Multiple Imputation

15 October 2013
Biostatistics 210

UNOS Data

- Predictors of death in kids with kidney tx
- Some data on 9775 kids (465 deaths)
- A number of missing predictors
  - cold ischemia
  - # HLA loci
  - age of donor

Missingness Mechanism

- MCAR: missing data is independent of value of data
- NMAR: missing data is dependent on value through variables we don't have
- MAR: missing data depends on value through data we have observed and we are going to use

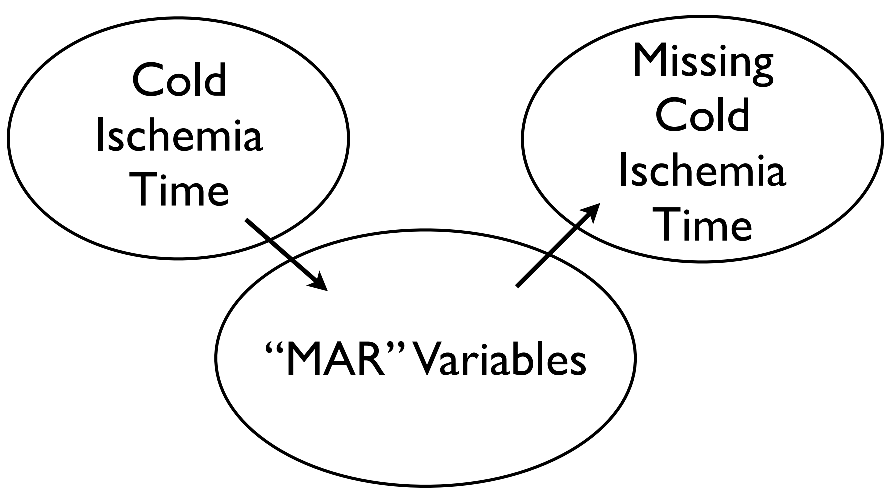
MAR Modeling

- MAR is wrt a series of variables
- Generally want to choose more rather than fewer: to make sure bias is eliminated
- Modeling requires insight into missing data
- Can't verify MAR assumption based on the data

Why <u>Multiple</u> Imputations?

- Don't know the value
- Single imputation: treats value as known
- Want to represent uncertainty
- Multiple draws from distribution

MAR implies MI



Missingness only associated with missing values through "MAR" variables

Association of Cold Ischemia and "MAR" Variables same if Cold Ischemia missing or not

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

MAR Assumption

- Assume that cold_ischemia is MAR
- That values MAR conditional on available data: txtype, HLA loci, age of recipient, age of donor, year of transplant, and survival
- Use a regression model as the basis for predictions

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

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`

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

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

Single Variable

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

Predictive Model

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


------------------------------------------------------------------------------
    cold_isc |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       death |    .243987   .3871391     0.63   0.529    -.5149169    1.002891
      txtype |   18.49092   .2235349    82.72   0.000     18.05273    18.92911
             |
      hlamat |
          1  |   .6966437   .3575722     1.95   0.051    -.0043006    1.397588
          2  |   .4241767   .3550638     1.19   0.232    -.2718505    1.120204
          3  |   .7843253   .3517806     2.23   0.026     .0947341    1.473916
          4  |   .9951523    .394421     2.52   0.012     .2219737    1.768331
          5  |   1.636238   .5308462     3.08   0.002     .5956272    2.676849
          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
------------------------------------------------------------------------------
```

Imputation Output

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

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

------------------------------------------------------------------
                   |              Observations per m
                   |----------------------------------------------
          Variable |   Complete   Incomplete   Imputed |     Total
-------------------+-----------------------------------+----------
          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

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

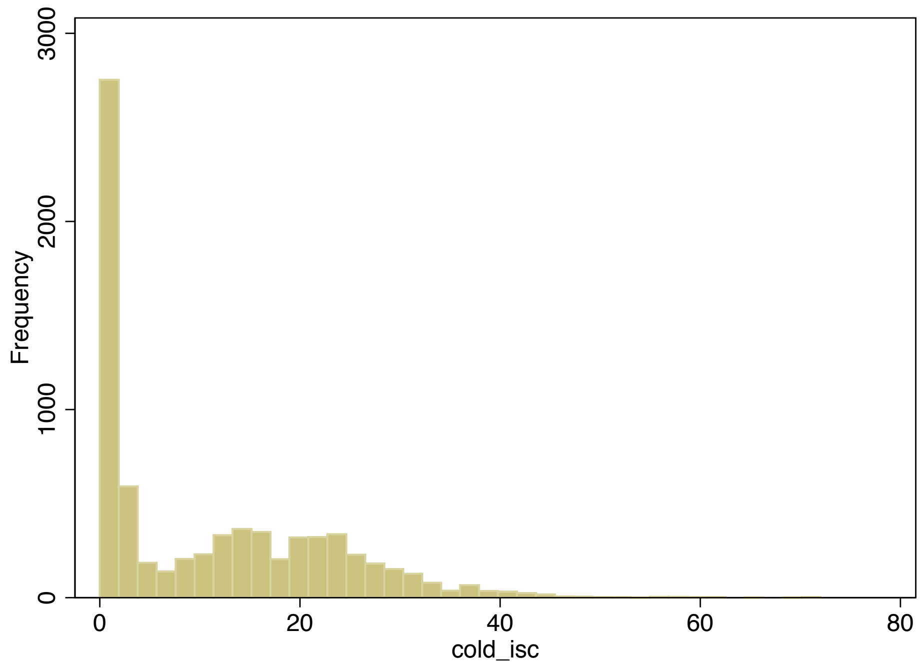
Results

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

Multiple-imputation estimates                    Imputations     =         20
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
      txtype |   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
------------------------------------------------------------------------------
```

