Mitigating Cancer-Related Cognitive Impairment in Older Adults with Cancer: Memory and Attention Adaptation Training-Geriatrics

(MAAT-G) Phase I

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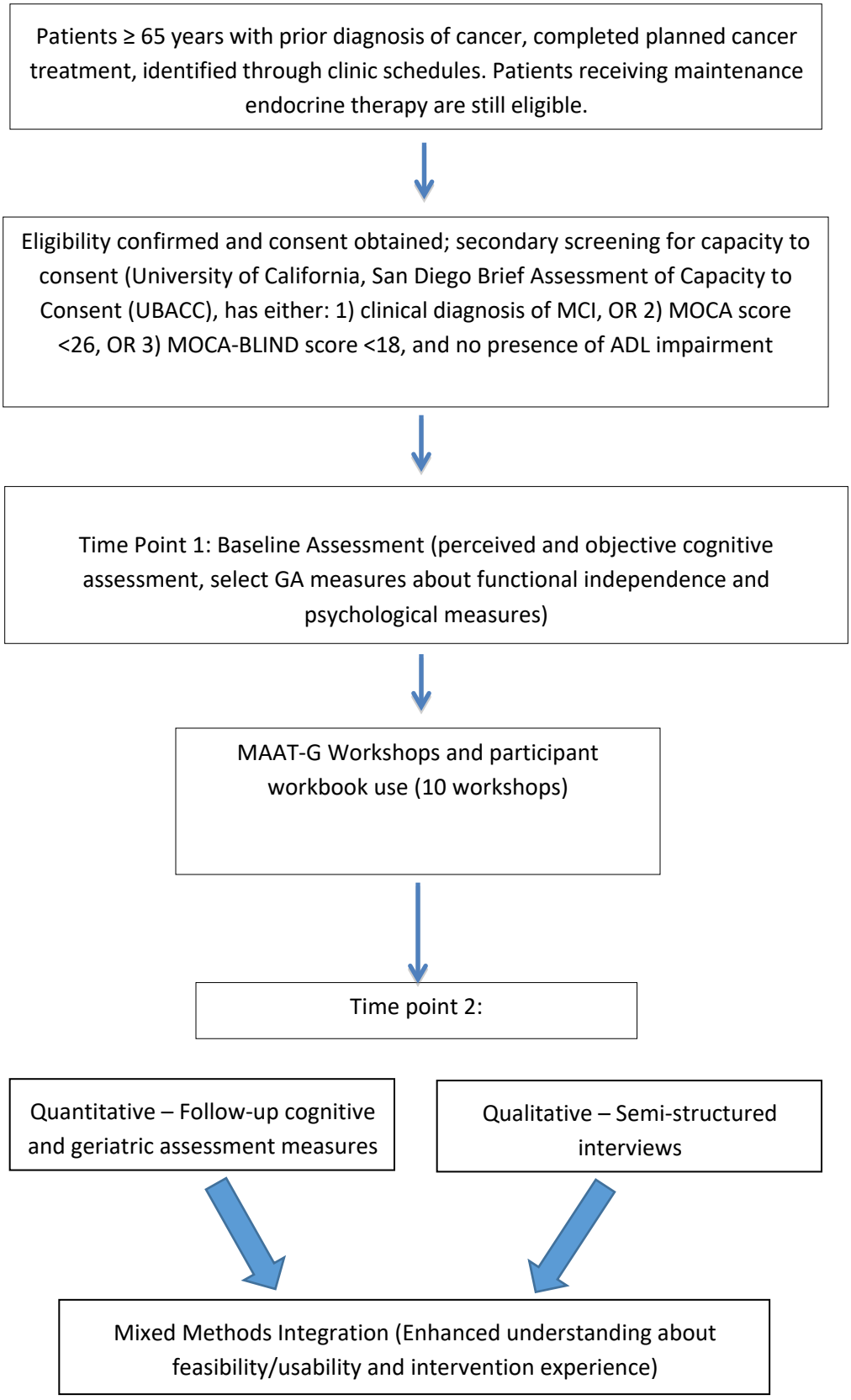
1.0 STUDY SCHEMA



2.0 SPECIFIC AIMS

Older cancer survivors are a rapidly growing population; in the United States there are >10 million cancer survivors aged ≥65. Older cancer survivors experience long-term side effects from their diagnosis and prior therapy, such as Cancer-Related Cognitive Dysfunction (CRCD).[1,2] CRCD is a prevalent side effect and creates difficulties in memory, attention and executive function. Up to 35% of cancer survivors experience CRCD symptoms months to years after completion of their cancer therapy.[3,4] In older cancer survivors with Mild Cognitive Impairment (MCI), the long-lasting effects of CRCD may be contributing to their cognitive difficulties. CRCD symptoms may represent a reversible component of a patient's cognitive decline and an intervention targeting CRCD in this population may afford improvements in perceived and objective cognitive function.

Prior studies evaluating non-pharmacologic interventions (e.g. Cognitive Training) for older adults with MCI have demonstrated improvement in cognitive and neuropsychiatric symptoms.[5-9] Memory and Attention Adaptation Training-Geriatrics (MAAT-G) is a cognitive-behavioral therapy (CBT)-based intervention for CRCD. Providing MAAT-G to older cancer survivors with MCI who are at greatest risk for developing progressive cognitive decline may afford improvements in perceived and objective cognitive function and alter the trajectory of cognitive symptoms by addressing the reversible components of CRCD. MAAT-G provides instruction and practice with adaptive behavioral coping skills, stress management techniques, and compensation strategies for CRCD. MAAT-G is delivered by a trained clinician (e.g. clinical psychologist, registered nurse) via videoconferencing during a series of ten workshop sessions.

Cancer-related cognitive dysfunction (CRCD) is a significant problem. Our group and others have demonstrated that CRCD affects up to 75% of patients during treatment and can create difficulties in attention, processing speed, executive function and memory.[10-12] Older adults are at greater risk of developing CRCD;[2,13-16] half of women aged ≥65 receiving adjuvant chemotherapy for breast cancer report worsening of cognition, and 25% have measurable declines on neuropsychological testing six months post-chemotherapy.[17,18] Patients with localized breast cancer have excellent overall survival but are at risk for CRCD as a long-term side effect of therapy.[3,19,20] For older adults, CRCD can compromise functional independence (e.g. Instrumental Activities of Daily Living [IADL]).[21] The etiology of CRCD likely involves multiple factors including host factors (e.g. age, cognitive reserve), biologic factors (e.g. cortisol-mediated stress response), clinical factors (e.g. comorbidities) and psychological factors (e.g. coping mechanisms).[11,22-27] While alleviating or preventing CRCD is important to older adult patients and their caregivers, interventions tailored to them do not exist.[28] Developing CRCD interventions for older adults is a high-priority area of research for the NIA.[29-32]

