Study Protocol and Statistical Analysis Plan

Title of Study: Parent Resource About Pediatric Clinical Trials
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Study Protocol

Objectives:

To develop and test the effectiveness and safety of medical and behavioral treatments for children and adolescents, pediatric clinical trials are needed. However, some clinical trials experience difficulty with recruitment of families due to a number of reasons, such as time or travel limitations, potential risks to child, mistrust, or lack of information. Providing relevant and high-quality information to parents can positively contribute to decision-making as well as recruitment and enrollment in future clinical trials. The Pediatric Clinical Trials (PCT) Pocket Guide is an interactive, online resource designed to increase parents' awareness and understanding of clinical research and their ability to communicate with others about research, and willingness to participate in a clinical trial. The objective of this project is to examine the feasibility of the PCT Pocket Guide in a randomized controlled trial with parents of children between the ages of 7 and 17 years. Parents will complete pre- and posttest assessments, which will provide information on the acceptability, appropriateness, and feasibility of the PCT Pocket Guide and a preliminary test of the Pocket Guide's efficacy for improving outcomes related to knowledge, attitudes, self-efficacy, trust, and willingness and likelihood of participating in pediatric clinical trials.

Design:

The study type is interventional and the study model is parallel assignment with a 1:1 allocation ratio and superiority framework to examine the feasibility of the PCT Pocket Guide. The randomized controlled trial will be conducted online at two time points: 1) baseline/pretest and 2) posttest (two weeks after pretest). The study questionnaires will be programmed into an online data collection system. The resources (intervention and active control) will also be completed online by participants. Participants will be randomized, stratifying based upon race/ethnicity (white and not Hispanic/Latino; nonwhite and/or Hispanic/Latino) to one of two conditions: 1) intervention (access to PCT Pocket Guide) or 2) active control (access to control materials compiled from a NIH-supported website). Participants are randomized and enrolled based on: 1) time study forms (i.e., consent) were completed, 2) confirmation of email addresses, 3) their reported demographics collected in the eligibility screener questions, 4) address verification, and 5) indication that they learned about the study from one of the targeted school districts. One of the Co-Principal Investigators will generate the allocation sequences using a random number generator in Excel, assign participants to condition (either intervention or active control) according to those sequences, and enroll participants in the study. The allocation sequence will be stored in a folder on a secure, password-protected server. All participants will be assigned a unique ID number that will be associated with their data (questionnaires; resource use) in place of their name. All personally identifiable information (PII) will be saved on iRT's password protected server, and kept separate from data.

Methods:

Sample and Recruitment.

Parents of children aged between 7 and 17 years will be recruited for the study from across the United States. To be eligible to participate in the study, the following criteria must be met: a) adult participant is a parent or legal guardian of adolescent participant child between ages 7 and 17; b) parent has access to a computer or tablet or smart phone with internet connection (as the resources and questionnaires are web-based); c) participant's child attends school where recruitment flyers have been sent or report that they heard about the study from one of the study recruitment partners; 4) parent is fluent in English or Spanish; and 5) parent has not allowed their child to participate in a clinical trial in the past. A study recruitment website will contain information about the research study and study team contact information that interested parents can review. The website will include a link to the study's eligibility screening questions. Parents will be asked to indicate their race, ethnicity, sex, and child/children's ages to assist in ensuring a diverse sample of participants. Parents will also be asked to respond to questions about previous clinical trial participation and trust related to clinical trials. Parents will also be asked which language they would prefer to use for the study (English or Spanish) and this information will be used as part of the enrollment process to enroll eligible parents in the study in their preferred language. Parents will also be asked where they heard about the study (e.g., social media, school, community or health organization) and will be asked to specify which school or organization. Study flyers will be used to recruit parents; we will identify school districts with diverse student populations and share the recruitment flyers via PeachJar, a digital flyer service within school districts. The English versions of the study materials and resources will be translated into Spanish.

Procedure.

Parents who are eligible to participate in the study will be given access to the online consent form. Parents will read the consent form and provide online consent by typing their names into a text box, providing contact information, and clicking a button to indicate consent. They will have the option to download and/or print the forms to retain a copy for their files. Interested participants who decide to complete the forms will be told that in an attempt to have a diverse sample, they may not be invited to participate. Potential parents will be provided with the contact information of the researchers and may contact them to ask any questions they may have about the study. If they contact the research team and have not yet been screened for eligibility, they may be screened using the same set of questions on the recruitment website over the phone with a project staff member. On the consent form, participants will be asked for their preferred email address to receive study communications and incentives (i.e., gift cards) over the study period. Before receiving communications at this email address, they will need to verify that they can receive emails at this address by clicking a link that is emailed to them. Parents will also be asked on the consent form to agree to receiving study communication via text. Before receiving text communications at their phone number, they will need to verify that they can receive texts at their number by clicking on the verification link that is sent via SMS message. Only parents with completed study forms will be permitted to participate in the study. iRT project staff will

determine whether or not the address the parent has provided in the consent form is real such as a Google search.

