# Development of Culturally Sensitive and Patient-Centered Feedback for Alzheimer's Dementia Risk Disclosure

**NCT04309500**

**IRB Approval Date: January 26, 2022**

**Uploaded: 09/29/2022**

# SHARE(D) Study Protocol

**FULL STUDY TITLE:** **Development of Culturally-Sensitive and Patient-Centered Feedback for Alzheimer's Dementia Risk Disclosure**

**SHORT STUDY TITLE:** **The SHARE(D) Project: Sharing Alzheimer's Risk Estimates with Diverse Populations**

Protocol Amendment Number: 01 Original
Authors: *ARF*
Issue Date: 01 May 2019

02 Amendment
Authors: *ARF*
Issue Date: 20 November 2019

03 Amendment
Authors: *ARF*
Issue Date: 8 May 2020

04 Amendment
Authors: *ARF*
Issue Date: 12 August 2020

05 Amendment per IRBMED requested changes
Authors: *ARF*
Issue Date: 02 November 2020

06 Amendment
Authors: *ARF*
Issue Date: 10 November 2021

07 Amendment
Authors: ARF
Issue Date: 3 January 2022

Secondary Registry Numbers: UMIRB: IRBMED HUM00178869 (Stage I)
UMIRB: IRBMED TBD (Stage II)
Clinical Trials: NCT04309500 (Stage II)

Sources of Support: NIH/NIA R03 AG063222-01

Contact for Public/Scientific Queries: *ARF* [rahmanam@med.umich.edu]

Trial Sponsor: NIH/NIA

Address: Neuropsychology Section, Department of Psychiatry
2101 Commonwealth Blvd., Suite C
Ann Arbor, MI 48105
(734) 936-3180

Public Title: The SHARE(D) Project: Sharing Alzheimer's Risk Estimates with Diverse Populations

Countries of Recruitment: United States of America

Problem(s) Studied: Dementia – Alzheimer's Type (DAT) risk disclosure

| | |
|---|---|
| Intervention: | Stage I: Observational study (needs assessment); no intervention<br><br>Stage II: Behavioral Intervention: personalized Dementia-Alzheimer's type risk disclosure feedback |
| Key Inclusion Criteria: | Stage I: Human volunteers who are consensus diagnosed as cognitively healthy or with Mild Cognitive Impairment (MCI) with ability to consent; ≥ 65 years of age; first-language English; identified co-participant who is cognitively healthy, has known the participant for ≥ 5 years, and has at least weekly phone/in-person contact with the participant<br><br>Stage II: Same as Phase I, plus participants must have a negative baseline screen for clinically significant depression or anxiety on standardized measures and already be followed by a medical provider. |
| Key Exclusion Criteria: | Stage I & II: Significant uncorrected sensory impairment, severe neurologic or psychiatric diagnosis; consensus diagnosis of dementia |
| Study Type: | Interventional, single-group design |
| Primary purpose: | Stage I: Complete assessment of needs, preferences, and rationale regarding DAT risk disclosure in participants and their family members of diverse racial-ethnic backgrounds<br><br>Stage II: Develop and pilot personalized DAT risk disclosure protocols with participants and family members of diverse racial-ethnic backgrounds; investigate initial outcomes including comprehension/recall of results, satisfaction, and psychological reactions immediately following risk disclosure and at 1- and 6-weeks following risk disclosure |
| Phase: | I/II (Stage II Behavioral Intervention Study) |
| Date of First Enrollment: | Stage I: 10/22/19<br>Stage II: 10/1/20 (anticipated) |
| Target Sample Size: | Stage I: up to 120 (60 participant/co-participant dyads)<br>Stage II: 20 (10 participant/co-participant dyads) |
| Recruitment Status: | Stage I: Currently recruiting<br>Stage II: Currently recruiting |
| Primary Outcomes: | Stage I:<br>(a) Interest in different levels of risk disclosure feedback<br>(b) Preferences for different levels of risk disclosure feedback<br>(c) Perceived personal threat of DAT<br>(d) Perceived benefits of/rationale for risk disclosure<br>(e) Perceived barriers to risk disclosure<br>(f) Importance of risk disclosure feedback elements<br><br>Stage II:<br>(a) Comprehension/recall of personal risk information<br>(b) Psychological distress (mood, anxiety, and event-specific distress)<br>(c) Satisfaction with feedback process (exploratory) |

**SECTION 1: Roles & Responsibilities - Contributorship**

**Annalise Rahman-Filipiak, Ph.D. (*ARF*) – Principal Investigator**

**Affiliations:** **University of Michigan, Department of Psychiatry**
**Contact:** **rahmanam@med.umich.edu**
**Roles & Responsibilities:**

Design conception and initiation
Preparation of protocol and revisions
Managing correspondence with clinical trials office
Publication of study reports
Preparation of manuscripts
Recruitment and screening of patients
Data collection
Data entry, verification
Statistical Analyses
Regulatory and compliance management/adverse event reporting

**Benjamin Hampstead, Ph.D., ABPP-CN (*BMH)* – Co-Investigator**

**Affiliations:** **VA Ann Arbor Healthcare Systems, Mental Health Service**
**University of Michigan, Department of Psychiatry**
**Contact:** **bhampste@med.umich.edu**
**Roles & Responsibilities:**

Design conception and initiation
Mentorship

**J. Scott Roberts, Ph.D. (*JSR*) – Co-Investigator**

**Affiliations:** **University of Michigan, School of Public Health**
**Contact:** **jscottr@umich.edu**
**Roles & Responsibilities:**

Design conception and initiation
Mentorship

**Mary Lesniak, B.S. (ML) – Research Associate**

**Affiliations**: **University of Michigan, Department of Psychiatry**
**Contact:** **marles@umich.edu**
**Roles & Responsibilities:**

Preparation of protocol and revisions
Managing correspondence with clinical trials office
Preparation of study reports
Preparation of manuscripts
Recruitment and screening of patients
Data collection
Data entry, verification
Statistical Analyses
Regulatory and compliance management/adverse event reporting

*ARF* conceived of the study, developed and refined the study protocol, and is responsible for study implementation, including data collection, entry, and management under the mentorship and direction of *BMH* and *JSR* and with assistance from ML*. BMH* will assist with development and psychometric evaluation of measures used in the study, as well as clinical characterization of participants. *JSR* will assist with development and adaptation of measures from the REVEAL study to the SHARE(D) Project, as well as integration of needs assessment information into Stage II feedback protocols. *ARF* will complete statistical analysis, prepare manuscripts and presentations, with editing input from *BMH* and *JSR*. *ARF* will manage the clinical trial registry, preparation of institutional review board materials, administrative duties, and auditing/reporting requirements for the various agencies associated with the study.

**Roles & Responsibilities – Sponsor(s)/Funder(s)**

This project was supported via an R03 award granted to ARF from the NIH/NIA. The funding source had no role in the design, execution, analyses, or interpretation of the study, nor will it have a role in the decision to submit results.

## SECTION 2: INTRODUCTION

### SECTION 2.1: Background & Rationale

As of 2018, an estimated 5.5 million Americans have late-onset dementia due to Alzheimer's disease (DAT), and another 11.6 million have Mild Cognitive Impairment (MCI)[1], with proportionately higher prevalence per capita in ethnic minorities[1-2]. Improved knowledge of health and lifestyle contributions to DAT trajectories have made early detection and disclosure of DAT risk a priority for researchers and clinicians alike. In fact, early disclosure of elevated risk would save an estimated $172,000 per patient[3] and $8 trillion nationally[1] in healthcare costs via health behavior change and long-term planning. Given that African Americans incur significantly higher dementia-related costs than any other demographic[4], early DAT risk feedback could be proportionately more beneficial for this population, yet occurs less frequently in these communities[5].

Literature suggests that between 50-90% of individuals are interested in receiving dementia risk feedback[6,7]. In this context, there is a gap between the rapid advancement of techniques to quantify DAT risk[8] and development of empirically-supported methods to communicate this information to patients. A survey of the current AD risk disclosure literature revealed three critical knowledge gaps that build on our experience and inform the aims of this project.

**Need 1: Feedback regarding personal DAT risk is undermined by a lack of knowledge about the type(s) of information patients and their families want to receive - and why.** With the acceptance of the Amyloid-Tau-Neurodegeneration (A/T/N) model of Alzheimer's disease (AD)[9], there is increased focus on how biomarkers may increase risk for the phenotypic presentation of AD (i.e., DAT). Advanced methods of detecting AD-related changes in genes, brain structure and function, biomarker burden, and cognition have expanded our ability to predict an individual's risk for future decline[8,10-11]. However, little is known about whether patients would prefer to receive this more advanced (but experimental) information, as opposed to clinically-available (i.e., familiar) information. Most published studies in this area disclose DAT risk based on data gathered in clinical visits, such as family and personal medical history, subjective symptoms, and cognitive screening or neuropsychological testing. These studies have found that the vast majority of participants are interested in this feedback for long-term planning purposes[6,7].

