ACCOUNTING FOR MONOTONE ATTRITION IN A POSTPARTUM DEPRESSION CLINICAL TRIAL

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ABSTRACT

Longitudinal studies in public health, medicine and the social sciences are often complicated by monotone attrition, where a participant drops out before the end of the study and all his/her subsequent measurements are missing. To obtain accurate non-biased results, it is of public health importance to utilize appropriate missing data analytic methods to address the issue of monotone attrition.

The defining feature of longitudinal studies is that several measurements are taken for each participant over time. The commonly used methods to analyze incomplete longitudinal data, complete case analysis and last observation carried forward, are not recommended because they produce biased estimators. Simple imputation and multiple imputation procedures provide alternative approaches for addressing monotone attrition. However, simple imputation is difficult in a multivariate setting and produces biased estimators. Multiple imputation addresses those shortcomings and allows a straightforward assessment of the sensitivity of inferences to various models for non-response.

This thesis reviews the literature on missing data mechanisms and missing data analysis methods for monotone attrition. Data from a postpartum depression clinical trial comparing the effects of two drugs (Nortriptyline and Sertraline) on remission status at 8 weeks were re-analyzed using these methods. The original analysis, which only used available data, was

replicated first. Then patterns and predictors of attrition were identified. Last observation carried forward, mean imputation and multiple imputation were used to account for both monotone attrition and a small number of intermittent missing measurements. In multiple imputation, every missing measurement was imputed 6 times by predictive matching. Each of the 6 completed data sets was analyzed separately and the results of all the analyses were combined to get the overall estimate and standard errors. In each analysis, continuous remission levels were imputed but the probability of remission was analyzed. The original conclusion of no significant difference in probability of remission at week 8 between the two drug groups was sustained even after carrying the missing measurements forward, mean and multiple imputations. Most drop outs occurred during the first three weeks and participants taking Sertraline who live alone were more likely to drop out.

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1.0 INTRODUCTION

Longitudinal studies are a major contributor to the fields of public health, medicine and social sciences. The defining feature of this type of study is that several measurements are taken for each participant over time (Diggle, et. al, 1994). However, longitudinal studies are often complicated by the occurrence of attrition, i.e. when participants drop out before the end of the study (Little and Rubin, 2005). Attrition happens for many reasons, including termination of participation due to lack of effectiveness of the assigned treatment or side effects (Hogan, et. al, 2004).

We consider a monotone pattern of attrition where once a participant drops out all subsequent measurements are missing. The properties of methods used to deal with attrition depend heavily on the nature of the attrition mechanism(s). The different types of attrition mechanisms are:

a. Missing completely at random (MCAR) where "the probability that a response is missing is completely independent of both observed data and the unobserved data for that case" (Little and Rubin, 2005).
b. Missing at random (MAR) where "missingness depends on the values recorded prior to dropout, but not on values after drop out" (Little and Rubin, 2005).
c. Non-random (MNAR) if it is neither MCAR nor MAR where missingness is related to the missing measurements (Schafer and Graham, 2002).

In a longitudinal data setting where attrition is monotone, MCAR requires attrition to be independent of measurements at any occasion while MAR allows attrition to be dependent on measurements at occasions prior to attrition. In this setting, MAR is called non-informative or ignorable, while MNAR is called informative (Schafer and Graham, 2002). We consider methods to analyze the outcome of interest in a study of postpartum depression (PPD), which is remission (defined as 17-item Hamilton Rating Scale for Depression (HRS-D) score ≤ 7), after accounting for monotone attrition in a PPD clinical trial.

1.1 POSTPARTUM DEPRESSION

Many prospective, cross-sectional and retrospective studies reported that during the first postpartum year more than 10% of new mothers experienced a major depressive episode (Stowe et. al, 1995). According to the criteria of the Diagnostic and Statistical Manual of Maternal Disorders-IV (DSM-IV) and Research Diagnostic Criteria, PPD was found to occur in 8% to 12% of mothers within the first 9 weeks of childbirth (Stowe et. al, 1995).

Different studies have identified various risk factors for developing PPD. Some found progesterone, cortisol, estrogen, prolactin and thyroid function to be significantly different between postpartum depressed women and non-depressed women while others did not (O'Hara et. al, 1991; O'Hara, Schlechte, et. al, 1991; Murray and Cooper, 1997). These contradictory results can be attributed to several reasons, including inconsistencies in postpartum mood timing and measurement, overly simplistic hormonal models to account for the variability of postpartum mood and lack of adjustment for important psychological, social and biological factors. Other studies attempting to link gynecological and obstetric problems to PPD showed mixed results as

well, probably due to the use of different stress measures (Murray and Cooper, 1997). However, stressful life events such as unemployment, serious illness in a family member, problematic marital relationships, a family history of psychopathology and lack of social support from spouse, family and friends were found to play an important role in PPD in several studies (Campbell et. al, 1992; O'Hara et. al, 1983; Murray and Cooper, 1997).

1.2 THE NORTRIPTYLINE VS. SERTRALINE STUDY

Wisner et al. conducted a clinical trial comparing treatment of PPD with two medications, Sertraline (SERT) and Nortriptyline (NTP). The study was funded by the National Institute of Mental Health (NIMH). It is a double blind 8-week trial with a 16-week continuation phase. This study included postpartum women between the ages of 15 and 45 who presented for treatment within 3 months of birth, had an acute onset of PPD within one month of delivery or chronic depression throughout pregnancy, and had an HRS-D score of 18 or higher at baseline. The study was conducted at three sites: Pittsburgh, PA; Cleveland, OH and Louisville, KY. The primary outcome of interest is remission, which is based on a 17-item HRS-D questionnaire. Every week, each participant was interviewed with the HRS-D questionnaire from which a total score was obtained. Participants are considered to be in remission from depression if their total score is less than or equal to 7 (Wisner et al., 2006, in press).

From the 420 women who called to find out about the study, 337 were scheduled for a screening interview, 206 were found to be eligible and 109 enrolled in the study. Of these 109 participants, 54 were randomly assigned to NTP and 55 to SERT; 95 had follow up data for 4

weeks, 83 for 8 weeks and 29 had at least 20 weeks (Figure 1). The percentage of participants who completed the study did not differ across sites (Wisner et al., 2006, in press).

Figure 1. Randomization and follow up of participants in the Nortriptyline and Sertraline study (excerpt from Figure 3 in Wisner et al., 2006, in press)

Despite randomization, significantly more non-whites were assigned to SERT than to NTP (p=0.02, Table 1). Forty percent of participants taking SERT were non-white compared to 18.5% taking NTP.

Table 1. Demographic variables for subjects by drug group
(excerpt from Figure 6 in Wisner et al., 2006, in press)

	SERT (N=55)		**NTP (N=54)**		**significance**
Race	N	%	N	%	
White	33	60.0%	44	81.5%	*p=0.02
Non-white	22	40.0%	10	18.5 %	

*Fisher's exact test

1.3 STATEMENT OF THE PROBLEM

The original analysis of Nortriptyline vs. Sertraline study did not consider methods to deal with missing measurements and only used available data. The revised multivariable analysis of the data from this study addresses the question of whether the probability of remission at week 8 differs for participants treated with SERT compared to participants treated with NTP, accounting for monotone attrition. We restrict our analysis to the first 8 weeks of data because participants in Louisville only had 8 weeks of data. In particular we will:

i. Review relevant methods and results from the original analysis of the Nortriptyline vs. Sertraline study
ii. Review approaches to account for monotone attrition
iii. Review methodology for predicting time to withdrawal
iv. Replicate the original Nortriptyline vs. Sertraline analysis
v. Identify patterns and predictors of attrition

vi. Compare alternative analytic strategies (Last observation carried forward (LOCF), mean imputation and multiple imputation (MI)) to account for the monotone attrition

vii. Compare the results of the revised analysis to the results of the original analysis

We will impute the quantitative HRS-D variable using all available observations over time. However, as in Wisner et al. we will assess treatment effects in terms of the probability of remission at week 8.

2.0 REVIEW OF THE LITERATURE

2.1 RELEVANT METHODS AND RESULTS FROM NORTRIPTYLINE VS. SERTRALINE STUDY

The primary question was whether the probability of remission in participants treated with SERT differed from that in participants treated with NTP. It was hypothesized that probability of remission in participants treated with SERT would be significantly higher than in participants treated with NTP. In the analysis of primary outcome for the first 8 weeks, 14 of the 109 participants in the study were excluded because they provided no follow-up data beyond one week; only 95 participants actually were included in the analysis. For participants who withdrew or dropped out of the study, data was used until the week of withdrawal (Wisner et al., 2006, in press). Age, marital status, race, living status, social problems, compliance with medication, employment status, education level and parity were compared across the three sites. Age, marital status, race, living status and education level differed across the three sites and therefore were included in the multivariable logistic regression model.

$$\Pr(HRSD \leq 7) = \beta_0 + \beta_1 * SERT + \beta_2 * Age + \beta_3 * Married + \beta_4 * Race + \beta_5 * i.Education + \beta_6 * Living\_status$$

Education level is a categorical variable with 4 levels: 9 to 11 years of education (baseline), completed high school (HS), some college, and completed college; living status is a binary variable (live with another adult (baseline) and live alone); marital status also is binary (not

married (baseline) and married), as are race (white (baseline) and non-white) and drug assignment (NTP (baseline) and SERT).

The multivariable analyses of remission in the first 8 weeks using all available data showed no significant difference in probability of remission between the two drug groups at week 8 for the 95 participants followed at least one week ($p=0.82$). Therefore we fail to reject the null hypothesis that probability of remission in participants taking SERT is higher than those taking NTP (Wisner et al., 2006, in press).

2.2 METHODS FOR ANALYZING MONOTONE ATTRITION

The commonly used methods to analyze incomplete longitudinal data are complete case analysis and LOCF. Complete case analysis is not recommended because too much power and precision are lost by considering only the complete cases. Moreover, such analysis can produce biased estimators (Mazumdar et. al, 1999, Molenberghs et. al, 2004). Although the LOCF method applies the intent-to-treat principle, it is based on an unrealistic assumption that post drop out measurements would be the same as the last observed measurement (Mazumdar et. al, 1999, Molenberghs et. al, 2004).

2.2.1 SIMPLE IMPUTATION

In simple imputation, "missing values are filled in and the resultant completed data are analyzed by standard methods" (Little and Rubin, 2005). The most commonly used simple imputation procedures are:

a. Mean imputation: where missing measurements are replaced with the average of the observed measurements. This method preserves the mean of the observed measurements, but overstates the sample size and underestimates the variance. It also distorts covariances between variables (Schafer and Graham, 2002).
b. Hot deck imputation: nonrespondents' data are filled with measurements from actual respondents. In a simple univariate hot deck, each missing measurement is replaced by a random draw from the observed measurements. This method assumes no parametric model, and partially solves the problem of understating uncertainty because the variability in the measurement is preserved. However, correlations and other measures of association are still distorted (Schafer and Graham, 2002).
c. Regression imputation: where "missing variables for a unit are estimated by predicted values from the regression on the known variables for that unit" (Little and Rubin, 2005). This method overstates the strength of the relationship between dependent and independent variables and therefore is not recommended for analyses of covariance or correlations (Schafer and Graham, 2002).

These simple imputation procedures have some advantages, such as their efficiency in retaining cases, which helps to keep the power of the study high. On the other hand, implementing these procedures might be difficult in multivariable settings and might produce biased estimators. Also, because the imputed measurements are treated as known, the imputation uncertainty is not taken into account (Mazumdar et. al, 1999, Schafer and Graham, 2002).

2.2.2 MULTIPLE IMPUTATION

MI procedures address the disadvantages of the simple imputation procedures (Little and Rubin, 2005). First, MI increases the efficiency of estimation. Second, valid inferences that reflect the additional variability due to the missing measurements can be obtained. Third, MI allows the straightforward study of the sensitivity of inferences to various models for non-response (Rubin, 1987). For data sets with both intermittent and monotone missing data, Yang et al. (2005) suggest imputing intermittent missing values and dropouts in a sequential order i.e. imputing missing values as they come in order in the data set.

In MI, each missing measurement (Y_{mis}) is replaced by a vector of $m \geq 2$ imputed values. An appropriate regression model, based on the type of missing measurement, is used to impute each missing value given a set of predictor variables (X). As a result, m completed data sets are created, which can be analyzed separately using standard methods. The results of these m completed data analyses are then combined using Rubin's rule to obtain overall estimates and standard errors. According to Rubin's rule, the overall estimate is simply the average of the m estimates. So if Q represents a regression coefficient to be estimated; the overall estimate of the m estimates of Q is $Q' = m^{-1}\sum_{j=1}^{m} Q^{(j)}$. The variance of this estimate is the modified sum $T = U' + (1 + m^{-1})B$ of the average within imputation variance $U' = m^{-1}\sum_{j=1}^{m} U^{(j)}$ and the between imputations variance $B = (m-1)^{-1}\sum_{j=1}^{m}[Q^{(j)} - Q']^2$ (Rubin, 1987).

2.3 METHDOLOGY FOR PREDICTING TIME TO WITHDRAWAL

Survival analysis involves examining the predictors of time to some event such as withdrawal. The key feature of such an analysis is that all participants may not experience the event (i.e. some observations may be censored). The data first need to be set up as survival data by specifying a failure variable (withdrawal), a time variable (weeks) and a unique identification variable for each participant. Significant predictors of attrition are identified by fitting separate Cox models for each variable. Then a Cox model is fit with the identified significant univariate predictors, using backward stepwise approach with a pre-specified p-value. Eliminating non-significant predictors is important because the inclusion of too many predictors in the model may inflate the standard errors of the regression coefficients (Vittinghoff et. al, 2005).

3.0 METHODS

3.1 REPLICATING ORIGINAL NORTRIPTYLINE VS. SERTRALINE ANALYSIS

Table 2 shows the distribution of the participants who were and were not included in the original analysis of Nortriptyline vs. Sertraline study. The 14 participants were not included in the original analysis because they either had only one week of data or dropped out for personal reasons. However, the 5 participants with less than 3 weeks of data were included in the analysis because they dropped out due to either side effects or sickness (Wisner et al., 2006, in press).

