MINDFULNESS-BASED DEMENTIA CARE PARTNER PROGRAM TO REDUCE DEPRESSIVE SYMPTOMS

Principal Investigator:

Leah R. Hanson, PhD
Senior Research Investigator, Senior Director of Neuroscience Research
HealthPartners Institute

Supported by:
The National Institute on Aging

Grant Number: 5U54AG063546-03 subaward 00001963

IMPACT ID FY21_Pilot2_Hanson

NCT05617300

Version 1.3
May 19, 2023

TABLE OF CONTENTS Page

1.1 PRÉCIS

Study Title

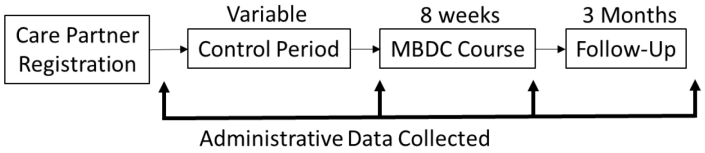
Mindfulness-Based Dementia Care Partner Program to Reduce Depressive Symptoms

Objectives

1. To assess the feasibility, acceptability, and fidelity of implementation of the MBDC program
2. To determine the feasibility of obtaining clinical outcome measures
3. To assess the willingness of participants to share access to healthcare utilization records

Design and Outcomes

This study will use a stepped wedge incomplete design with random assignment to accommodate continuous enrollment of participants and a rolling schedule of existing MBDC courses. Course participation includes the voluntary sharing of information through answering questions related to burden and mood as part of an administrative data collected at four points as illustrated below:



Interventions and Duration

The Mindfulness-Based Dementia Care (MBDC) program is an adaptation of Mindfulness-Based Stress Reduction (MBSR) for CPs of people living with Alzheimer's disease and related dementias. The web-based, group intervention consists of nine sessions including weekly two-hour classes and a half-day retreat. Participants learn from certified instructors how to incorporate mindfulness practices into day-to-day life to help cope with the challenges and stresses of dementia care. Courses currently are part of the memory clinic programs at all three of the pilot sites. Participants will be a part of the study for about 7 months including 8 weeks of intervention, a variable pre-intervention control period, and a 3-month follow-up period.

Sample Size and Population

130 adult CPs of people living with Alzheimer's disease or related dementia will be recruited to enroll in the MBDC program. Recruitment will occur as part of standard of care in three specialty care memory clinics. Eight or more MBDC courses will be held over the course of one year. During registration, CPs will self-select two options for a preferred day and time to meet for the group class. CPs will be randomly assigned to one of the two preferred day/times to assess the feasibility of randomization in a full scale embedded pragmatic clinical trial.

1 STUDY OBJECTIVES

1.1 Primary Objective

The primary aim of this study is to assess the feasibility, acceptability, and fidelity of implementation of the Mindfulness Based Dementia Care (MBDC) program.

1.2 Secondary Objectives

The second aim of this study is to determine the feasibility of obtaining clinical outcome measures. The third aim of this study is to explore the feasibility of obtaining online consent for research access to care partner (CP) and person living with dementia (PLWD) healthcare utilization records.

2 BACKGROUND AND RATIONALE

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

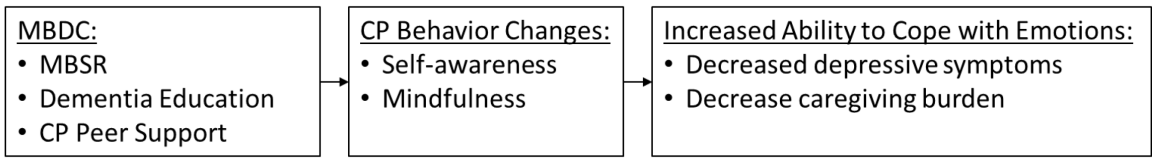
More than 11 million people provide unpaid care for people living with dementia (PLWD) in the United States.[1] While there are certain positive aspects of being a care partner (CP) and caregiving, coping with the PLWD's progressive loss of memory and ability to function in daily life can be particularly challenging and stressful. The increased burden and chronic stress of caregiving can lead to increased risk of mental health issues, as well as physical health changes.[2,3,4] Compared to non-CPs, CPs have been shown to have increased incidence of chronic conditions, including heart disease and hypertension, as well as higher utilization of healthcare services.[2,5] CPs also experience high rates of anxiety and depression.[6] Increased depressive symptoms are associated with higher CP healthcare utilization.[7] In a recent meta-analysis, depression was prevalent in 34% and anxiety in 44% of CPs of PLWD.[8] The odds of having depression were 1.5 times higher for females than males and 2.5 times higher for spousal CPs.[8]

2.2 Study Rationale

Mindfulness Based Stress Reduction (MBSR) is a group-based, standardized program that is both psychoeducation and skills-based, which uses mindfulness meditation practices to help people better cope with their emotions.[9] MBSR has been studied as a complimentary therapy to reduce stress and manage symptoms in a wide range of conditions including chronic pain, fibromyalgia, cancer, anxiety and depression.[10-12] Mindfulness based interventions, including MBSR, have been shown to decrease symptoms of depression.[13,14] MBSR is safe, with no reported adverse events. A recent review focused on the ability of mindfulness-based interventions to support caregivers of older adults, assessing depression, anxiety, burden, stress, and quality of life.[15] Three randomized controlled trials, including a total of 135 CPs, demonstrated lower level of depressive symptoms in MBSR groups compared to active control groups.[16-18] There was also some evidence for improvements in anxiety, stress, and overall wellbeing.[19] Importantly, MBSR has been tested with the intervention delivered to CPs by community-based instructors.[16] Thus, MBSR has shown Stage III efficacy in the NIH Stage Model for Behavioral Intervention Development and readiness for Stage IV testing.

There are still several challenges to a full-scale study of MBSR in CPs of PLWD including phased enrollment of courses,[20] its lack of dementia and CP specific education and support, and the unavailability of pragmatic clinical outcomes. The Presence Care Project (www.presencecareproject.com), a community-based non-profit organization, has developed a version of MBSR designed specifically for CPs of PLWD called Mindfulness Based Dementia Care.[21] Mindfulness Based Dementia Care (MBDC) is an nine-week group program, which includes both formal and informal mindfulness practice, role play, and lectures, combined with dementia-specific education and CP peer support. MBDC is recognized as a Dementia Care Program on the Best Practice Caregiving website, a partnership between Benjamin Rose Institute on Aging and Family Caregiver Alliance. MBDC participants learn how to incorporate mindfulness practices into day-to-day life as a CP to help cope with the challenges and stresses of dementia care. CPs participating in MBDC make changes to their thinking, becoming more self-aware and mindful. These behavior changes are thought to lead to an increased ability to cope with emotions as measured by decreased depressive symptoms and CP burden (Figure 1).

