STU#: STU00217555

**PROTOCOL TITLE:** **P**henotyping **A**dherence **T**hrough **T**echnology-**E**nabled **R**eports and **N**avigation: The PATTERN Study

**PRINCIPAL INVESTIGATOR:**

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**VERSION DATE:**

*07.09.24*

## STUDY SUMMARY:

| | |
|---|---|
| Investigational Agent(s) (Drugs or Devices) | NA |
| IND / IDE / HDE # | |
| Indicate Special Population(s) | ☐ Children<br>☐ Children who are wards of the state<br>☐ Adults Unable to Consent<br>☐ Cognitively Impaired Adults<br>☐ Neonates of Uncertain Viability<br>☐ Pregnant Women<br>☐ Prisoners (or other detained/paroled individuals)<br>☐ Students/Employees |
| Sample Size | 107 to 110 |
| Funding Source | NIA: Northwestern Pepper Center |
| Indicate the type of consent to be obtained | ☒ Written<br>☒ Verbal/Waiver of Documentation of Informed Consent<br>☒ Waiver of HIPAA Authorization<br>☐ Waiver/Alteration of Consent Process |
| Site | ☐ Lead Site ( For A Multiple Site Research Study)<br>☐ Data Coordinating Center (DCC) |
| Research Related Radiation Exposure | ☐ Yes<br>☒ No |
| DSMB / DMC / IDMC | ☐ Yes<br>☒ No |

**OBJECTIVES:**

We will adapt and pilot test a technology-enabled, primary care strategy for routinely monitoring medication use and adherence among older adults with multiple chronic conditions and polypharmacy. As part of the monitoring process, we will phenotype adherence challenges and link patients to appropriate clinic-based resources to address identified concerns. The study we will be adapting from is an ongoing trial (TAKE IT), IRB approved as STU00204465. Our specific aims are:

**Aim 1: Adapt the PATTERN intervention for use in primary care using input from key stakeholders**
In months 1 to 8, we will conduct key informant interviews with primary care patients (up to N=15), clinicians and administrators (up to N=15) to learn how the intervention, originally designed for a resourced, subspecialty setting, should be refined to meet new user needs. These activities will be guided by the Agency for Health Care Research and Quality's MCC Model and informed by the expertise of the Northwestern Pepper Center's **Design**, **Measurement**, and **Analytics Cores.**

**Aim 2: Assess the PATTERN intervention's feasibility and acceptability for use in primary care.**
In months 9 to 24, we will implement a 2-arm, patient-randomized pilot study at one or more NM internal medicine practices. Adults over 65 (N=80) with an upcoming primary care visit (within the next ~1 week, with MCC and polypharmacy, defined as taking ≥8 chronic medications, will be recruited over 6 months, and followed for 6 months (n=40 per study arm). Interviews will evaluate participants' experiences with the PATTERN intervention, regimen knowledge, and adherence (via self-report) utilizing a post-visit survey. The specific flags per question on the survey (the point at which someone is classified as having a phenotyped adherence concern) will be determined by the participating practice. Fidelity (receipt of portal assessment and time to completion, care response to adherence concerns, etc.) and clinical outcomes will be captured in the EHR.

## BACKGROUND:

The population of adults over 65 in the U.S. is growing at a rate 3-fold higher than those under 65, presenting unique challenges to primary care practices. Older adults are more likely to have multiple chronic conditions (MCC), and associated polypharmacy (often defined as taking ≥ 5 prescription medications). As a result, problems with treatment adherence are common; prior estimates have found 30 to 50% of community-dwelling, older adults over 65 demonstrate poor medication adherence. These individuals are at subsequent greater risk for suboptimal treatment benefits and adverse drug events, which are also more likely to occur in primary vs. specialty care, and among older adults with MCC. Studies have also shown that inadequate adherence is associated with poorer health-related quality of life, higher healthcare costs and increased mortality risk.

The Model of Medication Self-Management, co-developed by Northwestern faculty, has facilitated the deconstruction of patient medication use and was further developed to categorize adherence barriers as **cognitive** (e.g., forgetfulness), **psychological** (e.g., health literacy, depression, motivation), **medical** (e.g., acute illness), **regimen** (e.g., side effects, complex dosing schedules), **social** (e.g., transportation, support) and **economic** (e.g., cost). Given this heterogeneity, interventions should be informed by a patient's own report of perceived barriers to address their specific concerns.