Table 2. Distribution of participants who were and were not included in original Nortriptyline vs. Sertraline analysis

Weeks of data	Included in Analysis		Total
	Yes	No	
< 3	5*	14**	19
3-4	7	0	7
5-8	34	0	34
12	9	0	9
16-19	11	0	11
> 20	29	0	29
Total	95	14	109

*included in analysis because dropped out due to either side effects or sickness.
**not included in analysis because only had one week of data or dropped out for personal reasons.

The original analysis by Wisner et al. will be replicated using Stata. The logit command in Stata, which fits logistic regression models for binary outcomes, will be used to fit the probability of remission at week 8 in a model with drug assignment, marital status, living status, age, education level and race as predictors. Only interactions of significant predictors will be

tested. Box plots will be used to summarize the distributions of HRS-D for the two drug groups over time.

3.2 IDENTIFYING PATTERNS AND PREDICTORS OF ATTRITION

To better understand the pattern of missingness, the cross sectional time series commands in Stata will be used to summarize the patterns of attrition by drug group. Chi-square tests will be used to compare participants included and not included in the original analysis by drug group. Reasons for attrition by week will be cross-tabulated.

From previous studies, it was established that drug assignment (whether someone is on SERT or NTP) was a significant predictor of attrition (Wisner et al., 2006, in press). The first aim is to identify significant predictors of attrition other than drug assignment. Using Stata 9, the data will be set up as a survival data by using week number as the time variable, participant's number as the identification variable and whether participant remitted or not as the failure variable. First, univariate analysis of drug assignment, race, marital status, education level, living status and age at a significance level of 0.05 will be done. Then a Cox model will be fit including those variables found to be significant as well as drug assignment. Because the time to attrition is discrete, the exact partial method will be used to account for the tied attrition times. The non-significant predictors in the model will be removed by a backward stepwise approach using a p-value of 0.05 and only interactions of predictors remaining in the model will be tested. Kaplan-Meier curves will be used to summarize time to attrition by the identified significant predictors and drug assignment.

3.3 APPROACHES TO ACCOUNT FOR MONOTONE ATTRITION

3.3.1 SIMPLE IMPUTATION

Although the LOCF method is not recommended, it will be used as a comparison to other methods. Using Stata, the last recorded HRS-D score will be carried forward until week 8 for each participant with missing measurements. Also for comparison, we will use mean imputation to account for monotone attrition. For each participant, the mean HRS-D score of earlier weeks will be used to fill in missing measurements at later weeks. However, the mean HRS-D score measurements of later weeks will not be used fill in missing measurements at earlier weeks. This method automatically accounts for intermittent missing as well.

After that, a logistic regression model will be fit to the probability of remission at week 8 with drug assignment, race, marital status, education level, living status and age as predictors. Box plots will used to summarize the distributions of HRS-D for the two drug groups over time.

3.3.2 MULTIPLE IMPUTATION

MI will be done using the Stata 9 programs ICE (imputation by chained equations) and UVIS (univariate imputation sampling) (Royston, 2005). The ICE approach is based on each conditional density of a variable given all other variables. It has several advantages, including no assumed multivariate joint distribution, use of different kinds of weights and ease of use (Stata library).

Before doing any imputations, the DRYRUN option in ICE will be used to make sure that all the variables are treated appropriately in the imputation model, i.e. continuous variables are treated as continuous variables and modeled using a linear model while dummy variables are

created for categorical and binary variables (which are modeled using logistic regression).

Because the data are longitudinal, each participant's HRSD measurements at week 8 will be treated as the outcome variable in the imputation model and earlier HRSD measurements will be included as predictors in the imputation model along with race, age, education level, marital status, living status and drug assignment. In addition, dummy variables will be created for each participant number and week number and will be included in the imputation model with the other predictors to account for correlation within each participant. UVIS will be used to impute $HRSD_{mis}$ at week 8 based on identified predictors (race, education level, marital status, living status, drug assignment and age), earlier HRSD measurements, participant number and week number by predictive matching. Predictive matching imputes each $HRSD_{mis}$ randomly from a set of $HRSD_{obs}$ whose predicted values are closest to the predicted value for the $HRSD_{mis}$ from the regression model (Stata library). It is similar to Hot Deck imputation but gives better estimates of standard errors. Because HRS-D is a continuous variable, UVIS will use a linear regression model for the imputation. The default number of imputations is 5 but 6 that was randomly chosen, will be used in this analysis. There is still no clear reason for the choice of number of imputations (Royston, 2005). ICE calls UVIS for every variable with missing values, therefore earlier $HRSD_{mis}$ will be imputed 6 times as well using a linear regression model with race, age, education level, marital status, living status, drug assignment, earlier HRSD measurements week number and participant number as covariates (Royston, 2005). Because education level is a categorical variable with some missing values, ICE will call UVIS again after imputing $HRSD_{mis}$ to impute values for observations with missing education 6 times using an ordinal logistic regression (ologit) model with race, age, marital status, living status, drug assignment, HRSD, participant number and week number as predictors. After all $HRSD_{mis}$ and $education_{mis}$ are

imputed, we will have 6 complete data sets, which will be analyzed separately. The results of each analysis will be combined by a logistic regression model using the MICOMBINE option using Rubin's rule to obtain the overall estimates and standard errors. The DETAIL option in MICOMBINE will be used to show each of the 6 models modeled for each complete dataset. The β coefficients, standard errors and 95% confidence intervals will be summarized for each predictor in each imputation model and in the overall model. In addition, scatter plots of observed and imputed values will be shown for some of the participants.

4.0 RESULTS

4.1 ORIGINAL NORTRIPTYLINE VS. SERTRALINE ANALYSIS

The analysis of probability of remission in the logistic regression model containing drug assignment, living status, marital status, race, education level and age showed that no significant difference in the probability of remission between the two drug groups at week 8 (p=0.82) (Table 3). This finding confirms what was found by Wisner et al (2006, in press).

$$\Pr(HRSD \leq 7) = \beta_0 + \beta_1 * SERT + \beta_2 * Age + \beta_3 * Married + \beta_4 * Race + \beta_5 * i.Education + \beta_6 * Living\_status$$

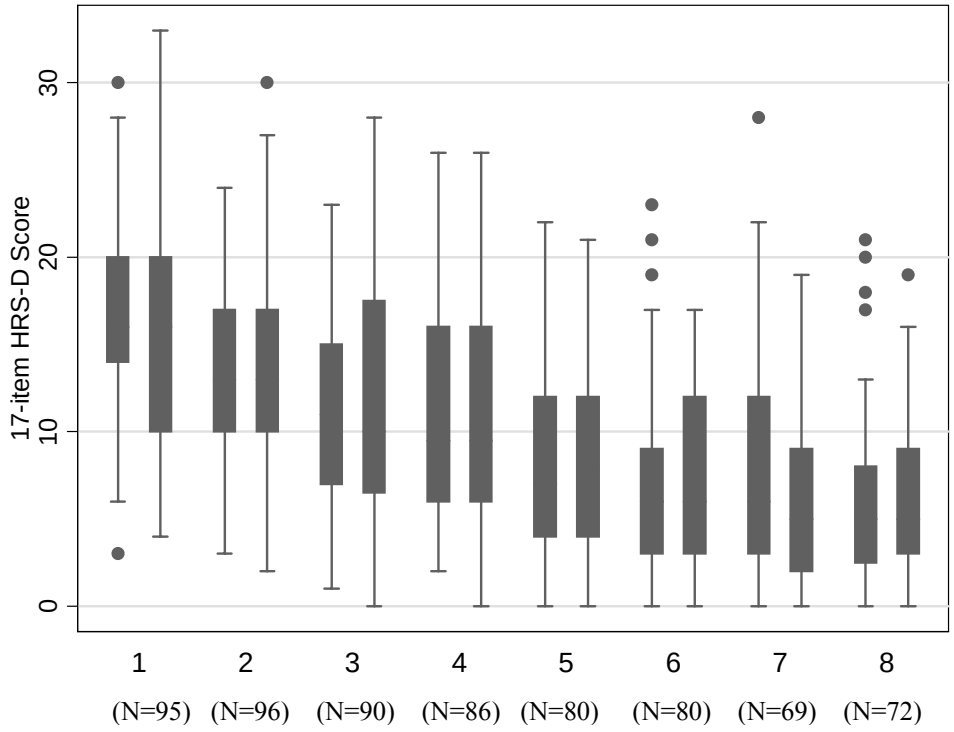
Table 3. Original logistic regression Nortriptyline vs. Sertraline analysis (N=62)

predictors	β coefficient	Standard error	p-value	95% Confidence interval	
SERT	0.14	0.59	0.82	-1.03	1.30
Age	-0.06	0.06	0.35	-0.18	0.06
Married	-0.07	0.85	0.93	-1.74	1.59
Non-white	0.37	0.82	0.65	-1.24	1.98
Completed HS	0.47	1.14	0.68	-1.77	2.72
Some College	1.03	1.01	0.31	-0.95	3.02
Completed College	1.52	1.13	0.18	-0.70	3.74
Constant	1.48	1.46	0.31	-1.37	4.34

*Living status variable was dropped by Stata from the model

Figure 2 shows the box plots of HRS-D scores by drug assignment over time. The number of participants with HRS-D scores was not constant at every week. At week 1 and week

2, 95 and 96 participants had HRS-D scores respectively while at week 9 only 72 participants did.



At each time point, first box represents NTP and second box represents SERT.
Figure 2. Box plots of HRS-D scores by drug assignment over time

4.2 PATTERNS AND PREDICTORS OF ATTRITION

Table 4 summarizes the characteristics of participants who were and were not included in the original analysis. In participants taking SERT, there was a significant difference between those included and not included in the original analysis with regard to both race ($p = 0.04$) and living status ($p < 0.001$). The same was observed in participants taking NTP with significant differences in race ($p = 0.03$) and living status ($p < 0.001$).

Table 4. Comparison of participants included and not included in original Nortriptyline vs. Sertraline analysis

	SERT				NTP			
	In (N=44)		Out (N=11)		In (N=51)		Out (N=3)	
Race	N	%	N	%	N	%	N	%
White	30	68.2	3	27.3	43	84.3	1	33.3
Non-white	14	31.8	8	72.7	8	16.0	2	66.7
Education level								
9 to 11 years	7	17.0	3	33.3	9	19.6		
Completed HS	6	14.3	1	11.1	5	10.9		
Some college	17	40.5	4	44.4	17	37.0	1	50.0
Completed college	12	28.6	1	11.1	15	33.3	1	50.0
Living status								
Alone	2	4.5	6	54.5	1	2.0	2	67.0
With adult	20	45.5	7	64.0	17	33.3	2	67.0
Marital Status								
Married	24	54.5	4	36.3	34	67.0	1	33.3
Not married	20	45.5	7	64.0	17	33.3	2	67.0
Age								
Mean	27.6		27.2		28.0		30.3	
Range	16 39		20 35		15 42		22 38	
Standard deviation	6.2		5.5		6.7		8.3	

A total of 37 participants, 23 (41.8%) from SERT and 14 (26.0%) from NTP, dropped out for various reasons. Figure 3 shows the reason and time of attrition during the first 8 weeks by drug assignment. For participants taking SERT, most dropouts occurred during weeks 1 and 3 while the number of dropouts in participants taking NTP was evenly distributed over the weeks. In participants taking SERT, side effects was the most cited reason for dropping out (8, 35.0%) while got manic and got sicker were the most cited reason for dropping out in participants taking NTP (3, 22.0% each).

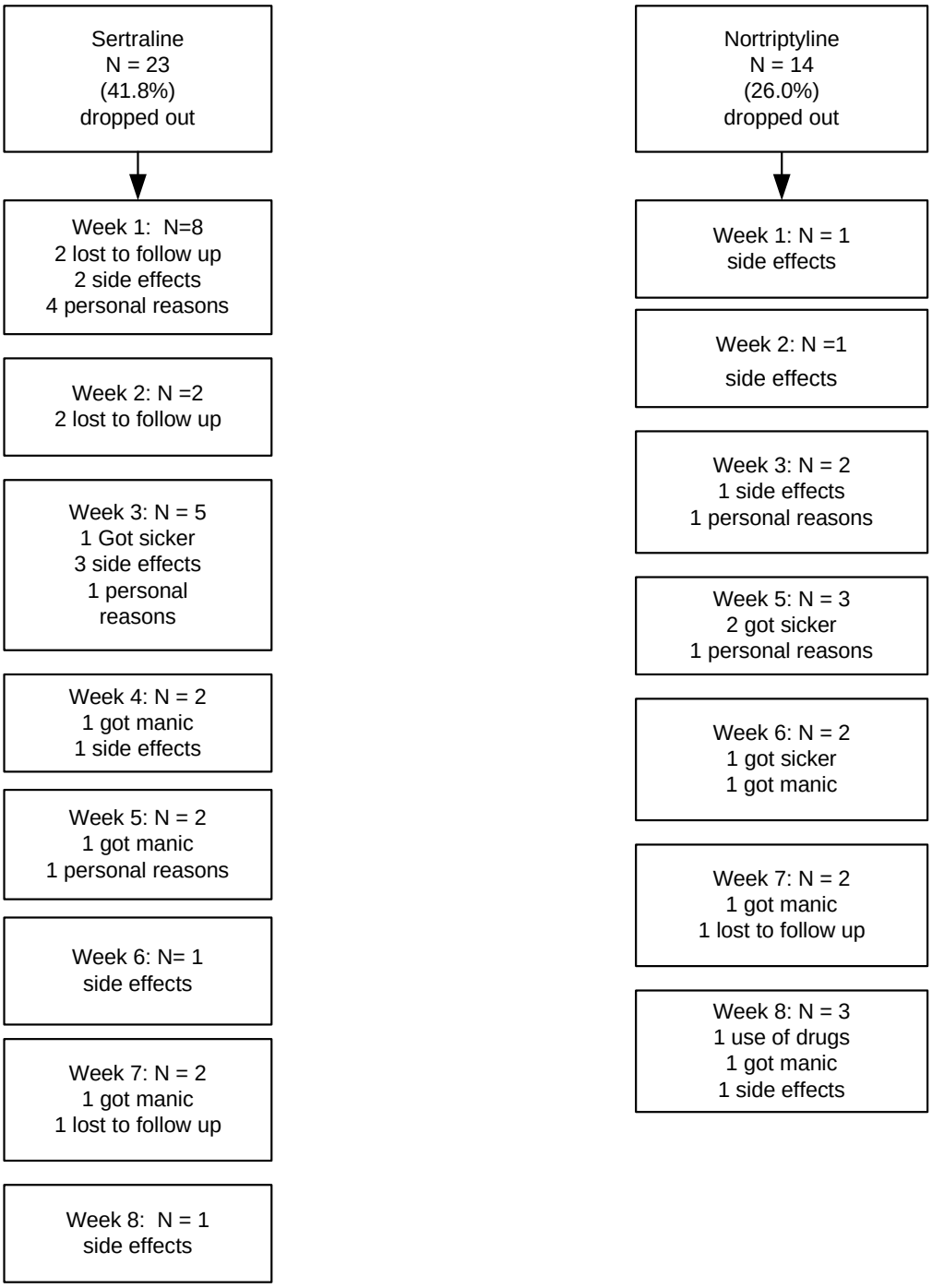


Figure 3. Reason and time to attrition by drug assignment.

