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A new framework for managing and analyzing multiply imputed data in Stata

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Abstract. A new set of tools is described for performing analyses of an ensemble of datasets that includes multiple copies of the original data with imputations of missing values, as required for the method of multiple imputation. The tools replace those originally developed by the authors. They are based on a simple data management paradigm in which the imputed datasets are all stored along with the original data in a single dataset with a vertically stacked format, as proposed by Royston in his ice and micombine commands. Stacking into a single dataset simplifies the management of the imputed datasets compared with storing them individually. Analysis and manipulation of the stacked datasets is performed with a new prefix command, mim, which can accommodate data imputed by any method as long as a few simple rules are followed in creating the imputed data. mim can validly fit most of the regression models available in Stata to multiply imputed datasets, giving parameter estimates and confidence intervals computed according to Rubin's results for multiple imputation inference. Particular attention is paid to limiting the available postestimation commands to those that are known to be valid within the multiple imputation context. However, the user has flexibility to override these defaults. Features of these new tools are illustrated using two previously published examples.

Keywords: st0139, mim, mimstack, ice, micombine, miset, mifit, multiple imputation, missing data, missing at random

1 Introduction

The presence of missing data raises challenges for many statistical analyses, especially those based on multivariable methods where the absence of values on just one or two variables for a case will, in general, render that observation unusable in standard methods of analysis. Loss of observations from the analysis dataset in this way raises two potential threats: first, that of bias due to selection processes that may be related to the variables or—more importantly—to the associations of interest, and second, that of loss of precision (or power) due to reduction in the available sample size. Over the past two decades, considerable literature has arisen on statistical approaches to handling missing data: in particular, see the influential texts by Little and Rubin (2002) and Schafer (1997).

The leading general approach to the problem now appears to be the method of multiple imputation (MI). Briefly, this method has two distinct stages. First, a set of copies of the original dataset must be created, in which each of the missing values is imputed using an appropriate modeling procedure. Second, standard analyses are performed on each of these completed or imputed datasets, and the results (in the form of whatever parameter estimates are of substantive interest—typically regression coefficients) are then combined according to Little and Rubin's theory (2002) to obtain a set of final estimates and standard errors. This process has been outlined in more detail in an earlier article (Carlin et al. 2003).

Although at first glance MI may appear cumbersome for use in everyday data analysis, with appropriate software tools the method is not difficult to apply. Recent publication of software both for performing imputation and for analyzing the imputed datasets has led to an upsurge of usage in applied research papers. The boundaries for safe application of the method have not been fully delineated although it is well understood that the standardly available approaches all rely on an assumption that the missing data can be regarded as missing at random. This assumption is a tricky one to characterize clearly in many applications, especially those involving large datasets with many variables (Potthoff et al. 2006). Furthermore, there are a number of possible approaches for performing imputation (Schafer 1997; van Buuren, Boshuizen, and Knook 1999). Although we think the method is very effective and reliable in many situations, the underlying assumptions need to be considered carefully in any application, and further research is needed to better define the types of problems where reliable answers can be expected.

In order to facilitate better research on MI and its validity in the context of departures from assumptions, as well as to facilitate more widespread adoption of the method in practice, we have developed a comprehensive new architecture for managing the process of data analysis using MI in Stata. Within this new framework, users are able to apply all the commonly used estimation commands available in Stata, including those based on the svy prefix, providing a substantial extension of the previously available tools for MI analysis. We have also refined and extended the available postestimation commands, including an implementation of predict for multiply imputed data. These advances are provided in the form of a new prefix command, mim, which this article introduces.

2 Overview

In this section, we give an outline of our approach and relate the new structure to previous work by the authors.

2.1 Background

Earlier publications described a system for managing imputed datasets and performing combined analyses in Stata (Carlin et al. 2003) and described a command for creating imputations using the method of "chained equations" (ice) along with another command (micombine) for combined analyses (Royston 2004, 2005a, 2005b). The latter publications were a substantial advance on the former for two reasons: (1) they provided a method for performing the imputations, and (2) they highlighted the fact that the MI process could be handled in Stata by storing imputed versions of a dataset in a stacked format within a single dataset.

The earlier mitools package of commands (Carlin et al. 2003) had no facility for generating imputed values (which had to be generated externally, for example, by using the freeware NORM from http://www.stat.psu.edu/~jls/misoftwa.html) and assumed that the imputed datasets were to remain distinct files. The mifit command in that package performed combined analysis for a range of regression commands by repeatedly loading each imputed dataset, storing the results obtained, and performing the combined calculations at the end. The package also introduced methods for postestimation in the MI framework (commands milincom and mitestparm) and was a first attempt to create a general environment for flexible management of imputed datasets. However, the architecture adopted meant that a special-purpose command needed to be written to perform manipulations (recoding, transformation, etc.) within each imputed dataset because this required successive reloading of the datasets.

