CommunityRx-Dementia (CRx-D) Study Protocol
NCT04146545
Final approved version:
November 30, 2023

Study Protocol

Table of Contents

CommunityRx-Caregiver (CRx-C; CommunityRx-Dementia; CRx-D)

Study Protocol: Original Approved Version (pre-test only)

Note: Per the recommendation of The University of Chicago's Institutional Review Board, the first submission of this study's protocol included only the study's pre-test protocol. Following completion of the pre-test, again per the IRB's recommendation, the pre-test version was amended for the full trial.

Principal Investigators: Stacy Tessler Lindau, MD, MAPP and Elbert Huang, MD, MPH

UCHICAGO IRB # 20-0301

ClinicalTrials.Gov Identifier NCT: NCT04146545

Version Approved: 2/1/2019

TITLE: CommunityRx-Caregiver (CRx-C)
PIs: Stacy Tessler Lindau, MD, MAPP; Elbert Huang, MD, MPH
Co-I: Katherine Thompson, MD

A. Background

More than 16 million unpaid family and friend caregivers care for a rapidly growing population of home-dwelling people with Alzheimer's disease and related dementias (ADRD) in the US.[1] ADRD caregivers have poorer physical health than their peers and high rates of burden (46%) and depression (30-40%).[1] Stigma and social isolation are common.[2,3] Randomized, controlled efficacy trials of intensive caregiver support, such as REACH-I,[4] II[5] and NYU Caregiver Intervention,[6] reduce caregiver burden and improve well-being and quality of life, but have not made linkage with community resources a primary focus. Unmet resource needs are major drivers of low caregiver self-efficacy, in turn a key factor in the pathway linking caregiver support to health outcomes.[7,8] A low-intensity, high quality resource referral process that addresses the full range of caregiver and care recipient resource needs would facilitate broad adoption and dissemination of intensive support interventions and may itself independently promote caregiver self-efficacy and other important health outcomes.

Federal law calls for connecting caregivers to community resources[9–13] (e.g. ADRD education, support groups, respite care), with special concern for reducing health disparities.[9,14] In parallel, CMS is testing, in the broader population, routine clinical assessment and referral for unmet health-related social needs (HRSNs) (e.g. food, housing, interpersonal safety, social support).[15,16] Although the demands of caregiving commonly produce financial strain,[17] HRSNs have largely been overlooked by caregiver support interventions.[4–6,18] Our work shows that even in higher poverty communities, supportive resources are available, but hard to find and access.[19] Scalable, "whole-person"[20] resource referral solutions are needed to efficiently manage and promote the health and well-being of ADRD caregivers and persons with dementia (PWD) with and without unmet HRSNs. Different from previous caregiver intervention studies that recruit caregivers accompanying a PWD at healthcare or community activities,[4–6,18] this study aims to promote caregiver health and well-being by intervening with caregivers at the point of their own primary healthcare. The target population on Chicago's South Side is predominantly African American. Half have unmet HRSNs. The overall objective of the proposed research is to evaluate the impact of CommunityRx-Caregiver (CRx-C), a scalable information technology-based intervention, developed with the target community, to address unmet community resource needs.

The CRx-C intervention is a caregiver-centered adaptation of CommunityRx (CRx), an information-based intervention that systematically matches people to nearby community resources for HRSNs, caregiving and other self-care needs.[19] In two studies (one in press at AJPH), we see that half of CRx recipients share resource information with others, acting as natural disseminators of intervention benefits.[19]

We hypothesize that connecting caregivers to community resources will increase self-efficacy, reduce unmet needs and promote better downstream health outcomes. CRx-C focuses on caregivers, but also assesses, by proxy, care recipient community resource use, health and healthcare utilization. The current study aims to pretest the administration of the intervention and data collection protocols to inform the design of a larger randomized controlled trial.

B. Purpose

The purpose of this research is to promote caregiver health and well-being by intervening with caregivers of people with dementia. The long-term goal of this research is to promote public health and alleviate suffering among a growing population of ADRD caregivers and PWD. To this end, we will evaluate the impact of CommunityRx-Caregiver (CRx-C), a scalable information technology-based intervention, developed with the target community, to address unmet community resource needs.

The over-arching aims of the program of research are:
Aim 1: Among caregivers with unmet HRSNs, evaluate the effects of CRx-C versus usual care on caregiver self-efficacy (primary outcome) and secondary outcomes: psychosocial (unmet needs, social isolation, well-being, burden, depression, stress), behavioral (community resource use), health and healthcare utilization.

Aim 2: Among all caregivers (those with and without unmet HRSNs), evaluate acceptability of the intervention as well as the effects of CRx-C versus usual care on the health care experience, including satisfaction with care (primary outcome), experiences of stigma during clinical care and likelihood of sharing community resource information with others.

Findings will yield an understanding of how best to leverage ADRD caregivers' or care recipients' healthcare visits to identify, support and improve outcomes for caregivers, including psychosocial characteristics, behaviors, health and healthcare. Results will inform whether and how CRx-C should be implemented in practice and explore how best to sensitively and effectively intervene to support all ADRD caregivers.

This pretest study aims to identify optimal processes for administering the planned intervention and to optimize the efficiency and flow of baseline and follow-up survey administration and interval communications with participants. Findings from this pretest will be presented to the CommunityRx-Caregiver Advisory Board which consists of a diverse sub-group of ADRD caregivers and other community stakeholders. Their input and feedback will be used to inform the larger randomized trial.

C. Methodology

The first step in the proposed program of research is to pretest the single-blind, randomized controlled trial procedures and administration of the intervention and data collection procedures to inform the design of a larger randomized controlled trial (RCT).

Interviewers will administer both in-person and telephone-based surveys; self-administration of a web-based follow-up survey will also be offered. For pretest, we will enroll 10 caregivers of people with ADRD, both with and without unmet health-related social needs (HRSNs). All human subjects will be consecutively screened for inclusion and enrolled as described in Section P. Recruiting Methods. Following screening, participants will be screened for unmet HRSNs and then randomly assigned to either usual care or usual care plus CommunityRx-Caregiver. Usual care is described below in Section G. Use of Controls or Placebos.

CommunityRx-Caregiver (CRx-C): Caregivers randomized to the intervention will receive CRx-C in addition to usual care. CRx-C will be initiated by the Community Resource Specialist (a member of the research team) at the baseline (index) primary care visit (primary care, geriatrics, ob/gyn clinics). The intervention will include: (a) a brief, structured educational intervention about common resource needs among ADRD caregivers (e.g., "It is recommended that we talk with caregivers of people with dementia about community resources that may be helpful. Many caregivers benefit from resources like support groups or respite care. It is also common for caregivers to need help with things like food or rent and utility support."); (b) delivery and review of a personalized resource "prescription" (HealtheRx-C) for vetted resources near the caregiver's preferred location to address HRSNs (e.g. food, housing, interpersonal safety and social support) and ADRD caregiver needs (e.g. ADRD education, support groups, respite care, advance care planning); (c) demonstration of use of an online Community Resource Finder that participants can use to find and share community resources (for HRSNs, caregiving and any self-care needs), give feedback and request additional resource information; and (d) coaching on how to activate community resources, including how to reach the Community Resource Specialist (a member of the research team), and (e) a series of text messages to which the subject can respond and communicate with the Community Resource Specialist.

In addition to the printed "HealtheRx-C" delivered at the time of the baseline visit, the HealtheRx will be texted to the participant within 24 hours, and emailed to them. Instructions on how to access the online resource finder will also be emailed to the participant after their baseline visit.

The proposed CommunityRx-Caregiver intervention includes a proactive text messaging protocol; we will pretest the first 30 days of the text messaging protocol to ensure its smooth operation.

All caregivers randomized to the intervention will receive, in addition to the educational component and review and receipt of the HealtheRx, a series of timed text messages from the Community Resource Specialist offering ongoing community resource linkage support. At any time, a participant can reply "stop" to stop receiving text messages from the CRx-C Community Resource Specialist. The participant can also text the Community Resource Specialist for assistance as desired. The specialist will respond to text messages within 24 hours during regular work days and within 48 hours of weekends or holidays. Table 1 below describes the frequency and content of automated text messages sent to caregivers who do not reply "stop." The content of these messages is based on a text messaging experiment conducted during the original Centers for Medicare and Medicaid Innovation Health Care Innovation Award CRx study.

Table 1. Frequency and content of CRx-C automated text messages

Frequency	Time frame	Content
Once	Within 24 hours of check-out from caregiver's outpatient visit	Hi [PARTICIPANT NAME]! It's your resource navigator from the CommunityRx study at UChicago Medicine. Text or call me to find caregiving & other resources.
		Here is your resource list: [URL link]. For HELP reply or call XXX-XXX-XXXX. Reply STOP to end messages
Weekly	Between baseline and 30 days post check-out from the outpatient visit	Hi from the CommunityRx study at UChicago Medicine. Do you have any caregiving or other resource needs? For HELP reply or call XXX-XXX-XXXX. Reply STOP to end messages

All caregivers enrolled in this study will receive text messages to support scheduling and reminders for follow-up surveys.

