PROTOCOL TITLE: **MY DOSE COACH TITRATION & MAINTENANCE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS ON BASAL INSULIN**

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TABLE OF CONTENTS

ABBREVIATIONS

ADR	Adverse Drug Reaction
AE	Adverse Event
AESI	Adverse Event of Special Interest
App	Application
BG	Blood Glucose
BGM	Blood Glucose Monitor
BMI	Body Mass Index
CFR	Code of Federal Regulations
CRF	Clinical Research Form
DDS17	Diabetes Distress Scale
DCES	Diabetes Care and Education Specialist
DM	Diabetes Mellitus
DMSRQ-SF	Diabetes Medication System Rating Questionnaire-Short Form
DSMP	Data Safety Monitoring Plan
EMR	Electronic Medical Records
Endo	Endocrinologist
FDA	Food and Drug Administration
FPG	Fasting Plasma Glucose
GCP	Good Clinical Practice
GEE	Generalized Estimating Equations
HbA1c	Hemoglobin A, Glycated hemoglobin
HCP	Health Care Professional
ICH	International Conference on Harmonization
ICSR	Individual Case Safety Report
IND	Investigational New Drug
iOs	iPhone Operating System
IRB	Institutional Review Board
LS	Least Squares
MDC	MyDoseCoach App
MDC-T	MyDoseCoach App Titration Module
MDC-M	MyDoseCoach App Maintenance Module
PC	Primary Care
PCP	Primary Care Provider
PI	Principle Investigator
SAE	Serious Adverse Event
SMBG	Self-monitoring Blood Glucose
SOC	Standard of Care
T2DM	Type 2 Diabetes Mellitus

UPDI	University of Pittsburgh Diabetes Institute
UPMC	University of Pittsburgh Medical Center
US	United States
USPS	United States Parcel Service

Note to Reviewers: ***The health care professional portion of the study (related to the secondary objective and study aim 3) will be evaluated as a separate study submission.***

1 OBJECTIVE, SPECIFIC AIMS, BACKGROUND, AND SIGNIFICANCE

1.1 Objective

1.1.1 Primary

To demonstrate that patients who are trained on and use the MyDoseCoach titration (MDC-T) phone application (app) to titrate insulin will have greater improvements in hemoglobin A1c (HbA1c) and more likely to achieve glycemic control at 3 months as compared to usual care practice, and those who do attain glycemic goals, are able to maintain glycemic control for an additional 3 months using the MDC Maintenance (MDC-M) app.

1.1.2 Secondary

To examine the feasibility of integrating digital solutions into clinical workflow and acceptability of MDC-T and MDC-M by health care professionals (HCPs) and patients.

1.1.3 Hypothesis

Patients using MDC-T will reach individualized fasting plasma glucose (FPG) and HbA1c targets and MDC-M will help patients to maintain glycemic targets at 6 months from baseline.

1.2 Specific Aims

1.2.1 Aim 1

To determine the effect of MDC-T on helping patients with T2DM, who are new to titrating insulin, to improve glycemic control and achieve target goals as compared to patients who titrate insulin with traditional usual care processes.

1.2.2 Aim 2

To determine if patients with T2DM can maintain glycemic control when reaching target goals after using insulin titration guided by the MDC-T.

1.2.3 Aim 3

To examine the feasibility of integrating digital solutions into clinical workflow and the acceptability of MDC (T and M) by HCPs and patients.

1.3 Background

1.3.1 Type 2 Diabetes Mellitus and Challenges in Meeting Treatment Goals

Despite the increasing body of knowledge of diabetes treatment strategies, a majority of patients with T2DM are still in a persistent state of poor glycemic control and unable to meet target goals [1]. Inertia surrounding insulin initiation and titration is a specific problem. Physicians may be reluctant to initiate and titrate insulin owing to a belief about patient risk, including associated concerns about patient competence, and resource issues [2,3].

Most patients with T2DM are seen in a primary care (PC) setting [4], which presents challenges in overcoming clinical inertia and facilitation of intensified therapies. A provider's decision to delay therapy in many cases may be related to fears over inadequate time, educational resources and added workload [5-8]. A survey of physician attitudes found that they consider diabetes more difficult to treat than other chronic diseases as it requires more monitoring and medication adjustment to achieve treatment goals [7]. Physicians also report that there is inadequate support for the increased time and effort required for treating diabetes patients, and neither clinics nor patients can afford what it takes for comprehensive care [5-9].

Various approaches have been proposed to help overcome clinical inertia, including support of patient self-management, and education for both physicians and people with diabetes [10-13]. It has been recommended that patient education should specifically target the concerns surrounding the intensification of therapy [14,15]. Our team conducted a 12-month cluster randomized controlled trial *Practice Intensification via Office Transformation* (PIVOT) to explore the feasibility and effectiveness of a diabetes care and education specialist (DCES)-led provider/patient intervention to support pharmacotherapy advancement in PC. Findings support the value of DCES-led education to reduce clinical inertia while highlighting the heterogeneity of practice models with recognition that clinical inertia in PC is a complex issue that requires continued exploration [13,16].

In an era of more tightly controlled health care resources, health systems and payers, including the University of Pittsburgh Medical Center (UPMC) and its' integrated payer the UPMC Health Plan, have already begun to seek ways to examine approaches that shift roles and include non-physician practitioners to address the problems. In partnership and supported by our own UPMC Health Plan, a *Diabetes High Risk Program*, was designed for diabetes patients at high risk for complications and unplanned care to receive DCES planned visits in underserved rural and urban practices. Two DCESs were introduced as members of PC teams, identified and provided individualized self-management education to DM patients considered at high risk (i.e., hemoglobin A1C $\geq$9%, DM-related emergency room visit or hospitalization, or reported barriers to care, e.g. medication adherence). Patients who participated in the program had significant improvements in glycemia that were sustained for one year [17].

DCESs are well suited to support skills necessary to achieve glycemic target goals and considered experts in teaching patients medication taking skills [18,19]. Presently, paper-based guides are available in which clinicians/educators rely on to help their patients in determining and recording appropriate insulin doses. The paper-based titration tool is prepared as a worksheet with steps to determine the next insulin dose. Determining insulin doses in practice

today is often a matter of trial and error, as the dose is tailored to a patient's individual therapeutic needs. A provider determines an appropriate dosage for the first time based on weight and blood glucose records. The patient is then expected to consult their provider and/or a DCES (if available) to teach him/her how to adjust the insulin dose, based on their BG levels and given a paper-based scale/algorithm to guide them on dose change doses. The patient is expected to assume the "lion's share" of the effort to initiate and titrate insulin using their "worksheet" with limited or unpredictable follow up. Unfortunately, this process often sets the stage for reluctance and fear of insulin initiation and delays titration with implications for long-term poor self-management and adherence.

