Study Protocol and Statistical Analysis Plan

Title of Study: Web-based Resource for Children and Adolescents About Clinical Research
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Table of contents

Study Protocol

Objectives:

DigiKnowIt News: Teen (*DKIN: Teen*) is an interactive educational website designed to educate adolescents (aged 12 to 17) about pediatric clinical research. The main objective of the study is to examine the feasibility of *DKIN: Teen* and its impact on adolescents' knowledge about pediatric clinical trials; self-efficacy about making decisions about participation in clinical research; positive attitudes and beliefs towards participation; and fears related to participating in clinical trials.

Design:

A small randomized controlled trial design will be conducted online at two time points: 1) baseline/pre-test and 2) post-test (one week after pre-test). The study questionnaires will be programmed into an online data collection system and the intervention itself is also completed online.

Participants will be randomly assigned to one of two conditions: 1) intervention (youth will receive access to *DKIN: Teen* right away) or 2) wait-list control (youth will not have access to the intervention between pre-test and post-test assessments; after completing the post-test questionnaire, youth will be given the option to review *DKIN: Teen*).

Methods:

Sample and Recruitment. Youth between the ages of 12 and 17 will be recruited for the study. To be eligible to participate in the study, the following criteria must be met. Youth in the study must: 1) be between the ages of 12 and 17 years; 2) understand English because the resource and questionnaires are in English; 3) have access to a computer or tablet with internet access for the duration of the study as the intervention and questionnaires are web-based; 4) *NOT* currently be in or have previously participated in a clinical trial. This study will investigate if the intervention improves attitudes and decision-making of youth who have not yet participated in a clinical trial; thus, excluding those who have already had the experience of being in a clinical trial. Youth will be recruited from across the United States via flyers and a study website in addition to recruitment efforts via Peachjar (digital flyer service used by school districts) and pediatric health organizations and advocacy groups. Efforts will be made to ensure that the intervention and wait-list control groups have about equal amounts of boys and girls as well as healthy youth and youth with varying chronic diseases/disorders and represent diversity in race and ethnicity.

Procedure. Parents of interested adolescents will visit the study recruitment website to learn more about the study and respond to the study eligibility screening questions. Parents will be notified onscreen immediately if their child is eligible to participate in the study, and if so, will be given access to online permission and assent forms. They will be instructed to review the forms together so they can decide about participation. 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. Families can contact the research team about any questions they might have after they have reviewed and signed the forms. Participants and their parents will be instructed to read the permission and assent forms and provide online permission and assent by typing their names into a text box, providing contact information, and clicking a button to indicate permission (parent) or assent (youth), rather than providing a signed hard copy of the forms. They will have the option to download and/or print the forms to retain a copy for their files. Only participants with permission and assent will be permitted to participate in the study. Eligible youth who have assent and have parent permission will be sent an email invitation to participate to their parent by project staff members if there is space for them in the study depending on their demographic characteristics.

Participants will be randomized, stratifying based upon gender (boy/girl/non-binary), race/ethnicity (white/nonwhite), and health status (healthy/chronic illness), to either the intervention group (*DKIN: Teen*) or wait-list control group. A research team member will enroll the participants into their assigned groups using an online study management system. All participants will be assigned a unique ID number that will be associated with their data in place of a name. Parents will receive an enrollment email from the study management system with a link for participating youth to complete the online pretest questionnaire. Next, parents of youth participants in the intervention group will be emailed instructions on how to access *DKIN: Teen*. Youth will be asked to review as much of it as they want within one week. *DKIN: Teen* is expected to take about 1 hour to fully complete and can done in more than one sitting. Project staff members will monitor website usage through a Learning Management System (LMS). Participants in the wait-list control group will receive business-as-usual, which in this case is no information to review about clinical trials.

About one week after completing the pretest, all parents will receive a link for youth participants to access the online posttest. At the end of the posttest, the youth in the intervention group will also receive the Consumer Satisfaction Questionnaire to give feedback about the website. Youth participants in the wait-list control group will have the option of reviewing *DKIN: Teen* after their posttest data have been collected through an email link to their parents. After a week, the wait-list control group will also have the opportunity to complete the Consumer Satisfaction Questionnaire. Parents will receive automatic email reminders from the study management system if their teen has not completed the questionnaires or has not accessed *DKIN: Teen*. The research team will also call a parent or send a check-in email to a parent if there is no response following the automatic reminder. Youth will receive $20 for the completing the pretest questionnaire and $30 for completing the posttest via gift cards. At the end of the study, responses on the online questionnaires will be downloaded from the online data collection system and saved on a secure, password-protected network in preparation for statistical analyses.