The Memory and Attention Adaptation Training (MAAT) intervention shows promise for targeting modifiable factors of CRCD.[19,33-35] MAAT provides instruction and practice with adaptive behavioral coping skills, stress management techniques, and compensation strategies for episodes of cognitive failure (e.g. lapses in memory, attention). MAAT is a series of eight manualized workshops delivered by a trained clinician via video-conferencing combined with a participant workbook. In younger cancer survivors (i.e. those who have completed chemotherapy), MAAT improves self-perceived cognition (Functional Assessment of Cancer Therapy–Cognition [FACT-Cog], d=0.52), verbal memory (California Verbal Learning Test 2 (CVLT), d=-0.63) and processing speed (Symbol Digit Subtest of Telephone Based Neuropsychological Status [TBANS], d=0.5).[19,33] These cognitive functions are particularly important for older adults. MAAT has been adapted to meet the unique needs of older adults and we have evaluated the usability of MAAT-G in older adults with cancer receiving systemic therapy. However, more data is

needed regarding the usability of MAAT-G in patients with pre-existing cognitive impairment. Because MCI is clinically underdiagnosed, we will utilize an abnormal cognitive screening result (Montreal Cognitive Assessment [MOCA]) to define our population. The MOCA has demonstrated a sensitivity of 80-90% for detecting MCI in older adults using a scoring cutoff of <26,[36,37] with a specificity of 81-87% for excluding patients with normal cognition.[36,37]

Study Objective:

Primary Objective: We will test the feasibility of delivering the adapted MAAT (MAAT-Geriatrics [G]) in older adults with breast cancer receiving adjuvant chemotherapy by determining usability of the intervention using the System Usability Scale (SUS).

Second Primary Objective: Evaluate the feasibility of MAAT-G in older cancer survivors with mild cognitive impairment by determining consent rate, intervention adherence rate, and study completion rate in this specific population (n=35).

1. Hypothesis: We will achieve a consent rate of >70%, intervention adherence rate >75%, and study completion rate of >75%.

Secondary Objective: To obtain descriptive feedback on the usability of the intervention and guide further adaptation, qualitative interviews with patients and their caregivers (if available) will be conducted at completion of the intervention.

Tertiary Objective:

2. Examine the pre-post change in perceived and objective cognitive function in older cancer survivors with MCI.
    1. Hypothesis: Older cancer survivors with MCI receiving MAAT-G will demonstrate improvement in perceived and objective cognitive assessment.
3. Enhance our understanding of the usability of a telehealth CRCD intervention (including barriers and facilitators) for older cancer survivors with MCI and the perceived MAAT-G intervention effect through integration of quantitative data (from tertiary objective) with qualitative data from semi-structured interviews of patients and caregivers.

3.0 BACKGROUND AND RATIONALE

3.1. Cancer-related cognitive dysfunction (CRCD) is a prevalent clinical problem; older adults are at greater risk of experiencing CRCD with cancer treatment, especially chemotherapy.[2,10-16,22,38,39]
Symptoms of CRCD include problems with memory, attention and executive function.[11] CRCD is common; in the largest CRCD study to date, patients with breast cancer receiving adjuvant chemotherapy reported significantly greater cognitive difficulties from pre-chemotherapy to 6 months post-chemotherapy, compared to age-matched controls (mean change FACT-Cog score -10.4 in patients versus mean change +1.5 in controls).[10,11,22] Older patients, particularly those with lower cognitive reserve, may be most vulnerable to the effects of chemotherapy on cognition.[13-15,38,39] Ahles and colleagues observed that the subgroup of older patients with low baseline cognitive reserve prior to adjuvant chemotherapy for breast cancer had the largest decline in processing speed post-treatment.[13] Twenty-five percent of older women with breast cancer receiving chemotherapy develop cognitive decline from pre- to six months post-chemotherapy (defined as decline in 1 standard deviation in $\geq$ two neuropsychological domains)[18], and half report worsening of their cognition.[17] The effects of CRCD can be long-term; up to 35% report CRCD months to years after completing therapy; cross-sectional studies of older breast cancer survivors demonstrate lower performance in multiple areas of neurocognitive function compared to age-matched controls without cancer, even several years after treatment.[3,20]

3.2 There is a large and growing number of older cancer survivors in the United States. Of the nearly 17 million cancer survivors in the U.S., 64% (approximately 10.7 million) are aged 65 and over.[78] This increase in older cancer survivors is due in part to improvements in cancer treatment, in addition to the aging demographics of our population. However, cancer therapy incites side effects, some of which can be long term and exacerbate other comorbid conditions.[40] One prevalent side effect is CRCD.[2,10-16,22,38,39] CRCD affects up to 75% of patients during treatment, creating difficulties in memory, attention and executive function.[2] CRCD is a significant concern for older cancer survivors, as older adults with lower cognitive reserve are most vulnerable to the effects of cancer treatment on cognition.[2,13,32] Ahles and colleagues observed that older patients with low baseline cognitive reserve prior to adjuvant chemotherapy for breast cancer had the largest decline in processing speed post-treatment.[13] For many patients, the effects of CRCD can be long-term and up to one-third of cancer survivors report CRCD symptoms months to years after completing therapy.[3,20] This is particularly relevant for older adults, who are most susceptible to CRCD, as the deleterious effects of CRCD may contribute to loss of functional independence (e.g. Instrumental Activities of Daily Living [IADL]).[21]

3.3 MCI is also a prevalent condition in older adults[41], including older cancer survivors. The prevalence of MCI in community-dwelling older adults aged 71 and older is up to 22%.[420] MCI has also been observed in older cancer survivors.[43,44] For example, using the National Institute on Aging/Alzheimer's Association (NIA/AA) criteria for MCI in a cohort of breast cancer survivors who received chemotherapy, 43% of patients met diagnostic criteria for MCI.[81] The relationship between the risk of cancer and risk of dementia is unclear, with some studies demonstrating higher rates of dementia in cancer survivors[4,45,46] and other reporting lower rates.[47,48] Although this relationship is not fully understood, several indicators suggest that older cancer survivors are at greater risk of developing cognitive problems following cancer treatment, as compared to their younger counterparts.[2,13,32,46] In a recent Surveillance, Epidemiology and End Results (SEER) registry analysis including over 3.5 million cancer survivors, long-term cancer survivors ($\geq$ 10 years) were observed to be more likely to die from Alzheimer's disease (AD) compared to

the general population (OR 1.13; 95% CI 1.12-1.15) and those who were aged 70+ at time of cancer diagnosis were most likely to develop AD (OR 1.29; 95% CI 1.26-1.31).[46] In older cancer survivors with MCI, the long-lasting effects of CRCD may be contributing to their cognitive difficulties. An intervention targeting the reversible components of CRCD in older cancer survivors with MCI may afford improvements in perceived and objective cognitive function. Because MCI is underdiagnosed, we will also utilize the MOCA in our screening process to identify potentially eligible patients that do not have a clinical diagnosis of MCI but have a MOCA score consistent with MCI. The MOCA has demonstrated a sensitivity of 80-90% for detecting MCI in older adults using a scoring cutoff of <26,[36,37] with a specificity of 81-87% for excluding patients with normal cognition.[36,37]

3.4. Multiple factors are likely involved in the etiology of CRCD including host factors (e.g. age, cognitive reserve)**,** biologic factors (e.g. cortisol-mediated stress response), clinical factors (e.g. comorbidities) and psychological factors (e.g. coping mechanisms).[11,22-27] CRCD can be conceptualized using a diathesis stress model, whereas under routine and low stress conditions, cognitive failures of daily life (e.g. mental lapses in memory, attention) are likely to occur with less frequency and when they do, they are readily managed.[35] However, under periods of sustained physical and psychological stress (allostatic overload) such as chemotherapy, there may be dysregulation of the stress response leading to more frequent cognitive failures.[26] The threshold for allostatic overload is variable and depends on an individual's self-regulatory capacity (i.e. an individuals' limited fund of "mental energy" to attend to self-regulatory behaviors such as decision-making, attentional demands, and emotional regulation).[49,50] Coping involves monitoring self-regulatory capacity and recognizing situations of allostatic overload that require adjustment/adaptation of behaviors.[27] Maladaptive coping mechanisms can lead to further negative effects on cognition.[51] Additionally, individuals possess varying abilities to compensate for cognitive stressors; however, compensatory strategies can be taught.

