UNIVERSITY OF ROCHESTER MEDICAL CENTER

WILMOT CANCER INSTITUTE

A telehealth advance care planning intervention for older patients with acute myeloid leukemia and myelodysplastic syndrome

July 11th, 2022

Study Principal Investigator:

Kah Poh (Melissa) Loh, MBBCh BAO
Division of Hematology/Oncology
University of Rochester Medical Center
James P Wilmot Cancer Center
601 Elmwood Ave, Box 704
Rochester, NY 14642
Email: Kahpoh_loh@URMC.Rochester.edu

Study Co-Investigator:

Benzi Kluger, MD
Department of Neurology
University of Rochester Medical Center
601 Elmwood Ave, Box 704
Rochester, NY 14642
Email: Benzi_Kluger@URMC.rochester.edu

Sally Norton, PhD, RN
School of Nursing
University of Rochester Medical Center
601 Elmwood Ave, Box 704
Rochester, NY 14642
Email: Sally_Norton@URMC.rochester.edu

Thomas Carroll, MD, PhD
Department Medicine
University of Rochester Medical Center
601 Elmwood Ave, Box MED
Rochester, NY 14642
Email: thomas_carroll@URMC.rochester.edu

Marissa LoCastro
James P Wilmot Cancer Center
601 Elmwood Ave, Box 704
Rochester, NY 14642
Email: Marissa_LoCastro@URMC.Rochester.edu

Study Personnel:

Terri Lloyd
James P Wilmot Cancer Center
601 Elmwood Ave, Box 704
Rochester, NY 14642
Phone: (585) 276-5652/ Fax: (585) 273-1042
Email: Terri1_Lloyd@URMC.Rochester.edu

Jessica Bauer
James P Wilmot Cancer Center
601 Elmwood Ave, Box 704
Rochester, NY 14642
Phone: (585) 276-6562/ Fax: (585) 273-1042
Email: Jessica_Bauer@URMC.Rochester.edu

1.0 Background

1.1. Acute Myeloid Leukemia (AML) and Myelodysplastic syndrome (MDS) are a disease of the aging

Approximately 20,000 and 10,000 people are diagnosed with AML and MDS each year. Over 60% of AML and MDS cases are diagnosed in adults aged ≥60 years.[1,2] For fit older patients with AML (i.e., without significant comorbidities or disabilities), the standard first-line treatment consists of intensive inpatient chemotherapy. Intensive chemotherapy provides the best chance for durable remission, but it is associated with a high treatment-related mortality (60-day mortality: 15-20%).[3,4] Intensive therapy is utilized in <1% of older patients with AML seen in the community oncology setting due to the need for hospitalizations.[6] In the last decade, lower-intensity outpatient treatments with reduced treatment-related mortality rates and potentially similar efficacy have become available.[5-10] These treatments have permitted more older patients with AML, including those with comorbidities and disabilities, to receive leukemia-directed therapy.[11] Management of MDS may consist of observation, growth factors, transfusion, or chemotherapy in the outpatient setting. AML and MDS are generally incurable except with the use of hematopoietic stem cell transplantation, for which many older adults are not candidates due to advanced age and comorbidities. In older patients with AML or high-risk MDS, outcomes are poor, with median overall survivals ranging from 6-12 months.

1.2. Patients with hematologic malignancies receive more aggressive care at the end-of-life (EOL) compared to those with solid tumors.

Previous studies have established quality indicators to guide optimal care at the end of life (EOL).[12,13] These quality indicators include healthcare utilization [emergency department (ED) visits, hospitalizations, intensive care unit (ICU) admissions, life-sustaining treatments (LSTs), chemotherapy administration, and receipt of transfusion] at EOL, completion of Medical or Physician Orders for Life-Sustaining Treatment (MOLST/POLST) forms, utilization of palliative care and hospice services, and place of death. Compared to patients with solid tumors, patients with hematologic malignancies (including AML and MDS) are more likely to visit the ED, be hospitalized, be admitted to ICU, and to receive LSTs, transfusions, and chemotherapy at the EOL.[14-16] In addition, they are less likely to complete MOLST/POLST forms in a timely fashion, less likely to receive palliative care and hospice services, and more likely to die in the hospital.[14,16] Therefore, interventions are needed to improve EOL care for patients with hematologic malignancies.

1.3. Advance care planning (ACP) may improve EOL care for older patients with AML and MDS

Advance care planning (ACP) is a process that supports adults in understanding and sharing their personal values, life goals, and preferences regarding medical care. These decisions can then be recorded in MOLST/POLST forms to guide surrogate decisions makers if the patient loses decision-making capacity. Our preliminary data suggest that among adults aged ≥70 years with AML and MDS seen at the Wilmot Cancer Institute (WCI) and its affiliated community centers, most MOLST forms were completed late in the disease course; median times from MOLST completion to death were 18 days and 75 days, respectively, for AML and MDS. Approximately

42% completed MOLST >30 days prior to death. Compared to patients who completed MOLST ≤30 days prior to death or never completed MOLST, those who completed MOLST >30 days prior to death were less likely to be admitted to the ICU and to utilize LSTs at the EOL, indicating that early MOLST completion may be associated with better EOL care. Interventions to improve access to ACP and MOLST/POLST completion can therefore be expected to improve EOL care.

1.4. Evidence-based interventions can improve access to ACP but they are not tailored to older adults with AML and MDS.

The Serious Illness Care Program is an evidence-based intervention to enhance EOL conversations between physicians and patients with advanced cancer.[17] It consists of the Serious Illness Conversation Guide as well as training and system-level support for physicians to conduct ACP conversations. In a phase III randomized trial, compared to the control arm, more patients and physicians in the intervention arm had serious illness conversations (96% vs. 79%) and these conversations occurred 2.4 months earlier and were more comprehensive and patient-centered.[17] However, <10% of patients had hematologic malignancies.

1.5. Telehealth may improve access to ACP.

Telehealth refers to the practice of caring for patients remotely when the provider and patient are not physically present with each other. Telehealth allows for improved patient access, but its adoption has been slow due to barriers such as lack of insurance coverage and patient/provider unfamiliarity.[18] The coronavirus pandemic has stimulated rapid increase in the use of telehealth visits in cancer care. Infrastructure and regulatory changes to facilitate telehealth visits have been implemented, including insurance reimbursement and education/support to assist older adults and providers. Therefore, telehealth provides an attractive modality improve access to ACP among older adults with AML and MDS.

1.6. Overall goal

The long-term goal of this proposal is to improve ACP access, patient-reported outcomes, and EOL care in older patients with AML and MDS via a telehealth-delivered ACP intervention. The objective of this one-year project is to adapt and assess the feasibility and usability of a telehealth-delivered ACP intervention for older patients with AML and MDS. The optimization of the ACP intervention will be guided by the Center for eHealth and Wellbeing Research (CeHRes) Roadmap that emphasizes structural stakeholder involvement.

2.0 Aim and Hypothesis

2.1. Primary Aim

To incorporate telehealth into an evidence-based ACP intervention that is adapted for older patients suffering from AML and MDS utilizing qualitative interviews with patients, their caregivers, and oncology and palliative care providers

Findings from Aim 1 will be used to inform Aim 2. Aim 2 will be done following completion of Aim 1.

