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January 5, 2026

Re: NCT03384134

To Whom it May Concern:

The following study protocol documents for NCT03384134 have been submitted in ClinicalTrials.gov:

1. Study protocol and statistical analysis plan – IRB 1344504_1921 – December 28, 2023
2. Informed consent documents

Sincerely,

A handwritten signature in black ink, appearing to read "M. Fortier", is written over a light gray rectangular background.

Michelle A. Fortier, PhD

Treating Pain in Children with Cancer: A 21st Century Innovative Approach (Pain Buddy)

CHOC Children's Hospital (Reviewing IRB, Participant Recruitment)

UC Irvine (CMU relying IRB, No Patient Recruitment)

St. Jude Research Hospital (Sub-Site-Participant Recruitment, Independent IRB)

PI: Michelle Fortier, PhD

Sponsor: National Cancer Institute (NIH)

October 21, 2021

Abstract:

Approximately 12,000 children are diagnosed with cancer in the United States each year and the majority of these children will experience moderate to severe pain and disabling symptoms such as fatigue and nausea during the course of their illness. The overwhelming majority of children undergoing treatment for acute lymphoblastic leukemia (ALL), the most common of childhood cancers, report pain throughout the first year of treatment following diagnosis, most frequently in the legs, abdomen, head/neck, and back. Pediatric cancer patients also report distress due to undesirable physical and psychological symptoms such as lack of energy, insomnia and worry. However, there are extremely limited controlled studies of children's cancer pain and data regarding the effectiveness of pain and symptom management strategies, particularly in the home setting. Recently there has been a national push toward involving health information technology, including electronic medical records, personal health records, and decision-support in order to minimize the gap between evidence and practice. There is preliminary empirical evidence that the use of computer-based decision-support positively impacts management of chronic pain and symptoms and can lead to significant improvements in clinical care, including use of appropriate treatment. Accordingly, through use of mobile technology a monitoring ambulatory protocol (electronic pain diary), called Pain Buddy, has been developed to quantify the prevalence and intensity of daily pain and symptom episodes in children with cancer as well as understand the contextual factors that impact the experience of children's cancer pain. Pain Buddy is a user interface (application) which contains a personalized avatar (Pain Buddy) to guide children and parents through daily diary entries using mobile devices. Study Aims: Primary Aim: Determine if Pain Buddy is more effective than an attention control in reducing pain severity among children ages 8-18 years old undergoing outpatient cancer treatment. *Secondary Aims:* Examine the impact of Pain Buddy on symptom-related distress, health-related quality of life, functional status, and satisfaction with treatment experience. Determine whether baseline characteristics of children (emotional functioning) and parents (stress, attitudes regarding analgesic use for children) moderate the effect of Pain Buddy on pain severity. To examine how parents and children report anxiety and depressive symptoms of children (RCADS sample). The purpose of this study is to examine the feasibility of the ambulatory monitoring protocol, called Pain Buddy, in documenting children's pain, symptoms and quality of life while receiving outpatient chemotherapy and effectiveness of Pain Buddy in reducing pain severity. The long term goal of Pain Buddy is to help doctors, nurses, and parents get the information they need to give children treatments for pain and symptom management that work. Using Pain Buddy, we aim to quantify the prevalence and intensity of daily pain and symptom episodes in children at home, data that will be used to develop a psychosocial intervention to be delivered electronically to children at home with a goal of improving quality of life. Secondary aims also include examining children's quality of life pre- and post- Pain Buddy and satisfaction with the use of Pain Buddy. This project has the potential to improve the quality of life of tens of thousands of children suffering from cancer each year using transformative mobile health information technology based approach to pain assessment and management. Phase 1 and 2 of the study are now complete. Phase 3 methods are described below.

Background & Significance:

Approximately 12,000 children are diagnosed with cancer in the United States each year and the majority of these children will experience moderate to severe pain and disabling symptoms such as fatigue and nausea during the course of their illness. The World Health Organization (WHO) guidelines for Cancer Pain Relief and Palliative Care in Children acknowledge the large proportion of cancer patients that experience pain and the “widespread inadequacy” of pain management efforts. The overwhelming majority of children undergoing treatment for acute lymphoblastic leukemia (ALL), the most common of childhood cancers, report pain throughout the first year of treatment following diagnosis, most frequently in the legs, abdomen, head/neck, and back.¹⁻² Children treated with chemotherapy often experience painful conditions, including mucositis, infection, and peripheral neuropathy due to the aggressive nature of treatment protocols.³ Pediatric cancer patients also report distress due to undesirable physical and psychological symptoms such as lack of energy, insomnia and worry⁴⁻⁵. However, there are extremely limited controlled studies of children’s cancer pain and data regarding the effectiveness of pain and symptom management strategies, particularly in the home setting.

Nonetheless, evidence suggests that cancer pain and symptoms are poorly controlled,⁶⁻⁹ with fewer than 30% of parents perceiving pain treatment as successful in end of life care of their child.¹⁰ Furthermore, lack of symptom alleviation leads to increased distress and poorer quality of life. Reasons for under treatment of pain and symptoms are complex and are related to deficits in the process of assessment and management of pain and symptoms in these children and lack of access to non-pharmacological interventions.^{4, 11} In fact, parents and children report that despite pain, fatigue and other symptoms being a common concern, assessments for these symptoms are not performed in a systematic manner.¹²⁻¹³ Specifically, barriers to adequate pain management may include misunderstanding about the use of analgesia in children (i.e., fears of addiction), lack of understanding of pain expression in children, misunderstanding of the effects of opioid medication in children, and lack of education of the benefit of non-pharmacological strategies for pain management.¹⁴ Thus, despite evidence that the “vast majority of patients with cancer pain can be made comfortable,”¹⁵ tens of thousands of children with cancer suffer significant pain that is not relieved by available interventions. This is compounded by the fact that increasing numbers of children currently receive chemotherapy on an outpatient basis due to advances in healthcare and changes in the medical-economical environment. This shift in care has now placed the burden of children’s pain and symptom management upon parents at home.

Unfortunately, despite the existence of symptom management guidelines, pediatric cancer pain and other symptoms that affect a child’s quality of life are currently poorly controlled. Part of this problem stems from difficulties translating guidelines to actual practice.^{16,17} Interventions targeting care of children in the home setting are seriously lacking, particularly psychosocial interventions. The American Pain Society (APS) guidelines for cancer pain¹⁸ include a need to recognize and treat pain promptly, involve patients in the pain management plan, continually assess and adjust the plan, and monitor processes and outcomes of pain management.⁶ However, traditional efforts to manage pediatric chronic conditions, such as increasing intensity of therapy and support from healthcare providers are difficult to incorporate into routine medical practice and not attractive to pediatric patients.¹⁹ Therefore, it is necessary to find innovative ways of engaging children and teens in their healthcare that are feasible to implement.

Recently there has been a national push toward involving health information technology, including electronic medical records, personal health records, and decision-support in order to minimize the gap between evidence and practice.^{17, 20-21} Indeed, there is preliminary empirical evidence that the use of computer-based decision-support positively impacts management of chronic pain and symptoms²² and can lead to significant improvements in clinical care, including use of appropriate treatment.²²⁻²⁵ For example, text messaging (TM) is a simple, efficient system and over half of teens in the U.S. have mobile phones and over a third report using TM²⁶ and these numbers are increasing. Text messaging is beginning to be used as a modality to engage teens in their healthcare and improve health outcomes.^{19, 27-29} In addition, TM programs are well-received by children.¹⁹ From a translational standpoint, TM technology is easily adopted, implemented, and maintained; requires little cost; and

reduces time required by staff to support pediatric healthcare management.¹⁹ Moreover, electronic means of assessment (e.g., personal digital assistants, Smartphones) have been shown to greatly increase adherence to monitoring health information data.³⁰

Because of the limited data on the experience of pain and symptom management in children with cancer, including how symptoms are assessed by parents, how often pain medication is given, what nonpharmacological strategies are used, and factors that impact parental pain and symptom management practices, there is a pressing need for research in this population. The lack of systematic assessments in children with cancer has hindered development and testing of new and innovative pain and symptom management interventions.

Accordingly, through use of mobile technology a monitoring ambulatory protocol (electronic pain diary), called Pain Buddy, has been developed to quantify the prevalence and intensity of daily pain and symptom episodes in children with cancer as well as understand the contextual factors that impact the experience of children's cancer pain. Pain Buddy is a user interface (application) which contains a personalized avatar (Pain Buddy) to guide children and parents through daily diary entries using mobile devices. The Pain Buddy application was developed in collaboration with the California Institute for Telecommunications and Information Technology (Calit2) at UCI and has been designed to be used with children age 8-18, receiving outpatient chemotherapy, as well as their parents. Pain Buddy will capture real time pain data from patients and that will ultimately allow for remote monitoring of patient symptoms. Remote symptom monitoring in real time will provide an opportunity for implementation of appropriate interventions, thereby introducing the potential to decrease pain and symptoms and improve quality of life in children with cancer. The use of symptom monitoring and skills training will further increase patient engagement in healthcare.

Related to the pain and symptoms experienced by children with cancer, there is also an increased likelihood that children will experience heightened activation of their innate immune response due to a number of factors including surgery, chemotherapy, and radiation, which are all associated with significant damage and destruction of tissue.⁴⁹ Gaps exist regarding inflammation in the pediatric oncology literature: Understanding prevalence during cancer treatment, characterizing its relationship with cancer pain and negative psychosocial symptoms, and determining whether it can be altered in children with cancer. Research on adult cancer survivors indicates that psychosocial interventions have the potential to affect long-term positive change in immune functioning, however no research to our knowledge has specifically measured the effect of psychosocial intervention on inflammation among children with cancer.⁵⁰ Furthermore, no research has been conducted in children with cancer to assess the efficacy of a mobile health (mHealth) symptom management intervention, such as Pain Buddy, in reducing inflammation. Thus, the non-invasive measurement of inflammatory biomarkers via saliva during the Pain Buddy intervention period may provide important information regarding immune health – and potential changes in immune functioning – in children undergoing cancer treatment.

Because children and teens really enjoy using electronic devices, like iPods, cell phones, and computers, Pain Buddy will be downloaded onto their personal handheld electronic device (cell phone, iPad, or tablet) That way, children can carry around Pain Buddy at all times to complete daily diary entries.

The long-term goals of this research are to develop a usable, engaging electronic decision-support pain and symptom management intervention for children receiving outpatient chemotherapy using Smartphone technology and to examine the efficacy of the electronic decision-support intervention on children's pain and quality of life. These long-term goals will be accomplished through assessment of the data collected from patients, parents and physicians using the ambulatory monitoring protocol.

Primary Aim:

- Determine if Pain Buddy is more effective than an attention control in reducing pain severity among children ages 8-18 years old undergoing outpatient cancer treatment.

Secondary Aims:

- Examine the impact of Pain Buddy on symptom-related distress, health-related quality of life, functional status, and satisfaction with treatment experience.

- Determine whether baseline characteristics of children (emotional functioning) and parents (stress, attitudes regarding analgesic use for children) moderate the effect of Pain Buddy on pain severity.
- To examine how parents and children report anxiety and depressive symptoms of children (RCADS sample).
To assess the types of medication that were used to manage pain and symptoms, specifically opioid usage.

Tertiary Aims:

- Use qualitative interviews to gain a rich description of previous Pain Buddy participants' experience using the application. with a particular focus on better understanding reasons for low and high pain diary adherence. (Focus Group)
- Assess high and low diary adherence among Hispanic/Latino participants and to investigate ways that Pain Buddy can be adapted and refined to be more culturally adapted. (Focus Group)
- Gather qualitative data from interviews with adolescents in order to develop and integrate a social support component to the Pain Buddy intervention.
- Assess concentrations of inflammatory biomarkers via saliva sampling among participants and their parents in the Pain Buddy intervention and attention-control groups. (NIH supplement project)
- Determine how inflammatory biomarkers are related to pain and patient- and parent-reported psychosocial outcomes (e.g., anxiety symptoms reported on the RCADS). (NIH supplement project)
- Examine whether the Pain Buddy intervention is related to observable changes in inflammation among children with cancer. (NIH supplement project)

Purpose:

The purpose of this study is to examine the feasibility of the ambulatory monitoring protocol, called Pain Buddy, in documenting children's pain, symptoms and quality of life while receiving outpatient chemotherapy and effectiveness of Pain Buddy in reducing pain severity. The long term goal of Pain Buddy is to help doctors, nurses, and parents get the information they need to give children treatments for pain and symptom management that work. Using Pain Buddy, we aim to quantify the prevalence and intensity of daily pain and symptom episodes in children at home, data that will be used to develop a psychosocial intervention to be delivered electronically to children at home with a goal of improving quality of life. Secondary aims also include examining children's quality of life pre- and post- Pain Buddy and satisfaction with the use of Pain Buddy. This project has the potential to improve the quality of life of tens of thousands of children suffering from cancer each year using transformative mobile health information technology based approach to pain assessment and management. Phase 1 and 2 of the study is now complete. Phase 3 methods are described below.