Royston's focus was on developing the ice command as an implementation of the method of "multiple imputation using chained equations", or "MICE" (Van Buuren, Boshuizen, and Knook 1999), with the micombine command provided to allow inferences to be obtained by combining analyses over the resulting imputations. Again, a wide range of regression estimation commands was accommodated. Stata's ereturn commands were used to allow the standard Stata postestimation commands test and testparm to work as might be expected, using estimated regression coefficients and the variance—covariance matrix obtained by pooling across the imputed datasets.

It seems clear that the best environment for managing the method of MI in Stata is based on storing the imputed datasets in stacked form in a single dataset, as in ice and micombine. The mim prefix command described in this article provides a new integrated framework for MI in Stata using this paradigm. To be compatible with mim, a dataset must contain two variables mj and mi that index, respectively, the individual datasets within the stack and observations within the datasets. Thus mi should contain the same value i for each observation from the ith individual across datasets, with the datasets being identified by mj taking the values $0, 1, \ldots, m$ for the original data (mj = 0) and

each of the imputed datasets. Most \min subcommands use only the imputed data (so ignore cases for which $\min j = 0$), but retaining the original data in the stack enables parallel manipulation and transformation of variables within incomplete and imputed data. Retaining the original data also allows complete-case analyses to be performed by applying the restriction $\inf \min_{j=0}$.

2.2 Estimation for MI datasets

mim is designed mainly for the creation of combined parameter estimates from an ensemble of imputed datasets. It allows the creation of combined estimates for regression coefficients obtained from any command that has the standard Stata estimation command structure. All commonly used commands, including those taking the svy prefix, are recognized directly by the mim prefix command, and others can also be used by specifying the category (fit) option with mim (see section 3). In the latter case, the user must take responsibility for the results because mim will not automatically reflect any nonstandard characteristics of commands that are not in the recognized list. While most Stata estimation commands—including those using multiple-equation models—should work seamlessly with mim, the user should pay attention to a command's handling of any ancillary parameters. Often these are calculated on the log scale but back-transformed for display purposes, and the associated t or z statistics, and their p-values, are sometimes suppressed. When a command that has these characteristics but is not in the recognized list is used with mim, all parameters will be displayed on the same scale in which they are calculated, and the corresponding t statistics and p-values will be displayed, whether or not they are valid. This behavior is consistent with Stata's ereturn display command.

2.3 Postestimation with MI

The method of MI was developed with a focus on the canonical activity of estimating regression models. We have maintained this focus here although Rubin's rules can be applied to any estimand for which approximate normality of the estimate is reasonably assured (and in a later release of \min , we plan to provide a more generic capability to create combined estimates for any user-defined scalar estimator). Rubin's combination rules have been shown to work well for scalar estimands, especially when a small-sample adjustment is applied to the degrees of freedom used for the t reference distribution (Barnard and Rubin 1999) (and assuming that the method of imputation is proper; Rubin [1996]). For standard fitting of regression models, the scalar approach is adequate because the estimation of each coefficient in the linear predictor may be treated separately from the other coefficients, using each coefficient's estimated standard error or variance.

^{1.} These are regress, mean, proportion, ratio, logistic, logit, ologit, mlogit, probit, oprobit, poisson, glm, binreg, nbreg, gnbreg, blogit, clogit, cnreg, mvreg, rreg, qreg, iqreg, sqreg, bsqreg, stcox, streg, xtgee, xtreg, xtlogit, xtnbreg, xtpoisson, xtmixed, svy: regress, svy: mean, svy: proportion, svy: ratio, svy: logistic, svy: logit, svy: ologit, svy: mlogit, svy: probit, svy: oprobit, and svy: poisson.

However, several subsidiary estimation tasks or hypothesis tests that involve more than one coefficient are often of interest. These are managed for all standard estimation commands in Stata with a range of auxiliary commands under the heading of postestimation. We believe that some, but not all, of these standard postestimation commands can be validly translated to the MI context with our current understanding of MI. mim currently has the facility to handle lincom, testparm, and predict, which respectively provide estimates for linear combinations of the regression parameters, Wald-type hypothesis tests for groups of regression coefficients considered simultaneously, and estimates of predicted values for the units of the original dataset. (Note that postestimation methods relying on likelihood comparisons (lrtest) are not applicable because MI does not involve calculation of likelihood functions for the data.)

The MI version of lincom is straightforward; it simply requires application of Rubin's rules to the (scalar) linear combination that is of interest. However, multiparameter hypothesis testing is less straightforward because it is not clear that a valid pooled variance—covariance matrix (in a multiparameter problem) can always be obtained by a simple averaging process (Schafer 1997). We have implemented an MI version of testparm using the method of Li, Raghunathan, and Rubin (1991), but in this first release we have not provided a full translation of the test command, of which testparm is a special case with a more limited range of syntax. Users may apply any of Stata's postestimation commands that rely on the standard structure of Stata's returned results (in particular the vector of estimates e(b) and variance-covariance matrix e(V)) by requesting that MI values of these quantities be placed in the standard returned results. mim does not do this by default because we do not believe that there is adequate theory to support all the possible resulting calculations and, in particular, because of the difficulty just mentioned of ensuring a valid variance—covariance matrix. The user is referred to help mim for details of the objects returned in e() when mim is used with an estimation command.

