# Clinical Interventional Study Protocol (CISP)

# FULL PROTOCOL TITLE

**Reducing Inappropriate Medication Use for BPSD and Improving Health Outcomes in PLWD**

**Principal Investigator:**
Helen C. Kales, MD
Joe P. Tupin Endowed Professor and Chair of the Department of Psychiatry and Behavioral Sciences at University of California, Davis

**Supported by:**

**The National Institute on Aging**

FY22_Pilot2_Kales

**Study Intervention Provided by: N/A**

**Sponsor of IND/IDE: N/A**

*(Any modification to the protocol should be annotated on the coversheet or in an appendix. The annotation should note the exact words that are changed, the location in the protocol, the date the modification was approved by the Executive Committee, and the date it became effective.)*

**Version 1**

**November 15, 2022**

**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 |
|---|---|---|
| | | |
| | | |
| | | |
| | | |
| | | |
| | | |
| | | |

**TABLE OF CONTENTS**

Page

## PRÉCIS

**Intervention Structure, Implementation Protocol, Fidelity/Adherence Monitoring Plan:**
In this study, we will refine and pilot the application of DICE in 4 primary care clinics by: (a) leveraging existing clinic staff to deliver DICE to care partner-PLWD dyads; (b) using electronic resources to identify and recruit PLWD-care partner dyads based on clinically relevant and minimum inclusion/exclusion criteria; and c) evaluating clinically relevant outcomes using the electronic medical record (EMR). DICE will be implemented in four large primary care clinics within the UCD Health System over a 6-month period (n=100 PLWD-care partner dyads; 25 dyads per site, allowing comparison of implementation and outcomes by site characteristics). Key "study champions"at each of the four primary care clinics will be the licensed practical nurse assigned to each clinic who will serve as the Onsite DICE Coordinator (ODC).

As a minimal risk study embedded in primary care practices, we plan to obtain a waiver of informed consent for PLWD, care partners and clinic staff in order to reduce introduction of artificial care resources or biases wherever possible. Additionally, a HIPAA waiver will be obtained for subject identification (see a. below) and outcome ascertainment from the EMR. There will be minimal PHI data collected. At the time the agreement is finalized, the IRB of Record to make the HIPAA determinations, or if necessary UC Davis IRB will make the HIPAA determinations before releasing the acknowledgment of a reliance on an external IRB.

We have arranged with University of California Davis LVN supervisors (Ms. Elder and Ms. Skillsky) to do a 6-hour training for all of the LVNs on a single day. This will be a hybrid of in person (kick off session and ending brainstorming session) and watching the online modules together in a campus auditorium. ODCs will then use the approach in a "test" case in study months 2-3 during which they will engage in as needed coaching with a DICE trainer (a geriatric psychiatrist and education specialist) to ensure they are using the approach with fidelity. The DICE trainer will also be available as needed for coaching during the remainder of the study for approach related questions. Manualization and training with follow-up coaching have been shown to be effective implementation strategies that can enhance fidelity of implementation of an evidence-based program. Other clinic personnel (social workers and PCPs) will also receive the manual, an email overview of the study, and be invited to train using the website or at the on-site training. Following training and case consultation, the ODCs will then use the DICE Approach for any PLWD they encounter during the 6-month study period (months 4-9). Primary outcome metrics will be collected using the electronic medical record and by estimating time spent in the approach and strategies extracted from clinic notes.

The ODC will meet with the PLWD-Care partner dyad by phone to determine if any BPSD are present. If no BPSD are currently present, the ODC will educate the care partner about DICE, including minimizing risk factors to prevent behaviors, and plan to continue monitoring (26) for BPSD during the 6-month study period. If BPSD are occurring, then the "Describe" and "Investigate" Steps of DICE will be triggered.

Each step of DICE will be documented by the ODC in their clinic note within the EMR. In the "Describe" step, the ODC will obtain an accurate characterization of the behavior and the

context in which it occurs as well as quantify the frequency and severity of the most troublesome behavior (as defined by the care partner) using the one-item question we have used in prior trainings (16, 17): "Please rate from 0 to 4 the severity and frequency of the behavior (0=none or never; 1=mild and/or occasionally; 2=moderate and/or sometimes; 3=severe and/or frequently; and 4=very severe and/or daily). If the severity and frequency are different, pick the higher score (e.g. a behavior that is daily but mild should be scored as a 4)". In the "Investigate" step, the ODC will identify possible underlying and modifiable causes of the behavior.

With information obtained in the "Describe" and "Investigate" steps, the ODC will work with the care partner to create and implement a treatment plan to manage BPSD. The ODC will brainstorm with the care partner (e.g. what are activities the PLWD enjoys) and instruct the care partner in behavioral and environmental strategies. These approaches could include enhancing effective communication with the PLWD, creating meaningful activities, dealing with environmental challenges including ensuring safety, and simplifying tasks and creating structured routines. The ODC will also consult with other relevant clinic personnel on the Create treatment plan as needed; for example, a plan may involve having the provider assess and manage infection, constipation or pain. From prior experience with DICE, these first three steps (Describe, Investigate, Create) can be accomplished in 30 minutes.

Following the "Create" step, and in a 2-week follow-up contact by telephone, the ODC will engage in the "Evaluate" step with the care partner, during which the ODC will determine if recommended strategies were used and their effectiveness. Effectiveness will be measured by repeating the frequency/severity question asked of the care partner in Describe so that the impact of the strategy can be assessed quantitatively comparing the pre- and post-strategy scores at 2 weeks' time; any downward movement of the score will be categorized as effective. , If the DICE generated strategies were effective, the ODC will monitor and surveil for BPSD with monthly contact. If the DICE generated strategies were not effective, the ODC will problem-solve with the care partner and other team members to determine if a) strategies were used and if so correctly; or b) if strategies are not effective and additional "Create" recommendations are needed. Additionally, the DICE trainer (MB) will be available to ODC for coaching regarding the DICE Approach as needed during the study period.

## Study Title

**Training Dementia Care Professionals to Help Care Partners Improve the Management of BPSD Using the DICE Approach**

## Objectives

**Primary:** To pilot a clinical implementation of The DICE Approach to not only provide clinicians tools to address behavioral issues with PLWD patients via their caregivers but also to determine the feasibility of ascertaining and analyzing the primary (psychotropic medication use) and secondary clinical outcomes (hospitalizations, ED visits and nursing home placement of PLWDs), including whether they differ for participants of color.

**Secondary:** To inform the design of a future large-scale ePCT, including its relevance to people from diverse racial, ethnic, socio-economic, and educational backgrounds who are living with dementia and their care partners. DICE is centered around reducing the "knee-jerk" use of psychiatric medications for sedation among PLWD, particularly when the underlying causes of BPSD (e.g. infection; pain; stressful environment) have not been explored.

**Design and Outcomes**

In this study, we will refine and pilot the application of DICE in 4 primary care clinics by: (a) leveraging existing clinic staff to deliver DICE to care partner-PLWD dyads; (b) using electronic resources to identify and recruit PLWD-care partner dyads based on clinically relevant and minimum inclusion/exclusion criteria; and c) evaluating clinically relevant outcomes using the electronic medical record (EMR). DICE will be implemented in four large primary care clinics within the UCD Health System over a 6-month period (n=100 PLWD-care partner dyads; 25 dyads per site, allowing comparison of implementation and outcomes by site characteristics). Key "study champions"at each of the four primary care clinics will be the licensed practical nurse (LVN) assigned to each clinic who will serve as the Onsite DICE Coordinator (ODC).

Aim 1:
Feasibility measures will include: 1) rate of enrollment of PLWD-care partner dyads; 2) number of contacts between ODCs and dyads; and 3) time requirements for ODCs implementing DICE (as estimated by the ODCs and corroborated by clinic notes).