Methods:

Study Design: The first phase of this study was a prospective, observational cohort study, the second phase was a randomized control trial (RCT), and the current phase is a large-scale randomized control trial (RCT) to extend the research findings of phase 2.

Procedures: Following electronic informed consent and HIPAA authorization, participants will be randomized to the intervention or control group using a blocked randomization scheme stratified by age group. Patients will be randomized at a 1:1 ratio with equal numbers randomized to the intervention and control groups.

- **Control Group.** Children in this condition will continue with the care that has been prescribed for cancer- and chemotherapy-related pain and symptoms, which may include medications, medical visits, physical interventions, etc. Participants in this condition will complete daily pain diaries using Pain Buddy, but will not receive skills training or remote monitoring of data. However, patients who are part of the control group will still be able to call the Oncology clinic or physician on call to discuss any matters of pain or illness in a timely fashion. 25 participant-dyads in this condition will also be asked to collect saliva samples to assess inflammatory biomarkers.
- **Pain Buddy Group.** Children in this condition will continue with the care that has been prescribed for cancer- and chemotherapy-related pain and symptoms, which may include medications, medical visits, physical interventions, etc. Participants in this condition will complete daily diaries using Pain Buddy and will also be taught cognitive and behavioral coping skills, like deep breathing, imagery, and relaxation, to deal with pain and symptoms. The skills will be taught through the skills section of the Pain Buddy Program. Pain and symptom information, collected daily by Pain Buddy, will be sent to a health care provider on the oncology treatment team, who will contact patients when symptom thresholds (Memorial Symptom Assessment Scale (MSAS), see appendix 1) are triggered and will instruct the patients on best ways to control pain and symptoms. 25 participant dyads in this condition will also be asked to collect saliva samples to assess inflammatory biomarkers.

The Memorial Symptom Assessment Scale (MSAS) outlines the symptom thresholds for the diary entries, which are triggered by frequency, severity, and distress of symptoms being entered on the daily diaries, as well as the age of the child. An alert may not be sent the same day, but after a particular symptom is reported for a number of consecutive diary entries (see appendix 1). For example, a child may report “sweats,” five diary entries in a row, for which then an alert will be sent to the health care provider. The designated study health care provider will contact the parent and patient directly to discuss ways to manage their symptom and pain. All communication between the health care provider and patient will be documented on the patient’s electronic medical record and communicated to study staff via the secure message center accessible on Power Chart. Before starting every diary entry, there is a message that children in both groups (intervention and control) must acknowledge that informs them that this device is not designed to provide medical advice nor is it a substitute for a nurse or doctor. If participants are experiencing symptoms they would like to discuss, they need to call their doctor. If they are experiencing a medical emergency, they should dial 911. This warning message serves as reminder for participants in either group to reach out to a health care professional for immediate attention or advice rather than relying on the mobile application.

Children in both groups will be asked to complete measures at Baseline (T_1), at end of intervention period (T_2), and at 6 months follow-up (T_3) to assess anxiety and depression (RCADS), health related quality of life (PedsQL), beliefs about pain (PCS), functional impairment (CALI-21), abilities to perform activities while in pain (PSES), pain anxiety (CPASS), and their satisfaction with the intervention (TEI). 50 children and their parents in total (25 in each group) will additionally be asked to collect 9 saliva sample at T_1 , + 2 days, T_2 , + 2 days, and T_3 + 2 days. Following completion of the baseline packet, children will be instructed to complete the pain and symptom diary twice per day for 60 days. The daily diaries will include measures about coping (CSQ), pain (APPT), other symptoms that may have been bothersome or stressful (MSAS), since the last time they completed the diary and use of coping mechanisms (intervention questionnaire). Additionally, patients in the Pain Buddy group will also complete the cognitive/behavioral interventions and have contact with a health care provider, as needed. The daily pain and symptom diaries will take children approximately 5 minutes to complete each time for a total of 10 minutes per day or a total of 600 minutes for all 60 days. The T_1 , T_2 , and T_3 measures are expected to take children 30 minutes to complete for a total of 90 minutes. Each saliva sample is expected to take children and parents no longer than 1 minute to complete, for a total of 9 minutes.

Patients will be recruited in person, via phone or via conferencing call (ZOOM). Informed consent, HIPAA authorization, and parent and child measures (T_1 , T_2 , and T_3) will be completed electronically using REDCap. At the time of recruitment, a research team member will also verbally introduce the optional saliva sample collection portion of the Pain Buddy study. Patients are not required to complete the optional saliva sample collection in order to participate in the Pain Buddy study. Any questions regarding what is expected of patients and parents for the saliva sample collection will be answered by a research team member. A separate informed consent form for the saliva collection portion of the study, which contains additional details relevant to saliva sampling for both patients and their parents, will be completed electronically using REDCap. Saliva sampling can be completed in the hospital or at home by the patient and parent at $T_1 + 2$ days,, $T_2 + 2$ days,, and $T_3 + 2$ days, either independently or with the assistance of a Pain Buddy research team member. Daily diary input will be completed using the Pain Buddy application. Research Electronic Data Capture (REDCap) is a mature, secure web application for building and managing online surveys and databases and is widely used in university research. REDCap ensures the security and privacy of survey and account data stored in their systems through several tools including SSL encryption and meets privacy standards set by the Health Insurance Portability and Accountability Act (HIPAA). In accordance with HIPAA compliance, IP addresses will be masked from the survey author (see page 7 for details on e-consenting via REDCap). All information entered into the mobile device is immediately encrypted and will be rendered inaccessible or uninterpretable to anyone outside of project staff. This protects the information entered by study participants in the event of mobile device loss, but also protects participants from potentially prying siblings and friends. If a participant suspends their diary entry sometime in the sequence of item presentations, the electronic diary will time-out after 30 minutes, reset the screen and advance to the next scheduled assessment offering another privacy safeguard. All diary information recorded is identified by a unique subject ID code and no identifying information is collected as part of the mobile device.

At baseline, parents will complete measures about their child's symptoms and distress (MSAS), their own anxiety (STAI), parental stress (PSS), attitudes about medication administration (MAQ, PPEP), their child's anxiety and depressive symptoms (RCADS), their child's health related quality of life (PedsQL), their child's beliefs about pain(PCS), their child's functional impairment (CALI-21), the ability of their child to perform activities while in pain (PSES), their response to their children's pain(ARCS),their satisfaction with the intervention (TEI), their health beliefs (HBS), and an oral health log (for parent-child dyads collecting saliva) using REDCap or paper forms if they prefer.

At the time of recruitment (in person, phone or via ZOOM), both parents and children will be given instructions on how to complete Informed consent, HIPAA authorization and measures via REDCap, as well as how to use Pain Buddy. Data will be downloaded periodically to a .csv (Comma Separated Values) file and stored on a secure network in the research office. Access to the file will be limited to authorized study staff and will not include any identifying information.

Participants in both groups will receive the Pain Buddy download link and reminders to complete diaries via Google Voice texting services. In order to remain HIPAA compliant, no Protected Health Information (PHI) or Personally Identifiable Information (PII) will be communicated over Google Voice. An educational component will be included at the bottom of each message sent that instructs participants not to send any PHI or PII in their response to the messages. Participants may also be contacted by phone or email (method chosen by participant) by the study coordinator to remind them to complete the REDCap questionnaires at the end of the intervention period, and at 6-month follow-up.

Participants in both the control and intervention groups will be compensated \$5 per week for completing at least 10 out of 14 diaries per week. If participants complete at least 10 diaries per week for the 8-week diary portion of the study they can earn up to \$40 in the form of a gift card.). Participants in the intervention condition can earn an additional \$25 if they complete at least 40 CBT (5 exercises per week) exercises throughout the 8-week study period. After parent-child dyads complete all 3 study questionnaires, participants will receive a \$50 gift card at each time point (baseline, 60 days, and 6-month follow-up). Parent-child dyads in both groups who are part of the 50 subjects asked to collect 9 saliva samples across the study ($T_1 + 2$ days,, $T_2 + 2$ days,, and $T_3 + 2$ days,). Participant dyads who

provide saliva samples will receive a \$5 gift card per completed sample for a total of up to \$90). Participants in the control group can be compensated up to \$ 280 in the form of a gift card for completion of all of the parts of the study (Diary, T1, T2 and T3 measures and saliva samples). Participants in the intervention group can be compensated up to \$305 in the form of a gift card for completion in all parts of the study (Diary, Skills, T1, T2, T3 measures and saliva samples).

Separate consent forms have been created to give participant dyads the ability to opt out of the saliva collection component while still participating in the other study components (diary and focus group/individual interviews).

Participants will receive Pain Buddy “coins” for completing diaries and skills training which can be used to acquire virtual accessories for their avatar as well as play mini games and access other features of the Pain Buddy program.

Medication Information: Self-report data will be collected on medication that was used to manage pain and symptoms on the Coping Intervention Questionnaire in the daily diaries. Additionally, we will extract prescription analgesic information from the participant’s electronic medical record which will include: medication name, dosage, quantity, date prescribed and prescribing physician.

Dosage Time: Data will be collected about the time use of each activity and screen on Pain Buddy. Any activity usage, time spent practicing skills, using the reward coin store, minigame or program features and participant’s visual and decoration choices will be recorded. Data regarding the time the program used and preferences will be collected.

Relaxation Skills: Relaxation skills teaching time is built into the program; the Pain Buddy program will trigger skills practice if the child reports clinically significant symptoms where different relaxation skills (e.g., deep breathing) will be taught to children by the program. Weekly reminder triggers will also occur to give children time to practice relaxation skills every week.

Upon completion of the 60 days, patients will be notified that their participation in the study is over. Patients in the experimental group will be notified that a health care provider will no longer be monitoring their symptoms and they will no longer receive contact from the health care provider or our study team, but can continue to use the Pain Buddy program if they wish. Data collection of their diary entries will also cease, as well as any other activity tracking of their program use.

NRC health data will also be analyzed to explore responses associated with better patient experience as well as the role of clinical factors as captured by the treatment the patient received.

RCADS sample procedures: Parent and child dyads will be asked to complete measures on REDCap on day of recruitment. Parents will be asked to complete demographic information, information regarding their child’s anxiety and depressive symptoms (RCADS) as well as a parent self-reported measure of perceived stress (PSS). Children will be asked to complete questions regarding their anxiety and depressive symptoms (RCADS).

Participants in the RCADS group will be contacted by phone, email or text (method chosen by participant) by the study coordinator to remind them to complete their questionnaire.

Data will be downloaded periodically to a .csv (Comma Separated Values) file and stored on a secure network in the research office. Access to the file will be limited to authorized study staff and will not include any identifying information. The parent-child dyad will be awarded a \$10.00 gift card upon completion of the study

Parent-Child Dyad Focus Group/ Individual Interview Procedures:

40 parent and child dyads who previously used the Pain Buddy application will be asked to participate in a focus group/individual interview consisting of a 60-minute discussion. Questions will ask about their general impression of the app, what specifically they liked about the app, things they would change and

what impacted their high and/or low adherence. Participant dyads who identified as Hispanic/Latino will be asked to identify factors that can help refine and adapt the application to be culturally adapted.

Patients will be asked if they have any questions concerning the study and all questions will be answered thoroughly and candidly.

If participants in either group express interest, the researcher will document the participant's availability to participate in a focus group or individual interview. The researcher will ask both parent and child questions about their experience using the Pain Buddy application. Researchers will be taking field notes as well as audio recording the discussion for transcription and analyses of themes. The focus group discussion or individual interviews will be conducted either via video conferencing call (Zoom), via telephone, at the OPI and 5th floor oncology unit located at CHOC Children's or at the UCI Center on Stress and Health located at 505 S. Main St. Suite 940 Orange, CA 92868. Participants dyads who complete participation in the adherence focus group or individual interview will be compensated with a \$50 Target gift card.

Child/Teen Focus Group/ Individual Interview Procedures:

24 Children/teens may be asked to participate in a second 30-minute interview that will ask how a social support component could enhance the program.

Patients will be asked if they have any questions concerning the study and all questions will be answered thoroughly and candidly.

If participants express interest, the researcher will document the participant's availability to participate in a focus group or individual interview. The researcher will ask child/ teen questions related to social support and how it can enhance the Pain Buddy application. Researchers will also show participants a beta version of the social support website we are developing to gather initial feedback on its features. Researchers will be taking field notes as well as audio recording the discussion for transcription and analyses of themes. The focus group discussion or individual interviews will be conducted either via video conferencing call (Zoom), via telephone, at the OPI or 5th floor oncology unit located at CHOC Children's or at the UCI Center on Stress and Health located at 505 S. Main St. Suite 940 Orange, CA 92868. Participants who complete participation in the social support focus group or individual interview will be compensated with a \$25 Target gift card.