Figure 1. Intervention Framework



MBDC is currently being taught at memory care clinics in the United States by Presence Care certified instructors. The cost of conducting a MBDC course is estimated to be in the range of $3,000-$4,000, depending on the site. Healthcare systems have typically supported the cost of instruction through clinic operational funds or philanthropy.

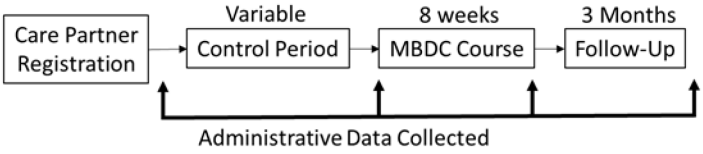
3 STUDY DESIGN

Design: The overall goal of this proposal is to test the feasibility of implementing MBDC to guide subsequent evaluation of effectiveness of the MBDC intervention in a full-scale embedded pragmatic clinical trial (ePCT). This study will use a stepped wedge incomplete design with random assignment to accommodate continuous enrollment of participants and a rolling schedule of initiating MBDC courses. We aim to examine the effects of MBDC on depressive symptoms and burden in CPs of PLWD. CPs will be referred to MBDC from three healthcare settings and surrounding community partners. MBDC program registration and collection of administrative data will occur via Presence Care's web-based platform. MBDC courses will be taught in groups via web-based video calls by Presence Care certified instructors, including one by an African American trainee. Eight or more courses will be taught over 9 months. Upon registering, CPs will select two preferred days/times for class and will be randomized to one of them. Participants may not be assigned to the instructor at their memory clinic. With up to 15 participants anticipated per course, a total of up to 130 CPs will be enrolled. Administrative data will be collected at the time of registration, prior to the MBDC course, immediately following the MBDC course, and 3 months later (Figure 4). The

administrative data collected will be used as pragmatic outcomes in this study. Participants will be a part of the study for about 7 months including 8 weeks of intervention, a variable pre-intervention control period, and a 3-month follow-up period. We will request a waiver of informed consent for this study. We will also request a partial HIPAA waiver of authorization for use of electronic health record data for recruitment purposes. The administrative data collected by Presence Care is not protected health information; no HIPAA authorization/waiver is required, but the data obtained by the research team from Presence Care for research purposes will be covered by a data use agreement.

Study population: The study population consists of CPs of PLWD from three settings. Multiple strategies described below will be used to increase the diversity of CP participating in MBDC.

Figure 4. *Study Design*



Settings: The three healthcare settings that will refer CPs to MBDC in this pilot include:

- the HealthPartners Center for Memory & Aging in St. Paul, MN;
- the Ray Dolby Brain Health Center at California Pacific Medical Center, a Sutter Health affiliate in San Francisco, CA; and
- the University of Michigan – Alzheimer's Disease Research Center in Ann Arbor, MI.

Challenges to conducting ePCTs in CPs include the lack of pragmatically available clinical outcomes and the complexity of collecting and harmonizing data across multiple, diverse healthcare systems. MBDC evaluation data is currently being collected at the three pilot sites in different ways. To overcome these challenges, we will partner with Presence Care to develop and implement a permanent centralized process for MBDC class registration and administrative data collection on their website. This upgraded infrastructure will enable the collection of common administrative data, including questionnaires with clinical outcomes, for long-term use in evaluation of the program.

Randomization scheme: At the time of enrollment (registration on the Presence Care site), a CP will be presented with several currently enrolling class options (multiple days/times of week) and asked to select two that work with their schedule. They will then be randomly enrolled in one of the two selected courses, allowing for randomization on the class level while still accommodating the participant's schedule. If a CP declines the assigned MBDC course, they will be allowed to self-select a course or to withdraw. As randomization is planned for the full-scale ePCT, it is important to determine acceptability of this component of implementation. This is balanced with the health care settings needs to support care partners experiencing stress.

Intervention Structure and Implementation Protocol: MBDC group sessions will be held virtually via web-based video calls. Presence Care certified instructors will facilitate the sessions according to the MBDC protocol. Nine sessions including 8 weekly classes (2 hours each) and a retreat (4 hours) will cover several topics (Table 1). The session taught by the African American instructor may include in-person group meetings in that community church setting.

Table 1. MBDC Session Topics

CLASS	TOPIC
1	Introduction to Mindfulness-Based Dementia Care -and one another!
2	Attitudinal Foundations & Beginning Practice
3	Living Grief & Self-Compassion
4	Coming to Our Senses
5	Everyday Communication
6	Being with Difficulty
7	(Retreat) Deepening Practice -Day of Mindfulness
8	Caring for Yourself
9	Reflecting Backward & Practicing Forward

The core course content for each session will be recorded for individuals who are unable to attend the live session. In this pilot, a phone option for CP participation will also be made available. There is currently a group of MBDC graduate meeting weekly by phone. Many of the CPs participating prefer the phone interaction vs. video call. We will explore whether phone participation increases access for participants with lower socioeconomic status and describe any differences in the intervention fidelity.

Instructors will reach out to CPs that miss class sessions with an email checking in and include a link to the recording. CPs will be asked to watch the session and send the instructor a summary about the content to make up the session. Instructors may withdraw CPs who miss more than 3 sessions. CPs will be mailed one chapter of the MBDC workbook for each class (Appendix 1). The CP workbook is currently available in English for in-person and virtual classes. Presence Care is currently in the process of updating the in-person Spanish MBDC workbook for the virtual class mode. Upon completion of the course, participants will be offered the opportunity to participate in a variety of mindfulness maintenance activities, such as weekly, guided virtual group meetings of MBDC graduates.

The Presence Care website will be upgraded to include a permanent infrastructure for centralized registration and administrative data collection. Data collection will be completed through Research Electronic Data Capture (REDCap) and will include clinical outcomes and program evaluation questionnaires. REDCap is a secure web-based system used for data collection and is compliant with federal regulations (21 CFR Part 11, FISMA, HIPAA, and GDPR). A Presence Care administrator will have access to the entire dataset and each instructor will have access to their participants' data. A data use agreement between Presence Care and HealthPartners Institute will be executed for the research use of data. Through this agreement, the HealthPartners biostatistician will have access to a limited data set through the REDCap portal.

Data sources, elements, and collection protocol: Table 2 details the data elements collected. The main data source for this project is the Presence Care administrative database. All CP and PLWD data will be entered by the CP either into the website or given verbally to HealthPartners research support staff over the phone. There will be no

transfer of data from healthcare settings to Presence Care. All questionnaires will include the same items, with an addendum added to the third questionnaire, which will include course evaluation and a theoretical assessment of willingness to share healthcare utilization data. Our Aim 3 goal is to determine whether CPs will be willing to consent online to share their insurance information evaluate healthcare utilization in future studies. The question would be "In the future, we wish to study how the MBDC affects health care utilization. If we were to do so, would you be willing to provide your Medicare ID number to help us understand how this program affects your health? Please note that we are not asking you to provide this information now, nor are collecting your utilization data." A second question will ask if they are a legally authorized individual for the PLWD, and if so, would they theoretically consent to also sharing the Medicare ID of that individual. We will not collect the Medicare ID number but ask theoretically if they would consider participating and offer the choices of "yes/no/I don't know".

