

Multiple Imputation

VGSM, Chapter 11

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Last Week

- Missing data grouped by relationship between missingness and its value
- MCAR/MAR and NMAR
- MAR is the assumption where most action is
- Motivates multiple imputation
- Model-based guesses at missing data

UNOS Dataset

- Data on 9775 pediatric kidney transplants from 1990-2002
- Followed for transplant outcomes
465 deaths
- Predictors: age, age of donor, year, HLA loci, txtype
- Cold ischemia time: missing in 23%

Multiple Imputation

1. Assume data MAR
2. Develop predictive model for missing data
3. Sample from predictive model
4. Make multiple complete datasets
5. Analyze datasets
6. Synthesize results

Selecting MAR Variables

- Bias is the biggest threat
 - More predictors make MAR plausible
 - Include the outcome
- Unimportant covariates: little cost
 - probably not much gained
- Any predictor in model -- include impute
 - possible some that aren't

Modeling Choice

- Specify a parametric model for imputations
- cold_ischemia: continuous variable but also has many "0" s
- Many missing values like to be "0"
- Difficult distribution to model
- Try Normal distribution

Predictive Model

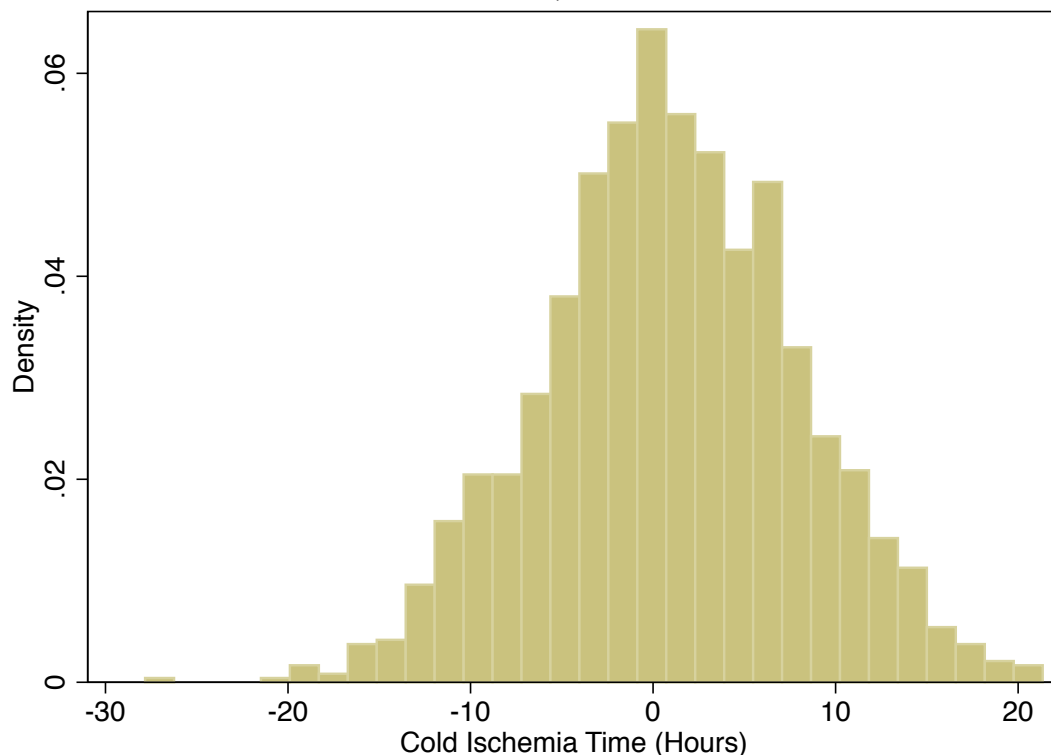
```
. . xi: reg cold_isc txtty death i.hla age_don age year
i.hlamat      _Ihlamat_0-6      (naturally coded; _Ihlamat_0 omitted)
```

