Developing a Pain Identification and Communication Toolkit (PICT) for Family Caregivers of Persons with Dementia

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TITLE: Developing a Pain Identification and Communication Toolkit (PICT) for Family Caregivers of Persons with Dementia

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All external collaborators will be consulting on study design and working with completely de-identified data.

1.1 Study Objectives

1.1.1 Objectives

Objective 1: To develop and refine PICT, an intervention to train family caregivers of PWD how to administer an observational pain assessment tool and communicate the results to health care providers.

Objective 2: To evaluate the feasibility and acceptability of the finalized version of PICT among family caregivers of PWD and health care providers

Objective 3: To test the preliminary efficacy of PICT on 1) caregiver ability to identify pain symptoms; and 2) caregiver efficacy in communicating with health care providers

1.1.2 Hypotheses / Research Questions

Hypothesis 1: As this study objective involves intervention development only, no hypotheses are given.

Hypothesis 2a (feasibility): 70% or more of participants will meet the benchmark for feasibility, defined by participant retention and adherence to the intervention.

Hypothesis 2b (acceptability): 70% or more of participants will meet the benchmark for acceptability, defined by participant ratings on questionnaires related to "helpfulness," "future use," and "overall comprehension" of the intervention content.

Hypothesis 3: PICT will be more effective than an attention control for improving caregivers' ability to identify pain in PWD and to initiate pain related-communication with health care providers.

2. Background and Significance

Dementia afflicts more than 5 million older adults (ages 65 and older) in the United States,[1] the majority of whom reside in the community.[2] Up to 60% of affected individuals suffer from pain,[3,4] with similar prevalence estimates across dementia subtypes (e.g., Alzheimer's disease, vascular dementia).[5] Although best practice guidelines have emphasized the importance of routine pain assessment of older persons with dementia (PWD),[6] pain remains severely under-detected and undermanaged in this population.[7,8] Untreated pain has profound effects on individuals' quality of life,[9,10] and is associated with numerous adverse outcomes, including physical impairment,[11] depression,[12,13] social isolation,[14,15] increased health service use,[16] and disruptions to family functioning.[17,18] One of the greatest barriers to detecting and treating pain in PWD is impaired communication.[19] As dementia progresses, the capacity to communicate effectively about one's pain diminishes;[20] individuals may be unable to understand or verbally articulate their discomfort, and instead express their pain through non-verbal behaviors (e.g., facial expressions, agitation).[21] In such cases, self- reports of pain are not feasible and behavioral assessment is recommended.[22,23] Family caregivers (spouses; adult children; other close relatives) are well situated to detect PWD's pain symptoms and communicate those symptoms to health care providers. Nearly 80% of community-dwelling PWD receive help from a caregiver.[24,25] These caregivers are in frequent, if not constant, contact with PWD[26] and are highly involved in their disease management activities.[27,28] Unlike health care providers who are likely to see the patient in a single

context (the treatment visit), caregivers have the opportunity to observe the PWD in diverse situations (e.g., at rest, during transfers, after the administration of pain medication), which is necessary not only for identifying the presence of pain, but also for determining under what circumstances it is likely to occur. Caregivers have frequent opportunities to communicate their observations to providers as companions to PWD at their doctor's visits.[29,30] Indeed, providers commonly turn to family members who are familiar with the patient for help interpreting the patient's pain,[31-33] but caregivers are sometimes reluctant to bring up pain-related concerns with providers.[34,35] While studies indicate that caregivers are fair or poor judges of PWD's pain and disregard non-verbal pain behaviors when unaided by pain assessment tools,[20,36] recent research shows that laypersons (caregivers and non-caregivers) are able to differentiate painful from non-painful experiences effectively when provided standardized tools to facilitate behavioral observation.[37,38] This research has predominantly been conducted in highly controlled experimental settings (observations of video-recorded actors); few studies have investigated how observational tools may be used by caregivers actively caring for PWD's in real-world clinical contexts.[39,40] Further, while research has documented caregivers' frustration regarding pain-related communication with health care providers,[41,42] there exist few interventions to help caregivers of PWD to articulate their pain-related concerns to medical professionals.

3. Study Design and Methods

3.1 Overall Design

This study includes the following phases: 1) intervention manual development; 2) Interviews; 3) field-testing; and 4) pilot randomized trial.