Acceptability will be measured by the acceptance rates of the ODC's recommendations of strategies for BPSD (generated by use of DICE) among dyads, as well as by other providers within the primary care practice. Exit interviews of participants (ODCs, other providers and care partners) will be conducted to further deepen the knowledge of intervention acceptability and implementation challenges.

Clinical outcomes: all UCD clinical sites (inpatient and outpatient) use the same EMR (EPIC), so ascertaining clinical outcomes will be uniform across clinics. The primary clinical outcome is the feasibility of measuring psychotropic medication use. Mean PLWD participant psychotropic medication use during the intervention period will be compared to historical controls (mean rate of medication use among PLWD for the four participating clinics in the 6 months prior to the intervention).

Aim 2: Secondary clinical outcomes will be the feasibility of measuring rates of hospitalizations, ED visits and nursing home placement ascertained from the EMR. Mean PLWD participant health care utilization during the intervention period will be compared to historical controls (mean rate in the 6 months prior to the intervention). The feasibility of obtaining the nursing home placement variable from the EMR will be established during this pilot study by ascertaining nursing home placement from care partners and then determining if it subsequently is recorded in the EMR.

**Interventions and Duration**

The DICE Approach intervention will be piloted for 6 months during the study period. As above, mean PLWD participant psychotropic medication use during the intervention period will be compared to historical controls (mean rate of medication use among PLWD for the four participating clinics in the 6 months prior to the intervention). Secondary clinical outcomes(Aim 2) will be the feasibility of measuring rates of hospitalizations, ED visits and nursing home placement ascertained from the EMR. Mean PLWD participant health care utilization during the intervention period will be compared to historical controls (mean rate in the 6 months prior to the intervention).

**Sample Size and Population**

Study aim 1: We will examine data across 4 clinics to assess the feasibility of a multi-site study. We selected 25 dyads per clinic as our sample size (total n=100) to have the ability to examine feasibility measures within clinic as well as across clinic with some accuracy. For example, the degree of accuracy around an enrollment rate of 75% overall is 18% (width of the 95% confidence interval), allowing us a tighter margin of error overall. Within clinic, accuracy is larger (width of 95% confidence interval 36%), suggesting more uncertainty, but allowing us to examine clinic-specific enrollment to ensure that there is consistency across clinics.

An exploratory analysis will the subjects enrolled in the study (n= 100 PLWD) as described above, will be compared on [measures] with historical controls (n=100 PLWD) .

**STUDY TEAM ROSTER**

**Principal Investigator:** **Helen C. Kales, MD –** Joe P. Tupin Endowed Professor and Chair of the Department of Psychiatry and Behavioral Sciences at University of California, Davis (UC Davis)

2230 Stockton Blvd. Suite 212
Sacramento, CA 95817
Office (916) 703-3143
Main (734) 680-9981
hckales@ucdavis.edu

**Main responsibilities/Key roles:** Dr. Kales will be responsible for 1) overall scientific direction and oversight; 2) resolving methodological questions; 3) contributing to study analyses, and 4) preparing research reports and manuscripts for peer-reviewed publication and dissemination. She will execute these functions through regular contact with the other investigators and staff. Human subjects research will be conducted at the UC Davis site in the health system clinics. All data will be stored at UCD on our secure servers and data sharded with DU or sponsors will be de-identified data only.

**Co-Investigators:** **Leslie McClure, PhD –** Professor & Chair, Department of Epidemiology & Biostatistics, Drexel University (DU)

3215 Market Street
Nesbitt Hall 535
Philadelphia, PA 19141
Office (267) 359-6218
Lam439@drexel.edu

**Main responsibilities/Key roles:** Dr. McClure will provide statistical and study design expertise to the project, including generating the randomization scheme, assisting with data management with a de-identified dataset provided to her by the UC Davis team, and cleaning, analysis and dissemination.

**Laura N. Gitlin PhD, -** Distinguished University Professor and Dean, Drexel University

College of Nursing and Health Professions
Drexel University
1601 Cherry Street, Mail Stop 10501
10th Floor Room 1092

Philadelphia, PA 19102
Main (215) 260-0968
Lng45@drexel.edu

**Main responsibilities/Key roles:** Dr. Gitlin is a close collaborator of Dr. Kales having worked on two NIH (NINR and NIA) R01 clinical trials together as well as a partner in the development of The DICE Approach. She will work closely with Dr. Kales on key aspects of study methodology (design, implementation), interpretation of results and manuscript preparation.

**Project Manager:** **Vince Kern,** Project Analyst 4, University of California Davis

3267 Shawnee Tr.
Pinckney, MI 48169
(734) 245-5858
vkern@ucdavis.edu

**Main responsibilities/Key roles:** Mr. Kern will work under the direction of Dr. Kales to: 1) assist in general management and objectives of the study, including day-to-day management of project activities; 2) troubleshoot and assist with the website for ODC and other clinic staff training; 3) oversee the RA (including submitting and maintaining regulatory documentation subject ascertainment from the EMR, coordinating clinic staff DICE trainings and consultation with Dr. Blazek, facilitating clinic DICE rollout, data collection and data cleaning); and 4) coordinate and participate in all study meetings related to operations, site updates, study supervision and assessment reliability.

**Consultant:** **Mary Blazek, MD**

4260 Plymouth Rd.
Ann Arbor, MI 48109
(734) 764-6831
mblazek@med.umich.edu

Main responsibilities/Key roles: Dr. Blazek will assist with the planning and implementation of DICE training in the UC Davis primary care sites as well as serve as consultant to the Onsite DICE Coordinators (ODCs) for cases in the months post-training. She will also contribute to manuscripts for peer-reviewed publication and dissemination.

**Research Assistant: TBD**

## PARTICIPATING STUDY SITES

**University of California, Davis: Helen C. Kales, MD –** Joe P. Tupin Endowed Professor and Chair of the Department of Psychiatry and Behavioral Sciences at University of California, Davis

All non-exempt human subjects activities will occur at UC Davis.

**Drexel University:** **Leslie McClure, PhD –** Professor & Chair, Department of Epidemiology & Biostatistics, Drexel University

**Laura Gitlin, PhD** - Distinguished University Professor and Dean, Drexel University

Drexel's activity falls in an exempt category and as such they will seek an exemption from their IRB and will not need to cede to Advarra.

## 1 STUDY OBJECTIVES

1.1 **Primary Objective:** To assess the feasibility and acceptability of the ePCT protocolized version of DICE that will guide the subsequent evaluation of the effectiveness of the intervention in a full-scale ePCT. DICE will be implemented in four large primary care clinics within the UCD Health System over a 6-month period (n=100 PLWD-care partner dyads; 25 dyads per site, allowing comparison of implementation and outcomes by site characteristics). Feasibility measures will include: 1) rate of subject enrollment (PLWD-care partner dyads); 2) number of contacts between ODCs and dyads; and 3) time requirements for ODCs implementing DICE. Acceptability will be measured by the acceptance rates of the ODC's recommendations of strategies for BPSD (generated by use of DICE) among dyads, as well as other providers within the primary care practice. Exit interviews of participants (ODCs, other providers and care partners) will be conducted to further deepen the knowledge of intervention acceptability and implementation challenges.

**Secondary Objectives:** To determine the feasibility of ascertaining and analyzing the primary (psychotropic medication use) and secondary clinical outcomes (hospitalizations, ED visits and nursing home placement of PLWDs) from the existing health system-wide electronic medical record (EMR) which will subsequently be used in a full-scale

effectiveness ePCT. Clinical outcomes for PLWD participants will be measured after the 6-month DICE implementation period using the EMR and compared to corresponding outcomes for the four participating clinics in the 6 months prior to the intervention ("historical control"; all PLWD in the four participating clinics):
2a) To determine the feasibility of measuring psychotropic medication use (primary outcome) within the EMR. Mean participant psychotropic medication use during the intervention period will be compared to historical controls (mean rate of medication use for participating clinics in the 6 months prior to the intervention).
2b) To determine the feasibility of measuring hospitalizations, ED visits and nursing home placement (secondary outcomes) using the EMR. Mean participant health care utilization during the intervention period will be compared to historical controls (mean rate in the 6 months prior to the intervention).

