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1. Objectives

We will perform a pragmatic, two-arm, multi-site randomized controlled trial of 1,350 older adults (50 years and older) with either 1) advanced cancer (defined as metastatic solid tumor) or 2) end-stage organ failure defined as New York Heart Association (NYHA) Class III or IV Heart Failure; End Stage Renal Disease defined as GFR < 15 ml/min/m^2 or on dialysis; or chronic obstructive pulmonary disease (COPD) defined as oxygen-dependent or FEV_1 < 50% who present to the Emergency Department (ED), along with 675 of their primary caregivers, to compare nurse-led telephonic case management to facilitated, outpatient specialty palliative care. We will compare the effectiveness of two distinct palliative care models that vary by provider type (nurse versus physician-led) and mode of delivery (telephonic versus in-person or telehealth): a) nurse-led telephonic case management; and b) facilitated, outpatient specialty palliative care. Both models of care provide supportive care services to the older adult within their current home environment. Both approaches are standard of care and the main difference

is the delivery of care by provider type. The telephonic nurse intervention arm provides palliative care services to older adults over the phone and is delivered by licensed nurses. The outpatient arm provides palliative care services to older adults and the patients have the option to receive care by attending in-person clinic visits or telehealth visits. The outpatient arm is delivered by physicians. The primary objective to be addressed is to compare both interventions on quality of life in patients with serious, life-limiting illness. Secondary objectives for this proposal include evaluating the effectiveness of both interventions on healthcare use in the 12 months following enrollment, loneliness, and symptom burden in patients. Furthermore, we will compare the impact of the interventions on several caregiver outcomes, including caregiver strain, caregiver quality of life, and bereavement. Randomization will be at the patient level and will be stratified by site and disease (cancer versus end-stage organ failure).

Overall, we seek to discover when caring for older adults with serious, life-limiting illness discharged home after an ED visit, how effectively does nurse-led telephonic case management enhance quality of life in patients and primary caregivers and reduce healthcare utilization, loneliness, symptom burden, caregiver strain, and bereavement when compared with facilitated, outpatient specialty palliative care? We hypothesize that patients randomized to nurse-led telephonic case management will have greater improvements in quality of life and lower healthcare utilization, loneliness, and symptom burden than those referred to outpatient specialty palliative care. We also hypothesize that caregivers will experience greater quality of life and less psychosocial and physical strain and bereavement in the nurse-led telephonic group.

2. Background

Most persons with a serious, life-limiting illness do not receive the care they prefer at the end of life.[1-3] The vast majority of Medicare beneficiaries (86%) prefer to spend as much time as possible at home, and to optimize control of pain and other burdensome symptoms.[1] While some are able to achieve these goals, many individuals, especially those who belong to vulnerable populations—including racial and ethnic minorities—spend their final days in and out of the ED and the hospital. This group often receives intensive, life-sustaining therapies (***e.g.,*** cardiopulmonary resuscitation) that are unlikely to prolong life or enhance quality of life, and many die in the hospital or intensive care unit (ICU).[4] While this may sometimes reflect an informed patient choice, more often it does not.[5,6] Over three-quarters of patients with serious illness would not choose a treatment if it resulted in severe functional or cognitive impairment.[7] Patients' main concerns at the end of life include maintaining control, relieving burdens, and strengthening family relationships.[8]

According to the World Health Organization, palliative care is "an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual". Multiple studies have shown that palliative care services improve patients' symptoms and the quality of end-of-life care across a broad range of illnesses. Patients receiving palliative care services are often able to remain cared for and supported at home, leading to greater

patient and family satisfaction, and less prolonged grief and posttraumatic stress disorder among bereaved family members.[9-14] Palliative care also lowers costs by reducing unnecessary hospitalizations, diagnostic and treatment interventions, and avoidable intensive and ED care.[15-19] The ENABLE II trial demonstrated higher scores for quality of life and mood in patients with life-limiting cancer and a prognosis of one year who received a psycho-educational palliative intervention in addition to standard care.[16] Another randomized trial demonstrated that comprehensive outpatient palliative care improves symptom management and patient satisfaction.[20] Patients with late-stage COPD and heart failure who were randomly assigned to in-home palliative care, as compared with usual care, reported greater satisfaction with care and were more likely to die at home.[21] Given these benefits, there is a need to change the paradigm for management of patients with serious, life-limiting illness and extend it beyond specialty palliative care in patients with advanced cancer to enable more individual patients and populations to benefit.

