Technologically Enhanced Coaching (TEC): A Program for Improving Diabetes Outcomes

NCT01855399

Data Analysis Plan

6/4/12

3.7 Analyses

Unit of Analysis and Sample Size Calculation

Patients within pairs (peer-peer coach dyads) will be the primary unit of analysis for the study. Thus, we calculated the sample size to adjust for the likely correlation between members of the pairs (intraclass correlation, or rho) in the intervention group. Accordingly, we calculated the sample size to provide 80% power to detect a difference between experimental groups of 0.5% in A1c with an alpha of .05, two-tailed.[95] We conducted the power analysis using the methods of Cohen and, based on the within-pair ICC of our prior reciprocal peer support intervention, adjusted for a within-pair intraclass correlation of 0.03 as implemented in STATA 12 software.[96] We estimated the standard deviation of a decline in A1c in this population (1.45) using data from our prior randomized controlled trials.[9,40] To provide the needed power, 148 subjects will be needed in each group (after attrition) and 74 peer mentors (clusters) across both groups (37 in each group). To conservatively allow for up to 15% attrition, a rate higher than occurred in any of our prior VA diabetes RCTs, we will recruit 174 patients for each arm, for a total of 348 patients, and a total number of 87 peer mentors. The estimate of the standard error of the change in BP was estimated from a database of actual BPs obtained in routine clinical practice for 24,000 patients with diabetes and hypertension in one large service network in the VA over a 24-month period in FY 2004-2005. It depends on both the variation in BP change at the person level and variability within person between measurements. We estimated the standard error for the change in blood pressure as 17 mmHg. Our target sample size will provide 90% power to detect a difference between experimental groups of 5 mmHg and differences between each of our key patient-centered outcome measures.

Approach to All Analyses

We will follow international guidelines for analysis and reporting of clinical trials.[97] In the first phase (data verification), we will examine the distribution of all study variables to assess extreme values, missing data, variances, possible coding errors, skewness, and type of distribution. We will examine baseline data for clinically important differences across the two study groups for potential prognostic indicators, such as patients' age, race, comorbidities, and baseline use of services. Although we do not anticipate any imbalances due to the randomization, any differences between experimental arms in baseline characteristics will be included as covariates in analyses comparing outcomes. In the second phase of our outcomes analyses, we will evaluate possible bivariate associations between patients' experimental condition and the outcomes, as well as between each covariate and the outcomes, prior to fitting multivariable models. This will be done to determine unadjusted measures of effect, assess possible confounders, and anticipate any collinearity in subsequent analyses. In the final phase we will fit multivariable models to identify main effects.

Analysis Plans by Aim

Aim 1: Test the effectiveness of a technology-enhanced peer coaching (TEC) program in improving glucose control relative to peer support alone. Our past experience in similar patient populations

suggests that the primary endpoint from the trial (change in A1c) will be close to normally distributed. To assess the primary endpoint for Specific Aim 1 (change in mean HbA1c from baseline to 6 months), we will use a general linear mixed regression model:

where i represents the patient, l represents the intervention, j is the pair-group, βl are parameters estimated from the data, Xil is the value of the lth fixed effect (peer support versus usual care) for the ith patient, bj are parameters estimated from the data, Zij is the value of the jth random effect (pairs) for the ith patient, and εi is the residual error.[99] We anticipate that members of peer coach-peer partner pairs in both arms, because of their interactions with each other, might show a positive intraclass correlation (ICC), a component of the variance attributable to the group. As recommended for group-randomized trials, the mixed model analyses will thus address potentially inflated type I errors that could occur if such clustering were not taken into account.[97] If patients in either arm drop out of the study or request reassignment to another peer coach, they will be analyzed according to their initial pairing in an intent-to-treat analysis.

After unadjusted changes in A1c are determined, further analyses using mixed-model ANCOVA will adjust for confounding effects of any variables that differed substantially between treatment arms. Both unadjusted and adjusted means with 95% confidence intervals will be reported for both arms. While the primary endpoint is the mean difference between baseline and 6-month A1c concentrations, subsequent analyses will be conducted to determine whether the intervention additionally affects the difference between baseline and 12-month A1c (i.e., the sustainability of any treatment effects) using a repeated-measures mixed model ANCOVA.

We will follow the same approach to comparing the observed usual care group with the peer support alone group. However, there is a higher likelihood of imbalances as the usual care group is observational, although they are drawn from the same eligibility pool as the participants. Therefore, we will include several key covariates in the analysis, including baseline A1c, age, gender, and race. We will also examine the data for differences in other potential prognostic indicators, such as baseline medication or service use, and include these variables in the regression if necessary. We will also need to examine whether biases may be caused by missing A1c data. Although the very high level of A1c testing in VHA is likely to lead to few missing data points, we will conduct sensitivity analyses using two approaches. In the first, we will assume that those with missing A1c levels at the end of the study had no improvement in their A1cs. In the second, we will use multiple imputation methods to fill in missing A1c values.