# 2 BACKGROUND AND RATIONALE

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

Managing behavioral and psychological symptoms (BPSD) is one of the most challenging aspects of caring for a person living with dementia (PLWD), causing intense care partner (family and formal provider) burden and upset, and posing threats to their health and well-being. Importantly, PLWD with BPSD are at risk for increased hospitalization rates, emergency department (ED) visits and nursing home placement. Potentially preventable hospitalization (PPH) encompasses hospitalizations for conditions that, with optimal access to outpatient care and management, should be unnecessary (e.g. urinary tract infection). Notably, dementia has been associated with the greatest additional PPH risk in patients with less medical comorbidity, belying the notion that patients with dementia are at increased risk for hospitalization simply because they are more medically ill.

A key factor in increased PPH risk is thought to be the presence of BPSD. The potential influence of BPSD on healthcare outcomes is conceptually depicted in Figure 1, which suggests that modifiable patient, environmental and care partner factors impact this relationship/ PWLD typically live in the community and are followed in primary care settings. However, Primary Care Physicians (PCP's) largely lack the time, training, and access to dementia care expertise and delivery care systems to effectively manage the nearly ubiquitous BPSD. Although the FDA has not approved any medications to treat BPSD, it is common clinical practice to use psychiatric medications such as antipsychotics to try to control them. However, antipsychotics show only limited efficacy in improving behavioral symptoms and have significant risks including side effects and mortality resulting in FDA black box warnings regarding their use for this purpose. Moreover, care partners frequently manage multiple BPSD simultaneously, and that can be a "moving target"—aggression may co-occur with or be replaced with wandering, and so on. Thus, the very nature of BPSD makes a simple "magic bullet" medication solution impossible, ineffective and inappropriate.

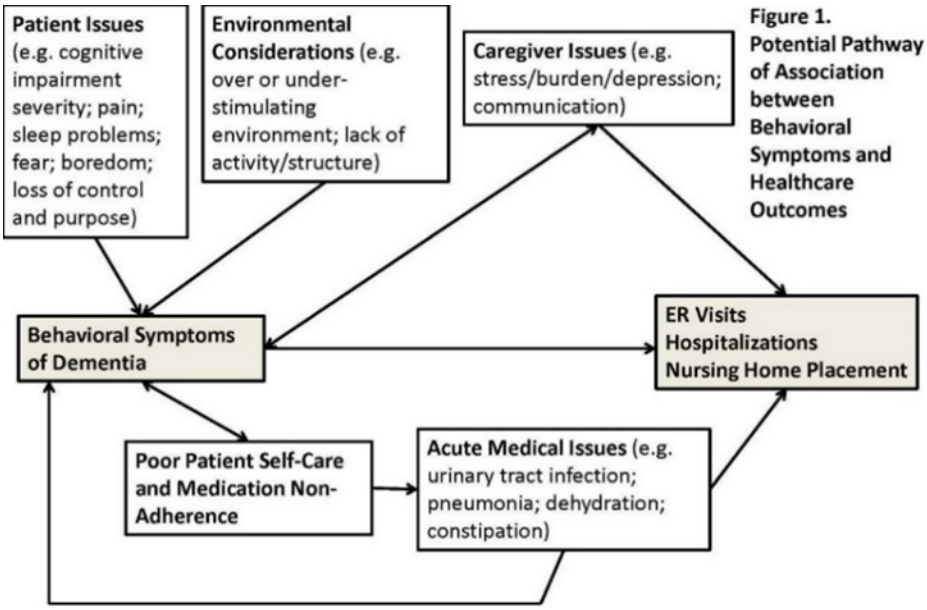


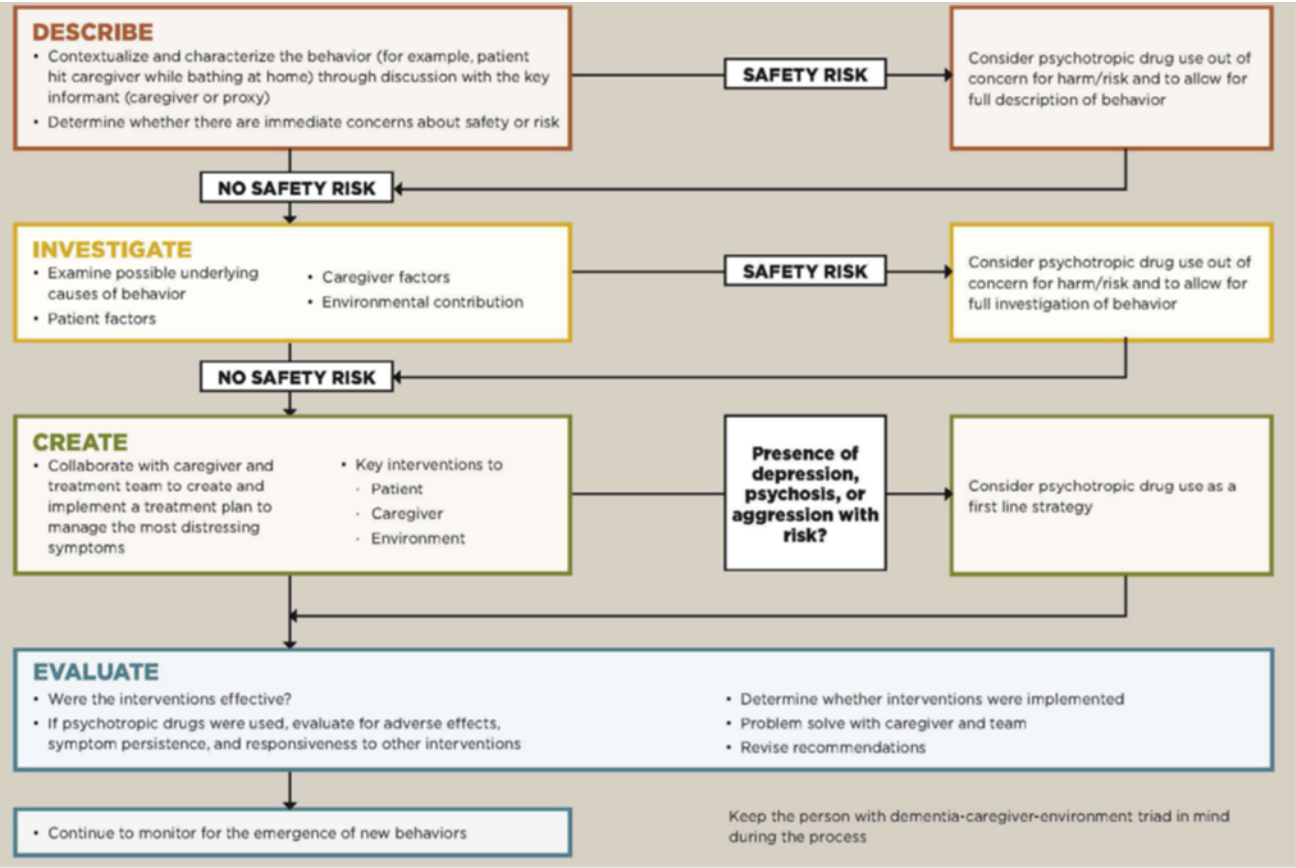

**Figure 1. Potential Pathway of Association between Behavioral Symptoms and Healthcare Outcomes**

## 2.2 Study Rationale

Nonpharmacologic strategies are recommended by multiple medical organizations and expert groups as the preferred first-line treatment approach to reduce inappropriate medication use in managing BPSD, except in emergency situations such as when behaviors could lead to imminent danger. Unfortunately, effective nonpharmacological strategies for BPSD have not been translated into real-world clinical management and standard care. Through a process of expert consensus and review of the existing evidence, we previously developed a low-cost, pragmatic, patient-centric, evidence-informed algorithm approach ("DICE"), to manage BPSD. DICE protocolizes an approach that has been tested in various randomized trials.

