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SPECIFIC AIMS

Persistent disparities based on race/ethnicity and socioeconomic status in healthcare are well documented in the United States (IOM 2003, AHRQ 2015, Williams 2016). Social determinants of health are key drivers of health disparities, especially in the elderly. T2DM is a chronic disease that is highly prevalent in the elderly, associated with significant racial/ethnic disparities, and impacted by social determinants of health (Walker 2016, Williams 2016, Walker 2015). Elderly individuals with diabetes have high multimorbidity, complex treatment regimens, impaired functional status and are often impacted by psychosocial determinants of health such as food insecurity, housing insecurity, competing needs, stress/coping, cognitive dysfunction, limited social and financial resources, and social isolation (Young-Hyman 2016, Tomaka 2006, Billimek 2012, Nicklett 2013). These factors create challenges for lifestyle and medical management (Kirkman 2012).

Behavioral activation is a cognitive behavior therapy, originally developed to address depression, that has shown promise in individuals with chronic medical conditions, including T2DM (Lejuez 2001, Lejuez 2011, Schneider 2016, Kaltman 2016, Weiss 2015). The focus on identifying and increasing the incorporation of activities into a patient's daily schedule, lends behavioral activation to incorporation into treatment for patients with diabetes (Lejuez 2011). In fact, several pilot studies suggest behavioral activation can be effective in improving self-care behaviors and adherence to treatment recommendations for patients with diabetes (Schneider 2016, Kaltman 2016, Weiss 2015). However, Latina/os and African Americans experience a number of barriers (e.g., language, culture, stigma) and, as a result, consistently underutilize and prematurely terminate behavioral treatments compared to other cultural groups (Alegria 2010). Several meta-analyses have concluded that culturally-adapted treatments improve outcomes in comparison to un-adapted treatments among racial/ethnic minority groups (Smith 2011; Griner 2006). This suggests that there is opportunity to address health care disparities by culturally adapting behavioral interventions and making them more relevant to better address the behavioral health needs of these traditionally underserved populations.

The aims of this randomized efficacy trial are:

Aim: To test the efficacy of Home DM-BAT on glycemic control (hemoglobin A1c).

Hypothesis: Low income, minority seniors with poorly controlled T2DM randomized to Home DM-BAT will have significantly greater improvements glycemic control (hemoglobin A1c) at 12 months of follow-up compared to the control group (in-home, supportive therapy - ST).

Scientific Premise. Persistent disparities based on race/ethnicity and socioeconomic status in healthcare are well documented in the United States (IOM 2003, AHRQ 2015, Williams 2016). Social determinants of health are key drivers of health disparities, especially in the elderly. T2DM is a chronic disease that is highly prevalent in the elderly, associated with significant racial/ethnic disparities, and impacted by social determinants of health (Walker 2016, Williams 2016, Walker 2015). Elderly individuals with diabetes have high multimorbidity, complex treatment regimens, impaired functional status and are often impacted by psychosocial determinants of health such as food insecurity, housing insecurity, competing needs, stress/coping, cognitive dysfunction, limited social and financial resources, and social isolation (Young-Hyman 2016, Tomaka 2006, Billimek 2012, Nicklett 2013). These factors create challenges for lifestyle and medical management (Kirkman 2012). Behavioral activation is a cognitive behavior therapy, originally developed to address depression, that has shown promise in individuals with chronic medical conditions, including T2DM (Lejuez 2001, Lejuez 2011, Schneider 2016, Kaltman 2016, Weiss 2015). Preliminary data from our group has demonstrated that 8 sessions of culturally-modified, manualized, diabetes-modified, behavioral activation treatment that incorporates: 1) diabetes education, 2) addresses social determinants of health (e.g. food insecurity, housing insecurity, competing needs, stress/coping etc.), and 3) brief behavioral activation treatment achieved maintenance of glycemic control in older adults with T2DM. The proposed study will test new strategies for improving clinical outcomes for T2DM in minority elders by addressing both diabetes-specific factors and social determinants of health that impede optimal health in this population.

Study Overview. This study will evaluate the efficacy of 8 sessions of in-home, telephone-delivered, culturally-modified, manualized diabetes-modified, behavioral activation treatment (Home DM-BAT) delivered by trained diabetes nurse educators among low income, ethnic minority seniors (age ≥65 years of age) with poorly

controlled T2DM (HbA1c $\geq 8\%$), living in independent, subsidized, assisted senior housing facility or community dwelling elderly adults in the greater Milwaukee area and surrounding counties that have high African American/Hispanic populations. 200 low income, minority seniors will be randomized to Home DM-BAT (n=100) or the control condition (in-home, telephone-delivered supportive therapy -ST) (n=100) to control for attention. The intervention includes 8 weekly intervention sessions and 10 monthly booster sessions delivered via telephone. The individual sessions will last 30-45 minutes based on our prior preliminary studies. Study assessments will be at baseline, 3-, 6-, 9-, and 12-months of follow-up. Primary analyses will be conducted at 12 months post-randomization.