All caregivers will complete an interviewer-administered baseline survey and phone- or web-based follow-up surveys at 7 days and one month after the index visit. Surveys will elicit self-reported data in the following domains: caregiver status, caregiver sociodemographic characteristics (e.g., age, race/ethnicity, sex and gender), caregiver-reported care recipient demographics (e.g. age, race/ethnicity), employment, household composition, income and insurance status, stage of dementia of the care recipient; psychosocial characteristics (e.g., caregiver self-efficacy, unmet health-related social and caregiving needs, burden, depression, stress and well-being); behaviors (e.g., use of resources, use of the Community Resource Finder, resource information sharing, activation of the Community Resource Specialist); health and healthcare use (e.g., physical health and health-related quality of life and healthcare utilization); and healthcare experience (e.g., satisfaction with care, stigma). Caregivers will be asked a limited number of questions as proxy for the care recipient to assess: well-being, community resource needs and use, health and healthcare utilization.

If needed to supplement healthcare utilization data, we will obtain health insurance claims for the participant. The informed consent/assent process will inform study participants of the rationale for accessing these data and request participants' permission to do so.

D. Duration

The duration of this protocol is approximately 6 months. This will allow for enrollment of participants into the pretest, preliminary data analysis and presentation of findings to the CommunityRx-Caregiver Advisory Board. WE will provide feedback to inform our trial design.

E. Location

Research under this protocol will be conducted by researchers in the Departments of Obstetrics and Gynecology and Medicine at the University of Chicago (located at 5841 S. Maryland Ave., Chicago, IL, 60637). Additional research (e.g., data preparation and analyses) will be conducted in Dr. Stacy Lindau's research laboratory, located in the Medical Center 2050, rooms R-311 and R-315 and Dr. Elbert Huang's research offices, located in the Medical Center 2007, Room B214.

F. Special Precautions

Protected health information (PHI) will be collected for research purposes and special precautions will be made to protect these data. In addition to the unique identifier applied by the REDCap computer-assisted personal interviewing (CAPI) software, we will use the caregiver's name, telephone number and email address to facilitate scheduling and completion of the follow-up surveys. We will use the caregiver's name and medical record number (MRN) to access their electronic medical record to assess health and healthcare utilization and whether caregiver status was documented by the caregivers' medical providers. From EMR data, we will access the participant's health insurance payer and unique beneficiary identification to obtain their health insurance claims, if needed. We will compensate caregivers for their participation in the follow-up surveys by gift card, and will use the caregiver's name and address for compensation payment purposes.

Certain survey data elements collected in the REDCap database will be sent securely to NowPow, a systematic resource referral platform, to generate the HealtheRx and to Mosio, a secure text messaging platform, to facilitate the proactive text messaging protocol and manage survey scheduling and reminders for all participants. Elements of PHI sent to NowPow to generate a personalized HealtheRx include: participant name, participant home address, date of birth and other non-PHI data elements. Data will be securely transferred from REDCap to NowPow through a custom secure integration created by the Center for Research Informatics. In addition to other non-PHI data elements, respondent address is necessary to better tailor the community resource information provided on the personalized HealtheRx. Elements of PHI sent to Mosio to facilitate the text messaging protocol and scheduling/reminders include: participant name, telephone number and date of enrollment in the study.

Metadata generated by use of the NowPow system will be provided to the research team via a secure file transfer protocol (sFTP) on a regular basis (see documentation below). NowPow is a company serving dozens of blue chip health systems using rigorous data protocols and therefore operates its technology in a manner that meets the strict HIPAA and security criteria standards of these organizations.

Because PHI will be accessed and collected for this program of research, there is a risk of loss of confidentiality. To protect confidentiality, we will implement a plan to protect data in all its forms from improper use and disclosure using HIPAA compliant policies and procedures; see Section N. Procedures to Maintain Confidentiality for more information.

Use of SFTP Server
NowPow will transfer files to the Lindau Lab by uploading them via Secure File Transfer Protocol (SFTP) to a dedicated location on a secure server; the files will then be retrieved by personnel in the Lindau Lab. All files will be end-to-end encrypted using a public RSA key generated by the Lindau Lab.

The SFTP server is maintained by the Research Computing Group in the Department of Public Health Sciences (Ryan Carter, Systems Administrator). It is located in a secure server room within the Billings Hospital building. The room is a dedicated server room with raised floor, redundant cooling and appropriate power and fire suppression systems. Access to the room is controlled and monitored via keycard, and a video surveillance system is used to continuously monitor access from within. In addition to machines belonging to Public Health Sciences, the room also houses systems belonging to the fMRI Unit and the Cancer Center. Only systems administrators from these three groups have access.

The SFTP server is located on a dedicated machine running only the SFTP service. All remote access to the SFTP server (both user and administrator access) requires key-based authentication (password authentication is disabled). The server is configured to place all users in their own “chrooted jail” upon login which strongly limits their access to a single root directory (i.e., the system can no longer reference paths outside that directory). In this case, this will be a dedicated directory created for use by NowPow and the Lindau Lab. Backups are encrypted and stored in a secure, physically separate location within the hospital. Backups are transferred to that location electronically. At no time are backups stored on portable media (e.g., tape or USB drives) or taken off-site.

G. Experimental controls and use of placebos

Caregivers in this study will be randomized to either usual care or usual care plus the CommunityRx-Caregiver intervention.
The usual care study arm for caregivers who are patients includes typical clinic visit procedures, including, but not limited to: meeting with a Patient Service Representative, receipt of a printed after visit summary (AVS), notification of any financial obligations and scheduling any future visits as appropriate. Usual care may also include information about community resources from the patient's healthcare team.

Usual care for caregivers who are not patients but accompany a person with dementia for their care may experience procedures and information similar to those described above.

H. Type and number of experimental subjects

Individuals will be approached for enrollment using methods described below in Section P. Recruiting Methods. Individuals will be consecutively approached, screened for inclusion, recruited for study participation and participate in the informed consent process. Following enrollment, caregivers will be assessed for HRSNs using the CMS Accountable Health Communities tool and stratified by HRSNs (no HRSN vs. ≥1 HRSN) and randomized to either usual care or usual care plus the CommunityRx-Caregiver (CRx-C) intervention. We will enroll up to 10 caregivers in the pretest.

Inclusion criteria:

- Resides in the target geographic region of the study
- Self-identifies as a caregiver of a home-dwelling person with Alzheimer's disease or other related dementia using an adaptation of the Behavioral Risk Factor Surveillance Survey caregiver module
- Has access to a cell phone and provides the research interviewer with the cell phone number
- Agrees to receive text messages from the study

Exclusion criteria:

- Minor caregivers who are not emancipated minors according to Illinois State law

I. Statistical analysis

The purpose of this research is to pretest our intervention administration and data collection procedures. We will collect baseline, one-week, and 30-day survey data. To this end, preliminary descriptive statistics will be used to summarize, overall and by study arm, sociodemographic characteristics and primary and secondary outcomes at each measured time point. The mean, standard deviation, median, and inter-quartile range will be generated for continuous variables; frequency counts and percentages will be generated for categorical variables. We will evaluate the pretest data for missingness, systematic item non-response, and out of range values and prepare our data management analytic code.

Analysis of RCT data: Descriptive statistics will be used to summarize, overall and by study arm, sociodemographic characteristics and primary and secondary outcomes at each measured time point. The mean, standard deviation, median, and inter-quartile range will be generated for

continuous variables; frequency counts and percentages will be generated for categorical variables. The main analyses will follow the principle of intent-to-treat. Additional a priori quantitative analyses will be conducted as needed to answer the research questions.

J. Potential risks and benefits

This program of research involves no more than minimal risk or no more risk than is encountered in routine medical and psychological examinations. The risks of participation in this protocol include a potential loss of confidentiality or psychological or emotional discomfort associated with the interview questions. Every effort will be made to ensure subject confidentiality and that risks due to loss of confidentiality are minimal compared to the protocols in place to protect human subjects' data. To date, more than 113,000 individuals have participated in CommunityRx intervention studies with no known adverse events or breaches of confidentiality. All data collected from human subjects will be collected using standard survey procedures. Whenever possible, the surveys will be conducted in a private room in the clinical setting, via telephone or online. Psychological and/or emotional discomfort associated with the survey questions is possible. Subjects will be informed that they can decline to answer any question and can terminate the survey at any time. Explanatory statements will be included in the surveys to help the interviewer monitor and respond appropriately to discomfort, including termination of the survey if necessary. Alternatives to participation include not participating in the research; participation is completely voluntary. Additional protections against these risks are described in Sections M and N, Informed Consent and Confidentiality, respectively.

There is no direct benefit to human subjects involved in the research beyond the information provided during usual care and the CommunityRx-Caregiver intervention. Participants, however, may gain personal satisfaction in contributing to research to address the humanitarian issue of unmet needs among caregivers of PWD. Potential risks include a breach of confidentiality and are both minimal and reasonable in relation to the anticipated benefits to research participants and people with dementia.

K. Monitoring of safety

The proposed data collection presents no more than minimal risk or no more risk than is encountered in routine medical or psychological examinations. As described, no surveys will be conducted without explicit documentation of informed consent and individuals will be provided with appropriate information about confidentiality when enrolling in the study and will indicate acceptance of these risks upon consent. Because we are not proposing a multi-site clinical trial, a Phase III trial, or a drug study, this study will not employ a Data and Safety Monitoring Board. Procedures are in place to ensure confidentiality and provide full informed consent as discussed below.

