklist, along with the patient's medical record number, will be accessible to the PI, co-investigators, and the Study Coordinator. It will also be accessible to the Research Informatics Core when the patient is discharged from the ICU. The study team will ensure the existence of an index, preferably the patient's MRN, that connects the CGM data with the EPIC clinical information pertaining to the EPIC encounter.
- If signs of infection or dermatitis at the site of sensor insertion are observed the sensor will be removed.
- The removal of the device (when it has reached its 10-day expiration or when a patient is transferred out of the ICU) or when dermatitis or infection at the site of sensor insertion is observed will follow these steps.
    - First the adhesive films holding the sensor in place will be removed using the techniques used to remove a Band-Air or any medical adhesive tape.
    - The sensor will be lifted off the skin and discarded in a biohazards container.
    - The insertion site will be inspected for dermatitis or infection or retention of the sensor wire and, if present, the ICU medical staff and the PI or Study Coordinator will be notified so that appropriate care may be given. In addition to being reported to the PI, the nature of all adverse events, including nature, extent, and severity, will be extracted from the AE tab we are placing in EPIC (See Figures 3 and 4) by the Research Informatics Core for statistical analysis.
    - If there is bleeding from the sensor insertion site, a sterile gauze pledget will be applied to the site and held in place with a piece of medical tape. Any bleeding would be expected to be similar in quantity to that which occurs after administration of a flu shot.
- If a sensor should fall off, be bumped off, or need to be removed because an MRI scan needs to be performed, it will subsequently be replaced at a fresh site as described above, and this will be documented as in Figure 4.

- AEs that require medical intervention (pain, infection, and rash, in particular) will be handled per protocol by removal of the device; these AEs will be treated using appropriate medical care as determined by the team caring for the patient. Minor AEs (*e.g.* the device fell off or had to be removed due to imaging procedures or stopped working or had to be moved to a new location for to patient positioning requirements) will be handled by replacement of the device with a new one by nursing staff. The Study Coordinator and PI will be notified of these events and ensure that the protocol is

