Official Title: Expanding Technology-Enabled Nurse Delivered Chronic Disease Care (EXTEND)

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Standard Research Summary

Purpose of the Study

Aim 1: Compare the effectiveness of the two 12-month EXTEND interventions for PPDM and hypertension. *Hypothesis 1a:* Compared to EXTEND, EXTEND Plus will improve primary (HbA1c) and secondary outcomes (e.g., blood pressure, weight, self-management measures) at 12 months; *Hypothesis 1b:* The relative effects of each intervention will be sustained at 24 months; *Hypothesis 1c:* Subgroup analyses will identify characteristics associated with high responsiveness to each intervention.

Aim 2: Guide scaling and dissemination of the EXTEND interventions by: (A) interviewing patients and stakeholders to clarify implementation barriers, facilitators and process requirements; (B) comparing intervention costs against potential reimbursement mechanisms; and (C) understanding the role of climate change and other social drivers of health on diabetes self-management and intervention engagement.

Aim 3: Explore the value of combining mobile monitoring and EHR data for predicting patient safety events (hospitalizations, emergency visits) in the EXTEND study cohort over 24 months.

Addendum Aims:
AAim 1: Characterize climate vulnerability using validated measures (e.g., Wet Bulb Globe Temperature (WBGT), Climate Vulnerability Index) in the EXTEND study cohort.

AAim 2: Examine associations between climate vulnerability and SDOH-related variables in the EXTEND study cohort.

AAim 3: Quantify the climate impact of the EXTEND and EXTEND Plus interventions by examining between-arm differences with in-person care utilization and translating to travel miles avoided, gallons of gas saved, and CO2 emissions prevented.

AAim 4: Extract social determinants of health (SDOH) from the EHR clinical notes of EXTEND participants who completed AHC-HRSN screening using large language models (LLMs) and encoder-based NLP models, compare model-extracted SDOH against patient-reported AHC-HRSN responses, and test whether an LLM-augmented SDOH lexicon and few-shot prompting improve extraction performance

Background & Significance

- Should support the scientific aims of the research

Chronic diseases like diabetes and hypertension require complex self-management, including self-monitoring of health data, regulation of diet and activity, frequent medication-taking, and navigating psychosocial concerns. When the demands of chronic disease self-management exceed patients' self-management capacity, poor control ensues. For many patients, receiving chronic disease care via a clinic-based delivery model provides insufficient self-management support, resulting in persistent poor control.

As an example of a clinic-refractory chronic disease, 12% of all patients with type 2 diabetes exhibit a continually elevated hemoglobin A1c (HbA1c) despite receiving clinic-based care. We have previously defined patients maintaining a HbA1c ≥8.0% for ≥1 year despite clinic-based care as having 'persistent poorly-controlled diabetes mellitus' (PPDM). Over 85% of patients with PPDM have comorbid hypertension, and most use hard-to-manage, complex insulin regimens. Clinic-based care often fails to resolve PPDM because the factors that complicate self-management in PPDM cannot be addressed with the infrequent patient-provider contact that is practical in clinic. Without better treatment options, patients with PPDM remain at high risk for preventable complications and costs, and comorbid hypertension further magnifies these risks.

Telehealth has the potential to improve management of clinic-refractory chronic diseases relative to clinic-based care alone because it facilitates patient-provider contact and better supports self-management. Our prior work shows that nurse-delivered telehealth interventions incorporating telemonitoring, self-management support, and medication management can lower HbA1c even among clinic-refractory patients

with PPDM. Excitingly, emerging mobile monitoring technologies could enhance telehealth for clinic-refractory chronic diseases, either by generating multiple streams of health data to facilitate patient self-management, or by integrating mobile monitoring data to into a nurse-delivered telehealth intervention.

While mobile monitoring-enabled telehealth holds promise for clinic-refractory chronic diseases, evidence gaps currently prevent routine use in clinical practice. First, the effectiveness of mobile monitoring technologies as aids to self-management in clinic-refractory chronic diseases is unproven. Second, the effectiveness of mobile monitoring-enabled telehealth interventions in clinical practice is uncertain; practical use would rely on delivery by clinical staff and automated integration of data into the electronic health record (EHR), each of which has seldom been accomplished. Third, barriers and facilitators to scaling of mobile monitoring-enabled telehealth interventions within and across systems are poorly understood. Fourth, reimbursement mechanisms for mobile monitoring-enabled telehealth are limited, so there is little evidence supporting sustainability in clinical practice. Given these uncertainties, mobile monitoring-enabled telehealth interventions are not used in practice – even where they are needed most, for clinic-refractory chronic diseases.

Addendum:
Patients with PPDM and hypertension are particularly susceptible to the impacts that climate change may have on their health. Heat waves, air pollution, extreme weather events, and changes in pathogen transmission all due to climate change can have severe consequences for these patients The rise in ambient temperatures can increase the risk of dysregulated glucose levels for people using glucose-lowering medication. Air pollution is linked to an increase in risk of insulin resistance and complications from diabetes such as chronic low-grade inflammation. Extreme weather conditions can pose challenges such as reduced access to primary care, hospitals, and medication in addition to high levels of psychological stress. Further, viral, bacterial, and fungal infections have been found to be worsened by climate change. Conversely, nearly 5% of the world's greenhouse gas emissions are associated with the health healthcare industry. The management of diabetes and its complications account for a substantial proportion of health services, thus producing large quantities of carbon emissions and plastic waste.

Design & Procedures

- Describe the study, providing details regarding the study intervention (drug, device, physical procedures, manipulation of the subject or the subject's environment, etc.). Discuss justifications for placebo control, discontinuation or delay of standard therapies, and washout periods if applicable. Identify procedures, tests and interventions performed exclusively for research purposes or more frequently than standard of care. Include alternative therapies, concurrent therapies discontinued per protocol, risk benefit ratio, and use of tissue/specimens. Discuss monitoring during washout periods if applicable. Include brief description of follow-up, if any.

This active comparator, effectiveness-implementation RCT will compare EXTEND to EXTEND Plus in a population with PPDM and hypertension (N=220). Our primary effectiveness analyses of these 12-month interventions will occur at 12 months, and persistence of effect will be examined out to 24 months (Aim 1). We will inform future scaling/dissemination in clinical practice by interviewing key stakeholders (n=40) regarding implementation barriers/facilitators and comparing program costs and reimbursement pathways (Aim 2). Finally, we will examine combined mobile monitoring and EHR data as a means to predict patient safety events in the EXTEND cohort over 24 months (Aim 3).