Study Population & Recruitment Plan

Study Sites: The study sites for this study are residents of independent, subsidized, assisted senior housing facility or community dwelling elderly adults in the greater Milwaukee area and surrounding counties that have high African American/Hispanic populations.

Recruitment Strategy: After obtaining approval from the Institutional Review Board, we will use multiple complementary approaches to identify eligible study subjects. The first method will consist of referral from administrators and staff members at the senior housing sites (**see attached letters of support**). The PI will meet with the appropriate administrators at the senior sites to receive approval to conduct the study at the identified sites and recruit residents to participate in the study. In addition, the PI will provide a study overview, explain the study procedures, and discuss logistics for conducting the study at the senior housing sites. The administrators and staff members will be asked to recommend residents who they deem appropriate (i.e., poorly controlled glucose, motivated, history of participating in prior studies, and/or interest in research) to participate in the study. After receiving permission to approach those individuals, they will be invited to the baseline visit to assess eligibility. The second method will include the posting and distribution of recruitment flyers throughout the senior housing sites and to residents, respectively. The third approach will be to advertise the study via multiple strategies to community dwelling elderly adults that are eligible for the study within the community. The fourth approach will consist of referrals from residents and community dwelling elderly adults in response to recruitment flyers and advertisements. Those interested in participating in the study will be contacted for screening. If eligibility criteria are met, the baseline/enrollment visit will be scheduled. In addition, after obtaining IRB approval for a partial waiver of HIPAA, the final approach will be to query clinic billing records. Search criteria will include patient demographics and ICD coded diagnosis to allow identification of subjects with ICD-10 codes consistent with a diagnosis of T2DM. Identified eligible participants will be sent recruitment and informational letters. We have successfully used these approaches in our past and current research. Other approaches will include local advertisement on relevant media, billboard, and organizational sites. The final method used will include the enrollment of study champions across the senior community who will actively identify and refer potential study subjects to the study. The study champions will be community members recruited into this study to serve as champions for a duration of 12 months, eligibility criteria discussed further below. As HOME DM-BAT is a community-based study, the use of study champions will serve as a complementary method that will be drawn in part from prior methodology in community based participatory research (Minkler and Wallerstein, 2008). Specifically, as community members, the champions will have an understanding of the barriers and facilitators that many seniors with diabetes experience and will therefore be able to facilitate recruitment into the study as a champion. As the champions will be participating in the research process through recruitment and retention, all champions will be compensated for their time, see details below. Champions will undergo a formal informed consent process and will complete a screening survey as well as an exit survey at the completion of the study. Once champions are enrolled, they will undergo three sequential training sessions to prepare them for their champion role. These training sessions will include: 1) overview of the study goals and objectives, 2) ethical considerations for research, and 3) procedures for recruitment into a research study. The study champions will have ongoing communication with members of the study team during the recruitment process to provide a forum for updates. In addition, champions will have their HbA1c measured as a part of the enrollment procedure. While the HbA1c level will not serve as an exclusionary factor, it will provide information on diabetes management for study champions, which prior evidence has shown this to be an important factor when enrolling participants as facilitators for research procedures (Long, 2012).

Participant Payment: Participants will receive \$10 for completion of screening, \$15 for completion of baseline, and \$25 for completion of 3, 6, 9, and 12-month assessments for a total payment of \$125.

Patient Eligibility Criteria: The study inclusion and exclusion criteria are as follows

Inclusion Criteria: 1) Age ≥ 65 years of age; 2) Self-identified as Black/African American or Hispanic; 3) Clinical diagnosis of T2DM verified by an HbA1c $\geq 8\%$ at the screening assessment; 4) Able to communicate in English or Spanish; and 5) Resident of independent, subsidized, assisted senior housing facility or community dwelling elderly adults in the greater Milwaukee area and surrounding counties that have high African American/Hispanic populations.