An ongoing Northwestern trial ('TAKE IT'; R01DK110172) has been able to leverage an electronic health record (EHR) platform and its linked patient portal (Epic, MyChart [MyNM]) to: 1) routinely engage new adult kidney transplant recipients via monthly portal-based adherence

assessments; 2) flag and phenotype reported adherence concerns; 3) alert care teams via secure messaging of the specific adherence concern(s); and 4) mobilize available resources tailored to identified barriers (e.g. SMS text reminders for cognitive barriers, a comprehensive medication review via phone or video telehealth to address regimen complexity, social work referral for social or economic concerns, etc.) following a standard protocol. A planned, preliminary review of the TAKE IT strategy's fidelity has found that most (83%) intervention participants complete the assessments, with 35% reporting one or more adherence barriers (regimen-related (45%), cognitive (27%), medical (20%), and psychological (16%)). Among patients reporting barriers, the care team was mobilized in 96% of cases with an acknowledged response. *No disparities have been found by age in terms of portal assessment completion*.

While the TAKE IT trial is still active, it shows promise as a feasible and acceptable means to engage patients beyond the point of care, specifically in the context of monitoring regimen adherence, and mobilizing care teams. Another recent PCORI trial co-led by Northwestern Pepper faculty utilized a similar means of monitoring treatment adherence, including phenotyping concerns and patient needs among older adults with asthma. Intervention participants exhibited significantly better medication adherence and quality of life at 12 months.

We will adapt the already-built TAKE IT strategy for use in primary care, targeting older adults with MCC and polypharmacy (using Medicare Part D medication therapy management criteria of ≥8 medications). This intervention, renamed as the PATTERN study (**P**henotyping **A**dherence **T**hrough **T**echnology-**E**nabled **R**eports and **N**avigation) will be pilot tested at one or more Northwestern Medicine (**NM**) primary care practices to determine its acceptability, feasibility, and preliminary fidelity.

**STUDY ENDPOINTS:**

Regimen adherence utilizing a post-visit survey as measured by ARMS- D and/or ASK-12 is the **primary outcome** of interest.

| **Variable** | **Instrument(s) or Measure(s)** | **Source** | **Timing & Window** | | |
|---|---|---|---|---|---|
| | | | **Screener** | **Post Visit Survey** | **6M** |
| **Outcome Measures** | | | **Phone** | **Phone** | |
| Medication Adherence | ASK-12 and ARM-D | self-report | | x | |
| Clinical outcomes | HbA1c | chart / EDW | | x | x |
| | Cholesterol panel | chart / EDW | | x | x |
| | systolic/diastolic blood pressure | chart / EDW | | x | x |
| Acceptability | Qualitative | Theoretical Framework of Acceptability | | x | |

**Secondary outcomes** include clinical outcomes (e.g. A1c, blood pressure, cholesterol panel). Relationships between adherence and potential confounders (age, comorbidity, regimen complexity, internet use, dose of intervention, health literacy, patient activation, social support) will also be examined. Acceptability and fidelity/feasibility will also be examined. This may include examining how many participants in the intervention arm completed the adherence questionnaire and how many of those indicating an adherence challenge were responded to in some way by the clinic.

## STUDY INTERVENTION

The goal of TAKE IT is to optimize adherence and to detect problems earlier to improve health outcomes in kidney transplant centers. TAKE IT includes the following intervention components that will be adapted and piloted for use in the PATTERN study for primary care among adults aged 65 and older with polypharmacy and multiple chronic conditions:

1. **An adherence assessment** that requests patients to report on their medication use, providing a link between the health center and patient beyond routine in-person visits. This assessment will identify patients at risk of non-adherence and categorize their adherence concern(s) as: cognitive, psychological, regimen, medical, social, economic.

2. **Care Alert Notifications** directed to the health center (i.e. to a nurse coordinator or whomever the health center prefers) if an adherence related problem is identified by the routine adherence assessment. This person can then activate appropriate staff to respond.

## PROCEDURES INVOLVED:

For PATTERN, the goal is to phenotype medication adherence challenges of patients aged 65 and older who have an upcoming primary care visit (within the next ~1 week) and are prescribed 8 or more medications to treat multiple chronic conditions in primary care. The processes for our key informant research activities (Aim 1) and the pilot study (Aim 2) are described in detail below.

**Aim 1** is cross-sectional and qualitative. During Aim 1, the Northwestern research team will solicit opinions from key informants (clinicians, administrators, patients) about the adaptation of the TAKE-IT intervention to the PATTERN study. Using feedback from those individuals, one-time interviews, the research team will work with EHR analysts to adapt the platforms used in TAKE IT to meet the needs of PATTERN.