Table 2. Data elements collected. All items will be a permanent part of Presence Care administrative data collection.

Data Forms	**Time Point Collected**	**Entered By**	**Detailed Data Elements**
Class Registration	Initial Registration	CP	Name, Address, Date of Birth, Phone Number, Referral Source, Race, Ethnicity, Language, Education, Length of Caregiving, Relationship to PLWD, Preferred Classes, Emergency Contact
		CP (about PLWD)	Name, Type of Residence, Date of Birth, Dementia Diagnosis
Questionnaire 1,2, 3, 4	Initial Registration (Q1), Week before MBDC (Q2), Week after MBDC (Q3), 3 months after MBDC completion (Q4)	CP	Clinical Outcome Scales: Depressive Symptoms (CES-D-10[22]) and Caregiver Burden (6-item Zarit Burden Interview, ZBI-6[24])
			CP Behavior Change Measures (: Self-Compassion (The State Self-Compassion Scale Short Form, SSCS-S)[25] and Mindfulness (The 5-Item Mindful Attention Awareness Scale – State)[26]
Questionnaire 3 only	Week after MBDC	CP	Course Satisfaction Assessment of willingness to share healthcare claims for CP and PLWD
Presence Care	Throughout MDBC sessions	Instructor	Class assigned, dates of classes, attendance, mode of attendance, instructor name
Automated Information	Throughout MBDC sessions	REDCap	Date of Registration, Date of Questionnaires Completion, Mode of Registration and Collection of Data
Post-Implementation Data	Following completion of all MBDC sessions	Clinic Directors	Healthcare Setting Stakeholder Interviews of Memory Clinic Directors

Outcomes: To assess the feasibility, acceptability, and fidelity of implementation of the MBDC program, the Aim 1outcomes will include: number of CP participants contacted

for recruitment, number of CP enrolled, missingness in the class registration materials, response rate to the four questionnaires, completeness of the administrative generated data, CP attendance and module completion rates. To determine the feasibility of obtaining clinical outcome measures, the Aim 2 outcomes will include response rates and completeness of data for Depressive Symptoms (CES-D-10[22]) and Caregiver Burden (6-item Zarit Burden Interview, ZBI-6[24]). To explore the feasibility of CP sharing access to healthcare utilization records, the Aim 3 outcome will include the number of CPs who are express willingness for theoretical use.

4 SELECTION AND ENROLLMENT OF PARTICIPANTS

4.1 Inclusion Criteria

During the online MBDC registration process, CPs will be asked yes/no questions to determine eligibility based on the inclusion/exclusion criteria. Branching logic within the survey will prompt messaging for those are ineligible and trigger an exit from the registration process. In addition, instructors will confirm eligibility of CPs during the check-in calls.

Participants must meet all the following inclusion criteria to participate in this study

- Age ≥18 years
- Self-identify as being an informal CP providing caregiving to a PLWD
- Register for an MBDC course through the Presence Care Website

4.2 Exclusion Criteria

All candidates meeting any of the exclusion criteria at baseline will be excluded from study participation.

- Previous participation in an MBDC program.
- Does not speak and understand either English.

4.3 Study Enrollment Procedures

Recruitment: Each pilot site has an established Presence Care certified instructor with 3-7 years of experience teaching MBDC to CPs referred by the memory clinic in their health system. In preparation for a future larger study, we will train one new MBDC instructor as part of this pilot. MBDC courses are ongoing, with systems in place at each site for referring CPs, and classes being held virtually due to the COVID-19 pandemic. . Participants will be referred from memory care clinics at each of the three aligned healthcare settings using flyers. Flyers are handed out by clinicians (physicians, advance-practice providers, neuropsychologists) during clinic visits to those CPs they feel would benefit from the program. Referrals using flyers at clinics may also occur during conversations with non-clinician staff (social work, Care Ecosystem). Flyers are posted on the clinic website and public spaces in the clinic. Partnerships with community-based programs surrounding the pilot sites are also in place including sharing MBDC flyers with local day programs and the Alzheimer's Association. Interested CPs referred to the MBDC program will visit the Presence Care website to register using the centralized system.

In addition to the current practices above, this pilot will use additional strategies to maximize the participation of diverse CPs in our communities. In addition, at HealthPartners, we will request a waiver of consent to identify PLWD through the electronic health record and healthcare claims data, and mail letters with MBDC flyers to families with over-sampling of non-white and Hispanic patients. The study team programmer will identify patients using ICD-10 diagnostic codes for dementia or mild cognitive impairment (F00-F03, G30-G31.9) documented at least two outpatient or inpatient encounters or if present on to the problem list (a list of diagnoses on a patient's electronic health record dashboard) in the electronic health record. At HealthPartners, patients can opt out of use of their data for research. We will exclude patients from mailings who have declined permission for their medical records to be used in research. CPs interested in participating will be directed to visit the Presence Care website to register using the centralized system.

Randomization scheme: As described above in Section 3, at the time of enrollment (registration on the Presence Care site), a CP will be presented with several currently enrolling class options (multiple days/times of week) and asked to select two that work with their schedule. They will then be randomly enrolled in one of the two selected courses, allowing for randomization on the class level while still accommodating the participant's schedule.

Consenting: Participation in the MBDC program will be completely voluntary. We plan to seek a waiver of informed consent for all aspects of the study. Please see section 11.2 for details.

5 STUDY INTERVENTIONS

5.1 Interventions, Administration, and Duration

MBDC group sessions will be held virtually via web-based video calls with a phone option available. Presence Care certified instructors will facilitate the sessions and use the MBDC participant Workbook (Appendix 1). Nine sessions including 8 weekly classes (2 hours each) and a half-day retreat (4 hours) will cover several topics (Table 1).

The core course content for each session will be recorded for individuals who are unable to attend. As taught in the Presence Care certification, instructors will reach out to CPs that miss class sessions with an informal email including a link to the recording. CPs will be asked to watch the session and send the instructor a brief summary about the content in order to make up the session. CPs will be emailed one chapter of the MBDC workbook for each class (Appendix 1). The CP workbook is currently available in English for in-person and virtual classes. Presence Care is currently in the process of updating the in-person Spanish MBDC workbook for the virtual class mode. Upon completion of the course, participants will be offered the opportunity to participate in a variety of mindfulness maintenance activities, such as weekly, guided virtual group meetings of MBDC graduates.

5.2 Handling of Study Interventions

Instructors are already trained and certified by Presence Care Project. All instructors will

use the MBDC participant workbook (Appendix 1). Class attendance will be recorded by instructors in the REDCap database.

