RESEARCH PROTOCOL

Continuous Glucose Monitoring for Hyperglycemia in Critically Ill Patients

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1. **Project Title:** Continuous Glucose Monitoring for Hyperglycemia in Critically Ill Patients

2. **Abstract:**

The investigators intend to conduct prospective, randomized comparative trial of patients admitted to the intensive care unit (ICU) at the North Florida/South Georgia Veterans Health System who received continuous glucose monitoring (CGM) vs standard glucose monitoring. This study will examine several outcomes for patients in the ICU with hyperglycemia. The primary outcome of the study will be the percentage of time in target range (blood glucose 70-180 mg/dL). Secondary outcomes will include percentage of time in clinically significant hypoglycemic (BG < 54 mg/dL), hypoglycemic (BG 54-69 mg/dL), hyperglycemic (BG 181-250 mg/dL), and clinically relevant hyperglycemic (BG >250 mg/dL) ranges; ICU length of stay, ICU mortality, 30-day mortality, costs associated with monitoring, mean BG, glucose variability between the two groups (% coefficient of variation = SD/mean BG*100%), and patient satisfaction. An evaluation will be done to assess the proportions of patients with new infection, acute kidney injury (AKI), agitation, delirium, and pain. Correlation between CGM values and whole blood values for blood glucose will be evaluated.

3. **Background:**

Diabetes mellitus (DM) is a common comorbidity among hospitalized patients with over 25% reporting a history of the disease. Furthermore, stress-induced hyperglycemia is common in critically ill patients. Among these patients, glucose control is a necessity to avoid further complications. Inpatient hyperglycemia has been associated with a longer length of stay, increased risk of infection, and increased mortality. Hypoglycemia can be more severe in hospitalized patients and can also increase length of stay and mortality. The current standard for glucose monitoring involves point-of-care (POC) blood glucose finger sticks or arterial/venous whole blood sampling. These methods have limitations and continuous glucose monitors (CGMs) offer a potential alternative.

Continuous glucose monitors (CGMs) were originally designed for use in the home and outpatient setting, with less data on its application in the hospital or critical care settings. Until April 2020, CGMs were not approved for inpatient use. To support COVID-19 healthcare efforts, the FDA allowed for the use of continuous glucose monitoring (CGM) systems for the treatment of patients in various healthcare facilities. This remote glucose monitoring allowed for conservation of personal protective equipment (PPE) and reduction of potential exposure of staff from multiple point-of-care glucose checks. Compared to the POC checks every one to two hours, CGM systems can provide blood glucose readings multiple times each hour, allowing for remote monitoring and the ability to detect urgent changes in blood glucose.

Several studies have evaluated the use of CGM among hospitalized patients with DM and have shown positive results when compared to traditional POC glucose

monitoring. Most studies have found the use of CGM can help minimize the number of hypoglycemia episodes and overall improve patient care. Similar studies have been done in the intensive care unit (ICU) with favorable results; however, these studies had smaller sample sizes and limited external validity. While there is consensus on the superiority of CGM detecting hypoglycemic blood glucose levels, the effects on other patient outcomes in the critically ill remain uncertain.

4. Study Purpose:

The purpose of this study is to compare the use of CGM versus POC glucose monitoring in the critical care setting for differences in glycemic control and other important ICU outcomes.

5. Research Plan:

a. Study Design:

i. Prospective, single-center, randomized comparative trial

b. Study Sample:

i. Adult patients at North Florida/South Georgia Veterans Health System anticipated to be admitted to an ICU for a minimum of 48 hours after enrollment

ii. A minimum sample size was calculated to be a total of 88 patients (44 per group), but will continue to enroll patients for a maximum of 2 years or a maximum of 300 patients

1. Anticipated mean POC % time in range of 58% (based on current rates in our facility) with a standard deviation of 20%
2. Anticipated mean CGM % time in range of 70% (based on CGM interpretation guidelines)
3. 80% power, 5% alpha

c. Inclusion Criteria:

i. Patients age 18-89

ii. Past medical history of any diabetes mellitus **OR** patients with at least 1 measured BG of 180 being treated with insulin (subcutaneous or infusion)