Among biological risk factors, apolipoprotein episilon-4 (APOe4) allelic status[8,12] and positron emission tomography (PET) based amyloid burden[5,7,13-15] have received the most attention in the risk disclosure literature, albeit in cognitively healthy individuals primarily. These studies indicate that patients' desire for risk information is high but varies as a function of how much they know about DAT and AD biomarkers[16-18]. There exists great variability in reasons for requesting risk disclosure, ranging from basic curiosity to family planning[6-7,16-17]. Additionally, post-disclosure, even cognitively healthy participants have difficulty understanding feedback language (e.g., interpreting a "positive" biomarker as a "good" outcome[12]). Comparing across these single-source risk disclosure studies may be misleading, however, as none have directly compared what type of feedback patients would want to receive given a menu of all possible risk factors. In the absence of such a study, we suggest that clinical, genetic, and biomarker feedback is likely to be processed differently by patients. Genotype and family history are static, representing non-modifiable susceptibility. Cognitive test scores represent concrete measurements of changes that may already be apparent to patients and caregivers. In contrast, biomarkers are unfamiliar measurements of the individual's underlying level of AD pathology and are probabilistic rather than deterministic for a diagnosis of DAT. In light of these differences, the need to compare patient preferences for different sources of risk feedback is critical.

**Advancement 1: This study will conduct a needs assessment of diverse patients' and informants' risk disclosure preferences.** Aim 1 will evaluate patient and informant preferences for different sources of information used to determine DAT risk (see Table 1). Our inclusion of both patients and informants is especially relevant given our[19] and others'[20-22] work showing discrepancies in self- and informant-rated cognitive deficits. The proposed project will include a sample that is racially diverse (see Advancement 2), unlike prior studies that have focused primarily on White older adults. Furthermore, the sample will include both cognitively symptomatic (MCI) and intact older adults, rather than focusing on healthy populations alone. Results will describe the unique disclosure needs of African-American and White participants and their families.

**Need 2:** To date, most feedback protocols have taken a one-size fits all approach to DAT risk disclosure, ignoring known strengths and challenges faced by racial-ethnic minority populations. Not only must we understand the type and amount of information patients want during DAT risk disclosure (Advancement 1), but also how and why racial groups differ in their preferences. Discussions of racial disparities in DAT prevalence tend to focus only on differences in biological risk factors (e.g., genetics, cardiovascular health), ignoring the complex epigenetic interplay between biology and environment. Sociocultural and socioeconomic differences (i.e., early educational differences, bias in cognitive testing, delayed/inadequate health care services, cultural stigma surrounding diagnosis) account for significant variance in DAT diagnosis and treatment in minority populations, even after controlling for biological risk factors[2]. One such sociocultural difference may be the extent to which African American individuals request, have access to, and utilize DAT risk disclosure in early stages of the AD course. The sparse literature on the topic indicates that African Americans may be less interested in DAT risk feedback[23], yet reasons why are unknown. Greater understanding of African-American perspectives on risk disclosure will facilitate better communication and treatment, which in turn may alleviate the larger health disparities faced by this population.

**Table 1. Sources of DAT Risk Information Used in Feedback**

| |
|---|
| Level 1: No information provided (no feedback) |
| Level 2: Standard Clinical Information<br>• Reported Family History<br>• Subjective Cognitive Complaints (Self + Informant)<br>• Neurological Examination<br>• Neuropsychological Evaluation |
| Level 3: Neurodegeneration<br>• Structural MRI (3D T1/T2)<br>• FLAIR |
| Level 4: Genetic Information<br>• APO-E ε4 allelic status |
| Level 5: A/T Biomarker Information<br>• Amyloid PET (PiB)<br>• Tau PET ($^{18}$F Flortaucipir) |

**Advancement 2: The proposed needs assessment will investigate recipient-specific factors that influence DAT risk disclosure preferences in African-American and White participants and informants.** The few studies examining risk disclosure preferences in non-White populations[16-17,23-24] suggest that African-American individuals are more likely than White counterparts to decline feedback about DAT risk. More nuanced preferences about amount, type, and reasons for feedback in African-American versus White participants remain unknown. Similarly, the *reasons* behind this discrepancy have never been directly studied. For White participants, personal characteristics such as general or dementia-specific anxiety[6,18,24,25] and knowledge of AD biomarkers, symptoms, course, treatments[24,25] influence preferences for type and amount of feedback. These same factors – perceived vulnerability to DAT and DAT knowledge – appear to be lower in African-American individuals[24] but it is unclear if these group differences drive the decreased desire for DAT risk disclosure. We will directly evaluate patient characteristics that contribute to feedback preferences in a sample of African-American and White participants using an application of the Health Belief Model (HBM)[26]. More specifically, we will study how perceived vulnerability to DAT, perceived seriousness of DAT, perceived benefits of DAT risk disclosure, and perceived barriers to effectively using DAT risk information shape feedback preferences.

**Need 3: Our ability to effectively communicate DAT risk to participants and informants is limited by a lack of empirically-supported methods that integrate multiple risk factors.** Existing studies have often taken a "siloed" approach that fails to integrate the multiple sources of DAT risk. Several studies have analyzed pre-disclosure desire to learn about a specific risk factor[6,7,16-18], or reactions to real[12] or simulated[12] single-source risk disclosure. Many provide guidelines for single risk-factor feedback[7,12,27-30], though these suggestions are abstract and drawn from investigations of mostly White, highly educated participants. To date, no study has developed a feedback protocol that integrates multiple DAT risk factors (clinical, genetic, neuroimaging, and biomarker) and can be adapted to meet the needs of racially diverse patients.

**Advancement 3: This study will produce preliminary person-centered, culturally-informed protocols for communicating multi-factorial DAT risk, with specific adaptations in style or content based on patient-specific factors.** Aim 2 will integrate the results of the existing literature and the Aim 1 needs assessment into practical feedback protocols, with initial piloting. Our approach not only attempts to replicate prior findings on psychological reactions to risk disclosure, but also extends the literature (a) by assessing protocol effectiveness in terms of patient and informant comprehension, recall, and satisfaction (exploratory), and (b) by comparing African American and White older adults' reactions to feedback. The project will result in a

preliminary series of standardized protocols with specified adaptations (e.g., additional psychoeducation modules or language changes for impaired individuals) that can be integrated based on individual needs.

## SECTION 2.2: Objectives & Hypotheses of the pilot study

**Objective 1: to investigate the preferences and needs of racially diverse participants, and their respective informants, in regards to receiving feedback about their risk for DAT.** We will leverage the robust Michigan Alzheimer's Disease Research Center (MADRC) infrastructure to recruit older adults who are asymptomatic (i.e., cognitively intact) or in the early stage of disease progression (Mild Cognitive Impairment [MCI]), half of whom will be African American. Utilizing mixed qualitative and quantitative methods in the Stage I Needs Assessment, we will systematically evaluate three questions:

**1.1 Do African-American and White participants or co-participants differ in their interest in receiving certain types of DAT risk information?** The study will evaluate group differences in participant and co-participant interest in and actual preference for feedback at five levels: (1) no information about AD risk, or risk information based on (2) standard clinical measures, (3) genetic information, (4) quantitative structural neuroimaging, (5) amyloid and tau PET. Exploratory analyses will assess whether group differences also exist based on clinical research diagnosis (normal vs. MCI), and whether participants and their co-participants agree.

**1.2 Do African-American and White participants or co-participants differ in their perspectives on/rationale for certain types of DAT risk feedback?** This study will assess whether African-American and White participants and co-participants identify different primary reasons for risk disclosure (i.e., basic curiosity, emotional reason, financial planning, medical planning, legal planning, social/family planning, or other). Exploratory analyses will assess whether group differences also exist based on clinical research diagnosis (normal vs. MCI), and whether participants and their co-participants agree.

**1.3 Which characteristics predict risk disclosure interest in African-American vs. White participants and co-participants?** This study will evaluate whether African-American and White participants and co-participants differ in their perceived threat of DAT, perceived benefits of risk disclosure, and perceived barriers to using risk information. We will also determine whether different factors (including personal demographic characteristics and the aforementioned perceived threat, benefits, and barriers) predict risk disclosure interest in different groups. Exploratory analyses will assess whether group differences also exist based on clinical research diagnosis (normal vs. MCI), and whether participants and their co-participants agree.

