GENERALIZED LINEAR MIXED MODELING TO EXAMINE THE RELATIONSHIP BETWEEN SELF EFFICACY AND SMOKING CESSATION

by

Craig S. Parzynski

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This thesis was presented

by

Craig S. Parzynski

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and approved by

Thesis Advisor:

Carol K. Redmond, ScD, Professor, Department of Biostatistics

Graduate School of Public Health, University of Pittsburgh

Committee Members:

Cynthia A. Conklin, PhD, Assistant Professor, Department of Psychiatry

School of Medicine, University of Pittsburgh

Kenneth A. Perkins, PhD, Professor, Department of Psychiatry

School of Medicine, University of Pittsburgh

Ada O. Youk, PhD, Assistant Professor, Department of Biostatistics

Graduate School of Public Health, University of Pittsburgh

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Craig S. Parzynski, M.S.

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The relationship between self efficacy and smoking cessation is unclear. Self efficacy is often viewed as a causal antecedent for future abstinence from smoking, a primary outcome of cessation studies. However, recent research has questioned whether the participant's report of self efficacy is a reflection on previous abstinence success or failure rather than a precursor. To elucidate the dynamic relationship between self efficacy and abstinence status, two generalized linear mixed models were developed. The first examined the ability of self efficacy to predict next day's abstinence, while the second examined the ability of abstinence to predict self efficacy ratings taken later that same day. All data came from a 2 x 2 crossover trial examining how interest to quit smoking and monetary reinforcement for abstinence affect the short term effects of medication on abstinence from smoking. Participants received both medication and placebo conditions in consecutive phases in a counter-balanced order, with an ad lib smoking washout period in between. Abstinence from smoking and self efficacy was recorded daily during both medication phases. Participants were 124 smokers, mean age 31.1(SE: 1.0), who smoked on average 16.3 (SE: 0.5) cigarettes per day and had a mean FTND score of 4.6 (SE: 0.1). The sample was comprised of 56.5% females. Results indicate that self efficacy is both a predictor of, and a reflection on abstinence status. Models were validated using bootstrapping

procedures. These procedures revealed only a small amount of bias in the models. The effects observed in this study may be constrained by the timing of assessments as well as the duration of the cessation attempt.

Public Health Importance: Tobacco use accounts for 443,000 deaths each year. Therefore, the development of successful clinical assessments to monitor smoking cessation efforts is of the utmost importance. Self efficacy is a measure of confidence to quit smoking. This study shows that the relationship between self efficacy and smoking cessation is bi-directional which may be influenced by the timing of assessments. Understanding this relationship may lead to more successful use of self efficacy as a clinical tool during smoking cessation attempts.

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1.0 INTRODUCTION

1.1 SMOKING CESSATION AND SELF EFFICACY

Tobacco use accounts for 443,000 deaths each year and is the leading preventable cause of death in the United States (CDC, 2006; CDC, 2008). More deaths are caused each year in the U.S. by tobacco use than by all deaths from human immunodeficiency virus, illegal drug use, alcohol use, motor vehicle injuries, suicides, and murders combined (CDC, 2008). An estimated 46 million adults smoke cigarettes (CDC, 2009). Several modes of treatments including behavioral, pharmacological, and cognitive therapies have been successful, at least in part, in treating nicotine addiction. However, these different therapies fail to elucidate the underlying cognitive mechanisms that lead to successful behavior change. Understanding the cognitive mechanisms that lead to behavior change may clarify specific processes that can be targeted during interventions for nicotine addiction.

One prominent cognitive based approach to behavior change is Bandura's social-cognitive theory (Bandura, 1977, 1997) which emphasized the concept of self efficacy. Self efficacy is a person's perceived personal capability of performing in a manner that achieves a goal in a given situation. It is most often seen as an influencing factor in behavior change and is often assessed in nicotine addiction treatment. Essentially individuals who have high confidence in their ability initiate successful behavior change in a certain situation (i.e. high self efficacy) will be more likely to change their behavior than those who have low confidence (i.e. low self efficacy) in their capability to successfully change.

In current literature, self efficacy is assumed to be an antecedent to subsequent behavior change, i.e. high self efficacy is believed to predict successful behavior change while low self efficacy predicts a higher likelihood of failure. Traditionally, self efficacy has been measured prior to a smoking cessation attempt and then used as a predictor of cessation success. Particularly, this has been the case in one's ability to successfully initiate and maintain tobacco cessation (Gwaltney et al., 2009). Studies using such methodology have shown limited success depending on latency between the self-efficacy measure and outcome assessment (Gwaltney et al., 2009). Baseline measures of self efficacy taken weeks or months prior to the treatment outcome have shown varying correlations. However, when self-efficacy measures are taken immediately prior to or during the quitting process (i.e. proximal to cessation outcome measures) a positive relationship between measures of self efficacy and post-treatment abstinence (O'hea et al., 2004; Baldwin et al., 2006; Gwaltney et al., 2009) and a negative relationship with smoking cessation outcomes such as number of lapses and likelihood of relapse (Van Zundert et al., 2010; Shiffman et al., 2000) emerges. When self efficacy and cessation outcomes are measured concurrently during the quitting process an interesting question arises. Is self efficacy the driving force of successful behavior change? Or in fact are self-efficacy measures taken during the quit process a reflection on prior cessation success? Specifically is abstinence on one day predictive of future self efficacy? Is self efficacy predictive of future ability to abstain? Or is there a dynamic process in which abstinence success increases self efficacy which breeds future successful abstinence?

Gwaltney and colleagues (Gwaltney et al., 2009) found that self efficacy assessed before the quit date wasn't as strongly related to abstinence status as self-efficacy assessed after the quit date. Furthermore, self-efficacy was only weakly associated with subsequent abstinence status

unless smoking behavior was controlled for. Still other research has suggested a reciprocal role of self efficacy with outcome expectations, urges, and coping in which all of these factors interplay to affect use, cessation, and relapse (Niaura, 2000). However, to our knowledge only one study has attempted to examine the causal relationship of self efficacy and treatment outcomes directly. Romanowich et al (2009) constructed two structural equation models to examine if self efficacy predicted treatment success (reduced carbon monoxide levels) or if in fact self efficacy is merely a result of prior behavior change. The first model examined if baseline self efficacy predicted subsequent reductions in carbon monoxide (CO) levels (i.e. reduced smoking behavior) while the second model examined if reductions in carbon monoxide readings predicted changes in self efficacy pre-to post-treatment. Results indicated that baseline self-efficacy measures were not significantly correlated with subsequent reductions in CO, however reductions in CO did predict subsequent later increases in self efficacy. The authors therefore concluded that, rather than being a cause of behavior change, as self-efficacy theory proposes, self efficacy may be a cognitive response to behavior change, suggesting that change in smoking behavior leads to changes in self efficacy. However, this study was limited by the use of only two measures of self efficacy, baseline and endpoint. Those measures were taken distal in time to the CO measures. Additionally, Romanowich et al. (2009) used contingency management procedures for all subjects, such that those successful in reducing CO measures were rewarded monetarily (with increasing compensation for continued success) which could confound outcome measures of CO.

As a result of these limitations further examination of this relationship between self efficacy and smoking cessation is warranted. The current study will expand upon Romanowich et al. (2009) by examining the directional relationship between self efficacy and treatment success

over several time points in a 2x2 crossover trial (a trial in which participants receive both medications). Furthermore, our examination will evaluate the potential of monetary reinforcement and quit interest to confound this relationship by investigating the interaction between self efficacy and these variables.

1.2 CROSSOVER TRIAL DESIGN

A cross-over trial is a specific research design in which each unit, or subject, receives multiple experimental treatments, one at a time. This type of design differs most notably from traditional parallel clinical study designs, in which participants are randomly assigned to receive just one treatment or another. In a crossover trial the treatment effects are within subjects instead of between subjects and participants are randomized to treatment sequences. For example, in a clinical drug trial, one participant would be randomly assigned to receive the active medication followed by the placebo drug while another would get the placebo first, followed by the active medication. In each of these cases, the same participant crosses over to the next drug and measurements are taken on the same participant in each period. This often happens after a wash out period, or a period of time used to extinguish the effects of the first drug, so that the effects of the second drug can be studied independently. In the crossover design each sequence, s, has p # of periods, and is made up of combinations of t # of treatments (Jones & Kenward, 2003).

1.3 STATISTICAL CONSIDERATIONS FOR CROSSOVER TRIALS

The traditional aim of the crossover trial design is to compare the effects of the individual treatments, not the sequences themselves. In general, we denote the response of the *k*th subject in

period j of sequence i as y_{ijk}. We can then construct a model in which we assume that y_{ijk} is the observed value of random variable Y_{ijk}. For a continuous outcome we assume that Y_{ijk} can be represented as a linear model in the following form: $Y_{ijk} = \mu + \pi_j + \tau_{d[i,j]} + s_{ik} + \varepsilon_{ijk}$

Where:

μ : an intercept;

π_j : an effect associated with period j, j = 1,…,p;

$\tau_{d[i,\ j]}$: a direct treatment effect associated with the treatment applied in period j of sequence i,

$d[i, j]$ = 1,…,t;

s_{ik} : an effect associated with the kth subject in sequence i, i = 1,…,s, k = 1,…,n_i; and

ε_{ijk}: a random error term, with mean zero and variance σ^2.

This model can be changed to accommodate dichotomous outcomes by using the logit (or log of the odds) of the linear model. That is, we will express the linear model in logarithmic terms. This allows us to bypass the assumption of linear modeling that the relationship between the Y variable and the X variable forms a linear relationship. Using logit modeling we predict the probability of $Y_{ijk.}$ which can be expressed by: $\Pr(Y_{ijk}) = \frac{1}{1+e^{-(\mu+\pi_j+\tau_{d[i,j]}+s_{ik})}}$ where $Y_{ijk} \sim BIN(n_i, p_i)$ for i = 1,…,m and $\Pr(Y_{ijk}) = p_i = E\langle \frac{Y_{ijk}}{n_i} | X_i \rangle$. Therefore, taking the logit we retrieve the linear model $logit(\Pr(Y_{ijk})) = \ln\left(\frac{Pr(Y_{ijk})}{1-Pr(Y_{ijk})}\right) = \mu + \pi_j + \tau_{d[i,\ j]} + s_{ik}$.

When analyzing such models, an important distinction regarding the subject effect, s_{ik}, must be made. The effects can be assumed to be unknown fixed parameters or they can be assumed to be realizations of random variables. In the linear modeling case, subject effects

assumed to be fixed can be analyzed using the generalized linear model with ordinary least squares (OLS) procedures, with mean zero and variance σ_S^2. When the subject effects are termed as random, generalized linear mixed modeling techniques using restricted maximum likelihood (REML) or other types of estimation must be used. This distinction is less restrictive in non linear models with dichotomous outcomes because in both instances parameters are estimated using maximum likelihood estimation. However in the random effects case specific procedures such as the Newton-Raphson method are employed to account for modeling of the random effects.

One problem that often arises in crossover designs is the use of repeated measures. In OLS regression all observations assume independent errors therefore errors should be uncorrelated, however in repeated measures designs, measurements taken adjacent in time are likely to be more correlated than distant observation altering the usual covariance structure. This is likely to affect inferences being made. In order to control for this error, the above model can be expanded to incorporate different covariance structures by expansion of the generalized linear model ($g(\mu) = X'\beta + \varepsilon$) to the generalized linear mixed model ($g(\mu) = X'\beta + Z'v + \varepsilon$), where $g(\mu)$ is function of a random variable y with an assumed distribution, $X'\beta$ denotes fixed effects, Zv denotes random effects and ε is a vector of unobserved random errors. Additionally, Z is a known design matrix of random effects and v is a vector of unknown random effects parameters.

In this model we assume:

1) $E(v) = 0$ and $Var(v) = G$;
2) $E(Y \mid v) = X\beta + Zv$ and $Var(Y \mid v) = R$;

Using this model we can specify the structure of G or R to account for correlated data. For dichotomous outcomes we assume a binomial distribution with a logit link function:

$\Pr(Y) = \frac{1}{1+e^{-(X'\beta + Z'v)}}$. Applying this to our original model, $Y_{ijk} = \mu + \pi_j + \tau_{d[i,j]} + s_{ik} + \varepsilon_{ijk}$, the fixed effects represented by β will contain the treatment and period effects (π_j and $\tau_{d[i,\ j]}$, respectively) while the subject effects (s_{ik}) will be represented by Z as a random effect. The same is true in the model of the continuous outcome variables; however we can also model repeated measures in the R variance-covariance matrix in addition to the random effects, Z. Other fixed and random effects can be added to the model accordingly.

1.4 OBJECTIVES

Using data from a 6-week crossover study of short-term smoking cessation in response to medication versus placebo, the proposed study will examine the direction of the relationship between self efficacy and abstinence collected over 5 days of attempted smoking cessation per medication condition. The primary objectives of this study are as follows:

1) To apply generalized linear mixed modeling techniques to examine the relationship between self efficacy and smoking cessation, specifically abstinence from smoking.
2) To determine if self efficacy is predictive of subsequent next day cessation success (i.e. abstinent or not abstinent), as traditional self efficacy theory would suggest, or if cessation success is predictive of subsequent same day self efficacy levels, as suggested by the findings of Romanowich et al. (2009).

2.0 METHODOLOGY

2.1 PARTICIPANTS

Participants were included in the study if they were between the ages of 18 and 65, smoked at least 10 cigarettes per a day for a year or more, had a carbon monoxide (CO) reading ≥ 10ppm, and currently were not in the process of quitting. Intention to quit was measured by asking potential participants if they intended to quit within the next 2 months, 4 months, 6 months, or a year. Those who intended to quit between 2 and 6 months were excluded from participation. Those who stated that they intended to quit within the next 2 months (< 2 months) were labeled as "high" in current quit interest, and those who stated they had no interest of quitting in the next 6 months (> 6 months) were labeled as "low" quit interest. (A key aim of the larger study was to determine whether level of quit interest would affect response to medication.) Participants were recruited through local media. Advertisements stated that the study was "an evaluation of the short term effects of varenicline on smoking behavior" and that it was "not a treatment study". Interested participants were phone screened and scheduled for an in person interview if eligibility criteria were met.

2.2 MEASURES

Participant characteristics were gathered at the initial in person interview prior to entry into the trial. This included demographic data (age, ethnicity, race, education), health information

(height, weight, bmi) and smoking history (cigarettes per a day, years smoking, previous quit attempts). The Fagerstrom Test for Nicotine Dependence (FTND; Heatherton et al., 1991) was used to assess participants' degree of nicotine dependence. The FTND yields a score from 0 – 10 with 10 indicating severe dependence. Carbon monoxide (CO) levels were assessed at every visit. Abstinence during the quit week (abstinence status) was defined as a participant reporting not smoking in the last 24 hours and having a CO measurement ≤ 4 ppm. Self efficacy was assessed at all clinic visits during the participants quit attempt using one question in the Intention to Quit questionnaire, developed for the study. The question asked the participant to rate on a scale from 0 to 100 how confident you are with each statement, "I am confident I will not smoke at all tomorrow".

