REPRODUCIBILITY AND TRANSPARENCY OF RESEARCH

Replication of Research Findings
The PI is familiar with reporting requirements of federally funded research. In order to ensure that other groups can replicate our research, several strategies will be employed.

Progress Reports:
• **Annual progress reports**, following annual Advisory Board meetings, will be composed by the study PI. These will follow PCORI recommended formatting.

• Within 3 months of the end of the 3-year study period, we will generate a **complete study report**. This will include detailed description of the final study design and procedures, a description of the primary and secondary hypotheses that we tested, final sources and methods used for determining exposure, outcomes and all potential covariates used in the analyses, final copies of all relevant documents for the study (e.g. survey materials, interview guides, questionnaires, etc.), an explanation of power calculations used for determining the sample size (including any post-hoc calculations for exploratory stratified analyses), a detailed explanation of the statistical analyses used, final programming code used to create all variables, to define the final study population and for conducting all analyses, and a detailed data dictionary.

In addition to providing these reports to PCORI, the report will also be made freely available to any researcher who requests them and to the Advisory Board (as well as being posted on the related website, described above and below). We will also reference these reports and their availability in any conference presentations or peer manuscripts arising from the study.

**ClinicalTrials.gov Registration:**
This study will be registered on ClinicalTrials.gov. We will update the registration as per this website’s procedures (e.g. when the study changes from “planned” to “recruiting” to “closed for recruiting”). Registration will preclude any study procedures. As they become available, we will update the project’s registration to reflect the availability of the annual progress reports describing the study procedures.
PROTECTION OF HUMAN SUBJECTS

Risks to Human Subjects

Human Subjects Involvement, Characteristics, and Design:

Sites to be included are the following:

Each site has its own Institutional Review Board (IRB) that will oversee the study. At each site, patients will be consented, enrolled and followed over time using the procedures described below. The role of the site-PI at each site is to oversee the process of patient and caregiver recruitment and enrollment, assure that all rules regulating human subject research are followed, and to remain in contact and work with the PIs to assure efficient and ethical conduct of the research plan. Training of the coordinators, research assistants, and other stakeholders directly involved in the conduct of the study is discussed below.

Adequacy of Protection Against Risks

Protections Against Risk: All of the hospitals have their own IRB. We will seek approval of the project from the Colorado Multiple Institutional Review Board (COMIRB), and then the site-PIs will work with the core investigator team to obtain IRB approval for the project at each site. All IRB concerns will be addressed prior to enrollment of study subjects at any one site. The PI will obtain and have on file a written assurance from each site that risks to human subjects, and protection against these risks, are addressed at a level equal to or higher than that described in the current proposal.

Patients and Caregivers. As noted above, there are few risks to the patient or caregiver for the proposed study, and these risks relate primarily to the psychological nature of discussing the patient’s serious illness. The coordinators (or research assistants) will stop any data collection where the caregiver or patient appears to become emotionally upset, and all patients/caregivers will also be told they can terminate study participation at any point. A protocol for addressing extreme emotional reactions will be in place should such a situation arise.

Clinicians. There are limited risks to site personnel who provide their demographic and training information to the researchers. If a clinician objects to providing any of the information requested, she/he may refuse. Likewise a clinician who gives consent at one point for his/her data to be collected may at any time rescind that permission and information will be expunged from the database. For the qualitative interviews, clinicians will be providing information about their experiences and comfort with the intervention. Clinicians will thus be able to “self-censor” and not provide any data that they do not wish to reveal. In addition, when the audio-tapes are transcribed, the PI will remove any potentially identifying information to assure that the data are anonymous. Clinicians will be instructed not to reveal any identifying information about any patients during the course of the interviews, and if they do so mistakenly, this information will be deleted from the transcripts.

