Smartphone Technology to Alleviate Malignant Pain (STAMP) (NCT03717402)

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PROTOCOL TITLE:

Smartphone Technology to Alleviate Malignant Pain (STAMP): development and piloting of a novel mHealth intervention to support cancer patients, nurses, and physicians in opioid management

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2.0 Background

Pain is a common, distressing, and costly complication of cancer. Pain affects approximately half of all patients on treatment, a third of patients after treatment completion, and 75-90% of patients in the terminal phase of illness.[1, 5, 17-19] Nearly 60% of these patients experience moderate to severe pain,[1, 5] for whom opioids are recommended.[20, 21] Pain has devastating consequences for patients' quality of life, mood, relationships, and functional wellbeing.[5] Cancer pain also has major impact on health systems, being among the most common reasons for emergency room,[22, 23] and hospital-based care.[24, 25] Approximately 25% of acute care episodes for cancer pain are potentially avoidable,[10, 24, 25] underscoring need for strategies to bolster outpatient management

Despite effective therapies and evidence-based treatment guidelines,[20, 26, 27] cancer pain is often poorly managed.[4, 6, 28] Guideline-driven management - which includes a stepwise treatment approach, use of standing and as-needed opioids, with frequent monitoring and titration – is able to relieve symptoms for the vast majority of patients.[3] Unfortunately, cancer pain is often poorly controlled.[2-6, 28] Over 40% of patients are prescribed pain regimens insufficient for their symptom severity.[4, 6, 28] This may be due to clinicians' underestimation of pain,[6, 29] gaps in clinical knowledge, and lack of time/resources needed to reassess and adjust management.[15, 30]

Managing cancer pain is complicated and stressful for patients and caregivers. Patients are often given multiple pain medications, at variable doses, making self-management confusing and difficult.[9] Although most patients are reticent to take opioids, they are advised to "stay ahead of their pain"[20, 26] – a proactive approach that requires repeated coaching. Patients must also cope with opioid side effects such as constipation, nausea, and sedation.[12, 31] Constipation is notable because it is nearly universal and requires patients to become facile using and titrating various laxatives, usually with little guidance. When management strategies are ineffective, patients frequently avoid calling for help, not wanting to "bother" clinicians; therefore, problems are often not recognized or acted upon until routine clinic visits. These everyday challenges highlight the critical need for interventions to support patients, caregivers and providers in the outpatient management of cancer pain.

Systems enabling electronic symptom self-assessments are a promising strategy to alleviate cancer pain. Patient reported outcome (PRO) assessments of cancer symptoms have been demonstrated to improve symptom-related quality of life,[32-35] reduce hospitalization,[32] and possibly extend survival.[36] Prior interventions have coupled PRO's to self-management support,[33, 34, 37, 38] clinician alerts,[32, 35, 39] and occasionally to clinician

management recommendations.[15, 16, 40] Sadly the application of PRO's to cancer pain are underdeveloped[7] due to several critical barriers. First, cancer pain fluctuates greatly based on medication use, activity, and other factors. To convey useful data to clinicians, assessments must be much more nuanced than existing PRO's. Second, to enable helpful management recommendations, systems must accurately capture medications, assess and account for their effects. Lastly, new platforms are needed to harness these data to generate clinical decision support (CDS) for both patients and providers. We propose developing an mHealth application capable of assessing pain-specific PRO's and medication use, conveying this data to care teams, and offering tailored management advice to patients and clinicians around pain and opioid side effects. The STAMP application could be not only an effective tool for cancer pain, but a powerful platform for future symptom interventions.

3.0 Objectives*

Overall Research Goal: To leverage the study team's expertise in oncology, nursing, palliative care, clinical decision support, and informatics, to develop **STAMP** (**S**martphone **T**echnology to **A**lleviate **M**alignant **P**ain): a novel mHealth application to support cancer patients and providers in the management of chronic cancer pain with opioids. Grounded in Wagner's Chronic Care Model, STAMP will support patient self-management through education, PRO assessment and medication reminders; offer tailored decision-support to both patients and providers; and thereby promote productive interactions between patients and care teams. Specifically, the study aims of this project are to:

Aim 1: *Develop STAMP, a novel mHealth app to optimize management of chronic cancer pain with opioids.*

Focus groups and iterative usability testing will inform functionalities and user interfaces. The patient application will track symptoms, provide multimedia education, offer behavioral and medication advice for pain and common opioid side effects. Importing medications and key clinical data from the electronic health record will enable tailored self-management support for patients, and specific management recommendations for clinicians. Within the clinician portal of STAMP, a dashboard will present trended symptom data, opioid use, and specific recommendations for poorly controlled symptoms. Severe symptoms will prompt patients to contact their care team, and trigger clinical alerts. Summary reports (with trended symptom data, opioid-use data, and management recommendations) will be distributed to oncologists prior to clinic visits, facilitating productive interactions and timely medication adjustments.

Aim 2: *Conduct pilot testing of STAMP among patients initiating or titrating opioids for moderate to severe cancer pain, and their cancer care providers.*

STAMP will be piloted among 5 oncologists and 20 ambulatory advanced cancer patients who have recently initiated or titrated a short and long-acting opioid for

moderate to severe pain. Patients will use the app for an 8-week period, during which time their symptoms, opioid use, quality of life, use of and satisfaction with STAMP will be assessed via 1) app-based symptom self-assessments, 2) longitudinal surveys, and 3) semi-structured interviews. Chart abstraction will assess patient outreach resulting from STAMP alerts, management changes prompted by its clinician-directed management suggestions; and care utilization (e.g. ER visits or hospitalizations for pain). Results will be used to refine the intervention, and apply for R01 funding to conduct a randomized trial evaluating the impact of STAMP on severity of cancer pain, symptom related quality of life, distress, care satisfaction, and healthcare utilization.

4.0 Inclusion and Exclusion Criteria*

The eligibility criteria vary for each activity. See section 5.0 below for more details.

5.0 Protocol Activities

There are 5 protocol activities, each detailed in section 5.0.

- Activity 1 – Content development (interviews and working groups)
- Activity 2 – Programming and testing of app algorithms
- Activity 3 – User Acceptability Testing
- Activity 4 – Pilot Testing
- Activity 5 – Patient Qualitative Interviews

5.1 Activity 1 – Content development (working groups and interviews)

PLEASE NOTE: Activity 1 was originally approved as NHSR via protocol #17-375. As of 7/31/19, protocol #17-375 is now COMPLETE. All future content development activities will fall under activity 1 of this protocol.

Brief description of activity:
Since fall 2018, patient and clinician working groups have assisted the project team in content development for the application, including development of educational materials and survey elements that will be included in the ultimate STAMP application. This work has been determined NHSR via protocol #17-375. Beginning with the protocol amendment, version 4, July 31, 2019, Activity 1 will be amended to be human subjects research, but exempt from full-board review. Upon receipt of IRB approval, the study team will be consenting and enrolling participants for interviews and focus groups to help refine previously developed content.

Activity 1 participants will take part in focus groups or individual qualitative interviews with the study team. Focus groups and qualitative interviews involving patients and providers will be conducted to help refine content previously developed for the STAMP app. Both focus groups and individual interviews will be set up to assist the study team in testing application study assessments and education. These focus groups and

interviews will ensure the content is understandable and meets the needs of our target users. The focus groups and interview participants will also review preliminary app wireframes and design concepts to ensure that iterations of the app are found useful to patients and clinicians.
A study team member will take hand-written notes during all interviews and focus groups to record feedback. The interviews will also be audio recorded to facilitate the team's ability to document participant feedback; however, all audio recordings will be destroyed after comparison to hand-written notes, and will not be electronically stored, or directly referenced during future manuscript development.
The "About STAMP/App Roadmap" document (Appendix U) describes a broad overview of the functionalities of the proposed STAMP application.

Participants will fall into one of four eligibility cohorts:

Cohort A = Patient Content Testing through semi-structured interviews

Cohort B = Patient Wireframe Testing through individual interviews or focus groups

Cohort C = Clinician Content Interviews/Focus Groups

Cohort D = Clinician Wireframe Testing through individual interviews or focus groups

Semi-structured interviews with participants in Cohort A will focus on the understandability and clarity of application content, using an interview guide (see Appendix L). Application content includes survey elements, educational materials about pain management and patient educational videos about pain management and opioids(Appendices P,Q, and V, respectively). These interviews will use standard cognitive interviewing techniques to make iterative revisions to survey elements that will ultimately be integrated into the STAMP application. Up to 20 participants will be consented (see Appendix JA) and enrolled into this cohort, or fewer, depending upon when the content is considered clear/acceptable to patients and no new major themes arise during interviews. After their interview is complete, participants will receive a $25 Amazon gift card.

Qualitative interviews with patient participants in Cohort B will involve presenting wireframes (Appendix R) of the application and receiving their feedback on the "look and feel" of the application and their ability to interpret and navigate the various screens, using an interview guide (see Appendix L). Participants will be asked to provide feedback on the usability and display but will not specifically be asked about content. The content in the wireframes will include previously vetted materials, seen in Appendices P and Q. Up to 20 participants will be consented (see Appendix JB) and enrolled in this cohort, or until thematic saturation has been achieved. After their interview is complete, participants will receive at $25 Amazon gift card.