We have also provided a limited implementation of Stata's predict command under the mim prefix. This produces estimates of predicted values at each observation in the estimation dataset by treating the estimand $X_i\beta$ for each observation i as a scalar parameter to which the Rubin combination formulas are applied. This calculation will often use values of X_i that are missing in the original data. A more general approach to prediction, which would allow predictions to be created for "synthetic" observations (appended as new rows of data), is a more complex task that we have not yet addressed. It requires a method for creating a joint inference for the vector β of regression coefficients in a linear predictor and then applying this to whatever set or sets of X values are specified.

2.4 Data manipulation with MI datasets

The final category of subcommands that mim handles are those that manipulate and transform data. Our experience is that, for practical work with complex datasets, it is essential to have the capacity to work flexibly with data after imputation has been performed. For example, imputation may be performed on raw variables that must

then be categorized or transformed in various ways to be used in planned analyses. With the previous mitools, imputed datasets were stored separately, so a command for managing manipulation of each imputed dataset in an ensemble was needed. In the mim environment, most data manipulations (generate, replace, recode, etc.) can be simply applied to the single stacked dataset. Assuming that the original data with missing values has been retained in the stacked mim dataset (with mj = 0), the specification of data transformations should appropriately allow for any missing values, i.e., in general by explicit exclusions such as "if var!=.".

mim was specifically programmed for three data manipulation commands (reshape, append, and merge) that cannot simply be applied to the stacked dataset because they require that proper attention be paid to the repeated dataset structure. The sortorder() option is required for the use of merge, in order to guarantee preservation of the observation identifier across merged datasets, because the _mi index must be dropped while the data manipulation is performed.

As with estimation commands, other data manipulation commands may be applied at the user's discretion by specifying the option category(manip), which essentially allows a command to be applied to each dataset separately, with the resulting datasets stacked back into the same structure as used originally. Note, however, that certain data transformations, such as those that generate new observations (e.g., expand), may produce meaningless results in the context of an MI dataset.

The mim prefix also supports two newly written utility subcommands: check and genmiss. The former provides a check as to whether the dataset in memory has a mim-compatible structure containing the indexing variables mj and mi. The main checks are that nonmissing values must be constant across imputed datasets and that all missing values must have been imputed. genmiss creates an indicator variable to contain the missing/observed status of a selected variable. These utility subcommands require that the original dataset with missing values has been included in the stacked dataset.

While mim is designed to facilitate the handling of multiply imputed datasets, the user should be aware of a number of other utilities that are available in Stata for managing and manipulating missing data more generally. These range from the user-written command mvpatterns, which enables a detailed summary of patterns of missing data, to various usages of standard Stata functions. In particular, the rowmiss function of egen is a handy tool for identifying the extent to which missing data affect observations in a dataset, as for example in egen int nmiss = rowmiss(varlist) if _mj==0, which would create a variable containing the number of missing values in varlist.

Finally, the mim package includes one auxiliary command, mimstack, which creates a mim-compatible dataset from an appropriate set of imputed datasets, with or without the original incomplete data.

3 Syntax

$ exttt{mim} \ igl[\ , \ mim_options igr] \colon \ com^{-1}$	mand				
$\label{eq:mim_problem} \texttt{mim} \ \big[\ \textit{,} \ \textit{replay_options} \big]$					
$mim_options$	description				
General					
<pre>category(fit manip)</pre>	specify whether $command$ is estimation or data manipulation				
<u>noi</u> sily	display output from execution of <i>command</i> within each of the imputed datasets				
Estimation (valid only for esti	mation commands)				
dots	display progress dots during model fitting				
<u>noind</u> ividual	suppress capture of results from each application of $command$				
<u>st</u> orebv	fill the standard list (e(b), e(V), etc.) of returned results for estimation commands with MI estimates				
Manipulation (valid only for d	ata manipulation commands)				
${\color{red} { ext{so}}}$ rtorder(${\color{blue} varlist}$)	one or more variables that uniquely identify the observations in a given imputed dataset following each execution of <i>command</i>				
$replay_options$	description				
<u>cl</u> earbv	clears the standard list (e(b), e(V), etc.) of returned results for estimation commands, but leaves intact all other items returned by mim				
j(#)	fills the standard list $(e(b), e(V), etc.)$ of returned results for estimation commands with the estimates corresponding to imputed dataset $\#$				
$reporting_options$ ${ t st}$ orebv	level() and eform options supported by <i>command</i> same as for estimation, unless j() option is specified				

xi is allowed as a prefix to mim but not as a prefix to command. svy is allowed as a prefix to command. version is allowed as a prefix to command.

