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CLINICAL STUDY PROTOCOL

i-Matter: Investigating an mHealth texting tool for embedding patient-reported data into diabetes management

Study Number

s18-01044

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Synopsis

Primary Objective

To compare the efficacy of MJS DIABETES vs. usual care (UC) on HbA1c reduction at 12-months.

Secondary Objectives (if applicable)

1. To compare the efficacy of MJS DIABETES vs. UC on adherence to self-care behaviors.
2. To evaluate the potential mediators of the intervention effects (diabetes knowledge, self-efficacy, outcome expectation, and patient-provider communication) on adherence to self-care behaviors and HbA1c reduction.

Primary Outcome Variables

The primary outcome, mean reduction in levels of HbA1c, will be extracted from patients' medical records.

Secondary and Exploratory Outcome Variables (if applicable)

The secondary outcomes are: 1) adherence to self-care behaviors (assessed with the Summary of Diabetes Self-Care Activities questionnaire) and 2) the theoretical mediators

of capability (assessed with the diabetes knowledge scale), motivation (assessed with the diabetes self-efficacy and outcomes expectations scales) and opportunity (assessed with the Interpersonal Processes of Care survey).

Study Duration

The study duration is 5 years. The formative phase will be 12 months and the clinical efficacy trial will be the remaining 4 years. Participants enrolled in the clinical efficacy trial will participate in the trial for 12 months. The approximate start date for the trial is September 1, 2018 and the approximate end date is August 31, 2023.

Study Design

Using a mixed-methods design, the proposed study will be conducted in two phases: 1) A formative phase, based on user-centered design and 2) a clinical-efficacy phase.

For the formative phase, we will use a mixed methods observational design to refine the study intervention.

For the clinical efficacy phase, we will conduct a single-blinded, phase 3 randomized controlled trial.

Study Population

The study population will include primary care providers and patients with uncontrolled type 2 diabetes (T2D) receiving care in the network of Family Health Centers (FHCs) and Faculty Group Practices (FGPs) at NYU Langone Health.

PCP Eligibility Criteria

Inclusion Criteria: (a) Fulltime primary care provider (MD/DO, NP) practicing at the participating FHC and/or FGPs and (b) provides care to at least five patients with a diagnosis of T2D.

Exclusion Criteria: Refuse to participate

Patient Eligibility Criteria

Inclusion Criteria:

- Have a diagnosis of T2D for ≥6 months;
- Have uncontrolled T2D defined as HbA1c >7% documented in the EHR on at least two visits in the past year;
- Fluency in English or Spanish;
- Be willing to send/receive text messages; and
- Be > 18 years of age.

Exclusion Criteria:

- Refuse or are unable to provide informed consent;
- Have acute renal failure, end stage renal disease (ESRD) or evidence of dialysis, renal transplantation, or other ESRD-related services documented in the electronic health record (EHR);
- Have significant psychiatric comorbidity or reports of substance abuse (as documented in the EHR);
- Are pregnant or planning to become pregnant within 12 months;
- Currently participate in another T2D study; or
- Plan to discontinue care at the clinic within the next 12 months.

Number of Participants

Formative Phase

Patients: 36 patients with uncontrolled T2D

Providers: 14 primary care providers

Clinical Efficacy Trial [Sample includes new participants that did not participate in the formative phase]

Patients: 282 patients with uncontrolled T2D

Providers:14 primary care providers

Abbreviations

Abbreviation	Explanation
AHRQ	Agency for Healthcare Research and Quality
DSMP	Data Safety Monitoring Plan
EHR	Electronic Health Record
HbA1c	Hemoglobin A1c
mHealth	Mobile Health
MJS	Modern Journal System
NP	Nurse Practitioner

PCP	Primary Care Provider
PHI	Personal health information
PI	Principal Investigator
PRO	Patient-reported outcome
RCT	Randomized controlled trial
SMBG	Self-monitoring blood glucose
T2D	Type 2 diabetes
TAM3	Technology Acceptance Model-version 3
UC	Usual Care
UCD	User-centered design

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1 - Introduction

1.1 Introductory Statement

This document is a protocol for a human research study. The purpose of this protocol is to ensure that this study is to be conducted according to ICH GCP guidelines (CRF 21 Part 312), applicable government regulations and Institutional research policies and procedures.

2 - Background

2.1 Background/prevalence of research topic

Although the prevalence of type 2 diabetes [T2D] has remained steady in recent years, T2D remains a significant cause of morbidity and mortality, particularly in vulnerable populations who continue to suffer disproportionately higher rates of complications. For example, only 53% of patients with T2D meet American Diabetes Association hemoglobin A1c (HbA1c) target of <7%. The number of patients who fail to meet this target is even higher in safety-net primary care practices - a place where most vulnerable populations receive their care. To date, the care of patients with T2D has focused largely on patient self-management (adoption of healthy lifestyle, medication adherence) and the use of clinical parameters such as HbA1c levels to determine treatment effectiveness. Although several meta-analyses support the link between improvements in patient self-management and reduction in HbA1c, their effect sizes are modest at best (-0.43% reduction in HbA1c), particularly among vulnerable populations (only -0.31% reduction in HbA1c).

3 - Rationale/Significance

3.1 Problem Statement

A major limitation of the current type 2 diabetes literature is the lack of focus on patients' perspectives of the physical and psychosocial impact of T2D on their daily lives as well as their ability to manage the disease and adhere to the recommended treatment regimen. Importantly, psychosocial factors (e.g., distress), which are not often captured in clinical practice, are of utmost importance to T2D patients' health behaviors. Measures of patient-reported outcomes (PROs) are a standardized and quantifiable approach that allows the collection and integration of data on patients' perspective into the clinical management of T2D. Despite the central role PROs play on T2D patients' ability to manage their disease, PCPs overestimate how frequently they assess PROs in the clinic visit, as compared to patients (76% vs. 55%, respectively). However, if we are to make an impact on the growing burden of T2D on patients and the broader society, treatment strategies must seek to balance primary care providers' (PCP) pursuit of glycemic control against patients' emotional, physical, and social experiences with their disease. In order to be successful such strategies must possess the following qualities:1) provide data that is actionable by primary care providers (PCPs); 2) support patient engagement in their care both within and outside the practice; 3) improve clinical outcomes; and 4) be integrated within the clinic workflow, as part of the electronic health record (EHR). Practice-based trials that evaluate the efficacy of integrating PROs into the care of T2D patients in safety-net primary care

practices, is at its embryonic stage.

3.2 Purpose of Study/Potential Impact

Although achieving glycemic control is of clinical importance, it is the daily experiences of living with T2D that drive patients' decisions to adhere to treatment recommendations and become engaged in their care. Even with the most efficacious treatments, failure to incorporate patients' perspective of their disease into clinical decision-making will make achieving the outcomes desired by patients and PCPs unattainable. Thus, an ideal opportunity to improve patient outcomes is being missed in primary care practices, especially among vulnerable populations who suffer disproportionately higher rates of complications. To date, PROs have been associated with improvements in quality of life, better patient-provider communication, and reduced emergency department visits among patients with chronic diseases. Despite these benefits, practice-based studies that incorporate PROs into diabetes care have lacked patient and PCP involvement in their development thus, they fail to meet the unique needs and preferences of patients, and lack the technical infrastructure to support their integration into the clinic workflow, greatly limiting their impact. If successful, this study will lay the foundation for developing a disseminable strategy for improving clinical and functional outcomes in patients with T2D. Specifically, this study will provide much needed evidence in three vital areas: 1) the facilitators and barriers to using mHealth platforms to record and track PROs for diabetes management; 2) the conditions under which mHealth interventions 'work' in primary care settings and the

organizational, individual and technical factors that are required to support their use; and 3) the theoretical drivers that underlie mHealth interventions to improve outcomes. These results should have important population health value for patients, providers, healthcare systems and policy makers by identifying the optimal set of tools and procedures to effectively collect and monitor PROs in patients' daily lives and as part of routine clinical care.

3.3.1 Potential Benefits

The intervention is expected to benefit the patients by improving adherence to self-care behaviors, reducing their cardiovascular risk profile, increasing their role as active participants in the management of their health, and potentially improving their diabetes control. The intervention is expected to benefits PCPs by improving communication with their patients helping to inform treatment-decisions for effective management of T2D. The knowledge gained from this study will also provide key academic, community, and policy stakeholders a patient-centered intervention approach for chronic disease management that has potential for broad dissemination, ultimately contributing to a reduction in the burden of T2D in vulnerable populations and the broader society.

3.3.2 Potential Risks

Though we expect the level of risk due to this project to be minimal, potential risks may include the following:

Violation of participant privacy and confidentiality: There is a potential risk to the PCPs and

patients with regards to violations of privacy and confidentiality, since text messages, emails, and recordings of interviews, focus groups, and real patient-PCP clinic visits will be used as a source of data. To mitigate this issue, all recorded sessions will be conducted in a private room in the FHC or FGP. Also, when sending recruitment information by email: Send Safe secure email will be used to contact patients. NYU Langone does not permit sending any patient health information via unencrypted email.

Privacy and Security Protections for Participants: To mitigate any breaches in security or privacy as it relates to the Modern Journal System (MJS) DIABETES intervention, we will adhere to policies by the Federal Office of the National Coordinator for Health IT as well as the principles of the Markle Framework for Networked Personal Health Information and the technical specifications of the O-Auth protocol for user authentication. Based on these sources, the Privacy and Security Plan will include:

- Development of explicit policies governing the access to individual PRO data in the MJS intervention (e.g., limited to study staff who require it for authorized, legitimate, and documented purposes)
- A firm policy prohibiting the study staff or consultants (i.e., Rip Road, Dr. Rosal) from access to individual patient health records, except for specific purposes of research approved by the IRB
- Encryption of all sensitive user data within the MJS mobile platform and EHR interface to prevent unauthorized access and disclosure in the case of a physical

loss. No personal health information (PHI) will be collected through the MJS platform.

- Regular training and reminders sent to study staff and consultants about system security and the need to follow related protocols to protect the confidentiality of user information. Policies will also be established for handling violations to security protocols, if they arise.
- A protocol outlining regular risk assessments and system audits to ensure a secure transmission of patients' data, including use of encryption protocols such as Secure Socket Layer (SSL) technology. The inclusion of Dr. Pasco as a co-I on the proposal will ensure that these Privacy and Security guidelines are in accord with norms and existing practices within the clinic.