Randomization:
Randomization will occur following the baseline appointment. We will not blind participants to arm assignment because they will receive information on both arms during consent. In order to assure blinding of research assistants conducting outcome data collection, randomization will be managed by the project coordinator. We will use a computer-generated, blocked randomization, stratified by clinic (DPC, Duke Endocrinology, and Duke Outpatient Clinic) and HbA1c

EXTEND procedures.
Participants randomized to EXTEND will receive four mobile monitoring devices to facilitate chronic disease self-management, including a glucose meter and test strips, a BP cuff, a home scale, and an accelerometer. Patients will receive a FDA-cleared glucometer (OneTouch Verio Reflect), a FDA-cleared blood pressure cuff (Withings BPM Connect), a wireless scale (Withings Body), and a wrist-worn accelerometer (Withings Pulse HR). These devices all have associated apps so that data from the devices can be pulled into a smartphone via Bluetooth. These data are retrieved by Validic and then transferred to Duke's data lake hosted by DHTS. When retrieved from the data lake, data will be stored in PACE for analysis. Unless advised differently by your primary providers, participants are encouraged to check their blood glucose 1-4 times daily (based on how often you take diabetes medications), measure BP daily, weigh daily, and monitor activity daily. These data are not monitored by our staff, and EXTEND patients do

not receive additional telehealth services. The EXTEND group continues chronic disease care with their existing providers during the study and are instructed at baseline to address management questions via their primary clinics' established avenues (as would be the case for any patient using mobile monitoring in clinical practice). Our team will provide technical support throughout the study. Our primary rationale for designing EXTEND as an active comparator trial is that all participants must have PPDM, so have thus established themselves as non-responders to clinic-based care. As such, a usual care (UC) control would be inappropriate. Moreover, although mobile monitoring devices are increasingly common, their evidence as aids to patient self-management in clinic-refractory chronic diseases is limited; our chosen approach will thus allow for a much-needed, rigorous examination of mobile monitoring's clinical impact in a clinic-refractory population. Finally, our active comparator approach will permit data collection for Aim 3, our novel examination of using mobile monitoring data to predict patient safety events.

NOTE: Participants who use a continuous glucose monitor may continue using it as directed by their primary providers; at study outcome visits, we will ask for permission to access the continuous glucose monitor data using standard Duke clinic approaches, and analyze it for study purposes.

EXTEND Plus procedures.
For EXTEND Plus, each intervention component (mobile monitoring, self-management support, and medication management) is administered by clinical registered nurses (RNs), as would be the case in clinical practice. For the EXTEND Plus' medication management component, RNs also work in conjunction with a PharmD study clinician affiliated with their clinic. The PharmD with prescribing privileges is the one who ultimately optimizes the medications, as is current standard of practice. RN and PharmD training is comprised of sessions led by the study PIs; training processes are guided by our pilot work. RNs and PharmDs receive copies of the EXTEND Plus manual containing study materials and procedures. Research staff do not participate in delivering EXTEND Plus, though they do manage research tasks (enrollment, outcome assessment, tech support). All participants continue care with their existing providers during the study. The RNs deliver EXTEND Plus via scheduled telephone encounters throughout the 12-month intervention. The initial encounter frequency is every two weeks, but may be extended to every four weeks for patients achieving treatment goals or at the EXTEND Plus team and patient's discretion. In addition to contacting patients by phone, the EXTEND Plus team may utilize other standard, Duke-approved approaches to interact with patients, including MyChart and patient-provided email addresses. Per American Diabetes Association (ADA) guidelines, HbA1c goals are individualized based on age, comorbidities, and hypoglycemia risk; most patients will target <7.0% to <8.0% (as should also be the case for EXTEND patients). BP targets follow ADA guidelines; most will target BP <140/90 mmHg, and for those with atherosclerotic cardiovascular disease (ASCVD) or a 10-year ASCVD risk ≥15%, a BP goal of <130/80 mmHg may be considered.

NOTE: Although the EXTEND Plus team will receive notifications about abnormal blood glucose, BP, weight, and activity readings at least once every business day, data will not be monitored 24/7. For any concerns about abnormal blood glucose, BP, weight, or activity readings, or any other urgent concerns, participants should reach out to the EXTEND Plus team and/or their primary clinic team. Also, participants who use a continuous glucose monitor may continue using it as directed by their primary providers; the EXTEND Plus team can use continuous glucose monitor data to help with diabetes management. At study outcome visits, we will also ask for permission to access the continuous glucose monitor data using standard Duke clinic approaches, and analyze it for study purposes.

The three EXTEND Plus intervention components are detailed below:

- Mobile monitoring.
    - Patients receive the same four mobile monitoring devices as in EXTEND; data are likewise compiled on the patient's smartphone and ultimately pulled into Duke's data lake hosted by DHTS. For EXTEND Plus, mobile monitoring data will be available in the EHR for viewing by the RN interventionists. At each every-two-week intervention encounter, the RN contacts the participant by phone to review interim mobile monitoring data, reconcile medications, and assess self-reported medication adherence. The RN then compiles this information into an EHR-based report (using templates developed during our pilot work). Patients check self-monitored blood glucose (SMBG) 1-4 times daily based on their treatment regimen, measure BP daily, weigh daily, and monitor activity daily.
- Self-management support.
    - This component utilizes behavioral strategies rooted in social cognitive theory, and content refined during >10 trials by co-investigator Hayden Bosworth. We have adapted this content for EXTEND Plus through our pilot work. Our approach builds patients' self-management capacities by focusing on knowledge and self-efficacy, key determinants of chronic disease control. This self-management support component addresses common issues underlying PPDM and hypertension using a module-based approach. RNs deliver a module by phone during roughly every other intervention encounter; modules utilize patient-centered strategies such as tailoring and goal setting, and all material is at an 8th grade reading level. Module topics include use of SMBG, BP monitoring, developing a diet plan, medication adherence, hypoglycemia and hypotension self-management, self-managing insulin, and more (we have developed 20 unique modules). In addition, this intervention component

addresses diet and activity self-management during each encounter, with an aim to enhance diabetes and BP control by targeting >5% weight loss via a 500-750 Calorie/day deficit. Our every-two-week contact frequency and 12-month duration is consistent with ADA recommendations, and a recent review supports the effectiveness of lifestyle content delivered as part of a multifactorial phone intervention. An early module focuses on developing an individualized diet plan; diets will incorporate Dietary Approaches to Stop Hypertension (DASH) principles, and because isocaloric diets are similarly effective regardless of macronutrient composition, composition is tailored to patient preferences. As per ADA guidelines, our self-management component encourages ≥150 minutes of moderate-to-vigorous intensity physical activity per week. Our pilot work corroborates the impact of our self-management support component; we saw a significant improvement in diabetes self-care versus control, and patients cited "establishment of new routines" and "greater awareness of blood sugar" as benefits of participation.