**1.4 Which components of feedback do African-American and White participants or co-participants see as most important?** This study will evaluate whether African-American and White participants and co-participants differ in their perspectives on the relative importance of different component of risk disclosure (e.g., educational materials, visual aids, follow-up coordination with providers). Exploratory analyses will assess whether group differences also exist based on clinical research diagnosis (normal vs. MCI), and whether participants and their co-participants agree.

**Objective 2: to develop person-centered, culturally-informed protocols for disclosure of different combinations of Alzheimer's dementia risk factors.** Building on the results of Objective 1, we will produce protocols for communication of DAT risk, with attention to specific adaptations in style or content based on the above noted individual factors. In particular, protocols will specify (a) effective methods of communicating risk conferred by each data source, (b) information designed for patients versus informants, (c) psychoeducation needs, and (d) resource/support needs. Through piloting in Stage II, we will evaluate three outcomes in both participants (those receiving the feedback) and co-participants:

**2.1 Comprehension and recall of personal risk disclosure information**

**2.2 Psychological reactions to personal risk disclosure information**

**2.3 Satisfaction with the feedback process (exploratory)**

**SECTION 2.3: Trial Design**

The Stage I Needs Assessment is an observational study with no intervention or randomization. Stage II will involve a clinical trial, with the risk disclosure feedback serving as the behavioral intervention. The study will use a single-group design. All 10 participant-co-participant dyads (5 Non-Hispanic African-American, 5 Non-Hispanic White) will receive feedback about the participant's DAT risk. Outcomes will be measured immediately following feedback and at 1- and 6-weeks following risk disclosure. For more information regarding design, see *Methods* section.

## SECTION 3: METHODS

## SECTION 3.1 Participants: Inclusion & Exclusion Criteria

### 3.1.1 Stage I

***Participants*** (those identified as the person who would hypothetically receive DAT risk feedback) will be recruited from the Michigan Alzheimer's Disease Research Center's University of Michigan Memory and Aging Project (UM-MAP), Testing High Definition transcranial Direct Current Stimulation (HD-tDCS) as Treatment of Mild Cognitive Impairment Project (STIM), or Dementia in African American Population Phenotyping from Potential Elevated Risk (DAPPER) project.

Participants will include up to 60 older adults, age 65+ years who have completed an initial evaluation as part of the University of Michigan Memory and Aging Project (UM-MAP), the Testing High Definition transcranial Direct Current Stimulation (HD-tDCS) as Treatment of Mild Cognitive Impairment (STIM) project, or as part of the Dementia in African American Population Phenotyping from Potential Elevated Risk (DAPPER) project. Consistent with the diversity-related goals of this study, 25 of these participants will be self-reported Non-Hispanic African-American, and 25 will be self-reported Non-Hispanic White. As exploratory analyses will look at the role of cognitive impairment, approximately 50% of the sample will be consensus-diagnosed as either cognitive healthy or with Mild Cognitive Impairment (MCI; single- or –multiple domain, amnestic or non-amnestic forms) through their participation in UM-MAP, STIM, or DAPPER. Exclusion criteria include current or historical neurologic disorder (e.g., Alzheimer's dementia or other neurodegenerative dementia, Parkinson's disease, seizure disorder, tumor, multiple sclerosis) or neurologic injury (e.g., significant stroke or moderate-severe head injury, defined by loss of consciousness > 5 minutes, presence of significant post-traumatic amnesia, or the need for extended hospitalization or intervention). Participants with motor symptoms indicative of a neurodegenerative etiology other than Alzheimer's disease will also be excluded. Participants with severe mental illness (i.e., bipolar disorder, thought disorder, psychosis) or anyone deemed to meet criteria for current substance use disorder will be ineligible for participation in this study.

***Co-Participants*** (those who are currently serving as a caregiver to the participant, or would hypothetically serve in this role should the need arise) include up to 60 adults, age 18+ years. Co-participants must be cognitively healthy, as defined by consensus diagnosis if they are also enrolled in UM-MAP, STIM, or DAPPER, by neuropsychological evaluation within 12 months of study participation, or by cognitive screening (MoCA) prior to study enrollment. As it is critical that co-participants can reliably and validly report on their perspectives or thoughts about their respective participants, co-participants must have known the participant for ≥5 years and have at least weekly phone or in-person contact with the participant.

### 3.1.2 Stage II

***Participants*** (those identified as the person to receive DAT risk feedback) will include a subset of 10 older adults (65+) drawn from the Stage I Needs Assessment, all of whom have available neuropsychological performance information, magnetic resonance imaging (structural) information, positron emission tomography (PET) amyloid and/or tau information, and apolipoprotein e genetic information already collected as part of UM-MAP, STIM, or DAPPER. Participants will meet all of the inclusion/exclusion criteria applicable for Stage I. Additionally, participants must be negative for mood or anxiety diagnosis and negative on mood measures prior to enrollment in Stage II. Participants must also be currently followed by a medical provider (primary care physician, geriatrician, family doctor). These additional inclusion criteria minimize the likelihood of significant psychological risks following feedback, and facilitate clinical coordination of care between study staff and clinical providers in the event that significant psychological distress does occur.

***Co-Participants*** (those who are currently serving as a caregiver to the participant, or would hypothetically serve in this role should the need arise) include 10 adults, age 18+ years. Similarly, participants must meet criteria from the Stage I Needs Assessment. Additionally, if the participant has

an active legally authorized representative (LAR) or power of attorney (POA) for medical decisions and/or research, that individual must serve in the role of co-participant, and must provide documentation of this legal designation prior to enrollment of the dyad in the study. If the participant does not have an enacted LAR/POA, any individual meeting the above criteria can serve as the co-participant.

All study-related activities will occur at the University of Michigan through virtual visits.

## SECTION 3.2 Recruitment Strategy

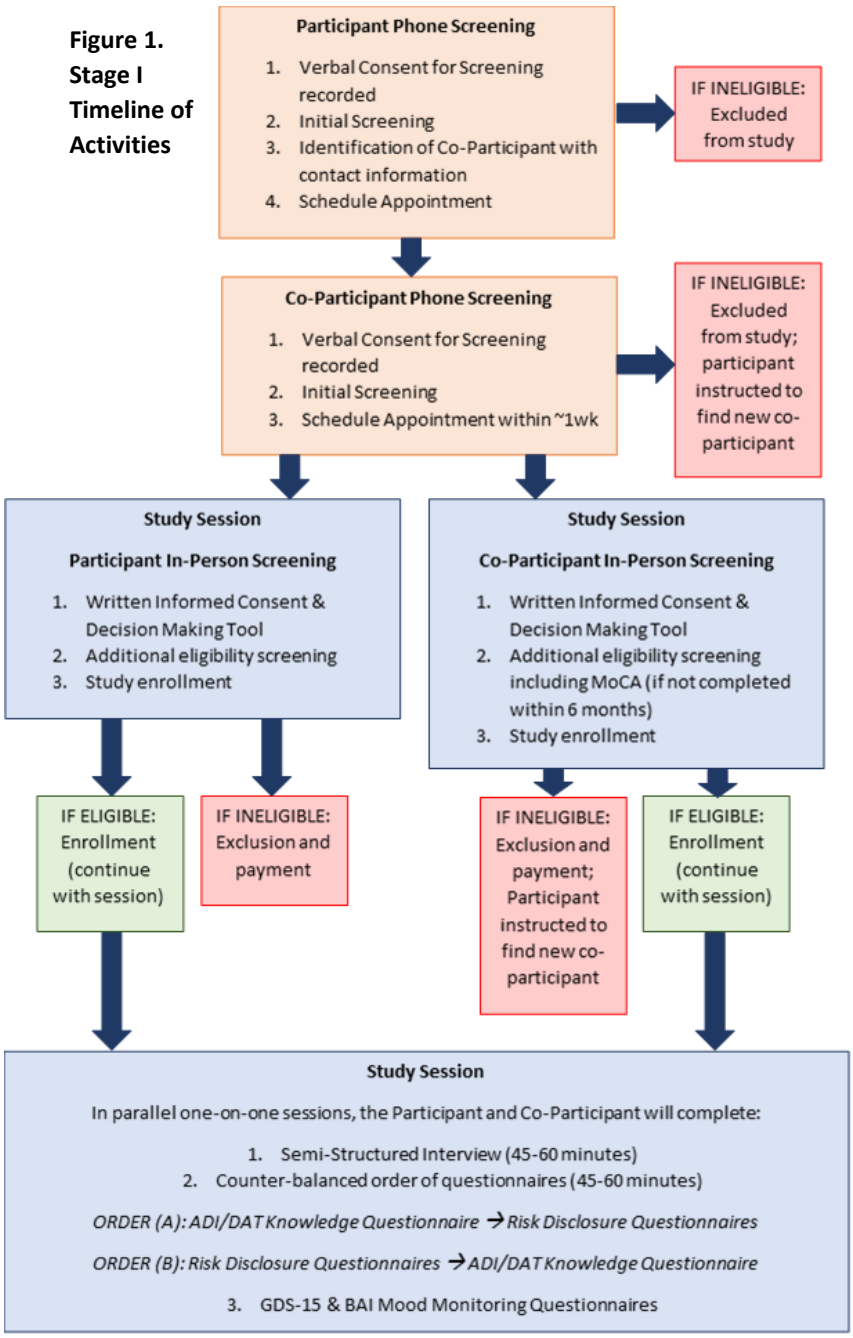
**3.2.1 Stage I:** Participants will be recruited from UM-MAP, STIM, or DAPPER. The MADC recruits participants from several sources including the MADC Memory Disorders clinic, community screening events, and external referrals. UM-MAP, STIM, or DAPPER participants interested in research are maintained in an IRB-approved database, which is available by request to the PI and her study team.