3. Setting of the Human Research

This study will be conducted in the Emergency Departments and observation units at the following sites:

- NYU Langone Tisch Hospital, New York, NY
- Bellevue Hospital Center, New York, NY
- NYU Langone Hospital – Brooklyn, Brooklyn, NY
- NYU Langone Hospital-Long Island – Mineola, NY
- Beaumont Hospital – Royal Oak, Royal Oak, MI
- Beaumont Hospital – Troy, Troy, MI
- Brigham and Women's Hospital, Boston, MA
- The Ohio State University Wexner Medical Center, Columbus, OH
- University of Florida Shands Hospital, Gainesville, FL
- Yale New Haven Hospital, New Haven, CT
- University of California Los Angeles, Los Angeles, CA
- University of California San Diego, San Diego, CA
- University of California Irvine, Irvine, CA
- Weill Cornell Medicine, New York, NY
- Hackensack University Health, Hackensack, NJ
- Atlantic Health, Morristown, NJ
- Northwestern University, Chicago, IL
- Rush University, Chicago, IL
- Henry Ford Health System, Detroit, MI

In a leadership transition, this research will be overseen by a multiple PI format. Dr. Corita Grudzen, will serve as Multiple PI (mPI) from Memorial Sloan Kettering Cancer Center (MSKCC) via subcontract, and Dr. Keith Goldfeld will serve as Contact PI and mPI from NYU Langone Health. In this, MSKCC will be added as a project site solely for data analysis, and will not be actively recruiting additional subjects.

4. Subject Identification, Recruitment, and Consent

a) Methods and Procedures

This is a pragmatic, two-arm, multi-site randomized controlled trial with patient-level randomization and stratification by site and disease (cancer versus end-stage organ failure) to compare nurse-led telephonic case management to facilitated, outpatient specialty palliative care for older adults with serious, life-limiting illness and their primary caregivers. Prior to the start of patient enrollment, the PI at each site will notify all treating physicians at their clinical site via email of the study parameters in order to allow physicians to opt out of routine participation by their patients. If the site PI does not hear from the primary care physician and/or oncologist that s/he wishes to opt out of routine participation, the site PI will assume they are willing to have their patients enroll should they meet the inclusion criteria.

Patients

Patients will be screened in the ED or observation unit at each site. For sites with no observation unit, patients who are admitted as inpatient for two midnights or less will also still be eligible to participate. Patients will also be screened from a generated report capturing all patients over age 50, visiting the ED, admitted or discharged, within 24 hours. Patient MRN will be collected from the 24-hour report and ED Trackboard and stored in REDCap if patients meet all initial qualifying criteria. The MRN will be expunged from REDCap once a patient either declines participation or reaches the disqualification state from the study after 48 hours. Patient MRN will not be recorded for subjects who opt out of research participation listed in their EHR. Research coordinators will be responsible for collecting, logging, and expunging MRN from REDCap. The data analyst will run a quarterly report to ensure data expungement. Qualifying conditions include 1) advanced cancer (defined as metastatic solid tumor) or 2) end-stage organ failure defined as New York Heart Association (NYHA) Class III or IV Heart Failure; End Stage Renal Disease defined as GFR < 15 ml/min/m^2 or on dialysis; or chronic obstructive pulmonary disease (COPD) defined as oxygen-dependent or FEV_1 < 50%. Only patients discharged or likely to be discharged per provider from the ED home will be approached.

The RA will then approach the patient and ask face-to-face questions or call the patient over the phone to ensure that the patient meets all eligibility criteria that could not be obtained in the electronic health record. The recruitment process can thus be either in-person or telephonically depending on if the patient has been already discharged from the ED or not. Only patients who are discharged or likely to be discharged home are eligible to participate.