1.4 Significance

Appropriate titration of basal insulin and ensuring that patients adhere to health care professional (HCP) recommended therapeutic regimens is critical to the achievement and maintenance of glycemic targets in the management of T2DM. Therefore, Sanofi has developed the MDC (T&M) app for guiding titration and supporting maintenance of therapy.

1.4.1 MyDoseCoach Application

MDC is an FDA-approved digital solution comprising a smartphone app for people with T2DM and web portal for healthcare professionals (HCPs). The **MDC Basal Titration Module** (MDC-T) provides a digital alternative to the manual titration model that is typically used for dose modification of longer-acting basal insulin for patients with T2DM. This allows the HCP to tailor the dosing instructions to the individual patient based on the HCP's independent professional judgment. The HCP defines an individualized longer-acting basal insulin titration plan that is used in MDC to give dose recommendations to the user based on their FBG readings and hypoglycemic event data. MDC provides similar functionality as a paper-based tool, while automatically calculating the median FBG value and instructing the patient on the next appropriate insulin dose according to a dose plan and dose adjustment rules set by their HCP.

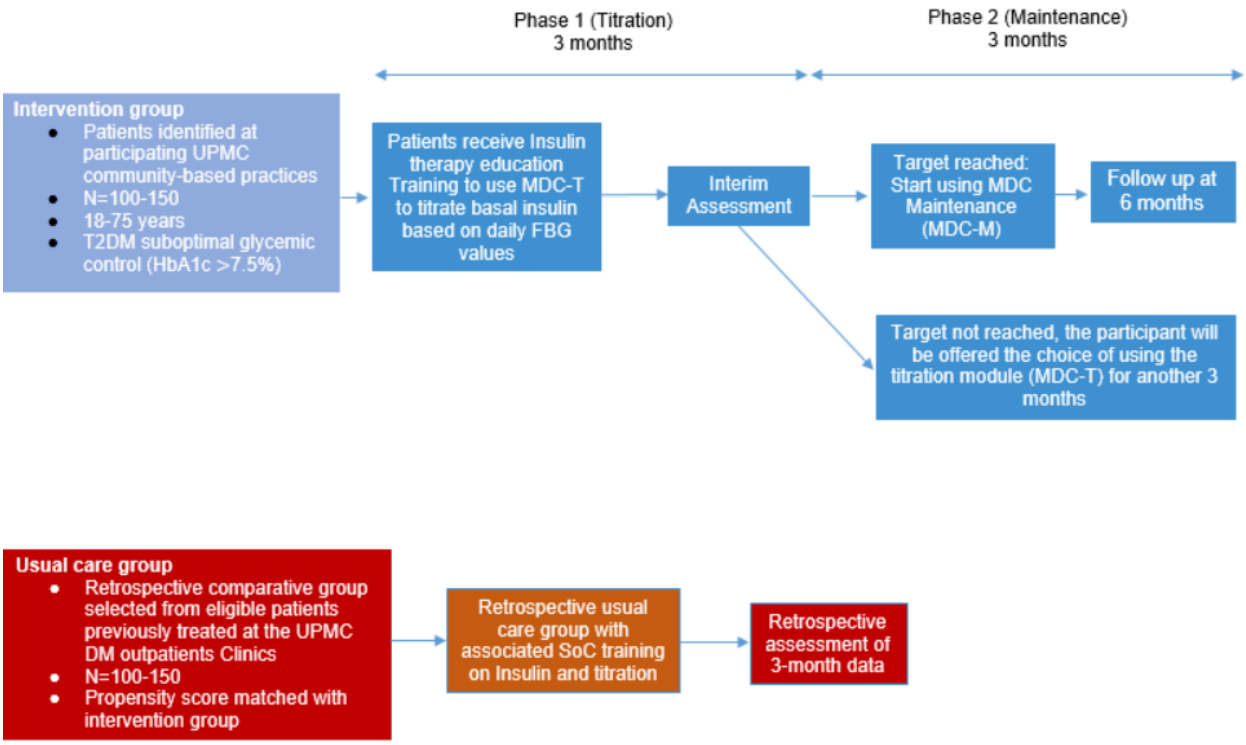
The MDC app is also designed to support patients in maintaining proper insulin dosing to help ensure ongoing glycemic control. Like the titration module, the **MDC Maintenance Module** (MDC-M) is intended for use by HCP's and patients to enable logging of insulin and non-insulin medication use and BG measurements and provide dosing and measurement reminders.

2 RESEARCH DESIGN AND METHODS

2.1 Classification and Methodological Designs

This study is a 6-month open label non-randomized trial with a prospective intervention group and a retrospective usual care group that includes two phases: Phase 1 (titration) will be used to determine effectiveness of MDC-T during insulin titration after 3 months. This is followed by Phase 2 (maintenance), a 3-month observational period for patients from the intervention group who reach titration targets, to determine effectiveness of their use of the MDC-M in helping patients maintain their glycemic targets. An overview of the study design in shown in the following figure.

Figure 2.1. Study Design



2.2 Detailed Description of Study Design

2.2.1 Setting

UPMC, headquartered in Pittsburgh, Pennsylvania, is one of the largest integrated health systems in the US, with more than 30 academic, community and specialty hospitals and 600 outpatient sites serving diverse populations throughout the region and beyond. UPMC is closely affiliated with the University of Pittsburgh and together support training for medical residents, clinical trials and other academic research. UPMC's reach and impact are extended through its Health Plan Insurer Services Division, which partners with UPMC and additional community network providers. UPMC is also a recognized innovator in health technology, including developing and applying data-driven approaches to provide patient-centered care. Central to these efforts is UPMC's Clinical Data Warehouse that contains all data points documented within the EMR system for every patient entering a UPMC facility, including but not limited to office visits, hospitalizations, medications, labs, and geographical information. The Department of Clinical Analytics aims to empower UPMC's health care professionals by providing access to interpretable visualizations of their own patient data. Such applications have facilitated both operational- and research-based endeavors, that ultimately improve patient care. For these reasons and more, UPMC provides an ideal "community laboratory" to examine methods that promote access and best practice to the patients it serves.

2.2.2 Heath Care Providers

HCPs who deliver diabetes care and education (e.g., endocrinologists, nurse practitioners, physician assistants and/or DCESs) at participating study sites will be invited to recruit/consent patients, train and support patients on use of the MDC, obtain study data as well as provide their own perspectives on the MDC app. Prior to initiating patient enrollment, participating HCPs will be fully trained on the MDC app and all study procedures, roles and responsibilities.

2.2.3 Intervention Group

Phase 1 (Titration)

Baseline Visit

Patients assigned to the intervention group will meet with a DCES and receive insulin therapy education according to current standard of care procedures (e.g., how to use an insulin pen, when and where to administer insulin, etc.). Whereas DCESs typically provide patients with written titration instructions prepared by the physician provider, for the intervention, DCESs, another HCP and/or a trained clinical research coordinator will train patients to use MDC-T for titration guidance. The physician provider will prepare an individualized titration algorithm, including a dose plan and dose adjustment rules that will be embedded in MDC-T. The DCES, another HCP, and/or clinical research coordinator will demonstrate to the patient how to use the MDC Titration Module to determine and guide dosing adjustments.