**3.2.2 Stage II:** Participants will be recruited to Stage II through invitation, only. The study team will review dyads who complete the Stage I Needs Assessment, screen these cases for any interim changes that might impact eligibility of the participant or co-participant, and contact dyads to determine interest in engaging in the second stage of the study. Specifically, following Stage I, the study team will contact the parent studies (UM-MAP, STIM, and DAPPER) via the MADRC 'cohort discovery' data request pipeline to confirm who among the list of interested Stage I participants have (a) annual research evaluation information with resulting cognitively normal or mild cognitive impairment diagnosis, and (b) at least one of the following: PET amyloid and tau biomarker data, apolipoprotein E genotype, or Neuroquant volumetric neuroimaging from MRI. Of note, none of these biomarker data will actually be accessed by the SHARE(D) research team for recruitment; the actual biomarker and personal health data will be requested only following informed consent from the participant and co-participant.

## SECTION 3.3 Procedures

**3.3.1 Stage I** – for a visual timeline of Stage I Activities, see Figure 1.

**Figure 1. Stage I Timeline of Activities**




**Session Description:**

After telephone screening for eligibility, participants will be scheduled for a study session (ideally in parallel) within approximately one week as availability allows. This session will be 90-to-120-minutes, one-on-one with a study team member.

In March 2020, the global Covid-19 pandemic resulted in research ramp-down and restrictions on in-person research visits. To protect the health of our participants, particularly given their vulnerable status as older adults, we determined that it would be best not to continue in-person research visits, and to instead adapt this protocol to allow for virtual visits. Therefore, during telephone screening, participants will be offered the opportunity to complete the Stage I session as a video or phone visit. Interested participants will be asked whether they have adequate access to and familiarity with a laptop, tablet, or computer to engage in a video visit session in which they will complete questionnaires and interviews using video-conferencing software. Participants who do not have access to this technology or do not feel comfortable completing the visit over video will be offered the opportunity to complete the session over the phone. Those that decline phone or video visit, but remain interested in the study will be deferred for scheduling until a time that it is deemed safe by research administration for participants to engage in in-person research.

In-Person Sessions: At the initiation of the session, participants/co-participants will complete written informed consent and the decision-making tool to ensure that they are cognitively capable of doing so. Additional screening criteria will then be reviewed. Co-participants without recent neuropsychological or cognitive evaluation (within 6 months) will also be screened using the MoCA.

Video Conferencing Sessions: Participants and Co-Participants who are interested in engaging in a video visit will be asked about their access to and comfort with technology for the session prior to scheduling. Participants and Co-Participants must utilize a desktop or laptop computer, or a tablet with a screen at least 9.7 inches in diagonal width to ensure that they are able to view the questions completely. Additionally, participants/co-participants must have access to a stable, secure internet connection (not public wi-fi) and a quiet, private space where they will be uninterrupted for the duration

of the 2-hour appointment. Participants and Co-Participants who meet the above criteria will be sent separate links to engage in a secure video conference session through the BlueJeans or Zoom for Health applications. Both applications are free, HIPAA-compliant services.

Phone Conferencing Sessions: Participants/co-participants who are interested in engaging in a virtual visit but do not have access to the required technology or otherwise feel uncomfortable with a video visit will be offered the opportunity to complete the session via phone.

> Informed Consent for Virtual Visits: The informed consent document will be emailed to participants and co-participants at the time of scheduling, to provide the recipient enough time to review the document. Prior to other study activities, a study team member will set up a phone call to review the consent paperwork together. At this phone appointment, a study team member will explain each section of the informed consent document, pausing to answer questions or clarify misunderstandings. In parallel with the procedures used in in-person sessions, the study team member will also use the Decision-Making Capacity Tool to ensure that the individual providing consent is able to fully understand the decision he/she is making prior to providing consent. After the informed consent document has been reviewed, eligible participants/co-participants will be asked to provide electronic signature on this form. This can be completed through two methods: (a) the patient can download, sign, scan, and email the form back to the study team member, who will additionally sign as witness and study representative, or (b) the Signnow platform will be used to provide electronic consent. SignNow is a secure platform offered through University of Michigan, which is HIPAA-compliant and approved by Health Information Technology Services (HITS). A copy of the form, with all signatures, will be emailed to the participant/co-participant.
>
> Co-Participant Screening for Virtual Visits: As noted above, all co-participants must be cognitively intact based on screening or recent evaluation. In lieu of in-person screening, co-participants will be asked to complete a brief phone or video screen (the Blind version of the Montreal Cognitive Assessment [MoCA]) after informed consent, but prior to other study activities. As with in-person visits, co-participants whose scores fall below the cutoff for impairment will be considered ineligible for study participation. Their respective participants will also be asked to delay scheduling of their virtual visit until they can identify another interested and eligible co-participant.

Ineligible participants or co-participants will be excluded, but paid for their time. Eligible participants and co-participants will be included in the research study, and will continue the session to complete questionnaires and a semi-structured interview. The semi-structured interview will be recorded, as the qualitative responses from participants/co-participants will be analyzed as secondary outcomes in th study. In-person sessions are recorded using a secure, HIPAA-compliant voice recorder, with all sessions transferred to a secure drive, password protected, and deleted from these recorders immediately after the session. Virtual visit interviews will be recorded using BlueJeans, Zoom for Health, or using the voice recorder with the phone call on speakerphone; similarly, these audio files will be de-identified, transferred to a secure drive, and password protected. Participants and co-participants will also complete a Beck Anxiety Inventory and Geriatric Depression Scale – 15 Item after these procedures, in order to monitor anxiety and mood (see Section 3.5.1 Monitoring). All in-person sessions will take place in the PI's (ARF) laboratory at the University of Michigan. All virtual sessions will be completed by study team members either at the Rahman laboratory, or in a secure, private location. Individuals will receive $20 compensation for their participation in the study, paid via check after the session.

***Conceptual Model.*** The conceptual model for understanding feedback preferences is adapted from the Health Belief Model[30], (Figure 1). The resulting model contains three domains: 1) Perceived Threat of AD (i.e., perceived vulnerability to and seriousness of an AD diagnosis); 2) Feedback Expectancies

(i.e., rationale for learning about risk, perceived barriers to learning about or dealing with risk information); and 3) Feedback Preferences (i.e., the type of risk disclosure desired).

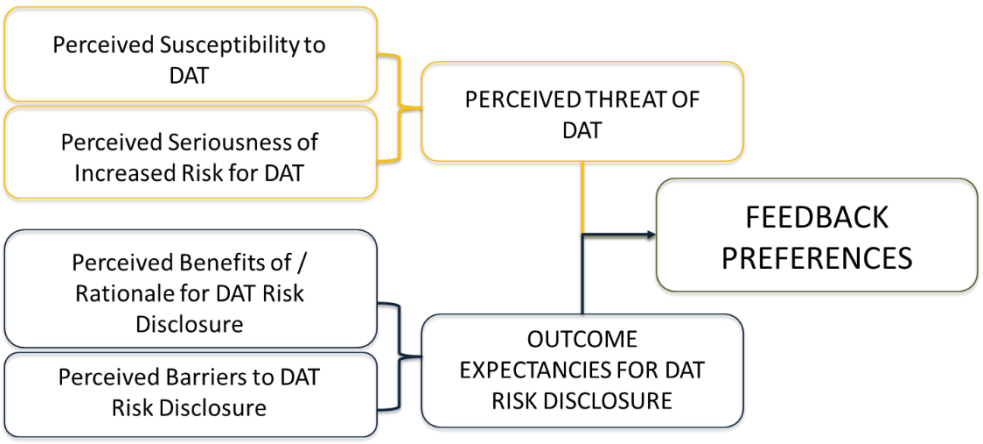



**Figure 2. Conceptual Model for Risk Disclosure Preferences**

**Primary Outcomes:**

***Questionnaires:*** In addition to the qualitative information gathered during the semi-structured interviews (see below), several formal questionnaires will be administered to provide quantitative information:

*HBM Components.* We have developed the Anticipatory Dementia Inventory (ADI), a 50-item Likert-style measure of DAT-specific worry based on the HBM. Items relate to perceived vulnerability to DAT, perceived seriousness of a diagnosis, and expectations about ability to deal with a diagnosis, with responses ranging from strongly disagree to strongly agree. This measure has previously been validated for use with racially diverse older adults through the PI's graduate work (paper in preparation).

