EMBEDDED CLINICAL TRIAL OF PATIENT PRIORITIES CARE AMONG PERSONS LIVING WITH MCI AND DEMENTIA

Principal Investigator:

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PROTOCOL VERSION TRACKING

When making changes to an approved and “final” protocol, please provide a summary of the changes, with the date, at the front of the protocol. Update the version number and date with each change.

Date	Version #	Summary of changes to protocol

PRÉCIS

Study Title

Embedded Clinical Trial of Patient Priorities Care Among Persons Living with Mild Cognitive Impairment (MCI) or Dementia

Objectives

Aim 1 Demonstrate the feasibility of identifying a diverse cohort of eligible patient/care partner dyads and implementing the PPC program by trained facilitators (e.g. social worker, nurse, nursing assistant). Implementation endpoints demonstrating feasibility will include:

1. Identification of care partners for 50% of eligible persons living with dementia or MCI (PLWDM),
2. Documentation of PPC discussion in 35% of eligible participants in the electronic health record (EHR), which will be ascertained using a Natural Language Processing model, and
3. Evaluation of implementation endpoints (acceptability, appropriateness, feasibility, fidelity, and potential for future adoption of the intervention) assessed through chart review and semi-structured participant interviews with some patients, patient-care partner dyads, facilitators, and clinicians.

Aim 2 Demonstrate feasibility of pragmatically assessing the following clinical outcomes using the EHR among enrolled patients and patient- care partner dyads measured up to 2 months after documented PPC discussion: days at home (primary clinical outcome), total medications, and new referrals to specialist physicians. We have defined the “days at home” variable to include data two months prior (pre-visit days at home) to the PPC visit, as well as two months after the visit (post-visit days at home). Days at home are days that are spent at home instead of in a hospital or long-term care facility.

Aim 3 Examine key feasibility measures across racial, ethnic, and socioeconomic subgroups including: 1. Quantitative measures of enrollment of eligible dyads, documented PPC discussions, and clinical outcomes measures, and 2. Qualitative measures ascertained from chart review and participant interviews, including acceptability and appropriateness.

Design and Outcomes

This study proposes to implement Patient Priorities Care (PPC) in three primary outpatient clinics. Clinicians at three participating sites will be provided with training in PPC. The research team and clinicians will work together to identify patients on the clinic schedule who would be suitable for a PPC visit. The study team will access the EHR to review patient records for the two months following the patient’s clinical visit, to determine whether a PPC visit was documented, as well as related clinical outcomes (see aims). A select group of clinicians, patients,

and care partners will also be interviewed to help identify what aspects of the program are effective and what further refinement of the PPC program is required to best serve the needs of PLWDM and care partners. The study is designed to demonstrate feasibility of a pragmatic approach to implementing PPC, as well as our ability to collect meaningful and pragmatic outcomes. If we can demonstrate the ability to identify care partners for patients, evidence of PPC conversations in the EHR, and evidence that diverse racial, ethnic, and socioeconomic groups are equally engaged in the program, then we anticipate the development of a fully embedded pragmatic clinical trial.

Interventions and Duration

The PPC intervention is comprised of a two-step process that can involve 1-2 clinic staff:

1. Priorities identification with a facilitator prior to seeing their physician or advanced practice provider(s) either: 1-2 weeks prior to or in tandem with the outpatient clinic visit.
2. Alignment of patient priorities with their medical care plan in collaboration with their clinician (typically a physician or advanced practice provider). Consistent with local clinical practices, the facilitator and clinician will be identified by clinic leadership for each eligible participant.

A facilitator for the first step of the intervention may be any member of the clinical team. The clinician in the second step must be the patient's physician or advanced practice provider.

Following training of facilitators and providers, the research team will begin to review the clinic schedule to identify individuals that qualify to receive the PPC intervention, based on the inclusion criteria provided. When possible, these lists will be automated to identify patients based on inclusion criteria that can be found within the patient's EHR.

The intervention will consist of the following steps:

1. Research staff will either mail the PPC packets to PLWDMs on behalf of the clinic or will provide the clinic staff with packets to mail directly to patients. The packet will include a letter from the patient's clinic. The packet will provide the PLWDM with information about PPC in a paper format and will include instructions to access materials in an electronic format. The paper packet will be mailed to the patient approximately 1-4 weeks prior to their next clinic visit, Access to online electronic materials will be available (myhealthpriorities.org) for participants and care partners. These materials will not include information about the patient's medical history or any other protected health information. No identifiable participant information will be stored on the electronic site.
    - The research team will notify providers via the EHR or secure messaging to indicate which patients have been mailed a PPC packet. The method of notification will be determined based on the provider's preference.

2. Facilitators will determine the best method to engage with patients based on clinical environment. They will use clinical judgment and the EHR to determine when and how to engage care partners during this step. Options might include:
   - sending reminder by text, phone call, and/or EHR message to patients and/or care partners 1-2 weeks prior to the next clinic appointment to
     - engage in discussion about the PPC packet and/or
     - encourage the patient and/or care partner to complete the worksheet
   - engaging in PPC discussions on the day of the appointment in tandem with the clinician visit but prior to seeing the clinician

3. Research staff will send patients electronic nudges approximately one to five day(s) prior to their clinic visit to complete PPC goal setting and bring any necessary materials to their clinic visit. These nudges will be sent as clinical reminders on behalf of the clinic staff, using the electronic patient portal, and will be automated when possible.

4. Clinic staff will provide a reminder about PPC to the patient and/or care partner, using an integrated approach during the clinic check-in workflow. Check-in staff will provide the patient and/or care partner with a copy of the PPC packet that was previously mailed to them, if they did not bring it to their appointment. When possible, EHR notifications will be automated to alert clinic staff when a patient and/or care partner who requires this check-in reminder, is on the clinic schedule.

5. Research staff will provide a reminder in the EHR appointment note to alert clinic check-in staff about patients that should receive a PPC packet. These packets will be prepared and delivered (or mailed) to each clinic, by research staff.

6. Patient EHR records will be evaluated for two years prior to the clinic visit for purposes of ascertaining eligibility and suitability to engage in PPC. Other data will be collected from the patient's medical record for two years prior to the clinic visit and outcomes data will be collected for two months after the clinic visit.

*PEP Talks (**P**erspectives on **E**mbedded **P**atient Priorities Care **Talks**)*
Semi-structured, audio-recorded participant interviews will also be conducted with a selection of facilitators, clinicians, patients, and care partners. These interviews will be conducted within 1 day and 3 months of the clinic visit. We will oversample for minority representation for these interviews. We anticipate completing interviews with up to approximately 30 participants.

Sample Size and Population

Patients will be recruited from geriatric, neurology, and primary care outpatient

clinics in three different health systems. To ensure diversity in our study population, we have purposefully engaged health systems that have higher racial and ethnic minority patient populations from the surrounding area. One of our sites is a federally qualified healthcare center, which enables oversampling for socioeconomic diversity.

A total of 160 patients or patient-care partner dyads will be identified as eligible from the geriatrics or primary care practices of three health care systems. Eligible PLWDM and their care partners will be identified through the EHR.

While pilot studies typically do not warrant power calculations, a target sample size can be estimated to ensure the results support progression to a full trial. Based on Lewis et al's red zone/green zone criteria, with an anticipated proportion for the upper red zone cut-off of 40% and the lower green zone cut-off of 50% for a one-sample test and 80% power (Aim 1), we will aim to recruit 160 patients or patient-care partner dyads. To meet criteria for progression to a full ePCT, we will aim to meet the recruitment goals described herein.

STUDY TEAM ROSTER

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Main responsibilities/ Key roles: Implementation and management of the proposed study including allocating funds, supervision of participating clinics and research staff at IU in identification of potential participants and data collection, overseeing data extraction and analysis, and oversight to maintain confidentiality, privacy, and security of the data

Co-Investigators: **Rafael Samper-Ternent, MD, PhD**

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Main responsibilities/ Key roles: Dr. Samper-Ternent will be responsible for the local implementation and management of the proposed study including overseeing data extraction and analysis and will ensure the data is protected and secure. He will supervise local research staff in identification of potential participants and in data collection, including consenting select patients and patient-care partner dyads for interviews.