All patients will be asked to complete a baseline survey to assess behavioral and psycho-social factors that may influence diabetes self-management. In addition, patients will receive a three-month supply of insulin pens (Lantus (U100) Solostar Pen or Toujeo (U300) Solostar Pen, as per treating Physician).

Patients will be instructed to return for a three-month follow-up clinic visit, as is standard of care for patients new to insulin.

Month 3 Visit

At the three-month appointment, the DCES or another HCP will assess the patient's experiences with titration and MDC-T, which will be documented using a study-specific survey. If the patient successfully reached their glycemic target, they will be invited to participate in Phase 2 of the study (maintenance).

For those patients who do not reach target at 3 months, the DCES/HCP will partner with the patient (and physician provider, as needed) to assess the patient's ability and interest in continued use of the MDC-T app and determine the best course of action (either return to usual care or continued participation in the study). If deemed eligible, the patient will continue to have access to the MDC-T app with continued guidance from their respective HCP, in regards to insulin therapy recommendations. They will be asked to complete follow-up surveys at months 3 and 6, as well as permit access to pertinent medical record information (e.g., HbA1c values) for the duration of the study. Patients who stay in the study and continue to use the MDC-T app will receive another three-month supply of insulin pens (Lantus (U100) Solostar Pen or Toujeo (U300) Solostar Pen, as per treating Physician).

Phase 2 (Maintenance)
Patients who are successful in reaching their glycemic target and agree to continue participation, will be transitioned into Phase 2 of the study at their three-month clinic visit. At this time, the HCP (endocrinology provider and/or DCES) will introduce and train patients how to use the MDC-M app to support glycemic control. Patients will receive another three-month supply of insulin pens (Lantus (U100) Solostar Pen or Toujeo (U300) Solostar Pen (as per treating Physician) and asked to return for the final follow-up visit at six months (routine clinic visit). They also will be asked to complete follow-up surveys at months 3 and 6 to assess changes in behavioral and psychosocial factors that influence diabetes self-management as well as their acceptability and satisfaction with their experience using the MDC app. When possible, surveys will be completed at clinic visits. However, surveys may also be made available electronically or via mail should visits occur remotely (e.g., via telemedicine) or a patient cannot complete at a face-to-face visit (e.g., time constraints).

The DCES and endocrinology provider will be available throughout the course of the study to respond to any question or concerns that the patient may have regarding insulin titration, insulin dosing, and the MDC app specifically.

2.2.4 Usual Care Group

A retrospective comparative group will be selected from eligible patients who previously were treated at the UPMC Diabetes Outpatient Clinics. This group was chosen for two reasons. First, patients seen at the UPMC Diabetes Specialty Outpatient Clinics have the most robust data available regarding insulin titration, including HbA1c and FBG and, for many patients, BG meter readings. Secondly, this particular group establishes a standard of specialty care against which to compare MDC and will uniquely inform the benefit of this digital tool. We postulate that if MDC produces outcomes, at the very least, equal to those of specialty practice, the likelihood of benefit to PC care is high. Patients in the usual care group will be identified using EMR data accessed through the UPMC Clinical Data Warehouse. As detailed in the Statistical Analysis Plan, propensity score matching will be used to pair intervention and usual care participants.

2.2.5 Study Calendar

Study phase	**Phase 1 (Titration)**		**Phase 2 (Maintenance)**
Visits	**1**	**2**	**3**
Time point	**Baseline**	**3 Months**	**6 Months**
Visit window		**±2 weeks**	**±4 weeks**
Study Specific Procedures			
Informed Consent	X		
Eligibility	X		
MDC Installation and Education	X	X[1]	
Patient Surveys[3]	X	X	X
Health Care Provider Surveys[4]	X	X	X
Reports of Technical Issues		X	X

Clinical Care/EMR Data Abstraction			
Demographics[5]	X		
Patient History[6]	X		
Vital signs[7]	X	X	X
Lab work[8]	X	X	X
Self-monitoring blood glucose (SMBG)		X	X
Provider visits (and Endocrinology escalation visits)		X	X
Hypoglycemic events	X	X	X
Hospital stays	X	X	X
Adverse events	X	X	X

1. Education on MDC-M app only for those participants who were able to reach target FBG/A1c transition to maintenance.
2. Diabetes Medication System Rating Questionnaire-Short Form (DMSRQ-SF), Diabetes Distress Scale (DDS17) at all time points; Usability and Satisfaction surveys as 3 and 6 months.
3. Health care provider perspectives and experiences on insulin dosing survey at baseline and usability and satisfaction survey at 3 months and completion of the study.
4. Participant name, age, gender, race, ethnicity, contact information, location, marital status, employment status, education level, health insurance information
5. Diabetes duration, diabetes-related medication, diabetes-related hospitalizations, hypoglycemic events within the past year, co-morbidities
6. Blood pressure, weight, BMI
7. Fasting blood glucose, HbA1c, cholesterol, lipids (if available in clinical records); baseline values may have been collected and recorded up to nine months prior to study start (e.g., lipid panels are usually conducted once a year).

2.3 Insulin Management System

Clinical and research components of clinical care are delineated in the table below. The information included in the “Routine Clinical Care (not on study)” column represents the routine care a patient with diabetes would undergo when starting an insulin regimen without being on a research study. The information in the “Routine Clinical Care (on study)” column represents the procedures the research participants will receive as routine clinical care while on this study and not related to the research component. The procedures in the “Study Research” column represents the investigational component of this research study being evaluated and would not be included as part of the patient’s routine clinical care.

Table. Clinical and Research Components of Patient Visits

	Routine Clinical Care (not on study)	Routine Clinical Care (on study)	Study Research
Phase 1 – Titration	• Insulin pen (or syringe and needles) • Paper dosage algorithm • Blood glucose meter	• Insulin pen (Lantus (U100) Solostar Pen or Toujeo (U300) Solostar Pen (as per treating Physician)) • Dosage algorithm • Blood glucose meter	• Use of MDC-T app (to support insulin dosage algorithm) •

Phase 2 - Maintenance	• Insulin pen • Blood glucose meter	• Insulin pen (Lantus (U100) Solostar Pen or Toujeo (U300) Solostar Pen (as per treating Physician))Blood glucose meter •	• Use of MDC-M app •

2.3.1 Phase 1 - Titration

- Lantus (U100) Solostar Pen or Toujeo (U300) Solostar Pen (as per treating physician)
- MyDoseCoach Titration App (MDC-T)
- Blood Glucose Meter (any meter allowed)

2.3.2 Phase 2 - Maintenance

- Lantus (U100) Solostar Pen or Toujeo (U300) Solostar Pen (as per treating physician)
- MDC-M app
- Blood Glucose Meter (any meter allowed)

2.4 Outcome Assessment

The MDC app will be evaluated using a combination of clinical, behavioral, psychosocial, provider, patient and process measures, in addition to MDC analytics, as described in this section.

