Application of behavioral economic strategies to enhance recruitment into a pediatric randomized clinical trial

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PROTOCOL TITLE: Recruitment and behavioral economic strategies

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Revision History

Revision #	Version Date	Summary of Changes	Consent Change?

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1.0 Study Summary

Study Title	Application of behavioral economic strategies to enhance recruitment into a pediatric randomized clinical trial
Study Design	Prospective, randomized, double-blind clinical trial
Primary Objective	To determine the impact of the application of behavioral economic strategies on recruitment of pediatric patients into a randomized clinical trial assessing the impact of technology-based interventions on postoperative pain management
Secondary Objective(s)	N/A
Study Population	Patients 12-18 years of age presenting for surgery that requires postoperative admission and usually requires narcotic administration.
Sample Size	800
Study Duration	3 years

2.0 Methods

2.1 One of the largest challenges faced in clinical trials is patient recruitment. It is often associated with one of the largest costs of the trial and inability to enroll in a clinical trial can ultimately result in under-enrollment and failure of the trial to yield results.[1] According to data from the Institute of Medicine, more than 40% of National Cancer Institute-sponsored clinical trials do not reach the minimal accrual of patients when enrollment closes due to challenges with recruitment.[2] Underpowering studies because of enrollment difficulties will result in clinical trials that are not appropriately powered to answer the initial hypothesis, often resulting in participants being exposed to the risks associated with a clinical trial without any actual benefit.[3] Furthermore, challenges with recruitment may result in a very homogeneous study population, resulting in difficulty in applying results of a study to a larger, broader population.1 Over time, many strategies have been attempted to help enhance clinical trial enrollment, including offering financial incentives.[4] Financial incentives, however, may not be the best way to enhance enrollment as high financial incentives are often perceived to be associated with high risk and there are ethical concerns about payments made to subjects.[5]

2.2 Despite plaguing clinical trials, there are not many strategies that have effectively been shown to increase recruitment and enrollment into clinical trials.[6] A recent meta-analysis attempted to identify

strategies to improve recruitment into trials. Of the 72 strategies assessed in the literature, only two showed some benefit: Using open trials rather than blinded, placebo trials; and using telephone reminders to people who do not respond to a mailed invitation.[6] The first is obviously contrary to the goal of a study and may influence its results and the second showed a very modest improvement of only 6% (95% CI 3% to 9%). As such, no clear strategies currently exist.

2.3 Behavioral economics (BE), a method of economic analysis that applies psychological insights into human behavior to explain economic decision-making, has broad applicability and its techniques offer a novel way that may be applied to try to help enhance study recruitment and enrollment. While many often assume that BE relates to how to optimize use of financial incentives and penalties, BE strategies can also provide insight into messaging and presentation of information, such as recruitment for clinical trials. Few studies have assessed the use of BE techniques for clinical trial recruitment and enrollment, including "nudges" and framing, to help enhance patient enrollment.[1,7,8] To our knowledge, this type of study has never been done in a pediatric population, which increases the complexity of enrollment as patients themselves are often not the ones consenting to participate and not only do the participants need to be convinced to participate but also their parent(s).[6] We are applying BE-based messaging and presentation strategies to patient recruitment and determining whether these strategies may enhance patient recruitment into a pediatric randomized clinical trial. We are looking at recruitment into both the intervention (VR-BF) as well as control (Manage My Pain) arm because in order for a trial to be successful, you must be able to successfully recruit not only into the intervention arm, but also into the control arm.

2.4 The goal of this study is to determine the impact of using a BE-informed recruitment video versus a similar recruitment video using a standard biological approach on teenagers' decision to enroll in a clinical study assessing the use of technology-based interventions to improve postoperative pain management into both the intervention as well as control arm. We will also assess the impact of the BE-informed script on the intention to adhere to the treatment, acceptability of the intervention, and perception of treatment burden, risk, and perceived efficacy assessed via patient survey. We hypothesize that using the BE-informed approach will enhance enrollment as well as the intention to adhere to treatment, acceptability of the intervention, and perceived efficacy while decreasing the perception of treatment burden and risk.

2.5 This is a single center, prospective, randomized, double-blinded clinical trial that will be conducted in two stages. Phase 1 will focus on patients that would be enrolled into a biofeedback-based virtual reality (VR-BF) arm and Phase 2 will focus on patients that would be enrolled into the control arm of a clinical trial with a control intervention, Manage My Pain application. Prior to beginning recruitment in Phase 1, we will create a script and film the videos associated with those scripts. Information learned in Phase 1 may result in slight modifications of the script and videos.

