Study Protocol and Statistical Analysis Plan

Study title: Harnessing mobile technology to deliver tailored, brief pain-CBT for advanced cancer patients on opioids for pain

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Principle Investigator/ Institution(s):

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PROTOCOL TITLE:

Harnessing mobile technology to deliver tailored, brief pain-CBT for advanced cancer patients on opioids for pain

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1.0 Objectives*

1. As a pain psychologist and palliative care researcher, I developed develop a novel mHealth intervention that harmonizes psychological and pharmacological support for advanced cancer pain. **I adapted core components of pain-CBT and integrated them into STAMP (Smartphone Technology to Alleviate Malignant Pain),** an existing NINR-funded cancer pain mHealth intervention. STAMP enables patients with advanced cancer to track their pain, opioid use, and side effects. It delivers tailored education and self-management advice while facilitating clinician monitoring and patients' proactive outreach. Having developed an extensive suite of multi-media cancer pain psycho-education covering core pain psychology principles, I seized a strategic opportunity to refine and integrate pain-CBT treatment into medically oriented self-management support in STAMP. Capitalizing on mHealth technology, I strove to destigmatize pain psychology through a potentially scalable model that can disseminate behavioral treatments for advanced cancer pain paired with their palliative care pain management plan. My aim is to:

- Determine feasibility and acceptability of the STAMP+CBT app: up to 15 patients with advanced cancer pain will be recruited from outpatient palliative care clinics at a major cancer center to participate in a single-arm, 6-week study of STAMP+CBT (4-week intervention period and a 2-week post intervention period). Surveys at baseline, 4 weeks (end of intervention period), and 6 weeks (end of 2-week post intervention period) will explore trends in pain specific intensity, self-efficacy, and catastrophizing, physical function, opioid use, and quality of life. End-of-study interviews will identify facilitators and barriers to usability, acceptability, and satisfaction of the app. The primary outcome will be feasibility evaluating 1) app retention rates and 2) completion of app exercises.

2.0 Background*

1. *Describe the relevant prior experience and gaps in current knowledge.* **Between 39% to 75% of patients with cancer suffer from pain, with the highest burden of symptoms occurring among those with advanced disease.**[1] Poorly managed pain can be devastating to patients' psychological health, physical functioning, social connectedness, and quality of life.[2,3] Opioids are the cornerstone of treatment;[4] however, up to 60% of patients experience inadequate relief.[5,6] Side effects (e.g. constipation and fatigue) are extremely common and often prevent patients from engaging in their

lives.[7,8] Effective non-pharmacologic treatments are greatly needed to mitigate the burden of advanced cancer pain.[9]

Chronic pain is a multidimensional construct involving dynamic relationships between biological, psychological, behavioral and social factors.[10] Although the biological basis of cancer pain is indisputable, psychological and behavioral factors impact many dimensions of the pain experience.[11–13] For example: patients' beliefs about pain, self-efficacy, affect, perceived stress, and sleep contribute substantially to pain severity and pain-related disability.[11–13] Moreover, beliefs surrounding cancer pain and opioid treatment, including stoicism, fears of addiction, and ambivalence undergird patients' many critical pain self-management needs including optimal use of opioids and productive communication with care teams.[2,14–16] New approaches are needed to address psychological factors that influence cancer pain and opioid use.[17]

Numerous psychological treatments have been proven beneficial for chronic non-cancer pain, with growing evidence of benefit for cancer pain.[18–21] The most efficacious programs address both emotional and evaluative aspects of pain while teaching pain coping skills.[22–25] Cognitive behavioral therapy for pain (pain-CBT) is the most widely utilized psychological treatment for chronic pain, with meta-analyses demonstrating small to moderate improvements in pain severity and daily functioning.[26] Pain-CBT differs from traditional CBT as it targets pain-specific psychological processes through pain psycho-education, cognitive restructuring to challenge maladaptive pain cognitions (e.g. pain catastrophizing), building emotional awareness, and by teaching coping skills to improve physical function and relaxation exercises to reduce muscle tension and stress reactivity.[27–29]

While the broad goals of pain-CBT are highly relevant to advanced cancer pain, its mode of delivery and certain emphases require modification to be suitable for advanced cancer patients. For example, cognitive restructuring exercises in pain-CBT focus on challenging and modifying "catastrophic" appraisals of pain such as "something must seriously be wrong."[27] This is insensitive to advanced cancer patients' realities – for whom worsening pain often truly signifies cancer progression and the terminal phase of illness.[30] Another problematic aspect of traditional pain-CBT is its focus on minimizing opioid use, yet this is fundamentally the reverse in advanced cancer where opioids are required. Practically, traditional pain-CBT involves months of in-person therapy, which is too taxing and frankly infeasible for this population. A few studies have sought to modify pain-CBT for general cancer populations. Although they use telehealth to overcome barriers to delivery, these interventions

continue to employ lengthy online sessions (e.g. 45-60 minutes).[31–33] Early data suggest these programs are feasible and acceptable to patients;[31–33] however, to our knowledge, none tailor pain-CBT specifically for advanced cancer patients, and none integrate pharmacologic management.[20]

Mobile health technology (mHealth) is a promising strategy to tailor, deliver, and ultimately disseminate psychological interventions for advanced cancer pain.[34,35] Mobile health overcomes many of the practical barriers that limit patients' access to traditional behavioral therapies while serving as a logical response to the severe shortages of trained therapists.[36] Smartphone delivery co-localizes support at home where patients have the greatest need.[37] Developing a smartphone intervention that combines medical support with pain self-management support has great potential for scalability to advanced cancer populations.

2. **Development of an mHealth tool to support opioid management for advanced cancer pain**. Under the mentorship of Drs. Enzinger and Tulsky, I have substantially contributed to the development of STAMP, a patient-facing smartphone application and web-based research portal designed to optimize the management of advanced cancer pain with opioids (IRB #18-504). The app hosts patients' specific analgesics (including dose and frequency), which are integrated throughout the application features (e.g. symptom surveys, tailored feedback). Daily surveys assess pain and related symptoms (e.g. pain, opioid use, pain interference, constipation/ laxative use, stress, and sleep) using adaptive survey logic and alternating schedules to minimize survey burden. Patients receive feedback and tailored education based upon their reported symptoms (e.g. links to pain psycho-education), including advice to contact their care team for concerning symptoms. As part of this project, I have led the development of an extensive suite of multi-media cancer pain education covering medication support (e.g. using short and long-acting opioids, managing side effects, opioid safety); pain psychology (e.g. pain perception, pain and the stress response); health behaviors and pain (e.g. sleep hygiene); and skills training (e.g. activity pacing/ relaxation recordings). Content is presented in multiple engaging formats (e.g. written texts with paired illustrations, 2-D animated videos, audio-recordings, games), using real-world examples, everyday language (7th grade reading level), and metaphors to support important concepts (See Appendix C).

