ASCENT / 23-004139

Pilot Test of a Pain Management Intervention Preparatory to a Future Pragmatic Trial (ASCENT)

NCT06063603

Document Date: 10/03/2023

IRB Minimal Risk Protocol Template

General Study Information

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Study Title: Pilot Test of a Pain Management Intervention Preparatory to a Future Pragmatic Trial (ASCENT)

Protocol version number and date: October 3, 2023 V4

Research Question and Aims

Hypothesis

This study will adapt intervention components that were previously validated in several pragmatic clinical trials: E2C2 (#18-007779), NOHARM (#20-004839) and COPE (#11-008151), for remote delivery to rural dwelling and Hispanic Cancer Survivors. We will refine the sociocultural, linguistic, IT, and clinical aspects of the intervention through iterative design cycles. We recognize that the needs of the targeted subgroups are heterogeneous and may require patient-specific matching of language, IT modes, extent of portal-based delivery, among other aspects, in order to optimize patient engagement and experience. Intervention components will be integrated and tested in a future parallel group, two-arm randomized clinical trial at six Mayo Clinic sites. The full trial is anticipated to begin later this year under a separate IRB application.

We hypothesize that an iteratively refined, EHR-based modular approach that combines specific intervention components in accordance with a patient's sociocultural, IT, and linguistic needs, will demonstrate fidelity, usability, and acceptability among our target population of Hispanic, rural dwelling, and rural dwelling Hispanic cancer survivors experiences moderate or worse pain.

Aims, purpose, or objectives

To refine and pilot test components of a validated collaborative care model-based intervention aimed at improving pain control among rural dwelling and Hispanic cancer survivors. The intervention will align pain care with evidence-based best practices and address SDOH and other barriers to patients' receipt of appropriate care. The pilot will emphasize sociocultural, linguistic, and IT adaptation of the intervention for the target demographic to inform the implementation of the future Achieving Equity through SocioCulturally-informed, Digitally Enabled Cancer Pain ManagemeNT (ASCENT) randomized control trial.

Background

Cancer pain is a key case study in health disparities in the US. Cancer pain is prevalent, undertreated, and remains a major cause of suffering, impairment, and disability for millions of Americans. Individual pain interventions and care models show promise for cancer pain in controlled settings. Unfortunately, typical approaches too often target limited aspects of the whole, fail to consider health disparities populations (HDPs), and are unable to serve broad and diverse populations. This situation will only worsen with time. For example, by 2030, the number already underserved Hispanic cancer survivors in the U.S. will increase to 4 million.

Hispanic and rural-dwelling cancer survivors stand to benefit the most from EHR innovations, as each of these HDPs experience profound disparities in pain outcomes, including marked under- and over-prescribing of opioids. Additionally, Hispanics not only comprise a steadily growing proportion of cancer survivors, but are also increasingly immigrating to rural communities, potentially placing them at "double risk" for poor outcomes. Digitally-facilitated solutions are especially well matched for these disparities, and can be customized to address the overlapping, yet distinct, needs of these HDPs. Doing so would provide a vital proof of concept and may illustrate the promise of digitally based, patient-centered approaches to mitigating other disparities.

This preparatory pilot study will allow iterative refinement of intervention components and study procedures to optimize their sociocultural and linguistic appropriateness, feasibility, and acceptability. The study will optimize patient-facing cancer pain support components of an EHR-facilitated, evidence-based bundle in a manner that meets the diverse needs of the target sample.

Study Design and Methods

Methods

In this pilot, we will test our ASCENT intervention at the following Mayo Clinic locations: Rochester, Arizona, Florida, Mankato, Eau Claire and La Crosse. For this minimal risk study without in-person patient contact, patients can be recruited from the previously mentioned locations, but research activities are only being conducted at Mayo Clinic Rochester and Mayo Clinic Arizona. We will recruit three groups of individuals: Rural, Hispanic, Rural & Hispanic. Participants who are experiencing cancer-related pain and who meet inclusion criteria will be recruited and will have the opportunity receive additional education material in an initial mailing as well as support from Pain Care Managers (PCMs) and Community Health Workers (CHWs) to manage their pain. The study team will provide as much material as possible in Spanish for participants who speak only Spanish or prefer to read in Spanish. The study team includes members who speak Spanish fluently. These members may include, but are not limited to study coordinators, PCMs, CHWs, and other support staff. If a patient speaks only Spanish and the team member does not, a telephone interpreter will be utilized. PCMs and CHWs will follow a validated pain management algorithm that includes evidence based and guideline-endorsed best practices for managing cancer related pain and addressing Social Determinants of Health (SDOH) barriers to receipt of recommended care. The ASCENT interventions in this pilot protocol and the future randomized trial align with the NCCN guideline for the management of cancer-related pain.