If there is space in the study, consented and verified participants will be randomly assigned to either the intervention group or active control group based on a randomly generated number table. When the study starts, parents will receive an enrollment email/text from the study management system via the parent's email address (and text message) with a link for the participating parent to complete the online parent pretest questionnaire within one week. If the parent completes the questionnaire, they will be eligible for a $20 gift card. Upon completion of the pretest questionnaire, parents will receive a message at the end of the questionnaire informing them of their next steps in the research study.

a. Participants in the intervention group will then be provided via email/text with a link to access the resource (PCT Pocket Guide). They will be asked to review the resource within two weeks.
b. Participants in the active control group will be provided via email/text with a link to access the control materials [articles and videos compiled from a NIH-supported website (Children and Clinical Studies) into one online resource]. They will be asked to review the resource within two weeks.

Project staff members will monitor resource usage by groups through the LMS. Parents who complete the resources within 2 weeks will receive a $25 gift card. Approximately two weeks after completing the pretest questionnaire, participants will receive an email and text with a link to access to their online posttest questionnaire. This questionnaire will include the same questions and instructions at pretest as well as consumer satisfaction questions. If the parent completes the questionnaire, they will receive a $30 gift card. Participants will receive automatic email/text reminders from the study management system if they have not completed the questionnaires or not accessed their assigned online resource.

Measures.

Implementation

The Learning Management System (LMS) will record the amount of time that participants spend with the parent resource (PCT Pocket Guide; active control) and the specific components that were reviewed.

Consumer Satisfaction

Data will be collected on participant feedback about the resource they review through a posttest consumer satisfaction questionnaire (CSQ). The CSQ will consist of the Acceptability of Intervention Measure (AIM), Intervention Appropriateness Measure (IAM), and Feasibility of Intervention Measure (FIM), which are 4 items each using a 5-pt. Likert scale (1=Completely disagree to 5=Completely agree) and have good discriminant validity and reliability (Weiner et al., 2017). Higher scores indicate greater acceptability, appropriateness, and feasibility. Participants will also be asked to rate their satisfaction with the resource's content, format, and usability using a 5-point Likert scale (1 = Strongly disagree to 5 = Strongly agree) with higher

scores indicating greater satisfaction with the resource. Participants will also respond to open-ended questions about what they liked best and least and any suggestions for changes for their assigned resource.

Outcomes

Likelihood of participation in clinical trials. Parents will be asked to respond to one question about the likelihood of allowing their child to participate in a clinical trial (i.e., "If your child were asked to be in a clinical trial, how likely would you be to let them participate?") and will respond using a 5-point Likert scale (1 = Not likely at all; 2 = Not very likely; 3 = Moderately likely; 4 = Very likely; 5 = Extremely likely). Parents will also be asked to respond to one question about the likelihood of their fear preventing them from allowing their child participate in a clinical trial (i.e., "How likely is it that your fearful or anxious feelings could stop you from allowing your child to participate in a clinical trial in the future?"). Parents will respond using a 5-point Likert scale (1 = Not likely; 2 = Somewhat likely; 3 = Moderately likely; 4 = Very likely; 5 = Extremely likely).

Willingness to participate in a clinical trial. Parents will review up to five research protocols related to a fictitious disease ('meditis') and respond to questions about their willingness to let their child participate in each research study (i.e., "If your child had meditis, would you agree to enroll them in this study?"; 1 = Definitely not to 7 = Definitely yes; and "If you had to say for sure, what would your answer be?"; 0 = No; 1 = Yes). Parents can also describe the reason for their decision in an open-ended space. Parents will also be asked about decision-makers in the decision to participate (i.e., "Who should make the final decision on whether or not your child will participate in this research study?"; 1 = my child; 2= mostly my child; 3 = joint decision; 4 = mostly me; 5 = me). The final two questions will ask about the risk and benefits of participating in each study (i.e., "Overall, how risky is this study for your child?"; "Overall, how beneficial is this study for your child?"; 1 = Not at all to 7 = Extremely). This measure is adapted from Brody et al. (2005).