2.4.1 Clinical Data/EMR Abstraction

Intervention Group
Phase1 (Titration) Clinical: HbA1c will serve as the primary outcome and clinical measure to determine the impact of the MDC-T app on glycemic control from baseline to 3 months. Related measures to be collected will include: Change in FBG from baseline to 3 months, rate of patients who attained individualized titration target, the time it took to attain titration target and number and type of hypoglycemic events, which are defined as follows:

- Mild/asymptomatic hypoglycemia – blood glucose <70 mg/dl and no symptoms;
- Moderate/symptomatic hypoglycemia – blood glucose <70 mg/dl and symptoms;
- Severe/symptomatic hypoglycemia – requires assistance of another person to resuscitate because blood glucoses are too low to maintain consciousness.

Hypoglycemic data will be collected in the following ways:

1) ask the patient to contact study team if/when it happens,

2) ask patient at each study visit,
3) review of MDC information,
4) review of EMR,

Data will be collected on an AE form for each patient and reported if an SAE. In addition, blood pressure, cholesterol and BMI data will be retrieved from the patient's EMR record.

Phase 2 (Maintenance) Clinical: HbA1c will serve as the primary outcome to determine the longer term impact of MDC-M app on maintenance of glycemic control from 3 months to 6 months for those patients achieving glycemic targets during the MDC-T titration phase. Related measures to be collected will include the number of patients who maintained individualized glycemic targets, change in FBG from 3 months to 6 months, and record of reported hypoglycemic events (following same definitions and data collection plan as described for Phase 1). Additionally, blood pressure, cholesterol and BMI data will be retrieved from the patient's EMR record.

All of the aforementioned data will be collected for the intervention group in accordance with the study calendar in section 2.2.5.

Control Group
A majority of the data is also expected to be available within the EMR for the control group. HbA1c, FBG, blood pressure, cholesterol, and BMI data should be recorded and accessible for patients. In addition, many patients also have BG meter readings. At a minimum, we will select patients who have HbA1c values that correspond to baseline [index date = date of insulin initiation] and follow-up time points/time frames that correspond with those described in the study calendar (section 2.2.5). EMR records, including notes, downloads, and related documented data will be reviewed to identify and classify hypoglycemic events according to already aformentioned definitions.

2.4.2 Health Care Provider/Clinical Workflow-Related Outcomes

Clinician experiences and perspectives on insulin dosing previous to the study will be collected at baseline and the usability of and satisfaction with the MDC will be assessed through a study-specific satisfaction survey (provider version). DCESs will keep logs detailing experiences (including triage/escalation to the need for an endocrinologist visit) and logistical issues, particularly those related to technology and disruption of workflow. In addition, at the end of the study, discussions s will be organized with UPMC HCPs and staff to review study findings and elicit additional perspectives on effective ways to integrate the app into clinical workflow in clinical practice.

2.4.3 Patient-Related Outcomes

Patient usability of MDC to titrate insulin and maintain glycemic control will be tracked relying on the devices inherent data analytics. Patient satisfaction will be assessed using study specific acceptability and satisfaction surveys (patient version) and the validated Diabetes Medication System Rating Questionnaire-Short Form (DMSRQ-SF) [20]. Diabetes medication system refers to the medication taken as well as the devices and supplies required to administer the medication. The DMSRQ-SF includes 20 items to assess convenience, negative events,

interference, self-monitoring of blood glucose burden, efficacy, social burden, psychological well-being, treatment satisfaction and treatment preference [20].

Other patient data to be collected will include demographics, diabetes-related information (e.g., duration, medications, etc.), and their level of diabetes distress, which will be evaluated at baseline and follow-up with the 17-item Diabetes Distress Scale (DDS17). The DDS17 assesses four dimensions of distress – emotional, regimen, interpersonal and physician [21], and has shown a consistent pattern of relationships with HbA1c, diabetes self-efficacy, diet and physical activity in multiple samples of patients with T2DM [22].

2.5 Study Endpoints

2.5.1 Primary Endpoint

Change in HbA1c at 3 months as compared to patients using standard of care.

2.5.2 Secondary Endpoints

2.5.2.1 Phase 1 (Titration)

- Change in HbA1c from baseline to 3 months within and between groups
- Proportion of patients reaching HbA1c <7% at 3 months as compared to patients using SOC
- Change in FPG from baseline to 3 months within and between groups
- Patient-reported changes in behavioral and psychosocial outcomes from baseline to 3 months (survey)
- Patient-reported acceptability of and satisfaction with MDC-T (survey)
- Provider-reported acceptability of and satisfaction with MDC-T (survey)
- Rate of escalation to Endo (Endocrine visits) for patients using MDC-T
- Safety end points (including hypoglycemia, any untoward adverse events)
- Number and type of technical complaints

2.5.2.2 Phase 2 (Maintenance)

- Proportion of patients maintaining their individualized HbA1c goal at 6 months as compared to the number of patients at target HbA1c at start of maintenance phase (month 3)
- Proportion of patients maintaining HbA1c <7% at 6 months compared to number of patients at target HbA1c <7% at start of maintenance phase (month 3)
- Change in HbA1c from baseline and 3 months to 6 months
- Change in FPG from baseline and 3 months to 6 months, if available
- Adherence to HCP recommended treatment plan
- Patient-reported changes in behavioral and psychosocial outcomes from baseline or 3 months to follow up time points (survey)
- Safety end points (including hypoglycemia, AEs)

- Number and type of technical complaints

2.6 Statistical Analysis

2.6.1 Power and Sample Size Justification

The primary objective of this study is to estimate the difference in HbA1c between the study treatment groups at 3 months. The sample size justification is based on precision estimate (i.e., confidence interval for the HbA1c difference between groups). The expected standard deviation for the 3-months change from baseline in HbA1c is 1.5. With 109 patients in the interventional arm and 109 patients in the retrospective control arm, the treatment effect, expressed as the LS means difference between arms, would be estimated with an expected precision of ± 0.40. Additionally, this sample size allows for a sufficient number of patients after drop-out, loss to follow-up and/or missing data to enter the maintenance phase (Phase 2) of the study. Based on previous research and experiences with insulin titration, an anticipated 70% of patients (n=76) will enter Phase 2 of the study.

2.6.2 Data Analysis

Patients will be matched 1:1 on a propensity score based on baseline demographics and clinical characteristics to improve the comparability of the interventional and retrospective groups. A logistic regression model will be used to estimate the propensity score and those baseline variables that influence treatment assignment will be included in the model. In this analysis, the following variables will be used to calculate the propensity score: age, gender, baseline BMI and baseline HbA1c. Other factors that may be included are race and number of comorbid conditions. Once the propensity score is calculated, a greedy nearest neighbor algorithm will be used for matching to form pairs of subjects from intervention and control groups with similar propensity scores. This means that for a given treated subject, the closest untreated subject within the specified caliper distance is selected for matching to the treated subject.