Once eligibility is confirmed, the RA will discuss with the patient what active participation in this study means (review verbal consent, randomization to an intervention, potential benefits, risks of participation), the purpose and limitations of the study (what will and will not be tested, confidentiality, what will be done with the results), and requirements of the study (duration of participant involvement, follow-up data collection 3 months, 6 months, and 12 months post-enrollment). If the patient agrees to participate, the patient's primary care physician and/or oncologist will also be notified that the patient is being enrolled in a study of palliative care and that they should expect a follow-up phone call from a palliative care provider or nurse. For patients and caregivers that will be consented in person, verbal consent will be obtained, but

subjects will be asked to sign the standalone HIPAA authorization form. The verbal consent process is an accommodation due to the COVID-19 environment making it difficult for this specific study population to process paperwork including signing and mailing back documents. Since the intervention is occurring in the environment available to each study subject and all subjects will receive a standard of care palliative care intervention, verbal consent is ethical.

For patients and caregivers that will be consented over the phone, the study team has requested a waiver of signed HIPAA authorization and all information will be presented verbally. The RA will review the consent form with the participant, either in-person or over the phone, and obtain verbal consent using the provided key information sheet, HIPAA authorization form and consent document; the subject will verbalize comprehension of the consent form and study enrollment. For subjects that choose to participate, a copy of the informed consent form, HIPAA form, and the key study information sheet will be mailed to the subject.

After informed verbal consent is obtained, a baseline survey to assess demographics and patients' quality of life, loneliness, and symptom burden will be conducted at bedside. Patients may also opt to complete the baseline surveys over the phone, email, or postal mail after informed verbal consent is obtained if they do not wish to complete it in the ED. Patients will be randomized to either telephonic nurse-led case management or facilitated, outpatient specialty palliative care after the baseline survey is administered. The baseline surveys will not interfere with emergency care and the interviews will be paused or stopped if the patient requires a diagnostic test or other medical intervention, or needs to speak with a nurse, physician, or other provider. The interview will continue when it will not interfere with any medical care. Patients will receive a $40 gift card upon completion of the baseline survey and a $20 gift card for every follow-up survey completed via phone, email, or postal mail after 12 weeks, 6 months, and 12 months following enrollment. Multiple phone numbers (*e.g.,* mobile, home, and work) along with email addresses and emergency contacts will be collected in order to secure various ways to keep in contact with the patient. Follow-up surveys can also be completed by the patient's caregiver or emergency contact collected at the time of consent, at patient's discretion. Reimbursement for up to $25 per visit to offset the costs of copay or travel, for either in-person and telehealth visits, will also be given in the form of a gift card to those randomized into the facilitated, outpatient palliative care clinic arm of the study. Patients randomized to the facilitated, outpatient palliative care arm are expected to attend monthly visits for up to 6 months.

Primary caregivers

RAs will approach primary caregivers of all eligible enrolled patients. RAs will engage in the same conversation as patients with primary caregivers regarding the scope of the study, their role in the study, and their rights as a participating subject in human subjects research. If the caregiver is present with the patient at bedside, the RA will obtain verbal informed consent and signed HIPAA authorization, and a copy of the informed consent will be provided to the caregiver. If the caregiver is not present at bedside, the RA will call the caregiver to obtain verbal consent and all information will be presented verbally using the key information sheet, HIPAA form, and informed consent document. A patient does not need to have a primary

caregiver in order to participate in the study and all primary caregivers have the opportunity to decline participation if they do not want to participate.

