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SUMMARY STATEMENT
(Privileged Communication)

Release Date: 06/24/2011

Application Number: 1R01NR012757-01A1

Principal Investigators (Listed Alphabetically):
GREEN, MICHAEL J. MD (Contact)
LEVI, BENJAMIN H.

Applicant Organization: PENNSYLVANIA STATE UNIV HERSHEY MED CTR

Review Group: NRCS
Nursing and Related Clinical Sciences Study Section

Meeting Date: 06/07/2011
Council: OCT 2011
Requested Start: 12/01/2011

RFA/PA: PA09-122
PCC: DCGNA
Dual PCC: 2MBB
Dual IC(s): CA

Project Title: Preparing Family Caregivers of Very Ill Patients for End-of-Life Decision Making

SRG Action: Impact/Priority Score: 25
Percentile: 11

Human Subjects: 30-Human subjects involved - Certified, no SRG concerns
Animal Subjects: 10-No live vertebrate animals involved for competing appl.
Gender: 1A-Both genders, scientifically acceptable
Minority: 1A-Minorities and non-minorities, scientifically acceptable
Children: 1A-Both Children and Adults, scientifically acceptable
Clinical Research - not NIH-defined Phase III Trial

END:
RESUME AND SUMMARY OF DISCUSSION: This highly significant study addresses the burden in family caregivers to make advanced care decision for patients with life threatening illnesses. The study will evaluate different modes of experiences and preparedness of family caregivers as surrogate decision makers in a controlled randomized trial intervention. If successful the study can be used widely in surrogate decision making for advanced care planning and is likely to reduce stress and burden currently experienced by this population group. During the discussion the reviewers noted a strong team with many years of experience in advanced care planning but previous collaboration is not clear. The strategy is innovative and the preliminary finding significant. Minor weaknesses for the reviewers were in the measurement scale that only includes conscious patients; lack of expertise in qualitative analysis; and poor time allocation for investigators involved in recruitment roles. Overall the strengths outweigh the weaknesses of this application.

DESCRIPTION (provided by applicant): Surrogate decision-making by family caregivers is highly stressful and emotionally burdensome, in part because caregivers often feel unprepared to make surrogate decisions. It is not known which advance care planning (ACP) process best prepares caregivers for this role. The main purpose of this study is to evaluate whether family caregivers of patients with life-threatening illnesses are better prepared and have better experiences with surrogate decision-making: 1) when they engage in a structured ACP process together with patients (versus when patients engage in ACP alone); and 2) when they use an online decision aid for ACP (versus using standard ACP). In doing so, we will also examine: 3) interactions between these factors. Using a 2 x 2 factorial design, 200 patient/family-caregiver dyads will be enrolled in a randomized, controlled trial, and assigned to 1 of 4 groups: Group 1: Standard ACP Alone, where the patient (but not family caregiver) uses standard ACP materials to engage in ACP; Group 2: Decision Aid Alone, where the patient (but not family caregiver) uses the decision aid to engage in ACP; Group 3: Standard ACP Together, where the patient and family caregiver use standard ACP materials together; and Group 4: Decision Aid Together, where the patient and family caregiver use the decision aid together. There will be 3 study visits: Visit 1, where patients (+/- family caregivers) engage in ACP using either standard materials or the decision aid; Visit 2, where patients and family caregivers independently complete hypothetical vignettes and then caregivers are interviewed; and Visit 3, where family caregivers (but not patients) are interviewed about their experience with, and sense of preparation for, surrogate decision-making. We hypothesize that engaging in ACP Together (patient + family caregiver) will be superior to patients engaging in ACP Alone, and that using the online Decision Aid will be superior to using Standard ACP. We further anticipate that engaging in ACP Together using the Decision Aid (Group 4) will be superior to the other 3 groups with regard to family caregiver: 1) self-efficacy; 2) knowledge; 3) depth of communication about ACP; 4) agreement between their decisions on the vignettes and patients' decisions; 5) understanding of how surrogate decisions should be made; and 6) satisfaction with the ACP process. We also expect that compared to Groups 1-3, family caregivers in Group 4 will report: 7) less distress; 8) less decisional conflict; 9) greater satisfaction with decisions; and 10) better experiences with surrogate decision-making. Achieving our study aims will determine whether family caregivers who use an online decision aid to engage in ACP Together with patients who have life-threatening illnesses are better prepared and have better experiences with surrogate decision-making. If the answer is yes, as we anticipate, this research has the potential to address a critical public health concern by establishing a readily accessible, reliable, and cost-effective mechanism for family caregivers and patients to engage in advance care planning that works.