- Medication management.
    - Our medication management approach has two key features associated with high impact; it facilitates frequent contact between patients and intervention staff, and allows EXTEND Plus clinicians to modify medications. As above, after each encounter, the RN compiles a report summarizing interim mobile monitoring data, reconciled medication list, self-reported medication adherence, and the self-management and diet/activity content delivered. The RN relays this report to the PharmD study clinician via the EHR, who considers treatment changes based on diabetes and hypertension medication protocols developed during our pilot work. We target: 1) fasting blood glucose 90-150 mg/dL and pre-prandial blood glucose 140-180 mg/dL (may be tailored for individual goals or hypoglycemia); and 2) BP <140/90 mm Hg (or 130/80 for high-risk patients as above). The PharmD notifies the RN of any recommendations via a template addendum to the EHR report, and the RN contacts the participant by phone to implement changes. Primary providers are alerted to changes via the EHR.
    - Of note, the RN does not optimize the medications. They compile the report and send this information in the EHR to the PharmD to optimize medications according to protocols. This role of the PharmD is current standard of practice and within their scope of practice.

Follow-up:
Follow-up assessments will occur at 3-, 6-, 9-, 12-, 18-, and 24-months. Each follow-up will include a brief, in-person assessment (HbA1c, blood pressure, weight) with or without additional completion of follow-up surveys. Patients may complete these surveys remotely through REDCap or in person, if preferred; surveys will become available 1-2 weeks before the 6-, 12-, 18- and 24-month assessments.

Participants will be sent a CGM data retrieval email to start gathering CGM data from participants who have a CGM (continuous glucose monitor). Participants will be given or mailed a Thank You note at their 24-month mark in the study. Participants will be sent emails when they reach their 12- and 24-month timepoints alerting them of this benchmark. Amendment 26 updated the email that goes out to all participants when they hit 24-months in the study

Addendum:
Cross-sectional survey of the study cohort assessing climate vulnerability and social determinant of health (SDOH) measures. Participants will complete a REDCap survey during an outcome visit from the parent trial (preferred method) or through an e-mail to participants with a survey link (second and third attempts).

AAim 4: Secondary analysis of EHR clinical notes from enrolled participants who completed the AHC-HRSN screening, with no new patient contact or data collection. Clinical notes are extracted from the EHR into PACE, where large language models (gpt-5.5, gpt-5-mini, Gemma 4, grok 4.1, Qwen 3.5, and Kimi) and encoder-based NLP models are used to extract SDOH for comparison against participants' AHC-HRSN survey responses.

Selection of Subjects

- List inclusion/exclusion criteria and how subjects will be identified.

Aim 1: Eligible participants will meet the following criteria: 1) type 2 diabetes by ICD-10 code (E11.xx) or treatment with glucose-lowering medication or mention in clinical notes; 2) 30-75 years old (to assure a type 2 diabetes population that will benefit from tighter control); 3) Poor diabetes control as indicated by at least 1 HbA1c ≥8.0% with NO HbA1c less than 8.0% over the 6 months; 4) At least 1 appointment (office visit, appointment, initial consult, telemedicine) at primary clinic site over the past year; 5) Hypertension by ICD-10 code (I10-I16) OR treatment with blood pressure-lowering medication OR

mention in clinical notes; 6) Poor hypertension control as indicated by a clinic systolic BP >140 AND/OR diastolic BP >90 over past year; 6) use an Apple iPhone or Android smartphone; 7) can provide informed consent. For feasibility, we will focus on patients who speak/read English during this trial. Participation will not require in-home Internet – a smartphone data plan will be adequate, which will promote racial and socioeconomic diversity (see section A.7).

Patients will be excluded if they: 1) have dementia, psychosis, or life-limiting illness; 2) have had an acute coronary event in past year; 3) have had a hypoglycemic seizure/coma over the past year; 4) reside in a nursing home; 5) use an insulin pump; 6) are or plan to become pregnant; and 7) are unable or unwilling to use necessary technology to participate in the study.

We have worked with Duke Primary Care (DPC) and Duke Endocrinology to derive conservative estimates of potentially eligible patients for EXTEND. DPC cares for 22,000 patients with type 2 diabetes; ~15% have PPDM (n=3,300), and 28% of these have poorly-controlled hypertension (n=924). Duke Endocrinology cares for 12,000 patients with type 2 diabetes; ~35% have PPDM (n=4,200), and 28% of these have poorly-controlled hypertension (n=1,176). Thus, well over 2,000 patients should initially meet our inclusion criteria, and this group will self-renew as new individuals develop PPDM and uncontrolled hypertension. Based on our team's recruitment record and close alignment with DPC and Duke Endocrinology, enrolling 220 patients will be highly feasible. We will include the Duke Outpatient Clinic as an additional study site in order to help address clinical needs at this clinic and to provide a larger pool of patients from which to recruit.

Aim 2: Qualitative interviews will be conducted with Duke Health Technology Solutions (DHTS) staff and EXTEND study staff who developed and implemented processes and procedures to facilitate the start of the EXTEND trial within Duke University Health System (DUHS). Data collected in these interviews will be used to identify the pre-implementation characteristics and activities that should be completed prior to implementing a telehealth intervention within a large academic health care system.

Addendum:
All participants in the parent trial. All enrolled patients will have the option to complete a 10–15-minute survey to help us understand the role of climate change and other social drivers of health on diabetes self-management and intervention engagement.

Subject Recruitment and Compensation

- Describe recruitment procedures, including what method(s) will be used, when the study will be introduced to potential participants and by whom. If any follow-up contact is planned, describe the proposed method and timing. Describe how you will ensure that subject selection is equitable and all relevant demographic groups have access to study participation (per 45 CFR 46.111(a) (3)). Include information about how many DUHS participants will be recruited. If participants are to be compensated and/or reimbursed, provide specific prorated amounts to be provided for expenses such as travel and /or lost wages, and/or for inducement to participate.

Patient Recruitment. For Aim 1, we will enroll 220 patients using IRB-approved processes. Staff will identify potentially eligible patients through EHR screening. Those who have activated MyCharts will first receive a MyChart research message with contact opt-out instructions. All potential patients will then receive an informational email. Staff will contact patients who do not opt out, screen them for eligibility, and schedule a baseline appointment if appropriate. Eligible patients will provide informed eConsent through REDCap before the baseline appointment or at the baseline appointment, if preferred; for others, reason for ineligibility will be recorded in a de-identified database. Following eConsent, patients will receive their baseline surveys, which can be completed remotely before their baseline visit or at their baseline assessment. The baseline visit will also include clinical assessments (POC or lab/clinic-based HbA1c, BP, weight, height);patients with HbA1c <7.5% at the time of this baseline assessment will be excluded from the study prior to being randomized due to their improved diabetes control. Once eligibility is confirmed, staff will orient participants, distribute mobile monitoring devices, and send a welcome email with details regarding which group they've been randomized into. Each enrollee will receive a copy of the consent in their email from REDCap (see Recruitment and Retention). For Aim 2, 20 enrolled patients will be asked to complete qualitative interviews during the study and all enrolled patients will be asked to complete an optional survey regarding climate change and other social drivers.