Exclusion Criteria: 1) Mental confusion at screening assessment suggesting significant dementia; 2) Participation in other diabetes research; 3) Alcohol or drug abuse/dependency at screening assessment; 4) Active psychosis or acute mental disorder at screening assessment; and 5) *Life expectancy <12 months at screening assessment based on medical history and comorbidity screen used in prior studies.*

Description of the Home DM-BAT Intervention: A trained nurse educator will deliver the manualized Home DM-BAT intervention via telephone. Subjects will receive 8-weekly sessions of behavioral activation and monthly booster sessions from months 3-12. Home DM-BAT is extremely suitable to standard diabetes management approaches because it targets important diabetes management behaviors (medication taking, physical activity, healthy eating, and self-monitoring of glucose and BP). Moreover, Home DM-BAT specifically attempts to incorporate contingencies of environmental reinforcement for positive health behaviors, with a focus on medication adherence and other diabetes specific healthy behaviors including physical activity, healthy eating, abstinence from smoking, and involvement in pleasurable activities that the patient chooses, such as spending time with friends, spirituality, or volunteer work. These supplemental activities are directed at improving overall emotional well-being. All intervention sessions will be delivered by telephone at times that do not interfere with previously scheduled activities. Each individual session will last 45 minutes and will include 15 minutes for a previously tested diabetes education/skills training intervention based on ADA guidelines, 30 minutes for diabetes-tailored behavioral activation and to address social determinant of health issues.

Control Group (GHE+ST): Patients randomized to the control group will receive in-home, telephone-delivered 8-weekly sessions of combined general health education (GHE) and supportive therapy (ST) and monthly booster sessions from months 3-12. Given that this is an effectiveness trial, the control group was designed to match the intervention group for both content and attention. The GHE component matches the diabetes education component of Home DM-BAT and ST component matches the behavioral activation component of Home DM-BAT. In addition, delivering GHE/ST to the control group will reduce attrition, maintain blinding, and maintain community trust. The control group will not receive diabetes education, address social determinants of health, or behavioral activation. **We have used the GHE+ST modules successfully in prior RCTs.**

Data Collection Strategy

Personnel: Nurse diabetes educators (NDE) will deliver the interventions; study staff will conduct screening, consent, enrollment procedures, and questionnaire administration. **Data collection will occur at locations convenient to the patient including the senior housing facilities, participants homes, MCW research facilities, or appropriate community locations. The RAs will travel to the sites to administer study questionnaires, while the study nurses and/or phlebotomists will perform blood draws. Blood specimen will be hand carried using appropriate safety containers by nurses and/or phlebotomists at the end of each visit to MCW lab for analysis in compliance with MCW standard operating procedures.**

Data Management: The MCW REDCap system will be used for data management. REDCap (Research Electronic Data Capture) is a secure, web-based application designed exclusively to support data capture for research studies initiated at Vanderbilt University (<http://project-redcap.org/>). REDCap provides: 1) an intuitive interface for data entry (with data validation); 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages (SPSS, SAS, Stata, R); 4) procedures for importing data from external sources; and 5) advanced features, such as branching logic and calculated fields. We have used REDCap successfully for multiple clinical trials.

Patient Randomization: A permuted block randomization method will be used to assign subjects to one of the two intervention groups: (a) Home DM-BAT intervention; and (b) Control (GHE/ST). Block size will be varied to minimize the likelihood that the blind will be broken. The randomization will be stratified by baseline HbA1c levels (8-10% vs. >10%).

Sample Size and Power. For comparing the difference in outcome means for Home DM-BAT versus GHE/ST in an **individually-randomized design**, with 80 participants per group, there will be 85% power to detect a *standardized* effect size ranging from **0.34 to 0.39 for the primary endpoint at 12 months** [assuming level of significance $\alpha=0.05$ (two-tailed)]; To account for missing information in the ITT sample and the dilution effect of ITT analyses, we increase the sample size by 20% to achieve a final ITT sample size of 100 participants randomized 1:1 to each treatment group (**total N=200 randomized participants**).

PROTECTION OF HUMAN SUBJECTS

1. RISKS TO THE SUBJECTS

Potential Risks

Potential risks to the participants include possible violation of each participant'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.

Confidentiality: This will be maintained by keeping participant folders in locked file cabinets in the investigator's locked office. Only participants' unique identification numbers will be recorded in folders and on data forms. The database will remain on the MCW computer system using unique ID numbers, rather than names, and will be password-protected.

