**mHealth for Diabetes Adherence Support**

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TABLE OF CONTENTS

1.0 Project Summary/Abstract 3

2.0 Background/Scientific Rationale 3

3.0 Objectives/Aims 6

4.0 Eligibility 8

5.0 Subject Enrollment 10

6.0 Study Design and Procedures 11

7.0 Expected Risks/Benefits 21

8.0 Data Collection and Management Procedures 25

9.0 Data Analysis 28

10.0 Quality Control and Quality Assurance 28

11.0 Data and Safety Monitoring 28

12.0 Statistical Considerations 30

13.0 Regulatory Requirements 34

References 36

# 1.0 Project Summary/Abstract

Many African-Americans and Latinos with diabetes do not achieve recommended diabetes goals placing them at high risk for complications. Team-based models of care can help in reaching goals of therapy. Additionally, mobile health (mHealth) technologies can further improve outcomes among those more difficult to reach. This study will evaluate the impact of a team-based, mHealth intervention designed to improve medication adherence, healthy eating, and physical activity behaviors. We will compare this mHealth approach with usual care.

Clinical pharmacists and health coaches (HC) will deliver our proposed team-based intervention. mHealth delivery includes mobile phone text messaging, secure videoconferencing, and HC home visits. Pharmacists will focus on medication reconciliation and adherence. Health coaches will help identify psychosocial and environmental challenges to adherence in a culturally-sensitive manner. Together, they can assist in goal-setting, problem-solving, negotiation of competing priorities, and provide social support leveraging mHealth technologies.

Preliminary data from our research group supports the role of health coaches partnering with clinic-based pharmacists in improving diabetes outcomes in minorities. In the proposed mHealth intervention, patient-pharmacist videoconferencing will eliminate the need for in-person visits with a pharmacist, which is impractical for many low-income patients. In addition, our pilot work suggests that text messaging is a preferable means of communication and may facilitate more frequent contact with patients.

We propose a randomized, controlled trial to evaluate the effectiveness of an mHealth diabetes adherence support intervention delivered by clinical pharmacists and health coaches. We will randomize 220 patients through UI Health to either: (1) mHealth diabetes adherence support through clinical pharmacists and health coaches; or (2) usual care. After one year, patients completing the mHealth intervention will be monitored for an additional year while the usual care group receives the mHealth approach. Outcomes include medication adherence, hemoglobin A1c, blood pressure, and LDL-cholesterol levels. The specific aims include: (1) evaluate the effectiveness of an mHealth diabetes adherence support intervention delivered by clinical pharmacists and health coaches to African-American and Latino adults with uncontrolled type 2 diabetes; (2) evaluate the maintenance of improved diabetes behaviors as well as clinical outcomes one year after completing the intervention; (3) evaluate the cost and cost-effectiveness of mHealth diabetes adherence support compared to usual care; and (4) evaluate the reach, adoption, and implementation of mHealth diabetes adherence support based on the RE-AIM framework.

# Project Summary for the mDAS Sleep Sub-study Supplement

As part of the parent R01 described above, Dr. Alana Biggers will conduct a smaller sub-study that is funded with a diversity supplement award to the R01. The award supports Dr Biggers gaining structured and unstructured experiences in research training over two years. With support of a mentored research study, she will investigate mobile health (mHealth) evaluation of sleep within the context of Type 2 diabetes. Sleep quality and duration are modifiable risk factors that can help people improve diabetes control and reach diabetes goals. Although poorly understood, African-Americans and Latinos often report poorer sleep quality and/or duration and may be more susceptible to the metabolic effects of poor sleep. Additional research is needed to understand sleep behaviors and the possible impact on the health and well-being of these populations. Currently, sleep is rarely assessed by clinicians and behavioral interventionists. mHealth technologies can potentially improve the evaluation and study of sleep in these populations. This study will characterize sleep (quality, duration, and patterns) among African-Americans and Latino-Americans with uncontrolled diabetes, evaluate the effectiveness of mHealth in monitoring sleep and explore the relationships between sleep and diabetes outcomes. mHealth exploration includes mobile phone text messaging, wrist actigraphy use, and self-report surveys of sleep. Preliminary data from this study will inform the development of remotely-delivered approaches to sleep assessment and intervention (e.g., promotion of sleep hygiene). Initially, Dr. Biggers will lead a cross-sectional study of 40 participants to assess and explore the impact of sleep using mHealth.

The specific aims of this proposed study include: (1) explore subjective daily sleep quality, duration, and pattern of 40 inner-city African-American and Latino-American patients with poorly controlled type 2 diabetes (hemoglobin A1c>8%); (2) evaluate the feasibility and acceptability of objectively measuring sleep quality, duration, and patterns and sedentary behaviors via mHealth; and (3) explore the relationships between subjective and objective measures of sleep quality, duration, and patterns, as well as the relationship between sleep measures and glycemic control (i.e., hemoglobin A1c), quality of life, depression, and sedentary behaviors. Ultimately, this research may help demonstrate a potential role of mHealth evaluation of sleep, leading to innovative, behavioral strategies to improve diabetes-related outcomes.

# 2.0 Background/Scientific Rationale

Diabetes affects approximately 13% of African-American and Latino adults in the United States.[9](#_ENREF_9) Aggressive management of blood glucose, blood pressure, and cholesterol through medication and lifestyle adherence are necessary to minimize adverse health outcomes.[17](#_ENREF_17) However, barriers to adherence contribute to the fact that fewer than 20% of these ethnic minorities actually reach all therapeutic goals.[8](#_ENREF_8),[18-24](#_ENREF_18) As a result, improvement in minority diabetes management remains a priority for research.[25](#_ENREF_25)

Medical nutrition therapy, physical activity, and pharmacotherapy are essential components of diabetes self-management.[26](#_ENREF_26) Adherence to diet and physical activity is low for a majority of Americans including those with type 2 diabetes.[27](#_ENREF_27),[28](#_ENREF_28) Similarly, adherence to medication is poor:[29](#_ENREF_29) 20-30% of prescriptions are never filled, and 50% of medications for chronic disease are not taken as prescribed.[30-32](#_ENREF_30) Self-management among low-income, minority populations is often more problematic due to extensive barriers such as low health literacy, depression, lack of social support, poor patient-clinician communication, and limited access to healthcare.[16](#_ENREF_16),[20](#_ENREF_20),[21](#_ENREF_21),[33-39](#_ENREF_33) Latinos may face additional barriers such as low English proficiency and other cultural issues. Low adherence may reduce treatment modifications and intensification contributing to poor diabetes control.[22](#_ENREF_22),[23](#_ENREF_23) Systematic reviews of interventions designed to improve medication adherence found few studies that improved clinical outcomes.[30](#_ENREF_30),[31](#_ENREF_31),[40](#_ENREF_40),[41](#_ENREF_41) Sample sizes were small, and minorities (especially Latinos) were underrepresented. Further research is necessary to identify effective interventions that improve adherence in ethnic minority populations.

The *patient-centered medical home* (PCMH) approach has been endorsed widely[42](#_ENREF_42),[43](#_ENREF_43) and involves diverse health professional teams working collaboratively with primary care physicians to provide high levels of care, access, communication, care coordination and integration.[42](#_ENREF_42)

*Clinical pharmacists* improve glycemic control in diabetes management with their expertise in medication management and ability to adjust therapy in collaboration with providers.[44-49](#_ENREF_44) Clinical pharmacists are widely accepted in this role; most state boards of pharmacy authorize collaborative drug therapy management protocols between clinical pharmacists and prescribers.[49](#_ENREF_49),[50](#_ENREF_50) For example, Project IMPACT: Diabetes is a national research initiative supporting pharmacists working in community-based diabetes care teams, involving 25 underserved communities across the U.S.[4](#_ENREF_4) Pharmacist-led interventions enhance adherence to chronic disease medication through patient education, use of adherence aids, and addressing medication-related issues (e.g., drug interactions and cost).[31](#_ENREF_31),[51-55](#_ENREF_51) Our research with low-income minority patients suggests that in-person pharmacist visits are not feasible for many patients due to the added travel burden, cost, and time from work. Also, few studies of pharmacist-based models of care have included Federally Qualified Health Centers (FQHCs) or focused on low-income minority populations.[49](#_ENREF_49)

*Health coaches* (HCs) are increasingly included as members of the medical home for vulnerable groups as their involvement contributes to improvement in diabetes self-management and A1c levels.[56-63](#_ENREF_56) The Patient Protection and Affordable Care Act (ACA) formally recognizes the role of HCs in health promotion and education, disease management, patient navigation, improving health literacy, and advocacy.[64](#_ENREF_64) UI Health has representation on the Illinois Department of Public Health (IDPH) Community Health Worker Advisory Board to support implementation across Illinois. Trained HCs are trusted by patients, understand socio-cultural barriers, and can help increase the relevancy of disease self-management to individuals who are struggling to manage competing priorities. Our research demonstrates that HCs can successfully collaborate with clinical pharmacists in addressing lifestyle and medication adherence.[16](#_ENREF_16)

Mobile health (mHealth) includes “the use of mobile computing and communication technologies in health care and public health.”[65](#_ENREF_65) Our mHealth approach includes tablet computer videoconferencing and cell phone text messaging components.

While the presence of mHealth applications is exploding in healthcare, few studies have explored the impact of videoconferencing on chronic disease management. Systematic reviews of Internet-mediated communication technologies fail to show clear effects on health due to variation in study design and technologies, heterogeneous study populations, and variability in contact frequency.[66-68](#_ENREF_66) In diabetes care, technology-based interventions focus on transmission of blood glucose values with less attention on addressing barriers to self-management.[69](#_ENREF_69) Empirical data suggest that videoconferencing in diabetes care is practical, potentially cost-effective, and reliable for disease management.[69](#_ENREF_69),[70](#_ENREF_70) Video conferencing with clinical pharmacists to promote medication adherence is a growing model in rural practice (e.g., Department of Veterans Affairs[1](#_ENREF_1) and Kaiser Permanente[2](#_ENREF_2)) but not well studied, particularly with mobile devices or involving urban, low-income minority patients.[71](#_ENREF_71),[72](#_ENREF_72) Our study will focus on low-income African-Americans and Latinos and explore the use of videoconferencing between patients and clinical pharmacists, facilitated by HCs.

Text messaging interventions in diabetes management have shown mixed results and inclusion of low-income minorities has been low.[73-78](#_ENREF_73) Few formal randomized controlled studies of text messaging exist.[79](#_ENREF_79) One recent study showed short-term, modest improvement in cardiovascular risk factors in Australians with coronary heart disease.[80](#_ENREF_80) While there are no clear, specific intervention components shown to improve outcomes, follow-up contact, individualized frequency, and tailored support likely improve acceptability and responsiveness by users.[81](#_ENREF_81),[82](#_ENREF_82) Our study will include daily, tailored text messages with HC follow up to provide social support, improve self-efficacy, and adherence. Furthermore, the proposed study utilizes inexpensive technologies for text messaging and video conferencing, with greater potential for widespread adoption in underserved communities.