The Lindau Lab has listed the Principal Investigators and study coordinator phone numbers on all study correspondence and forms. The purpose of the phone numbers is to provide respondents with a number to call if they have questions about any aspect of the study. If concerns regarding a participant's safety are endorsed within the health-related social needs screening, REDCap will deliver an alert to the research assistant (RA) after survey completion that the participant screened positive for safety concerns, without revealing the survey contents. With the participant's permission, the RA will alert an appropriate member of the clinical staff, including social work, or Drs. Lindau, Huang or Thompson such that they can connect the participant to resources to

support their safety. During the study, should a subject express intent to harm themselves or others, we will contact a health or public safety professional. We will give only the subject's name, contact information, and why we feel he or she is at risk of harming themselves or others. This report will not be linked to his or her survey information. Subjects have the right to refuse to speak to the mental health professional. If the survey procedures results in the observation or suspicion of elder or child abuse, all research personnel will act in compliance with Illinois State law in regards to mandatory reporting of abuse.

Research staff will strictly adhere to the procedures for enrolling participants and collecting data as outlined by the investigators. At the conclusion of the study, all hard copy materials, with the exception of the consent copies, will be destroyed and electronic files will be deleted or archived in password-protected files. Informed consent documents will be stored for at least 6 years following the completion of the study (defined by the last publication related to the study). Due to the small sample sizes associated with the pretest, these data will not be made publicly available.

L. Payment

Caregivers enrolled in the pretest will receive $25 in compensation for completion of the baseline interview (approximately 25 minutes) and $25 in compensation each for completion of the one-week and 30-day follow-up surveys (approximately 30 minutes). Compensation will not be prorated for partial completion of surveys but every effort will be made to allow for ample time to complete the surveys and participants can refuse to answer any question they do not want to answer. Participation is voluntary.

M. Informed Consent

We will obtain written informed consent as follows:
Caregivers 18 years of age or older: We will obtain written informed consent from all caregivers 18 years of age or older.

Caregivers 17 years of age and younger: We will obtain written informed consent from all caregivers younger than age 18 who are eligible to consent for participation in research. Caregivers ages 17 years of age and younger will be eligible to participate if they are an emancipated minor under Illinois state law (750 ILCS 30/5).

Research interviewers will guide caregivers through the informed consent document, providing statements to address: that the study involves research; the study's purpose, duration, procedures followed, risks and benefits, alternatives to participation, and confidentiality of records; to whom they should direct questions or contact in case of research-related injury; and statements regarding voluntary participation, refusal to participate, and discontinuation of participation. The researcher will provide adequate time for the potential subject to ask questions and will answer these questions before requesting the caregiver's signature to document consent. The informed consent process for caregivers enrolled in the study will take place in the clinic waiting room or the caregivers' exam room following recruitment, depending on the timing of their visit.

No surveys with human subjects will be conducted without explicit documentation of the informed consent process executed with each participant. Informed consent documents will be iterated using approved consent documents from the recently completed CRx pragmatic clinic trial of patients (N=411) receiving care in the University of Chicago's Primary Care Group and Emergency

Departments. The consent documents for that study were adapted from consent documents developed in collaboration with a literacy consultant and members of the community. Consent forms will be printed in large font and written in easily understandable language. Consent forms will be printed in duplicate, with a copy each going to the respondent and to Lindau Laboratory receipt control. Paper forms will be kept secure in locked cabinets in locked rooms. Consent documents will be received at the Lindau Laboratory by Ms. Abramsohn, Director of Research and Data Governance, to confirm participation in the study for data collection, validation, and data analysis purposes. A final copy of all consent documents will be submitted to the IRB for review and approval.

N. Confidentiality

The proposed research with human subjects, as presented above, presents no more than minimal risk or no more risk than is encountered in routine psychological examinations. Any potential risks may be due to emotional or psychological discomfort associated with the surveys or a breach of confidentiality. As described in detail above, no surveys will be completed without explicit documentation of informed consent and written authorization for the use and disclosure of identifiable data will be sought and obtained for all subjects enrolled in this study. All individuals will be provided appropriate information about privacy and confidentiality when enrolling in the study and will indicate acceptance of these risks upon consent/authorization.

The Lindau Laboratory has strict and secure procedures for protecting against and minimizing potential risks to human subjects' data. All survey data will be entered directly into REDCap, a password-protected database managed by the Center for Research Informatics (CRI) at the University of Chicago (cri.uchicago.edu). CRI provides a HIPAA-compliant data storage and computing environment that has achieved security accreditation by the Biological Sciences Division's Risk Management Group. Data will be saved to the secure servers in the Department of Ob/Gyn at the University of Chicago via a secure wireless connection on a secure, password-protected tablet, or research staff will enter REDCap data directly on OB/Gyn departmental computers using the secure, password-protected Ob/Gyn internet network. Data are backed up at the end of each collection day. Data will never be stored locally on the tablets.

REDCap will integrate electronically with NowPow (www.nowpow.com) to facilitate generation of the HealtheRx. Data will be pushed from REDCap to NowPow via a custom secure integration to create the participant's profile in NowPow, including name, address, date of birth and other non-PHI data. Any data sent to NowPow from REDCap to generate the personalized HealtheRx will be assigned a secondary unique ID in order to prevent any connection to the subjects' responses in REDCap. NowPow is seamless, secure and HIPAA-compliant. Data are backed up automatically and encrypted in-transit, at-rest, and end-to-end. De-identified metadata will be transferred to researchers in the Lindau Laboratory using a secure file transfer protocol (SFTP); details described above. All devices used by researchers to collect or access research files will be encrypted. Only approved research analysts in the Lindau Laboratory will have access to files that link participant's PHI to their unique identifiers for the purposes of creating analytic datasets.

REDCap will integrate electronically with the Mosio texting platform (www.mosio.com) to facilitate the text message protocol for human subjects in the intervention group and manage survey scheduling and reminders for all participants. To this end, REDCap will push the subject's name, telephone number and date of enrollment to Mosio via REDCap's secure API. Mosio provides a

secure messaging and data storage environment and has been approved for use by the University of Chicago Information Security Office. Only approved researchers in the Lindau Lab will have access to data stored by Mosio and will have the ability to securely download data directly to computers within the Ob/Gyn network.

All hard copies of project materials will be stored in locked file cabinets in locked offices at University of Chicago. Servers in the University of Chicago Department of Ob/Gyn are protected through a combination of a Microsoft-based firewall technology and the physical barrier of a Linksys router that is installed between the server and its internet connection. Laptop computers used to collect data will be encrypted and password protected. All data transmitted to secure servers will be encrypted. Analytic files will either be de-identified prior to analysis or limited to the minimum amount of data necessary to accomplish the intended research purposes per the HIPAA Privacy Rule. Any analytic datasets will limit the use or disclosure of PHI to the minimum necessary, if any at all, to accomplish the intended research purposes. Only IRB-approved researchers on this protocol will have access to data. These controls meet or exceed the strictness of practices legislated and enforced by the University of Chicago Biological Sciences Division and hospitals for protected health information.

Procedures are in place to ensure confidentiality and provide informed consent as discussed above. Numeric coding of surveys/interviews and secure containment of files that link participant's responses from PHI will also minimize this risk. Finally, the Lindau Laboratory will provide a contact phone number that will be included on all study correspondence and forms. The purpose of this phone number is to provide respondents with a single number to call if they have questions about any aspect of the study.

O. Bibliography

Bibliography included in online submission, View 8.1.

P. Recruiting methods

As we have done in prior trials in this setting, we will consecutively approach patients in the waiting rooms of the SSSC, PCG and Ob/Gyn for inclusion in the pretest and full RCT. Researchers will approach potentially eligible participants and explain that they may be eligible for a research study and, if interested, further screen for eligibility. If interested in participating and available at that time, the researcher will complete the informed consent process with the caregiver.
We will also attempt to recruit individuals who are accompanying patients with dementia for their care. Potential participants will be identified using administrative data (to identify patients with a diagnosis of Alzheimer's Disease and other related dementias living in the 27 ZIP code CommunityRx target geography) and through verifying discussions with nursing and other members of the care team, including patient service representatives and social workers. Participants who are not patients will be approached for participation in the study in a number of ways:

1) <u>In advance of the PWD's appointment via telephone</u>: Often included in the patient's EMR is the name and telephone number of their primary caregiver. In addition to accessing and viewing the patient's EMR for the eligibility criteria listed above (ZIP code and problem list), we will access and view the demographics section of the EMR for the caregiver's name and telephone number (usually specified in the notes section or listed as the emergency contact) and confirm with nursing and other members of the clinical staff to verify. We will obtain this information directly from the EMR or

from a request made to the Analytic Core Request System under the Center for Research Informatics.

2) Posting recruitment flyers in relevant waiting rooms and via social networks: We will recruit caregivers of people with dementia using recruitment flyers with study contact information posted in relevant clinic waiting rooms and shared via social networks. We will share this recruitment flyer with relevant community groups dedicated to supporting caregivers of PWD, including the Alzheimer's Association and the South Side Healthy Aging Resource Experts (SHARE) Network, among others, and allow and encouraging caregivers who have completed participation to take recruitment flyers to share with their social networks. We will also share the recruitment flyer through various social media and other outlets. Interested caregivers will then reach out to someone on the research team for further eligibility screening.