Tables 5 and 6 summarize the different data patterns in terms of weeks of available data in the SERT and NTP groups of the PPD study. Table 5 shows the time patterns of the observed outcomes for participants on SERT. Twenty six (47.3%) SERT participants had complete

outcome data, 4 (7.2%) dropped out after the second week, 2 (3.6%) dropped out after the first week, 2 (3.6%) dropped out after the fourth week, 2 (3.6%) dropped out after the sixth week, 1 (1.8%) dropped out after the third week, 1 dropped out after the fifth week (1.8%) and 1 dropped out after the seventh week (1.8%). In addition, outcome data was intermittently missing for 6 (11.0%) of participants.

Table 5. Available data pattern in Nortriptyline vs. Sertraline study for participants on Sertraline

Participants		**Data pattern**
N	**%**	
26	47.3	11111111
4	7.2	11……..*
2	3.6	1……..*
2	3.6	1111……*
2	3.6	111111…*
1	1.8	111……..*
1	1.8	11111…..*
1	1.8	1111111..*
3	5.4	111111..1**
2	3.6	111…111**
1	1.8	1111.111**
1	1.8	.1……***
1	1.8	.11……..***
8	14.5	.....
55	**100.0%**	**Total**

*monotone attrition (1=observed, . = missing)
**intermittent attrition (1=observed, . = missing)
***monotone and intermittent attrition (1=observed, . = missing)

Table 6 shows the data patterns for those on NTP. Thirty one (57.4%) NTP participants had complete outcome data, 3 (5.5%) dropped out after the fourth week, 2 (3.7%) dropped out after the second week, 2 (3.7%) dropped out after the fifth week, 2 (3.7%) dropped out after the sixth week, 2 (3.7%) dropped out after the seventh week and 1 (1.8%) dropped out after the first. In addition, outcome data was intermittently missing for 6 (11.0%) participants.

Table 6. Available data pattern in Nortriptyline vs. Sertraline study for participants on Nortriptyline

Participants		Data pattern
N	**%**	
31	57.4	111111111
3	5.5	1111……..*
2	3.7	11……..*
2	3.7	11111…....*
2	3.7	111111…..*
2	3.7	1111111…*
1	1.8	1……..*
4	7.4	111111…1**
1	1.8	1…111111**
1	1.8	1111…111**
1	1.8	1111…11.***
3	5.5	…1111111
1	1.8	…….
54	**100.0%**	**Total**

*monotone attrition (1=observed, . = missing)
**intermittent attrition (1=observed, . = missing)
***monotone and intermittent attrition (1=observed, . = missing)

Tables 5 and 6 show some intermittent missing HRSD measurements in each drug group. Therefore, it is necessary to account for this type of attrition as well as monotone attrition.

Table 7 summarizes the week when each participant dropped out and the reason why. Week 1 and 3 accounted for the highest number of attritions with 9 (24.0%) and 7 (19.0%), respectively. They were due primarily to side effects and personal reasons.

Table 7. Reason of attrition by week number

Week Number	Reason for attrition (N / %)						Total
	Use of drugs/ Alcohol	Got sicker	Got manic	Lost to follow-up	Side effects	Personal Reasons	
1				2 22.2%	3 33.3%	4 44.4%	9
2				2 66.7%	1 33.3%		3
3		1 14.29%			4 57.1%	2 28.6%	7
4			1 50.0%		1 50.0%		2
5		2 40.0%	1 20.0%			2 40.0%	5
6		1 33.3%	1 33.3%		1 3.33%		3
7			2 50.0%	2 50.0%			4
8	1 25.0%		1 25.0%		2 50.0%		4

The univariate survival analysis of drug assignment, race, marital status, education level, living status and age showed that only drug assignment ($p = 0.04$), race ($p = 0.001$), marital status ($p = 0.0005$), education level ($p=0.04$) and living status ($p < 0.001$) were significant predictors of attrition. A Cox model was fit including these predictors. Using a backward stepwise approach, only drug assignment and living status remained significant in the model ($p = 0.07$ and $p < 0.001$ respectively) (Table 8). The interaction between drug assignment and living status was not significant ($p = 0.16$). Table 8 shows that participants taking SERT or living alone are more likely to drop out.

Table 8. Significant predictors of attrition in Cox model analysis

Analysis	Significant predictors	β coefficient	Hazard ratio	Standard error of hazard ratio	p-value	95% Confidence interval of hazard ratio	
	SERT	0.66	1.93	0.69	0.07	0.95	3.89
	Live alone	2.20	9.01	3.58	<0.001	4.14	19.62

Figure 4 shows the Kaplan-Meier survival curve of time to attrition by drug assignment and living status. This figure shows that participants taking SERT and living alone drop out more quickly, followed by those taking NTP and living alone, those taking SERT and living with an adult and those taking NTP and living with an adult.

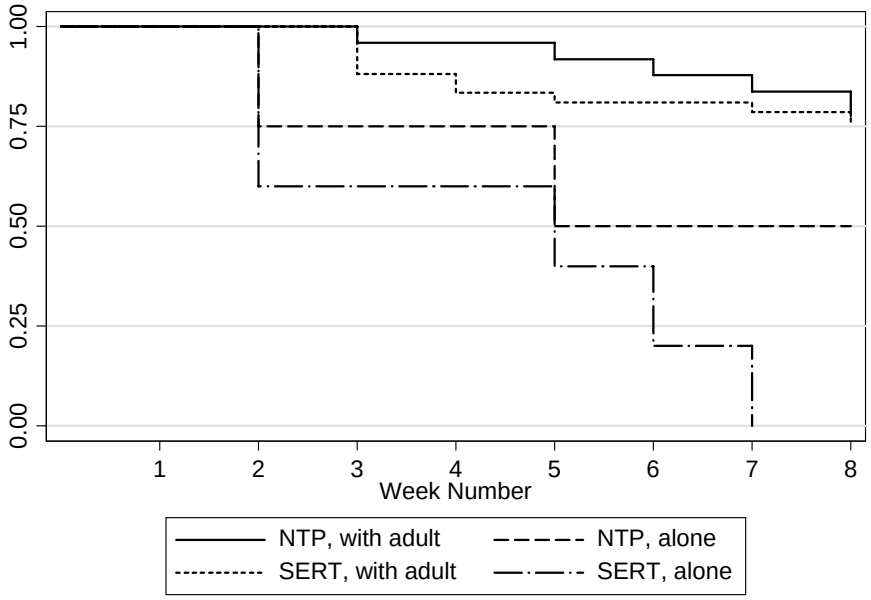


Figure 4. Kaplan-Meier survival curve of time to attrition by drug assignment and living status.

4.3 MONOTONE ATTRITION ANALYSIS

4.3.1 SIMPLE IMPUTATION

4.3.1.1 LOCF

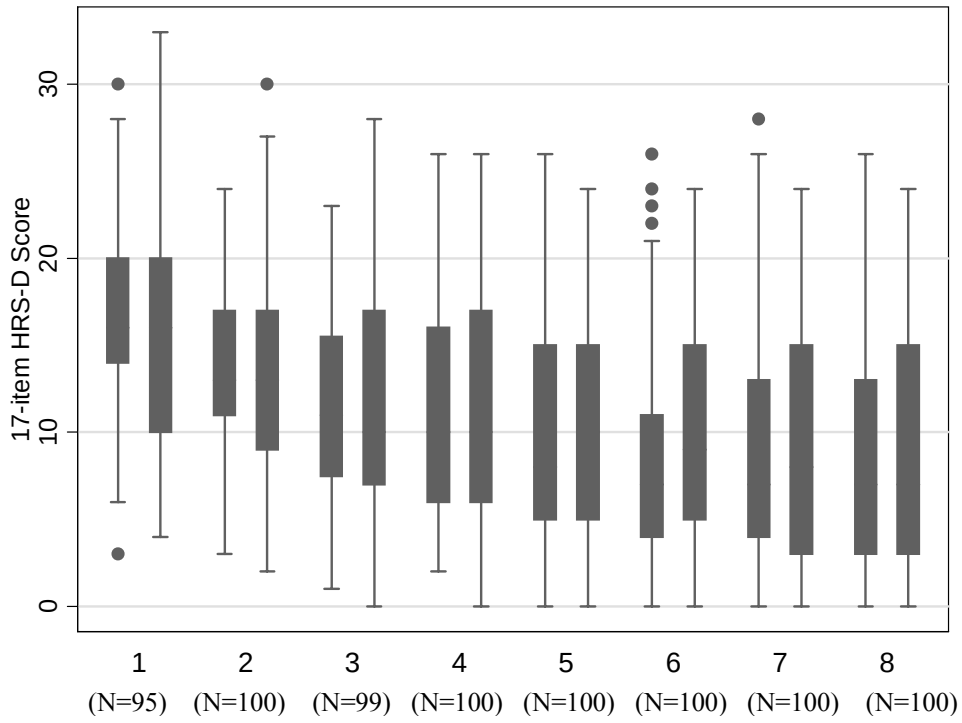
After undergoing LOCF, the logistic regression model showed that there was no difference between the two drug groups in predicting the probability of remission at week 8 (p=0.89) (Table 9). It should be noted that even after LOCF, there was still some missing measurements for some participants such as those who did not have a measurement at week 1.

$$\Pr(HRSD \leq 7) = \beta_0 + \beta_1 * SERT + \beta_2 * Age + \beta_3 * Married + \beta_4 * Race + \beta_5 * i.Education + \beta_6 * Living\_status$$

Table 9. Logistic regression analysis results after LOCF (N=93)

predictors	β coefficient	Standard error	p-value	95% Confidence interval	
SERT	0.06	0.43	0.89	-0.79	0.91
Age	-0.03	0.04	0.43	-0.12	0.05
Married	0.14	0.62	0.82	-1.08	1.35
Non-white	-0.27	0.57	0.63	-1.38	0.84
Completed HS	-0.23	0.83	0.77	-1.86	1.40
Some College	0.30	0.68	0.65	-1.03	1.63
Completed College	0.28	0.83	0.74	-1.34	1.90
Live alone	-0.69	0.87	0.43	-2.41	1.02
Constant	2.05	1.15	0.07	-0.20	4.29

Figure 5 shows the box plot of HRS-D scores by drug assignment after LOCF was carried out. The graph shows that there is no apparent differences between the two drug groups even after the missing measurements were filled in.



At each time point, first box represents NTP and second box represents SERT.
Figure 5. Box plots of HRS-D scores after LOCF by drug assignment over time

4.3.1.2 Mean Imputation

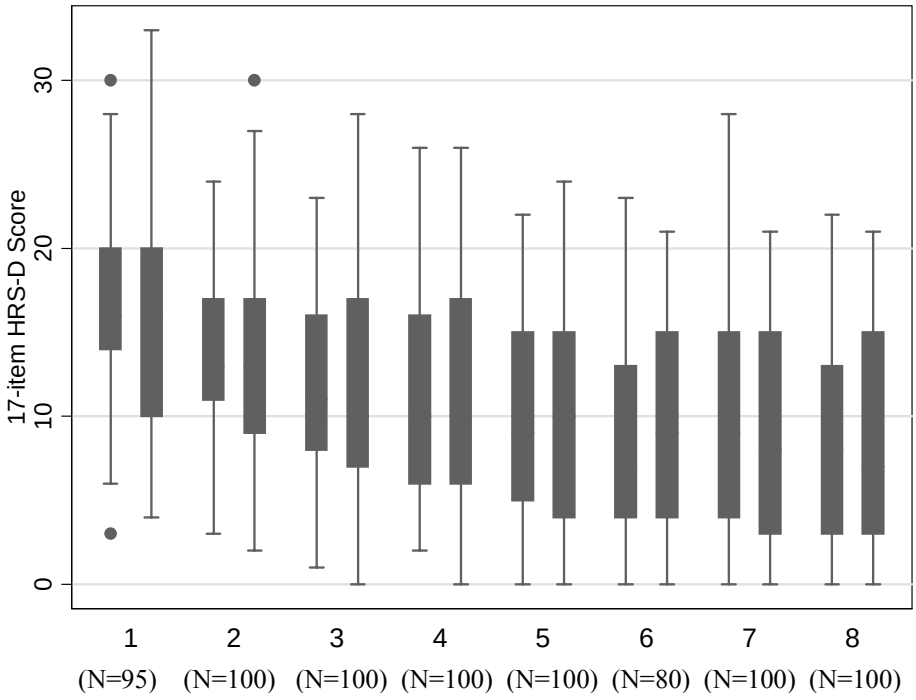
After performing mean imputation using the mean HRS-D scores for each participant, the logistic regression model showed that there was no significant difference between the two drug groups in predicting the probability of remission at week 8 (p=0.96) (Table 10). In this case, some measurements were still missing for some participants such as those with no week 1 measurements.

$$\Pr(HRSD \leq 7) = \beta_0 + \beta_1 * SERT + \beta_2 * Age + \beta_3 * Married + \beta_4 * Race + \beta_5 * i.Education + \beta_6 * Living\_status$$

Table 10. Logistic regression analysis results after mean imputation (N=93)

predictors	β coefficient	Standard error	p-value	95% Confidence interval	
SERT	0.25	0.44	0.57	-0.61	1.11
Age	-0.04	0.05	0.42	-0.13	0.05
Married	0.28	0.62	0.65	-0.94	1.50
Non-white	-0.31	0.57	0.58	-1.43	0.80
Completed HS	0.23	0.84	0.78	-1.40	1.87
Some College	0.73	0.68	0.29	-0.93	2.32
Completed College	0.69	0.83	0.40	-0.93	2.32
Live alone	-0.39	0.88	0.66	-2.12	1.34
Constant	0.41	1.07	0.70	-1.68	2.52

Figure 6 shows the box plot of HRS-D scores by drug assignment after mean imputation was carried out. At each time point, no significant differences between the two drug groups are apparent even after the missing measurements were filled in.



