Study Title: Technology Intensified Diabetes Education Study in African Americans With Type 2 Diabetes

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SPECIFIC AIMS

Diabetes Mellitus affects approximately 24 million adults in the United States (NIH 2008). African Americans (AA) with Type 2 diabetes (T2DM) have higher prevalence of diabetes, poorer metabolic control and greater risk for complications and death compared to White Americans (NIH 2008). There is strong evidence that self-management interventions that include diabetes education and skills training are effective at improving metabolic control in diabetes (Norris 2002). Recent findings indicate that patients with diabetes, especially ethnic minority patients, prefer telephone-delivered diabetes education to group visits or internet-based education (Sarkar 2008). Preliminary data from our group suggest that a culturally-tailored telephone-delivered diabetes education and skills training intervention (Egede 2010) is an effective strategy to improve metabolic control in AA patients with T2DM. However, no large RCT has tested whether providing feedback to patients using novel technology like the FORA 2-in-1 Blood Glucose and Blood Pressure monitor leads to improvements in glycemic and blood pressure control or whether using the feedback to tailor and augment diabetes education and skills training are effective at improving metabolic control.

Aim 1: To test the efficacy of a technology-intensified diabetes education/skills training (TIDES) intervention using the FORA 2-in-1 and Telehealth System for diabetes in improving HbA1c levels in AAs with poorly controlled T2DM.
Aim 2: To test the efficacy of the TIDES intervention in improving BP control and quality of life in AAs with poorly controlled T2DM.

RESEARCH STRATEGY

Approach. The overarching aim of this proposal is to test the efficacy of a technology-intensified diabetes education/skills training (TIDES) intervention in AAs with poorly controlled T2DM. 200 patients will be randomly assigned to two groups of 100 patients each; TIDES intervention group and usual care group. Each patient will be followed for 12 months, with study visits at baseline, 3, 6, 9, and 12 months. The primary outcome will be HbA1c at 12 months post-randomization while the secondary outcomes will be blood pressure control and quality of life at 12 months post-randomization.

Study Population & Recruitment Plan

The study sites for this study are MUSC general medicine, endocrine, family medicine, and community primary care clinics. The investigative team has access to patients in these clinics and letters of support from key physician collaborators in each of these clinics are attached.
Patient eligibility criteria: The study inclusion and exclusion criteria are as follows
Inclusion Criteria: 1) Age ≥21 years; 2) Clinical diagnosis of T2DM and HbA1c ≥8% at the screening visit; 3) Self-identified as AA; 4) Subject must be willing to use the FORA monitoring system for 12 months; 5) Subjects must be able to communicate in English; and 6) Subjects must have access to a telephone (landline for data uploads) for the study period.
Exclusion Criteria: 1) Mental confusion on interview suggesting significant dementia; 2) Participation in other diabetes clinical trials; 3) Alcohol or drug abuse/dependency; 4) Active psychosis or acute mental disorder; and 5) Life expectancy <12 months.

Description of Intervention: Patients will be assigned the FORA 2-in-1 Telehealth System and provided glucose test strips to allow testing at least once a day. The glucose and BP readings will be used to tailor and reinforce behavior change during weekly telephone-delivered diabetes education sessions. Subjects will receive: 1) the FORA system for self-monitoring; 2) weekly telephone-delivered diabetes education/skills training; 3) patient activation; and 4) patient empowerment. The intervention will be delivered by telephone once a week for 12 weeks with each session lasting ~30 minutes.

Assessments: Patients will be assessed at baseline, 3-months, 6-months, 9-months, and 12-months post randomization. Assessments will include valid and reliable scales administered by the study team. Participants will receive $25 for completing each visit.

Patient Randomization: A permuted block randomization method will be used to assign subjects to one of the two intervention groups. Block size will be varied to minimize the likelihood that the blind will be broken. The randomization will be stratified by clinical site, and baseline HbA1c levels (8-10% vs. >10%).

Sample Size and Power. With 80 subjects randomized to each of the two intervention groups, we will have 85% power to detect at least a 0.4 standardized effect size (difference in comparison group means in sd units) for continuous outcome measures.