Source	SS	df	MS	Number of obs =	7347
Model	611905.778	11	55627.798	F(11, 7335) =	1126.79
Residual	362116.493	7335	49.3683017	Prob > F =	0.0000
				R-squared =	0.6282
				Adj R-squared =	0.6277
Total	974022.271	7346	132.592196	Root MSE =	7.0263

cold_isc	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]
txttype	18.49092	.2235349	82.72	0.000	18.05273 18.92911
death	.243987	.3871391	0.63	0.529	-.5149169 1.002891
_Ihlamat_1	.6966437	.3575722	1.95	0.051	-.0043006 1.397588
_Ihlamat_2	.4241767	.3550638	1.19	0.232	-.2718505 1.120204
_Ihlamat_3	.7843253	.3517806	2.23	0.026	.0947341 1.473916
_Ihlamat_4	.9951523	.394421	2.52	0.012	.2219737 1.768331
_Ihlamat_5	1.636238	.5308462	3.08	0.002	.5956272 2.676849
_Ihlamat_6	1.722591	.560876	3.07	0.002	.6231127 2.822069
age_don	.0153432	.0067599	2.27	0.023	.0020918 .0285946
age	.0286415	.0161681	1.77	0.077	-.0030526 .0603356
year	-.2486191	.0229721	-10.82	0.000	-.2936511 -.2035872
_cons	495.8731	45.87233	10.81	0.000	405.9501 585.796

Normal Imputations

Mean 1, SD =7



Misspecified Distribution

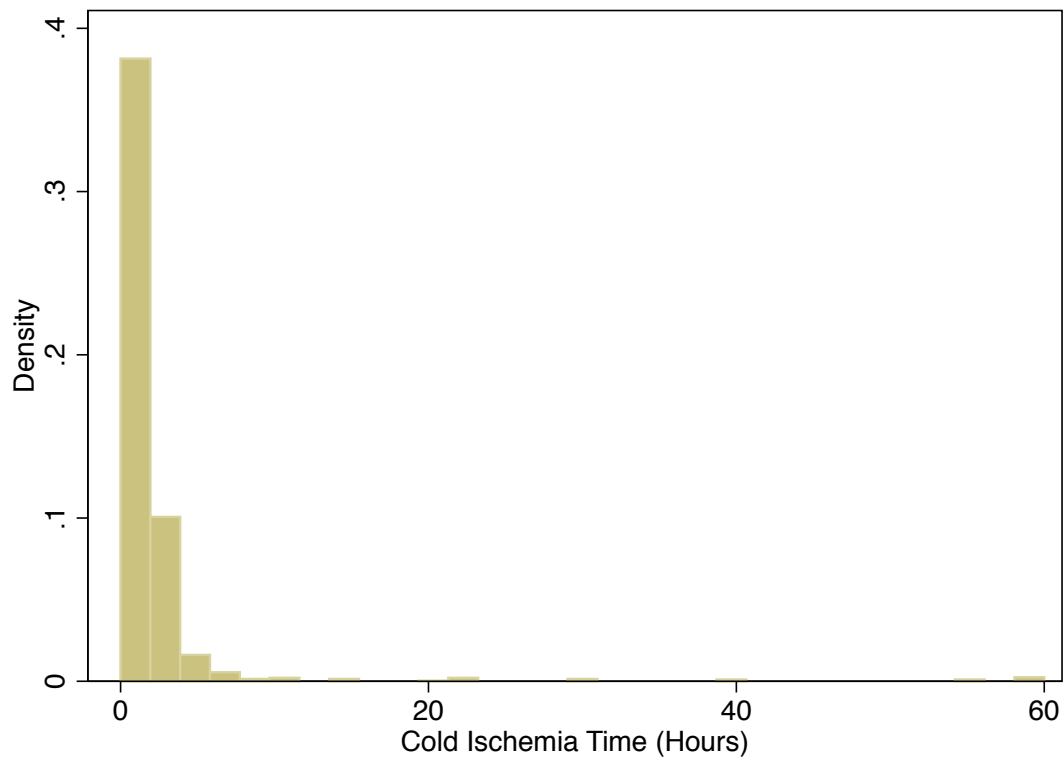
- Minimal effect
- Most important to get moments correct
means, SD, covariance of imputed data
- Unappealing to get implausible values
- Option to force plausible value