Server/REDCap Information

REDCap E-consent: REDCap accounts are provided by UCI Health Sciences, and require special permission to distribute and access surveys. Traditional hard copy Informed consent/assent and HIPAA authorization will be phased out and will be collected via REDCap. Participant dyads will be able to see and read through the Informed Consent and HIPAA Authorization forms as it is stamped and approved by CHOC IRB, they will have ample time to read through and ask any questions they may have pertaining to their participation in the study. Once they have read through, there will be designated fields for parent name and signature, along with participant name and signature.

What is e-Consent? Electronic-Consent (e-Consent) is a platform for consenting research participants either on site or at home using a computer-based consent form rather than traditional paper documentation. Consent forms can be implemented in a REDCap survey via computer, mobile phone, or tablet.

How the e-Consent Framework works: The 'Auto-Archiver + e-Consent Framework' survey option adds two things to the typical survey-taking process. 1) Before a participant completes the survey, an extra certification page is added to end of the Informed Consent form and HIPAA authorization that displays an in-line PDF copy of their responses in which they will be asked to confirm that all

information in the document is correct. Once they confirm all is correct, the survey will then be marked as complete. The survey will not be considered complete until they fulfill the certification step. (screenshots of certification page have been added to the IRB package) 2) Upon completion of the survey, a static copy of their responses in the form of a consent-specific PDF will be stored in the project's File Repository. The consent-specific PDF will have the values of the e-Consent Framework Options inserted at the bottom of each page in the PDF. These values (i.e., name, date of birth, etc.) are added to the PDF as extra documentation of the identity of the person who is consenting. The participant will receive an email auto generated from REDCap with a message that reads "Thank you for participating in the Pain Buddy Study. Attached you will find a copy of the consent forms you signed. If you have any questions, please contact the Pain Buddy study coordinator. Contact information is found below. Study Coordinator: Lessley Torres Direct Line: 714-456-2835 Painbuddy@CHOC.org UCI Center on Stress & Health 505 S. Main St. Ste 940 Orange, CA 92868" (a copy of the auto generated message has been uploaded for IRB review).

Why is this called a 'framework'?

The 'e-Consent Framework' is referred to as a 'framework' because enabling this option alone does not provide an e-Consent process but merely provides the general framework or mechanism to allow you to provide e-Consent to patients/subjects. As a survey administrator, you must still create your e-Consent survey and all the questions in it, including name, date of birth, and how you wish to capture the signature. This framework allows you to implement your e-Consent process by providing standardized tools (certification screen + automatic storage of consent form as a 'hard-copy' PDF) while still providing the ability to customize your survey how you wish.

How can the 'signature' process be handled for e-Consent?

Patients/subjects can 'sign' their consents by typing in their name or by utilizing REDCap's 'Signature' field type (i.e., 'wet signature') on the survey.

What is e-Consent version and type?

e-Consent version and type are both free-form text fields whose value will be inserted at the footer of each page in the PDF. Versioning of a form is a concept whereby you may give it a number or alpha-numeric designation to represent the current version or state of the form. So if the form is modified AFTER data collection begins, then it is recommended that a new version be applied. For example, the first version might simply be '1', and after collecting the consent of a few participants, a co-investigator or aim of the study is modified or added, which represents a new version of the form, thus will increment the version to '2' (and so forth).

REDCap Questionnaires: REDCap accounts are provided by UCI Health Sciences, and require special permission to distribute and access surveys. Collected survey data will be downloaded periodically as a .csv (Comma Separated Values) password protected file. This file will be stored on a secure UCI network accessible only through UCI Health Sciences ID Login from within the research office located at 505 S. Main Street, Suite 940, Orange, CA 92868. Access to the file will be limited to authorized study staff listed on the personnel chart and RI worksheet. Content on the CSV file is numerical data, and variable code names for the question items. Copies of the CSV files and PDFs of the questionnaire have been uploaded to the IRBNet package for committee review. This data is stored separately from the e-consent forms and they do not download on the same excel sheet. Rather electronic versions of the consent forms are stored in the REDCap file repositories accessible only by users with special privileges.

Pain Buddy Diary Data Security: The following security measures have been implemented for application-side security/privacy/confidentiality: Data remotely received from the electronic diary will be stored on an encrypted application server housed at UCI- California Institute for Telecommunication and Information Technology (Calit2) located at 4100 Calit2 Building Irvine, CA. 92697. This server is dedicated solely for Pain Buddy diary data storage and security. The server is maintained by Calit2. All data transmitted from the application is over the HTTPS protocol. IP address of this server is not shared with any parties outside of UCI Calit2 or UCI Health Sciences for security purposes. All diary

information recorded is identified by a unique subject ID code assigned to each participant at the beginning of the study. There is no identifying information collected as part of the mobile diary such as name, age, gender, diagnosis. Collected diary data will be downloaded periodically as a .csv (Comma Separated Values) password protected file. This file will be stored on a secure UCI network accessible only through UCI Health Sciences ID Login from within the research office located at 505 S. Main Street, Suite 940, Orange, CA 92868. Access to the file will be limited to authorized study staff listed on the personnel chart and RI worksheet and will not include any identifying information. Content on the CSV file is solely de-identified numerical data, and variable code names for the question items. Copies of the CSV files and PDFs of the questionnaire have been uploaded to the IRBNet package for committee review.

Protected Health Information (PHI): PHI obtained prior to participant signing the electronic HIPAA authorization (i.e. tracking sheet, appointment schedules) will be stored on a CHOC server network share drive specific to our center (UCI CSH), accessible only through the CHOC portal. Recruitment PHI is on a password-protected file that is accessible only by authorized study staff listed on the personnel chart and RI worksheet. After e-consent is obtained, active participant PHI will be stored on a secure UCI network known as SharePoint accessible only through UCI Health Sciences intranet and UCI Health Science ID Login from within the research office located at 505 S. Main Street, Suite 940, Orange, CA 92868. The main UCI Health Sciences SharePoint server is housed on premises at the UC Irvine Medical Center located at 101 The City Dr. S, Orange, CA 92868. IP address for the server is not shared with any parties outside of UCI Health Sciences for security purposes.

Collection, Storage, and Assay of Saliva: The PI, co-PIs, and study coordinators will ensure proper safe collection and storage of saliva, oversee shipment of saliva samples from CHOC research freezer to the UCI Institute for Interdisciplinary Salivary Bioscience Research (IISBR), and oversee analysis of samples conducted by IISBR staff. Consistent with current best practice protocol for salivary inflammatory biomarkers, whole saliva samples will be collected using an unstimulated passive drool technique.⁵¹ Participants will be instructed to avoid eating or brushing their teeth for one hour prior to each collection. Participants will rinse their mouths thoroughly with water before a sample is collected, and they will wash their hands for 20 seconds immediately prior to collecting the sample. Anyone assisting with the collection will also practice the same hand hygiene. Participants will then passively drool into a collection vial for three minutes or until 0.80 milliliters of fluid is collected. Samples will be immediately capped and sealed, and the outsides of the collection tubes will be disinfected with an appropriate EPA-approved product. Samples will then be placed in a secondary container such as a sealed plastic bag with absorbent material for potential spills, or a freezer box. Participants and any assisting will once again wash hands for at least 20 seconds after collecting the saliva sample. Samples will be immediately placed in the on-site freezer and stored at -80°C until transferred to IISBR and assayed. All samples will be assayed for salivary IL-1 β , IL-6, TNF- α , and CRP using highly sensitive enzyme immunoassays (Salimetrics, IISBR).

Analysis Methods

Data Analysis: Data analysis will be performed with SPSS 19.0 (SPSS Institute, Chicago, IL). The license for SPSS 19.0 is owned and paid for by the UCI Center on Stress & Health, located at 505 S. Main St. Suite 940, Orange, CA 92868 and is renewed on a yearly basis. The following are the CSV file names in which are periodically downloaded, and are to be used for data analysis using SPSS 19.0. Description of survey data collected is found below on pages 9-12. Copies of the files have been uploaded to IRBNet for committee review.

- 1) Painbuddy_REDCap CSV file_completed measures:
 - a. This file extracts the numerical data from the measures collected from parent (English and Spanish) and child at baseline, 60 day and 6 month follow up.
- 2) Painbuddy_section1_MSAS_8_9
 - a. This file is the diary data collected for participants in the 8-9 age groups. The reason for separate files from other age group is due to different measure structure that is appropriate for this age/reading level.

- 3) Painbuddy_section1_MSAS_10_18
 - a. This file is diary data collected for participants in the 10-18 age groups. The reason for separate files is due to the different measure structure that is appropriate for this age group.
- 4) Painbuddy_section2 APPT
 - a. This file collects pain report prompted by the responses from section 1. If the child does not experience pain, then this section is not prompted and no data is collected
- 5) Painbuddy_section3_intervention
 - a. This file collects pain report prompted by the responses from section 1 and 2. If the child does not experience pain, then this section is not prompted and no data is collected.

All multi-item survey measures will be tested for reliability using Cronbach's alpha and construct validity will be assessed comparing baseline survey measures with clinical outcomes using Pearson product-moment correlation coefficients. The study is a single blind stratified randomized controlled trial, stratified by site and age group. We will initially use generalized estimating equations to examine treatment groups on primary outcome (pain) and secondary outcome measures (quality of life, functional status, satisfaction) allowing for strata effects (site, age group) and adjusted for patient and parent covariates and independent variables as appropriate. The models will take the form: $Y_i = \beta_0 + \beta_1 x_{1ij} + \beta_2 x_{2i} + \beta_3 x_{3i}$ where Y_i is the outcome measure for the i th patient, β_0 is the overall study population intercept, x_1 is the intervention for the i th patient at the j th time, β_1 is the treatment effect of interest, x_2 is a vector of indicators for the strata (site/risk group) to which the i th patient belongs, β_2 is a vector of strata effects, x_3 is a vector of appropriate covariates, β_3 is a vector of estimated effects for the covariates. In addition, we will apply mixed effects linear regression models to explore the impact of treatment on time-varying outcomes. These models will allow for random individual intercepts and time-trends to address the repeated measures on individuals.

Power Analysis and Data Analysis

The study would have sufficient power with $\alpha = 0.05$, $\beta = 0.80$ to detect a difference between treatment groups of 20% (mean = 56.0 vs. 45.4) in VAS scores, with 138 patients in each intervention group. This difference corresponds to an effect size (ES) of 0.34 and is the minimum clinically relevant difference in pain scores noted by Tsze et al.⁶⁶ However, because this intervention targets children with cancer related pain, and based on pilot data, we anticipate a larger difference between groups of at least 25% (ES = 0.42), requiring 88 patients per group ($\alpha = 0.05$, $\beta = 0.80$). Based on pilot study results, and because we will randomize within sites, we have accounted for only a small degree of site level clustering [intraclass correlation coefficient (ICC) = .01], and have modified the sample size accordingly for a total of 90 per group. To account for approximately 15% study attrition, we will initially recruit 103 patients per group. Similar power estimates with other secondary outcome variables yield smaller sample sizes.

Heterogeneity of Treatment Effects: While we have no specific hypotheses regarding subgroups that may differentially benefit from the Pain Buddy intervention, with approximately equal numbers of boys and girls, with $\alpha = .05$, we have 80% power to detect a between gender difference in response of 40% (ES=.68) with 34 patients of each gender in treatment vs. control groups. We will test the gender*treatment group interactions in the models described above, examining the parameter estimates for the interaction term as well as the variance explained by models with and without that interaction.

Salivary Biomarkers: Comparisons of baseline characteristics between the intervention and control groups will be conducted using univariate ANOVA and t -tests. Chi-square analyses will be used for categorical baseline variables. Possible covariates such as oral health, salivary flow rate, and sample pH that may be correlated with salivary inflammatory biomarkers will be assessed using Pearson product-moment correlations. Identified covariates will be used in subsequent analyses. Repeated-measures ANCOVAs will be utilized to examine if there are significant differences overall in biomarker

levels and MSAS, APPT, RCADS, and PedsQL reports individually between Pain Buddy treatment groups across the 3 assessment timepoints. Associations between longitudinal changes in inflammatory biomarker levels and child self- and parent-reported measures will be investigated across all subjects using stepwise multivariate linear models, with change in child- and parent-reported measures as the dependent variables. Interaction terms will be added to the models to test if the effect of change in inflammatory biomarkers differs between intervention groups.

Missing Data: To address the potential for differential attrition and within subject missing data, we will conduct sensitivity analyses of our models to missing at random and not missing at random assumptions and different treatments of missing data, e.g. intention-to-treat vs. per protocol analyses. We will use multiple imputation and maximum likelihood estimation methods to address potential missing data within subjects for all study variables. We will also examine the sensitivity of study conclusions to inclusion of imputed variables vs. complete data.