Part 1 – Testing the ASCENT Intervention Components

Intervention

Potentially eligible participants will be identified using data found in the Epic EHR Chronicles database, including qualifying appointments, ethnicity, RUCA highly rural zip code, and cancer diagnoses (Approved in IRB# 22-008103). Patients who meet the electronic criteria listed in this protocol will receive information about our study and a pain Numeric Rating Scale (NRS) questionnaire via the patient portal, Welcome tablet functionality, or Interactive Voice Response (IVR). We are seeking a waiver of consent due to the volume of patients this would involve across the 6 participating sites, and the fact that symptom monitoring is considered a best practice in caring for cancer survivors. IVR is an automated telephone service provided by an external vendor (RevSpring). Research coordinators will attempt to enroll and formally consent patients who endorse

pain ≥5/10 and who respond to this initial outreach. Recruitment calls will also be made to screen patients who do not respond for pilot eligibility (See Recruitment & Consent section for more details). Patients will be able to opt out of hearing more information or being contacted by a study coordinator at multiple points in the trial recruitment and enrollment procedures. After consent, participants may be sent additional education materials in an initial mailing. The engagement, intake, visit 2, final visit, and follow up calls will be recorded for fidelity monitoring. All study visits will be conducted via telephone or video call.

We will test prototype recruitment scripts in English and Spanish. At the end of the recruitment process, participants will be queried about their experience. For each call, CRCs will indicate sections of the script that seemed wordy, awkward, confusing, or prompted questions from prospecive participants. We will additionally record recruitment conversations. Tapes will be reviewed by Hispanic and rural dwelling citizen scientist ASCENT team members, ASCENT implementation scientists, and CRCs.

All data used to direct the IVR calls is maintained on Mayo Clinic servers and no data are released to RevSpring. RevSpring has been used by the Mayo Clinic Spine Center to securely administer follow-up patient reported outcome measures to over two thousand patients. The ASCENT pain NRS questionnaire responses will reside on our server and will not go outside of the firewall. Data going to the RevSpring platform is transient in nature and is purged once the results are uploaded into Epic. TAP approval has been granted to RevSpring's IVR system and there are Business Associate Agreements (BAA) and Information Security Agreements (ISA) in place, which covers how PHI can be used and stored.

Recruitment Call: The research coordinator will formally recruit interested and eligible participants. Eligibility criteria include a pathologically confirmed solid or liquid cancer diagnosis, excluding acute leukemia, within 15 years of study enrollment; pain rated ≥ 5/10; and a PH8-8 score of ≤ 9. The pilot study will be described to eligible patients. Patients who consent ot participate will be asked questions to determine their access to and facility with technological devices, and the extent to which they can access broadband internet. Should the participant need a device to participate in the visits described in this protocol, the study team will send one to them for temporary use. The research coordinator will then schedule a time for the participant to meet with the Pain Care Manager (PCM) and Community Health Worker (CHW) either via telephone or video visit.

Engagement Call: The CHW will meet with the participant via video visit or telephone to discuss the ASCENT study, gain an initial understanding of the patient's pain, and introduce the practice of keeping a pain journal. The CHW will also obtain patients' SDOH background to identify barriers that may impact their ability to access pain treatment. The CHW will review first and second-line treatment options so that the patient is aware of the treatment options available to them. This conversation will be informed by a "Conversation Guide" bundle developed for the study.

Intake Visit: The PCM and CHW will meet with the participant via video visit or telephone to discuss the cancer-related pain they are experiencing (PCM), as well as obtain their SDOH background to help identify barriers that may impact their ability to access pain treatment (CHW). The PCM and CHW will work with the patient to develop an action plan to help address their pain by utilizing a "Conversation Guide" bundle developed for the study. This guide will share approved patient education materials for self-guided pain management, provide information on online tools, (such as our study website) and structure interaction between the participant and PCM/CHW. Participants will be able to receive the

Conversation Guide in a variety of formats per their preference (portal, paper mailing, web, email, etc). The conversation between the PCM and the participant will lead the PCM to make suggestions/referrals from the below Tier 1 and Tier 2 interventions, which consist of 6 treatment domains.

