Statistical Analyses and Data Management Procedures

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| TRIAL FULL TITLE | Improving Communication for Cancer Treatment: Addressing Concerns of Older Cancer Patients and Caregivers (COACH) |
| ClinicalTrials.gov ID: | NCT02107443 |
| SAP VERSION | 0.3 |
| SAP VERSION DATE | Last edited on 2018, June 21st |
| TRIAL STATISTICIANS | Charles Heckler, PhD (charles_heckler@URMC.Rochester.edu)<br>Eva Culakova, PhD (Eva_Culakova@URMC.Rochester.edu)<br>Javier Bautista, MS, MBA (Javier_Bautista@URMC.Rochester.edu) |
| TRIAL + INVESTIGATORS | Supriya Mohile, MD (supriya_mohile@urmc.rochester.edu)<br>Arti Hurria, MD (ahurria@coh.org)<br>William Dale, PhD, MD (wdale@medicine.bsd.uchicago.edu) |
| SAP AUTHOR | Charles Heckler, PhD (charles_heckler@URMC.Rochester.edu)<br>Nikesha Gilmore, PhD (Nikesha_gilmore@urmc.rochester.edu)<br>LianLian Lei (Lianlian_lei@urmc.rochester.edu) |

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# 1 Abbreviations and Key Sources

| **Abbreviations** | |
|---|---|
| AE | Adverse Event |
| ADL | Activities of Daily Living |
| BLUP | Best Linear Unbiased Predictors |
| BOMC | Blessed-Orientation Memory Concentration Test |
| C | Caregiver |
| COACH | Communication On Aging and Cancer Health |
| CRA | Caregiver Reactions Assessment |
| CTSQ | Cancer Treatment Satisfaction Questionnaire |
| E | Exploratory |
| FACT-G | Functional Assessment of Chronic Illness Therapy-G |
| GA | Geriatric Assessment |
| GAD | Generalized Anxiety Disorder |
| GDS | Geriatric Depression Scale |
| HCCQ | Health Care Climate Questionnaire |
| HCCQ-age | Health Care Climate Questionnaire modified for age-related communication |
| HRQoL | Health Related Quality of Life |
| IADL | Instrumental Activities of Daily Living |
| ICC | Intracluster Correlation |
| IRB | Institutional Review Board |
| IRR | Inter Rater Reliability |
| KPS | Karnofsky Performance Status |
| MAR | missing at random |
| MCMC | Markov chain Monte Carlo |
| MDASI | MD Anderson Symptom Inventory |
| MNAR | missing not at random |
| MUIS | Mischel Uncertainty in Illness Scale |
| NCI | National Cancer Institute |
| OARS | Older American Resources and Services |
| PCORI | Patient Centered Outcomes Research Institute |
| PEACE | Peace, Equanimity, and Acceptance in the Cancer Experience |
| PEPPI | The Perceived Efficacy in Patient-Physician Interactions |
| PI | Principal Investigator |
| Phys | Physician |
| PHQ-2 | 2-Item Patient Health Questionnaire |
| Pt | Patient |
| SPPB | Short Physical Performance Battery |
| S2 | Secondary Aim 2 |
| S3 | Secondary Aim 3 |
| URCC NCORP | University of Rochester Cancer Center NCI Community Oncology Program |
| URoch | University of Rochester |

| | |
|---|---|
| VOICE | Values and Options in Cancer Care |

| **Key Sources** | |
|---|---|
| Prop_PCORI | Research Grant Proposal to PCORI (CD-12-11-4634) |
| Protocol URCC 13070 | Improving Communication for Cancer Treatment: Addressing Concerns of Older Cancer Patients and Caregivers (COACH) |
| Reg_CT | ClinicalTrials.gov registration (NCT02107443)<br>National Library of Medicine's Health Services Research projects in progress (HSRP20143249) |

# 2 Introduction

## 2.1 Summary

This study will evaluate whether a standardized geriatric assessment (GA) administered through a novel web-based approach can facilitate communication of age-related problems that could influence outcomes important to the older cancer patient and his/her caregivers. Adults, age ≥ 70 with an advanced solid tumor malignancy in the University of Rochester Cancer Center NCI Community Oncology Program (URCC NCORP) network are eligible. Oncology physicians who practice at sites within the URCC NCORP network are eligible to participate in the study and are enrolled. Their eligible patients then undergo the informed consent process; those patients who agreed to participate in this study undergo a clinical assessment consisting of socio-demographic characteristics and GA.

## 2.2 Intervention to be studied

This is a cluster randomized study within the URCC NCORP network evaluating whether GA summary plus GA-driven recommendations can improve patient satisfaction with communication regarding age-related issues between patients, oncology physicians, and caregivers and improve discussion about age-related issues during a clinic consultation. Secondary aims are to determine if the intervention improves patient-reported quality of life, improves caregiver burden, and caregiver satisfaction with communication.

## 2.3 Study Objectives

This study will evaluate whether a standardized geriatric assessment (GA) administered through a novel web-based approach can facilitate communication of age-related problems that could influence outcomes important to the older cancer patient and his/her caregivers. A Geriatric assessment (GA) is a compilation of survey-based and assessment tools to assess geriatric domains such as comorbidity, functional status, nutrition, physical performance, cognition, and social support, which measures aging related issues that can affect the quality of life of an older patient with cancer. GA can better predict tolerance to cancer treatment and adds important age-related information that is not routinely captured by oncologists. Adults, age ≥ 70 with an advanced solid tumor malignancy in the University of Rochester Cancer Center NCI Community Oncology Program (URCC NCORP) network will be eligible. Eligible patients should choose one caregiver to participate. The study has received support from the Patient Centered Outcomes Research Institute (PCORI) under their "Communication and Dissemination" portfolio. In addition, the National Cancer Institute (NCI) review was required which led to changes in the aims and statistical plan.

### 2.3.1 Primary Aim (*as specified by NCI*)

To determine if providing geriatric assessment (GA) summary plus GA-driven recommendations to patients, their caregivers and oncology **physicians improves patient satisfaction with communication with the oncology physician** regarding age-related concerns.

*Primary hypothesis:* Patient satisfaction with communication with the oncology physician about age-related issues will be significantly higher in the intervention group compared to the control group.

The NCI primary outcome, patient satisfaction regarding communication about age-related issues as measured by a modified Health Care Climate Questionnaire (HCCQ-age), will be obtained by the Telephone Team, via a phone call administered by trained personnel blinded to group assignment within 1 to 7 days of the baseline audio-recorded clinic consultation. The HCCQ-age will be mailed (with a return envelope) if a telephone call is not feasible. If the responses to the survey are not able to be obtained before the 4-6 week assessment, the HCCQ-age at 4-6 weeks will be utilized.

#### 2.3.2 Secondary Aim 1 (*Primary Aim as specified by PCORI*)

To determine if providing GA summary plus GA-driven recommendations to patient, their caregivers, and oncology physicians increases discussions about age-related issues during clinic consultation.

*Primary hypothesis:* A higher number of age-related issues will be discussed and addressed in the intervention group.

The outcome measure for this aim is the number of age-related discussions that occur in the consultation clinic visit between the patient, oncology physician, and caregiver. The clinic visit will be audio-recorded.

#### 2.3.3 Other Secondary Aims

##### 2.3.3.1 Secondary Aim 2

To determine whether initially providing patients, their caregivers, and oncology physicians with GA summary plus GA-driven recommendations prior to their treatment influences **quality of life of older patients** receiving treatment and their caregivers.

##### 2.3.3.2 Secondary Aim 3

To determine whether providing patients, their caregivers, and oncology physicians with GA summary plus GA-driven recommendations influences **caregiver satisfaction with communication** about age-related issues.