Following study enrollment, a baseline survey will be administered. If they are enrolled in-person, caregivers will also have the option to complete the baseline surveys over the phone, email or postal mail after informed consent is obtained, if they do not wish to complete it in the ED. Baseline surveys will collect information pertaining to caregiver strain, caregiver quality of life, and demographics. Caregivers will receive a $40 gift card after completing the baseline survey and will receive a $20 gift card for each completed subsequent survey at 3 months, 6 months, and 12 months after enrollment.

b) Inclusion and Exclusion Criteria

Patients

English or Spanish-speaking older adults ages 50 years and older who have one or more qualifying serious, life-limiting conditions and who are scheduled for ED discharge, observation status, or inpatient stay for two midnights or less will be eligible to participate. The patient sample will only include older adults 50 years and over, as the comorbidity scoring tools that predict short- and long-term mortality were derived and validated in this population.[22-26] Older adults' disease progression and physical functioning differ from those of children and younger adults with serious, life-limiting illness, making comparisons regarding patient-oriented outcomes across the life span problematic. Qualifying conditions include: 1) advanced cancer (defined as metastatic solid tumor) or 2) end-stage organ failure defined as New York Heart Association (NYHA) Class III or IV Heart Failure; End Stage Renal Disease defined as GFR < 15 ml/min/m^2 or on dialysis; or chronic obstructive pulmonary disease (COPD) defined as oxygen-dependent or FEV_1 < 50%. Patients must have health insurance, reside within the geographical area, and have a working telephone. We will exclude those who have dementia listed in the EHR problem list, received hospice services in the last six months, have received 2 or more palliative care consults or visits in the last 6 months, and those who reside in or are being discharged to a skilled nursing or assisted living facility or chronic care hospital. No specific genders and racial and ethnic origins will be excluded from this study. Children, pregnant women, prisoners, and other vulnerable populations will not be recruited.

Primary Caregivers

English or Spanish-speaking primary caregivers (relative OR friend who has contact with the patient at least two times per week (not home health aide)) ages 18 years and older will be eligible to participate. Primary caregivers can provide verbal informed consent either in-person or telephonically. Caregivers must possess a working telephone. The caregiver sample will exclude individuals less than 18 years old because the unique stresses a child caregiver experiences are outside of the scope of this study. No specific genders and racial and ethnic origins will be excluded. Children, pregnant women, prisoners, and other vulnerable populations will not be recruited.

c) Number of Subjects

We will recruit a total of 1,350 patients with serious, life-limiting illness and 675 of their primary caregivers in eighteen EDs across the country. Sample size for patients was based on simulation methods to estimate power based on the primary outcome, a change in quality of life for patients, as measured by FACT-G from enrollment to 6 months. The change in quality of life between enrollment and 6 months is our primary outcome, though additional data points at 3 months will be collected as we found in our prior palliative care clinical trial that patients often died prior to 6 month follow-up. Power analyses were also performed to estimate the number of caregivers needed to detect a difference in caregiver strain measured by the Modified Caregiver Strain Index between the two groups.

d) Study Timelines

The total duration of patient and caregiver participation in this study will be 12 months. Baseline surveys will be performed at enrollment, and follow-up surveys will occur at 3 months, 6 months, and 12 months post enrollment. Follow up surveys will include measuring outcomes of quality of life, loneliness, and symptom burden in patients, and caregiver strain, caregiver quality of life, and bereavement (if patient death occurs) in caregivers.

e) Endpoints

The **primary outcome** is to compare both interventions on quality of life in patients. The **secondary outcomes** are to compare the effectiveness of both interventions on healthcare utilization, loneliness, and symptom burden in patients, and caregiver strain, caregiver quality of life, and bereavement in caregivers. These outcomes were selected from input by our clinical and research collaborators, PCORI program staff, and our Study Advisory Committee, including patient representatives, clinicians, researchers, and stakeholder representatives from a large Medicare Advantage Plan, the American Cancer Society, the American Society of Nephrology, and the American Heart Association.

f) Specimen Banking

N/A

g) Data Management and Confidentiality

We will use a centrally managed REDCap database to collect and house study data for patients and caregivers at all sites. Study data will be entered directly into REDCap in real-time via iPads or laptop computers which are password-protected, secured and managed by the study site. Paper surveys will be used if unavoidable (Spanish-speaking patient surveys, Wi-Fi connectivity issues in ED) and will be transposed into REDCap at study sites at earliest convenience and stored in a locked cabinet. The Senior Research Coordinator will conduct all data management and data quality assurance activities required by the survey data, as well as de-identify the data for analyses.