4 Options

4.1 General

category(fit | manip) is not required for the estimation and data manipulation commands that are listed in section 2. However, it is required when any other command is used to specify the type of command that is being passed to mim: either estimation (category(fit)) or data manipulation (category(manip)).

noisily specifies that the results of the application of *command* to each of the individual imputed datasets should be displayed.

4.2 Estimation

dots specifies that progress dots should be displayed.

noindividual specifies that capture of the estimation results corresponding to the fitting of the given estimation command to each of the individual imputed datasets should be suppressed.

storebv specifies that the standard list of returned results for estimation commands be filled using the MI results, forcing the MI coefficient and covariance matrix estimates into e(b) and e(V), respectively. This enables subsequent application, at the user's discretion, of Stata postestimation commands that use these quantities directly.

4.3 Manipulation

sortorder(varlist) must specify a list of one or more variables that uniquely identifies the observations in each of the datasets in a mim-compatible dataset after command has been applied to the given dataset (varlist cannot include _mi because the _mj and _mi variables are dropped from each dataset prior to the call to command). This option is not valid for append and reshape but is mandatory for all other data manipulation commands.

4.4 Replay

- clearby specifies that the standard list (e(b), e(V), etc.) of returned results for estimation commands be cleared. All other (eclass) items returned specifically by mim are left intact.
- j(#) specifies that the standard list (e(b), e(V), etc.) of returned results for estimation commands be filled with the estimates from the #th imputed dataset.

reporting_options may include any level() and eform options supported by command.

storebv specifies that the standard list (e(b), e(V), etc.) of returned results for estimation commands be filled with the MI estimates, unless the j() option is specified.

(There are no mim_options for mim: predict, mim: check, and mim: genmiss.)

5 Example: Adolescent health cohort study

Our first illustration uses a dataset adapted from an adolescent health cohort study that was used by Carlin et al. (2003) to introduce the original mitools commands. Imputation was performed for this study using the stand-alone package NORM, based on fitting a multivariate normal distribution (followed by appropriate rounding of categorical variables). This produces imputations in separate files, which we may combine into a mim format by applying mimstack. Imputations were performed separately for males and females in order to preserve interactions with gender, so we first load and stack five imputed datasets (smif*.dta) with the female participants, followed by a similar process with the male participants:

```
. mimstack, m(5) sortorder(id wave) istub(smiF) clear
. save smifimp5, replace
file smifimp5.dta saved
. mimstack, m(5) sortorder(id wave) istub(smiM) clear
. save smimimp5, replace
file smimimp5.dta saved
```

We then join the two mim datasets into one by using mim: append, at the same time creating a variable sex to identify the two genders. The check utility is used to verify that we have created a dataset in mim-compatible format.

```
. use smifimp5, clear
. gen byte sex = 1
. mim: append using smimimp5
. replace sex = 0 if sex == .
(3420 real changes made)
. label define sexlb 0 "male" 1 "female"
. label values sex sexlb
. mim: check
........
PASS
. save smiall, replace
file smiall.dta saved
```

The mim dataset smiall.dta is now ready for analysis and will remain in memory during the course of subsequent mim commands.

(Continued on next page)

. describe

Contains data from smiall.dta

obs: 7,020 vars: 12

vars: 12 13 Mar 2008 07:48 size: 140,400 (86.6% of memory free) (_dta has notes)

variable name	storage type	display format	value label	variable label
_mj	byte	%8.0g		imputation identifier
_mi	int	%8.0g		observation identifier
id	long	%9.0g		
wave	byte	%9.0g		survey wave
mmetro	byte	%9.0g		school in metro area
parsmk	byte	%9.0g		either parent smokes
drkfre	byte	%16.0g	drkfre	drinking frequency
alcdos	byte	%21.0g	alcdos	av units/drinking day
alcdhi	byte	%9.0g		drank >=5 units at least once
smk	byte	%13.0g	smk	smoking status
cistot	byte	%9.0g		CIS total score
sex	byte	%8.0g	sexlb	

Sorted by: _mj _mi

When using MI, it is sometimes useful to informally examine the variation in values across imputed datasets. This can be done with standard Stata syntax by using the _mj index. For example, one could examine the distribution of drinking frequency (a four-category variable) among imputed and nonimputed cases by running tables as follows:

- . mim: genmiss drkfre
- . by _mj: tabulate drkfre _mim_drkfre, col (output omitted)