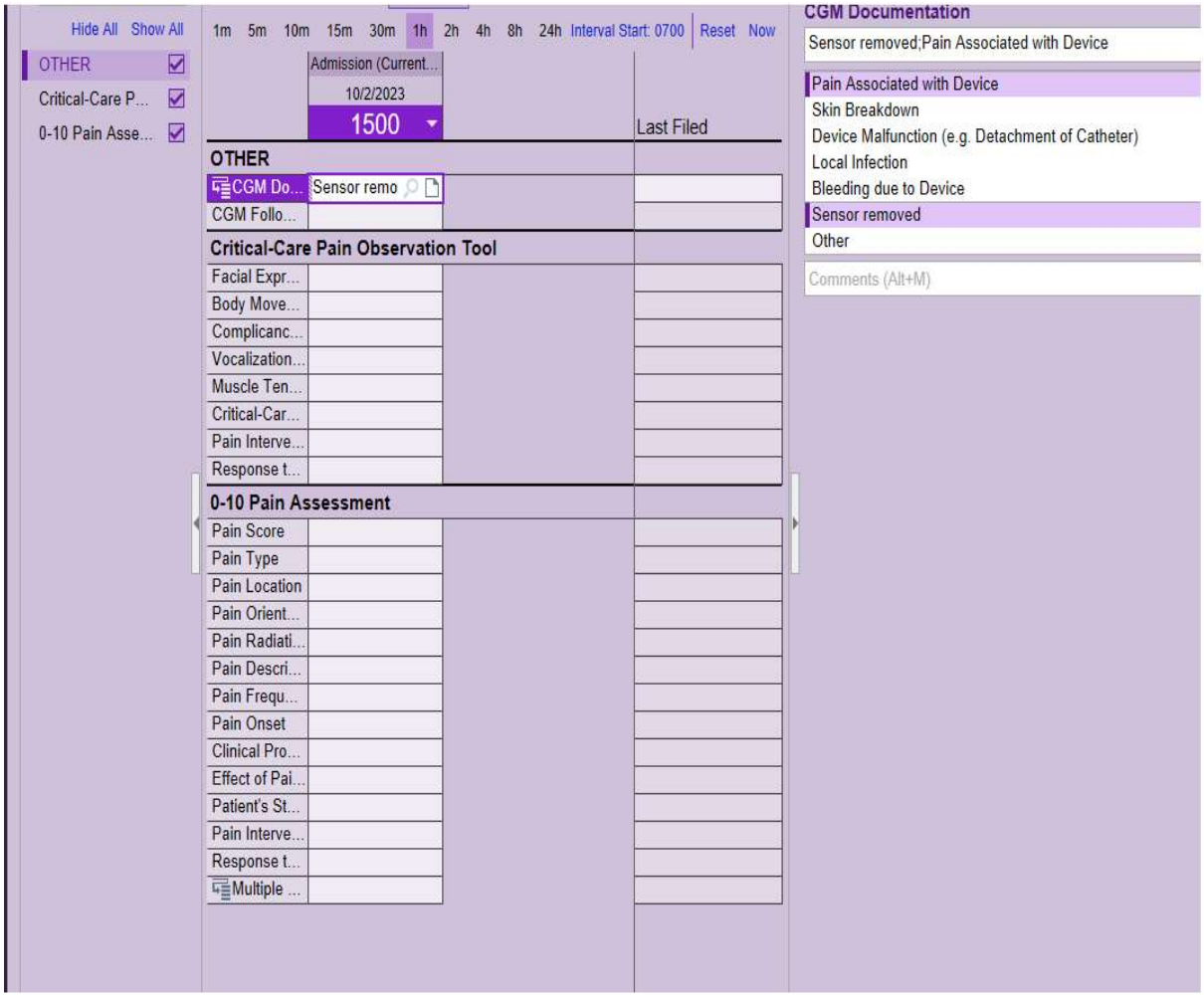


Figure 3. The Adverse Events and Pain Scale recording Tab that has been created in EPIC. The Critical Care Pain observation Test (CPOT) with be used for intubated patients and 0 to 10 Pain Assessment Score for non-intubated patients.

followed. The PI plans to be in touch regularly in person, by phone, by text, or by email, with the Director of 6- and 7-ICU and the Head Nurses of 6-ICU and 7-ICU to coordinate the response to AEs. As noted in the protocol, the probability of a serious AE, based on the widespread use of CGM in outpatients, is estimated to be extremely low. The Study Coordinator will be in daily contact with 6- and 7-ICU nursing staff to ensure that the protocol is followed and to determine the dates of study entry and study exit (e.g.

discharge from the ICU) for each subject. Neither the Study Coordinator nor the PI will provide direct patient care.

- There are no written notes created as part of this study. Adverse events for statistical analysis and eventual reporting in the scientific literature will be extracted from EPIC and analyzed by the RIC. Glucose concentration data obtained during routine care will be extracted from EPIC by the RIC. CGM data will be transmitted with no patient identifiers directly to the Dexcom cloud website and downloaded by the RIC staff to compare with the routine care glucose concentration data. AE data for analysis will be extracted from the EPIC study tabs shown in figures 3 and 4. These are all the data necessary for the conduct of the research. The Study Coordinator will provide the RIC staff with the patient medical record number and dates when in the study to enable the RIC staff to perform their tasks.
- All data collection and extraction during sensor use and after sensor removal, both from medical record and from the iPad that will record CGM readings will be performed by personnel of the Research Informatics Core in accordance with IRB regulations.
- Data analysis will be performed by Dr. Bruce Barton of the Research Informatics Core in collaboration with the PI.
- Study investigators will have no access to data that are not de-identified after the patient is discharged from the ICU.
- However, there exists the risk that the UMMHC electronic records system, computers used by the UMass Clinical Research Core and the UMass Research Informatics Core could be breached and expose patient data. These risks are believed to be small but are non-zero.

- This is a study of devices, comparing standard care glucose measurement with CGM measurement. No randomization is involved. Study participants are not required to participate actively in the study, only to allow the CGM to be placed.