Predictive Means Matching

- Linear regression fit to missing data
 $E(Y_{\text{mis}}) = \beta_0 + \beta_1 x_1 + \dots + \beta_p x_p$
- Sample from “posterior” of β | Data
- With each beta calculate predictions
for all observations
- Impute Y_{mis} from observed values k
nearest neighbors
- Forces plausible value
must specify k — *Stata default, $k=1$*

PMM Imputations

Mean 2, SD =6



Missing Data

Variable	Obs	Mean	Std. Dev.	Min	Max
hlamat	9541	2.57363	1.378919	0	6
age_don	9662	31.29952	13.38866	0	73
age	9766	11.64653	5.291385	0	18
cold_isc	7525	10.85967	11.51735	0	72
death	9775	.0475703	.2128662	0	1
prevtx	9702	1.1443	.3514119	1	2
txtype	9775	.4733504	.4993148	0	1

Multiple Missing Variable

- Can be handled by multiple imputation
- Means developing a model for several variable simultaneous
- Two main ways to do this
 - assume variables are normal
so called multivariate normal
 - “chained” regression equal
so called iterative chained equations

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Multivariate Normal Imputation

- Treats all variables as normal
- Imputes using linear regression
imputes well for linear
- Can be coaxed to do binary and ordinal
- Can't impute for unordered categorical

Chained Imputation

- Regression model for each missing variable
- “ICE”: iterative chained equations
- Combined for multivariate imputations
- Builds a multivariate distribution
- Separate models: gives big flexibility

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Possible Imputation Models

- Continuous: regress, pmm
- Binary: logit
- Ordinal: ologit
- Nominal: mlogit
- Discrete: poisson, nbreg
- Continuous+threshold: truncreg

separate models for each missing variable

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3. Make multiple complete datasets

Imputing in Stata

- Extensive suite of capabilities
- Data management
- Creating imputations
- Analyzing and synthesizing

mi package

- Powerful package for missing data
- Extensive capabilities
lots of choices, appear esoteric
- Can handle multiple missing predictors
- Presents results in easy to read format

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mi set

- Must declare data to be “mi set”
- `mi set mlong`
- Stores the imputations in long format
just governs how imputations are stored
- There is also `mi stset` & `mi xtset`

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mi register

- Must declare variable as needing or not needing imputation
- `mi register imputed cold_isc`
- `mi register regular death hlamat age_don age year`
- Says `cold_isc` will be imputed and others not

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mi impute

- This command actually does the imputations
- Can impute single or multiple variables
- Specifies:
 - predictors used for imputation
 - statistical model for imputation
 - number of imputations

imputing and analysis happen in separate steps

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Imputing Cold Ischemia

- `mi impute regress cold_isc = death txttype i.hlamat age_don age year , add(20) rseed(123)`
- Use linear regression to impute cold_isc
- Predictors: death, txttype, etc
- `add(20)` = 20 imputations
- `rseed( )` = sets a random seed
means you can replicate imputations very very useful

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Imputation Output

```
. mi impute regress cold_isc hlamat age_don age death year prevtx  
txttype , add(50) rseed(123)
```

```
Univariate imputation          Imputations =      50  
Linear regression              added =      50  
Imputed: m=1 through m=50      updated =       0
```

Variable	Observations per m			Total
	Complete	Incomplete	Imputed	
cold_isc	7347	2020	2020	9367

(complete + incomplete = total; imputed is the minimum across m of the number of filled-in observations.)

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Predictive Mean Matching

```
. mi impute pmm cold_isc hlamat age_don age death year prevtx
txttype , add(50) rseed(123)
```

```
Univariate imputation                    Imputations =      50
Linear regression                        added =          50
Imputed: m=1 through m=50                updated =          0
```

Variable	Observations per m			Total
	Complete	Incomplete	Imputed	
cold_isc	7347	2020	2020	9367

(complete + incomplete = total; imputed is the minimum across m of the number of filled-in observations.)