Manual development: The Pain Identification and Communication Toolkit (PICT) will be documented in a manual for health care providers and a workbook for caregivers. The provider manual will provide instruction on using the Pain in Advanced Dementia (PAINAD) assessment tool to detect pain in persons with dementia (PWD) and education on specific strategies to promote effective communication between family caregivers and providers, with an emphasis on fostering culturally competent interactions with PWD and their caregivers. The caregiver workbook will include instructions for how to identify pain symptoms using the PAINAD, information on differentiating between pain and dementia symptoms, strategies for effective communication with health care providers, as well as a Question Prompt List (QPL) to help facilitate action planning and culturally appropriate medical visit interactions. A research team comprised of two geriatricians, a geriatric nurse, a gerontologist, and developmental psychologist with extensive experience in conducting research in area of clinical communication will assemble the initial versions of the provider manual and caregiver workbook.

Interviews: As part of the manual development, interviews will be conducted with family caregivers (n=25) and health care providers (n=20) in-person in private offices at WCMC/NYP or over the telephone. The participant, in special circumstances (e.g. scheduling issues) may opt to have the interview take place in a private location convenient to them. All interviews will be recorded and transcribed by a certified, secure, and WCM-approved transcription agency. Participants will be recruited at WCM/NYP locations including the Center on Aging and Weill Cornell Medical Associates. Participants may also be recruited from WCM/NYP geriatric and palliative care support groups. The primary objectives of the interviews are to: a) adapt the PAINAD for use with caregivers by asking them to comment on its format and content; and b) generate an initial question pool for the Question Prompt List (QPL). The secondary objective of elucidating concerns about using a QPL to

encourage caregivers to ask questions (e.g., increasing visit time) and ways to address those concerns (e.g. instructing caregivers to ask only questions that are of particular concern). The interviews will also address formatting considerations of the caregiver workbook and provider manual (e.g. font size, language that is easy to understand, space for notes). Caregivers will also be asked to fill out a brief questionnaire that will be sent to participants along with the PAINAD tool by email or postal mail, or given to the participant prior to their interview. The questionnaire will include demographics, caregiving role, and patient health questions. Participants will be provided a self-addressed stamped envelope to mail this survey back; or they can use the WCMC secure file transfer to email back the questionnaire.

Field testing. Once initial versions of the PICT manual and workbook are developed, they will be iteratively field-tested and vetted by family caregivers (n=25 per iteration) and health care providers (n=20 per iteration). Participants will be recruited at WCM/NYP locations including the Center on Aging and Weill Cornell Medical Associates. After reviewing the PICT workbook, caregivers will complete a brief questionnaire about the content, format, and perceived utility of PICT, as well as ways to enhance its cultural relevance. They will also complete a brief (15-20 minute) semi-structured interview to clarify their perspectives. Health care providers will answer a similar set of questions. Results from this first field-test will inform the modified version of PICT and will address key issues, such as the feasibility of using research nurses (and other practice staff) to administer the intervention, anticipation of participant burden for caregivers, and adequacy of PICT format and instructions. Study procedures will be repeated (including IRB approval) with a new sample of caregivers (n=25) and providers (n=20). Results from the second field-test will be used to create the finalized intervention of PICT. Prior research indicates that a feasible intervention should be generated after two iterations.

Pilot testing. Family caregivers will be randomly assigned to PICT (n=50) or a control (usual care) condition (n=50).

Participants in both conditions will be asked to complete an identical pre-test questionnaire. The questionnaire will be sent to via email or postal mail, and/or will be scheduled to be completed over the phone. We will ask about the participant's background, caregiving role, and comfort speaking with health care providers. It will take approximately 15-20 minutes to complete.

Intervention condition. Participants in the intervention condition will be contacted by a member of the study team to start the PICT workbook. The PICT workbook consists of four sessions and will be completed over the telephone with a study team member. Sessions are conducted once a week and last approximately 30-60 minutes each. Participants will also be asked to read sections or the PICT workbook and complete exercises between sessions. The reading and exercises will take 10-15 minutes to complete. After the final session of the intervention, a study team member will contact the participant by telephone to complete another set of questionnaires (at 12 weeks after the pre-test questionnaire). The questionnaire will be sent to via email, postal mail, or will be scheduled to be completed over the phone. The post-test questionnaires will take approximately 20 minutes to complete and will ask about the participant's comfort and confidence in communicating with health care providers, behaviors he or she observes in the recipient, and views of the PICT workbook. Participants will also be asked to participate in a 20-30 minute telephone interview to elaborate their responses to the questionnaire. Participants must agree to be audiotaped to participate in the study.