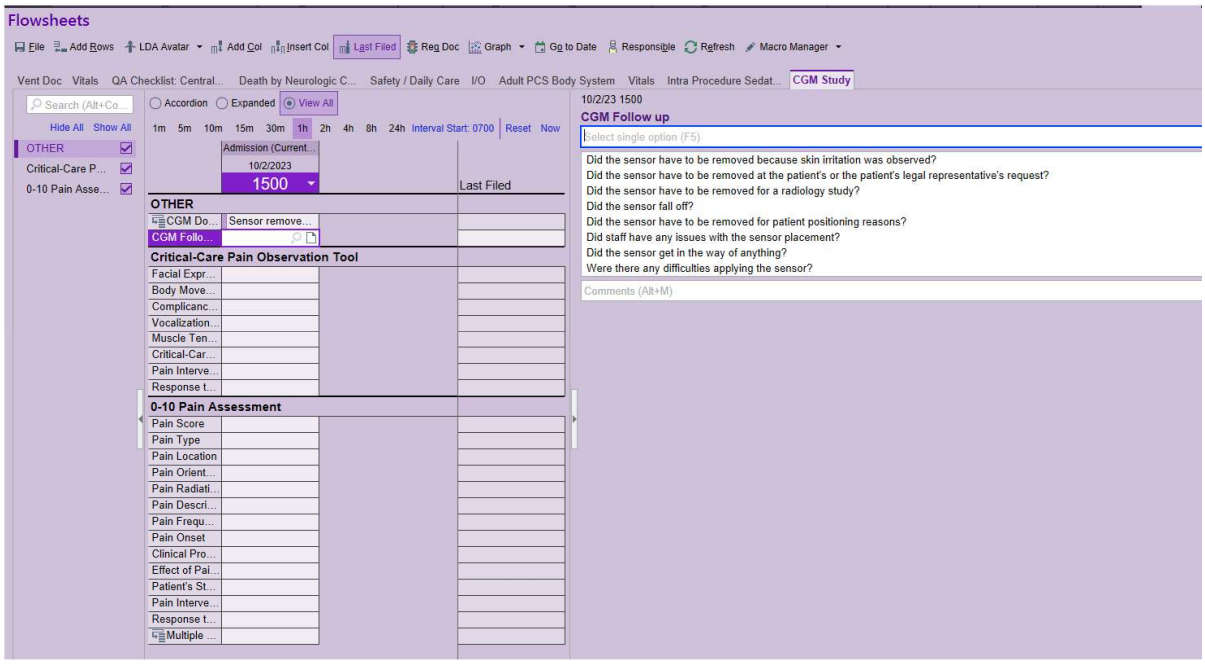


Figure 4: CGM-related pain and "other events" assessment sub-tab for the Pain item shown in Figure 3.

- The nature and timing of activities to be completed by study staff, nursing staff, and other clinical staff are as follows:
  1. Before the study begins, study staff (PI, co-investigators, and study coordinator) will provide the devices, teach nursing staff how and where to apply the devices, teach nursing staff how to remove the devices, teach nursing staff how to record AEs using the EPIC tab shown above, identify patients appropriate for enrollment in the study, obtain informed consent, address any questions and concerns raised by nursing staff or physicians, and assume overall responsibility for the conduct of the study.
  2. When a study patient has been enrolled and is in an ICU bed, nursing staff who work in 6- or 7-ICU will apply the CGM devices, pair the devices by Bluetooth with the cell phones, remove devices, record any AEs in EPIC, and notify study staff of any AEs, questions, or concerns. They will also provide routine patient care to enrolled ICU patients, not using any data generated by the CGM.
  3. Other ICU clinical staff (physicians, physician assistants) provide routine patient care of enrolled ICU patients. They will not use any data generated by the CGM, will address any AEs identified by nursing staff and respond as appropriate based on their medical training, They will notify study staff of any questions or concerns.

*For **medical record review**,*
NA

Humanitarian Use Device *(HUD)*
NA

12. DATA AND SPECIMEN BANKING*

- No biological specimens will be collected or banked.
- Glucose concentration data from the CGM sensor/transmitter will be transmitted by Bluetooth to a UMMMC-supplied iPhone and then by encrypted Wi-Fi to an iPad located in the ICU. Data extraction from the iPad into the study database stored along with blood sugar laboratory values from the electronic medical record will be stored in an anonymized database maintained by the Research Informatics Core.
- The Apple cell phones to be used are encrypted, are managed by UMMMC) and will used the encrypted UMMMC Wi-Fi network. Data that is obtained by or transmitted to the Research Informatics Core will be kept secure by the Core. The information in the transmission does not readily identify a subject.
- There are no plans to destroy the deidentified results database, as the deidentified results will be used form the basis of 1) a publication of the results and 2) additional studies of CGM in UMass ICUs
- By deidentification is meant that there will be no protected health information banked or recorded permanently. This means there will be no dates, zip codes or any of the 18 HIPAA identifiers listed at https://privacyruleandresearch.nih.gov/pr_08.asp .