2.3 EXPERIMENTAL DESIGN

The study was designed as a crossover trial of one within subject factor (medication: varenicline vs. placebo) and two between subject factors: 1) current intrinsic quit interest (high or low as previously described) and 2) abstinence reinforcement (payment of $12 for abstinence or no monetary reinforcement). The study was 6 weeks long, consisting of two 3-week medication phases. A phase consisted of a baseline ad libitum smoking week (week1), a dose run up week while continuing to smoke (week 2) and a final week of taking medication while attempting to abstain from smoking (week 3). Week 1 of the 2nd phase served as the washout period prior to the start of the 2nd medication. During this washout period, participants were given no medication and required to return to smoking. Subjects who wished to continue being abstinent could not continue in the study; however, no subjects refused to resume smoking. The order of

medication administration (varenicline first or placebo first) was randomized and counterbalanced between subjects. Week 1 and 2 consisted of 3 clinic visits (Monday, Wednesday, Friday) while week 3 consisted of 5 daily visits (Monday to Friday). Daily assessments included levels of carbon monoxide, withdrawal, and craving. Self efficacy was collected daily during week 3 of both phases. For more detail see Perkins et al. (2010).

2.4 MEDICATION ADMINISTRATION

Varenicline and placebo tablets (matched in size and appearance) were obtained from pharmaceutical manufacture Pfizer (New York). During the week 2 run up of medication, participants were instructed to take .5 mg pills once a day for 3 days, followed by .5 mg tablets twice a day for 4 days. The participant was then instructed to take the full recommended dose of 1mg, twice daily, during week 3, the quit week. These instructions were the same regardless of which medication was being administered. Medication compliance was assessed via pill counts at each visit. Compliance was high with 98% of participants adherent to the regimen.

2.5 DATA ANALYSIS

2.5.1 Model Building

Generalized linear mixed modeling techniques were used to develop two models. The primary questions of interest are as follows: 1) Are self-efficacy measures taken on a single day (Monday – Thursday) predictive of abstinence status on the following day (Tuesday-Friday)? 2) Does abstinence status on a single day (Monday – Thursday) predict self-efficacy measures taken later

that same day (Monday – Thursday)? Secondary questions of interest are: 1) Do the outcome measures (self efficacy or abstinence status) differ by period (the time in the study)? 2) Do the outcome measures differ by medication received (placebo vs. varenicline)? 3) Do the outcome measures differ by quit interest (high vs. low)? 4) Do the outcome measures differ by abstinence reinforcement (monetary reinforcement vs. no monetary reinforcement)? 5) Do self efficacy or abstinence status as predictors interact with these variables? 6) Are age, CPD, or FTND significant predictors of the outcomes?

In order to address the first primary question a generalized linear mixed model with self efficacy as the predictor variable and abstinence status (quit or not quit) as the outcome variable was developed. We assumed that abstinence status follows a binomial distribution and that the relationship between the covariates and the outcome are through the logit link function. To address the first of four secondary questions of interest we included main effects of dose order, medication, intrinsic quit interest, and abstinence reinforcement (variable names are period, drug, txstatus, and reinforce, respectively). To address whether or not the relationship between self efficacy and abstinence status varies by these different conditions, interactions in which each main effect is crossed with self efficacy were included. These interactions were examined individually first. Only those significant at $p < .05$ were retained. Finally, to control for the correlations between repeated measures among subjects within periods, the subject ID number X period interaction was included as a random effect. The first model (Model 1) takes the form:

$$\Pr(Quit) = \frac{1}{1 + e^{-(X'\beta + Z'v + \varepsilon)}} \text{ where}$$

$$X' = \begin{bmatrix} 1 \\ Period \\ Drug \\ TxStatus \\ Reinforce \\ Self\ Efficacy \end{bmatrix}, \beta = \begin{bmatrix} \beta_0 \\ \beta_1 \\ \beta_2 \\ \beta_3 \\ \beta_4 \\ \beta_5 \end{bmatrix}, Z' = [SubjectIDxPeriod], v = [v_1]$$

Additionally, variables that potentially confound the relationship between self efficacy and abstinence status were considered for inclusion in the model as fixed effects; these included age, FTND, and cigarettes per a day (CPD). Because they were not the primary variables of interested their contribution to the model and their ability to confound the predictor of interest was evaluated prior to their entry into the final model by assessing their ability to predict abstinence status and by examining their effect on the estimation of the coefficients of self efficacy. Covariates with p-values $\leq$ .10 were included in the final model along with any variables that confound self efficacy's prediction of abstinence status.

In this model predictor variables were paired with a time-lagged abstinence status variable (Abstinence (T-F)) such that self-efficacy measures from Monday were paired with abstinence status from Tuesday, while self-efficacy measures from Tuesday were paired with abstinence status from Wednesday, etc. Because data were collected Monday through Friday, four day pairings for each participant were possible for each medication, therefore each participant had 8 total measures (See Tables 1 & 2 in Appendix A for data structure and for ancillary variable information including variable and distributional summaries).

To answer the second primary question a model similar to Model 1 was developed, however self efficacy, a continuous variable, was used as the outcome variable of interest.

Therefore, a generalized linear mixed model incorporating abstinence status as the primary predictor variable of interest was developed. As in the first model, main effects of dose order, medication, intrinsic quit interest, and abstinence reinforcement were included in the model and then crossed with abstinence status to obtain interaction effects. Within period subject effects were entered as a random effect to account for correlations among repeated measures within subjects contained within periods. The second model (Model 2) takes the form: $Sefficacy = X'\beta + Z'\nu + \varepsilon$ where X', β, Z and ν are as above except the outcome is now self efficacy and abstinence is now a predictor.

Similar to the first model, age, FTND, and CPD were assessed for their contribution to the model and their ability to confound the estimation of the coefficients for abstinence status. These variables were included in the final model based on the criteria previously described. Again, interactions were assessed on an individual basis and those with p-values < .05 were retained for the final model.

Unlike the first model, data were not time lagged with the outcome variable. Therefore, abstinence status from Monday was paired with self-efficacy measures taken later on Monday, similarly abstinence status on Tuesday were paired with self-efficacy measures taken later Tuesday, and so on. It is important to note that abstinence status on Friday was not be paired with self efficacy data on Friday because subjects were not required to maintain abstinence on the weekend, therefore, the self efficacy question "I am confident I will not smoke at all tomorrow" was not applicable. Figure 1 provides a conceptual representation of Models 1 and 2.

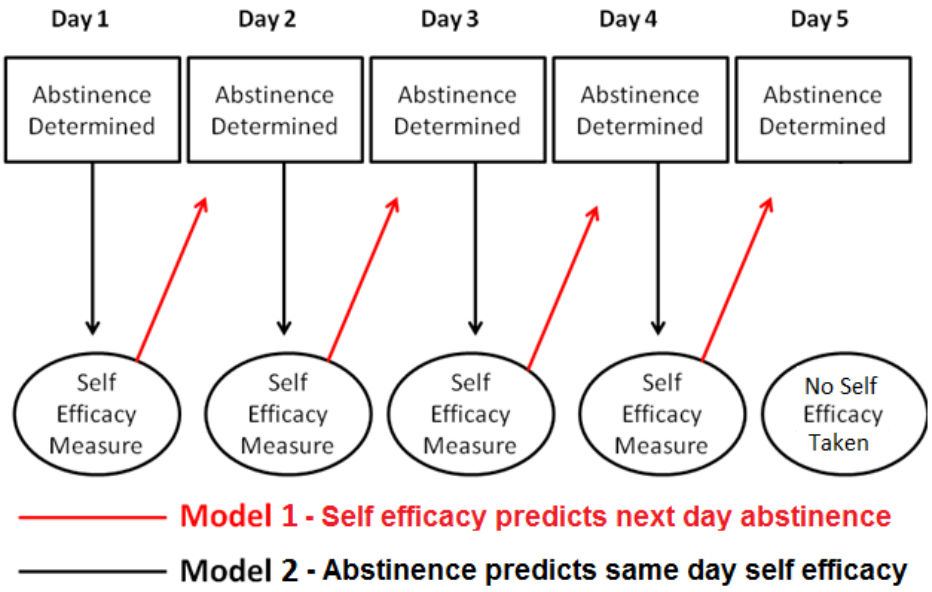

Figure 1. Conceptual depiction of Models 1 and 2 for a given treatment period.

Between subject factors, intrinsic quit interest and abstinence reinforcement, as well as within subject factors, drug and period, were entered into the model as fixed effects, regardless of their significance, to control for the study design. Interactions containing these variables that are nonsignificant were dropped for the final model. Appendix A contains summaries of all variables in the data set. Appendix B contains variable moments and boxplots.

2.5.2 Model Assumptions

Assumptions of these models include:

1) the vector of unknown random effects (ν) is multivariate normal with mean vector 0 and covariance structure *G*;

2) the vector of unobserved random errors (ε) is multivariate normal with mean 0 and covariance structure *R* (a repeated measures structure);

3) ν and ε are uncorrelated;

The error variance covariance structure estimating *G* and *R* was selected based on guidelines provided by Kinkaid, 2005. First the models were run with unstructured covariance, followed by the compound symmetry structure, and lastly other covariance structures were fitted based on the experimental design. One particular structure that was examined given the design of the data is Autoregressive(1). This covariance structure has homogeneous variances and correlations that decline exponentially over time. This structure suggests that two time points proximal in time are more correlated than those further away in time. This covariance structure is consistent with the time based daily measures of self efficacy in the present design and was a good fit for the model. Model fitting statistics, Akaike's Information Criteria and Schwarz's Bayesian Criteria, were used to compare covariance structure fit. As recommended, the structure that performs better than the compound symmetry structure was selected for the final model.

2.5.3 Missing Data

The data was assumed to be missing at random (MAR). For a data point to be considered MAR the expected value of that point should be unaffected by whether or not the observation is missing (Brown & Prescott, 2006). Therefore, we assumed that any missing observations are unrelated to abstinence status as an outcome, although the patterns of missingness may be related to other observable data (e.g. demographic characteristics). Since the missing observations are conditional on other observable data, the missing mechanism is assumed independent and

deemed ignorable. This is a plausible assumption for our data as there are few missing data points (less than 1%) and no evidence that these points are not MAR, where the missingness pattern is related to unobservable data. The MAR assumption is necessary for generalized linear mixed models (Brown & Prescott, 2006).

2.5.4 Model Diagnostics and Evaluation

The residuals and random effects were plotted against their corresponding predicted values to examine whether the residual variance was constant across observations and to visually assess outliers. Normal probability plots were used to assess the normality of the residuals and random effects. For Model 1, data were in its Bernoulli form, therefore plots of the random effects vs. predicted values were utilized to assess for outliers (Brown & Prescott, 2006)

For Model 2 (Abstinence predicts next day self efficacy), an iterative influence analysis was used to identify influential observations in which observations were removed and the model was refit resulting in an iterative re-estimation of the covariance parameters. Influential subjects were evaluated by using the likelihood distance measure. This procedure entails computing the full parameter estimates, then removing a subject and computing the parameter estimates of the reduced data. The likelihood distance gives the amount by which the log-likelihood of the full data changes if one were to evaluate it at the reduced-data estimates (Schabenberger, 2004). Points deemed to be influential were further evaluated suing Cook's D and MDFFITS, a multivariate version of Cook's D in which multiple points can be removed. Large values of these statistics indicate that the change in the parameter estimate is large relative to the variability of the estimate (Schabenberger, 2004). Outliers having influence on the model were

removed, and the model was refit. The final results report the models both with and without outliers included in the analysis. As the above options are not available when fitting generalized linear mixed models with binary data (Model 1), identified outlying observations in the self efficacy predicts abstinence model were removed and influence on the model assessed.

The final models were evaluated through a bootstrapping procedure in which 1000 bootstrap samples of size 123 were drawn with replacement. The bootstrap estimates were the mean of the 1000 estimates. These estimates were compared to the original sample estimates in order to estimate bias. Each sample maintained the frequency distributions of the design variables such that each sample had the same representation of participant randomization as well as the same representation of high versus low quit interest participants and monetarily reinforced versus not monetarily reinforced participants. This method produces a frequency distribution of the estimates whose expected value should be near the one observed in the original sample. Large values of bias, as well as original estimates outside the 95% confidence interval of the bootstrapped estimates, are evidence of lack of model fit and validity.

3.0 RESULTS

3.1 DEMOGRAPHIC CHARACTERISTICS

Participants were 124 smokers, mean age 31.1(SE: 1.0), who smoked on average 16.3 cigarettes per a day (SE: 0.5) and had a mean FTND score of 4.6 (SE: 0.1). The sample was comprised of 56.5% females. One participant had missing data for self efficacy across all days and therefore was excluded from the analyses. Therefore, 123 participants were included in the analysis. For the analysis 46.3% of participants had high quit interest and 47.1% received monetary reinforcement. Randomization to the two sequences of receiving treatment was approximately equal (51.2% vs. 48.8%). Mean self efficacy scores and percentage of individuals abstinent by day collapsed across the two periods are presented in Figure 2. Overall, a decreasing trend in mean self efficacy and the number of individuals who were abstinent on a given day was observed. Mean self efficacy ranged from 59.9 (SE: 1.97) on Day 1 (Monday) to 57. 6 (SE: 2.13) on Day 4 (Thursday). The percentage of individuals abstinent ranged between 28.6% and 36.9%, the lowest % abstinent individuals was on the final day of the periods (Friday), while the highest percent abstinent individuals was on the second day of the two periods (Tuesday).

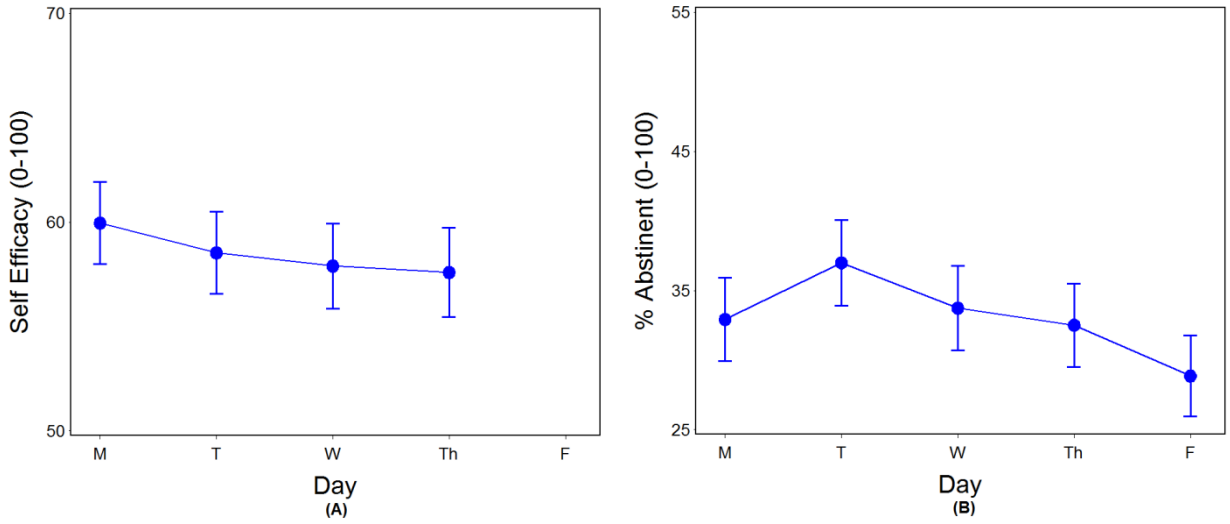

Figure 2. (A) Mean self efficacy scores by day. (B) % of participants abstinent from smoking by day.

