Multiple imputation for missing data in life course studies

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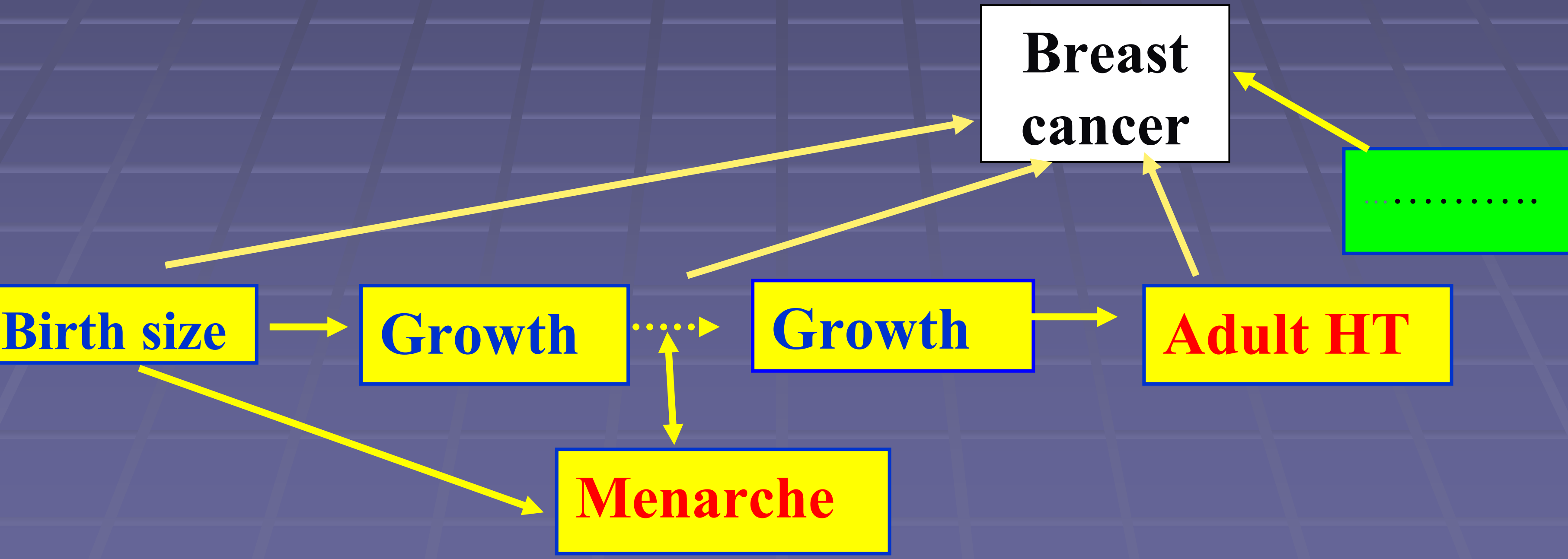
- Motivating example
- Types of missingness and common strategies
- Multiple imputation
- A suite of MI programs

Motivating example

- Breast cancer aetiology:
  - Several established risk factors (adult HT, menarche)
  - New focus on early life and childhood growth



LIFE COURSE

MRC 1946 birth cohort (N=2187):

repeated anthropometric measures in childhood

Childhood height measured at:	N	% missing
2 yrs	1782	18.5
4 yrs	1944	11.1
7 yrs	1925	12.0
11 yrs	1862	14.9
15 yrs	1689	22.8
ALL	904	41.3

Pattern and type of missingness

Data: $Y=(y, X_1, \ldots, X_p) = (Y_{obs}, Y_{mis})$

	y	X_1	X_2	…	X_p
1			•		
2					
3		•		•	
4			•		
…			•	•	•
…					•
n	•				

MCAR:

Pr (missing) = not $f(Y_{obs}, Y_{mis})$

MAR:

Pr (missing) = $f(Y_{obs})$

NMAR:

Pr (missing) = $f(Y_{obs}, Y_{mis})$

Strategies

1. Analyse only those with complete data
2. Available case analysis
3. Inclusion of a “missing value” category
4. Use methods not requiring complete data
5. Replacing missing value with imputed

Strategies

1. ~~Analyse only those with complete data~~ X
2. ~~Available case analysis~~ X
3. Inclusion of a "missing value" category

Biased even when data are MCAR

(Greenland and Finkle 1995)

confounder	RR_E
Level 1	1.45
Level 2	2.03
NK	1.51
overall	1.75

Strategies

1. X Analyse only those with complete data
2. X Available case analysis
3. X Inclusion of a "missing value" category
4. Use methods not requiring complete data
5. Replacing missing value with imputed