At each time point, first box represents NTP and second box represents SERT.
Figure 6. Box plots of HRS-D scores after mean imputation by drug assignment over time

4.3.2 MULTIPLE IMPUTATION

The DRYRUN showed that education level, which is a categorical variable, was treated as a continuous one by default. Therefore, dummy variables were created for the variable. In addition, dummy variables were created for race, marital status, living status and drug assignment to ensure that they are not being treated as continuous variables in the imputation model. Moreover, dummy variables were created for each participant number and week number to account for the correlation within each participant. Using a linear regression model, each $HRSD_{mis}$ at week 8, which was treated as the outcome variable in the imputation model to account for the longitudinal aspect of the data, was imputed 6 times based on race, living status, marital status, drug assignment, education level, participant number and week number by predictive matching. Using HRSD at week 8 as the outcome variable and creating dummy variables for participant number ensured that each participant's $HRSD_{mis}$ are linked and therefore earlier $HRSD_{mis}$ are imputed 6 times by predictive matching by predictive matching using a linear regression model with race, martial status, living status, drug assignment, week number and participant number as predictors. Each $education_{mis}$ was imputed 6 times by predictive matching as well, using an ologit model with race, marital status, living status, drug assignment, HRSD, week number, participant number and age as predictors. Stata created a new data set including the newly imputed HRSD and education level variables. The MICOMBINE option was used to combine the results of all $HRSD_{mis}$ imputations by a logistic regression model with race, education level, living status, drug assignment, age and marital status as predictors.

$$P(HRSD \geq 7) = \beta_0 + \beta_1 * SERT + \beta_2 * Age + \beta_3 * Married + \beta_4 * Race + \beta_5 * i.Education + \beta_6 * Living\_status + \beta_7 * HRSD$$

The DETAIL option in MICOMBINE showed each of the individual 6 models fit for each complete dataset. Table 11 shows the coefficient estimates, standard errors and confidence intervals for all the predictors in each of the 6 imputation models. The overall coefficient estimate for each variable was the average of the individual six estimates for that variable. The coefficient estimates varied considerably from one model to another but the standard errors did not vary as much. For the education level variable, the β coefficients were negative in some imputations and positive in others.

Table 11. Coefficient estimates, standard errors and confidence intervals for each variable in each imputation model

Imputation number	Variable	B coefficient	Standard error	95% Confidence interval	
1	SERT	0.27	0.16	-0.06	0.60
2	SERT	0.19	0.17	-0.14	0.52
3	SERT	0.37	0.17	-0.04	0.70
4	SERT	0.22	0.17	-0.11	0.55
5	SERT	0.29	0.18	-0.04	0.62
6	SERT	0.37	0.17	-0.05	0.70
Overall	SERT	0.28	0.19	-0.08	0.65
1	Age	-0.03	0.02	-0.07	0.001
2	Age	-0.04	0.02	-0.07	-0.004
3	Age	-0.05	0.17	-0.08	-0.01
4	Age	-0.04	0.02	-0.07	-0.002
5	Age	-0.03	0.02	-0.07	-0.003
6	Age	-0.03	0.02	-0.07	0.0005
Overall	Age	-0.04	0.02	-0.07	-0.002
1	Married	-0.11	0.24	-0.59	0.37
2	Married	-0.24	0.25	-0.73	0.24
3	Married	-0.05	0.24	-0.43	0.53
4	Married	-0.20	0.24	-0.28	0.67
5	Married	-0.03	0.24	-0.45	0.51
6	Married	-0.03	0.02	-0.48	0.47
Overall	Married	-0.01	0.29	-0.59	0.56
1	Non-white	0.17	0.23	-0.28	0.62
2	Non-white	0.18	0.23	-0.27	0.63
3	Non-white	0.37	0.23	-0.08	0.83
4	Non-white	0.09	0.22	-0.35	0.53
5	Non-white	0.52	0.23	-0.06	0.98
6	Non-white	0.35	0.23	-0.11	0.80
Overall	Non-white	0.28	0.29	-0.29	0.84
1	Education 9-11 years	-0.70	0.38	-1.45	0.04
2	Education 9-11 years	-0.64	0.37	-1.37	0.09
3	Education 9-11 years	-0.72	0.37	-1.45	0.004

Table 11 continued					
4	Education 9-11 years	0.38	0.41	-1.41	1.18
5	Education 9-11 years	-1.03	0.43	-1.86	-0.19
6	Education 9-11 years	-0.37	0.46	-1.27	0.53
Overall	Education 9-11 years	-0.51	0.66	-1.81	0.07
1	Education Completed HS	-0.12	0.40	-0.90	0.65
2	Education Completed HS	0.15	0.42	-0.68	0.98
3	Education Completed HS	-0.44	0.38	-1.18	0.30
4	Education Completed HS	0.52	0.40	-0.27	1.32
5	Education Completed HS	-0.95	0.43	-1.80	-0.11
6	Education Completed HS	-0.39	0.45	-1.27	0.49
Overall	Education Completed HS	-0.20	0.69	-1.56	1.15
1	Education Some college	0.14	0.34	-0.53	0.82
2	Education Some college	0.21	0.35	-0.48	0.91
3	Education Some college	-0.03	0.33	-0.68	0.61
4	Education Some college	0.54	0.36	-0.17	1.25
5	Education Some college	-0.32	0.38	-1.07	0.43
6	Education Some college	0.18	0.41	-0.62	1.00
Overall	Education Some college	0.12	0.48	-0.82	1.06
1	Education Completed college	0.42	0.36	-0.29	1.13
2	Education Completed college	0.46	0.37	-0.27	1.19
3	Education Completed college	0.20	0.34	-0.46	0.87
4	Education Completed college	0.91	0.38	-0.16	1.65
5	Education Completed college	-0.18	0.41	-0.98	0.61
6	Education Completed college	0.25	0.41	-0.40	1.00
Overall	Education Completed college	0.34	0.54	-0.72	1.41
1	Live alone	0.41	0.35	-0.28	-1.10
2	Live alone	0.17	0.34	-0.50	0.85
3	Live alone	0.43	0.36	-0.26	1.13
4	Live alone	0.52	0.35	-0.17	1.20

Table 11 continued					
5	Live alone	0.20	0.35	-0.49	0.90
6	Live alone	0.30	0.36	-0.40	1.00
Overall	Live alone	0.34	0.38	-0.41	1.09
1	Constant	1.51	0.56	-0.40	2.62
2	Constant	1.66	0.55	0.58	2.74
3	Constant	1.80	0.56	-0.70	2.89
4	Constant	0.83	0.58	-0.30	1.96
5	Constant	1.83	0.60	0.66	3.01
6	Constant	0.30	0.36	-0.40	1.00
Overall	Constant	1.49	0.71	-0.10	2.88

Table 12 shows the overall model after using MICOMBINE to combine the results from the 6 imputations. Even after doing MI, there is still no significant difference between the two drug groups in predicting remission (p=0.13).

Table 12. Overall logistic regression model after combining 6 imputed data sets (N=100)

Predictors	**β coefficient**	**Standard error**	**p-value**	**95% Confidence interval**
SERT	0.28	0.19	0.13	-0.08 0.65
Age	-0.04	0.02	0.04	-0.07 -0.002
Married	-0.01	0.30	0.96	-0.19 0.56
Non-white	0.28	0.29	0.33	-0.29 0.84
Education 9-11 years	-0.51	0.66	0.44	-1.81 0.79
Education Completed HS	-0.20	0.69	0.77	-1.56 1.14
Education Some college	0.12	0.48	0.80	-0.72 1.41
Education Completed College	0.34	0.38	0.37	-0.41 1.09
Live alone	0.34	0.38	0.89	-0.41 1.09
Constant	1.50	0.71	0.04	0.10 2.88

Figure 7 shows the observed and imputed measurements for participants 1006 and 1060 by week number. These participants have similar missingness pattern but 1006 is on NTP while 1060 is on SERT. Each missing measurement was imputed 6 times.

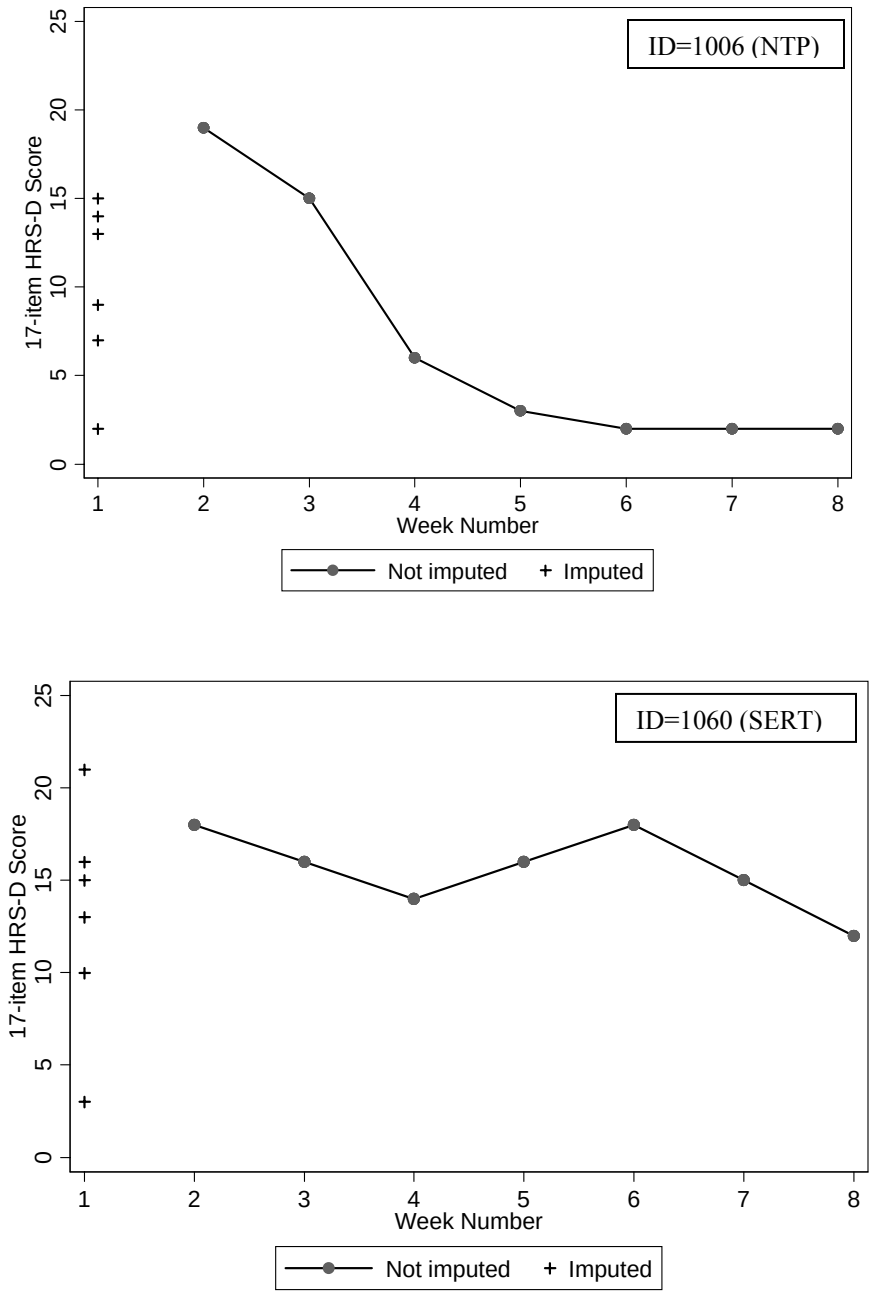


Figure 7. Observed and imputed HRSD measurements for participants 1006 and 1060 by week number

Figure 8 shows the observed and imputed measurements for participants 11021 and 10017 by week number. These participants have similar missingness pattern but 11021 is on NTP while 10017 is on SERT. Each missing measurement was imputed 6 times.