The DICE Approach systematically guides care partners and clinicians alike through the assessment and management of BPSD and teaches new transferrable problem-solving skills (Figure 2). We have manualized and developed both in-person and online care partner module-driven training in DICE. The trainings have now been delivered to hundreds of care partners nationally (Michigan, California, North Carolina, Pennsylvania, Wisconsin) and internationally (UK) where they have shown positive impact (18,19). The manual (20) has sold over 500 copies to date since 2017 and the training website released in 2020 (21) has over 500 subscribers.

The training approach was created with an eye towards wide-spread implementation and dissemination. The goal was to create a short training (6 hours, as opposed to weeks or months in other trainings) to minimize the time spent learning the approach. Given that prior studies have shown that brief mental health training programs can be effective for producing new skills in both professional providers (22) and family care partners (23), we created a training program aimed broadly at anyone (provider, family or professional care partner) caring for PLWD.




The training uses a modular format comprised of 8 sections:

1. What is dementia?
2. Behaviors in dementia
3. Describe step (learning to create a complete symptom description to guide assessment and management of behaviors)
4. Investigate step (identifying, examining and ruling out possible underlying and modifiable causes of behavior)
5. Create step (learning how to use behavioral and environmental strategies to manage behavioral symptoms; strategies based upon those nonpharmacologic approaches with the strongest evidence base, family caregiver interventions, which include caregiver education and support, training in stress reduction/cognitive reframing and specific skills in problem solving)
6. Evaluate step (assessing whether recommended strategies were or were not effective)
7. Learning about medications
8. Caring for the caregiver

The companion manual follows the modular format of the trainings. Training has been designed to be interactive, incorporating videos and hands-on learning and systematically moves trainees through a problem-solving approach to identify appropriate and tailored strategies to address the presenting BPSD (18). DICE has been designed to be algorithmic, easy to remember and helpful to create good habits and problem-solving. Strategies generated are based on patient and care partner profiles and the environmental context of behavioral occurrences. The approach includes guidance on the most judicious and appropriate use of psychotropics for BPSD, and expands the discussion of medications beyond psychotropics to other medications for the underlying causes

of BPSD (e.g. pain, infection, constipation). Thus, in the approach, pharmacologic, non-pharmacologic strategies or their combination may be recommended (1). Given that in-person trainings are both time and personnel intensive, we subsequently used the lessons learned from the in-person trainings to create a training website that is accessible 24/7 while retaining the interactive format (via e-simulations of various clinical situations both to teach the approach and test knowledge following training).

The DICE approach is ready for a pilot embedded pragmatic trial: it is manualized; there is a brief, tested, and accessible training program; it is designed for use by clinicians from any discipline; and its outcomes (mitigating negative effects of BPSD) reflect what matters to all stakeholders, including reduced inappropriate medication use. **Figure 2** describes the DICE Approach in more detail.

## 3 STUDY DESIGN

There are no public-facing marketing materials for this study.

In this study, we will refine and pilot the application of DICE in 4 primary care clinics by: (a) leveraging existing clinic staff to deliver DICE to care partner-PLWD dyads; (b) using electronic resources to identify and recruit PLWD-care partner dyads based on clinically relevant and minimum inclusion/exclusion criteria; and c) evaluating clinically relevant outcomes using the electronic medical record (EMR). DICE will be implemented in four large primary care clinics within the UCD Health System over a 6-month period (n=100 PLWD, care partner n= 100) dyads; 25 dyads per site, allowing comparison of implementation and outcomes by site characteristics). Key "study champions" at each of the four primary care clinics will be licensed practical nurse assigned to each clinic who will serve as the Onsite DICE Coordinator (ODC).

Secondary outcomes: EMR data collection: To determine the feasibility of ascertaining and analyzing the primary (psychotropic medication use) and secondary clinical outcomes (hospitalizations, ED visits and nursing home placement of PLWDs) from the existing health system-wide electronic medical record (EMR) which will subsequently be used in a full-scale effectiveness ePCT. Clinical outcomes for PLWD participants will be measured after the 6-month DICE implementation period using the EMR and compared to corresponding outcomes for the four participating clinics in the 6 months prior to the intervention ("historical control" n=100; compared to the sample of PLWD n=100. The total study sample size N= 100.

As a minimal risk study embedded in primary care practices, we plan to obtain a waiver of informed consent for PLWD, care partners and clinic staff in order to reduce introduction of artificial care resources or biases wherever possible. Additionally, a HIPAA waiver will be obtained for subject identification (see a. below) and outcome ascertainment from the EMR. There will be minimal PHI data collected.

We will work with each clinic site to allow ODC's the dedicated time (at least 6 hours) to engage in the online training during month one of the study. Because we want to have the least impact

on clinic schedules, ODCs will be permitted to do the training at their own pace asynchronously (e.g. all ODCs need not do the training at the same time). ODCs will then use the approach in a "test" case in study months 2-3 during which they will engage in as needed coaching with a DICE trainer (a geriatric psychiatrist and education specialist) to ensure they are using the approach with fidelity. The DICE trainer will also be available as needed for coaching during the remainder of the study for approach related questions. Manualization and training with follow-up coaching have been shown to be effective implementation strategies that can enhance fidelity of implementation of an evidence-based program. Other clinic personnel (nurse care navigators and PCPs) will also receive the manual, an email overview of the study, and be invited to train using the website. Following training and case consultation, the ODCs will then use the DICE Approach for any PLWD they encounter during the 6-month study period (months 4-9). Primary outcome metrics will be collected using the electronic medical record and by estimating time spent in the approach and strategies extracted from clinic notes.

## 4 SELECTION AND ENROLLMENT OF PARTICIPANTS

**Study Population:** English-speaking (as discerned from the EMR) PLWD-Care partner dyads from the 4 participating clinics will be recruited. Dyads in the participating clinics will be identified in the following way:

- via warm handoff from a clinic provider to the ODC via the current standard of care for working with caregivers of PLWD regarding behavioral concerns, ODCs will be notified of the potential study participant by either of the two methods of ascertainment by the study RA. The ODC will then contact the care partner who is identified in the EMR as the responsible person or family member for the PLWD by telephone participation in the DICE program. We will also track the proportion of PLWD without a caregiver listed for study tracking.

**Setting:** Participants will be recruited from four primary care clinics in the Primary Care Network (total of 13) at University of California Davis. Clinics have been selected for the number of PLWD seen annually in each clinic. Below is preliminary information obtained on the potential subject population for the four study clinics from FY 1/1/2021-12/31/2021:

| | Midtown | Elk Grove | ACC | FCC |
|---|---|---|---|---|
| **>65 years old Dementia** | 63 | 67 | 66 | 76 |
| **Race/ethnicity** | | | | |
| White | 40 (63.55) | 35 (52.2%) | 40 (63.5%) | 27 (35.5%) |
| Black | 11 (17.5%) | 14 (20.9%) | 11 (17.5%) | 11 (14.5%) |
| Asian | 8 (12.7%) | 10 (14.9%) | 8 (12.7%) | 25 (32.9%) |
| Other | 4 (6.4%) | 8 (11.9%) | 4 (6.3%) | |
| | | | | **13 (17.1%)** |

### 4.1 Inclusion Criteria

Participants must meet all inclusion criteria to participate in the study:

DICE participants

1) Person living with dementia (as defined by chart diagnosis) and their care partner
2) Care partner age >18 as defined in the EMR
3) Care partner English speaking

Historical controls

1) Person living with dementia (as defined by chart diagnosis)

### 4.2 Exclusion Criteria

1) Age of care partner <18 (this age group is rarely the responsible or legal party for PLWD)
2) Non-English speaking

### 4.3 Study Enrollment Procedures

PLWD-Care partner dyads from the 4 participating clinics will be recruited via warm handoff from a clinic provider. The ODC will then contact the care partner who is identified in the EMR as the responsible person or family member for the PLWD by telephone to discuss participation in the DICE Program. Participants will be recruited from four primary care clinics in the Primary Care Network (total of 13) at University of California Davis. Clinics have been selected for the number of PLWD seen annually by clinic social workers who are embedded in each clinic. As a minimal risk study embedded in primary care practices, we plan to obtain a waiver of informed consent for PLWD, care partners and clinic staff in order to reduce introduction of artificial care resources or biases wherever possible. There will be minimal PHI data collected.