Protections against Violations of Confidentiality: As part of the process involved in obtaining written informed consent, all patients/PCPs will be reminded that their responses are confidential and that they may refuse to participate in the project or withdraw at any time without explanation, and further, that such an action will in no way affect their future interactions with the FHC and/or FGP. To ensure confidentiality, data will be associated with an individual participant only by an assigned identification number, the code for which will be kept in a locked drawer. Only members of the research team will have access to the participants' personal information file. All computers containing confidential data will meet security requirements established by the HIPAA Security Rules, and established by the Office of Management and Budget (OMB) in OMB Circular No. A-130, Appendix III

Office of Management and Budget (OMB) in OMB Circular No. A-130, Appendix III - Security of Federal Automated Information Systems. Specifically, all electronic interview data will be saved on a secure server housed by NYULMC and backed up daily or weekly depending upon the receipt of data. PHI will be confined to a secure server that is not connected to the Internet. All computers will be password protected and on a private LAN network. No file and database servers are accessible to the public through the Internet. Prior to inclusion in any data set (internal and external), data will be stripped of all identifying information.

Since text messages will be transmitted in this study, a variety of measures will be used to reduce information security risk. Patients' text responses will be securely handled via Rip Road's HIPAA compliant hardware infrastructure. Rip Road follows a set of well-developed policies and procedures vetted by top healthcare organizations in the management and protection of all data tracked through MJS. Patient information will be de-identified for administrative views and for analysis within the Rip Road system. Text messages will not identify patients as having a specific disease or include any PHI information such as patients' name. Patients will be informed that their data are stored, without identifiers, in the highly secure HIPAA-compliant Cloud. They also will be informed that there is a remote possibility that the Cloud or their mobile account could be hacked and that information about study activities (communications, recorded behaviors) could be disclosed. However, these data are not sensitive in nature. Devices will be configured with a participant ID and no other personal identifiers. It is possible that a participant could lose their mobile phone or leave it in a public location with the screen turned- on, enabling others to view personal information.

To address this, we will assist the participant in enabling a screen saver that is activated when the mobile phone has been idle for 5 minutes, as well as a 4-digit password that must be entered each time the device is turned-on. They will also be instructed on how they can turn off home screen notifications if they choose to. Finally, all study staff will be trained in the NYULMC Research Practice Fundamentals, which include training in issues of confidentiality and requires trainees to sign a confidentiality agreement.

Anxiety: There is a potential risk that participants (PCPs and patients) may feel anxious during the audiotaped sessions. To mitigate this issue, the research assistant (RA) who collects the data will be trained to act professionally and address all patients' concerns. Participants will also be informed that they do not need to answer any questions that they are not comfortable with. To insure privacy during the completion of study measures, participants will complete questionnaires in a room with the door closed. In regards to the taped sessions, PCPs/patients will be reminded that the tapes are only for research purposes and will not influence their relationship with the FHC and/or FGP. Moreover, they will be reassured that the tapes will be saved in a secure and confidential database that only the study staff will have access to, and that have the right to ask that the tapes be deleted if they feel sensitive information was discussed during the sessions that they do not want the research team to hear.

Hyper- or hypoglycemia: Since this study is recruiting patients with uncontrolled T2D, occasionally someone may have low blood sugar or high blood sugar during their study participation. All patients will have a PCP as part of this study; however, it is quite

conceivable that a patient reports blood glucose data that will require more aggressive management. When problems arise suggesting the need to re-evaluate the medication regimen, participants will be referred to their provider of record, or local emergency room as appropriate.

4 - Study Objectives

4.1 Hypothesis

Among 282 patients with uncontrolled type 2 diabetes (HbA1c levels > 7%), those randomized to MJS DIABETES, compared to UC, will:

Hypothesis 1 (Primary Aim): Exhibit a higher mean reduction in HbA1c at 12-months.

Hypothesis 2a (Secondary Aim 1): Report higher rates of adherence to self-care behaviors at 12 months.

Hypothesis 2b (Secondary Aim 2): Report greater improvement in diabetes knowledge, self-efficacy and outcome expectation; and more collaborative patient-provider communication, which in turn will be associated with higher rates of adherence and higher mean reduction in HbA1c at 12 months.

4.2 Primary Objective

To compare the efficacy of MJS DIABETES vs. usual care (UC) on HbA1c reduction at 12-months.

4.3 Secondary Objectives (if applicable)

3. To compare the efficacy of MJS DIABETES vs. UC on adherence to self-care behaviors

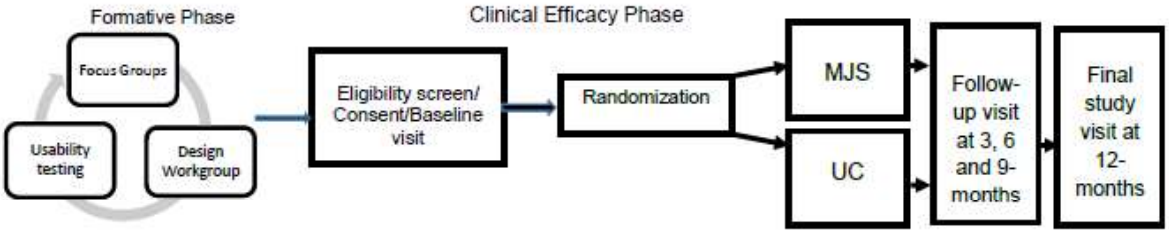
behaviors.

4. To evaluate the potential mediators of the intervention effects (diabetes knowledge, self-efficacy, outcome expectation, and patient-provider communication) on adherence to self-care behaviors and HbA1c reduction.

5 - Study Design

5.1 General Design

Using a mixed-methods design, the study will be conducted in two phases: 1) A formative phase, based on user-centered design and 2) a clinical-efficacy phase (see Figure).



The goals of the formative phase are three-fold: First, we will use focus groups to adapt MJS STATWISE to the needs of the PCP and T2D patients, including Spanish-speaking patients. Second, we will conduct a design workshop to integrate MJS DIABETES into the EHR system and patient's lives. Third, we will evaluate the usability of MJS DIABETES in a subset of T2D patients and their PCPs in order to optimize the tool's performance and workflow integration prior to the clinical efficacy trial. For the clinical efficacy phase, we will conduct a RCT trial to evaluate, among a sample of 282 patients with uncontrolled T2D, the efficacy of the adapted MJS DIABETES versus UC on reduction in the levels of HbA1c (primary outcome) and adherence to self-care behaviors (secondary outcome). In addition,

we will examine the role of diabetes knowledge, self-efficacy, outcome expectations, and patient-provider communication as potential mechanisms of the effect of the MJS DIABETES on HbA1c and adherence to self-care behaviors (secondary outcome). Patients randomized to MJS DIABETES will receive and respond to daily PROs via text messages and report SMBG (if insulin-dependent) over the course of the 12-month study. They will also receive feedback and motivational messages based on patterns of their PROs. Finally, patients and PCPs will receive journal reports that visually display the PROs to encourage decision-making and patient engagement during their clinic visits. PCPs will be able to view the PRO reports via the MJS-EHR interface during clinic visits with the patient or to track patients' PROs between clinic visits. Patients randomized to the UC arm will receive standard diabetes treatment as determined by their PCP.

Phase 2 of the study will not begin until all materials for this phase have been fully developed. These materials will then be submitted to the IRB via a modification for review and approval.

The primary outcome is mean change in HbA1c from baseline to 12 months. Secondary outcomes include 1) changes in patient adherence to self-care behaviors, (e.g., lifestyle behaviors, medication regimen); and 2) theoretical mediators of diabetes knowledge (capability), patient-provider communication (opportunity) and diabetes self-efficacy and outcomes expectations (motivation).

5.1.1 Study Duration (if applicable)

The study duration is 24 months. The formative phase will be the first 12 months of the trial to refine the study intervention. The clinical efficacy phase will be 12 months and there will be six patient visits: screening/consent, baseline, 3-month, 6-month, 9-month, and 12-month follow-up.

5.1.2 Number of Study Sites

The study will be conducted at the network of 10 safety-net Family Health Centers (FHC) and Faculty Group Practices (FGPs) at NYU Langone Health.

5.2.1 Primary Outcome Variables

The primary outcome, mean reduction in levels of HbA1c, will be extracted from patients' medical records. We will use the average of 3 glucose readings over the prior 3 months surrounding the study visit date to calculate mean levels of HbA1c.

5.2.2 Secondary and Exploratory Outcome Variables (if applicable)

The secondary outcomes are:

1) Patient adherence to diabetes self-care behaviors (e.g., dietary behaviors, medication adherence, foot care), which will be assessed with the self-report measure Summary of Diabetes Self-Care Activities questionnaire

2) The theoretical mediators: (a) Patient capability assessed with the self-report diabetes knowledge scale, (b) patient motivation assessed with the self-report diabetes self-efficacy and outcomes expectations scales, and (c) patient perceptions of opportunity (patient-

provider communication) assessed with the self-report Interpersonal Processes of Care survey.

5.3 Study Population

The study will be conducted at the network of 10 safety-net Family Health Centers (FHC) and Faulty Group Practices (FGPs) at NYU Langone Health. English and Spanish are the most common languages spoken with approximately 62% of patients self-identified as Latino, 21% as Black, and 13% as White. Majority of patients have Medicaid. In 2015, the FHCs provided care to 5,218 patients with T2D. Of these patients, 58% had an HbA1c>7% (n=3,026). The FGP consists of at least 657 additional eligible private practitioners in 351 private practices. Approximately, 55% of patients have poor diabetes control.

Selection rationale: The prevalence of T2D has grown to epidemic proportions and is largely considered one of the most significant public health problems in the US, in terms of morbidity, mortality, and economic burden. While a great deal of effort has been spent assisting PCPs in delivering guideline-concordant care to achieve glycemic control, less has been spent facilitating patient's perspective of their disease into care. As a result, an ideal opportunity to improve patient outcomes is being missed in primary care settings, especially among vulnerable populations who suffer disproportionately from its complications. Thus, this study will include diverse English and Spanish-speaking patients who receive care in safety-net practices.

5.3.1 Number of Participants

Fourteen PCPs and 36 patients with uncontrolled type 2 diabetes (T2D) from the network of Family Health Centers (FHCs) and Faculty Group Practices (FGPs) at NYU Langone Health will be recruited for participation in the formative phase of the study.

Fourteen PCPs and 282 patients with uncontrolled T2D from the network of FHCs and FGPs at NYU Langone Health will be recruited for participation in the clinical efficacy phase of the study. To mitigate bias, PCPs and patients that participated in the formative phase will be excluded from participating in the clinical efficacy phase.

To meet our patient recruitment goals, we will begin by screening 3,026 patients. We estimate that 40% of screened patients (n=1,210) will satisfy the inclusion criteria, and that 50% of the will have an A1c>7% at baseline visit (n=605). We estimate that approximately 55% of those 363 patients will agree to participate, leaving 282 for our study after accounting for attrition.

5.3.2 Eligibility Criteria/Vulnerable Populations

PCP Eligibility Criteria

Inclusion Criteria: (a) Fulltime primary care provider (MD/DO, NP) practicing at the participating FHCs or FGPs and, (b) Provide care to at least five patients with a diagnosis of T2D.

Exclusion Criteria: Refuse to participate

Patient Eligibility Criteria

Inclusion Criteria:

- Have a diagnosis of T2D for ≥6 months;
- Have uncontrolled T2D defined as HbA1c >7% documented in the EHR on at least two visits in the past year;
- Fluency in English or Spanish;
- Be willing to send/receive text messages; and
- Be > 18 years of age.