Analysis Plan
We will use a generalized linear models (GLMM) approach as the general analytic framework for inferential analyses for the Primary/Secondary efficacy aims. In addition to accommodating a wide range of distributional assumptions [dichotomous/categorical (e.g., binomial), continuous (e.g., normal), ordinal, count (e.g., Poisson). GLMM is equivalent to a linear mixed effect model (MEM) approach. MEM analyses estimate individual change in outcome for each subject in addition to estimating average change in outcome within each of the individual a, b, c, d intervention groups. The basic modeling procedure will involve using the longitudinal measurements of HbA1c (primary) separately as the dependent (outcome) variable, with intervention group (fixed effect), time (random effect), and time by intervention as the primary independent variable*s*.

Project Timeline: The study duration is four years (48 months). Months 1-6 will be used for startup, Months 7-30 will be used for participant enrollment and intervention delivery, Months 31-42 will be used for participant follow-up and Months 43-48 will be used for data analysis. We will randomize 200 patients in 4 cohorts of 50 patients every 6 months with an average of 9 randomized patients per month.

PROTECTION OF HUMAN SUBJECTS

1. RISKS TO THE SUBJECTS

a. Human Subjects Involvement and Characteristics

The overarching aim of this proposal is to test the efficacy of a technology-intensified diabetes education/skills training (TIDES) intervention in AAs with poorly controlled T2DM. 200 patients will be randomly assigned to two groups of 100 patients each; TIDES intervention group and usual care group. Each patient will be followed for 12 months, with study visits at baseline, 3, 6, 9, and 12 months. The primary outcome will be HbA1c at 12 months post-randomization while the secondary outcomes will be blood pressure control and quality of life at 12 months post-randomization.

Study clinics: The study sites for this study are MUSC general medicine, endocrine, family medicine, and community primary care clinics.

Participant Payment: Randomized participants will receive $50 for completion of baseline, 3, 6, 9, and 12 month assessments for a total payment of $250. Those considered ineligible at baseline will receive $10 and not be randomized.

Patient eligibility criteria: The study inclusion and exclusion criteria are as follows
Inclusion Criteria: 1) Age ≥21 years; 2) Clinical diagnosis of T2DM and HbA1c ≥8% at the screening visit; 3) Self-identified as AA; 4) Subject must be willing to use the FORA monitoring system for 12 months; 5) Subjects must be able to communicate in English; and 6) Subjects must have access to a telephone (landline for data uploads) for the study period.
Exclusion Criteria: 1) Mental confusion on interview suggesting significant dementia; 2) Participation in other diabetes clinical trials; 3) Alcohol or drug abuse/dependency; 4) Active psychosis or acute mental disorder; and 5) Life expectancy <12 months.

b. Sources of Materials

1. Research Material & Data: Sources of research material include medical history, research questionnaires, blood pressure readings, and blood specimens. The questionnaires will obtain information about demographics, clinical history, diabetes self-care, resource use, depression, and quality of life. Patients will provide ~10cc of blood for laboratory testing.

***2. Linkages to Subjects*:** Subjects will provide identifying information in addition to research data. Paper documents pertaining to this study will be stored in locked file cabinets in both the clinical center and the data management center, and data will be entered into secure, password-protected web databases developed for this study. A database of name, contact address, telephone number, and other research identification numbers will be stored separate from the study database, for purposes of audit by the sponsor (NIH) and MUSC IRB, if necessary. Access to study data will be limited to research personnel.

3. Collection of Data and Specimens:

Personnel: Two full-time masters-level trained diabetes educators (DEs) will deliver the interventions; two full-time research assistants (RAs) will conduct screening, consent, enrollment procedures, and questionnaire administration; a full-time data entry clerk (DC) will be responsible for data entry; and a part-time masters-level statistician will be responsible for data management (DM).

c. Potential Risks

Potential risks to the patient include possible violation of the patient's privacy, discomfort with questions on the research questionnaire, discomfort and bleeding from blood draws, discomfort with BP measurement, and psychological distress. Details on how these risks will be minimized are discussed under adequacy of protection against risks below.