#### 2.3.4 Exploratory Aims

Exploratory aims will evaluate (1) whether the number of discussions about age-related issues during the clinic visit correlates with patient satisfaction, (2) whether the intervention increase the proportion of age-related concerns that are acknowledged and addressed, and (3) if communication about age-related issues influences how patients, caregivers, and oncology physicians make decisions for cancer treatment. An additional exploratory aim will examine the impact of the intervention on survival.

## 3 Study Methods

### 3.1 General Study Design and Comparators

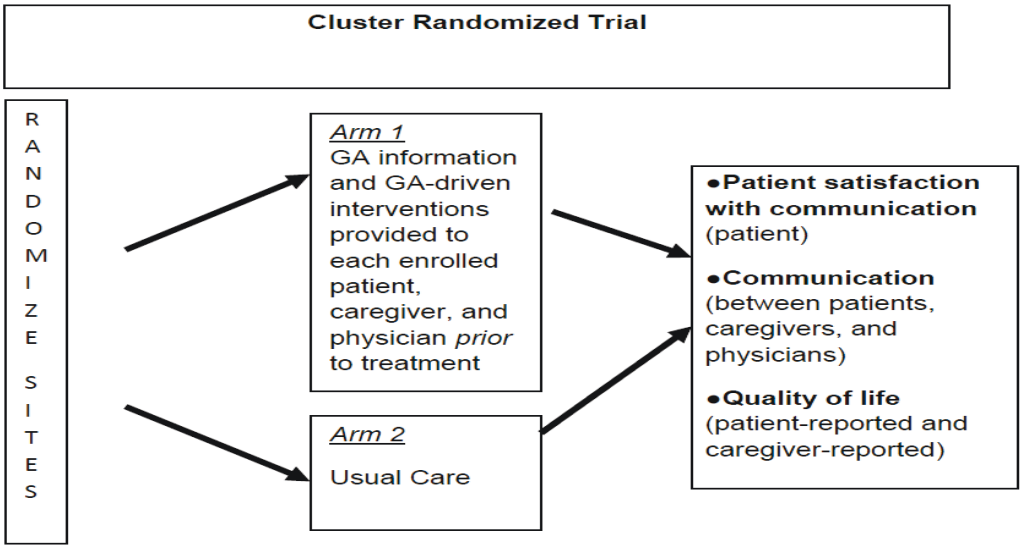
The study design is a cluster randomized clinical trial. The intervention is designed to try to improve communication about age related concerns between oncology physicians, patients and their caregivers. Study subjects include oncologists, patients and their caregivers. Sites within the URCC

NCORP network are randomized prior to the enrollment of any subjects at any site. Sites in both arms (control and intervention) will conduct the GA on all subjects. Physicians at sites randomized to the intervention arm will be provided with a GA summary and GA-driven recommendations. Since the GA is not part of community oncology physicians' standard of care, a usual care comparator arm is appropriate and will allow for the accurate and appropriate assessment of how the intervention can improve communication about age-related issues and outcomes compared to current clinical practice. This study design is similar to previous studies that evaluated the impact of providing summarized HRQoL information to patients and oncology physicians on communication and outcomes. Usual care was the comparator arm in these cluster randomized studies.

## 3.2 Study design

The study is designed as a cluster randomized trial because a care of service model is applied to each patient by the oncology team. If a cluster randomized design were not undertaken, there would be contamination in that oncology physicians could choose the care of service model if they were exposed to patients randomized to both arms. Given rapid changes that can occur in oncology practice with new supportive care and treatment agents, it is important to compare outcomes in the same time frame as would be possible in a cluster randomized study design compared to a "pre" versus "post" intervention study design.

The chart below depicts the study schema.




## 3.3 Inclusion-Exclusion Criteria and General Study Population

### 3.3.1 Entry Criteria for Oncology Physicians

Oncology physicians must work at a NCORP practice site with no plans to leave that NCORP practice or retire at the time of enrollment into the study.

### 3.3.2 Entry Criteria for Patients

#### 3.3.2.1 Inclusion Criteria for Patients

**3.3.2.1a** Male or female 70 years of age or older

**3.3.2.1b** Diagnosis of an advanced solid tumor malignancy (advanced cancer) or lymphoma. In most situations, this would be a stage IV cancer. A patient with a diagnosis

of stage III cancer or lymphoma is eligible if cure is not possible or anticipated. Clinical staging without pathological confirmation of advanced disease is allowed.

Must be considering or currently receiving any kind of cancer treatment (any line), including but not limited to hormonal treatment, chemotherapy, monoclonal antibody therapy, or targeted therapy. Patients who are considering therapy are eligible even if they ultimately choose not to be on therapy. Patients with a history of any previous cancer treatment, including radiation and/or surgery are eligible. A patient may also be enrolled on a treatment trial and participate in this study, if all other inclusion and exclusion criteria are met.

**3.3.2.1c** Have at least one geriatric assessment domain meet the cut-off score for impairment other than polypharmacy.

**3.3.2.1d** Have visits planned with the oncology physician for at least 3 months and be willing to come in for study visits.

**3.3.2.1e** Able to provide informed consent or, if the oncology physician determines the patient to not have decision-making capacity, a patient-designated health care proxy (per institutional policies) must sign consent by the baseline visit.

**3.3.2.1f** Subject has adequate understanding of the English language because not all GA measures have been validated in other languages.

#### 3.3.2.2 Exclusion Criteria for Patients

**3.3.2.2a** Have surgery planned within 3 months of consent. Patients who have previously received surgery are eligible.

**3.3.2.2b** Have already made a decision to not undergo any cancer treatment (e.g., being followed in best supportive care or hospice).

### 3.3.3 Entry Criteria for Caregivers

A caregiver can be anyone, age 21 or over, who is able to understand spoken English and understand the study process and provide informed consent. One caregiver for each patient will be eligible and must be chosen by the patient. For the purposes of this study, a caregiver is defined as a valued and trusted person in a patient's life who is supportive in health care matters by providing valuable social support and/or direct assistive care. The caregiver accompanies the patient to medical appointments, is able to listen and give thoughtful advice and may be a family member, partner, friend, or professional caregiver. The expectation is approximately 80% of patients will have a caregiver.

#### 3.3.3.1 Inclusion Criteria for Caregivers

**3.3.3.1a** Selected by the patient when asked if there is a "family member, partner, friend or caregiver [age 21 or older] with whom you discuss or who can be helpful in health-related matters;" patients who cannot identify such a person ("caregiver") can be eligible for the study. A caregiver need not be someone who lives with the patient or provides

direct hands-on care. A caregiver can be any person who provides support (in any way) to the patient.

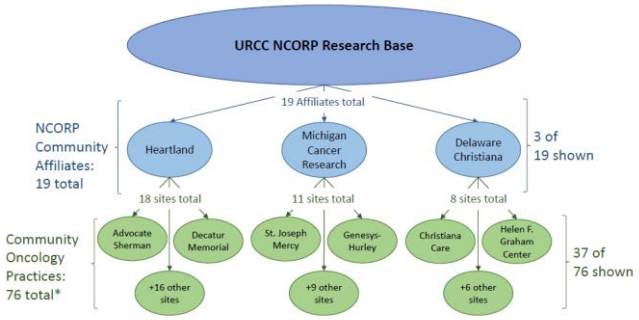
**3.3.3.1b** If a health care proxy signs consent for or with a patient, and wants to participate in the caregiver portion of the study, this same person will always be the caregiver selected. If a health care proxy does not want to enroll as a caregiver in the study or, if enrolled, chooses to stop their own participation in the caregiver portion of the study, but is able to assist the patient in completing the study, the patient can still participate. In other words, the health care proxy can choose NOT to participate in the caregiver portion of the study. This does not preclude the patient from participating in the patient portion of the study with the health care proxy's assistance.