Exclusion Criteria:

- Refuse or are unable to provide informed consent;
- Have acute renal failure, end stage renal disease (ESRD) or evidence of dialysis, renal transplantation, or other ESRD-related services documented in the EHR;
- Have significant psychiatric comorbidity or reports of substance abuse (as documented in the EHR);
- Are pregnant or planning to become pregnant within 12 months;
- Currently participate in another T2D study; or
- Plan to discontinue care at the clinic within the next 12 months.

We are targeting social and economically disadvantaged patients due to the high prevalence of T2D and related complications in this population.

We are also targeting employees of the FHCs and FGPs. Primary care physicians (PCP) who agree to take part in this study will not be recruited or consented by any individuals in a supervisory position. Moreover, PCPs will be informed that their decision to participate or to not participate in the study will have no effect on their employment at the FHCs or FGPs.

6 - Methods

6.1.1 Description of Intervention

Formative Phase (Phase 1): Based on the methodology employed in our previous mHealth studies, we will use the evidence-based user-centered design (UCD) approach to systematically gather and incorporate feedback from patients and PCPs for selection and adaption of the appropriate PROs for use in MJS DIABETES. We will use the UCD approach to also optimize and integrate the MJS report into the workflow of the EHR. The formative phase will occur in three sequential steps (Table 2): 1) Focus groups to adapt MJS to diverse patient and PCP needs, including those of Spanish-speaking patients; 2) A design workshop to understand the workflow processes for patients and PCPs and integrate MJS DIABETES into the EHR and patient workflow processes; and 3) Evaluate the usability of MJS DIABETES in a subset of T2D patients and their PCPs to optimize the tool's

performance and workflow integration. The outcome of this phase will be a refined, integrated, and well-tested technology-based PRO system for T2D whose efficacy will be evaluated in the clinical trial efficacy phase.

Table 2. Formative Phase: User centered design (UCD) Tasks and Methods

Step	Methods	Participants	Outputs
1. Adapt	Focus Groups: • 2 English-speaking patient groups • 2 Spanish-speaking patient groups • 2 PCP groups	6-8 patients per group 4-7 PCPs per group	Summary document that specifies: • Refined PRO content • Needs, preferences, and barriers/facilitators of use
2. Integrate	Design Workshop • Workflow mapping • Problem/opportunity analysis • Story mapping EHR Integration	4 patients 4 PCPs	Design specification document that specifies: • Clinic workflow/patient journey maps • Essential features of MJS tool • MJS prototype
3. Evaluate	Usability testing sessions	4 patients 4 PCPs	• Fully functional MJS DIABETES intervention

Focus groups: We will conduct audiotaped focus groups with patients and PCPs. Four focus groups will be conducted with patients (two with English-speaking patients; two with Spanish-speaking patients; 6-8 patients per group) and two focus groups will be conducted with PCPs (4-7 PCPs per group). Each focus group will be conducted via WebEx, be audiotaped, and last for approximately 2 hours in duration. Patient focus groups will be conducted to identify the barriers and facilitators to uptake of the MJS intervention and inform the initial program content. Patients will be asked to identify the most important symptoms, complications, side effects, and health-related quality of life concerns associated with their T2D and treatment experiences of T2D using validated patient reported outcome

measures (e.g., Diabetes Health Profile (DHP)-18) as a guide. In addition, the goal of the focus groups with Latino patients is to culturally adapt the PROs collected in the MJS intervention to needs, experiences and preferences of Spanish-speaking Latino patient users. The PCP focus group will be conducted to elicit feedback on the PROs identified in the patient focus groups, visual representations and placement of the PROs in the EHR, and barriers and facilitators to use in the PCP workflow. All audiotapes from the focus groups and interviews will be transcribed verbatim (and translated into English for the Spanish-speaking groups).

Design Workshop Upon completion of the focus groups, the study team will convene a one-day design workshop in collaboration with Rip Road to further develop the MJS PRO content and ideal workflow integration. The workshop will consist of 4 PCP and 4 patient representatives from the focus groups described above. The workshop will be led by co-I Dr. Mann and guided by a UCD protocol that sequentially leads the group through a variety of activities designed to elicit feedback on key components of the MJS adaptation (e.g. paper mock ups of tool design) as well as the proposed clinic workflow/patient journey (e.g., patient "day in the life" map) integration of MJS. Following the design workshop, Rip Road will partner with the study team to embed the MJS-EHR visualizations into Epic.

Usability Sessions: Once the prototypes are created, we will evaluate the workflow processes of the bilingual MJS diabetes intervention via usability testing with a purposive sample of patients and PCPs drawn from the focus group participants. Four patients and four PCPs will complete individual usability sessions with a beta version of the intervention

to provide preliminary performance data on its functioning. Table 4 describes the metrics that will be collected during the testing sessions. Patients and PCPs will also suggest refinements to the mock content and workflow/user journey map from the PCP and patient perspectives —— providing key feedback on topics such as potential disruption to the clinic workflow, impact of using interpreter services on discussions of the PRO report, and placement/presentation of the report in the EHR. Our previous studies suggest that we will need four patient and four PCP cycles of usability sessions to reach saturation. Each usability session will be approximately one hour in duration. The primary output of this step is the fully functional, integrated MJS DIABETES intervention for testing in the clinical efficacy trial.

Table 4. Usability metrics	
1.	**Task success (effectiveness):** % of given task that users successfully complete without critical errors
2.	**Time-on task (efficiency):** Time taken to complete a given task, measured from the time the user clicks/ texts "begin task" to when she clicks/texts "end task"
3.	**Computer/ Mobile phone inputs (efficiency):** Raw count of inputs (texts. Mouse clicks, keyboard strokes) and length of the navigation path to complete task
4.	**Task completion survey**: Post- task ratings of difficulty in a usability test
5.	**System Usability Scale**: 10-item survey that provides a comprehensive assessment of subjective usability with satisfaction score
6.	**Perceived ease of use**: 4-item survey that assesses the degree of effort that users perceive is needed to use the tool
7.	**Perceived Usefulness**: 4-item survey that assesses the perceived benefits and drawbacks of the tool on performing tasks/ job functions
8.	**Relevance**: 2-item survey that assesses the relevance of the tool on performing tasks/ job functions
9.	**Report Quality**: 3-item survey that assesses the users evaluation of the quality of the report provided by the tool
10.	**Result Demonstrability**: 2-item survey that assesses the users perceived ability to explain or talk about the tool with others
11.	**Communication**: 2-item survey assesses the whether the users communication with healthcare provider improved after using tool
12.	**Behavior Intention of use**: 4-item survey that assesses the likelihood of using the tool within a specific time frame

Description of MJS DIABETES intervention (Phase 2)

Phase 2 of the study will not begin until all materials for this phase have been fully developed. These materials will then be submitted to the IRB via a modification for review and approval.

Patient intervention: MJS DIABETES is comprised of 5 components: 1) PRO assessments, sent via text message; 2) adherence text message assessments; 3) data-driven feedback text messages 4) motivational text messages; and 5) journal reports that visually display PRO data.

MJS helps patients (and their provider) see how their diabetes symptoms and psychosocial functioning are changing overtime. Participants who enroll in the study agree to have messages sent to their phone based on one of several PRO categories. These include: (1) diabetes quality of life; (2) overall emotional health; (3) lifestyle behaviors; (4) medication adherence; and (5) physical functioning. PRO questions will be sent on a daily or weekly basis, depending on the PRO (i.e., adherence is a daily measure while quality of life is sent on a weekly basis). The list of potential PROs that will be sent to patients over the course of the 12-month study and their primary questionnaire source are shown in the Table below. No PHI will be collected in the MJS DIABETES tool. All data is a numerical response that is anonymous.

Potential MJS PROs	Scaling	Source
Over the past week, how would you rate your level of fatigue because of your diabetes?	0 (not at all tired)-10 (extremely tired) scale	Global Health PROMIS Tool
How would you rate your sleep quality over the past 7 days?	0 (very poor)-10	NIH PROMIS Sleep

	(excellent) scale	Quality
Over the past week, how often were you able to take your diabetes medication on time?	Never Rarely Sometimes Often Always	Diabetes self-management questionnaire
How many of the last seven days have you followed a healthful eating plan for diabetics?	0-7 days	Summary of Diabetes Self-Care Activities
In general, my present quality of life is	As good as it can be Good Quite good Neither good or bad Quite bad Bad As bad as it could possibly be	Audit of Diabetes Dependent Quality of Life
Over the past week, how often were you been bothered by emotional problems such as feeling anxious, depressed or irritable because of your diabetes?	Never Rarely Sometimes Often Always	Global Health PROMIS Tool
Over the past week, what percent of the time did you take all your diabetes medications as your doctor prescribed?	0-100%	Self-Rating Scale Item
On how many of the last seven days did you take the correct number of (pills/injections) for this medication?	0-7 days	Summary of Diabetes Self-Care Activities
Over the past week, how often did you eat [favorite unhealthy food]?	Always Often Sometimes Rarely Never	Perceived Dietary Adherence Questionnaire

On how many of the past 7 days did you eat lots of sweets or other foods rich in carbohydrates?	0-7 days	Perceived Dietary Adherence Questionnaire
How effective are you in coping with your diabetes?	1 (not at all) to 5 (extremely effective)	Appraisal of Diabetes Scale
How many times over the past week did you eat desserts like cookies, cakes and muffins or other sweets? Do not include sugar free kinds.	Never 1 time 2-3 times 4 or more times	NHANES Dietary Screener Questionnaire
How many times over the past week did you refined carbohydrates like white bread, white flour tortillas, dinner rolls and bagels?	Never 1 time 2-3 times 4 or more times	NHANES Dietary Screener Questionnaire
On how many of the past 7 days did you space carbohydrates evenly throughout the day?	0-7 days	Perceived Dietary Adherence Questionnaire
Over the past week how well could you control your emotions?	Not at all Poorly Fairly well Very well Extremely well	Thrive Questionnaire
In general, how would you rate your mental health, including your mood and your ability to think?	Poor Fair Good Very good Excellent	Global Health PROMIS Tool
How much was the quality of life of your life affected by the time required to control your diabetes?	0 (Not at all affected) – 10 (as bad as I can be)	Patient-reported outcome-Quality of Life
Over the last week, did you experience any weight gain because of your diabetes	Always Often	Diabetes Impact Measurement Scales

	Sometimes Rarely Never	
Over the last week, did you feel irritable or moody because of your diabetes	Always Often Sometimes Rarely Never	Diabetes Impact Measurement Scales

In addition to the PRO questions, patients will receive feedback via motivational and data-driven text messages. These text messages are designed to activate patients in their care via continued participation in the MJS program, and to provide them feedback data on patterns in their responses for self-reflection.