The widespread use of cell phones and text messaging among low income and minority populations has allowed HCs to increasingly adopt technology in their work.[83](#_ENREF_83) To date, most of this research has been conducted outside of the U.S. utilizing technology for field-based data collection, sending reminders, providing health education, and communication.[13](#_ENREF_13) Within the U.S., integration of low-cost technologies into community-based HC interventions remains an emerging area of research.[84](#_ENREF_84)

Despite widespread use of mobile devices, little is known about the effectiveness of the technology to improve health care delivery or outcomes.[81](#_ENREF_81) Systematic reviews show preliminary value of text messaging, patient education apps, and videoconferencing in chronic disease management, but most studies have been small in size, underpowered, low in quality, and include motivated, non-minority subjects.[65](#_ENREF_65),[69](#_ENREF_69),[70](#_ENREF_70),[78](#_ENREF_78),[79](#_ENREF_79),[85-88](#_ENREF_85) Our work will provide needed evidence on the impact of mHealth diabetes adherence support delivered to low-income minority patients with uncontrolled diabetes.

# 2.1 Background/Scientific Rationale for mDAS Sleep Sub-study Supplement

Diabetes is a leading cause of death and disability in the US costing $45 billion in direct medical costs and reduced productivity. 6 Diabetes disproportionately affects minority populations 7 especially African-Americans and Latino-Americans. Studies have shown that lifestyle intervention can reverse and/or improve diabetes control. 8 While healthy eating and physical activity are well-studied behaviors in diabetes self-management, sleep is increasingly being recognized as a potential modifiable factor that can also lead to increased diabetes control. Studies have shown that people with short sleep duration, long sleep duration, or poor quality sleep have worse glycemic control, even without sleep-disordered breathing such as obstructive sleep apnea. 1,2 Poor sleep quality and duration can lead to weight gain and impaired glucose tolerance. 9–11 For these reasons, sleep is an essential lifestyle component to study in diabetes self-management.

It is well established that African-Americans, Latinos, and other ethnic and racial minorities are more likely to develop diabetes and develop complications from the disease. 7 It is possible that poor sleep duration and quality contribute to these health disparities. Data exploring sleep quality within minority populations is very limited. However, existing data suggest that African-Americans are more likely to have worse sleep quality and shorter sleep duration compared to whites 4, whereas Latinos are more likely to have shorter sleep duration compared to whites. 4 Additional research is needed considering that these groups are also more likely to report psychosocial stress that contributes to inconsistent sleep patterns. 12,13 Furthermore, these populations are more likely to have nonstandard and non-day work hours (e.g., shift work) that contribute to inconsistent sleep and an increased risk of diabetes. 14–18 Further sleep research involving minority populations with diabetes is strongly justified and long overdue.

Despite evidence supporting a strong relationship between sleep and glycemic control, the mechanisms underlying the link are not well understood. Both diabetes and poor sleep are associated with more depression, lower quality of life, and more sedentary behavior. 19–26 In addition, socio-environmental factors secondary to poverty (e.g., neighborhood violence, social isolation, etc.) may result in higher levels of chronic stress that contribute to the link. The proposed study will explore these pathways by collecting detailed subjective and objective sleep assessments in patients with diabetes in addition to depression, quality of life, and physical activity (which are assessed in the parent grant). This study will begin to provide a nuanced understanding of the complex relationships between these highly relevant variables.

Little is known about the utility of mHealth to objectively evaluate sleep. The gold standard for studying sleep is polysomnography. 27,28 Unfortunately, this method is cumbersome and not feasible in a real-world setting. mHealth devices provide an opportunity to evaluate sleep in a natural setting. This is particularly valuable in mHealth intervention studies, including the parent study, where mobile assessments and interventions are incorporated. A few popular low-cost commercial activity trackers (e.g., Fitbit and Garmin) are widely available, however, they overestimate polysomonography total sleep time and sleep onset latency or underestimate wake after sleep onset. 29 Alternatively, wrist actigraphs represent evidence-based activity trackers that serve as comparable alternatives to polysomongraphy for measurement of sleep in the home. Actigraphs provide accurate measures of total sleep time, sleep percentage, movement, and wake after sleep onset. 27,28,30 In addition, their value may further improve with supplementary data from text message-prompted sleep diaries and selected questionnaires. 27 Together, the mHealth and traditional approaches can be used to evaluate home sleep environments and support efforts to develop sleep interventions.

The overall objectives of this supplement are to evaluate the feasibility and acceptability of mobile health approaches to assessing sleep duration and quality within minority populations known to have poor control of their type 2 diabetes. We will explore the relationships between sleep (duration, quality, and patterns), glycemic control, depression, quality of life, and sedentary behavior. Findings from this study will provide critical preliminary data to support Dr. Biggers’ application for a career development award. Dr. Biggers’ goal is to establish an on-going line of research as an independent investigator focused on developing sleep hygiene interventions to improve sleep duration and quality in minority populations with diabetes.

# 3.0 Objectives/Aims

We propose a randomized, controlled trial to evaluate the effectiveness of an mHealth Diabetes Adherence Support (*mDAS*) intervention delivered by clinical pharmacists and health coaches. This proposal is in response to NIH PA-14-334: Advancing Interventions to Improve Medication Adherence. We will randomize 220 patients through the University of Illinois Hospital & Health Sciences System (UI Health) to either: (1) mHealth diabetes adherence support (*mDAS*) through clinical pharmacists and HCs; or (2) usual care. After one year, patients completing the mHealth adherence intervention will be monitored for an additional year while the usual care group receives *mDAS*.

The specific aims include:

|  |  |
| --- | --- |
| **Aim 1:** | To evaluate the *effectiveness* of *mDAS* delivered by clinical pharmacists and HCs to African-American and Latino adults with uncontrolled type 2 diabetes. We will compare *mDAS* and usual care through the following outcome measures: hemoglobin A1c, blood pressure, LDL-cholesterol levels, and medication adherence. |
| **Aim 2:** | To evaluate the *maintenance* of improved clinical outcomes and medication adherence one year after intervention completion. |
| **Aim 3:** | To evaluate the cost and cost-effectiveness of *mDAS* compared to usual care. |
| **Aim 4:** | To evaluate *reach*, *adoption*, and *implementation* of *mDAS* (RE-AIM framework) |

# 3.1 Objectives/Aims for mDAS Sub-study Sleep Supplement

Sleep quality and duration are increasingly being recognized as modifiable risk factors for improving diabetes control. Studies have shown that short sleep duration (less than 7 hours), long sleep duration (more than 8 hours), and poor quality of sleep are associated with impaired glucose tolerance and insulin resistance. This increases the risk of developing diabetes and worsens glycemic control among those with type 2 diabetes. 1–3 Research specifically targeting sleep among low-income African-Americans and Latinos is lacking; however, available data suggest that these groups are more likely to experience problematic sleep patterns resulting in detrimental metabolic effects of poor sleep. 4 In addition, clinicians rarely assess sleep 5, though they are available to intervene on sleep hygiene. Collectively, these factors support the need to further investigate sleep in low-income minority populations with diabetes with intentions of developing remotely-delivered sleep assessment and intervention. The overall objectives of this study are to characterize sleep quality and duration among African-Americans and Latino-Americans with uncontrolled diabetes, evaluate the effectiveness of mHealth in monitoring sleep quality and duration, and explore the relationships between sleep and glycemic control.

The specific aims of this proposed study include:

**Aim 1**: To explore subjective daily sleep quality, duration, and patterns of 40 inner-city African-American and Latino-American patients with poorly controlled type 2 diabetes (hemoglobin A1c≥8%). Sleep quality, duration, and patterns will be measured by a validated sleep questionnaire, a mHealth version of a validated consensus sleep diary, and a home sleep environment questionnaire.

**Aim 2:** To evaluate the feasibility and acceptability of objectively measuring sleep quality, duration, and patterns and sedentary behaviors via mHealth. Study participants will wear an Actigraph Watch for seven days (including nights) and report their experiences with the device and assess its acceptability.

**Aim 3:** To explore the relationships between subjective and objective measures of sleep quality, duration, and patterns, as well as the relationships between the sleep measures, glycemic control (i.e., hemoglobin A1c), quality of life, depression, and sedentary behaviors.

Hypotheses 3a: Poorer sleep quality, duration, and patterns will be associated with higher hemoglobin A1c levels.

Hypotheses 3b: Poorer sleep quality, duration, and patterns will be associated with a lower quality of life, depression and more sedentary behaviors.

# 4.0 Eligibility

###### 4.1 Inclusion Criteria

* Self-identified as Latino/Hispanic or African-American
* Verbal fluency in English or Spanish
* Latest A1c ≥ 8.0% (within 3 mo)
* History of Type 2 Diabetes (> 1 year)
* Between the ages of 21 and 75 years
* Unlimited mobile phone/text messaging plan with ability to reply to text messages
* Home environment capable of video conferencing with wireless signal per patient’s report of cell phone reception in the home
* Receives primary care at clinical site for at least one year, with one visit during past year
* Able and willing to provide informed consent (agree to data collection requirements, accept randomization, agree to home visitation with HC and pharmacist involvement, and participate for two years)

###### 4.2 Exclusion Criteria

* Unable to verbalize comprehension of study or impaired decision making
* Lives outside Chicago (3+ months/year)
* Family/household member already participating in same study
* Plans to move from the Chicago area within the next two years
* Pregnant or trying to get pregnant
* Currently receiving regular pharmacist support through Medication Therapy Management or equivalent
* Unable to send/read text messages on mobile phone
* History of, or planned, gastric bypass or transplant surgery
* History of bipolar or psychotic disorder
* Other severe comorbidities that require complex, aggressive, or palliative treatment, e.g., stage 4 or greater renal disease, liver failure, cancer (other than nonmelanoma skin cancer), terminal illness
* Investigator discretion for safety concerns

Supplement Sleep sub-study is offered only to English-speaking participants but no additional inclusion/exclusion apply.

# 5.0 Subject Enrollment

University of Illinois Hospital and Health Sciences System (UI Health) includes both inpatient and outpatient facilities serving a diverse population in Chicago. UI Health has 19 ambulatory centers staffed by Family Medicine and Internal Medicine PCPs and includes Mile Square FQHCs where care is provided independent of ability to pay. Four to six clinical sites will participate. All sites share access to the EMR, Cerner Powerchart, and employ clinical pharmacists through the UIC College of Pharmacy Practice.

We will employ the following recruitment/enrollment methods:

1. Passive Advertising: We will distribute study advertisement materials throughout UI Health, including clinical environments. Individuals will call research assistants (RAs) for eligibility assessment by phone.
2. Active Recruitment from Registries: The research assistants will work from a physician-approved list of patients with diabetes and A1c ≥ 8 identified from the electronic medical record. We will send letters informing patients that they may be eligible for the study and may opt-out of further contact. After one month, those who do not opt out will be contacted by the RAs to assess interest and eligibility.
3. Active Recruitment in Clinical Sites: On-site RAs will receive additional referrals directly from staff or patients interested in the study. In these situations, RAs will discuss the study and assess eligibility in a private exam room within the clinic before or after a clinical encounter.
4. Diabetes Health Registry: RAs will call by phone individuals completing the Diabetes Health study (IRB 2011-0099) who indicated willingness to be contacted regarding future studies.