**3.3.3.2 Exclusion *Criteria for Caregivers***

**3.3.3.2a** Caregivers unable to understand the consent form due to cognitive, health, or sensory impairment will be excluded.

### 3.3.4 Randomization

NCORP practice sites will be randomized within a 2-arm cluster randomized design utilizing NCORP practice sites as the unit of randomization (see Figure to the right). A NCORP practice site is defined as any practice location within an overarching NCORP designation (NCORP Community Affiliate) where oncology physicians and study staff work independently (i.e., do not cross over into another practice site). Practice sites are randomized to one of either control (receiving only the GA without summary provided to oncology physician) or intervention (receiving the GA plus geriatric assessment recommendations with a summary provided to the oncology physician) study arm by means of a computer–generated randomization table, determined using R software provided by Dr. Charles Heckler, the lead biostatistician of the URCC NCORP Research Base (Appendix A).




**Notes**: Schematic depicts relationships between the URCC NCORP Research Base, Community Affiliates, and sites; *Randomization occur at the level of the Community Oncology Practice

Sites are randomized on a continual basis due to a variety of factors (i.e., a new NCORP Community Affiliate has been added to the URCC NCORP Research Base network, a new oncology practice site has been added to an existing NCORP Community Affiliate, or an oncology practice site that is a currently affiliated with an NCORP Community Affiliate has expressed interest in participating in the COACH study). Past accrual to URCC studies (or NCORP Cancer Control studies if URCC accrual information is not available for new Affiliates and sites) is used to stratify each practice site as a **large** accruing (20 or more accruals/year) site or a **small** accruing (less than 20 accruals/year) practice site in order to assure balance in the randomization. The general assumption will be that any new site will be considered "small", unless it is determined based on past accruals that they are large. For new oncology practice sites that meet the definition for being independent (i.e., physicians and staff that do not cross over into another site), the next unassigned randomization allocation, from the randomization table will be used to assign their study arm (Appendix A). The randomization table takes into account size of the practice site.

If a new oncology practice site is added at a later time during the study with physicians/staff that also see patients (cross over) at both or multiple practice sites, the new practice site will be assigned to the same study arm as the already randomized practice site where the physician/staff also sees patients.

Once sites have IRB approval on file with the Research Base and at least one member of research staff is trained on all study procedures, they are notified of their randomization allocation by an email from the study PI, Dr. Mohile. Practice sites names and randomization assignments are saved in the database, this is used to link to which arm each study patient belongs to during patient registration.

The original sample size calculation (see next section) was based on the randomization of the 16 NCORP oncology practice sites. During study startup, as the structure of the new NCORP affiliates unfolded, more practice sites than was anticipated were interested in participating. The original protocol included the ability for more sites to participate, since the increase in the number of the clusters also increases the statistical power of the study.

## 3.4 Sample Size

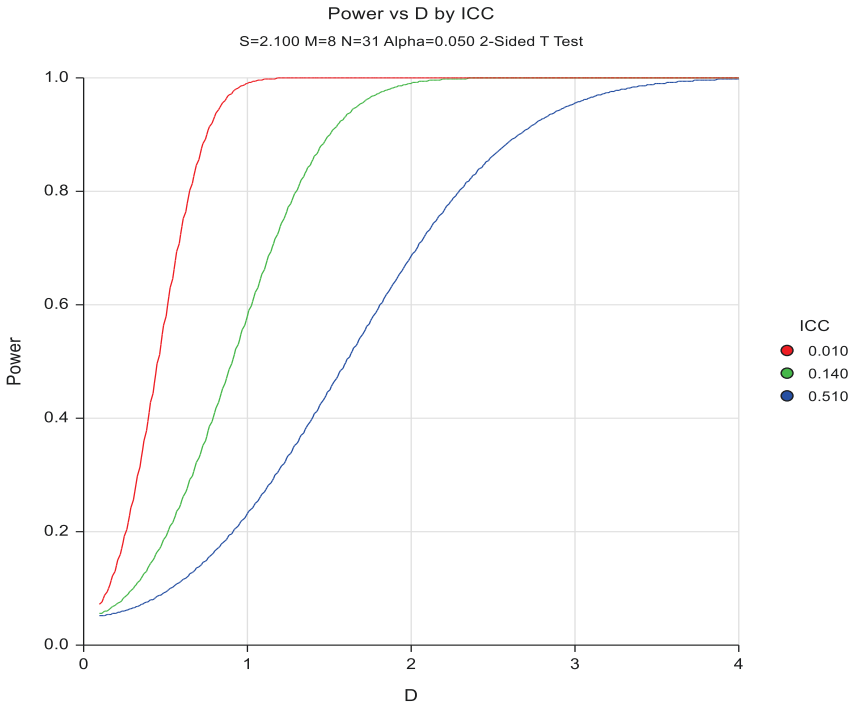
### 3.4.1 Sample Size for NIH-specified Primary Aim

We will utilize the modified HCCQ to address patient satisfaction with communication regarding age-related issues (HCCQ-age). Based on an analysis of the VOICE study, the standard deviation estimate of HCCQ was 2.1. The Intracluster Correlation (ICC) was 0.14 with a 95% confidence interval from 0.01 to 0.51. Because of the large amount of uncertainty in the ICC, we calculated power curves for ICC={0.01, 0.14, 0.51}, with ICC=0.51 being the most conservative. This design (8 sites per arm and 31 subjects per site) has 80% power at the 0.05 significance level to detect a change in HCCQ of 0.6, 1.3 and 2.3 for ICC={0.01, 0.14, 0.51}, respectively. Since the best estimate of the ICC is 0.14, the expected detectable difference is 1.3. This corresponds to an effect size of 0.62. The range of the HCCQ-age scores is 7 (worst possible) to 35 (best possible). Analyses will be based on the HCCQ variables being a continuous variable. We will use a generalized mixed model to confirm robustness. The sample size figure below shows the power for a range of detectable differences (D) for ICC=0.01, 0.14 and 0.51. Small changes in satisfaction scores have been interpreted in other studies to be meaningful given a focus on achievement of high satisfaction scores and the link with reimbursement. In addition to evaluating HCCQ-age using the total score as a continuous variable, we will compare the results for each question as a dichotomous variable (5 vs <5). If the distribution is skewed, we will consider treating HCCQ-age as an ordinal variable in analyses.

Accounting for a small dropout rate of 5% (based on our observational cohort data), the targeted accrual will be **528 patient subjects total.** The dropout rate reflects patients who sign consent but withdraw prior to the audio-recorded baseline visit and capture of HCCQ-age (which will occur within 7 days of baseline visit). To date out of 479 evaluable patients we currently have received 407 baseline HCCQ-ages; 4-6 week HCCQ-ages will be substituted per protocol for 33 patients; there are 19 patients that have no baseline HCCQ-age because they either died or withdrew before the 4-6 week visit, this brings us to a current total of 440 baseline HCCQs to be used in the per protocol analysis.

Though the COACH study sample size is 528 patient/caregiver dyads, there is no cap on the number of physicians enrolled. A total of 2 participants withdrew between screening and their baseline visit. Of the 413 patients enrolled, 159 have completed the study and all study requirements, 21 completed the study with some missing data, and 101 are still active. To date of the patients enrolled 48 withdrew, 61 expired, 21 their status is being determined and 4 participants are lost to follow-up. Due to the frailty of the subjects in this population, it is not

**Figure 1: Sample Size for NIH-specified Primary Aim**




unusual that many stop the study early due to progressive illness.