5.3 Concomitant Interventions

5.3.1 Allowed Interventions

Not Applicable

5.3.2 Required Interventions

Not Applicable

5.3.3 Prohibited Interventions

Previous participation in an MBDC program.

5.4 Adherence Assessment

Adherence to the intervention is defined as attendance of >75% of classes (or watching video makeup) for at least 6 of 9 sessions.

6 STUDY PROCEDURESSTUDY PROCEDURES

6.1 Schedule of Study Activities

Assessment	Registration (Q1)	Randomization	Instructor Check-In	Pre-Course Survey (Q2)	MBDC Course	Post-Course Survey (Q3)	Follow-Up Survey (Q4)
Timing		4 wk before course	2-3 wk before course	Sent 10 days before course		Sent 3 days after course	Sent 3 mo after course
Inclusion/Exclusion Criteria Participation Questions on Website	X		X				
Course Registration (CP, contact info, referral source, demographics, caregiving info, PLWD info, preferred course times/dates)	X						
Clinical Outcome Scales	X			X		X	X
CP Behavior Change Measures	X			X		X	X
Assignment to Course (course information)		X					X
Check-in with Instructor			X				
Course Attendance					X		
Course Satisfaction						X	
Assessment of Willingness to Share Healthcare Claims Access						X	
REDCap Automated Data Collection (dates of registration, randomization, questionnaire completion, etc.)	X	X	X	X	X	X	X
Adverse Events	X	X	X	X	X	X	X

6.2 Description of Evaluations

There are no research visits in this pragmatic trial. Below we describe the administrative data collection occurring as part of course registration and follow-up.

6.2.1 Screening Evaluation

Registration

Care partners referred using flyers that are interested in the MBDC program will be directed to register on the Presence Care website. The website will contain information about the MBDC course and what is expected for participation. It will also include screening questions regarding the inclusion/exclusion criteria. When CPs confirm their interest, they will be directed to answer questions regarding their demographics, contact information, referral source, caregiving information, PLWD information, and preferred course times/dates. Next, there will be questionnaires that include the clinical outcome scales and behavior change measures.

In this pragmatic clinical trial, enrollment is considered the act of completing registration for MBDC on the Presence Care Website.

There is a variable time period between CP registration and randomization. In this pilot, we also include a phone option for registration with a staff member. For this pilot, we will use a HealthPartners research staff member to speak with CPS and enter the information given to them verbally into the Presence Care website registration link. We will assess the use of these phone services to determine if this is mode is needed for the full scale ePCT.

6.2.2 Enrollment, Baseline, and/or Randomization

Randomization

Four weeks before a course is scheduled to start, CPs will be randomized to attend one of the two indicated as preferred days/times. They will be contacted by email of their assignment or by phone if that was the mode of registration. If a CP declines the assigned MBDC course, they will be given the option to choose their preferred day and time. We are assessing the feasibility of randomization and do not want to withhold the MBDC program from those for whom this is not feasible.

Instructor Check-In

About two or three weeks prior to the course initiation, instructors will contact participants for a brief phone call (approximately 15 min) to discuss the MBDC program. They will review the inclusion/exclusion criteria, ensure the program is a good fit, and confirm that the CP understands the time commitment involved. These check-ins are a normal part of teaching MBDC.

Pre-Course Survey

Ten days prior to course initiation, CPs will receive an email with a link to a questionnaire. There will be 3 automated reminders (every 3 days) if the survey is not

completed. HealthPartners research staff will similarly call CPs who registered via phone to obtain that data.

MBDC Course Participation

CPs will participate virtually in the live MBDC courses. Each course consists of nine sessions including 8 weekly classes and a 4-hour retreat. An extended session, like a retreat, is a protocolized part of any Mindfulness-Based curriculum. In our experience, attendance for this session is strong, and participant feedback is quite positive. Based upon stakeholder feedback, we have reduced the regular 8-hour retreat to a 4-hour session. During the pandemic, we found that the online version of this retreat is powerful in a different way than the in-person version. MBDC offers a bridge between mindfulness practice and the dementia care exchange. Participants find that they can practice in their own home, with their loved one present, and often intermittently interrupting. During the sessions, care partners are encouraged to include any disruptions and challenges in everyday life and caregiving, and to practice right where they are, as they are with no special conditions needed. In this pilot, we will evaluate the retreat, reasons why not attended, and add a question about the retreat length to the course satisfaction survey. We will be able to adapt through the phased implementation of the courses, to find the best length to meet the needs of care partners in preparation for the implementation of a full scale ePCT.

6.2.3 Follow-up Visits

Post-Course Survey (Q3)

Three days after course completion, CPs will receive an email with a link to a questionnaire. This survey will include clinical outcome scales and behavior change measures in addition to course satisfaction questions and healthcare claims access questions. There will be 3 automated reminders (every 5 days) if the survey is not completed. Research assistants will call CPs who registered via phone to obtain the data.

After the conclusion of all MBDC courses, the study team will conduct a one-hour interview with the director of the specialty clinic at each Memory Clinic Directors. Topics of conversation will include their perspectives on recruitment for MBDC in the clinic and opportunities for improving processes.

6.2.4 Completion/Final Evaluation

Follow-Up Survey (Q4)

Three months after course completion, CPs will receive an email with a link to a questionnaire. In the survey, there will be a statement of implied consent prior to the clinical outcome scales and behavior change measures. There will be 3 automated reminders (every 5 days) if the survey is not completed. Staff will call CPs who registered via phone to obtain the data.

7 SAFETY ASSESSMENTS

7.1 Specification of Safety Parameters

This pragmatic study has limited data available for safety parameters. We will monitor depressive symptoms and caregiver burden measured as part of the administrative data. If significant increases are observed between registration and the pre-course questionnaire, we will discuss whether the delay period is detrimental to CPs. If significant increases are observed between the pre and post course surveys (the opposite results than we expect), we will discuss whether MBDC implemented in this manner is either not effective or doing harm and make changes.

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

There is a small potential for increased stress as a part of participation in the MBDC program. There is a rare chance that instructors may encounter CPs with exhibiting concerning levels of stress or anxiety. Instructors will reach out to these individuals and document this as an AE in the REDCap database. As part of their teaching responsibility, instructors obtain emergency contact information and the address of CPs in the rare case it is needed during MBDC sessions.

7.3 Adverse Events and Serious Adverse Events

AE Definition: AE is any untoward or unfavorable medical occurrence in a human 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.

SAE Definition: SAEs consist of 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 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.

AEs for this study include: No AEs are expected. More than 150 CPs have completed the MBDC program with no reports of adverse events. There is a small potential for increased stress as a part of participation in the MBDC program.

SAEs for this study include: No SAE are expected. More than 150 CPs have completed the MBDC program with no reports of adverse events.