3.5. Memory and Attention Adaptation Training (MAAT) is a cognitive-behavioral therapy (CBT)-based intervention for CRCD. MAAT was designed as a practical and short-term CBT intervention to help cancer survivors learn adaptive, compensatory skills for chemotherapy-related memory dysfunction. In the literature, cognitive rehabilitation involves 2 broad approaches. This distinction is important and remains a source of debate. Traditional cognitive rehabilitation, or a "retraining" approach, emphasizes practice and drill of cognitive exercises to promote neuro-circuitry repair of damaged brain regions. However, some investigators contend performance at everyday tasks requiring memory (e.g., "memory related disability") does not improve with the retraining approach or generalize or "transfer" to daily living. By contrast, a "compensatory strategy" approach emphasizes direct teaching of adaptive skills on everyday tasks, which require memory, to minimize the impact of memory dysfunction on daily quality of life and function. We believe the compensatory strategy approach is advantageous to the retraining approach as it may be completed in a shorter format better suited to adult survivors. It overlaps with theoretical principals of CBT; learning new behaviors and cognitions to promote therapeutic, adaptive change. Compensatory strategies used in MAAT include self-awareness training (self-monitoring record keeping to identify "at risk" situations where cognitive failures may occur), Self-Instructional Training (SIT), or a method of "self-talk" to enhance on-task attention, mnemonic strategies to enhance retention and retrieval for daily working memory, and organizational and social skills training such as keeping a simplified schedule or active listening skills. Self-regulation skills of applied relaxation training and activity scheduling/pacing are also included. The overarching aim of MAAT is to enhance self-management and coping with cognitive failures in daily life to minimize impact on survivor quality of life.

As a CBT-based intervention, MAAT focuses on an individual's psychological response to injury as compared to the biological events triggering CRCD. MAAT is a series of manualized workshops delivered by a trained clinician via video-conferencing, supplemented by a participant workbook, which provide instruction and practice with adaptive behavioral coping skills, stress management techniques, and compensation strategies.

3.6. The **scientific premise** of this new research is that CRCD is a significant problem, particularly for older cancer survivors with MCI, and interventions to improve cognitive outcomes are needed. We are expanding the eligibility criteria for this study to test an intervention for CRCD that is adapted specifically for use in older adults to determine the feasibility of delivering the intervention in an expanded population, older cancer survivors with MCI.

Table 1: Association between abnormal cognitive screen and other GA impairments in older adults with cancer.

GA Domain	Abnormal Mini-Cog (% with impairment)	Normal Mini-Cog (% with impairment)	P-value
Physical function			
ADL	34%	24%	**0.024**
IADL	64%	52%	**0.006**
Falls	28%	25%	0.449
TUG	47%	34%	**0.003**
Comorbidity	68%	62%	0.184
Polypharmacy	88%	82%	0.059
Nutrition – MNA	60%	56%	0.451
Psychological			
GDS	29%	19%	**0.001**
GAD-7	14%	6%	**0.0009**
Social Support	23%	32%	**0.039**

3.7 Preliminary Studies:

3.7a. Abnormal cognition is common in older adults with cancer.[52] In a large, multi-site study of older adults with cancer (N=541), our team demonstrated that 33.5% of patients had an abnormal cognitive screen (Mini-Cog). Patients with an abnormal Mini-Cog were more likely to have impairments in other Geriatric Assessment (GA) domains **(Table 1)**.[53]

3.7b. It is feasible to study behavioral interventions in clinical trials for older adults with cancer receiving chemotherapy.[54] A pilot RCT testing the feasibility of implementing GA-guided management interventions for older adults with cancer receiving chemotherapy was conducted by the PI at the University of Rochester Wilmot Cancer Institute. 71 older adults were enrolled (75% of approached patients consented); 89% completed the 3-month follow-up assessment. A subset of older adults receiving chemotherapy experienced cognitive decline; in analysis of the Clock Draw Test, 15% demonstrated significant decline at 6-week follow-up.

3.7c. We have adapted an existing telehealth CRCD intervention specifically for use in older adults. To refine and adapt MAAT for older adults, we used the Contextual, Cohort-based, Maturity, Specific Challenge (CCMSC) model for adapting CBT- based interventions for older adults.[55] Subsequently, we made further refinements to MAAT-G using feedback from key stakeholders through a series of focus groups with members of

Table 2: MAAT-G Adaptations Using CCMSC Model

CCMSC Model Component and Goal	Example of Adaptations Incorporated into the MAAT-G intervention through the CCMSC model and stakeholder feedback
Social Context Factors: Appreciate that older adults may have distinctive social context, including specific environments (e.g. age-segregated housing, aging services networks).	1. A section was added to the clinician's manual to educate clinicians on social context factors and how this may influence compensatory strategies for older adults. 2. A screening question was added to the clinician's manual to inquire about social supports to encourage clinicians, patients and caregivers to consider all available resources for compensatory strategies.
Cohort-based Considerations: Understand that membership in a birth-defined group may impact abilities, beliefs, attitudes and personality.	1. A section was incorporated into the clinician's manual to educate on cohort-based factors and how this may influence coping mechanisms and stress response. 2. The patient workbook was adapted throughout to minimize complex terminology to account for potentially lower education levels of older cohorts. 3. Examples of scenarios of cognitive overload were adjusted throughout the manual (e.g. references to job-type examples were changed to more social-based examples of working tasks that might be more consistent with activities of older adults who may be retired) 4. Technology support materials were developed to encourage inclusion of patients with limited technology background
Consider Aspects Related to Maturity Factors: Appreciate cognitive strengths of older adults but understand that some may have pre-existing cognitive impairment. Appreciate influence of previous life experiences on emotional responses.	1. A section was added to the clinician's manual to educate clinicians on maturity factors and its effect on pace of information receipt, coping mechanisms and stress response. 2. MAAT-G was extended to 10 workshop sessions (from 8) to decrease the amount of new material presented during each workshop session. 3. Complexity of examples presented in the workshop sessions was reduced. 4. Font type and sizing was adjusted in the workbook to accommodate for potential visual impairment.
Acknowledge Specific Challenges: Appreciate how symptoms and comorbidities can impact psychosocial function.	1. A step was added to the clinician manual to screen for hearing loss to allow clinician to proactively adapt volume and rate of speech while delivering intervention. 2. Information about volume control highlighted in the technology support manual for patients. 3. Font type and sizing was adjusted in the workbook to accommodate potential visual impairment.