Data Safety. Data collection and storage has been planned where it is improbable that participant confidentiality will be breached. All patients will be given a unique identification number, and only one master list linking the names to patient identification at each site will be maintained at the University of Colorado. Only the blinded Lead Research Assistant will have access to this list. Each site will also have a list of locally enrolled patients, and this list will be used by the site-PI and lead coordinator at each site to determine issues related to patient follow up. All lists linking patient identification to patient identifying information will be kept in
double-locked locations (e.g. locked filing cabinet in locked office). These identification numbers will be used for data collection, data tracking, and data entry, so the secure aggregated database will not actually have any patient identifiers in it. Likewise, all clinicians will be given a unique identification number, and the lists linking this identification number to the clinician’s identity will be stored in a double-locked location. (Each site will keep their own clinician list; there will be no master list linking clinician identification to identifying information for qualitative analysis). Each site will maintain their own consent forms in a double-locked location as well.

All data transmitted to the coordinating center will be via a secure virtual private network (VPN) that is currently an option for University of Colorado Denver email correspondence. While we do not anticipate that any data will need to be sent in hard copy, if this becomes the case, all data will be sent via a secure fax line to which only the project manager at University of Colorado has access. This will not only reduce errors in the recording of the data, but also assure that there are no paper copies of forms that might pose a risk to patient or caregiver privacy. All reporting and/or publication of data will be in aggregate form. All additional protection of participant confidentiality mandated by the Heath Insurance Portability and Accountability Act (HIPAA) and local IRBs will be strictly followed. Additionally, we will observe the following data safeguarding procedures: 1) training staff at all sites on data sensitivity and data safeguards being employed to assure confidentiality; 2) storing and processing sensitive (although expunged of identifiers) hardcopy of any data or printouts in a centralized location; 3) securing sensitive hardcopy in locked files; 4) destroying all identifiable linkages to data after data accuracy has been verified and final analyses have been computed, and 5) protecting the database by encrypted password. All research instruments and electronic databases will be stripped of all identifying information (name, address, social security number, patient identification/medical record number, etc.). The core investigator team will be making site visits throughout the project, and during these visits will audit to make sure that each facility is in compliance with all rules and regulations relating to human subject research.

Data and Safety Monitoring Plan: The PI, in cooperation with the core investigator team and COMIRB, will monitor the safety of the implemented project. We have assembled a panel of clinicians who are experts in DT LVAD, communication, decision making, and palliative care. Many of these individuals have been involved in prior clinical studies of interventions to improve quality of care. As per COMIRB Recommendations and Policies Manual, all serious adverse events (SAEs), regardless of treatment group or relationship to the research, will be reported to the IRB within 24-hours in a full written report. Similar procedures will be carried out at each individual institution in accordance with their local IRB policy. SAEs will also be reported annually in the IRB application for continuation or termination of the research. All expected non-serious adverse events that occur at a greater frequency or severity than anticipated and all unexpected non-serious adverse events will be reported to the IRB within 15 working days and summarized annually in the IRB application for continuation or termination of the research. All expected adverse events will be reported annually to the IRB in the application for continuation or termination. The PI and co-investigators are versed in these reporting procedures as they are currently required for all research. All investigators and staff involved in this project have completed an extensive course and passed a certifying exam on the protection of human subjects in research. All of the site-PIs and coordinators will complete training at their local institutions to assure compliance with their local IRBs (most have done so already). In addition, patient and caregiver leads will complete appropriate coursework through COMIRB.

In accordance with PCORI policy regarding Data and Safety Monitoring we will establish a data and safety monitoring plan (DSMP) for this multi-site clinical trial. This 5-member board will be appointed in conjunction with and after consultation with the program officer at PCORI. The role of the DSMP and board is to oversee the trial, assess its interim outcomes, and report both unexpected results and adverse events to the program officers at PCORI as well as to each of the local IRBs at each hospital. Each IRB will be informed at the time of application for IRB approval of the existence of and members of the DSMP board. The members of the DSMP
board will be determined after the outcome of the grant application has been decided but before the project is sent to any IRB for approval. Review will occur annually. (The Advisory Panel is not the same as the DSMB.)