Participants will receive compensation for time and travel in the form of $75 for completing the baseline assessment and $50 for each completed follow-up assessment ($375 total). Additionally, patients will be able to keep all mobile monitoring devices provided for the study (glucometer, BP cuff, scale, and activity

tracker) after the 12- month intervention (approximate value $287). Finally, patients in both groups will receive 3 months of glucose strips at baseline and the 3-, 6-, and 9-month assessments (approximate value $240). If available, additional glucose strips may be provided after the 12-month period. The 20 patients participating in Aim 2 will also receive $50.

Participants will be eligible to receive study materials including a water bottle, phone wallet, folder, and tote bag. These are for patients to put all of the devices in a bag and to facilitate engagement with self-monitoring over time.

Staff Recruitment. For Aim 2, we will recruit up to 50 DUHS staff members for qualitative phone interviews, including prescribers, case managers/nurses, administrators, and information technology specialists. The PIs will identify appropriate participants from DUSON, DOCR, DPC, Duke Endocrinology, Duke Outpatient Clinic, and the DUHS Digital Strategy Office, and will initiate e-mail contact after obtaining leadership approval. Input on EXTEND's implementation and dissemination will be sought from interviewees; each will provide verbal consent before beginning. Input on EXTEND's implementation and dissemenation will be sought from interviewees throughout the study.

EXTEND study team members will not be compensated for completing a qualitative interview. We will compensate DHTS staff with $50 for completing a qualitative interview.

Aim 2: Precise description of the group or individual(s) to be enrolled:

1. DHTS Staff (n=6-8) members who assisted in the development of processes and procedures for the implementation and conduct of the EXTEND study.
2. EXTEND study team individuals (n=4) who worked with DUHS Of note, we will not interview the EXTEND study MPIs (n=2).

Relationship of the group or individual(s) to the study team, including supervisory relationships:

1. DHTS staff do not have any direct, or supervisory relationships with the study team conducting the interviews.
2. EXTEND study team individuals who are conducting the qualitative interviews do not have any supervisory relationships over the EXTEND study staff who will be interviewed. All data from the study team interviews will be de-identified. Interview data will be aggregated among all EXTEND study staff interviews and not reported individually.

These interviews are being conducted with Duke Health Technology Solutions (DHTS) and EXTEND study staff from the Duke University Schools of Nursing (DUSON) and Medicine. Both teams worked together to implement procedures to facilitate the EXTEND trial within Duke University Health System (DUHS). We are conducting these interviews with DUHS staff because DUHS Staff developed the capability to prescribe remote monitoring devices to patients and subsequently pull data from the devices into Duke's electronic health record (EHR). These data are then visualized and used for clinical care. We are conducting interviews with the EXTEND study team as EXTEND study team members worked with DUHS to select the remote monitoring devices and ensure data from the companies that distribute these devices are useful for care delivery and patient self-management. The 2 primary goals of these interviews are to: (1) better understand barriers and facilitators to implementing the EXTEND trial's data management processes and procedures in regards to workflow, data flow, and device selection; (2) better understand the activities that were undertaken to implement EXTEND's data management processes and procedures in regards to workflow, data flow, and device selection. These interviews will help us identify the following:

- Workflow: Generalizable steps taken to complete tasks (e.g., who does what and when, timeline of activities)
- Data flow: Patient generated health data (PGHD) collected from patients' devices; these data can be combined with other data from the EHR to be aggregated into clinically meaningful information to influence clinical decision-making
- Device selection: Devices, products, and tools selected for use in EXTEND Plus

Importance of including this group or individual(s) in the study

1. DHTS staff developed the capability to prescribe remote monitoring devices to patients and subsequently pull data from the devices into Duke's electronic health record. .
2. EXTEND study team individuals selected the remote monitoring devices and ensure data from the companies that distribute these devices are useful for care delivery and patient self-management. These data are then visualized and use for clinical care. EXTEND study team individuals (n=14) We will not interview the study MPIs (n=2).

Who will consent the group or individual(s) and how the possibility of coercion will be minimized:
A clinical research coordinator (from the Duke University Department of Population Health Sciences) and /or a trained PhD student from the Duke University School of Nursing from the EXTEND qualitative study

team will consent the members of the EXTEND study team and DHTS staff. These two individuals do not currently attend EXTEND study team meetings and do not have supervisory relationships with the EXTEND study staff.

Process for ensuring objective analysis of study results, particularly for friends and family members.
Data collection, analysis, interpretation, and dissemination will be led by an EXTEND co-investigator with qualitative and implementation expertise. All data collection, analysis, interpretation, and dissemination activities will be conducted by the EXTEND qualitative team which includes a clinical research coordinator from the Department of Population health Sciences and a Duke University School of Nursing PhD student. We will follow scientifically rigorous and valid qualitative methods principles when analyzing these interview data, which will include EXTEND study staff.
Analysis of these qualitative data will begin after the first three interviews and this analysis will guide future data collection. The analysis process will be iterative, as initial analysis will inform interview guide questions and probes. The qualitative team will meet weekly during interviewing, coding, and analysis to identify emerging areas, refine the interview guide, and address emergent questions. All transcripts will be de-identified and will not contain information with the interviewee's name to ensure objectivity during coding and analysis Throughout coding and analysis, the qualitative team will work closely together. The findings will be discussed with the EXTEND MPIs and other EXTEND study team members to ensure reliability and validity of the interpretation during weekly and monthly meetings. Importantly, the qualitative team will present an interim analysis, and then final analysis, to the larger EXTEND study team to obtain feedback and ensure findings are reliable and valid. Validity and reliability of findings and the iterative generation of codes will be ensured by working closely with the clinical research coordinator, PhD student, qualitative co-investigator, and EXTEND MPIs. The qualitative coding team will: provide rich descriptions of all codes and themes; discuss codes and coding until consensus is reached for each code and theme; and present any discrepant information. The codebook will describe the creation of the codes and emerging themes and be an audit trail of our actions. Regular meetings will ensure accuracy of coding, validity and reliability, higher level code development, and emerging findings.

Addendum:
Patients who complete the optional climate and social driver survey will receive an additional $50.

Subject's Capacity to Give Legally Effective Consent

- If subjects who do not have the capacity to give legally effective consent are included, describe how diminished capacity will be assessed. Will a periodic reassessment occur? If so, when? Will the subject be consented if the decisional capacity improves?

We will not include subjects who do not have the capacity to give legally effective consent

Study Interventions

- If not already presented in the Design & Procedures section, describe study-related treatment or use of an investigational drug or biologic (with dosages), or device, or use of another form of intervention (i. e., either physical procedures or manipulation of the subject or the subject's environment) for research purposes.

This information is presented above

Risk/Benefit Assessment

- Include a thorough description of how risks and discomforts will be minimized (per 45 CFR 46.111(a) (1 and 2)). Consider physical, psychological, legal, economic and social risks as applicable. If vulnerable

populations are to be included (such as children, pregnant individuals, imprisoned persons or cognitively impaired adults), what special precautions will be used to minimize risks to these subjects? Also identify what available alternatives the person has if he/she chooses not to participate in the study. Describe the possible benefits to the subject. What is the importance of the knowledge expected to result from the research?

