Trial Title: Cardiovascular Outcomes of an Adapted Evidence-Based Intervention for Rural African Americans: Heart Matters Trial

Internal Reference Number / Short title: Heart Matters

ClinicalTrials.gov: NCT02707432

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Other Study ID Number: UNC IRB - 13-2576

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Funder:	National Heart Lung and Blood Institute (Grant Number 1R01HL120690)
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No potential conflicts of interest.

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1 KEY TRIAL CONTACTS

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2 LAY SUMMARY

Cardiovascular disease (CVD) is the leading cause of death in the US, however African American residents of rural areas in the south and southeast regions have the highest prevalence of CVD of any group. African Americans carry a significant burden of CVD risk factors that often co-occur; this burden is amplified in rural communities. CVD disparities at the intersection of race and geography are driven by individual risk behaviors and complicated by factors such as limited access to quality healthcare, socio-economic inequities, limited healthcare infrastructure and environmental barriers to behavior change. Interventions to ameliorate CVD burden in rural African American communities will require placing the individual in the context of the larger community and taking advantage of new technologies to support behavior change. However, how best to integrate mobile technology into existing evidenced based interventions (EBIs) is still an emerging field and social and physical environmental factors important in rural communities are rarely considered in existing EBIs. The proposed study will address this gap in the literature by determining the feasibility and efficacy of adapting an EBI to consider the environment in important in rural African American communities and determining the acceptability of mobile technology in these communities to support behavior change. The proposed study is built on the

strong foundation of Project GRACE's 8-year history of designing and testing interventions using a community-based participatory research (CBPR) approach, and individual and collaborative expertise in community-based CVD outreach, service and research. We have developed a phased CBPR study with a long-term goal to reduce rates of CVD in Eastern NC. The overall objective of this proposal is to assess feasibility of implementing an EBI, adapted to the needs and interests of a rural community in order to plan a large scale study. To that end our specific aims are to 1) expand and sustain a Project GRACE CVD coalition of community and academic stakeholders to develop successful CVD risk prevention strategies in rural communities; 2) conduct a mixed-method community needs and assets assessment based on: a) assemble, review and assess existing sources of CVD data; b) identification of community strengths and resources using a web-based survey of community, faith based, social service and healthcare organizations; c) determine the acceptability of components of CVD risk reduction EBIs and community members' perceptions of possible targets for intervention using focus group interviews; d) determine specific family influences (barriers and facilitators) on acceptability of EBI acceptability; 3) adapt PREMIER, a multi-component EBI using intervention mapping; and 4) conduct a small-scale randomized control trial to assess a) efficacy; and, b) feasibility and adaption of implementing adapted PREMIER in rural settings.

3 SYNOPSIS

Trial Title	Cardiovascular Outcomes of an Adapted Evidence-Based Intervention for Rural African Americans: Heart Matters Trial		
Internal ref. no. (or short title)	Heart Matters		
Trial registration	NCT02707432 Date of registration: March 14, 2016 https://clinicaltrials.gov/ct2/show/NCT02707432?term=corbie&draw=2&rank=2		
Funder	National Heart, Lung, and Blood Institute (NHLBI; 5R01HL120690)		
Trial Design	Randomized, controlled trial		
Trial Participants	African American adults (21 years or older) with at least one risk factor for cardiovascular disease.		
Sample Size	140		
Planned Trial Period	Total length of the project is 18 months. Participant's involvement will be a 12-month intervention with a 6-month follow-up.		
Planned Recruitment period	March 27, 2017 – February 28, 2019		
	Objectives	Outcome Measures	Timepoint(s)
Primary	To determine the effect of an adapted intervention, Heart Matters, on cardiovascular clinical outcomes.	Body weight	6 months
Secondary	To determine the effect of Heart Matters on secondary cardiovascular clinical	Systolic and diastolic blood pressures	6 months

	outcome		
Intervention(s)	Lifestyle modification consisting of interactive group and individual visit sessions targeting physical activity, weight loss, and nutrition.		
Comparator	No comparator intervention due to delayed control design.		