PUBLIC HEALTH RELEVANCE: If the aims of this project are achieved, we will have shown that an advance care planning intervention can decrease the considerable distress experienced by family caregivers who serve as surrogate decision-makers for their seriously-ill loved ones. Furthermore, we will have identified a practical, exportable strategy for helping millions of caregivers prepare for their roles as surrogate decision-makers.
CRITIQUE 1:

Significance: 3  
Investigator(s): 2  
Innovation: 1  
Approach: 4  
Environment: 1  

**Overall Impact:** This application has potential to significantly affect ACP involvement by surrogate decision makers. It is innovative and has an excellent team, although reallocation of time commitments could strengthen the team. The methods proposed are generally quite good with the exception of using shared decision making rather than surrogate decision making as the event to be assessed. The environments proposed are excellent.

1. Significance:

   **Strengths**
   
   - Difficulties for surrogate decision makers are well documented in the literature. An intervention that does not require time from clinicians would be cost-effective if it is successful.

   **Weaknesses**
   
   - Given the stress placed on surrogate decision making when patients are incapacitated in this study, the decision to define "engaging in decision-making on behalf of the patient" as including shared decision making when the patient has capacity is a single moderate weakness. This is particularly true as the primary outcome instrument is a scale for unconscious patients.

2. Investigator(s):
3. Innovation:

Strengths
- Web-based interventions to support surrogates are not particularly innovative, but the approach here to allow multiple comparisons and across different diagnoses, geography, and ethnicity/race is innovative.
- The interactive nature of the decision aid, with audio and video clips, is innovative.

Weaknesses
- None noted

4. Approach:

Strengths
- The use of 4 groups will allow for comparisons of alone vs. together and good standard ACP vs. the decision aid.
- The use of MAUT and self-efficacy as conceptual frameworks is a strength.
- It is admirable to plan to interview caregivers after an experience of decision making.
- The definition of caregiver to include close friends and the explanation for how the decision maker from whom data are collected can confer with others represent good decisions.
- The inclusion of patients’ prior completion of an advance directive as well as diagnosis, race/ethnicity, and study site is a strength to the quantitative analysis.
- The qualitative analyses are more clearly described in this submission.

Weaknesses
- Given the stress placed on surrogate decision making when patients are incapacitated in this study, the decision to define “engaging in decision-making on behalf of the patient” as including shared decision making when the patient has capacity is a single moderate weakness. This is particularly true as the primary outcome instrument is a scale for unconscious patients.
- On page 103 the applicants note that they have enrolled 9% of referred patients, yet they anticipate enrolling 17% without an explanation of the difference.

5. Environment:

Strengths
- Access to clinical sites is excellent, evidenced by co-Is with recruitment responsibilities and letters of support.
- Research support in both sites is good.
- The Boston site allows recruitment of minority participants.

Weaknesses
- None noted.
Protocols for Human Subjects:
Acceptable Risks and/or Adequate Protections
- Risks and protections are well presented.

Data and Safety Monitoring Plan (Applicable for Clinical Trials Only):
Acceptable
- An excellent plan is described.

Inclusion of Women, Minorities and Children:
G1A - Both Genders, Acceptable
M1A - Minority and Non-minority, Acceptable
C3A - No Children Included, Acceptable
- Appropriate plans are in place for recruitment of women and minorities.
- Children are appropriately excluded
- Although all outcomes are measured for caregivers, patients are also included in the intervention and data collection. There should be an enrollment table for patients, not just for caregivers, for a total of 400 participants.