Semi-structured interviews and focus groups with clinician participants in Cohort C will involve discussing content of the application and receiving feedback regarding the acceptability of that content. These interviews will focus on potential patient symptom reports within the application, and reviewing messages that patients may receive in response to those symptoms (e.g. to contact their care team for uncontrolled symptoms) to ensure that they are clear, appropriate, and meet current standards of clinical practice (Appendix S). The interviews and focus groups will be conducted using a guide (see Appendix M). Up to 20 total clinicians in this cohort will participate, either in individual interviews or in groups of 3-8 clinicians, until thematic saturation has been achieved. For this cohort, there will be a waiver of signed consent, and each participant will receive a study information letter (Appendix K).

Semi-structured interviews and focus groups with participants from Cohort D will involve presenting wireframes of the clinician portal of the application (Appendix T) and receiving feedback on its "look and feel" and their ability to interpret and navigate various screens. The content in the wireframes will include previously vetted materials, seen in Appendix S. The interviews and focus group will be conducted using a guide (see Appendix M). Up to 20 total clinicians in this cohort will participate, either in individual interviews or in groups of 3-8 clinicians, until thematic saturation has been achieved. For this cohort, there will be a waiver of signed consent, and each participant will receive a study information letter (Appendix K).
Human Subjects Research Category (NHSR, exempt, expedited, full review): All human subjects research described in activity 1 is considered **exempt**. Exempt status for human subjects research involving cohorts A & C is explained by 45 CFR 46.101(b)(2), which states that research involving the use of survey procedures (e.g. survey pretesting) is considered exempt as long as the research poses little risk to the participants and information is recorded in a manner that the subjects cannot be identified. Exempt status for cohorts B & D is justified based upon 45 CFR 46.101(b)(6), because it involves standard procedures used in consumer acceptance studies, namely wireframe testing to ensure that the application is laid out in a user-friendly manner. Similarly, these activities are negligible risk and data will be stored in hand-written/typed notes and will not include any identifying information. Audio recordings of focus groups and interviews will be used for note-taking purposes only, and will be destroyed after the interviews/comparison with note-taking, and will not be stored in study files. All other identifiable information will not be captured.

Informed Consent: Written consent will be obtained from all patient participants (Cohorts A and B)). Separate consents will be utilized for patient content testing and wireframe testing: Patient participants selected for content testing (Cohort A) will be consented using the patient content consent (Appendix JA). Participants who will be testing wireframes (Cohort B) will be consented using the wireframe consent (Appendix JB) A waiver of informed consent is being requested for all clinician participants (Cohorts C and D). Instead, these participants will be given a study letter (Appendix K).
Methods that will be used to identify potential subjects: All potential participants will be identified by the study PI or through direct referral from the study team investigators or other DF/HCC clinicians.

In addition, under a HIPAA waiver previously granted for this study, study staff will look in the electronic medical record and scheduling systems to identify potentially eligible patients who meet the eligibility criteria for Cohorts A and B. Study staff may also query Epic,

administrative/operations/billing databases, order entry databases, and/or cancer registry databases to identify potentially eligible participants.

Activity 1 Eligibility: Focus groups and interviews will include patients, oncologists, oncology nurses, advance practice nurses, palliative care practitioners, or pharmacists. All groups and interviews will be supported by a member of the study team (PI, Co-I, project manager and/or research assistant).

Cohort A & Cohort B (Patients**) Inclusion Criteria:**

- Age ≥ 21 years
- Patient diagnosed with a metastatic or locally advanced solid tumor malignancy
- Current or previous outpatient use of opioids for cancer pain
- Own a smartphone

Cohort A & Cohort B (Patients**) Exclusion Criteria:**

- Cognitive impairment
- Inability to speak English
- History of substance abuse

Cohort C & Cohort D (Clinicians**) Inclusion Criteria:**

Clinicians caring for outpatients with cancer (medical oncologists, oncology nurses, advance practice providers, palliative care practitioners, etc.) working at DF/HCC

Cohort C & Cohort D (Clinicians**) Exclusion Criteria:**

- Unwilling to participate

Number of subjects: Up to 20 patients in Cohort A will take part in cognitive content testing interviews, and up to 20 patients in Cohort B will take part in wireframe testing. Up to 20 clinicians in Cohort C will take part in interviews or focus groups, and up to 20 clinicians in Cohort D will take part in wireframe testing.

When, where, and how potential subjects will be recruited: For Cohorts A and B (Patients), the clinical/study staff will approach patients in-person during a clinic visit to see if they are interested in participating in either the content testing or the wireframe testing. If a patient is interested in participating, the site will have the participant sign consent (Appendices JA or JB) and set up a time for an interview. For Cohorts C and D (Clinicians), the study PI or his/her designee will send emails/call/discuss in-person to all potential working group and/or interview participants. If interested, the clinicians will be given a study letter (see Appendix K) explaining the expected participation, they will be given a brief demographic survey and the interview/focus group will be scheduled.

Materials that will be used to recruit subjects: None.

Duration of subject's participation in the study: All interviews or focus groups will be in-person or via phone participation and will take approximately 30-60 minutes.

Duration anticipated to enroll all study subjects: We anticipate that it will take six months to enroll all participants.

Study design: Qualitative interview/user acceptability testing.

Description of all research procedures being performed: Participants in Cohorts A and C will help test study assessments and educational content. During interviews, participants will also provide feedback on iterations of the developed mobile app (wireframes) in Cohorts B and D. To elaborate:

<u>Cohort A</u>
After signing consent (Appendix JA), all patient participants will take part in a one-on-one interview with the study team. The interviewer will show application content (Appendices P, Q and V) and follow the developed interview guide (see Appendix L). Interviews will take approximately 30-60 minutes and can be conducted in-person or over the phone. Upon completion of the interview, the study team will complete a limited structured chart abstraction (Appendix N) to collect basic non-identifiable clinical/demographic information, including the following:

- Gender
- Age
- Ethnicity
- Race
- Education
- Cancer type
- Opioid Use
- Treatment receiving
- Seeing Palliative Care

<u>Cohort B</u>
After signing consent (Appendix JB), all patient participants will take part in a one-on-one interview with the study team. The interviewer will show application wireframes (Appendix R) and follow the developed interview guide (see Appendix L). Interviews will take approximately 30-60 minutes and can be conducted in-person. Upon completion of the interview, the study team will complete a limited structured chart abstraction (Appendix N) to collect basic non-identifiable clinical/demographic information, including the following:

- Gender
- Age
- Ethnicity
- Race
- Education
- Cancer type
- Opioid Use
- Treatment receiving

- Seeing Palliative Care

Cohort C

After verbal consent and review of the study letter (see Appendix K), all clinician participants will take part in either a one-on-one interview or a focus group with the study team. The interviewer will show application content (Appendix S) and follow the developed interview guide (see Appendix M). Participants will also complete a brief demographic survey, collecting non-identifiable information only (e.g. age cohort, years in practice, clinical role) – see Appendix O. Interviews or focus groups will take approximately 30-60 minutes and can be conducted in-person or over the phone.

Cohort D

After verbal consent and review of the study letter (see Appendix K), all clinician participants will take part in either a one-on-one interview or a focus group with the study team. The interviewer will show application wireframes (Appendix T) and follow the developed interview guide (see Appendix M). Participants will also complete a brief demographic survey, collecting non-identifiable information only (e.g. age cohort, years in practice, clinical role) – see Appendix O. Interviews or focus groups will take approximately 30-60 minutes and can be conducted in-person or over the phone.

Monitor subjects for safety or minimize risks: The risk to participants is minimal with the primary risk being loss of confidentiality/privacy. To monitor the risk of loss of confidentiality/privacy, the study team will ensure that the STAMP 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.

What data will be collected and how:

- Interview data: Verbal feedback will be collected from all focus group and interview participants regarding their understanding and acceptability of survey elements, other app content, and app wireframes. A study team member will take hand-written and/or typed notes of all interviews/focus groups. Additionally, these interviews will be audio-recorded to supplement and confirm accuracy of hand-written notes. Audio recordings will be destroyed immediately after comparison to hand-written notes (within 5 business days of the actual interview), will not be stored on any physical or virtual file, and will not be directly referenced during future manuscript development.
- Demographic surveys: Cohorts C & D (clinicians) will complete a brief survey (Appendix O) assessing demographic and professional characteristics (e.g. clinical role, age cohort, years in practice), without any direct or indirect identifiers.
- Chart abstraction: for cohorts A & B (patients), the team will complete a limited structured chart abstraction (Appendix N) to collect basic non-identifiable clinical/demographic information (e.g. age cohort, diagnosis, etc.)

Long-term follow-up: Not applicable for this activity.

5.2 Activity 2 – Programming and Testing of App Algorithm

Brief description of activity: Using all of the feedback and content developing during activity 1,
the study team will work with an application developer to finalize content and build the STAMP app.

Human Subjects Research Category (NHSR, exempt, expedited, full review): Not Human Subjects Research.

Informed Consent: Not applicable.