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Main responsibilities/ Key roles: Implementation of Natural Language Processing model to evaluate outcomes.

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1 STUDY OBJECTIVES

1.1 Primary Objective

The primary aim is to demonstrate the feasibility of identifying a diverse cohort of eligible patient/care partner dyads and implementing the PPC program by trained facilitators, as measured in three parts:

- Identification of care partners for 50% of eligible PLWDM.
- Documentation of PPC discussion in 35% of eligible participants in the EHR, which will be ascertained using a Natural Language Processing (NLP) model.
- Evaluation of implementation endpoints related to accessibility, appropriateness, feasibility, fidelity, and potential for future adoption of the intervention as assessed through chart review and semi-structured participant interview with some patients, patient-care partner dyads, facilitators, and clinicians.

1.2 Secondary Objectives

Aim 2 Demonstrate feasibility of pragmatically assessing the following clinical outcomes using the electronic health record (EHR) among enrolled patients and patient- care partner dyads measured up to 2 months (60 days) after documented PPC discussion: days at home (primary clinical outcome), total medications, and new referrals to specialist physicians. We have defined the "days at home" variable to include data two months (60 days) prior (pre-visit days at home) to the PPC visit, as well as two months (60 days) after the visit (post-visit days at home). Days at home are days that are spent at home instead of in a hospital or long-term care facility.

Aim 3. Examine key feasibility measures across racial, ethnic, and socioeconomic subgroups including: 1. Quantitative measures of enrollment of eligible dyads, documented PPC discussions, and clinical outcomes measures, and 2. Qualitative measures ascertained from chart review and participant interviews including: acceptability and appropriateness.

2 BACKGROUND AND RATIONALE

2.1 Background on Condition, Disease, or Other Primary Study Focus

High quality medical care must consider the patient and what is most important to them. A major challenge for outpatient care is delivering care that is consistent with patient goals. Although challenging, this includes patients with dementia and mild cognitive impairment. Many people with mild cognitive impairment or dementia report their goals and values are not discussed during clinic visits with their primary care provider. Their care partners experience similar dissonance between a clinician's focus and their goals.

Patients with dementia or mild cognitive impairment (MCI) are at higher risk for care that does not match their goals, especially if they have comorbid conditions. The burden of multiple chronic diseases can be staggering for people living with dementia or mild cognitive impairment. Without identifying their health goals, there is a risk of them receiving burdensome medical care.

Eliciting their care priorities early in the progression of cognitive impairment can

make this process easier and ensures care is aligned with their values. This proposal aims to ameliorate this gap in medical care by conducting a pilot study of implementation of Patient Priorities Care, an evidence-based program for helping the goals and values of patients and care partners to become fully integrated into the medical care plan.

2.2 Study Rationale

Because of the nature of this disease process, persons living with dementia or mild cognitive impairment (PLWDM) may eventually need to rely on others to make medical decisions for them. If clinicians can improve their ability to identify what matters most to patients and their care partners, this can alleviate patient and care partner stress as they adjust to the challenges of living with mild cognitive impairment or dementia.

Patient Priorities Care has been tested and demonstrated to reduce treatment burden in a population of elders with and without mild cognitive impairment or dementia.

The original study of PPC showed significant effects of PPC on documentation of priorities-based decisions and reduced treatment burden and demonstrated that PPC is successful in a mixed population of patients with and without cognitive impairment and dementia. Feasibility of the PPC model has also been demonstrated in a general ambulatory care setting. Foundational to PPC model is the identification of “SMART” (specific, measurable, actionable, realistic, and timely) goals. The SMART goals approach to care, including goals attainment scaling, has been demonstrated as an appropriate means of identifying realistic healthcare goals for patients with dementia. Efficacy of PPC has been demonstrated in stage III trials that included patients with MCI and early dementia.

Training materials for healthcare providers have been vetted and tested in several studies. Patient Priorities Care has also developed patient-facing materials both on paper and online that have been vetted and tested in multiple studies and with diverse populations. These materials enable the patient and care partner to identify and elaborate on their healthcare goals and facilitate communication between them and their clinician. Furthermore, there are materials and additional training resources available to help the clinician identify how to best integrate patient priorities into the care plan.

This study proposes to implement Patient Priorities Care in several primary care and geriatrics clinics by training the clinicians. A select group of clinicians, patients, and care partners will also be interviewed to help identify what aspects of the program are working and what further refinement of the Patient Priorities Care program is required to best serve the needs of patients and care partners.

Patient Priorities Care (PPC) is an approach to health decision-making that is designed to help adults with multiple chronic conditions identify their health priorities and inform their health professional to align their health care with these priorities.

There are two steps to the PPC process:

1) facilitator discussion of priorities and

2) integration of priorities into the patient's care plan.

A facilitator for the first step of the intervention may be any PPC-trained clinician identified by the clinical team, such as a social worker, physician, or advanced practice provider (such as a physician's assistant, or nurse practitioner). We are asking the clinical sites to identify who will serve as facilitators. The clinician in the second step must be the patient's physician or advanced practice provider. A physician or advanced practice provider may be both facilitator AND clinician in this two-step plan.

Due to the embedded design of the PPC intervention, the proposed risks are generally no greater than those that one might expect during a routine clinical visit with a primary care provider. One finding from the intervention's initial study, was that there is a slightly increased risk of individuals receiving the intervention to be prescribed psychotropic medications. To address this concern, the training protocol includes education on risks of antipsychotics.

There is also a small risk of feeling uncomfortable responding to a question during the participant interview. To mitigate this risk participants will be advised that they may choose to decline a question or end the interview at any time and for any reason.

The evidence based PPC intervention is designed to help medically complex adults with multiple comorbidities and their care partners to realign medical care with their goals and values. PPC increases documentation of priorities-based decisions and reduces patients' treatment burden and unwanted care by up to 30%.

This is a pilot study with a goal of eventually evaluating this program in a full embedded pragmatic clinical trial. To ensure the program's protocols are ready for the full trial this study must demonstrate an ability to identify care partners of patients, identify evidence of Patient Priorities Care in the electronic health record, and demonstrate evidence that diverse racial, ethnic, and socioeconomic groups are equally engaged in the program. Additionally, the study must demonstrate that important clinical outcomes can be assessed including medication burden, specialist referral burden, and days at home away from the hospital or a long-term care facility. These outcomes will be assessed for two months (60 days) following the PPC visit. Finally, the information obtained from the interviews with clinicians, facilitators, patients, and care partners, will help the study authors decide whether a full trial would be beneficial.

3 STUDY DESIGN

This pilot study is a single arm, pragmatic trial.

Objectives

Aim 1 Demonstrate the feasibility of identifying a diverse cohort of eligible patients or patient-care partner dyads and implementing the PPC program by

trained facilitators (e.g. social worker, nurse, nursing assistant). A total of 160 patients or patient-care partner dyads (~ 50% white, 45% Black, and of those 6% Hispanic/Latino) will be identified as eligible from the geriatrics or primary care practices of three health care systems. Eligible PLWDM and their care partners will be identified through the EHR implementation endpoints demonstrating feasibility will include:

- Identification of care partners for 50% of eligible PLWDM,
- Documentation of PPC discussion in 35% of eligible participants in the EHR, which will be ascertained using an established Natural Language Processing model, and
- Evaluation of implementation endpoints (acceptability, appropriateness, feasibility, fidelity, and potential for future adoption of the intervention) assessed through chart review and semi-structured participant interviews with some dyads and clinicians.