Vertebrate Animals:
Not Applicable (No Vertebrate Animals)

Biohazards:
Not Applicable (No Biohazards)

Resubmission:
- The applicants have been extremely responsive to the prior critique, in amazing detail in the space allowed.

Budget and Period of Support:
Recommended budget modifications or possible overlap identified:
- It would seem beneficial to the study science to increase time for Dr. Penrod and decrease allocations for Drs. Farace, Almokadem, and Schubart.

CRITIQUE 2:
Significance: 2
Investigator(s): 2
Innovation: 2
Approach: 2
Environment: 1
Overall Impact: The highly qualified and productive investigative team proposes a well-designed randomized trial to test their computer aided advance care planning (ACP) program with patients or with patients and family members together compared to standard advance care planning tool with patients alone or with patients and family together. The problem is highly significant and if successful, the intervention holds tremendous promise to improve advance care planning. The application includes several innovative components. The study design and methods are strong. The analysis plan is underdeveloped for the secondary aims but clearly describes plans for using findings from the mixed methods approach to make meaning of results. Despite a few minor flaws, the applications strengths outweigh the weaknesses.

1. Significance:

Strengths
- The focus on ACP for patients with stage 4 lung cancer, advanced pulmonary or cardiac disease is highly significant.

Weaknesses
- None noted.

2. Investigator(s):

Strengths

3. Innovation:

Strengths
- The factorial design with patient and patient together with family caregivers who would serve as surrogate decision makers is innovative for palliative care research.
- Measures of both self efficacy and concordance of decisions on vignettes is also innovative for palliative care research.

Weaknesses
- None noted.

4. Approach:

Strengths
- Application builds logically on the MPIs early ACP intervention research.
- Strong research design, measures, and analysis plan for the primary aim.
- Thoughtful approach to ACP intervention and active control condition.

Weaknesses
• It is not clear from the application if the randomization plan will balance groups a specified periods to prevent long runs to one of the groups, which is possible without a permuted block randomization plan.
• Lack of measurement of patient-family discussion about ACP reduces the likelihood of using this variable as a process variable that could have explanatory power.
• It is not clear from the application how fidelity of the interventions are documented and used in the analysis.
• Rationale for the 3 group analysis model excluding group 4 (Aid/Together) is not clear given study aims.
• It is not clear from the analysis that the study is powered sufficiently for the secondary aims.

5. Environment:
Strengths
• Research and clinical resources and facilities to support the research are strong at the two data collection sites.

Weaknesses
• None noted.

Protocols for Human Subjects:
Acceptable Risks and/or Adequate Protections
• Well crafted human subjects section with adequate protections.

Data and Safety Monitoring Plan (Applicable for Clinical Trials Only):
  Acceptable
  • Outstanding data and safety monitoring plan.

Inclusion of Women, Minorities and Children:
G1A - Both Genders, Acceptable
M1A - Minority and Non-minority, Acceptable
C1A - Children and Adults, Acceptable
  • Protections are adequate.

Vertebrate Animals:
Not Applicable (No Vertebrate Animals)

Biohazards:
Not Applicable (No Biohazards)

Resubmission:
• The investigators were responsive to the prior review. The changes strengthen the application.
Budget and Period of Support:
Recommended budget modifications or possible overlap identified:

Budget is adequately justified. It is not clear if GCRC is a CTSA supported resource, but even if it is not, it seems inappropriate to change facilities fee to use space when ICR rate should cover it.

Additional Comments to Applicant (Optional):

- The investigators may want to reconsider use of the Beck Depression Scale because of it's confound with cancer symptoms which can overestimate the depression.

CRITIQUE 3:

Significance: 2
Investigator(s): 1
Innovation: 2
Approach: 2
Environment: 1

Overall Impact: The proposed investigation has the potential to have a significant influence on the field of advance care planning and advance care planning research. It addresses an important and understudied issue, preparing surrogate decision makers for the surrogate decision making role. The investigators are highly qualified and the research and clinical environments are excellent. Concerns about innovation and approach are minor.

