Multiple Imputation in Practice

Aprroaches for handing categorical and interaction variables

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Outline

- Background of multiple imputation (MI)
- Challenges to the user
- How SAS, Stata, and R handle these challenges
- Real world example using software
- General guidelines and conclusion

Some background: Patterns of missingness

There are 3 main categories for describing missing data pattern

- Missing completely at Random (MCAR)
 Missingness is unrelated to any factor
- Missing at Random (MAR)
 Missingness depends only on observed values
- Not Missing at Random (NMAR)
 Missingness is related to unobserved values

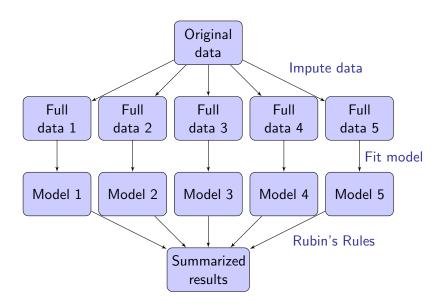
Some background: Multiple Imputation (MI)

MI is a simulation-based method for filling in missing values using observed data (valid if MAR)

Typical MI approach involves 3 basic steps

- Imputation
- Model fitting
- Summarize estimates using Rubin's Rules (Rubin, 1987)

Some background: Multiple Imputation (MI)



Algorithm: JM vs FCS

Joint Modelling (JM)

- Specify joint model, usually under multivariate normal (MVN)
- Derive posterior predictive distribution i.e. distribution of unobserved values conditional on observed data

Fully Conditional Specification (FCS)

- Designed to handle variables of mixed type
- Specify conditional model for each missing variable
- Impute data on a variable-by-variable basis

van Buuren (2007) compares the two methods in greater detail

Challenges - User has to make decisions

- Variables to include in the imputation model
- Number of imputations
- Model selection
- Longitudinal data
- Variables of mixed type
 - Especially nominal categorical variables such as race
- Derived variables
 - Higher order terms (X^2)
 - Interaction effects $(X_1 \times X_2)$
 - Propensity scores

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Why is nominal categorical variable a challenge?

Even though nominal categorical variables (e.g. race) are usually coded as numerical, the values are purely representative.

They are converted into dummy variables in the regression model.

In the imputation model, do we enter them as

- One class variable?
- Series of dummy variables?

How does each method handle categorical variables?

Joint Modelling (JM)

- If the imputation model is $Y, X_{Age}, X_{Male}, X_{Race}$
- The imputed value will not necessarily be a whole number

	Original Data				Imputed Data 1			
ID	Age	Male	Race		ID	Age	Male	Race
1	60	1	2		1	60	1	2
2	50		3		2	50	1.2	3
3		0		\rightarrow	3	44.4	0	-1.1
4	40	0			4	40	0	4.3
5	55	1	1		5	55	1	1

Options

- Use these values (not an option for Race)
- Round the values (rounding at 0.5 is not recommended for binary variables, Horton 2003)
- Use dummy variables in the imputation model as you would in your regression model

Making use of dummy variables in the imputation model

Joint Modelling (JM)

What does your regression model look like?

$$Y = \beta_0 + \beta_1 Age + \beta_2 Male + \beta_3 Black + \beta_4 Asian$$

Original Data						Imputed Data 1				
ID	Age	Male	Black	Asian		ID	Age	Male	Black	Asian
1	60	1	1	0		1	60	1	1	0
2	50		0	1		2	50	1.2	0	1
3		0			\rightarrow	3	44.4	0	0.1	0.2
4	40	0				4	40	0	0.3	1.5
5	55	1	0	0		5	55	1	0	0

Options

- Use these values
- Round the values (rounding at 0.5 is not recommended for binary variables, Horton 2003)



How does each method handle categorical variables?

Joint Modelling (JM)

Rounding options for binary variables

- Bernaards (2006) Calculate cut-off value based on a normal approximation to the binomial distribution
- Yucel (2008) Observed proportions
- Demirtas (2009) Round at 0.5, run logistic regression model to use as a refinement

Rounding options for categorical variables

- Allison (2000) Missing Data
- Song (2009) Correction of Bias in Imputing Missing Values of Categorical Variables
- Yucel (2011) Gaussian-Based Routines to Impute Categorical Variables in Health Surveys

These methods are not implemented in most software.



How does each method handle categorical variables?

Fully Conditional Specification (FCS)

- Specify a set of imputation models for each variable
 - Use linear regression to impute age
 - Use logistic regression to impute sex
 - Use multinomial regression to impute race

	Original Data					Imputed Data 1				
ID	Age	Male	Race		ID	Age	Male	Race		
1	60	1	2		1	60	1	2		
2	50		3		2	50	1	3		
3		0		\rightarrow	3	44.4	0	1		
4	40	0			4	40	0	3		
5	55	1	1		5	55	1	1		

Imputed data are ready to be analyzed.

How to handle interaction variables?