We have developed and tested three types of data-driven feedback messages that were automatically sent to patients on a weekly basis describing patterns in their PRO assessments over the past week. The high/low comparison messages compared the lowest (shortest) value reported (to date) to previous weeks, in which higher (longer) value were reported. The weekly average comparison messages compared changes in patients' mean PRO ratings for the current week as compared to the previous week. The re-occurring values messages also compared multiple weeks over time, data from single days during the week to days in previous weeks, and multiple [single] days over time. We use a rule-based algorithm that searches for these patterns in patient's data on a weekly basis. Specifically, the high/low comparison and re-occurring value messages will be sent if the appropriate patterns in the data are identified for the current week. If no patterns in the data are

identified, the weekly average comparison message will be sent as the default message each week. Example messages from our pilot include the following:

Comparison High/Low Message: Last [day of the week] your average FATIGUE score was a "[numerical fatigue score]." That is the lowest score you have reported in the past [#] of weeks.

Comparison Multiple day Message: In the past week your FATIGUE scores have been: "[day of week – numerical fatigue score for that day]"; "[day of week – numerical fatigue score for that day]"; and "[day of week – numerical fatigue score for that day]".

Average PRO value Message: Your average FATIGUE score this week was a "[numerical fatigue score]", compared to your average fatigue score of "[numerical fatigue score]", last week.

Motivational messages are also automatically generated and delivered via a pre-specified algorithm. There are two categories of motivational messages: (1) Response-based (i.e., sent in response to high/low compliance in replying to assessment entries) and (2) % completed (i.e., sent after specified time intervals of participation). Example messages include:

Low Compliance Message (always triggered if 3 consecutive days are missed): We haven't heard from you in the last 3 days. Text HELP if you need assistance in the journaling program.

Good Compliance Message: You have answered 10 text messages in a row for the

Good Compliance Message: You have answered 12 text messages in a row for the journaling program. Keep it up!

% Completed Message 1: You have responded to 85% of the messages over the past 4 weeks in the journaling program.

% Completed Message 2: Congratulations! You are halfway through the journaling program.

Mobile Opt-in/Opt out Process: After completing informed consent, patients randomized the intervention condition will meet with the RA to receive training on how to use the intervention and opt in to receive SMS messages. Per carrier policies to opt in, patients must provide their mobile numbers and carrier information. Once their information has been added to the system, they will receive a SMS asking them to reply to confirm their participation. To confirm, patients will need to reply via text message.

This step verifies their mobile number and joins them to the intervention. They will receive a welcome message.

To cancel or opt out of the program at any time, patients will be required to send the word 'STOP' to any program message. This information is communicated to the patient at the time of registration, via a Mobile Terms and Conditions document – which they will be required to sign. The opt out information is also communicated to them within the first program confirmation SMS, as well as once a month, in a SMS message sent as part of their subscription service.

All additional carrier compliance terms will also be adhered to. A HELP message, and an invalid response message will be developed. Carrier specific rate information will be included in messages as required.

Patients will then be instructed on how to respond to the SMS messages and asked to demonstrate their ability to understand.

Journal report: After the first week, and every 2 weeks thereafter, patients will receive a journal report that visualizes their responses to the text message questions in straightforward graphs and displays the adherence responses in a calendar. The reports are intended to help patients reflect on changes in their responses overtime, and discuss how their symptoms and functioning have changed in between visit.

PCPs: The EHR-integrated journal reports will provide PCPs with quantitative assessments of the extent to which patients are adhering to their T2D regimen, the psychosocial factors that may inhibit adequate glycemic control, and the diseases impact on their functional status. Reports of patient PRO data will be uploaded to the EHR every two weeks. Providers will be able to access reports of patients' PRO data via the MJS-EHR interface during visits with the patient or asynchronously to track patients' PROs between visits. Based on our pilot data, we will encourage providers to use the reports to support patient engagement and shared decision-making in the clinic visit, set priorities for the visit, and discuss trends in PRO data as they relate to behavioral and clinical outcomes. Prior to the initiation of the trial,

all participating PCPs will receive standardized training in the MJS-EHR interface functionalities as well as best practices for patient-centered discussions of the data visualizations (Table 6). The ability to receive and review PRO reports between clinic visits may also offer several opportunities to improve patient care such as by: reducing critical information gaps about patients' condition or symptoms; supplementing existing clinical data; providing PCPs with a comprehensive view of patients' ongoing experience of their

illness (symptoms, function and well-being); as well as meeting meaningful use requirements for two-way electronic communications.

Description of UC group

Patients randomized to the UC group will receive standard diabetes treatment recommendations as determined by their PCP. Rationale for UC condition: The UC group was designed to mimic usual care as delivered in primary care practices. We believe that including an alternate approach such as an attention control condition would defeat the purpose of this trial, which is to compare the efficacy of an innovative approach to collect and track PROs for diabetes self-care in real-world practice-based settings with particular attention to its integration into standard clinical practice.

Table 6. Treatment Fidelity Strategies

Element	Strategy
Study design	Conduct usability testing in Phase 1 of MJS Ensure MJS is consistent with TAM and SCT theoretical constructs Develop protocol for identifying and resolving technical problems during the study Distribute password protect study cell phones to ensure UC group patients are not given access to the MJS program during the study Limit access to the MJS EHR interface via a password protected portal Develop system prompts that direct PCPs to the appropriate interface (MJS vs. UC) for the patient being seen Embed quality control checks into the EHR to track whether UC patients receive the intervention despite the system prompts.
Participant training	Patient: 1:1 in-person training in the use of MJS using a standardized manual. Handout outlining program expectations, instructions on how to read the journal report, a toll free study phone number, and a link to an internet-based video that reviews the training content PCP: Internet-based, standardized training videos that will be archived and available for booster trainings. Training topics will include: demonstrating how to view and print MJS journal reports for use with participating patients during clinic visits, explaining how to interpret the reports, and best practices for patient-centered

	discussions about the data visualizations in the report
Intervention delivery	Continuous monitoring of MJS EHR interference and texting program to ensure program is working correctly and being delivered consistently Immediate resolution of technical difficulties
Intervention receipt	Collection of patient (i.e., # of texts delivered, error messages received, time to complete PRO messages) and PCP (i.e., # of MJS EHR interface log ins) usage metrics
Enactment of intervention skills	Audiotape a random sample of 20% of clinic visits to assess use of the journal report Collection of patient (i.e., # of texts sent in response to PROs messages, TAM3 survey about use behavior) and PCP (i.e., EHR data observing their time interacting with the MJS interface) engagement metrics

6.1.2 Method of Assignment/Randomization

This project has a hierarchical study design with each patient nested within a PCP thus, randomization will occur within PCP. The study statistician (Dr.Li) will oversee randomization, which will be carried out using a SAS macro after completion of the consent procedures and baseline data collection. Patients will be randomly allocated to either the intervention (MJS DIABETES) or UC at a 1:1 ratio. A random number from 0 to 1 will be used to determine to which group the subject is assigned. The standard cut score will be set at 0.5 for the first n subjects from the same PCP. Those who receive a random number between 0 and 0.5 will be assigned to the UC group and those with a random number greater than 0.5 will be assigned to the MJS group. The balance between the groups within each PCP will be carefully weighted after the total number of subjects from a PCP reaches a number greater than n. Before the randomization procedure, the number of subjects randomized to each arm of the study for each PCP will be estimated using SAS macro programs. If more than the n subjects are randomized initially, the cut score for the next subject is equal to the ratio of the experimental arm (n1) to the subjects already randomized

(m) for that PCP (n1/m). The randomization log will be stored in a secure file, and will be password protected. Once a patient has met eligibility criteria and provided consent, the program manager will call the study statistician for the patient's group assignment. As is true for most behavioral interventions, the patient cannot be blinded to the group assignment. However, it is plausible that study staff could bias the study outcome by knowing the patient's group assignment. To mitigate the potential for this bias, the RA that is responsible for data collection will be blinded to the patients' group assignments and study hypotheses (i.e., single blind design).

6.1.3 Selection of Instruments/Outcome Measures

Table 7 describes the measures that will be administered and their timing. Below, we describe each measure in detail.

HbA1c level: will be assessed as the difference between HbA1c at baseline and 12 months. HbA1c levels will be extracted from patient's clinic EHR. HbA1c levels will be calculated as the average of all available clinic measurements for the 90 days surrounding the targeted study visit dates. If a participant does not have an HbA1c value within the EHR for any particular follow-up visit, a lab test will be scheduled to obtain a measure. Clinic HbA1c measurements made during 6 months prior to randomization will be treated as the baseline period.

Medication adherence: will be assessed at baseline and 12 months. The Voils Self-Reported Medication Nonadherence Measurement will be used to assess the extent of nonadherence

and reasons for nonadherence.To estimate patients' adherence to a medication regime, the Proportion of Days Covered (PDC) metrics will be used. PDC metric is defined as a ratio of following: Numerator- days patient took drug/ Denominator- number of days between the first fill of the medication during the measurement period and the end of the measurement period.

Charlson Comorbidity Index- is a method of categorizing comorbidities of patients based on the International Classification of Diseases (ICD) diagnosis codes found in administrative data, such as hospital abstracts data. Each comorbidity category has an associated weight (from 1 to 6), based on the adjusted risk of mortality or resource use, and the sum of all the weights results in a single comorbidity score for a patient. A score of zero indicates that no comorbidities were found. The higher the score, the more likely the predicted outcome will result in mortality or higher resource use

Patient adherence to self-care behaviors will be assessed with the well-validated Summary of Diabetes Self-care Activities Measure. For this measure, patients are asked to indicate how many of the past seven days (response range 0 -7 days) they practiced the following self-care behaviors: follow a general diet, follow a diabetes specific diet, be physically active, monitor blood glucose, engage in foot care, and smoke (scored as a yes or no response). In the analyses, we will examine each behavior separately due to studies showing that engaging in one of the self-care behaviors does not correlate with practicing another behavior. The Cronbach's alpha for the scales range from 0.69 to 0.84).

Patient knowledge (capability): will be assessed with the Diabetes Knowledge Scale, which contains 2 sections that are each scored separately. The general knowledge segment of the test has 14 items and is appropriate for adults with type 1 and type 2 diabetes. An additional 9 items constitute the insulin use subscale that is appropriate for adults with type 2 using insulin. The test's readability was measured by the Flesch-Kincaid grade level; the reading level was calculated at the fourth-grade reading level. The coefficient alphas indicate that the scale is reliable for both the general test (.77) and the insulin use subscale (.84).

Patient self-efficacy (motivation): will be assessed with the 12-item Diabetes Self-efficacy Scale, which is assessed using a 10-point response from "1 = not at all confident" to "4 = very confident." For each item patients rated their confidence in their ability to perform a recommended self-care routine. Responses are summed to obtain an overall self-efficacy score, and for ease of interpretation, are transformed the score to a 100-point scale with a higher score representing greater self-efficacy. The scale has a standardized Cronbach α of 0.78, across diverse race/ethnicity populations and health literacy levels.