Patient and caregiver name, mailing address, date of birth, telephone number, MRN, and email address will be entered into REDCap and assigned a non-identifiable study ID number. No other PHI will be collected in the survey nor assigned to this study ID. Contact information and MRN

will only be used for the purpose of facilitating clinical care or locating participants to complete surveys or receive study compensation.

Data collection, secure data transfer, and storage have been designed to minimize the risk of a patient or caregiver participant's breach of confidentiality. All patients and caregivers will be assigned a unique study ID number and only one master list correlating to subject identifiers will be maintained at each site. RAs at each site will retain access to the list for intervention assignment, follow-up interviews, and chart abstractions. All lists linking participant IDs to subject identifiers will be stored in double-locked locations (e.g., locked filing cabinet in a locked office, or encrypted electronic file on a secure server). The ID numbers will be used for data collection, data tracking, and data entry, so the secure aggregated database will not contain any patient identifiers. Data use agreements will be established between the host institution (NYU School of Medicine) and the other sites to ensure that only the minimally necessary data is shared with the primary institution and nurse case managers. Secure data transfer from each site to NYUSoM research team will occur using encrypted electronic files via a secure connection, as delineated in the data use agreements.

To minimize research-associated risk and protect the confidentiality of participant data, all investigators and staff involved in this project will complete extensive courses and pass certifying exams on the protection of human subjects in research through CITI training and HIPAA certification.

As a result of a contract modification with PCORI, data will be stored long term with University of Michigan's Patient-Centered Outcomes Data Repository (PCODR) via the Inter-university Consortium for Political and Social Research (ICPSR) platform. Data repositories are best practices for advancing research and the sole purpose of this storage will be as such.

All data is currently housed at NYU, and NYU will be responsible for submitting the secure transfer, as approved by NYU legal entities via an appropriate data use agreement. This dataset will include de-identified full dataset, study protocol, metadata, data dictionary, full statistical analysis plan and analytic code. This data package will be de-identified in accordance with the HIPAA Privacy Rule or comparable applicable regulations prior to the transfer to ensure participant privacy and safety. PI, Dr. Goldfeld will be overseeing the transfer process. There is a vetting process in place that other researchers who want to use this dataset will need to abide by. Dr. Goldfeld will be consulted when requests to use the de-identified dataset come in and will be closely involved in the approval process.

This dataset will not include participants' name, any personal information (telephone number, address, e-mail address), health related information (including disease and insurance status), or individual responses to any surveys completed.

Subjects will be notified of the data transfer via mail, and will be provided the opportunity to opt out. If subjects contact our team and do not want their de-identified data transferred, the data analyst will remove them from the dataset for transferring purposes.

h) Provisions to Monitor the Data to Ensure the Safety of Subjects

The mPIs, in cooperation with Co-Is, and the NYUSoM IRB will monitor the safety of the proposed project. A Data Safety Monitoring Plan (DSMP) will be created for this study. The data analyst will be responsible for the oversight of all data and producing an interim analysis report midway through participant enrollment. The project manager will inform the mPIs immediately of any harmful, unexpected serious adverse events (SAEs) related to the research—these will also be reported to the IRB within 24 hours in a full written report. Other SAEs will be reported annually in the IRB application for continuation or termination of the research. All expected SAEs, 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 NYU PI within 15 working days and summarized annually in the IRB application for continuation or termination of the research. The mPIs and Co-Is will be versed in these reporting procedures, as they are currently required for all research conducted at each respective site.

i) Data Analysis

The analytic plan accounts for the nested structure of the data, assesses normality assumptions of dependent variables, and addresses issues related to missing data, study participation bias, and baseline covariate balance. We address each of these in turn. All analyses will be conducted by the biostatistician in R 4.3.1 (R Foundation for Statistical Computing, Vienna).