Aim 2 Demonstrate feasibility of pragmatically assessing the following clinical outcomes using the EHR among enrolled patients and patient- care partner dyads measured up to 2 months (60 days) after documented PPC discussion: days at home (primary clinical outcome), total medications, and new referrals to specialist physicians. We have defined the “days at home” variable to include data two months (60 days) prior (pre-visit days at home) to the PPC visit, as well as two months (60 days) after the visit (post-visit days at home). Days at home are days that are spent at home instead of in a hospital or long-term care facility.

Aim 3 Examine key feasibility measures across racial, ethnic, and socioeconomic subgroups including: 1. Quantitative measures of enrollment of eligible dyads, documented PPC discussions, and clinical outcomes measures, and 2. Qualitative measures ascertained from chart review and participant interviews, including acceptability and appropriateness.

Design and Outcomes

This study proposes to implement Patient Priorities Care (PPC) in three primary care and geriatric clinics. Clinicians at three participating sites will be provided with training in PPC. The study will be introduced to the clinical team by the respective site PIs (Dr. Carnahan or Dr. Samper-Ternent). Training materials are available on the PPC website. All clinical staff (facilitators and providers) are requested to watch two videos (https://patientprioritiescare.org/training/). Participants who will be facilitators are asked to also complete the online module under facilitator training. Instructions to access these trainings will be provided. Clinicians who will be aligning health priorities and goals are asked to complete the online module under clinician training. The time commitment is approximately 90 minutes total. Additionally, we will monitor the initial encounter notes and help participants with setting SMART goals and executing care alignment by facilitating individual huddles and consultation with national experts on PPC. SMART stands for specific, measurable, actionable, reliable, and time bound. SMART goals give specificity so they can be used in decision-making.

The research team will review EHR documentation for each scheduled patient that meets minimum inclusion criteria and review clinician documentation to

verify the presence of MCI or dementia in at least two clinical encounters in the last two years. The study team will access the EHR to review patient records for the two months following the patient's clinical visit, to determine whether a PPC visit was documented, as well as related clinical outcomes (see aims). The study team will partner with local EHR experts to automate as much of this process of identification, nudges, and review as is feasible. A select number of clinicians, patients, and care partners will also be interviewed to help identify what aspects of the program are working and what further refinement of the PPC program is required to best serve the needs of patients and care partners. The study is designed to demonstrate feasibility of a pragmatic approach to implementing PPC, as well as our ability to collect meaningful and pragmatic outcomes. If we can demonstrate the ability to identify care partners for patients, evidence of PPC conversations in the EHR, and evidence that diverse racial, ethnic, and socioeconomic groups are engaged in the program, then we anticipate the development of a fully embedded pragmatic clinical trial.

4 SELECTION AND ENROLLMENT OF PARTICIPANTS

Sample Size and Population

Patients will be recruited from geriatric and primary care clinics in three different health systems. To ensure diversity in our study population, we have purposefully engaged health systems that have higher racial and ethnic minority patient populations from the surrounding area. One of our sites is a federally qualified healthcare center, which ensures oversampling for socioeconomic diversity.

While pilot studies typically do not warrant power calculations, a target sample size can be estimated to ensure the results support progression to a full trial. Based on Lewis et al's red zone/green zone criteria, with an anticipated proportion for the upper red zone cut-off of 40% and the lower green zone cut-off of 50% for a one-sample test and 80% power (Aim 1), we will aim to recruit 160 patients or patient-care partner dyads.

We will include dyads whenever feasible, but so as not to exclude isolated adults, many who may be from historically underrepresented groups, we will allow for individuals whose physicians determine they have the capacity to understand the intervention to also participate on their own. Given that clinicians would see these individuals in clinic on their own anyway, clinician determination of capacity to participate is a pragmatic approach. This means that we act under the assumption that patients who require a care partner will have already included them in previous visits and/or provider communications (and we anticipate that this will be documented in the EHR), whereas patients who attend clinic visits independently and have no documentation indicating the involvement of a care partner in their medical decisions, or a need for one, will be determined to have the capacity to also participate in a PPC visit. PPC is designed such that even those with MCI or early dementia can engage in meaningful discussions with their provider about their preferences.

Dementia and MCI

To identify individuals with dementia and MCI, we will use two or more instances of use of an ICD-10 code for either diagnosis in the EHR within 24 months. Typically, we would include instances of these billing codes within a year of each other, but due to the COVID-19 pandemic, we recognize that there may be less frequent clinical visits and less robust billing. We will use the following billing codes: F01.50, F01.51, F02.80, F02.81, F03.90, G30.0, G30.1, G30.8, G30.9, G31.01, G31.09, G31.1, G31.2, F41.81, G31.84 and F03.91.

Health Equity

To ensure diversity of our study population, we have purposefully engaged health systems that have higher racial and ethnic minority patient populations than the surrounding area. Furthermore, one of our sites is at a Federally Qualified Healthcare center, which ensures oversampling for socioeconomic diversity. Purposeful oversampling such as this is a well-established method for ensuring a strong signal in research data from underrepresented groups.

4.1 Inclusion Criteria

Patient Inclusion Criteria

Patients must meet all of the following criteria to participate in this study:

- 40 years or older
- English-speaking
- Receiving care with a participating physician
- Has a scheduled outpatient care visit within 1-2 months (60 days)
- Individual has a diagnosis of MCI or dementia

Definition: To identify individuals with dementia and MCI, we will use two or more instances of use of an ICD-10 code for either diagnosis in the EHR within 24 months. Typically, we would include instances of these billing codes within a year of each other but, due to the COVID-19 pandemic, recognize that there may be less frequent clinical visits and less robust billing. Diagnostic codes include:
- F01.50, F01.51, F02.80, F02.81, F03.90, G30.0, G30.1, G30.8, G30.9, G31.01, G31.09, G31.1, G31.2, F41.81, G31.84 and F03.91.

Care Partner Inclusion Criteria

Care partners must meet all of the following criteria to participate in the study:

- 18 years or older
- English-speaking

A note about inclusion of care partners: Clinician determination of a patient's capacity to participate in a visit independently is part of a pragmatic approach. This means that clinic staff will determine when a care partner is needed. Generally, we act under the assumption that patients who require a care partner will have already included them in previous visits and/or provider communications (and we anticipate that this will be documented in the EHR), whereas patients who attend clinic visits independently and have no documentation indicating the involvement of a care partner in their medical

decisions, or a need for one, will be determined to have the capacity to also participate in a PPC visit.

4.2 Exclusion Criteria

Participants who meet any of the following criteria will be excluded from the study:

- Is not community-dwelling- e.g. lives in a nursing home
- Is enrolled in hospice
- Individuals who decline to receive the PPC intervention (i.e. decline to have the PPC conversation) will be excluded from the study.
    - Note that declining to receive the PPC intervention will in no way impact the care that patients receive now or in the future.

4.3 Study Enrollment Procedures

Patients will be identified by research staff using the EHR and other administrative data provided by the participating clinical site. The EHR will be accessed by research staff at each clinical site. Clinic schedules will be reviewed to identify patients with upcoming appointments who meet criteria for inclusion. Providers may also notify research staff if they are aware of an upcoming appointment with an individual who would be eligible for PPC.

Providers and facilitators will be notified when patients have been mailed a PPC packet via their preferred method of communication (ex: EHR or other secure messaging). They will not be responsible for pre-screening patients for inclusion in this mailing.

Recruitment efforts will be recorded by research staff at each clinical site in a screening log. Reasons for exclusion will be tracked.

5 STUDY INTERVENTIONS

5.1 Interventions, Administration, and Duration

The PPC intervention is comprised of an initial two-step process that can involve 1-2 clinic staff:

1. *Priorities identification* with a facilitator prior to seeing their physician or advanced practice provider(s) either: 1-2 weeks prior to or in tandem with the outpatient clinic visit.
2. *Alignment of patient priorities with their medical care plan* in collaboration with their clinician (typically a physician or advanced practice provider). Consistent with local clinical practices, the facilitator and clinician will be identified by clinic leadership for each eligible participant.