Q. Notification of physician

Notification of the caregiver's treating physician for permission to enroll will occur using a multi-pronged approach. First, we will educate all treating physicians and residents working in the target clinics about the study during the pretesting phase and give treating physicians the opportunity to opt out of study participation. Secondly, we will use these education sessions to identify how treating physicians wish to be contacted for permission (e.g., via text, email, phone, text page or through the electronic medical record system). We will use that communication as documentation of treating physician permission. Lastly, we will also educate nursing staff about the study. Nurse engagement will be helpful should we need to reach a treating physician during clinical rounds.

R. Anticipated coordination

Inter-departmental faculty coordination will be facilitated by regular research meetings attended by Drs. Lindau and Huang (PIs) and other Co-Investigators and key personnel. Faculty will also regularly communicate by email and phone calls as necessary. Co-Principal Investigator Dr. Elbert Huang (Professor of Medicine) will oversee enrollment of ADRD caregivers in the Primary Care Clinic. Co-Investigator, Dr. Katherine Thompson (Associate Professor of Medicine – Geriatric and Palliative Medicine) practices at the South Shore Senior Center (SSSC) and will oversee enrollment of ADRD caregivers there where many caregivers receive care. She provided a letter of support for this research. We have successfully fielded data collection efforts in both of these clinical sites as well as in the Department of Ob/Gyn.

S. Pregnancy test

Not applicable.

T. Exclusion of women, minorities and/or children

This study will not exclude women, minorities or children.

U. Drugs

No drugs will be given to subjects as part of this study.

CommunityRx-Caregiver (CRx-C; CommunityRx-Dementia; CRx-D)

Study Protocol: Final Approved Version

Note: Per the recommendation of The University of Chicago's Institutional Review Board, the first submission of this study's protocol included only the study's pre-test protocol. Following completion of the pre-test, again per the IRB's recommendation, the pre-test version was amended for the full trial. The below includes the most recent approval version.

Principal Investigators: Stacy Tessler Lindau, MD, MAPP and Elbert Huang, MD, MPH

UCHICAGO IRB # 20-0301

ClinicalTrials.Gov Identifier NCT: NCT04146545

Version Approved: 11/30/2023

TITLE: CommunityRx-Caregiver (CRx-C)
PIs: Stacy Tessler Lindau, MD, MAPP; Elbert Huang, MD, MPH
Co-I: Katherine Thompson, MD

A. Background

More than 16 million unpaid family and friend caregivers care for a rapidly growing population of home-dwelling people with Alzheimer's disease and related dementias (ADRD) in the US.[1] ADRD caregivers have poorer physical health than their peers and high rates of burden (46%) and depression (30-40%).[1] Stigma and social isolation are common.[2,3] Randomized, controlled efficacy trials of intensive caregiver support, such as REACH-I,[4] II[5] and NYU Caregiver Intervention,[6] reduce caregiver burden and improve well-being and quality of life, but have not made linkage with community resources a primary focus. Unmet resource needs are major drivers of low caregiver self-efficacy, in turn a key factor in the pathway linking caregiver support to health outcomes.[7,8] A low-intensity, high quality resource referral process that addresses the full range of caregiver and care recipient resource needs would facilitate broad adoption and dissemination of intensive support interventions and may itself independently promote caregiver self-efficacy and other important health outcomes.

Federal law calls for connecting caregivers to community resources[9–13] (e.g. ADRD education, support groups, respite care), with special concern for reducing health disparities.[9,14] In parallel, CMS is testing, in the broader population, routine clinical assessment and referral for unmet health-related social needs (HRSNs) (e.g. food, housing, interpersonal safety, social support).[15,16] Although the demands of caregiving commonly produce financial strain,[17] HRSNs have largely been overlooked by caregiver support interventions.[4–6,18] Our work shows that even in higher poverty communities, supportive resources are available, but hard to find and access.[19] Scalable, "whole-person"[20] resource referral solutions are needed to efficiently manage and promote the health and well-being of ADRD caregivers and persons with dementia (PWD) with and without unmet HRSNs. Different from previous caregiver intervention studies that recruit caregivers accompanying a PWD at healthcare or community activities,[4–6,18] this study aims to promote caregiver health and well-being by intervening with caregivers at the point of their own primary healthcare. The target population on Chicago's South Side is predominantly African American. Half have unmet HRSNs. The overall objective of the proposed research is to evaluate the impact of CommunityRx-Caregiver (CRx-C), a scalable information technology-based intervention, developed with the target community, to address unmet community resource needs.

The CRx-C intervention is a caregiver-centered adaptation of CommunityRx (CRx), an information-based intervention that systematically matches people to nearby community resources for HRSNs, caregiving and other self-care needs.[19] In two studies (one in press at AJPH), we see that half of CRx recipients share resource information with others, acting as natural disseminators of intervention benefits.[19]

We hypothesize that connecting caregivers to community resources will increase self-efficacy, reduce unmet needs and promote better downstream health outcomes. CRx-C focuses on caregivers, but also assesses, by proxy, care recipient community resource use, health and healthcare utilization.

B. Purpose

The purpose of this research is to promote caregiver health and well-being by intervening with caregivers of people with dementia. The long-term goal of this research is to promote public health and alleviate suffering among a growing population of ADRD caregivers and PWD. To this end, we will evaluate the impact of CommunityRx-Caregiver (CRx-C), a scalable information technology-based intervention, developed with the target community, to address unmet community resource needs.

The over-arching aims of the program of research are:
Aim 1: Among caregivers with unmet HRSNs, evaluate the effects of CRx-C versus usual care on caregiver self-efficacy (primary outcome) and secondary outcomes: psychosocial (unmet needs, social isolation, well-being, burden, depression, stress), behavioral (community resource use), health and healthcare utilization.

Aim 2: Among all caregivers (those with and without unmet HRSNs), evaluate acceptability of the intervention as well as the effects of CRx-C versus usual care on the health care experience, including satisfaction with care (primary outcome), experiences of stigma during clinical care and likelihood of sharing community resource information with others.

Aim 3: Among a purposeful sample of caregivers, assess: (a) experiences with CRx-D; (b) the role of stigma in disclosing needs and accessing resources; and (c) experiences sharing resource information with others.

Findings will yield an understanding of how best to leverage ADRD caregivers' or care recipients' healthcare visits to identify, support and improve outcomes for caregivers, including psychosocial characteristics, behaviors, health and healthcare. Results will inform whether and how CRx-C should be implemented in practice and explore how best to sensitively and effectively intervene to support all ADRD caregivers.

The pretest study aims to identify optimal processes for administering the planned intervention remotely or in-person and to optimize the efficiency and flow of baseline and follow-up survey administration and interval communications with participants. Findings from this pretest will be presented to the CommunityRx-Caregiver Advisory Board which consists of a diverse sub-group of ADRD caregivers and other community stakeholders. Their input and feedback will be used to inform the larger randomized trial.

C. Methodology

The first step in the proposed program of research is to pretest the single-blind, randomized controlled trial procedures and administration of the intervention and data collection procedures to inform the design of a larger randomized controlled trial (RCT). Given the pause of in-person medical visits and shelter-in-place orders due to the COVID-19 pandemic, we will pretest remote recruitment and consent procedures as well as remote intervention delivery. Interviewers will administer telephone or video-based surveys; self-administration of a web-based follow-up survey will also be offered. We will enroll up to 404 caregivers of people with ADRD, (both with and without unmet health-related social needs (HRSNs),10 caregivers enrolled in the remote pretest, 344 caregivers in the RCT for a 12-month follow-up, and an additional 50 male caregivers in the RCT for a 3-month follow-up. All human subjects will be consecutively screened for inclusion and enrolled

as described in Section P. Recruiting Methods. Following screening, participants will be screened for unmet HRSNs and then randomly assigned to either usual care or usual care plus CommunityRx-Caregiver. Usual care is described below in Section G. Use of Controls or Placebos.

CommunityRx-Caregiver (CRx-C): Caregivers randomized to the intervention will receive CRx-C in addition to usual care. CRx-C will be initiated by the Community Resource Specialist (a member of the research team) at the baseline (index) primary care visit (primary care, geriatrics, ob/gyn clinics or at the conclusion of a telemedicine visit). The intervention will include: (a) a brief, structured educational intervention about common resource needs among ADRD caregivers (e.g., "It is recommended that we talk with caregivers of people with dementia about community resources that may be helpful. Many caregivers benefit from resources like support groups or respite care. It is also common for caregivers to need help with things like food or rent and utility support."); (b) delivery and review of a personalized resource "prescription" (HealtheRx-C) for vetted resources near the caregiver's preferred location to address HRSNs (e.g. food, housing, interpersonal safety and social support) and ADRD caregiver needs (e.g. ADRD education, support groups, respite care, advance care planning); (c) demonstration of use of an online Community Resource Finder that participants can use to find and share community resources (for HRSNs, caregiving and any self-care needs), give feedback and request additional resource information; and (d) coaching on how to activate community resources, including how to reach the Community Resource Specialist (a member of the research team), and (e) a series of text messages to which the subject can respond and communicate with the Community Resource Specialist.