The EXTEND trial will use a data and safety monitoring plan including a Data and Safety Monitoring Board (DSMB) as approved by NINR. We will develop standard management practices to protect data, confidentiality and promote security. We will develop procedures for identifying, reviewing and reporting adverse events and unanticipated problems. We do not plan to enroll vulnerable populations such as children, pregnant women, prisoners or cognitively impaired adults.

Participants volunteer to enroll in this study and by not participating it will have no impacts on their plan of care at Duke.

Potential Risks

- Hypoglycemia is an expected adverse effect of diabetes medical therapy, particularly insulin treatment (which will be common in our study population). It is possible that attempting to improve glycemic control in this study will increase the risk of hypoglycemia versus standard care. However, we have mitigated this possibility by utilizing relatively liberal blood glucose targets (fasting blood glucose 90-150 mg/dL, pre-prandial blood glucose 140-180 mg/dL) and individualized HbA1c goals, which may be further relaxed for evidence of hypoglycemia. Further, all patients will be provided with detailed instructions for hypoglycemia management at study outset, and study staff will ensure that patients have access to glucose gel or tabs for hypoglycemia self-treatment, and a glucagon emergency kit for treatment of complicated hypoglycemia if deemed appropriate (i.e., for patients using insulin who have another person in the home to administer glucagon if needed).
- BP will be measured at screening and at each subsequent in-person follow-up. Along with the possibility of high BP, dietary changes and/or weight loss can result in low BP in participants who take BP medications. If the participant's systolic BP is <90 or ≥ 190 mmHg or their diastolic is <60 or ≥ 110 mmHg, a specific protocol will be followed as described below in section 2 (Protection Against Study Risks).
- There is a small risk of minor discomfort or bruising at the site of the upper arm automatic BP cuff. To prevent this, participants will receive the appropriately sized cuff based on their upper arm circumference. Participants will also review information on how to contact the research staff if additional questions, concerns, or new discomfort arise.
- There are small risks of injury or heart problems due to increased participation in physical activity. The study physician (Dr. Crowley) will be available to answer participants' questions during their participation. Participants will also be instructed to consult with their physician/health care team if they have any new health problems or symptoms.
- There is a small risk of inadvertent disclosure of participant data. As our standing operating procedure, we have policies and procedures in place to protect the confidentiality and security of participant data.
- When answering questionnaires during sensitive questions about personal issues may make participants uncomfortable. Participants do not have to answer any question they do not wish to, as will be explained during the consent process and during subsequent visits. Participants could become psychologically distressed during telehealth calls. If necessary, any individual experiencing notable psychological distress will be discussed with Drs. Crowley and Shaw.
- No reproductive risks are expected. Participants are excluded if pregnant or planning to become pregnant. If a participant becomes pregnant during the study, they will be withdrawn from the study.
- There are few potential risks associated with the measures or mobile data to be collected. There is a small risk of inadvertent disclosure of participant data. At enrollment, we will ensure that all sharing options with third party services such as online social networks or other fitness apps are disabled. Participants will be encouraged not to share information with third party services such as online social networks or other fitness apps. However, some participants may opt to do this. Thus, all participants will be encouraged to read the privacy statement for the mobile devices and decide for themselves what information they would like to share.

Protections Against Risk.

Detection of clinically significant problems. It is possible that clinically significant problems not caused by study participation will be detected by study staff. Subjects entering the study will have a history of hypertension and type 2 diabetes so we expect to see abnormal systolic and diastolic values, as well as abnormal glucose values. All values that reach a safety threshold (<90 or >180 systolic BP, <40 or >110 diastolic BP) will be reported to the subjects' care provider.
Protection against risk of abnormal blood glucose. In order to mitigate the risks of treatment-associated hypoglycemia, we are limiting our population to patients <70 years old and those without complicating conditions such as recent cardiac events. Additionally, we are using relatively liberal blood glucose

treatment targets (fasting blood glucose 90-150 mg/dL, pre-prandial blood glucose 140-180 mg/dL) and individualized HbA1c goals, which may be further relaxed as warranted for evidence of hypoglycemia. Further, all patients will be provided with detailed instructions for hypoglycemia management at study outset, and study staff will ensure that patients have access to glucose gel or tabs for hypoglycemia self-treatment, and a glucagon emergency kit for treatment of complicated hypoglycemia if deemed appropriate (i.e., for patients using insulin who have another person in the home to administer glucagon if needed). Finally, patients in the nursing intervention group will receive extensive education regarding hypoglycemia prevention and treatment during the study, which will increase their ability to self-manage any hypoglycemic events that occur.

Participants who have an alert glucose reading during study visits will be assessed for cardiovascular symptoms during the visit. At the screening visit and subsequent visits, if the participant's glucose is ≥400, the participant will be asked if they have any of the following: lightheadedness, dizziness, blurred vision, shortness of breath, or chest pain. If she/he has any of these symptoms, the participant will be advised to go to the emergency room. Study staff will call an ambulance unless the participant objects or has someone else to transport them to the emergency department. The study clinician will then be paged and made aware of the situation. If the participant does not have any of the listed symptoms, they will be advised to contact their primary care provider on the same day. If the participant's glucose is <70, they will be asked if they have any of the following: dizziness, lightheadedness, confusion, chest pain, or shortness of breath. If the participant has any of these symptoms, the participant will be advised to go to the emergency room. Study staff will call an ambulance unless the participant objects or has someone else to transport them to the emergency department. The study physician will then be paged and made aware of the situation. In the absence of the listed symptoms, the participant will be advised to contact their primary care provider within 24 hours.

Protection against risk of abnormal blood pressures. All participants will have poorly-controlled hypertension, and thus will likely be taking hypertension medications prescribed by their health care providers at the outset of the study. It is likely that we will also detect abnormal BP values as a result of increased monitoring during the study. Because of potential high and low BP values, subjects in the intervention arm may have their current hypertension regimen adjusted. Safety monitoring of BP will occur in the context of home BP monitoring as well as BP measurement during data collection visits. An average SBP at any study visit or during home BP monitoring >180 mm Hg and/or diastolic >110 mm Hg will be considered an alert value and trigger assessment by a study clinician. Furthermore, an average BP at any study visit or during a home BP monitoring < 90 systolic or <40 diastolic will also be considered an alert value and trigger an assessment by a study clinician. When participants who have an alert reading at home, the study nurse and clinician will contact them directly to assess cardiovascular symptoms. If at any time participants have symptoms of acute end organ damage (e.g. current chest pain, dyspnea at rest, new onset of blurry vision, or new neurological deficits consistent with a stroke) in the context of an elevated BP measurement (SBP >180, and/or DBP >110), they will be advised and assisted to seek emergency medical care. For participants in the intervention group whose average SBP >180 and DBP >110 or SBP < 90 or DBP < 40 but do not have acute symptoms, the primary provider will be notified and medications will be changed as deemed appropriate by the study team. Follow-up contact with the study staff will occur within one week.