13. Data Analysis and Management*

- Data entry into the Epic EMR will happen in the course of routine care. Data extraction from Epic into the study database will be performed by Research Informatics Core personnel.
- Data from the CGM sensor/transmitter will be transmitted by Bluetooth to a cell phone and then by Wi-Fi to an iPad located in the ICU nursing station. Data extraction from the iPad into the study database will be performed by Research Informatics Core personnel.
- Data analysis will be performed collaboratively by Research Informatics Core personnel and the Principal Investigator.
- Comparison of glucose concentration in hyperglycemic ICU patients as determined in the course of routine care and recorded in EPIC, with glucose concentrations as measured by the Dexcom G7 CGM. Comparisons will use two standard analytic tools for comparing glucose measurement devices, the Clarke Error Grid and the calculation of Mean Absolute Relative Difference (MARD). The MARD, in particular, will generate a percentage indicative of covariance and is not sensitive to type 1 or 2 errors.
- Statistical Power Considerations/Number of subjects
    - A typical patient in the ICU will generate approximately 5-8 glucose readings daily using current methodology.
    - The average 6-ICU stay for respiratory patients with hyperglycemia is 4-5 days with a median length of stay of approximately 3 days. The median and average lengths of stay in 7-ICU are approximately the same.
    - Conservatively, each patient will generate 15-40 routine care glucose data points.
    - To obtain 400-600 routine care datapoints, we plan to enroll 24 study subjects.
    - The CGM will generate a reading every 5 minutes. The three CGM datapoints flanking a ‘usual care’ datapoint will be averaged.

  - The reported MARD for the G7 in outpatient use is 8%; 400-600 readings will be adequate to determine if similar accuracy applies to ICU use or not.
- *Describe any procedures that will be used for quality control of collected data.*
  - The Research Informatics Core (RIC) will download digital data. The Research Informatics Core supports investigators by creating innovative solutions to enable the seamless integration of the multiple layers of medical expertise with the vast landscape that is this dense data environment. Together, the investigator and RIC produce the rigorous analysis outcomes necessary for data-intensive research projects (https://www.umassmed.edu/research-informatics/). RIC personnel are not involved in ICU care and do not overlap with ICU staff. Research Informatics Core personnel will also input Qualitative Data recorded in EPIC as described above (Section 11). As shown in Figure 4, examples of qualitative data to be recorded in EPIC include:

    >Did the sensor have to be removed because skin irritation was observed?
    >Did the sensor have to be removed at the patient's or the patient's legal representative's request?
    >Did the sensor have to be removed for a radiology study?
    >Did the sensor fall off? Did the sensor have to be removed for patient positioning reasons?
    >Did nursing staff have any issues with the sensor placement?
    >Did the sensor get in the way of anything?
    >Did nursing staff suggest a better placement for the smart phone?
    >Were there any difficulties applying the sensor?
    The Research Informatics Core will have responsibility for assuring the integrity and accuracy of all data collected.

14. PROVISIONS TO MONITOR THE DATA TO ENSURE THE SAFETY OF SUBJECTS*

- This research uses a device that is already FDA approved for outpatient use and involves only Minimal Risk. The data generated by the CGM will not be used for patient care.
- For safety monitoring, the sensor will be inspected visually for signs of infection or dermatitis on every nursing shift as described in Section 11.
- Patients able to communicate with nursing staff will be asked if the sensor is causing pain or discomfort.
- The following Stopping Rule will be used: If signs of infection or dermatitis (redness, exudation, tenderness) at the site of sensor insertion are observed the sensor will be removed and not replaced.

15. WITHDRAWAL OF SUBJECTS WITHOUT THEIR CONSENT*

Withdrawal of subjects will consist of removal of the G7 CGM. Reasons that this might happen include:

Accidental dislocation of the device.
Skin irritation.
Skin infection.
At the request of ICU providers in the event that the device is perceived to interfere in some way with routine care.

Removal of the CGM will have no impact on patient care.

16. RISKS TO SUBJECTS*

- Each application of the CGM device may cause transient discomfort comparable to that which will be caused by the fingerstick glucose measurements that are part of routine care. Most subjects will have only one sensor applied.
- The sensor may cause skin irritation (most likely due to the adhesive used), and it will have to be removed. Removal of the G7 device due to skin irritation is estimated by UMMMC Diabetes Center of Excellence personnel to be necessary in no more than 10% of cases.
- The device may be associated with a skin infection and will have to be removed.
- As the data from the CGM will not be used for patient care, there is very little risk of adversely impacting usual medical care.
- Study subjects will not incur any costs for the sensors, smartphones, or research procedures.
- There is very little risk of bleeding caused by application of the sensor; according to the manufacturer this potential risk is "rare". However, because the sensor penetrates the skin slightly, there is a risk of bleeding from the puncture site at the time of removal. We estimate that this risk is comparable to the risk of bleeding after receiving a flu shot.
- Risk of sensor wire detachment. The manufacturer reports that no G7 sensor wires (3 mm in length), which penetrate the skin, have detached in clinical studies; however, there is a remote chance a sensor wire could break or detach and remain under the skin. Sterile detached sensor wires are unlikely to pose a significant medical risk. If a sensor wire breaks off or detaches, remains under your skin, ICU medical staff will be contacted and standard procedures for foreign body removal implemented.