3.2 MODEL 1: SELF EFFICACY PREDICTS NEXT DAY ABSTINENCE

The first model assessed whether self efficacy from Monday through Thursday predicted abstinence the following day on Tuesday through Friday. The model was as follows:

$$\Pr(Quit) = \frac{1}{1+e^{-(X'\beta+Z'v+\varepsilon)}} \text{ where}$$

$$X' = \begin{bmatrix} 1 \\ Period \\ Drug \\ TxStatus \\ Reinforce \\ Self\ Efficacy \end{bmatrix}, \beta = \begin{bmatrix} \beta_0 \\ \beta_1 \\ \beta_2 \\ \beta_3 \\ \beta_4 \\ \beta_5 \end{bmatrix}, Z' = [SubjectIDxPeriod], v = [v_1]$$

3.2.1 Model 1 Covariance Structure Selection

The method of estimation using the GLIMMIX procedure in SAS v.9.2 was adaptive Gauss-Hermite Quadrature. This method does not allow the inclusion of R side effects; therefore for

this model a random intercept accounting for the differences between subjects within periods was used. The estimated variance component for this model was 7.47 indicating a large amount of information was recovered between subjects within periods. This method adequately accounts for the repeated measures aspect of the design; however it does not model a specific variance covariance pattern for the residuals, the R portion of the model variance.

3.2.2 Model 1 Variable Selection

Each covariate was assessed in a univariate model, those variables with $p < .20$ were included in the initial model. Age and CPD variables were not included in the initial model ($p = .498$ and $p=.979$, respectively). The initial model was fit with the main effects of FTND, quit interest, monetary reinforcement, period, drug, and self efficacy. The model was re-run to assess age and CPD as confounding variables. Model estimates did not differ greatly with the inclusion or exclusion of age or CPD, therefore age and CPD were removed from the model. The interactions between self efficacy and quit interest, monetary reinforcement, period, and drug as well as a crossover interaction (period X drug) were evaluated in the initial model. Of the interactions only the period X drug interaction was found to be significant ($p < .0001$). All other interactions were non-significant at the level $p > .25$. Therefore, only the period X drug interaction was retained in the final model while all other interactions were dropped. The final model was:

$$\Pr(Quit) = \frac{1}{1 + e^{-(X'\beta + Z'v + \varepsilon)}} \text{ where}$$

$$X' = \begin{bmatrix} 1 \\ Period \\ Drug \\ TxStatus \\ Reinforce \\ Self\ Efficacy \\ FTND \\ Treatment\ X\ Period \end{bmatrix}, \beta = \begin{bmatrix} \beta_0 \\ \beta_1 \\ \beta_2 \\ \beta_3 \\ \beta_4 \\ \beta_5 \\ \beta_6 \\ \beta_7 \end{bmatrix}, Z' = [SubjectIDxPeriod], v = [v_1]$$

3.2.3 Fixed effects for Model 1

Results of the final model indicated that the main effects of FTND (p = .032), self efficacy (p < 001), treatment seeking status (p = .019), and reinforcement status (p = .001) were all significant. Specifically, the log odds of being abstinent decreased by -0.328 for every unit increase in FTND. In terms of self efficacy, for every 10 unit increase the log odds of being abstinent the following day increased by 0.514. Those with high treatment seeking, i.e. those looking to quit within the next two months, had a log odds 1.12 higher than a comparable individual with low quit interest, i.e. intending to quit in greater than the next 6 months. Finally an individual who was monetarily reinforced had a log odds of being abstinent of 1.58 compared to an otherwise similar individual who was not reinforced. It should be noted that these estimates are subject specific indicating that estimates compare a subject to themselves. Finally, the interaction between period and treatment was significant indicating a crossover effect, therefore the treatment effect depended on the period in which it was received. Table 1 provides parameter estimates, standard errors and p-values for Model 1. Figure 3 provides a plot of the increase in the log odds of abstinence for every unit increase in self efficacy with 95% confidence bands.

Table 1. Parameter estimates, standard errors and p-values for Model 1.

Effect	Estimate	Std. Error	p-value	95% CI Lower Bound	95% CI Upper Bound
Intercept	-5.108	0.753	<.001	-6.591	-3.626
FTND	-0.329	0.153	0.033	-0.631	-0.027
Self Efficacy	0.051	0.007	<.001	0.037	0.066
Monetary Reinforcement (Yes = 1)	1.589	0.495	0.002	0.615	2.563
High / Low Interest to Quit (High = 1)	1.122	0.479	0.020	0.178	2.066
Period (Period 2 = 1)	2.053	0.720	0.005	2.267	5.230
Treatment (Varenicline =1)	3.749	0.752	<.001	0.635	3.471
Treatment x Period	-4.146	1.019	<.001	-6.154	-2.139

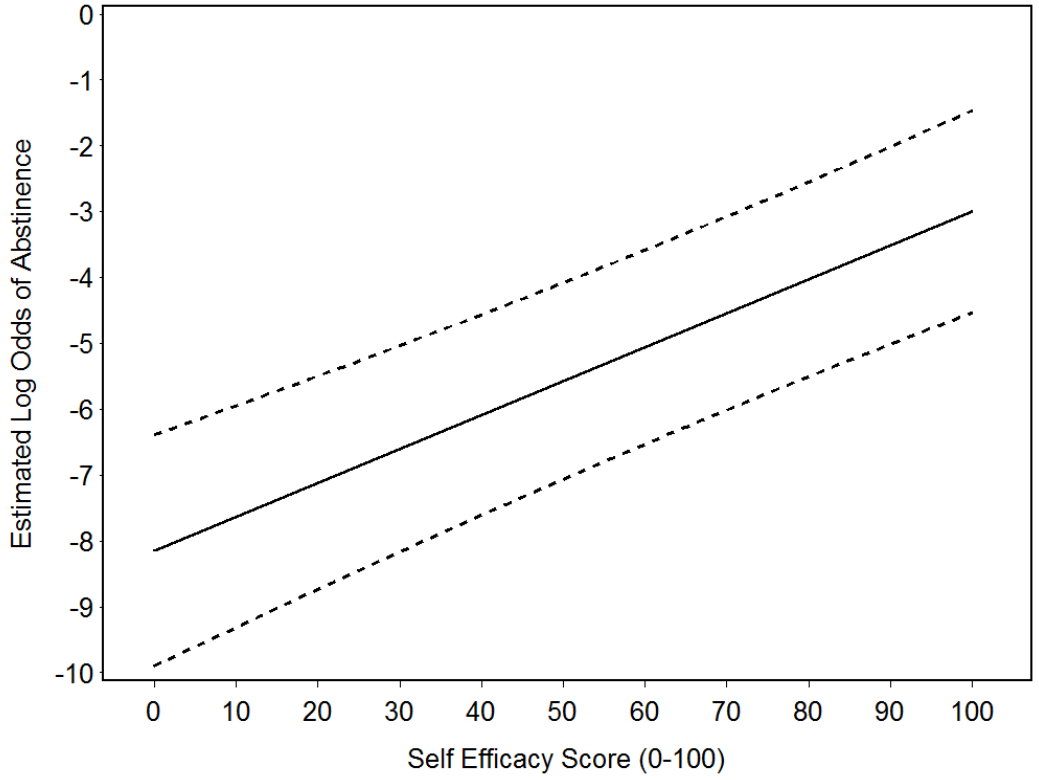

Figure 3. Estimated log odds of abstinence per 10 unit increase in self efficacy.

3.2.4 Model 1 Diagnostics

Given the data is in Bernoulli form, plots of the residuals versus their predicted values were not generated. A plot of the estimated random effects versus their predicted values showed no evidence of outliers. The normal probability plot of the random effect indicates a small amount of deviation from normality; however this does not appear to be a major issue. There is no evidence of systematic deviation from normality and therefore there is no evidence to reanalyze the data utilizing different assumptions. See Appendix C for Model 1 diagnostic and influence plots.

3.2.5 Bootstrapped Estimates for Model 1

The model was refit using 1000 bootstrap replicates of n = 123. All 1000 replicates maintained the frequency distributions of the design variables: Monetary Reinforcement, Quit Interest, and Sequence of Treatment Administration. Results of the bootstrapping procedure revealed only a small amount of bias in the original estimates. Table 2 provides a summary of the bias, bootstrap standard errors and 95% confidence intervals. The primary predictor of interest, self efficacy, had the smallest amount of bias (0.001), while the estimate for the intercept had the largest amount of bias (1.037). The 95% confidence intervals for the bootstrapped estimates are also provided. All of the original estimates fall within the confidence limits for each bootstrapped estimate indicating no evidence for lack of model validity.

Table 2. Bootstrap estimates, bias and standard error for Model 1.

Effect	Original Estimate	Bootstrap Estimate	Bias	Bootstrap Std. Error	95% CI Lower Bound	95% CI Upper Bound
Intercept	-5.11	-6.14	1.037	0.86	-8.15	-4.74
FTND	-0.33	-0.43	0.097	0.19	-0.81	-0.10
Self Efficacy	0.05	0.05	0.001	0.01	0.03	0.07
Monetary Reinforcement (Yes = 1)	1.59	1.97	-0.380	0.60	0.80	3.25
High / Low Interest to Quit (High = 1)	1.12	1.33	-0.204	0.47	0.39	2.21
Period (Period 2 = 1)	2.05	2.53	-0.477	0.76	1.21	4.26
Treatment (Varencline =1)	3.75	4.56	-0.810	0.82	3.13	6.41
Treatment x Period	-4.15	-5.04	0.895	1.25	-7.94	-2.73

3.3 MODEL 2: ABSTINENCE PREDICTS SAME DAY SELF EFFICACY

The second model examined whether abstinence during the trial was able to predict self efficacy taken later the same day. The model was as follows:

$Sefficacy = X'\beta + Z'v + \varepsilon$ where:

$$X' = \begin{bmatrix} 1 \\ Period \\ Drug \\ TxStatus \\ Reinforce \\ Abstinence \end{bmatrix}, \beta = \begin{bmatrix} \beta_0 \\ \beta_1 \\ \beta_2 \\ \beta_3 \\ \beta_4 \\ \beta_5 \end{bmatrix}, Z' = [SubjectIDxPeriod], v = [v_1] \text{ and}$$

$$\varepsilon \sim MVN[0, R], R \text{ has a specific covariance stucture}$$

3.3.1 Model 2 Covariance Structure Selection

To model the repeated measures nature of the data, the full model was fit using 5 different covariance structures. The order was as follows: 1) Unstructured 2) Compound Symmetry 3) Autoregressive (1) 4) Autoregressive (1) with random subject effects, and 5) Toeplitz. The AIC

and BIC statistics of the 5 models are shown in Table 2. The fixed effects results across the 5 structures did not differ. The Autoregressive(1) with random subject effects was selected as the final covariance structure because it estimated the least number of parameters and had estimates most similar to the unstructured covariance structure. Additionally, this structure exhibited the best AIC and BIC statistics indicating the best goodness of fit for the model.

Table 3. AIC and BIC values for 5 variance-covariance structures fit to the model.

	Structure name	AIC	BIC
1	Unstructured	8444.7	8479.8
2	Compound Symmetry	8500.3	8507.3
3	Autoregresive (1)	8452.8	8459.8
4	Autoregresive (1) w/ random subject effects*	8438.0	8448.5
5	Toeplitz	8439.9	8453.9

* selected for the final model

The autoregressive (1) structure with random subject effects specifies that the covariance between observations on the same subject comes from two sources. First, any two observations share a common contribution simply because they are on the same subject. Second, the covariance between observations decreases exponentially with time (Little et al., 2000).

3.3.2 Model 2 Variable Selection

Each covariate was assessed in a univariate model, those variables with $p < .20$ were included in the initial model. Age and CPD variables were not included in the initial model ($p = .638$ and $p=.531$, respectively). The initial model was fit with the main effects of FTND, quit interest, monetary reinforcement, period, drug, and abstinence. The model was re-run to evaluate age and

CPD as confounding variables. Model estimates did not differ with the inclusion or exclusion of age, therefore age was removed from the model. However, CPD became significant and was retained in the model. The interactions between abstinence and quit interest, monetary reinforcement, period, and drug as well as a crossover interaction (period X drug) were then included in the model individually to start. Those interactions not reaching significance were excluded from the final model. Of the interactions only the period X drug interaction was found to be significant ($p < .01$). All other interactions were non-significant at the level $p > .25$. Therefore, only the period X drug interaction was retained in the model while all other interactions were dropped.

The final model was:

$Sefficacy = X'\beta + Z'\nu + \varepsilon$ where:

$$X' = \begin{bmatrix} 1 \\ FTND \\ CPD \\ Period \\ Drug \\ TxStatus \\ Reinforce \\ Abstinence \\ Treatment\ X\ Period \end{bmatrix}, \beta = \begin{bmatrix} \beta_0 \\ \beta_1 \\ \beta_2 \\ \beta_3 \\ \beta_4 \\ \beta_5 \\ \beta_6 \\ \beta_7 \\ \beta_8 \\ \beta_9 \end{bmatrix}, Z' = [SubjectIDxPeriod], \nu = [\nu_1] \text{ and}$$

$$\varepsilon \sim MVN[0, R], R\ has\ a\ AR(1) covariance\ stucture$$

3.3.3 Fixed Effects for Model 2

Results from the final model indicated main effects of FTND (Z = -4.76, $p < .001$), CPD (Z = 1.37, $p < .002$), quit interest (Z = 2.95, p = .003), and abstinence (Z = 3.64, $p < .001$). Main effects of monetary reinforcement were nonsignificant (Z = 1.84, p = .065). The treatment X

period interaction was significant (Z= -2.69, p = .007) indicating the presence of a crossover effect on self efficacy. Parameter estimates and standard errors are provided in Table 4. Those with high quit interest had higher self efficacy than those with low quit interest. Furthermore, those who were abstinent from smoking on a given day had higher self efficacy than those were not abstinent (Figure 4). Finally, the treatment X period interaction indicated that those who received the placebo during period 1 had significantly lower self efficacy than those who received the placebo in period 2. Also those who received placebo in the second period had significantly higher levels of self efficacy compared to those who received varenicline in the second period. The estimated coefficient for FTND was $\hat{\beta}_1 = -5.843$ suggesting that as nicotine dependence increases self efficacy decreases. Additionally, the estimated coefficient for CPD was $\hat{\beta}_2 = 1.184$, therefore as CPD increased self efficacy also increased.

Table 4. Parameter estimates, standard errors and p-values for Model 2.