*Knowledge of AD/DAT.* DAT knowledge will be measured through a multiple-choice quiz about DAT symptoms, course, causes, treatments, and risk factors. This quiz will be developed in Quarter 1 of the first funding year via monthly study-team meetings.

*Risk Disclosure Interest and Preferences.* In addition to the open-ended preference/rationale questions administered in the interview, we will utilize a questionnaire asking participants and co-participants to rate their level of interest in receiving feedback based on each risk factor (Table 3; e.g., "How interested are you in knowing about your/your family member's risk for Alzheimer's Dementia based on your genotype?"), on a continuous scale ranging from 1 (no interest) to 5 (very interested). Participants and co-participants will also use a checklist to state which information they would want to receive, selecting as many of the DAT risk information sources as desired (e.g., "Would you choose to receive feedback about your/your family member's risk for DAT based on genotype? Yes or No?")

*Risk Disclosure Rationale.* Participants will also be provided with a list of reasons for risk disclosure cited in prior literature and asked to rank the primary reason/purpose for risk disclosure.

*Importance of Risk Disclosure Elements.* Participants and co-participants will also complete a questionnaire asking them to rate the importance of different empirically supported elements of risk disclosure protocols cited in the published literature (e.g., How important do you think it is that educational materials are provided as part of your risk disclosure feedback?). Responses will be on a continuous scale from 1 (not at all important) to 5 (extremely important).

The order of questionnaires and interview questions will be counter-balanced to avoid potential reciprocal priming effects (e.g., discussing perceived vulnerability to DAT may influence feedback preferences).

For video sessions, the above questionnaires will be presented as Microsoft Powerpoint slide shows, with one question on each slide. The study team member will share his/her screen, and advance the slideshow, asking each questions clearly, to facilitate ease of comprehension for participants.

**Secondary Outcomes:**

***Semi-Structured Interviews:*** Although the quantitative methods above will be the primary source of information for the current project, we believe that the inclusion of qualitative methods will provide richness and context to the results. Furthermore, the inclusion of open-ended questions and qualitative coding methods will remove bias against minorities implicit in validated measures and allow for identification of risk disclosure concepts or perspectives not covered in these measures. The interviews will incorporate risk disclosure questions adapted from Co-Investigator Roberts' Risk Evaluation and Education in Alzheimer's Disease (REVEAL) Study, a successful multi-site trial of risk disclosure needs in older adults. We will also include novel questions that relate to the three domains of the HBM to study patient and co-participant characteristics that influence preferences. During the interview, they will have the opportunity to freely discuss what sources of DAT risk they would prefer to receive about themselves or, in the case of co-participants, about their loved ones, and how they plan to use that specific risk information. This open-ended approach will not limit responses to only presumed reasons for risk disclosure drawn from the past literature.

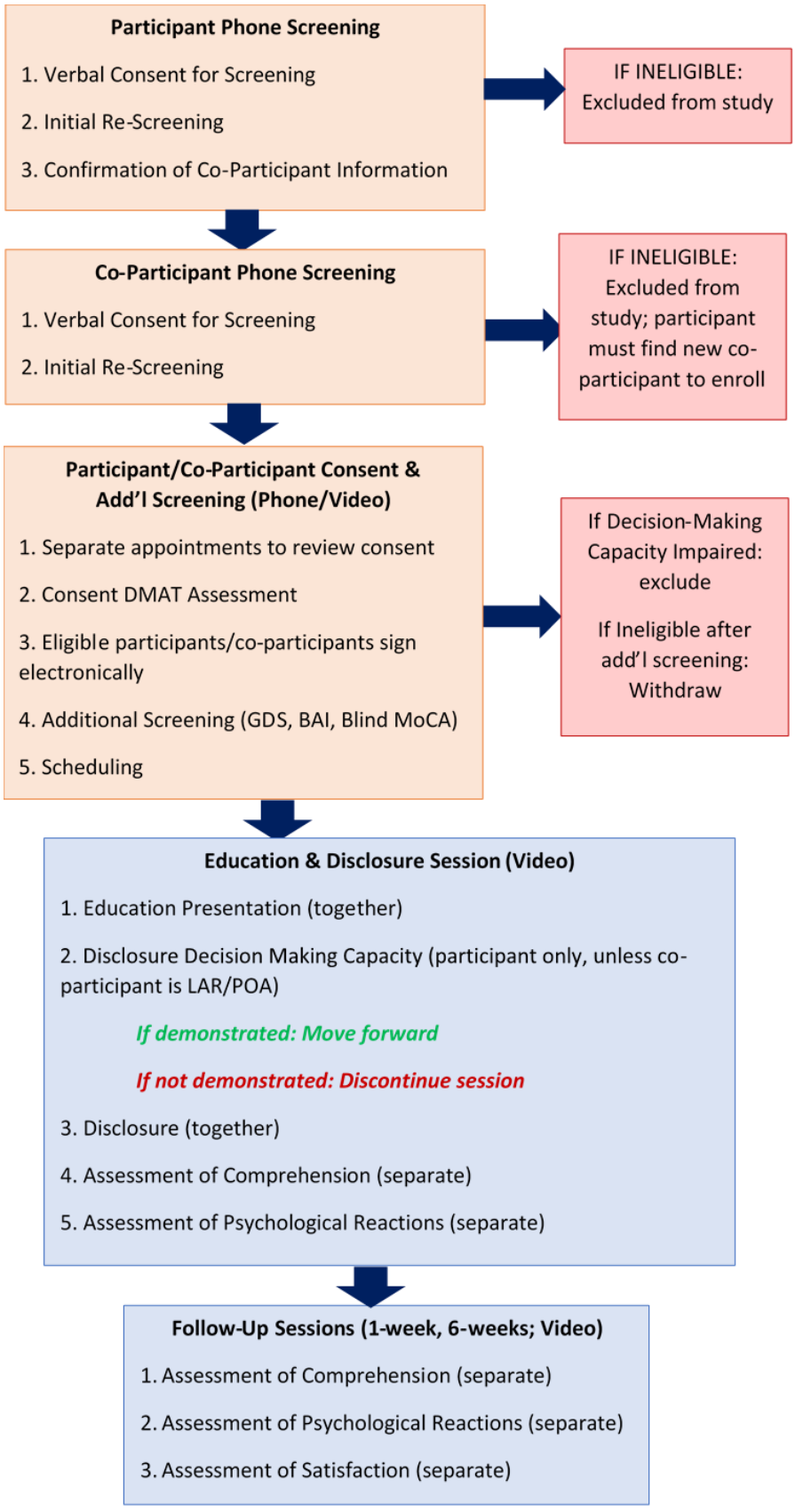
**3.3.2 Stage II -** for a visual timeline of Stage II Activities, see Figure 3.

Preliminary Screening: Following study team review of the participant's and co-participant's medical record to ensure no interim changes make either part ineligible, the study team will also access the participant's prior MADRC study involvement to determine whether they have adequate information for risk disclosure. Specifically, the study team will communicate with the MADRC UMMAP, STIM, and DAPPER teams to determine if the participant has (a) complete cognitive testing and research diagnosis and (b) recent (within 12 months) data for at least one additional biomarker, including MRI Neuroquant reports, PET amyloid and tau, or APOE genetic results. If the participant meets these criteria, the study team will send an email introducing the study (see 'SHARE(D)' Stage II Email Script') and begin contacting the participant via phone (see 'SHARE(D) Stage II Oral Script').

