Title: Comparison of 3 versus 6-Month Use of Professional Continuous Glucose Monitoring in the Treatment of Poorly Controlled, Non-Insulin Using T2DM Patients in a Primary Care Setting

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Research Abstract Proposal

Comparison of 3 versus 6-Month Use of Professional Continuous Glucose Monitoring in the Treatment of Poorly Controlled, Non-Insulin Using T2DM Patients in a Primary Care Setting

Primary Objective:

1. To determine whether 3-month versus 6-month professional CGM utilization improves time spent in target range of 70-140mg/dl in patients with poorly controlled T2DM not treated with insulin.

Secondary Objectives:

1. To determine whether 3-month versus 6-month professional CGM utilization improves hemoglobin A1c in patients with T2DM not treated with insulin.

2. To determine whether 3-month versus 6-month professional CGM utilization leads to more treatment intensification.

Background

For prescribers, the hemoglobin A1c (HbA1c) lab value is the most common monitoring used in primary care to assess diabetes control and determine if pharmacotherapy modification is warranted. For patients with type 2 diabetes (T2DM), self-monitoring blood glucose (SMBG) results may be performed to evaluate diabetes control, but these results must be communicated to the clinician in an effective and timely manner for the data to be useful in creating a patient-centered plan.[1] Structured SMBG plans that include a 7-point glucose profile over 3 days (fasting, pre and 2-hour post-meal, and bedtime) has demonstrated improved glycemic control in poorly controlled T2DM patients (HbA1c ≥ 7.5%) not treated with insulin.[2] In this study, prescribers were more likely to make treatment changes when structured SMBG occurred compare to no structured SMBG. However, structured SMBG protocols are rarely implemented in primary care offices. Overall, the usefulness and cost-effectiveness of SMBG in T2DM patients treated with non-insulin therapies is conflicting and the American Diabetes Association (ADA) has assigned it an evidence-based grade of "E" for expert opinion.[1,3] Professional continuous glucose monitoring (CGM) could represent another opportunity for prescribers to assess glycemic control over a 3-day period.

Professional CGM measures interstitial glucose every 5 minutes via a glucose-oxidaseimpregnated membrane during a 3–5 day period.[4] The patient wearing professional CGM is blinded to the repeated measurements and the data is stored for retrospective analysis. The durable equipment used to perform professional CGM is owned and maintained by the practice site or clinician and can be used regularly with a variety of patients. Currently, insurance companies often determine the use of professional CGM in T2DM and frequency of use is variable. There is no data available comparing glycemic control in non-insulin treated patients with T2DM when professional

CGM is utilized at different frequencies or examining the best use of professional CGM in this subset of patients. This population represents a significantly large number of patients who are typically treated in primary care settings without an endocrinologist. The results of this trial could assist Medtronic in marketing professional CGM products to primary care providers.

Given the usefulness of the glycemic data provided by professional CGM, I hypothesize that patients who wear the professional CGM at 3-month intervals when spend more time in target range that those wear it at 6-month intervals. This hypothesis will be addressed in the following specific aims:

Specific Aims:

1. **To determine the percent time spent in target range of 70-140mg/dl in poorly controlled patients with T2DM not treated with insulin.**
   Patients not receiving any insulin treatment with an HbA1c ≥ 7.5% before their scheduled primary care appointment will be invited to participate in the study and wear professional CGM for at least 3 days at either 3 intervals (baseline, 3-month and 6-month) or 2 intervals (baseline and 6-month). After removal, the downloaded report will provide quantitative data to determine the percent of time spent in the target range. The 6-month data will be analyzed to determine if frequency of professional CGM wear positively affects time spent in target range.

2. **To determine the hemoglobin A1c levels in poorly controlled patients with T2DM not treated with insulin.**
   Patients who consent to the study will have their HbA1c levels measured in our central lab at the clinic and recorded in the electronic medical record (EMR). This data is easily retrievable for reporting and would be analyzed to determine if frequency of professional CGM wear would positively affect HbA1c levels.

3. **To determine treatment modification in poorly controlled patients with T2DM not treated with insulin.**
   The EMR documents current and previous medication therapies including newly prescribed medications, increased or decreased dosage changes or termination of prescribed medication. Only FDA-approved medications for the treatment of type 2 diabetes will be monitored. The type of treatment modification and their frequencies can be retrieved from the EMR and analyzed to determine if frequency of professional CGM wear affects these outcomes.

Sample Size and Rationale

A calculated sample size of 20 patients will be needed to detect a 15% effect size (e.g., mean of 60% vs. 75% of time in target range) with a standard deviation of 10 and 90% power. Assuming a 25% drop out, planned enrollment is 25 patients with poorly

controlled T2DM (defined as last two consecutive HbA1c values between 7.5 – 10%) and who have not received insulin within the last 3 months.