To illustrate a more targeted analysis, we generate a binary variable drkreg and obtain estimates of the frequency of regular drinking at each wave by using the command mim: proportion. (proportion is a Stata estimation command—available from release 9—and so has been incorporated into the standard mim structure, making it unnecessary to have a separate command such as mici in the previous mitools.)

```
. gen drkreg = (drkfre >= 2) if drkfre != .
(163 missing values generated)
. forvalues num = 1/6 {
  2. dis "wave: " `num
  3. mim: proportion drkreg if wave==`num´
  4. }
wave: 1
Multiple-imputation estimates (proportion)
                                                           Imputations =
Proportion estimation
                                                           Minimum obs =
                                                                              195
                                                           Minimum dof =
                                                                            180.3
                    Coef. Std. Err.
                                               P>|t|
                                                        [95% Conf. Int.]
                                                                            MI.df
                                          t
           0
                  .876923
                            .023918
                                      36.66
                                               0.000
                                                         .829728
                                                                  .924118
                                                                            180.3
           1
                  .123077
                            .023918
                                       5.15
                                               0.000
                                                         .075882
                                                                 .170272
                                                                            180.3
  (output omitted)
```

Issuing the command mim on its own replays the last set of results produced by a mim estimation command, in this case for wave==6:

. mim Multiple-imputation estimates (proportion) Proportion estimation					<pre>Imputations = Minimum obs = Minimum dof =</pre>	5 195 35.2
	Coef.	Std. Err.	t	P> t	[95% Conf. Int.]	MI.df
0	.644103 .355897	.040777 .040777	15.80 8.73	0.000	.561336 .726869 .273131 .438664	35.2 35.2

The MI (combined) estimates are displayed using a standard Stata format with a few variations to convey important information about the MI results. The number of imputed datasets is shown, and under this we have the minimum number of observations available for each of the separate analyses. In many cases (including the example shown here), the number of observations will be identical across imputed datasets, but this is not the case if the estimation is performed on a subset of the data defined by restriction according to a variable that is subject to missing values. In that case, the sample used for estimation will generally differ across imputations. Displaying the minimum sample size is a conservative approach; for some purposes, the user may prefer to obtain the average to display in tables of results. The final column in the table contains the approximate degrees of freedom (Barnard and Rubin 1999) that are used for defining the t multiplier underlying the confidence interval calculation. This column also gives a useful index of the extent to which missingness has affected the information available for the estimation of each parameter. The value "Minimum dof" gives the minimum of the "MI.df" across the effects that have been estimated (as well as across the datasets of varying size, if applicable). In this example of proportion applied to a binary variable, the standard error and associated degrees of freedom are identical for each of the two complementary proportions.

The variation in results underlying the combined estimate, across imputed datasets, could be examined by replaying the single imputation results, as follows:

```
. forvalues num = 1/5 {
  2. mim, j(`num')
  3. }
  (output omitted)
```

An important feature is that mim can take the xi prefix to generate interactions and dummy variables in the standard way. We illustrate this with a logistic regression that examines evidence for a different rate of change with wave between the sexes by fitting an interaction model. The (incorrect) independent-observations likelihood is used for estimation (i.e., the standard logistic command) with standard errors obtained by the robust sandwich method in order to allow for correlation between repeated measures on the same subjects.

```
. xi: mim: logistic drkreg i.sex*wave, cluster(id)
                                       (naturally coded; _Isex_0 omitted)
i.sex
                  _{	t Isex_0-1}
                  _IsexXwave_#
                                        (coded as above)
i.sex*wave
Multiple-imputation estimates (logistic)
                                                            Imputations =
                                                                                5
Logistic regression
                                                           Minimum obs =
                                                                             1170
                                                           Minimum dof =
                                                                            228.7
               Odds Rat. Std. Err.
                                          t
                                               P>|t|
                                                         [95% Conf. Int.]
      drkreg
                                                                            MI.df
                  .522541
                            .203362
                                       -1.67
                                               0.096
                                                         .243466 1.12151
                                                                            975.9
     _Isex_1
                 1.22544
                            .071734
                                       3.47
                                               0.001
                                                         1.09194 1.37526
                                                                            228.7
        wave
                  1.03796
IsexXwave 1
                            .084476
                                        0.46
                                               0.647
                                                         .884479 1.21807
                                                                            391.7
```

This model may be used to illustrate the use of mim: lincom; we estimate the odds ratio for regular drinking among males as follows:

```
. mim: lincom wave + _IsexXwave_1
Multiple-imputation estimates for lincom
                                                                 Imputations = 5
 (1) wave + _{IsexXwave_1} = 0
      drkreg
               Odds Rat. Std. Err.
                                              P>|t|
                                                        [95% Conf. Int.]
                                                                           MI.df
                                         t
         (1)
                 1.27195
                            3.37316
                                       0.09
                                               0.928
                                                        .006988 231.506
                                                                           997.9
```

We note again that mim recognizes the logistic command and so by default returns estimates in exponentiated form, labeled appropriately as odds ratios. When a similar logistic regression model is estimated using the generalized estimating equations method, the default display of the estimates is in the log scale, i.e., as the coefficients in the linear predictor. However, exponentiated coefficients may be obtained as usual by using the eform option.