Descriptive statistics (e.g., demographics, duration of diabetes, etc.) will be used to describe the study groups. Baseline comparisons will be examined using standardized mean differences. A linear mixed model will be used to adjust the fixed effect of baseline FBG and the random effect of matched pairs, allowing to estimate the treatment effect with 95% CI. . Generalized estimating equations (GEE) for binary outcomes will be for binary outcomes to compare the change in slopes of outcomes of interest between the two groups and account for matched pairs . In addition, for the intervention group only, descriptive statistics will be used to summarize other data (e.g., patient and provider surveys, MDC metrics, etc.), and thematic analysis of any qualitative findings will be made.

Phase 1 (Titration): For the intervention group only, using a descriptive statistical approach, a primary assessment of titration outcomes will be built into the study at 3 months to evaluate the MDC-T app using a combination of clinical data, provider and patient feedback and process data (including patient/provider study-specific efficiency and satisfaction surveys, DE logs, validated DMSRQ-SF and MDC analytics).

Phase 2 (Maintenance): For the intervention group only, using a descriptive statistical approach, an assessment of maintenance outcomes will occur to compare the percentage of patients at goal between the study treatment group at 6 months. Clinician and patient experiences and perspectives on the usability of and satisfaction with MDC-M will be assessed through various means including study-specific efficiency and satisfaction surveys.

3 HUMAN SUBJECTS

3.1 Subject Population

Intervention participants will be identified in a consecutive manner at participating UPMC community-based PC practices, outpatient clinics and inpatient units. Study participants will include adult male and female T2DM patients, 18 to 75 years old, with T2DM and suboptimal glycemic control (HbA1c > 7.5%) who are recommended to start titrating basal insulin and willing and able to use the MDC app.

The retrospective comparative group will be selected from eligible patients who previously were treated at the UPMC Diabetes Outpatient Clinics. This group will be chosen for two reasons. First, patients seen at the Diabetes Outpatient Clinic have the most robust data available regarding insulin titration, including HbA1c and FBG and, for many patients, BG meter readings. Secondly, this particular group establishes a standard of specialty care against which to compare MDC and will uniquely inform the benefit of MDC. Patients in the usual care group will be identified using EMR data accessed through the UPMC Clinical Data Warehouse.

3.2 Inclusion Criteria

3.2.1 Intervention Group

- Patient receiving care at a UPMC Diabetes Outpatient and/or Inpatient settings
- Adult male and female patients 18 to 75 years old
- HbA1c > 7.5%
- Recommended to start self titration of basal insulin
- Access to and able to use an iOs or Android enabled device and have reliable internet access
- Willing and able to use the MDC app
- Able to comprehend basic diabetes survival skills, signs and symptoms of hypoglycemia and treatment of BG

3.2.2 Usual Care Group

- Adult male and female patients 18 to 75 years old
- HbA1c > 7.5%
- Started on basal insulin in a UPMC Diabetes Outpatient facility within the past three years of study start

- Has blood glucose data available in EMR (At least two HbA1c measurements corresponding to baseline and a subsequent time point after insulin titration) FBG readings)

3.3 Exclusion Criteria

- Pregnant or breastfeeding
- Patients unwilling to use MDC app

4 IRB APPROVAL

The Investigator will obtain, from the University of Pittsburgh Institutional Review Board (IRB), prospective approval of the clinical protocol and corresponding informed consent form(s); modifications to the clinical protocol and corresponding informed consent forms, and advertisements (i.e., directed at potential research subjects) for study recruitment.

The only circumstance in which a deviation from the current IRB-approved clinical protocol/consent form(s) may be initiated in the absence of prospective IRB approval is to eliminate an apparent immediate hazard to the research subject(s). In such circumstances, the Investigator will promptly notify the University of Pittsburgh IRB of the deviation. The Investigator should also notify the sponsor of this event.

The University of Pittsburgh IRB operates in compliance with FDA regulations at 21 CFR Parts 50, 56 and 812, also in conformance with applicable International Conference on Harmonization (ICH) Guidelines on Good Clinical Practice (CGP).

5 RECRUITMENT AND INFORMED CONSENT PROCEDURES

5.1 Recruitment Methods

5.1.1 Intervention Group

Intervention participants will be identified at participating UPMC community-based PC practices, outpatient clinics and inpatient units. A diabetes healthcare provider or staff member (e.g., endocrinologist, PCP, DCES) will identify patients who meet the following inclusion criteria – age, elevated HbA1c, and recommended to start basal insulin – and briefly introduce the patient to the study. The patient may be identified first from a clinic schedule or during the course of their visit. If the patient is interested in learning more about the study, a study investigator (who may also be a diabetes healthcare provider) will provide a more thorough description and a copy of the informed consent for review.

5.1.2 Health Care Group

HCPs (provider participant) who already provide diabetes care and education as part of the patient's routine clinical care will be involved in recruiting individuals for participation in this research study. The PI will formally invite HCPs to join the study, either in person or electronically (via email). A brief overview of the study, the risks and an explanation of their

involvement will be discussed with the potential provider participant. The PI, who is a nurse and DCES, works with and familiar with the HCPs that will be invited to be the provider participants for this study. If an HCP is interested in participating, they will be presented with the consent form.

5.2 Participant Informed Consent Procedures

There are 3 options for obtaining consent:

1) Consent process may take place within the diabetes outpatient or primary care setting (Diabetes endocrine satellite clinics or participating primary care sites) or during an inpatient stay.
2) Consent process may take place by videoconferencing.
3) Consent process may take place by telephone.

Consent will be obtained prior to performing any of the research interventions/interactions.

5.2.1 Consenting in the Outpatient Practice or Inpatient Setting

Potential participants will be presented with the research study and if interested will be presented with the informed consent form. If a potential participant is identified prior to an outpatient clinic visit, they may be presented with the research study by phone and if interested the consent may be sent to them by mail or email for them to review prior to their clinic visit.

Potential participants are ensured that their decision to participate is totally voluntary and in no way will jeopardize their diabetes care or education services. Patients will be given sufficient time to come back to the study team regarding any questions that they may have and their decision. After reading/explaining the consent and study procedures, the study team member will ask the participant if they have any questions (general) and then re-review the study procedures one more time to ensure that they are fully understood.

5.2.2 Process for Videoconferencing Consenting

- Study staff sends two copies (one to send back and one to keep) of the consent (via email or USPS) to the potential participant and schedules a video diabetes education visit to occur about a week later. In addition to the consent forms, they will also be provided a self-addressed, stamped envelope.
- During the video visit, the participant must have a hard copy in front of them as the study staff reads it, and if they agree, will sign in front of the study staff by video.
- The participant will hold up their signed signature page and study staff will take a “screen shot” – print it out to be attached to the study staff signed consent form. Another option is for the patient to take a picture of their signed signature page and upload into their MyUPMC account for the study staff to access.
- The participant will be instructed to mail their original signed copy of the consent form to study staff using the self-addressed, stamped envelope.