17. POTENTIAL <u>DIRECT</u> BENEFITS TO SUBJECTS*

NA

18. VULNERABLE POPULATIONS*

- Students and employees of UMass Chan Medical School and UMass Memorial Medical Center, pregnant persons, and prisoners will be excluded.

- ***Adults unable to consent:***
    - *How will you determine whether an adult has the capacity to consent?*
        - Patients admitted to either 6- or 7-ICU may be alert and oriented or may be cognitively impaired for many reasons including hypoxia, intubation, hypotension, neurological injury, and sedation. Determining the mental competency of patients admitted to an ICU is done routinely by ICU staff, often in the setting of clinical decision making. If ICU staff determine that the patient is competent to contribute to decision making involving their own care, then they will be approached to participate in the study by persons who are experienced in explaining medical research using appropriate language.
    - *Who will provide permission for the subject to participate? (See* HRP-013 SOP: Legally Authorized Representatives Children and Guardians*.)*

- Legally authorized representatives

- *Describe the assent process:*
  NA
- *If the impairment may be temporary, when and how will you obtain the subject's later consent?*
  - If an ICU patient's impairment is temporary and a CGM is in place, that person will be re-consented, told that the device was placed with the assent of their LAR, and asked if the device can remain in place until discharge from the ICU or, if they prefer, to have it removed.
  - No patient will at any time be forced or coerced in any way to participate in the study.

  If a participant regains capacity to consent and then declines to participate in the research, in agreement with the IRB Committee's understanding as communicated to us, the existing data will be maintained because the study is FDA regulated and data collection occurred with informed consent.
- *Explain how subjects will be closely monitored.*
  - All subjects in the ICU are, by definition, monitored closely by nursing staff and physicians.
  - Specific safety monitoring of the CGM will be performed at least once per nursing shift as described in Section 11.
- *Confirm that subjects will be withdrawn from the research if they appear to be unduly distressed.*
  - CGMs will be removed from research subjects at their request or if the CGM appears to staff to be causing stress.
- *See* HRP-417 CHECKLIST: Cognitively Impaired Adults *to ensure that you have provided sufficient information.*
  - HRP-417 has been consulted and all sections considered with regard to this low-risk study that does not affect the subjects' medical care. Because many diabetic patients admitted to the ICU are seriously ill and cannot, at least initially provide consent due to cognitive impairment due to their condition (sedation, hypoxia, etc.) the study objectives cannot be met in a timely fashion with only research involving only cognitively unimpaired subjects who can give consent personally.

19. MULTI-SITE RESEARCH*
NA

20. COMMUNITY-BASED PARTICIPATORY RESEARCH*
NA

21. SHARING OF RESEARCH RESULTS WITH SUBJECTS*

- There are no plans to share with study subjects the key results of the study, *i.e*. the correlational comparison of CGM glucose data with glucose data obtained in the course of routine care.

22. SETTING

- The study will be conducted in UMMMC 6-ICU and 7-ICU on the University Campus. Both 6- and 7-ICU have 16 beds. Like all UMMMC ICUs, both 6- and 7-ICU are connected electronically to the central UMMMC "eICU" (see section 23).
- Placement of the G7 CGM and its paired cell phone and charger will be overseen by the ICU nursing staff and Study Coordinator. A small security device will be used to prevent theft of the iPhone. Specifically, an I3C Hardware Security Cable Lock will be attached to the back of each Anker 313 Wireless Charger (Stand) [QI-certified for iPhone] device. Each iPhone is then placed on the charging stand and secured to the charging stand with a plastic electronic zip tie. The other end of the Security Cable Lock will be looped around a secure point in the room within 6 ft of the patient. Actual secure point may vary between each room. See Figure 5.



Figure 5

- The CGMs purchased for this study will be stored in the ICU supplies closet.

23. RESOURCES AVAILABLE

Describe study personnel.