Participants who have an alert BP reading during study visits will be assessed for cardiovascular symptoms during the visit. At the screening visit and subsequent visits, if the participant's systolic BP is ≥190 or diastolic is ≥110, the participant will be asked if they have any of the following: stroke symptoms (weakness on one side of body or loss of vision in one eye, loss of balance, trouble talking), headache, lightheadedness, dizziness, blurred vision, shortness of breath, or chest pain. If she/he has any of these symptoms, the participant will be advised to go to the emergency room. Study staff will call an ambulance unless the participant objects or has someone else to transport them to the emergency department. The study clinician will then be paged and made aware of the situation. If the participant does not have any of the listed symptoms, they will be advised to contact their primary care provider on the same day. If the participant's systolic BP is <90, they will be asked if they have any of the following: dizziness, lightheadedness, recent falls, chest pain, or shortness of breath. If the participant has any of these symptoms, the participant will be advised to go to the emergency room. Study staff will call an ambulance unless the participant objects or has someone else to transport them to the emergency department. The study physician will then be paged and made aware of the situation. In the absence of the listed symptoms, the participant will be advised to contact their primary care provider within 24 hours.

Protection against risk of loss of privacy. There is a small risk of inadvertent disclosure of participant data. Measures will be taken to maintain privacy during in-person sessions.

Protection against risk of other patient discomforts. Sensitive questions about personal issues may make participants uncomfortable. Participants are not required to answer any question they do not wish to, as will be explained during the consent process and during subsequent visits. Some participants could become distressed during telephone calls. This risk is unlikely given the previous research literature and our experience in our prior studies. Study personnel may consult the study physician, and the study team will attempt to determine whether the study is exacerbating a distressing condition; if so, the participant may be withdrawn from the study for their safety.

Potential Benefits of the Proposed Research to Human Subjects and Others

- All participants will receive some level of intervention, as all participants will receive mobile monitoring devices that can be used to further self-management and will transmit data to their health record; thus, we expect all to derive some benefit from participation. This instruction exceeds standard of participant care available to people in the community and involves no direct cost to participants. Participants may learn skills that help them improve HbA1c, SBP/DBP, and reduce weight by adhering to prescribed medication recommendations, dietary recommendations and participating in regular physical activity.
- Those randomized to the EXTEND Plus intervention will receive telehealth services every 2-4 weeks. This has the potential to provide substantial benefit to participants' clinical outcomes, self-care, medication adherence, self-efficacy, and more.
- Although the participants themselves might not derive direct benefit, knowledge gained from the study will assist in the treatment of others with T2DM and hypertension.

Costs to the Subject

- Describe and justify any costs that the subject will incur as a result of participation; ordinarily, subjects should not be expected to pay for research without receiving direct benefit.

There are no costs to the subjects for participating in this study.

Data Management, Analysis and Statistical Considerations

- Describe endpoints and power calculations. Provide a detailed description of how study data will be analyzed, including statistical methods used, and how ineligible subjects will be handled and which subjects will be included for analysis. Include planned sample size justification. Provide estimated time to target accrual and accrual rate. Describe interim analysis including plans to stop accrual during monitoring. Phase I studies, include dose escalation schema and criteria for dose escalation with definition of MTD and DLT.
- **For external collaborators/personnel** who are NOT ENGAGED in the research but are handling de-identified or a limited data set of **Duke** data, include their name, role and a description of the data.

Hypothesis 1a: Compared to EXTEND, EXTEND Plus will improve primary (HbA1c) and secondary outcomes (e.g., blood pressure, weight, self-management measures) at 12 months. We will assess the overall effects of the interventions on HbA1c at 6 and 12 months via two-group t-tests. To understand the differential HbA1c effect between study groups from baseline to 12 months, we will plot HbA1c vs. time (0, 3, 6, 9, 12 months) by study group. To test hypothesis 1a, we will build linear mixed models (LMM) that include fixed effects for linear and/or quadratic time (depending on trends from empirical plots and best fit assessed by statistical indices). Models will also include time-by-group interaction terms, randomization stratification variables, and to account for within-participant correlations over time, a random intercept and random slope for time. Any baseline variables that statistically differ between study groups will be included as model covariates. We will test the null hypotheses that the time by intervention parameter is 0. Secondary outcomes will be tested and modeled similarly to the primary outcome. If any outcome has a heavily skewed distribution, we will appropriately transform the data or use a generalized linear mixed model with an appropriate link function.

Hypothesis 1b: The relative effects of each intervention will be sustained at 24 months. To assess the sustainability of intervention effects, we will perform paired t-tests on primary and secondary outcomes within each intervention group between 12- and 18-month, and 12- and 24-months. To examine between-group effects, we will also construct LMM as for hypothesis 1a, with the inclusion of 18- and 24-month time points.

Hypothesis 1c: Subgroup analyses will identify characteristics associated with high responsiveness to each intervention. In order to explore differences in intervention effects based on patient characteristics identified as markers for engagement in our pilot work (age, sex, race/ethnicity), we will use ANCOVA to ascertain significant interactions between these variables and intervention effects on primary/secondary outcomes.

Missing data. Based on our pilot study, we anticipate no more than 20% missing values in longitudinal outcomes, owing to dropout or missed follow-up assessments. LMM will be fitted with a full maximum likelihood method using all available data. Although we anticipate little missingness for covariates, we will also explicitly address missing data using multiple imputation procedures when needed. We will conduct sensitivity analysis with and without multiple imputation; additional detail may be found in Form E.

Intent-to-treat (ITT). Our primary analysis fulfills the ITT principle, which states all randomized participants must be included and analyzed in the group to which they were randomized. HbA1c will be measured pre-randomization, so we do not expect missing baseline HbA1c or study arm variables in the randomized sample.

Power calculations. For our primary outcome, we performed power analyses using PASS (NCSS, LLC. Kaysville, Utah). Based on existing telemonitoring studies, we conservatively assumed an HbA1c reduction of 0.5% at 12 months in the EXTEND arm. For EXTEND Plus, our pilot data suggest a reduction of 1.3% at 12 months. Thus, we conservatively predict a between-arm HbA1c difference of 0.8% by 12 months. Based on prior work, we conservatively assumed a 20% dropout by 12 months, an HbA1c standard deviation (SD) of 1.6, and a within-patient correlation of 0.5 for HbA1c between baseline and at 12-month follow-up. These conservative estimates indicate that 110 patients per arm will provide 90% power to detect a between-arm difference in HbA1c change of 0.8% (Cohen's d=0.5) at 5% alpha level. Ad-hoc power analysis for secondary outcomes are provided in form E.

Consideration of effect modification by social and biological variables. As per hypothesis 1c, we will assess for heterogeneity of treatment effect based on key patient variables (age, sex, race/ethnicity).