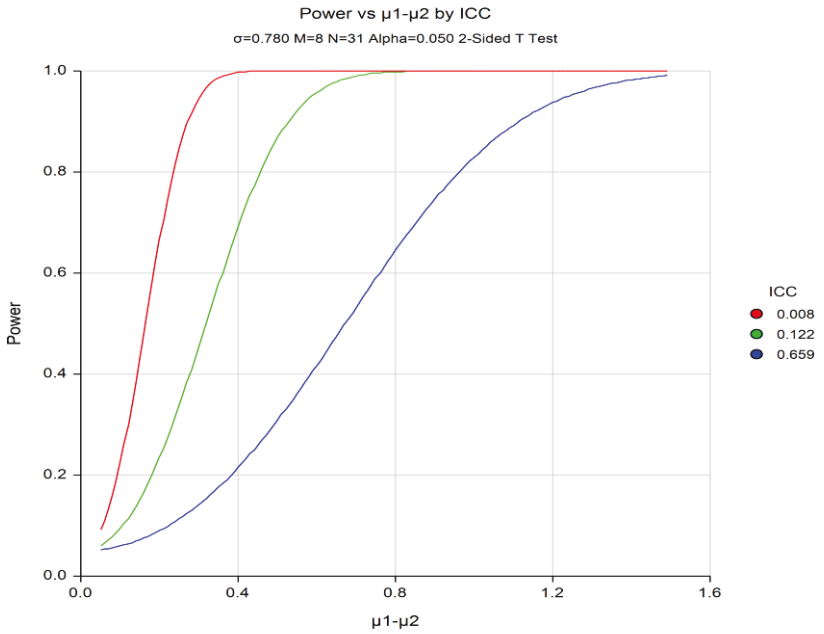
***As of February 1, 2017, we have 68 practice sites participating in the COACH study; the increased practice site clusters should provide better statistical power. The total patient sample size is the same, and accrual will cease when our target is met.***

### 3.4.2 Sample Size for PCORI-Specified Primary Aim

The primary focus for the PCORI analysis is the number of discussions related to geriatric domains, as measured by the GA, brought up and addressed during the audio-recorded baseline visit. In our preliminary data from a multicenter study, the median number of discussions was 1 in 32 audio-recorded conversations between older patients, their caregivers, and oncology physicians. This preliminary work allowed us to calculate the intracluster correlation (ICC) amongst 8 different sites for the assessment of the secondary outcome, number of discussions related to geriatric domains. The ICC was 0.122 with a 95% confidence interval from 0.008 to 0.659. Because of the large amount of uncertainty in the ICC, we calculated power curves for ICC={0.008, 0.122, 0.659}, with ICC=0.659 being the most conservative. This design (with 8 NCORP sites per arm and 31 evaluable subjects per NCORP) has 80% power at the 0.05 significance level to detect a change of 0.235, 0.456 and 0.962 in the mean number of discussions for ICC={0.008, 0.122, 0.659 } respectively, assuming a standard deviation of 0.78 .

Since the best estimate of the ICC is 0.122, the expected detectable difference is 0.122. This corresponds to an effect size of 0.59.

**Figure 2: Sample Size for PCORI Specified Primary Aim**




## 3.5 Data Sources

### 3.5.1 Audio-recordings

As part of baseline procedures, a clinic visit for both arms will be audio-recorded for the analysis of content. All enrolled patients (Arm 1 and Arm 2 groups) will have one office visit with their participating oncology physician audio-recorded (baseline visit). All parties present for recorded office visits, including: enrolled patients, any accompanying caregivers, family or friends, the oncology physician, and any other physicians or health care providers not participating in the study will be fully aware that the conversation is being audio-recorded and will provide verbal assent immediately before any recording begins, in addition to the prior written consent of enrolled subjects (oncology physicians, patients, and caregivers).

### 3.5.2 Patient Surveys

Patients will complete surveys prior to the start of treatment at screening and baseline, within 1 to 7 days after baseline via a follow-up call, at 4-6 weeks, 3 months, and 6 months. All surveys have been utilized in our pilot work with older patients with cancer and other age-related health conditions. As is often true for patients with advanced disease, missing data will be assumed to be *not* random; sicker patients tend not to complete surveys. We have included approaches to missing data in the statistical section of the protocol.

### 3.5.3 Oncology Physician Surveys

Oncology physicians will complete a baseline survey prior to or when their first patient consents to the study and a brief follow-up survey at the end of the study. After the audio-recorded

baseline clinic visit, oncology physicians will be asked about potentially important covariates or moderators, including disease and treatment characteristics.

#### 3.5.4 Caregiver Surveys

Caregivers will complete surveys at the same time points as patients. In addition, we will ask caregivers to assess satisfaction with communication and care, satisfaction with decisions, and caregiver burden (both personal and economic).

#### 3.5.5 Clinic Notes, Chart Abstraction and Claims

If there is missing information or conflicting medical information from the surveys, we will obtain medical records in order to verify information about disease location, pathology, stage, and metastases from clinic notes. We will request information from the CRA on recommendations made and implemented. In order to assess health care utilization (e.g., adverse events such as hospitalizations) for future work on examining cost-effectiveness of the intervention, permission to obtain Medicare claims for future research to examine cost-effectiveness, quality of care, and health care utilization will be asked on the consent form. Claims will not be obtained for any individual patient until the patient has completed study procedures. All consent and research procedures for obtaining Medicare claims will be followed: http://www.cms.gov/Research-Statistics-Data-and-Systems/Computer-Data-and-Systems/Privacy/Researchers.html

Permission to obtain claims is voluntary. Patients will be able to decline this procedure at the time of consent or later in writing. Declining consent for obtaining claims data from Medicare does not preclude patients from participating in this study.

### 3.6 Data Cleaning and Protocol Management

#### 3.6.1 General Protocol Management Procedures

Standard URCC NCORP data management procedures are followed.

#### 3.6.2 Data Cleaning Procedures-Access Database

Data checks are performed on a regular basis by the statistical staff to ensure the accuracy of survey completion and the data review process using the SAS program. These checks include determining: any inconsistency in different questions within the same measure, inconsistency in multiple sections in each form, and inconsistency between the baseline form and follow up forms. They also include checks for missing data in the database.

Inconsistency or missing data would arise if the study participant (clinical research associate, physician, patients, and/or caregivers) misunderstood the question or made errors in completing the forms. Errors may also arise during data entry procedures.

On completion of all checks, tables containing all errors are sent to the URCC NCORP Research Base protocol management team and handled according to pre-approved data management plans. Generally, any inaccuracies in the data base due to data entry errors are fixed immediately. If the error however is due to a site or participant error, a query is issued to the appropriate site study staff.

#### 3.6.3 Coding Schema for Transcripts of Audio Recordings (Appendix B)

The coding schema includes definitions for each code and the specific steps the coders performed during the coding process. The coding procedures involve an initial reading of the transcript to identify specific geriatric concerns and the initiator of the concerns, followed by a second reading, in which response quality and interventions implemented due to concerns are identified.

Five coders were involved in the coding process, with 20 percent of the transcripts coded by all five coders to establish and maintain inter-rater reliability; the remaining transcripts were all dually coded. For each transcript, whether dually coded or coded by the entire coding team, a consensus was agreed upon and a final coding table created for that transcript. These final consensus tables are what will be utilized in the analysis of the data.

Due to the coding schema involving a conditional coding structure, inter rater reliability involved percent agreement in 3 coding areas: number of geriatric concerns, the category of geriatric domain discussed, and the physician's response quality. For number of geriatric concerns, the percent agreement was calculate using the difference in numbers between each coder and the consensus. An average of all coder agreement was calculated for category of geriatric domain and physician response quality. If inter-rater agreement percentages fell below 70%, the coding team would meet for additional training. The principal investigator remained involved in the coding process and provided guidance or adjudication when necessary. (See Appendix B for a more detailed description of coding).