SCOREboard, our older adult patient advisory group. SCOREboard members, the majority who are cancer survivors, reviewed and provided feedback on workshop content, relevance to older adults, optimizing feasibility for delivering workshops concurrent with cancer treatment, and aspects related to technology support for older adults (see **Table 2** for details of MAAT-G adaptations).

3.7d. To date, the usability of MAAT-G has been evaluated in four older adults receiving systemic treatment for breast cancer. Regarding recruitment to the usability study, 4/4 approached patients consented to the study (100% consent rate). The mean age of patients enrolled is 73.3 (range 67-77). Two patients self-describe as limited technology knowledge. There was 100% capture of baseline assessment measures; these measures included perceived and objective cognitive assessment as well as selected GA measures of functional independence and psychological status. All four patients completed all study procedures and MAAT-G workshop sessions on schedule (e.g. 100% intervention adherence). However, none of these patients had a pre-existing diagnosis of cognitive impairment, and based upon the scientific rationale outlined above, we are expanding the eligibility criteria for this usability study to evaluate usability of MAAT-G in a population of older cancer survivors with a clinical diagnosis of MCI, a MOCA score < 26, or a MOCA-BLIND score < 18.

4.0 SUBJECT ELIGIBILITY

The eligibility criteria are aimed at identifying older cancer survivors. As above, if patients are able and willing to identify a caregiver, caregivers will also be consented to participate in study processes.

4.1. Patient Inclusion Criteria:

1. Be age 65 or older

2. Able to provide informed consent. All patients will be assessed using the University of California, San Diego Brief Assessment of Capacity to Consent (UBACC)[56] – a score >14.5 will define ability to independently provide informed consent. For patients scoring <14.5, or if investigators have additional concerns, we will require that their health care proxy participate in the consenting process and sign an informed consent and patients will required to provide assent.

3. Able to read and understand English

4. Have a prior diagnosis of cancer of any stage. Patients must have completed their planned cancer treatment. Patients are permitted to be receiving maintenance therapy (e.g. endocrine therapy).

5. Have a clinical diagnosis of MCI, a score <26 on the Montreal Cognitive Assessment (MOCA), or a score <18 on the Montreal Cognitive Assessment-BLIND (MOCA-BLIND). If the patient had a MOCA evaluation completed as a part of routine clinical care in the preceding 6 months prior to consent date, this may be used for eligibility purposes.

6. Be independent in Activities of Daily Living (ADL)

4.2. Patient Exclusion Criteria:

1. Have surgery planned within 3 months of consent

2. Patients who do not have decision-making capacity (as determined by UBACC as described above) **AND** do **NOT** have a previously designated health care proxy (established prior to their cognitive impairment) available to sign consent

3. Have an ADL dependence

We anticipate enrolling 39 patients (35 patients consented in the MCI cohort). Because the usability of telehealth in populations with pre-existing cognitive impairment is less well established, we are proposing a larger sample size for a better estimation of usability and feasibility of this study). Enrolled patients will also be allowed to enroll with a caregiver although patients without a caregiver can also enroll. Therefore, we do not have a target enrollment for caregivers. We are proposing a larger sample size for better estimation of usability and feasibility in the expanded eligibility criteria (which is a more diverse population of older cancer survivors with any cancer type).

4.3 Entry criteria for caregivers:

A caregiver can be anyone, age 21 or over, who is able to understand spoken English, understand the study process and provide informed consent. One caregiver for each patient will be eligible and must be chosen by the patient. For the purposes of this study, a caregiver is defined as a valued and trusted person in a patient's life who is supportive in health care matters by providing valuable social support and/or direct assistive care.

4.3.1. Inclusion criteria for caregivers:

1. Selected by the patient when asked if there is a "family member, partner, friend or caregiver [age 21 or older] with whom you discuss or who can be helpful in health-related matters;" patients who cannot identify such a person ("caregiver") will remain eligible for the study.

4.3.2 Exclusion criteria for caregivers

2. Caregivers unable to understand the consent form due to cognitive, health or sensory impairment will be excluded

If patients possess independent capacity to consent, they do not require a caregiver to consent in order to participate in the study.

5.0 IDENTIFICATION, RECRUITMENT, AND CONSENT PROCEDURES

Subjects will be enrolled at the University of Rochester Wilmot Cancer Institute (including Strong Memorial Hospital, Highland Hospital, and Pluta Cancer Center sites) and Myers Cancer Center in Dansville. Patients will be recruited from the medical oncology clinics at these sites. The clinic schedules of oncologists and their advanced practice providers (APPs) will be screened for eligible patients.

To ensure appropriate safety precautions when conducting in-person study procedures, the process for conducting in-person visits outlined in the Guidance for Human Subject Research will be followed.

5.1. Patient and Caregiver Identification, Recruitment, and Consent Procedures:

Potential patients will be identified in multiple ways. First, at all sites for accrual, study participants will be identified by their treating physician, the nurses that work with the physicians, and the study coordinator. The study coordinator works closely with the physicians and nurses to monitor patients and identify those patients that are anticipated to begin cancer treatment. With permission from oncology providers, we will screen for eligible patients from clinic schedules. The study coordinator contacts the physician (or their designee) and lets them know that a patient may be eligible for the study. The physician (or their designee) then confirms if the patient is a good study candidate or not. If there is a question about eligibility, the principal investigator will be contacted and will meet with the patient and/or health care proxies, review the medical records, and perform an assessment of eligibility if necessary. Afterwards, the study coordinator will meet with the patient, and explain the details of the study. Study staff will introduce the study to the patients and provide adequate time to read the consent.

For patients at the Dansville location, the study coordinator will contact the physician (or their designee) to let them know that a patient may be eligible for the study. The physician then confirms if the patient is a good study candidate or not and affirms that the patient has decision making capacity. The physician or a member of the study team then mentions the study to the patient during the visit. If the patient expresses interest, a member of the study team will consent the patient and provide the patient with the necessary materials to participate in the study. If the patient would like to consider the study further, the study team at Myers Cancer Center (Dansville) can provide the patient with an informational consent and with their permission, a member of the MAAT-G study team will contact the patient at a later date to follow-up.

Recruitment of caregivers: If patients are agreeable to participating in the study, patients will be asked if there is a "family member, partner, friend or caregiver [age 21 or older] with whom you discuss or who can be helpful in health-related matters;" to participate as a caregiver. If patients are unable to identify a caregiver, they will still be able to participate, as long as they have independent capacity to consent as described above. If patients are able to identify a caregiver, a member of the study team will give the patient a contact form that summarizes the purpose of the study, what the study would entail for the caregiver, and study coordinator's contact information. If the caregiver is interested in participating, s/he will contact the study coordinator using the contact information provided on the contact form. The study coordinator is not allowed to initiate the first point of contact with the caregiver.