Qualitative Data: There is no power analysis for qualitative data approaches but rather standard sample size to ensure data saturation, which tends to be between 20-40 people. The qualitative portion of the study will be analyzed inductively and thematically. The interviews will be recorded and will be transcribed verbatim. Two researchers will do the initial individual coding of the interview transcripts for two interviews to identify recurring themes. Once a consensus is agreed on for themes, the rest of the interviews will be coded by the same two researchers. When the analysis is complete, the identified themes and quotes will provide insight into child's reasons for high and/or low symptom diary adherence. The interviews will be conducted in the language preferred by the participant. Researcher will check for intercoder reliability for agreement on coding.

Measures: Each measure has been selected based on the model outlined in specific aims. Preliminary data on the applicability of these measures for the age and SES range of this cohort are available from our own or our collaborators' experience.

Coversheet and Additional Information sheet (*Medical record abstraction*) Information will be collected from patient medical records including age, weight, diagnosis, protocol/ roadmap code, person completing study measures, patient status, patient type, and whether patient completed chemotherapy. We will also be collecting information on prescribed medications (inpatient and outpatient) including medication name, dosage, quantity, date prescribed and prescribing physician. Additionally, we will be collecting the number of interventions received on an inpatient and outpatient setting, including but not limited to, the frequency and durations of psychological services, rehabilitation services, palliative care, and pain related interventions.

Demographic (*parent self-report*) Baseline demographics will be collected including gender, race, ethnicity, parents' education, occupation, age and income, etc. Regarding ethnicity and culture, the demographics form inquires about detailed information, including cities and countries of parents' previous residence, languages spoken in the home, and parents' and children's primary and secondary languages. In addition, we collect detailed socioeconomic status (SES) information including parent education, occupation, income, and area of residence (i.e., zip code), which will allow us to geocode for detailed SES information regarding the city/county in which participants reside. Completed using REDCap.

Demographic (*young adult self-report*) 18 year olds that are participating without a parent-dyad will complete baseline demographics about themselves. This will include gender, race, ethnicity, education, occupation, age and income. Regarding ethnicity and culture, the demographics form inquires detailed information about cities and countries of residence, primary and secondary languages spoken in the home, and education. Completed at baseline using REDCap.

Daily Diary:

Memorial Symptom Assessment Scale (MSAS) 7-12 (child self-report) is an 8-symptom instrument that evaluates whether or not the child experienced a particular symptom since the prior diary entry. If

the child says “yes” to having experienced any of the symptoms, then the child is prompted to describe the frequency (*i.e. a very short time, a medium amount or a lot*), severity (*i.e. a little, a medium amount or a lot*) and distress (*i.e. not at all, a little, a medium amount or very much*) experienced due to the symptom.³² Completed twice daily, once in the morning and once in the evening using Pain Buddy.

Memorial Symptom Assessment Scale (MSAS) 10-18 (child self-report) is a 30-symptom instrument that evaluates whether or not the child experienced a particular symptom. If the child says “yes” to having experienced any of the symptoms, then the child is prompted to describe the frequency (*i.e. a very short time, a medium amount or a lot*), severity (*i.e. a little, a medium amount or a lot*) and distress (*i.e. not at all, a little, a medium amount or very much*) experienced due to the symptom. The MSAS 10-18 is comprised of 3 subscales: psychological (PHYC *i.e. “difficulty concentrating or paying attention”*), physical (PHYS *i.e., “pain”*) and general distress index (GDI *i.e., “how much did it [the symptom] bother you?”*). The alpha coefficients of the PSYCH, PHYS and GDI subscales were 0.83, 0.87 and 0.85 respectively, suggesting internal consistency between the items.⁴ Completed twice daily, once in the morning and once in the evening using Pain Buddy.

Adolescent Pediatric Pain Tool (APPT)³³ (child self-report 8-17) is a multidimensional pain instrument that is reliable and valid. The first part of the measure includes a body outline for the front of the body and another outline for the back of the body and patients are asked to mark any areas that they are experiencing pain on. Secondly, pain intensity is also assessed on a word-graphing rating scale, which is a 100-mm horizontal line that ranges from “no pain,” “little pain,” “medium pain,” “large pain” and “worst pain.” Lastly, the third part of the measure contains a list of 67-words representing four domains of pain. These domains include: sensory (represent pressure or pain sensation *i.e. “aching,” “stinging”*), affective (represent unpleasant emotions of pain *i.e. “screaming,” “deadly”*), evaluative (represent intensity of pain *i.e. “miserable,” “uncontrollable”*) and temporal (represents duration and pattern of pain *i.e. “constant,” “on and off”*). A percentage is calculated for each domain (by dividing the words circles by the number of words possible in each category) as well as a total score for the number of words recorded out of 67 possible words. Completed twice daily, once in the morning and once in the evening using Pain Buddy.

Coping Interventions Questionnaire: A 12 item questionnaire asking about coping strategies child tried to manage their pain including distraction, CBT and any medications patient used. Completed twice daily, once in the morning and once in the evening using Pain Buddy.

Coping efficacy (CSQ): Two items from the Coping Strategies Questionnaire {Rosenstiel, 1983 #2680} will be used to measure coping efficacy. The items are answered on a 7-point scale and are: 1) “Based on all the things you did to cope, or deal with your pain today, how much control do you feel you had over it?” and 2) Based on all the things you did to cope, or deal with your pain today, how much were you able to decrease your pain?” Completed twice daily, once in the morning and once in the evening using Pain Buddy.

State-Trait Anxiety Inventory (STAI) (*parent self-report*). This is a widely used self-report anxiety assessment instrument for adults. To date, over 1,000 studies using the STAI have been published in peer reviewed literature.³⁸ Standard scores for children and adults are available. The questionnaire contains two separate, 20-item, 4-point self-report rating scales for measuring trait and state anxiety. Total scores for situational and trait anxiety range from 20 to 80 each; higher scores denote higher levels of anxiety. Test-retest correlations for the STAI trait are high and range from 0.73 to 0.86. Validity of the adult instrument was examined in two studies in which the STAI was given under high- and low-stress conditions to large samples of students.³⁸ For our purposes, only the one page Trait section of the questionnaire will be administered and utilized. Completed at baseline using REDCap.

Medication Attitude Questionnaire (MAQ)(*parent self-report*). This questionnaire was developed to examine attitudes about using pain medication for treating children’s pain. The instrument consists of 27 items each rated on a seven-point Likert-type scale that ranges from strongly disagree to strongly agree. Parents are instructed to consider analgesia as any medication prescribed for a specific event or over-the-counter analgesia any time. Internal consistency (Cronbach’s Alpha) for the overall scale is reported between 0.68 and 0.73 and for the four subscales the coefficients are reported between 0.63

and 0.75.³⁹⁻⁴⁰ A factor analysis with Varimax rotation suggested a 3-factor solution, explaining 52% of the MAQ variance. The factors were *Appropriate-Use* (e.g., “Giving children pain medication for pain teaches proper use of drugs”), *Side-Effects* (e.g., “Side effects are something to worry about when giving children pain medication”), and *Avoidance* (e.g., “Pain medication works best if saved for when the pain is quite bad”).⁴⁰ Completed at baseline using REDCap.

Parental Pain Expression Perceptions (PPEP) (*parent self-report, questions 17-25 on measure MAQ*). Our research group developed a nine-item questionnaire to evaluate parental perceptions regarding pain expression in children based on previous research and a review of the literature.⁴⁰ These items were examined for content validity by a group of experts that included pediatric practitioners, pediatric researchers, and parents. The PPEP was designed to assess parental attitudes regarding the manner in which children express pain emotionally and behaviorally. A factor analysis with Varimax rotation of the PPEP suggested a 3-factor solution, explaining 69% of the variance. The factors were *Active, Loud Behaviors* (e.g., “Children always express pain by crying or whining,” “Children who are playing are not in pain”); *Attention-Seeking* (e.g., “Children complain about pain to get attention,” “Children exaggerate pain”); and *Quiet, Withdrawn Behaviors* (e.g., “Children who are quiet are not in pain”). The Cronbach’s Alpha, calculated for the whole measure (0.79) suggested internal consistency between the items.⁴⁰ Completed at baseline using REDCap.

Parental perception of the effects of untreated pain in children. (*Last section of the measure MAQ*) To examine parental perception of the effects of untreated pain in children, parents will be asked to respond “yes” or “no” to the following two questions: “Do you think that untreated pain can cause physical damage?” and “Do you think that untreated pain can cause psychological damage?”⁴⁰ Completed at baseline using REDCap.

Perceived Stress Scale (PSS)⁴¹ (*parent self-report*) The PSS is a widely used 14-item self-report measure of perceived stress. Parents will be asked to rate statements such as “In the past month, how often have you been upset because of something that happened unexpectedly?” and “In the past month how often have you felt that things were going your way?” Subjects rate the items on a 5-point Likert-type scale with higher scores reflecting greater perceived stress. Seven items are reverse-keyed and items are summed to obtain the final score. The PSS has been shown to have adequate reliability and validity.⁴¹ Completed at baseline, 60 days, and 6 month follow-up using REDCap..

The Revised Child Anxiety and Depression Scale (RCADS) (*parent report*).³⁴ RCADS contains a 10-item major depressive disorder subscale and a 5-item generalized anxiety disorder subscale. T-scores are calculated based on gender and grade in school. Good internal consistency has been demonstrated. One-week test-retest reliability was good, and validity has been shown through correlations with other measures.³⁴ Completed at baseline, 60 days, and 6 month follow-up using REDCap.

The Revised Child Anxiety and Depression Scale (RCADS) (*child self-report*).³⁴ RCADS contains a 10-item major depressive disorder subscale and a 5-item generalized anxiety disorder subscale. T-scores are calculated based on gender and grade in school. Good internal consistency has been demonstrated. One-week test-retest reliability was good, and validity has been shown through correlations with other measures.³⁴ Completed at baseline, 60 days, and 6 month follow-up using REDCap.

Pediatric Quality of Life Inventory Version 4.0 (PedsQL)³⁵ (*child self-report, ages 8-12, 13-18; parent report child ages 8-12, 13-18*) The PedsQL measures health related quality of life (HRQOL) in children 2-18 years of age. This 23-item scale is applicable to healthy children as well as children with acute or chronic illnesses. The inventory is divided into 4 categories: physical, emotional, social and school, on a 5-point likert scale ranging from 0=never to 4=almost always (i.e. “I have trouble sleeping”). Higher scores on the scale suggest a better HRQOL. Internal consistency reliability for the total scale score is .88 for the child self-report and .90 to .93 for the parent report.³⁵⁻³⁶ Completed at baseline, 60 days, and 6 month follow-up using REDCap.

Pediatric Quality of Life-Cancer Module³⁷ (*child self-report, ages 8-12, 13-18; parent report child ages 8-12, 13-18*) The PedsQL Cancer Module is administered along with the generic core scale in

order to get a better understanding of a child's health related quality of life (HRQOL) due to cancer. This 27-item multidimensional scale encompasses of 8 categories: pain & hurt, nausea, procedural anxiety, treatment anxiety, cognitive problems, perceived physical appearance and communication. Also on a 5-point likert scale, this measure is scored exactly like the PedsQL with 0 being never to 4 being almost always and higher scores on the scale suggest a better HRQOL. The internal consistency reliability for the PedsQL Cancer Module Scale is .72 for the child self-report and .87 for the parent report.³⁷ Completed at baseline, 60 days, and 6 month follow-up using REDCap.

Pediatric Quality of Life-Fatigue Module³⁷ (*child self-report, ages 8-12, 13-18; parent report child ages 8-12, 13-18*). The PedsQL Fatigue Module is administered along with the generic core scale in order to get a better understanding of a child's health related quality of life (HRQOL) due to fatigue. This 18-item multidimensional scale encompasses of 3 categories: general fatigue, sleep/rest fatigue, cognitive fatigue. Also on a 5-point likert scale, this measure is scored exactly like the PedsQL with 0 being never to 4 being almost always and higher scores on the scale suggest a better HRQOL. The internal consistency reliability for the PedsQL Fatigue Module Scale is .89 for the child self-report and .92 for the parent report.³⁷ Completed at baseline, 60 days, and 6 month follow-up using REDCap.

Satisfaction Questionnaire (TEI)⁴² (*parent report/patient report*) Patients and their parents will provide ratings of satisfaction regarding their experience using the Pain Buddy application with questions such as "How satisfied were you with your experience using the Pain Buddy Diary". Patients and parents will rate their experience on a Likert-type scale with anchors of *Not at All Satisfied* to *Very Satisfied*. Likewise, parents will provide a rating of how satisfied they were with their child's diary use and experience using a Likert-type scale with anchors *Not at All Satisfied* and *Very Satisfied*. In addition to these quantitative responses, patients and parents will be asked for qualitative impressions of their experience using the Pain Buddy diary application. Completed at day 60 and 6 month follow up using REDCap.

Content and Usability Measure: (*parent report/patient report*) Assessment of content and usability by participants will be collected using methods similar to those used by other investigators in the study of utility of electronic interventions.^{28, 34} Ratings of content will be provided in response to queries such as "How useful or helpful was the information provided in this module?" on a Likert-type scale with anchors of *Not at All* and *Very Much*. Likewise, patients will provide a rating of how easy or difficult the module was to use on a Likert-type scale with anchors *Very Easy* to *Very Difficult*. In addition to these quantitative responses, parents will be asked for qualitative impressions of the program. In reviewing each module, patients will be asked to respond to open-ended questions querying "What did you like best about this module?" and "What did you like least about this module?" Completed at day 60 and 6 month follow up using REDCap.