MI Dataset

```
tabulate _mi_m
```

_mi_m	Freq.	Percent	Cum.
0	9,367	18.82	18.82
1	2,020	4.06	22.88
2	2,020	4.06	26.94
3	2,020	4.06	31.00
4	2,020	4.06	35.06
5	2,020	4.06	39.12
6	2,020	4.06	43.18
7	2,020	4.06	47.23
8	2,020	4.06	51.29
9	2,020	4.06	55.35
10	2,020	4.06	59.41
11	2,020	4.06	63.47
12	2,020	4.06	67.53
13	2,020	4.06	71.59
14	2,020	4.06	75.65
15	2,020	4.06	79.71
16	2,020	4.06	83.76
17	2,020	4.06	87.82
18	2,020	4.06	91.88
19	2,020	4.06	95.94
20	2,020	4.06	100.00
Total	49,767	100.00	

← original data

← imputation "10"

9,347 record dataset
becomes 49,767
records

Chained Syntax

- `mi register imputed hlamat age_don age cold_isc prevtx death txttype`
register everything
- `mi impute chained (pmm) cold_isc (ologit) hlamat (regress) age_don (regress) age (logit) prevtx = death txttype, add(50) rseed(897)`
- *(method) variable = nonmissing*
- Very flexible syntax

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Chained Output

```
. mi impute chained (pmm) cold_isc (ologit) hlamat (regress) age_don (regress) age (logit)
prevtx = death txttype, add(20) rseed(897) dots
```

Conditional models:

```
    age: regress age i.prevtx age_don i.hlamat cold_isc death txttype
  prevtx: logit prevtx age age_don i.hlamat cold_isc death txttype
  age_don: regress age_don age i.prevtx i.hlamat cold_isc death txttype
    hlamat: ologit hlamat age i.prevtx age_don cold_isc death txttype
  cold_isc: pmm cold_isc age i.prevtx age_don i.hlamat death txttype
```

Performing chained iterations:

```
  imputing m=1 through m=20 .....10.....20 done
```

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mi impute reply

```
Multivariate imputation          Imputations =      20
Chained equations                added =      20
Imputed: m=1 through m=20       updated =       0

Initialization: monotone        Iterations =     200
                                burn-in =      10

cold_isc: predictive mean matching
hlamat: ordered logistic regression
age_don: linear regression
age: linear regression
prevtx: logistic regression
```

Variable	Observations per m			Total
	Complete	Incomplete	Imputed	
cold_isc	7525	2250	2250	9775
hlamat	9541	234	234	9775
age_don	9662	113	113	9775
age	9766	9	9	9775
prevtx	9702	73	73	9775

(complete + incomplete = total; imputed is the minimum across m of the number of filled-in observations.)

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Multiple Imputation

1. Assume data MAR
2. Develop predictive model for missing data
3. Sample from predictive model
4. Make multiple complete datasets
5. Analyze datasets
6. Synthesize results

Analyze and Synthesize

Source of Uncertainty

- Predictive distn of cold_isc
 - $\text{cold_isc}_i = \alpha + \beta_1 * x_1 + \beta_2 * x_2 + \dots + \beta_p * x_p + \epsilon_i$
- Sources of uncertainty
 1. prediction: ϵ_i
 2. parameters: $\beta_1, \beta_2, \dots, \beta_p$
 3. form of model: *predictors, transformation*
- Imputation deals with 1 & 2

Result of 1st Imputation

Logistic regression

Number of obs = 9367

LR chi2(12) = 168.53

Prob > chi2 = 0.0000

Pseudo R2 = 0.0491

Log likelihood = -1633.2037

death	Odds Ratio	Std. Err.	z	P> z	[95% Conf. Interval]	
cold_isc	1.000987	.0065701	0.15	0.881	.9881921	1.013947
age_don	.9979897	.0039913	-0.50	0.615	.9901974	1.005843
age	.9584817	.0090968	-4.47	0.000	.9408171	.9764779
year	.8574911	.0130516	-10.10	0.000	.8322883	.8834571
prevtx	1.109361	.14694	0.78	0.433	.8557115	1.438197
txtype	1.248548	.2388952	1.16	0.246	.8580995	1.816656
hlamat						
1	1.004009	.199318	0.02	0.984	.6803856	1.481562
2	.818982	.1662035	-0.98	0.325	.5502147	1.219036
3	.6860487	.1422434	-1.82	0.069	.4569506	1.030008
4	.6296867	.1537688	-1.89	0.058	.3901773	1.016218
5	.8229399	.2596461	-0.62	0.537	.4434097	1.527323
6	.8010403	.2694053	-0.66	0.509	.414361	1.548566