2.6 Patients will be identified prior to surgery by assessing the operating room schedule after being booked for surgery. In Phase 1, for the VR-BF intervention, patients and parents will be approached and asked if they would like to hear about an upcoming study with a technology that is under development but not yet available but that we would like to obtain their feedback as the study will involve patients having surgery similar to the one that he/she is undergoing. Although the literature suggests that patients should not be told that this is a hypothetical study to avoid bias ("self-prophecy") associated with telling them they do not have the opportunity to participate in the study,[1,7] it would be unethical in this situation to tell a family about a study that would potentially be of interest and then tell them that the patient is not eligible as the study does not exist, particularly in the stressful setting they are. However, to minimize social desirability bias, they will be explicitly be informed that the survey is one-time and anonymous and that answers/opinions will not impact clinical care in any capacity. In addition, the survey will be done on paper and placed by the patient into a collection box with other papers/surveys, emphasizing the anonymity of results and avoiding things like time stamps on electronic records that may make anonymity less believable to the patient and family. Patients in Phase 1 will be randomized to 1 of 2 groups: VR-BF recruitment video using a BE-based script and one using a standard biological approach. A total of 400 patients, 200 per group, will be recruited in this phase. Following agreement to participate and consent, subjects will be shown 1 of the 2 recruitment videos based upon randomization and then given a standardized survey assessing the decision to enroll and other components of acceptability.

2.7 The process for Phase 2 will be the same as Phase 1 with the exception of how the families are approached. Because Manage My Pain is commercially available and free on the app store (iOS and Android platforms), patients and families will be asked if they would like to hear about an upcoming study being offered to patients having surgery similar to the one that their child is undergoing. They

will not explicitly be told that this is a hypothetical study to avoid the "self-prophecy" bias[1,7] but, in order to avoid disappointment and the ethical concerns, they will be informed that they are free to download the application and use it if they so desire at the conclusion of the study visit.

2.8 The surveys will not collect any data that may identify the patient to remain anonymous.

3.0 Data Banking

3.1 All data collected during this study will be stored in a secure location, and only the collaborators directly involved with this research project will have access to this information. In addition, all electronic files will be stored on a secure, password-protected network.

3.2 Data will be stored for 6 years after the study is completed.

3.3 Data will not be stored for future use.

4.0 Inclusion and Exclusion Criteria

4.1 *Inclusion:*

- Patients between the ages of 12-18 years of age
- Patients able to read, understand, and speak English
- Patients undergoing surgery requiring postoperative admission
- Patients undergoing surgery that requires narcotic administration

4.2 *Exclusion:*

- Patients outside of the age range
- Patients with history of developmental delay, uncontrolled psychiatric conditions, or neurological conditions (i.e., epilepsy, motion sickness, nausea/vomiting)
- History of severe vertigo or dizziness
- History of chronic pain
- Patients that use opioids or benzodiazepines chronically
- Patients with conditions that would preclude placement of a VR headset, including craniofacial abnormalities or undergoing surgeries of the head and neck.

5.0 Vulnerable Populations

5.1 This research involves children but does not involve greater than minimal risk under 21 CFR §50.51/45 CFR §46.404.

5.2 All data collected during this study will be stored in a secure location, and only the collaborators directly involved with this research project will have access to this information. In addition, all electronic files will be stored on a secure, password-protected network.

5.3 The subjects will not be exposed to greater than minimal risk.

5.4 Parents/legal guardians will be asked to give verbal informed consent and children over the age of 9 years will provide verbal assent.

6.0 Number of Subjects (Records)

6.1 800.

7.0 Recruitment Methods

7.1 No recruitment materials will be used. Patients will be identified using the operating room schedule. The study coordinator, PI, or sub-investigators will screen and identify appropriate participants based on the operating room schedule's noted location of their preop room. No names or other identifying information will be recorded. Screening participants will occur according to the protocol defined inclusion and exclusion criteria.

8.0 Withdrawal of Subjects

8.1 Patients may withdraw from the study at any time.

8.2 There are no anticipated circumstances under which subjects will be withdrawn from the research without their consent.

9.0 Data Management and Confidentiality

9.1 All data collected during this study will be stored in secure password protected computer files (REDCap) and secure locked cabinets to which only trained members of the research team and collaborators directly involved with this research project will have access.

9.2 The data will be stored for the duration of the study and retained for 6 years after the study is completed per NCH as this meets both HIPAA and OHRP regulations.

9.3 No data will be transmitted to or from external institutions.

9.4 Subjects will be assigned a study identification number and no identifiers will be entered into REDCap.

10.0 Provisions to Protect the Privacy Interests of Subjects

10.1 With this being an anonymous survey, there will be nothing linking subjects to their survey responses. Subject information will not be given to any other investigators. Subjects and their information will be closely monitored and guarded by study staff; there will be limited access to patients and their information by trained study staff; and subject information will only be shared and discussed between study staff specific to this study.

10.2 No PHI will be recorded for this study from patient records. Access to the patients' charts will be limited to only recruitment phase to

assess inclusion/exclusion criteria by the research team who have completed all the necessary training.

10.3 We will only be publishing de-identified research information.

11.0 Economic Burden to Subjects

11.1 There will be no costs to subjects and subjects will not receive any compensation.

12.0 Consent Process

12.1 The consent process will begin in the preoperative surgery unit on the day of surgery, by PI, Sub-Investigators, Study Coordinators, and/or trained research staff.

12.2 The study will be thoroughly explained to the patient and their family. There will be ample time allotted for questions and answers. An explanation of voluntary participation will take place, and the family will be asked if they are interested in participating in the study. The patient will then be enrolled in the study with the understanding that they can elect to stop the study and be withdrawn from the study at any time.