2. ADEQUACY OF PROTECTION AGAINST RISKS

b. Protection against Risk

1. Participants will be protected against potential risks as follows:

a. *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 research participants. RAs will be trained by the PI to identify patients who meet criteria for depression on the PHQ-9. Participants who screen positive for depression will be notified during the visit and verbally instructed to seek care from their Primary Care Provider (PCP). They will also be given the Suicide Prevention National Hotline: 1-800-SUICIDE (784-2433), and told to call if they experience acute worsening of symptoms before they can be seen by their PCP.

b. *Venipuncture (blood drawing):* To reduce the risks of discomfort and bruising, venipuncture will be performed by the nurse educator and discarded per routine lab policy/procedures at an appropriate laboratory. To reduce the risk of fainting, blood will be drawn while participants 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.

c. *Blood Pressure Measurement:* To lessen any associated risks, BP measurements will be performed by the study nurses utilizing a standardized protocol. Participants with elevated BP will be advised to contact their PCP. Those with potentially life-threatening BP readings will be sent to a local emergency room for treatment.

d. *Administration of Research Questionnaires:* Some participants might feel uncomfortable or be offended by detailed questions about emotional or physical health status and impairment, and healthcare utilization. All participants will be informed during the consent process 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.

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

2. Participants requiring medical or other professional intervention for study-related events will be provided with appropriate and timely medical guidance by the designated medical monitor. If adverse events occur during the conduct of this study, they will be reported to the MCW IRB in accordance with the appropriate guidelines. The results of participants' clinical assessments will be available within a few weeks of their study visit. The

designated medical monitor will review and inform participants of these results by phone and, at their request, also advise their personal PCP of the results.

3. 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 PI, study data coordinator/data entry clerk, and 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 data coordinator/data entry clerk. 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' identities will not be revealed. A file of names, contact addresses, telephone numbers, and other research identification numbers will be stored separately on paper and on computer, for purposes of audit by the sponsor (NIH/NIMHD) and MCW IRB, if necessary.

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

The intervention is expected to benefit patients, by 1) increasing their knowledge of diabetes, 2) activating and empowering them to better care for their diabetes, 3) improving blood glucose, blood pressure, and blood lipid control, and 4) reducing their risk developing complications of diabetes. Patients in the supportive therapy group will benefit by increasing their general health knowledge.

4. IMPORTANCE OF THE KNOWLEDGE TO BE GAINED

Key drivers of health disparities and key areas for interventions are the social determinants of health, or the economic and social conditions that influence health status. Considerable evidence now exists linking social determinants to a range of health outcomes, especially in chronic diseases such as type 2 diabetes, where a clear majority of minorities and the elderly are affected at alarming rates. Given the need to address multiple medical concerns during brief and often short, clinical visits, psychosocial factors are often not discussed extensively, resulting in the need for alternative approaches for addressing psychological well-being in elderly patients. Behavioral activation is a cognitive behavior therapy recommended as a cost-effective alternative to more intensive psychological therapies when treating patients with chronic and comorbid conditions. Evidence suggests behavioral activation can be effective in improving self-care behaviors and adherence to treatment recommendations for patients with diabetes. Therefore, this study has been designed particularly for elderly patients with diabetes. If successful, the findings of this study will demonstrate an alternative approach for addressing psychological stressors, lessening the impact of social determinants of health on outcomes, and improving general well-being by increasing social activities and decreasing social isolation among seniors with poorly controlled type 2 diabetes.

DATA AND SAFETY MONITORING PLAN

Quality assurance and data integrity

The PI will be responsible for monitoring quality assurance and data integrity. Meetings with the PI, co-investigators, and study staff will take place weekly throughout the study. At each meeting the team will discuss recruitment and accrual, protocol questions, retention, and data entry concerns. Enrollment numbers will be maintained and reported to the study team on an ongoing basis, along with information on reasons for exclusion, dates of completion of the study, and demographic summaries. All research staff will have training in human subjects research, including data integrity and protection of confidentiality, and will follow standard procedures such as storage of hard copies of assessments and other data in locked file cabinets and separation of consent forms and identified master lists in separate locations. Study files will be maintained on an MCW server that provides nightly backup procedures and HIPPA compliant firewalls.

Assessments will be administered by trained personnel using validated surveys on standardized collection forms. Training of study staff on administration of self-report measures and standard operating procedures will be done by the PI and co-investigators. Completed forms will be checked manually for missed entries, invalid responses, and corrected as necessary before the participant leaves. Accuracy of data entry will be ensured by RedCAP database field controls, and quarterly audits on data records to ensure accurate and complete data

collection.

Safety monitoring

The safety monitoring plan will include an internal Data Safety Monitoring Committee (DSMC) and the institutional IRB. The purpose of the DSMC 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 DSMC will be made to the IRB in the yearly progress unless the nature of a particular event is such that it bears reporting to IRB immediately.

DSMC: The internal DSMC will consist of the PI, biostatistician, co-investigators on the proposal, and the 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.

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 DSMC.