5.1.1. *Informed Consent:* Informed consent will be obtained from the patient by a member of the study team in person during a clinic visit. The member of the study team uses the informed consent document as a written aid and goes over every detail of the study with the patient and/or health care proxy in person and recruits them to the study. Members of the study team, the oncologist and the nurses are available to answer any questions the patient may have about any aspect of the study prior to consenting and throughout the entire study period. Patients may choose to sign the informed consent immediately on the day the study information is presented to them or they may choose to take the informational consent form home and discuss it with others. If they want to participate in the study, they can sign it the next time they meet with a member of the study team. If the patient is participating in a telehealth visit and expresses interest, the member of the study team will ask patient for his/her permission to be mailed an informational consent for their review.

5.1.2. *Verbal Informed Consent:* If the patient or caregiver cannot meet in person with a member of the study team to sign the informed consent, a member of the study team will verbally consent the subject. A member of the study team will use the verbal consent script, then sign and date it to confirm that s/he followed the script and the subject agreed to participate in the study. Following the completion of verbal consent with the subject, the member of the study team will mail or email the subject a study information sheet that summarizes what the study entails and the subject's involvement in it.

Waiver of documentation of consent:
We are requesting for waiver of documentation of consent as the research involves no more than minimal risk to the subjects (patient or caregiver) and involves procedures for which written consent is normally not required outside the research context. The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality.

Alteration of HIPAA Authorization:
We are requesting an alteration of HIPAA authorization. We will provide an information sheet to subjects (patient or caregiver) who provided verbal consent. Verbal consent will allow for reduction of in-person visits, thus maximizing the safety of both subjects and study staff. Nonetheless, when possible and if we are able to coordinate study and clinic visits, we will obtain written informed consent.

The study cannot be conducted without the use of protected health information (PHI) as we have to link patient reported data with medical history collected on electronic medical record. We have adequate plans to protect the PHI from improper use and disclosure. We will destroy identifiers after completion of the study for 7 years. We will not reuse or disclose the PHI to another person or entity other than the study investigators. The waiver will not adversely affect the privacy rights of the individual and the research cannot be practicably done without access to the use of the PHI.

5.1.3. *Baseline Measures and Study Procedures:* The baseline measures will then be performed and study procedures will occur. The patient must be determined to have decision-making capacity to provide informed consent by their treating oncologist.

5.1.4. *Human Subject Protection:* Ethical standards for human subjects will be strictly followed in accordance with the University of Rochester Research Subject Review Board Investigator Guidance policy and the University of Rochester Policy on Enrollment of Adult Decisionally Incapacitated Research Subjects and Permission of Authorized Representatives.

Patients with MCI may be considered a vulnerable population but are necessary to answering our research questions. For all patients, we will formally assess capacity to consent using the University of California San Diego Brief Assessment of Capacity to Consent (UBACC), adapted for our study. Following the informed consent process, decisional capacity for clinical research participation will be confirmed with the UBACC. The UBACC is a 10-item scale that can be administered by a Bachelor Degree-level research coordinator. The UBACC determines patient's understanding of key aspects of the consent process (e.g. purpose of study, risks of study). A UBACC total score >14.5 will be considered confirmed for decisional capacity for clinical research. For patients scoring <14.5, or if investigators have additional concerns, patients Health Care Proxy can participate in the consenting process and sign an informed consent. We will also require that patients who fail the screen or cases where investigators have additional concerns give consent, or at minimum assent if fully informed

consent is not possible. If a patient does not have a designated Health Care Proxy and scores <14.5 on the UBACC, they will be unable to participate.

Once consented is confirmed, if the patient does not have a clinical diagnosis of MCI a member of the study team will administer MOCA to the patient. If a member of the study team is able to administer the MOCA in person, the following scoring will be used: The traditional paper-pencil MOCA (i.e. 30-point MOCA scoring total) will be used for in person assessment and if the MOCA score is ≥26, the patient is informed that they are not eligible to participate in the study and will be considered a screen failure. If the MOCA score is <26, the patient is eligible to continue. If a member of the study team cannot administer the MOCA in person (e.g. when verbally consenting patients over the phone), s/he will follow up with the patient over the phone and administer the MOCA-BLIND and use the following scoring: The MOCA-BLIND scoring total is 22-point; if the MOCA-BLIND score is ≥18, the patient is informed that they are not eligible to participate in the study and will be considered a screen failure. If the MOCA-BLIND score is <18, the patient is eligible to continue. We utilize the MOCA (or MOCA-BLIND) in our screening process to identify potential cognitive impairment since MCI is underdiagnosed. The 30-point MOCA has demonstrated a sensitivity of 80-90% for detecting MCI in older adults using a scoring cutoff of <26, [57] with a specificity of 81-87% for excluding patients with normal cognition. [57] The 22-point MOCA-BLIND has demonstrated a sensitivity of 63% for detecting persons who are affected with MCI, and a specificity of 98%.[97]

A member of the study team must also identify whether the patient is independent in Activities of Daily Living (ADL) using the ADL questionnaire. The ADL questionnaire will be verbally asked to patients for both in person and phone assessments. If the patient has ADL impairment, the patient is not eligible and will be considered a screen failure. Because we are aiming to target older cancer survivors with MCI, we are excluding patients with ADL impairment whereby their cognitive impairment may be more consistent with dementia, similar to methods in other studies targeting patients with MCI. [77]

For patients that provide informed consent, the following components as described above will be subsequently assessed to confirm eligibility:

1. UBACC score >14.5; or for patients scoring <14.5 a health care proxy available to provide informed consent and patient able to provide assent
2. Established diagnosis of MCI or MOCA sore <26 or a MOCA-BLIND score <18
3. No presence of ADL impairment

If patients meet all of the above criteria the will be permitted to continue with the study. For patients that do not meet the above criteria, they will be considered a screen failure.

5.1.5. *Participation:* Current, state, federal, and institutional regulations concerning informed consent will be followed. Participation in this study is voluntary. Participants are free not to take part or to withdraw at any time, for whatever reason, without risking loss of present or future care they would otherwise expect to receive. In the event that a patient does withdraw from the study, the information they have already provided will be kept in a confidential manner. Participants may discontinue participation in the study at any time if they decide they do not wish to take part any longer. Participants may be withdrawn from the study by research personnel if it is deemed in their best interest to no longer participate.

5.1.6. *Duration:* Patients who consent to the study will be in this study for 8 months. Patients will be consented to actively participate, receive phone calls or meet with the research study team for up to 8 months after their initial visit. The research team may contact patients in the future to gain further information first hand regarding patients' overall health and treatment. Dr. Magnuson may decide to take patients off the study without their consent if the study is stopped. Additionally, patient data will be kept for a period of 10 years at URMC, even after the study is closed or a patient passes away. It will be maintained in a locked database with password access only (See Section 8).

6.0 REGISTRATION AND RANDOMIZATION

6.1. Registration:

To register a participant and caregiver who meets the eligibility criteria and who has signed the informed consent document, study staff will enter the information outlined in section 6.2 in the OnCore database.

6.2. Information Requested at Registration:

6.2.1 First name
6.2.2 Last name
6.2.3 eMRN
6.2.4 Birth Date
6.2.5 Gender
6.2.6 Race
6.2.7. Ethnicity

6.3. Initial Assessment:

After consent procedures are completed, the patient, with the help of the study coordinator, will complete a baseline assessment (See section 7). For phase I of this study, there will not be randomization of subjects.