Aim 2A (qualitative interviews). Interviews will be transcribed verbatim using an approved transcription service. Identifying information will be removed from all transcripts. We will conduct thematic analysis[133] using NVivo qualitative data analysis software or Microsoft Excel and Microsoft Word; analyses of patient and stakeholder transcripts will be conducted separately but will follow the same process. First, after three patient/stakeholder interviews, we will begin preliminary analyses to inform refinement of questions in each interview guide, which will enhance the value of future data collection.[134] First-level coding will be guided by a priori codes addressing conceptual model constructs (perceived burden, patient capacity, etc., see Figure 2) and will explore barriers and facilitators related to the interventions (Appendix A and B). Codes will be examined in the context of PPDM and hypertension, experiences during the EXTEND interventions, impressions of EXTEND Plus' three intervention components, and general thoughts on implementing and disseminating EXTEND.[133] Then, using matrices, we will identify similarities and differences across patient/stakeholder characteristics.[135,136] Our coding team will: 1) assure the validity and reliability of findings and the iterative generation of codes by working closely with the research team;[137] 2) provide rich descriptions of all codes and themes; 3) reach consensus through discussion for each code and theme; 4) triangulate data from quantitative and qualitative sources; and 5) present any discrepant information.[137] We will conduct a second analysis of the qualitative data using CoPilot and DukeGpt to identify how generative AI can supplement the conduct of qualitative research in clinical research. To facilitate this analysis, we will upload de-identified note sheets to the Duke-approved Microsoft CoPilot and DukeGpt. For all documents uploaded to CoPilot and DukeGpt we will remove: (1) the 18 HIPPA identifiers; and (2) create dummy study IDs. Once the documents are uploaded, we will use prompts to summarize the findings. We will then compare these findings to the human-generated findings.

Aim 2B (health economic analyses). Our economic analyses seek to: 1) determine intervention costs (see section C.14) and compare by trial arm; 2) simulate the impact of recent and proposed changes in Medicare and Medicaid reimbursement on the business case for the EXTEND interventions; and 3) estimate the budget impact of implementing the EXTEND interventions within DUHS. Within each intervention arm, we will evaluate unadjusted and covariate-adjusted differences in direct costs by age, sex, and race. The association of patient characteristics with patient-level direct costs will be evaluated using a generalized linear model (SAS PROC GLM) with family and link function to fit the distribution of the outcome. Budget impact will be evaluated by comparing the expected costs of system-wide intervention implementation against expected revenues. Expected costs will be estimated by calculating per patient incremental costs of the intervention and then multiplying by the number of eligible patients in DUHS. Expected Medicare fee-for-service (FFS) revenues will be estimated by multiplying the number of eligible reimbursable services by the CMS reimbursement. Sensitivity analyses will assess the impact of varying the length, number, and timing of EXTEND services on FFS revenue eligibility. We will also simulate outcomes under different reimbursement models using probabilistic sensitivity analyses; Monte Carlo simulations will be conducted in Excel using Crystal Ball. If there is a difference in utilization and indirect costs between the interventions, we will estimate the expected change in per capita spending that may impact financial performance for health systems participating in ACOs.
** Zhang Zhang, Ph.D., MSc, a post-doctoral fellow at Johns Hopkins Bloomberg School of Public Health, will not be engaged in research but will help co-author upcoming papers by reviewing de-identified, aggregate data, which has already been analyzed by the study team for use in publications.

Aim 3: Explore the value of combining mobile monitoring and EHR data for predicting patient safety events in the EXTEND study cohort over 24 months. We will use a novel and computationally efficient two-step approach to dynamically predict time-to-event for each outcome (hospitalization, emergency visits) based on current and historical data, with a moving time window. In the first step, functional principal component analysis (FPCA) will be used to reduce data dimension and capture individual trajectories from intensive longitudinal data collected through multiple mobile monitoring devices. Trajectories for each individual's

mobile health devices will be summarized as a set of FPC scores. In the second step, we will build a time-varying Cox regression model for each outcome, including FPC scores as new covariates. These Cox models will also include as covariates all relevant baseline demographics (e.g., age, sex, race/ethnicity), clinical data (e.g., medical comorbidities, medication prescriptions) and utilization variables (e.g., Endocrinology referral, PCP type (MD/NP/PA), clinic location, prior ED visit and hospitalization). Group LASSO will be used for variable selection. To assess the predictive model performance, we will calculate and report weighted time-dependent area under the curve (AUC). Dynamic expected Brier scores will be calculated to assess the accuracy of individual risk prediction. DUHS is highly interested in this novel approach for using mobile monitoring and EHR data to predict patient safety events, and will work with our team to implement and disseminate this approach as part of clinical care.

Addendum:
AAim 1: We will undertake a comprehensive characterization of the climate vulnerability of the EXTEND study cohort. This characterization will utilize a robust heat stress index using Wet Bulb Globe Temperature (WBGT) and the Climate Vulnerability Index (CVI). We will utilize historical climate data to construct a geographical representation of WBGT values across the study area, providing a perspective on climate vulnerability grounded in the living conditions experienced by each participant over an extended period. This method allows for a deep understanding of the patterns of heat stress that participants might be exposed to in their geographical locations. Additionally, the WBGT calculated from nearby weather stations and the Real-Time Mesoscale Analysis (RTMA) will allow for highly local, individual-level analysis of the threat of extreme heat on cohort members. The RTMA, managed by NOAA's National Centers for Environmental Prediction, is a tool offering hourly high-resolution analyses of near-surface weather conditions, leveraging both conventional and satellite-derived observations. To refine our analysis, we will integrate WBGT data from the study area with the specific dates and times of participants' appointments. This approach will allow us to quantify the extent of heat exposure that participants were able to avoid through the use of telehealth services instead of in-person visits to the clinic, thereby demonstrating the role of telehealth in reducing vulnerability to heat stress during extreme weather events.

The CVI is a quantitative assessment of specific vulnerabilities, risks, and disparities related to climate change by census track. CVI integrates four baseline vulnerabilities that reduce resilience (health, social /economic, infrastructure, and environment) and three climate change risks that may adversely affect individuals and communities (health, social/economic, extreme events). The CVI will be calculated for all participants based upon their home address.

AAim 2: Area Deprivation Index (ADI) and CMS Social Needs Screening Tool results will be summarized descriptively, with each domain operationalized ordinally. We will examine unadjusted, cross-sectional associations between each SDOH domain and each climate vulnerability measure, respectively (WBGT and Climate Vulnerability Index). To account for the ordinal nature of the ADI and CMS SDOH variables, we will utilize Kruskal-Wallis tests. We will then assess adjusted associations between SDOH domains (independent variables) and climate vulnerabilities (dependent variables) using linear regression models that include demographic variables as covariates.