- Research procedures can start via video visit after the study staff gets the screen shot of the participants signature page.

Potential participants are ensured their decision to participate is totally voluntary and in no way will jeopardize their diabetes care or education services. Patients will be given sufficient time to come back to the study team regarding any questions that they may have and their decision. After reading/explaining the consent and study procedures, the study team member will ask the participant if they have any questions (general) and then re-review the study procedures one more time to ensure that they are fully understood.

6 POTENTIAL RISKS AND BENEFITS

6.1 Potential Risks

The potential risks associated with participation in the study are of low frequency and of low/acceptable risk level.

There is little likelihood of physical risk because of participation in this study. Patients will not undergo any clinical procedures beyond those used during usual diabetes care. Collection of clinical data will follow usual care procedures and be performed by trained clinical staff. As is usual, patients may experience some physical discomfort during clinical procedures.

MDC is prescribed by the HCP with a therapy plan. A detailed risk analysis (user and product) has been conducted to evaluate all possible risks to the end user. An example of such a risk is how likely an overdose, attributed to an incorrect dose recommendation, will lead to serious hypoglycemia.

All such risks have been mitigated in the design of all the products and/or via risk control measures to prove that the produce is safe for use.

Within the context of this study, a favorable benefit-risk balance for the provided Sanofi medicinal products (Toujeo and Lantus) is already well established. The use of both drugs in this study is according to the approved National Product Label.

Patients are at low risk for psychological harm as no research procedures are performed in addition to usual care except for the addition of technological support and the administration of questionnaires. The only potential risk is that patients may not fully understand the technology process or experience frustration. Clinical personnel will be asked questions that have low psychological risk and may refuse to provide answers to any questions they are not comfortable answering or if in any way they feel that answering questions may jeopardize their employment or practice communications. Clinical personnel also run the potential risk of frustration with the technology process or perceive additional burden or experience disappointment with any unintended technological challenges in the process.

There is little social risk associated with this study. Patients are at low risk to social harm as no research procedures are performed in addition to usual care except for the addition of the

technology. For clinical personnel, questions will not go beyond the topic of healthcare delivery. HCP participants may perceive that feedback may be used to rate their performance; however, this is not the case and all responses will be kept anonymous. HCP participants may find the additional of technology to pose a potential disruption in office workflow.

There is a small possibility of a breach of confidentiality. Procedures will be put in place to minimize this risk. All participant questionnaires will be de-identified and kept in a double locked environment (paper questionnaires) or a secure server (electronic questionnaires).

6.2 Alternative Treatments

Patients who decline participation in this study will receive usual care for insulin dosing.

6.3 Potential Benefits

This study may contribute to the participants' ability to better self-manage their diabetes and provide valuable information on a process that has the potential to add evidence for broad best practice guidelines and policy. We are enthusiastic about the opportunity to implement a model MDC app that helps patients perform titration effectively to achieve their target goal and maintain improvement as compared to the current manual practice.

7 RISKS MANAGEMENT PROCEDURES

The nature of this study places patients at low risk to physical, psychological or social harm. Patients will not undergo any procedures beyond usual care except for the addition of access to clinical, health, and self-management support delivered through technology. Patients and clinical personnel who participate will be free to refuse to respond to any survey questions. All responses will be kept anonymous and not linked to any identifying information.

Only the minimum amount of data necessary for answering the proposed research questions will be extracted from the medical records. Patients will be assigned unique, study-specific identifiers. No clinical data will be linked to medical record numbers. A file linking patients to subject identifiers will be stored separately and securely from de-identified patient clinical data. Clinician participant data will be collected anonymously. Any identifying information will be eliminated from surveys. All research data will be stored on encrypted and password protected network drives. Access to patient-level data will be limited to members of the research team involved in data collection. All other members of the research team will review de-identified data.

All research interventions/activities will be conducted in private. The collection of sensitive information about subjects is limited to the amount necessary to achieve the aims of the research, so that no unneeded sensitive information is being collected.

Any paper records with patient identifying information will be store behind a double locked environment. An electronic password-guarded study database may be used under the supervision of the Investigator for this protocol with data being entered anonymously with a subject code behind a UPMC and/or University of Pittsburgh's secure computer server. Information linking subject identifiers with the coded subject number will be stored under password protection on computers in locked areas, with access only to the database manager.

All staff will sign confidentiality statements. Access to the database will be limited to the data manager and staff under the supervision of the Investigator.

All staff involved in this study are properly credentialed and instructed in the areas of testing, confidentiality, and safety.

The PI will retain the data for the entire period of this study and will retain the specified records and reports for up to seven years at least seven years after final reporting or publication of the study. If the subject and/or legal representative decide to withdraw or be withdrawn from study participation, they may request that the study data and samples be destroyed. Subject names or other directly identifiable information will not appear on any reports, publications, or other disclosures of clinical study outcomes.

8 REPORTABLE EVENTS

Each patient will be carefully monitored for adverse events by the investigator.

8.1 Definitions

8.1.1 Adverse Event (AE):

Any untoward medical occurrence in a patient or clinical investigation subject administered a product and which does not necessarily have to have a causal relationship with this intervention.

8.1.2 Adverse Event of Special Interest (AESI)

An adverse event of special interest (AESI) is an adverse event (serious or non-serious) of scientific and medical concern specific to the Sponsor's product or program, for which ongoing monitoring and rapid communication by the Investigator to the Sponsor may be appropriate. Such events may require further investigation in order to characterize and understand them. AESIs may be added or removed during a study by protocol amendment.

The AESIs are listed below:

- Pregnancy of a female subject entered in a study as well as pregnancy occurring in a female partner of a male subject entered in a study with Sanofi medicinal products or devices;
    - Pregnancy occurring in a female participant entered in the clinical trial or in a female partner of a male participant entered in the clinical trial. It will be qualified as an SAE only if it fulfills one of the seriousness criteria.
    - In the event of pregnancy in a female participant, Sanofi medicinal products or devices should be discontinued.
    - Follow-up of the pregnancy in a female participant or in a female partner of a male participant is mandatory until the outcome has been determined
- Symptomatic overdose (serious or non-serious) associated with Sanofi medicinal products or devices. An overdose (accidental or intentional) associated with the Sanofi medicinal product or devices is an event suspected by the Investigator or spontaneously notified by the participant (not based on systematic drug count) and defined as any dose

administration which, in the Investigators opinion based on clinical judgment, is considered significantly greater than the prescribed dose of insulin.

Of note, asymptomatic overdose has to be reported as a standard AE.