Options for JM and FCS

- Impute then transform
- Transform then impute
 - Active imputation

Additional options for FCS

Passive imputation

von Hippel (2009) suggests to *transform then impute*, rather than *impute then transform*

Options for Interactions: Active vs Passive imputation

Active Imputation

- Assumes the interaction variable to be another independent variable
- Include the interaction variable in the imputation model with all other variables including the main effects

Passive Imputation

- Passively imputes the interaction variable
- interaction variables are used to impute other missing values but not the main effects

MI by FCS	Vars in Imp Model				
Variable	Active	Passive			
X_1	Y, X_2, I_{12}, Z	Y, X_2, Z			
X_2	Y, X_1, I_{12}, Z	Y, X_1, Z			
$I_{12}:X_1\times X_2$	Y, X_1, X_2, Z	_			
Z	Y, X_1, X_2, I_{12}	Y, X_1, X_2, I_{12}			

How does each method handle interaction variables?

Active Imputation

• The relationship between the interaction effect and the main effects are not necessarily internally consistent

Original Data					Imputed Data 1			
ID	Age	Male	$Age \times Male$		ID	Age	Male	$Age \times Male$
1	60	1	60		1	60	1	60
2	50				2	50	1	40
3		0		\rightarrow	3	44.4	0	2
4	40	0	0		4	40	0	0
5	55	1	55		5	55	1	55

How does each method handle interaction variables?

Passive Imputation

• The relationship between the interaction effect and the main effects is preserved

Original Data					Imputed Data 1			
ID	Age	Male	$Age \times Male$		ID	Age	Male	$Age \times Male$
1	60	1	60		1	60	1	60
2	50				2	50	1	50
3		0		\rightarrow	3	44.4	0	0
4	40	0	0		4	40	0	0
5	55	1	55		5	55	1	55

Another Challenge

• Interaction between two nominal categorical variables

Interaction variables

Simple case

Binary × Binary

Slightly more complicated case

Binary × Multi-level Categorical

Most complicated case

Multi-level Categorical \times Multi-level Categorical

When interaction is Binary \times Binary

Race:
$$X_1 = \begin{cases} 1, & \text{if White} \\ 0, & \text{Other} \end{cases}$$
 Drug: $X_2 = \begin{cases} 1, & \text{if drug A} \\ 0, & \text{if drug B} \end{cases}$

Interaction:
$$I_{12} = X_1 \times X_2 = \begin{cases} 1, & \text{if White \& drug A} \\ 0, & \text{All other} \end{cases}$$

Regression model:
$$Y = \alpha + \beta_1 X_1 + \beta_2 X_2 + \beta_{12} I_{12} + e$$

Form of Interaction Variables in Imputation Model

	JM	FCS
Active	<i>I</i> ₁₂	specify 'logistic' for I_{12}
Passive	_	derive from X_1 and X_2

When interaction is Categorical \times Binary

If no interaction...

We create dummy variables for X_1

$$X_{W} = \begin{cases} 1, & \text{if White} \\ 0, & \text{Otherwise} \end{cases} X_{B} = \begin{cases} 1, & \text{if Black} \\ 0, & \text{Otherwise} \end{cases}$$

Regression model without interaction:

$$Y = \alpha + \beta_1 X_W + \beta_2 X_B + \beta_3 X_2 + e$$

When interaction is Categorical \times Binary

By introducing an interaction term between X_1 and X_2 ...

Model:

$$Y = \alpha + \beta_1 X_W + \beta_2 X_B + \beta_3 X_2 + \beta_4 X_W X_2 + \beta_5 X_B X_2 + e$$

Interaction is also the product of two main effects

Interaction:
$$I_{12} = X_1 \times X_2 = \begin{cases} 1, & \text{if White \& drug A} \\ 2, & \text{if Black \& drug A} \\ 0, & \text{All other} \end{cases}$$

Form of Interaction Variables in Imputation Model

	JM	FCS
Active	$X_W X_2, X_B X_2$	specify 'multinomial' for I_{12}
Passive	_	derive from X_1 and X_2

Race:
$$X_1 = \begin{cases} 1, & \text{if White} \\ 2, & \text{if Black} \\ 0, & \text{Other} \end{cases}$$
 Drug: $X_2 = \begin{cases} 1, & \text{if drug A} \\ 2, & \text{if drug B} \\ 0, & \text{if drug C} \end{cases}$

Model without interaction:

$$Y = \alpha + \beta_1 X_W + \beta_2 X_B + \beta_3 X_{DA} + \beta_4 X_{DB} + e$$

Race:
$$X_1 = \begin{cases} 1, & \text{if White} \\ 2, & \text{if Black} \\ 0, & \text{Other} \end{cases}$$
 Drug: $X_2 = \begin{cases} 1, & \text{if drug A} \\ 2, & \text{if drug B} \\ 0, & \text{if drug C} \end{cases}$

Model without interaction:

$$Y = \alpha + \beta_1 X_W + \beta_2 X_B + \beta_3 X_{DA} + \beta_4 X_{DB} + e$$

Model with interaction:

$$Y = \alpha + \beta_1 X_W + \beta_2 X_B + \beta_3 X_{DA} + \beta_4 X_{DB}$$
$$+ \beta_5 X_W X_{DA} + \beta_6 X_W X_{DB}$$
$$+ \beta_7 X_B X_{DA} + \beta_8 X_B X_{DB} + e$$