Tasks that will be completed by the study team:

- Finalize the specifications for the STAMP app:
    - **Basic concept**: Patient-facing mobile phone app with clinician web-based portal to help advanced cancer patients and cancer care providers better co-manage chronic cancer pain with opioids. The patient facing mobile phone app will:
        - Support symptom management
            - Prompt patients to report symptoms using surveys that utilize branching logic
            - Offer symptom coaching and behavioral advice (for pain and opioid side effects) in response to mild to moderate symptoms
            - Alert patients to contact their clinicians in response to severe symptom reports
            - Track symptoms over time
        - Support medication use
            - Host patient's individual pain medication list
            - Host patients' laxative plan
            - Link medications to medication-specific education
            - Daily surveys will integrate patients' specific opioid medications into items assessing medication use and pain control
            - Provide education around symptom management
              Content library will host education covering the following
                - Written, video, illustrations, and audio-recorded formats
                - Self-managing pain
                - Proper use of opioid/non-opioid analgesics
                - Opioid side effects & opioid safety
                - Understanding opioid addiction versus tolerance and dependence
                - Constipation management
                - Behavioral strategies for managing pain (e.g. meditations, activity pacing, goal setting)

        - Basics of pain psychology
      - Education about specific medications will be linked to patients' "medicine cabinet" function
      - Educational content will be pushed to patients based on their daily symptom reporting. This includes advice to call care providers for any severe symptoms.
        -
    - The clinician facing portal is deigned to be monitored by a clinic nurse, and will include:
      - A dashboard which includes all patients assigned to that nurse
        - Severe symptoms are flagged using a color-coded system
        - Nurses can indicate need for contact and last point of contact, facilitating population management
      - Individual patient views
        - Will present patient's granular symptom data and symptom trends
        - have generative capacity for a summary report (pdf or printable) to be distributed prior to clinical encounters
- Finalize the algorithms that control what the STAMP does in response to user inputs.
- Finalize STAMP's patient-facing content.
- Finalize STAMP's clinician-facing content.
- Obtain necessary permissions or licensing agreements.
- Finalize STAMP training materials:
  - Patient-facing training materials (when and how to use STAMP).
  - Clinician-facing training materials (when and how to use STAMP).
- The final STAMP app will be HIPPA compliant and compliant with DFCI security and privacy standards
- During the app build, graphics designers will develop wire frames for the STAMP user interfaces. The study team will present these wire frames to the participants in the study work groups (outlined in Activity 1). Group participants will review the wireframes and provide feedback on their visual appeal, readability, ease of navigation, and usefulness. Results will be used to modify the wireframes, which will be re-tested if necessary, prior to programming the STAMP application.

Table 1. Here is a sample of what the proposed patient-facing app will look like:

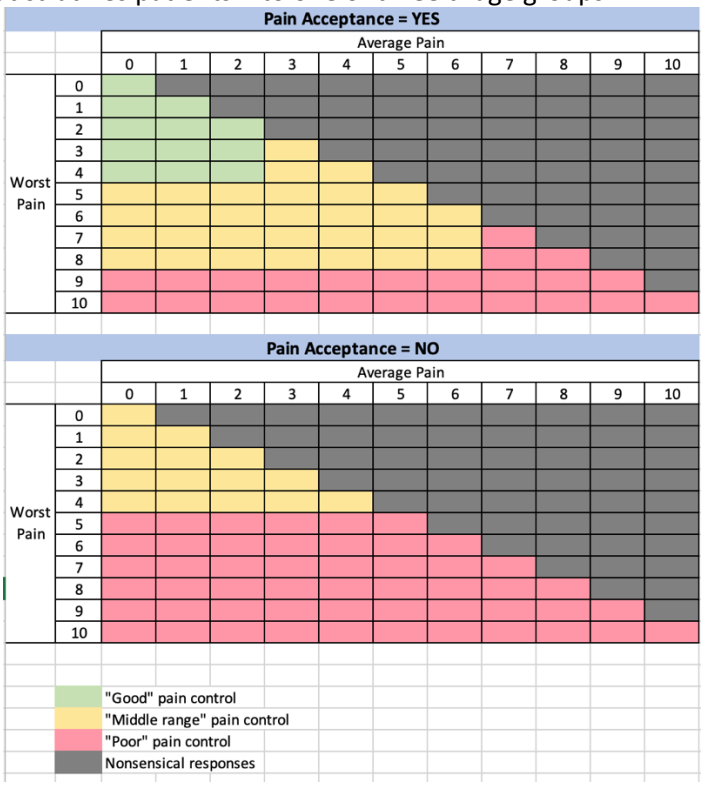
Example of the STAMP App Response Tools for Pain
SURVEY QUESTIONS *(for pain)*
1. In the last 24 hours, what was your pain at its **best**? 0 1 2 3 4 5 6 7 8 9 10
2. In the last 24 hours, what was your pain at its **worst**? 0 1 2 3 4 5 6 7 8 9 10
3. In the last 24 hours, what was your pain on **average**? 0 1 2 3 4 5 6 7 8 9 10

SURVEY DEPLOYMENT RULES & ADAPTATIONS

- Survey initial deployment timing: 1 day after study enrollment
- Frequency of surveys: 7 times per week

SYMPTOM CLASSIFICATION (threshold for action – will depend on the symptom and response)

Pain algorithm that stratifies patients into one of three triage groups:



SYMPTOM EDUCATION FOR PATIENTS (selected examples adapted from ACS)

Talk with your cancer team about your pain – where it is, when it began, how long it lasts, what it feels like, what makes it better, what makes it worse, and how it affects your life.
Take your pain medicine exactly as prescribed. Check with your cancer team if this schedule needs to be adjusted.
As the pain is relieved with medicines, **increase your activity level.**
Don't wait until the pain is severe before taking medicine for breakthrough pain.
Keep track of any other side effects that you notice. Discuss them with your cancer team.
Call your cancer team if: 1) you have new or worse pain, 2) you can't take anything by mouth, including the pain medicine, 3) you do not receive any pain relief, or 4) you become constipated, nauseated or confused.

Table 2. Summary of STAMP app functionalities that will be designed and built:

The main patient-facing tools will include the following (accessed via computer or app):
1. **Messaging** → Reminders about when surveys are available

2. **Alerts** → Notifications instructing patients to immediately contact their care team if severe or potentially dangerous symptoms are reported.
3. **Daily Symptom Reporting** → Surveys that will allow patients to report symptoms
4. **Visualizations** → Patients will be able to review their daily surveys, and trended symptom data
5. **Education** → Evidence-based symptom management tools, ranging in form (long-form texts, quick, bite-sized tips, videos, swipe-through texts)
6. **Activities** → Recorded relaxation exercises/meditations and quizzes
7. **Medication List** → House patient medications (opioids, laxatives, etc.)

The main clinician/staff-facing tools will include (accessed via computer or app):

1. **Alerts** → Systems to highlight severe symptoms within clinician portal
2. **Visualizations** → Display previously reported PROs for a given patient
3. **Reports** → Display patients who are enrolled in the program, view results across multiple patients, and identify patients who did not report PROs on schedule. Include a copy/paste report for use in medical records/email that draws from application data

5.3 Activity 3 – User Acceptability Testing and Focus Groups

Brief description of activity: Once the application has been built, the study team will conduct laboratory user acceptability testing and field user acceptability testing (UAT). UAT will be conducted through individual interviews with patients and oncology providers. This activity will allow the study team to test the preliminary application in both laboratory and "real life" environments, in order to solve any unforeseen programming and design challenges before conducting a pilot trial of the intervention.

Participants in Activity 3 will fall into one of three eligibility cohorts:

Table 3. Brief description of Activity 3 Cohorts

Cohort	Description	Components of Participation
Cohort A = Patient Laboratory UAT	Participants will include DFCI patients presenting to any solid-tumor clinic 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 anticipate conducting UAT with 5-6 patient participants, and no more than 12 participants. Each participant will receive a $25 gift card upon completion of the study activity.	• Participants observed while interacting with the mobile application • Semi-structured interview, using guide (Appendix WA) • Validated usability survey (Appendix ZA) • Medical Record Abstraction (Appendix XA)

Cohort B = Patient Field UAT	After completion of Cohort A, the study team will conduct Patient Field UAT. Participants will include patients with advanced gastrointestinal cancer who are using opioids for cancer pain and followed longitudinally within the DFCI gastrointestinal cancer center (GCC). 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 anticipate conducting UAT with up to 12 participants. Each participant will receive a $50 gift card upon completion of the study activity.
		• Onboarding visit with study team member
		• Participants will use app at home for up to one week on own mobile device
		  ○ Daily symptom assessments
		  ○ Review of educational resources
		• Post-use interview, using open-ended question guide (Appendix WB)
		• Validated usability survey (Appendix ZB).
		• Post-use medical record abstraction (Appendix XB)

Cohort C = Clinician UAT	Participants will include palliative and oncology physicians, mid-level providers, and nurses from across DFCI solid tumor programs. Concurrent to Cohort A testing, we will conduct UAT of the web-based clinician portal of the application with relevant clinicians. We will conduct clinician UAT with up to 10 clinicians.	• Clinicians observed while interacting with the clinician-facing web portal • Semi-structured interview, using guide (Appendix WC) • Demographics Survey (Appendix Y) • Validated usability survey (Appendix ZC).

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

Informed Consent: Waiver of documentation of consent. Before participating in user acceptability testing, participants in Cohorts A, B and C will be provided with a letter (Appendices VA, VB, VC , respectively) reviewing all elements of informed consent, as well as the option not to be observed. They will be notified that participation is completely voluntary and can be stopped at any time for any reason. If they want to participate, they will provide verbal consent after reviewing the study letter in detail with a member of the study team. These study letters include all elements of informed consent. These research activities involve no more than minimal risk to the subjects. Additionally, this activity does not involve any procedures for which written consent is normally required outside of the research context.

Methods that will be used to identify potential subjects:

Under a HIPAA waiver, study staff will look in the electronic medical record and scheduling systems 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.