Prior to conducting the outcome analyses, we will compare patients in each intervention arm (nurse-led telephonic care and specialty, outpatient palliative care clinic) with respect to baseline socio-demographic characteristics (age, gender, race, education, etc.) and functional status. We will assess whether any adjustments will need to be made in the final statistical models based on whether the differences are clinically meaningful.

To account for nesting in the data structure (patients nested in hospitals), we will use mixed effect multi-level models to estimate effect sizes. We anticipate two sources of variation. First, there will be regional (site) variation in the outcomes independent of the intervention. This means that even though the telephonic arm is centrally delivered, there may still be clustering at the site level. Second, there will be variation in how specialty, palliative care outpatient clinics deliver the clinic intervention arm, which will add an additional source of variation for this arm alone. As a result, we expect variation in the *effect* of the telephonic intervention across sites due to these sources of variation.

Various models will be created to estimate these effects. For the primary analysis, a linear mixed effect model will be made, as quality of life for patients will be a continuous variable. For secondary analysis, linear mixed effect models will be created for loneliness, symptoms burden, caregiver strain, caregiver quality of life, and bereavement, as these outcomes are continuous as well. Test Poisson and negative binomial mixed effects models will be generated for analysis of healthcare utilization since this outcome will be a count variable. All analysis will be tested using α-level of 0.05.

In all models, we will conduct an Intent-to-Treat (ITT) analyses. We also plan to perform sensitivity analyses with group assignments per protocol (in addition to a traditional intention to treat) to test whether receipt of nurse-led telephonic care or a visit to the palliative care

outpatient clinic impacts our outcomes. We will interpret the results and evaluate the performance of different statistical data analysis plans from both statistical and clinical perspectives. These more advanced statistical methods are able to rigorously capture the complex data structure, efficiently borrow information across different patient subgroups, significantly boost power in the statistical inference, and fully explore the rich information in the collected patient cohort.

j) Withdrawal of Subjects

Patient and caregiver participants may withdraw from participation in the study at any time upon verbal or written request. An investigator may terminate participation if s/he decides it would be in the best interest of the participant to no longer proceed in the study.

5. Risks to Subjects

Risks

The study involves obtaining demographic and other survey data from patients and caregivers to determine the effectiveness of the interventions on quality of life, loneliness, healthcare utilization, and symptom burden in patients, and caregiver strain, caregiver quality of life, and bereavement in caregivers. The survey instruments pose no physical, financial, or legal risk to patients or caregivers. Answering some of the questions may be psychologically difficult for patients and families because they involve discussing the potential for worsening health and the possible death of the patient. Past studies of patients near the end of life demonstrate that enrolling patients in research studies similar to this project do not harm patients or caregivers, and many studies report that patients are actually helped by participating in these types of projects. The risks of discussing death, dying, and bereavement with terminally ill patients is minimally stressful and often helpful. The study team has substantial expertise in assessing patients who become upset during the survey, and an established protocol will be used should this situation occur. All RAs will be trained on recruitment and interview/communication techniques to be used in the ED and during telephone follow-up. Should a patient experience emotional distress as a result of study participation, the RA will immediately inform the physician (when in the ED) or study mPI (when conducting telephone surveys). We have carefully considered the respondent burden in designing our project and all surveys will last less than 20 minutes. Our surveys are similar in number and content to that used in previous studies of patients with advanced illness.

Protection Against Risks

This proposed study contains minimal risk for the patients and caregivers involved. A breach of confidentiality and the psychological discomfort in discussing serious illness constitute the primary risks to the enrolled patients and caregivers. Patients and caregivers will be informed that information collected during interviews will be kept confidential and only be available to the research team. Additionally, participants will be advised that they can refuse to answer any question or stop the interview at any point. All RAs will be trained on recruitment and interview

techniques to be used in the ED and during telephone follow-up. Should a patient experience emotional distress as a result of study participation, the RA will immediately inform the physician (when in the ED) or study mPI (when conducting telephone interviews). The interview will conclude if the patient or caregiver appears emotionally distressed. If, at any time, a participant expresses verbal or nonverbal reluctance to participate, the interview will be terminated and the participant will be withdrawn from the study. Of note, these extreme emotional reactions are very rare and the literature supports that conversations with patients tend to be helpful and not harmful. Throughout the course of the study, the mPI will monitor the safety of all study participants. A DSMP will also be established for this study for the protection of subjects. A DSMP will replace a Data Safety Monitoring Board (DSMB), as this study is minimal risk. Death is already expected in patients with advanced disease, and there are also no known potential Serious Adverse Events.