A facilitator for the first step of the intervention may be any member of the clinical team. The clinician in the second step must be the patient's physician or advanced practice provider.

5.2 Handling of Study Interventions

Following training of facilitators and providers, the research team will begin to review the

clinic schedule to identify individuals that qualify to receive the PPC intervention, based on the inclusion criteria provided.

The **intervention** will consist of the following steps:

1. Research staff will provide the PLWDM with information about PPC in a paper format with instructions to access materials in an electronic format. The paper packet will be mailed to the patient approximately 1-4 weeks prior to their next clinic visit, Electronic materials will be available online (myhealthpriorities.org). These materials will not include information about the patient's medical history or any other protected health information. No identifiable participant information will be stored on the electronic site.
    - The research team will notify facilitators and clinicians via the EHR or secure messaging to indicate which patients have been mailed a PPC packet. The method of notification will be determined based on the provider's preference.
2. Facilitators will determine the best method to engage with patients based on clinical environment and information found in the EHR. They will use clinical judgment to determine when and how to engage care partners during this step. Options might include:
    - phone calls to patients and/or care partners 1-2 weeks prior to the next clinic appointment
        - engage in discussion about the PPC packet
        - encourage the patient and/or care partner to complete the worksheet
    - engaging in PPC discussions on the day of the appointment in tandem with the clinician visit but prior to seeing the clinician
3. Research staff will send patients electronic nudges (reminders through the patient portal) approximately one to five day(s) prior to their clinic visit to engage in PPC goal setting and bring any necessary materials to their clinic visit. These nudges will be sent as clinical reminders on behalf of the clinic staff, using the electronic patient portal, and will be automated when possible.
4. Staff will provide a reminder about PPC to the patient and/or care partner, using an integrated approach during the clinic check-in workflow, in which check-in staff will provide the patient and/or care partner with a PPC packet. Research staff will provide a reminder in the EHR appointment note to alert clinic check-in staff about patients that should receive a PPC packet. These packets will be prepared and delivered (or mailed) to each clinic, by research staff.
5. Patient EHR records will be evaluated for two years prior to the clinic visit for purposes of ascertaining eligibility and suitability to engage in PPC. Other data will be collected from the patient's medical record for two years prior to the clinic visit and outcomes data will be collected for two months after the clinic visit.

PEP Talks (Perspectives on Embedded Patient Priorities Care Talks) Interviews

Semi-structured, audio-recorded participant interviews will also be conducted with a selection of facilitators, clinicians, patients, and care partners. These interviews will be conducted between 1 day and 3 months of the clinic visit. We will oversample for

minority representation for these interviews. We anticipate completing interviews with up to approximately 30 participants. Participants will be offered a $20 incentive for completing this interview.

5.3 Concomitant Interventions

5.3.1 Allowed Interventions

Not applicable

5.3.2 Required Interventions

Not applicable

5.3.3 Prohibited Interventions

Not applicable

5.4 Adherence Assessment

Documentation of PPC discussion in 35% of eligible participants in the EHR will be ascertained using a Natural Language Processing (NLP) model. Participating clinicians will be trained to utilize the vendor “dot phrases” (pre-defined, templated language or EHR equivalent) to prompt the beginning of their PPC documentation. These dot phrases will then be incorporated into the NLP model to identify when PPC is documented within the clinical text. The NLP model will be trained to identify the dot phrases and extract details related to words following the phrase. For example: “patient care priorities were discussed, and patient wishes to…” A common script for identification of these dot phrases will be developed by the primary site and shared with the secondary site for local implementation. For the site that utilizes a different EHR vendor, a similar model will be employed ensuring the clinicians are trained to utilize similar language or programmatically input the equivalent of dot phrases. This will ensure the NLP model identifies the documentation.

6 STUDY PROCEDURES

6.1 Schedule of Study Steps

Study Steps	Screening: Pre-Visit (up to 8 weeks prior)	Outreach: Pre-Visit (1-4 weeks prior)	Outreach: Pre-Visit (1-2 weeks prior)	Outreach: Pre-Visit (1-5 days prior)	Intervention : Visit 1 (Day 0)	Follow-up: Post-Visit (2 months post visit)	Follow-up: Post-Visit (up to 3 months post visit)
Inclusion/Exclusion Criteria	X						
Mail PPC packet		X					
Review PPC packet			X				
Care partner assessment			X				
Send reminder (nudge) to patients			X	X			
Send nudge to facilitators and clinicians (per clinic preference)			X	X	X		
Provide PPC Packet at check-in					X		
Facilitator PPC Conversation (Step 1)			X		X		
Provider PPC Care Alignment (Step 2)					X		
Patient EHR/chart review	X				X	X	
Adverse Events					X	X	
Semi-structured qualitative interview (PEP Talks)							X

*Consistent with clinical practice the research team will have the ability to contact clinic staff by email, phone, EHR messaging, or other secure messages as needed to communicate about patients and/or care partners who are eligible for PPC.

6.2 Description of Evaluations

6.2.1 Screening Evaluation

These evaluations occur to determine if the candidate is eligible for the study.

Consenting Procedure

We will apply for a waiver of informed consent for most participants in this study because the intervention will be embedded within the standard clinical procedures.

A subset of clinicians and patients and care partners will experience traditional informed consent in order to participate in semi-structured, audio-recorded interviews with research staff as part of qualitative data collection. See Section 5.2 (PEP Talks) for details.

Screening

Trained research staff at each clinical site will conduct screening via the EHR and clinic schedule up to approximately 8 weeks prior to the clinic visit. Inclusion and exclusion criteria will be verified by research staff via the EHR by looking back in the patient's record for up to 2 years prior to the scheduled clinic visit. This review will occur up to 2 months prior to the patient's scheduled clinic visit. Screening and list generation will be automated where feasible.

6.2.2 Enrollment, Baseline, and/or Randomization

Enrollment

Due to the nature of the PPC model, there is no formal enrollment procedure or baseline research interview. Rather, patients will be considered enrolled if they meet inclusion criteria and a PPC packet is mailed to them.

- Note: a patient may decline to participate in the PPC intervention at any time. Declining to receive the PPC intervention will in no way impact their clinical care that patients receive now or in the future.
  - Individuals who inform their provider or other clinical staff that they wish to decline to receive the PPC intervention will be excluded from the enrolled patient list and will not be included in outcomes assessments for the study.

Baseline Assessments

The clinic visit is the reference point by which we will assess patient outcomes.

The PPC conversation will include two steps:

1. Priorities identification with a facilitator
2. Alignment of patient priorities with their medical care plan in collaboration with their physician or advanced practice provider(s).

Consistent with local clinical practices, the facilitator and clinician will be identified by clinic leadership for each eligible participant. A facilitator for the

first step of the intervention may be any member of the clinical team. The clinician in the second step must be the patient's physician or advanced practice provider.
Because the primary outcome is documentation in the EHR, the assessment for documentation will occur approximately two months (60 days) after the patient's clinic visit.

Randomization
Not applicable

6.2.3 Follow-up Visits
Not applicable

6.2.4 Final Evaluation

- Post-Clinic Visit up to 60 days (2 months post visit):
  - Research staff at each clinical site will identify and confirm documentation of the PPC visit in the EHR. Currently available reporting tools will be used to automate extraction of as much of this information as possible, and further automation of data collection using the NLP model will be implemented as available.
  - Research staff will record any Adverse Events experienced by the patient as applicable.
- Post-Clinic Visit up to 90 days (3 months post visit):
  - Conduct semi-structured interviews with some PLWDM, Care Partners and Clinicians (PEP Talks section 5.2)
  - Adverse Events

7 SAFETY ASSESSMENTS

Participant safety will be monitored, however, due to the nature of the study, the risks encountered during the PPC conversation are no greater than those expected during a routine clinic visit. Patient safety will be monitored at the clinician level since the conversation takes place during a routine clinic visit.