Interaction is NOT the product of two main effects

Interaction:
$$I_{12}^* = \begin{cases} 1, & \text{if White \& drug A} \\ 2, & \text{if White \& drug B} \\ 3, & \text{if Black \& drug A} \end{cases} \neq X_1 \times X_2$$

$$4, & \text{if Black \& drug B} \\ 0, & \text{All other} \end{cases}$$

Interaction is NOT the product of two main effects

Interaction:
$$I_{12}^* = \begin{cases} 1, & \text{if White \& drug A} \\ 2, & \text{if White \& drug B} \\ 3, & \text{if Black \& drug A} \end{cases} \neq X_1 \times X_2 = \begin{cases} 1 \\ 2 \\ 4 \\ 0 \end{cases}$$
On All other

Interaction is NOT the product of two main effects

Interaction:
$$I_{12}^* = \begin{cases} 1, & \text{if White \& drug A} \\ 2, & \text{if White \& drug B} \\ 3, & \text{if Black \& drug A} \end{cases} \neq X_1 \times X_2 = \begin{cases} 1 \\ 2 \\ 4 \\ 0, & \text{All other} \end{cases}$$

Form of Interaction Variables in Imputation Model

] JM	FCS
Active	$X_W X_{DA}, X_W X_{DB}, X_B X_{DA}, X_B X_{DB}$	specify 'multinomial' for I_{12}
Passive	_	derive from X_1 and X_2

Interaction variables - Summary

JM

- Convert interaction variable into dummy variables
- Multiply impute the data containing dummy variables
- Use imputed dummy variables in the scientific model

FCS

- Compute interaction variable
- Multiply impute the interaction variable as one class variable
- Onvert interaction variable into dummy variables to include in the scientific model

Software choices

SAS - PROC MI and PROC MIANALYZE

JM

Recently introduced FCS in version 9.3

No option for passive imputation

Stata - ice and micombine

FCS

Option for passive imputation

R - mice and pool

FCS

Option for passive imputation

There are many more choices but we will focus on these commands

SAS - PROC MI JM

- Pros
 - User-friendly
 - Computationally efficient
- Cons
 - No passive option

SAS - PROC MI FCS

- FCS Modelling Options
 - discrim (discriminant function method)
 - logistic (logistic regression method)
 - regress (linear regression method)
- Pros
 - User-friendly
- Cons
 - FCS option is still in experimental stage
 - Logistic option only for ordinal logistic regression
 - Discrim option only utilizes continuous variables as predictors
 - Computationally inefficient
 - No passive option

Stata - ice

- FCS Modelling Options
 - regress (regression method)
 - logit (logistic regression method)
 - ologit (ordinal logistic regression method)
 - mlogit (multinomial logistic regression method)

Pros

- User-friendly
- Passive option available

Cons

- For multi-level (usually 6 or more), ice often gives an error for mlogit option (can use the persist option to ignore the error)
- Passive option in ice needs care for specifying interaction between two multi-level nominal categorical variables

Passive option in ice

Command:

```
*manually generate interaction variable
gen int = 0
replace int = 1 if x1 == 1 & x2 == 1
replace int = 2 if x1 == 1 & x2 == 2
replace int = 3 if x1 == 2 & x2 == 1
replace int = 4 if x1 == 2 & x2 == 2
ice x1 x2 int z y, passive(int:x1*x2)
cmd(x1 x2:mlogit) saving(imp.dta) m(10)
```

Even if we explicitly create the interaction beforehand, because the passive option computes int by multiplying x1 and x2, int will only have 4 levels (0, 1, 2, 4) after imputation

Passive option in ice

Reassign values for X_2

$$X_1 = \begin{cases} 0 \\ 1 \\ 2 \end{cases} \qquad X_2 = \begin{cases} 0 \\ 3 \\ 5 \end{cases} \qquad X_1 \times X_2 = \begin{cases} 0 \\ 3 \\ 5 \\ 6 \\ 10 \end{cases}$$

```
*passive imputation
ice x1 x2 int z y, passive(int:x1*x2)
cmd(x1 x2:mlogit) saving(imp.dta) m(10)
*analytic model
micombine logit y b0.x1 b0.x2 b0.int
```

R - mice

- FCS Modelling Options
 - norm.nob (Linear regression)
 - norm (Bayesian linear regression)
 - logreg (Logistic regression)
 - polyreg (Polytomous/unordered regression)
 - Ida (Linear discriminant analysis)
- Pros
 - Flexible
 - Passive option available
 - Automatically creates dummy variables for factor variables
- Cons
 - Categorical variables need to be factor variables [as.factor()]
 - · Passive option requires intricate coding

Example Data

Breast Cancer Care from Two Different Hospitals

ID	Hosp	Mastectomy	AgeDx	Stage	YearDx	Race
1	1	1	64	1	2008	1
2	0	0	47	NA	1999	NA
3	0	0	80	NA	2009	1
4	1	1	55	3	2003	1
5	1	0	60	NA	2009	1
6	1	0	58	1	2009	1

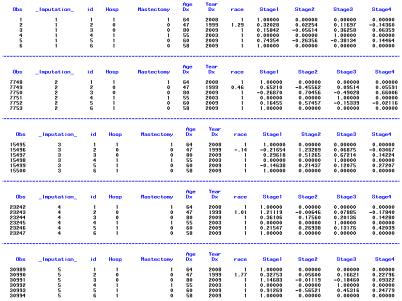
- Total *N* = 7747
- Missing variables Stage (26%), Race(13%)
- Overall missing proportion 31%
- Logistic regression model
 - Outcome Mastectomy
 - \bullet Predictors Hospital, Age, Stage, Year, Race, Hospital \times Stage