Informed Consent for Virtual Visits: The informed consent document will be emailed to participants and co-participants at the time of scheduling, to provide the recipient enough time to review the document. Prior to other study activities, a study team member will set up a phone call or video session to review the consent paperwork together. At this phone appointment, a study team member will explain each section of the informed consent document, pausing to answer questions or clarify misunderstandings. The study team member will also use the Consent Decision-Making Capacity Tool to ensure that the individual providing consent is able to fully understand the decision they are making prior to providing consent. After the informed consent document has been reviewed, eligible participants/co-participants will be asked to provide electronic signature on this form. This can be completed through two methods: (a) the patient can download, sign, scan, and email the form back to the study team member, who will additionally sign as witness and study representative, or (b) the Signnow platform will be used to provide electronic consent. SignNow is a secure platform offered through University of Michigan, which is HIPAA-compliant and approved by Health Information Technology Services (HITS). A copy of the form, with all signatures, will be emailed to the participant/co-participant. Only following receipt of this informed consent document will actual biomarker data be requested and received from the parent study teams (UMMAP, STIM, DAPPER) for integration into the disclosure protocols.

Additional Screening & Scheduling: Following receipt of the signed informed consent documents, both the participant and co-participant will be asked to complete the GDS-15 and BAI via phone or video (these can be conducted on the same call used to complete the consent documentation). Any individuals who score above the cutoffs for these measures will be ineligible to take part in the study, per eligibility criteria noted above. Additionally, all co-participants must be cognitively intact based on screening or recent evaluation. Co-participants who do not have recent screening or cognitive testing in their medical/research records will be asked to complete a brief phone or video screen (the Blind version of the Montreal Cognitive Assessment [MoCA]) on this call. Co-participants whose scores fall below the cutoff for impairment will be considered ineligible for study participation. Their respective

**Figure 3. SHARE(D) Stage II Timeline of Activities**




participants will also be asked to delay scheduling of their virtual visit until they can identify another interested and eligible co-participant. Once this secondary screening of the dyad has been completed, the study team will schedule all three sessions for each subject.

**Session Description:**

Education & Disclosure Session:

During this session, participants and co-participants will complete the follo.wing steps, summarized in Table 2:

1. Educational Module – participants and co-participants will be shown an interactive presentation covering the following topics:

a. Alzheimer's disease

b. Dementia-Alzheimer's Type

c. Available treatments for AD/DAT

d. Available biomarkers or indicators of DAT risk: how they are collected, what information is shared, and what the meaning of this information is relative to risk for AD and DAT

e. Risks of learning one's personal DAT biomarker status

f. Benefits of learning one's personal DAT biomarker status

This module will include multiple opportunities for either member of the dyad to ask questions.

2. Disclosure Preferences & Decision-Making Capacity Assessment – The educational module contains several 'checks for understanding' after each section to determine whether the participant fully demonstrates decision-making capacity for risk disclosure. As per the Disclosure Decision-Making Assessment Tool (DDMAT), the study team member will make notes about the participant's responses, provide corrections, clarifications, or prompts if needed, re-assess after this additional information has been provided, and then assess whether the ultimate

response demonstrates full understanding, appreciation, rationale, and communication (elements of decision-making capacity).

Of note, if the participant has a LAR/POA co-participant, that individual must demonstrate decision making capacity for the participant to receive risk disclosure, and agree with this decision. Regardless of whether the LAR/POA wants the participant to complete risk disclosure, the study team will not move forward with sharing the participant's risk information with either party unless assent is provided by the participant.

If the participant or designated LAR/POA does not demonstrate full decision making capacity, the study team will not move forward with risk disclosure, and the dyad's involvement in the study will be complete.

3. Risk Disclosure: the study team have developed a flexible disclosure protocol that provides written and graphic representations of the participant's health information and risk indicators. The protocol will be adapted using standardized instructions prior to the session, to personalize each protocol to the participant. Personalization will be based on demographic factors and geographic location of the patient's home (to ensure identified resources are close by and accessible), and research diagnosis and level of risk (to ensure that appropriate recommendations and resources are given). Additionally, we will adapt the protocol based on which of the following indicators the participant and/or LAR/POA requested after the education module (provided these are available from prior study participation):

- **DAT risk based on standard clinical procedures**: a review of cognitive strengths, weaknesses, and impairments relative to age-, sex- and/or race-matched normative data (using qualitative ranges from severely impaired to above average), in the context of the participant's medical and family history; disclosure of clinical research diagnosis (cognitively healthy or MCI); qualitative discussion about the increased risk for conversion to dementia based on an MCI diagnosis
- **AD risk based on apolipoprotein-e ε4 genotype**: disclosure of genotype (ε4 positive [homozygous/heterozygous] or negative); quantitative (percent or odds ratio) risk for Alzheimer's disease based on lifetime cumulative risk curves integrating race, gender, and genotype information (REVEAL study[31])
- **AD risk based on structural T1/T2/FLAIR magnetic resonance imaging (MRI)*:** quantitatively graded interpretation of atrophy (primarily in mesial temporal structures) based on age- and sex-matched normative comparisons drawn from the Neuroquant/Lesionquant program (Cortech labs: https://www.cortechslabs.com/products/neuroquant/); disclosure of any incidental findings; qualitative discussion regarding risk of underlying AD pathology based on imaging, and associated potential for DAT.
- **AD risk based on positron emission tomography (PET) amyloid and tau*:** qualitative interpretation (i.e., Elevated vs. Not Elevated) of the presence or absence of significant burden for either of the abnormal proteins; discussion that elevation on either/both proteins may indicate underlying AD pathology that may or may not develop into DAT.

*Given the lack of validated quantitative models of DAT risk conferred by these factors[8], only qualitative information regarding risk for developing or converting to DAT (the phenotypic presentation of AD) will be provided at this time. Particular attention will be given to differentiating the presence of AD pathology (i.e., positive amyloid and tau burden or indications of significant atrophy) from the actual development of symptoms (aMCI, DAT).

The disclosure protocol includes a summary of the above indicators; however, no summative or combined risk estimate is provided, as such an estimate is not empirically supported. Following this summary, the protocol includes general recommendations and next steps for healthy aging (e.g., taking care of physical and emotional health, staying cognitively and socially engaged) and a list of informational and support resources. As with the Education Module, the disclosure protocol will include multiple 'checks for understanding' after each section to ensure that information communicated is being comprehended accurately by the participant and co-participant.

4. Immediately following risk disclosure, the participant and co-participant will complete outcome measures and a brief psychological risk assessment with a clinical psychologist utilizing the recall assessment and impact of events scale documents. Both parties will also complete a checklist of requested resources or supports from the region- and service-specific list developed in SHARED Stage I. Participants and/or LAR/POAs will also be asked whether they would like a written summary of the information provided; if so, this report will be prepared after the visit and sent via mail to the participant or LAR/POA. No results will be uploaded in the participant's medical record; however, they are welcome to share the results with their medical providers independently.

| Table 2. Proposed Order & Components of Disclosure Sessions |
|---|
| 1. Initial Consent |
| 2. Education Module |
| 3. Assessment of Disclosure Preferences |
| 4. Assessment of Disclosure Decision-Making Capacity |
| 5. Personal Risk Disclosure<br>- Clinical Predictors of DAT Stage (Cognitive Testing, Research Diagnosis)<br>- Structural MRI-conferred AD Risk (qualitative)<br>- APOE-conferred AD Risk (quantitative)<br>- PET Amyloid and Tau-conferred AD risk (qualitative) |
| 6. Recommendations |
| 7. Participant & Caregiver Resources |
| 8. Risk Assessment & Follow-Up (as needed) |
| 9. Outcomes Assessment<br>- Comprehension<br>- Mood/Psychological<br>Satisfaction (exploratory) |

Follow-Up Sessions:

Outcome measures and psychologist risk assessment will also be repeated at 1-week and 6-weeks post-feedback. Participants and co-participants will also be encouraged to call the PI (ARF) or ML with any additional concerns or questions between these sessions. All sessions will take place in via phone or virtual visit. Participants and/or co-participants who complete some but not all sessions will receive pro-rated payment ($10 per session, $30 total), paid as a check after the sessions.

**Primary Outcomes**

**Comprehension and recall of personal risk disclosure information** will be measured as accuracy scores on a series questions about the patient's results and the meaning of different messages provided during feedback in regards to AD/DAT risk (i.e., "My Attention was [Normal/Impaired/Don't Know]"). The questionnaire will result in two scores: a Personal Information score and a Meaning of Information score (as it is possible that an individual may accurately remember his/her own information, but misinterpret it, or may understand the meaning of risk information, but incorrectly recall his/her own feedback).

**Psychological reactions to personal risk disclosure information** will be measured both in terms of general mood and anxiety, as well as feedback-specific distress.