**Aim 1: Key Informant Interviews with Clinicians and Administrators (up to N=15)**

Specifically, this will entail:

1) Individual, one-time interviews with eligible clinician and administrator participants, lasting ~45 minutes.
2) Participants will be screened and provide an online informed consent prior to participation.

3) Trained Northwestern research assistants will use semi-structured interview guides to conduct the interviews; interviews will be conducted over a secure video-based web platform (either Zoom or Microsoft Teams), as some questions may ask participants to view and respond to potential PATTERN study materials (e.g., adherence assessment).
4) In general, questions will explore participants opinions on: whether the assessment should be conducted among any patient meeting previously described eligibility criteria, or if it would better to focus on a smaller subset of patients with multiple morbidities more likely to result in medication adherence challenges; how clinicians prefer to address phenotyped adherence challenges, and whether they think their practice is ready to implement such an intervention. Additional questions related to intervention adaptation may be iteratively added should new topics arise in the initial interviews.
5) At the conclusion of the interviews or online after the consent is completed, participants will complete a brief demographic questionnaire.
6) All participant responses to the demographic questionnaire will be recorded on a RedCap survey.
7) Audio-recordings of the interviews will be used for analysis purposes using a rapid approach to qualitative analyses previously used by the research team.
8) The research team will then synthesize the data from recordings and RedCap and update the intervention adaptation.

**Aim 1: Key Informant Interviews with Patients (up to N=15)**

Specifically, this will entail:

1) Individual, one-time interviews with eligible patient participants lasting ~45 minutes.
2) Participants will be screened and provide verbal informed consent prior to participation.
3) Trained Northwestern research assistants will use semi-structured interview guides to conduct the interviews; interviews will be conducted over a secure video-based web platform (either Zoom or Microsoft Teams), as some questions may ask participants to view and respond to potential PATTERN study materials (e.g., adherence assessment).
4) In general, questions will explore participants opinions about: the acceptability of monthly assessments; the perceived likelihood that pilot study participants will complete assessments as instructed; the utility of health center resources that could be linked to identified and phenotyped adherence challenges. Additional questions related to intervention adaptation may be iteratively added should new topics arise in the initial interviews.
5) At the conclusion of the interviews, patients will complete a brief demographic questionnaire and validated measures of health literacy and patient activation.
6) All participants' responses to the questionnaire will be recorded on a RedCap survey.
7) Audio-recordings of the interviews will be used for analysis purposes using a rapid approach to qualitative analyses.
8) The research team will then synthesize the data from recordings and RedCap and update the intervention adaptation strategy further.

**Aim 1: Key Informant Audio Recording**

All key informant interviews (Aim 1) will be audio recorded using the Zoom or Microsoft Teams videoconferencing software. Prior to recording the interview, study participants will be asked to

turn their video cameras off so only their audio is recorded. Specifically, the Northwestern research team will record the interview portions where participants are offering suggestions or giving us feedback on the adaptation of the TAKE IT intervention into the PATTERN study (as described above). We will not record any identifiable information (ex: medical records or responses to demographic questionnaires). Due to Zoom recording recommendations made by NUIT, interviews conducted with the Zoom software will be recorded to the Zoom Cloud. Recording to the Zoom Cloud, rather than directly to one's computer, prevents the recorded files from becoming corrupted and diminishing the quality of the recording (ex: failed recording where not everything is recorded).

The Zoom Cloud or Microsoft Teams recordings will be downloaded and saved onto secure FSM department servers. Only authorized research personnel will have access to the data. The recordings may be used solely by the Northwestern research team for analysis purposes only. Recordings from the qualitative research activities will be analyzed using a rapid approach to qualitative analysis. De-identified notes may be taken as needed. The recordings and notes will be stored on the FSM department servers for the duration of the study. At the conclusion of the study, all recordings will be destroyed.

If a participant is not willing to be audio recorded, then they will be unable to participate in the Aim 1 study activities. No pilot study activity will involve audio or visual recording; those activities will take place over the phone through a Northwestern phone line.

**Aim 2: Pilot study (N=80; n=40 per arm)**

For **Aim 2**, we will conduct a patient-randomized controlled trial at one Northwestern Medicine primary care practice and followed for 6 months. A total of 80 participants will be recruited and randomly assigned via REDCap once a primary care appointment is scheduled to either the PATTERN arm or usual care (N=80, n=40 per) arm. Usual care refers to the normal standard clinical practices at the participating practice(s).