Effect	Estimate	Std. Error	p-value	95% CI Lower Bound	95% CI Upper Bound
Intercept	41.378	4.045	< .001	33.411	49.346
FTND	-5.843	1.228	<.001	-8.263	-3.423
CPD	1.184	0.373	0.002	0.449	1.919
Abstinent (Yes = 1)	5.753	1.579	<.001	2.653	8.852
Monetary Reinforcement (Yes = 1)	6.190	3.360	0.065	-0.430	12.810
High / Low Interest to Quit (High = 1)	9.963	3.375	0.003	3.314	16.612
Period (Period 2 = 1)	16.585	4.776	0.001	7.176	25.993
Treatment (Vareincline =1)	7.995	4.749	0.092	-1.361	17.351
Treatment x Period	-18.284	6.795	0.007	-31.670	-4.898

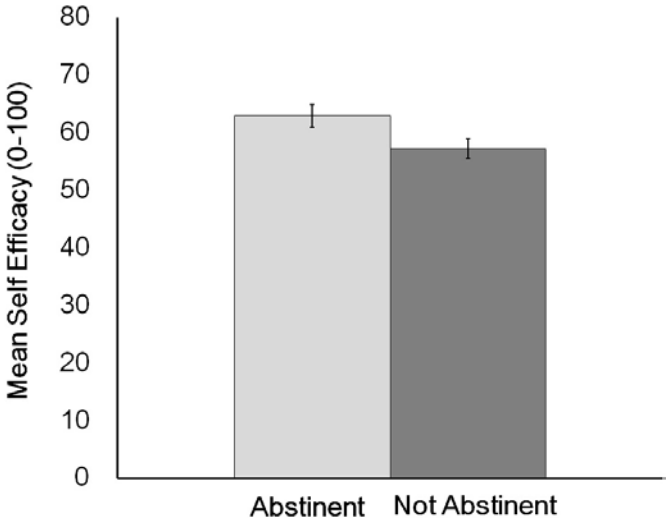

Figure 4. Adjusted self efficacy means for abstinent vs. not abstinent smokers.

3.3.4 Model 2 Diagnostics

Inspection of the residuals indicated that the model tends to under predict self efficacy at lower levels and over predicts self efficacy at higher levels. There was no evidence of deviations from normality for the residuals or random effects. Examination of the residuals revealed six potential influential points with residuals greater than ± 2. Therefore, observations 13, 22, 32, 51, 116 and 120 were examined for their influence on the model. Graphs of influence diagnostics are presented in Appendix C. Observations 32 and 51 had the highest Cook's D and MDFFITS statistics, while observation 22 exerted the most influence on covariance parameters as evidenced by the Cook's D, MDFFITS COVTRACE and COVRATIO for the covariance parameter estimates. Additionally, observations 22 and 32 had outlying values on the plot of Restricted Likelihood Distance indicating that these points influenced the log-likelihood the most. Observation 13, 116 and 120 appeared to exert minimal influence on the model in all plots

of influence statistics. Based on these influence diagnostics, the model was rerun excluding observations 22, 32 and 51. See Appendix C for Model 2 diagnostic and influence plots.

3.3.5 Removal of Influential Observations from Model 2

The three influential points identified (observations 22, 32 and 51) in our influence analysis were removed concurrently to examine their combined effect on the model. As a result, the standard errors for all estimates increased marginally, but the pattern of significant results remained the same. Estimates for most variables changed < 20%, however the estimate for our primary predictor of interest, abstinence, decreased from 5.752 to 4.310, a 25% decrease. However, abstinence remained a significant predictor of same day self efficacy ($p < .004$). Additionally, there were changes in the estimates for treatment and monetary reinforcement that were greater than 20%. Table 5 presents the estimates, standard errors, p-values and percentage change for the model after excluding the influential cases. Evaluation of the influential cases revealed no evidence of incorrect data entries. Therefore, we have no reason to exclude these cases.

Table 5. Parameter estimates, standard errors, p-values, and % change for Model 2 excluding influential points.

Effect	Estimate	Std. Error	p-value	95% CI Lower Bound	95% CI Upper Bound	% Change
Intercept	39.469	4.167	< .001	31.259	47.678	-4.6
FTND	-6.171	1.257	<.001	-8.647	-3.694	5.6
CPD	1.116	0.402	0.002	0.324	1.908	-5.8
Abstinent (Yes = 1)	4.310	1.506	<.001	1.353	7.268	-25.1
Monetary Reinforcement (Yes = 1)	7.661	3.442	0.065	0.879	14.442	23.8
High / Low Interest to Quit (High = 1)	11.124	3.470	0.003	4.287	17.962	11.7
Period (Period 2 = 1)	18.128	4.875	0.001	8.522	27.733	9.3
Treatment (Varenicline =1)	10.326	4.854	0.092	0.764	19.889	29.2
Treatment x Period	-21.881	6.953	0.007	-35.579	-8.182	19.7

3.3.6 Bootstrapped Estimates for Model 2

The model was refit using 1000 bootstrap replicates of n = 123. All 1000 replicates maintained the frequency distributions of the design variables: Monetary Reinforcement, Quit Interest, and Sequence of Treatment Administration. Results of the bootstrapping procedure revealed only a small amount of bias in the original estimates of model 2. Table 6 provides a summary of the bias, bootstrap standard errors and 95% confidence intervals. CPD had the smallest amount of bias, -0.005, while the estimate for monetary reinforcement had the largest amount of bias, -0.314. The primary predictor of interest for Model 2, abstinent, had a bias of 0.037. The 95% confidence intervals for the bootstrapped estimates are also provided. All original estimates fell within the 95% bootstrapped confidence intervals indicating no evidence for lack of model validity.

Table 6. Bootstrap estimates, bias and standard error for Model 2.

Effect	Original Estimate	Bootstrap Estimate	Bias	Bootstrap Std. Error	95% CI Lower Bound	95% CI Upper Bound
Intercept	41.38	41.07	0.310	3.78	33.64	48.36
FTND	-5.84	-5.92	0.072	1.19	-8.30	-3.66
CPD	1.18	1.19	-0.005	0.36	0.51	1.93
Abstinent (Yes = 1)	5.75	5.72	0.037	2.24	1.41	10.61
Monetary Reinforcement (Yes = 1)	6.19	6.50	-0.314	3.49	-0.35	13.48
High / Low Interest to Quit (High = 1)	9.96	10.05	-0.082	3.25	3.62	16.46
Period (Period 2 = 1)	7.99	7.92	0.076	3.75	1.01	15.50
Treatment (Varenicline =1)	16.58	16.72	-0.133	3.29	10.20	23.00
Treatment x Period	-18.28	-18.53	0.244	6.84	-32.55	-5.95

4.0 DISCUSSION

4.1 PRIMARY QUESTIONS

Two models were developed to answer the primary questions of interest. First, to address whether self efficacy is a significant predictor of next day abstinence, a generalized linear mixed model using the logit link and assuming the binomial distribution was fit. Our analysis indicated that increases in self efficacy were indicative of increases in the probability that a smoker would be abstinent the following day of the crossover trial. To answer the second primary question of interest, whether a smoker's abstinence on a single day is predictive of self-reported self efficacy taken later that day, a generalized linear model with identity link, assuming the normal distribution, was fit. Our analysis again indicated that abstinence was a significant predictor of same day self efficacy such that those who were abstinent had higher mean scores of self efficacy. Therefore, these results are indicative of a dynamic process in which abstinence is predictive of self efficacy taken the same day, and self efficacy is predictive of next day abstinence.

These results are contrary to previous clinical research in which self-efficacy measures taken on smokers attempting to quit or cut down smoking were determined to be more strongly influenced by previous smoking behavior (Gwaltney et al., 2009; Romanowich et al., 2009). Romanowich et al. (2009) found that baseline self-efficacy measures were not significantly correlated with subsequent reductions in CO, however reductions in CO did predict subsequent later increases in self efficacy. While Gwaltney et al. (2009) suggested that self-efficacy assessed

before the quit date wasn't as strongly related to abstinence status as self-efficacy assessed after the quit date. Our results, however, suggest that self efficacy is both a preceding factor in determining behavior change, as Bandura suggested, and a dependent factor influenced by previous behavior, as seen in previous studies (Gwaltney et al., 2009; Romanowich et al., 2009).

Though our results differ from previous results, this might be the result of two methodological differences between this study and other studies. Previous research has assessed self efficacy only before or after the start of a quit attempt and typically distal in time from abstinence assessment (Gwaltney et al., 2009). However, this study had multiple assessments of self efficacy proximal in time to the evaluation of abstinence. Though previous studies have shown mixed results of the self efficacy's ability to predict future abstinence, this study indicates that time of the assessment could be an important factor in determining the relationship of self efficacy with abstinence. Our research suggests that measuring self efficacy closer in time may yield a stronger relationship between self efficacy and subsequent abstinence. Additionally, this study was designed as a simulated quit attempt over a short period of time, specifically a week of quitting for each treatment period, while many other studies utilize self efficacy to predict prolonged abstinence status which may produce different results than in this simulated study. Our results may only be valid when examining self efficacy's relationship with abstinence over short intervals of simulated quit attempts.

4.2 SECONDARY QUESTIONS

Using the two models, several secondary questions were addressed. In particular, we examined whether the outcome variables (self efficacy or abstinence) differed by period, medication, quit

interest, and monetary reinforcement, and whether any of these variables interacted with the primary predictors of interest (self efficacy or abstinence). Additionally, we were interested in examining whether age, FTND or CPD were significant covariates in either of the models.

The results indicated that in both models period and medication interacted indicating a crossover effect. Therefore, individual main effects for period and medication could not be explored. In both models the outcome variables differed by when the treatment was received (period 1 or period 2). When predicting abstinence, monetary reinforcement and quit interest were both indicative of a greater probability of being abstinent the following day such that those who were monetarily reinforced or had a high quit interest had greater odds of abstinence. When predicting self efficacy, high quit interest, but not monetary reinforcement was indicative of higher self reported self efficacy. No interactions between the primary predictors of interest and these variables were observed in either of the two models. Additionally, age was not a significant predictor of either self efficacy or abstinence. CPD was a significant predictor of self efficacy such that increases in CPD led to increases in self efficacy. FTND was a significant predictor of both self efficacy and abstinence, such that increases in nicotine dependence were indicative of decreases in both self efficacy and the odds of abstinence.

While these questions were secondary to the primary hypothesis, they provide additional information about factors related to the outcomes of interest. Having high quit interest improved the odds of being abstinent. This is not surprising, as one would expect individuals with a greater interest in quitting to be more successful in their quit attempt. These results are aligned with the primary analysis of this data, in which those with high quit interest increased abstinence in the varenicline arm of the study compared to those with low quit interest (Perkins et al., 2010). Additionally, monetary reinforcement also was predictive of increased odds of abstinence. This

is consistent with previous research using contingency management. These procedures have been shown to be a successful method for increasing abstinence rates (Stitzer et al., 1986). This study also confirmed the Perkins et al. (2010) result of a crossover effect, in which the effect of medication order was significant. As the primary hypothesis of interest was not the effect of treatment, the crossover effect was retained in the model to control for its effect. Finally, higher levels of nicotine dependence as measured by the FTND were associated with decreased odds of abstinence. This is not surprising given the addictive nature of nicotine. As past research has confirmed, those who are more dependent are less likely to abstain (Courvoisier & Etter, 2010).

Research examining the relationship between smoking measures and self efficacy is scant. Therefore, our study provides insight into factors that can possibly affect self-efficacy measures. Level of quit interest, CPD and FTND were all factors found to be associated with self efficacy. The relationship of these variables with self efficacy should be further evaluated and validated for use as covariates in analyses using self efficacy as a predictor.

4.3 LIMITATIONS

Given that this study was a secondary analysis, an inherent limitation of the study was that sample size was based on power needed to detect a significant difference in the primary outcomes of interest. The primary strength of crossover trials is that the comparison of treatments within subjects reduces variance and subsequently reduces the number of patients needed to detect a clinically relevant significant difference. This study was a 2 x 2 crossover trial designed to examine how quit interest and monetary reinforcement can affect responses to treatment during a simulated quit attempt. Quit interest and monetary reinforcement were both

between subject factors, therefore the number of subjects needed to detect a significant difference in the responses of these groups would be larger than if only within subjects factors were included. Given the nature of the design, this secondary analysis may have been powered to detect relatively small differences in outcomes. Therefore, the results of this study should be examined in the context of clinical relevance rather than statistical significance.

4.4 CONCLUSIONS

Overall, this study provides evidence that self efficacy is predictive of abstinence and that abstinence predicts self efficacy, however these effects may be constrained by the timing of assessments as well as the duration of the cessation attempt. Future research could be developed to examine how timing of assessments and duration of quit attempts affects the relationship observed in this study. Additionally, our study confirmed previous research about factors that influence abstinence and identified new factors that may be important as covariates when using self efficacy as a predictor in analyses. Future research should be undertaken to validate the relationships between quit interest, CPD, FTND and self efficacy. Determining the timing and usefulness of self-efficacy measures may help discern when their use is most valid. Researchers need to be aware of how previous behaviors influence self efficacy and may want to consider entering previous behavior, such as previous abstinence, as covariates in these models.

APPENDIX A

VARIABLE SUMMARIES AND FREQUENCY DISTRIBUTIONS

Table 7. Example of the data structure in long format of first two subjects.

ID	Period	Day	Medication	TxStatus	Reinforce	Age	FTND	CPD	Sefficacy (M-Th)	Abstinence (M - Th)	Abstinence (Tu-F)
1001	1	1	0	1	1	22	4	13	40	0	0
1001	1	2	0	1	1	22	4	13	40	0	0
1001	1	3	0	1	1	22	4	13	40	0	0
1001	1	4	0	1	1	22	4	13	40	0	0
1001	2	1	1	1	1	22	4	13	50	1	1
1001	2	2	1	1	1	22	4	13	50	1	1
1001	2	3	1	1	1	22	4	13	60	1	1
1001	2	4	1	1	1	22	4	13	70	1	1
1002	1	1	1	1	0	24	8	22.9	.	0	0
1002	1	2	1	1	0	24	8	22.9	20	0	0
1002	1	3	1	1	0	24	8	22.9	20	0	0
1002	1	4	1	1	0	24	8	22.9	30	0	0
1002	2	1	0	1	0	24	8	22.9	30	0	0
1002	2	2	0	1	0	24	8	22.9	30	0	0
1002	2	3	0	1	0	24	8	22.9	.	0	0
1002	2	4	0	1	0	24	8	22.9	.	.	.

TxStatus = Intrinsic Quit Interest (1 = High interest)
Reinforce = Abstinence reinforcement (1=Monetary Reinforcement)
Medication = (1=Varenicline)
Sefficacy = Self efficacy measure: a combination of itq4_mon – itq_thurs for placebo and varenicline weeks

Table 8. Variable summaries.