1. Significance:
Strengths

- Surrogate decision making is often necessary near the end of life. This process is often quite stressful for surrogate decision makers, who are often family caregivers. While there has been a fair amount of work in enhancing the advance care planning process, little attention has been pain to preparing the surrogate decision maker for the process of surrogate decision making. An intervention that facilitates the surrogate decision making process, decreasing the stress and burden of surrogate decision making, enhancing the experience for the patient and, ideally, enhancing the likelihood that the patient will receive care congruent with his/her expressed wishes.

Weaknesses

- None identified.

2. Investigator(s):
None identified.

3. Innovation:
Strengths
- Decision aid utilizes multi-attribute theory to translate individuals' values and goals into a medical decision.
- Decision aid will be easily disseminated, should it be shown to achieve the goals of enhancing advance care planning.

Weaknesses
- There are other existing web-based, print and DVD-based advance care planning aids that have been demonstrated to enhance patient decision making around end-of-life issues (e.g. work done by Angelo Volandes).

4. Approach:
Strengths
- Clearly stated aims and hypotheses. The addition of Aim 3 is a particular strength as it allows teasing out the effect of the decision aid vs. the patient and caregiver doing advance care planning together.
- Builds on the investigators' prior funded investigations.
- Relevant conceptual framework.
- Recruitment goals are feasible and realistic.
- Data collection is well-described.
- Analyses clearly described.

Weaknesses
- The proposed approach will not evaluate the combination of standard ACP + the decision aid. It is possible that, for example, initially completing the decision aid may prepare the surrogate and/or patient to then have an effective advance care planning discussion with their health care provider.
- Is there a potential need to provide a “booster” exposure if there is a long interval between the initial intervention and the surrogate decision making event?

5. Environment:
Strengths
- Excellent study environment with both outstanding research resources and clinical setting, with particular attention paid to enhancing minority recruitment.

Weaknesses
- None identified.

Protections for Human Subjects:
Acceptable Risks and/or Adequate Protections
Data and Safety Monitoring Plan (Applicable for Clinical Trials Only):
Inclusion of Women, Minorities and Children:
G1A - Both Genders, Acceptable
M1A - Minority and Non-minority, Acceptable
C1A - Children and Adults, Acceptable

Vertebrate Animals:
Not Applicable (No Vertebrate Animals)

Biohazards:
Not Applicable (No Biohazards)

Resubmission:
- The investigators have adequately addressed the prior reviewers' comments.

Budget and Period of Support:
Recommend as Requested

THE FOLLOWING RESUME SECTIONS WERE PREPARED BY THE SCIENTIFIC REVIEW OFFICER TO SUMMARIZE THE OUTCOME OF DISCUSSIONS OF THE REVIEW COMMITTEE ON THE FOLLOWING ISSUES:

PROTECTION OF HUMAN SUBJECTS (Resume): ACCEPTABLE

INCLUSION OF WOMEN PLAN (Resume): ACCEPTABLE

INCLUSION OF MINORITIES PLAN (Resume): ACCEPTABLE

INCLUSION OF CHILDREN PLAN (Resume): ACCEPTABLE

COMMITTEE BUDGET RECOMMENDATIONS: The budget was recommended as requested.

NIH has modified its policy regarding the receipt of resubmissions (amended applications). See Guide Notice NOT-OD-10-080 at http://grants.nih.gov/grants/guide/notice-files/not-od-10-080.html. The impact/priority score is calculated after discussion of an application by averaging the overall scores (1-9) given by all voting reviewers on the committee and multiplying by 10. The criterion scores are submitted prior to the meeting by the individual reviewers assigned to an application, and are not discussed specifically at the review meeting or calculated into the overall impact score. For details on the review process, see http://grants.nih.gov/grants/peer_review_process.htm#scoring.