Research activities (described in detail below) will include an adherence assessment (for those in the Pattern arm) and a post-visit survey (for both arms) which will be conducted over the phone via a Northwestern phone line.

***Adherence assessments (part of the intervention)***

Adherence assessments will be automatically delivered to patients randomized to the intervention arm with an upcoming appointment to report medication challenges via MyChart.

***Post-visit interviews***

1) Potential participants who have an upcoming primary care visit (within the next ~1 week) will be called via a Northwestern telephone line to be recruited for the study. After confirming eligibility via phone, the participant will provide an electronic informed consent or verbal consent prior to participation. Individuals for whom have technology issues and electronic consent is not practical due to technological challenges, will be subject to verbal HIPAA/Alteration of HIPAA. The RC will schedule the post-visit survey

about 2 to 4 weeks after the patient attended their primary care visit and will inform the participant that it will be about a ~30 minute phone interview.
2) The RC will schedule interviews at the convenience of patients.
3) Patients may receive a phone call as a reminder to attend their scheduled study visit.
4) At the end of the phone interview there are open-ended questions for participants randomized to the intervention. These will be audio recorded, with the participant's permission, using a handheld audio recorder, Zoom, or Teams. The participant will be reminded that only that portion of the interview will be audio recorded.
5) The RC will turn off the audio recording, thank the patient, and confirm the delivery process for compensation.
6) The RC will thank the patient and confirm the delivery process for compensation.

**Aim 2: Audio Recording**
All participants randomized to the intervention will be asked a short series of open-ended questions to assess their acceptability of the intervention. These open-ended questions will be audio recorded using a hand-held audio recorder, Zoom, or Teams. Prior to recording the interview, study participants will be reminded that a portion of the interview will be audio recorded. Specifically, the Northwestern research team will record the end of the interview where participants are discussing their acceptability of the intervention. We will not record any identifiable information (ex: medical records or responses to demographic questionnaires).

All audio recordings will be downloaded and saved onto secure FSM department servers. Only authorized research personnel will have access to the data. The recordings may be used solely by the Northwestern research team for analysis purposes only. Recordings from the qualitative research activities will be analyzed using a rapid approach to qualitative analysis. De-identified notes may be taken as needed. The recordings and notes will be stored on the FSM department servers for the duration of the study. At the conclusion of the study, all recordings will be destroyed.

If a participant is not willing to be audio recorded, then detailed notes will be taken.

## DATA AND SPECIMEN BANKING
NA

## SHARING RESULTS WITH PARTICIPANTS
NA

## STUDY TIMELINES

**Total Study Duration**
In total, this is a 24-month study.

**Aim 1: Key Informant Interview Duration**

All key informant participants will be involved in the project for the length of their one-on-one interview on a single day. This is estimated to be up to one hour, including approximately 30 – 45 minutes for content solicitation, and 15 minutes or less for completion of the demographic questionnaire.

**Aim 2: Pilot Study Duration**
Once enrolled via rolling enrollment process, they will be followed for a total of 6 months, with a study interview about 2 to 4 weeks after their primary care visit. REDCap will be used to facilitate study tracking.

Procedures for analyses will be set up in ample time before the end of the study such that all data can be rapidly analyzed once the last participant clears the 6-month follow-up (patients will be interviewed about 2 to 4 weeks after primary care visit but some clinical data will be captured at 6 months from the EDW).

## INCLUSION AND EXCLUSION CRITERIA

**EDW data for Recruitment**
The study team will download the EDW report with the names and contact information of potentially eligible patients for Aims 1 and 2. Upon receiving the list of potentially eligible participants, the Northwestern study team will contact, screen, recruit, consent, and interview eligible participants. All patient/participant data will be saved on the project folder within the FSM network. The study team will receive the following patient contact information:

- Patient name
- Date of Birth
- Gender
- Home and cell phone number
- Mailing address
- Email
- Medical record number
- Clinic name
- Primary care visit date (within the next ~1 week)
- PCP name

The above indicates that we are requesting partial HIPPA waiver for recruitment of patient participants for Aims 1 and 2 (see consent procedures on pages 16 and 17 below). This is to be sure we are contacting, screening and enrolling participants for whom this research is tailored.

We are also requesting a waiver of documentation of consent for Aim 1 because this research presents no more than minimal risk (see consent procedures on pages 16 and 17 below). The procedures for Aim 1 are individual remote interviews, during which the participants will be instructed that their participation is voluntary and they may skip any question or stop the interview at any point if they feel uncomfortable. Questions, however, are designed to inform

our intervention, rather than to solicit deeply personal information from the participants. Furthermore, the research does not involve procedures for which written consent is normally required outside of research context.