The Principal Investigator (PI) will be responsible for ensuring participants' safety on a daily basis. Quarterly meetings between study sites will review any safety concerns and will review coordination of safety information between sites. In addition, the NIA IMPACT Collaboratory Safety Officer (SO) will oversee all data and safety monitoring activities for this study. The SO will be determined by NIA. The SO will act in an advisory capacity to the NIA Director to monitor participant safety, to evaluate the progress of the study, and to review procedures for maintaining the confidentiality of data, the quality of data collection, management, and analyses. Advarra IRB will conduct the ethical review required for the protection of human subjects. NIA PO, in consultation with the SO, will make a determination regarding the level and format of data and safety

monitoring this study requires, i.e. how often reporting is required.

Refer to the **IMPACT Collaboratory DSMB Charter** for details.

There are three potential risks to participation in the study. First, a past study of the PPC intervention found that there is a slightly increased risk of individuals receiving the intervention to be prescribed psychotropic medications. Psychotropic medications can include antidepressants and antipsychotics, the latter which has been overprescribed and inappropriately prescribed to individuals with dementia. To address this concern, the training protocol includes education on risks of antipsychotics. Second, there is the risk of potential breach of confidentiality. Third, individuals who participate in semi-structured interviews following the PPC conversation, may encounter questions that they would prefer not to answer. If this occurs, the participant can decline to respond. Additionally, participants may choose not to participate in an interview. There will be no penalty for providers not participating and all patients and care partners will be informed that choosing not to participate will not affect their clinical care.

7.1 Specification of Safety Parameters

Not applicable

7.2 Methods and Timing for Assessing, Recording, and Analyzing Safety Parameters

All adverse events, unanticipated problems and potential risks will be monitored and collected on an ongoing basis, and throughout the study by the research staff. Events, which are anticipated because they are related to the worsening or advancing of the underlying disease, or symptoms related to the disease, will be monitored through patient or care partner report. Events related to any patient, care partner, and provider loss of privacy or confidentiality, or related to fatigue, frustration, or distress related to completing the intervention will be assessed by the research staff via monitoring of the delivery of the study protocols and procedures within the EHR and by patient and care partner reports to the research staff.

Adverse Events and Serious Adverse Events

Adverse Event (AE): Any untoward or unfavorable medical occurrence in a clinical research study participant, including any abnormal sign (e.g. abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the patient's involvement in the research, whether or not considered related to participation in the research.

Serious Adverse Event (SAE): Any adverse event that:

- Results in death
- Is life threatening, or places the participant at immediate risk of death from the event as it occurred
- Requires or prolongs hospitalization
- Causes persistent or significant disability or incapacity
- Results in congenital anomalies or birth defects
- Is another condition which investigators judge to represent significant hazards

Unanticipated Problem (UP) Definition: any incident, experience, or outcome that meets all of the following criteria:

- unexpected, in terms of nature, severity, or frequency, given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the study population;
- related or possibly related to participation in the research;
- suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

For all participants, adverse events will be collected starting at enrollment and continue until after the participant has completed the study.

Unanticipated problems, that do not meet the definition of an adverse event, will be documented in a study log that will be stored in a secure electronic folder behind the university fire wall. Details in the log may include participant study ID, date that the problem was reported or discovered by the study, a description of the problem, and a corrective plan and measures to prevent reoccurrence.

Adverse events associated with this study are likely to be infrequent.
The IMPACT Collaboratory adverse event form will be used by research staff to report all adverse events caused by the intervention.

AEs for this study include: Some participants may feel increased stress or anxiety while participating in the intervention. Breach of confidentiality would also constitute an AE.

SAEs for this study include: PLWDM have an increased risk of hospitalization, nursing home admission, and death at baseline and these SAEs may occur during the course of the study.

7.2.1 Reporting Procedures

The content of the data and safety monitoring report will include study status, recruitment, enrollment, and retention information and participant descriptive information. Safety and quality information will be reported using study quality reports for Co-PIs that will contain:

- Summary of adverse events, participant descriptive information, and an explanation of how each event was handled,
- Summary of complaints and how each complaint was handled,
- Subject retention, including the number and reasons of participant withdrawals,
- Summary of protocol violations and how each was handled. Reports will be submitted to the IRB on an as-needed basis.

All adverse events will be initially judged by the PI (Carnahan) based on three criteria:

1. expectedness (expected, unexpected),

2. relatedness to participation in the study (definitely related, possibly related, not related), and

3. severity (mild, moderate, severe).

These judgments will be circulated to the study team and reported to the Program Official as noted below.

- All **adverse events that are serious** (SAE) **and unexpected** (i.e., have not been previously reported for the study's intervention) will be reported to the IMPACT Collaboratory Regulatory and Data Team Leader (Dr. Julie Lima), NIA IMPACT Collaboratory PO (Dr. Partha Bhattacharyya), and the IMPACT Collaboratory project's Safety Officer (SO) within 48 hours of the study's knowledge of SAE.
    - Only those adverse events that are serious (SAE), unexpected, ***and related to the intervention*** must also be reported to Advarra IRB. Unexpected and ***unrelated*** SAEs will be reported to Advarra IRB on a case-by-case basis if requested by the IMPACT Collaboratory project's Safety Officer (SO) or NIA IMPACT Collaboratory PO.
- All deaths will be reported to IMPACT Collaboratory Regulatory and Data Team Leader (Dr. Julie Lima), NIA IMPACT Collaboratory PO (Dr. Partha Bhattacharyya), and the IMPACT Collaboratory project's Safety Officer (SO) within 24 hours of study's knowledge of death.
    - Advarra IRB does not require the specific reporting of death outside of the SAE reporting requirement above, but they will be notified on a case-by-case basis if requested by the IMPACT Collaboratory project's Safety Officer (SO) or NIA IMPACT Collaboratory PO.
- All unanticipated problems (UPs) will be reported to the IMPACT Collaboratory Regulatory and Data Team Leader (Dr. Julie Lima), Advarra IRB, NIA IMPACT Collaboratory PO (Dr. Partha Bhattacharyya), and the IMPACT Collaboratory project's Safety Officer (SO) within 48 hours of the study's knowledge of the event.
- The summaries of all previously reported unexpected and related SAEs, deaths, and UPs, as well as all other SAEs and AEs will be reported to IMPACT Collaboratory Regulatory and Data Team Lead (Dr. Julie Lima), Advarra IRB, NIA IMPACT Collaboratory PO (Dr. Partha Bhattacharyya), and the IMPACT Collaboratory project's Safety Officer (SO) at a minimum every 6

months, or at a frequency requested by the IMPACT Collaboratory project's Safety Officer (SO) or NIA IMPACT Collaboratory PO.

Severity of Event

- **Mild:** Awareness of signs or symptoms, but easily tolerated and are of minor irritant type causing no loss of time from normal activities. Symptoms do not require therapy or a medical evaluation; signs and symptoms are transient.
- **Moderate**: Events introduce a low level of inconvenience or concern to the participant and may interfere with daily activities, but are usually improved by simple therapeutic measures; moderate experiences may cause some interference with functioning
- **Severe**: Events interrupt the participant's normal daily activities and generally require systemic drug therapy or other treatment; they are usually incapacitating

Expectedness of Event

- **Unexpected** - nature or severity of the event is not consistent with information about the condition under study or intervention in the protocol, consent form, product brochure, or investigator brochure.
- **Expected** - event is known to be associated with the intervention or condition under study.

Unexpected events will be subject to expedited reporting requirements as described in the NIA Guidance on Clinical Trials.