In qualitative feedback with 15 patients with advanced cancer pain, the education was considered to be far better than previously received education. Feedback included: "We need to be heard…this is really validating," "the visuals are amazing… I'm able to see a lot

of what you are putting into words," and "the app is intending to move people from…sort of suffering in silence…to find that balance between pain and opioids." The STAMP app is currently being piloted and will be completed by fall 2021.

Qualitative patient interviews regarding pain self-management and attitudes toward psychological treatment. I recently completed in-depth, semi-structured, qualitative interviews with 26 ambulatory advanced cancer patients using opioids to manage chronic pain. The majority (23/26) discussed how stigma of opioids impacted their pain management and willingness to use opioids. Most were also eager for behavioral tools to help manage pain; however, none had any prior exposure. Many expressed that they would be most likely to engage in behavioral treatment if it was recommended by their palliative care/oncology team and integrated into their overarching cancer pain plan. Smartphone delivery was viewed as an attractive way to learn behavioral skills (16/20), as very few patients felt capable of attending traditional in-person therapy. This preliminary data points toward the need for accessible psychological cancer pain support that acknowledges the psychological complexity of opioid-use, while supporting both medical and behavioral aspects of pain self-management.

3. To our knowledge, this will be the first adaptation of pain-CBT content specifically for patients with advanced cancer pain. Existing adaptations of pain-CBT content[32] have taught CBT-derived pain coping skills for mixed cancer cohorts,[31] and for transplant patients.[33] STAMP+CBT now adapts critical components of pain-CBT content to address common concerns of advanced cancer patients, while ensuring a realistic level of engagement for this population.This strategy is conceptually appealing because many pain self-management strategies (e.g. optimal use of breakthrough opioids, engaging in safe physical activity) involve interrelated psychological, behavioral, and medical processes. This approach also destigmatizes psychological treatment for pain, as it is integrated with their opioid management, including support from their cancer care team.

Using smartphones to deliver psychological pain treatment is innovative. Most evidence based, mHealth behavioral pain interventions have utilized tablets[31,32] and/or video-conferencing to deliver traditional 50-minute, module-based treatments. These interventions do not fully employ the unique capabilities of mHealth to tailor psychological treatments[37] and present content in engaging, empathic ways[38,39] (e.g. through gamification, quizzes). STAMP+CBT will leverage mHealth tailored software to integrate

engaging media (e.g. audio, videos, graphics), and user-centered design (e.g. positive aesthetics, playful interface).

4. STAMP+CBT content and resources were developed in a previous study (IRB 20-453). For the previous study, the team used qualitative feedback and results to help develop modifications to standard pain-CBT content too add them to the original STAMP app for a new pain mobile app that includes cognitive behavioral therapy for pain geared to cancer patients (STAMP+CBT). This section of the study has been completed, all content has been finalized and modifications to the application content for STAMP+CBT have been developed. This content can be reviewed and referenced in appendices D, F, Y, Z.

In the study described above interviews were used because they produce qualitative results; therefore, the portion of the study did not employ statistical analyses. The study team instead reviewed the qualitative feedback from patients and clinicians across three previous cohorts A, B, and C and found common themes. The study team used the common themes from participant responses to guide modifications of the application and its content. The goals of these previous cohorts was to identify and address any problems with the pain-CBT education and resources. For instance, participants requested revising technical psychological labels (e.g. "catastrophizing") to improve literacy, in addition to shortening length of text, adding an option for daily opioid tracking, and increasing the presence of visuals throughout the app. Furthermore, most patients endorsed the content as being usable, informative, convenient to access, and relevant to their cancer pain experiences.

3.0 Inclusion and Exclusion Criteria*

3.1 **Participant engagement will be referenced as "Pilot Cohort" in this protocol.**

PILOT COHORT Inclusion Criteria:

- Age ≥ 18 years
- Patients diagnosed with an active cancer diagnosis, either undergoing active cancer treatment or receiving treatment for an advanced cancer or are receiving palliative care
- Treatment managed at participating clinic (DFCI outpatient palliative care, gastrointestinal cancer center, and DFCI satellite clinic Merrimack Valley or Londonderry)

- Chronic pain related to cancer or treatment (≥ pain score of 4)
- Has an active prescription for at least one opioid medication to treat their cancer pain (i.e. not for post-surgical pain)
- Own a compatible smartphone (android) or is willing to use an android device provided by the study team
- Completes baseline survey

Pilot Cohort Exclusion Criteria:

- Patients in survivorship: patients who have completed their treatment regimens, are not actively receiving treatment for an advanced cancer, or have a cancer that is in remission
- Cognitive impairment that would interfere with study participation, as judged by treating clinician
- Inability to speak English: the intervention has not yet been translated to Spanish
- History of opioid use disorders
- Enrolled in hospice
- Currently hospitalized
- Use of transmucosal fentanyl, given safety concerns and ongoing risk mitigation program required to prescribe these (TIRF REMS).
- Pain primarily related to a recent surgery

3.2 We will exclude adults who are unable to consent, individuals who are not yet adults (infants, children, teenagers), pregnant women, and prisoners.

4.0 Study-Wide Number of Subjects*

N/A

Please find the summary of study-wide number of subjects below:

Cohort	Maximum # of participants
Pilot Cohort	Up to 15 patients
Total accrual	Up to 15 participants

5.0 Study-Wide Recruitment Methods*

Recruitment methods are outlined for this Pilot Cohort in Reference section 21.

6.0 Multi-Site Research*

N/A

7.0 Study Timelines*

1. *Describe:* Patients in this Pilot Cohort will be in the research study for 6 weeks total including: a 4-week intervention period and 2-week post intervention period. Patients will use the app for a total of 4 weeks (4-week intervention period), and will complete surveys at baseline, 4 weeks (end of intervention period), and at 6 weeks (end of 2-week post intervention period).
    - We anticipate enrolling 1-2 patients per week during the pilot period, and should thus complete the study within 4-5 months.
2. *The study timeline may change due to unforeseen circumstances. The estimated date for the investigators to complete this study (complete primary analysis) is October 31, 2022.*

8.0 Study Endpoints*

8.1 ENDPOINT 1: The primary objective is to determine feasibility and acceptability of STAMP+CBT. Specifically, we will evaluate patients' adherence to daily and weekly comprehensive symptom self-assessments within the STAMP+CBT app. We will calculate patients' overall adherence rate and 95% confidence interval. Defined using precision analysis, we will consider the intervention to be **feasible** if ≥70% of subjects complete ≥4 of the 6 pain-CBT modules and completes 50% of surveys by the end of 4 weeks (completion of the 4-week intervention study period; completion of the 2-week post intervention period will be exploratory).[40,41] The intervention will be considered **acceptable** if ≥80% of the acceptability items are rated 4 or higher/5; lower ratings will lead to app refinements. Other feasibility measures will assess time to accrual, participation rates, study retention and completion rates, and the number of patients who continue to review app content between weeks 5-6 (post-intervention period) . Power calculation: With 10 patients, we will be able to estimate these proportions with margins of error (half of a 95% confidence interval) of approximately 18% or less assuming that the feasibility threshold of 70% is reached. This margin of error is small enough so that proportion estimates relevant to study feasibility will be

accurate and provide informative guidance for future, larger studies. Using **qualitative** framework analysis methods, we will explore barriers/facilitators, suggested changes to content, acceptability of intervention engagement, and whether app use continues after completion. Although power is not sufficient in this pilot, we will explore associations between levels of engagement and changes in pain severity/interference, opioid use, catastrophizing, sleep, mood, and pain self-efficacy.