## 5 STUDY INTERVENTIONS

### 5.1 Interventions, Administration, and Duration

This is a single group intervention. We have arranged with University of California Davis LVN supervisors to do a 6-hour training for all the LVNs on a single day. This will be a hybrid of in person (kick off session and ending brainstorming session) and watching the online modules together in a campus auditorium. ODCs will then use the approach in a "test" case in study months 2-3 during which they will engage in as needed coaching with a DICE trainer (a

geriatric psychiatrist and education specialist) to ensure they are using the approach with fidelity. Manualization and training with follow-up coaching have been shown to be effective implementation strategies that can enhance fidelity of implementation of an evidence-based program. Other clinic personnel (social workers and PCPs) will also receive the manual, an email overview of the study, and be invited to train using the website or at the on-site training. Following training and case consultation, the ODCs will then use the DICE Approach for any PLWD they encounter during the 6-month study period (months 4-9). Primary outcome metrics will be collected using the electronic medical record and by estimating time spent in the approach and strategies extracted from clinic notes.

As part of the DICE program, the ODC will meet with the PLWD-Care partner dyad by phone to determine if any BPSD are present. If no BPSD are currently present, the ODC will educate the care partner about DICE, including minimizing risk factors to prevent behaviors, and plan to continue monitoring (26) for BPSD during the 6-month study period. If BPSD are occurring, then the "Describe" and "Investigate" Steps of DICE will be triggered.

Each step of DICE will be documented by the ODC in their clinic note within the EMR as is part of usual practice. In the "Describe" step, the ODC will obtain an accurate characterization of the behavior and the context in which it occurs as well as quantify the frequency and severity of the most troublesome behavior (as defined by the care partner) using the one-item question we have used in prior trainings (16, 17): "Please rate from 0 to 4 the severity and frequency of the behavior (0=none or never; 1=mild and/or occasionally; 2=moderate and/or sometimes; 3=severe and/or frequently; and 4=very severe and/or daily). If the severity and frequency are different, pick the higher score (e.g. a behavior that is daily but mild should be scored as a 4)". In the "Investigate" step, the ODC will identify possible underlying and modifiable causes of the behavior.

With information obtained in the "Describe" and "Investigate" steps, the ODC will work with the care partner to create and implement a treatment plan to manage BPSD. The ODC will brainstorm with the care partner (e.g. what are activities the PLWD enjoys) and instruct the care partner in behavioral and environmental strategies. These approaches could include enhancing effective communication with the PLWD, creating meaningful activities, dealing with environmental challenges including ensuring safety, and simplifying tasks and creating structured routines. The ODC will also consult with other relevant clinic personnel on the Create treatment plan as needed; for example, a plan may involve having the provider assess and manage infection, constipation or pain. From prior experience with DICE, these first three steps (Describe, Investigate, Create) can be accomplished in 30 minutes.

Following the "Create" step, and in a 2-week follow-up contact by telephone, the ODC will engage in the "Evaluate" step with the care partner, during which the ODC will determine if recommended strategies were used and their effectiveness. Effectiveness will be measured by repeating the frequency/severity question asked of the care partner in Describe so that the impact of the strategy can be assessed quantitatively comparing the pre- and post-strategy scores at 2 weeks' time; any downward movement of the score will be categorized as effective. If the DICE generated strategies were effective, the ODC will monitor and surveil for BPSD with monthly contact. If the DICE generated strategies were not effective, the ODC will

problem-solve with the care partner and other team members to determine if a) strategies were used and if so correctly; or b) if strategies are not effective and additional "Create" recommendations are needed. Additionally, the DICE trainer (MB) will be available to ODC for coaching regarding the DICE Approach as needed during the study period.

### 5.2 Handling of Study Interventions

See above.

### 5.3 Concomitant Interventions

Not applicable.

### 5.4 Adherence Assessment

Rather than adherence, in this pilot study, we will be examining feasibility and acceptability. Feasibility measures will include: 1) rate of enrollment of PLWD-care partner dyads; 2) number of contacts between ODCs and dyads; and 3) time requirements for ODCs implementing DICE (as estimated by the ODCs and corroborated by clinic notes).

Acceptability will be measured by the acceptance rates of the ODC's recommendations of strategies for BPSD (generated by use of DICE) among dyads, as well as by other providers within the primary care practice.

## 6 STUDY PROCEDURES

### 6.1 Schedule of Evaluations

| Assessment | Screening: | Baseline, Enrollment, Visit 1 (Day 0) | Followup, Visit 2 (Day 14) | Followup Visit 3 (Day44) | Followup Visit 4 (Day 74) | Followup Visit 5 (Day 104) | Followup Visit 6 (Day 134) | Followup Visit 7 (Day 164) |
|---|---|---|---|---|---|---|---|---|
| *Verification of dementia diagnosis and eligibility via inclusion/exclusion criteria* | X | | | | | | | |
| *Demographics* | X | | | | | | | X |
| *Current Medications* | X | X | X | X | X | X | X | X |
| *Hospitalizations* | | | | | | | | X |
| *Nursing Home Placement* | | | | | | | | X |
| *ED Visits* | | | | | | | | X |
| *Adverse Events* | | X | X | X | X | X | X | X |

### 6.2 Description of Evaluations

Please refer to Section 3.

#### 6.2.1 Screening Evaluation

Consenting Procedure

Not applicable. A waiver of informed consent will be sought as DICE will be part of any contact by the ODC with care partners about behavioral concerns in the PLWD. A waiver of information consent will also be requested for access to the EMR for the historical controls.

#### 6.2.2 Enrollment, Baseline, and/or Randomization

Enrollment

Enrollment will follow identification and meeting of inclusion and exclusion criteria.

#### 6.2.3 Follow-up Visits

Visits will be flexible and tailored to the needs of each care partner and PLWD as part of usual care. However, in general, Visit 1 will consist of meeting with the care partner over the phone to determine if any behavioral or psychological symptoms of dementia (BPSD) are present. If none are present, the ODC will educate the care partner about BPSD and the DICE Approach and create a plan for monitoring during the 6-month study period. If BPSD are present, the "Describe" and Investigate" steps of the DICE intervention will be triggered. Using this information during the same visit, the ODC will work with the care partner to create and implement a treatment plan. This visit will be accomplished in 30 minutes. Visit 2 will occur approximately 2 weeks after the first visit. The ODC will engage in the "Evaluate" step to determine if the treatment plan was implemented and its effectiveness. If effective, the ODC will monitor and surveil for BPSD with monthly contact. If not effective, the ODC will work with the care partner to create additional treatment strategies and then follow up at intervals between 2 weeks and 1 month as needed.

#### 6.2.4 Completion/Final Evaluation

At the final visit, an evaluation of the current effectiveness of DICE strategies will be performed. Exit interviews of participants (ODCs, other providers and care partners) will be conducted to further deepen the knowledge of intervention acceptability and implementation challenges. We will seek a waiver of informed consent for these interviews which will be conducted by study team members.

## 7 SAFETY ASSESSMENTS

The anticipated risks are very minimal given that this is a non-pharmacologic intervention being implemented to enhance usual care.