Imputations

Imputation #	OR txtype	SE(OR)
1	1.25	0.24
2	1.13	0.22
3	1.21	0.23
4	1.29	0.25
5	1.24	0.24
mean	1.22	0.24
SD	0.06	

Combining Imputations

$K = \text{Number of Imputations} = 5$

$$\begin{aligned}\text{MI Estimate} &= (OR_1 + OR_2 + \dots + OR_K) / K \\ &= 1.22\end{aligned}$$

$$\begin{aligned}\text{MI Variance} &= (1 + 1/K) * \{ SE(OR_k) \}^2 + \\ &\quad \{ \text{mean}(\{ SE_k(OR) \}^2) \} \\ &= (1 + 1/5) * \{ 0.06 \}^2 + \\ &\quad (0.24)^2 \\ &= .062\end{aligned}$$

$$\text{MI SE} = \text{sqrt}(\text{MI Variance}) = 0.25$$

Imputed Regression

the analysis step

- mi estimate, or : logistic death cold_isc
txty i.hlam age_don age year
- Fits a logistic regression with imputations
based on the last commands
- After “:” usual commands
- Need “or” to get odds ratios

Results

mi estimate, or: logistic death cold_isc age_don age year prevtx txttype i.hlamat

Multiple-imputation estimates Imputations = 5
Logistic regression Number of obs = 9367

death	exp(b)	Std. Err.	t	P> t	[95% Conf. Interval]	
cold_isc	1.002313	.0071502	0.32	0.746	.9883722	1.01645
age_don	.9979795	.0039896	-0.51	0.613	.9901907	1.00583
age	.9584372	.0090968	-4.47	0.000	.9407726	.9764335
year	.8578479	.0130779	-10.06	0.000	.8325948	.8838669
prevtx	1.108886	.1468931	0.78	0.435	.855321	1.437622
txttype	1.216516	.2422243	0.98	0.325	.8233093	1.797515
hlamat						
1	1.002488	.1990982	0.01	0.990	.679246	1.479555
2	.8181683	.1660688	-0.99	0.323	.549628	1.217914
3	.6849142	.1420574	-1.82	0.068	.4561307	1.02845
4	.6284968	.1535163	-1.90	0.057	.3893938	1.014419
5	.8206398	.2589599	-0.63	0.531	.4421287	1.523199
6	.7986734	.26867	-0.67	0.504	.4130751	1.544221
_cons	6.3e+131	1.9e+133	9.98	0.000	8.0e+105	4.9e+157

PMM Results

mi estimate, or: logistic death cold_isc age_don age year prevtx txttype i.hlamat

Multiple-imputation estimates Imputations = 5
Logistic regression Number of obs = 9367

death	exp(b)	Std. Err.	t	P> t	[95% Conf. Interval]	
cold_isc	1.002321	.0070415	0.33	0.741	.9886026	1.01623
age_don	.9979781	.0039895	-0.51	0.613	.9901895	1.005828
age	.9584332	.0090967	-4.47	0.000	.9407689	.9764293
year	.8577968	.0130501	-10.08	0.000	.8325966	.8837597
prevtx	1.108817	.1468895	0.78	0.436	.8552597	1.437547
txttype	1.216574	.2400089	0.99	0.320	.8263761	1.791016
hlamat						
1	1.002359	.1990838	0.01	0.991	.6791438	1.479398
2	.8180324	.1660531	-0.99	0.322	.5495211	1.217746
3	.6847243	.1420257	-1.83	0.068	.4559942	1.028187
4	.6284921	.1535049	-1.90	0.057	.3894033	1.014379
5	.8208394	.2589845	-0.63	0.531	.4422767	1.523429
6	.798598	.2686421	-0.67	0.504	.4130386	1.544066
_cons	7.1e+131	2.1e+133	10.00	0.000	1.0e+106	4.9e+157