12.3 As this is a minimal risk study and only involves completing a survey, we are requesting a waiver of documentation of informed consent. To keep this study completely anonymous with no PHI collected, it would not be feasible to obtain a signed, written, consent.

12.4 Potential subjects will be provided a written information sheet and verbal consent and assent will be obtained.

13.0 Setting

13.1 Potential subjects will be identified from the surgery schedule in Epic and recruited from the pre-op area of the surgery unit. Surveys will be completed on paper in the pre-op area which will be collected and submitted into REDCap.

14.0 Resources Available

14.1 The research team is comprised of a PhD research scientist, a research nurse, a research coordinator, and two research associates. All team members will meet with the PI, co-investigators, and the research team for a study start up meeting for training about the protocol, research procedures, and their duties and functions.

15.0 Protected Health Information Recording

1.0 Indicate which subject identifiers will be recorded for this research.

☐ Name
☐ Complete Address
☐ Telephone or Fax Number
☐ Social Security Number (do not check if only used for ClinCard)
☐ Dates (treatment dates, birth date, date of death)
☐ Email address , IP address or url
☐ Medical Record Number or other account number
☐ Health Plan Beneficiary Identification Number
☐ Full face photographic images and/or any comparable images (x-rays)
☐ Account Numbers
☐ Certificate/License Numbers
☐ Vehicle Identifiers and Serial Numbers (e.g. VINs, License Plate Numbers)
☐ Device Identifiers and Serial Numbers
☐ Biometric identifiers, including finger and voice prints
☐ Other number, characteristic or code that could be used to identify an individual
☒ None (Complete De-identification Certification Form)

2.0 Check the appropriate category and attach the required form* on the Local Site Documents, #3. Other Documents, page of the application. (Choose one.)

☐ Patient Authorization will be obtained. (Include the appropriate HIPAA language (see Section 14 of consent template) in the consent form OR attach the HRP-900, HIPAA AUTHORIZATION form.)
☒ Protocol meets the criteria for waiver of authorization. (Attach the HRP-901, WAIVER OF HIPAA AUTHORIZATION REQUEST form.)
☐ Protocol is using de-identified information. (Attach the HRP-902, DE-IDENTIFICATION CERTIFICATION form.) (Checked "None" in 1.0 above)
☐ Protocol involves research on decedents. (Attach the HRP-903, RESEARCH ON DECEDENTS REQUEST form.)
☐ Protocol is using a limited data set and data use agreement. (Contact the Office of Technology Commercialization to initiate a Limited Data Use Agreement.

*Find the HIPAA forms in the IRB Website Library, Templates.

Attach the appropriate HIPAA form on the "Local Site Documents, #3. Other Documents", page of the application.

3.0 How long will identifying information on each participant be maintained?

We will access PHI for recruitment purposes only, there will be no recorded identifying information. Survey results will be retained for 6 years after the research is complete which meets both HIPAA and OHRP regulations.

4.0 Describe any plans to code identifiable information collected about each participant. Subjects surveys will be assigned a study identification number and no identifiers will be entered into REDCap. There is no identifying information being recorded.

5.0 Check each box that describes steps that will be taken to safeguard the confidentiality of information collected for this research:

☒ **Research records will be stored in a locked cabinet in a secure location**

☒ **Research records will be stored in a password-protected computer file**

☐ **The list linking the assigned code number to the individual subject will be maintained separately from the other research data**

☒ **Only certified research personnel will be given access to identifiable subject information**

6.0 Describe the provisions included in the protocol to protect the privacy interests of subjects, where "privacy interests" refer to the interest of individuals in being left alone, limiting access to them, and limiting access to their information. (This is not the same provision to maintain the confidentiality of data.) Subject information will not be given to any other investigators. Subjects and their information will be closely monitored and guarded by study staff; there will be limited access to patients and their information by trained study staff; and subject information will only be shared and discussed between study staff specific to this study

Confidential Health Information

1.0 Please mark all categories that reflect the nature of health information to be accessed and used as part of this research.

☒ Demographics (age, gender, educational level)
☒ Diagnosis
☐ Laboratory reports
☐ Radiology reports
☐ Discharge summaries
☒ Procedures/Treatments received
☒ Dates related to course of treatment (admission, surgery, discharge)
☐ Billing information
☒ Names of drugs and/or devices used as part of treatment

☐ Location of treatment
☐ Name of treatment provider
☒ Surgical reports
☒ Other information related to course of treatment
☐ None

2.0 Please discuss why it is necessary to access and review the health information noted in your response above.
It is necessary to review the above health information to enable us to identify our patient population, ensure they meet the study inclusion and exclusion specifications. No confidential health information for use of recruitment will be recorded.

3.0 Is the health information to be accessed and reviewed the minimal necessary to achieve the goals of this research? ☒ Yes ☐ No

4.0 Will it be necessary to record information of a sensitive nature? ☐ Yes ☒ No

5.0 Do you plan to obtain a federally-issued Certificate of Confidentiality as a means of protecting the confidentiality of the information collected? ☐ Yes ☒ No