2.2. Secondary Aim

To assess the feasibility and usability of the adapted telehealth-delivered ACP intervention in a single-arm pilot study of 20 older patients with AML and MDS.

2.3. Hypothesis

The telehealth ACP intervention will be feasible and usable.

2.3.1 Feasibility and usability metrics

The usability and feasibility of the adapted telehealth-delivered ACP intervention will be evaluated based on the following:

a) Retention rate (percentage of patients who consented and completed the visit)
b) Telehealth Usability Questionnaire (total average of >5 will be considered usable)

3.0. Study Design and Population

3.1. Study Settings

Wilmot Cancer Institute (WCI), University of Rochester Medical Center (URMC) and its affiliated centers.

3.2. Study Type

Aim 1: Qualitative study (phase 1)

Aim 2: Single-arm pilot study (phase 2)

3.3. Study Population

Aim 1: We will gather feedback from older patients with AML/MDS (N=5-10), caregivers (N=up to 2 caregivers per patient and therefore up to a total of 20 caregivers), oncology physicians (N=5-10), oncology APP and nurses (N=5-10), palliative care physicians (N=5-10), as well as palliative care APP and nurses (N=5-10). Therefore, the total number of participants will be between 25 and 70.We anticipate thematic saturation will be reached with this number of participants based on past similar research.[19,20] For patients, we will consent up to 15 patients to account for screen fail or withdrawal.

Results from Aim 1 will be used to adapt the telehealth intervention for use in Aim 2. In other words, Aim 2 will occur after Aim 1 has been completed.

Aim 2: We will recruit 20 patients, their caregivers (up to 2 caregivers per patient), and oncology providers. We will consent up to 30 patients to account for screen fail or withdrawal.

3.4. Inclusion and Exclusion Criteria for Patients

Inclusion criteria:

Aim 1

- Age ≥60 years
- Have an AML or MDS diagnosis
- Able to provide informed consent
- English-speaking

Aim 2

- Age ≥60 years (conventional definition of older age in AML/MDS)
- AML or MDS diagnosis
- Being managed in the outpatient settings
- Able to provide informed consent
- English-speaking

Exclusion criteria
- None

3.5. Inclusion and Exclusion Criteria for Caregivers (Aims 1 and 2)

Inclusion criteria:
- Age ≥21 years
- Selected by patient when asked if there is a "*family member, partner, friend, or caregiver with whom you discuss or who can be helpful in health-related matters*"
- Able to provide informed consent
- English-speaking

Exclusion criteria
- None

3.6. Inclusion and Exclusion Criteria for Oncology Providers

Inclusion criteria:

Aim 1
- Oncologists, advanced care practitioners (APPs), and nurses who cared for at least one patient age ≥60 years with AML/MDS in the past year.

Aim 2
- Oncologists, advanced care practitioners (APPs), and/or nurses who will be conducting the telehealth-delivered ACP visit

Exclusion criteria
- None

3.7. Inclusion and Exclusion Criteria for Palliative Care Providers (Aim 1 only)

Inclusion criteria:

Aim 1
- Palliative care physicians, APPs, and nurses who cared for at least one patient age ≥60 years with AML/MDS in the past year.

Exclusion criteria
- None

3.8. Number of Subjects

Aim 1: We plan to enroll the following groups: older patients with AML/MDS (N=5-10), caregivers N=(up to 20), oncology (N=5-10) and palliative care physicians (N=5-10) as well as

oncology (N=5-10) and palliative care APPs and nurses (5-10). In prior qualitative studies of older patients, caregivers, and oncologists, we were able to successfully enroll similar numbers of participants in 3-6 months.[20,21] In addition to enrolling at WCI, we will also be recruiting patients and oncologists from WCI-affiliated community practices (e.g., Interlakes Oncology, Dansville, Pluta, Olean, Wellsville), to obtain feedback from community oncology settings.

Aim 2: We plan to enroll 20 patients total and their caregivers (up to 2 caregivers per patient if available) in 9 months. From 2012-2019, 4-7 oncologists saw >100 patients with AML or MDS aged ≥60 annually at WCI and its affiliated centers. In prior studies of similar populations, the recruitment rate was 65-75%.[20,22] Therefore, recruiting 20 patients and their caregivers over 9 months is feasible.

3.9. Gender of Subjects

The gender ratio of enrolled patients will be similar to that of the gender ratio of AML in older adults (approximately 1.2:1 to 1.5:1 male to female ratio).[23,24]

3.10. Age of Subjects

We will recruit patients with AML and MDS aged 60 and above (from date of consent, confirmed on electronic medical record).

3.11. Racial and Ethnic Origin

The Caucasian to Non-Caucasian ratio of individuals with AML is 5:1. In Rochester, New York, Whites, African Americans, and Hispanics make up approximately 65%, 30%, and 5% of the population (Race and Ethnicity in Rochester, NY statistical atlas). We expect these to be similar in MDS although data were not available. As enrollment is limited to English-speaking patients, we predict a higher percentage of whites. The study does not restrict enrollment based on race or ethnicity.

3.12. Vulnerable Subjects

Recruitment will exclude vulnerable populations such as fetuses, neonates, children, pregnant woman, prisoners, and institutionalized individuals. We will also exclude adults who are deemed to not have decisional capacity and those who lost their consent capacity during the study period, as per their treating oncologist.

4.0. Recruitment and Consent

Subjects will be enrolled at the URMC WCI, as well as WCI-affiliated sites, including Interlakes Oncology, Dansville, Pluta, Olean, and Wellsville.

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

4.1 Identification of Study Subjects, Recruitment, and Consent Procedures

Patients will be identified by treating physicians at WCI and WCI-affiliated sites, nurses of these physicians, and the study coordinator. The study coordinator will work closely with physicians and nurses to identify patients who have an AML or MDS diagnosis. Given permission from the oncologist, the study team will screen clinic schedules of these oncology providers. The study coordinator will contact the physician (or designee) and inform them of patient eligibility and ask permission to approach the patient. The principal investigator will address any eligibility questions that may arise.

For **in-person consent with patients**, below are the possible scenarios for obtaining consent.

1) Physician/Study Investigator makes the initial contact and provides consent form, and patient signs consent with the physician on the same day: After confirming with the physician (or their designee) that a patient is a potential candidate for the study, the study staff will provide a consent form to the treating physician/study investigator so he/she can provide it to the patient during an in-person clinic visit. The physician/study investigator will go over every detail of the study during the clinic visit with patient. If agrees, the patient will sign the consent form with the physician/study investigator during the same in-person visit.

2) Study staff makes the initial contact and provides consent form, and patient signs consent with the study staff on the same day: After confirming with the physician (or their designee) that a patient is a potential candidate for the study, the patient will be provided with an informed consent form by the study staff when they come in for an in-person clinic visit. The study staff will introduce the study to the patients and go over every detail of the study. If agrees, the patient will sign the consent form with the study staff during the same in-person visit with the study staff.