8.2 COMPREHENSIVE ENDPOINT: The study team will use qualitative and quantitative results to determine the feasibility and acceptability of this pain CBT mobile health app for patients with cancer. This feasibility study will inform final modification to the application and study procedures in preparation for a future efficacy study of the STAMP+ CBT mobile health app.

9 Procedures Involved*

9.1 STUDY PROCEDURES:

The content for the STAMP+CBT application can be reviewed and referenced in appendices D, F, Y, Z. Once app programming is completely finalized, patients in the Pilot Cohort will engage in the pilot study to evaluate app feasibility and acceptability.

9.2 Patients in the Pilot Cohort will pilot the application for 4 weeks (or 6 weeks if they request to review the content further, this will allow us to test the correct length of app use). The onboarding and monitoring protocol is available in Appendix S. In addition, the RA will contact participants after 4 weeks (end of intervention period), and 6 weeks (end of 2-week post-intervention period). The purpose of these contacts would be to schedule the end of intervention interview and confirm completion of survey assessments, as well as the final survey assessments at 6 weeks (end of 2-week post intervention period).

9.3 Participants will fall into only one eligibility category:

Pilot Cohort = Patient pilot testing

Table 1. Brief description of pilot cohort activities

Description	Components of Participation
Participants will include DFCI patients presenting to outpatient palliative care, GCC, or satellite (MV and LD) clinics with ongoing chronic cancer pain management issues. Participants will meet with the study team in person, over the phone, or via a compliant and secure video chat/screen-share platform (i.e. Zoom). We will conduct the pilot cohort with up to 15 patients. Each participant will receive a $25 gift card upon completion of the 4-week intervention period, and another $25 gift card upon completion of the 2-week post intervention survey. *The first 5 patients will onboard to the application and their involvement/feedback will focus on making final revisions onboarding for the application and study procedures. Therefore, the following 10 patients' data will be included for pilot study analysis and feasibility findings.*	• Use the STAMP+CBT mobile app for 4 weeks (intervention period, 4 weeks for content introduction, extended 2 weeks for review of content if patient's request this) • Engage with pain CBT content including a goal-setting module, relaxation exercises, and educational content • Daily and weekly reporting of pain, catastrophizing, mood, and sleep symptoms and painkiller usage and satisfaction through the app (Appendix U) • Complete survey assessments at baseline, 4 weeks (end of intervention period), and 6 weeks (end of 2-week post intervention period) assessing pain severity, self-efficacy and catastrophizing, physical function, opioid use, and quality of life outcomes. (Appendices P, Q, R) • End-of-intervention interview (4 weeks) assessing usability and acceptability (Appendix T) • Medical Record Abstraction (Appendix O)

PILOT COHORT:

The first few patients (up to 5) will onboard to the application and their involvement/feedback will focus on making final revisions to the mobile application and study procedures. All procedures will be the same for the 15 patients, however, data for the initial patients (up to 5) will not be included in final analysis as their involvement will be focused on revising final app bugs/iterations and modifications to study procedures before the pilot trial initiation. The following patients (up to 10) will be considered as the core pilot study participants to evaluate feasibility and acceptability of the application and study procedures.

Survey assessments

An RA will ask the patient to complete a baseline survey assessment after consenting, at the end of the 4-week intervention study period, and at the end of the 2-week post intervention period to assess key outcomes (pain severity/interference,[42] QOL[43]), potential mediators of intervention effects (catastrophizing[44], self-efficacy[45], perceived stress[46], anxiety/depression[47], sleep[48]), acceptability,[49] and usability[50]. The survey can be completed remotely though a link to a Partners Healthcare compliant electronic survey system (e.g. REDCap), over the phone with the RA, over Zoom with the RA,

in person with pen and paper or on a tablet. The Baseline survey will assess socio-demographics, barriers to pain management, pain severity, opioid use, pain and psychological symptoms, and quality of life, with metrics shown in Table 5. End of 4-week intervention period survey will largely replicate the baseline survey; additionally, patients will rate their satisfaction with STAMP+CBT using the 6-item Acceptability E-scale. Surveys will be used to assess pain and psychological symptom trajectory, medication use, and quality of life. See **Appendix P** for the Baseline survey items, **Appendix Q** for 4-week (end of 4-week intervention period) survey items, and **Appendix R** for 2-week (post intervention period) follow-up survey items. Additionally, a subset of patients (up to 10) will be invited for a qualitative interview focused on study burden, facilitators/barriers to app use, satisfaction, and perceived utility in order to guide future refinements to the app (see Appendix T) when they complete use of the app at 4 weeks (end of intervention study period).

Intervention

After the patient completes the baseline survey, the RA will meet with the patient (in person or virtually), to assist in either 1) downloading the application onto participants' mobile device or 2) providing/mailing the study phone to the participant. The RA will help to register the patient to the app and help set up any preferences. The RA will then conduct a 15-minute tutorial on the STAMP+CBT app and its intended use (Appendix S). The RA will also input the patient's pain medications from Epic, reconciling this list with the patient, and with the nurse navigator on the patient's care team if there are any discrepancies. As the nurse navigator is already a member of the care team, they'll have access to all Epic records and any documentation for this study included in Epic. The participant will also input their desired goal to work towards for the duration of the trial. During the trial, there is also a function in the app that allows participants to notify the research team if a medication or goal needs to be changed and reflected in the app. Final iterations to the app, research portal, and study procedures will be made following the initial few patients (up to 5) recruited to using the application. **Thereafter, we will begin recruiting patients (up to 10) for the pilot study cohort.**

Participants will utilize STAMP+CBT for 4-weeks (intervention study period). The 4 weeks will consist of all content introductions. Patients will also be offered the opportunity to continue their app use for the next 2 weeks (post-intervention period) until study completion (2 week follow up and survey), this will allow us to assess feasibility and acceptability of the appropriate length of use for the intervention. STAMP+CBT hosts and organizes patients' opioid/non-opioid analgesics. It has an extensive multi-media library of education content related to pain management (Appendix C)

and pain specific CBT concepts (Appendices C, D, and F). Content will be delivered on a schedule to ensure that patients receive all pain CBT and medication education available (Appendix U). STAMP+CBT prompts patients to take daily surveys for reporting of pain, pain catastrophizing, mood, opioid/pain medication use, and sleep symptoms and progress towards individualized goals (Appendix U). At the end of each survey, patients receive feedback according to their symptom severity, with links to tailored educational content about pain and psychological symptom management. (Appendix U). Patients also complete weekly surveys for reporting symptoms listed above as well as goal progress. If patients report any severe symptoms, they are instructed to contact their care team immediately, with a telephone number included on the application screen, see table 2, or to go the Emergency room/call 911 for a true medical emergency. If patients' pain is poorly controlled but not severe enough to be prompted to immediately contact their care team (for example if their average pain is above a 4 and not acceptable), they are reminded to contact their care teams if their symptoms worsen or they are concerned about it.