JM with Impute then Transform Approach in SAS

```
/* Proc MI JM Impute then Transform */
Edata dummy: set rawdat:
   if Stage ne . then do; *** create dummy variables for stage (ref: Stage 0);
   Stage1=(Stage=1):
   Stage2=(Stage=2);
   Stage3=(Stage=3):
   Stage4=(Stage=4);
   end:
   drop Stage;
Dproc mi data=dummy out=impdat im nimpute=5; *** multiply impute data;
  var Mastectomy Hosp AgeDx Stage1 Stage2 Stage3 Stage4 YearDx Race;
 run;
by imputation;
  model Mastectomy = Hosp AgeDx Stage1 Stage2 Stage3 Stage4 YearDx Race
                   Hosp*Stage1 Hosp*Stage2 Hosp*Stage3 Hosp*Stage4/link=logit dist=binomial covb;
  ods output parameterestimates=gmparms covb=gmcovb parminfo=gmpinfo:
 run:
mproc mianalyze parms=qmparms covb=qmcovb parminfo=qmpinfo; *** summarize estimates from each model;
     modeleffects Hosp AgeDx Stage1 Stage2 Stage3 Stage4 YearDx Race
                 Hosp*Stage1 Hosp*Stage2 Hosp*Stage3 Hosp*Stage4;
 run:
```

JM with Impute then Transform Approach in SAS



JM Using Active Imputation in SAS

```
/* Proc MI JM Active */
Edata active: set rawdat:
          if Stage ne . then do; *** create dummy variables for stage (ref: Stage 0);
            Stage1=(Stage=1):
            Stage2=(Stage=2);
            Stage3=(Stage=3):
            Stage4=(Stage=4);
           end:
           drop Stage;
           HospStage1 = Hosp*Stage1:
          HospStage2 = Hosp*Stage2;
           HospStage3 = Hosp*Stage3:
          HospStage4 = Hosp*Stage4;
Description of the proof o
        var Mastectomy Hosp AgeDx Stage1 Stage2 Stage3 Stage4 YearDx Race
                   HospStage1 HospStage2 HospStage3 HospStage4;
     run:

    proc genmod data=impdat jmact desc; *** build logistic regression model;
       by imputation;
       model Mastectomv = Hosp AgeDx Stage1 Stage2 Stage3 Stage4 YearDx Race
                                                               HospStage1 HospStage2 HospStage3 HospStage4/link=logit dist=binomial covb;
       ods output parameterestimates=gmparms covb=gmcovb parminfo=gmpinfo;
     run;
Eproc mianalyze parms=gmparms covb=gmcovb parminfo=gmpinfo; *** summarize estimates from each model;
                modeleffects Hosp AgeDx Stage1 Stage2 Stage3 Stage4 YearDx Race
                                                       HospStage1 HospStage2 HospStage3 HospStage4;
     run;
```

JM Using Active Imputation in SAS

2 1 2 0 0.43152 0.43952 -0.20955 -0.11642 0.22256 0.37967 -0.61139 0.00943 3 1 3 0 0.55556 0.37536 -0.25771 0.1811 0.31538 0.0573 -0.5745 0.0575 5 1 4 1 5 1 -0.47303 0.65655 -0.25771 0.1811 0.31538 0.0573 -0.34955 -0.5755 0.4275 0.												
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Results from Two Methods in SAS

		Proc MI JM	Impute then Tra	ansform		
0bs	Parm	Estimate	StdErr	LCLMean	UCLMean	Probt
1	Hosp	-0.020050	0.132546	-0.28908	0.24898	0.8806
2	AgeĎx	-0.016363	0.001926	-0.02014	-0.01259	< .0001
3	Stage1	0.109555	0.127272	-0.15390	0.37301	0.3983
4	Stage2	0.972660	0.105035	0.76617	1.17915	< .0001
5	Stage3	1.889572	0.154569	1.58624	2.19290	< .0001
6	Stage4	-0.194886	0.351248	-0.94089	0.55112	0.5869
7	YearDx	-0.027180	0.008945	-0.04481	-0.00955	0.0027
8	Race	-0.179914	0.063441	-0.30427	-0.05556	0.0046
9	Hosp*Stage1	-0.194767	0.178784	-0.56382	0.17428	0.2868
10	Hosp*Stage2	-0.421166	0.156632	-0.73248	-0.10985	0.0086
11	Hosp*Stage3	-0.577543	0.235492	-1.05436	-0.10073	0.0189
12	Hosp*Stage4	0.095694	0.381707	-0.68329	0.87468	0.8037
		Proc	MI JM Active			
0bs	Parm	Estimate	StdErr	LCLMean	UCLMean	Probt
1	Hosp	0.111996	0.141570	-0.18007	0.40406	0.4366
2	AgeDx	-0.016774	0.001947	-0.02059	-0.01296	< .0001
2 3	Stage 1	0.224637	0.126132	-0.03404	0.48332	0.0861
4	Stage2	1.158222	0.138978	0.86739	1.44905	< .0001
5 6	Stage3	2.108979	0.206800	1.68308	2.53488	< .0001
6	Stage4	-0.375647	0.397006	-1.20777	0.45647	0.3562
7	YearDx	-0.027291	0.008481	-0.04392	-0.01066	0.0013
8	Race	-0.193142	0.063511	-0.31763	-0.06865	0.0024
9	HospStage1	-0.328696	0.185086	-0.71408	0.05669	0.0905
10	HospStage2	-0.644039	0.178030	-1.00974	-0.27834	0.0012
11	HospStage3	-0.806307	0.222029	-1.24675	-0.36586	0.0004
12	HospStage4	0.273622	0.459300	-0.68893	1.23618	0.5585