In addition to the "HealtheRx-C" delivered at the time of the baseline visit or e-visit, the HealtheRx will be texted to the participant within 24 hours, and emailed to them. Instructions on how to access the online resource finder will also be emailed to the participant after their baseline visit.

The proposed CommunityRx-Caregiver intervention includes a proactive text messaging protocol; we will pretest the first 30 days of the text messaging protocol to ensure its smooth operation. During the full RCT, the proposed CommunityRx-Caregiver intervention will include proactive text messaging throughout the first 90 days of the study period.

All caregivers randomized to the intervention will receive, in addition to the educational component and review and receipt of the HealtheRx, a series of timed text messages from the Community Resource Specialist offering ongoing community resource linkage support. At any time, a participant can reply "stop" to stop receiving text messages from the CRx-C Community Resource Specialist. The participant can also text the Community Resource Specialist for assistance as desired. The specialist will respond to text messages within 24 hours during regular work days and within 48 hours of weekends or holidays. The content of these messages is based on a text messaging experiment conducted during the original Centers for Medicare and Medicaid Innovation Health Care Innovation Award CRx study; text message content will be submitted with this proposal for review.

The 344 caregivers enrolled in the RCT for a 12-month follow-up will receive text messages to support scheduling and reminders for follow-up surveys. All caregivers will be contacted at their 6 and 9 month study time point to verify their contact information is up-to-date. Caregivers will be entered into a raffle to win a $50 gift card if they verify their contact information is up-to-date at each of these study time points. Each verification (one at 6-months and one at 9-months) counts as one raffle entry.

The 344 caregivers enrolled in the RCT for a 12-month follow-up will complete an interviewer-administered baseline survey (by phone, video or online) and phone- or web-based follow-up surveys at 7 days, one month, 3 months, and 12 months after the index visit. The 50 additional male caregivers enrolled in the RCT for a 3-month follow-up will complete an interviewer-administered baseline survey (by phone, video or online) and phone- or web-based follow-up surveys at 7 days, one month, and 3 months after the index visit. Surveys will elicit self-reported data in the following domains: caregiver status, caregiver sociodemographic characteristics (e.g., age, race/ethnicity, sex and gender), caregiver-reported care recipient demographics (e.g. age, race/ethnicity), employment, household composition, income and insurance status, stage of dementia of the care recipient; psychosocial characteristics (e.g., caregiver self-efficacy, unmet health-related social and caregiving needs, burden, depression, stress and well-being); behaviors (e.g., use of resources, use of the Community Resource Finder, resource information sharing, activation of the Community Resource Specialist); health and healthcare use (e.g., physical health and health-related quality of life and healthcare utilization); and healthcare experience (e.g., satisfaction with care, stigma). Caregivers will be asked a limited number of questions as proxy for the care recipient to assess: well-being, community resource needs and use, health and healthcare utilization.

If needed to supplement healthcare utilization data, we will obtain health insurance claims for the participant. The informed consent/assent process will inform study participants of the rationale for accessing these data and request participants' permission to do so.

Following completion of their last follow-up survey, a purposeful sample of participants will be invited to complete an in-depth qualitative interview. Caregivers will be informed about the purpose of the study and, if interested, undergo informed consent (described below in Section M. Informed Consent). This interview will elicit caregivers' (a) experiences with and attitudes toward the components of the CRx-D intervention (screening for caregiver status and unmet needs, delivery of the CRx-D, text messaging and other communications with the community resource specialist and the Community Resource Finder tool); (b) experiences sharing resource information with others, and (c) the role of stigma in disclosing needs and accessing resources.

Additionally, we will conduct qualitative interviews with a purposeful sample of participants enrolled in the 3-month RCT focused on gender differences. This interview will elicit (a) ADRD caregiver support networks, particularly the effect on women caregivers of caregiving support provided and procured by men family and friends; (b) gender differences in ADRD caregiver coping mechanisms; and (c) familial gender roles related to ADRD caregiving.

D. Duration

The duration of this protocol is approximately four years. This will allow for ongoing recruitment of participants into the study, administration of baseline and all follow-up surveys and interviews and ongoing presentation of findings to the CommunityRx-Caregiver Advisory Board. The duration of this protocol will also allow enough time for data analysis and manuscript development.

E. Location

Research under this protocol will be conducted by researchers in the Departments of Obstetrics and Gynecology and Medicine at the University of Chicago (located at 5841 S. Maryland Ave., Chicago, IL, 60637). Additional research (e.g., data preparation and analyses) will be conducted in Dr. Stacy Lindau's research laboratory, using networked computers, located in the Medical Center

2050, rooms R-311 and R-315 and Dr. Elbert Huang's research offices, located in the Medical Center 2007, Room B214.

F. Special Precautions

Protected health information (PHI) will be collected for research purposes and special precautions will be made to protect these data. In addition to the unique identifier applied by the REDCap computer-assisted personal interviewing (CAPI) software, we will use the caregiver's name, telephone number and email address to facilitate scheduling and completion of the follow-up surveys. We will ask participants to provide us with an alternative contact (e.g., name, phone number, email address) that we can reach out to if we should lose contact with the enrolled caregiver. We will ask participants to tell this person that they have listed them as an alternative contact for this study. We will use the caregiver's name and medical record number (MRN) to access their electronic medical record to assess health and healthcare utilization and whether caregiver status was documented by the caregivers' medical providers. From EMR data, we will access the participant's health insurance payer and unique beneficiary identification to obtain their health insurance claims, if needed. We will compensate caregivers for their participation in the follow-up surveys and for study referrals by gift card, and will use the caregiver's name and, email and mailing address for compensation payment purposes. Individuals not enrolled in the study who refer an individual to the study who ultimately enrolls in the study will be compensated for this referral. We will use the individual's name, email or address for compensation purposes only.

Certain survey data elements collected in the REDCap database will be sent securely to NowPow, a systematic resource referral platform, to generate the HealtheRx and to Mosio, a secure text messaging platform, to facilitate the proactive text messaging protocol and manage survey scheduling and reminders for all participants. Elements of PHI sent to NowPow to generate a personalized HealtheRx include: participant name, participant home address, date of birth and other non-PHI data elements. Data will be securely transferred from REDCap to NowPow through a custom secure integration created by the Center for Research Informatics. In addition to other non-PHI data elements, respondent address is necessary to better tailor the community resource information provided on the personalized HealtheRx. Elements of PHI sent to Mosio to facilitate the text messaging protocol and scheduling/reminders include: participant name, telephone number and date of enrollment in the study.

Metadata generated by use of the NowPow system will be provided to the research team via Globus for secure file transfer on a regular basis (see documentation below). NowPow is a company serving dozens of blue chip health systems using rigorous data protocols and therefore operates its technology in a manner that meets the strict HIPAA and security criteria standards of these organizations.

Qualitative interviews will be audio recorded and transcribed. Qualitative interview audio recordings will be transcribed by Amazon Web Services (AWS) Transcribe. AWS Transcribe has been reviewed and approved by the BSD Information Security Office and deemed to be HIPAA-compliant. Interviews will be de-identified upon transcription.
Because PHI will be accessed and collected for this program of research, there is a risk of loss of confidentiality. To protect confidentiality, we will implement a plan to protect data in all its forms

from improper use and disclosure using HIPAA compliant policies and procedures; see Section N. Procedures to Maintain Confidentiality for more information.

Use of Globus for File Transfer
A Globus endpoint will be created by the Biological Sciences Division's Information Services pointing to the lindau-lab file share on PRFS. The endpoint will be configured to force encryption of the data channel. A dedicated subdirectory within the file share will be created, and a guest collection will be created permitting authorized users to access that subdirectory. NowPow will be granted access to that collection, and will use Globus (either the client or API) to transfer files into the dedicated subdirectory where they may be retrieved by an analyst in the Lindau Lab.

G. Experimental controls and use of placebos

Caregivers in this study will be randomized to either usual care or usual care plus the CommunityRx-Caregiver intervention.

The usual care study arm for caregivers who are patients includes typical clinic visit procedures, including, but not limited to: meeting with a Patient Service Representative, receipt of a printed after visit summary (AVS), notification of any financial obligations and scheduling any future visits as appropriate. Usual care may also include information about community resources from the patient's healthcare team.

Usual care for caregivers who are not patients but accompany a person with dementia for their care may experience procedures and information similar to those described above.

H. Type and number of experimental subjects

Individuals will be contacted for enrollment using methods described below in Section P. Recruiting Methods. Individuals will be contacted, screened for inclusion, recruited for study participation and participate in the informed consent process. Following enrollment, caregivers will be assessed for HRSNs using the CMS Accountable Health Communities tool and stratified by HRSNs (no HRSN vs. $\geq$1 HRSN) and randomized to either usual care or usual care plus the CommunityRx-Caregiver (CRx-C) intervention. We will enroll up to 404 caregivers, (10 caregivers enrolled in the remote pretest, 344 caregivers in the 12-month RCT (follow-up for 120months), and an additional 50 male caregivers in the 3-month RCT (follow-up for a 3-month follow-up).