Control condition. Caregivers in the control condition will receive an informational pamphlet about pain in dementia and a link to the Alzheimer's Association website. Twelve weeks after the participant completes the pre-test questionnaire, she or he will be contacted by a member of the study team to complete the post-test questionnaire. The questionnaires will be sent via email, postal mail, or will be scheduled to be completed over the phone and will take approximately 20 minutes to complete.

When caregivers express interest in the study through any recruitment method; they will be called and will be screened for eligibility which includes questions about care hours, length of care, distance, enrolled in hospice, access to internet, and must be cognitively intact (BOMC<=10). Any study data collected for potential participants that do not meet eligibility will be immediately deleted. Informed Consent and HIPAA authorization for caregivers and informed consent for providers will occur in-person at recruitment sites (by paper or REDCap), remotely (by mail, secure file transfer, or REDCap), or just prior to in-person interviews as outlined in the Informed Consent section. These processes will be the same for all phases of the study.

3.2 Interviews, Focus Groups, Surveys, and/or Observations

A. Administration

- *Timing and Frequency*
  - Interview and field-testing phases: Caregiver and healthcare professional subjects will complete a one-time 20-30 minute interview accompanied by a brief questionnaire. Interviews will be conducted by a research nurse or trained co-investigators.
  - Pilot testing phase: PICT will consist of 4 weekly 30-60-minute sessions delivered by a study team member. In between sessions, participants will have 10-15 minutes of reading and exercises to complete.
- *Location*
  Interview and field testing phases will take place in-person in private offices at WCMC/NYP or over the telephone. The participant, in special circumstances (e.g. scheduling issues) may opt to have the interview take place in a private location convenient to them.
  Pilot testing will take place over the telephone.
- *Procedures For Audio And Visual Recording*
  All interviews will be recorded and transcribed by a certified, secure, and WCM-approved transcription agency.
- *Person Identifiers*
  Co-investigators may review EPIC to identify potential participants who meet eligibility. Contact information and appointment information will also be collected for either in-person or letter (postal and email) recruitment. Only data from potential participants will be stored on secure servers. These data will be deleted upon completion of the study or immediately if a patient chooses not to participate in the study.

B. Study Instruments

Interview Phase 1

- Caregiver subjects
  - Screening questions
    - Caregiving questions
    - Brief cognitive screener (BOMC)
  - Brief Questionnaire – Caregiver
    - Demographics
    - Caregiving Questions
    - Patient Health Characteristics
  - Interview Guide – Caregiver
  - Field test questions - Caregiver
- Healthcare Professional subjects
  - Brief Questionnaire – Provider
    - Demographics
    - Medical practice questions
  - Interview Guide – Provider
  - Field test question – Provider

Pilot Test Phase

- Caregiver subjects in PICT (intervention) group
  - Pre-test Questions for All Caregiver Participants
  - Post-test Questions for Caregivers in PICT Group
  - Exit Interview Questions
- Caregiver subjects in control group
  - Pre-test Questions for All Caregiver Participants
  - Post-test Questions for Caregivers in Control Group

4. Study Design

4.1 Study Population

Healthy volunteers that are caregivers and healthcare providers of persons with dementia and pain.

4.2 Inclusion Criteria

Family Caregivers:

1. Age 21 or older
2. English speaking
3. Cognitively intact (BOMC ≤10)
4. Provides at least 8 hours of care per week to a person with dementia who also has a pain diagnosis
5. Has access to the internet

Healthcare professionals:

1. Currently providing clinical services to persons with dementia and/or chronic pain
2. Has provided these clinical services for at least 1 year

4.3 Exclusion Criteria

Family Caregivers:
1. Paid Caregiver
2. Age 20 or younger
3. Non-English speaking
4. Cognitively impaired
5. Does not provide at least 8 hours of care per week to a person with dementia who also has a pain diagnosis
6. Has provided care < 6 months
7. Currently enrolled in hospice
8. The patient to whom the caregiver provides assistance is enrolled in hospice

Healthcare professionals:
1. Not currently providing clinical services to persons with dementia and/or chronic pain
2. Has provided these clinical services for fewer than 1 year