Chart review will be performed to establish eligibility (type 2 diabetes and A1c 8% or higher in past three months). An RA will complete an initial screening interview with the potential patient, either over the phone or in person in the participating clinics. RAs will ask screening questions (see Eligibility Screening attachment) and document the screening and eligibility (see Screening and Contact Information Sheet attachment). If the patient is eligible and interested, the RA will review the study in detail, using an IRB approved consent form as guidance. The RA will inform patients that the research is being conducted to improve medication management in diabetes care and to find out if pharmacists and health coaches help people reach goals of therapy. The RA will discuss the study protocol in detail as part of consent procedures and use the “teach back” method to ensure participant comprehension. The RA will clarify that the research procedures are separate from routine clinical care and participation is completely voluntary. All subjects must have a mobile phone with text messaging plan. Any individuals without an unlimited plan will not be reimbursed for text charges. The RA will confirm the patient’s eligibility and willingness to meet with a health coach in their home. They will then obtain informed consent and HIPAA authorization. The patient will be offered a copy of the consent form for their own convenience.

Participants will then complete baseline data collection at the UIC Clinical Interface Core. All screening and study data will be recorded in REDCap. Screening reports will provide investigators with information regarding recruitment progress and reasons for ineligibility.

# 5.1 Additional Subject Enrollment and Methods for mDAS Sub-study Sleep Supplement

At the end of a regularly scheduled data collection point for the larger R01 study, English-speaking participants will be asked if they are interested in hearing the details of a sleep study (mHealth Supplement). Interested participants will be given a brief overview of the study and if they remain interested, at that time they will be fully consented for participation. If they are interested but unable to stay for the consenting process and/or additional data collection, another visit will be set up. Otherwise, after providing written informed consent, participants will complete a series of sleep related questionnaires that will be entered directly into REDCap. After completing the questionnaires, participants will be given a Philips Actiwatch with instructions for use. They will be asked to wear the watch for 7 consecutive days taking it off only if they are going to submerge it in water. They will also be reimbursed $10 for their additional time. Each day during the 7 day sleep period, they will answer daily questions through a survey about the previous night’s sleep quality and process. The participants will have the option of a) completing the consensus sleep diary survey questions via text using the myTapp messaging system, or b) completing a web-based online sleep diary survey using a secure application such as REDCap or Qualtrics. If the participants do not respond to the text message link, then research personnel will attempt to call the participant once to complete the day’s sleep diary. At the end of the 9 days, participants will be contacted by telephone to complete a brief post-study assessment (see measures) and to schedule a day/time to return the actiwatch. Participants will be given the option of coming into the CRC to drop off the Actiwatch or they can have an RA come to their house to pick up the device. They will receive an additional $30 when the Actiwatch is returned. Recruitment goal is 40 individuals; although we expect to have to approach at least 60 in order to get 40 who will complete the study.

# 6.0 Study Design and Procedures

A randomized, controlled trial will evaluate the effectiveness of *mDAS* delivered by a clinical pharmacist and HC versus a usual care group. We will recruit 220 patients from UI Health. We recognize that all participants will have uncontrolled diabetes and require additional support from their healthcare team. Consequently, our usual care group will receive additional resources to meet basic standards of diabetes care and establish clinical equipoise between the two study groups. The usual care group will receive a referral to a diabetes educator and clinical pharmacist for medication reconciliation. These individuals are on staff and available to any patient, yet under-utilized. This group will receive a one-page contact sheet with the names and phone numbers of their local healthcare team as well as paper-based, low-literacy diabetes educational information. After one year, patients who have completed *mDAS* will be monitored for an additional year with usual care to evaluate maintenance, while the usual care patients receive *mDAS*. After recruitment, subjects will be randomized to receive either: (1) *mDAS* delivered by a clinical pharmacist and HC via home visits, videoconferencing, and text messaging; or (2) usual care.Study condition allocation will be completed after consent and baseline data collection. Using the REDCap Randomization Module, a random sequence of 220 subject assignments will be used. Blocked randomization (with varying block sizes) by clinical site, ethnic group (African-American and Latino), and gender will balance the proportion of participants.

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###### 6.1 Overview of Participant Procedures

Recruitment and Randomization

1. Potential participants will be identified by one of four recruitment methods previously described.
2. RAs will screen patients for eligibility and discuss the study protocol in detail. If the patient is deemed eligible to participate he/she will complete written informed consent and HIPAA authorization.
3. Enrolled participants will schedule an appointment at the UIC Clinical Interface Core (CIC) to complete baseline data collection, which includes a blood draw.
4. Participants randomized to *mDAS* will receive the intervention component in Year 1, while participants randomized to *Usual Care* will receive it in Year 2. RAs will inform participants of assignment.

**Additional information for mDAS Sleep Sub-study Supplement**

1. English-speaking participants will be asked to participate in a sleep sub-study to evaluate his or her sleep for 9 days at one of the regularly scheduled data collection follow up visits for the parent study.
2. RAs will screen willing participants for the sleep sub-study for eligibility and discuss the study protocol in detail. If the patient is interested, he/she will complete written informed consent for the sleep sub-study and complete the questionnaires. He/she will take an actiwatch to wear day and night for 7 days. Each day, they will receive mytapp messages asking about their sleep quality and process the night before. The Actiwatch will be returned at patient’s convenience (drop it off or RA will pick it up). Reimbursement for the entire study is $40.

Usual Care Component

1. Participants will receive contact information for a diabetes educator and a clinical pharmacist for medication reconciliation.
2. Patients will receive a one-page contact sheet with the names and phone numbers of their local healthcare team as well as paper-based, low-literacy diabetes educational information.

*mDAS -* Pharmacist Component

1. Pharmacists will provide medication and disease management services to patients by following a Pharmacist Management Protocol (see attached).
2. The initial pharmacist videoconference will include medication reconciliation and review therapeutic goals.
3. Follow up videoconferences will occur every other month. The interval duration may increase/decrease based on individual preference and when subjects reach goals.
4. These subsequent visits will involve an evaluation of adherence, medication reconciliation, and a review of home glucose and/or blood pressure monitoring data, an evaluation of drug interactions and side effects, goal setting, basic lifestyle modifications, pillbox use, development of a low-literacy medication list, and other adherence aids.
5. Pharmacists will adjust therapy according to the plan of care under PCP guidance and notify PCPs of agreed upon modifications through EMR notifications. Side effects will be conveyed to the PCP (if the PCP is not available, the covering physician will be contacted as per Pharmacist management Protocol).
6. Pharmacists will forward all electronic progress notes to PCP EMR “Inbox” after each encounter.
7. If the PCP feels that the patient should not remain in the study the provider can inform the Co-PIs to disenroll the participant.

*mDAS -* Health Coach Component

1. All health coaches will receive standardized training/re-training via two educational curricula: (1) the *Diabetes Education Empowerment Program*; (2) Dr. Bodenheimer’s *Training Curriculum for Health Coaches*; and (3) PEARLS for problem solving in depression management.
2. The coaches will communicate with their patients through home visits, phone calls, clinic encounters, and text messaging. Coaches will use *mytapp* to schedule text messages (messages will be tailored to individual and reflect patient goals).
3. Coaches may evaluate food inventory, medication adherence, and insulin injection techniques. Coaches will check glucose levels and blood pressures as needed.
4. Coaches may show Living Well with Diabetes lessons via iPad for education.
5. Coaches will participate in goal setting procedures. They will use the Purple Binder to access community resources.
6. Coaches will facilitate videoconferencing with patients. A multidisciplinary meeting will include coaches and pharmacists to communicate on a weekly basis about active participant issues.
7. Coach activity will be collected on a standardized electronic form completed after every participant contact. Coaches will document contact in the EMR.

Crossover Transition

1. One year after enrollment, the participants receiving *mDAS* will have the intervention components phased out to assess maintenance. The participants in the usual care group during year 1 will receive *mDAS* support for the subsequent year to assess intensification.
2. Coaches will help participants enlist social support and community resources for long term assistance with medications.
3. Coaches may periodically be contacted by disengaged participants during the following year. These communications will be logged.

Retention

1. Monetary reimbursement for each data collection
2. Periodic phone calls to verify address and phone data
3. Use of secondary alternative contact information
4. Any “lost” individuals will be searched for using a comprehensive standardized web based search protocol which included:
   1. Five people locators
   2. Major social networking sites, specifically those with more minority involvement
   3. Department of corrections database
   4. These searches will be conducted on the target individual as well as secondary contacts
   5. All potential contact will be private. No study related information will be conveyed in public through these searches.

Health Coach Fidelity

1. To continuously evaluate the fidelity of the pharmacist and health coach components of the intervention, investigators will review health coach and patient medical records of 10% of participants randomly selected.
2. In addition, we will monitor health coach activities through encounter forms that include participant interactions and duration of time spent on activities.
3. Drs. Gerber and Sharp will attend multidisciplinary weekly meetings with health coaches and pharmacists and review active patient issues.

Data Collection

1. This research will be performed at the CCTS Clinical Interface Core.
2. Surveys will be conducted by interview format. This information is only being collected for research and will not be shared with others. This will take approximately 60 minutes.
3. We will draw some blood from each subject’s arm to measure Hemoglobin A1c and cholesterol profile. Each subject will be asked to fast (may drink water but may not eat food for 12 hours prior to the test). The amount of blood drawn will be about 6 ml (approximately one teaspoon).
   1. Briefly, a total of 6 ml of whole blood will be collected in one gold SST top vacutainer tube and one lavender EDTA tube on each of the blood draws.
   2. Once collected the blood will be delivered to the Alverno lab for processing.
4. Each subject’s height, weight, and blood pressure will be measured, similar to how this is done in the doctor’s office.
5. The subject will provide contact information for all of the pharmacies where prescriptions have been filled for the past year. The subject will allow study personnel to contact these pharmacies to collect information on the type, number, and dates of prescriptions filled.
6. Each subject will be asked to return after 6, 12, 18, and 24 months for similar testing (surveys, blood tests, height, weight, blood pressure).

**Additional Data Collection for mDAS Sub-study Supplement**

1. Each subject will be asked to complete surveys in interview format on personal sleep practices. The surveys include: Pittsburgh Sleep Quality Index, PROMIS Sleep-related Impairment Short Form 8a (8 items) and PROMIS Sleep Disturbance Short Form 8b (8 items), an assessment of sleep apnea and restless leg syndrome. This will take approximately 20 minutes. Patients will be compensated $10 for this initial sleep sub-study data collection.
2. The RA will provide instructional tutorial on using the wrist actigraphy (Actiwatch) to the participants. This will take approximately 5 minutes
3. Study participants will wear a wrist actigraphy for 7 days and 7 nights and answer custom questions on sleep after the participants wake up. The participant has the option of answering the questions via myTapp messages or through a web-based online sleep diary survey using a secure application such as REDCap or Qualtrics. These questions will be modified from a validated consensus sleep diary.
4. At the end of the 9 days, participants will be telephoned to complete a post-study evaluation and to schedule a day/time to return the actigraph watch.
5. Participants will be compensated $30 for sub-study completion by research personnel.