One protocol-mandated study staff outreach to patients will occur within a week of enrollment. An RA will call to assess any technical or usability problems with the app (e.g. how to access the app on their phone, where to find certain study areas, etc.). These technical discussions will be optional for the patient and more can be scheduled if requested. Thereafter, the RA will monitor the STAMP+CBT dashboard twice daily (Mon-Fri), for any patient reported severe symptoms (Table 2). If a patient reports one of these severe symptoms, the RA will contact the patient's nurse through a secure EPIC message to notify the patient's care team. Additionally, to assist in population management, a *tiered system notifications,* in the portal will indicate symptom severity, need for outreach and/or management changes (See Table 3). As an additional safety measure, the application always prompts the patients to contact their care team for any severe symptoms they report and there is no expectation for proactive clinician outreach. These procedures have been approved by participating clinic nurses. The application provides a direct link to call the Outpatient Palliative Care Clinic at DFCI.

To minimize the burden of the intervention on clinicians, there are no automated clinician alerts (i.e. email or in-basket message) for severe symptoms, rather, patients are prompted to call their care teams or 911 (emergency services) if they report severe symptoms (Table 2 and 3). Patients are reminded frequently throughout the application that the research portal is not monitored around the clock and therefore they should reach out for urgent needs. Reports (with summarized pain and psychological symptoms; opioid use data; side effects; patients' goals and reported goal attainment) will be sent to nurse managers, palliative care providers, and

oncologists to enable effective communication, opioid titration, and other management changes when prompted by the patient.

During the study patients will be asked to complete 3 survey assessments, one at baseline, one at the end of the 4-week intervention period, and another at the end of the 2-week post intervention period. Patients will also be invited to complete a short semi-structured interview about their experiences using the application (See Appendix T). See below for description of the surveys (Table 5).

Table 2. Severe Symptoms

Pain	• Worst pain = 9-10 • Worst pain = 7-10 and new pain
Red Flag Symptoms	• Severe weakness or fatigue • Lightheadedness or feeling like I was going to pass out • No gas or stool from my bottom (or ostomy) in the last 2 days • Vomiting 2 or more times in the last 24 hours • Fever of 100.5 or greater • New or worsening chest pain • New or worsening shortness of breath • New or worsening back pain • New numbness and weakness in one or both of your legs • Severe difficulty eating or drinking • Hallucinations/nightmares
Opioid Side Effects	• Hallucinations

Table 3: Report on Research Dashboard Based on Patient Responses

Relief with opioids	No relief OK Unsure Good relief
Pain Control	Poor Suboptimal Good
Other Severe Symptoms	Number of severe symptoms on Table 2 shown in red
Opioids need updating	Yes No
Mood	IF Patient responds to mood questions 17-20 with a total score of ≥12: Low Mood IF Patient responds to mood questions 17-20 with a total score of <12: High Mood
Catastrophizing	IF Patient responses to catastrophizing questions 12-16 with a total score greater than ≥10: High Stress IF Patient answers catastrophizing items 12-16 with a total score <10: Low Stress
Sleep	If sleep item 23 on the survey score ≥3 : Poor If score <3: Good
Goals need updating	IF Patient answers "No, it needs to be changed" in goal-setting section of weekly survey: Goal needs updating

**Note: The RA will check the portal twice daily and send an EPIC message to the patient's nurse for all responses in red needing urgent evaluation*

Chart Abstraction

The study team will complete a limited structured chart abstraction at baseline and at end-of-study to collect basic non-identifiable clinical/demographic information (See appendix O). Chart abstraction will assess clinical actions responding to STAMP+CBT data and healthcare utilization related to pain and symptom management (e.g. hospitalization, ER visits, urgent clinic visits for symptom management, psychosocial oncology social work, psychology, or psychiatry visits). As people with cancer have variable prognoses, they may pass away during a study; therefore, we want to be able to abstract and record if/when a patient passes away during or recently after their involvement. Should this situation arise, it can negatively influence outcomes of the study evaluation (feasibility/acceptability).

Chart Abstraction Information collected will include the following:

- **Demographics:** Gender, age, ethnicity, race
- **Cancer**: Patient's date of diagnosis, diagnosis (cancer type), stage at diagnosis, status of active curative or palliative treatment, history and date of surgery related to cancer, and whether patient has seen palliative care (yes/no)
- **Pain**: patient's last pain rating, type of pain, location of pain, surgeries or operations for pain, documented calls about pain.
- **Prescribed Pain Medicines**: Patient's prescribed short-acting opioid, long-acting opioid, and non-opioid pain medications, and length of time taking opioids.
- **Prescribed Anxiolytics**: Patients' prescribed anxiolytics and whether this was prescribed before or during the study
- **Prescribed Antidepressants**: Patients' prescribed antidepressants and whether this was prescribed before or during the study
- **Medication/Opioid side effects**: Constipation or related symptoms.
- **Clinic visits**: Unplanned or urgent clinic visits that include pain 6 months prior, during, and 6 months post-intervention, and social work, psychology, or psychiatry visits during study period
- **Mental Health Diagnoses**: Whether the patient has a mental health diagnosis and what mental health diagnosis the patient has.

Table 4: Summary of developed STAMP+CBT content (See Appendix F for further descriptions):

CBT for pain Modules	**Location of Content**	**Type of Content**
Adaptive surveys: Depression, stress, anxiety, catastrophizing, sleep, personalized goals	**Appendix B**	Survey items
Text or audio-visual content: **Appendix C:**		
Pain psychoeducation	**Appendix C** **Appendix D**	Written content Video content
Emotional awareness	**Appendix C**	Written content
Relaxation/ deep breathing	**Appendix C**	Written content
Stress and pain	**Appendix C**	Written content
Cognitive processes/restructuring for pain	**Appendix C** **Appendix D**	Written content Video content Behavioral Game: http://18.210.82.141/v31/
Goal setting	**Appendix C**	Written content
Activity setting	**Appendix C** **Appendix D**	Written content Video content
Opioid Education	**Appendix C** **Appendix D**	Written content Video content
Non-opioid analgesics education	**Appendix C**	Written content

Human Subjects Research Category (NHSR, exempt, expedited, full review):

Pilot Cohort: Expedited

Human subjects research designation for the Pilot Cohort is **expedited.**

Informed Consent: Written consent will be obtained from all participants (Appendix AD). After identifying potential eligible patients, we will contact the treating physician via email or phone to request permission to approach any patient. If the physician approves the approach, we will ask them to introduce the study to the patient at a regularly scheduled visit and ask permission for the research team to contact them to further explain the study and offer participation. If the physician denies approach, we will not approach the patient to offer study participation.