Recommendation in SAS

- Use JM FCS option is still experimental
- No need to round
- Use active imputation

```
/* ice active */

*import data
insheet using "C:\example.csv", clear

*create interaction
gen theintwhosp*stage

*active imputation
ice mastectomy hosp agedx stage yeardx race theint, saving(imp_active.dta) m(5) replace
use imp_active.dta, clear

*build logistic regression model and summarize
micombine logit mastectomy hosp agedx b0.stage yeardx race b0.theint
```

- . *active imputation
- . ice mastectomy hosp agedx stage yeardx race theint, saving(imp_active.dta) m(5) replace

#missing values	Freq.	Percent	Cum.
0	5,341	68.94	68.94
1	386	4.98	73.93
2	1,395	18.01	91.93
3	625	8.07	100.00
Total	7.747	100.00	

Variable	Command	Prediction equation
mastectomy hosp agedx yeardx race	logit	[No missing data in estimation sample] mastectomy hops ageds area yeardx theint
stage theint	mlogit mlogit	mastectomy hosp agedx yeardx race theint mastectomy hosp agedx stage yeardx race

Imputing

[Perfect prediction detected: using augmlogit to impute ${\tt stage}$]

Error #430 encountered while running -uvis-

I detected a problem with running uvis with command mlogit on response theint and covariates mastectomy hosp agedx stage yeardx race.

The offending command resembled:

uvis mlogit theint mastectomy hosp agedx stage yeardx race , gen([imputed])

With mlogit, try combining categories of theint, or if appropriate, use ologit

you may wish to try the -persist- option to persist beyond this error. dumping current data to ./_ice_dump.dta convergence not achieved r(430):

```
/* ice active */
*import data
insheet using "C:\example.csv", clear

*create interaction
gen theint=hosp*stage

*active imputation
ice mastectomy hosp agedx stage yeardx race theint, saving(imp_active.dta) m(5) replace persist
use imp_active.dta, clear

*build logistic regression model and summarize
micombine logit mastectomy hosp agedx b0.stage yeardx race b0.theint
```

- . *active imputation
- . ice mastectomy hosp agedx stage yeardx race theint, saving(imp_active.dta) m(5) replace persist

	ing	E	req.	Perc	ent		Cum.
	0	5	,341	68	.94		68.94
	1		386	4	.98		73.93
	2	1	,395	18	.01		91.93
	3		625	8	.07	1	00.00
To	tal	7	,747	100	.00		

Variable	Command	Prediction equation
mastectomy hosp agedx yeardx race stage theint	logit mlogit mlogit	[No missing data in estimation sample] mastecomy hosp ageds stage yeard'x theint mastecomy hosp ageds variety race theint mastecomy hosp ageds variety race mastecomy hosp ageds stage weards race

Imputing

[Perfect prediction detected: using augmlogit to impute stage]

[Perfect prediction detected: using augmlogit to impute stage]

.....2

[Perfect prediction detected: using augmlogit to impute ${\tt stage}$]

[persist option: ignoring error #430, not updating theint in cycle 7]

[Perfect prediction detected: using augmlogit to impute stage]

[persist option: ignoring error #430, not updating theint in cycle 3]

......
[persist option: ignoring error #430, not updating theint in cycle 9]

..4
[Perfect prediction detected: using augmlogit to impute stage]

[persist option: ignoring error #430, not updating theint in cycle 10]

(note: file imp_active.dta not found)

file imp_active.dta saved

. list in 7748/7753

	id	hosp	mastec~y	agedx	yeardx	stage	race	theint	_mi	_mj
7748.	1	1	1	64	2008	1	1	1	1	1
7749.	2	0	0	47	1999	1	1	0	2	1
7750.	3	0	0	80	2009	1	1	0	3	1
7751.	4	1	1	55	2003	3	1	3	4	1
7752.	5	1	0	60	2009	1	1	1	5	1
7753.	6	1	0	58	2009	1	1	1	6	1

. tab stage theint

			theint			
Total	4	3	2	1	0	stage
11,181	0	0	0	22	11,159	0
15,188	0	0	7	7,028	8,153	1
12,428	0	3	6,576	3	5,846	2
4,065	4	2,578	2	0	1,481	3
1,600	1,121	2	1	5	471	4
44,462	1,125	2,583	6,586	7,058	27,110	Total

```
/* ice passive */

*import data
insheet using "C:\example.csv", clear

*create interaction
gen theintwhosp*stage

*passive imputation
ice mastectomy hosp agedx stage yeardx race theint, passive(theint:hosp*stage) saving(imp_passive.dta) m(5) repuse imp_passive.dta, clear

*build logistic regression model and summarize
micombine logit mastectomy hosp agedx b0.stage yeardx race b0.theint
```

```
/* ice passive */

*import data
insheet using "C:\example.csv", clear

*create interaction
gen theint=hosp*stage

*passive imputation
ice mastectomy hosp agedx stage yeardx race theint, (passive(theint:hosp*stage)) saving(imp_passive.dta) m(5) reg
use imp_passive.dta, clear

*build logistic regression model and summarize
micombine logit mastectomy hosp agedx b0.stage yeardx race b0.theint
```