Name	Label	Values	Scale	Normality
ID	ID #	N/A	N/A	N/A
age	Age	18 – 65	Ratio	Not met
gender	Gender	Male Female	Nominal	N/A
cpd	Cigarettes Per Day	0 - ∞	Ratio	Not met
ftnd	Fagerstrom Test for Nicotine Dependence	0 – 9	Interval	No
white	White Ethnicity	0 = No 1 = Yes	Categorical	N/A
black	Black Ethnicity	0 = No 1 = Yes	Categorical	N/A
asian	Asian Ethnicity	0 = No 1 = Yes	Categorical	N/A

Table 8 (continued).

hispanic	Hispanic Ethnicity	0 = No 1 = Yes	Categorical	N/A
native	Native American Ethnicity	0 = No 1 = Yes	Categorical	N/A
doseorder	Medication Order	0 = Plac – Var 1 = Var – Plac	Categorical	N/A
txstatus	Treatment Seeking Status	0 = Non Treatment Seeker 1 = Treatment seeker	Categorical	N/A
reinforce	Abstinence Reinforcement	0 = No Reinforcement 1 = Monetary Reinforcement	Categorical	N/A
itq_4_mon_var	Self Efficacy Monday Varenicline Week	0 – 100	Interval	Not met
itq_4_mon_plac	Self Efficacy Monday Placebo Week	0 – 100	Interval	Not met
itq_4_tue_var	Self Efficacy Tuesday Varenicline Week	0 – 100	Interval	Not met
itq_4_tue_plac	Self Efficacy Tuesday Placebo Week	0 – 100	Interval	Not met
itq_4_wed_var	Self Efficacy Wednesday Varenicline Week	0 – 100	Interval	Not met
itq_4_wed_plac	Self Efficacy Wednesday Placebo Week	0 – 100	Interval	Not met
itq_4_thu_var	Self Efficacy Thursday Varenicline Week	0 – 100	Interval	Not met
itq_4_thu_plac	Self Efficacy Thursday Placebo Week	0 – 100	Interval	Not met

Table 9. Frequencies of variables.

	Percentage
Female	56.45%
White	81.45%
Black	15.32%
Asian	3.23%
Hispanic	1.61%
Native	2.42%
Plac – Var	50.81%
Treatment Seekers	45.97%
Monetary Reinforcement	46.77%

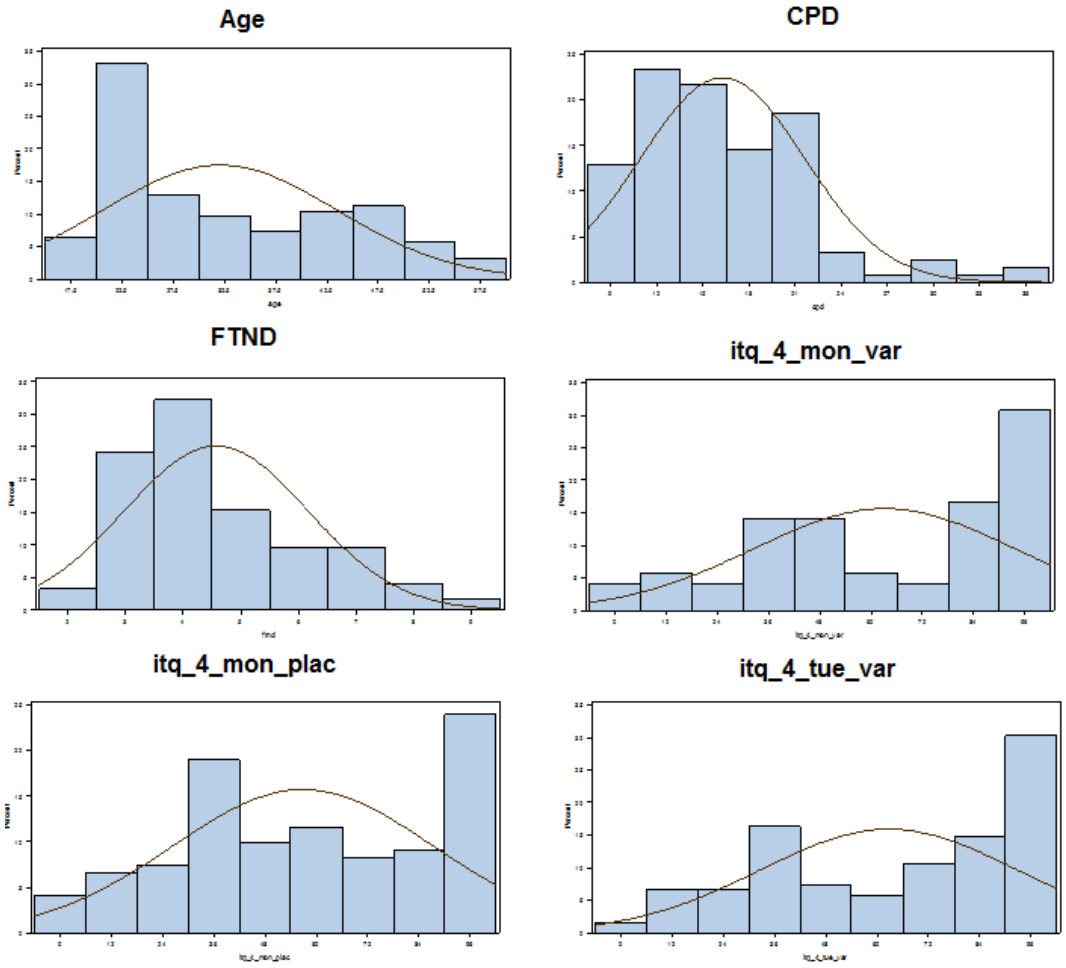

Figure 5 (continued).

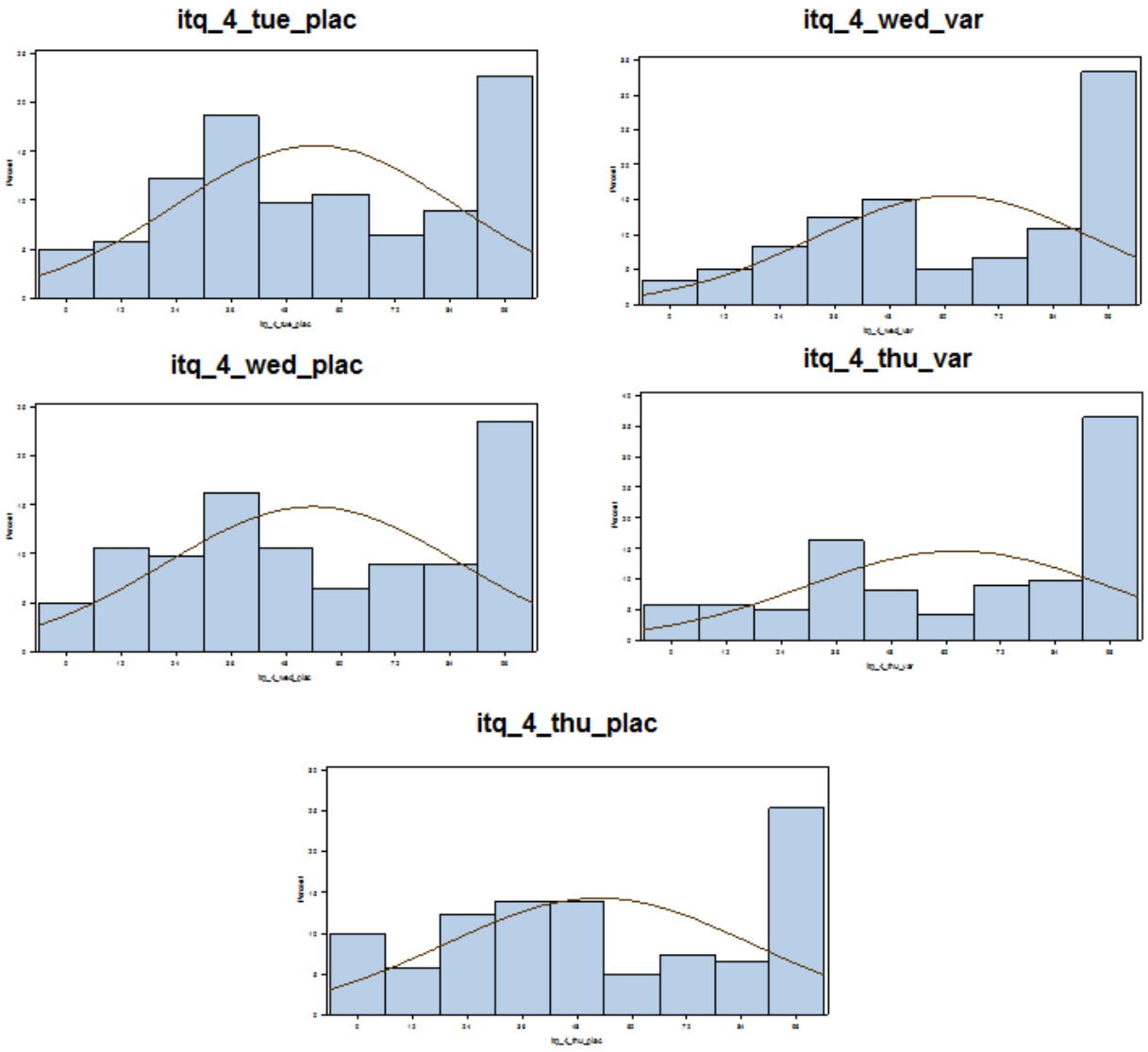

Figure 5. Histograms of variables.

APPENDIX B

VARIABLE MOMEMTS AND BOXPLOTS

Table 10. Variable moments.

Variable	N	Mean	Std Dev	Minimum	Maximum
age	124	32.0564516	11.3955507	18.0000000	58.0000000
cpd	124	16.2725000	5.3317543	8.8500000	35.0000000
ftnd	124	4.5725806	1.5884409	2.0000000	9.0000000
itq_4_mon_var	120	63.0833333	30.6455977	0	100.0000000
itq_4_mon_plac	121	56.8595041	30.4421051	0	100.0000000
itq_4_tue_var	122	62.7049180	30.0972771	0	100.0000000
itq_4_tue_plac	123	54.3902439	30.7060720	0	100.0000000
itq_4_wed_var	120	62.0000000	30.7770514	0	100.0000000
itq_4_wed_plac	123	53.9024390	32.3564711	0	100.0000000
itq_4_thu_var	123	62.4390244	32.8269547	0	100.0000000
itq_4_thu_plac	122	52.7049180	33.5265255	0	100.0000000
itq_4_fri_var	123	41.3008130	36.2360058	0	100.0000000
itq_4_fri_plac	121	32.8925620	33.1521245	0	100.0000000

Variable	N	Variance	Skewness	Kurtosis	Median
age	124	129.8585759	0.5722327	-1.0088355	28.0000000
cpd	124	28.4276043	1.2637285	2.1434100	15.0000000
ftnd	124	2.5231445	0.8053894	-0.0058891	4.0000000
itq_4_mon_var	120	939.1526611	-0.4644781	-0.9276209	70.0000000
itq_4_mon_plac	121	926.7217631	-0.1389198	-1.1053010	60.0000000
itq_4_tue_var	122	905.8460913	-0.4292560	-1.1218344	70.0000000
itq_4_tue_plac	123	942.8628549	-0.0384002	-1.1818233	50.0000000
itq_4_wed_var	120	947.2268908	-0.3779362	-1.1082189	70.0000000
itq_4_wed_plac	123	1046.94	-0.0390222	-1.3114296	50.0000000
itq_4_thu_var	123	1077.61	-0.4531232	-1.1583427	70.0000000
itq_4_thu_plac	122	1124.03	-0.0211993	-1.2959267	50.0000000
itq_4_fri_var	123	1313.05	0.3923751	-1.3085931	30.0000000
itq_4_fri_plac	121	1099.06	0.7877968	-0.6406118	20.0000000

Table 10 (continued).

Variable	N	25th Pctl	50th Pctl	75th Pctl	Quartile Range
age	124	22.0000000	28.0000000	42.5000000	20.5000000
cpd	124	12.2500000	15.0000000	20.0000000	7.7500000
ftnd	124	3.0000000	4.0000000	5.5000000	2.5000000
itq_4_mon_var	120	40.0000000	70.0000000	90.0000000	50.0000000
itq_4_mon_plac	121	30.0000000	60.0000000	80.0000000	50.0000000
itq_4_tue_var	122	30.0000000	70.0000000	90.0000000	60.0000000
itq_4_tue_plac	123	30.0000000	50.0000000	80.0000000	50.0000000
itq_4_wed_var	120	40.0000000	70.0000000	90.0000000	50.0000000
itq_4_wed_plac	123	20.0000000	50.0000000	80.0000000	60.0000000
itq_4_thu_var	123	30.0000000	70.0000000	90.0000000	60.0000000
itq_4_thu_plac	122	20.0000000	50.0000000	90.0000000	70.0000000
itq_4_fri_var	123	10.0000000	30.0000000	80.0000000	70.0000000
itq_4_fri_plac	121	0	20.0000000	50.0000000	50.0000000

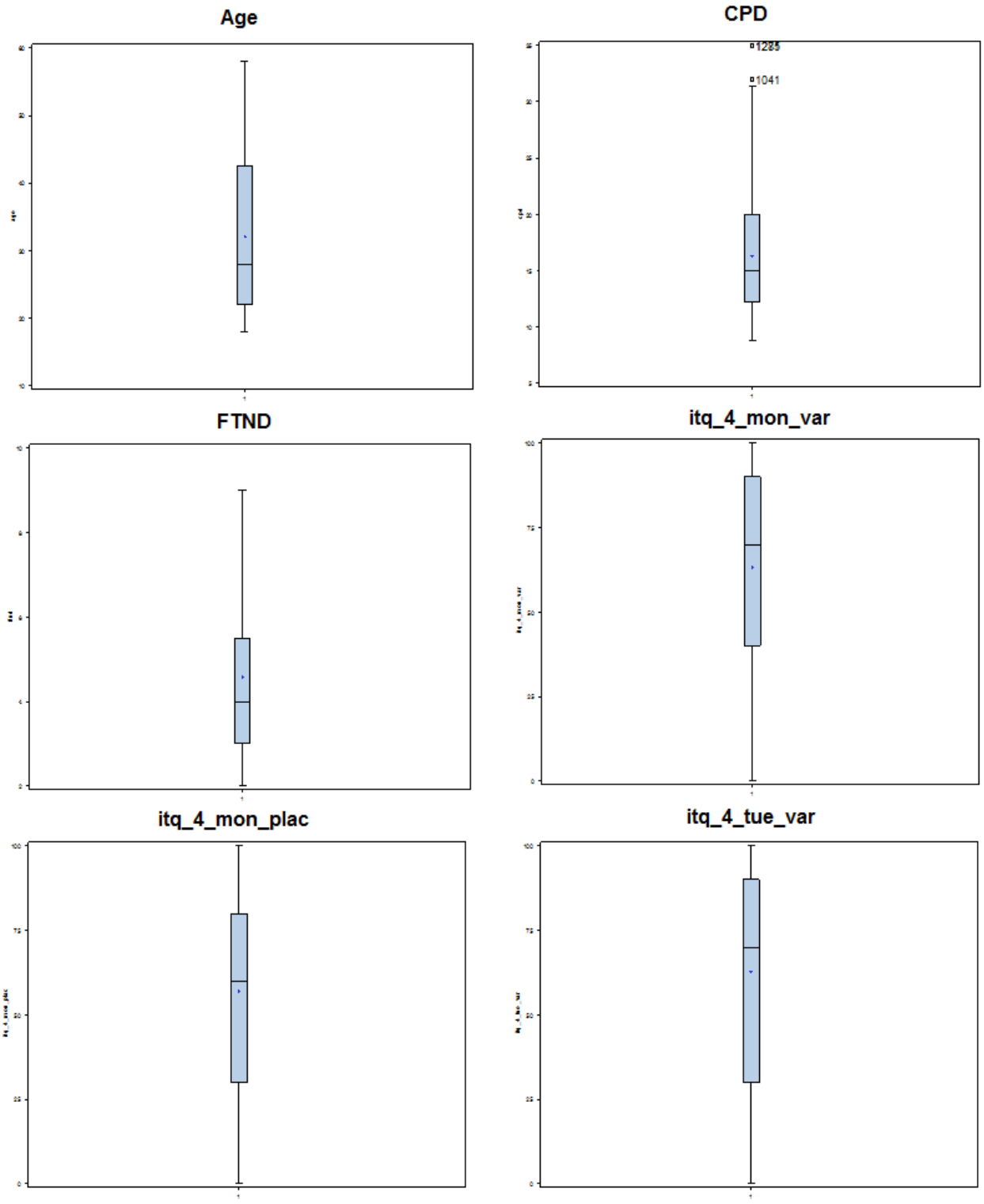

Figure 6 (continued).