**On the consent form, participants will be asked for permission to use the data collected within the larger mDAS study as part of the analyses in this sub-study. Patients are allowed to decline and still participate in this portion of the research.**

**Temporary modifications to data collection during COVID-19 pandemic**

Due to the COVID-19 pandemic and social distancing orders, the following modifications will be made until research operations allow adequate in-person contact.

* + - 1. Data collection surveys as described above will be conducted by telephone with the possibility of using Doximity (HIPAA secured videohealth) in some occasions.
      2. Subjects will be compensated for data collection visits with a gift card instead of cash. Gift cards will be purchased online from major online retailers and mailed directly to subjects.
      3. Subjects will be offered the option to complete the Hemoglobin A1c test and Cholesterol panel at home using FDA-approved home test kits from Home Access Health Corporation. Each test requires a finger stick using a lancet (provided) to produce 5 drops of blood for the sample. The total time required to complete the tests is 20-30 minutes. The following steps will be taken to inform subjects about the kits and obtain results remotely.
         1. Data collectors will call subjects to provide details about the kits and determine if they are willing and able to complete the lab tests at home.
         2. If so, coordinator will prepare one of each kit to be mailed to the subject. Coordinator will sanitize work surfaces thoroughly and wear gloves and a mask while packaging any kits.
         3. Each kit has an identification number which will be linked to the subject’s study ID. Home Access also requires a date of birth (DOB) to identify each sample. To protect the subject’s PHI, we will create a master list with shifted DOBs for subjects using the REDCap date shifting feature. With this feature, REDCap randomly shifts dates up to 364 days upon downloading the data. The shifted DOB and the study ID will be used to label the kits.
         4. A list of assigned kits with shifted DOBs and study IDs will be sent to Home Access via a secure FTP (sFTP) server. No PHI will be sent to Home Access.
         5. The subjects will complete the tests with guidance from the data collector (over the phone or Doximity) and mail them to the lab using the prepaid envelope provided by Home Access.
         6. Samples will be processed by Home Access and results will be sent daily to coordinator via sFTP server.
         7. A $20 gift card for completing the home test kits will be sent to subject once a result is confirmed.

Note that all subjects will have the option to decline home testing and wait until research operations resume and they can complete the blood draw per the usual protocol. Subjects who choose to wait will also be compensated $20 for completing the blood draw *only* for survey data collection visits completed during the COVID-19 pandemic. Once research operations resume, subjects will be paid as outlined in section *6.2 Transition and Retention.*

Evaluation of Pharmacist Activity and Medication Changes

1. Chart review by a research assistant will define the number of PCP and pharmacist encounters as well as the number of pharmacist- or physician-initiated medication changes.

###### Components of *mDAS*

*Videoconferences*. Pharmacist videoconferences 30-45 minutes in duration will be scheduled every other month or as needed. HCs will reserve videoconference appointments using an online system with dedicated days/times pharmacists are available. All patient encounters with pharmacists are remote via videoconferencing with HCs present in the home using VSee. Vsee transmits personal health information securely, is low cost, and is available for use on desktop computers and mobile devices (e.g., iPads). Similar to Skype, Vsee provides real-time person-to-person audio and video communications. However, it is most suitable for health-related communication, as it is FDA registered and HIPAA compliant (using 256-bit AES, Advanced Encryption Standard). Vsee uses “peer-to-peer” sessions so information is not stored on a server.

Videoconferencing will follow the American Telemedicine Association practice guidelines: (1) pharmacist and patient/HC identity verification; (2) informed consent; (3) physical environment (privacy, lighting, noise); (4) education and training (pharmacist and HC); (5) alternate communication (e.g., telephone contact in case of disruption of service); and (6) documentation in UI Health EMR (by pharmacist). All study pharmacists and HCs will receive standardized training on use of videoconferencing which includes scheduling, preparing the environment (home or pharmacist office), patient education on telehealth, and documentation. We will evaluate HC and pharmacist competency. All encounters will have contingency plans in place for technology problems (e.g., inadequate signal for video streaming), including use of mobile phones for all HCs. Videoconference content includes standardized medication and disease management.

*Pharmacist Services.* Pharmacist services follow a standardized Pharmacist Management Protocol. All participating clinical sites have clinical pharmacists providing in-person disease management services and follow a similar protocol. All participating pharmacists have faculty appointments in the UIC Department of Pharmacy Practice. The UI Health system is a teaching hospital and as such, pharmacists at participating sites train an ongoing rotation of pharmacy residents and students. With the patient’s permission, residents and students may observe clinical consultations performed by the pharmacist. Residents and students will not provide any clinical care to patients and will not perform any videoconference visits. They will not have any role in this study. The clinical pharmacist reconciles medications during the first encounter with assistance from the HC in the patient’s home. Follow-up *mDAS* pharmacist activities include evaluation of medication and lifestyle adherence, reviewing home glucose and/or blood pressure monitoring log data, identifying therapeutic goals, formulating an approved plan of care, assessing for changes in medications, and documenting the plan in the EMR.

In addition, pharmacists provide education related to medication (name and purpose of medications; time, strength, and method of administration); drug interactions and side effects; goals of therapy; basic lifestyle modifications; and use of pillbox, low-literacy visual medication lists, or other adherence aids. Pharmacists educate and encourage lifestyle changes based upon ADA nutrition and physical activity guidelines. They propose medication changes based on algorithms and protocols derived from national guidelines under physician guidance. Pharmacists will have access to home glucose monitor readings during the videoconference, as well as ambulatory blood pressures obtained by the HC during home visits. Pharmacists will set the goals for A1c and blood pressure collaboratively with PCPs (e.g., A1c ≤ 7%) as is the case in regular clinical practice within our setting*.* These procedures are currently followed with clinical pharmacists in ambulatory management of complex patients with uncontrolled diabetes.

Overall, there is mixed evidence regarding the benefits of aggressive glycemic control. In the proposed study, PCPs and pharmacists will adopt the ADA approach to individualized care, where the general goal for non-pregnant adults is A1c less than 7%. They may decide upon less stringent goals for those with a history of severe hypoglycemia, limited life expectancy, advanced complications, or extensive comorbid conditions. Pharmacists routinely monitor hypoglycemic events, address prevention and review treatment. This includes three steps: (1) addressing hypoglycemia with every patient contact; (2) applying principles of appropriate therapy (education, empowerment, frequent glucose self-monitoring, flexible medication regimen, individualized goals, professional guidance); and (3) considering risk factors for hypoglycemia. In addition, pharmacists will follow the 2013 American College of Cardiology/American Heart Association guidelines for lipid management (e.g., calculating 10 year atherosclerotic cardiovascular risk to determine statin intensity).

PCPs and pharmacists communicate routinely regarding patient care and are located in the same area within the medical setting. Pharmacists review EMRs including blood test results, clinical progress notes, problem and medications lists, drug allergies, hospitalization records, and emergency room reports. Non-urgent communication and electronic progress notes from each pharmacist encounter will be sent to the PCP through inbox messaging and note forwarding within the EMR. Pharmacist progress notes include a detailed list of medications, estimated adherence levels, and home glucose/blood pressure monitoring log information.

*Health Coaches.* The study includes both African-American and bilingual/bicultural Latino health coaches representative of the communities they serve. All of our current HCs are the first person in their families to earn an undergraduate college degree, come from low-income backgrounds, and recognize the importance of cultural-based norms.All HCs have an undergraduate degree in or related to Community Health with experience conducting home visits. They receive 80 hours of standardized training/retraining beginning with diverse Latino and African-American cultures in America and the influence of poverty upon health*.* HCs provide culturally sensitive support and tailor based on participant personal preferences. Fundamental education in diabetes includes the Diabetes Education Empowerment Program (DEEP) targeting literacy and cultural awareness and Dr. Thomas Bodenheimer’s Training Curriculum for Health Coaches. HCs shadow a clinical pharmacist to understand medication use, adherence, glucose and blood pressure monitoring, insulin injection, and medication reconciliation. On-going training is provided every two months on related topics that reinforce and expand the initial training.We provide training in videoconferencing (e.g., scheduling and practice encounters), text messaging (e.g., text application practice and standardized safety procedures), and conducting home visits in a culturally sensitive manner. HCs receive routine orientation to clinical operations and staff at their primary care locations.Standardized safety procedures related to text messaging and home visits are also addressed. Dr. Colleen Fairbanks, a consultant, provides training in motivational interviewing related to adherence. To evaluate clinical skills, the HCs will demonstrate reliable measurement of blood sugar, blood pressure, pulse, and administration of insulin (though HCs do not administer insulin to patients).

The HC component involves monthly home visits with on-going telephone support. Every other month a visit will include facilitation of the pharmacist videoconference, with the patient spending an additional time with the HC afterwards for reinforcement. HC visits including pharmacist videoconferencing will last 60-90 minutes total, while the HC visits without pharmacist involvement will last 30-45 minutes.

The HCs work with the pharmacist to evaluate adherence (e.g., check fill and expiration dates), assist in medication reconciliation, review home glucose and/or blood pressure monitoring data, and provide reinforcement of proper medication use. Finally, HCs debrief patients after pharmacist encounters to reinforce and clarify recommendations and plans. HCs and pharmacists will communicate with each other between videoconference encounters by phone or secure e-mail as needed to coordinate efforts. HCs provide pharmacists with valuable insights into culturally-influenced lifestyle issues and health beliefs.

Home visits include the HC, patient, and family members or co-residents as appropriate and permitted by the patient. This is particularly helpful when someone else prepares meals for the patient. HCs address nine critical content areas over the course of the one-year intervention: relationship building, diabetes education, medication reconciliation, adherence barriers, engaging social support, navigating the healthcare system, exploring emotions, movement or physical activity, and nutrition. HCs evaluate key points in each content area which guides their work with each patient. HCs can check blood pressure and blood sugar to share with the pharmacist and other providers. HCs will document summaries of all patient communication in the EMR through remote access and forward electronically to PCPs and pharmacists.

HCs will attend to lifestyle and medication adherence issues by identifying and tracking barriers, problem solving, goal-setting, and providing supportive accountability. Using motivational interviewing techniques, HCs help patients identify diabetes-related goals and create action plans. Many of our patients are socially isolated. An important HC role is to identify extended family, friends, or neighbors for support. HCs engage support for tangible tasks tailored to the patient and directed at positively impacting adherence.

Diabetes education is facilitated by our culturally appropriate multimedia education iBook, Living Well with Diabetes/Viviendo Bien con Diabetes (LWD). This iBook is available in English and Spanish and targets African-Americans and Latinos through video testimonials, food choices, and various lifestyle issues. HCs present specific chapters in LWD on a tablet computer along with other visual, low-literacy materials to reinforce specific diabetes self-management concepts. In addition, HCs can utilize available evidence-based tablet computer tools in decision support. HCs are trained on diabetic medical nutrition therapy and basic physical activity recommendations for those with poor mobility so that they can work with patients to set individual goals. Education will address realistic and achievable food choices, portion sizes, cooking preparation, relationships between medications-meals-glucose levels, and integration of movement into lifestyle.HCs routinely identify basic resource needs that they address by facilitating connections with food pantries, free park district activities, or assistance paying utilities. Additional relevant resources are identified using online databases, such as purplebinder.com and healtherx.org.