After a clinician has approved the study team to approach their patient, the patients may be approached in person during an upcoming clinic visit. Once approached, the RA will review the study letter and consent form with the patient (Appendices X and AD). The study letter will notify participants that engagement in the study is completely voluntary and can be stopped at any

time for any reason. The palliative care clinic in which patients are being recruited for this study have also largely remained remote with tele-health services. Few patients attend in-person clinic appointment for palliative care outpatient care. Therefore, if approaching patients at the clinic is not possible, eligible patients may be approached remotely via phone. If a patient is contacted by phone, the RA will send the study letter and consent forms through a secure and personalized link in the FDA and HSSH compliant Mass General Brigham/Partners REDCap database. The RA will attempt to contact a patient three times. If contact is not established, the RA will email a copy of the recruitment letter to introduce the study (Appendix AC). The letter encourages the patient to contact the research team if they are interested in participating in the study. If the patient then contacts the research team, the study letter and consent form will be reviewed with the patient before obtaining written consent. If the patient does not respond by email or if they opt of the study participation, they will no longer be contacted. **To account for patient understanding, the study letter will also be included in the app for review at any time.**

9.4 **MONITOR SUBJECTS FOR SAFETY AND MINIMIZE RISKS:** The risks to participants in the Pilot Cohort are minimal. The primary risk is loss of confidentiality/privacy. To monitor the risk of loss of confidentiality/privacy, the study team has ensured that the STAMP+CBT app is HIPAA compliant and meets the privacy and security standards set by DF/HCC, and will continue to do so with modifications in this study (IT approval received from Mark Tomlinson). In addition, all collected study data will be maintained in a secure location and personal identifiers will be removed. As described above, end of study interviews will be audio and video recorded, and transcribed for analysis of participant feedback. For the patients engaging in qualitative interviews, their video recorded data will be destroyed after manuscript publication.

<u>Risks to participants in the Pilot Cohort</u>

- Physical risks: Physical risks to subjects include if they feel reassured by the app's feedback/content and choose not to contact their care team for severe symptoms. It is also theoretically possible that patients are given medication advice that is either ineffective at relieving pain.
- Psychological risks: Reporting pain and psychological symptoms daily may be distressing for some patients. It may also be the case that reviewing psychological content may be distressing as awareness of cognitive and emotional factors relevant to pain will be acknowledged.

- Privacy risks: There is a risk of privacy violation or loss of confidentiality; however, this is anticipated to be minimal, and the study team is committed to guaranteeing adequate protection against risk as described in the following section.

9.5 **Data to be collected:**

9.5.1 Interview Data: Audio and video recordings of feedback will be collected from all interview participants regarding their perceived feasibility and acceptability of the mobile application as well as their experience with the app.

9.5.2 E-Acceptability (Survey) Data: Participants will complete an acceptability survey following review of finalized content (see Appendices I).

9.5.3 Chart Abstraction: Baseline demographic and clinical data will be collected from all patient participants via chart abstraction. Data will also be collected at the end of the pilot intervention. Data will include non-identifiable clinical/demographic information, including the following:

9.5.3.1 Gender
9.5.3.2 Age
9.5.3.3 Ethnicity
9.5.3.4 Race
9.5.3.5 Cancer type
9.5.3.6 Cancer stage
9.5.3.7 Opioid medications
9.5.3.8 Pain score during last visit (see Appendices O).
9.5.3.9 Health service utilization (e.g. ED visits, hospitalizations, unplanned urgent clinic visits, changes to opioid medications, psychosocial oncology visits)

9.5.4 Survey Assessment Data: Demographic, disease, medication, pain, mood, stress, and sleep data will be collected at baseline before the intervention, end of the 4-week intervention, and at the end of the 2-week post intervention period (see Appendices P, Q, R). T1 and T2 of Table 5.

9.5.5 Symptom Reporting: Individual pain, pain interference, pain medication use, stress, mood, and sleep symptoms as well as pain management data will be recorded for each participant over the course of the pilot intervention (Appendix U). Participants will report their symptoms and management daily and weekly.

9.6 **Long term follow-up:** Participants in the Pilot Cohort complete a survey assessment assessing quality of life, pain, psychological

measures, healthcare utilization, and app use at the end of the 2 weeks post-intervention (T3 of Table 5).

Table 5: Measures collected from patients at each of three survey timepoints

Measures collected via patient assessments		Survey			App data	Chart review
Assessment	**Measure**	**T1**	**T2**	**T3**		
Socio-demographics	Standard	x				
Clinical characteristics	Standard					x
Baseline cellphone use	MTUAS	x				
Pain severity/interference	BPI	x	x	x		
Opioid use/adherence	Self-report	x	x	x		
Quality of life	FACT-G	x	x	x		
Satisfaction	Novel metric		x			
Use of STAMP+CBT	-		x	x	X	
Usability	SUS		x			
Management changes	-					x
Healthcare utilization	-		x	x	X	x
Self-efficacy in managing symptoms	PROMIS	x	x			
Self-efficacy in managing medications	PROMIS	x	x			
Pain catastrophizing	PCS	x	x	x		
Stress	PSS	x	x	x		
Patient reported outcomes	PRO-CTCAE	x	x	x		
Depression and Anxiety	PROMIS	x	x	x		
Sleep Disturbance	PROMIS	x	x	x		

10 Data and Specimen Banking*

10.1 This study does not involve any specimen collection/banking of any kind. Personal health information will be collected as part of the study. The consent form informs the participants that data collected for this study may be used in the future. By consenting, participants agree. Participants will not be asked to provide additional informed consent for the use of de-identified information in future research. There is no scheduled date on which the audio recording and transcription information and data that is being used or shared for this research will be destroyed, because research is an ongoing process. However, the video recorded data will be destroyed after manuscript publication. Patients will not provide any data on their

personal symptoms' reports; no specific patient symptom data will be collected.

10.2 All data collected during this study will be stored and used for future research. Any personal identifiers will be removed so that information cannot be linked back to a patient. For the patients engaging in qualitative interviews, their video recorded data will be destroyed after manuscript publication.

10.3 Investigators can request the data collected from this study for new research. Data may also be shared with outside non-profit academic investigators as well as with for-profit pharmaceutical investigators or commercial entities with whom Dana-Farber collaborates such as the University of Oklahoma Health Sciences Center, Stephenson Cancer Center. Requests must be sent to the study chair (Dr. Desiree Azizoddin) and must be approved by the Dana-Farber IRB prior to sharing.