For **verbal consent with patients**, below are the possible scenarios for obtaining consent. All study procedures can be conducted remotely therefore in-person visits are not necessary if patients are not returning for in-person visits or to minimize in-person contacts.

1) Physician/Study Investigator makes the initial contact, study staff follows up with the patient on the phone, and patient provides verbal consent on the phone: After confirming with the physician (or their designee) that a patient is a potential candidate for the study, the physician/study investigator will confirm that the patient

is willing to speak with the study staff about the study. The study staff will then call the patient via phone. The study coordinator will use the verbal consent script as a written aid and will go over every detail of the study with the patient to recruit them for the study. Study staff will sign and date it to confirm that he/she followed the script and the patient agrees to participate in the study. An information sheet summarizing the study and patient's involvement will be mailed /emailed to the patient for their records.

For caregivers of alive patients, we will obtain verbal consent. They will be provided with an information sheet. The patient will identify a caregiver and makes the initial contact. After confirming with the patient that a caregiver is willing to speak with the study coordinator about the study, the study staff then call the caregiver via phone. The study coordinator will use the verbal consent script as a written aid and will go over every detail of the study with the caregiver to recruit them for the study. Study staff will sign and date it to confirm that he/she followed the script and the caregiver agrees to participate in the study. An information sheet summarizing the study and caregiver's involvement will be provided/mailed/emailed to the caregiver for their records.

For providers, we will discuss the study at research or staff meetings and solicit interest in participation. In addition, we will approach providers via email communications. An informational sheet will be emailed to the providers. We will obtain verbal consent if they agree to participate.

4.1.1. Informed Consent

Informed consent will be obtained from the patient by the study investigators or coordinators. Consent documents will be signed by the patient and maintained in the patient record with copies provided to the patient. For verbal consent, documents will be maintained in the patient record with copies provided to the patient. Verbal consent documents with caregivers and oncology/palliative care providers will also be maintained in separate records with copies provided to caregivers and oncologists.

Waiver of documentation of consent:

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

Alteration of HIPAA Authorization:

We are requesting an alteration of HIPAA authorization. We will provide an information sheet to patients, caregivers, and oncology providers who provided verbal consent. Verbal consent will allow for reduction of in-person visits, thus maximizing the safety of both patients and study staff. Nonetheless, when possible and if we are able to coordinate study and clinic visits, we will obtain written informed consent.

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

4.1.2. Human Subject Protection

The University of Rochester Research Subject Review Board Investigator Guidance policy will be used to ensure that ethical standards for human subjects are upheld.

4.1.3. Participation

Regulations at the state, federal, and institutional level will be adhered to in regards to informed consent. Study participation is completely voluntary. After consenting, participants may withdraw from the study at any time for any reason, and they may do so without any repercussions. Participants may also be withdrawn by study personnel if it is determined that it is not favorable for the patient. All information regarding consent and withdrawal will be kept confidential.

4.1.4. Duration

Aim 1: The qualitative section of this study involves interviewing consented patients and caregivers for 30-60 minutes. We will also interview oncology and palliative care providers. Study participants will be interviewed by the study team either in-person (in a private space) or via phone/zoom. Interviews will be audio-recorded, uploaded to Box, and subsequently deleted from the audio-recorder.

Aim 2: At baseline, study patients and consented caregivers will complete demographics and baseline measures. We will also collect demographic information from oncology providers. After the oncology providers undergo a skill-based training session of SICG (2-4 hours; duration to be determined based on feedback obtained from aim 1), a telehealth visit will be scheduled with the study participants, caregivers, and oncologist providers within 1-2 months of enrollment. Following the visit, all participants will complete post-intervention measures. Within 1-2 weeks after the telehealth visit, the study team will separately interview the patient, caregiver (if available), and oncology provider present at the telehealth visit via Zoom/phone or in-person.

All audio-recordings will be uploaded to Box, transcribed by a professional transcription service, and subsequently deleted from the audio-recorder. After the study is completed, all participant data will be maintained for 7 years at URMC and will be kept in a password-protected database.

5.0. Registration

For Aim 1 (qualitative), registration information for patients, caregivers, and providers will be collected and entered into REDCap.

For Aim 2, registration information for patients, caregivers, and oncology providers will be collected and entered into the OnCore Database:

5.1. Registration Information for Patients

- 5.1.1 Site
- 5.1.2 Most recent IRB approval date
- 5.1.3 Name of person registering study participant
- 5.1.4 Eligibility verification
- 5.1.5 Verification that consent form has been signed and date signed
- 5.1.6 Treatment facility (WCI vs. Other)
- 5.1.7 Participant's identification
  - 5.1.7.a First and last names
  - 5.1.7.b Birth date (MM/DD/YEAR)
  - 5.1.7.c Gender
  - 5.1.7.d Race
  - 5.1.7.e Medical Record Number
  - 5.1.7.f Ethnicity
  - 5.1.7.g Date of baseline visit

5.2. Registration Information for Caregivers

- 5.2.1 Participant's identification
  - 5.2.1.a First and last names
  - 5.2.1.b Birth date (MM/DD/YEAR)
  - 5.2.1.c Gender
  - 5.2.1.d Race
  - 5.2.1.e Five-digit zip code
  - 5.2.1.f Ethnicity
  - 5.2.1.g Caregiver's preferred and alternate phone numbers (and email address if patients consent to be contacted via email)

5.3. Registration Information for Oncology and Palliative Care Providers

- 5.3.1 Participant's identification
  - 5.3.1.a First and last names
  - 5.3.1.b Birth date (MM/DD/YEAR)
  - 5.3.1.c Gender
  - 5.3.1.d Race
  - 5.3.1.e Five-digit zip code
  - 5.3.1.f Ethnicity

5.4. Initial Assessment

In Aim 1, study patients will complete demographics and a 30-60 minutes interview. Patients and caregivers in Aim 2 will complete baseline assessments with the study coordinator and then schedule a telehealth visit.

6.0 Intervention

The original SICG intervention included clinical tools, training, and system changes (Table 1). The primary clinician tool was a structured communication guide called the Serious Illness Conversation Guide (SICG; https://www.ariadnelabs.org/wp-content/uploads/sites/2/2017/05/SICG-2017-04-21_FINAL.pdf). Patient tools included a preconversation letter given to the patient at study enrollment, which introduced the SICG, and a "Family Guide," outlining an approach for continuing the conversation with their family after the patient-clinician discussion. The clinician training included a 2.5-hour, skills-based training session on the SICG led by palliative care faculty. System changes included the following systematic components: (1) clinicians were asked the "surprise question," "would you be surprised if this patient died in the next year?"; (2) clinicians were sent email reminders and given the SICG by study staff the day before an outpatient visit; (3) an accessible, structured, EMR documentation template mirroring the SICG was provided, and clinicians were trained on its use; and (4) in-person, email-based, or telephonic clinician coaching on the SICG was provided by palliative care faculty.