**Screening of patients for key informant interviews (Aim 1) and participation in pilot study (Aim 2)**

Trained RCs will review the EDW report and only reach out to those who meet patient eligibility criteria. All criteria will be confirmed over the phone prior to moving forward with the consent process and scheduling the study interview.

**Aim 1: Key Informant Interviews with Clinicians and Administrators** (up to N=15)

To be eligible to participate in the key informant interviews for clinicians and administrators, participants must meet the following eligibility criteria:

- Be currently employed as a primary care clinician or administrator at a Northwestern Medicine primary care practice.

**Aim 1: Key Informant Interviews with Patients** ( up to N=15)

To be eligible to participate in the key informant interviews for patient participants must meet the following eligibility criteria:

- Be an adult aged 65 or older
- Speak English as their primary language
- Have a diagnosis of multiple chronic conditions (including diabetes, hypertension and hyperlipidemia)
- Be prescribed 8 or more medications
- Primarily responsible for administering own medication
- Receive medical care at a Northwestern Medicine primary care practice
- Have no severe, uncorrectable visual, hearing, or cognitive impairments that would preclude study consent or participation
- Have a phone
- Have access to video conferencing technology and willingness to have the call recorded
- Have an active email address.

**Aim 2: Pilot Study Patient Participants** (N=80, n=40 per arm)

To be eligible to participate in the pilot study participants must meet the following eligibility criteria:

- Be an adult aged 65 or older
- Speak English as their primary language
- Have at least 2 chronic health conditions
- Have an upcoming primary care visit (within the next ~1 week)
- Be prescribed 8 or more medications
- Primarily responsible for administering own medication
- Receive medical care at a participating Northwestern Medicine primary care practice
- Have no severe, uncorrectable visual, hearing, or cognitive impairments that would preclude study consent or participation

- Have access to the internet and a MyChart account
- Have an active email address; and
- Not interviewed as a key informant in Aim 1 activities.

## VULNERABLE POPULATIONS

We will not include any vulnerable populations in this research.

## PARTICIPANT POPULATION(S)

| Accrual Number: | Category/Group: (Adults/Children Special/Vulnerable Populations) | Consented: Maximum Number to be Consented or Reviewed/Collected/Screened | Enrolled: Number to Complete the Study or Needed to Address the Research Question |
|---|---|---|---|
| Study-wide | Aim 1: Adults | 50 | 27-30 |
| | Aim 2: Adults | 600 | 80 |
| Total: | Adults | 650 | 107-110 |

## RECRUITMENT METHODS

**Aim 1: Recruitment of clinicians and administrators**

We will identify potentially eligible medical directors and administrators via internal systems. Members of the Northwestern team, which may include members of the Northwestern Pepper Center, will send an email to potential participants describing the study. Potential participants may contact the study RA directly or complete the online consent with the link in the email. They will also be given the opportunity by email to opt out of being contacted for this activity. Those who express interest or do not opt out will be called or emailed by a research coordinator (RC), introduced to the study, screened, and scheduled for an individual, one-time interview to be held remotely over Zoom or Microsoft Teams. Online consent will take place prior to the interview.

**Aims 1 and 2: Recruitment of patients**

Potentially eligible patients will be identified via the EHR. A report containing contact information (name, dob, gender, phone number, address, email, medical record number, clinic name, clinic date ( Aim 2), and primary care provider name) will be downloaded from the EDW. An RC will review the report and then mail a letter to patients on the list, notifying them that a trained Northwestern RC will be telephoning to invite them to participate in a study. Patients will be given the opportunity to opt out of being contacted by calling a hotline number and leaving a message. Seven days after the letters have been mailed, an RC will call patients who did not opt out to ask screener questions to determine eligibility and, if eligible and interested, schedule their one-time interview (Aim 1).

An RC will contact potential participants via phone using a Northwestern phone line to invite them to participate in a study. Potential participants will be informed about the study and if

interested, the RC will continue to ask screener questions to determine eligibility and, if eligible consent and randomize, and schedule their one-time interview (Aim 2).