1. Enrollment will occur within 72 hours after being admitted to an ICU if history of diabetes
2. Enrollment will occur within 72 hours after developing hyperglycemia in ICU if no diabetes

d. Exclusion Criteria:

i. Pregnant patients

1. Female patients who report no known current pregnancy, will be considered to not have potential to be pregnant with one of the following:

a. History of surgical sterilization (methods include hysterectomy, bilateral tubal ligation, bilateral salpingectomy or bilateral oophorectomy)
b. Postmenopausal (defined as age greater than 62 years, or age 62 years or less than with amenorrhea for at least 12 consecutive months)
c. No sexual partners within previous 9 months who can father children (those who cannot father children include female partners; and male partners who are incapable of fathering children because of congenital anomalies, surgery, or medical treatment)
d. Reported consistent use of hormonal (oral contraceptives, implant, injection, patch, vaginal ring) or intrauterine device (IUD) contraception.

ii. Diagnosis of diabetic ketoacidosis (DKA)
iii. Diagnosis of hyperosmolar hyperglycemic state (HHS)
iv. Anticipated to require prone positioning while on insulin therapy
v. Any contraindications to CGMs based on manufacturer labeling
vi. BG above maximum reading for CGM (e.g. greater than 400 mg/dL)
vii. Receiving medication that could interfere with CGM readings (based on manufacturer specifications)
    1. Receiving any dose of hydroxyurea as this could falsely elevate the sensor readings (if applicable for specific CGM)
    2. Receiving greater than 1,000mg acetaminophen every 6 hours in any form as this could falsely elevate the sensor readings (if applicable for specific CGM)

e. Recruitment:

i. Patients who meet eligibility criteria for this study may be referred to the study team by a clinical staff member of the ICU team responsible for the clinical care of the patient. Study team members are ICU clinicians and may also be part of the team providing clinical care. Patients (or their authorized decision maker) will first be asked if they wish to learn about the study. If the patient is interested in participating in the study, the research team will contact the patient and provide details of study participation and informed consent.
ii. Patients will be provided information on standards of care. As a participant in this study, all care including medical procedures, diagnostic tests, monitoring, medications, treatments, and other care will be the same for all patients as those who do not participate in the study, with the exception of the method of glucose monitoring.

f. Randomization:

i. Study participants will be randomly assigned to one of the study groups after being found eligible for inclusion and giving consent to participate
ii. A randomization process, such as a computerized algorithm or random number generator will be used to assign patients a group upon inclusion
iii. Patients will be allocated 1:1 to the monitoring groups based on this randomization

g. Study Groups:

i. Group 1: POC group (Blinded to CGM)
    1. All patients will have Dexcom G6 Pro CGM sensor/transmitter placed per device instructions
    2. Nurses and all members of the medical treatment team will be BLINDED to the CGM blood glucose readings during the study period
    3. Glycemic management will be based on POC glucose values.
ii. Group 2: CGM group (Unblinded to CGM)
    1. All patients will have Dexcom G6 CGM sensor/transmitter placed per device instructions
    2. Nurses and all members of the medical treatment team will be UNBLINDED to the CGM blood glucose readings during the study period
    3. Glycemic management will be based on CGM values.

h. Study Outcomes

i. **Primary Outcome**
    1. Percentage of time in target range (BG 70-180mg/dL) [Appendix E]
        a. Comparison of CGM readings between both types of monitoring/treatment groups
ii. **Secondary Outcomes**
    1. Percentage of time in each range (Appendix E) [Comparison of CGM readings between both types of monitoring/treatment groups]
        a. Clinically significant hypoglycemic range (BG < 54 mg/dL)
        b. Hypoglycemic range (BG 54-69 mg/dL)
        c. Hyperglycemic range (BG 181-250 mg/dL)
        d. Clinically relevant hyperglycemic range (BG >250 mg/dL)
    2. ICU length of stay
    3. ICU mortality
    4. 30-day mortality

5. Costs associated with monitoring
6. Mean BG
7. Glucose variability for each group
    a. % coefficient of variation = SD/mean BG*100%
8. Patient satisfaction

iii. **Safety**

1. Proportion of patients with a new infection
2. Proportion of patients with new AKI (AKIN guidelines)
3. Proportion of patients with CAM-ICU positive delirium
4. Proportion of patients with agitation (RASS $\geq$ 2)
5. Proportion of patients with a positive pain score (CPOT vs DVPRS)
    a. Correlate pain score with timing of BG check for POC and at time of placement of CGM

i. Inpatient Hyperglycemia Management:

i. Hyperglycemia management will be directed by the ICU team per standard of care
ii. Standard nutritional guidelines are recommended. Nutritional care will be managed at the discretion of the providers
iii. IV insulin infusion targeting BG 140-180 mg/dL is preferred treatment, especially if NPO, on an inconsistent nutritional regimen, hemodynamically unstable, or in setting of organ dysfunction
    1. Will use validated protocol with computerized decision support tool (Appendix D)
    2. Converting from IV insulin infusion to SC insulin managed as described in Appendix D
iv. SC insulin regimen may be used based on the discretion of the treating ICU team, with dosing/agents recommended in Appendices A, B, and C
    1. Only recommended for patients on consistent nutritional regimen who are hemodynamically stable
    2. Daily insulin dose adjustments to the SC insulin regimen will be managed at the discretion of the treating ICU team, considering use of correctional insulin and concomitant factors (e.g. use of medications which increase blood glucose)

j. Hypoglycemia Management:

i. Managed per protocol in both groups.
    1. If able to eat/swallow, 15 grams of carbohydrates (glucose tablets/glucose gel) PRN
    2. If unable to eat/swallow or developed severe hypoglycemia, ½ ampule vs 1 ampule intravenous D50W PRN

3. If no intravenous access is available, 1mg glucagon subcutaneous PRN

ii. Additional treatment may be given after 15 minutes if the patient has an inadequate response to the glucose correction.

k. CGM Devices:

i. Two CGM devices will be used in this study, Dexcom G6 and Dexcom G6 Pro. Both devices are placed similarly onto patients. Both devices can be worn for same timeframe (10 days). Both devices can interact with same applications, smartphone, and manufacturer software (Dexcom Clarity). Both devices carry same manufacturer instructions for placement and use with specific medications and diagnostic procedures. Dexcom G6 can only be used in an Unblinded mode where CGM values are visible to the patient and clinical care team. Dexcom G6 Pro allows for a Blinded mode where CGM values are not visible to patients or the clinical care team.

ii. Dexcom G6
   1. Will be used in the CGM group
   2. Used only in Unblinded mode
   3. Sensor and transmitter are separate components

iii. Dexcom G6 Pro
   1. Will be used in the POC group
   2. Will be used in Blinded mode
   3. Sensor and transmitter are combination device

l. Blood Glucose Correlation:

i. CGMs will be calibrated if necessary, per manufacturer instructions with POC or venipuncture BG sample

ii. CGM and POC tests will be correlated with routine venipuncture monitoring on at recommended daily interval unless clinical suspicion of an inaccurate reading

m. POC Group Procedures:

i. CGMs will be placed on the abdomen (or other site) per manufacturer recommendations and can be at the discretion of placing provider.
   a. Placement at least 3 inches from insulin pump infusion or injection site
   b. Placement away from waistband, scarring, tattoos, irritation, and bones
   c. Placement in a location unlikely to be bumped, pushed, or laid on while sleeping
   d. CGMs will be removed prior to any surgery, computed tomography (CT) scan, or magnetic resonance imaging

(MRI), or other procedure as necessary per manufacturer instructions

ii. Patients, nurses, and other treatment team will be blinded to the CGM readings
    1. All treatment decisions for this group will be based on POC readings and venipuncture

iii. POC BG will be checked per protocol based on treatment received
    1. Every 1-2 hours per protocol if receiving an insulin infusion
    2. At least 3 times per day if receiving a basal:bolus insulin regimen

n. CGM Group Procedures:

i. CGMs will be placed on the abdomen (or other site) per manufacturer recommendations and can be at the discretion of placing provider.
    a. Placement at least 3 inches from insulin pump infusion or injection site
    b. Placement away from waistband, scarring, tattoos, irritation, and bones
    c. Placement in a location unlikely to be bumped, pushed, or laid on while sleeping
    2. Remote monitoring software will be set up for nursing staff
    3. All staff will be educated on using the monitoring software
    4. CGMs will be removed prior to any surgery, computed tomography (CT) scan, or magnetic resonance imaging (MRI), or other procedure as necessary per manufacturer instructions

ii. Nurses and treatment team will NOT be blinded to the CGM readings
    1. All treatment decisions for this group will be based on CGM readings, confirmatory POC readings (as necessary), and venipuncture

iii. Nursing staff will obtain a confirmatory POC for hypoglycemia alarms and administer appropriate therapy per protocol
    1. If a different reading is recorded, a venipuncture will be obtained