Table 1 SICG intervention components and description

Intervention Component	Description
Clinical tools	
SICG	The SICG was used by intervention clinicians to guide the conversation. SICG is a structured communication guide that provides clinicians with psychologically informed language to assess illness understanding and patient information preferences; share prognosis according to patient preferences; explore patient values, goals, and care preferences; and make a recommendation based on patient priorities.
Patient and family materials	Intervention patients were prepared ahead of the conversation with a written letter; patients were also given a Family Guide after a SICG conversation to support follow-up discussions with their family members.
Clinician training	
Skills-based training program of 2.5 hours	Structured training was delivered to intervention clinicians with standardized elements and individualized observation and feedback delivered by palliative care faculty.
System changes	
Patient identification using the "surprise question"[a]	The surprise question "Would you be surprised if this patient died in the next year?"[33] was applied at regular intervals by oncology clinicians to lists of their patients.
Reminders	Email reminders were provided to intervention clinicians to initiate conversations using the SICG during routine care visits in the outpatient setting.
SICG documentation template in an accessible advance care planning module in the EMR	A novel, structured, accessible template in the electronic medical record was developed to document serious illness conversations, and intervention clinicians were trained to use it.
Coaching on use of the SICG	Palliative care faculty offered coaching to intervention clinicians on use of the SICG by phone, email, or in person.

The intervention will be adapted based on feedback from stakeholders in Aim 1 and the protocol will be amended to include details of the intervention to be delivered in Aim 2.

7.0 Treatment Protocol

7.1. Study Outline

We will screen and consent eligible patients of treating physicians at WCI and WCI-affiliated centers.

For Aim 1, the study team will conduct an in-person or zoom/phone interview for 30-60 minutes. First, we will explain the rationale of the study. Second, we will conduct an interview to elicit preferences and information regarding the ACP intervention.

For Aim 2, the study subject and caregiver (if applicable) will complete demographics and baseline measures. Following this, a telehealth visit will be scheduled with their oncology provider within 1-2 months of enrollment. If the patient does not have access to an electronic device, the study team will provide them with a tablet that is preloaded with the zoom application and internet access (if needed). Instructions on how to use zoom on the tablet will be provided. The sole purpose of the tablet is to allow for a zoom visit to occur and no data will be obtained and stored. If the tablet is lost or broken, we will provide a replacement tablet (and the broken tablet will be collected). We will work with the University IT to restrict the use of the tablets to zoom only.

During the ACP visit, their oncology provider will discuss ACP and EOL care. This visit will be recorded. Prior to the visit, providers will be provided with a checklist of items to discuss and summary of aging-related vulnerabilities. After the visit, the study subject and caregiver (if applicable) will complete post-intervention measures. They will be asked to mail back the tablet or return the tablet in the next in-person visit.

Within 4 weeks (up to 12 weeks if needed) of the telehealth visit, we will conduct an interview with the patient and caregiver (if applicable) either in-person or via zoom/phone for 30-60 minutes. We will also conduct an interview with the oncology provider who enrolled the patient on the study. All parties present for the recorded visit, including: enrolled patients, any accompanying caregivers, family or friends, the oncologist, and any other physicians or health care providers not participating in the study will be fully aware that the conversation is being audio-recorded before any recording begins, in addition to the prior written consent of enrolled patients. Patients, caregivers, and oncology providers may receive copies of these recordings at their request. Participants will complete post-intervention measures within 4 weeks of the visit (up to 12 weeks if needed).

7.2. Assessments of the Participants

Demographic, clinical, and cancer characteristics will be collected on paper or via RedCap**.**

7.2.1. Demographics (Patient, Caregivers, and Providers)

Patient and caregiver's age, race, ethnicity, gender, highest level of education achieved, employment status, and marital status. Caregiver's relationship to the patient will also be inquired. This will only be collected at baseline.

Provider's age, race, ethnicity gender, years in practice since completion of training, and disciplines (e.g., oncology physician, palliative care physician, APP, nurse) will be collected.

7.2.2. Clinical and Cancer Characteristics (Patient)

ECOG performance status, comorbidity, medications, weight, height, BMI, diagnosis and date of diagnosis, prior hematologic malignancies, cytogenetic risk group, and treatment regimen will be abstracted from the medical records. This information will only be collected at baseline.

In addition, we will collect the following from the medical records. We have previously collected this information in a retrospective fashion and will use similar procedures to extract this information prospectively from the medical records.

- Rate of hospice enrollment (and timing relative to death)
- Rate of palliative care referral (and timing relative to diagnosis)
- Rate of chemotherapy administration within the last 2 weeks of life
- Completion of advance directives which include MOLST forms, living will, durable power of attorney for healthcare, and healthcare proxy forms. Documentation of ACP conversation in the electronic medical record will also be collected.
- Do no resuscitation order (and timing related to diagnosis and death)
- Percentage of patients who died from cancer with more than one emergency department visit in the last 30 days of life
- Percentage of patients who died from cancer admitted to the ICU in the last 30 days of life
- Hospitalization in the last 30 days of life (number of hospitalizations, reasons for hospitalizations)
- Use of life-sustaining treatments (e.g., mechanical ventilation, vasopressors, tracheostomy, dialysis for acute kidney injury, percutaneous endoscopic gastrostomy) in the last 30 days of life
- Transfusion in the last 7 days of life
- Place of death (home, hospital, facility, etc.)
- Inpatient mortality rate

7.2.3. Measures

Measures will be collected via in-person, or mailed to the participants.

7.2.3.1. Functional Status (Patient) – baseline only

Activities of daily living (ADL): ADLs are measures of self-care. ADL independence will be assessed using the Katz Index of Independence in Activities of Daily Living, commonly referred to as the Katz ADL. The Katz ADL is the most appropriate instrument to assess functional status as a measurement of the client's ability to perform activities of daily living independently. Clinicians

typically use the tool to detect problems in performing activities of daily living and to plan care accordingly. The Index ranks adequacy of performance in the six functions of *bathing, dressing, toileting, transferring, continence, and feeding.* Clients are scored yes/no for independence in each of the six functions. A score of 6 indicates full function, 4 indicates moderate impairment, and 2 or less indicates severe functional impairment.[25]

Instrumental Activities of Daily Living (IADL): Self-reported functional status will be assessed using the IADL subscale of the Multidimensional Functional Assessment Questionnaire: Older American Resources and Services (OARS). The IADL subscale consists of seven questions rated on a three-point Likert scale. It measures the degree to which an activity can be performed independently.[26]

Fall History: A self-reported history of falls in the past year will be recorded. A history of a recent fall has been demonstrated to be independently predictive of increased risk for chemotherapy toxicity in older cancer patients.[27]

7.2.3.2. Psychological Health (Patient and Caregiver) – baseline and post-intervention

General Anxiety Disorder-7: A 7-item screening tool for anxiety.[28]

Patient Health Questionnaire-9 (PHQ-2): A 9-item valid and reliable screening tool depression in the general population.[29]

Distress: A self-reported tool to screen for symptoms of distress, using a 0-10 rating scale.[30]

7.2.3.3. Social Support (Patient) – baseline only

OARS Medical Social Support: A 13-item questionnaire for patients regarding persons involved in medical social support as well as perception of overall support.[31,32]

Patients also self-report their living situation and their main social support.