## COMPENSATION FOR PARTICIPATION IN RESEARCH ACTIVITIES

Participants who consent to participate in the Aim 1 Key Informant Interviews, and those who participate in the Aim 2 pilot testing activities will be compensated for their time and effort. Participants will be paid at the completion of the interview via the PNC Stored Value Visa Card program (physical gift card) or via the Northwestern Visa Prepaid Card program (virtual gift card). Participants will be asked which payment type they prefer.

| **Study Activity** | **Payment Amount** |
|---|---|
| Aim 1: Key Informant interviews with clinicians and administrators | $100 |
| Aim 1: Key Informant interviews with patients | $30 |
| Aim 2: Pilot study participation | $50 (post-visit interview) |

## WITHDRAWAL OF PARTICIPANTS

There are no anticipated circumstances when a participant would be withdrawn from the study without their consent.

Participants can choose to withdraw from the study at any time. If a participant chooses to withdraw from the research, any data collected up until the point of withdrawal will still be utilized as it will not include identifying information. They will then not be contacted for further interviews or visits.

## RISKS TO PARTICIPANTS

Participation in this study puts subjects at a minimal risk of discomfort or inconvenience, as they are primarily responsible for providing their own opinions and suggestions about intervention adaptation (Aim 1), or experiences with their prescribed medication taking behaviors (Aim 2). Nevertheless, some of the questions may be upsetting or make participants feel uncomfortable; participants may experience a sense of unease or shame while they complete measures of health literacy (Aim 2). Finally, participation may result in a loss of privacy, since research and oversight staff may review research findings.

## POTENTIAL BENEFITS TO PARTICIPANTS

It is possible that subjects enrolled in the study may directly benefit from this study by having a better understanding of medication challenges and resources available for support. The results of this study may provide important information regarding how strategies can be implemented via available technology (e.g., the EHR) to phenotype and provide appropriate support to identified medication adherence challenges.

## DATA MANAGEMENT AND CONFIDENTIALITY

The proposed pilot study uses a 1:1 randomized design that assigns patients to PATTERN or usual care. We will accrue 80 patients (to allow consenting to occur until we have 80 interviews ), anticipating 90% retention for follow-up at about 2 to 4 weeks after primacy care visit, leaving a minimum 72 patients for primary analyses. High retention will be supported through close follow-up, and reminders.

As mentioned previously, regimen adherence during post-visit survey as measured by the ARMS-D and/or ASK-12 is the **primary outcome** of interest. **Secondary outcomes** include clinical outcomes (e.g. A1c, blood pressure, cholesterol panel). Relationships between adherence and potential confounders (e.g., age, comorbidity, regimen complexity, internet use, dose of intervention, health literacy, patient activation) may also be examined.

As a small pilot study, appropriate bivariate analyses (chi square, t-test) will be performed to compare outcome by study arm. Exploratory analyses will apply generalized linear models (GLMs), adjusting for confounders, specifying the logit link function for binary outcomes and identity link for continuous outcomes. Treatment group will be the independent variable of primary interest, with usual care specified as reference group. We will also include baseline value of the outcome and any potential confounding covariates noted in bivariate analysis. For outcomes measured per medication as described in the **Measurement table** above, a generalized estimating equation (GEE) approach will be employed to adjust standard errors for within-patient correlation. Should PATTERN demonstrate a significant - or non-significant trend suggesting an effect on outcomes, **secondary analyses** will examine if any of the potential confounders considered exhibit any effect modification.

To understand the fidelity of PATTERN, we will determine the extent to which the intervention was implemented as planned to optimize it for a future multi-site trial. We will capture data from patient self-report and the EHR. Patients receiving PATTERN will be asked whether they received the EHR message and visited the portal. From the EHR, we will determine if the portal assessment was completed, the prevalence and type of patient-reported adherence concerns, whether the clinic read portal responses, and the average time from assessment submission to clinician or staff review, and/or response. We will examine if receipt and completion of EHR assessments and deployment of adherence support tools increases participant knowledge and medication taking behaviors.

**Data Safety and Monitoring Board (DSMB).** Because this is a small pilot, a formal DMSB is not required. However, we will identify two members of the Northwestern Pepper Center who will be given responsibility to review protocols, procedures, and concerns related to research integrity, including an approval of the methods and analysis plan. The DSMB will be organized by Dr. Pack and include an appropriate research biostatistician with related expertise. Meetings will take place via video/teleconference.

We will register the trial protocol at ClinicalTrials.gov.

**Measures**

**Patient Characteristics.** We will include a socio-demographic/health questionnaire, and the Tangible Social Support survey to assess the extent/quality of social connections. The Consumer Health Activation Index (CHAI) will be included, and patients will be asked about their internet use.

**Regimen Complexity.** EHR data will identify the number of prescription medications an individual has been prescribed. This will serve as a proxy for medication regimen complexity.