Inclusion criteria:

- Resides in the target geographic region of the study
- Self-identifies as a caregiver of a home-dwelling person with Alzheimer's disease or other related dementia using an adaptation of the Behavioral Risk Factor Surveillance Survey caregiver module
- Has access to a cell phone and provides the research interviewer with the cell phone number
- Agrees to receive text messages from the study
- Has a personal email address.
- -Self-report their gender identity to be male or trans male/trans man (only for additional 50 caregivers enrolled in the 3-month RCT)

Exclusion criteria:

- Minor caregivers who are not emancipated minors according to Illinois State law

I. Statistical analysis

The purpose of this research is to pretest our intervention administration and data collection procedures. We will collect baseline and follow-up survey data. To this end, descriptive statistics will be used to summarize, overall and by study arm, sociodemographic characteristics and primary and secondary outcomes at each measured time point. The mean, standard deviation, median, and inter-quartile range will be generated for continuous variables; frequency counts and percentages will be generated for categorical variables. We will evaluate the survey data for missingness, systematic item non-response, and out of range values and prepare our data management analytic code.

Descriptive statistics will be used to summarize, overall and by study arm, sociodemographic characteristics and primary and secondary outcomes at each measured time point. The mean, standard deviation, median, and inter-quartile range will be generated for continuous variables; frequency counts and percentages will be generated for categorical variables. The main analyses will follow the principle of intent-to-treat. Additional a priori quantitative analyses will be conducted as needed to answer the research questions.

Qualitative interview data will be collected and analyzed using directed content analysis. Directed content analysis uses findings from extant literature to ask pointed questions about the concept under study and to structure coding of the qualitative data. We will operationally define codes in a codebook prior to data analysis. Initial analysis will begin with a full read of the interview transcripts for, upon first impression, instances of textual data that align with the codes in the codebook. Actual coding of textual data will occur upon second pass of the transcripts, using the codebook. Any textual data that were identified in the first-pass read of the transcript but not coded using the codebook will be given a new code. Two experienced qualitative researchers, Dr. Jerome and Emily Abramsohn, MPH, will use ATLAS.ti to independently analyze the qualitative data. After analysis of the first 5 interviews, using the principles of theoretical sampling, both the sample strata and the interview guide will be evaluated and, if needed, revised to ensure compatibility with emerging theory about the intervention. Drs. Lindau and Thompson, also experienced qualitative analysts, will read and code a sub-set of the transcripts and contribute their clinical expertise in interpretation of qualitative data. They will serve as adjudicators when consensus cannot be reached by the two primary coders. Based on our experience with prior qualitative studies, interviews with 44 caregivers (including 12 men recruited specifically from the 3-month RCT focusing on gender differences) will be sufficient to reach theoretical saturation given the pre-specified enrollment strata and allow for qualitative analysis by gender in accordance with the aims of the gender-focused supplement.

J. Potential risks and benefits

This program of research involves no more than minimal risk or no more risk than is encountered in routine medical and psychological examinations. The risks of participation in this protocol include a potential loss of confidentiality or psychological or emotional discomfort associated with the interview questions. Every effort will be made to ensure subject confidentiality and that risks due to loss of confidentiality are minimal compared to the protocols in place to protect human subjects' data. To date, more than 113,000 individuals have participated in CommunityRx intervention

studies with no known adverse events or breaches of confidentiality. All data collected from human subjects will be collected using standard survey procedures. The surveys will be conducted via telephone or online. Psychological and/or emotional discomfort associated with the survey questions is possible. Subjects will be informed that they can decline to answer any question and can terminate the survey or interview at any time. Explanatory statements will be included in the surveys and interviews to help the interviewer monitor and respond appropriately to discomfort, including termination of the survey or interview if necessary. Alternatives to participation include not participating in the research; participation is completely voluntary. Additional protections against these risks are described in Sections M and N, Informed Consent and Confidentiality, respectively.

There is no direct benefit to human subjects involved in the research beyond the information provided during usual care and the CommunityRx-Caregiver intervention. Participants, however, may gain personal satisfaction in contributing to research to address the humanitarian issue of unmet needs among caregivers of PWD. Potential risks include a breach of confidentiality and are both minimal and reasonable in relation to the anticipated benefits to research participants and people with dementia.

K. Monitoring of safety

The proposed data collection presents no more than minimal risk or no more risk than is encountered in routine medical or psychological examinations. As described, no surveys will be conducted without explicit documentation of informed consent and individuals will be provided with appropriate information about confidentiality when enrolling in the study and will indicate acceptance of these risks upon consent. Because we are not proposing a multi-site clinical trial, a Phase III trial, or a drug study, this study will not employ a Data and Safety Monitoring Board. Procedures are in place to ensure confidentiality and provide full informed consent as discussed below.

The Lindau Lab has listed the Principal Investigators and study coordinator phone numbers on all study correspondence and forms. The purpose of the phone numbers is to provide respondents with a number to call if they have questions about any aspect of the study. If concerns regarding a participant's safety are endorsed within the health-related social needs screening, REDCap will deliver an alert to the research assistant (RA) after survey completion that the participant screened positive for safety concerns, without revealing the survey contents. With the participant's permission, the RA will alert an appropriate member of the clinical staff, including social work, or Drs. Lindau, Huang or Thompson such that they can connect the participant to resources to support their safety. During the study, should a subject express intent to harm themselves or others, we will contact a health or public safety professional. We will give only the subject's name, contact information, and why we feel he or she is at risk of harming themselves or others. This report will not be linked to his or her survey information. Subjects have the right to refuse to speak to the mental health professional. If the survey procedures results in the observation or suspicion of elder or child abuse, all research personnel will act in compliance with Illinois State law in regards to mandatory reporting of abuse.

Research staff will strictly adhere to the procedures for enrolling participants and collecting data as outlined by the investigators. At the conclusion of the study, all hard copy materials, with the exception of the consent copies, will be destroyed and electronic files will be deleted or archived in

password-protected files. Informed consent documents (paper or electronic) will be stored for at least 6 years following the completion of the study (defined by the last publication related to the study). Due to the small sample sizes associated with the pretest, the pretest data will not be made publicly available.

L. Payment

Caregivers enrolled in the pretest will receive $25 in compensation for completion of the baseline interview (approximately 25 minutes) and $25 in compensation each for completion of the one-week and 30-day follow-up surveys (approximately 30 minutes).

The 344 caregivers enrolled in the RCT for a 12-month follow-up, will receive $20 in compensation for the completion of the baseline interview, 1-week, 1-month (about 30 minutes each). Caregivers will receive $30 gift card in compensation for the completion of the 3-month survey (about 40 minutes) and $50 gift card in compensation for completion of the 12-month survey (about 50 minutes).

Caregivers will be entered into a raffle to win a $50 gift card if they verify their contact information is up-to-date at each of these study time points. Each verification (one at 6-months and one at 9-months) counts as one raffle entry. Within 3 months of their check-in, they will receive an email notification about whether they are the raffle winner. If they're the winner, they will receive their compensation electronically or by mail within 4 weeks of email notification.

The additional 50 male caregivers enrolled in the 3-month RCT, will receive $20 in compensation for the completion of the baseline interview, 1-week, 1-month (about 30 minutes each). Caregivers will receive $30 gift card in compensation for the completion of the 3-month survey (about 40 minutes). To supplement recruitment of these male caregivers, we will compensate any individual ($25 gift card) who refers a caregiver to our study who then ultimately enrolls in the study.

All RCT caregivers will receive their compensation electronically or by mail within 4 weeks of completing each of the surveys.

Caregivers enrolled in the qualitative interviews will receive a $50 gift card by mail upon completion of the interview.

Compensation will not be prorated for partial completion of surveys but every effort will be made to allow for ample time to complete the surveys and participants can refuse to answer any question they do not want to answer. Participation is voluntary.

M. Informed Consent

We will obtain written or electronic informed consent as follows:

Caregivers 18 years of age or older: Until we are able to recruit in-person, we will obtain electronic informed consent from all caregivers 18 years of age or older using an e-consent process developed in partnership with REDCap and used previously by Dr. Huang's lab.
Following the guidance of the CDC and the University of Chicago Medical Center, we will not recruit participants in-person until we receive permission. If we are able to recruit in person, we will obtain written informed consent from all caregivers 18 years of age or older.

Caregivers 17 years of age and younger: We will obtain electronic or written informed consent from all caregivers younger than age 18 who are eligible to consent for participation in research. Caregivers ages 17 years of age and younger will be eligible to participate if they are an emancipated minor under Illinois state law (750 ILCS 30/5).

Research interviewers will guide caregivers through the informed consent document, providing statements to address: that the study involves research; the study's purpose, duration, procedures followed, risks and benefits, alternatives to participation, and confidentiality of records; to whom they should direct questions or contact in case of research-related injury; and statements regarding voluntary participation, refusal to participate, and discontinuation of participation. The researcher will provide adequate time for the potential subject to ask questions and will answer these questions before requesting the caregiver's signature to document e-consent. The informed consent process for caregivers enrolled in the study will take place in the clinic waiting room or the caregivers' exam room following recruitment, depending on the timing of their visit or prior to or following a telemedicine visit using a REDCap form e-mailed to participants. The researcher will walk the caregiver through the consent process via phone or video and, if the caregiver chooses to participate, the caregiver will electronically sign the consent form in REDCap by typing their full name into the signature field and verifying their identify by entering their date of birth or the care recipients' date of birth. A copy of the signed consent form will be shared with them via email. We are requesting a waiver of documentation of consent for participation in the qualitative interviews, and will obtain verbal consent immediately before the interview. Similar to the process for consent for participation in the RCT, researchers will guide caregivers through an informed consent script and ask for their verbal consent before proceeding with the interview. A copy of the informed consent script will be emailed to the participant for their records. The informed consent document is enclosed in this submission for review.