Aim 2: Assess the impact of the intervention on blood pressure and medication adherence as well as on key patient-centered outcomes, including patients' satisfaction and involvement with care, perceived social support, and diabetes-specific quality of life. For assessment of changes in systolic blood pressure and for the self-reported outcomes, we will use mixed effects models (similar to those in Aims 1) for

continuous outcomes, and generalized estimating equations (GEE) for ordinal outcomes with clustering.[98]

Aim 3: Identify patient characteristics associated with engagement in the intervention and mediators and moderators of the intervention's impact on patient outcomes. For these analyses, we will use multivariate modeling and path analyses.[99] Many of these outcomes will be measured using Likert scales. Thus, we will begin these analyses by developing contingency tables for ordered categorical data. We will then use generalized estimating equations (GEE), which are appropriate for modeling ordinal outcomes with correlated data.[99]

We will use both quantitative and qualitative methods. We will compare patient characteristics and attitudes of participants and those not willing to participate in the study. For example, using VA administrative data, we will compare the characteristics of study participants (mean age, race, most recent A1C, co-morbidities) with those of diabetes patients treated in each site's outpatient clinics. Eligible refusers will be asked whether they would consent to a brief survey in which we will record information helpful in assessing the intervention's reach, such as diabetes distress, perceived need for support, interpersonal attachment styles, reasons for not enrolling, and existing sources of social support.

We will model independent associations and pathways linking intervention exposure to outcomes using nested multivariate regression. Subsequent nested models will introduce potential mediators, and we will evaluate changes in the magnitude of the relationship between experimental condition and outcomes before and after the covariates are introduced. Analyses of potential moderators will use standard approaches to evaluate potential interactions between these covariates and patients' experimental condition.[100] Independent variables and moderators will be centered before testing interactions, so that multicollinearity between first order and higher-order terms will be minimized. Statistically significant interactions will be interpreted by plotting regression lines for high and low values of the moderator variable. Stata routines greatly facilitate the plotting of these relationships.[101]

To gain more in-depth understanding of factors associated with level of engagement in the intervention and with outcomes, along with examining baseline correlates of different levels of engagement using quantitative approaches with the baseline survey and clinical data, we will conduct and analyze semi-structured interviews conducted at the 6-month assessment. The use of the IVR platform will enable us to categorize patient-mentor dyads into different levels of frequency of contacts and duration of contacts ("engagement"). The IVR system records data on dates of all completed telephone contacts and duration of each telephone call into a data set in separate data fields. It is thus easy to examine the 'dose' of intervention engagement of each dyad, depending on how frequently and how long they spoke together. We will conduct semi-structured interviews with purposive samples of peer mentors and participants with different levels of intervention engagement (low, medium, and high). We will perform

a thematic analysis of the interview data with participants with different levels of engagement in the intervention (in both arms) using QSR NVivo, a qualitative data analysis package. Our overall approach to thematic analysis will be what Miller and Crabtree refer to as the “Editing Analysis Style,” which contains both deductive and inductive elements. Following this approach, two investigators will independently read interview transcripts, break down patient interview responses into individual segments that express a single idea or theme (e.g., particular ways respondents found the telephone calls useful or not useful) and label these phrases with appropriate codes. An iterative process will be used to compare results until agreement is reached on the categories and criteria for inclusion.[102] We will seek to examine in more depth factors contributing both to successful and unsuccessful peer mentor-partner matches.

3.7.5 Approach to Missing Data

Clinical trial analyses often are limited to patients with complete data. However, even in cases with low rates of attrition such as our prior VA diabetes RCTs, this strategy may yield overly optimistic effect size estimates. Problems adhering to the protocol or worse health status often are associated with missing data. Although we will conduct an initial analysis using only observed data, we will conduct a second analysis that imputes missing data. We will impute missing data using the method described by Lavori, Dawson, and Shera.[103] This uses logistic regression to model patients' likelihood of having outcome data and define strata within which outcome values are missing at random. We will then stratify patients according to these propensities and randomly sample from the observed outcome distribution and impute these values for missing data within each stratum. When data are missing for items within scales, we will use recommended imputation procedures rather than deleting patients list-wise from the analysis.[104] In addition, we will compare dropout rates in each arm, using the chi-square tests and compare subjects with complete follow-up to those with missing data with respect to observed baseline characteristics. Finally, we will repeat analyses assuming that all subjects with incomplete data had no improvements in their baseline A1cs as a conservative approach.