-1.67304

cons

5

132.3

-2.11679 -1.22929

```
. mim: xtgee drkreg sex wave, fam(binom) i(id)
Multiple-imputation estimates (xtgee)
                                                           Imputations =
                                                           Minimum obs =
                                                                             1170
                                                           Minimum dof =
                                                                             78.6
      drkreg
                   Coef. Std. Err.
                                              P>|t|
                                                        [95% Conf. Int.]
                                                                           MI.df
                -.493965
                             .23835
                                      -2.07
                                              0.040
                                                       -.964602 -.023328
                                                                           163.7
         sex
        wave
                 .219717
                            .038719
                                      5.67
                                              0.000
                                                        .142644 .29679
                                                                            78.6
```

We illustrate the multiparameter postestimation capabilities of mim by including further covariates in the model:

-7.46

0.000

.224338

```
. gen cisgp = cistot
(165 missing values generated)
. recode cisgp 0/5=1 6/11=2 12/100=3
(cisgp: 6300 changes made)
. xi: mim: xtgee drkreg sex wave i.cisgp, fam(binom) i(id) eform
i.cisgp
                  _Icisgp_1-3
                                       (naturally coded; _Icisgp_1 omitted)
Multiple-imputation estimates (xtgee)
                                                          Imputations =
                                                                               5
                                                          Minimum obs =
                                                                            1170
                                                          Minimum dof =
                                                                            74.1
```

drkreg	exp(b)	Std. Err.	t	P> t	[95% Con	f. Int.]	MI.df
sex	.558385	.133963	-2.43	0.016	1.18006	.895874	226.0
wave	1.28066	.052581	6.03	0.000		1.38983	74.1
_Icisgp_2	1.00571	.192688	0.03	0.976		1.4676	189.2
_Icisgp_3	1.77553	.353741	2.88	0.004		2.62857	255.8

```
. mim: testparm _Icis*
(1)
      _{\rm Icisgp_2} = 0
(2) _Icisgp_3 = 0
      F(2, 221.4) =
                          4.76
            Prob > F =
                          0.0095
```

A test of the overall null hypothesis of no differences between the three groups defined by the cisp variable (a categorical indicator of mental health) was obtained by using the mim: testparm command.

Because these data relate to measures taken on repeated occasions, some analyses may best be handled by reshaping the data to wide form. This is accomplished by using mim: reshape:

```
. gen drkany = (drkfre >= 1) if drkfre != .
(163 missing values generated)
. keep _mj _mi id wave drkany cisgp sex
. mim: reshape wide drkany cisgp, i(id) j(wave)
```

We can now obtain an estimate of the incidence of alcohol use between waves 1 and 2:

```
. mim: proportion drkany2 if drkany1 == 0
Multiple-imputation estimates (proportion)
                                                            Imputations =
                                                                                 5
Proportion estimation
                                                            Minimum obs =
                                                                               136
                                                            Minimum dof =
                                                                             122.6
                    Coef. Std. Err.
                                               P>|t|
                                                         [95% Conf. Int.]
                                                                             MI.df
           0
                  .696501
                            .040309
                                       17.28
                                               0.000
                                                         .616709
                                                                  .776292
                                                                             122.6
           1
                  .303499
                            .040309
                                       7.53
                                               0.000
                                                         .223708
                                                                  .383291
                                                                             122.6
```

Logistic regression can be used to examine the association between incidence and covariates of interest:

```
. xi: mim: logistic drkany2 i.cisgp1 if drkany1 == 0
                  _Icisgp1_1-3
                                       (naturally coded; _Icisgp1_1 omitted)
Multiple-imputation estimates (logistic)
                                                           Imputations =
Logistic regression
                                                           Minimum obs =
                                                                              136
                                                           Minimum dof =
                                                                            524.7
     drkany2
               Odds Rat.
                           Std. Err.
                                          t
                                               P>|t|
                                                         [95% Conf. Int.]
                                                                            MI.df
  _Icisgp1_2
                  .864098
                            .406523
                                       -0.31
                                               0.756
                                                         .343045
                                                                 2.17658
                                                                            642.2
                            .484563
                                               0.884
                                                                            595.8
  _Icisgp1_3
                  1.06857
                                        0.15
                                                         .438557
                                                                 2.60365
```

This analysis provides an example where the size of the imputed dataset used in each of the single-imputation analyses varies because the condition drkany1==0 produces a different set of observations (because drkany was subject to missingness and so varies across imputations).

6 Example: Breast cancer

We use a second example, taken from Royston (2004), to illustrate the use of ice to obtain multiply imputed data, followed by mim to handle and analyze the imputations.