### 7.1 Specification of Safety Parameters

NA

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

NA

### 7.3 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 participants' 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
- Causes persistent or significant disability or incapacity
- Results in congenital anomalies or birth defects
- Is another condition which investigators judge to represent significant hazards

No AE's or SAE's are expected based upon the study intervention. Hospitalizations and ED visits are secondary outcomes in the study and not considered adverse events. However, we will collect data on such events from the medical chart and caregiver report during visits and report them as needed.

### 7.4 Reporting Procedures

The primary investigator will be responsible for determining the severity and whether any AE or SAE is study related.

**Severity of Event**

For adverse events (AEs), the following guidelines will be used to describe severity.

- Mild – Events require minimal or no treatment and do not interfere with the participant's daily activities.
- Moderate – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- Severe – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious".

These terms should match those collected on the Adverse Event Form.

**Relationship To Study Intervention**

Given the nature of the intervention, a binary assessment (related/not related) will be used. No AE's or SAE's are expected based upon the study intervention. Hospitalizations and ED visits are secondary outcomes in the study and not considered adverse events.

AEs for this study include: Mild inconvenience due to the time taken for the intervention.

SAEs for this study include: Given the nature of the participant population based on age and comorbidities, death can reasonably be expected (unrelated to the intervention) in some PLWD.

### 7.5 Follow-up for Adverse Events

The occurrence of an adverse event (AE) or serious adverse event (SAE) may come to the attention of study personnel during visits with the ODC or study team review of the medical record.

We will distinguish between alerts and adverse events as developed by the NIH REACH initiative. Alerts refer to events occurring independently of the study and place the PLWD or care partner at risk. These could include a care partner medical emergency, PLWD driving, aggression in the dyad, suicidal ideation in a care partner or PLWD, etc. The Project Manager will keep a running record of alerts and dates of resolution. We will seek resolution of an alert within 48 hours of being notified of such and define resolution as the participant being contacted and informed of actions to resolve the presenting issue. Alert forms will be reviewed by Dr. Kales weekly during research administration meetings. Adverse events include hospitalization. ED visit, nursing home placement or death of a caregiver or PLWD. There are two levels of monitoring of adverse events. For AEs attributed to the study/intervention, notification of the PI, IRB, Safety Officer (SO) and NIA occurs within 24 to 48 hours of identification of the event, as per the DSMP and as noted in Section 7.7 below. For AEs not attributed to the study/intervention, the first level of monitoring occurs on a weekly basis and involves the following; a) the PI are notified of all non-emergency events at staff meetings with project directors at their respective sites; b) events are reviewed at weekly interviewer meetings at respective sites to assure that each has been managed appropriately and follow-up and resolution obtained); c) all events will be entered in a secure on-line data management system developed, and monitored at DU. The second level of review involves generating aggregate data reports that are provided to both PIs and SO twice yearly for review (or more frequently if they so choose). Data entry and an aggregate review facilitate a double check that events are resolved and assist in monitoring of the trial. Resolution of events is defined as the participant having been contacted and informed of actions to resolve the presenting issue.

### 7.6 Safety Monitoring

Given the minimal risk nature of the study embedded in usual care, NIA determined that a DSMB is not required. Rather, the IMPACT Collaboratory Safety Officer (SO) will be appointed to evaluate all study protocols and enrollment rates to ensure conformity to human subject procedures and patient safety in the trial. The SO will also review the study design, the IRB protocols, any adverse events, and interim reports of the ongoing study. Dr. Kales will be responsible for overseeing the preparation of data and data analyses for the SO. The Principal Investigator (PI) will be responsible for ensuring participants' safety on a daily basis. In addition, the NIA IMPACT Collaboratory SO will oversee all data and safety monitoring activities for this study. 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 SO, will make a determination regarding how often data safety monitoring reporting is needed.

### 7.7 Reporting schedule:

- 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.

## 8 INTERVENTION DISCONTINUATION

As a minimal risk study embedded in primary care practices, we plan to obtain a waiver of informed consent for PLWD, care partners and clinic staff in order to reduce introduction of artificial care resources or biases wherever possible. The DICE Approach will be delivered as part of routine care. It is possible that PLWD/care partners may drop out of routine outpatient care. If this occurs, we will continue to monitor and evaluate PLWD data.

## 9 STATISTICAL CONSIDERATIONS

### 9.0 General Design Issues

The overarching goal of this proposal is to refine and pilot the application of DICE in primary care clinics by: (a) leveraging existing clinic staff to deliver DICE; and (b) using electronic resources to identify and recruit PLWD-care partner dyads based on clinically relevant and minimum inclusion/exclusion criteria. We maximize a pragmatic approach and minimize a separate study infrastructure to evaluate feasibility and acceptability in order to prepare for a larger embedded pragmatic trial (ePCT). Licensed practical nurses embedded in four primary care practices at University of California Davis (UCD), whom we will refer to as "Onsite DICE Coordinators" (ODC), will coordinate behavioral management using DICE with care partner-PLWD dyads and other clinic providers. We will accomplish this goal through the following specific aims:

Aim 1. To assess the feasibility and acceptability of the ePCT protocolized version of DICE that will guide the subsequent evaluation of the effectiveness of the intervention in a full-scale ePCT. DICE will be implemented in four large primary care clinics within the UCD Health System over a 6-month period (n=100 PLWD-care partner dyads; 25 dyads per site, allowing comparison of implementation and outcomes by site characteristics). Feasibility measures will include: 1) rate of subject enrollment (PLWD-care partner dyads); 2) number of contacts between ODCs and dyads; and 3) time requirements for ODCs implementing DICE. Acceptability will be measured by the acceptance rates of the ODC's recommendations of strategies for BPSD (generated by use of DICE) among dyads, as well as other providers within the primary care practice. Exit interviews of participants (ODCs, other providers and care partners) will be conducted to further deepen the knowledge of intervention acceptability and implementation challenges.

Aim 2. To determine the feasibility of ascertaining and analyzing the primary (psychotropic medication use) and secondary clinical outcomes (hospitalizations, ED visits and nursing home placement of PLWDs) from the existing health system-wide electronic medical record (EMR) which will subsequently be used in a full-scale effectiveness ePCT. Clinical outcomes for PLWD participants will be measured after the 6-month DICE implementation period using the EMR and

compared to corresponding outcomes for the four participating clinics in the 6 months prior to the intervention ("historical control"; all PLWD in the four participating clinics):

2a) To determine the feasibility of measuring psychotropic medication use (primary outcome) within the EMR. Mean participant psychotropic medication use during the intervention period will be compared to historical controls (mean rate of medication use for participating clinics in the 6 months prior to the intervention).

2b) To determine the feasibility of measuring hospitalizations, ED visits and nursing home placement (secondary outcomes) using the EMR. Mean participant health care utilization during the intervention period will be compared to historical controls (mean rate in the 6 months prior to the intervention).

### 9.1 Sample Size and Randomization

We will examine data across 4 clinics in order to assess the feasibility of a multi-site study. We selected 25 dyads per clinic as our sample size (primary study sample- total n=100 PLWD), and their caregiver (n=100) in order to have the ability to examine feasibility measures within clinic as well as across clinic with some accuracy. For example, the degree of accuracy around an enrollment rate of 75% overall is 18% (width of the 95% confidence interval), allowing us a tighter margin of error overall. Within clinic, accuracy is larger (width of 95% confidence interval 36%), suggesting more uncertainty, but allowing us to examine clinic-specific enrollment to ensure that there is consistency across clinics.

To determine the feasibility of ascertaining and analyzing the primary (psychotropic medication use) and secondary clinical outcomes (hospitalizations, ED visits and nursing home placement of PLWDs) from the existing health system-wide electronic medical record (EMR) participants (the primary study sample of PLWD n=100) will be measured after the 6-month DICE implementation period using the EMR and compared to corresponding outcomes for the four participating clinics in the 6 months prior to the intervention (historical controls n=100); all PLWD in the four participating clinics), (N=300).