Activity 3 Eligibility:

Table 4. Activity 3 Eligibility

	Inclusion Criteria	Exclusion Criteria
Cohort A: Patient Lab UAT	• Patients diagnosed with a metastatic or locally advanced solid tumor malignancy • Age ≥21 • Currently on short AND/OR long–acting opioids • Own a smartphone • Has chronic pain as the result of cancer or cancer treatment	• Cognitive impairment • Inability to speak English • History of opioid use disorder
Cohort B: Patient Field UAT	• Patients diagnosed with a metastatic or locally advanced solid tumor malignancy • Age ≥21 • Currently on short- AND/OR long–acting opioids • Own a smartphone with a data plan, and have access to Wifi • Patient receiving longitudinal care at the DFCI gastrointestinal cancer center (GCC) • Has chronic pain as the result of cancer or cancer treatment	• Cognitive impairment • Inability to speak English • History of opioid use disorder
Cohort C: Clinician Lab UAT	• Oncology physicians, mid-level providers, and nurses from across outpatient DFCI palliative care and solid tumor programs.	• Unwilling to participate

Number of subjects: Up to 32 participants will take part in Activity 3, including up to 12 participants in Cohort A, up to 12 participants in Cohort B, and up to 10 participants in Cohort C.

When, where, and how potential subjects will be recruited:

Cohorts A & B: Potentially eligible patients will be identified by 1) referrals from clinic staff, or 2) by screening the EMR for outpatient solid tumor disease center 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 clinical/study staff will approach patients in-person during a clinic visit to see if they are interested in participating. Alternatively, the study staff can send eligible patients an introduction to the study via mail/email and call them to offer participation (Appendices VA or VB).

Interested participants will then review the study letter with a research team member (Appendix VA or VB) and if interested provide verbal consent. Next, they will set up a time for the interview (Cohort A) or initial study visit (Cohort B).

Cohort C: Clinicians will be recruited through interactions with the study PI and/or email invitation from the study team. The study PI or his/her designee will send emails/call/discuss in-person to all potential interview participants. If interested, the clinicians will be given a study letter (Appendix VC) explaining the expected participation and the interview/focus group will be scheduled.

Materials that will be used to recruit subjects: See Appendices VA and VB for study letters for Cohorts A and B.

Duration of subject's participation in the study:

- **Cohort A:** Patient Laboratory UAT and qualitative debriefing interviews will take approximately 30-60 minutes, and will occur in person, over the phone, or via a compliant and secure video chat/screen-share platform (i.e. Zoom).
- **Cohort B:** Patient UAT Field study will include patients using the application at home for up to one week at home. The initial study visit will occur in-person or via phone or secure video chat/screen-share platform (i.e. Zoom) and will take about 30 minutes, in which the participant will download the app be oriented to the app. Use of the application over this week will involve completing daily symptom surveys on the app, which have been designed to take no more than 5 minutes, and to review tailored feedback/symptom education that the app provides in response to reported symptoms. Patients can spend as long as they want to review education content also provided on the app. It is expected that it will take patients 1 minute to review brief pearls and 5-15 minutes to review more in-depth content (optional). Upon completion of the field UAT, participants will complete an in-person or over the phone interview with the study team which will take approximately 30 minutes.
- **Cohort C:** Clinician Laboratory UAT will take approximately 30-60 minutes and will occur either in-person, over the phone, or via a compliant and secure video chat/screen-share platform (i.e. Zoom).

Duration anticipated to enroll all study subjects: We anticipate that it will take three to six months to enroll all UAT participants. Analysis will start after the first patient is enrolled and continue after completion of all activities as needed to revise the application.

Study design: Qualitative interviews/user acceptability testing

Description of all research procedures being performed:

Cohort A – Patient Lab UAT: After providing consent, participants will schedule a time to take part in the study interview. Next, the interview will be conducted with the internal study team in a private room in DFCI, or remotely via a HIPPA-compliant secure video-chat platform (i.e. Zoom). Participants will be provided a study phone with the application already downloaded onto it, or they will be provided a link to temporarily download the STAMP application onto their own phone (depending upon patient preference). Participants will be recorded while asked to "think aloud" for 30-60 minutes as they use STAMP. Think-aloud is the most common health technology UAT method, identifying >70% of usability problems within the first few interviews. [104,105] Verbal/non-verbal data will be transcribed and analyzed qualitatively to identify themes related to usability concerns and in response to open-ended questions about the app.

Participants will then be guided through a semi-structured interview about the usability and acceptability of the application and subsequently complete a validated usability survey (the e-acceptability scale) (Appendix ZA). Medical record abstraction will then be completed for each enrolled participant (Appendix XA).

Detailed qualitative analysis is not appropriate for this aim. Rather, the goal is to identify and address any problems with the proposed application. Iterative revisions will occur in response to these themes, after which we will enroll additional patients. UAT will continue until no new themes emerge and usability scores are $\geq$ 3 out of 5. We anticipate conducting UAT with 5-6 patient participants, and no more than 12 participants. Each participant will receive a $25 gift card upon completion of the study activity.

Cohort B – Patient Field UAT: After completion of testing with Cohort A and modifying the application in response, the study team will conduct field testing with up to 12 participants. Participants in Cohort B will be asked to use the STAMP app at home for up to a week (on their own mobile device), which involves completing daily symptom assessments within the app and reviewing educational resources within the app as desired.

During the first study visit (remote or in-person), patients will download the app on their personal device using a secure email or text link, with assistance from the research assistant (RA) as needed. The RA will then review the primary app features and familiarize the participant to symptom reports and app capabilities. The RA and study nurse will input the participant's opioid regimen, other pain medications, and laxative medications to the "medicine cabinet" feature of the app. All medications will be reviewed with the patient and reconciled by the study nurse to ensure their accuracy.

The participant will then be asked to use the app on their own smartphone through this "test" phase, for up to one week at home. Use during this week will include completing a daily symptom survey (estimated to take <5 minutes) on the app and reviewing educational content they receive within the app in response to their surveys. Of note, if

the patient reports any severe symptoms within their daily survey, the application advises them to contact their clinical team (see Table 5 for a list of severe symptoms).

Following participant's use of the app at home, we will conduct an interview with them to evaluate perceived app functionality, usability, and acceptability, and complete modifications to the application (Appendix ZB). Interviews will be recorded for note-taking purposes. Each participant will receive a $50 gift card upon completion of the study activity.

A study research nurse from the Gastrointestinal Cancer Center (GCC) will monitor cohort B's app-reported symptoms within a web-based portal on a daily basis. The portal includes a color-coded system to highlight poorly controlled symptoms, allowing for more proactive outreach to patients. It also presents patients' symptom and medication-use data, facilitating triage calls and changes in management. This nurse who monitors the portal is part of the nurse navigators team for the GCC, and during usual care would be part of the team of people who contact patients for uncontrolled pain/symptoms and coordinate management decision. The nurse will follow usual clinical judgement regarding patient outreach and management changes and will notify participants' care team (i.e. physician or mid-level provider) if they think that further medical work-up or medication changes are required based upon reported symptoms.

A structured medical record abstraction will be completed for each enrolled participant at the end of the study period to assess any clinical interactions (i.e. phone calls, clinic visits), healthcare utilization (i.e. ER visit or hospitalization for pain), or changes in pain/symptom management over the one-week study period and the week after (Appendix XB).

Cohort C: Clinician Lab UAT: Concurrent to Cohort A testing, we will conduct UAT of the web-based clinician portal of the application with relevant clinicians. With similar methodology to Lab UAT for Cohort A, up to 10 clinicians will "think aloud" while reviewing the clinician interfaces of STAMP (pre-populated with a set of test cases, not real patient data). Clinicians will be directly observed by the study team using a secure video-based screen-sharing platform (i.e. Zoom), or in person. Sessions will be recorded to assist with note taking. Following "think aloud" testing, clinicians will undergo a brief semi-structured debriefing interview and complete a validated usability survey (modified acceptability e-scale) (Appendix ZC). Clinicians will also complete a demographics survey (Appendix Y).

Findings will inform iterative revisions with repeat testing as needed. If common barriers are observed, the tool will be modified and repeat field UAT will be conducted until STAMP is found to be usable to most patients and providers.

Monitor subjects for safety or minimize risks:
The risks to participants in cohorts A, B, and C are minimal. The primary risk is loss of confidentiality/privacy. To monitor the risk of loss of confidentiality/privacy, the study team will ensure that the STAMP 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. As described above, UAT interviews will be recorded for the purpose of note-taking only, and will be destroyed as soon analysis concludes.

First, it is important to note that patient symptoms are imported into the clinician portal and severe symptoms are highlighted in red. This portal will be monitored once or twice per day by the study nurse. Therefore, patient symptoms will be reviewed more often by there are team than with standard care practice and we anticipate they will receive earlier outreach for potentially worrisome symptoms.