First, the raw data containing missing values is loaded, and stset is used to specify a survival time structure for later analysis. This could have been done subsequently although the summary information provided would be potentially misleading because it would reflect the number of imputed datasets that were created. Second, five imputations of the missing values are created using ice (version 1.4.0; Royston 2007), saving the imputations to a new file, brcaeximp2b.dta. We use the match() option for the variable mx6 because it has an extremely skewed, semicontinuous distribution that makes it difficult to impute using a parametric model.

```
. use brcaex, clear
(German breast cancer data)
. stset rectime, fail(censrec)
     failure event:
                     censrec != 0 & censrec < .
obs. time interval:
                     (0, rectime]
                     failure
exit on or before:
      686 total obs.
        0 exclusions
      686 obs. remaining, representing
      299 failures in single record/single failure data
   771400 total analysis time at risk, at risk from t =
                                                                   0
                              earliest observed entry t =
                                                                   0
                                   last observed exit t =
                                                                2659
. ice mx1 mx4a mx5e mx6 mhormon lnt _d using brcaeximp2b, match(mx6) m(5)
> genmiss(m_) seed(101) replace
   #missing
     values
                   Freq.
                              Percent
                                             Cum.
          0
                     231
                                33.67
                                            33.67
          1
                     290
                                42.27
                                            75.95
          2
                     126
                                18.37
                                            94.31
          3
                      33
                                 4.81
                                            99.13
          4
                       6
                                 0.87
                                           100.00
      Total
                     686
                               100.00
   Variable
              Command
                        Prediction equation
              regress
                        mx4a mx5e mx6 mhormon lnt _d
        mx1
       mx4a
              logit
                        mx1 mx5e mx6 mhormon lnt _d
       mx5e
                        mx1 mx4a mx6 mhormon lnt _d
              regress
                        mx1 mx4a mx5e mhormon lnt _d
        mx6
              regress
    mhormon
                        mx1 mx4a mx5e mx6 lnt _d
              logit
        lnt
                         [No missing data in estimation sample]
                         [No missing data in estimation sample]
```

Imputing 1..2..3..4..5..(note: file brcaeximp2b.dta not found) file brcaeximp2b.dta saved

A plot of the distributions of observed and imputed values of one of the variables subject to missing data (mx1) illustrates the variability between imputations but reveals a similar distribution for the imputed values as for the observed, although one of the imputed distributions is somewhat different from the others (figure 1). Slightly different results will be obtained each time the imputation procedure is performed (unless the seed() option is used in ice); this is a natural feature of the method.

(Continued on next page)

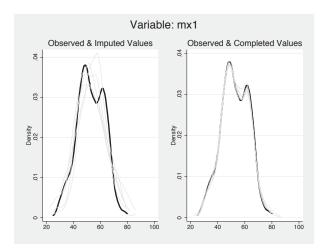


Figure 1. Frequency plots of the observed and imputed values of the variable mx1 in the breast cancer example. The left-hand panel superimposes the distribution of the five sets of imputed values (light-gray lines) on the distribution of the observed values (black lines), while the right-hand panel displays the distribution of the completed data—observed and imputed values combined—along with the incomplete observed data distribution.

Fractional polynomial transformations are applied to $\mathtt{mx1}$ and $\mathtt{mx6}$ for modeling purposes:

```
. use brcaeximp2b, clear
(German breast cancer data)
. fracgen mx1 -2 -0.5
-> gen double mx1_1 = X^-2
-> gen double mx1_2 = X^-0.5
   (where: X = mx1/10)
. fracgen mx6 0.5
-> gen double mx6_1 = X^0.5
   (where: X = (mx6+1)/1000)
```

The model is fitted in each imputed dataset and combined estimates are obtained:

```
. mim: stcox mx1_1 mx1_2 mx4a mx5e mx6_1 mhormon, nohr

Multiple-imputation estimates (stcox)

Imputations = 5

Minimum obs = 686

Minimum dof = 8.8
```

Coef.	Std. Err.	t	P> t	[95% Conf. Int.]	MI.df
36.459	19.3132	1.89	0.092	-7.38798 80.3059	8.8
-14.9337	8.25602	-1.81	0.103	-33.5639 3.69646	9.1
.5223	.290443	1.80	0.075	053744 1.09834	102.7
-1.86353	.273425	-6.82	0.000	-2.417 -1.31005	38.1
-1.97985	.440288	-4.50	0.000	-2.87119 -1.0885	38.0
422055	.163597	-2.58	0.016	757682086429	27.1
	36.459 -14.9337 .5223 -1.86353 -1.97985	36.459 19.3132 -14.9337 8.25602 .5223 .290443 -1.86353 .273425 -1.97985 .440288	36.459 19.3132 1.89 -14.9337 8.25602 -1.81 .5223 .290443 1.80 -1.86353 .273425 -6.82 -1.97985 .440288 -4.50	36.459 19.3132 1.89 0.092 -14.9337 8.25602 -1.81 0.103 .5223 .290443 1.80 0.075 -1.86353 .273425 -6.82 0.000 -1.97985 .440288 -4.50 0.000	36.459 19.3132 1.89 0.092 -7.38798 80.3059 -14.9337 8.25602 -1.81 0.103 -33.5639 3.69646 .5223 .290443 1.80 0.075053744 1.09834 -1.86353 .273425 -6.82 0.000 -2.417 -1.31005 -1.97985 .440288 -4.50 0.000 -2.87119 -1.0885