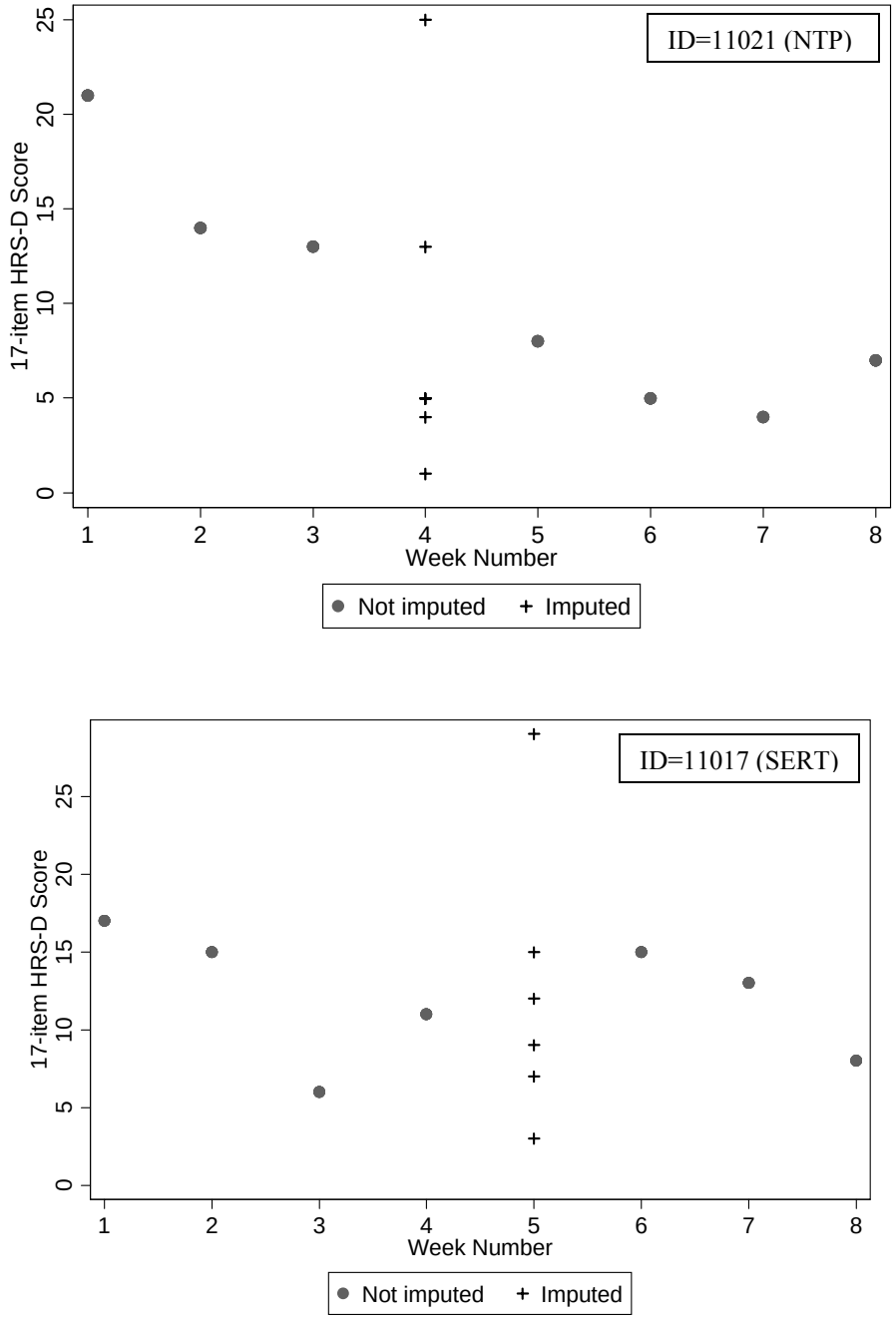


Figure 8. Observed and imputed HRSD measurements for participants 11021 and 11017 by week number

Figure 9 shows the observed and imputed HRSD measurements for participants 11003 and 11022 by week number. Both participants have same missingness pattern and are both on SERT.

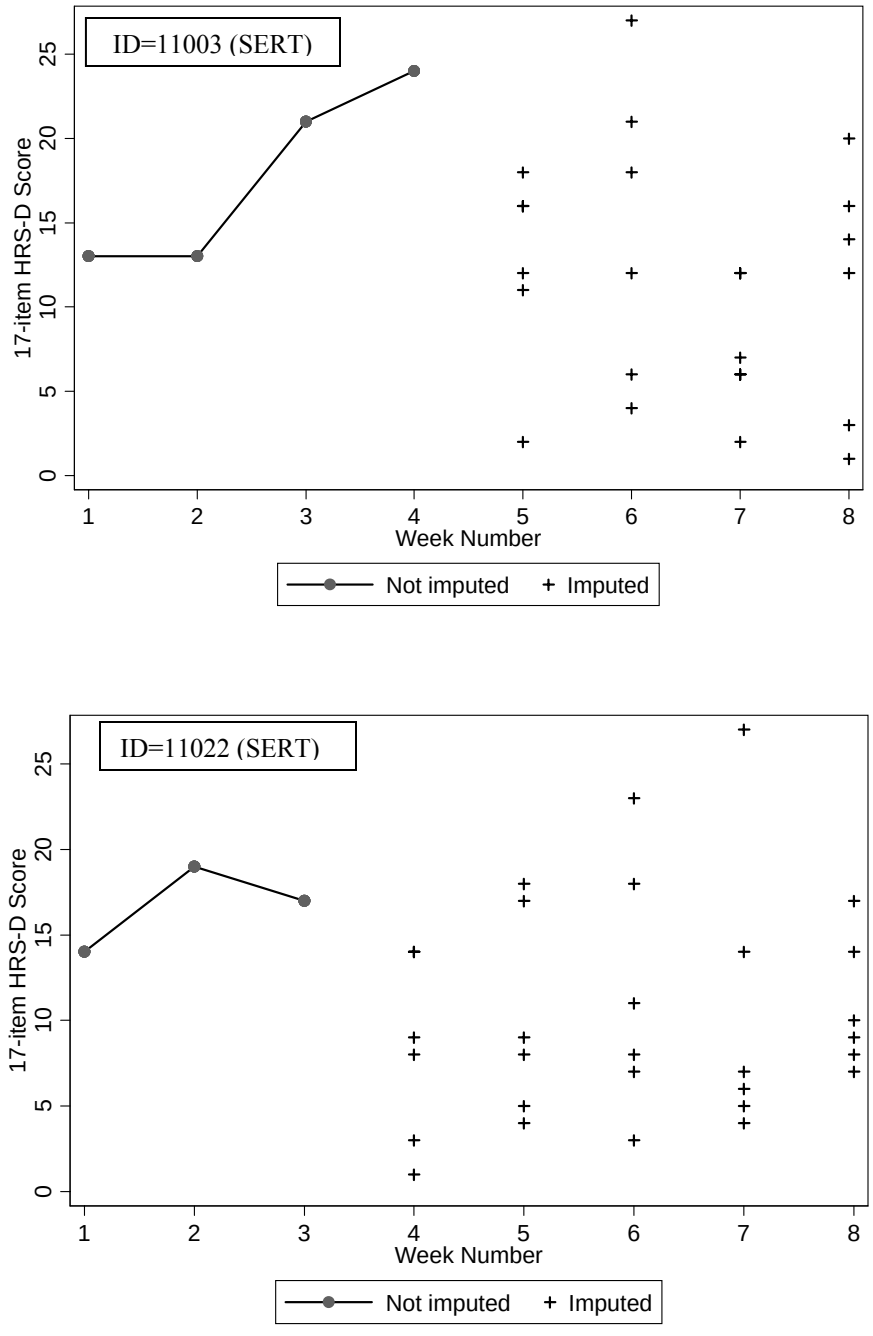


Figure 9. Observed and imputed HRSD measurements for participants 11003 and 11022 by week number

Figure 10 shows the observed and imputed HRSD measurements for participants 11027 and 11023 by week number. Both participants have same missingness pattern but 11027 is on NTP while 11023 is on SERT.

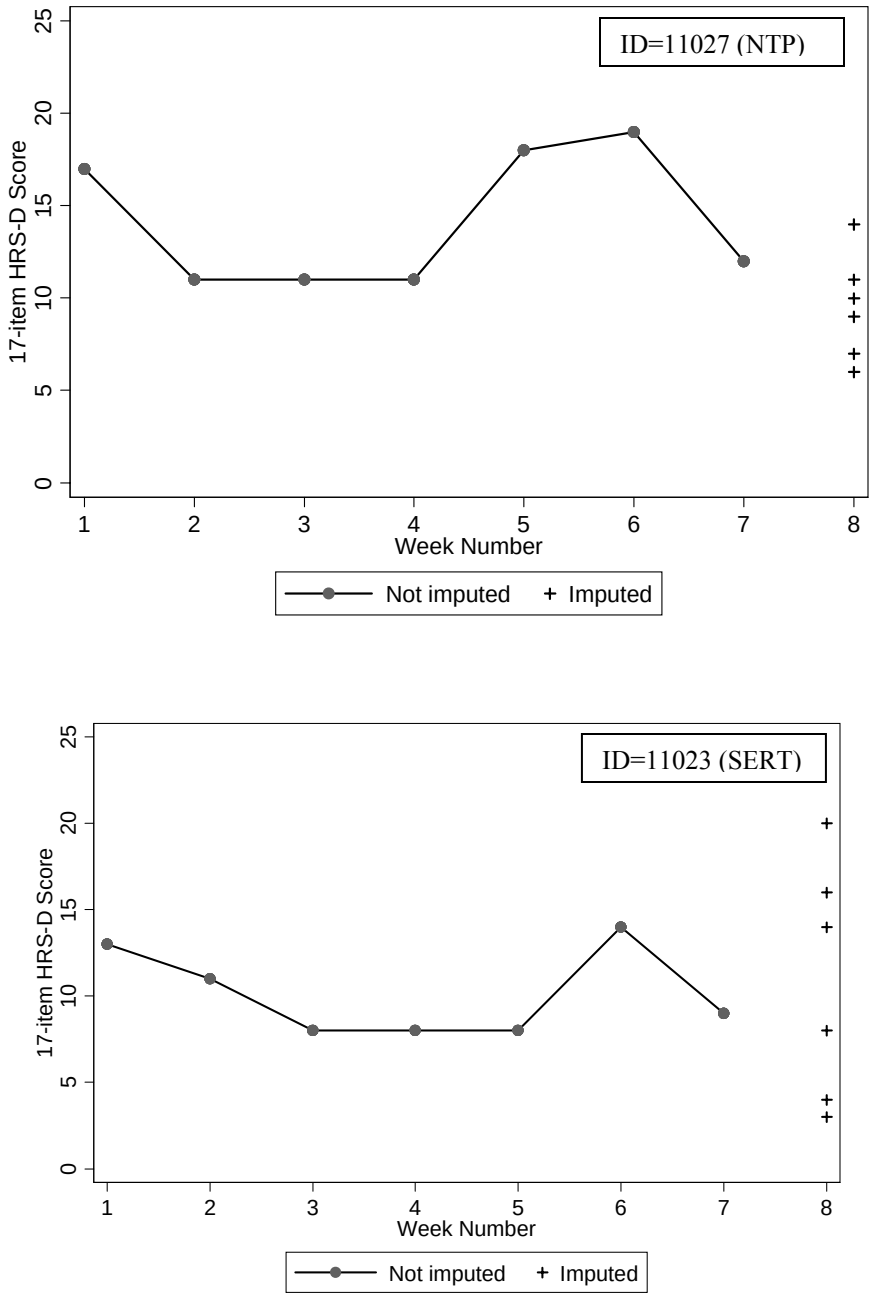


Figure 10. Observed and imputed HRSD measurements for participants 11027 and 11023 by week number

Table 13 compares the difference in HRS-D variable before and after LOCF, mean and MI by drug assignment at each week. LOCF and mean imputation gave generally similar estimated means. In weeks 1-4, MI gave smaller mean and standard deviation estimates than the original while larger estimates in weeks 5 through 7. At week 8, LOCF and mean esimates were higher than the original ones while MI esimates were similar to the original esimates. But suprisingly MI standard error estimates were slightly lower than original estimates at week 8.

Table 13. Comparison of HRS-D before and after LOCF, mean imputation and MI by drug assignment at each week

		SERT			NTP		
Week number	**Method**	**N**	**Mean**	**Standard deviation**	**N**	**Mean**	**Standard deviation**
1	Original	45	15.73	6.53	50	17.04	5.51
1	LOCF	45	15.73	6.53	50	17.04	5.51
1	Mean imputation	45	15.73	6.53	50	17.04	5.51
1	MI	47	15.58	6.45	53	16.68	5.74
2	Original	45	13.51	6.53	51	13.39	4.81
2	LOCF	47	13.36	6.51	53	13.61	4.87
2	Mean imputation	47	13.37	6.51	53	13.60	4.87
2	MI	47	13.36	6.44	53	13.37	4.93
3	Original	40	11.92	7.14	50	11.46	5.27
3	LOCF	47	12.06	6.77	53	11.75	5.39
3	Mean imputation	47	12.15	6.81	53	11.85	5.40
3	MI	47	11.83	7.03	53	11.38	5.31
4	Original	36	10.78	6.56	50	11.42	6.47
4	LOCF	47	11.40	6.65	53	11.72	6.47
4	Mean imputation	47	11.38	6.40	53	11.81	6.52
4	MI	47	10.81	6.41	53	11.34	6.46
5	Original	35	8.40	5.82	45	8.55	6.02
5	LOCF	47	10.11	6.55	53	9.89	6.77
5	Mean imputation	47	10.06	6.48	53	9.92	6.50
5	MI	47	9.12	6.00	53	9.10	6.12

Table 13 continued							
6	Original	35	7.71	5.35	45	7.38	5.33
6	LOCF	47	9.53	6.30	53	8.11	6.51
6	Mean imputation	47	9.40	6.06	53	8.77	6.06
6	MI	47	8.18	5.78	53	8.03	5.75
7	Original	30	6.80	6.10	39	7.82	6.60
7	LOCF	47	9.04	6.89	53	9.11	7.09
7	Mean imputation	47	9.23	6.52	53	9.57	6.65
7	MI	47	7.96	6.42	53	8.56	6.64
8	Original	32	6.41	5.15	40	6.32	5.31
8	LOCF	47	9.13	6.58	53	8.47	6.85
8	Mean imputation	47	8.83	6.21	53	8.45	6.21
8	MI	47	6.40	5.13	53	6.37	5.19

5.0 DISCUSSION

The original Nortriptyline vs. Sertraline analysis, which only used available data, was replicated. The same analysis was repeated after LOCF, mean imputation and MI and the results were compared. The continuous HRS-D levels were imputed but the assessment of treatment effects was done in terms of probability of remission. Predictors and patterns of attrition also were identified.

The same results were obtained from each analysis, i.e. there was no significant difference between SERT and NTP in predicting the probability of remission at week 8. However, MI gave larger standard error estimates than the other two methods earlier in participants taking SERT. Most drop outs occurred during the first three weeks, and participants taking SERT and living alone were more likely to drop out.

The study has both strengths and limitations. Some of the strengths are the relatively large sample size, which increases the power of the results, the use of different methods to account for monotone attrition and the fact that we actually looked at the individual imputations in MI. The fact that more non-whites were assigned to SERT than NTP is one limitation of the original study. Using ICE, which is relatively new, to do MI in Stata is another limitation because the MICOMBINE command does not recognize commands that would fit cross-sectional time series regression model which would be more appropriate for our data. SAS, which is another statistical software with more options for MI, could have been used instead.