Tier 1	Tier 2
Exercise	Integrative Medicine
Cognitive Behavior Therapy (CBT)	-Massage
Medicine	-Acupuncture
	-Mindfulness
	Spiritual Support
	Pain Clinic Referrals
	Palliative and Spiritual Care Referrals

Planning Visit: A second visit will take place approximately 2 weeks after the intake visit, depending on the availability of the participant, PCM and CHW. In this visit, the participant will give an update on their pain and additional resources may be suggested by the PCM and/or CHW.

Final Visit: The third visit will be the final visit between the participant, PCM and CHW and will take place approximately 4 weeks after the intake (depending on patient, PCM and CHW availability). Participant progress will be reviewed, final recommendations and referrals will be made.

Participant Surveys: After a participant has completed the three visits listed above, they will be sent a short survey via email, mail or portal to give feedback about their experience. Telephone may also be used to administer the survey. This feedback may help facilitate any necessary changes for the future ASCENT trial.

Follow Up Visits & NRS pain surveys: the CHW or PCM may conduct follow up calls between intake and visit 2 and/or between visit 2 and the final visit. As pain levels, SDOH barriers and level of needed assistance vary from patient to patient, these will be scheduled as needed on a participant-by-participant basis at the discretion of the PCM/CHW and participant. Additionally, the participant will receive regular pain NRS surveys via portal and/or IVR. CHWs and PCMs will check in with patients via portal or text message to see how patients are doing and if follow up visits are required.

Remuneration: Participants will be reimbursed for their participation in this study. They will receive $50 for the intake visit, $50 for visit 2, $50 for the final visit and $20 for the completion of the participant survey for a total of up to $170. No remuneration will be given for recruitment or follow up calls. Payment will be submitted within 2 weeks of study completion after which Mayo Accounting will process a check or direct deposit via payroll for Mayo Employees.

Care Manager Conferences: The ASCENT study team will work collaboratively with Medical Oncology, Social Work, Physical Therapy, Palliative Care, and other applicable areas to address patient needs. Care Manager Conferences will take place weekly during this pilot to ensure that participant situations require a collaborative approach can be addressed in a timely manner. During the conferences the PCM will present the patient's pain and related issues to an interdisciplinary group of pain specialists potentially including

Rehabilitation Medicine, Hospice and Palliative Medicine, Pain Medicine, and Pain Psychology. This is a best practice approach that is integral to clinical practices across the Mayo Clinic Enterprise. Participants will not be involved in these conferences but the feedback gathered will help the PCM/CHW assist the participant.

Recruitment & Consent

Using existing Patient Reported Outcome Measure (PROM) tools, potentially eligible participants with a scheduled encounter in Medical Oncology, Hematology, or Community Medicine will be identified via an EHR report, which the study coordinator(s) will regularly pull. Those with a patient portal will be sent a study invitation via portal message prior to their encounter. Nonresponders will receive the invitation during clinical registration on an Epic Welcome tablet. Patients who do not interact with the invitation via their protal of Welcome tablet will be sent the invitation by mail. Any follow-up recruitment attempts being will be conducted via portal message, telephone, or mail. Patients who do not have a portal set up will be initially invited to participate via Epic Welcome tablet. Non responders will be approached via mail or telephone, with follow-up recruitment attempts being done via telephone. Potential participants will not be contacted more than 3 times total.

We are seeking a waiver of signed informed consent as well as a waiver of signed HIPAA for this pilot protocol consonant with our intended approach to the eventual trial. Due to the minimal risk this study poses, as well as the complexities of recruiting rural and Hispanic populations and the likelihood of including undocumented Hispanic participants, we think a waiver is justified consistent with the intent of existing regulations.

Consenting will be conducted orally, at which point the participants will be screened for inclusion and exclusion criteria. The research coordinator will administer a few IT related questions to assess technology usage and fluency.

Part 2 – Qualitative Interviews & Focus Groups

Patient Interviews: A subset of participants (up to 40 total) will be recruited to take part in an interview about their experience in this pilot. Our goal is to reach thematic saturation. We will assume that thematic saturation has been reached when further observations and analysis reveal no new themes. Those who are interested will meet one time with a member of our study team via telephone or video. We are seeking approval for oral consent and waiver of HIPAA for the same reasons outlined in the intervention recruitment section of this protocol. Remuneration in the amount of $30 will be given for participation in this interview. The interview will be recorded and transcribed for data analysis purposes and stored on a secured server.