7 Conclusions

The field of MI data analysis is still young, but it is quickly growing and increasingly offers the possibility of more efficient and more informative analyses of important datasets, particularly in the social and health sciences. Following the success of our earlier package mitools (Carlin et al. 2003) and of the package ice for multiple imputation of missing values (Royston 2004, 2005b), our new package mim further rationalizes and advances the management and analysis of MI datasets. The approach used by mim requires all imputed copies of the dataset to be stored together in stacked format, allowing all analysis to take place using the single dataset in memory. This approach is conceptually appealing in that it reminds the analyst that the individual imputed datasets should not be taken too seriously on their own: it is only by analyzing the multiply imputed datasets and appropriately combining results that valid inferences may be obtained. In this sense, the imputed data are naturally viewed as an extension of the original data. Use of the mim framework does, however, require that the user not forget that they are using a multiply imputed dataset; it is easy to mistakenly apply commands to the entire stacked dataset with the illusion of having several times more observations than actually exist. Clearly, there is an inherent complexity in using MI, which requires that the user always needs to be alert to such issues.

While there is certainly room for further development of mim (for example, to extend the test postestimation command), we believe the current version already provides a rich set of facilities for the analysis of MI data and for research on MI inference. Examples of research questions with MI data include how to build multivariable models from a set of candidate variables and how to construct suitable model performance summaries and diagnostics. More broadly, important questions remain unanswered about the use of MI: for example, how sensitive are results to the use of inappropriate imputation methods, and are there ways in which users can check the validity of their imputations and resulting analytic conclusions? As mentioned in this article's introduction, the only imputation methods that are widely available in standard software assume that the data are "missing at random" according to Rubin's technical definition (Little and Rubin 2002). Although this assumption cannot, by definition, be tested in the data being analyzed, the user should consider whether it has a good basis in the context of his or her application, and it would be helpful to have more research on the sensitivity of results to departures from missing at random (e.g., Carpenter, Kenward, and White 2007).

We hope to be able to update mim on a regular basis as relevant research on handling statistical issues with MI data is published and in response to user queries and suggestions. We also hope that users will develop Stata implementations of alternative methods for imputation and make them compatible with the mim environment so that comparative analyses are facilitated. (For example, it would be valuable to have a Stata version of Schafer's NORM.) Therefore, we welcome user input to help us further develop mim.

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9 References

- Barnard, J., and D. B. Rubin. 1999. Small-sample degrees of freedom with multiple imputation. *Biometrika* 86: 948–955.
- Carlin, J. B., N. Li, P. Greenwood, and C. Coffey. 2003. Tools for analyzing multiple imputed datasets. *Stata Journal* 3: 226–244.
- Carpenter, J. R., M. G. Kenward, and I. R. White. 2007. Sensitivity analysis after multiple imputation under missing at random: a weighting approach. Statistical Methods in Medical Research 16: 259–275.
- Li, K. H., T. E. Raghunathan, and D. B. Rubin. 1991. Large-sample significance levels from multiply imputed data using moment-based statistics and an F reference distribution. Journal of the American Statistical Association 86: 1065–1073.
- Little, R. J. A., and D. B. Rubin. 2002. Statistical Analysis with Missing Data. 2nd ed. New York: Wiley.
- Potthoff, R. F., G. E. Tudor, K. S. Pieper, and V. Hasselblad. 2006. Can one assess whether missing data are missing at random in medical studies? *Statistical Methods in Medical Research* 15: 213–234.
- Royston, P. 2004. Multiple imputation of missing values. Stata Journal 4: 227–241.
- ——. 2005a. Multiple imputation of missing values: update. Stata Journal 5: 188–201.
- ———. 2005b. Multiple imputation of missing values: update of ice. Stata Journal 5: 527–536.
- ———. 2007. Multiple imputation of missing values: further update of ice, with an emphasis on interval censoring. *Stata Journal* 7: 445–464.
- Rubin, D. B. 1996. Multiple imputation after 18+ years. Journal of the American Statistical Association 91: 473–489.
- Schafer, J. L. 1997. Analysis of Incomplete Multivariate Data. London: Chapman & Hall.
- van Buuren, S., H. C. Boshuizen, and D. L. Knook. 1999. Multiple imputation of missing blood pressure covariates in survival analysis. *Statistics in Medicine* 18: 681–694.

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