No surveys or interviews with human subjects will be conducted without explicit documentation of the informed consent process executed with each participant. Informed consent documents will be iterated using approved consent documents from the recently completed CRx pragmatic clinic trial of patients (N=411) receiving care in the University of Chicago's Primary Care Group and Emergency Departments. The consent documents for that study were adapted from consent documents developed in collaboration with a literacy consultant and members of the community. Consent documents will be written in easily understandable language and, in addition to English will be translated into Spanish. We have hired bilingual Research Assistants to enroll participants who speak Spanish or will make use of the hospital Language Line for interpretation and translation. Confirmation of consent will be collected and stored in REDCap for the RCT, or documented in REDCap for the interview, and only accessible to approved researchers to confirm participation in the study for data collection, validation, and data analysis purposes. A final copy of all consent documents will be submitted to the IRB for review and approval.

N. Confidentiality

The proposed research with human subjects, as presented above, presents no more than minimal risk or no more risk than is encountered in routine psychological examinations. Any potential risks may be due to emotional or psychological discomfort associated with the surveys or a breach of confidentiality. As described in detail above, no surveys will be completed without explicit

documentation of informed consent and written authorization for the use and disclosure of identifiable data will be sought and obtained for all subjects enrolled in this study. All individuals will be provided appropriate information about privacy and confidentiality when enrolling in the study and will indicate acceptance of these risks upon consent/authorization.

The Lindau Laboratory has strict and secure procedures for protecting against and minimizing potential risks to human subjects' data. All survey data will be entered directly into REDCap, a password-protected database managed by the Center for Research Informatics (CRI) at the University of Chicago (cri.uchicago.edu). CRI provides a HIPAA-compliant data storage and computing environment that has achieved security accreditation by the Biological Sciences Division's Risk Management Group. Data will be saved to the secure servers in the Department of Ob/Gyn at the University of Chicago via a secure wireless connection on a secure, password-protected tablet, or research staff will enter REDCap data directly on OB/Gyn departmental computers using the secure, password-protected Ob/Gyn internet network. Data are backed up at the end of each collection day. Data will never be stored locally on the tablets.

REDCap will integrate electronically with NowPow (www.nowpow.com) to facilitate generation of the HealtheRx. Data will be pushed from REDCap to NowPow via a custom secure integration to create the participant's profile in NowPow, including name, address, date of birth and other non-PHI data. Any data sent to NowPow from REDCap to generate the personalized HealtheRx will be assigned a secondary unique ID in order to prevent any connection to the subjects' responses in REDCap. NowPow is seamless, secure and HIPAA-compliant. Data are backed up automatically and encrypted in-transit, at-rest, and end-to-end. De-identified metadata will be transferred to researchers in the Lindau Laboratory using a secure file transfer protocol (SFTP); details described above. All devices used by researchers to collect or access research files will be encrypted. Only approved research analysts in the Lindau Laboratory will have access to files that link participant's PHI to their unique identifiers for the purposes of creating analytic datasets.

REDCap will integrate electronically with the Mosio texting platform (www.mosio.com) to facilitate the text message protocol for human subjects in the intervention group and manage survey scheduling and reminders for all participants. To this end, REDCap will push the subject's name, telephone number and date of enrollment to Mosio via REDCap's secure API. Mosio provides a secure messaging and data storage environment and has been approved for use by the University of Chicago Information Security Office. Only approved researchers in the Lindau Lab will have access to data stored by Mosio and will have the ability to securely download data directly to computers within the Ob/Gyn network.

All hard copies of project materials will be stored in locked file cabinets in locked offices at University of Chicago. Servers in the University of Chicago Department of Ob/Gyn are protected through a combination of a Microsoft-based firewall technology and the physical barrier of a Linksys router that is installed between the server and its internet connection. Laptop computers used to collect data will be encrypted and password protected. All data transmitted to secure servers will be encrypted. Analytic files will either be de-identified prior to analysis or limited to the minimum amount of data necessary to accomplish the intended research purposes per the HIPAA Privacy Rule. Any analytic datasets will limit the use or disclosure of PHI to the minimum necessary, if any at all, to accomplish the intended research purposes. Only IRB-approved researchers on this protocol will have access to data. These controls meet or exceed the strictness

of practices legislated and enforced by the University of Chicago Biological Sciences Division and hospitals for protected health information.

Procedures are in place to ensure confidentiality and provide informed consent as discussed above. Numeric coding of surveys/interviews and secure containment of files that link participant's responses from PHI will also minimize this risk. Finally, the Lindau Laboratory will provide a contact phone number that will be included on all study correspondence and forms. The purpose of this phone number is to provide respondents with a single number to call if they have questions about any aspect of the study.

O. Bibliography

Bibliography included in online submission, View 8.1.

P. Recruiting methods

Given the shift to telehealth appointments at UCM and shelter-in-place orders due to the COVID-19 pandemic, we will pretest a remote recruitment strategy and enroll participants for the full RCT. The following strategies will be conducted to identify eligible caregivers:

1. Via Epic: We will use EPIC to view the schedule of outpatient visits at University of Chicago Medicine. We will use EPIC to identify patients on the clinic schedule that reside in the ZIP code target geography. We will contact patients by sending them a text message and calling their phone numbers recorded in Epic. We will attempt to recruit these patients within one week of their outpatient or telemedicine visit using the recruitment script and screening tool approved by the IRB. Eligible patients will set up a time with study staff to go through e-consent and complete the baseline survey.
2. Via collaboration with Clinical Research Informatics: We will work with CRI to identify eligible caregivers via a three-part process:

    Step 1: The study team will generate a list of patients that have an ICD 9 or 10 code of Alzheimer's disease or a Related Dementia and identify their primary or emergency contact. The study team will do this using the SlicerDicer tool available to physicians in Epic or via a request made to the Analytic Core Request System under CRI.
    Step 2: The study team will then contact the patient's primary or emergency contact to assess if they are also a patient of UCM, their caregiver status and request permission to re-contact them on the day of their next scheduled outpatient or telehealth visit (see approved Chart Review Screener Survey and Script).
    Step 3: This list of eligible caregivers that have given us permission to re-contact them will be shared with CRI again. CRI will set up a data-sharing warehouse that will be continually updated so that the study team can keep track of upcoming outpatient appointments of eligible caregivers. The study team will then contact these caregivers within 1 week of their healthcare visit to assess interest in the study and proceed with screening and enrollment.

This multi-step approach is necessary to identify caregivers at the point of their own healthcare – a primary focus of this study. If a patient is eligible and interested we will set up a time to contact them for e-consent, intervention delivery and to conduct the survey within one week of their outpatient or telehealth visit. If the patient is eligible, researchers will send them an e-consent form

using REDCap that is able to be filled out online. The e-consent process is one that has been developed successfully in Dr. Huang's research lab.

If we are able to safely approach patients in-person again, as we have done in prior trials in this setting, we will consecutively approach patients in the waiting rooms of the SSSC, PCG and Ob/Gyn for inclusion in the full RCT. Researchers will approach potentially eligible participants and explain that they may be eligible for a research study and, if interested, further screen for eligibility. If interested in participating and available at that time, the researcher will complete the informed consent process with the caregiver. We will also attempt to recruit individuals who are accompanying patients with dementia for their care. Potential participants will be identified using administrative data (to identify patients with a diagnosis of Alzheimer's Disease and other related dementias living in the ZIP code CommunityRx target geography) and through verifying discussions with nursing and other members of the care team, including patient service representatives and social workers. Participants who are not patients will be approached for participation in the study by:

3. Posting recruitment flyers in relevant waiting rooms and via social networks: We will recruit caregivers of people with dementia using recruitment flyers. These recruitment flyers include study contact information posted in relevant clinic waiting rooms and shared via social networks. Flyers also include a QR code that links to a password-protected data collection form in REDCap where interested individuals can enter information (name, phone number, preferred language and dementia caregiver status) so that we can reach out with more information about the study. We will share these recruitment flyers with relevant community groups dedicated to supporting caregivers of PWD, including the Alzheimer's Association and the South Side Healthy Aging Resource Experts (SHARE) Network, among others, and allow and encouraging caregivers who have completed participation to take recruitment flyers to share with their social networks. We will also share the recruitment flyer through various social media and other outlets. Interested caregivers will then reach out to someone on the research team for further eligibility screening. Participants who have completed the trial will receive this flyer in the mail following completion of their last survey and, if they gave us permission to recontact them, we will call them to follow up and encourage them to share their flyer with other caregivers they may know. We will also use the ITMs research profile website, https://bethenewnormal.org/, and researchmatch.org to post our study and to use it as a recruiting tool for eligible subjects (see recruitment materials uploaded to View 3.1 in AURA). To supplement this strategy, we will compensate individuals $25 for any referred person who ultimately enrolls in this study.
4. Receiving patient referrals from the My Diabetes, My Community (MDMC) trial: Dr. Elbert Huang and Dr. Stacy Lindau lead the My Diabetes, My Community trial - a three-arm parallel pragmatic randomized controlled trial among older, predominantly African American patients with type 2 diabetes seen at the University of Chicago. A dementia diagnosis and inability to complete the study on their own are two of the exclusion criteria for the trial. During screening, it is possible for research assistants to contact patients living with dementia or their caregivers. When a patient with dementia and their caregiver are identified and screen out in the MDMC trial, there is an opportunity to ask whether they would be interested in participating in another trial they may be eligible for - the CommunityRx-Caregiver trial. The MDMC research assistant would ask if the patient is interested in hearing more about a trial they may be eligible for and whether it is ok to share their phone number with the CommunityRx-Caregiver team. In receiving verbal consent to share their phone number with the CommunityRx-Caregiver team, the MDMC research

assistant will document this in the patients' screening data in REDCap and notify the MDMC Project Manager (PM). The MDMC PM will then flag this record to the CommunityRx-Caregiver PM. The MDMC PM, Jacqueline Kanoon, is an active study staff on the CommunityRx-Caregiver trial. A CommunityRx-Caregiver team member will then follow-up with the patient about participating in the CommunityRx-Caregiver study.

Once their participation in the RCT (either 12-month or 3-month) is complete, certain caregivers will be approached for inclusion in a qualitative interview. Researchers will contact caregivers by email, text message and phone. Research interviewers will explain that the caregiver may be eligible for a research study and, if interested, further screen for eligibility. Recruitment scripts for the various modes of contact have been submitted for review with this protocol. If eligible, researchers will guide participants through the informed consent process as described in Section M. Informed Consent.

Q. Notification of physician

Notification of the caregiver's treating physician for permission to enroll will occur using a multi-pronged approach. First, we will educate all treating physicians and residents working in the target clinics about the study during the pretesting phase and give treating physicians the opportunity to opt out of study participation. Secondly, we will use these education sessions to identify how treating physicians wish to be contacted for permission (e.g., via text, email, phone, text page or through the electronic medical record system). We will use that communication as documentation of treating physician permission. Lastly, we will also educate nursing staff about the study. Nurse engagement will be helpful should we need to reach a treating physician during clinical rounds.

R. Anticipated coordination

Inter-departmental faculty coordination will be facilitated by regular research meetings attended by Drs. Lindau and Huang (PIs) and other Co-Investigators and key personnel. Faculty will also regularly communicate by email and phone calls as necessary. Co-Principal Investigator Dr. Elbert Huang (Professor of Medicine) will oversee enrollment of ADRD caregivers in the Primary Care Clinic. Co-Investigator, Dr. Katherine Thompson (Associate Professor of Medicine – Geriatric and Palliative Medicine) practices at the South Shore Senior Center (SSSC) and will oversee enrollment of ADRD caregivers there where many caregivers receive care. She provided a letter of support for this research. We have successfully fielded data collection efforts in both of these clinical sites as well as in the Department of Ob/Gyn.

S. Pregnancy test

Not applicable.

T. Exclusion of women, minorities and/or children

This study will not exclude women, minorities or children.

U. Drugs

No drugs will be given to subjects as part of this study.

Changes to the CommunityRx-Dementia RCT protocol since Initial IRB Approval (Excluding Personnel Changes)

Per the recommendation of The University of Chicago's Institutional Review Board, V1 of this study's protocol, approved 2/11/2019, included only the study's pre-test protocol. Following completion of the pre-test, again per the IRB's recommendation, V1 was amended for the full trial (approved 11/3/2020). The below includes The majority of differences between V1 and V10 presented above include: a) planned differences between the pre-test protocol and full trial protocol (e.g., sample size, number of follow-up surveys) and b) revisions to allow remote enrollment of participants and remote administration of the intervention (conducted in person in the pre-test protocol) due to restrictions related to the COVID-19 pandemic (declared by the United States March 2020 and lifted May 2023). All changes were approved by the Institutional Review Board.

IRB amendment 1 (5/18/2020):	Allowed for remote protocols due to the COVID-19 pandemic, and included the following changes: • Chart review procedures to allow for remote recruitment, enrollment and intervention delivery • Minor edits to recruitment script related to screening using chart review • Change in consent process to document informed consent using electronic consent (E-consent) in REDCap; to conduct for the small group of pre-test participants

IRB amendment 4 (9/3/2020)	• Allowed study team to view upcoming appointments in UCM outpatient clinics for screening purposes via Epic schedules
	• Updated procedures with the Center for Research Informatics (CRI)
	  ○ Request permission to share study data with CRI to expedite recruitment in a remote setting due to COVID-19 e.g. identify primary contacts of ADRD patients who are also UCM patients
	  ○ CRI to set up data sharing warehouse to continually provide refreshed data on upcoming patient appointments (never implemented)
	• Minor edits to surveys

IRB amendment 8 (11/13/2020)	• Extended the pretest to the full RCT. • Extended study follow-up period to 12-months • Increased number of subjects enrolled • Addition of 3-month and 12-month surveys • Addition of 6-month and 9-month check-ins to verify contact information is up-to-date • Addition of qualitative interviews and verbal consent for these interviews • Permission to collect PHI for alternate contact if study team loses contact with enrolled subject

IRB amendment 9 (1/13/2021):	Included the following change: • Inclusion of non-English speakers • Inclusion of Spanish translated documents • Minor revisions to study surveys, recruitment script, and recruitment flyer
IRB amendment 11 (4/23/2021)	Included the following changes: • Expansion of recruitment efforts to larger geographical area; expanded zip code eligibility • Minor survey updates
IRB amendment 13 (6/23/2021)	Included the following changes: • Addition of COVID-related survey items to follow up surveys • Addition of chart review screening questions • Addition of study team's contact information to "The New Normal." ITM's website for research trials, researchmatch.org and similar organizations for recruitment purposes
IRB amendment 16 (9/19/2021)	Included the following change: • Addition of Care Recipient Living Situation questions to follow-up surveys
IRB amendment 20 (12/17/2021)	Included the following changes: • Revisions to the verbal consent for qualitative interviews regarding payment • Addition of recruitment scripts for qualitative interviews • Minor edits to the protocol to include recruitment collaboration between the "My Diabetes, My Community" Trial (IRB20-0870)
IRB amendment 21 (1/13/2022)	Included the following changes: • Addition of care recipient's gender and sex question to the 12-month survey • Clarification of age criteria to specify the study is recruiting caregivers age 18 and older and caregivers age 17 and younger if they are emancipated minors under Illinois State Law (750 ILCS 30/5) • Description of Mosio and NowPow data sharing
IRB amendments 22 (4/13/2022)	Include the following changes: • Updated consent form to reflect Dr. Lindau's updated conflict of interest statement • Updated qualitative protocol to include the use of Amazon Web Services to transcribe audio recordings • Minor additions to the 12-month survey

IRB amendments 26 (10/5/2022)	The study team was awarded an administrative supplement from the NIH to enroll an additional 50 male/men caregivers with a 3-month follow-up period. Changes included: • Addition of 50 men caregivers for shortened follow-up period (3-months) • Addition of gender screening question • New consent forms in English and Spanish for the supplement • Recruitment expansion to UChicago Medicine Ingalls Memorial • New recruitment flyers for additional men for the supplement • Slight modification of scripts and protocol for the recruitment of additional men
IRB amendments 27 (11/28/2022)	Include the following changes: • Addition of recruitment strategy in the community • Minor edits to consent documents, including an update to the study coordinator's name • Minor edits to the recruitment script tailored for men caregivers in the community
IRB amendments 29 (1/5/2023)	Inclusion of the Spanish version of recruitment flyers for the administrative supplement.
IRB amendments 31 (2/17/2023)	Inclusion of a QR code on the English and Spanish versions of the supplement recruitment flyers for the community that links to a password-protected data collection form in REDCap, where interested individuals can enter their name, phone number, preferred language, and dementia caregiving status, so that they can be contacted by a staff member with more information about the study.
IRB amendments 32 (3/23/2023)	Addition of supplementary recruitment strategies including snowball recruitment and compensation of successful referrals
IRB amendments 36 (7/21/2023)	Include the following changes: • Inclusion of recruitment materials to be promoted through "The New Normal" • Increase the number of participants included in the qualitative protocol for the parent trial
IRB amendments 38 (8/31/2023)	This amendment is to reach out to participants who gave us permission to re-contact them for future research, and contact them with a flyer about the SCORE Study "Social care patient-reported Outcomes Study" which aims to develop meaningful and valid patient-reported outcome measures reflecting patients' experience of social care (PROMs for social care.) UChicago staff will NOT have active involvement

	with potential participants in the SIREN SCORE study at UCSF. Any inquiries about that study will be directed to the UCSF study staff whose contact information is provided on the flyer.
IRB amendments 40 (9/15/2023)	This amendment proposes the use of UChicago's Globus for secure file transfer.
IRB amendments 43 (11/30/2023)	This amendment serves to remove the designation of waiver of consent for this study. There is no waiver of consent associated with this study.