4 ABBREVIATIONS

AE	Adverse event
PI	Principal Investigator
CT	Clinical Trials
GCP	Good Clinical Practice

5 BACKGROUND AND RATIONALE

Purpose: To determine the effect of an adapted intervention, Heart Matters, on cardiovascular clinical outcomes.

Background: African Americans in the rural southeast are disproportionately affected by cardiovascular disease and associated risk factors. Despite evidence-based cardiovascular interventions targeting clinical or behavioral risk factors, geographic and racial disparities persist and continue to widen. Cardiovascular disease (CVD) is the leading cause of death in the United States (US) with an estimated 50% of individuals in the US expected to have CVD by 2030. African American residents in rural areas of the south and southeast (also called the “stroke belt”) have the highest prevalence of CVD compared to other populations. Furthermore, CVD prevalence rates for residents of rural areas (13.1%) are higher compared to those in urban areas (11.2%) of the US. In the setting of geographic disparities, striking racial disparities in CVD risk factors, morbidity and mortality are exacerbated. African Americans are disproportionately affected by a higher burden of CVD risk factors: high blood pressure, diabetes, smoking, high cholesterol, and physical inactivity. This heightened risk is prevalent in both youth and older age groups and has increased over time. While CVD disparities at the intersection of race and geography are driven by a disproportionate burden of individual risk factors, racial disparities in rural settings are amplified by associated factors, such as limited access to quality healthcare services, socio-economic burden, dwindling resources, insufficient health infrastructure, and physical barriers to access to care. There are numerous evidence based interventions (EBIs) that have focused on reduction in CVD risk factors. These interventions have often focused on primary prevention of individual risk factors such as hypertension, diabetes, lipids, physical activity, and diet quality. Many of these have been developed in urban centers, and only a few have included participants that are reflective of geographic and racial disparities in CVD risk.

Given the burden of co-morbidities in rural African American populations, interventions targeting only one behavior or risk factor are likely to be less successful than those using intervention components and concepts impacting multiple behaviors. There is a need for culturally adapted interventions that address multiple behavioral risk factors for CVD. Using a Community-Based Participatory Research (CBPR) approach, our team adapted and will implement an EBI to improve cardiovascular risk in African Americans living in a rural underserved setting.

Participants: African Americans who reside in Edgecombe and Nash counties, aged 21 years or older, with at least one self-reported cardiovascular disease (CVD) risk factor.

Potential benefits for study participants include participation in long-term lifestyle modifications that may result in improved diet, nutrition, and physical activity patterns**,** which in turn should decrease blood pressure and lead to an overall reduction in cardiovascular and cancer morbidity.

Heart Matters Intervention: Heart Matters will use a lifestyle modification to reduce CVD risk factors and includes 26 interactive group sessions and 7 individual visit sessions over 12 months. Heart Matters lifestyle goals include: 1) reducing weight by 15 lbs. or another agreed upon goal, 2) limiting fat intake by consuming 20–50% or less of total calories from fat, 3) limiting daily sodium intake to 2300 mg or less, 4) accumulating 150 min of moderate-intensity exercise each week, 5) limiting alcohol intake; women are advised to consume no more than one alcoholic drink per day and men are advised to consume no more than two alcoholic drinks per day, and 6) diet and physical activity tracking.

Trained facilitators and co-facilitators will conduct 26 90-minute group sessions at each organizational site with 15–20 participants per group. Facilitators are members of the community who are teachers, coaches, or clergy members and have 30 min of group supervision of adherence to protocol for each session delivered. Co-facilitators are allied health professionals, such as nutritionists, nurses, and personal trainers who help deliver the educational content. All facilitators will participate in an extensive three-part training on intervention protocols and curriculum.