Adult Response to Children's Symptoms (ARCS)^{44, 45} (*parent report*) Assesses behaviors by parents or other adults in response to their children's pain. The ARCS consists of 29 items describing parents' responses to their children when the children are in pain. On the ARCS parent-report form, parents self-report on the frequency of their own use of each type of response to their children's pain. The internal consistency of each subscale was adequate (alpha reliability coefficients = .87, .67, and .79) for Protect, Minimize, and Encourage/Monitor. Completed at baseline, day 60, and 6 month follow up using REDCap.

Child Activity Limitations Interview (CALI-9)⁴³ (*parent report/patient report*) The CALI-9 is a 9 item likert-type assessment tool that can be used to rate pain-related limitations and track outcomes over time among youth with chronic pain. The measure includes both child and parent reports with a common factor structure and scoring that is easily interpretable. The CALI-9 can be used to assess limitations in active and routine domains, which may allow for better understanding of ways in which pain impacts the day-to-day functioning of children and adolescents with chronic pain. Completed at baseline, day 60, and 6 month follow up using REDCap.

Child Pain Related Self-Efficacy (PSES)⁴⁶ (*parent report/patient report*) The PSES is a 7-item measure that assess whether children are functioning normally when in pain. The Cronbach's

alpha measured at .89 for the child items and .90 for the parent items. This measure may help explain variance in assessment of self-management behaviors, including treatment adherence. Completed at baseline, day 60, and 6 month follow up using REDCap.

Child Pain Anxiety Symptom Scale (C-PASS) ⁴⁷ (*patient report*) The C-PASS is a 20- item scale for children adapted from the adult PASS-20. Children are asked to rate the extent to which they think, act, or feel on a scale from 0 ("never think, act or feel that way") to 5 ("always think, act, or feel that way"). The CPASS showed excellent internal consistency (alpha reliability coefficients = .90). Completed at baseline, day 60, and 6 month follow up using REDCap.

The Health Beliefs Survey (HBS) (parent- and child report) is a 3-item self-report measure of individuals' views of general health, which can be used for children, aged ten years to adulthood. Completed using REDCap.

The Household Material Hardship (HMH) survey ⁴⁸ (*parent report*) is a self-report measure designed to gain better understanding about financial situation of families at the start of their child's diagnosis of cancer and the subsequent impact of a child's cancer diagnosis on families' financial well-being. The survey is divided into sections that cover topics about family structure, housing, transportation, home utilities, food, employment, and financial supports. Completed using REDCap.

Saliva Sample

Oral Health and Food/Drink Log: Parents and patients collecting saliva samples will report on their oral health (e.g. any gum or dental issues) as well as any food or drink consumed, and any prescription or over the counter medication or mouth rinses before saliva sample collection, with a reported time.

RCADS Sample

Demographic (*parent self-report*) Demographics will be collected including gender, race, ethnicity, parents' education, occupation, age and income, etc. Regarding ethnicity and culture, the demographics form inquires about detailed information, including cities and countries of parents' previous residence, languages spoken in the home, and parents' and children's primary and secondary languages. In addition, we collect detailed socioeconomic status (SES) information including parent education, occupation, income, and area of residence (i.e., zip code), which will allow us to geocode for detailed SES information regarding the city/county in which participants reside. Completed at baseline using REDCap.

The Revised Child Anxiety and Depression Scale (RCADS) (parent report).³⁴ RCADS contains a 10-item major depressive disorder subscale and a 5-item generalized anxiety disorder subscale. T-scores are calculated based on gender and grade in school. Good internal consistency has been demonstrated. One-week test-retest reliability was good, and validity has been shown through correlations with other measures.³⁴ Completed at baseline using REDCap.

Perceived Stress Scale (PSS)⁴¹ (*parent self-report*) The PSS is a widely used 14-item self-report measure of perceived stress. Parents will be asked to rate statements such as "In the past month, how often have you been upset because of something that happened unexpectedly?" and "In the past month how often have you felt that things were going your way?" Subjects rate the items on a 5-point Likert-type scale with higher scores reflecting greater perceived stress. Seven items are reverse-keyed and items are summed to obtain the final score. The PSS has been shown to have adequate reliability and validity.⁴¹ Completed at baseline using REDCap.

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Multi-site RCT

Outcome/Construct:	Measure/Parameter:	Assessment Time Points
Child		
Child Symptoms and distress	MSAS	Morning and evening
Pain	APPT	Morning and evening
Coping	CSQ	Morning and evening
Use of coping mechanisms	Intervention questionnaire	Morning and evening
Anxiety and Depression	RCADS	Baseline, T2 and T3
Quality of Life	PedsQL	Baseline, T2 and T3
Child Pain Catastrophizing	PCS	Baseline, T2 and T3
Child Pain Interference	CALI-9	Baseline, T2 and T3
Child self-efficacy	PSES	Baseline, T2 and T3
Pain Anxiety	CPASS	Baseline, T2 and T3
Satisfaction	TEI	T2 and T3
Health Beliefs	HBS	Baseline and T3
Parent		
Demographics	Demographic questionnaire	Baseline
Anxiety	STAI-T	Baseline
Medication Attitudes	MAQ, PPEP	Baseline
Child's anxiety and depression	RCADS	Baseline, T2 and T3
Child's Symptom Assessment	MSAS	Baseline, T2
Child's Quality of Life	PedsQL	Baseline, T2 and T3
Parental Stress	PSS	Baseline, T2 and T3
Child Pain Catastrophizing	PCS	Baseline, T2 and T3
Child Pain Interference	CALI-9	Baseline, T2 and T3
Child self-efficacy	PSES	Baseline, T2 and T3
Parental response to pain	ARCS	Baseline, T2 and T3
Satisfaction	TEI	T2 and T3
Health Beliefs	HBS	Baseline and T3
Economic Impact Survey	HMH	Baseline

Saliva Sample

Outcome/Construct:	Measure/Parameter:	Assessment Time Points
Child		
Inflammation (CHOC only)	Salivary IL-1 β , IL-6, TNF-a, and CRP	Baseline + 2 days, T2 + 2 days, and T3 + 2 days,
Child's oral health	Oral health questionnaire	Baseline + 2 days,, T2 + 2 days, and T3 + 2 days,
Parent		
Inflammation (CHOC only)	Salivary IL-1 β , IL-6, TNF-a, and CRP	Baseline + 2 days,, T2 + 2 days, and T3 + 2 days,
Parent's oral health	Oral health questionnaire	Baseline + 2 days,, T2 + 2 days, and T3 + 2 days,

RCADS Sample

Outcome/Construct:	Measure/Parameter:	Assessment Time Points
Child		
Anxiety and Depression	RCADS	Baseline
Parent		
Demographic information		Baseline
Anxiety and Depression	RCADS	Baseline
Stress	PSS	Baseline

Focus Group Sample

Outcome/Construct:	Measure/Parameter:	Assessment Time Points
Child		
Evaluation of Pain Buddy	Interview Guide	6-months post completion of Pain Buddy participation
Social support component	Interview Guide	Post Baseline
Parent		
Evaluation of Pain Buddy	Interview Guide	6-months post completion of Pain Buddy study participation

Subjects: 206 parent parent-child dyads (206 children and 206 parents), ages 8-18, undergoing cancer treatment at CHOC Children's Hospital and St. Jude Children's Research Hospital, (Memphis, TN-independent IRB) will be recruited to participate in the randomized control trial. For this phase of the study, 103 children will be randomly placed in the Pain Buddy group and the other 103 will be randomly placed in the attention control group. All 206 children participating in the RCT will complete pain, symptom and use of coping mechanisms dairies twice a day for 60 consecutive days. The participants in the control group will have access to all Pain Buddy features except for remote monitoring of their diary data and cognitive behavioral skills-training. A contingency plan has been developed in conjunction with CHOC Oncology physicians which states that patients who are part of the control group will still be able to call the Oncology clinic or physician on call to discuss any matters of pain or illness in a timely fashion.

The children in the monitoring condition will receive standard of care for pain and symptom management (mediation, clinic visits etc.). In addition to receiving standard of care for pain and symptom management, participants in the Pain Buddy condition will have their daily diary data monitored remotely by a member of the UCI team who will then communicate it to the study health care provider. The UCI team will inform the health care provider to contact the patient/parent via telephone with treatment recommendations when pre-determined symptom criteria are met. Alerts will be responded to within a 24- hour period Monday through Friday during daytime office hours. Alerts triggered over the weekend will be responded to the following workday. All communication between the health care provider and patient will be documented on the patient's electronic medical record and communicated to study staff via the secure message center accessible on Power Chart. Children in the Pain Buddy condition will also receive cognitive-behavioral skills training to manage pain and symptom-related distress 1) when pre-determined symptom criteria are met and 2) when child initiates training and 3) Every week when application prompts child to complete the skill of the week. The cognitive-

behavioral skills training will be delivered via audio scripts and copies of the scripts have been submitted for IRB approval.

Inclusion Criteria:

- Between the ages of 8-18 years
- Are within 16 weeks of first time cancer diagnosis
- Currently undergoing outpatient treatment for cancer
- Have experienced a pain score of 30 or greater on a visual analog scale in the past month
- Patients who are able to speak, read, and write in English. Parents who are able to speak, read, and write in English or Spanish
- Have internet access to use Pain Buddy on their mobile devices (the internet will be used to securely send the pain information to the research team).

Exclusion Criteria:

- Cognitive impairment, such as a developmental delay that would impact the child's ability to use the Pain Buddy program.
- Children diagnosed with acute promyelocytic leukemia (APL) as the treatment protocols for these children are largely inpatient, precluding use of the intervention.

Potential participants will be identified through review of the Outpatient Infusion Center (OPI) and/or Cancer Institute appointment schedules at CHOC Children's. Subjects who are determined to be eligible by electronic review of the medical record including Roadmap will be approached by a trained research associate at their scheduled appointments or in the Oncology inpatient wing to discuss the purpose of the study, eligibility and study requirements. Contact information for study personnel and study information sheet will be provided to parent and child. The research associate will thoroughly describe the study and both the patient and parents will be asked if they are interested in participating. Patients and parents will be asked if they have any questions concerning the study and all questions will be answered thoroughly and candidly. If interested in the study, risks, benefits and alternatives to participation will all be explained and as part of eligibility criteria, children will be asked about pain experience in the previous month. Participants and children will also be informed that they are free to discontinue the study at any time, for any reason and without any adverse effects. Both English and Spanish speaking participants will be recruited for this study and all participants will be provided a study information sheet in either English or Spanish. A researcher fluent in either English or Spanish will be available to answer any questions the participant may have. Spanish forms have been submitted to the IRB for approval.

Saliva Sample

For the Saliva sample, 50 parent- in total (25 in each group) will additionally be asked to collect 3 saliva samples at T₁ + 2 days, T₂, + 2 days, and T₃ + 2 days. This sample group will still be provided with the Pain Buddy program and opportunities to be asked to participate in the Focus Group/Individual Interviews. All recruitment procedures remain the same as a listed above. This group will adhere to all inclusion and exclusion criteria listed above. However, we have separated this sample to allow participant dyads the flexibility to opt out of providing saliva samples, if they wish to. Thus, separate consent forms have been created.

RCADS Sample:

For the RCADS sample group, 40 parent-child dyads will be asked to complete measures that examine how they each report anxiety and depressive symptoms of the child. This sample group will not be provided with the Pain Buddy program and will solely be prompted to fill out questionnaires.

Inclusion Criteria:

- Between the ages of 8-18 years

- Are within 16 weeks of first time cancer diagnosis
- Currently undergoing outpatient treatment for cancer
- Patients who are able to speak, read, and write in English. Parents who are able to speak, read, and write in English or Spanish

Exclusion Criteria:

- Cognitive impairment, such as a developmental delay that would impact the child's ability to answer questionnaire.
- Children diagnosed with acute promyelocytic leukemia (APL) as the treatment protocols for these children are largely inpatient, precluding use of the intervention.

Potential participants will be identified through review of the Outpatient Infusion Center (OPI) and/or Cancer Institute appointment schedules at CHOC Children's. Subjects who are determined to be eligible by electronic review of the medical record will be approached by a trained research associate at their scheduled appointments to discuss the purpose of the study, eligibility and study requirements. Contact information for study personnel and study information sheet will be provided to parent and child. The research associate will thoroughly describe the study and both the patient and parents will be asked if they are interested in participating. Patients and parents will be asked if they have any questions concerning the study and all questions will be answered thoroughly and candidly. If interested in the study, risks, benefits and alternatives to participation will all be explained and as part of eligibility criteria, children will be asked about pain experience in the previous month. Participants and children will also be informed that they are free to discontinue the study at any time, for any reason and without any adverse effects. Both English and Spanish speaking participants will be recruited for this study and all participants will be provided a study information sheet in either English or Spanish. A researcher fluent in either English or Spanish will be available to answer any questions the participant may have. Spanish forms have been submitted to the IRB for approval.