AAim 3: We will calculate miles of travel for in-person care in each arm over the course of the study using GPS data to measure travel distance from each participant’s residence to their primary clinic. We will then use these travel distance figures to estimate total and mean per-patient travel time prevented, gasoline consumption prevented in gallons based on EPA figures (https://www.epa.gov/fueleconomy), and travel costs prevented in each arm based on AAA data (https://gasprices.aaa.com/). Based on gasoline consumption prevented, we will also use the EPA Greenhouse Gas Equivalencies Calculator to estimate total and mean per-patient GHG production prevented over the course of the study (https://www.epa.gov /energy/greenhouse-gas-equivalencies-calculator). We will summarize our findings using descriptive statistics and perform between-arm statistical comparisons using t-tests.

AAim 4: We will retrieve participants' EHR clinical notes covering the relevant study period and extract them from the EHR into PACE. All LLM inference will run through the Duke Health AI Studio API, which provides institutionally governed access to these models inside Duke's protected environment, so note text and PHI are not transmitted to public or external endpoints, and analysis code will be written in Python and run within PACE. Each model will extract SDOH domains that match the AHC-HRSN domains (for example housing instability, food insecurity, transportation, utilities, and interpersonal safety) from the clinical notes, and we will compare each model's note-derived SDOH against participants' self-reported AHC-HRSN responses, treating the survey as the reference standard. Agreement will be summarized per domain, including overall agreement, positive and negative concordance, and cases documented in notes but not reported on the survey or reported on the survey but absent from notes. We will also test whether an LLM-augmented SDOH lexicon and few-shot prompting improve extraction relative to a baseline prompt, comparing performance across models and prompting strategies. All note text will remain within PACE, analytic datasets will carry only the study ID with direct identifiers removed, and no note text will leave the protected environment.

[redacted], will not be engaged in research but will review preliminary results to help propose alternative modeling

approaches and interpret the findings. His contribution will be recognized in publications.

Data & Safety Monitoring

- Summarize safety concerns, and describe the methods to monitor research subjects and their data to ensure their safety, including who will monitor the data, and the frequency of such monitoring. If a data monitoring committee will be used, describe its operation, including stopping rules and frequency of review, and if it is independent of the sponsor (per 45 CFR 46.111(a) (6)).

Data and Safety Monitoring Board
We will convene and utilize a Data and Safety Monitoring Board (DSMB). These 5 voting members, which includes a Chair, will be external to the study team, with expertise in clinical research trials, diabetes and hypertension management, telehealth and biostatistics, ethics of clinical research, and expert in the work of DSMBs. The DSMB will also have an Executive Secretary who is not involved with the study team or study and who is a non-voting, ex-officio member of the DSMB with clinical trial expertise. The DSMB will be charged with reviewing safety and trial progress and providing advice with respect to study continuation, modification, and termination. Establishment and governance of the DSMB will follow recommendations by the Duke Health Institutional Review Board (IRB) and the NINR policy for data and safety monitoring of clinical trials. A charter as described in the NINR policy will be developed and approved by the DSMB. Meetings of the DSMB will encompass open, closed and executive sessions and summaries and minutes developed as described in the NINR policy for external DSMBs.

When serving on the DSMB for an individual protocol, a DSMB member has a conflict of interest if on the protocol under review he or she, or his/her spouse, domestic partner, or dependents:

- Serves as PI, co-investigator, key personnel, or likely author on publications resulting from the protocol under review (the DSMB may waive this requirement as needed);
- Is involved in monitoring, analysis, or evaluation of participants on the protocol under review;
- Is in a position that gives him or her the ability to influence the conduct of the protocol in any role other than that of a DSMB member;
- Has any intellectual property or financial conflict of interest with the protocol under review.

Certain other activities are not viewed as constituting conflicts of interest but must be reported annually to the DSMB chair. These include: the participation of a member in educational activities supported by the funding agency; the participation of members in other research projects supported by the funding agency; and occasional scientific consulting to the funding agency on issues not related to the product in the protocol and for which there is no financial payment or other compensation. Committee members who have a conflict of interest may answer DSMB member questions, but must remove themselves during sensitive discussions and recuse themselves from voting on the protocol in which they have a conflict, unless the DSMB (absent the member or staff person with a conflict of interest) determines that these guidelines should be waived. A DSMB member may be from the same department or research program as the MPIs whose protocol is under review if none of the above referenced conflict of interest criteria are present.

The DSMB will meet with the MPIs (Shaw & Crowley) and the study biostatisticians (Yang & Hatch) as shown in Table 1 below (more frequently if issues regarding enrollment or safety are encountered).

Contact PI (Shaw) will be responsible for submitting necessary reports to NINR.

Procedures
In providing oversight for the conduct of this study, the DSMB will meet at least annually as shown in Table 1 below (more frequently if issues regarding enrollment or safety are encountered). At these meetings, the DSMB will review protocol-specific reports created by statisticians using data pulled from REDCap. These standard reports will include an overview of study objectives, a review of actual and projected accrual rates, an evaluation of participant demographics for balance of randomization, a summary of any protocol amendments, and a summary of the number and seriousness of adverse events (AEs).

The DSMB meetings will consist of open and closed portions. During the open session, the PIs and their staff are invited to be present, and only aggregate data will be discussed to reduce the risk of misleading conclusions. The closed session will be restricted to DSMB members, administrative staff, and any

appropriate invited guests and will consist of discussion of accumulating data by assigned intervention arm when applicable. During the closed session, members will review the DSMB report prepared. The report will include the following items:

- Study progress (e.g. overall accrual, accrual rates)
- AEs, especially SAEs
- Data quality - to potentially address data quality, the DSMB reserves the right to review the data, accompanying source documentation, or other relevant study data materials, if requested.
- Impact of findings on the risk-benefit ratio

Table 1. Schedule of Monitoring Procedures

Activity	Frequency	Responsible Person	Shared with
Auditing 10% participant records for compliance with IRB and informed consent requirements	6 months after 1st enrollee, then annually thereafter during data collection phase	Center for Nursing Research (Bishop)	MPIs, research team, DSMB, IRB
Auditing 10% of participant records to verify source documents	6 months after 1st enrollee, then annually thereafter during data collection phase	Center for Nursing Research (Bishop)	MPIs, research team, DSMB, IRB
Auditing 10% of participant records to ensure adherence to protocol	6 months after 1st enrollee, then annually thereafter during data collection phase	Center for Nursing Research (Bishop)	MPIs, research team, DSMB, IRB
EXTEND-Nursing intervention fidelity assessment: *Encounters*	Weekly during intervention delivery	Project Coordinator (Pennington)	MPIs, research team, DSMB
EXTEND-Nursing intervention fidelity assessment: *Intervention Delivery*	Shadow 5-10 encounters by each RN to ensure consistency in intervention delivery	Project Coordinator (Pennington)	MPIs, research team, DSMB
EXTEND-Nursing intervention fidelity assessment: *Medication Management*	Periodic case review meetings (monthly the first 3 months of and quarterly to semiannually thereafter)	Project Coordinator (Pennington)	MPIs, research team, DSMB
Review of research protocol, trial progress, data integrity, recruitment/enrollment /retention, participant risk vs benefit, other factors as needed	Annually	DSMB	MPIs, research team, IRB, NINR