11 Data Management* and Confidentiality

11.1 Because interviews produce qualitative results, statistical analyses will not be employed for a portion of this study. The study team will review qualitative feedback from patients and find common themes related to app feasibility and acceptability. The study team will use the common themes derived from qualitative thematic analysis of the interview that review this feasibility study to guide further iterations of the application and study procedures for a future larger, efficacy study of the STAMP+CBT app.

11.2 Statistical analyses will be utilized in the pilot intervention portion of this study to ascertain feasibility and acceptability. We will measure time spent on the app per day and per week, completion rates for surveys and content review, and frequency of log-ons over the course of the pilot. The primary objective is to determine feasibility and acceptability of STAMP+CBT. Defined using precision analysis, we will consider the intervention to be feasible if $\geq$70% of subjects complete $\geq$4 of the 6 pain-CBT modules and patients will complete 50% of surveys by the end of 4-weeks (completion of the 4-week intervention study period and completion of the 2-week post intervention period).[40,41] A module will be considered complete if the participant engages in $\geq$70% of its content, including completing mHealth survey items, psycho-educational content, and app exercises. The intervention will be considered acceptable if $\geq$80% of the acceptability items are rated 4 or higher/5; lower ratings will lead to app refinements. Other feasibility measures will assess time to accrual, participation rates, and study retention and completion rates. Power calculation: With 10 patients, we will be able to estimate these proportions with margins of error (half of a 95% confidence

interval) of approximately 18% or less assuming that the feasibility threshold of 70% is reached. This margin of error is small enough so that proportion estimates relevant to study feasibility will be accurate and provide informative guidance for future, larger studies. Although power is not sufficient in this pilot, we will explore associations between levels of engagement and changes in pain severity/interference, opioid use, catastrophizing, sleep, mood, and pain self-efficacy.

11.3 The data the research team will access regarding app utilization will include; date and time of app log-ins, date of time of survey completion, survey responses, including clinical reporting of daily symptoms and medication usage, total app log-ins during intervention period, percent of surveys completed during intervention period, date time and frequency patients access external educational content.

11.4 PHI data will be collected using REDCap and the STAMP+CBT app.

11.4.1 **REDCap:** For this study, data and patient consent will be collected using the Partners instance of REDCap (redcap.partners.org). In collaboration with the Harvard Catalyst | The Harvard Clinical and Translational Science Center, REDCap (Research Electronic Data Capture) is a free, secure, HIPAA compliant web-based application hosted by Partners HealthCare Research Computing, Enterprise Research Infrastructure & Services (ERIS). Vanderbilt University, with collaboration from a consortium of academic and non-profit institutional partners, develops this software application for electronic collection and management of research and clinical study data. Data collection is customized for each study or clinical trial by the research team with guidance from ERIS REDCap administrators. REDCap is built around HIPAA guidelines and is 21 CFR Part 11 capable.

11.4.2 **STAMP+CBT app:** The final application will be HIPAA compliant and compliant with DFCI security and privacy standards. The application is built on the Insight Platform where data is secure on Microsoft Azure servers (see Appendix AA for further details on this application and Appendix AB for previous IRB approval research at the University of Oklahoma Health Sciences Center through their IRB).

Microsoft enterprise cloud services are also covered by FedRAMP assessments. Microsoft Azure and Microsoft Azure Government received a Provisional Authority to

Operate from the FedRAMP Joint Authorization Board; Microsoft Dynamics 365 U.S. Government received an Agency Authority to Operate from the US Department of Housing and Urban Development, as did Microsoft Office 365 U.S. Government from the US Department of Health and Human Services.

All data collected by the Insight Platform is encrypted during storage and in transit. The Insight platform has been approved for research at the University of Oklahoma Health Sciences Center through their IRB (See Appendix AB). Users of the OUHSC Insight Platform should confer with their institution's policies regarding restrictions associated with data collection and transfer between the Insight mobile application, Microsoft Azure servers, and users institutional servers. Data collected and stored by users is intended to be de-identified. Any data classified as PHI will require users institution to enter into an appropriate Business Associate Agreement.

Study specific procedures to maximize data security:

Controlled access: The REDCap and STAMP+CBT app administrators will set up all user accounts so that each user only has access to their own relevant participant data in a prototype model only.

Use of unique study ID numbers: REDCap automatically assigns unique study ID numbers to each new case.

Extensive training: All personnel involved in this study are required to complete and document completion of extensive protocol training. Furthermore, all research personnel are required to have valid certification of human subjects research training

Storage of Patient Research Data: All patient research data is subject to HIPAA regulations at the host institution.

Note: Interviews will be audio and video recorded using the HIPAA compliant platform, Zoom. The audio and video recordings will be stored in a password protected Dropbox business account. The audio recordings will be transcribed analysis of feedback. It is important to keep the facial features of patients in the videos as this provides important sociobehavioral analysis. To protect the identity of subjects, we will advise patients to modify their name on screen and use their initials when logging into zoom, instead of their full name. Patients' video recorded data will be destroyed after manuscript publication.

The STAMP+CBT app will use the Microsoft Azure cloud service with multilayered security for storage of research data collected (see appendix AA).

11.5 The staff at Dana-Farber will be responsible for monitoring the data for completion, accuracy, and compliance. All personnel involved in this study are required to complete and document completion of extensive protocol training. Furthermore, all research personnel are required to have valid certification of human subjects' research training.

12 Provisions to Monitor the Data to Ensure the Safety of Subjects*

This is a social behavioral research project, not a treatment protocol. The study involves minimal risk.

As such, the only adverse event that will be monitored and reported is psychological distress as determined by the treating oncologist or palliative care provider. For any patient who exhibits severe distress as result of the study procedures, the study research assistant will notify the patients' oncologist, palliative care provider, and/or social worker for appropriate response, including possible mental health referral if necessary. Furthermore, participants will be *reminded that participation is voluntary and can be stopped at any time for any reason. See the DSMP (Appendix N) for more details.*

12.1 Protection against physical risks: The study team has placed extensive protections against the aforementioned physical risks of the app. These protections significantly exceed the level of support and guidance that patients would receive with usual care. Moreover, patients' symptom reports will be reviewed daily by the study staff and shared with clinical nurse navigators that are part of the patients' care teams, which represents closer monitoring than usual care. Finally, the patient-facing app always instructs patients to contact their care teams and reminds them that the portal is not monitored continuously, or to call 911/go to an emergency room for medical emergencies. First, the application sets a low bar for instructing patients to contact their care teams for reported symptoms. This includes reporting any new pain, fever, new or worsening back pain, new or worsening chest pain, any pain rated $\geq$ 8 out of a 0 to 10 scale (See table 2 for the detailed list). Moreover, if patients report moderate to severe pain levels that do not meet the previous criteria, in addition to receiving education about their pain management, they are also reminded that their care team wants to hear from them if they are concerned about their symptoms or if their symptoms are not improving. A link to their care team's number is included in the application. This level of support is much greater than what patients have usually with routine care.