Knowledge. This measure will be created for the purposes of this study based on the content in the parent resource. Parents will respond to fact-based questions in multiple choice format that assess their knowledge about clinical research (e.g., "What does giving assent mean?"; "Once your child agrees to be in a clinical trial, can they stop before the trial is over?").

Familiarity with clinical trials. Parents will be asked to respond to one question about their familiarity with clinical trials ["How much do you know about pediatric clinical trials (research studies with children under 18)?"; 1 = I don't know anything; 2 = I know a little about them; 3 = I know some things about them; 4 = I know a lot about them; 5 = I know all there is to know about them.]

Attitudes and beliefs. Six items will assess their positive attitudes about clinical trials (e.g., How do you feel about kids participating in clinical trials?; 1=Not good at all; 2=Not very good; 3=Not sure; 4=Good; 5=Very good; α=.91; adapted from Madsen, Mirza, Holm, Hilsted, & Riis, 2002) and five items will assess their beliefs about positive aspects of pediatric clinical research (e.g., I believe that clinical trials can help kids; 1=Strongly Disagree; 5=Strongly Agree).

Decision Self-Efficacy. To assess self-efficacy for making decisions, parents will be asked to respond to 11 questions including confidence in obtaining information, asking questions, and making an informed decision ("Get the facts about the risk and side effects of each choice."). These items will be adapted to reflect a decision about their child's participation in a clinical trial. Parents will respond to each question using a 5-point Likert scale (0 = Not at all confident; 4 = Very confident; adapted from O'Connor, 1995).

Research trust/mistrust. Parents will be asked to respond to 10 items using a 5-point Likert scale (1 = Strongly Disagree; 5 = Strongly Agree) to assess research trust/mistrust. The measure has four factors, including General Trustworthiness; Perception of Deception; Perception of Exploitation; and Perception of Discriminatory Treatment (Smirnoff et al., 2018).

Statistical Analysis Plan

Data will be analyzed using SAS 9.4.

Preliminary analyses. Psychometric analyses will be conducted to examine the reliability, validity, and distributions of key variables and scales. Handling variables with poor reliability or validity will include modification or elimination of such variables from the analysis data sets. Variables with noticeably skewed distributions will be transformed or categorized to reduce the impact of non-normality on subsequent analyses. Descriptive statistics will also be conducted to examine the distributions, correlations, means, and standard deviations of the outcome variables. Preliminary analysis will include a test of equivalency between the intervention and control groups on demographic characteristics and baseline levels of primary outcome variables using chi-squared analyses for categorical variables and t-tests for continuous variables. Any characteristics that are nonequivalent will be added as covariates in the main analyses. Depending on the level of missingness, missing data will be multiply imputed at the item level. The imputation model will be estimated using the PROC MI procedure in SAS and will include all outcome items and demographic characteristics that will aid in estimating missing data values. Main analyses will be conducted on each of the imputed datasets.

Main Analyses. Parents' reports on the acceptability (AIM), appropriateness (IAM), and feasibility (FIM) of both the intervention (PCT Pocket Guide) and active control (NIH-supported website materials) will first be examined through descriptive statistics. Group mean scale scores greater than 3.0 will indicate more than a moderate amount of acceptability, appropriateness, and feasibility for each resource. Next, ANCOVAs will be used to compare AIM, FIM, and IAM scores looking at main effects of condition as well as interactions (parent gender, parent race/ethnicity, child age, research mistrust), including relevant covariates from the preliminary analyses. We will examine the resource completion rates (at least 70% complete) in the entire intervention group, as well as in subpopulations (parent gender, parent race/ethnicity, research mistrust, research familiarity), as another measure of feasibility. Finally, open-ended feedback about what was liked most, least, and suggested revisions will be coded into categories and summarized. The feedback will be used to create a list of necessary edits to increase the relevance of the resource for parents overall, and for subpopulations of parents.

Exploratory Analyses. To examine intervention effects on the outcome variables at posttest, multiple regression analyses will be used with condition (intervention; active control) as the independent variable. Pretest scores for each outcome will be included as predictor variables and outcome variable means will be reported as adjusted posttest scores. Analyses will be intent-to-treat. Demographic characteristics found to be non-equivalent between the two groups will be included as covariates in the regression models. In addition, moderator analyses will examine intervention effects for subpopulations (e.g., race/ethnicity, sex, research mistrust) to provide evidence regarding how the impact of the PCT Pocket Guide may potentially vary as a function of these characteristics.