Dist of Cold Ischemia Time



Predictive Means Matching

- Easy way to be faithful to quirky distns
- Imputes from observed distribution
- Choose match based on closest value of linear predictor
- Respect thresholds
- mi impute pmm cold_isc hlamat age_don age death year prevtx txtype , add(20) rseed(567)

Transformed Results

```
Multiple-imputation estimates                   Imputations     =         20
Logistic regression                             Number of obs   =       9367
                                                Average RVI     =     0.0091
                                                Largest FMI     =     0.1067
DF adjustment:   Large sample                   DF:     min     =    4339.77
                                                        avg     =   1.59e+10
                                                        max     =   1.24e+11
Model F test:       Equal FMI                   F(  12, 6.0e+06)=      13.07
Within VCE type:          OIM                   Prob > F        =     0.0000

------------------------------------------------------------------------------
       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
      txtype |   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
------------------------------------------------------------------------------
```


Models in MI Impute

mi impute *model*

- Continuous variable
  regress -- linear regression
  pmm -- non-parametric regression
  truncreg -- regression with a boundary
  (e.g., cold ischemia can’t be less than 0)
- Categorical
  logit -- logistic regression
  ologit -- ordered logit (order category)
  mlogit -- unordered logit (unordered)

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 10, clear
  complete dataset using imputation #10
  allows you to check imputation set

Imputation 10

```
. logistic death cold_isc age_don age year prevtx txtype 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
      txtype |   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

mi xeq

simpler approach

- mi xeq 10: summ cold_isc
  summarize cold_isc from imputation 10

```
m=10 data:
-> summ cold_isc

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


mi xeq

examining results

```
. mi xeq 10: logistic death cold_isc age_don age year prevtx txtype i.hlamat

m=10 data:
-> logistic death cold_isc age_don age year prevtx txtype 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
      txtype |   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
------------------------------------------------------------------------------
```

How Many Imputations

- Surprisingly few
- 50% missingness 5 draws is highly efficient
- Stata on UNOS data
  - 20 imputations in 6 sec.
  - 50 imputations in 16 sec.
  - 100 imputation in 31 sec.
  - 500 imputations in 360 sec.

50 Imputations

```
. mi estimate, or: logistic death cold_isc age_don age year prevtx txtype 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
      txtype |   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
------------------------------------------------------------------------------
```

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
      txtype |   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
------------------------------------------------------------------------------
```


Complete Case

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

Logistic regression                               Number of obs   =       7347
                                                  LR chi2(12)     =     109.63
                                                  Prob > chi2     =     0.0000
Log likelihood = -1355.1485                       Pseudo R2       =     0.0389

------------------------------------------------------------------------------
       death | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
    cold_isc |   1.001708   .0070643     0.24   0.809     .9879571    1.015649
     age_don |   .9976003   .0042907    -0.56   0.576      .989226    1.006045
         age |   .9693436   .0102045    -2.96   0.003     .9495481    .9895518
        year |   .8672756   .0150721    -8.19   0.000     .8382322    .8973253
      prevtx |   1.025197   .1484016     0.17   0.864     .7719559    1.361515
      txtype |   1.308204   .2723144     1.29   0.197     .8699419    1.967256
             |
      hlamat |
          1  |   1.116539    .253119     0.49   0.627       .71599    1.741169
          2  |   .9675642   .2217915    -0.14   0.886      .617393    1.516344
          3  |   .8108275   .1908674    -0.89   0.373     .5111603    1.286174
          4  |   .8051673   .2183204    -0.80   0.424     .4732423    1.369899
          5  |   .9409304   .3416137    -0.17   0.867      .461871    1.916877
          6  |    .892732    .331529    -0.31   0.760     .4311368    1.848533
------------------------------------------------------------------------------
```