- . *passive imputation
- . ice mastectomy hosp agedx stage yeardx race theint, passive(theint:hosp*stage) saving(imp_passive.dta) m(5) r

#missing values	Freq.	Percent	Cum.
0	5,341	68.94	68.94
1	386	4.98	73.93
2	1,395	18.01	91.93
3	625	8.07	100.00
Total	7,747	100.00	

Variable	Command	Prediction equation
mastectomy hosp agedx yeardx race stage theint	logit mlogit	[No missing data in estimation sample] mastectomy hosp agedx stage yeardx theint mastectomy hosp agedx yeardx race [Passively imputed from hosp*stage]

. use imp_passive.dta, clear

- . *passive imputation
- . ice mastectomy hosp agedx stage yeardx race theint, passive(theint:hosp*stage) saving(imp_passive.dta) m(5) r

#missing values	Freq.	Percent	Cum.
0	5,341	68.94	68.94
1	386	4.98	73.93
2	1,395	18.01	91.93
3	625	8.07	100.00
Total	7 747	100.00	

Variable Comman	i Prediction equation
mastectomy hosp agedx yeardx race logit stage mlogit	[No missing data in estimation sample] mastectomy hosp agedx stage yeardx theint mastectomy hosp agedx yeardx race [Passively imputed from hosp*stage]

. use imp_passive.dta, clear

. list in 7748/7753

	id	hosp	mastec~y	agedx	yeardx	stage	race	theint	_mi	_mj
7748.	1	1	1	64	2008	1	1	1	1	1
7749.	2	0	0	47	1999	0	1	0	2	1
7750.	3	0	0	80	2009	4	1	0	3	1
7751.	4	1	1	55	2003	3	1	3	4	1
7752.	5	1	0	60	2009	3	1	3	5	1
7753.	6	1	0	58	2009	1	1	1	6	1

. tab stage theint

	theint										
stage	0	1	2	3	4	Total					
0	9,815	0	0	0	0	9,815					
1	8,145	7,639	0	0	0	15,784					
2	5,882	0	7,118	0	0	13,000					
3	1,487	0	0	2,725	0	4,212					
4	455	0	0	0	1,196	1,651					
Total	25,784	7,639	7,118	2,725	1,196	44,462					

Results from the Two Methods in Ice

- . *active imputation
- . micombine logit mastectomy hosp agedx

Multiple imputation parameter estimates

mastectomy	Coef.	Std. Err.
mastectomy		
hosp	1109177	.1080544
agedx	0173094	.0019449
stage		
0	0	(empty)
1	.1335282	.1025934
2	1.103616	.1100777
3	2.087673	.23944
4	4561715	.3856415
yeardx	0285017	.0084972
race	1872521	.0709139
theint		
0	0	(empty)
1	.0284646	.1421275
2	3623982	.1397179
3	5782175	.2582078
4	.5624794	.4661046
_cons	57.34566	17.03261

7747 observations (imputation 1).

- . *passive imputation
- . micombine logit mastectomy hosp agedx

Multiple imputation parameter estimates

mastectomy	Coef.	Std. Err.
mastectomy		
hosp	0400464	.1114586
agedx	0165242	.0019731
stage		
0	0	(empty)
1	.1033335	.1112763
2	. 975499	.1098498
3	1.980216	.1814719
4	3110553	.2978437
yeardx	0279643	.0084428
race	1934281	.066012
theint		
0	0	(empty)
1	1572001	.148122
2	4194108	.1574878
3	6265811	.2145474
4	.2444306	.3547756
_cons	56.27944	16.92546

7747 observations (imputation 1).



Recommendation in Stata

- Study the output
 - Command
 - Predictor equation
- Use passive imputation
- Increase the number of imputation when using the persist option
- If using passive imputation, make sure all levels of interaction variable are present
- May be worthwhile to compare two approaches

```
### Active imputation
# Select variables used for imputation
toimp <- mydata[c("Hosp", "Mastectomy", "AgeDx", "stage", "YearDx", "race")]</pre>
# Create interaction
toimp$theint <- toimp$Hosp * toimp$stage
# Change to factor variables
toimp$stage <- as.factor(toimp$stage)</pre>
toimp$race <- as.factor(toimp$race)
toimp$theint <- as.factor(toimp$theint)</pre>
# Impute
imp_active <- mice(toimp, m=5, method=c("", "", "", "polyreg", "", "logreg", "polyreg"))</pre>
summary(imp_active)
# Summarize scientific model
result <- pool(with(data=imp_active.
  qlm(Mastectomy ~ Hosp + AgeDx + stage + YearDx + race + theint, family="binomial")))
summary(result)
```

```
> summary(imp_active)
Multiply imputed data set
mice(data = toimp, m = 5, method = c("", "", "", "polyreg", "",
    "logreg", "polyreg"))
Number of multiple imputations: 5
Missing cells per column:
      Hosp Mastectomy
                           AgeDx
                                      stage
                                                              race
                                                                        theint
                                                 YearDx
                                        2020
                                                              1011
                                                                          2020
Imputation methods:
      Hosp Mastectomy
                           AgeDx
                                       stage
                                                 YearDx
                                                              race
                                                                        theint
                                  "polvrea"
                                                          "logreg"
                                                                     'polvrea"
VisitSequence:
 stage race theint
            6
PredictorMatrix:
           Hosp Mastectomy AgeDx stage YearDx race theint
Hosp
Mastectomv
AgeDx
stage
YearDx
race
theint
Random generator seed value:
```