## 3.7 Study Variables

### 3.7.1 Table 1. COACH Patient Measures

| Measure | Aim | Screening Visit 00 | Baseline Visit 01 | Telephone Team Call[a] | 4-6 Weeks Visit 02 | 3 Months Visit 03 | 6 Months Visit 04 |
|---|---|---|---|---|---|---|---|
| Demographics | | Pt | | | | | |
| ADL | GA | Pt | | | Pt | Pt | Pt |
| IADL | GA | Pt | | | Pt | Pt | Pt |
| Fall History | GA | Pt | | | Pt (f/u) | Pt (f/u) | Pt (f/u) |
| OARS Physical Health | GA | Pt | | | Pt | Pt | Pt |
| OARS Comorbidity | GA | Pt | | | | | |
| OARS Medical Social Support | GA | Pt | | | | | |
| Social Activities | GA | Pt | | | Pt (1 item) | Pt (1 item) | Pt (1 item) |
| GAD-7 | GA | Pt | | | | | |
| GDS | GA | Pt | | | Pt | Pt | Pt |
| Patient-rated KPS | S1 | Pt | | | Pt | Pt | Pt |
| HCCQ | NIH 1° | | | Pt | Pt | Pt | Pt |
| HCCQ-age Communication | NIH 1° | | | Pt | Pt | Pt | Pt |
| Press-Ganey Pt Satisfaction | NIH 1° | | | | Pt | Pt | Pt |
| FACT | S1 | | Pt | | Pt | Pt | Pt |
| MDASI | S1 | | Pt | | Pt | Pt | Pt |
| Emotional Distress | S1 | Pt | | | Pt | Pt | Pt |
| PEACE | E | | Pt | | Pt | | |
| PEPPI | E | | Pt | | Pt | | |
| Control Preferences Scale | E | | Pt | | | | |
| MUIS- Complexity Subscale | E | | Pt | | Pt | Pt | Pt |
| Understanding of Disease | E | | Pt | | Pt | | |
| Survey Completion | | Pt | | | Pt | Pt | Pt |

**Note:** Screening and baseline can be combined. [a] A research staff member from the Telephone Team will call the patient within 1 to 7 days after the baseline audiorecorded visit."

**Abbreviations:** Pt (Patient); Phys (Physician); GA (Geriatric Assessment); NIH 1° ( NIH Primary Aim); E (Exploratory Aim); S1 (Secondary Aim 1); ADL (Activities of Daily Living); IADL (Instrumental Activities of Daily Living); GAD (Generalized Anxiety Disorder 7-Item Scale); Geriatric Depression Scale (GDS); KPS (Karnofsky Performance Status); PEACE (Peace, Equanimity, and Acceptance in the Cancer Experience); PEPPI (The Perceived Efficacy in Patient-Physician Interactions); MUIS (Mishel Uncertainty in Illness Scale); CTSQ (Cancer Treatment Satisfaction Questionnaire); FACTF (Functional Assessment of Chronic Illness Therapy); MDASI (MD Anderson Symptom Inventory).

### 3.7.2 Table 2. COACH Caregiver Measures

| Measure | Aim | Screening Visit 00 | Baseline Visit 01 | Telephone Team Call[a] | 4-6 Weeks Visit 02 | 3 Months Visit 03 | 6 Months Visit 04 |
|---|---|---|---|---|---|---|---|
| Demographics | | C | | | | | |
| Caregiver Reaction | S1 | C | | | C | C | C |
| OARS Comorbidity | S1 | C | | | | | |
| SF-12 | S1 | | C | | C (f/u) | C (f/u) | C (f/u) |
| Cost of Care | S1 | C | | | C | C | C |
| Ryff Environmental Mastery | S1 | | C | | C | C | C |
| PHQ-2 | S1 | | C | | C | C | C |
| GAD-7 Anxiety | S1 | | C | | | | |
| Health Care Climate Questionnaire-age Communication (caregiver) | S2 | | | | C | C | C |
| HCCQ-age Communication (patient) | S2 | | | | C | C | C |
| HCCQ-age Communication (general, caregiver) | S2 | | | | C | C | C |
| Press-Ganey Pt Satisfaction | S2 | | | | C | C | C |
| Distress Thermometer | S1 | C | | | C | C | C |
| PEACE | E | | C | | C | | |
| PECPI | E | | C | | C | | |
| Control Preferences Scale | E | | C | | | | |
| MUIS- Complexity Subscale | E | | C | | C | C | C |
| Understanding of Disease | E | | C | | C | | |
| AD8 | E | C | | | C (f/u) | C (f/u) | C (f/u) |

**Note:** Screening and baseline can be combined. [a] A research staff member from the Telephone Team will call the patient within 1 to 7 days after the baseline audiorecorded visit."

**Abbreviations:** C (Caregiver); CRA (Clinical Research Associate); Pt (Patient); Phys (Physician); GA (geriatric assessment); NIH 1° (NIH Primary Aim); I (Intervention); E (Exploratory Aim); S1 (Secondary Aim 1); S2 (Secondary Aim 2); PEACE (Peace, Equanimity, and Acceptance in the Cancer Experience); PEPPI (The Perceived Efficacy in Patient-Physician Interactions); MUIS (Mishel Uncertainty in Illness ScaleSF-12 (12-Item Short Form Health Survey); PHQ-2 (2-Item Patient Health Questionnaire); GAD (Generalized Anxiety Disorder 7-Item Scale); HCCQ (Health Care Climate Questionnaire); KPS (Karnofsky Performance Status); Blessed OMC (Blessed-Orientation Memory Concentration Test); SPPB (Short Physical Performance Battery).

### 3.7.3 Table 3. COACH Clinical Research Associate & Physician Measures

| Measures | Aim | Screening Visit 00 | Baseline Visit 01 | Telephone Team Call[a] | 4-6 Weeks Visit 02 | 3 Months Visit 03 | 6 Months Visit 04 |
|---|---|---|---|---|---|---|---|
| Audio-taped Pt-Phys Visit | PCORI 1° | | CRA | | | | |
| Screening Coversheet page 2[b] | | CRA | | | | | |
| Tumor & Treatment Characteristics | E | CRA | | | CRA (f/u) | CRA (f/u) | CRA (f/u) |
| Cancer Treatment History Form | PCORI 1° | | CRA | | | | |
| Physician rated KPS | S1 | CRA | | | CRA | CRA | CRA |
| Lab Screening Form | GA | CRA | | | | | |
| Polypharmacy | GA | CRA | | | | | |
| Polypharmacy High Risk Drug Review | GA | CRA | | | | | |
| BOMC Test | GA | CRA | | | | | |
| Mini-Cog | GA | CRA | | | CRA | CRA | CRA |
| Nutritional Status and MNA | GA | CRA | | | | | |
| Timed "Up and Go" | GA | CRA | | | | | |
| SPPB | GA | CRA | | | CRA | CRA | CRA |
| GA Scoring Guide to Detect Impairments | GA | CRA | | | | | |
| Physician Baseline Survey[c] | E | Phys | | | | | |
| Situational Vignettes[c] | E | Phys | | | | | |
| Physician Follow-Up Survey[d] | E | | | | | | Phys[d] |
| Treatment Decision Making Form | E | | Phys | | | | |
| Understanding of Disease -Physician | E | | Phys | | | | |
| **Study Related Forms[e]** | | | | | | | |
| Screening Log | | | | | | | |
| Patient Eligibility Screening Form | | | | | | | |
| Caregiver Eligibility Screening Form | | | | | | | |
| Patient Withdrawal Form | | | | | | | |
| Physician Withdrawal Form | | | | | | | |
| Caregiver Withdrawal Form | | | | | | | |
| URCC NCORP AE Report | | | | | | | |

**Note:** Screening and baseline can be combined. The measures/forms are not listed in the order of administration. [a] A research staff member from the Telephone Team will call the patient within 1 to 7 days after the baseline audiorecorded visit. [b] The Screening Coversheet page 2 collects patient information that will be used to establish survival status. [c] The Physican Baseline Survey will be administered via REDCap or paper form and the situational vignettes are collected as part of the Physician Baseline Survey. [d] The physician follow-up survey will be administered at the end of the study period. [e] These forms will be used for study documentation purposes.