*Text Messaging.* All text messages will be tailored by health coaches and sent through a custom software application (*mytapp*). Dr. Gerber developed *mytapp* for community-based health behavior research. *Mytapp* sends messages immediately or at a scheduled date/time, recurrent messages (daily, weekly, or weekdays), group messages, or multiple question surveys. *mytapp* requires a password for access and is restricted to trained research personnel. HCs receive training on *mytapp* and schedule messages for their patients regarding appointments, medications, and goals. The content of text messages will parallel our conceptual framework providing social support, competence, perceived barriers and benefits of treatment, and severity and susceptibility of complications. Health coaches will monitor their own patients’ responses for their cohort. Additionally, the project coordinator will monitor all *mytapp* activities including subject responses.

Goals set jointly by HC and patients are SMART (specific, measurable, achievable, relevant, and time-specific). Action plans are culturally tailored to subject individual needs, preferences, and resources. African-American HCs will highlight specific activities and resources in African-American communities. Likewise, Latino HCs include Spanish text messages (if Spanish is the preferred language) and different community-based resources and educational materials. Activity choices may include routine medication use, food choices, physical activity, stress reduction, smoking cessation, or other behavioral targets. Subjects indicate their level of confidence in success to help refine the frequency and intensity of activity though motivational interviewing techniques. HCs will help their patients anticipate barriers, discover potential solutions, and establish follow up plans. They employ problem-solving strategies and engage community resources as needed.

Text messaging will further enhance HCs’ ability to support their patients. They will direct messages to maintain motivation, elicit feedback on progress, and screen for barriers that may reduce chance of success. For example, a morning text message may ask a patient how they did on their goal the previous day. Responses may be “yes/no”, a rating scale, or other measure of activity. The subject will receive an automated response based on progress made, and additional messages (tips/problem solving messages) if not achieving goals. No more than seven messages will be delivered weekly, except for optional medication reminders.

|  |  |  |
| --- | --- | --- |
| **Example Text Message Templates** | | |
| **Message Type** | **Frequency** | **Example** |
| Medication Reminder | 1-4 times/day | “Hi, Ms. Brown, just checking to see if you took your morning pills.” |
| Refill Reminder | Monthly | “Make sure you don't run out. Check to see when a pill refill is due.” |
| Appointment Reminder | Variable | “Just a reminder that you have a doc’s appointment today.” |
| Goal Monitoring | Variable | “Remember your goal. Did you take your meds last night?” |
| Glucose Monitoring | Variable | “Hello, Mr. Marquez, have you had time to check your sugar today?” |
| Self-Efficacy | Weekly | “Taking your meds is within your control. You can do it.” |
| Motivation | Weekly | “You have come a long way! Keep up the good work!” |
|  |  |  |

**Temporary modifications to data collection during COVID-19 pandemic**

Due to the COVID-19 pandemic and social distancing orders, all pharmacist and health coach contact with participants will be made remotely and not in-person. This includes phone calls and Doximity video telehealth.

**Additional text messaging for mDAS Sub-study Supplement**

Participants in the sub-study will be asked to answer daily questions on their previous night’s sleep. They will complete the seven day sleep assessment surveys based on their preference by either text message surveys using myTapp or they will receive a text link to an online-based survey through a secure, web-based data collection application, such as REDCap or Qualtrics. The text messages will serve as a modified mobile consensus sleep diary for patients during the sleep period. The questions will include the following:

1. What time did you get into bed last night?
2. What time did you try to go to sleep?
3. How long did it take you to fall asleep?
4. How many times did you wake up, not counting your final awakening?
5. In total, how long did these awakenings last?
6. What time was your final awakening?
7. What time did you get out of bed for the day?
8. How would you rate the quality of your sleep? a) very poor, b) poor, c) fair, d) good, or e) very good? Please text the letter that corresponds to you (if using text message response).
9. In total, how long did you nap or doze?
10. Comments

Thanks for your participation.

Transition and Retention

Despite having "access" to healthcare, participants will be economically vulnerable individuals with uncontrolled diabetes. Ethically, we acknowledge that the "usual care" currently received often does not meet patients' needs or standards of care. Therefore, participants assigned to usual care will receive initial support to engage existing resources available through UI Health, such that healthcare providers will consider this an acceptable alternative upon randomization (clinical equipoise).

Upon randomization, participants will receive referrals to a diabetes educator and clinical pharmacist for medication reconciliation, adherence support, and education. Staff can schedule the visit at data collection. This is important as our prior work with medication reconciliation identified discrepancies in almost 60% of patients. A one-page list of clinic resources with names and direct telephone numbers (e.g., social worker) will be provided so they can more easily navigate the system. Finally, low-literacy, paper-based diabetes education information will be provided. At the end of year 1, these patients will cross-over and receive *mDAS*. Prior to this transition, HCs will work with the patients and their social support network to prepare them for the transition. Participants randomized to usual care will receive *mDAS* for one year.

*Retention strategies*. Participants will be reimbursed $30 for each data collection. Participants assigned to the intervention in year one will receive an additional $50 at 6 months and 12 months if they complete at least one videoconference before each data collection. Participants assigned to the intervention in year two will receive an additional $50 at 18 months and 24 months if they complete at least one videoconference before each data collection. Participants who complete all five data collection visits and videoconferences with the pharmacist as described above will receive up to $250 for completing the study.

*Additional Retention Strategies for mDAS Sleep Sub-study Supplement* Participants will be reimbursed an additional $40for participating in the sleep sub-study and turning in the wrist actigraph.

*Temporary modifications to compensation during the COVID-19 pandemic.* Participants may choose to be paid through their preferred electronic pay app (such as QuickPay/Zelle, Venmo, or Paypal) OR a gift card of their choice from a list of online retailers such as Walmart, Target, Amazon, or Visa. Gift cards will be issued in the amounts as described above for each data collection visit and can be mailed, emailed or texted depending on the vendor.

Due to social distancing orders, participants will have the option to complete their HbA1c and cholesterol profiles using a home test kit. They may also choose to wait and come in to the CRC for a blood draw once research operations resume. Because of the added time and effort required for each of these options, an additional $20 will be given to subjects for lab tests completed during the COVID-19 pandemic only. This additional incentive will not be offered once in-person interviews and phlebotomy resume.

Other retention strategies include: (1) periodic phone calls/ mailings to verify contact information; and (2) use of alternative contact information. We have developed a comprehensive standardized web-based search protocol that includes five people locators, major social networking sites including those with more minority involvement, and the department of corrections database. Searches are conducted on the target individual as well as alternative contacts.

# 7.0 Expected Risks/Benefits

Risks and Protections

The main risks include: (1) a small risk that subjects will have blood sugar or blood pressure levels that are too low or too high; (2) a small risk that the confidentiality of the subjects' records will be breached; (3) a small risk that subjects will feel annoyed by receiving study text messages; and (4) a small risk that a subject will experience pain or bruising at the site where blood is drawn for phlebotomy (less common risks include fainting, the formation of a small blood clot or swelling of the vein and surrounding tissue, bleeding from the site, and infection). It is unlikely that any of these risks would result in serious consequences. For all patients, an alternative to enrolling in the study is not participating (patients may continue usual health care services at UI Health outside of the study, including diabetes education).

Additional risks for those enrolled in the sub-study include a small risk the patients may develop a rash, irritation, or discomfort from wearing a wrist actigraph for 7 days/nights.

HIPAA regulations focus more on minimizing and managing risk rather than the actual information technology utilized. We will utilize a comprehensive approach to maximize data security for videoconferencing and text messaging services. Protected health information (PHI) will be exchanged through videoconferencing but not in text messaging. We will include an information privacy and security committee to advise, assist, and monitor our research policies using technology and for documentation. The committee will include an IT security expert, privacy official, and a clinician from UI Health. The committee will: (1) conduct a formal risk analysis; (2) develop a risk management strategy based on risk analysis; (3) implement strategy and train staff; and (4) monitor risk continuously. Text messages will have the health coach name pre-pended to messages to remind participants they come from health coaches (e.g., “Monique: Just a friendly reminder – it’s time for your meds, Carol.”). Patients will be reminded that text messages are sent in an automated fashion by computer. Thus, any replies may not be read immediately. Text messaging by patients should not be considered an Emergency Response System. Furthermore, they will be reminded that urgent health questions should be directed to their physician and not sent in a text message. HCs will monitor daily message feeds containing routine responses from patients.

*Extreme Blood Sugar or Blood Pressure Levels*: If a patient takes too much or too little medication, blood sugar and blood pressure levels may be too low or too high. The expected frequency of experienced side effects among participants is comparable as those receiving usual care taking the same medication. However, greater intensification of therapy could potentially increase this risk. To minimize risk, pharmacists and PCPs follow standard algorithms for glycemic and blood pressure management (i.e., American Diabetes Association and Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure) and use standard precautions in adjusting therapy: (1) addressing side effects (e.g., hypoglycemia) during every patient contact; (2) applying principles of aggressive therapy (education, empowerment, self- monitoring, flexible medication regimen, individualized goals, professional guidance); and (3) considering risk factors for hypoglycemia or hypotension. HCs also receive specific training on how to respond to extreme blood sugars and blood pressures if this occurs during a visit. They will be trained to respond in manner that is appropriate for their positions as trained lay-people.

Currently, at least one-third to two-thirds of patients with diabetes do not take their diabetes and hypertension medications correctly. In contrast, study participants will receive greater monitoring and support than other patients receiving usual care, which may help them take medication more properly. The study procedures will allow for medication adjustment in a logical, conservative fashion, whereas many patients may adjust therapies on their own, or with infrequent or ineffective provider contact, not adjust at all. All pharmacists and health coaches receive extensive training and monitoring to deliver appropriate assistance to patients. We have implemented additional protection with PCP (or covering physician) contact if necessary at any time, day or night. Based on the frequent contact and monitoring involved, participants have less extreme blood sugar or blood pressure levels than those receiving usual care.

*Poor Information:* It is possible that subjects may receive and act on inaccurate information or misinterpret accurate information given the team approach and novel communication methods utilized. However, it remains more likely that there is a greater risk of misinformation from providers when additional support is not available, especially due to language and cultural barriers. To address this, HCs receive training and ongoing evaluation to reduce the risk of providing misinformation. HCs serving Latino patients will be bilingual, and all communication as well as informational materials will be in either English or Spanish to avoid a potential language barrier. In addition, HCs work closely with pharmacists and communicate regularly, providing a means to obtain accurate information and receive prompt and clear answers to their questions. To address any possibility for subject concern regarding information received, we will encourage them to seek help from their primary care physician (PCP) and pharmacist if they are uncomfortable with any of the information provided by health coaches.

*Breach of Confidentiality:* There is a small risk of breach of confidentiality, regarding health information and collected research data. All research staff, including pharmacists and HCs, will have formal IRB human subject protection and HIPAA training. Additional HC training includes discussions on maintaining confidentiality of health information, including communication with health providers. For data collection, all subjects will be assigned a blind code number. These lists will be kept in a locked file and will not be shown to staff. Data collected from computer use files will have the name removed and the code number attached by the research coordinator. Project staff who have access to the data will not have access to subject names. No clinical staff who have direct contact with the subjects will have access to research data. Finally, there will be no personal information stored on the server itself; and all e-mail communication will be encrypted and secure.