4.4 Strategies for Recruitment and Retention
Overview of Caregiver Recruitment Procedures

Co-investigators will meet with health care providers who see patients at the Center on Aging, the Alzheimer's Disease and Memory Disorders Program, and Weill Cornell Internal Medical Associates to make them aware of the study protocol, including the plan to send recruitment letters (postal mail or email) to their patients' caregivers. During the meetings, the co-investigators will ask each provider to review his or her patient list and identify individuals who have both pain and dementia, as well as a family caregiver. When meeting with these healthcare providers, co-investigators will verify that the caregiver lives with the patient and/or obtain the caregiver contact information from the providers. Recruitment letters will then be sent by mail or email (when available) to the caregivers of the identified patients. Patients themselves will not be contacted, and every effort will be made to contact the caregiver directly. When possible, letters will be sent to the emergency contact (i.e., caregiver) if their telephone matches that of the patient, or by email. The recruitment letter will describe the study and advise caregivers that they may decline participation by emailing or placing a telephone call to the study team. Approximately 2 weeks after the initial letter (postal mail or email) is sent, caregivers who have not opted out will be telephoned or emailed by the trained co-investigator to confirm their interest.

For caregivers that care for a patient at recruitment sites, patients' medical records will first be reviewed by a trained co-investigator who will confirm whether or not they meet eligibility criteria (dementia and pain diagnosis). Recruitment site caregivers will be approached in the waiting room prior to their doctor's visit. The co-investigator will perform the consenting process either in the waiting room or a private office, if available.

Other caregivers will be recruited via caregiving resources and groups in the community including the WCM/NYP Geriatrics caregiver support groups, local community centers, senior service agencies, etc. Interested individuals will provide their name and contact details on a sign-up sheet.

Trained co-investigators will use the caregivers' preferred method of contact to inform them about the study (phone or email). The procedure outlined above (i.e., co-investigator mails/emails the consent form in advance and requests the signed consent form back prior to conducting the interview) will then be followed. If time allows, co-investigators may choose to have participants consent in-person at recruitment sites, and in that case, they will also be given the first survey to mail back at their convenience after consent is obtained.

Caregivers may also contact the study team to participate after seeing a recruitment flyer. The Guthrie Clinic also has agreed to be a recruitment site. They will be limited to posting and handing out WCM flyers to potential participants.

Additional efforts will rely on making study information available on online platforms. Online platforms may include, but are not limited to: caregiver/dementia interest pages on Facebook, participant registries, online bulletin boards, mobile apps and websites, etc. Methods include, but are not limited to: posting flyers, posting messages describing the project and inviting interested participants to contact study members (see "Social Media Posting" document), including study information in e-newsletters, etc. Permission from group administrators will be received prior to posting on any social media group platform. In addition, ResearchMatch.org will be added as a recruitment method.

Additionally, snowball recruitment method will be used to ask potential participants to share study information with other caregivers who may be interested in the study.

Trained co-investigators will use the caregivers' preferred method of contact to inform them about the study (phone or email). The procedure outlined above (i.e., co-investigator mails/emails the consent form in advance and requests the signed consent form back prior to conducting the interview or REDCap consent) will then be followed.

Interview and field testing phases: Caregiver participants will be compensated $15 after completing the study interview in the form of a ClinCard.

Pilot testing phase: Participants will be compensated $10 after completing the pre-test questionnaires and $30 after completing the post-test questionnaires. Participants in the PICT (intervention) condition will also receive $10 after each of the 4 sessions. Compensation will be paid in the form of a ClinCard.

Overview of Health Care Provider Recruitment Procedures
Health care providers will be informed of the opportunity to participate in the brief questionnaire and interview during practice site meetings and/or one-on-one conversations about the project.

5. Registration Procedures

5.1 Subject Registration (WCM only)

Subjects will be registered within the WRG-CT as per the standard operating procedure for Subject Registration.

5.2 Subject Registration (Sub-sites)

N/A

6. Study Procedures

6.1 Schedule of Assessments

Table 1. Schedule of trial events for interview and field testing phases

	Pre-study	Visit 1 (Interview)
Screening	X	
Informed Consent	X	X
Demographics and Questionnaire		X
Semi-structured Interview		X

Table 2. Schedule of trial events for the pilot test phase

	Pre-study	Week 1	Week 2	Week 3	Week 4	Post-study
Screening	X					
Informed Consent	X					
Demographics and Pre-test Questions		X				
Weekly Session *		X	X	X	X	
In-home reading *		X	X	X	X	
Post-test Questions						X
Exit Interview *						X

** denotes intervention participants only*

7.0 Data Reporting / Regulatory Considerations

7.1 Data Collection

The data collection plan for this study is to utilize REDCap to capture all treatment, toxicity, efficacy, and adverse event data for all enrolled subjects.