**Abbreviations:** C (Caregiver); CRA (Clinical Research Associate); Pt (Patient); Phys (Physician); GA (geriatric assessment); NIH 1°(NIH Primary Aim); I (Intervention); E (Exploratory Aim); PCORI 1° (PCORI Primary Aim); S1 (Secondary Aim 1); S2 (Secondary Aim 2); KPS (Karnofsky Performance Status); Blessed OMC (Blessed-Orientation Memory Concentration Test); SPPB (Short Physical Performance Battery),NCI: National Cancer Institute; URCC NCORP Research Base (University of Rochester Cancer Center NCI Community Oncology Research Program Research Base), AE (Adverse Event).

# 4 Statistical Analysis

## 4.1 Statistical Considerations

This is a cluster-randomized trial with NCORP practice sites being the clusters. Because of the cluster randomized study design, we will apply linear mixed model methodology. The outcome will be the response, and the arm will be the fixed effect. NCORP practice sites will be entered as a random effect independent of residual error. Estimation will be performed using Restricted Maximum Likelihood, and the null hypothesis of zero mean difference between arms will be tested using a F test. The specific NCORP practice site differences will be assessed graphically using Best Linear Unbiased Predictors (BLUP) of the mean response for each NCORP.

All regression analyses will include terms to control for study site and oncologist type. In addition, clinically important socioeconomic variables such as patient gender, age, race/ ethnicity, and cancer variables such as cancer type and treatment status will be used to control for patient-level covariates. In case a key covariate is found to be unbalanced between study arms, it will be included in the model as a potential confounder.

## 4.2 Analysis for NIH Primary Aim

The total HCCQ score will be the response, and the analysis will be as described in 4.1. The distribution of the data will be evaluated and if analysis will also include treating HCCQ score as an ordinal variable if warranted.

## 4.3 Analysis for PCORI Primary Aim

The analysis for PCORI Primary Aim will be the same as for NIH Primary Aim, using the number of discussions as the response.

## 4.4 Other Secondary Analyses

### 4.4.1. Secondary Aim 2

HRQoL will be assessed with the FACT-G and Caregiver HRQoL (burden) will be assessed with the Caregiver Reactions Assessment (CRA). We will include geriatric assessment impairment (at baseline and follow up) to evaluate if these influence patient-reported HRQoL differently in the intervention versus the control group. We will also compare whether the uptake of geriatric assessment recommendations influences patient reported HRQoL and caregiver burden. Data from the intervention arm will be fit to a linear mixed model with the FACT-G or CRA as the outcome, number and percent (number implemented/number recommended) of interventions as the fixed effect, and NCORP site as a random effect independent of residual error. Analyses will be adjusted for treatment status.

### 4.4.2. Secondary Aim 3

We will compare the effect of the intervention on caregiver satisfaction (the modified health care climate questionnaire-age for the caregiver) using the same linear mixed model methodology.

### 4.4.3. Exploratory Aims

In order to examine the relationship between observed communication from audio-recordings and patient satisfaction, we will evaluate the correlation between the numbers of discussions regarding age-related concerns from audio-recorded visits with patient satisfaction on HCCQ.

We will determine the association of baseline oncology physician and patient decision-making preferences on the likelihood of having a discussion related to geriatric domains. The analysis for PCORI Primary Aim will be used with the above characteristics added as independent variables. The statistical significance and estimated coefficients will be used to identify and interpret potentially important baseline features. Any conclusions will be considered to be hypothesis generating for further research.

We will also measure if the intervention influences the proportion of discussions during which an oncology physician responds appropriately to an older patient or caregiver-initiated discussion on age-related needs and concerns (e.g., oncology physician response/(number of patient and caregiver concerns)).

We will capture survival through the participant's medical record and verification with the primary team. We will follow participants for survival for 12 months after enrollment. We will obtain the date, location of death, and cause of death. If a site becomes aware that a study participant is deceased, they should complete the Withdrawal form which is available on the URCC NCORP website. Otherwise sites will be contacted approximately 1 year after each participant was enrolled to assess survival and asked to complete this form. We will determine the effect of the intervention on 12-month survival using log rank tests and survival plots.

We will also verify information with Medicare claims data if the participant provided permission to do this through initial consent. In order to assess health care utilization (e.g., adverse events such as hospitalizations) for future work on examining cost-effectiveness of the intervention, permission to obtain Medicare claims in the future was asked on the consent form. Claims will not be obtained for any individual patient until the patient has completed study procedures. All consent and research procedures for obtaining Medicare claims will be followed: http://www.cms.gov/Research-Statistics-Data-and-Systems/Computer-Data-and-Systems/Privacy/Researchers.html

Permission to obtain claims is voluntary and patients are able to decline this procedure at the time of consent. Declining consent for obtaining claims from Medicare for future research to examine cost-effectiveness, quality of care, and health care utilization did not preclude patients from participating in this study.

### 4.5 Missing Data

Every effort will be made to encourage and facilitate participants' completion of questionnaires, but because of dropout, missing data will occur. We will evaluate the patterns of missing data and associations of missingness with other available variables. Under the missing at random (MAR) assumption, the parameter estimates from the mixed model analyses will be unbiased. If the data are suspected to be missing not at random (MNAR), a sensitivity analysis using pattern-mixture models will be run to determine the impact on the results.

## 5 Description of Subject Disposition in Trial Report

Subject disposition will be described in CONSORT flow diagrams for patients, caregivers and providers (Appendix C includes data that will be used for the CONSORT flow diagram).

## 6 Reporting Conventions

Reporting conventions will accord with the most recent edition of the AMA Manual of Style. In particular, P-values ≥0.001 will be reported to 3 decimal places; p-values less than 0.001 will be reported as "<0.001". The mean, standard deviation, and any other statistics other than quantiles, will be reported to no more than 2 decimal places greater than the original data. Quantiles, such as median, or minimum and maximum will use the same number of decimal places as the original data. Estimated parameters, not on the same scale as raw observations (e.g. regression coefficients) will be reported to 3 significant figures.

## 7 Technical Details

Dr. Charles Heckler with the help of statistical support staff will perform all analyses using SAS and R software. We will use SAS and R programming code as appropriate, and will follow reproducible research conventions. All programs and results will be stored on a secure network drive.