Study Team Interviews: Up to 15 ASCENT study interventionalists will be interviewed and asked for feedback and experiences from this pilot. Recruitment will be done via email and the oral consent document will be attached to the email. A response to the invitation to schedule an interview will be regarded as an agreement to participate. No remuneration will be given for participation.

Provider Focus Groups: 2-3 focus groups will take place involving up to 15 Medical Oncology providers from the participating sites in this pilot. Although there is no action required of providers in this pilot study, they can view the PCM action plan. We want to look at the impact of this additional support to patients on provider workflow and obtain feedback about what they may like to see from the future ASCENT trial (e.g., how they want to be informed when their patients are enrolled in ASCENT, what information about their patients' pain management they would like to be alerted to and how). Recruitment will be done via email and the oral consent document will be attached to the email. A response to the invitation to schedule an interview will be regarded as an agreement to participate.No remuneration will be given for participating.

Intervention Fidelity

All of the above components of the intervention are regarded as "important" but not "essential" to the patient experience in the trial. We will assess fidelity by establishing check lists of essential elements for each touchpoint along the intervention trajectory including: recruitment, intake call, unscheduled CHW contacts, planning call, and scheduled PCM check-ins. For pilot activities all contacts will be recorded. Two individuals to review transcripts of the touchpoints and document whether >95% of essential elements are present. If an encounter includes fewer that 95% of the elements, the interventionalists will review training materials and role play the touchpoint with senior ASCENT team members.

Measurement

Refinement of Intervention Components:

Assessment of the usability and acceptability of specific intervention components and study processes will require data collection appropriate to these study components and will be tailored to each touchpoint. In addition to multi-stakeholder review of recorded interactions, CRC- and PCM-identified ineffective script sections, participant-reported experience, extent and nature of family/lay caregiver involvement, and fidelity checklists, touchpoint specific assessments will include:

Recruitment – proportion of opened and completed Epic questionnaires, proportion of patients calling the ASCENT 1-800 line to express interest.

Engagement and Intake Visits – proportion of patients who provide complete pain and SDOH histories, select a Tier 1 pain management option, and develop a SMART goal; proportion of patients requesting review of Tier 2 options, patient engagement with sections of the ASCENT Conversation Guide (assessed by PCMs and CHWs using 11-point numerical rating scales (NRS).

Planning Visit – proportion of patients requesting revisions to the recommended plan, proportion of patients completing SMART goal; category of pain intervention selected as initial focus of multi-modal pain care plan; type of participant-selected provider as PCM contact.

Final Visit – proportion of patients able to receive and initiate use of modality selected during the planning visit, category of barriers impeding receipt of recommended pain care, general assessment of ASCENT program (NRS).

Follow Up Visits & NRS pain surveys: Proportion of patients completing surveys by administration mode, cause of pain escalation (categorical), participant-perceived barriers (categorical).

PROM collection:

The following outcome measures will be collected at baseline (after consent but required before moving on to engagement) and when patients exit the pilot study after 4-5 weeks:

Measure	Domain
Primary	
BPI SF	Pain
Secondary	
PROMIS SF	Physical Function
EQ-5D-3L	QoL
PHQ-2	Depression
GAD-2	Anxiety
PROMIS SF	Sleep
Mediators	
PROMIS SF	Self-efficacy

These PROM data will be collected to evaluate the completeness and fidelity of outcome collection rather than to estimate intervention effectiveness. Maximizing PROM response rates and minimizing the proportion of incomplete surveys will be a key focus during our pilot activities. We will offer multiple administration modes for study completion including EHR portal, IVR, telephone interview, and printed questionnaires. The cost and logistics vary considerably across these modes. Their use and acceptance by highly rural and Hispanic individuals has not been characterized. We will therefore query patients regarding their preferred mode during the Recruitment call. After initiating a patients preferred mode we will assess the proportion of responders. We will follow up with non-responders to encourage them to trial an alternative mode. We will capture responses rates to initial and secondary administration modes across demographically-defined subgroups. For persistent non-response, we will attempt to collect PROM data via telephone interview with a CRC.

Risks and Benefits

The risks of the ASCENT pilot study are minimal as participants are being potentially offered additional support and expertise to manage cancer-related pain. Nothing in this trial will impede patients them from getting whatever pain modalities they and their team agree they need. The benefits to patients include the potential for safer and more guideline-concordant pain management and lower risk of opioid exposure and dependency.