- Principal investigator: Will have overall responsibility for the study. He is CITI certified and has been caring for patients with diabetes as a specialist since 1979. He has also served as local principal investigator in studies of non-invasive glucose meters and a candidate drug for the prevention of type 1 diabetes in the Clinical Research Center on the University Campus.
- Co-investigators: All co-investigators are CITI certified. They will assist the PI by bringing to bear detailed knowledge regarding the use of GGMs in outpatient care and the integration of medical devices into the "eICU" system at UMMMC. The eICU is a central monitoring facility that is staffed around the clock and receives information electronically on the multiple medical parameters (*e.g.*, pulse, blood pressure, oxygenation) for all patients in all ICUs in the UMMMC system. It has alarm systems

that alert eICU personnel to potential problems that are then communicated to the on-call caregiver in the ICU where the patient is located.
    - One Co-Investigator has more than 40 years of experience caring for persons with diabetes and is currently the Clinical Chief of Diabetes.
    - The second Co-investigator has more than a decade of experience as director of the eICU at UMMHC and is an experience4 ICU provider.
- Research coordinator: Will be appointed by the director of the Department of Medicine Clinical Research Core. All staff in the Clinical Research Core are CITI certified. The Director is an experienced ICU nurse and has headed the Clinical Research Core for many years. She will be responsible for the appointment of a Study Coordinator from among her staff. The Study Coordinator will enroll subjects and make daily rounds to record qualitative data/events as described above.
- At the 11/7/2023 meeting of the Convened IRB, the Committee determined that while the ICU nurses will be conducting research procedures, listing the ICU nurses as study staff or requiring CITI human subjects training for them would not add to the protection of the rights and welfare of subjects, and thus, as a one-time exception will not be required.
- Research informatics personnel: Will oversee the extraction of needed glucose data from Epic and the CGMs and create the identified master study database.
- The PI, an emeritus Professor of Medicine, works on site a minimum of 14 hours weekly. He will be available to the co-investigators and ICU staff by phone at all times during the study.
- In the event that the PI is not available, the Co-Investigator who is an MD and is the full-time Clinical Chair of Diabetes will assume his responsibilities and be available to address any issues that may arise.
- The second Co-Investigator is an MS, PA-C and is also available to ICU staff at all times in his role as Director of the eICU.
- The Research Coordinator will devote one to two hours per day to the study until completion.
- Describe your process to ensure that all persons assisting with the research are adequately informed about the protocol.
    - Everyone assisting with the research has been involved in its design and execution.
    - If approved, the first study procedure will be to meet with ICU physicians and staff. They have already been approached, together with the Director of 6- and 7-ICU, and, because of the potential of the CGM to improve care, save time, and reduce the pain inflicted on patients by fingerstick testing, enthusiasm has preliminarily been expressed.
- It is possible that a Pulmonary or Endocrinology Fellow in training may express a desire to participate in this study to assist the PI and Study Coordinator for educational purposes. Such an individual will be CITI certified, undergo instruction by the Study Coordinator, and participate only after approval of the IRB.

24. LOCAL RECRUITMENT METHODS

- A HIPAA waiver will be used to aid recruitment.
- No member of the study team will be providing direct patient care in the ICU and thus will not be able to invite their own patients.

- The decision to admit, and where to admit, a patient to a UMMMC ICU (from the emergency department, by transfer from another facility, or from a hospital floor) is made by the on-call attending physicians in collaboration with the eICU staff. Candidate study participants will be identified by Study Coordinator each morning by calling the eICU.
- At any one time, approximately half of the patients in 6- and 7-ICU have known or new onset diabetes.
- Admission to the ICU may occur at any time but the interval between admission and sensor placement has no bearing on this study.
- As placement of the CGM will play no role in medical care in the ICU, the length of time between notification of the Study Coordinator and confirmation of eligibility and initiation of informed consent procedures is not critical.
- The potential subject will be identified on the basis of 1) presence in a 6- or 7-ICU bed and 2) the presence of either known diabetes as an admission diagnosis or the observation of a plasma glucose concentration >200 mg, indicative of previously unrecognized diabetes.
- When a potential subject is identified by eICU and ICU staff, the study coordinator will confirm eligibility and then approach the patient to obtain informed consent. If the patient is unable to provide consent due to cognitive impairment or sedation, the patient's LAR will be approached to provide consent. It is common for ICU patients to be unable to provide consent for many procedures (*e.g.*, initiation of dialysis, intubation, extubation, etc.) and the judgment of ICU caregivers will be respected in matters concerning the ability of the patient to provide consent.
- Because it would be impossible to identify potential study subjects without following these procedures which must occur before a subject is approached, a HIPAA Waiver of Authorization has been completed and attached to this proposal, and an Appendix A document will be inserted into the medical record of any subject who is approach for study enrollment.
- There are no recruitment materials
- No payment or other compensation is planned.