2. ADEQUACY OF PROTECTION AGAINST RISKS

a. Recruitment and Informed Consent

We will use two complementary approaches to identify eligible study subjects. The first method will consist of systematic identification of AA patients with T2DM. After obtaining IRB approval for a partial waiver of HIPAA, we will use clinic-billing records over the previous 12-month period to identify AA subjects with ICD-9 codes consistent with a diagnosis of type 2 diabetes. The PI will share the goals of the study and inclusion/exclusion criteria with physicians and clinic staff during clinic administrative meetings. Physicians and clinic staff will be asked to refer appropriate subjects to the study research assistants. In addition, IRB approved recruitment flyers will be posted in prominent locations in the study clinics.

b. Protection against Risk

A. Patients will be protected against potential risks as follows:

1. Psychological Distress: Because we will be administering a questionnaire that measures the presence of depression, we will take several steps to ensure the safety of all research participants. RAs will be trained by the PI to identify patients who meet criteria for depression on the PHQ-9. Subjects' who screen positive for depression will be notified during the visit and verbally instructed to seek care from their primary health care provider (PCP). They will also be given the 24-hour MUSC crisis psychiatry telephone service and told to call if they experience acute worsening of symptoms before they can be seen by their PCP.

2. Venipuncture (blood drawing): To reduce the risks of discomfort and bruising, venipuncture will be performed by trained personnel. To reduce the risk of fainting, blood will be drawn while subjects are in a seated position. The amount of blood that will be drawn, approximately 10cc, is not considered to pose a health risk for most adults. .

3. Blood Pressure Measurement: To lessen any associated risks, blood pressure measurements will be performed only by trained personnel utilizing a standardized protocol. Subjects with elevated blood pressure will be evaluated by our designated medical monitor and referred to their primary care provider. Those with potentially life threatening blood pressure readings will be sent to a local emergency room for treatment.

4. Administration of Research Questionnaires: Some participants might be offended by detailed questions about emotional or physical health status and impairment, and healthcare utilization. All participants will be informed at the outset that they may terminate participation at any point. Our past research suggests that data collection using these measures can be conducted without undue psychological distress or exacerbation of symptoms among study participants.

5. Unknown risks: Subject participation in research may have other unknown risks. The researchers will advise subjects if they learn of emerging information that might alter subjects' decisions to participate in this study.

B. Subjects requiring medical or other professional intervention for study-related events will be provided with appropriate and timely medical guidance by the designated medical monitor. The medical monitor will have oversight on medical risks and will review all adverse events and report them to the IRB in accordance with the MUSC IRB Adverse Event Reporting Policy. The results of subjects' clinical assessments will be available within a few days of their study visit. The medical monitor will review and advise subjects of these results by phone and, at their request; will also advise their personal physician of the results.

C. To protect against the potential risk of loss of confidentiality and/or breach of privacy, data will be compiled using codes in lieu of personal identifiers. Access to study data will be limited to research personnel. Development of and security oversight for the electronic database for this study will be performed by the study statistician. Paper documents pertaining to this study will be stored in locked file cabinets and electronic data will be entered into secure, password-protected databases developed for this study by the research assistants. The PI will perform periodic review of the data entry process to ensure accuracy of recording. When study results are published or presented, only aggregate reports of the results will be used and participants' identity will not be revealed. A file of name, contact address, telephone number, and other research identification numbers will be stored separately on paper and on computer, for purposes of audit by the sponsor (NIH) and MUSC IRB, if necessary.

3. POTENTIAL BENEFITS OF THE PROPOSED RESEARCH TO THE SUBJECTS AND OTHERS

The intervention is expected to benefit patients, by increasing their knowledge of diabetes, activating and empowering them to better care for their diabetes, improving blood glucose and blood pressure control, and reducing their risk of developing complications of diabetes.

4. IMPORTANCE OF KNOWLEDGE TO BE GAINED

The proposed study is innovative for a variety of reasons. First, sophisticated information technology, such as the FORA system, offers the potential to address several of the barriers to effective care by providing reinforcement and positive feedback to patients that should increase adherence. Second, the culturally-tailored education and skills training intervention proposed in this study is innovative because it targets patient level factors for which there is strong evidence of differences between AAs and Whites with T2DM (i.e. diabetes knowledge, self-management skills, empowerment, and fatalism/perceived control

5. DATA AND SAFETY MONITORING PLAN

The data and safety monitoring plan will include an internal Data Safety Monitoring Committee (DSMC), a Data and Safety Monitoring Board (DSMB), and the institutional IRB. The purpose of the DSMC, DSMB, and IRB are to ensure the safety of participants and the validity and integrity of the data. Summaries of adverse events reports or patient safety concerns raised by the DSMB or IRB will be made to NIH in the yearly progress unless the nature of a particular event is such that it bears reporting to NIH immediately.