7.1.1 REDCap

REDCap (Research Electronic Data Capture) is a free data management software system that is fully supported by the Weill-Cornell Medical Center CTSC. It is a tool for the creation of customized, secure data management systems that include Web-based data-entry forms, reporting tools, and a full array of security features including user and group based privileges, authentication using institution LDAP system, with a full audit trail of data manipulation and export procedures. REDCap is maintained on CTSC-owned servers that are backed up nightly and support encrypted (SSL-based) connections. Nationally, the software is developed, enhanced and supported through a multi-institutional consortium led by the Vanderbilt University CTSA.

7.2 Regulatory Considerations

7.2.1 Institutional Review Board/Ethics Committee Approval

As required by local regulations, the Investigator will ensure all legal aspects are covered, and approval of the appropriate regulatory bodies obtained, before study initiation.

Before initiation of the study at each study center, the protocol, the ICF, other written material given to the patients, and any other relevant study documentation will be submitted to the appropriate Ethics Committee. Written approval of the study and all relevant study information must be obtained before the study center can be initiated or the IP is released to the Investigator. Any necessary extensions or renewals of IEC/IRB approval must be obtained for changes to the study, such as amendments to the protocol, the ICF, or other study documentation. The written approval of the IEC/IRB together with the approved ICF must be filed in the study files.

The Investigator will report promptly to the IEC/IRB any new information that may adversely affect the safety of the subjects or the conduct of the study. The Investigator will submit written summaries of the study status to the IEC/IRB as required. On completion of the study, the IEC/IRB will be notified that the study has ended.

Neither the Investigator nor BMS will modify or alter this protocol without the agreement of the other. All agreed protocol amendments will be clearly recorded on a protocol amendment form and will be signed and dated by the original protocol approving signatories. All protocol amendments will be submitted to the relevant institutional IEC/IRB for approval before implementation, as required by local regulations. The only exception will be when the amendment is necessary to eliminate an immediate hazard to the trial participants. In this case, the necessary action will be taken first, with the relevant protocol amendment following shortly thereafter.

Once protocol amendments or consent form modifications are implemented at the lead site, Weill Cornell Medicine, updated documents will be provided to participating sites. Weill Cornell Medicine must approve all consent form changes prior to local IRB submission.

Relevant study documentation will be submitted to the regulatory authorities of the participating countries, according to local/national requirements, for review and approval before the beginning of the study. On completion of the study, the regulatory authorities will be notified that the study has ended.

7.2.2 Ethical Conduct of the Study

The Investigators and all parties involved should conduct this study in adherence to the ethical principles based on the Declaration of Helsinki, GCP, ICH guidelines and the applicable national and local laws and regulatory requirements.

This study will be conducted under a protocol reviewed and approved by the applicable ethics committees and investigations will be undertaken by scientifically and medically qualified persons, where the benefits of the study are in proportion to the risks.

7.2.3 Informed Consent

A co-investigator or qualified designee must obtain documented consent according to ICH-GCP and local regulations, as applicable, from each potential subject or each subject's legally authorized representative prior to participating in the research study. Subjects who agree to participate will receive an oral consent document prior to speaking to a co-investigator.

Informed Consent will occur prior to their pre-test questionnaire, by oral consent for participants until virtual consent methods are approved by the WCM IRB. For oral consent, a member of the study team will review the ICF in-full (see Oral Consent Script attachment) by phone, allowing for questions and reminding the potential subject that participation is voluntary. Oral confirmation of consent to participate will be documented by the study team member.

Once virtual consent processes are established with the JCTO, we will submit an amendment with the IRB to conform to these new policies. We feel that with our older adult population, at a higher risk to COVID-19, that this is best practices in human subjects for participants not to leave their home in order to participate in this study. REDCap consent documents were previous approved in an earlier amendment and we are prepared to use these methods accompanied by a phone discussion as stated above for oral consent.

The initial ICF, any subsequent revised written ICF and any written information provided to the subject must approved by IRB prior to use. The ICF will adhere to IRB/IEC requirements, applicable laws and regulations.