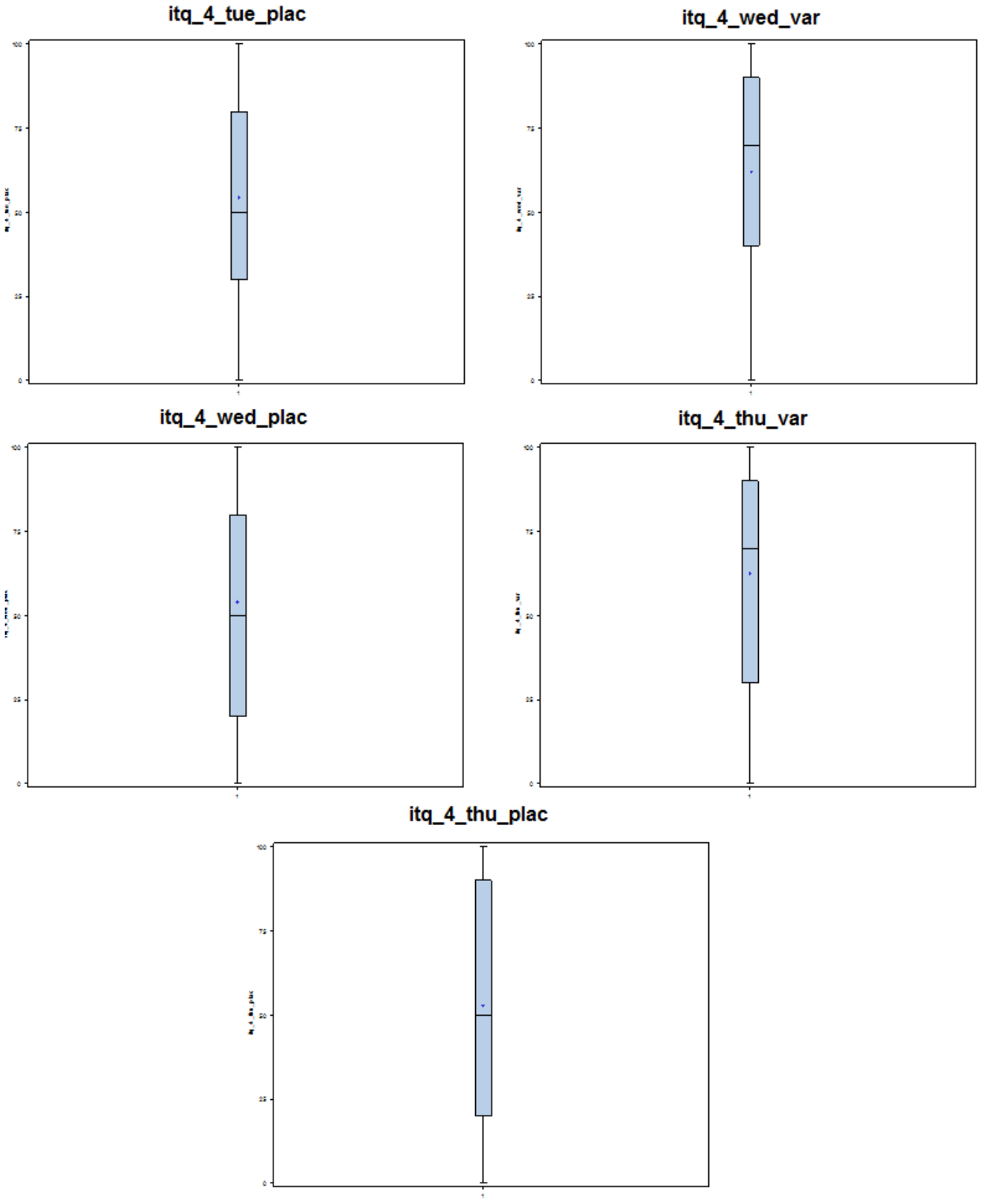

Figure 6. Boxplots of variables.

APPENDIX C

DIAGNOSTIC AND INFLUENCE PLOTS

Diagnostics for Model 1(Abstinence Predicts Next Day Abstinence)

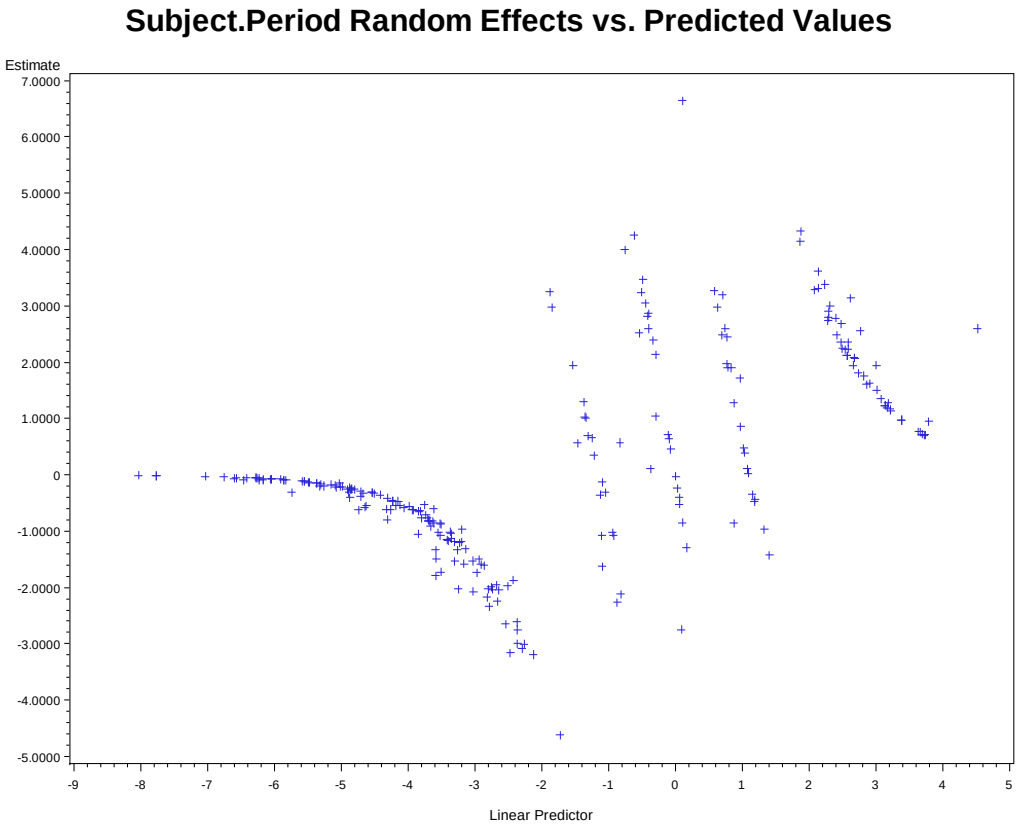

Figure 7. Plots of the random effect against its predicted values.

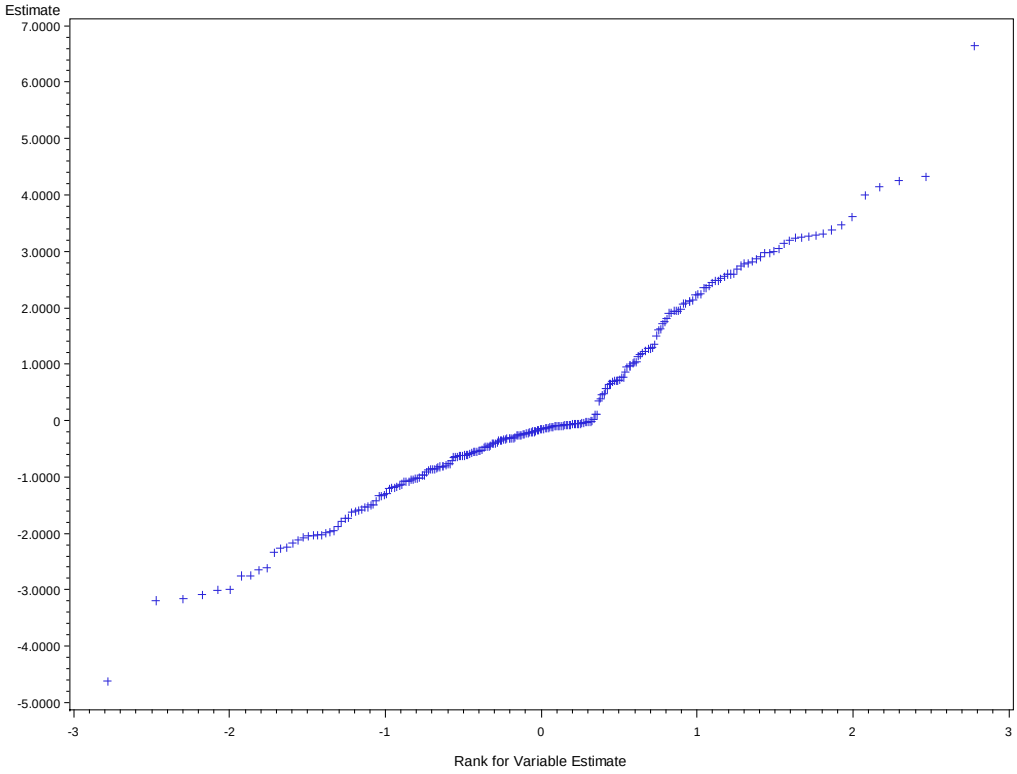

Figure 8. Normal plot of the random effects.

Diagnostics for Model 2(Abstinence Predicts Same Day Self Efficacy)

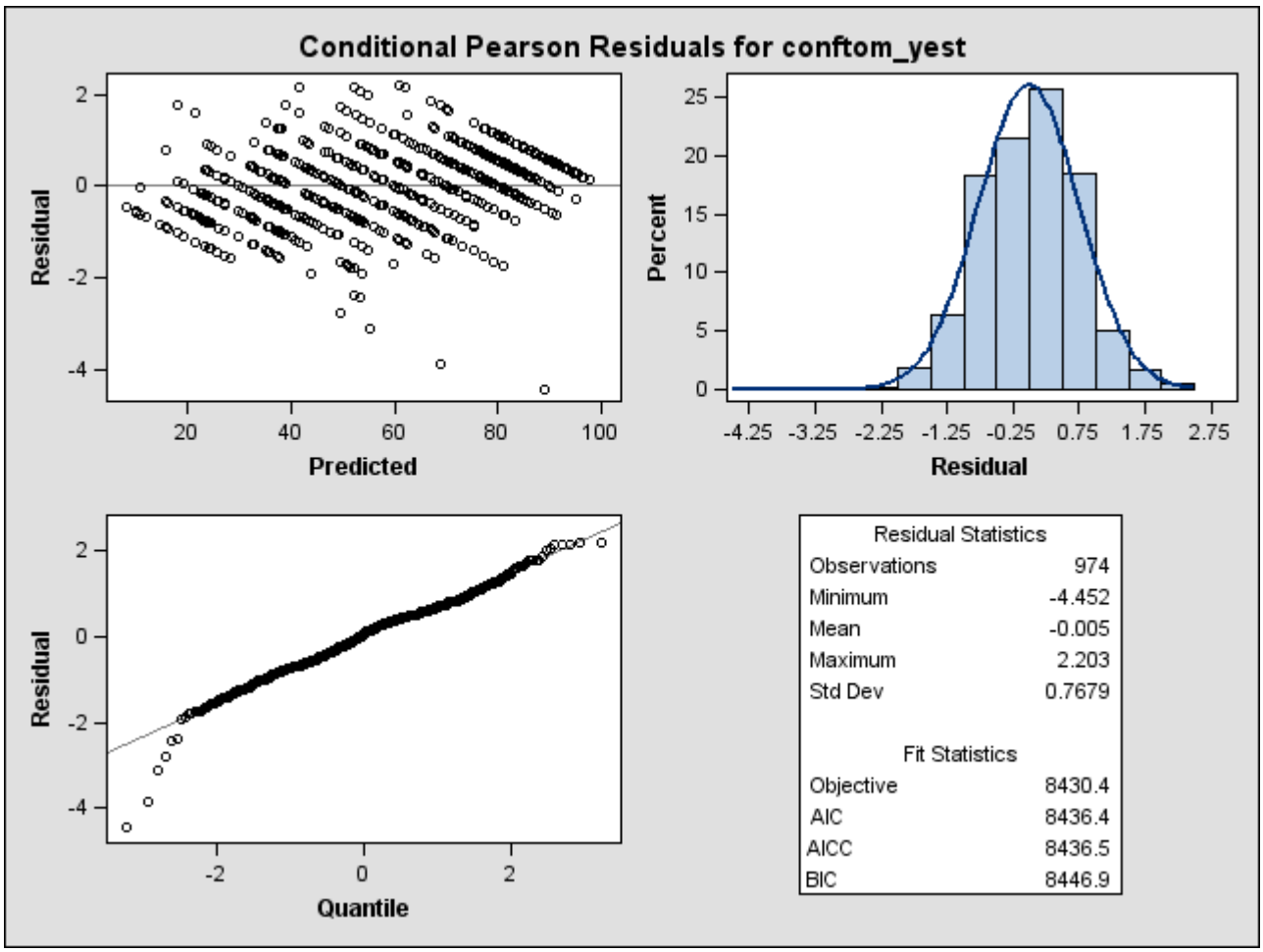

Figure 9. Residual and normal plots for conftom_yest (self efficacy).