*Videoconferences* will be conducted through VSee. VSee provides real-time person-to-person audio and video communications. It is most suitable for health-related communication, as it is FDA registered and HIPAA compliant. VSee uses 256-bit AES (Advanced Encryption Standard) and “peer-to-peer” sessions so information is not stored on a VSee server. Although VSee allows for local file storage which may be considered electronic personal health information (e-PHI), UI Health does not currently have electronic storage of such communications into the electronic medical record. Pharmacist notes abstracting the relevant details of the videoconference encounter will be recorded in the medical records. Overall, the risk of accidental disclosure of e-PHI is very small.

*Text messages* will not include any identifying information nor will any personal health information be disclosed by our team. Patients will be instructed not to use text messaging to share health information. Patients will be reminded that text messages are sent in an automated fashion by computer. Thus, any replies may not be read in a timely fashion. Text messaging by patients should not be considered an Emergency Response System. Furthermore, they will be told and reminded that urgent health questions should be directed to their physician and not sent in a text message. If an individual does share e-PHI through text messaging, the information will be permanently deleted and the patient will be educated regarding this process.

*Feeling annoyed by text messages*: Subjects will receive regular scheduled text messages during the study. Participants who no longer wish to receive reminders or text messages may reply with “STOP.” Twilio automatically will block *mytapp* from sending messages if this is received; thus, messages will be immediately discontinued without requiring contact with research team. However, patients have the option to re-subscribe with “START” again and resume messages. *mytapp* also color-codes blocked messages as “red” which will be easily detected by health coaches. This allows the HCs to identify problems including loss of mobile service.

*Phlebotomy:* Subjects may have pain or bruising at the site where blood is drawn for phlebotomy. Less common risks include fainting, the formation of a small blood clot or swelling of the vein and surrounding tissue, bleeding from the site, and infection. The Clinical Interface Core (CIC) employs health professionals for all phlebotomy services.*Home test kits*: Subjects may experience very brief discomfort after the finger stick and from squeezing drops of blood into the sample well. This will be comparable to the pain they experience when they undergo glucose testing. Alcohol pads, gauze and bandaids are provided with each kit to keep the site clean. Tips for minimizing discomfort and increase blood flow are included in the kit and instructional video online.

While unlikely, there is a slight risk that a participant may indicate thoughts of suicide or self-harm by scoring a 2 or 3 on item 9 of the PHQ-9 questionnaire. If this occurs, the data collector will contact Dr. Lisa Sharp on her cell phone immediately upon completion of the interview or during a break in the interview (if appropriate). Dr. Sharp is a trained clinical psychologist and as such will come to the CIC, meet with the patient and evaluate if further action is needed to ensure the participant’s safety. If Dr. Sharp is unable to be reached, Dr. Gerber will be paged or reached by cell phone. Dr. Sharp or Gerber will assess the participant including suicidal ideation, intent, and plan. Then, Dr. Sharp or Gerber will intervene appropriately, which may include providing resources for mental health support, facilitating referral to psychiatry, or immediately escorting the participant to the UI Health emergency room if urgent evaluation/intervention is needed to ensure personal safety, security, and stability.

Benefits

This study may provide additional, generalizable knowledge regarding the impact of the mHealth diabetes adherence support intervention, including HCs and clinical pharmacists in helping minority groups with uncontrolled diabetes. The expectations are that all subjects may potentially benefit from the support provided. In the United States, underserved African-American and Latino populations are disproportionately affected by type 2 diabetes and face greater barriers utilizing conventional health care. Many do not achieve their goals of normal blood sugar and blood pressure and remain at high risk for complications when compared with Whites. The discovery of newer approaches to improve their blood sugar and blood pressure control is needed. This study includes HCs, pharmacists and mobile health technology that combined may make these support services more accessible to this vulnerable population. In addition, this study will examine the cost and cost-effectiveness of mHealth diabetes adherence support. The risks taken on behalf of subjects are small compared with the importance of the knowledge gained in this study.

**Additional Benefits of mDAS Sleep Sub-Study Supplement:**

Patients will have no direct benefit from participation in the sleep sub-study. However, it will contribute to scientific knowledge related to the challenges underserved African-American and Latino populations face in diabetes care, poor sleep duration and quality, which may contribute to worse diabetes-related health outcomes. Data exploring sleep quality within minority populations is very limited. Existing data suggest that African-Americans and Latinos are more likely to have poor sleep quality due to either psychosocial stress or non-standard sleep hours contributing to inconsistent sleep patterns and an increased risk of diabetes. Further sleep research involving minority populations with diabetes is needed for discovery of better treatment options.

At the end of the study, each participant will receive a thank you letter with a synopsis of their sleep results. Each participant will receive their average number of hours of sleep per night, the target number of hours of sleep they should aim for per night, and some general sleep hygiene tips.

# 8.0 Data Collection and Management Procedures

Physiological and Survey Measures: The UIC Center for Clinical Translational Science (CCTS) Clinical Interface Core (CIC) will provide data collection services for all physiologic measures. Trained study RAs will conduct all surveys by interview in the CIC, in English or Spanish. These staff will receive training and practice on specific techniques for establishing professional rapport, answering potential questions, and maintaining cooperation of respondents. Laminated cards with Likert-type scale responses are provided as a visual reference to patients. RAs possess laptop computers and remotely access REDCap for data entry.The survey requires an average duration of 60 minutes. Subjects will receive compensation as previously described (Section 6.2) for travel and time at each collection point. Public transit cards will be provided when needed.

Control Variables (Time-Constant/Baseline):

1. *Socio-demographics* will include age, gender, self-reported race and ethnicity, country of origin, income, highest level of education, employment status, global health status, and insurance.
2. *Diabetes and Medical History* will include time since diabetes diagnosis, receipt of diabetes education, current therapy, diabetes complications, and co-morbid conditions.
3. *Health Literacy* will be assessed using three screening questions with high discriminatory power among English and Spanish speaking populations.
4. *Mobile phone use* and comfort sending text messages will also be assessed using five items.
5. *Environmental Surveys* that assess loneliness, social cohesion, and neighborhood safety will be administered.

Additional Control Variable for mDAS sub-study

1. *Medication History* will include reported pain medications, sleep aids, or psychotropic medications prescribed and/or taken.

Intermediate Variables (Time-Varying): Intermediate variables will be collected at five time points (0, 6-, 12-, 18-, and 24-months).

1. *Perceived severity* of diabetes and *perceived susceptibility* will be assessed through two items adapted from Bradley.
2. *Perceived benefits of therapy* will be measured by the five-item survey related to benefits of therapy.
3. *Depression* will be measured using the nine-item Patient Health Questionnaire (PHQ-9).
4. *Social Support* will be measured using an assessment of amount of total support received and satisfaction of support from family, friends and healthcare team.
5. *Self-efficacy* will be measured by the Stanford 8-item self-efficacy for diabetes survey.

Process Measures:

1. *HC Activity* will be collected on a standardized worksheet completed after every participant contact (by phone and in-person). Information will include mode, time, and content of contact, results of glucose or blood pressure self-monitoring, goals, life events, pharmacist interactions, and interventions. Dr. Sharp will review HC worksheets for intervention fidelity.
2. *Text Messaging*: Detailed information on text messages sent and received are stored in a *mytapp* database. Drs. Gerber and Sharp will login to *mytapp* to review message data monthly to ensure fidelity. Additionally, Dr. Biggers will login to mytapp to review message data from the sub-study weekly.
3. *PCP and Pharmacist Activity*: The pharmacist will reconcile medications as part of the intervention, and the reconciled list from the medical chart will be used as data to evaluate medication changes and overall complexity of therapy. Intensification of therapy will be defined as the number of increases in the dosage of antihypertensive, hypoglycemic agent, or insulin or the addition of a new agent since the baseline visit. Chart review will define the number of PCP visits and pharmacist videoconferences as well as the number of pharmacist- or physician-initiated medication changes.
4. *Patient Summary Evaluation*: Feedback will be collected from participants regarding their experience with the health coach, pharmacist, and videoconference technology. Individual responses will not be shared directly with the participant’s health coach or pharmacist. Evaluation will be collected at 12 months for participants who receive the intervention in Year 1 or 24 months for those who receive it in Year 2.

Physiologic Outcomes and Quality of Life:Physiologic outcomes will be collected at five time points (0, 6-, 12-, 18-, and 24-months). CIC research staff will perform phlebotomy, blood pressure, weight and height recordings while being blinded to subject group assignment.

1. *Hemoglobin A1c* and *fasting lipid profile* (total cholesterol, HDL, LDL, and triglycerides) will be obtained via phlebotomy. The A1c laboratory test has National Glycohemoglobin Standardization Program certification.
2. A calibrated digital scale will measure *weight*.
3. At baseline, a height stadiometer will measure body *height*, with subjects removing their shoes (for BMI assessment).
4. *Blood pressure* will be assessed on subjects sitting down for at least five minutes, following standard procedure. Extreme blood pressures are reported to Dr. Gerber per CIC protocol.
5. *Health Related Quality of Life* will be measured using the EQ5-D (general) and DDS4 (diabetes specific).

Medication Adherence and Behavioral Outcomes: Medication adherence will be assessed using self-report and objective measures.

1. A self-report *medication adherence* survey will be included for all diabetes medications (developed by Lu et al, AIDS Behav 2008; Gonzalez JS et al, Diabetes Care, 2013). This instrument includes three items.
2. *Pharmacy fill data* will provide a more valuable method of adherence evaluation. Each participant will provide contact information for all pharmacies where prescriptions have been filled for the past two years. A signed HIPAA authorization form allows research personnel to contact pharmacies for medication fill information. For each prescription, the medication name, date dispensed, dosage, frequency, quantity, and supply will be requested. The Proportion of Days Covered (PDC) will be calculated for all diabetes, hypertension, and hyperlipidemia medications.
3. The revised *Summary of Diabetes Self-Care Activities Measure (SDSCA)* will capture basic diet, exercise, blood sugar testing, foot care, and smoking with 11 core items.
4. *Alcohol misuse* will be assessed with the AUDIT-C brief screen. This instrument defines those with heavy/hazardous drinking behaviors.

Cost and Healthcare Utilization Data:We will conduct a cost-utility analysis comparing *mDAS* with usual care, following the guidelines for conducting pharmacoeconomic analyses by the Panel on Cost-Effectiveness and Medicine and the International Society for Pharmacoeconomics and Outcomes Research. We will conduct the analysis from the health-system perspective, and include the costs of running the program as well as the costs associated with patient health services utilization. Costs will include pharmacists and HCs (training and implementation), educational materials, tablet computers with data service, text messaging, and videoconferencing. Health services utilization will include costs associated with hospital admissions, emergency room visits, outpatient visits and prescription medications during the intervention period. Participants will be followed throughout the study to obtain data on their programmatic and healthcare services related costs. At data collection points, research assistants will obtain the necessary information from patients on healthcare use outside of UI Health. We will capture UI Health care information electronically from the hospital electronic records and billing data for enrolled subjects. We have previously analyzed similar UI Health data. Additional costs (salaries for HCs, etc.) will be estimated from prevailing internal costs at the time. Cost estimations for healthcare use will be based on national Medicare reimbursement rates (average DRG rates) for hospitalization, Medicare fee schedules for physician and other professional services, and Medicare’s Resource-Based Relative Value Scale for outpatient procedures. Since our study will span a period exceeding one year, appropriate costs will be discounted and adjusted for inflation.