Patient diabetes distress: will be assessed with the well-validated and widely used 17-item Diabetes Distress Scale, which is assessed using a Likert type scale from “1= not a problem” to “6= a very serious problem.” For each item patients rated the degree of distress the potential problem a person with diabetes may experience. To score, the sum of all the patient’s responses is divided by 17. A mean score of 3 or higher is considered a level of distress that needs medical attention. In the event of an elevated score, a message will be sent to the patient’s primary care provider and be noted in the patient’s study record.

Patient outcome expectations (motivation): will be assessed with the 20-item Outcome Expectations Questionnaire (adapted from McCaul et al., 1987), which assesses participants' perceptions of the positive and negative consequences of performing diabetes self-care behaviors (e.g., "If I exercise daily, my diabetes will be better controlled"). The measure has been previously validated in a diverse sample of patients with type 2 diabetes, The Cronbach α of the total scale is 0.86.

Patient-provider communication (opportunity): will be assessed with the Interpersonal Processes of Care Survey, a patient-reported, multidimensional instrument designed to assess interpersonal aspects of care. It is validated for patients of diverse racial/ethnic groups and available in Spanish and English. The IPC assesses 7 subdomains of communication, patient-centered decision making, and interpersonal style. As in previous studies, we will also include diabetes-specific communication items related to the fundamental areas of diabetes education including: diet ("how to plan your meals to improve your blood sugar"), foot care ("how to care for your feet"); physical activity ("how to exercise properly"); and other issues ("what is a good number for your blood sugar").

Patient demographic data will include race/ethnicity, place of birth, years in the US, primary language, age, gender, household income, education level, marital status, employment status, health insurance status, smoking and drinking behaviors, and medical comorbidity. PCP demographic data will include gender, race/ethnicity age, years of medical practice,

years practicing at the FHC or FGP, and how well they know the patient (range from very well to not at all).

Characteristics of disease and medication regimen: All patients will have their EHR reviewed at baseline and 12 months. Information extracted from the charts will include diabetes characteristics such as clinic HbA1c readings, duration of diabetes, evidence of target organ damage, changes in diagnosis, medical comorbidity, clinic appointment attendance, and other medications prescribed and their dosages. In addition, we will collect information on the number and classes of diabetes medications prescribed and dosages as this reflects the intensity of treatment by providers and will serve as a covariate in the analysis to allow us to account for the influence of medication management on changes in HbA1c over the course of the study.

Health Care Utilization: Will be assessed at 6 month and 12 month follow-ups. Health care utilization is a self-reported questionnaire that assesses the use of healthcare services such as hospitalization, clinic visits and emergency department visits for T2D care for every 6 months during the course of the trial.

Perceived usefulness: will be measured with a 4-item survey that are derived from the well-validated Technology Acceptance Model-version 3 (TAM3) survey that assesses the perceived benefits and drawbacks of the tool on performing tasks/job functions. This measure will be administered to patients and PCPs during the usability sessions during the formative phase as well as at the 12-month study visit. The internal consistencies of this scale is 0.94

scale is 0.94

Perceived ease of use: will be measured with a 4-item survey derived from the TAM3 survey that assesses the degree of effort that users perceive is needed to use the tool. This measure will be administered to patients and PCPs during the usability sessions during the formative phase as well as at the 12-month study visit. The internal consistencies of this scale is 0.93.

Relevance: will be measured with a 2-item survey derived from the TAM3 survey that assesses the relevance of the tool on performing tasks/ job functions. This measure will be administered to patients and PCPs during the usability sessions during the formative phase as well as at the 12-month study visit.

Report Quality: will be measured with a 3-item survey derived from the TAM3 survey that assesses the users' evaluation of the quality of the report provided by the tool. This measure will be administered to patients and PCPs during the usability sessions during the formative phase as well as at the 12-month study visit.

Result Demonstrability: will be measured with a 2-item survey derived from the TAM3 survey that assesses the users' perceived ability to explain or talk about the tool with others. This measure will be administered to patients and PCPs during the usability sessions during the formative phase as well as at the 12-month study visit.

Communication: will be measured with a 2-item survey derived from the TAM3 survey that assesses whether the users communication with healthcare provider improved after using

tool. This measure will be administered to patients and PCPs during the usability sessions during the formative phase as well as at the 12-month study visit.

Behavior intention of use: will be measured with a 4-item survey derived from the TAM3 survey that assesses the likelihood of using the tool within a specific time frame. This measure will be administered to patients and PCPs during the usability sessions during the formative phase as well as at the 12-month study visit.

Use behavior: Data on patient and PCP use of the MJS intervention will be extracted from the tool at the end of the clinical efficacy phase and include the following metrics: # of messages sent/received; time to respond; # of missed responses; # of errors, # views of the EHR report, # clicks within EHR report, time spent in EHR report, audiotaped clinic visit.

Physician communication: will be measured with two Physician Communication surveys. One is a 13-item survey which is assessed using a Likert type scale from “1= poor” to “5= excellent” and the other a 9-item survey which is assessed using a Likert type scale from “1= strongly agree” to “5= strongly disagree”. Both surveys will be used to see if the intervention had an impact on physician’s communication skills (which we hypothesize would impact patient self-management behaviors) and to determine whether there was any contamination across study arms.

Table 7. Study Measures

Variable	Measure	Data Source/Timing (months)
	Primary and Secondary Outcomes	
HbA1c	Average glucose levels over prior 3 months surrounding the study visit date	Electronic health record extraction Baseline, 3, 6, 9, 12

Self-care behaviors	Summary of Diabetes Self-care Activities Measure[11]	Patient self-report Baseline, 3, 6, 9, 12
	Covariates	
Demographics	*Patient* race/ethnicity, years in US, primary language, age, gender, household income, education level, marital status, employment status, health insurance *PCP* gender, race/ethnicity age, years of medical practice, years practicing at the FHC, and how well they know the patient (range: very well to not at all).	Patient and PCP Baseline
Characteristics of disease and medication regimen	T2D duration; target organ damage; medical comorbidities; #, class and doses of T2D medications other prescribed medications, Voils Medication Adherence, PDC metric, Charlson Comorbidity Index	Electronic health record extraction Baseline, 12
Health care utilization	Healthcare Utilization questionnaire measures patient hospitalizations, clinic visits and emergency department use for T2D every 6 months during the course of the trial.	Patient self-report 6, 12
	Theoretical Mediators	
Knowledge	Diabetes Knowledge Scale[12]	Patient self-report Baseline, 3, 6, 9, 12
Self-efficacy	Diabetes Self-Efficacy Scale[13]	Patient self-report Baseline, 3, 6, 9, 12
Outcome expectations	Outcome Expectations Questionnaire[14]	Patient self-report Baseline, 3, 6, 9, 12
Patient-provider communication	Interpersonal Processes of Care survey-Short form[15]	Patient self-report Baseline, 3, 6, 9, 12
Patient diabetes distress	Diabetes Distress Scale	Patient self-report Baseline, 3, 6, 9, 13
	Process Measures	
Perceived usefulness	TAM3 survey[5]	Patient and PCP self-report; 12 mos.
Perceived ease of use	TAM3 survey[5]	Phase 1 live usability testing Patient and PCP self-report; 12 mos.
Relevance	TAM3 survey[5]	Patient and PCP self-report; 12 mos.
Report Quality	TAM3 survey[5]	Patient and PCP self-report; 12 mos.
Result Demonstrability	TAM3 survey[5]	Patient and PCP self-report; 12 mos.
Communication	TAM3 survey[5]	Patient and PCP self-report; 12 mos.
Behavior Intention	TAM3 survey[5]	Patient and PCP self-report; 12 mos.
Provider Communication	Provider Communication survey	PCP Baseline and 12 mos.
Use Behavior	# of messages sent/received; time to respond; # of missed responses; # of errors, # views of the EHR report, # clicks within EHR report, time spent in EHR report, audiotaped clinic visit	Extracted from MJS program

6.1.4 Intervention Administration

Treatment Fidelity: will be based on the NIH Behavior Change Consortium Treatment Fidelity Guidelines. Treatment fidelity will be comprised of 4 elements: 1) study design; 2) participant training; 3) intervention delivery; 4) intervention receipt; and 5) enactment of intervention skills (Details of the treatment fidelity approach is outlined in Table 6 above).

6.1.5 Reaction Management

In the event that any of the participants (patients and PCPs) experience anxiety as a result of participating in the formative and/or clinical efficacy phases of this trial, we will provide a list of mental health services that are offered at no or low-cost through the NYU Langone Health network of participating FHCs and/or FGPs. If immediate attention is warranted, the clinic social worker and/or psychologist will be contacted.

6.2.1 Efficacy

The efficacy of the intervention will be assessed via the primary outcome, reduction in levels of HbA1c from baseline to 12 months. HbA1c levels will be abstracted from patients' medical record.

6.2.2 Safety/Pregnancy-related policy

Patients who are pregnant or planning to become pregnant in the next 12 months are excluded from participation in this trial.

6.2.2.1 Adverse Events Definition and Reporting

The Principal Investigator (PI) will be responsible for quality control including reviewing and reporting adverse events. The plan will comprise the following elements:

- Adverse events will be reported to the IRB.
- A detailed plan to address serious events that may arise during study visits, such as HbAic values that indicate a diabetic emergency, is in place. Critical blood sugar values are defined as: 300 mg/dl or higher OR less than 40 mg/dL). In the event that the RA encounters such readings at any point in the study visit process or via transmission of home readings, the following protocol will be triggered: (1) Let the participant know that these values are very high and recommend follow-up with his/her primary care provider; (2) Alert the study PI and contact the Project Manager to inform that such a reading has occurred; (3) Document all cases on Adverse Event Form. The Project PI and key personnel will meet every 6 months to review adverse events reports, participant complaints, if any, and dropout rates. Data will be provided at those meetings by the investigators on key variables that may indicate harm, including changes in HbA1c and cardiovascular risk profile.
- Any unexpected adverse reactions that are associated with the research and that are fatal or life threatening will be reported to the IRB within 24 hours of discovery. Any unexpected adverse events associated with the study that are moderate to severe in nature, but not life threatening, will be reported to the IRB in 5 days.

- Summaries of adverse events reports will be made to AHRQ/Merck in the yearly progress or report or, at the end of year 2, in the final report, unless the nature of a particular event is such that it bears immediate reporting to AHRQ/Merck.
- If a serious adverse event occurs as a result of the study, consideration will be given to stopping the study early. In the event of early stopping of the study, the IRB will be promptly notified.