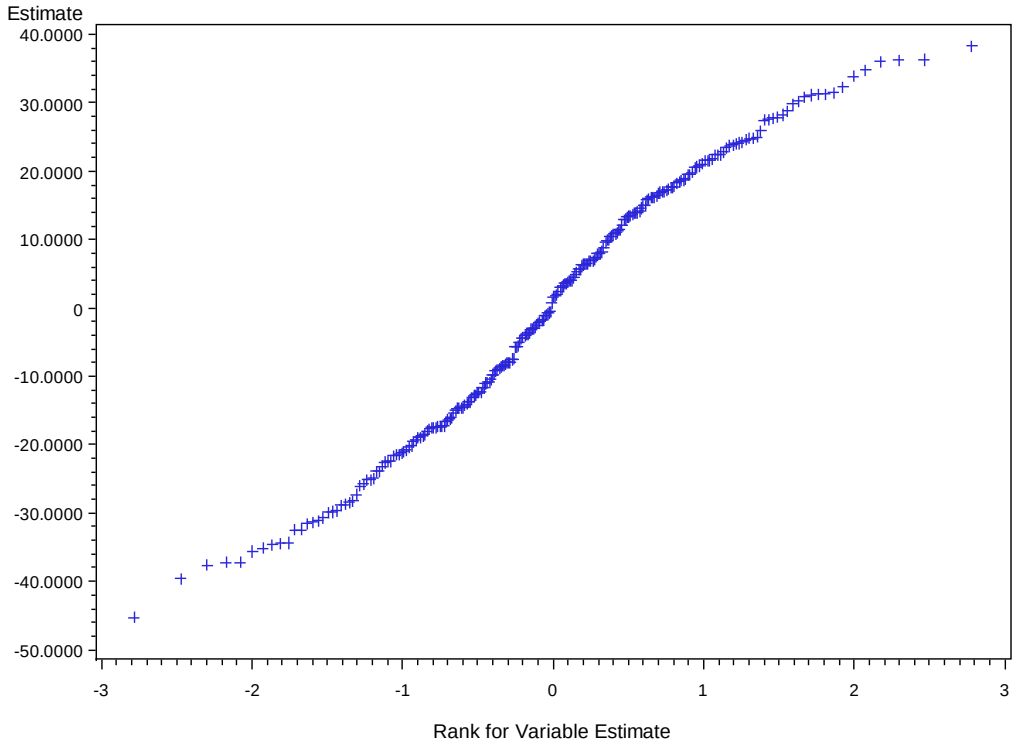

Figure 10. Normal plot of random subject x period effects.

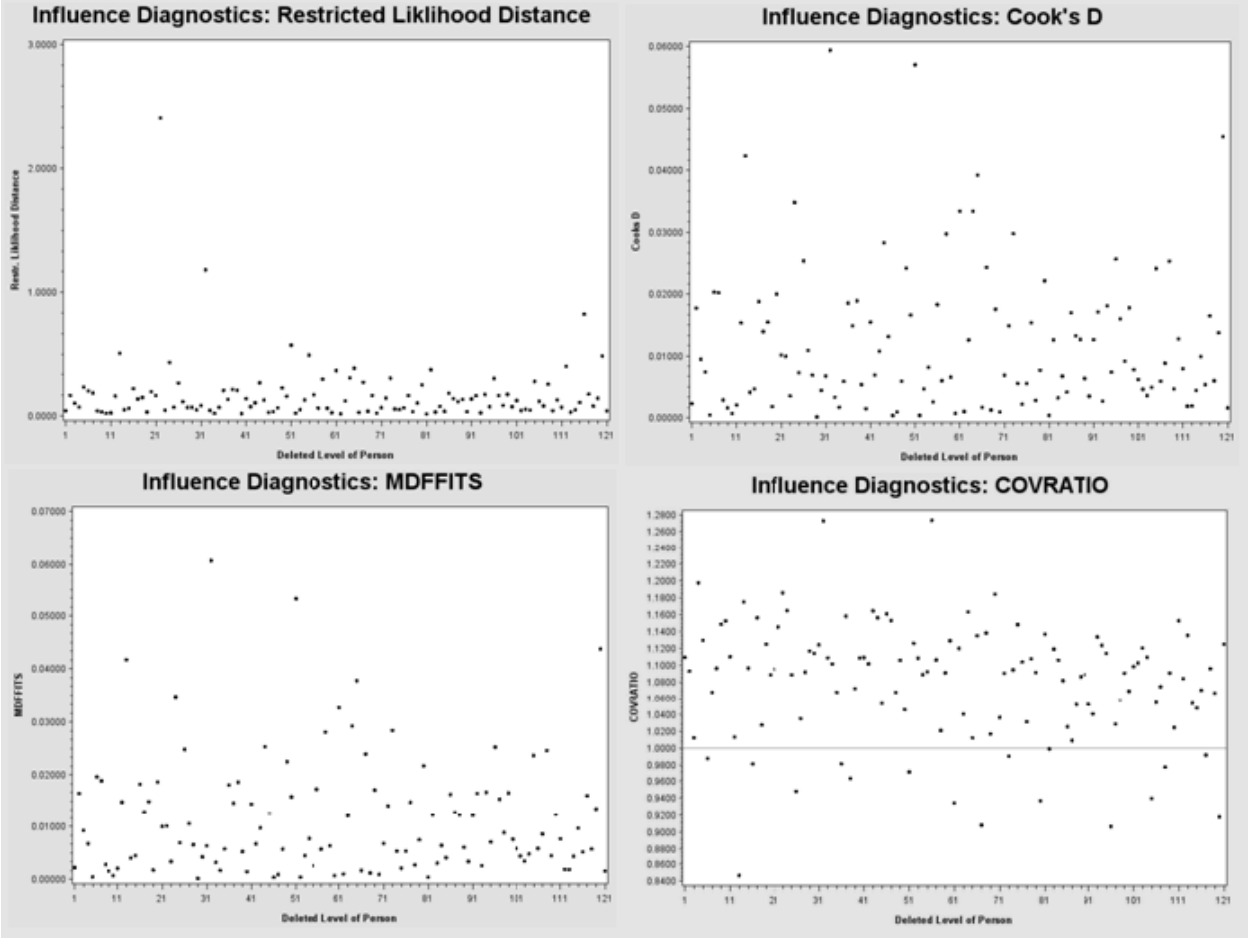

Figure 11. Influence diagnostics for fixed parameters.

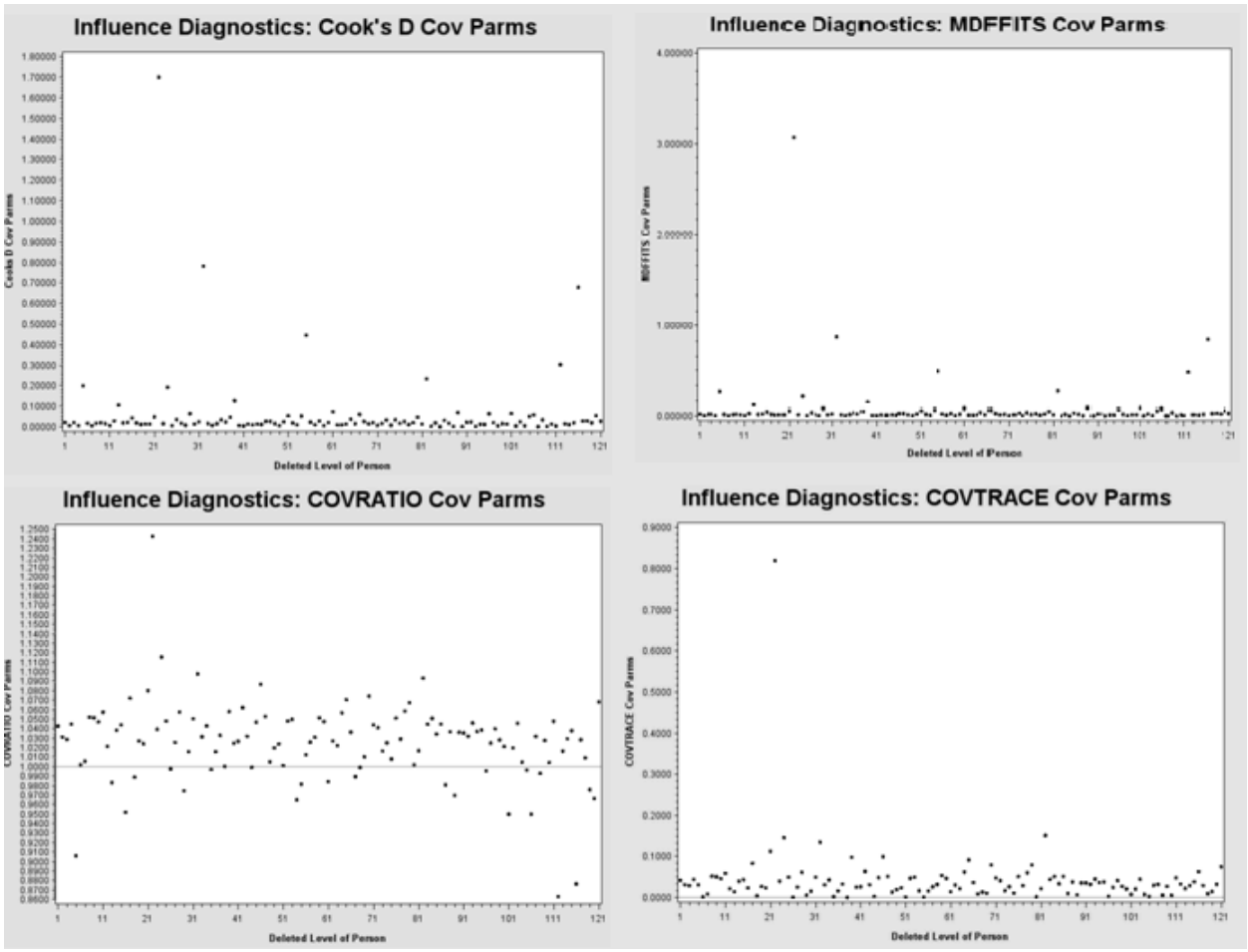

Figure 12. Influence diagnostics for covariance parameters.

APPENDIX D

GLOSSARY OF ACRONYMS

List of Acronyms used:

CO: Carbon monoxide

OLS: Ordinary least squares

REML: Restricted maximum likelihood

G: Variance-covariance matrix associated with the random effects

R: Variance-covariance matrix associated with the error residuals

FTND: Fagerstrom Test for Nicotine Dependence

CPD: Cigarettes per day

MAR: Missing at random

SE: Standard error

APPENDIX E

SAS SOURCE CODE

MODEL 1 CODE:

```
options ps=60 ls=80 nocenter nodate nonumber;

libname final "E:\Paper\SAS Data" ;

Data db3;
      infile 'E:\For K. Perkins\itq_craig_long.csv' dsd firstobs = 2;
      input subjectID education income doseorder txstatus reinforce age FTND
IntCLadder EndCLadder CPD
            period drug day CO_tdy CO_yest without_tdy without_yest
determined_tdy determined_yest
         permanent_tdy permanent_yest conftom_tdy conftom_yest confyear_tdy
confyear_yest
            abstinent_tdy abstinent_yest ;
      /*Creating Centered Continuous Variables*/
              age_cent = age - 32.0564516;
              FTND_cent = FTND - 4.5725806;
              CPD_cent = CPD - 16.2725;
              conftom_cent = conftom_yest - 58.4907598;
      label subjectID = 'ID#'
              period = 'Period'
              txstatus = 'Quit Interest'
              reinforce = 'Monetary Reinforcement'
              drug = 'Medication Type'
              conftom_yest = 'Self Efficacy (Mon-Thurs)'
              abstinent_tdy = 'Quit or Not (Tues-Fri)';
      if subjectID = 1246 then delete;
      if period = 1 then period2 = 0;
      else if period = 2 then period2=1;
      drop  education income IntCladder EndCladder CO_tdy CO_yest without_tdy
without_yest confyear_yest determined_tdy
              determined_yest permanent_yest permanent_tdy conftom_tdy
confyear_tdy abstinent_yest doseorder;
run;

%macro unimods1(name,cats,mod);
      Proc glimmix data=&name ic=pq method=quad;
      class subjectID period &cats;
      model abstinent_tdy(event='1') = &mod

                                                          / s dist=binary
link=logit ddfm=bw;
      random int / sub=subjectid(period);
run;
%mend unimods1;

/*UNIVARIATE MODELS*/
```

```
%unimods1(db3,,age_cent)
%unimods1(db3,,ftnd_cent)
%unimods1(db3,,cpd_cent)
%unimods1(db3,,conftom_cent)

/*INITIAL MODEL*/
%unimods1(db3,,ftnd_cent conftom_cent reinforce txstatus period2 drug)

/*ADDING EXCLUDED COVARIATES BACK IN MODEL*/
%unimods1(db3,,age_cent ftnd_cent conftom_cent reinforce txstatus period2
drug)
%unimods1(db3,,cpd_cent ftnd_cent conftom_cent reinforce txstatus period2
drug)
/*NO EVIDENCE OF MAJOR CONFOUNDING*/

/*ASSESSING INTERACTIONS*/
%unimods1(db3,,ftnd_cent conftom_cent reinforce txstatus period2 drug
period*drug)
%unimods1(db3,,ftnd_cent conftom_cent reinforce txstatus period2 drug
conftom_cent*drug)
%unimods1(db3,,ftnd_cent conftom_cent reinforce txstatus period2 drug
conftom_cent*period)
%unimods1(db3,,ftnd_cent conftom_cent reinforce txstatus period2 drug
conftom_cent*txstatus)
%unimods1(db3,,ftnd_cent conftom_cent reinforce txstatus period2 drug
conftom_cent*reinforce)

/*FINAL MODEL*/
ods output parameterestimates=final.fixed_abs solutionr=random;
Proc glimmix data=db3 ic=pq method=quad;
      class subjectID period;
      model abstinent_tdy(event='1') = ftnd_cent conftom_cent reinforce
txstatus period2 drug
drug*period2      / dist=binary link=logit ddfm=bw s;
      random int / sub=subjectid(period)s;
      output out=pred pred=pred student=resid;
run;


/*DIAGNOSTIC PLOTS*/
data pred2; set pred;
keep subjectID period pred; run;
proc sort data=pred2; by period subjectid ; run;
proc means data=pred2 noprint; by period subjectid; var pred;
output out=pred3 mean=re_pred N=freq; run;

proc sort data=pred3; by period subjectid; run;

data check; merge pred3 random; run;
proc gplot; plot estimate*re_pred;
title 'Subject.Period Random Effects vs. Predicted Values'; run;

Proc Rank out=norm normal=tukey; var estimate; ranks rank; run;
proc gplot data=norm; plot estimate*rank;
title 'Subject.Period Residuals - Normal Plot'; run;
```

```
/*BOOTSTAP PROCEDURE*/

Data db3_boot;
      set db3;
      if period=2 then do;
            if day=1 then day=5;
            if day=2 then day=6;
            if day=3 then day=7;
            if day=4 then day=8;
end; run;

/*TRANSPOSE TO WIDE*/

proc transpose data=db3_boot out=db3_boot1 prefix=conftom;
   by subjectid;
   id day;
   var conftom_cent;
run;

proc transpose data=db3_boot out=db3_boot2 prefix=abstinent;
   by subjectid;
   id day;
   var abstinent_tdy;
run;

data db3_boot3;
      set db3_boot;
      if day > 1 then delete;
      drop day age ftnd cpd conftom_cent period2 conftom_yest abstinent_tdy;
run;

data boot_wide;
    merge  db3_boot1(drop=_name_) db3_boot2(drop=_name_ _label_) db3_boot3;
    by subjectID;
      if drug = 0 then drug2 = 1;
      else drug2=0;
run;

proc print data=boot_wide(obs=20);
run;

/*MACRO TO SELECT 1000 REPLICATES OF THE DATA*/
%macro select (num,tx, re,dr);
data boot_wide&num;
      set boot_wide;
      if txstatus=&tx and reinforce=&re and drug=&dr;
run;

proc surveyselect data=boot_wide&num out=outboot&num
seed=123456
method=urs
samprate=1
```

```
outhits
rep=1000;
run;
%mend select;

%select(1,1,1,1)
%select(2,1,1,0)
%select(3,1,0,1)
%select(4,1,0,0)
%select(5,0,1,1)
%select(6,0,0,1)
%select(7,0,1,0)
%select(8,0,0,0)

data outboot9;
      set outboot1-outboot8;
      array daya {8} day1-day8;
      do i = 1 to 8;
            daya{i} = i;
      end;
      drop i;
run;

proc sort data=outboot9; by replicate; run;

/*CHECK FREQ DISTRIBUTIONS FOR ORIGINAL AND REPLICATE SETS*/
proc freq data=boot_wide; table txstatus*reinforce*drug; run;
proc freq data=outboot9; by replicate; table txstatus*reinforce*drug; run;

/*Return to long format*/
data boot_long;
 set outboot9;
 array conftom {8} conftom1-conftom8;
 array abstinent {8} abstinent1-abstinent8;
 array daya {8} day1-day8;
 do i = 1 to 8;
      conftom_cent=conftom{i}; abstinent_tdy=abstinent{i}; day=daya{i};
output;
end;
drop conftom1-conftom8 abstinent1-abstinent8 day1-day8 i;
run;

data boot_long2;
      set boot_long;
      if day > 4 then drug=drug2;
      if day > 4 then period=2;
      if day > 4 then day = day-4;
      if period = 1 then period2=0;
      else period2 = 1;
      drop drug2;
run;

proc print data = boot_long2 (obs=20);
run;
```

```
/*RUNNING MODEL TO GET BOOTSTRAP ESTIMATES*/
ods output parameterestimates=final.est_all ;
ods select parameterestimates;
Proc glimmix data=boot_long2 ic=pq method=quad;
      by replicate;
      class subjectID period;
      model abstinent_tdy(event='1') = ftnd_cent conftom_cent reinforce
txstatus period2 drug
drug*period2      / dist=binary link=logit ddfm=bw s;
      random int / sub=subjectid(period);
run;

      proc univariate data=final.est_all;
            class effect;
            var estimate;
            output out=final.final_boot mean=mean std=std pctlpts=2.5, 97.5
pctlpre=ci;
      run;
```