7.2.4 Compliance with Trial Registration and Results Posting Requirements

Under the terms of the Food and Drug Administration Modernization Act (FDAMA) and the Food and Drug Administration Amendments Act (FDAAA), the Sponsor-Investigator of the trial is solely responsible for determining whether the trial and its results are subject to the requirements forsubmission to http://www.clinicaltrials.gov. Information posted will allow subjects to identify potentially appropriate trials for their disease conditions and pursue participation by calling a central contact number for further information on appropriate trial locations and trial site contact information.

7.2.5 Record Retention

Essential documents are those documents that individually and collectively permit evaluation of the study and quality of the data produced. After completion of the study, all documents and data relating to the study will be kept in an orderly manner by the Investigator in a secure studyfile. Essential documents should be retained for 2 years after the final marketing approval in an ICH region or for at least 2 years since the discontinuation of clinical development of the IP. In addition, all subject medical records and other source documentation will be kept for the maximum time permitted by the hospital, institution, or medical practice.

8. Statistical Considerations

Interviews: Interview transcripts will be analyzed according to the constant comparative method, in which new concepts are compared to existing codes (labels that catalog key concepts), existing codes are refined, and a coding structure is developed in stages. This process will continue until theoretical saturation is reached - the point at which no new information is generated from additional interviews.

Pilot testing: statistical considerations. Feasibility will be examined in terms of rates of recruitment and number of sessions completed by participants in the intervention condition. Preliminary analyses to compare the intervention vs. control group on PWD and caregiver sociodemographic characteristics will be carried out in linear models (for continuous variables) and logistic-linear models (for categorical variables). The effectiveness of the intervention will be evaluated in a statistical model that includes treatment (control vs. intervention) and time of assessment (baseline vs. 4 weeks post intervention) as fixed classification factors; the interaction of treatment and time; covariates such as age and gender; and family caregivers (30 per treatment group) as levels of a random classification factor. The primary dependent variable (caregiver contacts primary care practice) is dichotomous, and analysis is by a logistic-linear mixed model with binomial error. Self-efficacy will be included in the model as a fixed classification factor (categorized in 2 levels) as will its interaction with treatment and time. Interactions with other key sociodemographic and clinical variables will also be examined.

9. Adverse Event Reporting Requirements

Adverse event (AE) monitoring and reporting is a routine part of clinical research. Safety is monitored by evaluation of adverse events reported by subjects or observed by investigators or research staff, as well as by other investigations such as clinical laboratory tests, x-rays, electrocardiographs, etc.

9.1 Adverse Event Definition

An adverse event (also referred to as an adverse experience) can be any unfavorable and unintended sign (e.g., an abnormal laboratory finding), symptom, or disease temporally associated with the use of a drug, and does not imply any judgment about causality. An adverse event can arise with any use of the drug (e.g., off-label use, use in combination with another drug) and with any route of administration, formulation, or dose, including an overdose.

9.1.1 Adverse Event Characteristics and Related Attributions

CTCAE term (AE description) and grade: The descriptions and grading scales found in the revised NCI Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 will be utilized for AE reporting. A copy of the CTCAE version 4.0 can be downloaded from the CTEP web site (http://ctep.cancer.gov).

- Attribution of the AE:
  - Definite – The AE *is clearly related* to the study treatment.
  - Probable – The AE *is likely related* to the study treatment.
  - Possible – The AE *may be related* to the study treatment.
  - Unlikely – The AE *is doubtfully related* to the study treatment.
  - Unrelated – The AE *is clearly NOT related* to the study treatment.

9.1.2 Recording of Adverse Events

All adverse events will be recorded on a subject specific AE log. The AE log will be maintained by the research staff and kept in the subject's research chart.

9.1.3 Reporting of AE to WCM IRB

All AEs occurring on this study will be reported to the IRB according to the IRB policy, which can be accessed via the following link: http://researchintegrity.weill.cornell.edu/forms_and_policies/forms/Immediate_Reporting_Policy.pdf.

9.1.4 Reporting Events to Participants
Not applicable

9.1.5 Events of Special Interest
Not applicable

9.1.6 Reporting of Pregnancy
Not applicable

10. Unanticipated Problems Involving Risks to Subjects or *Others*
Not applicable

10.1 Definition of Unanticipated Problems Involving Risks to Subjects or Others (UPIRTSO)
Not applicable

10.1.1 Unanticipated Problem Reporting
Not applicable

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