**Fidelity (Process Measures).**

**Receipt of adherence assessments.** During the post-visit survey, the RC will ask whether patients received the adherence assessments. We are only collecting these 1-time at the follow-up interview (not longitudinally).

**Use of Patient Portal.** During the post-visit interview, the RC will inquire whether patients used the portal to complete the adherence assessment which will be verified using EHR data.

**Care Alert Notification.** We will review EHR data on care alerts, and nurse follow up to identify whether adherence concerns were addressed by the care team. The RC will also ask patients if they received follow up, by whom, and what services were provided.

**Effectiveness Outcomes.** We will collect data on an array of knowledge, behavioral, and clinical outcomes.

**Medication Adherence.** Adherence will be measured using: 1) ARMS-D and/or ASK-12.

**Clinical Outcomes.** *Blood pressure* (continuous SBP; control (y/n): SBP<140 & DBP<90) and g*lycemic control (HbA1c)* will also be examined in those with hypertension and diabetes. The cholesterol panel will also be included.

## PROVISIONS TO MONITOR THE DATA TO ENSURE THE SAFETY OF PARTICIPANTS

NA: This study does not include more than minimal risk.

## PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF PARTICIPANTS

Participants will be informed in all cases about their rights as research subjects. They may withdraw at any time during the study without penalty or loss of any healthcare benefit or service to which they are entitled. Patients will be assigned a unique identification number. We will also attempt to reduce shame and performance anxiety as a result of interviews through extensive training of the interviewer(s).

Data collected includes online and verbal consent forms for Aim 1 and for Aim 2. It also contains information collected during the study interviews (demographics, audio recordings of key informant interviews (Aim 1), survey/interview information (Aims 1 and 2), as well as clinical data from the EDW (Aim 2).

A master study tracking database via REDCap will contain information linking participants to their study ID numbers. All survey data and demographics will be stored in REDCap. Downloaded data will not contain any identifiable information. Only participant ID numbers will appear on the survey. Only study investigators and authorized research personnel listed in the IRB will have access to the data.

Any information that could allow identification of individual participants, including the master list, will be kept strictly confidential in password-protected files on the FSM department servers, which are located in a HIPAA compliant data center and accessible only by the research team. Data will be stored on the Northwestern server for the length of the study. Personal Health Information (PHI) won't be reused in this study. All identifiable information, including interview recordings for both aims will be deleted upon completion of the study or destroyed at the earliest opportunity, whichever comes first.

## COMPENSATION FOR RESEARCH-RELATED INJURY

NA

## ECONOMIC BURDEN TO PARTICIPANTS

NA

## CONSENT PROCESS

**Aim 1:** Because this research places participants at minimal risk, and because Aim 1 is designed to solicit opinions about an intervention, verbal or online consent will be obtained for all Aim 1 participants, prior to their participation in the adaptation phase of the PATTERN study. For patient interviews, after contacting potentially eligible participants, but prior to conducing the one-time, individual interview over Zoom or Microsoft Teams, a trained RC will read the consent form aloud to the potential participant and reiterate key requirements (e.g., that the interview will be audio recorded). The potential participant will be informed that they are free to skip any questions or end the interview at any time without penalty. All information will be provided to the subjects in terms that they can fully understand. There will be no exertion of any overt or covert coercion. Once the RC is satisfied that the potential participant understands the consent process and the nature of their participation in the research study, the potential participant will be asked if they consent to participate. After verbal consent is obtained, the consent date and name of the research coordinator that obtained the consent will be recorded in REDCap by the RC prior to starting the interview. For clinician or admin interviews, eligible participants will receive an email with information on who to contact if they would like to learn more information about the study. The email will also have a link to an online consent, where they can review more information about the study. After consent, they will be contacted to schedule the qualitative interview.

**Aim 2:** Electronic or verbal consent with a HIPPA authorization will be obtained for all Aim 2 participants, prior to their participation in the pilot phase PATTERN study. Electronic consent will be prioritized. Individuals for whom an electronic consent is not practical due to technological challenges will be subject to verbal HIPAA/Alteration of HIPAA. Participants will

be provided with a copy of the consent form by the RC that can be emailed or mailed to the participant after consenting to participate. Once complete, the RC will reiterate the key aims and participant requirements (1 phone interview and the one adherence assessment), before giving the potential participant the opportunity to ask any questions they might have. The potential participant will be informed that they are free to withdraw at any time without penalty and all information will be provided to the subjects in terms that they can fully understand. There will be no exertion of any overt or covert coercion. Once the RC is satisfied that the potential participant understands the consent process and the nature of their participation in the research study, the potential participant will be asked to sign and date the online consent form. Participants will receive a signed consent form for their records by email. If an online consent cannot be obtained, we will proceed with a verbal consent. The consent date and name of the research coordinator that obtained the consent will be recorded in REDCap by the RC prior to starting the interview. Participants will receive a copy of the consent form for their records by mail or email depending on their preference.