Data Management

- Imputing creates phantom observations
- Data is only good for imputations
- Useful command -- “mi extract” creates a dataset based on one “imputation”
- *mi extract 0, clear
back to regular incomplete data*
- *mi extract l0, clear
complete dataset using imputation #l0
allows you to check imputation set*

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Imputation l0

```
. logistic death cold_isc age_don age year prevtx txttype i.hlamat
```

Logistic regression

Number of obs	=	9367
LR chi2(12)	=	168.51
Prob > chi2	=	0.0000
Pseudo R2	=	0.0491

Log likelihood = -1633.2127

death	Odds Ratio	Std. Err.	z	P> z	[95% Conf. Interval]	
cold_isc	1.000447	.0065814	0.07	0.946	.9876305	1.01343
age_don	.997997	.0039921	-0.50	0.616	.9902032	1.005852
age	.9584903	.0090981	-4.47	0.000	.9408232	.9764891
year	.8573443	.0130516	-10.11	0.000	.8321415	.8833103
prevtx	1.109332	.1469424	0.78	0.433	.855679	1.438175
txttype	1.261713	.2416046	1.21	0.225	.8668913	1.836355
hlamat						
1	1.004259	.1993966	0.02	0.983	.6805166	1.482015
2	.8191515	.1662461	-0.98	0.326	.5503179	1.219312
3	.6863007	.1423103	-1.82	0.069	.4570993	1.03043
4	.630004	.1538591	-1.89	0.059	.3903584	1.016771
5	.8238943	.259907	-0.61	0.539	.4439664	1.528949
6	.8018133	.2697156	-0.66	0.511	.4147099	1.550251
_cons	2.0e+132	6.1e+133	10.03	0.000	2.8e+106	1.4e+158

but this dropped all other imputations

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mi xeq

simpler approach

- mi xeq l0: summ cold_isc
summarize cold_isc from imputation l0

m=10 data:
-> summ cold_isc

Variable	Obs	Mean	Std. Dev.	Min	Max
cold_isc	9367	10.04335	11.53007	-20.96038	72

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mi xeq

examining results

. mi xeq l0: logistic death cold_isc age_don age year prevtx txttype i.hlamat

m=10 data:
-> logistic death cold_isc age_don age year prevtx txttype i.hlamat

Logistic regression	Number of obs	=	9367
	LR chi2(12)	=	168.51
	Prob > chi2	=	0.0000
Log likelihood = -1633.2127	Pseudo R2	=	0.0491

death	Odds Ratio	Std. Err.	z	P> z	[95% Conf. Interval]
cold_isc	1.000447	.0065814	0.07	0.946	.9876305 1.01343
age_don	.997997	.0039921	-0.50	0.616	.9902032 1.005852
age	.9584903	.0090981	-4.47	0.000	.9408232 .9764891
year	.8573443	.0130516	-10.11	0.000	.8321415 .8833103
prevtx	1.109332	.1469424	0.78	0.433	.855679 1.438175
txttype	1.261713	.2416046	1.21	0.225	.8668913 1.836355
hlamat					
1	1.004259	.1993966	0.02	0.983	.6805166 1.482015
2	.8191515	.1662461	-0.98	0.326	.5503179 1.219312
3	.6863007	.1423103	-1.82	0.069	.4570993 1.03043
4	.630004	.1538591	-1.89	0.059	.3903584 1.016771
5	.8238943	.259907	-0.61	0.539	.4439664 1.528949
6	.8018133	.2697156	-0.66	0.511	.4147099 1.550251
_cons	2.0e+132	6.1e+133	10.03	0.000	2.8e+106 1.4e+158

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mi extract

- Useful command
- Analysis not supported in mi estimate:
- Use “mi extract, `k’” looped for k
- Save results
- Analyze using published formulae
not optimal, but possible

How Many Imputations

- Feasibly many:
“50% missingness 5 draws is highly efficient”
- True but gives poor standard errors
better guideline 20-40
- Stata on UNOS data
 - 20 imputations in 6 sec.
 - 50 imputations in 16 sec.
 - 500 imputations in 360 sec.