Participants will have seven 60-min individual sessions throughout the intervention. Individual sessions will be pre-scheduled and conducted via phone by the facilitator. Using motivational interviewing techniques, facilitators will discuss participant's progress and challenges to making behavior changes. Participants develop an individualized action plan at the first individual visit and this plan is revisited in subsequent individual visit sessions in an effort to track individual progress.

6 OBJECTIVES AND OUTCOME MEASURES

Objectives	**Outcome Measures**	**Timepoint(s) of evaluation of this outcome measure (if applicable)**
Primary Objective To determine the effect of an adapted intervention, Heart Matters, on body weight.	Body weight measured by Tanita WB-800 Professional Digital Weight Scale	Body weight measurement at day 0 and 6 months after baseline.
Secondary Objectives To determine the effect of an adapted intervention, Heart Matters, on cardiovascular clinical outcomes.	Systolic and diastolic blood pressures are measured by the Omron HEM907XL-Automatic Digital Blood Pressure Monitor.	All secondary outcomes are measured at day 0 and 6 months after baseline.

7 TRIAL DESIGN

Heart Matters is a community-based randomized trial comparing the effects of implementing the adapted lifestyle modification intervention on cardiovascular clinical outcomes among African American participants in rural eastern NC.

To implement Heart Matters, we will cluster individual participants within organizations that we recruit to participate in the study and be host sites for the intervention delivery. We will randomize organizations to 2 start times: Time 1 Heart Matters Intervention Group (immediately after baseline data collection) and Time 2 6 month-delay Heart Matters Intervention Group (6 months after baseline data collection). Randomization by organization will reduce the likelihood of data contamination given the fact that rural communities tend to be smaller and participants may be familiar with each other.

The flow of the participant is: 1. Screening at community organization and pre-intervention data collection. 2. Randomization of organizations to treatment group or 6 month delayed intervention control, 3. 6 month assessment data collection.

Data collection procedures: After the consent process, eligible individuals will complete the baseline data collection in a community setting. All data collection will be completed by trained research staff from the partner community organizations, James McFarlin Community Development, Inc and Project Momentum, Inc. Data collection will include biometric and biomarker data as well as self-report behavioral data. Trained research staff will collect biometrics such as weight, height, grip strength, and balance. Trained research staff who are registered nurses will collect blood pressure and hemoglobin A1c. Study staff will record the biometric data on paper forms which will be entered into REDCap, a secure web-based application for data management. For participants with life-threatening A1c levels, they will be immediately transported to emergency services, and adverse event data will be documented by research staff. The baseline questionnaire will include behavioral measures and structured questions on demographics (e.g. age, race, marital status, SES), health history, medications, CVD risk factors. Data collectors will enter data from the paper questionnaire forms into REDCap.

8 PARTICIPANT IDENTIFICATION

8.1 Trial Participants

Participants with at least one risk factor for cardiovascular disease, living in one of two rural counties in eastern North Carolina, aged 21 years and older.

8.2 Inclusion Criteria

- Participant is willing and able to give informed consent for participation in the trial.
- African American adults aged 21 years or above.
- Self-reported with at least one cardiovascular disease risk factor of pre-diabetes or diabetes, hypertension, obesity, family history of early CVD, or prior diagnosis of CVD

8.3 Exclusion Criteria

The participant may not enter the trial if ANY of the following apply:

- Individuals who had significant cognitive impairment or unstable cardiovascular disease

- Cognitive impairment that limits informed consent

9 TRIAL PROCEDURES

9.1 Recruitment

9.1.1 Organizational Recruitment

We will recruit organizations to serve as recruitment and intervention sites from both counties (Edgecombe and Nash). We will invite potential organizations based on: (a) existing relationships through the Project GRACE consortium, (b) and a list of organizations beyond existing networks generated by our James McFarlin Community Development, Inc and Project Momentum, Inc collaborators. Knowing that CVD risk is high in older adult populations, the extended list will include senior health and civic organizations. Historically, faith based organizations reach a large segment of the minority community and are a trusted leader in the community. As a result, many organizations may be faith-based.