If a patient is unable to complete an electronic consent due to inability to use technology for electronic consent, we request a waiver of documentation of informed consent and an alteration to obtain verbal HIPAA Authorization, since this study presents no more than minimal risk of harm to participants. For patients that are unable to complete electronic consent, research cannot practicably be conducted without the waiver or alteration. Obtaining written consent is not feasible since this clinic-randomized study will recruit patients from clinics all over the Chicagoland area (including North and West suburbs). In order to maintain the sample size necessary for meaningful data, we need to request a waiver of documentation of informed consent and alteration to obtain verbal HIPAA Authorization. Additionally, it is important that we do not exclude older adults solely based on inability to use technology, decreasing the diversity of the population. After verbal consent and HIPAA Authorization is obtained, the consent date and the name of the research coordinator that obtained the consent will be recorded in Redcap by the RC prior to starting the baseline interview.

## NON-ENGLISH-SPEAKING PARTICIPANTS

Only English-speaking participants will be enrolled in this small pilot study.

## WAIVER OR ALTERATION OF CONSENT PROCESS

We will obtain a partial HIPPA waiver for recruitment of patient participants in Aim 1 and Aim 2. For Aim 2, all participants will provide a signed HIPPA wavier so that we may report clinical outcomes described above in the measurement sections. We want to be sure we are contacting, screening, and enrolling participants for whom this research is tailored.

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## PROTECTED HEALTH INFORMATION (PHI AND HIPAA)

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For Aim 2, all participants will provide a signed HIPPA wavier so that we may report clinical outcomes described above in the measurement sections.

## QUALIFICATIONS TO CONDUCT RESEARCH AND RESOURCES AVAILABLE

The Center for Applied Health Research on Aging (CAHRA) directed by Michael Wolf, MA, MPH, PhD, CAHRA serves as a research and education hub for geriatricians, gerontologists and aging health services researchers. This Center unites >70 faculty across clinical disciplines and from cognitive, behavioral, social and public health sciences throughout the university and the Northwestern Medicine health system. CAHRA's mission is to promote informed decision making and actions leading to optimal health and well-being among individuals and families over the life span.

Building off of Dr. Wolf's highly successful Health Literacy and Learning Program (HeLP), which was founded in 2004 to create a network of multidisciplinary faculty that could partner together to generate applied, innovative research that would help transform the delivery of healthcare for vulnerable patients (older adults are a specific target), CAHRA was launched in 2019 through an institution-created endowment and is now formally linked to IPHAM and the Department of Medicine. The Center is physically and strategically co-located on the same floor of the Arthur Rubloff Building as the Division of GIMG, as well as the Center for Behavioral Intervention Technologies (CBITs) and encompasses approximately 2,500 square feet of office space, in additional to dedicated research interview space.

The establishment of CAHRA demonstrates Northwestern's commitment to prioritizing aging research and to pursuing a leadership position in the field. The Center's six research programs are a reflection of the wide-ranging research portfolio of the Center's core faculty members: 1) Health Literacy & Learning, 2) Cognitive Aging, 3) Psychosocial Support, 4) Life Course Health, 5) Treatment Adherence, and 6) Measurement & Analysis. Together, CAHRA leads a robust research agenda to explore and understand the many factors that affect a person's ability to manage health throughout their life and use that knowledge to develop and disseminate interventions that support better health.

**Allison Pack, PhD MPH (Principal Investigator)** is a Research Assistant Professor in the Division of General Internal Medicine at Northwestern University's Feinberg School of Medicine and an early-stage investigator. She is health services researcher with expertise in applied qualitative methodology. Her research experience has largely focused on assessing the acceptability and feasibility of new HIV prevention and treatment modalities among diverse populations. More recently, her research has expanded to include a focus on health literacy and medication adherence for other chronic diseases. She has recently received funding as principal investigator for two other studies related to patient uptake and/or use of medications in primary care. With the award for this current study, Dr. Pack became a Pepper Center Fellow with the Claude D. Pepper Center at Northwestern University. This position affords her additional support from the Center's numerous cores and research faculty.

## MULTI-SITE OR COLLABORATIVE RESEARCH:

NA