Measures.

Knowledge. This measure has been created for the purposes of this study. Youth will respond to questions that assess their factual knowledge about clinical research (e.g., What is a clinical trial?). Questions are in multiple choice format (some questions have multiple correct answers), and the total score will be calculated.

Attitudes and Beliefs (adapted from Madsen, Mirza, Holm, Hilsted, & Riis, 2002). Youth will be asked to respond to questions that 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) and questions that assess their beliefs about positive aspects of pediatric clinical research (e.g., I believe that clinical trials can help kids; 1=Strongly Disagree; 2=Disagree; 3=Unsure; 4=Agree; 5=Strongly Agree).

Self-Efficacy (adapted from Bandura, 2006). Youth will be asked to respond to questions related to their self-efficacy for making decisions related to participation in clinical trials for two areas: 1) gathering information about clinical trials (e.g., Ask my parents questions for more information about clinical trials?); 2) communicating about clinical trials (e.g., Tell the researcher that I don't want to participate in the clinical trial, even if they really want me to do it). Youth will rate each question on a 5-point Likert scale (1 = I cannot do it at all; 5 = I know I can do it). Youth will be asked to respond to additional items to measure youths' confidence for participating clinical trials (e.g., I know what rights I have in a clinical trial. I know whom to ask if I need more information about a clinical trial.; 1=Strongly Disagree; 2=Disagree; 3=Unsure; 4=Agree; 5=Strongly Agree).

Procedural fears (adapted from Kowalsky, France, France, Whitehouse, & Himawan, 2014). Youth will be asked to respond to questions related to their perceptions of fear or anxiety about different types of medical procedures, including getting a needle in the arm, injection in the leg, getting a scan, and taking new medicine, on a 5-point Likert scale (1 = Not at all afraid or anxious, 2 = Somewhat afraid or anxious, 3 = Moderately afraid or anxious, 4 = Very afraid or anxious, 5 = Extremely afraid or anxious).

Fidelity of Implementation. iRT's LMS will record the amount of time that users spend on the website components and the specific components that were reviewed.

Consumer Satisfaction Questionnaire *(CSQ)* will assess satisfaction for each of the three components of the website in terms of: (1) content (e.g., The information in the Spotlights was interesting to me.); (2) format (e.g., I liked that there were games and activities I could play in the Investigations.); (3) usability (e.g., I could figure out how to make the Comics work.). Overall quality will also be assessed (e.g., I would recommend this resource to a friend that was considering participating in research.). Participants will rate each item on a 5-point Likert scale (1 = Strongly Disagree, 2 = Disagree, 3 = Undecided, 4 = Agree, and 5 = Strongly Agree).

Statistical Analysis Plan

Preliminary Analyses. Chi-squared analyses will be used to examine if the randomization process produced equivalent groups between the wait-list control and intervention groups with respect to gender, race, ethnicity, health status, and SES. A t-test will be used to examine if the randomization process produced equivalent groups between the wait-list control and intervention groups with respect to age. If any of these demographical variables are found to differ significantly between the two groups, they will be included as covariates in the main analyses. Finally, the outcome variables will be examined to see if the values are normally distributed.

Main Analyses. Intent-to-treat (ITT) analyses will focus on examining the feasibility of *DKIN: Teen* for making positive changes in youth outcomes related to participation in clinical trials. A series of single factor, condition (intervention, wait-list control) random effects ANOVA models will be used to examine if using *DKIN: Teen* impacts the posttest 1) knowledge, 2) attitudes, 3) beliefs, 4) self-efficacy, 5) fears related to participation as well as likelihood to participate and 6) likelihood that fears would prevent participation. Pretest scores for each outcome will be included as predictor variables; therefore, outcome variable means will be adjusted posttest scores. Because this study is not powered to find significant differences (i.e., p-values) between groups, small or larger effect sizes (Cohen's d) will be emphasized during interpretation as evidence of feasibility.