APPENDIX A

PROGRAMS FOR ANALYSIS

Table 2. Distribution of participants who were and were not included in original Nortriptyline-Sertraline Analysis

```
use "F:\withdrawals\sum_merged_report.dta"
tabulate wkns_out2 included95
```

Replicating original Nortriptyline vs. Sertraline study

```
use "F:\withdrawals\Final data.dta"
g remit=1 if hrsd<=7 & wk_number==8
replace remit=0 if hrsd>=8 & wk_number==8
replace remit=. if hrsd==. & wk_number==8
xi: logit remit sert age married living_status2 race i.education if
wk_number==8
```

Figure 2. Box plots of HRS-D scores by drug assignment over time

```
use "F:\withdrawals\Final data.dta"
iis id
tis wk_number
graph box hrsd, medtype(line) over(sert, label(nolabel)) over(wk_number)
ytitle(17-item HRS-D Score)
```

Table 4. Comparison of participants included and not included in original Nortriptyline vs. Sertraline analysis

```
use "F:\withdrawals\Final data.dta"
sort SERT
by SERT: tabulate LIVING_STATUS2 included if WK_NUMBER==0, chi2
by SERT: tabulate RACE included if WK_NUMBER==0, chi2
by SERT: tabulate EDUCATION included if WK_NUMBER==0, chi2
by SERT: tabulate MARRIED included if WK_NUMBER==0, chi2
by SERT: tabulate AGE included if WK_NUMBER==0, chi2
```

Table 5. Available data pattern in Nortriptyline vs. Sertraline Study for participants on Sertraline

```
use "F:\withdrawals\Final data.dta"
stset WK_NO, id(ID) failure(WITHDREW)
sort SERT
by SERT: xtdes
```

Table 6. Available data pattern in Nortriptyline vs. Sertraline Study for participants on Nortriptyline

```
use "F:\withdrawals\Final data.dta"
stset WK_NO, id(ID) failure(WITHDREW)
sort SERT
by SERT: xtdes
```

Table 7. Reason of Attrition by Week Number

```
use "F:\withdrawals\Final data.dta"
tabulate WK_NUMBER REASON if WITHDREW==1, col chi2
```

Identifying predictors of attrition

```
stset WK_NUMBER, id(ID) failure(WITHDREW)
sts test SERT
sts test RACE
sts test MARRIED
sts test EDUCATION
sts test LIVING_STATUS2
sts test AGE
xi: stcox SERT RACE MARRIED LIVING_STATUS2 i.EDUCATION, exactp
sw stcox SERT RACE MARRIED LIVING_STATUS2, exactp pr(.1) lockterm1
sw stcox SERT RACE MARRIED LIVING_STATUS2, exactp pr(.1) lockterm1 nohr

g SERTXLIVING_STATUS2=SERT*LIVING_STATUS2
stcox SERT LIVING_STATUS2 SERT*LIVING_STATUS2, exactp
```

Figure 4. Kaplan-Meier survival curve of time to attrition by drug assignment and living status.

```
use "F:\withdrawals\Final data set.dta"
stset WK_NUMBER, id(ID) failure(WITHDREW)

sts graph, by(SERT LIVING_STATUS2) ytitle(" ") xtitle(Week Number) xlabel(1 2
3 4 5 6 7 8) title(" ") legend(order(1 "NTP, with adult" 2 "NTP, alone" 3
"SERT, with adult" 4 "SERT, alone"))
```

Last observation carried forward

```
use "F:\withdrawals\Final data"
g REMITTED_LOCF=1 if WK_NUMBER==9 & HRSD_LOCF<=7
replace REMITTED_LOCF=0 if HRSD_LOCF>=8 | HRSD_LOCF<=7 & WK_NUMBER<8
replace REMITTED_LOCF=. if HRSD_LOCF==.
xi: logit REMITTED_LOCF SERT AGE MARRIED LIVING_STATUS2 i.EDUCATION RACE if
WK_NUMBER==8
```

Figure 5. Box plot of HRS-D scores after LOCF by drug assignment over time.

```
use "F:\withdrawals\Final data"
iis ID
tis WK_NUMBER
graph box sa17to_a, medtype(line) over(SERT, label(nolabel)) over(WK_NUMBER)
ytitle(17-item HRS-D Score)
```

Mean Imputation using mean HRS-D score for each participant

```
use "F:\withdrawals\Final data"
tabstat HRSD, stats(mean) by(ID)
g HRSD_MEAN = HRSD
tabstat HRSD, stats(mean) by(ID)
g REMITTED_MEAN=1 if WK_NUMBER==8 & HRSD_MEAN<=7
replace REMITTED_MEAN=0 if HRSD_MEAN>=8 | HRSD_MEAN<=7 & WK_NUMBER<8
replace REMITTED_MEAN=. if HRSD_MEAN==.
xi: logit REMITTED_MEAN SERT AGE MARRIED LIVING_STATUS2 RACE i.EDUCATION if
WK_NUMBER==8
```

Figure 6. Box plot of HRS-D scores after mean imputation by drug assignment over time.

```
use "F:\withdrawals\Final data"
iis ID
tis WK_NUMBER
graph box HRSD_MEAN, medtype(line) over(SERT, label(nolabel)) over(WK_NUMBER)
ytitle(17-item HRS-D Score)
```

Multiple imputation

```
use "F:\withdrawals\MI"
g HRSD9=.
replace HRSD9=HRSD if WK_NUMBER==8
drop if WK_NUMBER==8
ice HRSD9 HRSD SERT AGE MARRIED RACE EDUCATION LIVING_STATUS2, dryrun
tab SERT, gen(s)
tab MARRIED, gen(m)
tab RACE, gen(r)
tab EDUCATION, gen(e)
tab WK_NUMBER, gen(w)
tab ID, gen(i)
tab LIVING_STATUS2, gen(l)
ice HRSD9 HRSD s1 s2 AGE m1 m2 r1 r2 e1-e4 l1 l2 w1-w7 i1-i100, dryrun
ice HRSD9 HRSD s1 s2 AGE m1 m2 r1 r2 EDUCATION l1 l2 w1-w7 i1-i100 using
imp_final, sub(EDUCATION: e1 e2 e3 e4) m(6) match cmd(EDUCATION: ologit)

use "F:\withdrawals\imp_with_wk_id"
micombine regress HRSD9 HRSD SERT AGE MARRIED RACE e1-e4 LIVING_STATUS2 w1-
w8, detail
```

Table 12. Overall logistic regression model after combining 6 imputed data sets

```
use "F:\withdrawals\ imp_with_wk_id"
micombine regress HRSD AGE e1 e2 e3 e3 RACE LIVING_STATUS2 MARRIED SERT,
detail
```

Figure 7. Observed and imputed HRSD measurements for participants 1006 and 1060 by week number

```
use "F:\withdrawals\ imp_with_wk_id_for graphs"
twoway (connected HRSD WK_NUMBER if ID==1006 & imputed==0) (scatter HRSD
WK_NUMBER if ID==1006 & imputed==1, msymbol(plus) mcolor(black)
msize(medium)), ytitle(17-item HRS-D Score) ylabel(0 10 20 30) xtitle(Week
Number) xlabel(1 2 3 4 5 6 7 8) legend(order(1 "Observed" 2 "Imputed"))
twoway (connected HRSD WK_NUMBER if ID==1060 & imputed==0) (scatter HRSD
WK_NUMBER if ID==1060 & imputed==1, msymbol(plus) mcolor(black)
msize(medium)), ytitle(17-item HRS-D Score) ylabel(0 10 20 30) xtitle(Week
Number) xlabel(1 2 3 4 5 6 7 8) legend(order(1 "Observed" 2 "Imputed"))
```

Figure 8. Observed and imputed HRSD measurements for participants 11021 and 11017 by week number

```
use "F:\withdrawals\ imp_with_wk_id_for graphs"
twoway (connected HRSD WK_NUMBER if ID==1048 & imputed==0) (scatter HRSD
WK_NUMBER if ID==1048 & imputed==1, msymbol(plus) mcolor(black)
msize(medium)), ytitle(17-item HRS-D Score) ylabel(0 10 20 30) xtitle(Week
Number) xlabel(1 2 3 4 5 6 7 8) legend(order(1 "Observed" 2 "Imputed"))
twoway (connected HRSD WK_NUMBER if ID==1068 & imputed==0) (scatter HRSD
WK_NUMBER if ID==1068 & imputed==1, msymbol(plus) mcolor(black)
```

```
msize(medium)), ytitle(17-item HRS-D Score) ylabel(0 10 20 30) xtitle(Week
Number) xlabel(1 2 3 4 5 6 7 8) legend(order(1 "Observed" 2 "Imputed"))
```

Figure 9. **Observed and imputed HRSD measurements for participants 11003 and 11022 by week number**

```
use "F:\withdrawals\ imp_with_wk_id_for graphs"
twoway (connected HRSD WK_NUMBER if ID==1003 & imputed==0) (scatter HRSD
WK_NUMBER if ID==1003 & imputed==1, msymbol(plus) mcolor(black)
msize(medium)), ytitle(17-item HRS-D Score) ylabel(0 10 20 30) xtitle(Week
Number) xlabel(1 2 3 4 5 6 7 8) legend(order(1 "Observed" 2 "Imputed"))
twoway (connected HRSD WK_NUMBER if ID==2101 & imputed==0) (scatter HRSD
WK_NUMBER if ID==2101 & imputed==1, msymbol(plus) mcolor(black)
msize(medium)), ytitle(17-item HRS-D Score) ylabel(0 10 20 30) xtitle(Week
Number) xlabel(1 2 3 4 5 6 7 8) legend(order(1 "Observed" 2 "Imputed"))
```

Figure 10. **Observed and imputed HRSD measurements for participants 11027 and 11023 by week number**

```
use "F:\withdrawals\ imp_with_wk_id_for graphs"
twoway (connected HRSD WK_NUMBER if ID==11023 & imputed==0) (scatter HRSD
WK_NUMBER if ID==11023 & imputed==1, msymbol(plus) mcolor(black)
msize(medium)), ytitle(17-item HRS-D Score) ylabel(0 10 20 30) xtitle(Week
Number) xlabel(1 2 3 4 5 6 7 8) legend(order(1 "Observed" 2 "Imputed"))
twoway (connected HRSD WK_NUMBER if ID==11010 & imputed==0) (scatter HRSD
WK_NUMBER if ID==11010 & imputed==1, msymbol(plus) mcolor(black)
msize(medium)), ytitle(17-item HRS-D Score) ylabel(0 10 20 30) xtitle(Week
Number) xlabel(1 2 3 4 5 6 7 8) legend(order(1 "Observed" 2 "Imputed"))
```

Table 13. Comparison of HRS-D before and after LOCF, mean imputation and multiple imputation by drug assignment at each week

```
use "F:\withdrawals\Final data"
iis ID
tis WK_NUMBER
sort SERT WK_NUMBER
by SERT WK_NUMBER: xtsum HRSD
by SERT WK_NUMBER: xtsum HRSD_LOCF
by SERT WK_NUMBER: xtsum HRSD_MEAN
xtsum HRSD
xtsum HRSD_LOCF
xtsum HRSD_MEAN
use "F:\withdrawals\ imp_with_wk_id"
iis ID
tis WK_NUMBER
sort SERT WK_NUMBER
by SERT WK_NUMBER: xtsum HRSD
```

Data description

```
. describe

Contains data from C:\Documents and Settings\Yazan\My Documents\Flash
Drive\withdrawals\Final\Final data.dta
  obs:           981
 vars:            11                          26 Jun 2006 20:16
 size:        15,696 (98.5% of memory free)
-------------------------------------------------------------------------------
-
              storage  display     value
variable name   type   format      label      variable label
-------------------------------------------------------------------------------
ID              int    %8.0g                  Participant Identification
                                                Number
WK_NUMBER       byte   %8.0g                  Week Number
SERT            byte   %8.0g       sert       Sertraline
WITHDREW        byte   %8.0g                  Withdrew
HRSD            byte   %8.0g                  17-item Hamilton Rating Scale
                                                for Depression'
RACE            byte   %8.0g       race
LIVING_STATUS   byte   %8.0g       living_a
AGE             byte   %8.0g
EDUCATION       byte   %8.0g       education
MARRIED         byte   %8.0g       married
REASON          byte   %8.0g       reason    Reason participant withdrew
-------------------------------------------------------------------------------
Sorted by:  ID
```

Replicating original analysis

```
. xi: logit remit sert age married living_status2 race i.education if
wk_number==8
i.education       _Ieducation_0-3     (naturally coded; _Ieducation_0
omitted)

note: living_status2 != 0 predicts success perfectly
      living_status2 dropped and 2 obs not used

Iteration 0:   log likelihood = -37.351296
Iteration 1:   log likelihood = -35.954836
Iteration 2:   log likelihood = -35.942368
Iteration 3:   log likelihood = -35.942366

Logistic regression                               Number of obs   =         62
                                                  LR chi2(7)      =       2.82
                                                  Prob > chi2     =     0.9013
Log likelihood = -35.942366                       Pseudo R2       =     0.0377
------------------------------------------------------------------------------
       remit |      Coef.   Std. Err.      z    P>|z|    [95% Conf. Interval]
-------------+----------------------------------------------------------------
        sert |   .1381738   .5950206     0.23   0.816   -1.028045    1.304393
         age |  -.0581579   .0618452    -0.94   0.347   -.1793722    .0630564
     married |  -.0711458   .8501547    -0.08   0.933   -1.737418    1.595127
        race |   .3702204   .8223387     0.45   0.653   -1.241534    1.981975
_Ieducatio~1 |   .4776461   1.145306     0.42   0.677   -1.767112    2.722404
_Ieducatio~2 |   1.038034   1.014094     1.02   0.306    -.949553    3.025621
_Ieducatio~3 |   1.516912   1.133831     1.34   0.181   -.7053561    3.739181
```

```
       _cons |   1.483577   1.458196     1.02   0.309   -1.374435     4.34159
------------------------------------------------------------------------------
```