iv. CGMs will record the BG and transmit to a remote device
    1. The duration of CGM use for the study will be limited to 10 days (or the maximum duration allowable for use as recommended by the manufacturer)

v. CGMs are pre-set with the following alerts:
    1. Low-glucose alerts set to 70 mg/dL
    2. Urgent low alerts set to 55 mg/dL, with urgent low soon alerts set if BG is expected to be 55 mg/dL within 20 minutes
    3. High alerts set to 250 mg/dL

vi. BG readings less than 40 mg/dL are read on the CGMs as “LOW”. While the exact reading will be unable to be determined, the amount of time spent in the “LOW” reading will be recorded
    1. When this occurs, a confirmatory POC reading will be obtained. If these numbers differ, a venipuncture will be collected

o. Data Collection

i. **CGM Sensor Data**
    1. Clinical CGM data will be transmitted and evaluated using manufacturer software.

ii. The following will be obtained from the Computerized Patient Records System (CPRS):
    1. **Demographic Data:** age, sex, race, weight, height, comorbidities
    2. **Admission Data:** length of stay, diagnoses, mortality
    3. **Clinical Data:** vital signs, complete metabolic panel (BMP) and other serum electrolytes (magnesium/phosphate), complete blood counts, liver function tests, infection/microbiology results (gram stains/cultures/sensitivities/PCR or other microbiology identification), blood gases, other laboratory data need to assess treatment/diagnoses/severity of illness, blood glucose levels, antidiabetic treatments (including type of insulin and doses administered), other medications (including presence of additional medications [e.g. steroids, vasopressors, or any other medications that may affect blood glucose or the CGMs sensors]), sedation/agitation (e.g. Richmond Agitation Sedation Scale) scores, delirium (e.g. CAM-ICU) scores, pain (e.g. CPOT, DVPRS) scores, diet/nutritional regimen

iii. **Satisfaction survey data:** patient satisfaction survey

iv. **Cost Analysis:** a comparison will be conducted based on the costs of equipment, staff time, and other relevant costs related to glucose monitoring in each group

p. Privacy, Security, and Confidentiality:

i. Investigators will be responsible for maintaining patient privacy and confidentiality

ii. The principal investigator has the responsibility for security of the study

iii. Study data will be entered, managed, and stored securely using VA Research Electronic Data Capture (REDCap).

iv. Study data will be coded then de-identified for data analysis.

6. **Analysis Methods:**

   Descriptive statistics and inferential statistical methods will be used as appropriate to report findings of this study.

   To minimize risk of bias, data collection and analysis will be by performed by study team members not involved in the clinical care of the study participants, as possible.

7. **Possible Discomforts and Risks:**
   - Inaccurate measurement of BG which could lead to hypo- and hyperglycemia
   - CGMs are minimally invasive but could cause some patients mild physical pain or discomfort
   - Apart from the type of monitoring utilized, no further changes to patient care will be made. Investigators will not alter medication prescribing to deviate from standard of care. As such, no additional discomfort or risk to the patient caused by this study is expected.

8. **Possible Benefits:**
   - Reduction of serious hypoglycemia or other adverse events is the most relevant potential benefit of using CGM
   - Decreased point-of-care finger sticks compared to standard care. This may lead to benefits such as increased patient comfort and reduced costs.
   - Possible benefit of improved glycemic control with the ability to monitor glucose levels more carefully and adjust treatment as appropriate; this could lead to improved patient outcomes. We hypothesize the use of CGM will yield less cases of hypoglycemia and more glucose values at goal.

9. **Anticipated Costs:**

   GGM devices and other necessary equipment will be provided through a manufacturer sponsored grant. Administrative and regulatory expenses will be covered by a manufacturer sponsored grant. No other costs beyond investigator salary and those for routine clinical care are anticipated.

10. **Conflicts of Interest:**

    None of the investigators hold a patent or license for any material, object, or process involved with this research. None of the investigators own stock in or serve as consultants to any company involved in this research. The researchers will not receive payment or other financial incentive for conducting this study.

    The PI or any of the Sub-investigators have no real or potential conflict of interest with regards to this research project.