12.2 Protection against psychological risks: if in the course of their participation patients raise significant emotional distress, the appropriate care team members i.e. nurse navigator, physician, mid-level provider will be contacted to make appropriate social work or mental health referrals. Similar to that of physical risks, this app provides closer monitoring than what is provided for usual care for psychosocial needs; In addition to instructing patients to call their care team for advice, the RA will share patient's elevated symptoms with a nurse navigator, already assigned to patients' care teams, for follow up. As such, these nurse navigators, will have access to all health records and including any documentation for this study included in EPIC.

12.3 Protection against privacy risks: To monitor the risk of loss of confidentiality/privacy, the study team has ensured that the STAMP+CBT app is HIPPA compliant and meet the privacy and security standards set by DF/HCC. In addition, all collected study data will be maintained in a secure location and personal identifiers will be removed.

12.4 **To maximize data security, both REDCap and STAMP+CBT employ:**

- User Privileges - To ensure that users have access only to data and information that they are supposed to have within the application, user privileges are utilized within the software. Each user has their own account, and their user account will only have access to information that they themselves have created or to which administrators have granted them access.
- Password-protection & Authentication - Both systems are password protected and implement authentication to validate the identity of end-users that log in to the system.
- Logging and Audit Trail - Both systems maintain built-in audit trails that log all user activity and all pages viewed by every user.

12.5 Institutions will register eligible participants in the Clinical Trials Management System (CTMS) OnCore as required by DF/HCC Policy REGIST-101.

13 Withdrawal of Subjects*

13.1 Subjects who do not complete app onboarding within 3 weeks of study enrollment will be withdrawn from the research study without their consent.

13.2 These patients will be informed of their withdrawal from the study by study staff. The overall DF/HCC study PI, Dr. Desiree Azizoddin,

will make all decisions regarding early termination of the study. The study team will then notify all participants accordingly.

13.3 Patients will be notified by research staff if they will be partially withdrawn from the research, as reviewed in their study letter (Appendix X) as well.

14 Risks to Subjects*

14.1 There are risks to taking part in any research study. The primary risk of this study is loss of privacy or confidentiality. The risk of loss of privacy or confidentiality by using the STAMP+CBT app or taking part in this study is minimal. The study team has taken many steps to prevent any loss of privacy or confidentiality, including training of all clinic and research staff in best practices, rules, and regulations surrounding privacy and confidentiality, collecting research data using unique study ID numbers instead of names or other identifying information, and use of data collection systems that meet data security standards.

14.2 *Recruitment and Informed Consent:* Participants will only be approached if approval is received by their treating clinician. If the physician deems them unsuitable for the study, they will not be approached. Participants will be approached in clinic or by phone by the RA in a private and confidential manner. If the patient is eligible and interested in participation, the study letter and consent forms (Appendices X and AD) will be reviewed with the participant.

In the case of remote approach by phone, the RA will attempt to contact the patient 3 times. If the patient contact cannot be established, the RA will email a copy of the recruitment letter to the patient (Appendix AC). The recruitment letter encourages the patient to reach out to the study staff if they are interested in participating. If a patient reaches out to the study staff then the study letter and consent form will be reviewed before the patient provides written consent. During remote approaches by phone the study letter and consent forms will be sent by email through a secure and personalized link in the FDA and HSSH compliant Mass General Brigham/Partners REDCap database. While discussing the study letter and consent the study staff will emphasize that participation is voluntary and the participant may stop participating at any time. Consent discussions may take place over the phone or HIPAA compliant Zoom.

The study letter and consent forms for consent to participate will adhere to strict standards regarding its content. Required sections include: Introduction; Why is this research study being done? What

other options are there? What is involved in the research study? How long will I be in this research study? What are the risks or discomforts of the research study? What are the benefits of the research study? Can I stop being in the research study and what are my rights? What are the costs? What happens if I am injured or sick because I took part in this research study? What about confidentiality? Whom do I contact if I have questions about the research study?

15 Potential Benefits to Subjects*

15.1 Using the STAMP+CBT app and taking part in this research study may or may not benefit participants. We hope that by reviewing the content in the STAMP+CBT app, patients are able to learn to better manage their symptoms and the increased flow of information between a patient and their care team improves their experiences. We also hope the information learned from this research study will provide more information about how to best help patients and their care team work together during and between visits to achieve better symptom management in cancer patients.

16 Vulnerable Populations*

16.1 This research does not involve vulnerable populations of prisoners, children, cognitively impaired adults, or pregnant women. Prisoners, children, cognitively impaired adults, and pregnant women are excluded.

17 Community-Based Participatory Research*

N/A

18 Setting

18.1 This is a pilot study that will take place at the Dana-Farber Cancer Institute. The research procedures will all be conducted online through secure, HIPAA compliant portals (i.e. Zoom, partners email, etc.). The research team will identify and recruit potential subjects through outpatient palliative care, GCC, and satellite clinics including MV and LD. See section 22.0.

19 Resources Available

19.1 The research team is well-qualified to perform their duties. Dr. Azizoddin has extensive experience in conducting research studies in cancer distress screening, pain psychology, and education. She has deep knowledge of the clinical and research environments and the patient population and culture at DFCI.

19.2 This study team will be taking place under the Department of Psychosocial Oncology and Palliative Care (POPC) at Dana-Farber.

The POPC Department maintains its own server infrastructure and systems administration staff that provide data storage, data backup, and data security in support of large data analysis projects. The servers are configured as a virtual server pool with virtual server hosts connected to a centralized Storage Area Network (SAN) device. Server virtualization increases the efficiency and flexibility of the server pool while minimizing downtime and cost. The server pool currently has 20 processor cores and a data storage capacity of 9 terabytes. This server infrastructure has a dedicated Systems Administrator to optimize performance, maintain security patches, perform backups, and execute other related tasks. Researchers in the Division have access to additional resources through the Research Computing group. Research Computing provides a variety of services including file server space, backup services, website hosting, and support of some workstation computers.

All individuals in the study team will review the protocol and be updated on protocol procedures and study needs, at the beginning of study activation and throughout the study period.

20 Prior Approvals

20.1 The existing pain educational text and audio-visual content has been previously approved in the initial STAMP pilot study (DF/HCC IRB #18-504 and # 384-811).

20.2 The additional pain CBT content was developed during study procedures previously approved in DF/HCC IRB #20-453. This content can be viewed in appendices C, D, U, Y, and Z.

21 Recruitment Methods

21.1 *Identifying potential subjects:* Potentially eligible patients will be identified by 1) referrals from clinic staff, and 2) by screening the EMR for outpatient solid tumor or hematology disease center clinic schedules, 3) by screening the palliative care clinic schedules. Once the study team identifies a potentially eligible patient, the team will reach out to the treating clinician for permission to approach and offer engagement in the study. If the provider does not approve that the study staff approach a patient, the study staff with NOT approach the patient to offer engagement in the study. Patients will provide written consent on the consent form after viewing study letter according to IRB procedures (see Appendices X and AD).