7.2.3.4. Nutritional status (Patient) – baseline only

Self-reported weight loss in the past 6 months

7.2.3.5. Cognition (Patient) – baseline only

BLESSED (baseline only): A screening tool for cognitive impairment in older adults.[33]

7.2.3.6. Satisfaction with Communication (Patient and caregiver) – post-intervention only

Health Care Climate Questionnaire (HCCQ): A questionnaire assessing patients' and caregivers' satisfaction with patient-oncologist communication.[34,35]

Heard and understood question: A self-report measure for seriously ill patients and their caregivers to report how well they feel heard and understand.[36]

7.2.3.7. Therapeutic alliance (Patient) – post-intervention only

Modified Human Connection Scale: A survey to measure the extent to which patients and caregivers feel a sense of mutual understanding, caring, and trust with their physicians.[37]

7.2.3.8. Goal-Concordant care (Patient) – post-intervention only

SUPPORT Survey: The Study to Understand Prognoses and Preferences for Outcomes and Risk of Treatments (SUPPORT) survey to assess if patient values align with current medical care.[38]

7.2.3.9. Usability (Patient and caregiver) – post-intervention only

Telehealth Usability Questionnaire: A questionnaire assessing the usability of telehealth implementation.[39]

7.2.3.10 Peaceful Acceptance of Illness (Patient) – post-intervention only

PEACE Questionnaire: Peace, Equanimity, and Acceptance in the Cancer Experience (PEACE) questionnaire to measure the extent to which patients with advanced cancer have a sense of peaceful acceptance of their terminal illness.[40]

7.2.3.11. Acceptability (Patient and clinician) – post-intervention only

Patient Acceptability Questionnaire: A questionnaire used to assess the impact of the serious illness conversation on the patient's understanding and perception of their diagnosis.[41]

Clinician Acceptability Questionnaire: A questionnaire used implementation to assess the clinicians experience in using the SICP with patients.[41]

7.2.3.12 Confidence (Provider) – baseline and post-intervention

Clinician Confidence Questionnaire: A questionnaire used to assess clinician's self-perceived ability to implement the SICP in real practice.[41]

7.2.3.13. Health Literacy (Patient and caregiver) – baseline only

Cancer health literacy (CHLT-6): A brief instrument to determine whether an individual has limited cancer health literacy.[42]

7.2.3.14 Quality of Life (Patient and caregiver) – baseline and post-intervention

*Functional Assessment of Cancer Therapy-Leukemia (FACT-Leu)***:** *T*he FACT-Leu scale was created by combining the Functional Assessment of Cancer Therapy-General module (FACT-G) and a sub-scale made up of 17 leukemia-specific items.[43] It been tested and determined to be a valid, reliable, and efficient

instrument for evaluating leukemia-specific health-related QoL. This will be used for patients.

Caregiver Quality of Life Index-Cancer: The instrument self-reported health-related QoL.[44] This will be used for caregivers.

7.2.2.15. Disease Understanding (Patient, caregiver, and clinician) – baseline and post intervention

Disease Understanding – Patient (baseline and post-intervention): A questionnaire assessing patient's prognostic understanding of illness. They will also be asked if prognostic information was provided.

Disease Understanding – Caregiver (baseline and post-intervention): A questionnaire assessing caregiver's prognostic understanding of illness. They will also be asked if prognostic information was provided.

Disease Understanding – Provider (post-intervention only): A physician-facing questionnaire assessing patient prognosis. They will also be asked if prognostic information was provided.

7.2.2.16. ACP Engagement Survey (Patient) – baseline and post-intervention – Aim 2

ACP Engagement Survey: 15-item engagement survey that assess patient self-efficacy and readiness for identification of a medical decision maker, identification of personal values, and flexibility in decision making and communication with their physician.

7.2.2.17. Feasibility metrics

Feasibility metrics will be collected:

- Retention rate (percentage of patients consented to the study ultimately completing all study components) – primary metric
- Recruitment rate (percentage of patients who are approached and agree to enroll) will also be described

8.0 Data Handling and Statistical Considerations

8.1. Data Handling

8.1.1. The same protocols and procedures for data quality and control that are readily used for the NCI Community Oncology Research Program (NCORP) Research Base protocols currently being overseen by our office (which have accrued over 1,000 patients in the previous year) will be used for this study. Patients will fill out forms generated from RedCap and this information will be entered into RedCap (Section 9.5). Study personnel will perform BLESSED and the scores will be entered into RedCap.

8.1.2. It is anticipated that allowing for the appropriate number of evaluable participants and by checking self-report measures for completeness, we will have a full complement of data. Every effort will be made to encourage and facilitate participants' completion of all questionnaires and all items on the questionnaires for each study assessment. In the event that missing data occur, every effort will be made to contact participants via phone and obtain the data or to find out why the questionnaires or items are missing. The reasons for missing data will be documented. Missing questionnaire items will be treated in accordance with the documented scoring procedures. Although it is very unlikely that missing values will not occur randomly, we will confirm their randomness. Multiple imputation[45] will be applied to (1) give more accurate statistical tests and standard errors for key treatment effect parameters and to (2) give some indication of the sensitivity of the analyses to missing data. The causes and pattern of the missing data will be examined and taken into consideration in the design of future studies.

8.1.2. For audio-recordings, these will be uploaded to Box within a week of the interview/clinic visits and deleted from the digital audio recorder (Sony). The recordings will be transcribed by a professional transcription service, and the transcripts will be used for data analysis.

8.1.4. Data collected (both assessments and transcripts) will only be accessed by the following: 1) The research team and 2) The treating physician and their designee.

8.2. Data Analysis and Sample Size:

8.2.1. Analysis Plan for Aim 1

We anticipate thematic saturation will be reached with this number of participants based on past similar research (i.e., the point at which no new data emerge).[19,20] All interviews will be conducted and audio-recorded by study personnel and then transcribed by a professional transcription service. Two trained personnel ("coders") will extract and highlight themes from the transcripts. We will analyze the qualitative data using grounded theory and constant comparative methods, with coding to structure data into categories and create groups according to the broader issues or themes.[46] The themes will focus on EOL care as it relates to older patients with AML and MDS, barriers and challenges to ACP and MOLST completion, potential solutions and ideas, experience

with telehealth interventions, added values of the intervention, support and concerns for the proposed intervention, components of the intervention that are important to them, and their opinions about the intervention (e.g., delivery, format). We will keep an audit trail to establish trustworthiness. We will critically examine the data collection and analysis process, discuss emerging codes, and reach consensus on principal themes. These themes will be used to adapt the telehealth-delivered ACP intervention.