11. References:

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Appendix A. Weight-Based SC Insulin Dosing – PO diet eating full meals

- Age ≥ 70 years, eGFR <60mL/min, underweight, risk for hypoglycemia
    - Total Daily Insulin Dose = 0.2 units/kg
        - 0.1 unit/kg/day basal glargine
        - 0.03-0.05 units/kg/meal nutritional aspart
        - Correctional Aspart AC = Low (1 unit:50 mg/dL BG >150 mg/dL)
- Normal Body Weight (BMI 18.5-25)
    - Total Daily Insulin Dose = 0.4 units/kg
        - 0.2 unit/kg/day basal glargine
        - 0.07 units/kg/meal nutritional aspart
        - Correctional Aspart AC = Low (1 unit:50 mg/dL BG >150 mg/dL)
- Overweight or Obese (BMI >25)
    - Total Daily Insulin Dose = 0.5 units/kg
        - 0.25 unit/kg/day basal glargine
        - 0.08 units/kg/meal nutritional aspart
        - Correctional Aspart AC = Medium (2 units:50 mg/dL BG >150 mg/dL)

Additional Considerations:

- Aspart dose should be given immediately prior to meal. If it is unknown if patient will eat, hold aspart prior to meal and give after meal if patient consumes at least 50%. Give aspart dose within 15 minutes of first bite.
- If patient is expected not to eat or consumes less than 50% of meal: nurse to notify physician, hold scheduled nutritional aspart dose, continue basal glargine, and give aspart correctional sliding scale.
- Correctional aspart to be given in addition to nutritional aspart dose.
- If blood glucose is less than 100 mg/dl, nurse to hold nutritional/correctional insulin and notify physician. Basal insulin should be continued as prescribed unless instructed otherwise by physician orders.
- If patient has abrupt change in diet (e.g. made NPO for urgent procedure), nurse to notify physician. It is recommended to start dextrose containing IV fluids and continue basal insulin glargine to prevent rebound hyperglycemia. Insulin regimen should be re-evaluated by provider as warranted.
- Pre-meal blood glucose goal is 100-150 mg/dl.

Appendix B. Weight-Based SC Insulin Dosing –NPO, Liquid Diet Only, or Minimal Diet Intake

- Age ≥ 70 years, eGFR <60mL/min, underweight, risk for hypoglycemia
    - Total Daily Insulin Dose = 0.1 units/kg (100% Basal Glargine)
        - Correctional Regular insulin (every 6 hours) or aspart (every 4 hours) = Low (1 unit:50 mg/dL BG >150 mg/dL)
- Normal Body Weight (BMI 18.5-25)
    - Total Daily Insulin Dose = 0.2 units/kg (100% Basal Glargine)
        - Correctional Regular insulin (every 6 hours) or aspart (every 4 hours) = Low (1 unit:50 mg/dL BG >150 mg/dL)
- Overweight (BMI 25-30)
    - Total Daily Insulin Dose = 0.25 units/kg (100% Basal Glargine)
        - Correctional Regular insulin (every 6 hours) or aspart (every 4 hours) = Medium (2 units:50 mg/dL BG >150 mg/dL)
- Obese (BMI >30)
    - Total Daily Insulin Dose = 0.3 units/kg (100% Basal Glargine)
        - Correctional Regular insulin (every 6 hours) or aspart (every 4 hours) = Medium (2 units:50 mg/dL BG >150 mg/dL)

Additional Considerations:

- Dextrose containing maintenance IV fluids are recommended for patients with prolonged NPO status receiving scheduled insulin.
- If blood glucose is less than 100 mg/dl, nurse to hold basal insulin and notify physician.

Appendix C. Management of SC Insulin Dosing –Continuous tube feedings or PN

- Age ≥ 70 years, eGFR <60mL/min, underweight, risk for hypoglycemia
    - Total Daily Insulin Dose = 0.2 units/kg
        - 0.1 units/kg/day basal glargine
        - 0.025 units/kg every 6 hours nutritional regular insulin
        - Correctional Regular insulin every 6 hours = Low (1 unit:50 mg/dL BG >150 mg/dL)
- Normal Body Weight (BMI 18.5-25)
    - Total Daily Insulin Dose = 0.4 units/kg
        - 0.2 units/kg/day basal glargine
        - 0.05 units/kg every 6 hours nutritional regular insulin
        - Correctional Regular insulin every 6 hours = Low (1 unit:50 mg/dL BG >150 mg/dL)
- Overweight or Obese (BMI >25)
    - Total Daily Insulin Dose = 0.5 units/kg
        - 0.25 units/kg/day basal glargine
        - 0.06 units/kg every 6 hours nutritional regular insulin
        - Correctional Regular insulin every 6 hours = Medium (2 units:50 mg/dL BG >150 mg/dL)