Relative Efficiency

of MI compared to complete case

Variable	RE
cold_isc	1.00
txtype	1.27
age_don	1.22
age	1.21
year	1.33

Comparison

- Big gains unlikely for missing variables
- Instead seen in other variables
- Deleting them bias and loss of efficiency
- Bias: certain covs patterns left out
  recent years, living tx, younger recipients
- Efficiency: just lose numbers
- Imputed value not big diff here: not pred.

Did it work?

Compared to complete/available case analysis?

- No way to really know
- Must believe the MAR assumption
- No difference? Could be small % missing values
- Imputations close to overall mean for variables

Multiple Missing Variables

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

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
- Only implemented in Stata 12

Possible Imputation Models

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

separate models for each missing variable

Chained Syntax

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

mi impute reply

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

Conditional models:
               age: regress age i.prevtx age_don i.hlamat cold_isc death txtype
            prevtx: logit prevtx age age_don i.hlamat cold_isc death txtype
           age_don: regress age_don age i.prevtx i.hlamat cold_isc death txtype
            hlamat: ologit hlamat age i.prevtx age_don cold_isc death txtype
          cold_isc: pmm cold_isc age i.prevtx age_don i.hlamat death txtype

Performing chained iterations:
  imputing m=1 through m=20 .........10.........20 done
```

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

------------------------------------------------------------------
                   |               Observations per m
                   |----------------------------------------------
          Variable |   Complete   Incomplete   Imputed |     Total
-------------------+-----------------------------------+----------
          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.)
```


Chained Results

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

Multiple-imputation estimates                     Imputations     =         20
Logistic regression                               Number of obs   =       9775
                                                  Average RVI     =     0.0524
                                                  Largest FMI     =     0.2545
DF adjustment:   Large sample                     DF:     min     =     305.01
                                                          avg     =  345849.80
                                                          max     = 2868239.03
Model F test:       Equal FMI                     F(  11,68922.5) =       8.87
Within VCE type:          OIM                     Prob > F        =     0.0000

------------------------------------------------------------------------------
       death | Odds Ratio   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
    cold_isc |   1.009929   .0069456     1.44   0.152     .9963536    1.023689
     age_don |   .9904639   .0038147    -2.49   0.013     .9830154    .9979688
         age |   .9483929   .0084812    -5.93   0.000     .9319149    .9651624
      prevtx |   1.382299   .1809094     2.47   0.013     1.069402    1.786747
      txtype |    1.23375   .2337621     1.11   0.268     .8506975    1.789283
             |
      hlamat |
          1  |    1.04634   .1895773     0.25   0.803     .7335592    1.492486
          2  |   .8583751   .1603099    -0.82   0.414      .595238    1.237837
          3  |   .8070057   .1548374    -1.12   0.264     .5540192    1.175515
          4  |   .6971202   .1609292    -1.56   0.118     .4433924    1.096042
          5  |   .8441431   .2567099    -0.56   0.577     .4651095    1.532064
          6  |   .8949769   .2920161    -0.34   0.734     .4721403    1.696495
             |
       _cons |   .1035634   .0236399    -9.93   0.000     .0662056    .1620011
------------------------------------------------------------------------------
```

Multiple Imputation

- One method for handling missing data
- Can be various others: have a similar spirit
  averaging over distn for missing values
- Imputation is flexible and can be used in many problems
- Useful with missing predictor(s)
- Conceptually straightforward
- Lots of issues in practice

Issues in Modeling

- 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

Missing Values

- Important to explore and understand
- Informs model
- MAR assumption permits valid analysis
  missing depend on values thru observed data
- Missing data methods needed for validity and/or efficiency

Making Up Data?

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

Further Topics

- MAR assumption animates two other approaches
  - maximum likelihood approaches
  - inverse weighting
- Will discuss next week