8.2.2. Analysis Plan for Aim 2

Quantitative analyses: We anticipate that our proposed sample size will be sufficient based on prior research[22] and also published guidance on usability study.[47,48] We will employ descriptive statistics to summarize the data. Feasibility will be defined based on the retention rate (percentage of patients consented to the study ultimately completing all study components); >80% will be considered feasible. Recruitment rate (percentage of patients who are approached and agree to enroll) will also be described. Usability will be defined based on the Telehealth Usability Questionnaire completed by patients; total average of >5 will be considered usable.[49,50] We anticipate that about 20% of the participants will withdraw before post-intervention assessment due to death.[51] With 20 patients enrolled, we anticipate at least 16 patients to be evaluable. When we estimate retention rate and usability, a 95% CI will span approximately +/- 25%. For example, if we observe 12/16 (75%) patients complete the tasks, the CI will be 51-90%.

For other measures, these are being collected in preparation for a larger clinical trial in the future. As exploratory analyses, paired t-tests or McNemar's test will be used to evaluate change in measures from baseline to post-intervention.

Qualitative analyses will be per Aim 1. All audio-recorded interviews and clinic visits will audio-recorded by study personnel and then transcribed by a professional transcription service. The themes will focus on participant experience during the telehealth ACP visit and feedback which will be used to further optimize the study procedures and intervention.

For audio-recorded clinic encounters, we will assess EOL care concerns brought up by patients and caregivers. We will assess how the physician addresses these concerns. Quantitative analysis of the communication processes, including number of questions asked and topics discussed will be analyzed. We have previously used the same study procedures and coders will undergo extensive training and supervision by study investigators.

9.0 Data Management

9.1. Data Collection Table

9.1.1. Aim 1

a) Patient

	Eligibility and consent form	Assessment
Informed Consent	X	
Demographics		X
Clinical and Cancer Characteristics		X
Cancer Health Literacy (CHLT-6)		X
Qualitative Interview		X
Disease Understanding		X

b) Caregiver (if applicable)

	Eligibility and consent form	Assessment
Informed Consent	X	
Demographics		X
Cancer Health Literacy (CHLT-6)		X
Qualitative Interview		X
Disease Understanding		X

c) Oncology and Palliative Provider

	Eligibility and consent form	Assessment
Informed Consent	X	
Demographics		X
Qualitative Interview		X

9.1.2. Aim 2

a) Patient

	Eligibility and consent form	Baseline Assessment	Post-Intervention Assessment (within 4 weeks of the telehealth visit and up to 12 weeks)
Informed Consent	X		
Demographics		X	
Clinical and Cancer Characteristics		X	
Qualitative Interview			X
Activities of Daily Living (ADL), Instrumental Activities of Daily Living (IADL), Fall History		X	
Patient Health Questionnaire (PHQ-9), General Anxiety Disorder-7 (GAD-7), Distress		X	X
Nutritional Status		X	
OARS Medical Social Support		X	
Cognition (BLESSED)		X	
Health Care Communication Questionnaire (HCCQ), Heard and understood question			X
Therapeutic alliance Human Connection Survey			X
Cancer Health Literacy (CHLT-6)		X	
Telehealth Usability Questionnaire (TUQ)			X
Acceptability			X
ACP engagement survey		X	X
Peaceful acceptance of illness			X
Goal concordant care			X
Functional Assessment of Cancer Therapy-Leukemia (FACT-Leu)		X	X
Disease Understanding		X	X

b) Caregiver (if applicable)

	Eligibility and consent form	Baseline Assessment	Post-Intervention Assessment (within 4 weeks of the telehealth visit and up to 12 weeks)
Informed Consent	X		
Demographics		X	
Patient Health Questionnaire (PHQ-9), General Anxiety Disorder-7 (GAD-7), Distress		X	X
Qualitative Interview			X
Cancer Health Literacy (CHLT-6)		X	
Health Care Climate Questionnaire (HCCQ), Heard and understood question			X
Telehealth Usability Questionnaire (TUQ)			X
Caregiver Quality of Life Index-Cancer		X	X
Disease Understanding		X	X

c) Oncology provider

	Eligibility and consent form	Baseline Assessment	Post-Intervention Assessment (within 4 weeks of the telehealth visit and up to 12 weeks)
Informed Consent	X		
Demographics		X	
Qualitative Interview			X
Disease Understanding			X
Acceptability			X
Provider confidence survey		X	X

9.2. All hardcopy research records will be stored onsite in the URMC, in locked research files at the WCI. The Cancer Center is secured with electronic key cards. Offices within the Cancer Center are again secured by key and data is kept in locked file cabinets. Electronic research records are stored on the URMC's password secured and firewall protected networks. These are the same methods of security used for patient medical records. For audio-recordings, these will be uploaded to Box within a week of the interview and deleted from the audio recorder. All study

data will be kept for a period of 7 years after the study and all reports and publications are complete.

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

9.4. The study coordinator will assign a numerical study ID to each participant once they have signed the consent form (chronologically based on the data they signed consent i.e., 001, 002, 003…). All study forms and questionnaires will use this number and the participant's first, middle, and last initials as identifiers, to ensure data integrity. Other identifying information will not exist on these forms. A complete list of study participants with study ID, name, and contact information will be maintained separately. This linkage information will only be accessible to the study coordinator, study investigators, and the individuals responsible for maintaining the database.

9.5. Additionally, data on the socio-demographics, clinical, and cancer and treatment characteristics will be collected and managed by the research teams at URMC using REDCap electronic data capture tools hosted at URMC.[52] We will also evaluate the medical records for clinical characteristics and outcomes, and utilize REDCap to collect and manage this information.

> 9.5a. URMC provides the following information on the REDCap program: "Vanderbilt University, in collaboration with a consortium of institutional partners, has developed a software toolset and workflow methodology for electronic collection and management of research and clinical trial data, called REDCap (Research Electronic Data Capture). The REDCap system is a secure, web-based application that is flexible enough to be used for a variety of types of research. It provides an intuitive interface for users to enter data and real time validation rules (with automated data type and range checks) at the time of data entry. REDCap offers easy data manipulation with audit trails and functionality for reporting, monitoring and querying patient records, as well as an automated export mechanism to common statistical packages (SPSS, SAS, Stata, R/S-Plus). Through the REDCap Consortium, Vanderbilt has disseminated REDCap for use around the world. Currently, over 240 academic and non-profit consortium partners on six continents with over 26,000 research end-users use REDCap.[53]
>
> 9.5b. According to the Clinical and Translational Science Institute (CTSI), REDCap is supported with the following means. "The *CTSI Informatics Core*, a unit of the SMD *Academic Information Technology (AIT) Group,* will serve as a central facilitator for data processing and management. REDCap data collection projects rely on a thorough study-specific data dictionary defined in an iterative self-documenting process by all members of

the research team, with planning assistance from the *AIT-CTSI Informatics Core*. The iterative development and testing process results in a well-planned data collection strategy for individual studies."[46]

9.5c. The CTSI states that regarding security, "REDCap servers are housed in a local data center at the University of Rochester and all web-based information transmission is encrypted. REDCap was developed in a manner consistent with HIPAA security requirements and is recommended to University of Rochester researchers by the URMC Research Privacy Officer and Office for Human Subject Protection.[53]

10.0 Risks/Benefits

10.1. Risks

There is potential loss of confidentially associated with participation in the proposed study. In terms of loss of confidentiality, quantitative data from participants will need to be stored. Though rigorous and well-tested data safety and security guidelines will be observed, there is still a chance that confidentiality could be breached and sensitive medical information could become known to persons outside the research team.