Additional Considerations:

- If patient is receiving bolus enteral tube feedings, daily nutritional insulin dose should be evenly divided and given prior to each feeding.
- For cyclic enteral tube feeding or parenteral nutrition (e.g. nocturnal only), insulin dosing must be individualized and coincide with nutritional regimen.
- Correctional regular insulin is given in addition to nutritional regular insulin dose.
- If blood glucose is less than 100 mg/dl, nurse to hold nutritional/basal insulin and notify physician.
- If nutrition is interrupted: nurse to notify physician, start dextrose 5%/0.45% NaCl infusion at twice the rate of nutrition order, hold scheduled regular insulin, give glargine and correctional regular insulin.

Appendix D. Management of Intravenous Insulin Infusion

Excel tool (pictured below) developed using the algorithm of the paper-based IIP developed by the University of Pittsburgh Medical Center (UPMC).

- Initial IV insulin infusion rate based on initial BG level
- Adjusted IV insulin infusion rate based on current BG, change in BG from previous, and current IV insulin infusion rate
- Instructions for converting from IV insulin infusion to SC insulin are provided, based on the average hourly rate of IV insulin

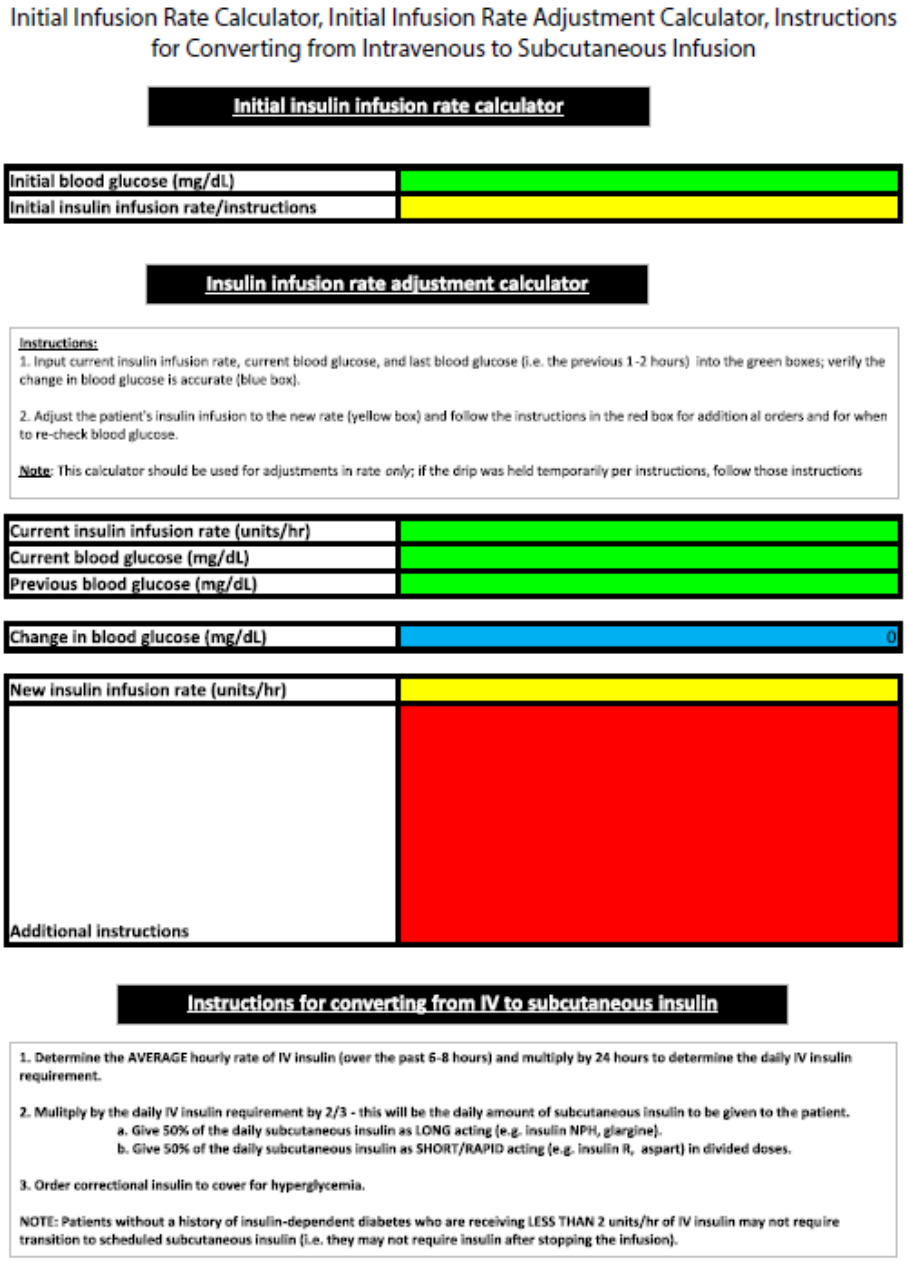

Figure 1: The nurse obtains a point-of-care blood glucose and manually enters the value into the tool. The tool then calculates the new insulin infusion rate and provides any additional instructions.

IV Insulin Infusion Titration

BG (mg/dL)	Current rate 0.1-3.9 units/hour	Current rate 4-6.9 units/hour	Current rate 7-10 units/hour	Current rate >10 units/hour*
<70	**(1) D/C insulin. Give 50mL (1 amp) D50 IV. Recheck BG in 15 min.** Repeat as necessary. (Do not restart insulin until at least 1 hr after D50.) Notify MD. If no continuous glucose, start IV fluid as per page 1. Restart insulin at 50% (half) previous rate when BG >140 AND it is at least 1 hr after D50. Recheck BG in 1 hr.			
70-99	**(2) D/C insulin.** Recheck BG in 1 hr and then hourly. When BG >140, restart insulin but decrease rate by 50% (half) and recheck BG in 1 hr.			
100-139	**(3.1)** If BG drop >25 mg/dl from last check, **D/C insulin.** Recheck BG in1 hr and then hourly. When BG >140, restart insulin but decrease rate by 50% (half) and recheck BG in 1 hr. **(3.2)** Otherwise, **decrease** by 0.5 units/hr (if current rate <0.5 units/hr, then D/C) and recheck BG in 1 hr.	**(4.1)** If BG drop >25 mg/dl from last check, **D/C insulin**. Recheck BG in 1 hr and then hourly. When BG >140, restart insulin but decrease rate by 2 units/hr and recheck BG in 1 hr. **(4.2)** Otherwise, **decrease** rate by 1 unit and recheck BG in 1 hr.	**(5.1)** If BG drop >25 mg/dl from last check, **D/C insulin**. Recheck BG in 1 hr and then hourly. When BG >140, restart insulin but decrease rate by 3 units/hr and recheck BG in 1 hr. **(5.2)** Otherwise, **decrease** rate by 1.5 units and recheck BG in 1 hr.	**(6.1)** If BG drop >25 mg/dl from last check, **D/C insulin**. Recheck BG in 1 hr and then hourly. When BG >140, restart insulin but decrease rate by 4 units/hr and recheck BG in 1 hr. **(6.2)** Otherwise, **decrease** rate by 2 units and recheck BG in 1 hr.