21.2 *Recruitment of potential subjects:* Under a HIPAA waiver, study staff will look in the electronic medical record, scheduling systems, and inpatient lists to identify potentially eligible patients who meet the eligibility criteria. Study staff may also query Epic, administrative/ operations/billing databases, order entry databases,

and/or cancer registry databases to identify potentially eligible participants. Study staff may also accept potential patient referrals from site clinicians, through palliative care, DFCI satellite clinics Merrimack Valley and Londonderry, and outpatient GCC clinic. Purposive sampling based on data from the electronic medical record (e.g., demographics, cancer stage, number of recent hospitalizations, number of prescription drugs) will be used to ensure that perspectives of diverse patients are included.

21.3 Patient approaches can occur through the following mechanisms dependent upon COVID-19 related research regulations and clinic operations at the time.

- In person approach: A research assistant (RA) will approach the patient in clinic to explain the study and offer participation. Interested participants will then review the study letter and consent form with a research team member (Appendices X and AD) and if interested provide written consent. The patient and RA will then set up a time for onboarding to the application.
- Remote approach: The clinician can introduce the study to the patient during a clinic visit and the RA will follow up by phone to explain the study and offer participation. The study letter and consent form will be sent electronically through a secure and personalized link in REDCap (Appendices X and AD). The RA will attempt to contact the patient three times. If no contact is established, the RA will email the participant a copy of the recruitment letter (Appendix AC). The recruitment letter introduces the study and encourages the patient to contact the study team if they are interested in participating. If the patient contacts the RA after the recruitment letter, the RA will review the study letter and consent form before obtaining written consent.

21.4 See study letter Appendix X, recruitment letter Appendix AC, and consent form Appendix AD for the Pilot Cohort.

21.5 A $25 giftcard will be provided upon completion of the 4-week intervention period, and another $25 gift card will be provided when patients complete the 2week post intervention period survey. Clinicians will not receive compensation for their engagement.

22 Local Number of Subjects

22.1 This project will ONLY be taking place at Dana-Farber and participating DFCI satellite clinics. Therefore, all study participants will be recruited on site and through remote approach and follow-up

(phone and zoom). In total, approximately 15 subjects will be accrued at DFCI and participating DFCI satellite clinics.

Activity	Maximum # of participants
Pilot Cohort	Up to 15

23 Provisions to Protect the Privacy Interests of Subjects

23.1 To protect PHI, the following measures will be taken. Patients will be approached and interviewed in private settings. All study form hard copies will use only de-identified unique study ID numbers and be kept in the patients' study files in locked drawers to which only the designated study team member has a key. All electronic data will be kept on secure, password protected servers as evaluated and managed by the Dana-Farber Department of Research Computing and IS.

Departmental and institute-wide policies enforce the protection of our electronic information, especially with regards to HIPAA regulations and the integrity of patient care. These policies also safeguard again theft, abuse, misuse, and any form of damage. The scope of protection includes information which is printed from or stored on a database, mainframe, server desktop, laptop, PDA, CD-ROM, hard disk, flash drive, optical platter, tape, smart phone, network, telephone, and other computer-enabled medical devices. These policies regulate usage of system IDs, passwords, e-mail accounts, anti-virus mechanisms, encryption, mobile devices, remote access, remote control software, and wireless devices. IS responsibilities and governance including firewall protection of all Dana-Farber internal networks and the internet, system evaluation, risk analysis, information access, regular review of user accounts, systems audit, regular review of remote access, and physical location access. Specific to this project, no data will be stored on laptops at any point and secure transfer protocols will be used for any electronic exchange of information. All staff/users receive mandatory institutional trainings on Information Security and must adhere to policies at all times.

Subjects will be approached for potential participation in private or by phone. They will also complete all study assessments in private and at their own comfort (remote completion). At each assessment, subjects will be reminded that they can skip any questions they do not wish to answer and are free to withdraw from the study at any time.

Study research assistants will have access to subject's medical records to abstract information as discussed in other sections of this protocol. RAs will only access information that is necessary to collect for the study protocol and will not be permitted to access the medical record for other purposes.

24 Compensation for Research-Related Injury

N/A

25 Economic Burden to Subjects

25.1 Costs that subjects may be responsible for because of participation in the research: Subjects participating in this study will be asked to complete online surveys using an internet-enabled device. Participants will have to use their own hardware (e.g., smartphone, tablet, computer) and their own WiFi or Data Plan which may cost them money; subjects are responsible for these costs. Devices and/or data plans may also be provided by the study staff to interested participants who do not own an android device.

Patient participants in the Pilot Cohort will receive a $25 gift card upon completion of the 4-week intervention period, and a second $25 gift card upon completion of the 2-week post-intervention survey.

26 Consent Process

26.1 Potentially eligible patients will be identified by 1) referrals from clinic staff, or 2) by screening the EMR for outpatient GCC or palliative care clinic schedules. Once the study team identifies a potentially eligible patient, the team will reach out to the treating clinician for permission to approach.

Once approved to approach, the study staff may approach patients in-person during clinic. Once approached the RA will review the study letter and consent form with the patient (Appendices X and AD). If it is not possible for the RA to meet the patient during a clinic visit, the clinician may introduce the study and the RA will follow up by phone. During a phone call the RA will explain the study and offer participation before obtaining written informed consent. During this phone call, the RA will email a copy of the study letter and consent form and the participant will provide written consent. The RA will send the study letter and consent forms through a secure and personalized link in the FDA and HSSH compliant Mass General Brigham/Partners REDCap database. The RA will attempt to contact a patient three times. If contact is not established, the RA will email a copy of the recruitment letter to introduce the study (Appendix AC). The letter encourages the patient to contact the research team if they are interested in participating in the study. If the patient then contacts the research team, the study letter and consent form will be reviewed remotely during a phone call with the patient before obtaining written consent. If the RA is

unable to establish contact with the patient after 3 call contacts and if the patients does not respond to the email recruitment letter, the patients will no longer be contacted

All interested participants will provide written consent after thorough review of the study letter and consent form. Next, they will complete the baseline survey to ensure enrollment in the study. Thereafter, the RA will coordinate with the patient to onboard with the pilot application. They will be notified that participation is completely voluntary and can be stopped at any time for any reason.

27 Process to Document Consent in Writing

27.1 Participants will be given a study letter and consent form to provide written consent. The research presents no more than minimal risk of harm to subject. The research procedures for this tech-based intervention will also primarily occur remotely given COVID-19 barriers to in-person care (the majority of outpatient palliative care visits continue to occur remotely). We will email the study letter and consent forms through a secure and personalized link in the FDA and HSSH compliant Mass General Brigham/Partners REDCap database. Additionally, a copy of the study letter will be housed in the app itself in the event that patients want to review this study letter after onboarding and during study participation for this mobile health app.

28 Drugs or Devices

N/A for this study.

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