*Depression:* Mood will be assessed using the self-administered Geriatric Depression Scale – Short Form (GDS-15)[32-33]. The GDS-15, a 15-item assessment of depressive symptoms, has been adapted to remove common depression symptoms often conflated with normal aging (i.e.,

somatic symptoms). It asks the participant to rate the presence of mood symptoms over the past two weeks.

*Anxiety:* The BAI[34], also validated for use with older adults[35] is a 21-item measure of the perceived severity ('not at all' to 'severely') at which the participant is experiencing anxiety symptoms over the past week.

*Feedback-Specific Distress*: We will utilize a revised version of the Impact of Genetic Testing for Alzheimer's Disease (IGT-AD) Scale, which itself is based on The Impact of Event Scale (IES) [36]. The scale will be specifically anchored to the 'life event' of receiving feedback; responses will be slightly modified to assess the impact of receiving any and all AD indicator results (not solely genetic information). The IES and IGT-AD have been utilized to measure test-related distress in previous risk disclosure studies[37-39], including REVEAL. Participants who have a negative score of 24 or more will be contacted by PI for follow-up with participant/co-participant.

**Exploratory Outcomes**

**Satisfaction with the feedback process** will be evaluated by determining how well participants' and informants' pre-test expectations are met. We will collect subjective, open-ended qualitative ratings of the utility of risk assessment using questions developed in the REVEAL study, such as "What was the overall impact that your risk information had on you?", "Would you recommend risk assessment for AD to your family or friends?", and "If you had it to do over again, would you choose to have risk assessment for AD?"

## SECTION 3.4 DATA MANAGEMENT & ANALYSIS

### 3.4.1 Data Management & Entry

Only IRB approved study personnel will have access to study documents/data. Signed consent paperwork and will be uploaded into the participant's medical record according to IRB standards and then stored in a binder, separate from all other study data. Electronic consent forms will be saved under password protection on the secure lab drive. Copies will be printed and stored in the aforementioned binder, away from all other study data. Data are kept in a locked file cabinet within a private office in an office suite (i.e., behind two locked doors). The participant's study ID number will be recorded on every paper page of the study documents.

The participants' biomarker data (beyond UM-MAP, STIM, or DAPPER diagnosis) will not be requested or stored as part of this study until completion of Stage I, to ensure no implicit bias in the manner in which needs assessment procedures are conducted based on participant risk. At this time, data from the 10 participants enrolled in the Stage II feedback piloting will be requested through the secure UM-MAP, STIM, or DAPPER Data Core avenue; de-identified participant information, coded with the UM-MAP, STIM, or DAPPER ID number, will be shared with the study team as a secure excel database. This file will reside on the University of Michigan secure server as a password protected file only accessible by approved study personnel.

### 3.4.2 Statistical Design

**Data Screening (Stage I & II)**

Prior to statistical analyses, data screening will be conducted. Initial steps will include a missing data analysis to determine randomness of missing data and range checks to assess for data quality. Additional screening for univariate and multivariate outliers, skewness and kurtosis will be conducted to inform needs for data transformation and statistical approach. Additionally, for Stage I data, we will compare outcomes in participants who completed in-person vs. video vs. phone visits to ensure that session modality did not impact interpretation of results.

## Statistical Approach

### 3.4.2.1 Stage I

**Primary Outcome 1.1 (Differences in risk disclosure interest and preferences):** To analyze the dichotomous yes/no interest outcomes, chi-squared analyses will be used to compare the proportion of African-American and White participants who endorse interest in receiving feedback at each level, for caregivers and patients separately. Given that there are five levels of risk disclosure feedback, five comparisons will be conducted; to account for the relatively small sample size, a conservative Bonferroni correction for multiple comparisons will be implemented ($\alpha = .05/5 = .01$). To analyze the Likert-style interest outcomes, either independent samples *t*-tests or Mann Whitney U tests will be used to compare mean interest level in African-American and White participants for each of the five risk disclosure levels, again using a Bonferroni correction. Further exploratory correlation analyses will determine agreement between caregiver and informant interest in African-American and White subgroups, separately.

**Primary Outcome 1.2 (Differences in risk disclosure rationale):** This study will assess whether African-American and White participants and co-participants identify different primary reasons for risk disclosure (i.e., basic curiosity, emotional reason, financial planning, medical planning, legal planning, social/family planning, or other), a Fisher's Exact test will be used, comparing frequency of reason endorsement. These analyses will be conducted for patients and informants separately; however, we will also explore agreement among dyad members.

**Primary Outcome 1.3 (Patient characteristics that influence preferences):** We will utilize a regression approach to determining patient characteristics and perspectives that shape level of interest. More specifically, we will create mixed linear models to quantify the fixed effects of four sets of variables (participant factors [demographics, baseline anxiety and depression, DAT knowledge], ADI Perceived threat of DAT, ADI Perceived benefits of this level of risk disclosure, ADI Perceived barriers to using this risk information), as well as the random effects attributable to the dyadic relationship. This approach will allow us to calculate the intra-class correlations representative of the effect of the dyadic relationship. Furthermore, given the likely effect of dyadic role ('patient' or informant) on perceived threat, perceived benefits, and perceived barriers, the interaction terms (e.g., role by threat, role by benefits, role by barriers) will also be included in the model. It is expected that the effect of the dyadic relationship will be significant; therefore, additional subgroup analyses examining predictors of risk disclosure interest in caregivers and patients *separately* will be conducted.

**Primary Outcome 1.4 (Differences in importance of risk disclosure components):** To analyze the Likert-style importance outcomes, either independent samples *t*-tests or Mann Whitney U tests will be used to compare mean interest level in African-American and White participants for each of the feedback components, again using a Bonferroni correction. Further exploratory correlation analyses will determine agreement between caregiver and informant interest in African-American and White subgroups, separately.

**Secondary Outcome (Qualitative Information from Semi-Structured Interviews):** In combination with the semi-structured interviews, we will therefore record and transcribe the narrative responses of patients and caregivers. After basic 'cleaning' of the data (removal of articles, non-content utterances, and additional identified 'stop' words), the text will be analyzed using R Statistical Software for most commonly used words or phrases by race. A Topic Modeling approach (akin to an exploratory factor analysis for text analysis) will be utilized to identify central themes (the 'factors') and associated terms or phrases (the 'items) by race.

### 3.4.2.2 Stage II

Given the nature of the study (pilot) and associated small sample size, descriptive statistics will be calculated, but no group comparisons will be completed.

**Primary Outcome 2.1 (Comprehension & Recall):** The Personal Information and Meaning of Information accuracy scores will be totaled for all participants. Mean, median, and standard deviation will be calculated. Exploratory analyses will evaluate trends in whether specific types of feedback information (e.g., neuroimaging vs. amyloid/tau burden) were better understood than others, and whether group differences exist (i.e., participants vs. co-participants, by race, by cognitive status).

**Primary Outcome 2.2 (Psychological Reactions):** Mean, median, and standard deviation of total scores on the GDS-15, BAI, and IES will be calculated. Change in total scores on the BAI and GDS-15 will be calculated by comparing Stage II scores with Stage I screening scores. Descriptive statistics will also be calculated for these change scores.

**Secondary Outcome 2.3 (Satisfaction):** Answers to the qualitative questions will be reviewed individually for suggestions and themes.

## SECTION 4: MONITORING

### 4.1 Risk Monitoring

#### 4.1.1 Stage I

It is not expected that discussing DAT risk disclosure preferences or needs will cause significant distress or exacerbation of mood symptoms; however, all participants in the Year 1 Needs Assessment will complete a brief measure of mood and anxiety, including the Geriatric Depression Scale – 15 Item version (GDS-15)[1] and the Beck Anxiety Inventory (BAI)[2] following participation in the semi-structured interview. A study team member will also be present in the room, or available virtually with the participant or co-participant for the entirety of the session to monitor distress. Each of the measures have empirically supported cut-off scores for determining clinically significant depression, anxiety, and event-related distress; individuals who endorse clinically significant depression or anxiety on the GDS-15 or BAI at the end of the session, or who appeared distressed during the session, will undergo a risk assessment and follow-up (see below). The study safety plan to determine need for risk assessment or intervention is included in Appendix A. Of note, for video or phone sessions, at the start of each session, the participant/co-participant will be asked to provide a call-back number in case he/she is disconnected from the technology, as well as current location; this information will not be stored in the participant's/co-participant's file, but will be used as a reference in case of emergency or safety issue.