### 9.2 Treatment Assignment Procedures

Not applicable

### 9.3 Interim analyses and Stopping Rules

Not applicable

### 9.4 Outcomes

Clinical outcomes: all UCD clinical sites (inpatient and outpatient) use the same EMR (EPIC), so ascertaining clinical outcomes will be uniform across clinics. The primary clinical outcome is the feasibility of measuring psychotropic medication use. Mean PLWD participant

psychotropic medication use during the intervention period will be compared to historical controls (mean rate of medication use among PLWD for the four participating clinics in the 6 months prior to the intervention). Secondary clinical outcomes will be the feasibility of measuring rates of hospitalizations, ED visits and nursing home placement ascertained from the EMR. Mean PLWD participant health care utilization during the intervention period will be compared to historical controls (mean rate in the 6 months prior to the intervention). The feasibility of obtaining the nursing home placement variable from the EMR will be established during this pilot study by ascertaining nursing home placement from care partners and then determining if it subsequently is recorded in the EMR.

### 9.5 Data Analyses

Data will be summarized with descriptive statistics to allow us to review the demographics and clinical characteristics of our enrolled participants, as well as to review implausible values. The extent of missing data will also be assessed as a key indicator of feasibility of collecting data from clinic notes and the EMR; additionally, we will ascertain whether baseline characteristics are associated with missingness in order to modify study procedures for the larger trial. Feasibility will be characterized by rate of enrollment (# enrolled/# invited to enroll), number of contacts between ODCs and dyads (summarized as averages/SDs across dyads), and time requirements (summarized as averages/SDs). We will examine these overall and by clinic, to ensure consistency across clinics. We will summarize data on medication use (binary: psychotropic use or not) for the four clinics overall prior to the study and for enrolled PLWD post-intervention and will compare them using mixed models with a logit link to analyze these pre-post data, accounting for correlation within clinic. Models will first be fitted in a crude fashion, secondarily we will include covariate adjustment as a means to inform design characteristics in the ePCT, recognizing we have limited power to make definitive conclusions from these analyses. We will similarly examine healthcare utilization (counts of hospitalizations and ED visits; binary measure of nursing home placement) once we ensure that these data are feasibly collected from the EPIC EHR.

Models will first be fitted in a crude fashion, secondarily we will include covariate adjustment to inform design characteristics in the ePCT, recognizing we have limited power to make definitive conclusions from these analyses. We will similarly examine healthcare utilization (counts of hospitalizations and ED visits; binary measure of nursing home placement) once we ensure that these data are feasibly collected from the EPIC EHR. In order to go on to the ePCT, we must meet two criteria. First, the primary feasibility outcome (enrollment rates) must be greater than 75%. Second, we must be able to show that the lower limit of the 90% confidence interval for testing the pre-post medication use is greater than a 25% decrease in the pre-study proportion. The former criteria is based on the observed enrollment rate in the pilot from the WeCareAdvisor study (17) of PLWD-care partner dyads; the latter is based on what is reasonable to assume will change in the shorter 6-month pilot and is clinically relevant.

## 10 DATA COLLECTION AND QUALITY ASSURANCE

### 10.2 Data Collection Forms

Data will be collected from the electronic medical record. ODCs will put information about the use of the DICE Approach into their routine clinical notes. Exit interviews will be collected on paper and uploaded into secure study files.

### 10.3 Data Management

The UCD study team will be responsible for data collection. Data from the clinical notes as well as outcomes will be downloaded onto a secure server. A waiver of authorization for PHI data will be completed by the study team. The Drexel CO-I will be responsible for data management and analysis of a deidentified data set that is transferred from UCD and securely stored at Drexel.

### 10.4 Quality Assurance

10.3.1 Training

The study will take place in usual clinic care. The only added training will be the training in the DICE approach as described above. PIs and study personnel will be trained in Good Clinical Practice and HIPAA for research purposes.

10.3.2 Quality Control Committee

Not applicable

10.3.3 Metrics

Not applicable

10.3.4 Protocol Deviations

Will be submitted as applicable.

10.3.5 Monitoring

Not applicable

## 11 PARTICIPANT RIGHTS AND CONFIDENTIALITY

### 11.1 Institutional Review Board (IRB) Review

This protocol 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

We request a waiver of informed consent for the use of electronic medical records for recruitment purposes and outcome ascertainment, enrollment, and participation in the program for the study subjects. We also request a waiver of informed consent through the use of

electronic medical records for historical controls. We offer the following justifications for the waivers of informed consent:

- *the research involves no more than minimal risk to the subjects*. This is an augmentation of usual care. The anticipated risks are minimal given that this is a non-pharmacologic intervention being implemented to enhance usual care by educating clinical staff on The DICE Approach. The training is done via The DICE Approach web-based training and its companion printed manual.
- *The research could not practicably be carried out without the requested waiver*. As part of usual care, it would be impossible to consent every dyad. As a minimal risk study embedded in primary care practices, we are requesting a waiver of informed consent for PLWD, care partners and clinic staff in order to reduce introduction of artificial care resources or biases wherever possible. Also, requiring consent would introduce artificial care resources and bias which would compromise scientific validity.
- *the research could not practicably be carried out without using such information;* collecting data on this augmentation of usual care is essential for this research. The knowledge to be gained is critical. Rates of psychotropic use are at all-time highs post-pandemic, putting PLWD at risk for morbidity, mortality and reduced quality of life. . We require identifiable information for recruitment purposes and for access to the EMR for the historical controls.
- *The waiver or alteration will not adversely affect the rights and welfare of the subjects*. This is an augmentation of usual care that is being adopted clinic wide. The main purpose of this study is to assess the feasibility and usability of this intervention in primary care and anticipate that it will benefit PLWD and their care partners.
- *There will be minimal PHI data collected and the HER data will be de-*identified prior to sending the data to the data analyst in the study. Requiring consent will introduce artificial care resources and bias which would compromise scientific validity.
- The clinicians and/or caregivers who will be applying the strategy post-training will be seeking outcomes and the PLWD will not be trained in The DICE Approach but rather be the recipient of the non-pharm behavioral strategies.
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation. At *the end of the study; no information will be provided directly to subjects. However, we plan to provide information about the results through departmental/HS electronic newsletters, through our CTSC study pages and we will utilize UCD CTSC resources to disseminate the findings to the community at large*.

Finally, please note that we do not consider the exit interviews to be a human subjects research activity requiring consent. They consist of Exit interviews of participants (ODCs, other providers and care partners) and will be conducted to further deepen the knowledge of intervention acceptability and implementation challenges.

### 11.3 Participant Confidentiality

In using the EMR data for subject identification and outcome ascertainment, we will request a full waiver of HIPAA authorization since we are not planning on getting direct authorization from the PLWD themselves. The HIPAA waiver is needed for the release or use of identifiable PHI by a covered entity for the purposes of research. The HIPAA authorization/waiver criteria that must be met are similar to, but distinct from the consent waiver requirements, and each criteria (provided below) must be stated and justified. Exit interviews will be linked to study ID only and no PHI will be collected.

Use or disclosure involves no more than minimal risk to the privacy of individuals because of the presence of at least the following elements:

- We will protect health information identifiers from improper use or disclosure. Any data 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 necessary for monitoring by IRB, the sponsor or persons working on behalf of the sponsor (i.e. IMPACT research study staff, the DSMB and/or Safety Officer), the NIA, and the OHRP.
- We will destroy identifiers at the earliest opportunity absent a health or research justification or legal requirement to retain them, and
- 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; Information will not be released without written permission of the participant, except as necessary for monitoring by IRB, the sponsor or persons working on behalf of the sponsor (i.e. IMPACT research study staff, the DSMB and/or Safety Officer), the NIA, and the OHRP.
- Research could not practicably be conducted without the waiver or alteration; As a minimal risk study embedded in primary care practices, we are requesting a HIPAA waiver for PLWD, care partners and clinic staff in order to reduce introduction of artificial care resources or biases wherever possible.