Process for identifying AEs, SAEs, and UPs: AEs, SAEs and UPs related to participation in the MBDC program will be collected by the instructors and entered into the Presence Care website database (REDCap system) where CP participation, such as attendance is collected. Entry of AEs, SAEs, and UPs will trigger an alert to the PI who will evaluate (and investigate if necessary), then categorize its severity, expectedness, and potential relatedness.

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 Safety Officer 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 Safety Officer 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 Safety Officer 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 Safety Officer 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 Safety Officer 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 Safety Officer at a minimum every 6 months, or at a frequency requested by the IMPACT Collaboratory Safety Officer or NIA IMPACT Collaboratory PO.

7.3.1 Reporting Procedures

All data and safety monitoring reporting will classify SAEs and AEs as to their severity, expectedness, and potential relatedness to the study intervention as per the definitions below:

Severity

- **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

- **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.

Relatedness

- **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.

7.3.2 Follow-up for Adverse Events

The occurrence of an adverse event (AE) or serious adverse event (SAE) may come to the attention of the instructor during MBDC program classes. Instructors will capture these events in the REDCap database and follow-up as needed with CP participants.

7.4 Safety Monitoring

A NIA-appointed Data and Safety Monitoring Officer will monitor this study.

8 INTERVENTION DISCONTINUATION

MBDC instructors may recommend a CP discontinue the program if participants are unable to meet the time commitment or have had a change in caregiving status. Care partners may withdraw voluntarily from participation in the study at any time and for any reason. There will be no replacement of subjects who discontinue early in this pilot study.

9 STATISTICAL CONSIDERATIONS

9.1 General Design Issues

Design choice and rationale

A stepped wedge trial design was chosen to ensure all participants had the opportunity to participate in the MBDC course. This trial design has each individual contribute control and intervention data, allowing for within participant comparisons. The stepped wedge trials also provides flexibility with rolling recruitment as opposed to the requirement to fill a class that starts on a particular date, which has been a barrier in other mindfulness trials.[26] An adaptive randomization schematic was chosen to ensure that the classes fill up at a relatively similar rate, another pragmatic concern to consider before attempting a larger study. For the secondary aim, shorter versions of the validated scales used to assess efficacy were chosen to align with the pragmatic nature of this work, ensuring participants spend minimum amount of time possible providing clinical outcome data.

Hypotheses and Outcomes

This pilot study will determine if it is feasible to implement the MBDC program with fidelity for testing in a full-scale ePCT. The primary feasibility progression criteria will be assessed using the previously described measures of feasibility, acceptability, and fidelity. For the progression criteria to be met with no modifications, we will require >75% participants attend (or watch video makeup) for at least 6 of 9 sessions. If that number is between 50% and 75%, we would recommend the study progress, however we will make modifications to increase adherence. We also define progression criteria based on the diversity of recruitment within the pilot. If our participants are not representative of the PWLD population's racial and ethnic demographics within each care system, we will recommend changes to the recruitment strategy to encourage a higher enrollment rate of CPs who represent these populations. If progression criteria are met, secondary feasibility measures including the completeness of the clinical outcomes will be used to help direct data collection approach in future trials.

The efficacy hypothesis is that participation in the MBDC course programming will reduce depressive symptoms and burden while increasing self-compassion and mindfulness in CPs for PLWD. These outcomes will be measured using the following assessments:

Clinical Outcome Scales for Efficacy:

Center for Epidemiologic Studies Depression Scale (CES-D): The Center for Epidemiologic Studies Depression Scale measures self-reported symptoms associated with depression. It has been validated for dementia and multiple other diagnoses, and it is sensitive to differences between caregivers and non-caregivers.[27] The 10-item version has been shown to retain the reliability and validity of the original 20-item scale in the elderly population.[28]

Zarit Burden Inventory: The Zarit Burden Inventory is an interview that evaluates caregiver burden through a self-report measure. The survey scores are positively correlated with behavior problems in older adults and depression scores of caregivers.[29] The shorten version of this scale, the ZBI-6, demonstrated comparable discriminative and internal consistency as the original 12-item versions.[30]

Clinical Outcomes for Behavior Change

The State Self-Compassion Scale Short Form: To evaluate self-compassion, participants indicated how often they acted in the manner stated in each of the items on a scare of 1 (almost never) to 5 (almost always). The survey evaluates self-kindness verses self-judgement, common humanity verses isolation, and mindfulness versus over-identification[31].

Mindful Attention Awareness Scale: This 5-item scale asks participations to indicate at what level they relate to specific experiences, aimed at measuring main characteristics of mindfulness.[25] Higher scores represented elevated levels of mindfulness expression.

9.2 Sample Size and Randomization

Sample size rationale: The sample size is largely determined by the logistics of the pilot award funding and time period. We plan to enroll up to 130 in MBDC courses offered during the study timeframe (up to 15 CP/course). While this pilot is not formally powered for efficacy, we estimate that a sample size of 120 would allow detection of a 3-point change in CES-D-10 scores associated with the intervention, assuming a modest correlation of scores within course session (ICC = .10) and CES-D-10 score standard deviation of 4, with 80% power and a two-sided alpha of 0.05. The results from the pilot will be used to better inform power-calculations for a large ePCT specifically to provide an estimate of the ICC associated with course cluster as this parameter is key in determining a study's power a-priori. Table 2 provides estimates of the current study's expected effect size with a range of assumptions for ICC value (0 to 0.3) and average CES-D-10 scores for the control period (10 to 15), as well as estimates for a hypothetical ePCT with a sample size of 450 (30 courses, 15 per course) maintaining at least 80% power.

Table 2A. Effect size estimates for pilot study and full ePCT with varying ICC

ICC	Effect Size: Difference in CES-D-10 change between control and intervention	
	Pilot Study N = 120, Courses = 8	**Large ePCT N = 450, Courses = 30**
0	2.68	1.32
0.1	2.99	1.49
0.3	2.86	1.44

9.2.1 Treatment Assignment Procedures

At the time of MBDC enrollment (registration on the Presence Care site), a CP will be presented with several currently enrolling class options (multiple days/times of week) and asked to select two that work with their schedule. Approximately 4 weeks prior to the course start date, they will then be randomly enrolled in one of the two selected courses, allowing for randomization on the class level while still accommodating the participant's schedule. An adaptive randomization schematic will be used to adjust the probability of class assignment based on CPs already enrolled in the trial. Since randomization is preferred in the full-scale ePCT, it is important to assess the feasibility of the acceptability of the random assignment in this pilot. Once a CP has registered for a MBDC course, there is variable delay period until there are enough people to fill the class. During this time, Presence Care will send regular emails updates to stay in contact. Once a class option is full, CPs will be notified, and the class will start. If a CP situation or schedule has changed and they decline the assigned course, they will have the option choose a preferred day and time so that we do not deny anyone access to this program.