7.0 TREATMENT PROTOCOL

7.1 Measures:

Patient measures will include *demographics, cognitive, psychological, and functional independence* measures. The battery was selected based upon our experience in prior studies.[10,33,58,59] Based upon experience in prior studies, we estimate the cognitive evaluation will take approximately 60 minutes to complete[10,12] and the demographics, psychological and functional independence measures will take approximately 20 minutes.

Demographics: Patient and caregiver demographics will be collected, including age, gender, race, ethnicity, marital status, education and socio-economic status will be captured. Cancer and treatment variables, comorbidities, and medications list will be collected from the medical record by study staff.

Cognitive Evaluation will include: 1) FACT-Cog[60], a validated patient reported outcome measure created to assess cognitive challenges identified by patients with cancer; 2) Controlled Oral Word Association (COWA)[61], a measure of verbal fluency evaluating expressive language and executive function; and 3) Hopkins Verbal Learning Test-Revised (HVLT-R)[62], a validated test of verbal learning and memory, (two different versions will be used-form 1 and form 2), and 4) Cognitive Difficulties Scale (CDS)[63]; a patient reported outcome measure to estimate how many and how often cognitive symptoms impact daily life in older adults with MCI. All measures are "paper and pencil" or verbally administered. COWA and HVLT-R require the study coordinator to administer the tests; they can be administered virtually so study coordinator will schedule a telephone or televideo meeting with the patient at the corresponding time points, as needed.

Psychological Assessment: will include Geriatric Depression Screen (GDS)[64] and Generalized Anxiety and Depression (GAD-7).[65]

Functional Independence: IADLs and ADLs will be measured.[66]

Usability will be assessed quantitatively with the System Usability Survey.[67,68]

Phase I semi-structured interview questions for patients and caregivers will focus on usability of MAAT-G (e.g. barriers and facilitators to intervention) and explore patient/caregiver experience with MAAT-G and their perception of how MAAT-G altered cognitive symptoms and functional independence

7.2 Recruitment and Retention Metrics:
These measures include: 1) Consent rate (proportion of participants enrolled of those approached), intervention adherence rate (proportion of enrolled participants that complete the 10 weekly MAAT-G sessions within the defined study window), and study completion rate (proportion of patients completing all study procedures including time point 2 assessment and interview). In order to better understand the usability and experience of older cancer survivors with MCI with engaging in a videoconferencing-based cognitive intervention, we will incorporate a quantitative usability measure (System Usability Scale) as well as additional qualitative questions highlighted in Table 3 (next page).

7.3 Study Procedures:
Baseline: Following informed consent, patients will undergo Time Point (TP) 1 assessment. Patients will be provided with a data-enabled tablet with HIPPA-compliant video-conferencing application and instructed on its use, participant workbook, and tablet instruction manual. At the time of enrollment, a member of the study team will assign each patient a unique meeting ID number within the tablet instruction

Table 3: Measures overview

	Timepoint 1 (Baseline)	Timepoint 2 (Post-Intervention)

Participant	• Demographics
	• Cognitive Assessment
	• Geriatric Assessment measures
	  • Functional independence
	  • Psychological Assessment
		• Cognitive Assessment
		• Geriatric Assessment measures
		  • Functional independence
		  • Psychological Assessment
		• System Usability Scale (SUS)
		• Semi-structured interviews
		  • Intervention versus active control perceived effects
		  • Telehealth experience
		  • Aspects of recruitment and retention and technology support

Caregiver	• Demographics	• Semi-structured interviews
		  • Intervention versus active control perceived effects on participant cognition and function
		  • Telehealth experience and aspects of caregiver support for telehealth participation
		  • Aspects of recruitment and retention and technology support

manual. This meeting ID number allows each patient to log on to the video-conferencing application and speak to the trained psychologist, psychology post-doctoral fellow, or psychology intern for the workshops. Study coordinators will train and support patients on the use of the tablet and video conferencing application. No data is being stored on the tablet itself. If patients consent to have sessions recorded, this will be done through the HIPPA-compliant Zoom software application. If participants do not have access to wireless internet, the tablet will be equipped with a data package for participant use for the purposes of this study. At completion of the study, patients will return the tablet to a member of the study team. If the tablet is lost or stolen during the study, no PHI will be stored on the tablet and thus would not be accessible. If the tablet is broken during the course of the study, we will provide participants with another tablet for use during the study period. The participant would contact a member of the study team with any concerns or problems with using the tablet, contact information will be provided during training on tablet use. The patient may elect to use their personal computer and decline the study ipad if that is their preference.

Intervention Period: The intervention period is 8-12 weeks; 10 weekly MAAT-G workshops will be delivered through video-conferencing on the tablet. MAAT-G workshops will be audio-recorded for fidelity review with patients' permission. (See section 7.5)

Follow-up: Within 4 weeks of intervention completion (approximately week 10-14), patients will undergo TP2 assessment.

Patient assessments will be performed by trained study coordinators. As a safety precaution due to COVID-19, patients may take surveys home for completion (e.g. demographics) and then mail back to study team in order to minimize the amount of in-person contact between coordinators and patients; the method of completing surveys at home has been successful in prior studies with good retention.[54,69] However, to encourage the completion of the surveys, the study coordinator will schedule a telephone or televideo meeting with the patient, as needed, to ensure patients' questions concerning the surveys are addressed. Study coordinators will score assessments and transcribe results into a database. Audio-recordings will be deleted following transcription.

Semi-structured interviews will be conducted by a trained study coordinator who is not responsible for any other component of the study. Interviews will be conducted with patients and if consented, will also be conducted with caregivers. As a safety precaution due to COVID-19, the interviews with the patients and caregivers will be conducted over the phone. These audio-recorded interviews will be conducted after completion of the intervention.

Location: MAAT-G participation will take place through video-conferencing. Participants will be encouraged to participate from their home or other private location. Due to COVID-19, the Department of Psychology is conducting clinical visits from their clinical office and home office locations until further notice. Wherever the location may be, individuals who are conducting the MAAT-G intervention will ensure privacy in a private room with a closed door. Participants will be provided with a HIPAA compliant tablet to use for participation in the intervention activities and the intervention will be delivered using HIPAA compliant video-conferencing technology provided by the University of Rochester. The coordinator will be in touch with patients by phone throughout the length of the study, serving as a liaison between patient and the trained clinician administering MAAT-G workshops. The coordinator will help organize the scheduling/rescheduling of workshop sessions and will be available for any patient questions.

7.4. MAAT-G Intervention

The MAAT-G intervention will be delivered by a trained clinician (e.g. psychologist, psychology post-doctoral fellow, psychology intern, or registered nurse) at the University of Rochester Medical Center. The intervention will be delivered through televideoconferencing and participants will be provided a tablet equipped with a HIPAA compliant televideoconferencing application to use for the MAAT-G workshop sessions. We will use the University of Rochester Zoom application which is HIPAA compliant. A tablet instruction manual will be given to patients to help guide them through how to use a tablet and how to navigate the Zoom application. A unique meeting ID number will be given to each patient to log in to the Zoom application. If participants do not have access to wireless internet, the tablet will be equipped with a data package for participant use for the purposes of this study. Participants will also be provided a workbook for skills practice in between workshop sessions. A summary of workshop content is provided in table 1 below. During workshop #2, the study coordinator or trained MAAT-G interventionist will provide patients a link to a Vimeo video. The coordinator will email the link to the patients a couple days before workshop #2. The Vimeo video has been created by the study team and talks patients through how to remain relaxed before stressful events occur. Study patients will be able to access the video without providing any personal information to the website.