Parent- Child Dyad Focus Group/ Individual Interview Sample:

For the focus group/individual interview sample, 40 parent-child dyads participants in the upper and lower quartiles for adherence of the intervention will be asked to participate in an audio recorded interview in order to understand barriers and facilitators to adherence. Questions will be asked about their experience using the Pain Buddy application, what they liked about the app, things they would change and what impacted their high and/or low adherence. Participant dyads who identified as Hispanic/Latino will be asked to identify factors that can help refine and adapt the application to be culturally adapted.

Inclusion Criteria:

- Parents and Children who were previously recruited and completed participation using the Pain Buddy application.
- Participants in the upper and lower quartiles for adherence to the intervention.
- Between the ages of 8-18 during the time they participated in the Pain Buddy study.
- Patients who are able to speak, read, and write in English. Parents who are able to speak, read, and write in English or Spanish.

Exclusion Criteria:

- Participants who did not participate in the Pain Buddy Study.
- Cognitive Impairment, such as a developmental delay that would impact the child's ability to answer questions about their experience.
- Parents or Children who do not speak English or Spanish.

Child/Teen Focus Group/ Individual Interview Sample:

For the focus group/individual interview sample, 24 child/teen participants between the ages of 12-18 will be asked questions about how a social support component could enhance the Pain Buddy application. Researchers will also show participants a beta version of the social support website we are developing to gather initial feedback on its features.

Inclusion Criteria:

- Children/Teens who were previously recruited and completed participation using the Pain Buddy application.
- Between the ages of 12-18 during the time they participated in the Pain Buddy study.
- Patients who are able to speak, read, and write in English.

Exclusion Criteria:

- Participants who did not participate in the Pain Buddy Study.
- Cognitive Impairment, such as a developmental delay that would impact the child's ability to answer questions about their experience.
- Children who do not speak English or Spanish.

Potential participants will be identified through review of the tracking list of previously consented participants of the Pain Buddy study. Subjects who previously participated in Pain Buddy will be approached by a trained research associate at their scheduled appointments to discuss the purpose of the study, eligibility and study requirements. Contact information for study personnel and study information sheet will be provided to parent and child. The research associate will thoroughly describe the study and both the patient and parents will be asked if they are interested in participating. Patients and parents will be asked if they have any questions concerning the study and all questions will be answered thoroughly and candidly. If interested in the study, risks, benefits and alternatives to participation will all be explained. Parents and children will also be informed that they are free to discontinue the study at any time, for any reason and without any adverse effects. Both English and Spanish speaking participants will be recruited for this study and all participants will be provided a study information sheet in either English or Spanish. A researcher fluent in either English or Spanish will be available to answer any questions the participant may have. Spanish forms have been submitted to the IRB for approval.

Risks and Benefits to Subjects: All subjects will be identified only by randomly assigned ID number that will be used on all study documents and data extracts. Subject privacy will be protected by our research staff to the greatest extent possible. All research documents, are stored in locked file cabinets in our locked research office at 505 S. Main Street, Suite 940, Orange, CA 92868. Only research team members have access to the files. Only authorized personnel have access to the research database, REDCap file repositories where e-consents are housed and study investigators will receive data extracts for analysis that contain no subject identifiers. Potential subjects will be reassured that their study participation is totally voluntary and their refusal will not affect their current or future medical and health care. Subjects may decide they do not want to participate or complete the study at any time. They may be dropped from the study and their questionnaires destroyed at their request.

Informed Consent: Potential subjects will be asked to review and sign the electronic informed consent and HIPAA authorization forms via REDCap. Participants will be provided electronic copies of their signed documents, all of which will include, 1) research/purpose/procedures, 2) risks, 3) benefits 4) alternatives, 5) confidentiality, 6) compensation for injury, 7) whom (and how) to contact study personnel, 8) the voluntary nature of human research and the ability to withdraw participation, 9) investigator termination of subject participation, 10) additional costs, 11) consequences of withdrawal, 12) reporting of significant new findings and 13) the approximate number of subjects to be enrolled. All collected research data will be identified only by a randomly assigned ID number

Potential participants will be provided contact information for study personnel and study information sheets will be provided to both parent and child. The research associates approaching parent-patient dyads will thoroughly describe the study and both the patient and parents will be asked if they have any questions concerning the study, and all questions will be answered thoroughly and candidly. If interested in the study, then risks, benefits, and alternatives to participation will be explained to eligible participants. Eligible participants will also be informed that they are free to discontinue the study at any time, for any reason, and without any adverse effects. By signing the electronic informed consent and HIPAA authorization and checking the certification form on REDCap it is understood that participant dyads are fully aware of what participation entails including the usage and transfer of their PHI from CHOC network over to a UCI protected network and server.

Recruitment Setting: Potential participants will be identified through review of the Outpatient Infusion Center (OPI) and/or Cancer Institute appointment schedules at CHOC Children's. Subjects who are determined to be eligible by electronic review of the medical record will be approached by a trained research associate at their scheduled appointments in the OPI, Cancer Clinic, or Inpatient Oncology wing to discuss the purpose of the study, eligibility and study requirements. Contact information for study personnel and study information sheet will be provided to parent and child. The research associate will thoroughly describe the study and both the patient and parents will be asked if they are interested in participating. Patients and parents will be asked if they have any questions concerning the study and all questions will be answered thoroughly and candidly. If interested in the study, risks, benefits and alternatives to participation will all be explained and as part of eligibility criteria, children will be asked about pain experience in the previous month. Participants and children will also be informed that they are free to discontinue the study at any time, for any reason and without any adverse effects.

Primary Language of prospective subjects: Both English and Spanish speaking participants will be recruited for this study and all participants will be provided a study information sheet in either English or Spanish. Children must be English speakers as the intervention is based in English; parents may be either English or Spanish speakers. A researcher fluent in both English and Spanish will be available to answer any questions the participant may have. Spanish forms have been submitted to the IRB for approval

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Appendix 1

Threshold of Symptom Alerts

The MSAS uses the following thresholds to determine the severity of symptoms, the number of times the symptoms were reported based on the age of the participants. For this study, health care providers will be notified when one or a combination of symptoms are entered into the diary.

Pain Buddy Symptom Alert Table

Symptom	Ratings
MSAS 7-12	
Overall Pain Rating	≥ 7.5
Pain	≥ A medium amount (Frequency) AND ≥ A medium amount (Severity) AND ≥ A medium amount (Bothersome/Distressing)
Tired	Three consecutive entries of: Almost all the time (Frequency) AND Very tired (Severity) AND Very much (Bothersome)
Itching	Three consecutive entries of: Almost all the time (Frequency) AND Very itchy (Severity) AND Very much (Bothersome/Distressing)
Vomiting	Three consecutive entries of: ≥ A medium amount (Frequency) AND ≥ A medium amount (Bothersome/Distressing)
Sleep	Five consecutive entries of: ≥ A medium amount (Bothersome/Distressing)
Feeling Sad	Five consecutive entries of: ≥ A medium amount (Frequency) AND ≥ A medium amount (Severity) AND ≥ A medium amount (Bothersome/Distressing)
Worried	Five consecutive entries of: ≥ A medium amount (Frequency) AND Very worried (Severity) AND ≥ A medium amount (Bothersome/Distressing)
MSAS 12-18	
Overall Pain Rating	≥ 7.5
Pain	≥ A lot (Frequency) AND ≥ Moderate (Severity) AND ≥ Somewhat (Bothersome/Distressing)
Drowsiness, Difficulty Swallowing	≥ A lot (Frequency) AND ≥ Severe (Severity) AND ≥ Quite a Bit (Bothersome/Distressing)
Problems with Urination	≥ A lot (Frequency) AND ≥ Severe (Severity) AND ≥ Somewhat (Bothersome/Distressing)
Shortness of Breath	≥ Sometimes (Frequency) AND ≥ Moderately (Severity) AND ≥ Somewhat (Bothersome/Distressing)
Cough	Three consecutive entries of: ≥ A lot (Frequency) AND ≥ Severe (Severity) AND ≥ Somewhat (Bothersome/Distressing)
Numbness	Three consecutive entries of: Almost Always (Frequency) AND Very Severe (Severity) AND ≥ Quite a bit (Bothersome/Distressing)
Vomiting, Diarrhea, Dizziness, Itching	Three consecutive entries of: ≥ A lot (Frequency) AND ≥ Severe (Severity) AND ≥ Quite a Bit (Bothersome/Distressing)
Nausea	Three consecutive entries of: ≥ A lot (Frequency) AND ≥ Moderate (Severity) AND ≥ Quite a Bit (Bothersome/Distressing)
Constipation	Three consecutive entries of: ≥ Moderately (Severity) AND ≥ Quite a Bit (Bothersome/Distressing)
Headache	Three consecutive entries of: ≥ Sometimes (Frequency) AND ≥ Moderately (Severity) AND ≥ Somewhat (Bothersome/Distressing)
Mouth Sores	Three consecutive entries of: ≥ Moderately (Severity) AND ≥ Somewhat (Bothersome/Distressing)
Lack of Energy	Five consecutive entries of: ≥ Sometimes (Frequency) AND ≥ Moderately (Severity) AND ≥ Somewhat (Bothersome/Distressing)
Nervousness	Five consecutive entries of: ≥ A lot (Frequency) AND Very Severe (Severity) AND ≥ Quite a Bit (Bothersome/Distressing)
Feelings of Sadness	Five consecutive entries of: Almost Always (Frequency) AND Very Severe (Severity) AND Very Much (Bothersome/Distressing)

Sweats	<i>Five consecutive entries of:</i> Almost Always (Frequency) AND Very Severe (Severity) AND $\geq$ Quite a Bit (Bothersome/Distressing)
Swelling in Arms or Legs	<i>Five consecutive entries of:</i> Very Severe (Severity) AND Very Much (Bothersome/Distressing)
Changes in Skin	<i>Five consecutive entries of:</i> Very Severe (Severity) AND $\geq$ Quite a Bit (Bothersome/Distressing)



CHILDREN'S HOSPITAL OF ORANGE COUNTY
INSTITUTIONAL REVIEW BOARD

Authorization To Use, Create and Disclose Health Information for Research

Study Title: Pain Buddy Treating Pain in Children with Cancer: A 21st Century Innovative Approach

In this form, the word "you" means both the person who takes part in the research and the person who gives permission to be in the research.

Purpose of this Authorization

We are asking you to take part in the research described in the consent form for the study whose title is identified above. To do the research described, the research staff at CHOC needs to use, create and/or disclose your health information during the course of this study. By law, we have to tell you how we do this and get your permission. This form describes what we will do with your information. Please read it carefully. If you agree with it, please sign your name at the bottom. You will get a copy of this form after you have signed it.

Description of Health Information that will be Used/Disclosed

With your permission, the health information that will be used, created and shared includes:

- All information about you that is collected during the research study. This might include the results of tests or exams that become part of the study records; diaries and questionnaires that you might be asked to fill out as part of the study, audio recordings from the focus group/individual interview and/or other records from the study
- All health information in your medical records that is needed for this research study. These might include the results of physical exams, blood tests, x-rays, diagnostic and medical procedures, prescribed medications and your medical history.

Person/Organization Authorized to Receive Your Health Information

We may share your health information with people at CHOC who help with the research. We may also share your health information with certain people and groups outside of CHOC. These may include:

- Dr. Michelle Fortier and the University of California, Irvine as well as: The sponsor of the study, *National Cancer Institute*, and its representatives.

- Government agencies of the United States and foreign countries, review boards, and others who watch over the safety, effectiveness, and conduct of the research
- Other researchers when a review board approves the sharing of the health information
- Others, if the law requires

Duration of Authorization and Future Use of Health Information

This authorization will expire 50 years from the date you signed it unless you revoke (cancel or withdraw) it sooner. If you sign this form, we will use, create, and share your health information until the end of the research or until the expiration date of your authorization, whichever comes first.

Your information may also be useful for other research studies. We can only use your information again if the CHOC Institutional Review Board gives us permission. This committee may ask us to talk to you again before doing the research. But the committee may also let us do the research without talking to you again if we keep your health information confidential.

The study Sponsor may use your health information to analyze and evaluate the results of the study. The Sponsor may also reanalyze the results of the study at a later date and combine them with results of other studies. However, your name will never appear on any sponsor forms, reports or publications or in any future disclosures by the Sponsor.

Your Privacy Rights in Research

You do not have to sign this authorization form. If you choose not to allow us to use your protected health information, you cannot participate in this research study. You will not be able to receive any research-related treatment described in the study consent form. We will discuss any non-research alternatives available to you. No matter what you decide you will still get your doctor's care and will not lose any of the benefits you have now.