Relationship to Study Intervention

- **Definitely Related**: The adverse event is clearly related to the investigational agent/procedure – i.e. an event that follows a reasonable temporal sequence from administration of the study intervention, follows a known or expected response pattern to the suspected intervention, that is confirmed by improvement on stopping and reappearance of the event on repeated exposure and that could not be reasonably explained by the known characteristics of the subject's clinical state.
- **Possibly Related**: An adverse event that follows a reasonable temporal sequence from administration of the study intervention follows a known or expected response pattern to the suspected intervention, but that could readily have been produced by a number of other factors.
- **Not Related**: The adverse event is clearly not related to the investigational agent/procedure - i.e. another cause of the event is most plausible; and/or a clinically plausible temporal sequence is inconsistent with the onset of the event and the study intervention and/or a causal relationship is considered biologically implausible.

7.2.2 Follow-up for Adverse Events

The occurrence of an adverse event (AE) or serious adverse event (SAE) may come to the attention of research staff during EHR review of documentation of clinic visits, or during semi-structured participant interviews.

All AEs including local and systemic reactions not meeting the criteria for SAEs will be captured on the appropriate case report form (CRF) and/or the IMPACT Collaboratory AE form, as necessary. Information to be collected includes event description, time of onset, qualified medical professional's assessment of severity, relationship to study product (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event. All AEs occurring while on study must be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. AEs characterized as intermittent require documentation of onset and duration of each episode.

7.3 Safety Monitoring

The NIA Guidelines on Data and Safety Monitoring generally require that a NIA-appointed Data and Safety Monitoring Board or Safety Officer monitor clinical trials. Please see the Data and Safety Monitoring Guidelines. This study has been assigned to a Safety Officer only.

The study PI will present their safety reports at the intervals described below. Safety reports will be provided to the SO and NIA PO.

Data will be presented in a blinded manner in SO reports. SO reports, data and discussion are confidential. Participant identities will not be known to the SO.

For the study, the frequency of DSM will proceed as follows:

1. Prior to the start of participant enrollment and data collection, the study PI must submit a DSMP for approval by the SO and/or the NIA PO;

2. Six months after the initiation of participant enrollment and/or data collection, the study PI must provide a DSM report to the SO, through submission to the IMPACT IRB and Regulatory Team. This interim report will be reviewed by the SO to determine whether there are any human subjects or data safety concerns; and

3. At the end of the study, the PI must submit a final DSM report to the SO, through submission to the IMPACT IRB and Regulatory team.

The SO will sign a Conflict of Interest Statement which includes current affiliations, if any, with pharmaceutical and biotechnology companies (e.g., stockholder, consultant), and any other relationship that could be perceived as a conflict of interest related to the study and / or associated with commercial interests pertinent to study objectives.

Safety Officer
Madhuri Reddy, MD, MSc
Geriatric Medicine Specialist, Hebrew SeniorLife
Dr. Reddy is a geriatric medicine specialist who specializes in chronic wound care and technology. She has a fellowship in chronic wound healing and uses evidence-based care to develop methods of prevention and management of pressure ulcers. Dr. Reddy previously served as the Chair of the Institutional Review Board at Hebrew Senior Life.

SO Responsibilities
The role of the SO is described in the **IMPACT Collaboratory DSMB Charter**.

A detailed list of SO responsibilities includes:

- Review the research protocol, informed consent documents and plans for data safety and monitoring;
- Recommend subject recruitment be initiated after receipt of a satisfactory protocol;
- Evaluate the progress of the trial, including periodic assessments of data quality and timeliness, recruitment, accrual and retention, participant risk versus benefit, performance of the trial sites, and other factors that can affect study outcome;
- Consider factors external to the study when relevant information becomes available, such as scientific or therapeutic developments that may have an impact on the safety of the participants or the ethics of the trial;
- Review study performance, make recommendations and assist in the resolution of problems reported by the PI;
- Protect the safety of the study participants;
- Report to NIA on the safety and progress of the trial;
- Make recommendations to the NIA and the PI concerning continuation, termination or other modifications of the trial based on the observed beneficial or adverse effects of the treatment under study;
- If appropriate, review interim analyses in accordance with stopping rules, which are clearly defined in advance of data analysis and have the approval of the DSMB;
- Ensure the confidentiality of the study data and the results of monitoring; and,
- Assist the NIA by commenting on any problems with study conduct, enrollment, sample size, and/or data collection.

8 INTERVENTION DISCONTINUATION

This is a one-year pilot study to establish feasibility with low anticipated risk. If there were unanticipated serious adverse events that were possibly or probably related to the study, we would review with the institutional review board and consider discontinuation.

9 STATISTICAL CONSIDERATIONS

9.1 General Design Issues

Aim 1 Demonstrate the feasibility of identifying a diverse cohort of eligible patient/care partner dyads and implementing the PPC program by trained facilitators (e.g. social worker, nurse, nursing assistant). A total of 160 patients or patient-care partner dyads (~50% White, 45% Black, and of those 6% Hispanic/Latino) will be identified as eligible from the geriatrics or primary care practices of three health care systems. Eligible PLWDM and their care partners will be identified through the EHR. Implementation endpoints demonstrating feasibility will include:

1. Identification of care partners for 50% of eligible PLWDM identified in Aim 1,
2. Documentation of PPC discussion in 35% of eligible participants in the EHR, which will be ascertained using review of electronic medical records and an established Natural Language Processing model,
3. Evaluation of implementation endpoints (acceptability, appropriateness, feasibility, fidelity, and potential for future adoption of the intervention) assessed through chart review and semi-structured participant interviews with some patients, patient-care partner dyads, facilitators, and clinicians.

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Aim 2 Demonstrate feasibility of pragmatically assessing the following clinical outcomes using the EHR among enrolled patients and patient- care partner dyads measured up to 2 months (60 days) after documented PPC discussion:

1. days at home (primary clinical outcome),
2. total medications, and
3. new referrals to specialist physicians.

We have defined the “days at home” variable to include data two months (60 days) prior (pre-visit days at home) to the PPC visit, as well as two months (60 days) after the visit (post-visit days at home). Days at home are days that are spent at home instead of in a hospital or long-term care facility.

Aim 3 Examine key feasibility measures across racial, ethnic, and socioeconomic subgroups including:

1. quantitative measures of enrollment of eligible dyads, documented PPC discussions, and clinical outcomes measures, and
2. Qualitative measures ascertained from chart review and participant interviews, including acceptability and appropriateness.
3. Deploy established algorithms for detecting social factors that may influence patient care priorities, such as housing instability, financial insecurity, or transportation concerns. These algorithms have been previously created and

validated across the care spectrum and will be deployed at the primary site in current form on the established natural language processing platform at Regenstrief Institute. All available clinical notes for the recruited cohort will be annotated by the software as either positive or negative for the social factors. This can then be incorporated into analyses.

Given the smaller recruitment size for the secondary site, keywords from the algorithms will be shared with the study team for manual chart extraction. This process will also be utilized as controls for the programmatic implementation at the primary site.

9.2 Sample Size and Randomization

While pilot studies typically do not warrant power calculations, a target sample size can be estimated to ensure the results support progression to a full trial. Based on Lewis et al.'s red zone/green zone criteria, with an anticipated proportion for the upper red zone cut-off of 40% and the lower green zone cut-off of 50% for a one-sample test and 80% power (Aim 1), 160 dyads is suggested as a sample size for the proposed study. To meet criteria for progression to a full ePCT, we will aim to meet the recruitment goals described below for each implementation outcome. In alignment with discussions with the IMPACT Collaboratory Consultation Team, we will not be randomizing for this study. We will plan in the subsequent Stage IV trial of this intervention to employ a randomized stepped wedge approach.

9.2.1 Treatment Assignment Procedures

Not applicable.

9.3 Interim analyses and Stopping Rules

Not applicable (no interim analysis for this one-year study)

9.4 Outcomes

9.4.1 Primary (clinical) outcome

1. Days at home is the primary clinical outcome we are measuring. We will survey for 2 months (60 days) before the PPC visit (pre-visit days at home), as well as for 2 months (60 days) after the PPC visit (post-visit days at home), utilizing data that is collected from the patient's electronic medical record.