MAAT-G workshop content **WORKSHOP VISIT:**	Content/Strategies:
1	1. Introduction to MAAT 2. Self-Awareness and monitoring of memory problems
2	1. Progressive Muscle Relaxation 2. Quick Relaxation
3	1. Self-Instructional Training 2. Verbal and silent rehearsal
4	1. Cognitive restructuring
5	2. Keeping a schedule 3. Memory routines
6	4. External cueing 5. Distraction reduction
7	6. Activity scheduling and pacing 7. Active listening
8	1. Fatigue management 2. Sleep improvement
9	3. Visualization strategies
10	4. Tying it all together

The University Advarra system will be used per WCI policy for study reimbursement for $30 per time point/workshop. The templated RSRB information for Advarra will be used for information for patients

for use of the gift card system. The study team will collect W-9 and send to University Accounts Processing for study payment documentation and sent to accountspayable@finance.rochester.edu. Following this, the participant W-9 will be shredded. W-9 information will not be kept by the study team.

7.5. Quality and Fidelity for MAAT-G:

A clinician manual for MAAT-G has been developed and will be used to standardize interventionalist behavior. Sessions will be audio-recorded and reviewed to ensure intervention fidelity and adherence to clinician manual (with patient's permission).

7.6. Potential risks:

A participant may become more aware of any attention or memory problem they are experiencing as a result of participation in this study, potentially increasing psychological stress. While this is unlikely to provoke significant problems, the PI (Dr. Magnuson) will be available for evaluation and referral to appropriate behavioral care if needed.

Risks to privacy using telehealth and telecommunications are a potential concern. We also recognize that while encryption of videoconferencing makes breeches of private information unlikely, not all risks to privacy can be completely eliminated. We will inform all participants using the telehealth equipment of this.

7.7. Potential benefits:

There may be no direct benefits to participation in this study. However, the study will provide useful information about the feasibility of enrolling and delivering a videoconferencing-based intervention to older cancer survivors with MCI and strategies for helping patients cope with memory and attention problems.

8.0 DATA MANAGEMENT

8.1. Data Handling and Statistical Considerations:

8.1.1. The same protocols and procedures for data quality and control that are readily used for prior studies conducted with the Geriatric Oncology Research Group and currently being overseen by our office. Data will be entered into REDCap (see section 8.3.5 below).

8.1.2. After entering into REDCap, data are audited visually for errors. R, SPSS and SAS will be used for the statistical analyses. Unless otherwise stated, all statistical tests will be performed at the two-tailed 5% level of significance. Likewise, 95% confidence intervals will be constructed for the estimation of effects.

8.1.3. The assumptions underlying all statistical analyses will be thoroughly checked using appropriate graphical and numerical methods.[70,71] In case of violations of distribution assumptions such as normality, appropriate nonparametric methods will be attempted.[72,73] If outliers or influential data are detected, the accuracy of the data will be investigated. If no errors are found, analyses may be repeated after

removing these cases to evaluate their impact on the results. However, the final analyses will include these data points.

8.2. Data Analysis and Sample Size:

Data Analytic Plan: The expanded population for the current amendment (N=35; patients meeting revised eligibility criteria) will be analyzed separately from the 4 patients in the original cohort.

Sample Size Considerations: A sample size of 35 patients will allow for the assessment of feasibility of delivering MAAT-G in this population[57] and also allow for thematic saturation of qualitative interviews. The effect size of MAAT-G in older adults with MCI is not known. MAAT has demonstrated a medium effect size (d = 0.52) on perceived cognition (FACT-Cog) in younger cancer survivors. [57] Using Repeated Measures Analysis of Variance (ANOVA) design and pre-post correlation of 0.5, and 25% attrition, [57] a sample size of n=25 evaluable patients will provide 80% power to detect an effect size of 0.52 at the significance level of 0.10. This sample size is appropriate for preliminary studies and will allow us to conduct Aim 2 analysis and evaluate distribution parameters (mean, standard deviation) of key measures of perceived and objective cognitive function to inform future studies.

Analysis Plan (Second Primary Aim): To evaluate feasibility of enrolling and delivering a videoconferencing-based intervention to older cancer survivors with MCI, we will calculate the proportion of: 1) approached patients who enrolled; 2) identified caregivers who enrolled; 3) enrolled patients who completed all 10 MAAT-G sessions on schedule [e.g. intervention adherence]; and 4) enrolled patients who completed timepoint 2 assessment [e.g. study completion]. We will consider the delivery of the telehealth-based intervention feasible if the following are met: 1) >70% of eligible patients that are approached agree to enroll; 2) >70% of identified potential caregivers agree to enroll; 3) >75% of patients complete the 10 MAAT-G sessions; and 4) >75% of patients complete the timepoint 2 assessment. This analysis on the patients enrolled from this amendment forward (e.g. analysis will only include older cancer survivors with MCI. Mean SUS score will also be calculated for all patients completing TP2 assessment. The SUS ranges 0-100; a score >68 is above average.[68]

Tertiary Objective Analysis Plan: To examine the pre-post change in perceived and objective cognitive function in older cancer survivors with MCI, we will utilize repeated measures ANOVA. Because this is a preliminary analysis with a small sample size primarily focused on feasibility, our goal with the analysis of Aim 2 is to estimate key distribution parameters (mean, median, standard deviation). We will also calculate the SUS (usability) score for each individual patient. The Usability Scale ranges 0-100; a score >68 is above average. [61]

Secondary Aim Analysis plan:

Qualitative Analysis of transcripts from participant/caregiver interviews will be analyzed for themes on barriers and facilitators to intervention participation. Potential themes include relevance of workshop content to older adults, potential barriers to using video-conferencing technology for the target population and mechanisms for minimizing this barrier, and/or the content and formatting of participant workbook to ensure relevance and usability for older adults.

Mixed Methods Integration: Qualitative and quantitative data will be integrated to develop a more complete understanding of the usability of MAAT-G . In addition, it will enhance our understanding of

the participant experience with MAAT-G and help to explore potential benefits beyond what is captured in qualitative tools alone. Data will be organized using MAXQDA joint displays.[74]

8.3. Records to be Kept:

8.3.1. *Data Collection Table:*

	SCHEDULE OF DATA COLLECTION	
FORM	**Baseline**	**Post-Intervention**
On Study Data (Patient and caregiver demographic information and clinical data)	X	
Eligibility confirmation components: **1. UBACC** **2. MOCA, MOCA-Blind, or diagnosis of MCI** **3. ADL**	X	
FACT-COG	X	X
Cognitive Difficulties Scale (CDS)	X	X
COWA	X	X
HVLT-R (two different versions-form 1 and form 2)	X	X
GDS	X	X
GAD-7	X	X
IADL Survey	X	X
SUS (usability measure)		X
Semi-structured interview with patient and caregiver (if enrolled)		X

8.3.2 All hardcopy research records will be stored onsite in the University of Rochester Medical Center, in locked research files at the James P. Wilmot Cancer Center. The Cancer Center is secured with electronic key cards. Offices within the Cancer Center are again secured by key and data is kept in locked file cabinets. Electronic research records are stored on the University of Rochester Medical Center's password secured and firewall protected networks. These are the same methods of security used for patient medical records. All study data will be kept for a period of 10 years after the study and all reports and publications are complete.