140-180	**(7.1)** If BG drop >50 mg/dl from last check, **D/C insulin.** Recheck BG in 1 hr and then hourly. Restart insulin (as long as BG>140), but decrease rate by 50% (half) and recheck BG in 1 hr. **(7.2)** If BG drop 25-50 mg/dl from last check, **decrease** rate by 50% (half) and recheck BG in 1 hr. **(7.3)** Otherwise, **make no changes**. If BGs 140-180 for 2 consecutive hours, recheck q2h.	**(8.1)** If BG drop >50 mg/dl from last check, **D/C insulin.** Recheck BG in 1 hr and then hourly. Restart insulin (as long as BG>140), but decrease rate by 2 units/hr and recheck BG in 1 hr. **(8.2)** If BG drop 25-50 mg/dl from last check, **decrease** by 2 units/hr and recheck BG in 1 hr **(8.3)** Otherwise, **make no changes**. If BGs 140-180 for 2 consecutive hours, recheck q2h.	**(9.1)** If BG drop >50 mg/dl from last check, **D/C insulin**. Recheck BG in 1 hr and then hourly. Restart insulin (as long as BG>140), but decrease rate by 3 units/hr and recheck BG in 1 hr. **(9.2)** If BG drop 25-50 mg/dl from last check, **decrease** by 3 units/hr and recheck BG in 1 hr **(9.3)** Otherwise, **make no changes**. If BGs 140-180 for 2 consecutive hours, recheck q2h.	**(10.1)** If BG drop >50 mg/dl from last check, **D/C insulin**. Recheck BG in 1 hr and then hourly. Restart insulin (as long as BG>140), but decrease rate by 4 units/hr and recheck BG in 1 hr. **(10.2)** If BG drop 25-50 mg/dl from last check, **decrease** by 4 units/hr and recheck BG in 1 hr **(10.3)** Otherwise, **make no changes**. If BGs 140-180 for 2 consecutive hours, recheck q2h.
181-250	**(11.1)** If BG drop >50 mg/dl, **decrease** rate by 50% (half) and recheck BG in 1 hr. **(11.2)** If BG drop 25-50 mg/dl from last check, make **no change** and recheck BG in 1 hr **(11.3)** Otherwise, **increase** rate by 1 unit/hr and recheck BG in 1 hr.	**(12.1)** If BG drop >50 mg/dl, **decrease** rate by 2 units/hr and recheck BG in 1 hr **(12.2)** If BG drop 25-50 mg/dl from last check, make **no change** and recheck BG in 1 hr **(12.3)** Otherwise, **increase** rate by 1.5 units/hr and recheck BG in 1 hr.	**(13.1)** If BG drop >50 mg/dl, **decrease** rate by 3 units/hr and recheck BG in 1 hr **(13.2)** If BG drop 25-50 mg/dl from last check, make **no change** and recheck BG in 1 hr **(13.3)** Otherwise, **increase** rate by 2 units/hr and recheck BG in 1 hr.	**(14.1)** If BG drop >50 mg/dl, **decrease** rate by 4 units/hr and recheck BG in 1 hr **(14.2)** If BG drop 25-50 mg/dl from last check, make **no change** and recheck BG in 1 hr **(14.3)** Otherwise, **increase** rate by 3 units/hr and recheck BG in 1 hr.
>250	**(15.1)** If BG drop ≥25 mg/dl from last check, make **no change** and recheck BG in 1 hr **(15.2)** Otherwise**, give** 2 units insulin IV push AND **increase** rate by 1 unit/hr. Recheck BG in 1 hr.*	**(16.1)** If BG drop ≥25 mg/dl from last check, make **no change** and recheck BG in 1 hr **(16.2)** Otherwise, **give** 2 units insulin IV push AND **increase** rate by 1.5 units/hr. Recheck BG in 1 hr.*	**(17.1)** If BG drop ≥25 mg/dl from last check, make **no change** and recheck BG in 1 hr **(17.2)** Otherwise, **give** 2 units insulin IV push AND **increase** rate by 2 units/hr. Recheck BG in 1 hr.*	**(18.1)** If BG drop ≥25 mg/dl from last check, make **no change** and recheck BG in 1 hr **(18.2)** Otherwise, **give** 2 units insulin IV push AND **increase** rate by 3 units/hr. Recheck BG in 1 hr.*