9.3 Interim analyses and Stopping Rules

No interim analysis is planned as this is a one-year pilot study. There are no statistical rules that would suspend MBDC program enrollment. The Safety Officer and NIA may decide to stop this study based upon review of data provided by the statistician.

9.4 Outcomes

9.4.1 Primary outcome

To assess the feasibility, acceptability, and fidelity of implementation of the MBDC program, primary outcomes will include: number of CP participants contacted for recruitment, number of CP enrolled, missingness in the class registration materials, response rate to the four questionnaires, completeness of the administrative generated data, CP attendance and module completion rates.

9.4.2 Secondary outcomes

To determine the feasibility of obtaining clinical outcome measures, secondary outcomes will include response rates and completeness of data for CED-D-10 and ZBI-6. To explore the feasibility of obtaining online consent for research access to CP

healthcare utilization records, exploratory outcomes will include the number of CPs who agree and consent to research access included on Questionnaire 3.

9.5 Data Analyses

Aim 1- Primary Feasibly Analysis: To assess the feasibility, acceptability, and fidelity of implementation of the MBDC program we will beginning by measuring the absolute number of potential CPs contacted for recruitment and the number of those who complete the online course enrollment. The total number of mailed flyers will be counted. Adding documentation of flyer distribution to the current clinic workflow is too large of a barrier for this pragmatic trial. An estimate of flyers distributed in the clinics will made by asking clinic directors for total numbers of flyers printed. These will be used to calculate the overall rate of program registration as well as broken down by referral site. The feasibility of collecting patient provided data will be evaluated by quantifying the missingness in the class registration materials as well the response rate to the four questionnaires. The completeness of the administrative generated data, including date of enrollment, course section, and attendance, will also be quantified. Fidelity of the intervention will be assessed by describing CP attendance and module completion rates as recorded by Presence Care staff. Completion patterns will be summarized overall and stratified by patient demographics and study site. The fidelity of the make-up video module offerings as a substitute for in-class participation will be evaluated by comparing course outcomes between CPs who completed the course fully in-class and those who utilized the make-up modules. Any differences in intervention fidelity associated with CP demographics will be described and discussed. Table 3 gives an example of how counts will be utilized to describe the recruitment, enrollment, and adherence. The 3-month post-intervention questionnaire will be sent to all CP participants and the response rate and patterns for CP with adequate follow-up time within the study timeframe will be described. We expect that 60% of participants will have at least 3-months to reply to these additional questionnaires before the final analytic data is aggregated.

Table 3.

	Counts for feasibility	Use in analysis
Participants contacted	N	Total number of targeted mailings Estimate of clinic flyer distribution using print rates
Participants who enroll and are randomized into MBDC course section	a	Recruitment rate: a/N
Participants who start MBDC course	b	Participation rate: b/N, compare to a/N
Participants who complete course (6/9 modules)	c	Completion rate: c/b, used as main progression criteria Overall successful enrollment rate: c/N
Number who complete each module in real-time – k = 1, …, 9	d_k	Module specific completion rate: d_k/b

Number who complete each module as a make-up session – k = 1, …, 9	e_k	Module specific make-up completion rate: e_k/b Compare to d_k/b to assess fidelity of make-up offerings
Number who complete each questionnaire – m = 1,2,3	f_m	Questionnaire specific response rate: f_m/a and/or f_m/b if $a \neq b$

Aim 2 - Secondary Feasibility and Efficacy Analyses: The completeness of the CED-D-10 and ZBI-6 outcomes will be quantified by calculating the rate of CPs that respond to all items on each scale (CES-D-10: 10 items, ZBI-6: 6 items) at each assessment. The rate of completion for both scales will be presented overall and stratified by questionnaire, site, and by CP demographics. As the current study design results in a non-uniform length of the control period, the weeks between Q1 and Q2 will be recorded and summarized for the sample to better understand how the design could scale to a larger ePCT. A preliminary efficacy analysis will utilize the total scores for the CES-D-10 (range: 0 to 30) and ZBI-6 (range: 0 to 24) calculated for all completed questionnaires. Both outcomes will be summarized at each questionnaire timepoint using means and/or medians, as appropriate. Change over the control (Q2-Q1) and intervention (Q3-Q2) periods will be calculated for each CP and summarized for the sample. Descriptive summaries will be provided for responses from CP who complete the 3-month follow-up questionnaire (Q4) within the 12-month study timeframe and before the final analytic dataset is defined. These responses will not be used in any of the formal inferential analyses.

Analysis will utilize linear mixed-models with random effects to account for clustering of data within MBDC course section as well as repeated measures within CPs to estimate the intervention effect on depressive symptoms and care-giver burden (Equation 1). In a scaled up ePCT, we expect the unit of randomization to continue to be course section, which is reflected in our choice of random effects. The model structure will be based on a standard ANCOVA used to evaluate change that adjusts for the pre-intervention measurement of the outcome variable with the post-intervention measurement as the model outcome. Each CP will contribute a pair of data points for the control period (Pre: Q1, Post: Q2) and intervention period (Pre: Q2, Post: Q3) which requires our random effects structure to account for repeated measurements within CPs. If there is no difference in change in efficacy outcomes, we expect Q2-Q1 = Q3-Q2. Each model will include covariates to adjust for possible confounding associated with CP demographics and CP history (age, race/ethnicity, socioeconomic measures, and length of caregiving). While the relative time of measurement is considered (pre/post) our analysis does not adjust for time over the course of the study, as we hypothesize any treatment effect would be time-agnostic within the year-long pilot study time frame. When an ePCT with a longer timeline is considered, this assumption will have to be revisited. A brief assessment of self-compassion and mindfulness scales outcomes will be performed using the responses collected from the "research only" section of the questionnaires. These results will help better understand the possible mechanisms between the intervention and clinical outcome for future ePCTs. These items will be removed at the conclusion of the pilot to decrease participant burden. All analysis will be performed in SAS 9.4 and significance determined using a two-sided alpha of 0.05.

