USING LATENT VARIABLES AND DIRECTLY OBSERVED TREATMENT TO IMPROVE THE DIAGNOSIS AND MANAGEMENT OF DEPRESSION AMONG HEMODIALYSIS PATIENTS

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Statistical analyses

Develop and validate hemodialysis-specific depression screening instrument. We will begin by using graphs and descriptive statistics to summarize demographic and medical characteristics as well as scores on our measures of depression (PHQ-9) and dialysis complications. Next, we will perform exploratory factor analysis of the nine PHQ-9 items to determine how many latent factors represent aspects of depression. It has been hypothesized that the PHQ-9 has a two factor structure representing somatic and affective domains of depression. However, our previous work on depression and multiple sclerosis suggested a single factor structure. We will use an oblique (geomin) rotation and will examine the eigenvalues, which represent the variance accounted for by each underlying factor, in a scree plot. The number of eigenvalues $\geq$1 represent unique latent factors. We will also use parallel analysis to calibrate our decisions regarding meaningful eigenvalues. This approach computes eigenvalues from a random dataset via Monte Carlo simulation with the same number of observations and variables as used in the factor analytics model. Further, we will use model fit criteria such as chi-square, comparative fit index (CFI), Tucker Lewis fit index (TLI), root mean square error of approximation (RMSEA), and standardized root mean square residual (SRMR) statistical test values to help determine the measurement properties of our latent constructs.

We will then use structural equation modeling to examine overlap between depressive symptoms and dialysis complications. Conducting these analyses involves four steps: 1) specifying the conceptual model, 2) estimating model parameters and assessing goodness of fit, 3) making any model modifications, and 4) testing hypotheses of interest. In particular, we will apply a measurement model with covariates which permits detection and adjustment for differential item functioning (DIF), i.e. when subgroups with the same latent trait have a different likelihood of responding to specific questions.[79] The initial model will include the factors representing aspects of depression, depressive symptoms, dialysis complications, and all the potential paths (referred to as DIF paths) connecting them. We will then make model comparisons and modifications to our initial model using multiple indices and statistics (e.g. chi-square, CFI, TLI, RMSEA, SRMR, modification indices) along with clinical input to establish the best fitting model, i.e. the most parsimonious model with all clinically relevant DIF paths of at least a small standardized path coefficient.[30] The results of these analyses will be standardized path coefficients which indicate the magnitude of the effect of one variable on another such as the impact of nocturnal cramps on sleep disturbance after adjustment for all other relationships in the model.[29] Both factor analysis and structural equation modeling will be performed with MPlus software.[80]

For clinical use, we will develop a hemodialysis-specific PHQ-9 (hdPHQ-9) free of overlapping symptoms to isolate the underlying dimension of depression. We will extract factor scores from the latent construct (or constructs) representing depression in the final best fitting model to form this adjusted scale. A factor score is an individualized score on a latent construct representing a scale of interest. These factor scores will be linearly transformed to fit the range of the original PHQ-9 (i.e. 0–27) using a probability integral transformation to maintain the interpretation and thresholds of the PHQ-9. This one-to-one transformation will result in similar distributions of PHQ-9 and hdPHQ-9 scores in the sample. However, certain individuals will have sizeable differences between the two scores. We will also develop a web app that will allow users to enter information for a patient and will automatically calculate the hdPHQ-9 score.

Finally, we will use bootstrapping in order to validate our hdPHQ-9. After developing our model

based on the entire sample, we will fit the model on a series of bootstrap datasets (each by resampling with replacement the same number of observations as the entire sample). From this

procedure we will: 1) obtain the average (as well as the 95% confidence interval) for each of the model parameters and fit indices across the bootstrap samples and 2) observe how the extracted hdPHQ-9 factor scores for each individual in the original data set vary across the models derived from each bootstrapped sample. Thus, bootstrapping validation can be used to understand if there is any bias and sampling variation in the model parameters and associated hdPHQ-9 scores due to overfitting in the final model.