> table(complete(imp_active)\$stage, complete(imp_active)\$theint)

```
## Passive imputation
# Make dummy variables for interaction
toimp$theint1 <- ifelse(toimp$theint == 1, 1, 0)
toimp$theint2 <- ifelse(toimp$theint == 2, 1, 0)
toimp$theint3 <- ifelse(toimp$theint == 3, 1, 0)
toimp$theint4 <- ifelse(toimp$theint == 4, 1, 0)
# Select variables in the imputation model
toimp2 <- toimp[c("Hosp", "Mastectomy", "AgeDx", "stage", "YearDx", "race"
                  , "theint1", "theint2", "theint3", "theint4")]
# Dry run to get meth and pred
ini <- mice(toimp2, max=0, print=FALSE)
# Save the methods and specify to passively impute the interactions
meth <- inismeth
meth["theint1"] <- "~I(Hosp*stage.1)"
meth["theint2"] <- "~I(Hosp*stage.2)"
meth["theint3"] <- "~I(Hosp*stage.3)"
meth["theint4"] <- "~I(Hosp*stage.4)"
# Remove interactions from predicting main effecs
pred <- inispred
pred[c("stage"), c("theint1", "theint2", "theint3", "theint4")] <- 0
# Impute
imp_passive <- mice(toimp2, m=5, method=meth, pred=pred, print=FALSE)
# Summarize scientific model
result <- pool(with(data=imp_passive.
  glm(Mastectomy ~ Hosp + AgeDx + stage + YearDx + race
      + theint1 + theint2 + theint3 + theint4, family="binomial")))
summary(result)
```

> ini\$meth												
Hosp	Mast	ectomy	AgeDx		stage vreg"	Ye	arDx	race logreg"	theint "pmm		theint3 "pmm"	theint4 "pmm"
> ini\$pred					, 5			5 5				
	Hosp	Mastectomy	AgeDx	stage	YearDx	race	theint1	theint2	theint3	theint4		
Hosp	0	0	0	0	0	0	0	0	0	0		
Mastectomy	0	0	0	0	0	0	0	0	0	0		
AgeDx	0	0	0	0	0	0	0	0	0	0		
stage	1	1	1	0	1	1	1	1	1	1		
YearDx	0	0	0	0	0	0	0	0	0	0		
race	1	1	1	1	1	0	1	1	1	1		
theint1	1	1	1	1	1	1	0	1	1	1		
theint2	1	1	1	1	1	1	1	0	1	1		
theint3	1	1	1	1	1	1	1	1	0	1		
فالمساك والما	-	4	4	- 4	4	-	4	4	4			

```
> summarv(imp_passive)
Multiply imputed data set
call:
mice(data = toimp2, m = 5, method = meth, predictorMatrix = pred.
    printflag = FALSE)
Number of multiple imputations: 5
Missing cells per column:
      Hosp Mastectomy
                            AgeDx
                                       stage
                                                  YearDx
                                                               race
                                                                       theint1
                                                                                   theint2
                                                                                              theint3
                                                                                                         theint4
                                        2020
                                                               1011
                                                                          2020
                                                                                      2020
                                                                                                 2020
                                                                                                            2020
Imputation methods:
                            Mastectomy
                                                    AgeDx
                                                                        stage
                                                                                           YearDx
                                                                                                                                 theint1
                                                                     "polvrea"
                                                                                                             "logreg" "~I(Hosp*stage.1)
           theint2
                               theint3
                                                  theint4
"~I(Hosp*stage, 2)" "~I(Hosp*stage, 3)" "~I(Hosp*stage, 4)"
VisitSequence:
  stage
           race theint1 theint2 theint3 theint4
PredictorMatrix:
           Hosp Mastectomy AgeDx stage YearDx race theint1 theint2 theint3 theint4
Hosp
                                                  Ô
Mastectomy
                                0
                                             0
                                                                           0
AgeDx
stage
YearDx
race
theint1
theint2
theint3
                                                                                   1
theint4
Random generator seed value: NA
```

```
> head(complete(imp_passive))
 Hosp Mastectomy AgeDx stage YearDx race theint1 theint2 theint3 theint4
                               2008
                    47
                               1999
                               2009
                               2003
                               2009
                               2009
> table(complete(imp_passive)$theint1, complete(imp_passive)$stage)
 0 1713 1415 2300 717 274
> table(complete(imp_passive)$theint2, complete(imp_passive)$stage)
 0 1713 2743 1045 717 274
> table(complete(imp_passive)$theint3, complete(imp_passive)$stage)
 0 1713 2743 2300 259 274
      0 0 0 458
> table(complete(imp_passive)$theint4, complete(imp_passive)$stage)
                        201
```