Protection of Human Subjects

Care will be taken to ensure that patients' data are protected. Data from chart review, patient-reported preferences, and patient-reported outcomes will be stored securely on password protected Mayo Clinic research servers. Clinicians will still be able to make professional judgments about the appropriateness of engaging patients in specific conversations about pain management throughout their post-surgical recovery, and may disregard EHR-prompts as appropriate.

Subject Information

Target accrual is the proposed total number of subjects to be included in this study at Mayo Clinic. A "Subject" may include medical records, images, or specimens generated at Mayo Clinic and/or received from external sources.

Target accrual: 140 (maximum). Accrual will depend on the nature and extent of sociocultural and linguistic tailoring, and the number of iterative design cycles. This total includes 40 participants for the pilot study itself, up to 40 participant interviews, up to 15 study team interviews and up to 45 providers for focus groups.

Subject population (children, adults, groups): Adults

Inclusion Criteria:

- A qualifying liquid or solid cancer diagnosis with visits at a participating Mayo site
- Age 18+
- NRS pain score of a 5+ out of 10
- Pain that developed (onset) or significantly worsened since cancer diagnosis
- Malignant Hematology including:
  - Lymphoma
  - Myeloma
  - Chronic Leukemias

Exclusion Criteria:

- PHQ8 score of 14 or more.
- Life expectancy less than 12 months
- Hospice enrollment
- Admitted to hospital from Long Term Care/SNF
- Acute Leukemias
- Primary brain tumors
- Confinement to a bed or a chair more than a third of waking hours because of health complications.

Review of medical records, images, specimens

Check all that apply (data includes medical records, images, specimens).

☐ Only data that exists before the IRB submission date will be collected.

Date Range for Specimens and/or Review of Medical Records:
Examples: *01/01/1999 through 12/31/2015*, or all records through *mm/dd/yyyy*.

Note: The Date Range must include the period for collection of baseline data, as well as follow-up data, if applicable.

☒ The study involves data that exist at the time of IRB submission **and** data that will be generated after IRB submission. Include this activity in the Methods section.
Examples

- The study plans to conduct a retrospective chart review and ask subjects to complete a questionnaire.

- The study plans to include subjects previously diagnosed with a specific disease and add newly diagnosed subjects in the future.

☐ The study will use data that have been collected under another IRB protocol. Include in the Methods section and enter the IRB number from which the research material will be obtained. *When appropriate, note when subjects have provided consent for future use of their data and/or specimens as described in this protocol*.

Enter one IRB number per line, add more lines as needed

☐ Data ☐ Specimens ☐ Data & Specimens _____

☐ Data ☐ Specimens ☐ Data & Specimens _____

☐ Data ☐ Specimens ☐ Data & Specimens _____

Data Analysis

Power analyses may not be appropriate if this is a feasibility or pilot study, but end-point analysis plans are always appropriate even if only exploratory. Provide all information requested below, or provide justification if not including all of the information.

Endpoints:
Optimized components and process
Our target endpoint is optimization of key study processes and intervention components. We will use modified, multi-stakeholder Delphi processes to determine when a study process/component has been optimized. A process/component will be considered optimized when 80% of Delphi process participants agree that sociocultural appropriatness, usability, patient-centricity, and acceptability have been optimized. After that point no further iterative refinement cycles will occur.

Response rates
Our goal is to achieve >90% response rates for PROM assessments, recruitment questionnaires, and remote pain assessments. Iterative design cycles will continue with different modes, delivery approaches, follow up for non-response, and preface text.

Qualitative data
We will incrementally and iteratively develop a coding scheme beginning with the first transcript. Categories, groups of content sharing common features, will be created and abstraction of the text will be accomplished by assigning category codes. Subcategories will be identified to further delineate the content. Finally, themes or ideas that cut across categories will be created. As new concepts emerge, they will be defined and added to the coding scheme. If data saturation is not reached we will consider the need for additional interviews.

Future trial endpoints
Primary: Brief Pain Inventory
Secondary: PROMIS Physical Function, Sleep Disturbance and Anxiety Computerized Adaptive Tests
We will assess the psychometric performance of the PROM study endpoints in target subgroups. In addition to calculating descriptive statistics for primary and secondary outcomes at baseline and when participants go off study, we will graph PROM scores in aggregate and by demographically-defined subgroups to assess for ceiling and floor effects and distribution of scores across the full trait range. Although the anticipated sample sizes will be limited, 20 Hispanics and 20 rural dwellers, we will compare measures of central tendency and variance in participants' PROM scores to those reported for other cohorts and used to calculate the full trial's sample size. This will clarify the whether review of the trial's power calculation is warranted.