Data Management: We utilize REDCap (Vanderbilt University) for data entry. Our data manager is experienced in form creation, export, and randomization functions. Data will be exported, cleaned, and analyzed in SPSS, SAS, or R. To address missing data, we will examine the data for patterns of missingness and potential bias in missingness (SPSS Missing Values). If data are not missing at random, we will apply one of several available imputation methods in a sensitivity analysis based on the nature and extent of missing data. We will determine effectiveness using intention-to-treat principles with actual imputation of missing data. This will allow us to appreciate the potential biases inherent in a “real-world” setting due to drop out and poor adherence to study procedures.

# 9.0 Data Analysis

Dr. Yinglin Xia will lead analytic measures in collaboration with Dr. Michael Berbaum, IHRP Methodology Research Core. Cost effectiveness analyses will be conducted in collaboration with Dr. Kevin Stroupe, Loyola University. Sustainability and RE-AIM assessment will involve Dr. Paul Estabrooks, consultant. Drs. Gerber and Sharp (Co-PIs) will coordinate all analytic activities with regular meetings and keep data, statistical code, analytic output on a shared drive at IHRP.Additionally Dr. Biggers, along with the co-PIs will coordinate all analytic activities for the sub-study with regular meetings and keep data, statistical code, and analytic output on a shared drive at IHRP.

# 10.0 Quality Control and Quality Assurance

To continuously evaluate the fidelity of both conditions, the PIs will review written logs maintained by the pharmacists and HCs that include visit dates, length of visits, visit content, and disposition (e.g., visit completed, patient unreachable, etc.).Weekly group meetings with HCs and PIs provide an opportunity to monitor the intervention delivery and on-going training. All technology-related difficulties are reported to the coordinator immediately and discussed in weekly meetings with the PIs. Dr. Sharp will maintain weekly involvement with HCs to provide support and incorporate structured training opportunities quarterly. Additionally, Dr. Biggers will maintain weekly involvement with research personnel to provide support and incorporate structed training opportunities for the sub-study data collection and equipment retrieval.

# 11.0 Data and Safety Monitoring

The Data and Safety Monitoring Plan (DSMP) for the proposed project has two goals: (1) to insure the safety of the participants; and (2) to produce high quality research while considering both risks and benefits. Overall, the study poses minimal risk to participants. Because of this low risk status, the DSMP focuses on close monitoring by the co-principal investigators (co-PIs) and a safety officer (SO), along with prompt reporting of excessive adverse events and any serious adverse events to the NIH and to the IRB at the University of Illinois at Chicago (UIC).

Although there are additional reports to be produced by the study coordinator as a result of this DSMP, there are no substantive changes to the study protocol that might require review by the NIH. Safety reports will be sent to the study statistician, the co-PIs, and the SO. A research assistant will be responsible for assembling the data and producing these reports, as well as assuring that all parties obtain copies of these reports.

The research team will meet weekly and continuously evaluate the progress of the trial, including periodic assessments of data quality and timeliness, participant recruitment and retention, participant risk versus benefit, subject complaints (if any), adverse events, and other factors that can affect study outcomes. Summaries of enrollment and withdrawals will be reviewed together.

The frequency of data review differs according to the type of data as follows:

*Qualifications and Responsibilities of the Safety Officer*: We will identify an independent safety officer (SO) for this trial. This individual will have an advanced medical degree and experience in human subject protection, research study design, and the adverse event review process. The safety officer will review the reports sent by the study coordinator (at the frequency outlined above in the table) and will use a checklist to determine whether there is any corrective action, trigger, or an ad hoc review that should be communicated to the study investigator, the UIC IRB, and the NIH.

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| **Data Type** | **Frequency of Review** |
| Subject enrollment | Quarterly during recruitment phase |
| Subject status (retention) | Biannually |
| Adverse event rates (injuries) | As they occur |

*Reporting of Subject Accrual, Adherence to Inclusion/Exclusion Criteria:* Review of the rate of subject accrual and adherence to inclusion/exclusion criteria will occur monthly during the recruitment phase by the co- PIs, SO, and the statistician. *Reporting of Adverse Events:* The research staff will be asked to report any problems the participants experience to the co-PIs either in person or by telephone. The safety officer (SO) will review, collate, and evaluate adverse events in real-time. Any adverse events reported to the IRB will also be reported to the NIH. All adverse events will be evaluated by the SO and the co-PIs within 72 hours; serious adverse events within 24 hours. Any study-related serious adverse event will be reported to the UIC IRB within 24 hours and the NIH within 2 weeks; all others will be included in the annual report to the NIH.

*Data Privacy and Security:* Formal training on data and participant safety is provided to all research staff involved in the data collection process, including health coaches. All staff and students involved in our research studies sign a confidentiality agreement stating that they are aware that any data they come in contact with is strictly confidential and is not to be discussed outside of the research project. They also complete the University of Illinois at Chicago online training on Human Subjects Protection (101) and the HIPAA Privacy Act. This will include the various modes of communication (e.g., telephone) and methods of maintaining confidentiality. At the UI Health and UIC research offices, all workstations require the use of a password in order to gain access. When leaving a workstation unattended, the user must log-out or lock their computer. Users are required to use screen savers that will be activated after ten minutes of inactivity and are password protected. All correspondence via fax must be stripped of patient identifiers. Before receiving a fax containing sensitive data, the sender must call the receiver to ensure the receiver is available to pick up the data. All e-mail with e-PHI will be sent securely through Cisco’s Registered Envelope Service (CRES). The coding system will be kept in a locked cabinet or drawer separate from the actual data. Research investigators performing the statistical analyses data will not have access to information that can connect up the actual identity of a study participant and their data. Information connecting a study participant’s name and study identifying number is kept in a locked file drawer in one of the co-PI’s office.

*VSee videoconferencing* uses “peer-to-peer” sessions so information is not stored on a VSee server. VSee uses 256-bit AES (Advanced Encryption Standard) for secure transmission of information. Text messaging will not be secure and will not contain e-PHI. However, *mytapp* includes multiple security measures. Limited subject information will be available on *mytapp*, such as name and study ID number, and telephone number stored in an encrypted PostgreSQL database. We utilize TLS (Transport Layer Security) with encryption for all *mytapp* interactions and interactions with Twilio. All information from Twilio to *mytapp* is validated against embedded digital signatures to ensure authenticity and prevent “spoofing.” A “PaperTrail” application provides a continuous audit trail to monitor *mytapp* use and all message activity.

We will utilize a comprehensive approach to maximize privacy and data security for videoconferencing and text messaging services. We will include an information privacy and security committee to advise, assist, and monitor our research policies using technology and for documentation. The committee will include an IT security expert, privacy official, and a clinician from UI Health. The committee will: (1) conduct a formal risk analysis; (2) develop a risk management strategy based on risk analysis; (3) implement strategy and assist in training staff; and (4) monitor risk continuously.

# 12.0 Statistical Considerations

To address missing data, we will examine the data for patterns of missingness and potential bias in missingness (SPSS Missing Values). If data are not missing at random, we will apply one of several available imputation methods in a sensitivity analysis based on the nature and extent of missing data. We will determine effectiveness using intention-to-treat principles with actual imputation of missing data. This will allow us to appreciate the potential biases inherent in a “real-world” setting due to drop out and poor adherence to study procedures.

Patients who share a single PCP might exhibit similarities that are not shared with patients attended by other PCPs. To address this, we will include random effects in the model for clinic site, PCP, and HC (though the small numbers of HCs may call for a fixed effect approach, or “insufficient replication”). To examine a stricter examination of effect, we will also do a “per protocol” analysis of complete cases. Completed cases will not be dependent on intermediate time point data collections (6 and 18 months). Potential selection bias will be corrected by including in our models covariates that are differentially related to study participation.

Primary Outcomes

Univariate comparisons between the two study groups for outcomes and covariates at baseline will be conducted using chi-square tests for categorical variables, Kruskal-Wallis tests for ordinal variables, and t-tests for continuous variables. Non-normal continuous data will be transformed prior to analysis.

In order to provide comprehensive analysis for H1, we will extend the usual analysis of crossover designs by including a longitudinal trend component in the first year. Thus, we can examine the time course (0, 6, and 12 months) as linear or quadratic over the first three measurements. This will allow us to investigate whether changes are made early, and at what rate they continue through the rest of the time period. This analysis permits the comparison of trends between the two conditions. In addition, we will regard subjects as a random effect and will use Gaussian mixed-model estimation (SPSS MIXED). We can then substitute treatment by period interactions for the carry-over effects, and the model can be reduced in a recommended sequence (first omit carry-over, then omit treatment, finally omit period). SPSS MIXED will also be used to explore patterned covariance structures such as compound symmetry and autoregression along with incorporating time-constant and time-varying covariates, such as health literacy or diabetes distress.

The primary analysis of all physiological outcomes jointly in the repeated measures design will be conducted in a general linear model framework. SPSS MANOVA (for repeated measures) will be used to explore the simultaneous impact of the treatment on multiple correlated dependent variables, including the use of Roy-Bargmann stepdown F-tests and discriminant function analysis as post hoc tests to identify subsets of outcome measures affected. MANOVA secondary analyses will explore the impact on results of inhomogeneous baseline variables. Group by time-trend interaction contrasts will be used to explore different group trajectories of change. The potential consequences of medication intensification (e.g., initiation of insulin) will be explored by evaluating changes in BMI and quality of life.

Exploratory subgroup analyses will follow a heterogeneity in treatment effects (HTE) framework. We will determine which subjects in the intervention group had the greatest improvement in outcomes, based on multiple pre-specified patient characteristics, including race (African-American or Latino), depression, comorbidities, baseline behaviors, health literacy, continuity of care, and social support. These analyses will also consider additional comparisons between subjects above and below median levels of videoconferencing and text messaging activity. Statistical tests will be implemented as interactions within the full data set.

If the intervention is effective, we will examine whether changes in self-efficacy, health beliefs, or social support serve as mediators for improved outcomes according to our conceptual framework. In addition, we will explore diabetes-related behaviors as well as medication treatment intensification as mediators using MPlus. To further identify the relative contributions of videoconferencing and/or text messaging, we will conduct meditational modeling with videoconferencing time, number of text messages, and HC contact time as mediating variables. This may describe any dose-response relationships between mHealth utilization and outcomes. We will compute bias-corrected bootstrap standard errors using MPlus. This offers accurate confidence intervals for mediation coefficients. Due to anticipated relationships between HC activity level and mHealth delivery, we plan to inspect correlations between mediators and incorporate any significant findings in model development. This analysis will demonstrate whether intervention effects are sensitive to mediators.Finally, given the sample size, observed (rather than latent) variables will be used in the mediation models. To enhance the power of mediation modeling, we will adopt an α=.10 Type I error criterion to improve the chances of finding promising mediators for future study.