9.4.2 Secondary (implementation) outcomes

1. Identification of care partners for 50% of eligible PLWDM,
    - To meet green zone criteria, we must identify care partners for 50% of eligible PLWDM.
    - The red zone threshold is 40%.
    - Should the sample fall in the amber zone between 40-50%, then we will determine whether acceptable amendments can be made to the protocol to warrant progression to a full ePCT.

2. Documentation of PPC discussion in 35% of eligible participants in the EHR, which will be ascertained using an established Natural Language Processing model,
    - To meet green zone criteria, we must identify PPC discussion in 35% of eligible participants. In the original study of PPC, 66.3% of visit notes indicated a PPC discussion. Because that was performed at a single institution under ideal conditions, we expect that our pragmatic pilot will have a lower recruitment rate for this aim than the original study. That said, the 65% green zone is associated with a sample size of 159 individuals, which would include our overall recruitment goal.
    - Should the sample fall in the amber zone between 25-35%, then we will determine whether there are amendments that can be made to the protocol to warrant progression.
3. Evaluation of implementation endpoints (acceptability, appropriateness, feasibility, fidelity, and potential for future adoption of the intervention) assessed through chart review and semi-structured participant interviews with some patients, patient-care partner dyads, facilitators, and clinicians (Table 1).

If themes emerge that indicate potential future successful full ePCT, then this will meet progression criteria.

We will use findings from Aim 3 to examine key feasibility measures across racial, ethnic, and socioeconomic subgroups to determine further adjustments that may be needed to tailor the intervention to a diverse population. We recognize that a “one size fits all” approach is inappropriate for many historically and structurally marginalized groups and that adjustments may need to be made to the flexibility of the overall intervention protocol. This may include identification of additional implementation or clinical endpoints for examination. Progression criteria for this aim is that we are able to determine the key feasibility measures for a minimum of the +/- 10% proportion of racial, ethnic, and socioeconomic subgroups that mirrors the populations seen in each health system. We will also conduct between-group comparisons on our measure of PPC documentation between Black v. White and those with financial insecurity vs. none (small sample sizes will preclude analysis of Hispanic patients and those with housing instability). If there are significant differences, we will make further adjustments prior to embarking upon a Stage IV ePCT of this intervention.

Table 1. Implementation outcomes and data sources

	Implementation outcomes	**Source of data**
Feasibility	Identification of sample Enrollment goals Feasibility of outcome ascertainment	Administrative data Qualitative interviews with clinicians, patients, and care partners NLP

Adoption	Utilization /intent to use	EHR Qualitative interviews with clinicians
Acceptability / appropriateness	Satisfaction with the intervention (content, delivery, credibility) Perceived usefulness and practicality	Qualitative interviews with clinicians, patients, and care partners
Fidelity	Adherence to implementation protocol Quality of implementation	Training records – completion /results- competency Checklist of adherence to protocol -EHR Qualitative interviews- barriers /facilitators to refine implementation strategy

9.5 Data Analyses

This is a feasibility pilot study, so the primary analyses are concerning feasibility and are described in section 9.4.

For the semi-structured participant interviews (PEP Talks) we will employ a five-stage framework analytic approach to identify key themes that emerge. Theme identification will start after the first two interviews and continue in an iterative process. We will purposefully oversample individuals from diverse socioeconomic and racial or ethnic backgrounds to ensure a strong signal from these traditionally underrepresented groups.

10 DATA COLLECTION AND QUALITY ASSURANCE

10.1 Data Collection Forms

Data for PEP Talks interviews will be collected by the research staff at each clinical site from the EHR.

Data collection forms will be designed and securely stored within REDCap or on a password protected, encrypted server at the Regenstrief Institute Indiana University (IU) Center for Aging Research or at the University of Texas- Houston (UTH), respectively. EHR data will be collected using site specific automated data repositories (e.g., Regenstrief Data Core in Indiana).

10.2 Data Management

The clinical sites will have no responsibility for data collection or management.

Data will be managed by the research team at the IU Center for Aging Research. Physical documents related to the study will be stored in a locked file cabinet, while electronic documentation will be stored on an encrypted, password-protected server at the Regenstrief Institute. Data collection instruments will be created in REDCap.

This project will utilize REDCap and the Dynamic Data Pull (DDP) module of REDCap. The Dynamic Data Pull (DDP) is a special feature for importing data into REDCap from an external source system. It provides an adjudication process whereby REDCap users can approve all incoming data from the source system before it is officially saved in the REDCap project. The DDP will only allow people with access to PHI to use it as it has a built-in check each time it is accessed. The DDP can only be enabled by a REDCap administrator who serves as an honest broker to PHI. Using the DDP requires using the Medical Record Number (MRN) as a key to automatically gather demographic and laboratory data and reduces data entry errors.

10.3 Quality Assurance

10.3.1 Training

Training for the research team will be provided by the IU Center for Aging Research, and its affiliates. Research staff will be trained in all aspects of good clinical practice and patient privacy and security. Facilitators and clinicians will additionally receive training in the delivery of PPC. Since facilitators will not be conducting research operations, additional training in human subjects research and/or GCP will not be required. Training materials are available on PPC website. All clinical staff (facilitators and providers) are requested to watch two videos (https://patientprioritiescare.org/training/). Participants who will be facilitators are asked to also complete the online module under facilitator training. Clinicians who will be aligning health priorities and goals are asked to complete the online module under clinician training. The time commitment is approximately 90 minutes total. Additionally, we will monitor the initial encounter notes and help participants with setting SMART goals and executing care alignment by facilitating individual huddles and consultation with national experts on PPC.

10.3.2 Quality Control Committee

Internal monitoring of the study will be utilized to ensure quality of the data being gathered for this study, when appropriate. For example, if research staff are documenting data from the EHR into REDCap, other members of the research team will periodically review some entries for accuracy.

10.3.3 Metrics

Go to section 9.4 for more information on quality assurance metrics.

10.3.4 Protocol Deviations

Quality assurance procedures include observing research activities for adherence to protocol. The research team has developed internal methods for quality assurance for any data that is recorded within our study documents and REDCap database. Any deviations to the protocol will be documented and reviewed by the study team at weekly meetings. Should a reportable deviation occur we will adhere to reporting requirements as outlined by the IRB and as noted in section 7 above.

10.3.5 Monitoring

Monitoring will include review and observation of data from clinical sites for the purpose of ensuring protocol compliance and data quality. The research team will be responsible for addressing any concerns identified through the monitoring process. Monitoring will also ensure the completion of documentation of informed consent for qualitative interview participants.

11 PARTICIPANT RIGHTS AND CONFIDENTIALITY

11.1 Institutional Review Board (IRB) Review

This protocol, relevant subject facing material, and the informed consent document(s) and any subsequent modifications will be reviewed and approved by the IRB or ethics committee responsible for oversight of the study.

11.2 Informed Consent Forms

Our study consists of two separate components – the embedded intervention and a set of semi-structured participant interviews.

Embedded PPC Intervention

The **intervention** consists of the PPC program, which will be embedded within clinical practice. We request a waiver of informed consent for recruitment, participation, and outcome assessment of participants, to include the use of EHR data for these purposes.

We offer the following justifications for the waiver of informed consent:

- the research involves no more than minimal risk to the subjects:
    a. Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. The embedded design of this study aligns with this definition. Furthermore, prior research supports the minimal risk designation of PPC. PPC is currently used as the standard of care in many outpatient care clinics.
- The research could not practicably be carried out without the requested waiver:
    a. Obtaining consent prior to implementation of the study would impact the scientific integrity of the trial, in that it is contradictory to the pragmatic design of the trial. This intervention is being integrated into routine clinical practice and obtaining consent would significantly interrupt the regular flow of patient care in the clinic. The consent process would not only be impracticable in a busy outpatient practice, but it runs the risk of skewing results as follows:
        i. It would be limited to less cognitively impaired PLWDM or

ii. to more cognitively impaired PLWDM who have an available care partner to consent to participate in research. This would impact the ability to obtain data about individuals with more cognitive impairment, who do not have a care partner to consent on their behalf.

b. Additionally, since patients and patient/ care partner dyads are identified using ICD-10 codes for MCI and dementia, the informed consent process would involve disclosure of the methods used to identify patients, and with that the risk of sharing protected health information (such as diagnosis) with an unauthorized party.