An additional theoretical risk for participants in Cohort B is that patients may feel reassured that their symptoms are being monitored and be less likely to call their care team. We have sought to mitigate this possibility in multiple ways. First, the application has clear disclaimers that the portal is not monitored continuously, and that it should not substitute calling care teams for worrisome symptoms. Secondly, when patients report potentially serious symptoms, they are specifically instructed to notify their care team by calling or paging after hours (the clinic number is included in the application). See below for the list of symptoms that prompts phone contact:

Table 5. 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
Constipation	• No bowel movement in four days • Haven't passed gas from bottom or ostomy • New or severe abdominal pain • Vomiting two or more times

Severe symptom notification:

> *"Your care team needs to know about your symptoms. Take a break from the survey and call them [link to clinic number]. If it's after hours, ask to have your doctor paged."*

Additionally, for less severe symptoms, patients are encouraged to call their care teams if they are worried about their symptom or if it is worsening. If patients report pain that is in a moderate range of severity, or if they report that it is unacceptable to them, they are presented with the following message:

> *"Below, you'll find some tips to help. Remember, your providers care about your pain. If this level of pain is not acceptable to you, or if you are worried about it, they want to hear from you. You can call them at [insert clinic number]."*

Finally, the patient-facing application contains clear disclaimers on each survey that the portal is not continuously monitored, using the following language:

> *"My Pain Pal is not constantly monitored. It is not monitored at all outside of regular business hours. For urgent problems, contact your care team by phone (link to clinic number) or call 911."*

An additional risk for Cohort B is running out of data on their smartphone's data plan; it is possible that using the study app could lead to extra charges from the smartphone carrier. For this reason, we recommend that participants are connected to Wifi while using the application. To mitigate this risk, eligibility criteria for this cohort outline that participants must have a smartphone data plan and access to Wifi.

What data will be collected and how:

- Symptom Reporting. Participant responses to the symptom reporting questions within STAMP will be collected for research purposes for Cohort A, and for both use in clinical care and for research purposes for Cohorts B. Cohort C data will only include hypothetical patient data related to clinical care.
- Interview Data (Cohorts A and B). Audio and video feedback will be collected from all interview participants regarding their understanding and acceptability of the mobile application.
- Interview Data (Cohort C). Verbal feedback will be collected from all interview participants in Cohort C. Clinicians will be asked to evaluate whether patients' needs are accurate, clear, and clinically appropriate when presented in the portal. Additionally, participant responses to usability and acceptability will also be collected.
- E-Acceptability (Survey) Data: Participants in all Cohorts (A, B, and C) will complete an acceptability survey (see Appendices ZA, ZB, and ZC, respectively)
- Demographics Survey: Clinicians in Cohort C will complete a non-identifiable demographics survey (Appendix Y).
- Chart Abstraction: Baseline demographic and clinical data will be collected from all patient participants (Cohorts A and B) via chart abstraction. Additionally, for cohort B an end-of-study abstraction will evaluate any clinical interactions or management changes related to pain management that might have been influenced by the application (see Appendices XA and XB).

  App Usage Data: Data on STAMP app usage by all user types will be collected.

Long-term follow-up: Not applicable for UAT.

5.4 Activity 4 – Pilot Testing

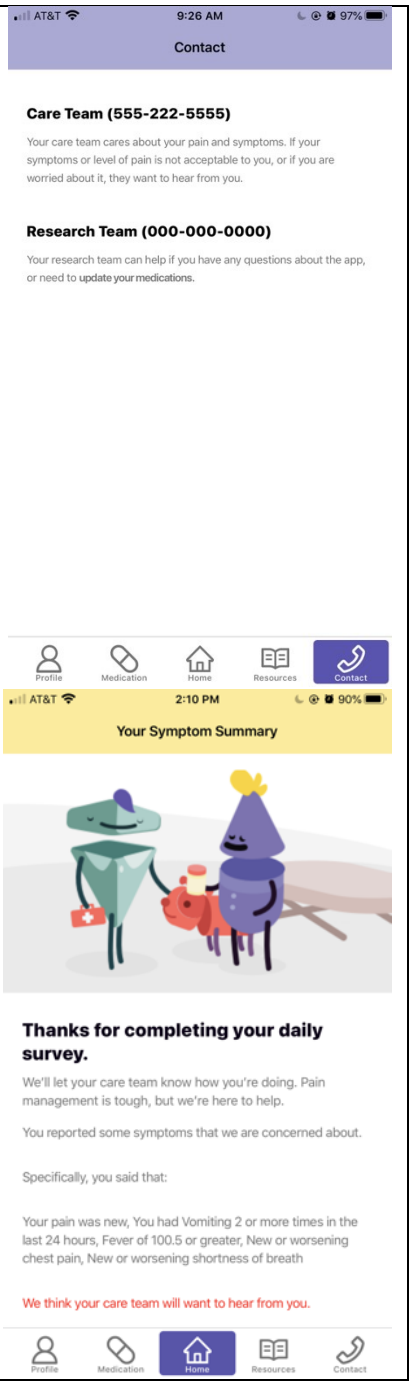
NOTE: A subsequent amendment will be submitted to conduct Activity 4

Pilot testing

Brief description of activity: A pilot study will be conducted at DFCI to demonstrate the utilization and efficacy of the STAMP app among patients with chronic cancer pain and their cancer care providers. This will be a single arm study with up to 20 patients. Patients with advanced solid tumors who are using opioids to manage chronic cancer pain will be recruited from outpatient clinics (GCC, palliative care), and they will be asked to use the app for 4 weeks. Once a patient is enrolled in the study, a research assistant (RA) will set up the app, putting in the patient's prescribed opioids and laxatives. Patient will have access to educational materials about pain management and patient educational videos about pain management and opioids (See Appendices P, Q, and V, respectively, approved 01/13/2020 - reference #321742) through the app. Patient will be prompted to take daily surveys for symptom reporting and medication updates. At the end of each survey patients receive, a summary of their symptom severity, with links to tailored educational content about pain management, and recommendations about how to safely titrate over-the-counter laxatives to manage opioid-induced constipation. This laxative advice operates within the parameters of normative and approved over-the-counter laxative use, and has been extensively reviewed, vetted, and approved by multi-disciplinary groups of clinicians. 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 6). 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. Finally, if they report any concerning abdominal symptoms (e.g. no bowel movement in 4 or more days, haven't passed gas from bottom or ostomy, new or severe abdominal pain, vomiting two or more times in the past 24 hours), patients are not given any laxative titration instructions and are instead advised to contact their care team for more advice. See Table 6 for detailed information on what symptom-reports prompt patients to contact their care team immediately and to view the message as presented in the app.

Table 6: "Red-Flag" symptoms that prompt a "call your care team" message when reported in the app

Pain	• Worst pain = 9-10 • Worst pain = 7-10 and new pain	
Severe 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	
Constipation	• No bowel movement in four days • Haven't passed gas from bottom or ostomy • New or severe abdominal pain • Vomiting two or more times	

The research team will monitor the portal where patient survey responses are presented. If a severe symptom is reported, the research team will contact the relevant nursing staff for clinical follow-up (as per the above paragraph, patients are always advised to contact their care teams for safety concerns, and there is no expectation for immediate nurse outreach). Nurses and physicians involved in the care of participating patients will also have access to patient-responses on the clinician portal. Patients will complete measures for their pain management, mood and barriers to pain management at baseline and at the

end of-study (see appendices AE and AI, respectively). An end-of-study semi-structured interview will assess adherence to STAMP's self-management recommendations, perceived usefulness of STAMP and its impact on care team interactions (see appendix AG for interview guide).

There will be a maximum of three attempts to contact the patient. During each attempt, the patient will be called, and if there is no response, a voicemail will be left [See Appendix AL for phone call and voicemail scripts]. Patients will be considered opted-out of the study if they do not respond to the maximum of 3 attempted contacts, or if they indicate that they would like to opt-out of the study during the call or their reply to the voicemail.

Nurse navigators, physicians and mid-level providers involved in the care of participating patients will also be offered participation in the study. Once they agree to participate, clinicians will be led by the research staff through an orientation to the clinician portal in which they will be able to monitor as part of their routine and usual care for their patients [See Appendix AD]. Clinicians will also complete a brief survey and semi-structured interview at end-of-study assessing satisfaction with STAMP and suggested enhancements (see appendices AK and AJ respectively).

Table 7: Report on Clinician Dashboard Based on Patient Responses

Relief with opioids	No relief OK Unsure Good relief
Pain Control	Poor Suboptimal Good
Last BM	Today Yesterday 2 days ago 3 days ago 4 or more days ago
Other Severe Symptoms	Number of severe symptoms on Table 6 shown in red
Opioids need updating	Yes No

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

Informed Consent: Written consent will be obtained from all patient participants (Appendix AH). A waiver of informed consent is being requested for all clinician participants. Remote consenting will be permitted if a patient cannot be approached at an upcoming clinic visit. We will contact treating physician via email or phone/zoom to request permission to approach the patients. If their physician approves, we will ask them to introduce the study to the patient at a regularly scheduled visit and ask permission of the patient for the research team to contact them to further explain the study and offer participation.

When a treating clinician gives permission to approach their patient for participation, the study team will call the patient to explain the study and offer participation. We will also send the patient a study letter via mail or via email (depending on the patient's preference), but we will not wait for receipt of the letter to approach the patient. If the patient returns an opt out card, they will not be contacted.

If a patient is being contacted by phone, the patient will be asked to confirm their identity and verify their personal information (i.e. date of birth, address). Consent forms will be sent by mail or electronically through a secure and personalized link in the FDA and HSSH compliant Mass General Brigham/Partners REDCap database. During the consent discussion, 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.

Methods that will be used to identify potential subjects:

Under a HIPAA waiver, study staff will look in the electronic medical record and scheduling systems 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. Clinicians will be identified through direct referral from the study PI.