*Notify MD when insulin infusion rate exceeds 10 units/hr or if 4 consecutive BGs are >250 mg/dL.

Reference:

- University of Pittsburgh Medical Center. Regular Insulin IV Infusion Protocol: Goal Blood Glucose 140–180 mg/dL. (Updated: Nov 30, 2009.) 2009. http://inpatient.aace.com/sites/all/files/UPMC_140-180_IV_Insulin_Protocol.pdf.

Appendix E. CGM Blood Glucose Target Ranges, defined in CGM interpretation guidelines:

- DM type 1/type 2
    - Time in Range (TIR)
        - BG 70-180 mg/dL
            - >70% of readings; >16 h, 48 min per day
    - Time Below Range (TBR)
        - BG <70 mg/dL
            - <4% of readings; <1 h per day
        - BG <54 mg/dL
            - <1% of readings; <15 min per day
    - Time Above Range (TAR)
        - BG >180 mg/dL
            - <25% of readings; <6 h per day
        - BG >250 mg/dL
            - <5% of readings; <1 h, 12 min per day

- Older/high-risk DM type 1/type 2
    - Time in Range (TIR)
        - BG 70-180 mg/dL
            - >50% of readings; >12 h per day
    - Time Below Range (TBR)
        - BG <70 mg/dL
            - <1% of readings; <15 min per day
    - Time Above Range (TAR)
        - BG >250 mg/dL
            - <10% of readings; < 2h, 24 min per day