In addition to partnering for participant recruitment, organizations will be host sites for intervention delivery. We will use the following inclusion criteria to evaluate each organization: kitchen space with refrigerator, stove and/or microwave, contact person from each organization available to open and close the building, and layout of how the used space should look at the conclusion of use. We will base final inclusion criteria on if the site could host the intervention for all 12 months.Of the original list of criteria, we will identify sufficient sites to meet sample size needed.

9.1.2 Individual Participant Recruitment

Community-based recruiters at James McFarlin Community Development, Inc and Project Momentum, Inc will work with organizational leaders to hold recruitment events at each organization. Outreach to individuals will be based on recommendations from organizational leaders and will include direct outreach and information sessions at each organization, distributing written materials/flyers, recruiting at organizational events and exploring the social networks of initial recruits.

9.2 Screening and Eligibility Assessment

We will obtain verbal informed consent from potentially eligible participants for the initial screening during which individuals will provide identifiable information (e.g. contact information) and provide medical history to determine if eligible or excluded. No re-screening or protocol waivers will be permitted. Medical history interview will ask about cardiovascular disease risk factors (pre-diabetes or diabetes, hypertension, obesity, family history of early CVD, or prior diagnosis of CVD) and cognitive impairment.

9.3 Informed Consent

After the eligibility screening, we will obtain written informed consent for each eligible participant who decides to enroll in the study. Community partners at James McFarlin Community Development, Inc and Project Momentum, Inc will be responsible for enrolling participants into the study.

9.4 Randomization

Participants in organizations will be randomized by a statistician into Time 1 (immediate intervention delivery after baseline data collection) and Time 2 (6 month delayed intervention delivery) under a matched pair in order to balance the sample size between Arm 1 and 2. Organizations will be paired based on the number of participants, and then randomly assigned one organization from each pair to each arm.

9.5 Blinding and code-breaking

There is no blinding or code-breaking in this trial.

9.6 Baseline Assessments

Immediately following the consent process, eligible individuals will complete the baseline data collection in a community setting. All data collection is completed by trained research staff from the partner community organizations, James McFarlin Community Development, Inc and Project Momentum, Inc. Data collection will include biometric and biomarker data as well as self-report behavioral data. Trained research staff will collect weight. Trained research staff who are registered nurses will collect blood pressure and hemoglobin A1c. Study staff will record the biometric data on paper forms which will be entered into REDCap, a secure web-based application for data management. For participants with life-threatening A1c levels, they will be immediately transported to emergency services, and adverse event data will be documented by James McFarlin Community Development, Inc and Project Momentum, Inc research staff.

Trained data collectors will conduct the structured survey. The baseline questionnaire will include behavioral measures and structured questions on demographics (e.g. age, race, marital status, SES), health history, medications, CVD risk factors. Data collectors will enter data from the paper questionnaire forms into REDCap.

9.7 Subsequent Visits

Data collection occurs at baseline and at each 6 month interval for 18 months.

9.8 Sample Handling

All samples for A1C will be disposed as biohazard material immediately after collection, reading, and recording is complete.

9.9 Early Discontinuation/Withdrawal of Participants

During the course of the trial a participant may choose to withdraw early from the trial at any time. This may happen for a number of reasons, including but not limited to:

- The occurrence of what the participant perceives as an intolerable adverse event.
- Inability to comply with trial procedures
- Participant decision due to circumstances outside of trial.

Participants may have the following two options for withdrawal;

1) Participants can withdraw from the study but permit data and samples obtained up until the point of withdrawal to be retained for use in the study analysis. No further data or samples would be collected after withdrawal.

2) Participants can withdraw completely from the study and withdraw the data and samples collected up until the point of withdrawal. The data and samples already collected would not be used in the final study analysis. (Any limits to this type of withdrawal where, for example analysis of their data or samples has already been integrated into interim results or dose escalation decisions etc. should be explained in the participant information sheet).

