PEP4PA - Peer Empowerment Program for Physical Activity in Low Income and Minority Seniors [R01HL125405]
October 7, 2020
Protocol ID: 150336

Statistical Analysis

Dr. Natarajan will be the lead statistician and be responsible for generating randomization allocation sequences, supervising data analysis, and developing and implementing novel methods. She will be blinded to intervention condition. Summary statistics will be calculated; groups will be compared on baseline characteristics; variables that are not balanced across study arms will be adjusted for in subsequent analyses. The primary analysis will use the intent-to-treat principle.

Aim1 & 2 Analysis Plan: Aim 1 will test the efficacy of the PEP4PA intervention on PA, and will compare the PA intervention group to the usual care control group on minutes/day of PA and % meeting NHANES criteria measured by accelerometry over 6-12 months. A mixed effects regression model will be used with post-intervention PA at 6 & 12 months as the dependent variable and intervention arm (active vs control) as the independent variable, with baseline PA as a covariate. Gaussian link function will be used for the continuous PA outcome; a binomial link will be used for the binary outcome (meeting vs not meeting guidelines). A random effect for site (center) and a subject-specific intercept (nested within site) will be added to the model to adjust variance estimates for clustering within site and within individuals over time. Additional covariates such as gender and age, and any factors found to be imbalanced between treatment arms at baseline will be included to examine the impact of covariates on estimated treatment effects. Aim 2 assesses the efficacy of the PEP4PA to improve physical functioning, blood pressure, depressive symptoms & quality of life and will compare these outcomes between treatment and control arms using the same approach as Aim 1.

Aim 3 Analysis Plan: Assess the incremental cost effectiveness ratio (ICER) of PEP4PA in terms of cost per MET hour and cost per QALY compared to usual programming in the control centers at 12 months. Drs. Shi and Gilmer will be the lead health economists on this project and will be responsible for supervising cost data collection and conducting CEA at 12 & 24 months. The CEA will follow well-established guidelines developed by Drummond et al., and Haddix et al., including identification of all relevant costs and consequences for the intervention, accurate measurement in appropriate effectiveness units, sound valuation, and sensitivity analysis to test uncertainties. The final outcome of the CEA is ICER, the ratio of the differences in costs and effectiveness. Two ICEA measures will be evaluated in this project: cost per MET hour and cost per QALY. To allow comparisons to other PA interventions, cost per QALY derived from this study will be compared to subjective thresholds of the value of health care ($50,000 per QALY).We propose to use $1.16 per MET hour cost, the median ICER of community support PA program in community setting, as a tentative cutoff for comparison. To account for non-parametric nature of the data, we will use bootstrap to create confidence intervals for the mean costs and effectiveness for the each comparison. A scatter plot of 5000 bootstrapped ICER will be generated by drawing a random sample with replacement. The CEA results will be presented in a cost-effectiveness acceptability curve. The uncertainty of the parameters will be explored in sensitivity analysis. The impact of time spent in the cost will be tested.

Aim 4 Analysis Plan: This aim assesses the efficacy of the PEP4PAintervention on other PA outcomes (step counts, sedentary time), psychosocial and lifestyle measures (cognitive/executive functioning, sleep quality), and walking routes (measured by GPS devices). As in Aim 1, mixed effects models will be fit for each outcome at 6 & 12 months (dependent variable), with adjustment for baseline level, group, and other covariates. In addition, because several of these outcomes are likely correlated (e.g., sleep, sedentary time), we will apply statistical methods for multiple outcomes i.e. O'Brien's test which is a weighted linear combination of t-statistics for each outcome and multivariate repeated measures models which will be used to examine treatment effects on the vector of outcomes over time.

Aim 5 (*Exploratory aims*) We will examine *quantitative* participant and intervention mediators and moderators (see Figure 1) of behavior change and implementation success. Moderators will be tested by including interaction terms between the putative moderator and treatment condition in the models. Mediation will be assessed using path analysis. To examine multiple mediators, we will extend the above analysis to a multiple mediation framework for multilevel data. We will apply bootstrap methods to resample and refit mediation models to compute standard errors and examine consistency of results. We will also fit Bayesian graphical networks (BN). Qualitative data will be reviewed using standard content analysis procedures. The 'authenticity' of emergent themes will be checked using validation procedures.

Aim 6 The modeling approaches in Aims 1-4 will be expanded to include the 18 and 24 month data.

Sample size estimates We determined sample size for the primary outcome (Aim 1) of improving PA over 12 months. In preliminary analysis of our MIPARC study, we observed (i) a mean 40 min/day difference between intervention and control groups for LMPA at 6 months (SD = 57 min/d), yielding an effect-size of 0.7, and (ii) an intraclass correlation (ICC) of 0.07 for center clustering effects on LMPA (in our pilot study in low-income seniors this ICC < 0.01). 12 sites and 28 subjects/site will yield 80% power (2-sided test α =0.05) to detect conservative effect-sizes between 0.41 to 0.56 for time-averaged standardized mean differences between arms assuming center clustering ICCs ranging from 0.05 to 0.1, and autocorrelations of 0.5 to 0.8 on within-subject repeated measures of PA. Also, under these assumptions, there is 80% power to detect percentages of 20%- 25% meeting guidelines in the intervention vs 5% (based on pilot data) in the control arms at follow-up. To allow for a worst-case attrition rate of 20% by 6 months (our RC retention rate is 91% at 6 months), we aim to recruit 408 participants (12 sites with 34/site).

Missing data All outcomes will be tested using an intent-to-treat framework. Our analytic approach using mixed-models will yield unbiased results even if some observations are missing as long as the data are "missing at random", i.e., the reasons for missingness can be predicted from observed measurements. In MIPARC differences between drop-outs and baseline factors were similar between treatment arms (i.e., treatment*arm interactions were not statistically significant). Thus, under similar assumptions the mixed model approach will give unbiased results in the proposed study. We will conduct sensitivity analyses to test for informative drop-outs and develop alternate approaches, e.g. pattern-mixture models.