Equation 1.

$$Change_{itk} = \beta_0 + \delta X_{itk} + \omega Pre_{itk} + \boldsymbol{\beta X_i} + \gamma_{0ik} + v_{0k} + \epsilon_{ik}$$

$i = \text{Participant Subscript}, 1, \ldots, N$
$k = \text{Cluster Subscript}, 1, \ldots, K$
$t = \text{time period}, 1 = \text{Control}, 2 = \text{Intervention}$
$\text{Change}_{itk} = \text{Change in efficacy outcome over period t}$
$\text{Pre}_{itk} = \text{Pre measurment from period t}$
For Control period: Pre = Q1, Change = Q2 - Q1
For Intervention period: Pre = Q2, Change = Q3 - Q1
$x_{itk} = \text{Binary indicator for intervention for patient i in k at time t}$
$\boldsymbol{X_i} = \text{Vector of covariates for pariticpant i}$
$\beta_0 = \text{General intercept of the model}$
$\delta = \text{Intervention effect (coefficient of } x_{itk})$
$\omega = \text{Baseline measurement adjustment effect (coefficient of } \text{Pre}_{itk})$
$\boldsymbol{\beta} = \text{Vector of coefficients associated with covarites in } \mathbf{X_i}$
$\gamma_{0ik} = \text{Participant-specific random intercept with mean zero and variance } \sigma_\gamma^2$
$v_{0k} = \text{Cluster-specific random intercept with mean zero and variance } \sigma_v^2$
$\epsilon_{itk} = \text{Random error with mean zero and variance } \sigma_\epsilon^2$

Aim 3 - Exploratory Feasibility Analysis: To explore the feasibility of obtaining online consent for research access to CP healthcare utilization records. The number of CPs who agree to access for themselves or the PLWED on Questionnaire 3 will be counted. While we will not specifically collect utilization data, the number of CPs who agree will inform the feasibility of including healthcare utilization as an outcome in a full-scale ePCT. Any differences in CP demographics between enrollees who opt-in and those who opt-out will be assessed.

10 DATA COLLECTION AND QUALITY ASSURANCE

10.1 Data Collection Forms

All data will be collected through the REDCap database embedded in the Presence Care website. If a course participant does not have access to a computer or the internet, there will be an option to speak with staff and complete the information via interview, which will be entered into the Presence Care website.

10.2 Data Management

All data will be entered directly into eCRFs in REDCap. The data system includes password protection and internal quality checks to identify data that appear inconsistent, incomplete, or inaccurate. Instructor logs from the MBDC classes will also be directly entered in REDCap.

10.3 Quality Assurance

10.3.1 Training

MBDC program instructors are operating under standard of care based on Presence Care training. Instructors will be trained on data entry in REDCap, for example documenting attendance, etc.

10.3.2 Quality Control Committee

Not applicable.

10.3.3 Metrics

Metrics for quality control include the following:

- Number of protocol deviations
- Number of data entry errors
- Number of technological issues with survey distribution

10.3.4 Protocol Deviations

It will be the responsibility of the PI to identify, document in REDCap, and report deviations as soon as possible.

10.3.5 Monitoring

The study team programmer will perform internal data quality checks on the data set provided through the Data Use Agreement with Presence Care. Should independent monitoring become necessary, the PI will provide direct access study data for the purpose of monitoring and auditing by the sponsor/funding agency, and inspection by local and regulatory authorities.

11 PARTICIPANT RIGHTS AND CONFIDENTIALITY

11.1 Institutional Review Board Review

This study will be using Advarra as a central IRB. Any institution considered engaged in human subject research activities will complete a local IRB application as needed to cede oversight of the project to the central IRB. Any modifications to this protocol will be reviewed and approved by the IRB.

11.2 Informed Consent Forms

We request a waiver of informed consent for all aspects of this study, to include the use of electronic medical records for recruitment purposes, randomization assignment, enrollment and participation in the MDBC program, and the use of the collected program data. We offer the following justifications for the waiver of informed consent:

1. *the research involves no more than minimal risk to the subjects*;

The mailing of an informational brochure to the patient about a program of potential interest to the family involves no more than minimal risk to the subject. People receive unsolicited mail from many sources including advertisement of services they are not interested in. In addition, the MBPD program is already offered as a standard program in some places. CPs who have completed the MBDC program to-date have provided overwhelmingly positive feedback about the program and its life-changing lessons (Figure 3). There have been no reported adverse events related to participation in MBDC. The randomization component is minimal risk as well, particularly since the CP will be given the option to choose their preferred day and time if they decline the randomly assigned MBDC course. We are assessing the feasibility of randomization and do not want to withhold the MBDC program from those for whom this is not feasible. Use of the administrative data will be governed by a data use agreement.

2. *The research could not practicably be carried out without the requested waiver;*

   The main purpose of this study is to assess the feasibility, acceptability, and fidelity of implementation of the Mindfulness Based Dementia Care (MBDC) program in practice. Participation is voluntary and participants can drop out at any time and are free to skip any questions during the data collection process. The centralized registration and administrative data collection process described herein is being created as a permanent part of MBDC through the Presence Care website. It would not be practicable to add research informed consent to this process as there is a possibility that the knowledge of being in a research study, or the burden of having to fill out extra paperwork would bias the feasibility, acceptability, and fidelity of implementation that we are hoping to measure.

3. *If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;*

   We require identifiable information for recruitment purposes. We could not mail without access to this identifiable information. Access to the administrative data from Presence Care will be governed by a data use agreement

4. *The waiver or alteration will not adversely affect the rights and welfare of the subjects;*

   While we are requesting a waiver of informed consent for research purposes, participation in the program is completely voluntary, as is answering any of the questions in the data collection activities. Participants can stop the program at any time. We include a statement as part of the administrative data set questionnaires that: 1) answering questions is voluntary; 2) their answers may be shared in a de-

identified way with researchers. A "yield" approach for empty data fields will be used in the survey software that triggers an alert asking for, but not requiring the completion of data elements

5. *Whenever appropriate, the subjects will be provided with additional pertinent information after participation*

   Information about the MBDC program is already present in each site's memory clinic newsletters and/or in notices in clinic common areas. We plan to invite patients, CPs, and families to a virtual, community presentation of the results of the study.

Finally, please note that we do not consider the stakeholder interviews mentioned in Table 2 to be a human subjects research activity requiring consent. They consist of interviews with memory clinic leaders to discuss perspectives on recruitment for MBCD and opportunities for improving processes.

We also request a partial HIPAA waiver of authorization for the use of HealthPartners EHR data for eligibility and recruitment purposes. We offer the following justifications for the partial HIPAA waiver:

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

   i) *An adequate plan to protect health information identifiers from improper use or disclosure,*

      The HealthPartners programmer will extract PHI data from the EHR and store on a secure server in a project folder that requires individual username permission to access. ;p]

   ii) *An adequate plan to destroy identifiers at the earliest opportunity absent a health or research justification or legal requirement to retain them, and*

      Identifiers will be destroyed after recruitment is complete. To ensure that we do not duplicate mailings to patients, we need to retain identifiers until recruitment is complete, and cannot destroy sooner.

   iii) *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*

      PHI will not be used or disclosed to a third party except as required by law. Section 11.3 provides more detail.

2) *Research could not practicably be conducted without the waiver or alteration; and*

HealthPartners research staff will be contacting potential participants via mail to inform them of the study and therefore, potential subjects will not be available to sign a HIPAA Authorization.

3) *Research could not practicably be conducted without access to and use of PHI.*

We require PHI information for recruitment purposes. We could not mail without access to this identifiable information.

11.3 Participant Confidentiality

To protect against risk of breach of confidentiality, we will use REDCap, which is a secure web-based system used for data collection and is compliant with federal regulations (21 CFR Part 11, FISMA, HIPAA, and GDPR).