# 8 Appendices

## 8.1 Appendix A: Randomization Schema

### 8.1.1 Current Sites Randomization Assignments

*Note: Practice Site Names and NCORPs are not included in this table in order to keep study PI and statistician blinded to the randomization allocations.* See sample below:

| Rand ID | Size | Randomization Allocation |
|---|---|---|
| 1 | Small | GA |
| 3 | Large | GA |
| 3 | Large | GA |
| 3 | Large | GA |
| 3 | Large | GA |
| 3 | Large | GA |
| 3 | Large | GA |
| 3 | Large | GA |
| 4 | Small | Control |
| 5 | Small | GA |
| 6 | Small | GA |
| 9 | Small | GA |
| 10 | Large | GA |
| 10 | Large | GA |
| 10 | Large | GA |
| 10 | Large | GA |
| 10 | Large | GA |
| 11 | Large | Control |
| 11 | Large | Control |
| 11 | Large | Control |
| 11 | Large | Control |
| 11 | Large | Control |
| 11 | Large | Control |
| 11 | Large | Control |
| 11 | Large | Control |
| 11 | Large | Control |
| 11 | Large | Control |
| 11 | Large | Control |
| 11 | Large | Control |
| 11 | Large | Control |
| 11 | Large | Control |
| 11 | Large | Control |
| 11 | Large | Control |
| 11 | Large | Control |

### 8.1.2 Future Sites Randomization Assignments

When new sites join the study, we first determine whether they are large or small based on their past accruals onto URCC NCORP or cancer control studies. After this determination, they are then assigned the next available practice site ID number and placed in either the “Small Site” or “Large Site” column.

## 8.2 Appendix B: Coding Schema

As part of coding procedures, a manual was developed which included definitions of age related concerns categorized within each GA domain, of who initiated the discussion, and the possible response qualities from the oncologist. Five coders each underwent 40 hours of in-person training with sub-investigators and the PI. In addition, all coders read and studied the coding manual. Coders transitioned from training to independent coding only after full consensus was met on all 25% training transcripts as a group.

The GA domains include physical performance, functional status, cognitive, comorbidity, polypharmacy, nutritional status, psychological status, and social support. Explicit discussions related to cognition (e.g., how is your memory?) were captured as well as implicit discussions (e.g., are you remembering to take your medications). Within each GA domain there are numerous age-related concerns, which are listed in the coding manual as subcodes, with the addition of an unspecified subcode for each concern. Developing the coding scheme for who initiated the concern involved identifying who initially brought up the concern during the clinic visit (e.g oncologist, patient, caregiver, other health care provider, friend, family member). For response quality coding, the coders identified whether an age-related concern was specifically asked about or only mentioned, and whether later acknowledged through a follow-up question, reflection, or validation. Then GA concerns were reviewed to detect whether or not they were appropriately addressed by the oncologist or not addressed (e.g. dismissed, ignored, shut down, minimized) at all.

The coding procedures consist of initially reading the transcript to look for the geriatric domains discussed, the identification of any age related concern, and determining who initiated those concerns during the clinic visit. The second reading of the transcript was to identify the response quality of each age related concern and any discussions of GA recommendations to address those concerns.

All coders were paired together rotating coding partners throughout the coding process to ensure groups did not drift in their coding process over time. Each coder coded independently. Then, each week met with his or her paired coder to complete one coding consensus table for each transcript. In addition, each week all five coders met and came to consensus concerning the transcripts designated for inter-rater reliability, creating a final consented coding table. Twenty percent of the transcripts were coded by all five coders to establish inter-rater reliability, with the remaining transcripts dually coded. The final consensus tables will be used to analyse the data.

Because all final codes were discussed and agreed upon by at least two trained coders, reliability and consistency of the codes throughout all observations is very high.

### 8.2.1 COACH Coder Interrater Reliability

To establish interrater reliability between all coders, 20% of all transcripts will be coded by all coders. These transcripts will be allocated over the entire duration of time coding is conducted to test for ongoing agreement among all coders. Transcripts are randomly assigned to each coder. Every 5$^{th}$ transcript is coded by all coders and will be used for IRR. If an overall agreement is not $\geq$ 70%, discrepancies will be identified and targeted training will take place. Also to prevent coding drift, the teams of coders will alternate. Review the table below to explain this strategy.

| Transcript # | Coder 1 | Coder 2 | Coder 3 | Coder 4 | Coder 5 |
|---|---|---|---|---|---|
| 1 | X | X | | | |
| 2 | | X | X | | |
| 3 | | | X | X | |
| 4 | | | | X | X |
| 5 | X | X | X | X | X |

Due to the conditional coding structure of this study, we will report percent agreements for 3 coding areas. These percent agreements will be calculated on the 20% of transcripts that are coded by all coders, since the remainder of transcripts are dual coded. The gold standard for the calculation of percent agreement will be the consensus coding, which will be reached by all coders.

### 8.2.2 % Agreement for 3 Coding Areas

(1) First is the percent of agreement on the **number of geriatric concerns mentioned** in the transcript, without regard to who initiated the conversation. This is calculated on the difference score between the coder and consensus and a percent of those coded correctly is divided by those coded incorrectly. The equation is as follows: consensus # - abs(coder # - consensus #) / consensus #) x 100). An average of all individual coders' agreements will be reported.

(2) Second is the percent agreement on **the category of geriatric domain discussed.** This will be calculated by each individual coder agreement with the consensus of whether each geriatric domain (a total of 8) was present or absent. An average of all coder agreements will be computed.

(3) Lastly is the percent agreement on **the physician's concern response quality.** Response quality will be considered for only the same concerns that all coders coded for individually. The agreement will be calculated based on the coder's agreement with the consensus codes on the three response quality categories: appropriately acknowledged, appropriately addressed, and dismissed. An average of all coder agreements will be computed.

### 8.2.3 Computation

We will compute percent agreement scores for the three defined areas. Information will be available in real time to allow for retraining if necessary and ongoing monitoring. All scores will be maintained in a data file and summary reports will be computed at study end (or when required). The table below provides an example of how all three percent agreements will be calculated. The three percent agreements are highlighted in blue.

Note the computation varies because area one is a count variable, and areas two and three are all dichotomous variables (yes/no). For the number of geriatric concerns mentioned, percent agreement is calculated on the difference score between the coder and consensus and a percent of those coded correctly divided by those coded incorrectly.

| Percent Agreement | Variable | Coder A | Coder B | Coder B | Consensus | A and Consensus | B and Consensus | C and Consensus | % Agreement |
|---|---|---|---|---|---|---|---|---|---|
| **# of Concerns** | Number of geriatric concern mentioned | 7 | 5 | 5 | 5 | 0% | 100% | 100% | 67% |
| **Geriatric Domain Mention** | Functional Status | 1 | 0 | 1 | 1 | 100% | 0% | 100% | 67% |
| | Nutritional Status | 1 | 1 | 1 | 1 | 100% | 100% | 100% | 100% |
| | Cognition | 0 | 0 | 0 | 0 | 100% | 100% | 100% | 100% |
| | Physical Performance | 1 | 1 | 1 | 1 | 100% | 100% | 100% | 100% |
| | Comorbidity | 0 | 0 | 0 | 0 | 100% | 100% | 100% | 100% |
| | Polypharmacy | 1 | 0 | 1 | 1 | 100% | 0% | 100% | 67% |
| | Social Support | 0 | 1 | 1 | 1 | 0% | 100% | 100% | 67% |
| | Psychological Status | 0 | 1 | 0 | 0 | 100% | 0% | 100% | 67% |
| | | | | | | | | | 83% |
| **Response Quality: Acknowledged** | Concern 1 | 1 | 1 | 1 | 1 | 100% | 100% | 100% | 100% |
| | Concern 2 | 0 | 0 | 0 | 0 | 100% | 100% | 100% | 100% |
| | Concern 3 | 1 | 1 | 1 | 1 | 100% | 100% | 100% | 100% |
| | Concern 4 | 1 | 1 | 1 | 0 | 0% | 0% | 0% | 0% |
| | Concern 5 | 0 | 0 | 1 | 1 | 0% | 0% | 100% | 33% |
| **Response Quality: Addressed** | Concern 1 | 0 | 0 | 0 | 0 | 100% | 100% | 100% | 100% |
| | Concern 2 | 0 | 0 | 0 | 0 | 100% | 100% | 100% | 100% |
| | Concern 3 | 0 | 1 | 0 | 1 | 0% | 100% | 0% | 33% |
| | Concern 4 | 1 | 1 | 1 | 1 | 100% | 100% | 100% | 100% |
| | Concern 5 | 0 | 0 | 0 | 0 | 100% | 100% | 100% | 100% |
| **Response Quality: Dismissed** | Concern 1 | 0 | 0 | 0 | 0 | 100% | 100% | 100% | 100% |
| | Concern 2 | 0 | 0 | 0 | 0 | 100% | 100% | 100% | 100% |
| | Concern 3 | 0 | 1 | 0 | 1 | 0% | 100% | 0% | 33% |
| | Concern 4 | 1 | 1 | 1 | 1 | 100% | 100% | 100% | 100% |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Concern 5 | 0 | 0 | 0 | 0 | 100% | 100% | 100% | 100% |
| **General Interventions** | Mention of Geriatric Assessment | 1 | 0 | 1 | 1 | 100% | 0% | 100% | 67% |
| | Assess values/goals for treatment outcome | 1 | 1 | 1 | 1 | 100% | 100% | 100% | 100% |
| | Elicit caregiver perspective/input | 0 | 0 | 0 | 0 | 100% | 100% | 100% | 100% |
| | Discussed health care proxy | 1 | 1 | 1 | 1 | 100% | 100% | 100% | 100% |
| | Goals of care preferences | 0 | 0 | 0 | 0 | 100% | 100% | 100% | 100% |
| | Confirm health care proxy in chart | 0 | 1 | 0 | 0 | 100% | 0% | 100% | 67% |
| | List emergency contacts in chart | 0 | 0 | 1 | 0 | 100% | 100% | 0% | 67% |
| | Confirm Advanced Directives in chart | 0 | 0 | 0 | 0 | 100% | 100% | 100% | 100% |
| | Discuss advanced directive | 1 | 1 | 1 | 1 | 100% | 100% | 100% | 100% |
| | Change chemo regimen | 0 | 0 | 1 | 1 | 0% | 0% | 100% | 33% |
| | | | | | | | | | 81% |