Table 8. Activity 4 Eligibility

	Inclusion Criteria	Exclusion Criteria
(Cohort A): Patient Eligibility	• Patient is cared for within participating clinic (PC and GCC) • Age ≥21 • Diagnosed with locally advanced, metastatic solid tumor, or multiple myeloma being managed with palliative intent • Chronic pain related to cancer or cancer treatment, persisting or at least two weeks • Average pain rating of ≥4/10 currently, or at least one day within the past week • Active prescription for short and/or long acting opioids	• Cognitive impairment that would interfere with study participation, as judged by treating clinician • Inability to speak English • History of opioid use disorders • Enrolled in hospice • Currently hospitalized • Use of opioids not supported by STAMP (e.g. transmucosal fentanyl, tapentadol, opioid/acetaminophen combinations, oxymorphone, buprenophine, leorphanol) • Pain primarily related to a recent surgery

	• Takes at least 1 opioid medication on most days
	• Own a compatible smartphone
	  • iPhone, have updated or willing to update it to the past 3 iOS version releases: iOS 12, iOS13, iOS 14).
	  • Android flagship devices with more than 5% market share, last 2 android version releases: Android 9 Pie and Android 10)
		• Currently has or has had recurrent bowel obstructions
		• The following special populations <u>are</u> excluded: adults unable to consent, prisoners, and pregnant women.

(Cohorts B and C): Clinician Eligibility	• Physicians and mid-level providers practicing in participating clinics and caring for a patient on the study • Nurse Navigators working within participating clinics	• Unwilling to participate

Number of subjects:

Cohort A: Up to 20 patients (the number of participants will depend on usability issues at 4 weeks) will be enrolled in the single-arm pilot study.

Cohort B: Up to 20 nurse navigators involved in the opioid management of patients in Cohort A.

Cohort C: Up to 20 physicians and mid-level providers responsible for opioid management of patients in Cohort A.

<u>When, where, and how potential subjects will be recruited:</u>

<u>Cohort A</u>: Potentially eligible patients will be identified by 1) referrals from clinic staff, and 2) by screening participating physician and mid-level providers' clinic schedules. After getting the treating clinicians' permission, the patient will be approached for participation. 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 with a research team member (Appendix AA) and if interested sign consent. Next, they will set up a time for onboarding to the application.

- Remote approach: A research assistant may join the patients' virtual visit to explain the study and offer participation. If it is not possible for the RA to join the virtual visit, the clinician can introduce the study and the RA will follow up by phone to explain the study and offer participation. Alternatively, the study staff will send eligible patients a study letter with an opt-out card via mail (Appendix AA). Unless the patient returns an opt-out card within 10 days, the RA will contact the patient by phone or email to explain the study and offer participation.

Consent forms to the patients will be sent either by mail or electronically through a secure and personalized link in the FDA and HSSH compliant Mass General Brigham/Partners REDCap database. During the consent discussion, study staff will emphasize that the study is voluntary, patients may withdraw from the study at any time, and that withdrawal of consent will not affect their medical treatment in any way. Consent discussions can be completed via phone or Zoom. A $20 incentive will be provided after signing consent and another $30 will be provided completing the baseline survey, totaling $50.

Cohorts B and C: Physicians, mid-level providers and nurses will be approached by the study team via email, phone or in-person. The study will be introduced to clinicians during scheduled departmental meetings. Any clinicians who are not able to attend these meetings will be individually introduced to the study. A study letter will be sent to via email, and a waiver for written documentation of informed consent will be requested for these cohorts (See appendix AB for clinician study letter)

Materials that will be used to recruit subjects: See Appendices AA and AB for study letters for Cohort A; and Cohorts B and C.

Duration of subject's participation in the study: Patients will be enrolled in the trial for 8 weeks: Using the application for 4 weeks and completing an end of study survey between 4 to 8 weeks.

Duration anticipated to enroll all study subjects: We anticipate that it will take three to six months to enroll all pilot study participants.

Study design: Single arm pilot study

Description of all research procedures being performed:

Baseline survey (Cohort A)

RA will ask the patient to complete a survey after signing consent [0-2 weeks], and at the end of study [4-8 weeks from intervention]. 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,[13] pain severity,[51] opioid use,[19] symptoms,[62] and quality of life,[63] with metrics shown in Table 9. Surveys will assess symptom

trajectory, medication use, and quality of life. End of study survey will largely replicate the baseline survey, additionally, patients will rate their satisfaction with STAMP using the 6-item Acceptability E-scale.[57] See Appendix AE for the Baseline survey items and Appendix AI for end-of-study survey items. Additionally, patients will invited for a qualitative interview to ask a few open-ended questions about their experience to guide future refinements to the app (see Appendix AG).

Intervention

Cohort A: All patients on Cohort A will use the STAMP mobile phone App for 4 weeks. See below for a description of the intervention.

Intervention (Cohort A): After the patient completes the baseline survey, the RA will meet with the patient (in person or virtually), to assist in downloading the application onto participants' mobile device, register the patient to the app and help set up any preferences. The RA will then conduct a 15-minute tutorial on the STAMP app and its intended use [Appendix AC]. The RA will also input the patient's pain medications and laxatives from Epic, reconciling this list with the patient, and with the patient's nurse navigator if there are any discrepancies. During the trial, there is also a function in the app that allows participants to notify the research team if a medication needs to be changes and reflected in the app.

Participants will *utilize STAMP for 4-weeks*. As reviewed in section 5.2 (Activity 2), STAMP hosts and organizes patients' opioid/non-opioid analgesics and laxatives. It has an extensive multi-media library of education content related to pain management (approved 01/13/2020 (reference #321742)). STAMP prompts patients to take daily surveys for symptom reporting and medication updates. At the end of each survey patients receive, a summary of their symptom severity, with links to tailored educational content about pain management, and recommendations about how to safely titrate over-the-counter laxatives to manage opioid-induced constipation. This laxative advice operates within the parameters of normative and approved over-the-counter laxative use, and has been extensively reviewed, vetted, and approved by multi-disciplinary groups of clinicians. 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 6. 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. Finally, if they report any concerning abdominal symptoms (e.g. no bowel movement in four days, haven't passed gas from bottom or ostomy, new or severe abdominal pain or vomiting two or more times), patients are not given any laxative titration instructions and are instead advised to contact their care team for more advice.

Two protocol-mandated clinician outreaches to patients will occur within a week of enrollment: 1) an RA will call to assess any technical or usability problems with the app, and 2) the nurse will review PRO's in the STAMP portal and call patients to discuss

symptoms, self-management challenges, assist patients in problem-solving, and offer medical advice. Thereafter, the RA will monitor the STAMP dashboard twice daily (Mon-Fri), and contact the patients' nurse for any symptom that is flagged as "Red" in the portal. To assist in population management, a *tiered system of color-coded flags (Red, yellow and green)* in the portal will indicate symptom severity, need for outreach and/or management changes (See Table 7). Of note, the system always prompts the patients to contact their care team for any severe symptoms and there is no expectation for proactive clinician outreach. These procedures have been approved by participating clinic nurses. Of note, nurses will also have access to this STAMP dashboard and be able to review patients' primary symptom reporting data through a personal log-in and secure password.

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. Patients are reminded frequently throughout the application that the clinician portal is not monitored around the clock and therefore they should reach out for urgent needs. Symptom data are visible within the clinician portal. *Reports*, (with graphical symptom overviews, opioid use data, side effects) will be sent to oncologists ahead of scheduled clinic visits to enable effective communication, opioid titration, and other management changes.

At the end of the 4-week period, patients will be asked to complete an end of study survey [4-8 weeks]. Patients will also be invited to complete a short semi-structured interview about their experiences using the application (See Appendix AG). See below for description of the surveys.

Clinicians' involvement in the study (Cohorts B and C): Participating nurse navigators will also undergo a 30-minute tutorial in which they get oriented to the clinician portal and how to find the information about the patients (appendix AD). The RA and study nurse will undergo more extensive trainings in use of the app and study procedures, led by the primary research team. The nurse navigators will be expected to reach out to their patients enrolled in the study within a week of enrolment after reviewing the PRO's in the STAMP portal. During this call, they will discuss symptoms and self-management challenges. They may also assist patients with problem solving and offer medical advice. After the initial check-in, the nurse navigators will be asked to monitor the portal daily (Mon-Fri) and contact their patients as necessary. The RA will also be monitoring the portal and reaching out the Nurse Navigators as necessary. Nurse navigators will be asked to fill out a usability survey at the end of their involvement. Physicians will receive reports from the app prior to seeing their patients who are enrolled in the study, and they be asked for feedback after their patients completing the study. Clinicians will be asked to fill out a survey and will be invited for a 30-minute interview at the end-of-study over the phone or via Zoom. 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.

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 AF). Chart abstraction will assess clinical actions responding to STAMP data, clinicians' adherence to STAMP CDS recommendations (methods previously described);[16] and healthcare utilization (e.g. hospitalization, ER visits, urgent clinic visits for symptom management.) Information collected will including 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, and history and date of surgery related to cancer, patient 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 Laxative Medications**: Patient's prescribed laxative medications.
- **Medication side effects**: Constipation or related symptoms.
- **Clinic visits**: Unplanned or urgent clinic visits 6 months prior, during and 6 months post-intervention
- **Mental Health Diagnoses**: Whether the patient has a mental health diagnosis and what mental health diagnosis the patient has.

Monitor subjects for safety or minimize risks:

Risks to Subjects

- 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 laxative titration advice that is either ineffective at relieving constipation, or results in side effective such as diarrhea or abdominal pain.
- Psychological risks: Reporting pain daily may be distressing for some patients.
- 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.