50 Imputations

```
. mi estimate, or: logistic death cold_isc age_don age year prevtx txttype i.hlamat
```

Multiple-imputation estimates		Imputations	=	50
Logistic regression		Number of obs	=	9367
		Average RVI	=	0.0126
DF adjustment:	Large sample	DF: min	=	2492.02
		avg	=	2.42e+10
		max	=	2.69e+11
Model F test:	Equal FMI	F(12, 3.2e+06)=		13.04
Within VCE type:	OIM	Prob > F	=	0.0000

death	exp(b)	Std. Err.	t	P> t	[95% Conf. Interval]	
cold_isc	1.001093	.0071376	0.15	0.878	.9871925	1.015189
age_don	.9979925	.003991	-0.50	0.615	.9902007	1.005846
age	.9584724	.0090979	-4.47	0.000	.9408057	.9764708
year	.8575193	.0130689	-10.09	0.000	.8322835	.8835204
prevtx	1.109199	.14693	0.78	0.434	.8555691	1.438017
txttype	1.245769	.2475528	1.11	0.269	.8438537	1.839111
hlamat						
1	1.003516	.1992915	0.02	0.986	.6799574	1.481042
2	.8187808	.1661875	-0.99	0.325	.5500469	1.218809
3	.6857152	.1422276	-1.82	0.069	.4566588	1.029664
4	.6294577	.153747	-1.90	0.058	.389994	1.015957
5	.822776	.2596321	-0.62	0.536	.4432816	1.527156
6	.8006779	.2693564	-0.66	0.509	.4140995	1.548143

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500 Imputations

Multiple-imputation estimates		Imputations	=	500
Logistic regression		Number of obs	=	9367
		Average RVI	=	0.0130
DF adjustment:	Large sample	DF: min	=	23812.19
		avg	=	1.54e+11
		max	=	1.54e+12
Model F test:	Equal FMI	F(12, 3.1e+07)=		13.02
Within VCE type:	OIM	Prob > F	=	0.0000

death	exp(b)	Std. Err.	t	P> t	[95% Conf. Interval]	
cold_isc	1.002006	.0070717	0.28	0.776	.9882409	1.015964
age_don	.9979834	.0039899	-0.50	0.614	.9901938	1.005834
age	.9584474	.009097	-4.47	0.000	.9407824	.9764441
year	.8577653	.0130703	-10.07	0.000	.8325267	.8837691
prevtx	1.109026	.1469091	0.78	0.435	.8554327	1.437797
txttype	1.223848	.2423487	1.02	0.308	.8301736	1.804205
hlamat						
1	1.002682	.1991348	0.01	0.989	.6793796	1.479836
2	.8183211	.1660985	-0.99	0.323	.5497324	1.218137
3	.6850761	.1420932	-1.82	0.068	.4562356	1.028699
4	.6287796	.1535788	-1.90	0.057	.3895769	1.014854
5	.8212404	.259145	-0.62	0.533	.4424569	1.524297
6	.7992063	.2688505	-0.67	0.505	.4133495	1.545256

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Approach to Imputation Model

- Inclusivity over parsimony
more predictor: MAR more plausible
- Will remove biases -- primary objective
- Two things to include: outcome, predictor in your analytic model
- Functional form tends not to be critical

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Making Up Data?

- No.
- Making a model for missingness
- Making guess at missing data
- Fully representing uncertainty
 - this is the key to its validity

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Maximum Likelihood (ML)

Based on implication #1

- Maximum likelihood valid for MAR data
as long as CMAR variables incorporated
- Works especially well for missing outcome
especially in longitudinal analysis
where attrition depends on previous values
- ML often fit with the EM algorithm
EM also iterative fills in missing data
- Imputation & analysis models consistent
MI and maximum like very similar

Disadvantages of ML

- Cumbersome for missing predictors
don't usual model their distribution
- Awkward if CMAR variables are not a part
of desired
- Lacks flexibility of MI

Inverse Weighting

Based on implication #1

- Model $\text{pr}(\text{non missingness} | C_{\text{MAR}})$
weight by chance of being observed
- Two step approach
not implemented in software
easy to mess up (my experience)
- Clear connection to complete data analysis
- Inefficient

3 Methods

- Same MAR assumption
- Inverse weight:
model missingness, data model flexible
- MI/ML:
model data, missingness model unspecified