Predictors of attrtion

```
. stset wk_number, id(id) failure(withdrew)

                id:  id
     failure event:  withdrew != 0 & withdrew < .
obs. time interval:  (wk_number[_n-1], wk_number]
 exit on or before:  failure

------------------------------------------------------------------------------
      809  total obs.
       86  obs. begin on or after (first) failure
------------------------------------------------------------------------------
      723  obs. remaining, representing
      109  subjects
       37  failures in single failure-per-subject data
      723  total analysis time at risk, at risk from t =         0
                            earliest observed entry t =         0
                                 last observed exit t =         8

. sts test sert

         failure _d:  withdrew
   analysis time _t:  wk_number
                 id:  id


Log-rank test for equality of survivor functions

              |   Events         Events
sert          |  observed       expected
--------------+-------------------------
Nortriptyline |        14          19.97
Sertraline    |        23          17.03
--------------+-------------------------
Total         |        37          37.00

                    chi2(1) =       4.08
                    Pr>chi2 =     0.0433

. sts test married

         failure _d:  withdrew
   analysis time _t:  wk_number
                 id:  id


Log-rank test for equality of survivor functions

        |   Events         Events
married |  observed       expected
--------+-------------------------
No      |        24          14.04
Yes     |        13          22.96
--------+-------------------------
Total   |        37          37.00

              chi2(1) =      12.03
```

```
              Pr>chi2 =     0.0005

. sts test race

         failure _d:  withdrew
   analysis time _t:  wk_number
                 id:  id


Log-rank test for equality of survivor functions

           |   Events         Events
race       |  observed       expected
-----------+-------------------------
White      |        18          28.18
Non-white  |        19           8.82
-----------+-------------------------
Total      |        37          37.00

                chi2(1) =      16.37
                Pr>chi2 =     0.0001

. sts test education

         failure _d:  withdrew
   analysis time _t:  wk_number
                 id:  id


Log-rank test for equality of survivor functions

                    |   Events         Events
education           |  observed       expected
--------------------+-------------------------
9-11 years          |        12           6.16
Completed HS        |         5           4.02
Some college        |        11          13.80
Completed College   |         7          11.02
--------------------+-------------------------
Total               |        35          35.00

                        chi2(3) =       8.26
                        Pr>chi2 =     0.0409

. sts test living_status2

         failure _d:  withdrew
   analysis time _t:  wk_number
                 id:  id


Log-rank test for equality of survivor functions

                  |   Events         Events
living_sta~2      |  observed       expected
------------------+-------------------------
Live with adult   |        24          34.18
Live alone        |        13           2.82
------------------+-------------------------
Total             |        37          37.00
```

```
                    chi2(1) =      43.07
                    Pr>chi2 =     0.0000

. sts test age

         failure _d:  withdrew
   analysis time _t:  wk_number
                 id:  id

Log-rank test for equality of survivor functions

       |   Events         Events
AGE    |  observed       expected
-------+-------------------------
15     |         0           0.40
16     |         1           0.21
18     |         0           0.40
19     |         4           2.93
20     |         4           2.20
21     |         4           1.55
22     |         0           1.61
23     |         5           2.89
24     |         0           1.21
25     |         0           2.02
26     |         1           1.69
27     |         1           1.79
28     |         1           1.28
29     |         1           1.21
30     |         3           2.04
31     |         2           2.02
32     |         1           1.69
33     |         3           1.40
34     |         2           2.36
35     |         3           2.30
36     |         0           0.81
37     |         0           0.81
38     |         1           1.38
39     |         0           0.40
41     |         0           0.40
-------+-------------------------
Total  |        37          37.00

           chi2(24) =      23.34
            Pr>chi2 =     0.4997



. xi: stcox sert married race i.education living_status2, exactp
i.education       _Ieducation_0-3     (naturally coded; _Ieducation_0 omitted)

         failure _d:  withdrew
   analysis time _t:  wk_number
                 id:  id

Iteration 0:   log likelihood = -121.82748
Iteration 1:   log likelihood = -112.12851
Iteration 2:   log likelihood = -103.67709
Iteration 3:   log likelihood = -102.90251
Iteration 4:   log likelihood = -102.90168
Iteration 5:   log likelihood = -102.90168
Refining estimates:
```

```
Iteration 0:   log likelihood = -102.90168

Cox regression -- exact partial likelihood

No. of subjects =          102                     Number of obs   =       672
No. of failures =           35
Time at risk    =          672
                                                   LR chi2(7)      =     37.85
Log likelihood  =   -102.90168                     Prob > chi2     =    0.0000

------------------------------------------------------------------------------
          _t | Haz. Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        sert |    1.93781   .7668102     1.67   0.095      .892242    4.208622
     married |   .8347885   .4440889    -0.34   0.734     .2942769    2.368082
        race |   1.651904   .7597636     1.09   0.275     .6706407    4.068925
_Ieducatio~1 |    1.04038   .6347849     0.06   0.948     .3146545    3.439934
_Ieducatio~2 |   .3973631   .1948057    -1.88   0.060      .152016    1.038689
_Ieducatio~3 |   .7226843   .4726825    -0.50   0.619      .200543    2.604292
living_sta~2 |   7.709659   3.971392     3.97   0.000     2.809086     21.1595
------------------------------------------------------------------------------

. sw stcox sert married race living_status2, lockterm1 pr(.05) exactp
(86 obs. dropped due to estimability)
                      begin with full model
p = 0.5749 >= 0.0500  removing married
p = 0.0715 >= 0.0500  removing race

Cox regression -- exact partial likelihood

No. of subjects =          109                     Number of obs   =       723
No. of failures =           37
Time at risk    =          723
                                                   LR chi2(2)      =     29.48
Log likelihood  =   -115.15593                     Prob > chi2     =    0.0000

------------------------------------------------------------------------------
          _t | Haz. Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        sert |   1.927684   .6919278     1.83   0.067     .9539014    3.895546
living_sta~2 |   9.011379   3.578441     5.54   0.000     4.137872    19.62481
------------------------------------------------------------------------------
. g sertXliving_status2=sert*living_status2

. sw stcox sert living_status2 sert*living_status2, lockterm1 pr(.05) exactp
(86 obs. dropped due to estimability)
                      begin with full model
p = 0.2151 >= 0.0500  removing sertXliving_status2

Cox regression -- exact partial likelihood

No. of subjects =          109                     Number of obs   =       723
No. of failures =           37
Time at risk    =          723
                                                   LR chi2(2)      =     29.48
Log likelihood  =   -115.15593                     Prob > chi2     =    0.0000

------------------------------------------------------------------------------
          _t | Haz. Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        sert |   1.927684   .6919278     1.83   0.067     .9539014    3.895546
```

```
living_sta~2 |   9.011379   3.578441     5.54   0.000    4.137872    19.62481
-------------------------------------------------------------------------------
```

Patterns of attrtion

```
. iis bagnum

. tis weeknum

. sort nort

. by nort: xtdes, patterns(20)

-------------------------------------------------------------------------------
-> nort = 0

  bagnum:  1004, 1008, ..., 11026                          n =         47
 weeknum:  1, 2, ..., 8                                    T =          8
           Delta(weeknum) = 1; (8-1)+1 = 8
           (bagnum*weeknum uniquely identifies each observation)

Distribution of T_i:  min      5%     25%       50%       75%     95%     max
                        1       1       5         8         8       8       8

     Freq.  Percent    Cum. |  Pattern
 -------------------------+----------
       26     55.32   55.32 |  11111111
        4      8.51   63.83 |  11......
        3      6.38   70.21 |  111111.1
        2      4.26   74.47 |  1.......
        2      4.26   78.72 |  111.1111
        2      4.26   82.98 |  1111....
        2      4.26   87.23 |  111111..
        1      2.13   89.36 |  .1......
        1      2.13   91.49 |  .11.....
        1      2.13   93.62 |  111.....
        1      2.13   95.74 |  1111.111
        1      2.13   97.87 |  11111...
        1      2.13  100.00 |  1111111.
 -------------------------+----------
       47    100.00         |  XXXXXXXX

-------------------------------------------------------------------------------
-> nort = 1

  bagnum:  1001, 1002, ..., 11028                          n =         53
 weeknum:  1, 2, ..., 8                                    T =          8
           Delta(weeknum) = 1; (8-1)+1 = 8
           (bagnum*weeknum uniquely identifies each observation)

Distribution of T_i:  min      5%     25%       50%       75%     95%     max
                        1       2       7         8         8       8       8

     Freq.  Percent    Cum. |  Pattern
 -------------------------+----------
       31     58.49   58.49 |  11111111
        4      7.55   66.04 |  111111.1
        3      5.66   71.70 |  .1111111
        3      5.66   77.36 |  1111....
        2      3.77   81.13 |  11......
```

```
        2      3.77   84.91 |  11111...
        2      3.77   88.68 |  111111..
        2      3.77   92.45 |  1111111.
        1      1.89   94.34 |  1.......
        1      1.89   96.23 |  1.111111
        1      1.89   98.11 |  1111.11.
        1      1.89  100.00 |  1111.111
 -------------------------+----------
       53    100.00         |  XXXXXXXX
```

Last observation carried forward

```
. xi: logit remit_locf sert age married living_status2 race i.education if
wk_number==8
i.education       _Ieducation_0-3     (naturally coded; _Ieducation_0
omitted)

Iteration 0:   log likelihood = -64.198998
Iteration 1:   log likelihood =  -62.64907
Iteration 2:   log likelihood = -62.648024
Iteration 3:   log likelihood = -62.648024

Logistic regression                               Number of obs   =         93
                                                  LR chi2(8)      =       3.10
                                                  Prob > chi2     =     0.9278
Log likelihood = -62.648024                       Pseudo R2       =     0.0242
------------------------------------------------------------------------------
  remit_locf |      Coef.   Std. Err.      z    P>|z|    [95% Conf. Interval]
-------------+----------------------------------------------------------------
        sert |   .0563616   .4347577     0.13   0.897   -.7957478    .9084711
         age |  -.0358329   .0457852    -0.78   0.434   -.1255702    .0539044
     married |   .1370477   .6205505     0.22   0.825   -1.079209    1.353304
living_sta~2 |  -.6959209   .8738721    -0.80   0.426   -2.408679    1.016837
        race |  -.2714913   .5684148    -0.48   0.633   -1.385564    .8425813
_Ieducatio~1 |  -.2357499   .8316188    -0.28   0.777   -1.865693    1.394193
_Ieducatio~2 |   .3033493   .6795667     0.45   0.655   -1.028577    1.635276
_Ieducatio~3 |   .2760922   .8274721     0.33   0.739   -1.345723    1.897908
       _cons |   1.003229   1.075961     0.93   0.351   -1.105616    3.112074
------------------------------------------------------------------------------
```

Mean imputation

```
. xi: logit remit_mean sert age married living_status2 race i.education if
wk_number==8
i.education       _Ieducation_0-3     (naturally coded; _Ieducation_0
omitted)

Iteration 0:   log likelihood = -64.414292
Iteration 1:   log likelihood = -62.392884
Iteration 2:   log likelihood = -62.390255
Iteration 3:   log likelihood = -62.390254

Logistic regression                               Number of obs   =         93
                                                  LR chi2(8)      =       4.05
                                                  Prob > chi2     =     0.8528
Log likelihood = -62.390254                       Pseudo R2       =     0.0314
------------------------------------------------------------------------------
  remit_mean |      Coef.   Std. Err.      z    P>|z|    [95% Conf. Interval]
```

```
-------------+----------------------------------------------------------------
        sert |   .2490395   .4374406     0.57   0.569   -.6083282    1.106407
         age |  -.0371703   .0459752    -0.81   0.419   -.1272801    .0529395
     married |   .2784031   .6219576     0.45   0.654   -.9406113    1.497418
living_sta~2 |   -.389262   .8810357    -0.44   0.659    -2.11606    1.337536
        race |  -.3136883   .5698107    -0.55   0.582   -1.430497    .8031202
_Ieducatio~1 |   .2332761   .8361935     0.28   0.780   -1.405633    1.872185
_Ieducatio~2 |   .7260593   .6830815     1.06   0.288   -.6127559    2.064875
_Ieducatio~3 |   .6945494    .830699     0.84   0.403   -.9335907    2.322689
       _cons |   .4155642    1.07413     0.39   0.699   -1.689692    2.520821
------------------------------------------------------------------------------
```