Data collection, secure data transfer, and storage have been designed to minimize the risk of a patient or caregiver participant's breach of confidentiality. All patients and caregivers will be assigned a unique study ID number and only one master list correlating to subject identifiers will be maintained at each site. RAs at each site will retain access to the list for follow-up interviews and chart abstractions. All lists linking participant IDs to subject identifiers will be stored in double-locked locations (*e.g.,* locked filing cabinet in a locked office, or encrypted electronic file on a secure server). The ID numbers will be used for data collection, data tracking, and data entry, so the secure aggregated database will not contain any patient identifiers. Data use agreements will be established between the host institution (NYUSoM) and the other sites to ensure that only the minimally necessary data is shared with the primary institution and nurse case managers. Secure data transfer from each site to the NYUSoM research team will occur using encrypted electronic files via a secure connection, as delineated in the data use agreements.

To minimize research-associated risk and protect the confidentiality of participant data, all investigators and staff involved in this project will complete extensive courses and pass certifying exams on the protection of human subjects in research through CITI training and HIPAA certification.

6. Potential Benefits to Subjects

The proposed study is designed to compare two methods of palliative care delivery for patients with serious, life-limiting illness—nurse-led telephonic case management and facilitated, outpatient specialty palliative care. These interventions may improve patient-centered outcomes including quality of life, loneliness, and symptom burden, and may reduce caregiver strain and bereavement and improve caregiver quality of life in primary caregivers. These interventions may also decrease future healthcare utilization (*e.g.,* ED visits and hospital admissions) and increase hospice use in patient participants. For patients with serious, life-limiting illness, visits to the ED are common. For these patients, the ED often represents a place of last resort to address both physical and/or psychosocial crises. As a result, emergency care has not adapted to the needs or goals of this patient population; seriously ill patients who prefer to have care delivered at home are often admitted because of inadequate care coordination or providers' fear

of ED revisits. This study will help align discussions for patients and providers regarding goals of care, end-of-life wishes, advance directives, pain and symptom management, and community resources. We hypothesize that patients randomized to nurse-led telephonic case management will demonstrate greater improvements in quality of life and reduced healthcare utilization and loneliness than those referred to outpatient specialty palliative care. We hypothesize that caregivers may also experience improved caregiver quality of life and less psychosocial and physical strain and bereavement. We hope to demonstrate the comparative effectiveness of a palliative care model so that payers and medical centers can incorporate such services into their institutions.

As PCORI asks investigators to make every reasonable effort to return aggregate results to study participants, participants will be mailed a document summarizing study findings.

7. Economic Impact to Subjects

There is no expected economic impact to patient and caregiver participants. As part of the inclusion criteria, all patient participants are required to possess health insurance in order to receive outpatient palliative care services.

8. Payments to Subjects

Patient and caregiver participants will receive a $40 gift card upon completion of the baseline interview at enrollment. Patient and caregiver participants will receive a $20 gift card for every follow-up survey milestone completed at 3 months, 6 months, and 12 months. Patient participants randomized to the outpatient palliative care group will be reimbursed up to $25 in the form a gift card to cover the cost of travel for each monthly palliative care visit for 6 months from enrollment. Patient participants who are randomized into the outpatient palliative care group and choose to attend the appointments via telehealth will not receive the $25 travel reimbursement as there is no cost of travel to cover.

9. Vulnerable Populations

Include	*Exclude*	*Vulnerable Population Type*
	X	Adults unable to consent
	X	Individuals who are not yet adults (*e.g.,* infants, children, teenagers
	X	Wards of the State (*e.g.,* foster children)
	X	Pregnant women
	X	Prisoners

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