In addition, the Investigator may discontinue a participant from the trial treatment at any time if the Investigator considers it necessary for any reason including, but not limited to:

- Ineligibility (either arising during the trial or retrospectively having been overlooked at screening)
- An adverse event which requires discontinuation of the trial or results in inability to continue to comply with trial procedures

9.10 Definition of End of Trial

The end of trial is the point at which all the data has been collected and entered and no participant contact is needed.

10 SAFETY REPORTING

Safety reporting will be addressed during routing study team meetings and additional as needed meetings or communication. The PI and study coordinator will report any safety issues to the IRB. The IRB will be notified of any safety issues that necessitate reporting and possible protocol changes. Progress reports will be provided to the IRB at least annually, or as requested. All unanticipated problems or serious adverse events involving risk to human subjects will be reported. All collaborators, students, and employees assisting in this research study will be informed about these obligations.

10.1 Adverse Event Definitions

Adverse Event (AE)	Any untoward medical occurrence in a participant to whom a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product.
Serious Adverse Event (SAE)	A serious adverse event is any untoward medical occurrence that: • results in death • is life-threatening • requires inpatient hospitalisation or prolongation of existing hospitalisation • results in persistent or significant disability/incapacity • consists of a congenital anomaly or birth defect*.

	Other 'important medical events' may also be considered a serious adverse event when, based upon appropriate medical judgement, the event may jeopardise the participant and may require medical or surgical intervention to prevent one of the outcomes listed above.

10.2 Adverse Events

In the event of an adverse event, the PI and study team will work with the IRB to determine a protocol for handling AE that may occur during the course of data collection and the intervention. Facilitators and data collectors will be trained to follow protocol procedures and report any AE to the primary investigator immediately.

11 STATISTICS

11.1 Statistical Analysis Plan (SAP)

The plan for the statistical analysis of the trial are outlined below. There is not a separate SAP document in use for the trial.

11.2 Description of Statistical Methods

Demographics and clinical measures will be described using means, standard deviations, frequencies, and percentages. T-tests will be used to compare group level characteristics of continuous variables. Pearson Chi-square tests will be used to compare categorical group comparisons. Treatment effects from baseline to 6 months post intervention will be analyzed using linear mixed effects models. Least square means differences will be used by finding the differences between baseline and 6-month outcomes, as well as differences in groups with corresponding 95% confidence intervals. Models will be adjusted for age, blood pressure medications, and cluster. All of the analysis will be implemented using SAS 9.4 (Cary, NC).

11.3 Sample Size Determination

Sample size for Heart Matters was calculated on the basis of observing a 1.8 kg difference (SD = 3.2) in the primary outcome – weight change – between two intervention groups from baseline to 6 months. We determined a sample of 102 would allow us to detect a 1.8 kg difference (SD = 3.2) in weight change between intervention and control groups, with 80% power and an α of 0.05. Accounting for attrition and intra-class correlation, due to a clustered randomized delayed intervention design, we plan to enroll 120 participants.

11.4 Analysis Populations

We will implement Heart Matters in Edgecombe and Nash counties; two counties in eastern North Carolina that are considered rural by urbanized area definitions with respective populations of 54,150 and 93,919. The two counties share one urbanized area, the city of Rocky Mount. Both have had a large prevalence of African Americans (56.7 and 40% of population, respectively) that experience significant health disparities with respect to cardiovascular disease. The sample is recruited through community organizations and

thus not considered a randomly selected sample representative of populations.

11.5 The Level of Statistical Significance

A p-value smaller than 0.05 will be considered statistically significant.

11.6 Procedure for Accounting for Missing, Unused, and Spurious Data

For all measures, scores will be calculated if an individual answered at least 60% of the items of a given measure. If an individual answered less than 60% of items, the data will be treated as missing for that measure only.