You may revoke this authorization at any time by notifying the principal investigator in writing at the address below. If you do revoke your authorization, any information previously disclosed cannot be withdrawn. Once information about you is disclosed in accordance with this authorization, the recipient may redisclose it and the information may no longer be protected by Federal privacy regulations. However, the recipient may be prohibited from disclosing substance abuse information under the Federal Substance Abuse Confidentiality Requirements.

IRB #: 181088

PI: Michelle Fortier, PhD

If you do revoke your authorization, you may need to leave the research study if all the necessary information has not been collected. We will tell you if this is the case. We may still use the information we have already collected. We need to know what happens to everyone who starts a research study, not just those people who stay in it.

A copy of CHOC's Notice of Privacy Practices will be given to you upon request.

Access to Protected Health Information Collected, Used, or Disclosed Under this Authorization

You have the right to see and copy your Personal Health Information related to the Study, by contacting the study doctor for as long as this information is held by CHOC. However, to ensure the scientific integrity of the Study, you agree that you may not be able to review some of your records related to the Study until after the Study has been completed.

Questions About this Authorization

If you have any questions, please ask the researcher. You can also call the CHOC Corporate Compliance Hotline at (877) 388-8588 with questions about the use of your health information.

Signature and Date

My signature below indicates that I am the parent/legal guardian of this child, and that he/she is not a ward of the state or other agency, that I am the Legally Authorized Representative (LAR) for the participant, or that I am a participant legally able to consent for myself. I have read the above information about the study, **Pain Buddy Treating Pain in Children with Cancer: A 21st Century Innovative Approach**. I agree to the use, creation, and sharing of my/my child's health information for purposes of the research study described in this form and the study consent form.

Name of Participant (printed)	Age
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Signature of Parent/Legal Guardian/Legally Authorized Representative (LAR) or Participant if 18 Years of Age or Older and able to sign	Date
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Printed Name of Parent/Legal Guardian/ Legally Authorized Representative (LAR) if Participant is under 18 Years of Age or unable to sign	Relationship
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Children's Hospital of Orange County
INSTITUTIONAL REVIEW BOARD

INFORMED CONSENT AGREEMENT

Pain Buddy Treating Pain in Children with Cancer: A 21st Century Innovative Approach

If you are a parent or legal guardian of a child who may take part in this study, permission from you is required. The assent (agreement) of your child may also be required. When we say "you" in this consent form, we mean you or your child; "we" means the study team and other staff.

You are being asked to take part in a research study. Before you give your consent to be a volunteer, it is important that you read the following information and ask as many questions as necessary to be sure that you understand what you will be asked to do. If you don't understand something in this consent form, please be sure to ask your study team to explain.

Investigators and Sponsor

Principal Investigator: *Michelle Fortier, PhD*

Co-Investigator(s): Haydee Cortes, BA, Lessley Torres, BA,

Sponsor: National Cancer Institute (NIH)

Human Research Participant's Bill of Rights

(For Medical Experiments)

The rights listed below are the right of every individual asked to participate in a research study.

You have the right:

1. To be told about the nature and purpose of the study.
2. To be told about the procedures to be followed in the research study, and whether any of the drugs, devices, or procedures is different from what would be used in standard practice.
3. To receive a description of any side effects, discomforts, or risks that you can reasonably expect to occur during the study.
4. To be told of any benefits that you may reasonably expect from the participation in the study, if applicable.
5. To receive a description of any alternative procedures, drugs, or devices that might be helpful, and their risks and benefits compared to the proposed procedures, drugs or devices.
6. To be told of what sort of medical treatment, if any, will be available if any complications should arise.
7. To be given a chance to ask any questions concerning the research study both before agreeing to participate and at any time during the course of the study.
8. To refuse to participate in the research study. Participation is voluntary. You may refuse to answer any question or discontinue your involvement at any time without penalty or loss of benefits to which you might otherwise be entitled. Your decision will not affect your right to receive the care you would receive if you were not in the experiment.
9. To receive a copy of the signed and dated written consent form and a copy of this form.
10. To be given the opportunity to freely decide whether or not to consent to the research study without any force, coercion, or undue influence.

QUICK SUMMARY OF RESEARCH STUDY

The purpose of this study is to examine the feasibility of the ambulatory monitoring protocol, called Pain Buddy, in documenting children's pain, symptoms and quality of life while receiving outpatient chemotherapy and effectiveness of Pain Buddy in reducing pain severity. We will also be looking at the types of medication that were taken to manage pain and symptoms from your electronic medical record as well as your patient experience data collected from NRC Health.

- You do not have to be in this study. Some other things you may be able to do are: Not participate
- If you join, you will be in this study up to 8 months (2 months actively and a follow up questionnaire 6 months after the end of the second month)
- You will be asked to complete questions about quality of life and how you are feeling at the beginning of the study, after 60 days, and at a 6 month follow up along with daily pain and symptom diaries twice a day for a consecutive 60 days.
- Benefits: Being in this study will not directly help you. We are hopeful information from this study might help others in the future
- The most important risks to know about are a potential loss of confidentiality.
- If you have any questions about or do not understand something in this form, you should ask the study doctor or study staff. You should also discuss your participation with anyone you choose to better understand this study and your options.
- Pain Buddy is not designed to provide medical advice nor is it a substitute for a nurse or doctor. If you are experiencing symptoms you would like to discuss, you need to call your doctor. If you are experiencing a medical emergency, please dial 911.

WHY IS THIS RESEARCH STUDY BEING DONE?

The purpose of this research study is to help researchers and healthcare providers better treat pain and disabling symptoms such as fatigue and nausea in children undergoing cancer treatment. Because of this, we want to understand how often children have pain and symptoms during cancer treatment, and find the best ways of controlling these symptoms. For this study we are using a native application, Pain Buddy, to measure children and/or teen's pain and symptoms. We will also look at the types of medications that were taken to manage pain and symptoms from your electronic medical record as well as your patient experience data collected from NRC Health.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Pain Buddy
Approximately 103 participants (parent-child dyads) will take part in the research at CHOC Children's and 103 participants at St. Jude Research Hospital. A total of 206 participants will be asked to participate across all study sites.
Focus Group/Individual Interviews
We will enroll 40 participants (parent-child dyads) at CHOC who previously participated in the Pain Buddy study.
We will enroll 24 participants (children/teens) at CHOC who previously participated in the Pain Buddy study. A total of 24 participants will be asked to participate across all study sites.

HOW LONG WILL THE STUDY GO ON?

The **Pain Buddy** study includes:

- 3 questionnaires which take about 30 minutes to complete, for a total of 90 minutes.
- Daily Diaries take 5 minutes to complete. Will complete two per day equaling 10 minutes a day for a total of 600 minutes over 60 days.

The **Focus Group/Individual Interview** includes:

- One, 60-minute focus group/individual interview, for a total of 60 minutes. And/or
- One, 30-minute focus group/individual interview, for a total of 30 minutes.

Inclusion Requirements:

You can participate in the **Pain Buddy** study if you meet the following inclusion criteria:

- Between the ages of 8-18 years
- Are within 16 weeks of first time cancer diagnosis
- Currently undergoing outpatient treatment for cancer
- Have experienced a pain score of 30 or greater on a visual analog scale in the past month
- Patients who are able to speak, read, and write in English. Parents who are able to speak, read, and write in English or Spanish
- Have internet access to use Pain Buddy on their mobile devices (the internet will be used to securely send the pain information to the research team).

You can participate in up to two **Focus Group/Individual Interview** sample studies if you meet the following inclusion criteria:

Pain Buddy usage Focus Group/ Individual Interview

- Between the ages of 8-18 years during your time of participation in the Pain Buddy Study
- Previously completed all parts of the Pain Buddy Study (T1, T2, T3).
- Patients who are able to speak, read, and write in English. Parents who are able to speak, read, and write in English or Spanish.

Social Support Focus Group/ Individual Interview

- Between the ages of 12-18 years during your time of participation in the Pain Buddy Study
- Previously completed Baseline of Pain Buddy Study (T1)
- Patients who are able to speak, read, and write in English.

Exclusion Requirements

You cannot participate in this study if you meet the following exclusion criteria:

- Cognitive impairment, such as a developmental delay that would impact the child's ability to use the Pain Buddy program.
- Children diagnosed with acute promyelocytic leukemia (APL) as the treatment protocols for these children are largely inpatient, precluding use of the intervention.

You cannot participate in the **Focus Group/Individual Interviews** sample study if you meet the following exclusion criteria:

- Did not previously participate or complete all required parts of the Pain Buddy study.
- Patients who cannot read, speak or write English. Parents- who cannot speak, read, or write English or Spanish (if applicable).

WHAT PROCEDURES ARE INVOLVED WITH THIS STUDY?

Before you can participate in the main part of the study...

You may need to have "screening" procedures. The screening process helps the researchers decide if you meet the study requirements listed below. The screening procedures include:

- Review of the appointment schedule at the Outpatient Infusion Center (OPI).
- Review electronic medical record to screen for exclusionary criteria listed above.

If the screening procedures show that you are eligible to participate in the study, and you choose to take part, then you will have the following procedures and tests done as listed below.

The main study tests and procedures include...

1. If you agree to participate, you will be randomly placed into the Pain Buddy group or the control group.
 - a. **Control Group:** Children and teens placed in the control group will complete pain and symptom diaries on Pain Buddy twice per day for 60 days and will receive standard of care for pain and symptom management (mediation, clinic visits etc.)
 - b. **Pain Buddy Group:** Children and teens placed in the Pain Buddy group will also complete pain and symptom diaries on Pain Buddy twice per day for 60 days and receive standard of care for pain and symptom management (mediation, clinic visits etc.). Children and teens placed in the Pain Buddy Group will also have his/her pain and symptom diary information forwarded to a healthcare provider, who can help you and your child figure out how to best manage his/her pain and symptoms. Children in the Pain Buddy condition will also receive cognitive-behavioral skills training to manage pain and symptom-related distress 1) when pre-determined symptom criteria are met and 2) when child initiates training and 3) Every week when application prompts child to complete the skill of the week.
2. Pain Buddy will be monitored by a member of the UCI research team and communicate alerts to the study healthcare provider. Alerts will be monitored and responded to Monday-Friday during daytime office hours. Any alerts triggered during evening/weekend times will be responded to the following business day.
3. Pain Buddy is not designed to provide medical advice nor is it a substitute for a nurse or doctor. If you are feeling symptoms you would like to discuss, you need to call your doctor. If you are experiencing a medical emergency, please dial 911. Participants in the control group can still call the Oncology clinic or the doctor on call to follow up on any symptoms they are experiencing.
4. We will also be reviewing your medical record to learn about the types of pain medications that you are prescribed.
5. Parent-Child Dyad Focus Group/Individual Interview- We will be asking 40 parent-child dyads to participate in a 60-minute audio recorded interview in order to understand barriers and facilitators to using Pain Buddy.
6. Children/Teens Focus Group/Individual Interview- We will be asking 24 children/teens to participate in a 30-minute audio recorded interview that asks for feedback on a social support website that could enhance Pain Buddy.

Time Point	Patient Tasks	Parent Tasks
Baseline (T1)	Questionnaires about general health, pain, anxiety and depression, quality of life	Questionnaires about child's general health, pain, anxiety and depression, quality of life
Completion of T1 questionnaire	\$50 Compensation	
Daily Diaries (60 Days)	- Daily pain diaries twice a day (1 in morning, 1 in afternoon) for a consecutive 60 days - Complete at least 10 out of 14 diaries per week.	No assessment
Skills training (60 days) (Pain Buddy Group ONLY)	Practice any 5 relaxation skills per week for 8 weeks (40 skills total).	No assessment

Month 2 (T2)	Questionnaires about general health, pain, anxiety and depression, satisfaction with program	Questionnaires about general health, pain, anxiety and depression, satisfaction with program
Completion of Daily Diaries	\$5 per week (if 10/14 diaries completed)	
Completion of Skills Training (Pain Buddy group only)	\$25 Compensation (if 40 skills completed at end of 60 days)	
Completion of T2 questionnaire	\$50 Compensation	
6-months post logging daily diaries (T3)	Questionnaires about general health, pain, anxiety and depression, satisfaction with program, saliva sample	Questionnaires about general health, pain, anxiety and depression, satisfaction with program, oral health/food log
Completion of T3 questionnaire	\$50 Compensation	

Focus Group/Individual Interviews

Time Point	Patient Tasks	Parent Tasks
4 to 6 months post T3 questionnaire. Parent child dyads may be asked to participate in a 60-minute audio recorded interview in order to understand barriers and facilitators to using Pain Buddy.	Discussion about experiences using Pain Buddy, average screen time, ways Pain Buddy can be improved, culturally adapted and reasons for high/low diary completion.	Discussion about experiences using Pain Buddy, average screen time, ways Pain Buddy can be improved and culturally adapted.
Completion of Parent-Child Dyad Focus Group/Individual Pain Buddy usage Interview	\$50 Compensation	
4 weeks post T1- Children/Teens may be asked to participate in a 30-minute audio recorded interview that asks how a social support could enhance Pain Buddy.	Discussion about how a social support component could enhance Pain Buddy.	No interview
Completion of Child/Teen Focus Group/Individual Social Support Interview	\$25 Compensation	

RETURN OF RESULTS

You will be informed of any significant findings that may influence your willingness to participate in this research study. You will also be informed if the study is discontinued before completion.