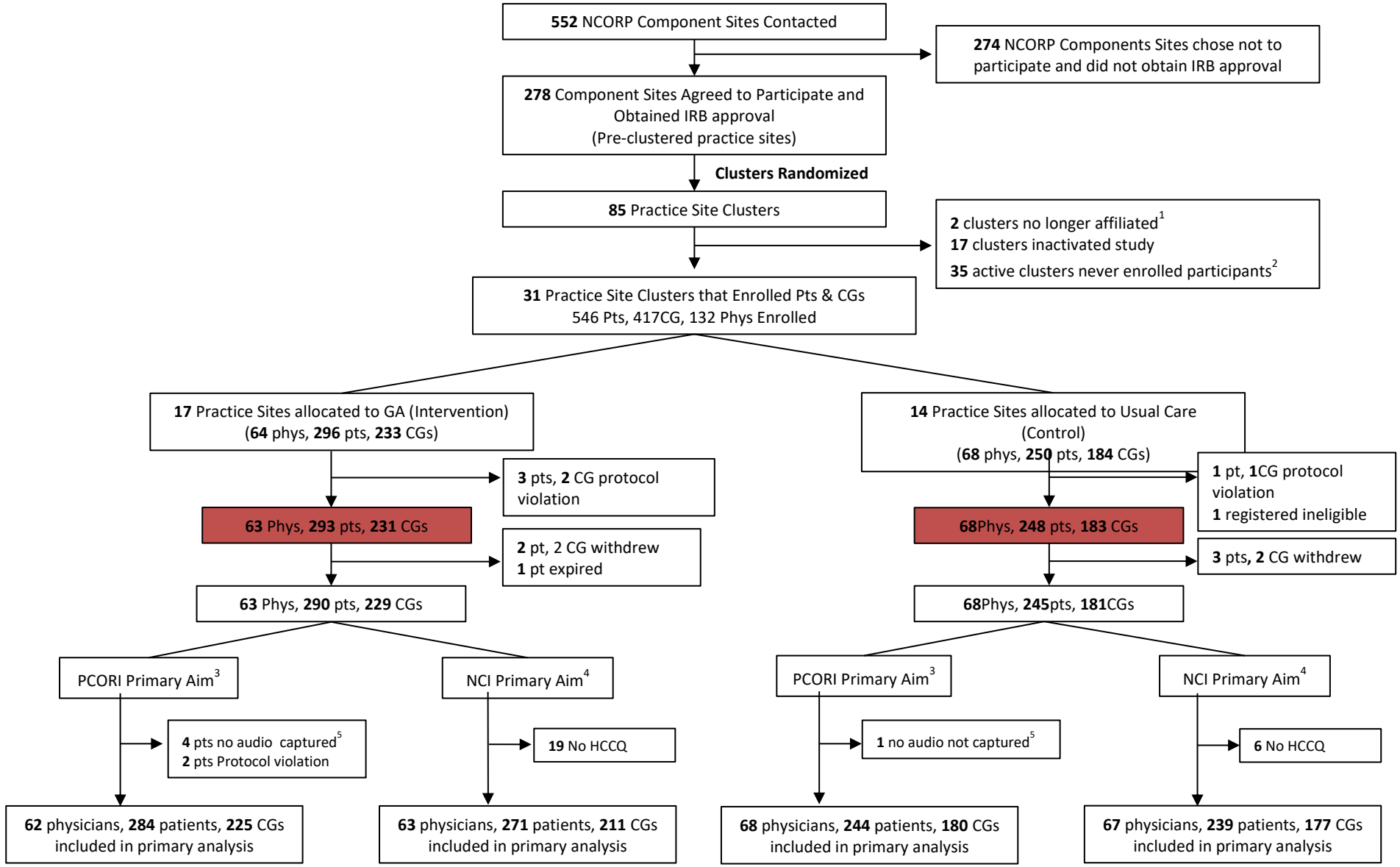
### 8.3 Appendix C: Data that will inform Consort Diagram

| COACH | Total S# Patients (Excludes Registration Errors) (Visit 0) | Enrolled (Excludes Registration Errors) | Total # Patients With Baseline Packets Received (Visit 1) | Total # Patients With 4-6 Week Packets Received (Visit 2) | Total # Patients With 3 Month Packets Received (Visit 3) | Total # Patients With 6 Month Packets Received (Visit 4) | Total Active with Missing Data (missing Forms) | Total Currently Active (excludes withdrawn and deceased) | Total Withdrawn | Total Deceased During Study | Total Deceased Post Study |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Patient | | | | | | | | | | | |
| Caregiver | | | | | | | | | | | |
| Totals | | | | | | | | | | | |

| COACH | Total # Screen Registered (Includes Registration Errors) | # Screen Failures (ineligible, deceased) | # Screen withdrawals | # Pending Enrollment (Screen Registered but not Enrolled) | # Registration Errors | # Enrolled |
|---|---|---|---|---|---|---|
| Patient | | | | | | |

| # Patients Withdrawn (w/d) or Expired during given assessment period | | | | | |
|---|---|---|---|---|---|
| Time period | Screen | Baseline | 4-6 Weeks | 3 month visit | 6 month visit |
| Withdrawn | | | | | |
| Expired | | | | | |

## 8.4 Appendix D: COACH Study Cluster Randomized CONSORT Flow Diagram






**1**-sites are no longer associated with their respective NCORP or with the URCC Research Base; **2**-clusters that maintained IRB approval but never actually enrolled any participants

**3**-discussions about age-related issues during clinic consultation-assessed using audios of baseline visit with physician

**4**-satisfaction with communication regarding age-related issues-assessed using HCCQ's collected at baseline.

**5**-irretrievable, site miscommunication, technical difficulty, or protocol violation