Sustainability

We expect a limited amount of decline in physiologic outcomes with the transition back to usual care. We will test the hypothesis that improvements in A1c, blood pressure, and LDL cholesterol will be maintained during the maintenance time period. The analyses will be conducted similarly as for H1, and will evaluate change in the initial intervention group one year after intervention completion.

Consulting with Dr. Paul Estabrooks, we will implement a *Sustainability Action Plan (SAP)* to integrate HCs and ensure provision of pharmacy telehealth at an organizational level beyond the period of grant funding. The first phase will identify existing organizational goals and activities that support integration of HCs and pharmacy telehealth approaches into routine clinical operations. Our healthcare system is actively testing HC/peer educator models in multiple locations of the network. In collaboration with these sites and other key stakeholders, we will adapt an existing sustainability checklist to evaluate the presence of specific factors that are needed to support on-going operations within the organization. The next phase involves identifying existing and needed resources within our organization to support delivery of the additional services at the end of the study. The cost-effectiveness data (Aim 3) will help guide this procedure. Working with the Illinois Healthcare Reform Implementation Council and our existing relationship with the Illinois Community Health Worker Advisory Board (see letter of support), we will share details on training and reimbursement for community health workers (aka health coaches) as set forth in the Affordable Care Act and Illinois Bill HB5412 (the board will propose training and certification processes for community health workers and advice legislators). Dr. Edwin Fisher (consultant), as the Global Director of Peers for Progress, is actively involved in legislation to provide peer support service reimbursement and will aid in identifying relevant stakeholders. The final step focuses on executing the outlined action plan.

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| **Table 4: RE-AIM Framework for Process Evaluation** | |
| **Reach** | Identify proportion of eligible population contacted, responded, participated, and excluded. Compare demographics and glycemic levels of eligible UI Health patients and study participants. Are the study participants representative of the clinical population? |
| **Effectiveness** | Determine change in hemoglobin A1c, blood pressure, and other outcomes (Aim 1). Are there unintended consequences of the intervention (e.g., negative impact on quality of life)? |
| **Adoption** | Conduct semi-structured interviews with randomly selected providers, staff, administrators, and health coaches across participating clinical sites (interview guides to be developed). Assess satisfaction and compare resources, setting, and intervention delivery across sites. |
| **Implementation** | Measure HC activity including encounters and phone calls completed, videoconferencing, and text messages delivered. Determine subject participation in intervention. |
| **Maintenance** | Implement Sustainability Action Plan (Aim 2). Evaluate change in outcomes one year after completion of the intervention and determine if positive outcomes were maintained. Assess drop-out rates and adverse events experienced. |

Process evaluation will provide support for the project’s potential as an intervention in a real-world setting. We will evaluate translation using the RE-AIM framework to determine dissemination potential and generalizability (Table 4). To assess adoption, we will conduct semi-structured interviews of providers, staff, and administrators, providing different perspectives. Chain sampling will help identify those most likely to be “information rich” and continue until saturation reached.

Pharmacist interviews: Up to 15 pharmacists who have participated in the mHealth for Diabetes Adherence Support study (IRB 2016-0380) will be individually interviewed to gather feedback on delivering the intervention and potential for adoption.

An email invitation will be sent to pharmacists describing the purpose of the interview and a summary of the procedures. Interested pharmacists will be scheduled for one-on-one interviews with Dr. Sharp or a research assistant. The interviews will take place in private room at the pharmacist’s clinical site or at a private campus location that is convenient for the pharmacist. A semi-structured interview guide will be used and content will focus on video conferencing, provider-pharmacist interactions, and interactions with health coaches. Interviews will be audio recorded. Names of the pharmacists will not be linked to their responses in order to maintain confidentiality. A brief demographic survey will be completed by the pharmacist and a number will be assigned to their interview. The interview will last approximately 30 minutes.

Interviews will be transcribed, coded and analyzed. Results will be used to inform the process evaluation component for the study (Aim 4) and future research involving clinical pharmacists, health coaches and the use of telehealth technology in health care.

Cost and Cost Effectiveness

We will obtain program and healthcare use data to estimate the cumulative costs from a health system perspective for each group over 24 months. To accommodate drop-outs and missing data (censoring) in the cost estimates, we will use a modification of survival analysis. To estimate average cumulative costs, we will divide the time interval following randomization into months, and then estimate cumulative costs to time T (i.e., 6, 12, 18, and 24 months) as: (T)= pt x ct, where pt is the probability of participating at month t, and ct is the mean cost at month t given participation at t. Patients participating at the end of follow-up contribute cost information from randomization to end of follow-up, while patients who drop out contribute costs from randomization through drop-out date (and then zero costs thereafter until end of subject follow-up). We will then discount to estimate the average present value of costs: (T) = , where r is the discount rate and Ŝt is the Kaplan-Meier estimator of the probability of participation to month t. We will use a discount rate of 3% per year and calculate (T) for subjects in both groups. For the cost-effectiveness analysis, we will calculate the incremental average costs resulting from *mDAS* vs. usual care and compare via a two-sample t-test for independent groups. Costs may not be normally distributed; however, if the sample is sufficiently large, t-tests on untransformed costs are appropriate.

Our effectiveness measures will include improvements in A1c, blood pressure, of cholesterol levels and projected quality-adjusted life-years (QALYs). Furthermore, a reduction in unnecessary healthcare utilization (emergency room visits and preventable hospitalizations) may result in cost savings. The incremental cost-effectiveness ratio (e.g., cost per change in A1c) of *mDAS* vs. usual care will be estimated at the end of 12 and 24 months. Cost per QALY will be determined from projections of continued mHealth involvement and assumptions concerning the continued effects of *mDAS* on outcomes over time. The QALY and utility estimates will be based on the Markov model developed by the Diabetes Cost-effectiveness Group at the CDC (using UKPDS data). Sensitivity analyses will estimate the impact of changes in factors such as age, induced health-care visits, incidence of complications, HC costs, physician time, and discount rates. We will discount both QALYs and costs at 3% per year to maintain equivalent treatment of the measures of costs and effectiveness over time. To compare discounted QALYs, we will integrate the area under the Kaplan-Meier curves for each study condition to obtain mean QALYs. The difference between the two areas will provide the incremental effectiveness from receiving *mDAS*.

The ratio of net costs (Δ costs) and net utility (Δ utility) will yield the incremental cost utility ratio between the *mDAS* and usual care groups. One-way sensitivity analyses will determine the impact of discount rate (0%-10%) on the cost utility ratio. We will also examine variability associated with the cost-utility ratio using a bootstrapping technique. The bootstrapping results will be presented using the acceptability curve approach. The acceptability curve shows the proportion of samples in which the intervention is considered cost-effective relative to a comparison condition given a maximum amount that a decision maker is willing to pay for the outcome (e.g., $50,000/QALY). Specifically, Net Benefit = (-1) \* (Net Costs) + (Net Effects) \* (Willingness to pay) is calculated and the proportion of samples with mean net benefit greater than zero is plotted across a range of willingness to pay values. If *mDAS* lowers costs and produces more health it will tend to have an acceptability curve over 50% across all levels of willingness to pay.

Sample Size Justification: Sample size calculations are powered to detect change in A1c. The ADA Technical Review of Diabetes Self-Management Education reported that successful education programs achieved reductions of 5-20% in A1c.[113](#_ENREF_113) The UKPDS 35 demonstrated that each 1% absolute reduction in mean A1c is associated with a 21% decrease in risk for any diabetes-related endpoint, a 21% decrease in diabetes-related deaths, a 14% decrease in risk for myocardial infarctions, and a 37% decrease in risk for microvascular complications. Based on our previous studies, we estimated a mean baseline A1c level of 10% with standard deviation of 1.8 and an effect size of (1.0/1.8) 0.56 for Aim 1. The cross-time correlation was estimated to be 0.30 with compound symmetry structure. We adjusted for clustering and assumed an intraclass correlation coefficient (ICC) of 0.01 with five clusters. This yielded a design effect of 1.34. Two-sided alpha of 0.05 and 80% power were assumed. Allowing for 20% drop-out, 220 patients will be required total.

UI Health billing data show there are 7,258adult African-Americans and Latinos with diabetes. We estimate that approximately half of these patients have an A1c level above 8.0% based on prior study. We anticipate recruiting 6% of the eligible diabetic population. We have successfully recruited a similar size of patients with type 2 diabetes using comparable recruitment methods.

# 12.1 Additional Statistical Considerations for mDAS Sub-study

Dr. Biggers will receive statistical/analytic support from the Methodology Research Core at the Institute for Health Research and Policy (IHRP) and statistician Dr. Yinglin Xia. Descriptive statistics will be summarized as mean (standard deviation) or median (range) for continuous variables, and as frequencies (proportions) for categorical variables. We will address the three specific aims as follows:

**Aim 1:** Descriptive statistics will be calculated for the PROMIS as well as sleep duration based on text-message responses. Response rates will be quantified per individual and overall in aggregate. Interviews will provide an inventory of potential barriers to sleep in the home (e.g., presence of television in bedroom). These will be categorized and quantified. Differences in race/ethnicity within the descriptive data will also be compared.

**Aim 2:** Feasibility and acceptability of using the Actiwatch to collect objective sleep data will be based on the average number of days and amount of time per day the Actiwatch was worn. In addition, research personnel will obtain qualitative information regarding barriers to wearing the device in the semi-structured phone interview. Drs. Biggers, Sharp, and Gerber will collaboratively determine a coding scheme to describe issues discovered.

**Aim 3:** Independent and dependent variables will be explored via histograms to identify extreme values and assess normalcy (some Actiwatch data may yield spurious values). We will determine correlations between subjective text-message sleep diary and objective Actiwatch data (e.g., total sleep time and bouts of wakening after sleep onset). In addition, we will examine correlations between sleep parameters (e.g., total sleep time) and hemoglobin A1c, depression, quality of life, and sedentary behavior. For continuous variables, Pearson corrections will be calculated (and Spearman rank for non-parametric variables). Partial correlation models will include covariates such as patient age, gender, race/ethnicity, income, and education level. We will explore additional models that include the number of days the Actiwatch device was worn. All hypothesis tests will be 2-sided with a significance level of 0.05.

# 13.0 Regulatory Requirements

*Informed Consent*: Research assistants will obtain informed consent for all participants. They receive training that includes observation of the entire consent process prior to patient encounters. The informed consent document will be stored in a locked cabinet within IHRP, accessible to research assistants, projects coordinator, and Co-PIs. Our personnel include a bilingual research assistant who will consent all Spanish-speaking participants.

*Subject Confidentiality*: All research staff, including pharmacists and HCs, will have formal IRB human subject protection and HIPAA training. Additional HC training includes discussions on maintaining confidentiality of health information, including communication with health providers. For data collection, all subjects will be assigned a blind code number. These lists will be kept in a locked file and will not be shown to staff. Data collected from computer use files will have the name removed and the code number attached by the research coordinator. Project staff who have access to the data will not have access to subject names. No clinical staff who have direct contact with the subjects will have access to research data. Finally, there will be no personal information stored on the server itself; and all e-mail communication will be encrypted and secure. During data analysis, when data integrity has been confirmed, identifiers will be destroyed. PHI will be included to the extent needed for study objectives, including medication use, and patients will provide consent for release.

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