Results from the Two Methods in Mice

```
> summary(result_active)
                est
                                        df Pr(>|t|)
                                                      lo 95
(Intercept) 57.6903 16.87418
                              3.419 5225.3 0.000634 24.6098 90.7707
Hosp
                    0.10195 -1.301 5666.8 0.193426 -0.3325
AgeDx
            -0.0177
                     0.00194 -9.084 5502.8 0.000000 -0.0215 -0.0138
stage2
             0.1418
                     0.10243 1.384
                                     216.3 0.167702 -0.0601
                                     113.6 0.000000
stage3
            1.0763
                     0.10915
                              9.861
                                                     0.8601
                                                             1.2925
stage4
            2.1375 0.18380 11.630
                                    101.6 0.000000 1.7729
stage5
            -0.4399 0.32853 -1.339
                                      91.7 0.183880 -1.0924
YearDx
            -0.0287
                     0.00842 -3.405 5266.6 0.000667 -0.0452
race2
            -0.2028
                   0.06612 -3.067
                                     362.3 0.002321 -0.3328
theint2
            0.0771 0.13658
                             0.565 1235.1 0.572418 -0.1908
theint3
            -0.3142
                    0.13615 -2.308 2425.0 0.021084 -0.5812 -0.0473
theint4
            -0.7338
                     0.23555 -3.115
                                      57.9 0.002857 -1.2054 -0.2623
theint5
             0.6219 0.40605 1.532
                                      42.6 0.133020 -0.1972
> summary(result_passive)
                                        df Pr(>|t|)
                est
                          se
                                                      lo 95
(Intercept) 55.2286 17.04365
                              3,240 1939,1
                                            0.00121 21.8027 88.6544
Hosp
            -0.0334
                     0.11867 -0.282
                                    113.0
                                            0.77870 -0.2685
AgeDx
            -0.0165
                     0.00195 -8.468 3961.4
                                            0.00000 -0.0203 -0.0127
                     0.12369 0.696
                                      23.2
stage2
             0.0862
                                            0.49303 -0.1696
             0.9823
                     0.10518
                                     204.1
                                            0.00000
                                                     0.7749
stage3
                             9.339
                     0.18385 11.090
                                            0.00000
stage4
             2.0390
                                     109.6
                                                    1.6746
                                            0.16595 -1.1611
stage5
            -0.4783
                     0.34063 -1.404
                                      54.4
                    0.00850 -3.228 1917.9
                                            0.00127 -0.0441 -0.0108
YearDx
            -0.0274
race2
            -0.1730
                     0.06825 -2.535
                                     160.4
                                            0.01221 -0.3078 -0.0382
theint1
            -0.1674 0.16427 -1.019
                                      41.3
                                            0.31403 -0.4991
theint2
                                            0.00247 -0.7291 -0.1575
            -0.4433
                     0.14526 -3.052
                                     311.5
theint3
            -0.6575
                     0.22347 -2.942
                                     179.5
                                            0.00369 -1.0985 -0.2165
theint4
             0.3676
                     0.37828 0.972
                                    100.1
                                            0.33350 -0.3829 1.1181
```

Recommendation in R

- Convert all categorical variables to factor variables using 'as.factor()'
- Study the imputation object, especially if using passive imputation
 - Method vector
 - Predictor matrix
- Use active or passive imputation
 - However, code for active imputation is far more simple
- May be worthwhile to compare two approaches

Comparison Across Software

Odds Ratios		SAS JM		Stat	a ice	R mice		
	CC	Active	Imp o Trf	Active	Passive	Active	Passive	
Hosp A Stage 0	1.00	1.00	1.00	1.00	1.00	1.00	1.00	
Hosp A Stage 1	1.17	1.12	1.25	1.14	1.11	1.15	1.09	
Hosp A Stage 2	2.99	2.65	3.18	3.02	2.65	2.93	2.67	
Hosp A Stage 3	8.73	6.62	8.24	8.07	7.24	8.48	7.68	
Hosp A Stage 4	0.69	0.82	0.69	0.63	0.73	0.64	0.62	
Hosp B Stage 0	1.00	1.00	1.00	1.00	1.00	1.00	1.00	
Hosp B Stage 1	1.00	0.92	0.90	1.18	0.95	1.24	0.92	
Hosp B Stage 2	1.85	1.74	1.67	2.10	1.74	2.14	1.71	
Hosp B Stage 3	4.13	3.71	3.68	4.52	3.87	4.07	3.98	
Hosp B Stage 4	0.33	0.91	0.90	1.11	0.94	1.20	0.90	
Age	0.99	0.98	0.98	0.98	0.98	0.98	0.98	
White vs Other Race	0.79	0.84	0.82	0.83	0.82	0.82	0.84	
Year	0.97	0.98	0.97	0.97	0.97	0.97	0.97	

Conclusion

- Do not treat imputed values as real Summarized estimates and inference are the most important
 - e.g. Do not create Table 1 from the imputed data
- Make sure you know what method/option is used
 - JM or FCS?
 - Active or Passive?
 - Interactions?
- Perform sensitivity analysis
 - Try a different approach
 - Increase the number of imputations
- Keep up with the literature
- Study the software manual

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4 D > 4 P > 4 B > 4 B > B 9 9 P

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