10.2. Benefits

There are no anticipated benefits to the participants.

10.3 Payments and Costs

Patients and caregivers participating will be paid $10 Wegmans gift cards. For Aim 1, participants will receive the Wegmans gift cards immediately following the interviews. For Aim 2, participants will be paid for completion of the post-intervention assessment. Oncology providers will not be reimbursed for their participation.

10.4 Funding Source

The study is funded by the Cancer and Aging Research Group and National Institute of Aging.

References

1. SEER Cancer Statistics Factsheets: Acute Myeloid Leukemia. National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/statfacts/html/amyl.html. .
2. Ma X, Does M, Raza A, Mayne ST. Myelodysplastic syndromes: incidence and survival in the United States. *Cancer*. Apr 15 2007;109(8):1536-42. doi:10.1002/cncr.22570
3. Burnett AK, Russell NH, Hills RK, et al. A comparison of clofarabine with ara-C, each in combination with daunorubicin as induction treatment in older patients with acute myeloid leukaemia. *Leukemia*. 2017//02/02 2017;31(2):310-317. doi:10.1038/leu.2016.225
4. Lancet JE, Uy GL, Cortes JE, et al. Final results of a phase III randomized trial of CPX-351 versus 7+3 in older patients with newly diagnosed high risk (secondary) AML. *Journal of Clinical Oncology*. 2016//05/05-20 2016;34(15_suppl):7000-7000. doi:10.1200/JCO.2016.34.15_suppl.7000
5. Kantarjian HM, Thomas XG, Dmoszynska A, et al. Multicenter, randomized, open-label, phase III trial of decitabine versus patient choice, with physician advice, of either supportive care or low-dose cytarabine for the treatment of older patients with newly diagnosed acute myeloid leukemia. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology*. 2012//07/07-20 2012;30(21):2670-2677. doi:10.1200/JCO.2011.38.9429
6. Juliusson G, Lazarevic V, Hörstedt A-S, Hagberg O, Höglund M. Acute myeloid leukemia in the real world: why population-based registries are needed. *Blood*. 2012//04/04-26 2012;119(17):3890-3899. doi:10.1182/blood-2011-12-379008
7. Khan C, Pathe N, Fazal S, Lister J, Rossetti JM. Azacitidine in the management of patients with myelodysplastic syndromes. *Ther Adv Hematol*. Dec 2012;3(6):355-73. doi:10.1177/2040620712464882
8. DiNardo CD, Pratz K, Pullarkat V, et al. Venetoclax combined with decitabine or azacitidine in treatment-naive, elderly patients with acute myeloid leukemia. *Blood*. Jan 3 2019;133(1):7-17. doi:10.1182/blood-2018-08-868752
9. Stein EM, DiNardo CD, Pollyea DA, et al. Enasidenib in mutant IDH2 relapsed or refractory acute myeloid leukemia. *Blood*. Aug 10 2017;130(6):722-731. doi:10.1182/blood-2017-04-779405
10. DiNardo CD, Pratz KW, Letai A, et al. Safety and preliminary efficacy of venetoclax with decitabine or azacitidine in elderly patients with previously untreated acute myeloid leukaemia: a non-randomised, open-label, phase 1b study. *The Lancet Oncology*. Feb 2018;19(2):216-228. doi:10.1016/s1470-2045(18)30010-x
11. Shahrokni A, Loh KP, Wood WA. Toward Modernization of Geriatric Oncology by Digital Health Technologies. *Am Soc Clin Oncol Educ Book*. Mar 2020;40:1-7. doi:10.1200/edbk_279505
12. Earle CC, Park ER, Lai B, Weeks JC, Ayanian JZ, Block S. Identifying potential indicators of the quality of end-of-life cancer care from administrative data. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. Mar 15 2003;21(6):1133-8. doi:10.1200/jco.2003.03.059
13. Odejide OO, Cronin AM, Condron NB, et al. Barriers to Quality End-of-Life Care for Patients With Blood Cancers. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. Sep 10 2016;34(26):3126-32. doi:10.1200/jco.2016.67.8177
14. Hui D, Didwaniya N, Vidal M, et al. Quality of end-of-life care in patients with hematologic malignancies: a retrospective cohort study. *Cancer*. May 15 2014;120(10):1572-8. doi:10.1002/cncr.28614
15. Earle CC, Landrum MB, Souza JM, Neville BA, Weeks JC, Ayanian JZ. Aggressiveness of cancer care near the end of life: is it a quality-of-care issue? *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. Aug 10 2008;26(23):3860-6. doi:10.1200/jco.2007.15.8253
16. Fletcher SA, Cronin AM, Zeidan AM, et al. Intensity of end-of-life care for patients with myelodysplastic syndromes: Findings from a large national database. *Cancer*. Apr 15 2016;122(8):1209-15. doi:10.1002/cncr.29913