DSMC: The internal DSMC will consist of the PI, biostatistician, co-investigators/consultants on the proposal, and a designated medical monitor.The functions of the DSMC will include: 1) provide scientific oversight; 2) review all adverse effects or complications related to the study; 3) monitor accrual; 4) review summary reports relating to compliance with protocol requirements; and 5) provide advice on resource allocation. The DSMC will meet quarterly and as necessary by telephone. The recommendations of the DSMC will be reviewed and the PI will take appropriate corrective actions as needed.

DSMB: In addition to the internal DSMC, a DSMB will be established. The DSMB will be made up of professional with appropriate expertise, willing to participate, and who do not have any conflicts of interest. The DSMB will include the following: 1) two experts in the area of diabetes, 2) a biostatistician with expertise in the conduct of clinical trials, and 3) two members with expertise in ethics and quality of life evaluation. The DSMB will meet annually. The DSMB will perform the following activities:

1) Review the research protocol and plans for data and safety monitoring.
2) Evaluate the progress of the interventional trial, including periodic assessments of data quality and timeliness, participant recruitment, accrual and retention, participant risk versus benefit, performance of trial sites, and other factors that can affect study outcome.

3) Monitors will also consider factors external to the study when interpreting the data, such as scientific or therapeutic developments that may have an impact on the safety of the participants or the ethics of the study.
4) Make recommendations to the internal DSMC, IRB, and funding I/C at NIH concerning continuation or conclusion of the trial.
5) Protect the confidentiality of the trial data and the results of monitoring.

The DSMB will have the authority to halt the trial if it perceives that harm is occurring due to the intervention. The DSMB will meet with the internal DSMC yearly to review adverse events reports, patient complaints if any, and dropout rates. Data will be provided at these meetings by the investigators on key variables that may indicate harm, including changes in glycemic control, blood pressure, depression, and self-reported adherence to medication regimen. The DSMB biostatistician will evaluate confidentiality and integrity of the data base, and the procedures for recording and storing confidential files. The DSMB will also review the elements of the plan to deal with emergencies.

Institutional IRB: The IRB will review and approve the funded protocol, review patient consent forms, ensure protection of patient privacy and safety, and monitor the study on an ongoing basis. Adverse events will be reported to the IRB as they occur. Annual reports to the IRB will indicate accrual rate, adverse events, new findings that may influence continuation of the study, and reports of the DSMB.

E. INCLUSION OF WOMEN AND MINORITIES

INCLUSION OF WOMEN

Both men and women will be included in this study. Based on the demographics of the study clinics, we estimate that women will constitute 50% of the sample.

INCLUSION OF MINORITY GROUPS

Only minority adults (African Americans) are included in this study. This is justified because of the high burden of diabetes and its complication in African Americans, and the paucity of data on effective interventions in this population.

F. TARGETED/PLANNED ENROLLMENT TABLE

TARGETED/PLANNED ENROLLMENT: Number of Subjects - 200			
Ethnic Category	**Sex/Gender**		
	Females	**Males**	**Total**
Hispanic or Latino	0	0	0
Not Hispanic or Latino	100	100	200
Ethnic Category Total of All Subjects*	100	100	200
Racial Categories			
American Indian/Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	100	100	200
White	0	0	0
Racial Categories: Total of All Subjects *	100	100	200

G. INCLUSION OF CHILDREN

Children (age <21) are excluded from this study. Children are excluded because type 2 diabetes is not common in children.

H. Resource Sharing Plans

Sharing of resources generated by this project is an essential part of our proposed activities and will be carried out in several different ways. We would wish to make our results available both to the community of scientists interested in diabetes research to avoid unintentional duplication of research.

Our plan includes the following:

Presentations at National Scientific Meetings: From the project, it is expected that approximately eight (8) presentations will be made at national meetings. There is an annual American Diabetes Association Scientific Meeting held in June of every year. This is a 4-6 day meeting in which interested persons present new information on a variety of topics related to diabetes. The PI will attend this meeting annually and present ~2 abstracts during each year of the grant.

Publications in Peer Reviewed Journals: Another important way we plan to share resources will be to publish our findings in peer-reviewed journals. We plan to publish an initial paper within the first 24 months to describe the study design and expected outcomes. We expect to begin analysis of baseline data by month 36 and publish at least 3 peer-reviewed papers during this time. We also intend to submit 6 manuscripts in the last 12 months with the goal of having at least 4 peer-reviewed publications within this timeframe. Thus, we expect to produce at least 8 peer-reviewed publications by the end of the 4-year study period in addition to final reports.

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