WHAT ARE THE POSSIBLE SIDE EFFECTS OR RISKS RELATED TO THE STUDY?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, researchers don't know all the side effects that may happen. Side effects may be mild or very serious.

You should talk to the research team about any side effects you experience while taking part in the study.

There is minimal risk to participating in this study. Risks and side effects related to the assessments include those which are:

Likely

- Mild discomfort or distress while remembering your cancer experience.

Less Likely

- Being uncomfortable or distressed while answering questions about yourself

Rare but serious

- Potential loss of confidentiality

Psychological discomforts: Possible discomfort(s) associated with the study are being uncomfortable or distressed while answering questions about your pain. If you do not wish to answer a question, you can skip it and go to the next question. If you do not wish to participate you can stop.

Incidental finding: There may be a risk of an unexpected finding from the study evaluations performed. If we find results that may affect your health, we will refer you to your primary care physician specialist.

Unknown risks: There may be risks related to the research that we don't know about yet. Any additional risks to which you may be exposed to, and any changes that are made to the study, as a result of any newly identified risks will be reported to you.

Confidentiality risk: With any study that collects personal health information or audio recording, there is a risk of loss of confidentiality of your health information. Persons conducting the study are required to comply with applicable laws and policies to protect your health information.

Benefits to Others or Society

There are no direct benefits from participation in the study. We are hopeful this study will benefit children who have pain due to chronic illness in the future.

WILL YOU BE PAID FOR TAKING PART IN THIS STUDY?

Compensation

You will be paid for taking part in this research study.

Control Group: You can earn \$5 per week for completing at least 10/14 core diaries per week. You can earn up to \$40 at the end of the 60 day diary period for completing the diary minimum. You will be paid \$50 in the form of a gift card for completing questionnaires at 3 different time points. There are 3 questionnaires to complete.. The total compensation for participation in the entire study is up to \$190).

Pain Buddy Group: You can earn \$5 per week for completing at least 10/14 core diaries per week. You can earn \$25 at the end of the 60 day diary period if you complete at least 40 skills training sessions (5 sessions per week. You will be paid \$50 in the form of a gift card for completing questionnaires at 3

different time points. There are 3 questionnaires to complete. The total compensation for participation in the entire study is up to \$215.).

Parent-Child Dyad Focus Group/Individual Interview: Parent-child dyads may be asked to participate in the focus group/individual interview. Those who agree to participate, will be paid \$50 in the form of a gift card after the interview is complete.

Child/Teen Focus Group/Individual Interview: Child/Teens may be asked to participate in a second focus group/individual interview. Those who agree to participate, will be paid \$25 in the form of a gift card after the interview is complete.

If you decide to withdraw from the study or are withdrawn by the research team, you will receive compensation for the questionnaires that you have completed.

The law requires that CHOC submit an IRS 1099 form for individuals to whom it provides compensation exceeding \$600 per calendar year. Compensation provided by this research study will count toward the annual total for this purpose.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

There will be no cost to you or your insurance company to participate in this study.

WHAT OTHER CHOICES DO YOU HAVE IF YOU DON'T WANT TO PARTICIPATE?

There are no alternative procedures available. The only alternative is not to participate in this study.

WHAT HAPPENS IF YOU WANT TO STOP TAKING PART IN THIS STUDY?

You are free to withdraw from this study at any time. **If you decide to withdraw from this study, you should notify the study team immediately.** The study team may also end your participation in this study if you do not follow instructions, miss scheduled visits, the study sponsor decides to stop the study or your safety and welfare are at risk.

If you experience any of the side effects listed above, if your health worsens, or if you are injured during the research, you may need to be withdrawn from the study, even if you would like to continue. The study team will make this decision and let you know if it is not possible for you to continue. The decision may be made to protect your safety and welfare, or because the research plan does not allow people who develop certain conditions to continue to participate.

If you choose to withdraw or are withdrawn from this research study, you may choose to end the continued use or disclosure of your protected health information (PHI) for research purposes. The request to end the use or disclosure of your PHI should be made in writing.

WHAT HAPPENS IF YOU ARE INJURED BECAUSE YOU TOOK PART IN THIS STUDY?

Emergency, Side Effects, Illness, or Questions About the Study

If you need medical treatment, get treatment and inform the person treating you that you are in this research study, and then let your study team know. If you have any questions about the study, or need to talk to the study team, you may call:

Monday – Friday 8:00am – 4:30pm **UCI Center on Stress & Health (714)456-0039**

You may leave a message with the secretary and the doctor will call you back.

Evenings, Weekends, & Holidays **CHOC Hospital 714-997-3000 or 800-992-2462 (CA only).**
Ask for the on-call physician for the **Oncology Department**. You may be asked to leave a message with the page operator, and the physician on-call will return your call as soon as possible.

If you are injured as a result of being in this study, CHOC will provide necessary medical treatment. The costs of the treatment may be covered by CHOC or the study sponsor, National Cancer Institute (NIH) or billed to you or your insurer just like other medical costs, depending on a number of factors. CHOC and the study sponsor do not normally provide any other form of compensation for injury, such as loss wages, disability, or discomfort. For more information about this, you may call the Office of Research Compliance at (714) 509-8869 or by email at ORC@choc.org.

HOW WILL INFORMATION ABOUT YOU AND YOUR PARTICIPATION BE KEPT?

Subject Identifiable Data

Identifiable information collected about you will be removed and replaced with a code. A list linking the code and your identifiable information will be kept separate from the research data. Personal identifiers will be retained 6 years following publication of data. Personal Identifiers will be used for recruitment purposes and to communicate with you during the course of the study.

Data Storage

Research data will be kept in paper format in locked file cabinets in our locked research office at the CHOC Commerce Tower at 505 S. Main Street, Suite 940, Orange, CA 92868. Only authorized individuals will have access to it.

Research data will be stored electronically on a secure password-protected UCI network.

Data Retention

The researchers plan to keep the research data indefinitely. Research data is de-identified

WHO WILL HAVE ACCESS TO MY STUDY DATA?

Information gathered about you while in this study will be kept confidential according to applicable laws and regulations by the study team, except that:

- Dr. Michelle Fortier and the University of California, Irvine and its representatives
- The Sponsor of the study, National Cancer Institute (NIH) and their representatives will receive information concerning the study and will have access to your medical records as they relate to this study.
- Certain agencies, either Federal or State may require your medical information concerning this study.
- Certain legal actions may require disclosure of your medical information.
- Your medical information may be released to the CHOC Institutional Review Board or its legally authorized representative.

While the study team will make every effort to keep your personal information confidential, it is possible that an unauthorized person might see it. We cannot guarantee total privacy.

Future Research

Any information shared for future research will **not** include your name or other personal identifying information.

ClinicalTrials.gov

ClinicalTrials.gov is a Web site that provides information about clinical trials. A description of this clinical trial will be available on <http://www.clinicaltrials.gov/>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Certificate of Confidentiality

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health (NIH). With this Certificate, researchers cannot be forced to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by National Cancer Institute which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

ARE THERE OTHER ISSUES TO CONSIDER IN DECIDING WHETHER TO PARTICIPATE IN THIS STUDY?

Investigator Financial Conflict of Interest

Your physician and others concerned with this study will not be reimbursed for their time and expense of doing this research

Participant Rights

You are agreeing to be in this research study by your own choice. You can decide not to be in the study at all or you can decide to stop being in the study even after the study has started. No matter what you decide you will still get your doctor's care and won't lose any other benefits you have now. You also won't be giving up any of your legal rights by signing this consent form.

It is important that you understand the details about this study. If you have any questions that haven't been answered, please be sure to ask the study team.

If you have any questions about your child's rights as a participant in a research study, please contact the CHOC Institutional Review Board for the protection of research participants through:

Office of Research Compliance
(714) 509-8869

This research project has been reviewed by an institutional review board for the protection of the rights of human participants in research projects, in accordance with federal regulations.



Children's Hospital of Orange County
INSTITUTIONAL REVIEW BOARD
PEDIATRIC ASSENT FORM

NOTE: A Pediatric Assent Form is necessary for patients 7-11 years of age.

Study Title: Treating Pain in Children with Cancer: A 21st Century Innovative Approach (Pain Buddy)

- I understand that I am being asked to be in this research study because my doctor and his/her helpers want to know what things make children feel better when they are getting cancer treatment.
- I understand that I will be asked to answer questions about how I am feeling at the beginning of the study, after 60 days, and at a 6 month follow up.
- I understand that I will complete Pain Buddy 2 times every day, once in the morning and once in the afternoon for 60 days.
- I understand that my parents will also answer questions about how they are feeling.
- I understand that I might be asked to talk about how much I liked and used Pain Buddy in a recorded interview.
- I understand that my medical record will be reviewed to learn about the type of medications I take.
- I understand that I may change my mind about being in this study and that nobody will be angry with me.
- I understand that Pain Buddy is not designed to replace my nurse or doctor.
- I understand that if I am feeling symptoms I would like to talk about I should call my doctor.
- I understand that if I am having a medical emergency I should dial 911.
- I understand that I can ask questions about what my doctor and his/her helpers are doing and things will be explained to me in a way that I will understand.
- I understand that the doctor doing this research is Dr. Fortier and I can call her at (714) 480-0039 if I need to ask a question.
- I understand that if I can't contact Dr. Fortier and I have questions or a complaint about the research study I can call the CHOC Institutional Review Board at (714) 509-8869.

Signature of 7 to 11 Year Old Participant

Date

Signature of Person Obtaining Consent
(Principal or Co-Investigator)

Printed Name

Date

☐ the child is not capable of providing assent in the Investigator's opinion due to altered mental status or physical incapacity, specifically: _____

DO YOU AGREE TO PARTICIPATE IN THIS STUDY?**Signature and Consent**

My signature below indicates that I am the parent/legal guardian of this child, and that he/she is not a ward of the state or other agency, that I am the Legally Authorized Representative (LAR) for the participant, or that I am a participant legally able to consent for myself. I have read the above information about the study **Treating Pain in Children with Cancer: A 21st Century Innovative Approach (Pain Buddy)**. I have had a chance to ask questions to help me understand what will be expected in this study. I agree to be in the study and I have been told that I can change my mind later if I want to. I have been told that by signing this consent form I am not giving up any of my legal rights. I have been informed that I will be given a signed and dated copy of this agreement which includes the Human Research Participant's Bill of Rights for my records.

Name of Participant (printed)

Age

Signature of Parent/Legal Guardian/Legally Authorized Representative (LAR) #1
or Participant if 18 Years of Age or Older and able to sign

Date

Printed Name of Parent/Legal Guardian/

Relationship

Legally Authorized Representative (LAR) #1 if Participant is under 18 Years of Age or unable to sign

Assent for Participants Ages 12 Through 17

My signature below means that I have read the above information about the study, **Treating Pain in Children with Cancer: A 21st Century Innovative Approach (Pain Buddy)**. I have had a chance to ask questions to help me understand what will be expected of me in this study. I agree to be in the study and I have been told that I can change my mind later if I want to. I have been told that by signing this consent form I am not giving up any of my legal rights. I have been informed that I will be given a signed and dated copy of this agreement and of the Human Research Participant's Bill of Rights for my records.

Signature of Participant

Date

A witness signature is required only if: (Researchers: check all that apply)

- ☐ Consent is obtained from the subject using the Short Form process, as approved by the IRB.
- ☐ The subject has decision-making capacity, but cannot read, write, talk or is blind.
- ☐ The subject's legal guardian/legally authorized representative (LAR) cannot read, write, talk or is blind.
- ☐ The IRB specifically mandated a witness signature for this study (e.g., high risk and/or invasive research procedures).

Note: The witness must be impartial (i.e. **not** a member of the participant's family, **not** a member of the study team).

For the witness/interpreter:

I confirm that the information in this consent form was accurately explained to and apparently understood by the subject or legally authorized representative and that informed consent was given freely.

Signature of Witness/Interpreter **Date**
(Record Interpreter Identification Number if phone/remote interpretation services used)

Printed Name of Witness/Interpreter
(If no witness signature is required, this witness signature section of the consent form may be left blank)

Investigator Signature

My signature below means I have fully explained the research study described by this form. I have answered the participant's and/or parent's/guardian's/Legally Authorized Representative's questions and will answer any future questions to the best of my ability. I will tell the person(s) taking part in this research of any changes in the procedures or in the possible harms/possible benefits of the study that may affect their health or their willingness to stay in the study.

Signature of Person Obtaining Consent **Printed Name** **Date**
(Principal or Co-Investigator)