6.2.3 Pharmacokinetics (if applicable)

Not applicable

6.2.4 Biomarkers (if applicable)

Not applicable

6.3.1 Study Schedule

In the formative phase, the total expected duration of participation for both patients and providers is 14 hours over the course of 12 months. The estimated time for each visit during this phase is as follows:

- Participation in 1 focus group: 2 hours
- Participation in the design workshop: 8 hours
- Participation in usability sessions: 4 hours

In the clinical efficacy phase, patients will participate in six study visits over the course of 12

months. The duration of the intervention is 12 months, inclusive of this time. The intervention includes receiving and responding to up to 3 daily text messages. It is estimated to take 2 minutes to respond to all text messages each day.

The estimated time for each study visit is outlined below:

- Screening: 10 minutes
- Consent/Baseline: 45 minutes
- Follow-up visits at 3, 6, 9: 30 minutes each visit
- Final study visit at 12 months: 60 minutes (patients) and 30 minutes (PCPs)

6.3.2 Informed Consent

Both patients and PCPs will provide informed consent to participate in either phase of this study. The protocol and consent will be approved by the New York University IRB.

Due to COVID-19 and to keep the safety of both our research team and research subjects, we will be collecting consent via telephone. A trained Research Assistant will schedule a time with eligible interested participants to go over the written consent via telephone. Research Assistants will email or mail a copy of the consent to participants in preparation for the telephone consent. After going over the written consent via telephone, research assistants will also send the consent via a RedCap link where the participant has the opportunity to read the consent and sign electronically, confirming that they read and

understood the consent. Research Assistants will also document on RedCap the time and date of the telephone consent and note that the consent process was done via telephone due to COVID-19.

PCPs: A trained RA will meet with PCPs that express interest to provide a fuller description of the study. During this meeting, the PCP will be given a fuller description of the study in clear, easy to-understand language, emphasizing the points made during the letter/telephone/email invitation. All PCPs will told that their responses are anonymous and confidential, that they may refuse to participate in the project or withdraw at any time without explanation and further, that such action will in no way affect their relationship with the primary care practice. If the PCP remains interested in participating, the RA will provide a copy of the consent form for him/her to read. PCPs will be asked to repeat back the salient points of the consent form to make sure that they understand the study they are agreeing to participate in. If the healthcare provider desires to participate, s/he will sign, and the RA will co-sign. PCPs will receive a copy of the signed informed consent. A second copy will be stored in a secure, locked filing cabinet in a dedicated room.

Patients: For phase 1 of the study, patient initial verbal consent will be conducted during a telephone call with a RA. During the telephone call the RA will give a fuller description of the study to the participant in clear, easy to-understand language, emphasizing the points made during the initial telephone call/letter/Epic invitation. All patients will be told that their responses are anonymous and confidential, that they may refuse to participate in the project

responses are anonymous and confidential, that they may refuse to participate in the project or withdraw at any time without explanation, and further, that such action will in no way affect their future interactions with their PCP. If the patient remains interested in participating, they will have the option to either complete the focus group in-person in a dedicated room or via a remote session using NYU's secure Webex conferencing platform. For patients opting to complete the focus group remotely, the RA will send a copy of the informed consent to them for signature and include a pre-stamped envelope with return address. The RA will also include a letter with their contact information so the patient can contact the RA to ask for help in reading the consent form. Patients will be asked to mail back their signed consent to the study team before their scheduled focus group. Once the informed consent is received by the RA, the RA will sign and mail a copy to the patient. The original consent will be stored in a secure, locked filing cabinet in a dedicated room.

For Phase 2 of the study, patient consent will be conducted during an in-person meeting with a RA in a private space at the FHC or FGP. During the meeting the RA will give a fuller description of the study to the participant in clear, easy to-understand language, emphasizing the points made during the initial telephone call/letter/Epic invitation. All patients will told that their responses are anonymous and confidential, that they may refuse to participate in the project or withdraw at any time without explanation, and further, that such action will in no way affect their future interactions with their PCP. If the patient remains interested in participating, they will be provided with a copy of the consent form to read; if the patient asks for help, or evidences a problem in reading the consent due to literacy issues, the RA will read and explain the consent him/her. Patients will be asked to

repeat back to the salient points of the consent form to make sure that they understand the study they are agreeing to participate in. Patients who exhibit any cognitive deficits will not be eligible to participate in this study. If the patient desires to participate, s/he will sign, and the RA will co-sign. Participants will receive a copy of the signed informed consent. A second copy will be stored in a secure, locked filing cabinet in a dedicated room.

The RAs on the project will have previous experience working on intervention trials and as part of this work have obtained informed consent from demographically diverse participants. Further, the RAs will be experienced with consenting Spanish-speaking participants. If the participants speak Spanish they will receive an IRB approved Spanish translated Consent form. The Spanish consent form will be explained by a Spanish-speaking RA. A modification will be submitted that contains only translated research materials, including the informed consent documents.

6.3.3 Screening

Trained RAs will be responsible for screening potentially eligible participants from the FHCs and FGPs. Once a potentially eligible patient is identified for this study, they will be screened by telephone using a standardized form that outlines the study's inclusion and exclusion criteria. Study staff will obtain verbal consent prior to beginning the eligibility screening. Only participants that meet all eligibility criteria will be scheduled for a subsequent face-to-face meeting to obtain written informed consent.

6.3.4 Recruitment, Enrollment and Retention

Providers will be recruited through in-service talks at the clinics. Four methods, described below, will be employed to recruit the maximum number of eligible patient participants. Signed informed consent will be obtained from participants who meet the study eligibility criteria.

Method 1: Recruiting Using EHRs through EPIC: We will use EPIC to identify potentially eligible patients seen in the FHC/FGPs, based on DRG codes indicating presence of type 2 diabetes. We will develop a roster of potentially eligible patients for each treating physician in the practice. Physicians will be asked to review the roster and indicate, for each patient, whether an intervention targeting tracking patient-reported outcomes via text messaging is appropriate. Lists of patients deemed appropriate (i.e., "yes") by the physician will be generated. Following permission from FHC/FGP treating physicians to recruit their patients to the study, patients will be approached and screened using the following process: (a) A letter signed by the treating physician and Dr. Schoenthaler will be sent to the treating physician's patients notifying them of the study, and informing that an NYULH clinical staff person will contact them to explore their willingness to consider participation, or that their patients can call directly to the study staff to ask about the study. (b) Study staff will call or email patients who agree to be contacted, describe the study and, if the patient expresses an interest, conduct preliminary screening by telephone. Verbal consent is obtained by study staff prior to eligibility screening. (c) For potentially eligible patients with active MyChart accounts that have agreed to be contacted for research and indicate yes under the “recruiting ok?” option on EPIC, study staff will send the already IRB approved email script

via Epic. The patient will receive the message via MyChart and it will automatically be noted on their EHR as an encounter message. (d) Written informed consent will be obtained with subsequent face-to-face visit for eligible participants. An IRB-approved waiver of authorization will be obtained prior to searching the EHR.

Method 2: Participant self-referral through EPIC EHR MyChart alerts: We will provide the NYULH Epic Research Integration team with a list of potentially eligible patients provided to us by NYULH DataCore services through an IRB-approved waiver of authorization. The Epic team will create weekly reports on upcoming appointments from this potentially eligible patient's list, and will send these patients an alert notification two weeks prior to these appointments. These alert will inform patients to check MyChart electronic record for a new message. A modification will be submitted with the alert text prior to starting the study.

We will provide a NYULH Epic Research Integration team with an IRB-approved patient-facing script to be posted in the Epic electronic health record patient portal (MyChart) with a brief study description and encouragement to discuss the study with their treating physician on their next appointment. After this encounter, the Epic Research Integration team will send a second alert to potential participants after their medical appointment for them to check MyChart for another IRB-approved message reminding patients to contact study staff for any questions or to express their interest to participate. At this point, study recruitment proceeds as per protocol: (a) study staff describe the study and, if the patient expresses an interest, conduct preliminary screening by telephone. Verbal consent is obtained by study

staff prior to eligibility screening. (b) Written informed consent will be obtained with subsequent face-to-face visit for eligible participants. A modification will be submitted with the alert text prior to starting the study.

Method 3: Self-referral from advertisements placed in the FHC/FGPs: IRB-approved fliers and brochures containing an overview of the study will be created and displayed in the clinical practice setting for those who may be interested. Interested patients will be provided with the phone number of the study staff that they may call to obtain additional information about the study. Those participants contacting the study office will be provided a brief description of the goals of the study and what their participation would entail. Those who remain interested will be screened to assure that they meet eligibility criteria and schedule an informed consent and eligibility visit. We will contact the patients' healthcare provider/agent to determine if their patient is fit to participate in the study. A modification will be submitted with flyers prior to starting the study.

Method 4: Physician referral: During the provision of routine ambulatory care, physicians will identify potentially eligible participants and ask about their interest in a study that proposes to examine how patient and providers talk about taking medications. Interested patients will be advised to contact the study by telephone to discuss possible enrollment. Interested patients will be provided with the phone number of the investigators that they may call to obtain additional information about the study. Those participants contacting the study office will be provided a brief description of the goals of the study and what their participation

would entail. Those who remain interested will be screened to assure that they meet eligibility criteria and schedule an informed consent visit.

Retention Plan

We will use several strategies to retain practices and participants while they are enrolled in the trial. These include: (1) Signed memorandum of understanding (MOU): We have found that this formal agreement ensures that the sites understand the purpose of the study and their roles and responsibilities for participation, which increases the likelihood of retention. The MOU also highlights the benefits of participating in the project. All sites will be asked to sign this agreement as part of the recruitment and enrollment process. (2) Identify a practice champion or key contact to act as a liaison: This is also crucially important to ensure fidelity to the implementation of the MJS DIABETES intervention into the clinic workflow. (3) Offer monetary incentives for participation. For patients, this includes offering appropriate incentives (including cell-phone data plan subsidies), time to complete study visits, periodic phone calls, and transportation to the sites (total incentive: Formative phase: $60; Clinical Efficacy trial: $50). PCPs in both phases will be offered an incentive of $50 for their time. (4) Maintain communication: For patients, following consent, we will request the names, addresses, and telephone numbers of two friends or relatives, so we can contact patients in the event of a missed appointment. This approach has been a helpful strategy in prior trials. We will implement additional strategies that have led to successful retention of racial/ethnic minority patients in clinical trials such as: provision of a toll-free study telephone number; flexible scheduling; and continuity of study staff to maintain a personal connection to the

study. We will also send reminders for upcoming study visits in the form of mailed letters, telephone calls, and secure messages sent through MyChart and doxcimity. For PCPs, we will maintain contact through an emailed newsletter for these sites that provides updates about national and statewide health care initiatives but does not discuss intervention-related information. We will also remind PCPs of the protocol at the monthly meetings.

To increase enrollment into the study, all participants will also be asked about their ability to receive text messages during the consent procedures. Those individuals who express concern about participating due to the fees associated with receiving text messages (due to either not having a text messaging plan or a limited allowance of messages per month) will receive reimbursement for the messages that are sent as part of the study. Patients who will accrue the most text messaging charges and do not have a text messaging plan will be reimbursed $25 in total.