MODEL 2 CODE:

```
options ps=55 ls=76 nocenter nonumber nodate;

libname final "E:\Paper\SAS Data";

Data db2;
      infile 'E:\For K. Perkins\itq_craig_long.csv' dsd firstobs = 2;
      input subjectID education income doseorder txstatus reinforce age FTND
IntCLadder EndCLadder CPD
            period drug day CO_tdy CO_yest without_tdy without_yest
determined_tdy determined_yest
         permanent_tdy permanent_yest conftom_tdy conftom_yest confyear_tdy
confyear_yest
            abstinent_tdy abstinent_yest ;
      /*Creating Centered Continuous Variables*/
             age_cent = age - 32.0564516;
             FTND_cent = FTND - 4.5725806;
             CPD_cent = CPD - 16.2725;
      if subjectID = 1246 then delete;
      if period = 1 then period2 = 0;
      else period2 = 1;
      drop  education income IntCladder EndCladder CO_tdy CO_yest without_tdy
without_yest confyear_yest determined_tdy
             determined_yest permanent_yest permanent_tdy conftom_tdy
confyear_tdy abstinent_tdy doseorder;
      label subjectID = 'ID#'
             doseorder = 'Dose Order'
             txstatus = 'Quit Interest'
             reinforce = 'Monetary Reinforcement'
             drug = 'Medication Type'
             conftom_yest = 'Self Efficacy (Mon-Thurs)'
             abstinent_yest = 'Quit or Not (Mon-Thurs)';
```

```
run;

%macro unimods(name, cat, model);
      proc mixed data=&name ic ;
            class subjectID &cat;
            model conftom_yest = &model
                  /s ddfm=bw;
            repeated / sub=SubjectID(period) type=un r rcorr;
      run;
%mend unimods;


/*UNIVARIATE MODELS*/
%unimods(db2,period,age_cent)
%unimods(db2,period,ftnd_cent)
%unimods(db2,period,cpd_cent)
%unimods(db2,period,abstinent_yest)

/*INITIAL MODEL*/
%unimods(db2,period reinforce txstatus drug,ftnd_cent abstinent_yest
reinforce txstatus period drug)

/*ADDING AGE BACK IN*/
%unimods(db2,period reinforce txstatus drug,ftnd_cent age_cent abstinent_yest
reinforce txstatus period drug)

/*ADDING CPD BACK IN*/
%unimods(db2,period reinforce txstatus drug,ftnd_cent cpd_cent abstinent_yest
reinforce txstatus period drug)
/*RETAINING CPD*/

/*CHECKING INTERACTIONS*/
/*perid x drug*/
%unimods(db2,period reinforce txstatus drug,
ftnd_cent cpd_cent abstinent_yest reinforce txstatus period drug period*drug)
/*abstinent*drug*/
%unimods(db2,period reinforce txstatus drug,
ftnd_cent cpd_cent abstinent_yest reinforce txstatus period drug
abstinent_yest*drug)
/*abstinent*reinforce*/
%unimods(db2,period reinforce txstatus drug,
ftnd_cent cpd_cent abstinent_yest reinforce txstatus period drug
abstinent_yest*reinforce)
/*abstinent*txstatus*/
%unimods(db2,period reinforce txstatus drug,
ftnd_cent cpd_cent abstinent_yest reinforce txstatus period drug
abstinent_yest*txstatus)
/*abstinent*period*/
%unimods(db2,period reinforce txstatus drug,
ftnd_cent cpd_cent abstinent_yest reinforce txstatus period drug
abstinent_yest*period)
/*ONLY PERIOD X DRUG IS SIG*/

/*SELECTING BEST FITTING COVARIANCE STRUCTURE*/
```

```
%MACRO aic(name, titl, cov ,com);
      ods select infocrit;
      proc mixed data=&name ic ;
            title "&titl Covariance Structure";
            class subjectID period txstatus reinforce drug abstinent_yest;
            model conftom_yest = age_cent FTND_cent CPD_cent abstinent_yest
reinforce txstatus period drug
                  period*drug
                / ddfm=bw;
            &com random int/ subject=subjectID(period);
            repeated / sub=SubjectID(period) type=&cov r rcorr;
      run;
%mend aic;

%aic(db2, Unstructured, un, *)
%aic(db2, Compound Symmetry, cs, *)
%aic(db2, AR 1, ar(1), *)
%aic(db2, AR 1 with random subject, ar(1), )
%aic(db2, Toeplitz, toep, *)
/*AIC for AR1 with random subject has best AIC/BIC*/

/*FINAL MODEL (remove comments to get lsmeans)*/
ods html;
ods graphics on;
ods output influence=influence solutionr=random solutionf=final.fixed_se;
proc mixed data=db2 ic;
            title'FINAL MODEL - Abstinence Predicts Same Day Self Efficacy';
            class subjectID period /*txstatus reinforce drug
abstinent_yest*/;
            model conftom_yest = FTND_cent CPD_cent reinforce txstatus
period2 drug abstinent_yest period2*drug
                  / s cl ddfm=bw outpm = resids influence(iter=5
effect=subjectID est) residual vciry; /*OUTPUTTING MARGINAL/CONDITIONAL RESID
w/ plots*/
            random int/ subject=subjectID(period) v vcorr s;
            repeated / sub=SubjectID(period) type=ar(1);
/*          lsmeans reinforce txstatus abstinent_yest period2*drug / diff;*/
      run;
ods graphics off;
ods html close;

/**********************/
/*                    */
/*Influence Diagnostics*/
/*                    */
/**********************/

/*ADDING OBSERVATION NUMBER VARIABLE*/
data influence2;
      set influence;
      obnum = _n_;
run;

/*NORMALITY OF RANDOM EFFECTS PLOT*/
proc rank data=random out=norm normal=tukey; var estimate; ranks rank; run;
```

```
proc gplot data=norm; plot estimate*rank;
title "Normal Plot of Random Subject Effect"; run;

/*PLOTTING INFLUENCE DIAGNOSTICS*/

%macro opts (label);
goptions reset=all;
symbol value=dot color=black height=.5;
axis1 label=(a=90 f="Arial/Bold"
"&label") minor=(n=5);
axis2 label= (f="Arial/Bold" "Deleted Level of Person")order=(1 to 124 by
10);
%mend opts;

/* Fixed Effects Influence Diagnostics*/
ods html;
ods graphics off;
%opts(Restr. Liklihood Distance)
proc gplot data=influence2;
      title 'Influence Diagnostics: Restricted Liklihood Distance';
      plot RLD*obnum /vaxis=axis1 haxis=axis2;
      run;

%opts(Cooks D)
proc gplot data=influence2;
      title "Influence Diagnostics: Cook's D";
      plot cookD*obnum /vaxis=axis1 haxis=axis2;
      run;

%opts(MDFFITS)
proc gplot data=influence2;
      title 'Influence Diagnostics: MDFFITS';
      plot MDFFITS*obnum /vaxis=axis1 haxis=axis2;
      run;

%opts(COVRATIO)
proc gplot data=influence2;
      title 'Influence Diagnostics: COVRATIO';
      plot covratio*obnum /vaxis=axis1 haxis=axis2 vref=1;
      run;

/*Covariance Parameter Influence Diagnostics*/

%opts(Cooks D Cov Parms)
proc gplot data=influence2;
      title "Influence Diagnostics: Cook's D Cov Parms";
      plot cookDcp*obnum /vaxis=axis1 haxis=axis2;
      run;

%opts(MDFFITS Cov Parms)
proc gplot data=influence2;
      title 'Influence Diagnostics: MDFFITS Cov Parms';
      plot MDFFITScp*obnum /vaxis=axis1 haxis=axis2;
      run;
```

```
%opts(COVRATIO Cov Parms)
proc gplot data=influence2;
      title 'Influence Diagnostics: COVRATIO Cov Parms';
      plot covratiocp*obnum /vaxis=axis1 haxis=axis2 vref=1;
      run;

%opts(COVTRACE Cov Parms)
proc gplot data=influence2;
      title 'Influence Diagnostics: COVTRACE Cov Parms';
      plot covtracecp*obnum /vaxis=axis1 haxis=axis2 vref=0;
      run;

ods graphics off;
ods html close;

Proc print data=influence2;
      var subjectID obnum;
run;

/*DROPPING INFLUENTIAL CASES TO SEE EFFECT*/

Data db2_del;
      set db2;
      if subjectID = 1028 then delete;
      else if subjectID = 1041 then delete;
      else if subjectID = 1265 then delete;
run;

ods html;
ods graphics off;
ods output solutionf=final.fixed_se_delobs;
proc mixed data=db2_del ic ;
            title' Examining removal of 3 points';
            class subjectID period;
            model conftom_yest = FTND_cent CPD_cent abstinent_yest reinforce
txstatus period2 drug  period2*drug
                  / s cl ddfm=bw;
            random int/ subject=subjectID(period) ;
            repeated / sub=SubjectID(period) type=ar(1);
      run;
ods graphics off;
ods html close;


/*BOOTSTAP PROCEDURE*/

Data db2_boot;
      set db2;
      if period=2 then do;
            if day=1 then day=5;
            if day=2 then day=6;
            if day=3 then day=7;
            if day=4 then day=8;
end; run;
```

```
/*TRANSPOSE TO WIDE*/

proc transpose data=db2_boot out=db2_boot1 prefix=conftom;
   by subjectid;
   id day;
   var conftom_yest;
run;

proc transpose data=db2_boot out=db2_boot2 prefix=abstinent;
   by subjectid;
   id day;
   var abstinent_yest;
run;

data db2_boot3;
      set db2_boot;
      if day > 1 then delete;
      drop day age ftnd cpd period2 conftom_yest abstinent_yest;
run;

data boot_wide;
    merge  db2_boot1(drop=_name_ _label_) db2_boot2(drop=_name_ _label_)
db2_boot3;
    by subjectID;
      if drug = 0 then drug2 = 1;
      else drug2=0;
run;

proc print data=boot_wide(obs=20);
run;

/*MACRO TO SELECT 1000 REPLICATES OF THE DATA*/
%macro select (num,tx, re,dr);
data boot_wide&num;
      set boot_wide;
      if txstatus=&tx and reinforce=&re and drug=&dr;
run;

proc surveyselect data=boot_wide&num out=outboot&num
seed=30459584
method=urs
samprate=1
outhits
rep=1000;
run;
%mend select;

%select(1,1,1,1)
%select(2,1,1,0)
%select(3,1,0,1)
%select(4,1,0,0)
%select(5,0,1,1)
%select(6,0,0,1)
%select(7,0,1,0)
%select(8,0,0,0)
```

```
/*Return to long format*/
data outboot9;
      set outboot1-outboot8;
      array daya {8} day1-day8;
      do i = 1 to 8;
            daya{i} = i;
      end;
      drop i;
run;

proc sort data=outboot9; by replicate; run;

/*CHECK FREQ DISTRIBUTIONS FOR ORIGINAL AND REPLICATE SETS*/
proc freq data=boot_wide; table txstatus*reinforce*drug; run;
proc freq data=outboot9; by replicate; table txstatus*reinforce*drug; run;

data boot_long;
 set outboot9;
 array conftom {8} conftom1-conftom8;
 array abstinent {8} abstinent1-abstinent8;
 array daya {8} day1-day8;
 do i = 1 to 8;
      conftom_yest=conftom{i}; abstinent_yest=abstinent{i}; day=daya{i};
output;
end;
drop conftom1-conftom8 abstinent1-abstinent8 day1-day8 i;
run;

data boot_long2;
      set boot_long;
      if day > 4 then drug=drug2;
      if day > 4 then period=2;
      if day > 4 then day = day-4;
      if period = 1 then period2=0;
      else period2 = 1;
      drop drug2;
run;

proc print data = boot_long2 (obs=20);
run;


/*RUNNING MODEL TO GET BOOTSTRAP ESTIMATES*/
ods output solutionf=final.est_all_se ;
ods output covparms=cparms;
ods select solutionf;
ods select covparms;
proc mixed data=boot_long2 ic;
            by replicate;
            title'Boot Strap Estimates';
            class subjectID period ;
            model conftom_yest = FTND_cent CPD_cent abstinent_yest reinforce
txstatus period2 drug period2*drug
                  / s cl ddfm=bw ;
```

```
            random int/ subject=subjectID(period) v vcorr s;
            repeated / sub=SubjectID(period) type=ar(1);
      run;

/*FINAL BOOT STRAP ESTIMATES*/
      proc univariate data=final.est_all_se;
            class effect;
            var estimate;
            output out=final.final_boot_se mean=mean std=std pctlpts=2.5,
97.5 pctlpre=ci;
      run;
```

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