To protect patient privacy, recruitment letters will be addressed to patients and mailed to the patient address. In case a patient may not be aware of a dementia diagnosis or not remember it, we will use sensitive language such as "information about a program of potential interest" and avoid statements that could cause alarm.

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 FDA, 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

This study will be approved by a central IRB and conducted in accordance with the Belmont Report and the Declaration of Helsinki.

13 COMMITTEES

Not applicable.

14 PUBLICATION OF RESEARCH FINDINGS

This trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals

15 REFERENCES

1. Alzheimer's Association. Alzheimer's disease facts and figures. Chicago, 2021: https://www.alz.org/media/Documents/alzheimers-facts-and-figures.pdf.
2. Pinquart M, Sörensen S. Correlates of physical health of informal caregivers: a meta-analysis. The Journals of Gerontology Series B: Psychological Sciences and Social Sciences. 2007;62(2):P126-P137.
3. Caceres BA, Frank MO, Jun J, Martelly MT, Sadarangani T, de Sales PC. Family caregivers of patients with frontotemporal dementia: An integrative review. Int J Nurs Stud. 2016;55:71-84.
4. Lavretsky H. Stress and depression in informal family caregivers of patients with Alzheimer's disease. 2005.
5. Rahman A, Anjum R, Sahakian Y. Impact of Caregiving for Dementia Patients on Healthcare Utilization of Caregivers. Pharmacy (Basel). 2019;7(4).
6. Ferrara M, Langiano E, Di Brango T, De Vito E, Di Cioccio L, Bauco C. Prevalence of stress, anxiety and depression in with Alzheimer caregivers. Health Qual Life Outcomes. 2008;6:93.
7. Zhu CW, Scarmeas N, Ornstein K, et al. Health-care use and cost in dementia caregivers: Longitudinal results from the Predictors Caregiver Study. Alzheimers Dement. 2015;11(4):444-454.
8. Sallim AB, Sayampanathan AA, Cuttilan A, Ho R. Prevalence of Mental Health Disorders Among Caregivers of Patients With Alzheimer Disease. J Am Med Dir Assoc. 2015;16(12):1034-1041.
9. Kabat-Zinn J. Mindfulness-based stress reduction (MBSR). Constructivism in the Human Sciences. 2003;8(2):73.
10. Fjorback LO, Arendt M, Ornbøl E, Fink P, Walach H. Mindfulness-based stress reduction and mindfulness-based cognitive therapy: a systematic review of randomized controlled trials. Acta Psychiatr Scand. 2011;124(2):102-119.
11. Hilton L, Hempel S, Ewing BA, et al. Mindfulness Meditation for Chronic Pain: Systematic Review and Meta-analysis. Ann Behav Med. 2017;51(2):199-213.
12. Mehta R, Sharma K, Potters L, Wernicke AG, Parashar B. Evidence for the Role of Mindfulness in Cancer: Benefits and Techniques. Cureus. 2019;11(5):e4629.
13. Hofmann SG, Sawyer AT, Witt AA, Oh D. The effect of mindfulness-based therapy on anxiety and depression: A meta-analytic review. J Consult Clin Psychol. 2010;78(2):169-183.
14. Marchand WR. Mindfulness-based stress reduction, mindfulness-based cognitive therapy, and Zen meditation for depression, anxiety, pain, and psychological distress. J Psychiatr Pract. 2012;18(4):233-252.
15. Murfield J, Moyle W, O'Donovan A. Mindfulness- and compassion-based interventions for family carers of older adults: A scoping review. Int J Nurs Stud. 2019:103495.

16. Whitebird RR, Kreitzer M, Crain AL, Lewis BA, Hanson LR, Enstad CJ. Mindfulness-based stress reduction for family caregivers: a randomized controlled trial. Gerontologist. 2013;53(4):676-686.
17. Brown KW, Coogle CL, Wegelin J. A pilot randomized controlled trial of mindfulness-based stress reduction for caregivers of family members with dementia. Aging Ment Health. 2016;20(11):1157-1166.
18. Oken BS, Fonareva I, Haas M, et al. Pilot controlled trial of mindfulness meditation and education for dementia caregivers. J Altern Complement Med. 2010;16(10):1031-1038.
19. Liu Z, Sun YY, Zhong BL. Mindfulness-based stress reduction for family carers of people with dementia. Cochrane Database Syst Rev. 2018;8(8):Cd012791.
20. Whitebird RR, Kreitzer MJ, Lewis BA, et al. Recruiting and retaining family caregivers to a randomized controlled trial on mindfulness-based stress reduction. Contemp Clin Trials. 2011;32(5):654-661.
21. Manteau-Rao M, Barrows K. Caring for a Loved One with Dementia: A Mindfulness-Based Guide for Reducing Stress and Making the Best of Your Journey Together. New Harbinger Publications; 2016.
22. Mohebbi M, Nguyen V, McNeil JJ, et al. Psychometric properties of a short form of the Center for Epidemiologic Studies Depression (CES-D-10) scale for screening depressive symptoms in healthy community dwelling older adults. Gen Hosp Psychiatry. 2018;51:118-125.
23. Bachner YG, O'Rourke N. Reliability generalization of responses by care providers to the Zarit Burden Interview. Aging Ment Health. 2007;11(6):678-685.
24. Higginson IJ, Gao W, Jackson D, Murray J, Harding R. Short-form Zarit Caregiver Burden Interviews were valid in advanced conditions. J Clin Epidemiol. 2010;63(5):535-542.
25. Pommier E, Neff KD, Tóth-Király I. The Development and Validation of the Compassion Scale. Assessment. 2020;27(1):21-39.
26. Brown KW, Ryan RM. The benefits of being present: mindfulness and its role in psychological well-being. J Pers Soc Psychol. 2003;84(4):822-848.
27. Radloff LS. The CES-D scale a self-report depression scale for research in the general population. *Applied psychological measurement.* 1977;1(3):385-401.
28. Irwin M, Artin KH, Oxman MN. Screening for depression in the older adult: criterion validity of the 10-item Center for Epidemiological Studies Depression Scale (CES-D). Arch Intern Med. 1999 Aug 9-23;159(15):1701-4. doi: 10.1001/archinte.159.15.1701. PMID: 10448771.
29. Zarit SH, Zarit JM. Zarit Caregiving scale. ZBI. 1980.
30. Higginson IJ, Gao W, Jackson D, Murray J, Harding R. Short-form Zarit Caregiver Burden Interviews were valid in advanced conditions. J Clin Epidemiol. 2010 May;63(5):535-42. doi: 10.1016/j.jclinepi.2009.06.014. PMID: 19836205.

31. Neff KD. The development and validation of a scale to measure self-compassion. *Self and identity.* 2003;2(3):223-250.