- The research involves using identifiable private information, and could not practicably be carried out without using such information in an identifiable format:

    a. It is necessary in this study to utilize identifiable information for the purpose of screening patients, mailing information about PPC, and assessing outcomes in the EHR after the PPC visit. These tasks would be impossible to complete without using identifiable information from the health systems' EHR.

- The waiver or alteration will not adversely affect the rights and welfare of the subjects:

    a. We believe that a waiver will not adversely impact participants. Because PPC is a well-established model of care that is used as the standard of care in many other clinics, we believe the waiver is justifiable and appropriate for this study. We believe that patients would find value in a model that helps align their priorities with their healthcare. Because this is an intervention designed to improve clinician-patient communication and identification of goals, it is highly unlikely that study participants would object if they knew of the waiver. However, potential participants are free to decline to participate in this discussion with their provider, without penalty. Declining to participate will in no way impact their clinical care now or in the future.

- Whenever appropriate, the subjects will be provided with additional pertinent information after participation

    Results will be shared via published manuscripts and any other applicable formats within the healthcare systems where the study is performed.

Semi-structured Participant Interview (PEP Talks)

We will conduct **semi-structured interviews (PEP Talks)** with a select group of

facilitators, clinicians, patients, and their care partners. Any patient, care partner, facilitator, or clinician who was involved in a documented PPC visit in a participating clinic is eligible to participate in a semi-structured interview (PEP Talk). Informed consent will be obtained for this activity. We will request a waiver of documentation of informed consent.

Consent forms will be Institutional Review Board (IRB)-approved. Research staff will review the consent document with individuals who are eligible to participate in these semi-structured interviews (PEP Talks). Research staff will explain the research study to the interviewee and answer any questions that may arise. A verbal explanation will be provided in terms suited to the participant's comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice, and that the quality of their medical care will not be adversely affected if they decline to participate in this study. Participants will have the opportunity to carefully review the consent form and ask questions prior to providing their consent. The participants will be offered a copy of the informed consent form, in person or by mail, so that they may discuss the study with their family or care partner or think about it prior to agreeing to participate. The informed consent process will be conducted by trained research staff.

PEP Talks with Patients and Care Partners

We will approach patients and care partners for participation by phone or mail. Patients or care partners who cannot consent for the interview will not be eligible to participate. We will determine capacity to consent for the interview using a consent verification process, which is outlined below.

We will utilize a teach back consent verification process with interview participants after reviewing the informed consent information. This process will involve questions about the topic under study, what the participant would be asked to do if enrolled, and the voluntary nature of the study. We will use a teach back approach in which participants will answer questions about the information in the informed consent. This information will be repeated up to three times. If the participant is unable to correctly answer each question after three attempts, the participant will be determined to be ineligible to participate in the interview.

These interviews will be conducted by phone, virtual meeting, or in person.

PEP Talks with Facilitators and Clinicians

We will approach providers who have participated in PPC implementation by phone, email, or in person during clinic to invite them to complete a semi-structured interview with research staff. There will be no penalties for declining to participate in the interview. For those who are interested, we will conduct informed consent as outlined above.

Documentation of Consent

All research activities including documentation of consent procedures will be recorded in the source document (including the date), by research staff at each clinic before the participant undergoes any study-specific procedures.

11.3 Participant Confidentiality

We also request a full HIPAA waiver of authorization for the use of EHR data for this study. We offer the following justifications for the HIPAA waiver:

- Use or disclosure involves no more than minimal risk to the privacy of individuals because of the presence of the following elements:
  - An adequate plan to protect health information identifiers from improper use or disclosure,
  - An adequate plan to destroy identifiers at the earliest opportunity absent a health or research justification or legal requirement to retain them, and
  - Adequate written assurances that the PHI will not be used or disclosed to a third party except as required by law, for authorized oversight of the research study, or for other research uses and disclosures permitted by the Privacy Rule;
- Research could not practicably be conducted without the waiver or alteration; and research could not practicably be conducted without access to and use of PHI as outlined in the prior section 11.2 and as follows:
  - Obtaining consent prior to implementation of the study would impact the scientific integrity of the trial, in that it is contradictory to the pragmatic design of the trial.
  - Additionally, since patients and patient-care partner dyads are identified using ICD-10 codes for MCI and dementia, the informed consent process would involve disclosure of the methods used to identify patients, and with that the risk of sharing protected health information (such as diagnosis) with an unauthorized party and/or disclosing information from the medical record that the patient and/or care partner has not been disclosed previously.
  - To minimize the risk of breach of confidentiality, all study materials will be regarded as strictly confidential. Paper study documents will be stored in a locked file cabinet in a secure office at the IU Center for Aging Research and at the University of Texas. Computerized data entry and data storage systems are on secure Indiana University and University of Texas servers and password protected and will be accessible only to study personnel. The participants will be informed that representatives of the IRB or other regulatory bodies may inspect their study records to verify the information collected and that all information will be handled in strictest confidence. All analyses from the study will be performed and reported in aggregate and will exclude any personally identifiable information. Data agreements will be established between University of Texas, Indiana University, and the Regenstrief Institute to facilitate access to identifiable protected health information as needed for the project. Access will be as specified per all applicable university policies and procedures, including but not limited to, secure transfer protocols, virtual private networks, and remote desktops.

Any data, specimens, forms, reports, video recordings, and other records that leave the site will be identified only by a participant identification number (Participant ID, PID) to maintain confidentiality. All records will be kept in a locked file cabinet. All computer entry and networking programs will be done using PIDs only. Information will not be released without written permission of the participant, except as allowed through a waiver of HIPAA authorization or the necessary for monitoring by IRB, the sponsor or persons working on behalf of the sponsor (i.e. IMPACT research study staff, or Safety Officer), the NIA, and the OHRP.

11.4 Study Discontinuation

The study may be discontinued at any time by the IRB, the NIA, the OHRP, the FDA, or other government agencies as part of their duties to ensure that research participants are protected.

12 ETHICAL CONSIDERATIONS

The research team will adhere to the following policies, guidelines, and ethical principles as described:

- Propose, conduct, and report research with integrity and honesty;
- Protect people and humanely treat animals involved in research or teaching;
- Learn, follow, and demonstrate accountability for meeting and ensuring compliance with the requirements of sponsors, regulatory bodies, and other applicable entities;
- Faithfully describe and transmit research data and findings;
- Protect rights to individual and University intellectual property;
- Ensure originality of work, provide credit for the ideas of others upon which their work is built, and be responsible for the accuracy and fairness of information published; and
- Fairly assign authorship credit on the basis of an appropriate array of significant intellectual contributions, including conception, design, and performance; analysis and interpretation; and manuscript preparation and critical editing for intellectual content.

13 COMMITTEES

IMPACT Collaboratory- Study oversight, sponsorship, and funding.

14 PUBLICATION OF RESEARCH FINDINGS

Publication of the results of this trial will be governed by the policies and procedures developed by the sponsor(s) of this study. Any presentation, abstract, or manuscript will be made available for review by the sponsor prior to submission. We will adhere to the IMPACT Collaboratory Publication and Acknowledgment Policy and Resource and Data Sharing Plan available on the IMPACT Investigator's Portal.

15 REFERENCES

Lewis M, Bromley K, Sutton CJ, McCray G, Myers HL, Lancaster GA. Determining sample size for progression criteria for pragmatic pilot RCTs: the hypothesis test strikes back! *Pilot Feasibility Stud.* 2021;7(1):40.