25. LOCAL NUMBER OF SUBJECTS

The median stay in 6- and 7-ICU is between 4 and 5 days; glucose in hyperglycemic patients is measured 4 to 6 times daily. An initial cohort of 24 patients is anticipated to yield 384 to 600 usual care measurements, which will be sufficient to analyze concordance with the CGM data.

26. CONFIDENTIALITY

- Protected Health Information (PHI, which will include only the patient medical record number, date of enrollment, and date of discharge from the ICU), will be obtained by the Study Coordinator designated by the Department of Medicine Clinical Research Core and stored on the Research Core's secure UMass Chan OneDrive SharePoint drive. Access to this drive is restricted to the Clinical Research Core.
- The Clinical Research Core Director has informed the Study Team that this is a permissible location.
- It is the policy of the Department of Medicine Clinical Research Core to destroy all PHI stored on their OneDrive SharePoint research drive two years after the conclusion of enrollment.

- PHI of individuals who do not enroll in the study will be recorded on the same Department of Medicine Clinical Research Core OneDrive SharePoint research drive to prevent reapproaching these patients multiple times. This PHI will be destroyed by Clinical Research Core personnel as soon as the study closes to enrollment.
- All PHI that is recorded by the Study Coordinator on the Department of Medicine Clinical Research Core secure SharePoint research drive will be permanently deleted by Core personnel. The Research Core has informed the Study Team that these data are permanently deleted and cannot be recovered.
- The only data being gathered are time-stamped glucose concentrations and information on any adverse events or sensor malfunctions. All this information is identified. Information regarding diagnoses and outcomes is handled as part of the Electronic Medical Record.
- The glucose data will be identified by data source, CGM vs. fingerstick vs. phlebotomy.
- The research database will be constructed by the Research Informatics Core and will have no patient identifiers. The Research Informatics Core will have responsibility for secure storage of the data.
- A Certificate of Confidentiality is not being sought.

27. PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF SUBJECTS

- The CGM, the size of a dime, is placed on skin of an extremity. There are no significant privacy issues that relate to the placement of the sensor.
- No protected health information is being accessed or analyzed.
- Confidentiality is addressed in Section 26.

28. COMPENSATION FOR RESEARCH-RELATED INJURY

- This is an internally funded study with very low device-associated risk.
- The University of Massachusetts Chan Medical School does not provide funds for the treatment of research-related injury. If a subject is injured as a result of participation in this study, treatment will be provided. Insurance carriers will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available.

29. ECONOMIC BURDEN TO SUBJECTS

None

30. CONSENT PROCESS

If you will be obtaining informed consent:

- *Explain how you will ensure that all study staff are familiar with and will follow* HRP-090 SOP: Informed Consent Process for Research
    - All study personnel are CITI certified and experienced in obtaining informed consent according to HRP-090.
    - The PI has downloaded HRP-090 and distributed it to study personnel.
    - ICU staff will determine using standard procedures if a candidate subject is capable of medical decision making, as this affects all aspects of ICU care, not just the CGM study. This determination will be used by the Study Coordinator to determine if consent should be obtained from the patient or the patient's LAR.

  - Interpreter services will be used when enrolling ICU patients whose primary language is Spanish.
- *Describe where the consent process will take place.*
  - For competent patients: In the ICU room after the patient is deemed to be stable by ICU staff.
  - For patients unable to consent: In a family waiting room adjacent to the ICU.
- *Describe any waiting period between recruiting the subject and obtaining consent such that subjects have sufficient time to consider whether or not to participate.*
  - Sensor placement is not a time-sensitive procedure and does not affect routine care in the ICU. There is no limit to the amount of time a patient or LAR has to consider participation.
- *Describe any process to ensure ongoing consent.*
  - If a patient/subject who was enrolled with an LAR regains capacity to consent as determined jointly by ICU staff and the Study Coordinator, the patient will be asked to consent to having the sensor remain in place after having the study explained using the approved consent form.

