Test Up Now Education Program

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Study Protocol and Statistical Analysis

Study Protocol

The TUNE-UP study is designed as a two-group pretest/posttest pragmatic randomized controlled trial. The study uses the parallel group, two arm superiority trial design with 1:1 allocation ratio. The pragmatic trial aims to test the effectiveness of the intervention in the setting of community health centers. To conduct the intervention trial, 115 participants were randomized at the time of enrollment following completion of the baseline survey. The two experimental arms are: 1) an intervention group which receives the adapted Screen to Save (S2S) educational materials, a tailored brochure for African Americans on colorectal cancer (CRC) screening with input from focus group research, and CHA in-person and cellphone education and counseling supplemented by text messages; and 2) a control group which receives the brochure only. Participants in both study arms received communication from their CHC to receive their stool-based testing kit. The primary outcome is CRC screening by 12-months post-intervention (i.e., receipt of the stool-based test). The intermediary CRC screening outcome is measured at 3-months. Secondary outcomes included CRC knowledge and CRC screening self-efficacy.

Study participants and setting

African American men and women aged 45 to 64 years were included in the study. Participants were screened for eligibility after contacting the project coordinator according to the following inclusion criteria: (1) 45-64 years of age, (2) self-identify as African American, (3) have a working cellphone, (4) resident of Florida, and (5) not up to date with CRC screening per established screening guidelines (i.e., no stool tests in > 9 months, no colonoscopy within 9 years, and no flexible sigmoidoscopy within 4 years) Exclusion criteria are: previous history of CRC, precancerous colorectal polyps, or co-morbid conditions, such as inflammatory bowel disease or Crohn's disease. The project coordinator reads the consent form and obtains verbal consent from eligible persons interested in participating in the trial. Participants receive the consent form signed by the project coordinator with complete information on the study and university contact information when meeting to complete the baseline survey. Based on recruitment and outreach, research participants are patients of one of two community health centers in the greater Tallahassee, Florida area and primarily reside in two North Florida counties: Leon or Gadsden.

Randomization and blinding

The study used the block randomization method. The trial randomized participants at the individual level, stratified by the two CHC sites, using a 1:1 ratio between intervention and control arms. The randomization algorithm used randomly permuted blocks with random block sizes for the purpose of assigning participants. The random selection of block sizes has the advantage of reducing selection bias. The randomization file was produced in SAS 9.4 by the biostatistician. The Principal Investigator informed the study coordinator of study arm assignment using ID numbers after the participant gave consent to participate in the study and completed the baseline survey. If a participant was assigned to the intervention arm, the study coordinator informed the CHA so the participant could be contacted to complete the intervention arm protocol.

Intervention and control groups

All participants received the tailored educational brochure at the initial visit when they completed the baseline survey with the Project Coordinator. The participants who were randomized to the intervention group viewed the S2S video, and the CHA explained the contents if there were questions. This was followed by two weeks of short CHA follow-up calls, concluding with three weeks of motivational text messages on CRC screening. Participants who were randomized to the control group received the educational brochure only. Both intervention and control groups received the FIT from their CHC either in the mail, in person, or during a scheduled patient visit. The CHCs were blinded to study arm.

Community health advisor and educational materials

One CHA was trained by the research team to deliver the 6-week intervention consisting of an initial face-to-face CRC educational presentation using the S2S video, two weeks of phone-call follow-up, and three weeks

of text message follow-up. The intervention was delivered by the CHA to African Americans in North Florida who are patients of the participating CHCs and were not up to date with CRC screening.

The adapted S2S PowerPoint developed by the research team was professionally produced into an approximately 11-minute video narrated by an African American woman. After the participant viewed the adapted S2S video on the CHA's tablet, the CHA asked if the participant wanted to discuss the video or ask any questions. After allowing 2-3 minutes for discussion, the CHA showed the participant a 5-minute FIT patient education video. This video walked the viewer through the steps of completing their at-home screening test. The video was obtained from the manufacturer of the FIT after the research team was informed by CHCs that it was the primary FIT they use. Once the participant finished viewing the second video, the CHA again engaged the participant to discuss any topics or questions the participant may have had. The CHA used a fidelity checklist to document completion of the week 1 educational presentation and make appropriate notes. In weeks 2 and 3 of the intervention, the CHA called the participant to ascertain receipt of the FIT from their CHC and the participant's completion of their FIT. Fidelity checklist phone scripts allow the CHA to document delivery of the calls and facilitated their use of motivational interviewing to address any barriers to completing the screening. In weeks 4-6 of the intervention, participants received one motivational text message per week to encourage them to complete their screening. The intervention was completed in 6 weeks or potentially earlier if the participant reports completion of their FIT.