8.1.3 New Safety Finding

Any (other than reportable individual case safety report (ICSR)) safety issue that may require expedited reporting because providing information that may lead to a change in the known risk-benefit balance for the product and as mentioned, but not limited to, in the following regulatory texts: Europe: Good Pharmacovigilance Practices, modules VI and VII; and US: FDA: 21 CFR Parts 312 Investigational New Drug Application- Section 312.32, (c) (1) IND safety reports.

8.1.4 Related Adverse Event, i.e. Adverse Drug Reaction (ADR)

There is a reasonable possibility according to the External Sponsor that the product may have caused the event.

8.1.5 Serious adverse event (SAE)

Any untoward medical occurrence that at any dose:

- Results in death
- Is life threatening, (Note: the term “life-threatening” refers to an event/reaction in which the patient was at risk of death at the time of the event/reaction; it does not refer to an event/ reaction which hypothetically might have caused death if it were more severe)
- Requires inpatient hospitalization or results in prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect, or
- Is a medically important event or reaction. Medical and scientific judgment should be exercised in deciding whether other situations should be considered serious, such as important medical events that might not be immediately life-threatening or result in death or hospitalization, but might jeopardize the patient or might require intervention to prevent one of the other outcomes listed in the definition above.

8.1.6 Unexpected related Adverse Event, i.e. Unexpected Adverse Drug Reaction (ADR)

An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g., Investigator's Brochure for an unapproved investigational medicinal product or package insert/summary of product characteristics for an approved product). An expected ADR with a fatal outcome should be considered unexpected unless the local/regional product labeling specifically states that the ADR might be associated with a fatal outcome.

8.1.7 Device Deficiencies

All inadequacies related to the identity, quality, durability, reliability, safety or performance of the medical device including malfunctions, use errors, and inadequate labelling.

8.1.8 Unanticipated Serious Adverse Device Effect

Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

8.1.9 Medical Device Reporting reportable event

- An event that user facilities become aware of that reasonably suggests that a device has or may have caused or contributed to a death or serious injury or
- An event that manufacturers or importers become aware of that reasonably suggests that one of their marketed devices:
  - *May have caused or contributed to a death or serious injury, or*
  - *Has malfunctioned and that the device or a similar device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.*

8.2 Obligations and Responsibilities of the External Sponsor

The External Sponsor shall be responsible for transmitting to Sanofi all AE's occurring with the use of Sanofi medicinal products.

All complaints and adverse events will be managed and reported in compliance with all applicable regulations and included in the final clinical study report.

For the intervention group:

- All AEs, regardless of seriousness or relationship to Sanofi Medicinal product and study medical devices (e.g., MDC app), spanning from the signature of the informed consent form until the end of the study as defined by the protocol for that patient, are to be recorded on the corresponding page(s) or screen(s) of the CRF.
- Any defect in the device or medical device complaint, with AE must be reported within 24 hours in case of potential Adverse Event or Serious Adverse Event or without AEs must be reported within 5 days by the Investigator in order for a product technical complaint to be completed. Appropriate information (e.g., samples, labels, or documents such as pictures or photocopies) related to product identification and product deficiencies may need to be gathered. The investigator will assess whether or not the quality issue has to be reported together with an AE or SAE.
- Whenever possible, diagnosis or single syndrome should be reported instead of symptoms. The Investigator should specify the date of onset, intensity, action taken with respect to Sanofi Medicinal product or Medical Device, corrective treatment/therapy given, additional investigations performed, outcome, and his/her opinion as to whether there is a reasonable possibility that the AE was caused by Sanofi Medicinal product(s), Medical Device or by the study procedure(s).
- The Investigator should take appropriate measures to follow all AEs until clinical recovery is complete and laboratory results have returned to normal, or until progression has been stabilized, or until death, in order to ensure the safety of the patients. This may imply that observations will continue beyond the last planned visit per protocol, and that

additional investigations may be requested by the monitoring team up to as noticed by the Sponsor.

- When treatment is prematurely discontinued, the patient's observations will continue until the end of the study as defined by the protocol for that patient.
- Laboratory, vital signs abnormalities are to be recorded as AEs only if:
  - Symptomatic and/or
  - Requiring either corrective treatment or consultation, and/or
  - Leading to Lantus (U100) or Toujeo (U300) discontinuation or modification of dosing, and/or
  - Fulfilling a seriousness criterion, and/or
  - Defined as an AESI

For the retrospective control group:
The Sponsor will transmit at the time of the analysis and at the latest the time of study report to Sanofi safety signals or conclusions with potential safety impact if any, based on data documented within the EMR.

8.2.1 Reporting Serious Adverse Events

SAEs will be reported as follows:

- SENDING (within 24 hours, preferably by fax or e-mail) the signed and dated corresponding page(s) from the CRF to the representative of the monitoring team whose name, fax number and e-mail address appear in the clinical trial protocol
- ATTACHING a photocopy of all examinations carried out and the dates on which these examinations were performed. Care will be taken to ensure that the patient's identity is protected and the patient's identifiers in the clinical trial will be properly mentioned on any copy of a source document provided to the Sponsor. For laboratory results, the laboratory normal ranges will be included
- All further documentation will be sent to the monitoring team within 24 hours of knowledge of the SAE. In addition, every effort will be made to further document any SAE that is fatal or life threatening within a week (7 days) of the initial notification.

Any SAE brought to the attention of the Investigator at any time after the end of the study for the patient and considered by him/her to be caused by the Sanofi Medicinal product(s)/study medical devices with a reasonable possibility, will be reported to the monitoring team.

8.2.2 Reporting Adverse Events of Special Interest

For AESIs, the Sponsor will inform Sanofi immediately (i.e., within 24 hours), as per SAE notification guidelines described previously

8.3 Sanofi Pharmacovigilance Contact

Fax/emails to be adapted in the final contract:
Email: CL-CPV-Receipt@sanofi.com
Or
Fax: to +33 1 60 49 70 70

8.4 Sanofi Product Technical Complaint Contact

Fax/emails to be adapted in the final contract:
Email: customerservice@agamatrix.com
Or
Fax: to 1-866-906-4197

9 DATA SAFETY MONITORING

9.1 Data Safety Monitoring Plan

A data and safety monitoring plan (DSMP) will be implemented by the PI to ensure that the confidentiality of the research data is maintained. The data and safety monitoring plan for the research information will involve quarterly monitoring by the PI of 1) the removal of direct identifiers from information contained within the electronic research database; 2) the security of the database linking the electronic research database linkage codes with subject identifiers; and 3) any conditions that may negatively impact the confidentiality of information contained within the electronic research database. In addition to the DSMP meetings, the research team will hold meetings to discuss the study (e.g., study goals; progress in data collection, coding, and analysis; identification and documentation of adverse events or subject complaints; violations of confidentiality) and address any issues or concerns at that time. The research staff will also submit annual reports to the IRB at the time of annual renewals.