- Research could not practicably be conducted without access to and use of PHI. We require PHI information for recruitment purposes and outcome ascertainment, enrollment, and participation in the program and for access to the EMR for the historical controls.

### 11. 4 Study Discontinuation

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

### 11.5 Ethical Considerations

All ethical principles as listed in the Belmont Report will be followed.

### 11.6 Committees

Not applicable.

### 11.8 Publication Of Research Findings

Publication of the results of this trial will be governed by the policies and procedures developed by the Steering Committee. Any presentation, abstract, or manuscript will be made available for review by the sponsor and the NIA 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.

## 12 REFERENCES

*References Cited*

*1. Kales HC, Gitlin LN and Lyketsos CG. State of the Art Review: Assessment and management of behavioral and psychological symptoms of dementia. BMJ: British Medical Journal. 2015; 350.*

*2. Kunik ME, Snow AL, Molinari VA, Menke TJ, Souchek J, Sullivan G, Ashton CM. Health care utilization in dementia patients with psychiatric comorbidity. Gerontologist. 2003;43(1):86-91.*

*3. Bartels SJ, Horn SD, Smout RJ, Dums AR, Flaherty E, Jones JK, Monane M, Taler GA, Voss AC. Agitation and depression in frail nursing home elderly patients with dementia - Treatment characteristics and service use. American Journal of Geriatric Psychiatry. 2003;11(2):231-8. doi: 10.1176/appi.ajgp.11.2.231.*

*4. Ng S, Morgan RO, Walder A, Biswas J, Bass DM, Judge KS, Snow AL, Wilson N, Kunik ME. Functional decline predicts emergency department use in veterans with dementia. American Journal of Alzheimer's Disease and Other Dementias. 2014.*

*5. Kunik ME, Snow AL, Davila JA, McNeese T, Steele AB, Balasubramanyam V, Doody R, Schulz PE, Kalavar JS, Walder A, Morgan RO. Consequences of aggressive behavior in patients with dementia. Journal of Neuropsychiatry and Clinical Neurosciences. 2010;22(1):40-7.*

*6. Maust DT, Kim HM, Chiang C, Langa KM, Kales HC. Predicting Risk of Potentially Preventable Hospitalization in Older Adults with Dementia. J Am Geriatr Soc. 2019*

*Oct;67(10):2077-2084. doi: 10.1111/jgs.16030. Epub 2019 Jun 18. PMID: 31211418; PMCID: PMC6896207.*

*7. Kales HC, Gitlin LN, Lyketsos CG. When Less is More, but Still Not Enough: Why Focusing on Limiting Antipsychotics in People With Dementia Is the Wrong Policy Imperative. J Am Med Dir Assoc. 2019 Sep;20(9):1074-1079. doi: 10.1016/j.jamda.2019.05.022. Epub 2019 Aug 6. PMID: 31399358.*

*8. Callahan CM, Boustani MA, Unverzagt FW, Austrom MG, Damush TM, Perkins AJ, Fultz BA, Hui SL, Counsell SR, Hendrie HC. Effectiveness of collaborative care for older adults with alzheimer diseasei n primary care: A randomized controlled trial. JAMA. 2006;295(18):2148-57. doi: 1001/jama.295.18.2148.*

*9. Boustani M, Sachs G, Callahan CM. Can primary care meet the biopsychosocial needs of older adults with dementia? Journal of General Internal Medicine. 2007;22(11):1625-7.*

*10. Maust DT, Kim HM, Seyfried LS, et al. Antipsychotics, Other Psychotropics, and the Risk of Death in Patients With Dementia Number Needed to Harm. JAMA Psychiatry. 2015; 72: 438-45.*

*11. Kales HC, Gitlin LN, Lyketsos CG; Detroit Expert Panel on Assessment and Management of Neuropsychiatric Symptoms of Dementia. Management of neuropsychiatric symptoms of dementia in clinical settings: recommendations from a multidisciplinary expert panel. J Am Geriatr Soc. 2014 Apr;62(4):762-9. doi: 10.1111/jgs.12730. Epub 2014 Mar 17. PMID: 24635665; PMCID: PMC4146407.*

*12. Nichols LO, Martindale-Adams J, Burns R, Graney MJ, Zuber J. Translation of a dementia caregiver support program in a health care system--REACH VA. Arch Intern Med. 2011;171(4):353-9. Epub 2011/03/02. doi: 171/4/353 [pii] 10.1001/archinternmed.2010.548 [doi]. PubMed PMID: 21357811.*

*13. Gitlin LN, Winter L, Dennis MP, Hodgson N, Hauck WW. A biobehavioral home-based intervention and the well-being of patients with dementia and their caregivers. JAMA. 2010;304(9):983-91. doi: 10.1001/jama.2010.1253.*

*14. Gitlin LN, Winter L, Dennis MP, Hodgson N, Hauck WW. Targeting and managing behavioral symptoms in individuals with dementia: A randomized trial of a*

*nonpharmacological intervention. Journal of the American Geriatrics Society. 2010;58(8):1465-74. doi: 10.1111/j.1532-5415.2010.02971.x.*

*15. Gitlin LN. The cost-effectiveness of a nonpharmacologic intervention for individuals with dementia and family caregivers: the tailored activity program. The American Journal of Geriatric Psychiatry. 2010;18(6):510-9. doi: 10.1097/JGP.0b013e3181c37d13*

*16. Kales HC, Kern V, Kim HM, Blazek MC. Moving Evidence-Informed Assessment and Management of Behavioral and Psychological Symptoms of Dementia into the Real World: Training Family and Staff Caregivers in the DICE Approach. Am J Geriatr Psychiatry. 2020 Dec;28(12):1248-1255. doi:1016/j.jagp.2020.08.008. Epub 2020 Aug 22. PMID: 32950366.*

*17. Walaszek A, Schroeder M, Albrecht T, LeCaire T, Endicott S, Marschall K, Felten K, Sayavedra N, Russmann S, Kern V, Blazek MC, Kales HC, Carlsson C, Mahoney J. Effectively training dementia care specialists and other dementia professionals using the DICE Approach with caregivers to improve the management of behavioral and psychological symptoms of dementia. Alzheimer's Dementia. 2021 Dec; 17 Suppl 8: e049782.*

*18. https://www.amazon.com/DICE-Approach-Caregiver-Managing-Behavioral/dp/1607855003*

*19. https://diceapproach.com/*

*20. Haddad M et al. The effect of a training programme on school nurses' knowledge, attitudes, and depression recognition skills: the QUEST cluster randomized controlled trial. Int J Nurs Stud 2018; 83: 1-10.*

*21. Haar K et al. Strong families: a new family skills training programme for challenged and humanitarian settings: a single-arm intervention tested in Afghanistan. BMC Public Health 2020; 20: 1-16.*

*22. Grodstein F, Chang CH, Capuano AW, Power MC, Marquez DX, Barnes LL, Bennett DA, James BD, Bynum JPW. Identification Of Dementia In Recent Medicare Claims Data, Compared To Rigorous Clinical Assessments. J Gerontol A Biol Sci Med Sci. 2021 Dec 17:glab377. doi: 10.1093/gerona/glab377. Epub ahead of print. PMID: 34919685.*

*McCarthy EP, Chang CH, Tilton N, Kabeto MU, Langa KM, Bynum JPW. Validation of Claims Algorithms to Identify Alzheimer's Disease and Related Dementias. J Gerontol A*

*Biol Sci Med Sci. 2021 Dec 17:glab373. doi: 10.1093/gerona/glab373. Epub ahead of print. PMID:*

**SUPPLEMENTS/APPENDICES - NONE**