Study Design

6-month, Prospective, Randomized, Single Center

Inclusion Criteria

- 18 years or older with a diagnosis of T2DM with a scheduled office visit with primary care provider within the next 4 weeks
- Last 2 HbA1c values between 7.5 – 10% measured in the last 12 months
- Treated with non-insulin therapies or therapeutic lifestyle changes
- Never worn professional CGM or have not worn in last 12 months
- Willing to perform requirements needed for professional CGM

Exclusion Criteria

- Current or previous treatment with any insulin within 3 months at baseline

Protocol or Study Plan

1. Identify patients via electronic medical record reporting based on inclusion criteria.
2. Contact and screen prospective participants either via phone call explaining the research project and objectives.
3. In patient expresses interest, complete the consent process and randomize participant into either 3-month or 6-month professional CGM.
4. **Baseline Visit**
    a. Assign de-identified code to participate for confidentiality protection.
    b. Measure demographic information, baseline HbA1c levels, baseline medication therapies and doses.
    c. Place professional CGM placement and provide patient education for successful 3-day wear.
    d. Schedule follow-up professional CGM placement visits at either
        i. 3-month and 6-month or
        ii. 6-month only.
    e. Confirm scheduled primary care physician follow-up appointment(s).
    f. After patient returns CGM, download 3 color copies of CGM reports (one for physician, patient and research records)
    g. Provide downloaded professional CGM reports to primary care physician prior to patient appointment for review. Inform physician a Certified Diabetes Educator (CDE) is available for consultation, as needed.
        i. Contingency Plan – if in the event any reading are < 40mg/dl or > 400mg/dl, the physician will be contacted that same day through

the EMR system instead of waiting till the next scheduled appointment

5. **3-Month Visit**
    a. if randomized to 3-month CGM arm
        i. Confirm patient CGM placement visit approximately 1 week in advance. ii. Place professional CGM placement and provide patient education for successful 3-day wear. iii. Record any new HbA1c results and changes to medication therapies and/or doses.
        iv. Confirm 6-month professional CGM placement visits.
        v. Confirm scheduled primary care physician follow-up appointment(s).
        vi. After patient returns CGM, download 3 color copies of CGM reports (one for physician, patient and research records)
        vii. Provide downloaded professional CGM reports to primary care physician prior to patient appointment for review. Inform physician a Certified Diabetes Educator (CDE) is available for consultation, as needed.
            1. Contingency Plan – if in the event any reading are < 40mg/dl or > 400mg/dl, the physician will be contacted that same day through the EMR system instead of waiting till the next scheduled appointment
    b. If patient is NOT scheduled to receive CGM, then at 3 months:
        i. Contact patient by telephone and ask to perform SMBG four times daily (before all meals and bedtime) for 3 days and bring the results to their scheduled physician visit
6. **6-Month Visit**
    a. Confirm patient CGM placement visit approximately 1 week in advance.
    b. Place professional CGM placement and provide patient education for successful 3-day wear.
    c. Record any new HbA1c results and changes to medication therapies and/or doses.
    d. Confirm scheduled primary care physician follow-up appointment(s).
    e. After patient returns CGM, download 3 color copies of CGM reports (one for physician, patient and research records)
    f. Provide patient with $50 gift card.
    g. Provide downloaded professional CGM reports to primary care physician prior to patient appointment for review. Inform physician a Certified Diabetes Educator (CDE) is available for consultation, as needed.
        i. Contingency Plan – if in the event any reading are < 40mg/dl or > 400mg/dl, the physician will be contacted that same day through the EMR system instead of waiting till the next scheduled appointment
7. Analyze and report data.

Schedule with key milestones

Fall 2016 – begin recruitment
Spring 2017 – all participants completed 3-month visit
Fall 2017 – all participants completed 6-month visit

Biostatistics and Data Analysis

Descriptive statistics including mean, standards deviation, frequency, etc. will provide the summary information for this study. A linear regression will be used to investigate if frequency of professional CGM wear (independent variable) positively affects time spent and HbA1C level (outcome variables) in target range. An appropriate transformation will be used if the normality is severely violated. Meanwhile, the significant changes of HbA1C overtime will be used to determine with a longitudinal data analysis. More specifically, repeated measure approach will be used for 3 intervals (baseline, 3-month and 6 month) and matched pair t-test will be used for2 intervals (baseline and 6-month). Frequencies of in treatment modification would be analyzed using Chi-Square test. A $p<0.05$ will be used to indicate statistically significant. All data analyses will be performed with SAS (version 9.4 Cary, NC, USA).

Start Date and End Date

October 1st 2016 – October 1st 2017 (approximate)

References

1. Bailey TS, Grunberger G, Bode BW, et al. American Association Of Clinical Endocrinologists And American College Of Endocrinology 2016 Outpatient Glucose Monitoring Consensus Statement. *Endocr Pract.* 2016 Feb;22(2):23161.
2. Polonsky WH, Fisher L, Schikman CH, et al. Structured self-monitoring of blood glucose significantly reduces A1C levels in poorly controlled, noninsulin-treated type 2 diabetes: results from the Structured Testing Program study. *Diabetes Care.* 2011 Feb;34(2):262-7.
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