17. Bernacki R, Paladino J, Neville BA, et al. Effect of the Serious Illness Care Program in Outpatient Oncology: A Cluster Randomized Clinical Trial. *JAMA Intern Med*. Jun 1 2019;179(6):751-759. doi:10.1001/jamainternmed.2019.0077
18. Almathami HKY, Win KT, Vlahu-Gjorgievska E. Barriers and Facilitators That Influence Telemedicine-Based, Real-Time, Online Consultation at Patients' Homes: Systematic Literature Review. *Journal of medical Internet research*. Feb 20 2020;22(2):e16407. doi:10.2196/16407
19. Loh KP, Abdallah M, Kadambi S, et al. Treatment decision-making in acute myeloid leukemia: a qualitative study of older adults and community oncologists. *Leuk Lymphoma*. Oct 11 2020:1-12. doi:10.1080/10428194.2020.1832662
20. Loh KP, Sanapala C, Digiovanni G, Mustian K, Klepin H, Janelsins M, Schnall R, Culakova E, Vertino P, Susiarjo M, Mendler J, Liesveld J, Mohile S. Qualitative study of a mobile health exercise intervention for older patients with myeloid neoplasms. Oral presentation at: University of Rochester Department Medicine Unmasked Conference; 27-29 May 2020, Rochester, New York, United States.
21. Loh KP, Kadambi S, Mohile SG, Mendler JH, Liesveld JL, O'Dwyer KM, Becker MW, McHugh C, Stock W, Majhail N, Wildes T, Duberstein PR, Klepin HD. Qualitative study of factors that influence treatment decision-making among community oncologists and older patients with acute myeloid leukemia (AML). Poster presentation at: American Society of Hematology Annual Meeting; 30 Nov-4 Dec 2018, San Diego, California, United States.
22. Loh KP, Ramsdale E, Culakova E, et al. Novel mHealth App to Deliver Geriatric Assessment-Driven Interventions for Older Adults With Cancer: Pilot Feasibility and Usability Study. *JMIR Cancer*. Oct 29 2018;4(2):e10296. doi:10.2196/10296
23. Acharya UH, Halpern AB, Wu QV, et al. Impact of region of diagnosis, ethnicity, age, and gender on survival in acute myeloid leukemia (AML). *J Drug Assess*. 2018;7(1):51-53. doi:10.1080/21556660.2018.1492925
24. Cartwright RA, Gurney KA, Moorman AV. Sex ratios and the risks of haematological malignancies. *Br J Haematol*. Sep 2002;118(4):1071-7. doi:10.1046/j.1365-2141.2002.03750.x
25. Shelkey M, Wallace M. Katz Index of Independence in Activities of Daily Living. *Home Healthcare Now*. 2001;19(5)
26. Graf C. The Lawton instrumental activities of daily living scale. *The American journal of nursing*. Apr 2008;108(4):52-62; quiz 62-3. doi:10.1097/01.Naj.0000314810.46029.74
27. Hurria A, Togawa K, Mohile SG, et al. Predicting chemotherapy toxicity in older adults with cancer: a prospective multicenter study. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2011;29(25):3457-3465. doi:10.1200/JCO.2011.34.7625
28. Löwe B, Decker O, Müller S, et al. Validation and standardization of the Generalized Anxiety Disorder Screener (GAD-7) in the general population. *Medical care*. Mar 2008;46(3):266-74. doi:10.1097/MLR.0b013e318160d093
29. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med*. Sep 2001;16(9):606-13. doi:10.1046/j.1525-1497.2001.016009606.x
30. Ownby KK. Use of the Distress Thermometer in Clinical Practice. *J Adv Pract Oncol*. Mar 2019;10(2):175-179.
31. Fillenbaum GG. *Multidimensional functional assessment of older adults : the Duke Older Americans Resources and Services procedures / Gerda G. Fillenbaum*. L. Erlbaum Associates; 1988.
32. Fillenbaum GG, Smyer MA. The development, validity, and reliability of the OARS multidimensional functional assessment questionnaire. *J Gerontol*. Jul 1981;36(4):428-34. doi:10.1093/geronj/36.4.428
33. Jayani RV, Magnuson AM, Sun CL, et al. Association between a cognitive screening test and severe chemotherapy toxicity in older adults with cancer. *J Geriatr Oncol*. Mar 2020;11(2):284-289. doi:10.1016/j.jgo.2019.10.004

34. Freytag J, Street RL, Jr., Xing G, et al. The ecology of patient and caregiver participation in consultations involving advanced cancer. *Psychooncology*. 2018;27(6):1642-1649. doi:10.1002/pon.4710
35. Gremigni P, Sommaruga M, Peltenburg M. Validation of the Health Care Communication Questionnaire (HCCQ) to measure outpatients' experience of communication with hospital staff. *Patient Education and Counseling*. 2008/04/01/ 2008;71(1):57-64. doi:https://doi.org/10.1016/j.pec.2007.12.008
36. Gramling R, Stanek S, Ladwig S, et al. Feeling Heard and Understood: A Patient-Reported Quality Measure for the Inpatient Palliative Care Setting. *J Pain Symptom Manage*. Feb 2016;51(2):150-4. doi:10.1016/j.jpainsymman.2015.10.018
37. Mack JW, Block SD, Nilsson M, et al. Measuring therapeutic alliance between oncologists and patients with advanced cancer: the Human Connection Scale. *Cancer*. Jul 15 2009;115(14):3302-11. doi:10.1002/cncr.24360
38. A controlled trial to improve care for seriously ill hospitalized patients. The study to understand prognoses and preferences for outcomes and risks of treatments (SUPPORT). The SUPPORT Principal Investigators. *Jama*. Nov 22-29 1995;274(20):1591-8.
39. Parmanto B, Lewis AN, Jr., Graham KM, Bertolet MH. Development of the Telehealth Usability Questionnaire (TUQ). *Int J Telerehabil*. 2016;8(1):3-10. doi:10.5195/ijt.2016.6196
40. Mack JW, Nilsson M, Balboni T, et al. Peace, Equanimity, and Acceptance in the Cancer Experience (PEACE): validation of a scale to assess acceptance and struggle with terminal illness. *Cancer*. Jun 2008;112(11):2509-17. doi:10.1002/cncr.23476
41. Bernacki R, Hutchings M, Vick J, et al. Development of the Serious Illness Care Program: a randomised controlled trial of a palliative care communication intervention. *BMJ Open*. Oct 6 2015;5(10):e009032. doi:10.1136/bmjopen-2015-009032
42. Dumenci L, Matsuyama R, Riddle DL, et al. Measurement of cancer health literacy and identification of patients with limited cancer health literacy. *J Health Commun*. 2014;19 Suppl 2(0 2):205-24. doi:10.1080/10810730.2014.943377
43. Cella D, Jensen SE, Webster K, et al. Measuring health-related quality of life in leukemia: the Functional Assessment of Cancer Therapy--Leukemia (FACT-Leu) questionnaire. *Value Health*. Dec 2012;15(8):1051-8. doi:10.1016/j.jval.2012.08.2210
44. Weitzner MA, Jacobsen PB, Wagner H, Jr., Friedland J, Cox C. The Caregiver Quality of Life Index-Cancer (CQOLC) scale: development and validation of an instrument to measure quality of life of the family caregiver of patients with cancer. *Qual Life Res*. 1999;8(1-2):55-63. doi:10.1023/a:1026407010614
45. Little R, Yau L. Intent-to-treat analysis for longitudinal studies with drop-outs. *Biometrics*. Dec 1996;52(4):1324-33.
46. Hsieh HF, Shannon SE. Three approaches to qualitative content analysis. *Qual Health Res*. Nov 2005;15(9):1277-88. doi:10.1177/1049732305276687
47. Nielsen J, Landauer TK. A mathematical model of the finding of usability problems. CHI '93 Conference on Human Factors in Computing Systems; 1993; Amsterdam, The Netherlands. 1993. pp. 206–213.
48. Virzi RA. Refining the Test Phase of Usability Evaluation: How Many Subjects Is Enough? *Human Factors*. 1992/08/01 1992;34(4):457-468. doi:10.1177/001872089203400407
49. Parmanto B, Lewis AN, Jr., Graham KM, Bertolet MH. Development of the Telehealth Usability Questionnaire (TUQ). *Int J Telerehabil*. Spring 2016;8(1):3-10. doi:10.5195/ijt.2016.6196
50. Layfield E, Triantafillou V, Prasad A, et al. Telemedicine for head and neck ambulatory visits during COVID-19: Evaluating usability and patient satisfaction. *Head Neck*. Jul 2020;42(7):1681-1689. doi:10.1002/hed.26285

51. DiNardo CD, Jonas BA, Pullarkat V, et al. Azacitidine and Venetoclax in Previously Untreated Acute Myeloid Leukemia. *N Engl J Med*. Aug 13 2020;383(7):617-629. doi:10.1056/NEJMoa2012971
52. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. Apr 2009;42(2):377-81. doi:10.1016/j.jbi.2008.08.010
53. Clinical & Translational Science Institute. REDCap. REDCap at the University of Rochester. Available at: Https://www.urmc.rochester.edu/ctsi/research-help/REDCap.cfm.