*If you will be obtaining informed consent from **non-English speaking subjects**:*

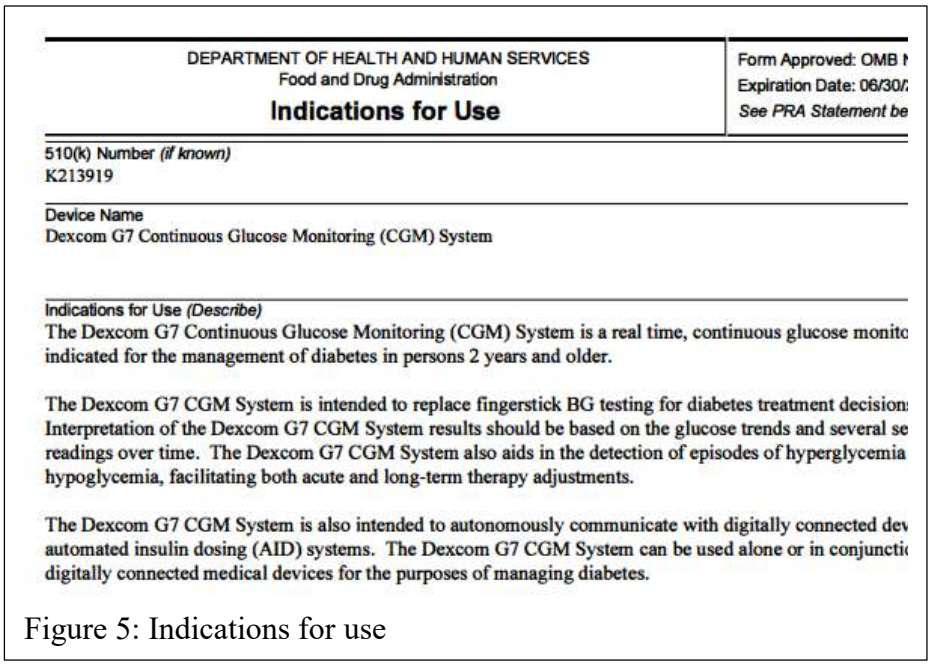
- *Explain whether you will use a translated consent form or a short form.*
  - The consent form will be translated.
- *If you will translate the consent form, indicate the languages.*
  - The consent form will be translated into Spanish only.

31. PROCESS TO DOCUMENT CONSENT IN WRITING

- Written Documentation of Consent will be obtained in accordance with HRP-091.
- All personnel in the Department of Medicine Clinical Research Core have received instruction in and are familiar with the process outlined in HRP-091
- The PI has downloaded HOP-091 from the eIRB website and distributed it to all other study personnel.

32. DRUGS OR DEVICES

- No drugs are being studied.
- The only device being studied is the Dexcom G7 CGM
- The Dexcom G7 is FDA approved for routine outpatient use and is low risk. Please see 510k FDA Premarket Notification K 213919 (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K213919)
- The use of this device is IDE exempt because the investigators attest that:
  - The device was not regulated as a drug before enactment of the Medical Device Amendments. (Transitional device.)
  - The device is FDA-approved/cleared.
  - The device is being used or investigated in accordance with the indications in the FDA approved/cleared labeling (Figure 5).



DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB N
Expiration Date: 06/30/2
See PRA Statement be

510(k) Number *(if known)*
K213919

Device Name
Dexcom G7 Continuous Glucose Monitoring (CGM) System

Indications for Use *(Describe)*
The Dexcom G7 Continuous Glucose Monitoring (CGM) System is a real time, continuous glucose monitc indicated for the management of diabetes in persons 2 years and older.

The Dexcom G7 CGM System is intended to replace fingerstick BG testing for diabetes treatment decision: Interpretation of the Dexcom G7 CGM System results should be based on the glucose trends and several se readings over time. The Dexcom G7 CGM System also aids in the detection of episodes of hyperglycemia hypoglycemia, facilitating both acute and long-term therapy adjustments.

The Dexcom G7 CGM System is also intended to autonomously communicate with digitally connected dev automated insulin dosing (AID) systems. The Dexcom G7 CGM System can be used alone or in conjunctic digitally connected medical devices for the purposes of managing diabetes.

Figure 5: Indications for use

  - The IDE-exempt status of the device was reviewed and confirmed at IRB Office Hours on 6/13/2023 with Andrea Robinson.
  - Devices will be obtained from a retail supplier at no cost to study participants and stored in the supplies closet in 6-ICU until used.
- All drugs and devices used in the research, the purpose of their use, and their regulatory approval status (e.g., FDA approved/cleared, investigational)
- All research procedures being performed and the order in which they are performed, including procedures being performed to monitor subjects for safety or minimize risks.