11.7 Procedures for Reporting any Deviation(s) from the Original Statistical Plan

Any deviations from the original statistical analysis plan will be reported in publications.

12 DATA MANAGEMENT

Data collection will include biometric and biomarker data as well as self-report behavioral data. Hard copy files of data will be retained in locked containers in locked rooms where approved study staff will have access. Data will be entered in REDCap, a secure web-based application for data management. All export of data from REDCap will adhere to university protocols to ensure data is safely stored on university approved servers.

12.1 Access to Data

Direct access will be granted to authorized representatives from the Sponsor, host institution and the regulatory authorities to permit trial-related monitoring, audits and inspections.

12.2 Data Recording and Record Keeping

Trained research staff will collect weight and other data collection except trained research staff who are registered nurses will collect blood pressure and hemoglobin A1c. Study staff will record the biometric data on paper forms, which will be entered into REDCap, a secure web-based application for data management. REDCap provides timestamped tracking to allow for an audit trail of all revisions to database codebook and data itself. Any quality assurance reviews and corrections to data entry will be tracked through REDCap.

Hard copy files will be stored at UNC. The participants will be identified by a unique trial specific number and/or code in any database. The name and any other identifying detail will NOT be included in any trial data electronic file. Informed consent documents and a document linking file that links participant ID to their name will be stored separately from all data.

13 QUALITY ASSURANCE PROCEDURES

13.1 Monitoring

Weekly meetings will be conducted with the team members during all stages of the study to review progress to date, any protocol deviations, data management, safety monitoring, and compliance.

13.2 Scientific Advisory Board

The Scientific Advisory Board will be comprised of PI, Co-Investigator, Project Manager, Biostatistician from the study two and 2 outside experts. The study team will provide a report to the scientific advisory board annually, and the board will discuss and make recommendations to support completion of scientific aims. As this will be a minimal risk study, this oversight is sufficient.

14 PROTOCOL DEVIATIONS

A trial related deviation is a departure from the ethically approved trial protocol or other trial document or process (e.g. consent process) or any applicable regulatory requirements. Any deviations from the protocol will be documented in a protocol deviation form and filed in the trial master file. The protocol deviations and completed forms will be presented to the PI and study team by the project coordinator during weekly meetings. The review will ensure any repetitive or single, but significant deviations be escalated to the IRB for assessment of whether a non-compliance /deviation may be a potential Serious Breach and determine any necessary response.

15 ETHICAL AND REGULATORY CONSIDERATIONS

15.1 Participant Confidentiality

To track participant outcomes across time while maintaining confidentiality, ID numbers will be used. A separate linking file will be maintained linking the IDs to the respondents' names. The surveys will be conducted using the mobile REDCap database, a password protected, firewalled database only accessible to the research team. Data will be collected using RedCap app. In case of computer problems, we will have paper copies of surveys available. All paper documentation will be maintained in locked files at UNC.

15.2 Expenses and Benefits

Participants will receive $195 in compensation for participation in data collection and intervention session attendance: $5 eligibility screening, $25 for baseline data collection, $15 for 6 month data collection, $20 for 12 month data collection, and $20 for 18 month data collection. Throughout the intervention, participants will receive a $15 cash incentive for attendance at Group Sessions 4, 8, 12, 16, 20, 24, and $20 at session 26.

16 PUBLICATION POLICY

The study PI is responsible for intellectual content on publications from the dataset collected for this study. Study PI should determine appropriate authorship and acknowledgements for all scientific publications. Institutional and funder policies should be adhered to. NHLBI should be acknowledged in all publications.

17 ARCHIVING

6 months after the main study outcomes paper is published, de-identified dataset will be available per institutional and federal guidelines. Data will be destroyed five years after the study

publications are complete. For electronic data, we will follow accepted techniques to permanently delete files. This will include destruction of linkage files, transcriptions, data files, web-based database files, digital interviews and all other electronic files. All paper files will be shredded at that time.

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