#### 4.1.2 Stage II

It is possible that patient and informant participants may experience psychological distress as a result of hearing feedback about their current cognitive status and risk for developing DAT, particularly if the feedback indicates elevated risk. Although DAT risk disclosure has been found to be generally safe and well-tolerated in the literature[3,4], we will conduct careful screening of mood, anxiety, and event-related distress utilizing psychometrically sound evaluations. Specifically, each participant and co-participant will repeat the GDS-15 and BAI, and complete the Impact of Event Scale (IES)[5] at the Year 2 disclosure session as well as at 1- and 6-week follow-up. Any clinically significant elevation of scores on the GDS-15 or BAI, a score of 24 or higher on the IES, and/or other indication of new or exacerbated mood symptoms will result in a more advanced evaluation during the feedback and follow-up sessions (see Appendix A). In addition, participants and co-participants will be given contact information for the study team and encouraged to call ARF or ML with any concerns or needs related to their reactions to the disclosure session.

**4.2 Safety Assessment:** In the case of safety concerns in either Stage, a risk assessment and follow-up will be conducted. A licensed psychologist (*ARF*, *BMH*, or *JSR*), who will be available during all sessions either in-person or virtually, will evaluate the patient's or informant's severity of psychological symptoms and risk of self-harm. The clinician will take additional action as needed to either provide immediate transfer to emergency care (in the case of active threat), or facilitation of clinical care or supportive resources, per participant request

(in the absence of active threat). All participants will also be provided with emergency contact cards with local, 24/7 resources if emergent mood issues arise between sessions. A summary of the project suicide safety plan is included in Appendix A.

**4.3 Adverse Events Reporting:** Participant mood and distress will be carefully assessed for the 50 Year I dyads using the Geriatric Depression Scale – 15 Item version (GDS-5) and the Beck Anxiety Inventory (BAI). These measures, in addition to the Impact of Event Scale (IES), will be administered to the patient and informant dyads receiving pilot feedback in Year 2 to determine (a) whether changes in mood or distress occur, and (b) whether these changes are attributed to study participation. The GDS and BAI have empirically supported cut-off scores for determining clinically significant depression, anxiety; scores will therefore be used to define the nature of any events (unanticipated vs. anticipated, adverse vs. serious adverse) and relationship of these events to study participation (related vs. unrelated). The IES does not have a validated cutoff; however, we will treat a score of 24 or higher as warranting additional study team follow-up.

Information regarding non-serious adverse events (i.e., an elevation in mood or anxiety symptoms as a result of study participation) will be reported directly to the PI, who will compile and submit a report to independent Safety Officer (SO). The SO for this project is Joshua Grill (jgrill@hs.uci.edu).). Similarly, serious adverse events that are determined to be unrelated to study participation will be reported to the PI, recorded in a secure study database, and reported to the SO. These summary reports will be submitted to the SO on a quarterly basis.

Unanticipated adverse events or serious adverse events deemed related to study participation (i.e., acute exacerbation or onset of severe depression or anxiety, hospitalization for emotional reasons, and/or preparation for or engagement in self-injurious behavior as a result of risk disclosure results) will be reported immediately to the study PI. Consistent with Office of Human Research Protection, Institutional Review Board guidelines for the study's parent institution, and NIA standards, serious study-related adverse events resulting in life-threatening outcome or death will be reported to the SO and NIA program officer as soon as possible, and within 24 hours of study PI knowledge of the event. Other serious study-related adverse events and unanticipated adverse events will be reported as soon as possible, and within 48 hours of study PI knowledge of the event. The PI, in conjunction with the SO, will review the case and relevant study data to determine whether the study should be halted or how it may be altered to promote safety.

Additionally, the SO will meet at least twice per year via telephone or video conferencing to review adverse events and their outcomes, and to generate recommendations for study protocol alteration for improved safety (or termination of the study, if deemed necessary).

## SECTION 5: ETHICS AND DISSEMINATION

### 5.1 Research Ethics Approval & Protocol Amendments

All procedures detailed above fall within the parameters approved by the University of Michigan institutional review board. Any changes to these parameters or procedures will be proposed to and approved by the IRB through formal amendments prior to implementation.

### 5.2 Consent or Assent

All consent forms and others requiring authorized signatures will be approved by the University of Michigan IRB. A study team member will review the consent form for the specific Stage. The team member will pause after each section to solicit and answer questions. Comprehension of the procedures, risks, benefits, and other aspects of the study will be checked using a decision-making tool (a brief measure asking the participant to use his or her own words to review the contents of each section of the consent form before signing). These procedures will be followed regardless of whether the consent is completed in person or remotely via electronic consent.

### 5.3 Confidentiality

Information gathered from individuals contacted for initial screening is entered into a recruitment database file that is stored in the shared drive (accessible only to approved lab personnel) and password protected. This

centralized file will contain only the necessary information for contacting and determining eligibility and interest in the study, as well as assigned ID numbers for enrolled participants. For information regarding security and confidentiality of data from enrolled participants, see '**Data Management & Entry**'.

Participants will be made aware prior to enrollment in Stage I that they will not receive feedback regarding their risk for DAT as part of the Stage I study. As mentioned above, a copy of the consent form is uploaded into the participant's University of Michigan electronic medical record as a 'Research Document' to communicate current research participation to medical providers.

### 5.4 Declaration of Interests

None of the study investigators have any financial or competing interests to declare.

### 5.5 Access to Data

Study data will remain housed within the Rahman laboratory at the University of Michigan and will only be available to authorized study team members or members of oversight committees (e.g., IRB).

### 5.6 Ancillary and Post-Trial Care

As noted above, there are procedures in place to alert the principal investigator and take any needed action to deal with serious adverse events or harms that occur during the study session. As stated in the consent form, participants are instructed to seek immediate medical attention for any serious adverse events that arise after the study session, rather than waiting to contact or hear back from study personnel. Participants are instructed that any medical appointments that are attended after the study will be billed through the patient's regular insurance avenues.

As this study is examining a non-clinical sample of healthy older adults, and DAT biomarker risk evaluation is not considered part of the standard of care for older adults, there is no obligation to provide a waitlist control or delayed access to treatment to individuals assigned to the sham condition.

### 5.7 Dissemination Policy

A summary of results from the current study will be uploaded within one year of study completion to clinicaltrials.gov. At this time, there are no plans to grant public access to the participant level dataset or statistical coding used to analyze data. Findings will be communicated in the form of scientific presentations at national meetings and publications in peer-reviewed scientific journals. There are no restrictions on publications. Authorship will be based on study contribution, considering efforts towards study design, data collection and management, statistical analysis and interpretation, and production of presentations and manuscripts.

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**Appendix A.** Safety Plan

***Note: For virtual visits, study team members will verify participants'/co-participants' call-back number and address of their current location at the outset of each session.**

**Potential Suicidal Ideation** indicated by:

- Negative answer to GDS #11, 'Do you think it is wonderful to be alive now?'
- Score > 5 on GDS-15 and/or Score > 16 on BAI
- Participant direct or indirect reference to suicidal ideation, intention, plan, or preparatory behaviors (e.g., giving away personal items, stock-piling medications)
- Informant concerns about changes in the participant's thoughts/speech/ actions consistent with depression

## Risk Assessment & Safety Planning

1. Principal Investigator completes assessment of:
    a. Current/past suicidal thoughts
    b. Current/past suicidal intention or plans
    c. Current/past preparatory behaviors
    d. Current/past suicidal actions or attempts
    e. Access to means
    f. Current supports/barriers to carrying out suicidal thoughts/plans
    g. Current reasons for living
    h. Current/past treatment for psychiatric issues, including contact information if available
2. If needed, consultation with Co-Investigators
3. **Study team determines whether active threat to self (need for hospitalization).**

### Active Threat

**In-Person Visit Protocol:**

1. Ann Arbor
    **a.** Call UM Psychiatric Emergency Services: 734-936-5900
    **b.** Call Huron Valley Ambulance for transport: 734-994-4111
2. Detroit
    **a.** Call 9-1-1
3. **Clinician remains with participant until they leave in ambulance.**

**Virtual Visit Protocol:**

1. Confirm participant phone #/current location.
2. If participant has friend/family present to safely transport to emergency department, proceed.
3. If no friend/family member present, stay on call with participant & call UM PES Care Manager:
    a. 8am-5pm: Page #34832 with your location, means of contacting you (phone, IM)
    b. After-hours: Call local police or SW at 734-936-5900 (will assist with contacting police).

### No Active Threat

1. **Provide resources:**
    **a.** Depression brochure
    **b.** Ann Arbor - Mental Health Resources and Washtenaw County Senior Resources lists
    (OR)
    Detroit - Community Resources for Seniors list
2. **Complete Safety Plan with patient**
3. **Encourage participant to follow up with own health care provider.**