8.3.3 All recorded data, such as the audio-recorded interviews/transcripts and the Zoom workshop sessions will be stored on the UR Box drive to assess fidelity of intervention delivery. Within the Box drive, data will be stored in a password protected folder with access restricted to the PI and a subset of

study team members. All personal identifiers will be deleted (e.g. de-identified) from the transcriptions of the audio-recordings. Once data is uploaded to the secure server, the data will be deleted from the audio recorders.

8.3.4. All data collected for the current study will be used in post hoc analyses as appropriate, including exploratory secondary analyses with data collected as described above. Data will not be used for future studies without prior consent of the patient. The patient's individual research record will not be shared with their treating physician, unless they provide consent or the patient's treating physician is a study physician, in which case they will have access to study data as a study co-investigator. Overall study results will be presented to participants, faculty and staff at the University of Rochester Medical Center after completion of the study. Study results will be presented at professional meetings and published.

8.3.5. The study coordinator will assign a numerical study ID to each participant once they have signed the consent form. All study forms and questionnaires will use this number and the participant's first, middle, and last initials as identifiers, to ensure data integrity. Other identifying information will not exist on these forms. A complete list of study participants with study ID, name, and contact information will be maintained separately. This linkage information will only be accessible to the study coordinator, study investigators, and the individuals responsible for maintaining the database.

8.3.6. Additionally, the data can be collected and managed by the research teams at University of Rochester Medical Center using REDCap[167] electronic data capture tools hosted at URMC.

8.3.6a. URMC provides the following information on the **REDCap program: "**Vanderbilt University, in collaboration with a consortium of institutional partners, has developed a software toolset and workflow methodology for electronic collection and management of research and clinical trial data, called REDCap (Research Electronic Data Capture). The REDCap system is a secure, web-based application that is flexible enough to be used for a variety of types of research. It provides an intuitive interface for users to enter data and real time validation rules (with automated data type and range checks) at the time of data entry. REDCap offers easy data manipulation with audit trails and functionality for reporting, monitoring and querying patient records, as well as an automated export mechanism to common statistical packages (SPSS, SAS, Stata, R/S-Plus). Through the REDCap Consortium, Vanderbilt has disseminated REDCap for use around the world. Currently, over 240 academic and non-profit consortium partners on six continents with over 26,000 research end-users use REDCap".

8.3.56. According to the Clinical and Translational Science Institute (CTSI), REDCap is supported with the following means. "The *CTSI Informatics Core*, a unit of the SMD *Academic Information Technology (AIT) Group,* will serve as a central facilitator for data processing and management. REDCap data collection projects rely on a thorough study-specific data dictionary defined in an iterative self-documenting process by all members of the research team, with planning assistance from the *AIT-CTSI Informatics Core*. The iterative development and testing process results in a well-planned data collection strategy for individual studies".

8.3.6c. The CTSI states that regarding security, "REDCap servers are housed in a local data center at the University of Rochester and all web-based information transmission is encrypted. REDCap was developed in a manner consistent with HIPAA security requirements and is recommended to

University of Rochester researchers by the URMC Research Privacy Officer and Office for Human Subject Protection.

9.0 DATA SAFETY AND MONITORING

This protocol should be considered low risk as the intervention is a cognitive behavioral therapy (CBT)-based intervention. CBT- based treatments are utilized in routine clinical care for use with community dwelling older adults. This study is designed to see if MAAT, a CBT-based intervention, is feasible to deliver to older adults cancer survivors with MCI and can improve cognitive outcomes for this population..

9.1. Adverse Event Reporting Requirements:

9.1.1. Adverse events will be reported using the URCC Adverse Event form and/or as required by the Cancer Center Clinical Trials Office.

9.1.2. Adverse events will be reported in accordance with the following guidelines:

	Grade 1	Grade 2			Grade 3				Grade 4		Grade 5	
	Unexpected and Expecte	Unexpected		Expect ed	Unexpected		Expected		Unexpe cted	Expect ed	Unexpect ed	Expect ed
		with hospit	witho ut		with hospi	witho ut	with hospit	witho ut				
Unrelated Unlikel	Not Required	Not Required	Not Required	Not Required	Not Required	Not Required	Not Required	Not Required	10 Calendar Days	Not Required	10 Calendar Days	10 Calendar Days
Possible Probabl	Not Required	10 Calendar	Not Required	Not Required	10 Calendar	10 Calendar	Not Required	Not Required	24-Hour; 5	10 Calendar Days	24-Hour; 5 Calendar	10 Calendar Days

Hospitalization is defined as initial hospitalization or prolongation of hospitalization for ≥ 24 hours, due to adverse event.

9.1.3. Adverse event reports will be submitted in one of the following ways:

(1) By email: (pdf)
(2) By mail:
(3) By fax:

9.1.4. An unexpected adverse event is defined as any adverse experience, the specificity or severity of which is not consistent with the risk information. This is a low risk study as interventions have been shown to improve outcomes of community-dwelling older adults. To reiterate, only adverse events attributed to the behavioral intervention will be captured and reported.

9.1.5. A serious event refers to any event in which the outcome results in any of the following: death, a life-threatening adverse experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability, incapacity, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a

serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. We anticipate that any serious events will be related to standard of care cancer treatment and not due to the MAAT-G intervention, which is designed to improve outcomes and focus on cognitive side effects of cancer treatment. To reiterate, only adverse events attributed to the behavioral intervention will be captured and reported.

9.1.6. Adverse events will be reported in accordance with institutional policies (University of Rochester, Research Subject Review Board, local IRB, URCC CCOP, CTO, and DSMB) as per their requirements.

9.2. Data Safety Monitoring:

9.2.1. All adverse events requiring reporting will be submitted to the current Project Coordinator as described in Section 9.1. Serious adverse event reports will be forwarded to the study chair and the Data Safety and Monitoring Committee (DSMC). Adverse events are entered into a protocol-specific spreadsheet.

9.2.2. Adverse event rates are monitored utilizing the spreadsheet. If a serious adverse event is reported frequently, the study chair will conduct a detailed review. The DSMC Committee Chair will be notified and will determine if further action is required.

9.2.3. The Data Safety Monitoring Committee (DSMC) will review study progress and cumulative reports of adverse events at annual meetings and as needed. An overall assessment of accrual and adverse events will enable the committee members to assess whether significant benefits or risks are occurring that would warrant study closure.

9.2.4. The URCC will notify the other sites immediately of any serious safety concerns identified by the DSMC.

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