Protection Against Risks

Recruitment and Informed Consent

Participants will be sent a study letter and given the option to opt out of the study. If they do not opt out, participants will be approached in by the RA in a private and confidential manner. If the patient is eligible and interested in participation, the study letter and consent form will be reviewed with and signed by the participant. The RA will keep all

signed documents in a password protected folder or locked cabinet, accessible only to the PI-designated study team member.

In the case of remote approach, Consent forms will be sent by mail or electronically through a secure and personalized link in the FDA and HSSH compliant Mass General Brigham/Partners REDCap database. During the consent discussion, 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 informed 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?

Protection against the 3 types of risk to this study:

- 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/or nurse navigators, 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.
    - 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 6 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.
    - Regarding constipation advice, our team developed algorithms that replicate typical advice given by care teams. These algorithms were generated from a rigorous development process guided by a multidisciplinary expert panel [DFCI protocol #18-662]. Furthermore, the algorithms are built off of titrating over-the-counter laxatives within the parameters of acceptable doses on the package instructions. The app will also not provide any laxative advice if the patient reports severe abdominal symptoms including not passing gas in the last 48 hours, new or severe abdominal pain, no bowel movement in 4 or more days,

vomiting 2 or more times in the past 24 hours.

- 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.

Protection against privacy risks: To monitor the risk of loss of confidentiality/privacy, the study team has ensured that the STAMP 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.

To maximize data security, both REDCap and STAMP 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. Auto-logout setting will automatically log a user out of the system if they have not had any activity (e.g. typing, moving the mouse) on their current web page for the set amount of time. This prevents someone else from accessing their account and their data if they leave a workstation without properly logging out or closing their browser window.

Logging and Audit Trail - Both systems maintain built-in audit trails that log all user activity and all pages viewed by every user.

What data will be collected and how:

- Study-related health information (including, demographics, cancer type, cancer stage, treatment plan, recent hospitalizations, prescription drugs) will be collected via medical record (and/or local cancer registry) review at baseline.
- Health service utilization (e.g. ED visits, hospitalizations, unplanned urgent clinic visits, changes to opioid medications) will be assessed by structured chart abstractions at end of study.
- Participant responses to the symptom reporting questions within STAMP will be collected for both use in clinical care and for research purposes.
- Data on STAMP usage by all user types will be collected.
- Patient survey at baseline and end of study
- Semi-structured patient interviews at end of study (Zoom or phone)
- Clinician survey at end of study

Measures collected via patient assessments	Survey	App data	Chart review

Assessment	Measure	T1	T2			
Socio-demographics	Standard	x				
Baseline cellphone use	MTUAS[66]	x				
Pain severity/interference	BPI[51]	x	x			
Opioid use/adherence[19]	Self-report	x	x			
Quality of life	FACT-G[63]	x	x			
Satisfaction	Novel metric		x			
Use of STAMP[57]	-			x		
Usability	SUS[68]		x			
Management changes	-					x
Healthcare utilization	-	x	x			x
Self-efficacy in managing symptoms	PROMIS[54]	x	x			
Self-efficacy in managing medications	PROMIS[54]	x	x			
Pain catastrophizing	PCS[67]	x	x			
Patient reported outcomes	PRO-CTCAE[53]	x	x			
Depression and Anxiety	PROMIS[54]	x	x			
Sleep Disturbance	PROMIS[54]	x	x			

Long-term study follow-up: Not applicable.

5.5 Activity 5 – Qualitative interviews with patients about pain management

NOTE: Amendment #3 covering Activity 5/ qualitative interviews was approved by the IRB in April 2019.

Brief description of activity: The study team will interview up to 30 patients (including DFCI inpatients and outpatients) about their experiences with a cancer diagnosis and chronic pain management. Interviews will be one-on-one, semi-structured, and conducted using the developed interview guide (see Appendix G). All interviews will be audio-recorded, transcribed, and coded for common themes. All patients for this activity will fall into one of two eligibility cohorts:

Cohort A = patients visiting DFCI for a regular appointment with ongoing chronic cancer pain management issues

OR

Cohort B = patients visiting DFCI via the outpatient care clinic or patients recently admitted to the DFCI inpatient clinic at BWH for an active pain crisis.

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

Informed Consent: Written consent will be obtained from all patient participants.

Methods that will be used to identify 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. 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.

Activity 5 Patient Inclusion Criteria:

- Patients diagnosed with a metastatic or locally advanced solid tumor malignancy
- English-speaking
- Age ≥21
- Patient visiting the DFCI outpatient clinic
  OR
  Patient admitted to the DFCI inpatient hospital
- Has chronic pain as the result of cancer
- Patients prescribed both a short-acting and long-acting opioid

Activity 5 Patient Exclusion Criteria:

- Long-standing history of chronic pain unrelated to cancer (i.e. arthritis) for which they were taking opioid pain medications before their cancer diagnosis
- Recent surgical procedure (less than 4 weeks prior) resulting in pain
- Inability to participate in a 60-90 minute interview, e.g. due to cognitive or physical limitations

Number of subjects: Up to 30 patients will take part in one-on-one interviews, OR interviews will be stopped once thematic saturation has been achieved.

When, where, and how potential subjects will be recruited: Potentially eligible patients will be identified by 1) referrals from clinic staff, and 2) by screening the EMR for outpatient solid tumor disease center clinic schedules, and 3) by screening the palliative care consult service inpatient lists. Once the study team identifies a potentially eligible patient, the team will reach out to the treating clinician for permission to approach for an interview. Patients will sign informed consent according to IRB procedures. A $25 incentive will be provided after study completion.

Materials that will be used to recruit subjects: NONE – if eligible, the study team will approach patients in-person to discuss.

Duration of subject's participation in the study: Patients will take part in a one-time, 1-hour interview with the study team. All interviews will be in-person or over the phone.

Duration anticipated to enroll all study subjects: We anticipate that the interviews will take 6 months to complete. Analysis will follow, thereafter.

Study design: Semi-structured, qualitative interview

Description of all research procedures being performed: After signing consent, all study patients will take part in a one-on-one interview with the study team. Prior to the interview, all patients will complete a one-time baseline survey (see Appendix I). The baseline survey involves demographic questions as well as validated pain measures. Patients can complete the survey via hard copy or online via REDCap. Once completing the baseline survey, patients will participate in the one-time interview. The interviewer will follow the developed interview guide (see appendix G). Interviews will take approximately one hour and can be conducted in-person or over the phone.

As the study team member asks the interviewee questions from the interview guide, s/he will audio-record their responses and take notes. The audiotape and paper onto which s/he records their responses will NOT contain an identifier of any kind (to elaborate, it will NOT contain the interviewee's name, MRN, SSN; only a study ID number). After conducting each interview, we will store the interview responses (paper and audiotape) in a locked drawer in our office (D-1011). Once the data has been entered into an electronic medium, the electronic files will be kept on a secure, password-protected server at Dana-Farber Cancer Institute. The audio-recordings will be transcribed verbatim, using a secure system. All audio-recordings and study materials will be kept for 5 years following study completion, at which time they will be destroyed.

Monitor subjects for safety or minimize risks: Not applicable.

What data will be collected and how: *(see appendix H)*

Basic demographic information (i.e. to explore gender or age stratification in qualitative results) will be collected from all participants via chart abstraction. Collected information will include:

- **Cancer**: Patient's date of diagnosis, diagnosis (cancer type), stage at diagnosis, status of active curative or palliative treatment, and history and date of surgery related to cancer
- **Pain**: Patient seen palliative care (yes/no), patient's last pain rating, type of pain, and location of pain.
- **Prescribed Pain Medicines**: Patient's prescribed short-acting opioid, long-acting opioid, and non-opioid pain medications, and length of time taking opioids.

Statistical Analysis: Because interviews produce qualitative results, statistical analyses will not be employed as part of this study. Qualitative thematic analysis will use a grounded theoretical approach in which two or more investigators will code transcripts and assign labels using an open coding approach. Investigators will name concepts and revise coding until consensus is reached. Analyses will be conducted using NVIVO analytic software, which the study PI will receive training in as part of this project.

ENDPOINT: The study team will use the qualitative results to help develop and modify a new pain mobile health app for cancer patients.

6.0 Study-Wide Number of Subjects*

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

Activity	Maximum # of participants
Activity 1	20 Cohort A patients 20 Cohort B patients 20 Cohort C clinicians 20 Cohort D clinicians
Activity 2	N/A
Activity 3	12 Cohort A patients 12 Cohort B patients 10 Cohort C clinicians
Activity 4	20 patients, 20 Nurse Navigators and 20 physicians and mid-level providers
Activity 5	30 patients
Total accrual	169 participants • 114 patients • 55 clinicians

7.0 Study-Wide Recruitment Methods*

Each activity utilizes slightly different recruitment methods. See section 5.0 for details.

8.0 Multi-Site Research*

Not applicable – this is NOT a multi-site research project.

9.0 Study Timelines*

The duration of an individual subject's participation in the study and the duration anticipated to enroll all study subjects varies by activity. See section 5.0 for details.

The first 5-6 quarters of the project will be dedicated to developing STAMP and conducting UAT. We anticipate enrolling 4-5 patients per week on our pilot, and should thus complete the study within 3-4 months. The study timeline may change due to unforeseen circumstances.

The estimated date for the investigators to complete this study (complete primary analyses) is August 31, 2021.