Multiple imputation

```
. micombine logit remit_mi sert age married race e1-e4 living_status2, detail

Iteration 0:   log likelihood = -445.32851
Iteration 1:   log likelihood = -434.98252
Iteration 2:   log likelihood = -434.94681
Iteration 3:   log likelihood = -434.94681

Logistic regression                                     Number of obs   =        700
                                                        LR chi2(9)      =      20.76
                                                        Prob > chi2     =     0.0137
Log likelihood = -434.94681                             Pseudo R2       =     0.0233
------------------------------------------------------------------------------
    remit_mi |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        sert |    .271626   .1677776     1.62   0.105    -.057212     .600464
         age |  -.0348888   .0174633    -2.00   0.046    -.0691161   -.0006614
     married |  -.1100332   .2446416    -0.45   0.653     -.589522    .3694556
        race |   .1690064   .2295638     0.74   0.462    -.2809303    .6189431
          e1 |  -.7014422   .3807919    -1.84   0.065    -1.447781    .0448962
          e2 |  -.1244925   .3963651    -0.31   0.753    -.9013538    .6523688
          e3 |   .1421278   .3444916     0.41   0.680    -.5330634    .8173189
          e4 |   .4231972   .3636436     1.16   0.245    -.2895311    1.135926
living_sta~2 |   .4119143   .3514338     1.17   0.241    -.2768833    1.100712
       _cons |   1.513611   .5652276     2.68   0.007     .4057849    2.621436
------------------------------------------------------------------------------

Iteration 0:   log likelihood = -446.02059
Iteration 1:   log likelihood = -435.83008
Iteration 2:   log likelihood = -435.78514
Iteration 3:   log likelihood = -435.78513

Logistic regression                                     Number of obs   =        700
                                                        LR chi2(9)      =      20.47
                                                        Prob > chi2     =     0.0152
Log likelihood = -435.78513                             Pseudo R2       =     0.0229

------------------------------------------------------------------------------
    remit_mi |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        sert |   .1894666   .1673572     1.13   0.258    -.1385475    .5174806
         age |  -.0383933   .0173967    -2.21   0.027    -.0724902   -.0042964
     married |  -.2439483   .2460207    -0.99   0.321    -.7261399    .2382433
        race |    .180851   .2319346     0.78   0.436    -.2737324    .6354344
          e1 |   -.640551   .3736983    -1.71   0.087    -1.372986    .0918843
          e2 |   .1494875   .4236126     0.35   0.724    -.6807779    .9797528
          e3 |   .2149666   .3548855     0.61   0.545    -.4805961    .9105294
```

```
          e4 |     .46044    .373735     1.23   0.218   -.2720671    1.192947
living_sta~2 |   .1706587   .3448578     0.49   0.621   -.5052501    .8465675
       _cons |   1.661602   .5523021     3.01   0.003    .5791097    2.744094
------------------------------------------------------------------------------

Iteration 0:   log likelihood = -448.05836
Iteration 1:   log likelihood = -434.93008
Iteration 2:   log likelihood = -434.87109
Iteration 3:   log likelihood = -434.87109

Logistic regression                               Number of obs   =        700
                                                  LR chi2(9)      =      26.37
                                                  Prob > chi2     =     0.0018
Log likelihood = -434.87109                       Pseudo R2       =     0.0294

------------------------------------------------------------------------------
    remit_mi |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        sert |   .3678606   .1681803     2.19   0.029    .0382332    .6974879
         age |  -.0466941   .0175035    -2.67   0.008   -.0810003   -.0123879
     married |   .0497887   .2445703     0.20   0.839   -.4295602    .5291376
        race |   .3714656   .2324675     1.60   0.110   -.0841624    .8270936
          e1 |  -.7232892   .3711625    -1.95   0.051   -1.450754    .0041759
          e2 |  -.4388097   .3778473    -1.16   0.246   -1.179377    .3017575
          e3 |   -.035481   .3273324    -0.11   0.914   -.6770408    .6060787
          e4 |   .2044431   .3406394     0.60   0.548   -.4631979    .8720842
living_sta~2 |   .4334122   .3568412     1.21   0.225   -.2659837    1.132808
       _cons |   1.799681   .5584138     3.22   0.001    .7052098    2.894152
------------------------------------------------------------------------------

Iteration 0:   log likelihood = -443.21363
Iteration 1:   log likelihood = -436.56584
Iteration 2:   log likelihood = -436.54357
Iteration 3:   log likelihood = -436.54357

Logistic regression                               Number of obs   =        700
                                                  LR chi2(9)      =      13.34
                                                  Prob > chi2     =     0.1478
Log likelihood = -436.54357                       Pseudo R2       =     0.0150

------------------------------------------------------------------------------
    remit_mi |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        sert |   .2178878   .1679547     1.30   0.195   -.1112974    .5470731
         age |  -.0363415   .0173814    -2.09   0.037   -.0704084   -.0022746
     married |   .1967933   .2415658     0.81   0.415   -.2766669    .6702536
        race |   .0895722   .2257755     0.40   0.692   -.3529397    .5320841
          e1 |   .3851511    .407939     0.94   0.345   -.4143947    1.184697
          e2 |   .5244122   .4039181     1.30   0.194   -.2672527    1.316077
          e3 |   .5404699   .3624929     1.49   0.136   -.1700031    1.250943
          e4 |   .9065902    .378793     2.39   0.017    .1641696    1.649011
living_sta~2 |   .5161831   .3486949     1.48   0.139   -.1672464    1.199613
       _cons |   .8297245   .5769292     1.44   0.150    -.301036    1.960485
------------------------------------------------------------------------------

Iteration 0:   log likelihood = -448.72483
Iteration 1:   log likelihood = -435.56886
Iteration 2:   log likelihood = -435.50406
Iteration 3:   log likelihood = -435.50405

Logistic regression                               Number of obs   =        700
```

```
                                                LR chi2(9)      =      26.44
                                                Prob > chi2     =     0.0017
Log likelihood = -435.50405                     Pseudo R2       =     0.0295

------------------------------------------------------------------------------
    remit_mi |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        sert |    .2890039   .1674615     1.73   0.084    -.0392146    .6172223
         age |   -.0344393   .0173988    -1.98   0.048    -.0685404   -.0003382
     married |    .0272098   .2450515     0.11   0.912    -.4530824     .507502
        race |    .5192792    .233976     2.22   0.026     .0606947    .9778637
          e1 |   -1.030142   .4264018    -2.42   0.016    -1.865875   -.1944102
          e2 |   -.9514855   .4312971    -2.21   0.027    -1.796812   -.1061588
          e3 |   -.3236886   .3834895    -0.84   0.399    -1.075314     .427937
          e4 |   -.1834053   .4065985    -0.45   0.652    -.9803238    .6135132
living_sta~2 |    .2053187   .3534515     0.58   0.561    -.4874335    .8980709
       _cons |    1.833621   .5983322     3.06   0.002     .660911     3.00633
------------------------------------------------------------------------------

Iteration 0:   log likelihood = -448.05836
Iteration 1:   log likelihood =  -436.7552
Iteration 2:   log likelihood = -436.70391
Iteration 3:   log likelihood =  -436.7039

Logistic regression                             Number of obs   =        700
                                                LR chi2(9)      =      22.71
                                                Prob > chi2     =     0.0069
Log likelihood =  -436.7039                     Pseudo R2       =     0.0253

------------------------------------------------------------------------------
    remit_mi |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        sert |    .3745607   .1675229     2.24   0.025     .0462218    .7028995
         age |   -.0333887   .0173108    -1.93   0.054    -.0673173    .0005399
     married |   -.0039184   .2444746    -0.02   0.987    -.4830798     .475243
        race |    .3481279   .2326404     1.50   0.135     -.107839    .8040948
          e1 |   -.3716112   .4581811    -0.81   0.417    -1.26963     .5264074
          e2 |   -.3885167   .4506427    -0.86   0.389    -1.27176     .4947267
          e3 |    .1858891    .411828     0.45   0.652    -.621279     .9930572
          e4 |    .2538755   .4101049     0.62   0.536    -.5499154    1.057666
living_sta~2 |    .2985123   .3571038     0.84   0.403    -.4013983     .998423
       _cons |    1.301454   .6289927     2.07   0.039     .0686512    2.534257
------------------------------------------------------------------------------

Multiple imputation parameter estimates (6 imputations)
------------------------------------------------------------------------------
    remit_mi |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        sert |    .2850676   .1866172     1.53   0.127    -.0806955    .6508307
         age |   -.0373576   .0181933    -2.05   0.040    -.0730158   -.0016994
     married |    -.014018   .2931792    -0.05   0.962    -.5886387    .5606027
        race |     .279717    .288825     0.97   0.333    -.2863695    .8458036
          e1 |   -.5136475   .6641685    -0.77   0.439    -1.815394    .7880989
          e2 |   -.2049008   .6910435    -0.30   0.767    -1.559321     1.14952
          e3 |     .120714   .4789186     0.25   0.801    -.8179492    1.059377
          e4 |    .3441901    .542198     0.63   0.526    -.7184985    1.406879
living_sta~2 |    .3393332   .3818089     0.89   0.374    -.4089985    1.087665
       _cons |    1.489949   .7099906     2.10   0.036     .0983929    2.881505
------------------------------------------------------------------------------
700 observations.
```

XTSTUM

```
. iis id

. tis wk_number

. sort sert wk_number

. by sert: xtsum hrsd8

-------------------------------------------------------------------------------
-> sert = Nortriptyline

Variable         |      Mean   Std. Dev.       Min      Max |    Observations
-----------------+--------------------------------------------+----------------
hrsd8    overall |  6.367475   5.188553          0       21 |     N =    2226
         between |             4.616891          0       21 |     n =      53
         within  |             2.449118  -1.108715 21.46271 |     T =      42
-------------------------------------------------------------------------------


-> sert = Sertraline

Variable         |      Mean   Std. Dev.       Min      Max |    Observations
-----------------+--------------------------------------------+----------------
hrsd8    overall |  6.401216   5.133407          0       21 |     N =    1974
         between |             4.245025          0       19 |     n =      47
         within  |             2.950611  -.9797366 21.44883 |     T =      42

. by sert wk_number: xtsum hrsd

-------------------------------------------------------------------------------
-> sert = Nortriptyline, wk_number = 1

Variable         |      Mean   Std. Dev.       Min      Max |    Observations
-----------------+--------------------------------------------+----------------
hrsd     overall |     17.04   5.510509          3       30 |     N =      50
         between |             5.510509          3       30 |     n =      50
         within  |                   0       17.04    17.04 |     T =       1
-------------------------------------------------------------------------------
-> sert = Nortriptyline, wk_number = 2

Variable         |      Mean   Std. Dev.       Min      Max |    Observations
-----------------+--------------------------------------------+----------------
hrsd     overall |  13.39216   4.808652          3       24 |     N =      51
         between |             4.808652          3       24 |     n =      51
         within  |                   0    13.39216 13.39216 |     T =       1
-------------------------------------------------------------------------------
-> sert = Nortriptyline, wk_number = 3

Variable         |      Mean   Std. Dev.       Min      Max |    Observations
-----------------+--------------------------------------------+----------------
hrsd     overall |     11.46   5.269125          1       23 |     N =      50
         between |             5.269125          1       23 |     n =      50
         within  |                   0      11.46    11.46 |     T =       1
-------------------------------------------------------------------------------
> sert = Nortriptyline, wk_number = 4

Variable         |      Mean   Std. Dev.       Min      Max |    Observations
-----------------+--------------------------------------------+----------------
```

```
hrsd     overall |     11.42   6.474723          2        26 |     N =      50
         between |              6.474723          2        26 |     n =      50
         within  |                    0      11.42     11.42 |     T =       1
-------------------------------------------------------------------------------
> sert = Nortriptyline, wk_number = 5

Variable         |      Mean   Std. Dev.       Min      Max |    Observations
-----------------+--------------------------------------------+----------------
hrsd     overall |  8.555556   6.017231          0       22 |     N =      45
         between |              6.017231          0       22 |     n =      45
         within  |                    0   8.555556 8.555556 |     T =       1
-------------------------------------------------------------------------------
-> sert = Nortriptyline, wk_number = 6

Variable         |      Mean   Std. Dev.       Min      Max |    Observations
-----------------+--------------------------------------------+----------------
hrsd     overall |  7.377778    5.33125          0       23 |     N =      45
         between |               5.33125          0       23 |     n =      45
         within  |                    0   7.377778 7.377778 |     T =       1
-------------------------------------------------------------------------------
> sert = Nortriptyline, wk_number = 7

Variable         |      Mean   Std. Dev.       Min      Max |    Observations
-----------------+--------------------------------------------+----------------
hrsd     overall |  7.820513   6.580961          0       28 |     N =      39
         between |              6.580961          0       28 |     n =      39
         within  |                    0   7.820513 7.820513 |     T =       1
-------------------------------------------------------------------------------
> sert = Nortriptyline, wk_number = 8

Variable         |      Mean   Std. Dev.       Min      Max |    Observations
-----------------+--------------------------------------------+----------------
hrsd     overall |     6.325   5.312721          0       21 |     N =      40
         between |              5.312721          0       21 |     n =      40
         within  |                    0     6.325    6.325 |     T =       1
-------------------------------------------------------------------------------
> sert = Sertraline, wk_number = 1

Variable         |      Mean   Std. Dev.       Min      Max |    Observations
-----------------+--------------------------------------------+----------------
hrsd     overall |  15.73333   6.531045          4       33 |     N =      45
         between |              6.531045          4       33 |     n =      45
         within  |                    0   15.73333 15.73333 |     T =       1
-------------------------------------------------------------------------------
> sert = Sertraline, wk_number = 2

Variable         |      Mean   Std. Dev.       Min      Max |    Observations
-----------------+--------------------------------------------+----------------
hrsd     overall |  13.51111   6.535297          2       30 |     N =      45
         between |              6.535297          2       30 |     n =      45
         within  |                    0   13.51111 13.51111 |     T =       1
-------------------------------------------------------------------------------
> sert = Sertraline, wk_number = 3

Variable         |      Mean   Std. Dev.       Min      Max |    Observations
-----------------+--------------------------------------------+----------------
hrsd     overall |    11.925   7.141024          0       28 |     N =      40
         between |              7.141024          0       28 |     n =      40
         within  |                    0     11.925   11.925 |     T =       1
-------------------------------------------------------------------------------
> sert = Sertraline, wk_number = 4
```

```
Variable         |      Mean   Std. Dev.       Min      Max |    Observations
-----------------+--------------------------------------------+----------------
hrsd     overall |  10.77778   6.560101          0       26 |     N =      36
         between |             6.560101          0       26 |     n =      36
         within  |                   0   10.77778 10.77778 |     T =       1
-------------------------------------------------------------------------------
> sert = Sertraline, wk_number = 5

Variable         |      Mean   Std. Dev.       Min      Max |    Observations
-----------------+--------------------------------------------+----------------
hrsd     overall |       8.4   5.816811          0       21 |     N =      35
         between |             5.816811          0       21 |     n =      35
         within  |                   0        8.4      8.4 |     T =       1
-> sert = Sertraline, wk_number = 6

Variable         |      Mean   Std. Dev.       Min      Max |    Observations
-----------------+--------------------------------------------+----------------
hrsd     overall |  7.714286   5.355434          0       17 |     N =      35
         between |             5.355434          0       17 |     n =      35
         within  |                   0   7.714286 7.714286 |     T =       1
-------------------------------------------------------------------------------
> sert = Sertraline, wk_number = 7

Variable         |      Mean   Std. Dev.       Min      Max |    Observations
-----------------+--------------------------------------------+----------------
hrsd     overall |       6.8    6.09918          0       19 |     N =      30
         between |              6.09918          0       19 |     n =      30
         within  |                   0        6.8      6.8 |     T =       1
-------------------------------------------------------------------------------
> sert = Sertraline, wk_number = 8

Variable         |      Mean   Std. Dev.       Min      Max |    Observations
-----------------+--------------------------------------------+----------------
hrsd     overall |   6.40625   5.154762          0       19 |     N =      32
         between |             5.154762          0       19 |     n =      32
         within  |                   0    6.40625  6.40625 |     T =       1
         within  |              1.45113   5.398148 25.56481 |     T =       6
-------------------------------------------------------------------------------
```

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