6.3.5 On Study Visits

Screening Visit: During this visit, trained RAs will use a standardized form to screen patients based on the study's inclusion and exclusion criteria. Verbal consent will be obtained prior to beginning the eligibility screening. Only patients that meet all eligibility criteria will be scheduled for the face-to-face consent/baseline visit. This visit should take 10 minutes.

Consent/Baseline Visit: At this visit, trained RAs will describe the study in easy-to-understand language. If the patient remains interested, the RA will obtain written informed

consent in the patient's preferred language (English or Spanish). Following informed consent, patients will complete the baseline study measures (see Measures Table 7). Finally, patients will be randomized to the intervention or control arms. This visit will take approximately 45 minutes.

Follow-up study visits at 3, 6, and 9-Months (post randomization): Patients will complete self-report measures with a bilingual RA. Patients in the MJS group will also be asked about any challenges to using MJS since their last study visit. The visit will be conducted either via telephone with a RA or REDCap, depending on the patient's preference. These visits will take approximately 30 minutes each.

6.3.6 End of Study and Follow Up

Final study visit at 12-Months (post randomization): Patients will complete the self-report measures and have their chart review completed. Patients in the MJS group will also complete measures regarding perceived use, ease of use and use behavior. Patients will also complete an exit interview where they will be queried about their experiences using the MJS tool over the past 12 months and recommendations for improvements. The visit will be conducted either via telephone with a RA or REDCap, depending on the patient's preference. This visit will take approximately one hour.

In addition, providers will be asked to complete, measures regarding perceived use, ease of use, use behavior and physician communication at 12 months. Providers will also complete an exit interview where they will be queried about their experiences using the MJS-EHR

interface over the past 12 months and recommendations for improvements. The PCP study visit will take approximately 30 minutes.

6.4.2 Sample Size Considerations

Formative phase: Sample size estimates for this phase are based on best practices for maximizing information power of qualitative research. Information power is determined by the specificity of the study aims, use of theory, and dialogue quality. It is recommended to begin with 4-8 participants and add to the sample, as needed to maximize information power.

Clinical Efficacy Phase: Power calculations are based on comparable studies using mHealth solutions to improve clinical and patient-reported outcomes in patients with T2D. We expect a group difference of 0.6%-1.4% between MJS DIABETES and UC groups at month 12 as suggested in Baron et al. This study compared the effects of a mHealth intervention on HbA1c and PROs including health-related quality of life and depression among a sample of 81 patients with T2D. Based on this study, we assume that a SD of HbA1c is 1.6%. Using a two-sample t test, for 80% power and 5% type I error, we can detect a 0.6% group difference with n=113 per group. With that same sample size, we are able to detect a 0.3% reduction in HbA1c for the MJS DIABETES group at month 12 compared to baseline. An attrition rate of 20% will ensure that 282 patients (141 per group) complete the study and

have adequate data. This attrition rate is comparable to other clinic-based T2D trials in vulnerable populations.

6.4.3.1 Primary Analyses

Our analytic plan to achieve our outcomes at each phase is as follows:

For the formative phase, focus groups will be transcribed (and translated in English) verbatim and coded using Atlas.ti. The analysis of the qualitative data from patient and PCP focus groups will be done in two parts: 1) A brief report of the predominant themes for immediate use in the design workshop, described below, and 2) content analysis of the sessions to be shared in future publications in order to advance the science on the use of PROs for diabetes management in primary care practices.

For the brief report, Dr. Schoenthaler and a trained RA will conduct a debriefing meeting after each focus group to create a summary that outlines the key barriers, facilitators, needs and workflow preferences among patients and PCPs. After completing all 3 focus groups, the RA will calculate the mean importance ratings for each of the PROs discussed by the patients and PCPs. The study team will use the mean scores in concert with recommendations for selection of PROs in diabetes research outlined by Reaney et al. to identify the appropriate PROs that will be collected in the clinical efficacy trial. The brief report will drive the development of workshop materials and exercises (draft MJS content, workflow maps), as described below.

For the content analysis, session transcripts will be analyzed by Dr. Schoenthaler and

consultant, Dr. Rosal, [who are experienced in qualitative research], using the constant comparison method. Specifically, the coders will independently review the transcribed focus groups to identify themes related to the design of the MJS intervention for English and Spanish-speaking patients, and PCPs, and barriers and facilitators to uptake. The coders will iteratively develop a codebook during this process to maintain coding consistency and transparency in coding decisions. Discrepancies in coding will be resolved through an interactive process of re-reading and discussing the transcripts until consensus is reached; the codebook will be updated to reflect any changes. Assessments of inter-rater agreement will be calculated using Krippendorff's alpha to ensure an acceptable level of agreement is reached (>0.80) between the coders. To evaluate the usability of MJS DIABETES, we will follow best practices for instant data analysis (IDA) of usability data. After each session, the study team will meet to brainstorm the usability and workflow issues (e.g., content, readability, navigation, alerting and visualizations) that were observed. Each identified issue will be then categorized as either: critical (unable to complete the task), severe (significant delay or frustration in task completion), or cosmetic (minor issue). Each of these issues will be mapped onto the transcribed audio and screenshots captured during the sessions to provide specific and detailed recommendations for refinement of the MJS mobile platform and EHR interface before proceeding to the next testing session. After completing all of the sessions, we will conduct affinity mapping to identify the major issues that were causing critical and severe errors in the testing sessions. This inductive process involves aggregating the separate issues identified in the brainstorming sessions into larger themes related to usability and workflow of MJS DIABTES. This creates a more synthesized and

comprehensive understanding of the most severe and frequent issues that must be addressed before testing MJS DIABETES in the RCT. Previous research have shown that using IDA can reduce the amount of time needed for analysis by 90%, while achieving 85% overlap in identifying critical usability issues compared to traditional qualitative analytic methods. The primary output of this step is the fully functional, well-integrated MJS DIABETES intervention for testing in the clinical efficacy trial.

For the clinical efficacy phase, the primary analysis is intent-to-treat (ITT). For the ITT approach, all patients that are randomly assigned to the intervention or UC groups will be included in the analysis, regardless of program and evaluation compliance. The primary outcome is the mean reduction, compared to baseline, in HbA1c at 12 months in the MJS diabetes intervention vs. UC arm. HbA1c will be treated as a continuous variable in this analysis. We will test the treatment X time interaction in a random effects linear regression model to test the time-specific differences in HbA1c at 12 months attributable to the intervention. We also will use the "lincom" command in Stata to estimate differences in time-specific changes from baseline. In additional analyses, we will adjust for covariates (e.g., ethnicity, gender, age, income, education, employment, insurance) unbalanced between the treatment arms at baseline at p=0.10.

6.4.3.2 Secondary Objectives Analyses

For secondary aim 1, analyses will examine the intervention effect individually on each self-care behavior and as a summary score at 12 months. The measures will be treated as continuous variables. As with the primary aim, we will test the treatment X time interactions

continuous variables. As with the primary aim, we will test the treatment x time interactions in a random effects linear regression model to test the time-specific differences in each of the individual self-care behaviors, and the summary score at 12 months. The "lincom" command in Stata will be used to estimate differences in time-specific changes from baseline. Adjustments for covariates will be made if randomization does not produce balanced groups. We will also estimate the proportion of patient and PCP use of MJS DIABETES as defined by number of PROs answered, error messages received, response times, number of EHR PRO reports accessed, clicks within the EHR PRO report, and retention rates over the 12-month study to calculate mean, median and standard deviation. We will perform statistical modeling to determine the direction and degree of association between change in PROs and change in the primary and secondary outcomes.

For secondary aim 2, we will estimate a just-identified path model using the robust weighted least squares estimator to investigate relationships among the theoretical mediators of diabetes knowledge, self-efficacy, and outcomes expectation and patient-provider communication and the adherence and HbA1c outcomes, Based on our conceptual model, we will test the direct effects from the theoretical constructs to the self-care behaviors (individually). In addition to the direct effects, the indirect effects from each variable to HbA1c via adherence will be estimated as the product of component direct effects and tested using bootstrapped 95% confidence intervals. Finally, we will estimate the direct effects of the predicted model of adherence on HbA1c reduction. Predicted probabilities of the secondary outcomes and HbA1c will be calculated from path model coefficients to elucidate the magnitudes of direct and indirect effects.

6.4.3.3 Safety/Pregnancy-related policy

Patients who are pregnant or planning to become pregnant in the next 12 months are excluded from this trial.

6.4.3.4 Analysis of Subject Characteristics

Baseline characteristics and outcomes will be summarized descriptively using mean values and standard deviation or frequency descriptions. During preliminary analysis, we will also examine: (1) comparability of treatment arms at baseline (based on Chi-squared statistics or t-tests, as appropriate) based on participant characteristics, (2) relationships between the response variables and potential covariates, and (3) predictors of missing data/drop-out. We will document any observed reasons for missing data during data collection.

6.4.3.5 Interim Analysis (if applicable)

Not applicable

6.4.3.6 Health economic evaluation

Not applicable

6.4.5 Handling of Missing Data

Univariate statistics and missing value analysis modules will be used to check the number and pattern of missing. We will use Little test to check the assumption of missing data completely at random (MCAR) or missing at random (MAR). Identified predictors of missing data will be included as covariates in a random effects framework, to provide unbiased

estimates of the intervention effect under an assumption of MAR (i.e., missingness depends on observed covariates but not on unobserved covariates). We will conduct sensitivity analyses to assess departures from this assumption.

7 - Trial Administration

7.1 Ethical Considerations

This study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki.

To mitigate any breaches in security or privacy as it relates to the MJS DIABETES intervention, we will adhere to policies by the Federal Office of the National Coordinator for Health IT as well as the principles of the Markle Framework for Networked Personal Health Information and the technical specifications of the O-Auth protocol for user authentication. Based on these sources, the Privacy and Security Plan will include:

- Development of explicit policies governing the access to individual PRO data in the MJS intervention (e.g., limited to study staff who require it for authorized, legitimate, and documented purposes).
- A firm policy prohibiting the study staff or consultants (i.e., Rip Road, Dr. Rosal) from access to individual patient health records, except for specific purposes of research approved by the IRB.
- Encryption of all sensitive user data within the MJS mobile platform and EHR interface to prevent unauthorized access and disclosure in the case of a physical loss. No PHI will be collected on the MJS platform.

- Regular training and reminders sent to study staff and consultants about system security and the need to follow related protocols to protect the confidentiality of user information. Policies will also be established for handling violations to security protocols, if they arise.
- A protocol outlining regular risk assessments and system audits to ensure a secure transmission of patients' data, including use of encryption protocols such as Secure Socket Layer (SSL) technology.

As part of their participation in this study, patients and providers will receive a small amount of payment to reimburse them for their time and effort. The payment is needed to reimburse patients and providers for the additional travel to the FHC/FGPs for study visits and additional time to participate.