10.0 Study Endpoints*

Analysis of activity 1 (Focus groups and interviews):

Because interviews produce qualitative results, statistical analyses will not be employed as part of this study. The study team will review qualitative feedback from both patients and clinicians across the four cohorts and find common themes. The study team will use the common themes to guide development of the application.

Analysis of activities 2 (application build) – Not applicable.

Analysis of activity 3 (user acceptability testing):

Patients that take part in UAT will complete a validated usability survey[57] and respond to open-ended questions about the app.[58, 59] Verbal/non-verbal data will be transcribed and qualitatively analyzed to identify common themes related to usability problems and comprehension. Detailed qualitative analysis is not appropriate for this aim. Rather, the goal is to identify and address any problems with the tools. After responsive revisions, additional patients will participate in additional testing. UAT will occur until no new themes emerge, and the average usability score exceeds 4 (out of 5 on a 5-point Likert scale).

With identical methodology, providers that take part in UAT will "think aloud" using the clinician interfaces of STAMP, with iterative revisions and repeat testing as needed. The think-aloud method is the most common form of UAT for health technology, and has been shown to identify >70% of usability problems within the first few interviews. [60, 61]

Analysis of activity 4 (pilot testing): The primary outcomes for the pilot study relate to feasibility and acceptability.

- Feasibility: Descriptive statistics will characterize the proportion of eligible days on study that they complete a STAMP symptom survey, and the number of times patients log into the application. Other metrics of feasibility will include the study participation rate (proportion of eligible patients approached who consent to the study), completion rates of each study assessment, and the proportion of patients who consent and enroll on study who complete the study.
- Acceptability: summary statistics will characterize acceptability ratings (e.g. mean and standard deviation), using #7 from our modified acceptability scale as our primary acceptability measure ("how would you rate your overall satisfaction with My Pain Pal App?", with response options ranging from 1-5). Summary statistics will also assess acceptability on domains of ease of use, understandability, enjoyability, time required for use, learning, helpfulness, and likely to recommend to another patient.
- Usability: summary statistics will characterize usability from the system usability scale
- Exploratory outcomes: we will examine the number of symptom alerts generated by STAMP, the proportion of alerts that result in clinical action (e.g. phone calls or clinic visits), and medication changes.

Exploratory analyses will evaluate patient's symptom trajectories using a marginal model with GEEs, and mixed-effects models with patient as the random and time as the fixed effect.[64]

Analysis of activity 5 (qualitative patient interviews): Because interviews produce qualitative results, statistical analyses will not be employed as part of this study. Qualitative thematic analysis will use a grounded theoretical approach in which two or more investigators will code transcripts and assign labels using an open coding approach. Investigators will name concepts and revise coding until consensus is reached. Analyses will be conducted using NVIVO analytic software, which the study PI will receive training in as part of this project.

ENDPOINT: The study team will use the qualitative results to help develop a new pain mobile health app for cancer patients.

11.0 Procedures Involved*

The study design, study procedures and safety monitoring varies by activity. See section 5.0 for details.

12.0 Data and Specimen Banking*

This study does not involve any specimen collection/banking of any kind.
Personal health information will be collected as part of this study.

All data collected during this study will be stored and used for future research. Any personal identifiers will be removed so that the information cannot be linked back to a patient.

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. Requests must be sent to the study chair (Andrea Enzinger) and must be approved by the Dana-Farber IRB as well as the NIH prior to sharing.

The consent form informs the participant 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 information and data that is being used or shared for this research will be destroyed, because research is an ongoing process.

13.0 Data Management* and Confidentiality

DF/HCC uses a clinical trial management system (CTMS) called OnCore, which is managed by the Office of Data Quality (ODQ).

- Activity 1 involves focus groups and interviews and is considered exempt research. We will NOT be collecting identifiable information from these participants. Therefore, we will not be using OnCore for participant registration.

- Activity 2 is NHSR; registration in OnCore is not applicable.
- Activity 3 involves user acceptability testing through interviews and focus groups. Patient participants will sign consent and we will collect basic demographic information. Patient participants WILL be registered in OnCore. For clinician participants, we will collect age group, gender, race, and ethnicity. We will NOT collect each participant's initials and date of birth. We will enter summary/batch accrual information into Dana-Farber's CTMS OnCore for Activity 3. Individual registration is not feasible as OnCore mandates DOB.
- Activity 4 involves pilot testing. Patient participants will sign consent and we will collect basic demographic information. Patient participants WILL be registered in OnCore. For clinician participants, we will collect age group, gender, race, and ethnicity. We will NOT collect each participant's initials and date of birth. We will enter summary/batch accrual information into Dana-Farber's CTMS OnCore for Activity 3. Individual registration is not feasible as OnCore mandates DOB.
- Activity 5 involves qualitative patient interviews. Patient participants will sign consent and we will collect basic demographic information. Patient participants WILL be registered in OnCore.

Data security: PHI data will be collected using multiple applications: REDCap and the STAMP app.

REDCap: For this study, data 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.

STAMP App: The final application will be HIPPA compliant and compliant with DFCI security and privacy standards

<u>To maximize data security, both REDCap and the STAMP App will employ:</u>

<u>User Privileges.</u> 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.

<u>Password-protection & Authentication.</u> Both systems are password protected and implement authentication to validate the identity of end-users that log in to the system.

Auto-logout setting will automatically log a user out of the system if they have not had any activity (e.g. typing, moving the mouse) on their current web page for the set amount of time. This prevents someone else from accessing their account and their data if they leave a workstation without properly logging out or closing their browser window.

Logging and Audit Trail. Both systems maintain built-in audit trails that log all user activity and all pages viewed by every user.

Study specific procedure to maximize data security:

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

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.

Quality control: The staff at Dana-Farber will be responsible for monitoring the data for completion, accuracy, and compliance.

14.0 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 questionnaire-based assessments and symptom reporting and monitoring. As such, the only adverse event that will be monitored and reported is psychological distress as determined by the treating oncologist. For any patient who exhibits severe distress as result of the study procedures, the study research assistant will notify the patients' oncologist and 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 F) for more details.

15.0 Withdrawal of Subjects*

Subjects who do not complete the baseline assessment within 1 week of study enrollment will be withdrawn from the research study without their consent. These patients will be informed of their withdrawal from the study by study staff.

The overall DF/HCC study PI, Dr. Andrea Enzinger, will make all decisions regarding early termination of the study. The study team will then notify all participants accordingly.

16.0 Risks to Subjects*

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 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 the NIH's data security standards.

17.0 Potential Benefits to Subjects*

Using the STAMP app and taking part in this research study may or may not benefit participants. We hope that by using the STAMP app, patients are able 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, caregivers, and their care team work together during and between visits to achieve better symptom management in cancer patients.

18.0 Vulnerable Populations*

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.

19.0 Community-Based Participatory Research*

Not applicable to this study.

20.0 Sharing of Results with Subjects*

Participants will be directed to clinicaltrials.gov for research study results.

21.0 Setting

This is a pilot study that will take place at Dana-Farber.

22.0 Resources Available

This study team will be taking place under the Population Sciences Division at Dana-Farber. The Population Sciences Division 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.

Additionally, the research team is well-qualified to perform their duties. Dr. Enzinger has extensive experience in conducting research studies in cancer disparities, health services, and education. She has deep knowledge of the clinical and research environments and the patient population and culture at DFCI.

23.0 Prior Approvals

Not applicable for this study.

24.0 Recruitment Methods

The recruitment methods vary by activity. See section 5.0 for details.

25.0 Local Number of Subjects

This project will ONLY be taking place at Dana-Farber. Therefore, all study participants will be recruited on site.

Activity	Maximum # of participants
Activity 1	20 Cohort A patients 20 Cohort B patients 20 Cohort C clinicians 20 Cohort D clinicians
Activity 2	N/A
Activity 3	12 Cohort A patients 12 Cohort B patients 10 Cohort C clinicians
Activity 4	20 patients, 20 nurse navigators and 20 physicians and mi-level providers
Activity 5	30 patients

26.0 Provisions to Protect the Privacy Interests of Subjects

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 Dana-Farber's secure, password protected servers as 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 They will also complete all study assessments in private. 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.

27.0 Compensation for Research-Related Injury

Not applicable for this study.

28.0 Economic Burden to Subjects

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 and/or report their symptoms from home 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 will not be provided by the study.

In Activity 1 (Cohorts A & B), up to 40 participants will each receive a $25 Amazon gift card at the conclusion of their interview.

In Activity 3, Cohort A, up to 12 participants will each receive a $25 Amazon gift card and for Cohort B, up to 12 participants will each receive a $50 Amazon gift card after participating in all research activities.

The 20 pilot study participants (activity 4) will each receive a $50.00 gift card at the conclusion of the study.

In Activity 5, up to 30 participants will each receive a $25 Amazon gift card at the conclusion of their interview.

29.0 Consent Process

Each activity utilizes slightly different consent methods. See section 5.0 for details.

30.0 Process to Document Consent in Writing

Each activity utilizes slightly different consent methods. See section 5.0 for details. Patient participants involved with Activity 1 (Cohorts A and B), and Activity 4 will provide written consent. Participants in Activity 3 will be given a study letter, and provide verbal consent, as we are requesting a waiver of documentation of written informed consent for these participants.

31.0 Drugs or Devices

Not applicable for this study.

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33.0 Study Appendices

Appendix A: Working Group Recruitment Email
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Appendix AG: Activity 4 – Qualitative Interview Guide (Cohort A)

Appendix AH: Activity 4 – Informed consent form (Cohort A)
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