Statistical analysis

All statistical analyses were performed using SAS 9.4. First, summary statistics were generated for all variables. Then bivariate analyses were conducted for key variables to compare differences between the intervention and control arms. Proportions calculated from categorical variables were compared using a chi-square test; means obtained continuous variables were compared using two-sample t-test. The multivariate analyses were conducted using the GEE procedure in SAS that implements the generalized estimating equations regression. Analyses were performed using an intent-to-treat approach that includes all participants randomized. Significance tests were two-sided and employed an overall significance level of $\alpha=0.05$. For each arm, the proportion of participants who receive CRC screening by 12 months was computed. The chi-square test was used to compare the two treatment arms for screening receipt. If the proportion of participants receiving CRC screening in the intervention arm is at least 15% higher than that in the control arm, the intervention will be determined to be effective. In addition, since our sample size gets small when participants are stratified by community health center or sex, we will use Fisher's exact test to assess the effect of the intervention. To assess the influence of key covariates (age, income, marital status, education, insurance status) on the primary outcome, logistic regression analysis was employed. In addition, to investigate treatment effects over time (baseline, 3 months, and 12 months), we will estimate hazard ratios by fitting Cox proportional models using time-varying covariates. In these models, the receipt of CRC screening will be regressed at each actual time point on time elapsed since baseline to test for an interaction between time and treatment group. The basic model will be repeated, adjusting for age, income, marital status, education, and any other significant covariates at baseline. To test the proportional hazard assumption, the Kaplan-Meier curve and the Schoenfeld residuals will be used for fixed and time-varying covariates, respectively.

Mediation and moderation analyses will be conducted to determine why and when variables are related, respectively. We will focus on specific mediators to include CRC perceived susceptibility, CRC self-efficacy, and CRC knowledge in the conceptual model.

The complexities of the relationships between the exogenous variables (X) and the endogenous variables (Y) as a function of the mediators will be examined using three separate regression models. We will ensure that the assumptions of continuous measurements (i.e., that all variables are measured on a continuous scale), normality (i.e., normal distribution of all variables), independence (i.e., that there is no correlation of errors from one observation to another observation), and linearity (i.e., evidence linear relationships among the variables) are met. We will assess direct causality and indirect causality using standardized regression coefficients (i.e., betas) to determine the direction and magnitude of the effect of one variable upon the other variable.

We will confirm that the mediators (i.e., CRC perceived susceptibility, CRC self-efficacy, and CRC knowledge) are caused by the exogenous variables X and are also the causes of the endogenous variables Y. We will also determine if X loses its significance when M is included in the model. Specifically, we will perform regression analyses and confirm the significance of the relationship between the exogenous (i.e., independent variable - IV) and endogenous variables (i.e., dependent variable - DV), the exogenous and mediator variable, the mediator and the endogenous variables in the presence of the IV, and lastly, we will confirm the lack of significance (or the meaningful reduction in effect) of the relationship between X and Y in the presence of the mediators.

Additionally, we will assess the moderator variables (i.e., sex, health literacy, family history of cancer) to determine under what condition (i.e., when) a given predictor X/independent variable (IV) is related to an outcome Y/dependent variable (DV). We will assess whether the moderation effect is enhancing (i.e., that is, increasing the moderator would increase the effect of the predictor on the outcome), buffering (i.e., that is, increasing the moderator would decrease the effect of the predictor on the outcome), or antagonistic (i.e., where increasing the moderator would reverse the effect of the predictor on the outcome). We will apply hierarchical multiple regression to examine the effects of the moderating variable. We will assess the interaction effect between X and M and whether or not such an effect significantly predicts the occurrence of Y. All variables will be standardized to facilitate data interpretation and avoid multicollinearity. We will fit a regression model predicting the outcome from both the predictor and moderator variables. We will check that both the effect of the predictor and the effect of the moderator, as well as the model (R2) are statistically significant. Then, we will fit another regression model that includes the interaction effect of the first model and check for a statistically significant R2 change and a statistically significant effect of the interaction term to determine if moderation is occurring (i./e., both are statistically significant).

Mediation analysis allows assessment of each covariate’s impact on the primary outcome independent of whether the intervention’s effect is significant; thus, adding to scientific understanding of the relevance of each. To examine the mediating effects on the primary outcome of each of the short items scored on a Likert-type scale, we will follow the strategy of Baron and Kenny. We will conclude that the candidate covariate is indeed a mediator of the effects of the intervention if: (1) the treatment group indicator is significant; and (2) the candidate covariate is significant, and the coefficient estimate of the treatment group indicator is smaller in absolute value than its counterpart in analysis.

To assess the impact of candidate moderators, we will use Cox proportional hazard model and other appropriate survival analysis models to investigate the primary outcome on treatment group, each candidate moderator, and the interaction of treatment and each candidate moderator at each measurement time point.