7.2 Institutional Review Board (IRB) Review

This study will be overseen by the NYU School of Medicine Institutional Review Board. All research staff will have completed and passed IRB and HIPAA training and will be thoroughly trained in appropriate consent procedures and the need to maintain strict confidentiality. All research protocols will be reviewed and approved by the IRB prior to gaining access to protected health information and subject recruitment

7.3 Subject Confidentiality

As part of the process involved in obtaining written informed consent, all patients/PCPs will be reminded that their responses are confidential and that they may refuse to participate in

the project or withdraw at any time without explanation, and further, that such an action will in no way affect their future interactions with the FHC or FGP. To ensure confidentiality, data will be associated with an individual participant only by an assigned identification number, the code for which will be kept in a locked drawer. Only members of the research team will have access to the participants' personal information file. All computers containing confidential data will meet security requirements established by the HIPAA Security Rules, and established by the Office of Management and Budget (OMB) in OMB Circular No. A-130, Appendix III - Security of Federal Automated Information Systems. Specifically, all electronic interview data will be saved on a secure server housed by NYULMC and backed up daily or weekly depending upon the receipt of data. PHI will be confined to a secure server that is not connected to the Internet. All computers will be password protected and on a private LAN network. No file and database servers are accessible to the public through the Internet. Prior to inclusion in any data set (internal and external), data will be stripped of all identifying information.

Since text messages will be transmitted in this study, a variety of measures will be used to reduce information security risk. Patients' text responses will be securely handled via Rip Road's HIPAA compliant hardware infrastructure. Rip Road follows a set of well-developed policies and procedures vetted by top healthcare organizations in the management and protection of all data tracked through MJS. Patient information will be de-identified for administrative views and for analysis within the Rip Road system. Text messages will not identify patients as having a specific disease or include any PHI such as patients' name.

Patients will be informed that their data are stored, without identifiers, in the highly secure HIPAA-compliant Cloud. They also will be informed that there is a remote possibility that the Cloud or their mobile account could be hacked and that information about study activities (communications, recorded behaviors) could be disclosed. However, these data are not sensitive in nature. Devices will be configured with a participant ID and no other personal identifiers. It is possible that a participant could lose their mobile phone or leave it in a public location with the screen turned- on, enabling others to view personal information. To address this, we will assist the participant in enabling a screen saver that is activated when the mobile phone has been idle for 5 minutes, as well as a 4-digit password that must be entered each time the device is turned-on. They will also be instructed on how they can turn off home screen notifications if they choose to. Finally, all study staff will be trained in the NYULMC Research Practice Fundamentals, which include training in issues of confidentiality and requires trainees to sign a confidentiality agreement.

7.4 Deviations/Unanticipated Problems

If any protocol changes are needed, the Principal Investigators will submit a modification request to the IRB. Protocol changes will not be implemented prior to IRB approval unless necessary to eliminate apparent immediate hazards to the research subjects. In such a case, the IRB will be promptly informed of the change following implementation (within 10 working days).

7.5 Data Quality Assurance

In accordance with procedures for Good Clinical Practice, the PI will be responsible for data quality control including reviewing protocol compliance, data collection and verification. Data will be reviewed monthly.

Since assessment data is all entered electronically, accuracy and completeness of the data is maximized through alerts and pop-ups if the data is inconsistent, out of range, or not entered. The data entry procedures include a secure intra-net log-in that is password protected and data entry will have data quality checks with the electronic data system. Outcome measure data that involve questionnaire responses are collected in the secure REDCap. Exit interview data will be collected via either a telephone interview with the RA or through REDCap, depending on the patient's preference. Safety data are collected in a separate database related to each participant.

At the outset of the study, an investigator meetings will be held to introduce investigators and study personnel to the study protocol, data collection forms, procedures and regulatory requirements. During the course of the study, the program coordinator will make routine site visits to review protocol compliance, compare data collection forms with individual subject's original source documents, assess test material accountability and ensure that the study is being conducted according to the pertinent regulatory requirements. The review of the subject's medical records will be performed in a manner to ensure that subject confidentiality is maintained.

7.5.1 Data Collection

Data collected in the study are divided into four categories: (1) outcomes, (2) covariates, (3) mediators, and (4) process measures. The measures table 7 provides information on the measure to assess each variable and timing of administration. All measures will be obtained by a trained RA using a standardized procedure. With the exception of the process measures, measures will be the same for both arms.

Data collection forms will be identified only with IDs; relating of ID code to names will require information kept under lock and key, and supervised by a designated high-level staff member. None of the analyses will permit individual identification. Only ID numbers will be used for communication with the RAs in the event of data anomalies. The clinical/research barrier will remain intact, in that it will not be necessary for the data-processing staff to know the identity of the participants.

7.5.1.1 Access to Source

It is assumed that all PHI will be collected after informed consent; as a result certain PHI (e.g., date of birth) that are necessary for analyses may be entered as part of the data set. Certain rules obtain for handling PHI: a) copies of hard copy data will be hand-delivered in a sealed envelope marked confidential (e.g., via messenger or directly by the RA) or sent via FEDEX to the RC; b) non-encrypted electronic data, e.g., lab values will be accessed using a project-specific password or uploaded to the NYU secure server; c) prior to electronic submission or upload to the NYU server, all data containing PHI will be encrypted using PGP or Silver Key encryption software (e.g., assessment data). PGP and Silver Key ensure

data safety by requiring digital keys for decryption; d) a security code will be required for access to fax transmissions. This secure fax machine is housed in a locked area. All project related fax transmissions will contain a confidentiality notice.

7.5.1.2 Data Storage/Security

Hard copy data and log sheets are kept in a locked storage area behind a locked, alarmed door. Electronic data will be backed up daily or weekly depending upon the frequency of receipt/ entry. The backup disks will be stored in a fireproof safe in a different location. All computers are password protected and are on a private LAN network. There are no servers that are accessible to the public through the Internet. A hardware-based firewall separation protects against hackers and unauthorized access to all electronic data not maintained on the server, providing protection against viruses, worms and Trojan horses transmitted over the Internet. The firewall contains anti-virus software (McAffee Anti Virus) to protect the network from threats of viruses contained in email attachments. Through "push-technology" this anti-virus software is automatically updated for all virus definitions and other updates. Secure internet communication is established through a VPN tunnel which is configured through the firewall.

7.6 Study Records

Study records will include all regulatory documents, protocols, consents forms, data collection forms, subject medical records, surveys, and transcripts from audio-taped interviews and video-recorded usability sessions.

7.6.1 Retention of Records

In accordance with 45 CFR 164.530(j)(1) of HIPAA, research records including signed consent forms that contain the HIPAA authorization will be retained for 6 years after the date on which the subject signed the consent form or the date when it last was in effect, whichever is later. In addition, we will maintain records of IRB activities for at least three years after completion of the research (45 CFR 46.115(b)).

7.7 Study Monitoring

The PI will be responsible for monitoring the study. As noted in the Data Safety Monitor Plan, the PI will monitor the study activities along with a designated medical monitor, internal committee and IRB.The PI will review the study for protocol compliance, data collection and verification on a monthly basis.

7.8 Data Safety Monitoring Plan

The purpose of the data safety monitoring plan (DSMP) is to ensure the safety of participants and the validity and integrity of the data. Personnel involved in the monitoring activities will include:

- The PI
- Designated medical monitor (a physician in our program who will provide consultation on medical risks and who will review adverse events)
- Internal Committee (The PI and the Co-Investigators on the present proposal)

- Institutional Review Board

The PI will be responsible for quality control including reviewing protocol compliance, data collection and verification. Data will be reviewed monthly. Specifically, the plan will comprise the following elements:

- Monitoring participant recruitment and retention rates and developing a database tracking system to ensure there is no differential attrition by race/ethnicity, age, or gender
- Ensuring patient confidentiality through the use of unique identifiers. In addition, all data will be saved on a secure server housed by NYU Langone Health and backed up daily or weekly depending upon the receipt of data. PHI will be confined to a secure server that is not connected to the Internet. All computers are password protected and on a private LAN network. Only IRB-approved study staff will have access to the data. No file and database servers are accessible to the public through the Internet. Prior to inclusion in any data set (internal and external), data will be stripped of all identifying information. Finally, we will obtain a Certificate of Confidentiality.
- Reporting of adverse events to the IRB and to AHRQ/Merck: Adverse events will be reported to the New York University IRB. Summaries of adverse events reports will be made to AHRQ/Merck in the yearly progress or report or, at the end of year 2, in the final report, unless the nature of a particular event is such that it bears immediate

reporting to AHRQ/Merck.

- A detailed plan to address serious events that may arise such as increased anxiety while taping interactions that may include sensitive information, survey assessments, or patient hyper- or hypoglycemia. The plan will include a step-by-step algorithm to deal with such events. The Principal Investigator will monitor the data and conduct safety reviews, at a specified frequency appropriate to the level of risk (every 3 months).
- Procedures for protocol adherence and deviations. If any protocol changes are needed, the PI will submit a modification request to the IRB. Protocol changes will not be implemented prior to IRB approval unless necessary to eliminate apparent immediate hazards to the research subjects. In such a case, the IRB will be promptly informed of the change following implementation (within 10 working days).
- Statistical review of the study will be conducted by the study statistician at the conclusion of Year 4. Interim analyses will be performed after half of the eligible sample has been randomized and completed the final study visit. However, if a serious adverse event occurs as a result of the study, consideration will be given to stopping the study early. In the event of early stopping of the study, the IRB will be promptly notified.

7.9 Study Modification

The study may be modified or discontinued at any time by the IRB, AHRQ, Merck, or other government agencies as part of their duties to ensure that research subjects are protected. If any protocol changes are needed, the PIs will submit a modification request to the IRB. Protocol changes will not be implemented prior to IRB approval unless necessary to eliminate apparent immediate hazards to the research subjects. In such a case, the IRB will be promptly informed of the change following implementation (within 10 working days).

7.10 Study Discontinuation

The study may be discontinued at any time by the IRB, AHRQ, Merck, or other government agencies as part of their duties to ensure that research subjects are protected. If a serious adverse event occurs as a result of the study, consideration will be given to stopping the study early. In the event of early stopping of the study, the IRB will be promptly notified.

7.11 Study Completion

The estimated completion date of this study is 08/31/2023. At that time, a progress report will be submitted to the IRB and the record will remain open for analysis of study data. Once all research-related interactions with participants are completed and collection and analysis of identifiable private data (as described in the IRB-approved protocol) are finished, the study will be closed with the IRB.

7.12 Conflict of Interest Policy

All study team members will complete a financial disclosure form. In the event a conflict that requires disclosure or management is identified, the PI will provide to the IRB in writing with

a summary of conflict and the conflict management plan.

7.13 Funding Source

This project will be funded by the AHRQ and Merck & Co., Inc.

7.14 Publication Plan

Publication of the results of this trial will be governed by the policies and procedures developed by the PI and study team. Any presentation, abstract, or manuscript will be made available for review by AHRQ and Merck prior to submission.