Sharing of data generated by this project is an essential part of our proposed activities and will be carried out in several different ways. We would wish to make our results available both to the community of scientists and health care providers interested in diabetes and ways to support patients in successful diabetes self-management. Specifically, we intend to present at national/international scientific meetings (e.g., the American Diabetes Association's Scientific Sessions), and in peer-reviewed journals (e.g., the DCES). In addition, we will also present our findings to local health care providers to inform best practices of diabetes care.

Data confidentiality will be closely supervised. All paper-based files will be stored in a locked file cabinet with limited access.

9.2 Frequency of Monitoring

The PI will review subject safety data as it is generated. The PI, sub-investigators, and the research staff will meet at least monthly to re-evaluate study goals, subject recruitment, data coding and retention, documentation and identification of adverse events, complaints and confidentiality of subjects. There will be an evaluation of the progress of the research study, including assessments of data quality, timelines, participant recruitment, accrual, and retention. The PI will also review the outcome and adverse event data to determine whether there is any change to the anticipated benefit-to-risk ratio of study participation and whether the study should continue as originally designed or should it be re-evaluated and changed.

10 WITHDRAWAL OF SUBJECTS

Participation in this research is completely voluntary. An individual's decision whether or not to participate in this research, or to later withdraw from it, will not affect his/her current or future medical care at UPMC or the relationship with the University of Pittsburgh. If a participant chooses to withdraw, any information collected about the participant up until the time of withdrawal will be kept, but no additional information will be collected.

Study investigators may choose to remove participants from the study if a participant is advised by their health care provider to discontinue insulin therapy or if a participant is no longer able to act independently to follow study procedures due to such reasons as mental/cognitive incapacity or moved to assisted living.

In addition, a subject may be considered "lost to follow" if they cannot be reached. Every attempt will be made to contact these participants and after 3 failed attempts a certified letter will be sent to the participant.

11 COSTS AND PAYMENTS

11.1 Costs

Item	Cost/Supplier
MyDoseCoach App (Titration and Maintenance)	Available free of charge from either the Google Play Store for android devices or App Store for iOS Apple devices
Lantus (U100) Solostar Pen or Toujeo (U300) Solostar Pen	Supplied free of charge by Sanofi

11.2 Payments

Patients will receive $20 for completing the baseline survey and $50 for each completed survey at 3 and 6 months. In addition, $100 per participant will be allotted for HCPs as remuneration for their time spent on study-related activities (e.g., consenting participants, survey administration, instructing patients on MDC, etc.).

12 REFERENCES

1. Khunti K, Wolden ML, Thorsted BL, Andersen M, Davies MJ. Clinical inertia in people with type 2 diabetes: A retrospective cohort study of more than 80,000 people. Diabetes Care 2013 Nov;36(11):3411-3417.
2. Peyrot M, Rubin RR, Lauritzen T, et al; International DAWN Advisory Panel. Resistance to insulin therapy among patients and providers: Results of the cross-national Diabetes Attitudes, Wishes, and Needs (DAWN) study. Diabetes Care 2005;28(11):2673-2679.
3. Wallace TM, Matthews DR. Poor glycaemic control in type 2 diabetes: A conspiracy of disease, suboptimal therapy and attitude. QJM 2000;93(6):369-374.

4. Janes G. Ambulatory medical care for diabetes. In: Group NDD (2nd ed.), Diabetes in America, Vol. 95-1468, Bethesda, Maryland: National Institutes of Health. 1995;541-552.
5. Del Prato S, Penno G, Miccoli R. Changing the treatment paradigm for type 2 diabetes. Diabetes Care 2009;32(Suppl 2):S217-S222.
6. Egede LE, Michel Y. Perceived difficulty of diabetes treatment in primary care: Does it differ by patient ethnicity? Diabetes Educ 2001;27(5):678-684.
7. Anderson RM, Fitzgerald JT, Gorenflo DW, Oh MS. A comparison of the diabetes-related attitudes of health care professionals and patients. Patient Educ Couns. 1993;21(1-2):41-50.
8. McBrien KA, Naugler C, Ivers N, et al. Barriers to care in patients with diabetes and poor glycemic control—A cross-sectional survey. PLoS One. 2017;12(5):e0176135. doi: 10.1371/journal.pone.0176135.
9. Parchman ML, Romero RL, Pugh JA. Encounters by patients with type 2 diabetes—complex and demanding: An observational study. Ann Fam Med 2006;4(1):40-45.
10. Chryala CA, Sherr D, Lipman RD. Diabetes self-management education for adults with type 2 diabetes mellitus: A systematic review of the effect on glycemic control. Patient Educ Couns 2016;99(6):926-943.
11. Siminerio LM. Approaches to help people with diabetes overcome barriers for improved health outcomes. Diabetes Educ 2008;34(Suppl 1):18S-24S.
12. Siminerio L. Overcoming barriers to better health outcomes in patients with diabetes; improving and balancing patient education and pharmacotherapy initiation. US Endocrinology 2010;4(2):42-44.
13. Krall J, Gabbay R, Zickmund S, Hamm ME, Williams KR, Siminerio L. Current perspectives on psychological insulin resistance: primary care provider and patient views. Diabetes Technol Ther 2015;17(4):268–274.
14. Ross SA. Breaking down patient and physician barriers to optimize glycemic control in type 2 diabetes. Am J Med 2013;126(9 Suppl 1):S38-48.
15. American Diabetes Association. Strategies for improving care. Diabetes Care 2016;39(Suppl 1):S6-S12.
16. Krall J, Durdock K, Johnson P, Kanter J, Koshinsky J, Thearle M, Siminerio L. Exploring approaches to facilitate diabetes therapy intensification in primary care. Clin Diabetes 2017;35(2):100-105.
17. Zupa MF, Arena VC, Johnson PA, Thearle MB, Siminerio LM. A coordinated population health approach to diabetes education in primary care. Diabetes Educ 2019;45(6):580-585.
18. Tshiananga JK, Kocher S, Weber C, Erny-Albrecht K, Berndt K, Neeser K. The effect of nurse-led diabetes self-management education on glycosylated hemoglobin and cardiovascular risk factors: A meta-analysis. Diabetes Educ 2012;38(1):108-123.
19. Siminerio L. Challenges and strategies for moving patients to injectable medications. Diabetes Educ 2006;32(Suppl 2):82S-90S.
20. Peyrot M, Xu Y, Rubin RR. Development and validation of the Diabetes Medication System Rating Questionnaire-Short Form. Diabet Med 2014;31(10):1237-1244.
21. Polonsky WH, Fisher L, Earles J, Dudl RJ, Lees J, Mullan J, Jackson RA. Assessing psychosocial distress in diabetes: Development of the diabetes distress scale. Diabetes Care 2005;28(3):626-631.
22. Fisher L, Hessler DM, Polonsky WH, Mullan J. When is diabetes distress clinically meaningful? Establishing cut points for the Diabetes Distress Scale. Diabetes Care 2012;35(2);259-264.