5 - Imputations

If MAR:

Idea: replace missing values with a "guess"

Analysis: same as with complete data

Two types, *many* variants:

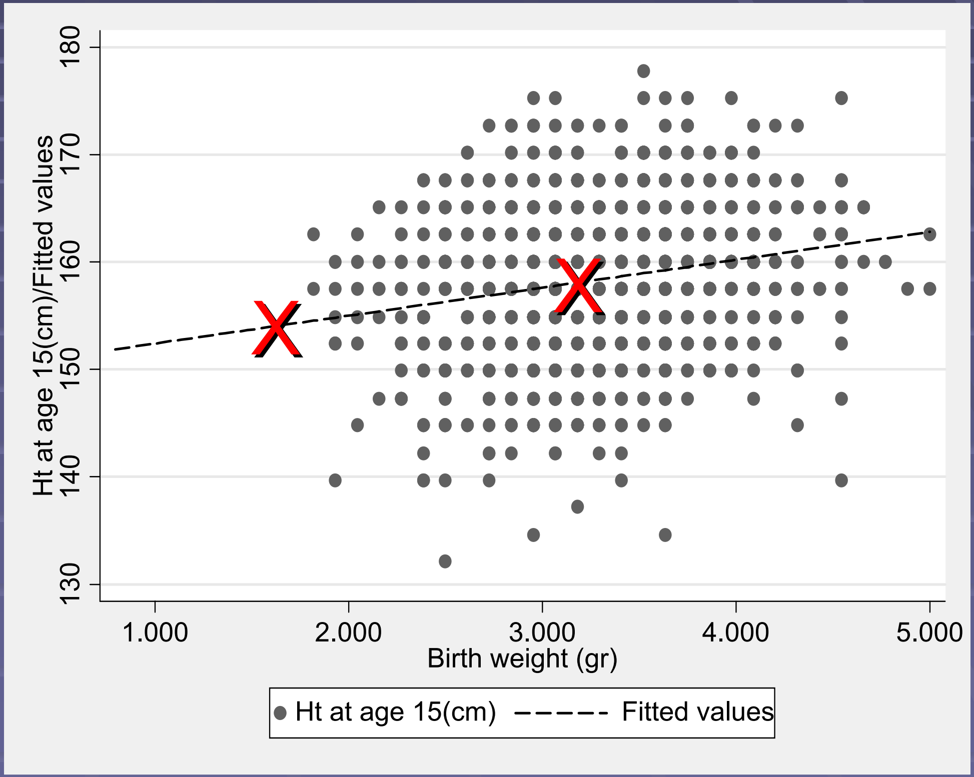
I. SINGLE IMPUTATION

II. MULTIPLE IMPUTATION

I - SINGLE IMPUTATION

a) from a regression model:

**eplace missing values
ith predicted**



not good:

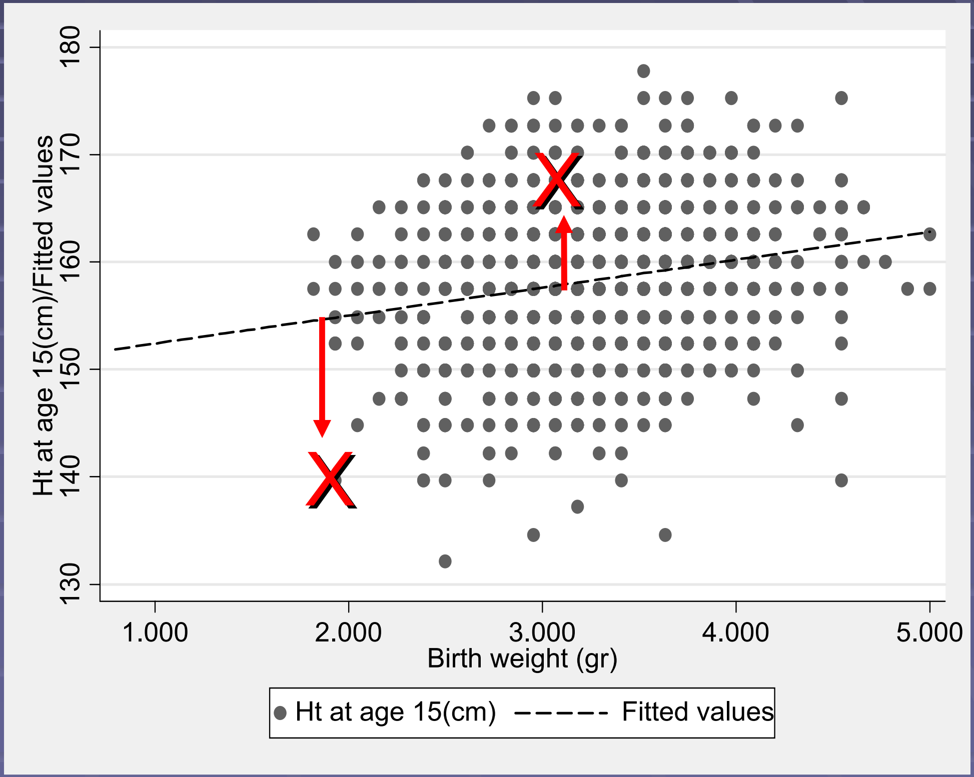
true data variation

impute.ado

SINGLE IMPUTATION

b) predicted value + random term

Size of random term depends on residual variance of the model



UNSATISFACTORY:

Still pretending the data are observed!

SINGLE IMPUTATION

c) Hot-deck

Replaces record with any missing values with another, but complete, selected at random

Not recommended if several records are incomplete

II - MULTIPLE IMPUTATION

Not one but several data sets are created

- **Each has a different set of random draws to replace missing value**
- **Separate analyses on each data set**
- **Results summarised**

PROBLEM:

generating a `proper' predictive distribution

More technically…..

•MI replacements are simulated draws from a predictive distribution of the missing data:

$$Y^*_{mis} \sim P(Y_{mis} \mid Y_{obs}, \theta^*)$$

$$\text{where } \theta^* \sim P(\theta \mid Y_{obs})$$

•Require a model for the complete data

$$P(Y \mid \theta)$$

• **Proper**, i.e. **reflect uncertainty** about missing data and the parameters

(Shafer, Multiple imputation: a primer. *Stat Methods in Medical Research*, 1999)

MI: three steps

A. Imputation of plausible values:

- Missing values replaced by imputed
- **m** times

B. Analysis of the imputed datasets

C. Combination of the results

B. Analysis

- Each dataset is analysed in the same way:

  e.g. : logistic regression
- Save :
  - Point estimates of the statistics of interest: log(OR) $= Q_{(l)}$
  - Their variance matrix: $U_{(l)}$

- All stored for $l = 1, 2, .., m$

C. Combination

Take the **m** sample estimates Q_j and variance U_j

For one parameter:

- Overall estimator: Mean (Q_j)
- Its variance: Mean(U_j) + (1+1/m) Var(Q_j)

For k parameters:

- Overall estimators: Mean ($\underline{Q}_j$)
- Variance matrix : (1+ r_1) Mean ($\underline{U}_j$)

$$r_1 = (1+1/m)\ \text{trace}[\ \text{var}(\underline{Q}_j)\ (\ \text{mean}(\underline{U}_j)^{-1}]\ /\ k$$

A. Imputation

Most difficult part

Say x_1 has missing values. Approaches:

i. Use draws from available observations of x_1

(unconditional draws)

ii. Use draws from regression models of x_1

(conditional draws)

iii. [**Hot-deck** imputation]

iv. **[Markov Chain Monte Carlo techniques]**

i) unconditional draws

$x_{1i} \sim N(\mu, \sigma^2)$, i=1,…,N

only $x_{11}\ x_{12} \dots x_{1a}$ observed, for a<N : (… obs)

For imputation run *l* …

1. Draw $\sigma^2_{(l)}$ f…
2. D…
3. … $N(\mu_{(l)}, \sigma^2_{(l)})$
4. … served $x_{11}\ x_{12} \dots x_{1a}$ plus imputed in st…

Not good for MAR

should condition on:

- **Factors affecting x_1**
- **factors influencing missingness**

ii) Simple conditional draws

Assume $x_{1i} \sim N(\beta_0 + \beta_1 x_{2i}, \sigma^2)$,

x_{2i} always observed , $x_2 \rightarrow$ missing mechanism, $X=[1\ \underline{x}2]$,

For imputation run *l* =*1*,…, *m*:

1. Draw $\sigma^2_{(l)}$ from $(a-2)\ S^2_{obs} / \chi^2_{(a-2)}$
2. Draw $(\beta_{0\ (l)}, \beta_{1\ (l)})$ from $N((\hat{\beta}_0, \hat{\beta}_1), \sigma^2_{(l)} (X'X)^{-1})$
3. Draw missing values from $N(\beta_{0\ (l)} + \beta_{1\ (l)}\ x_i, \sigma^2_{(l)})$
4. New dataset: observed plus imputed in step 3

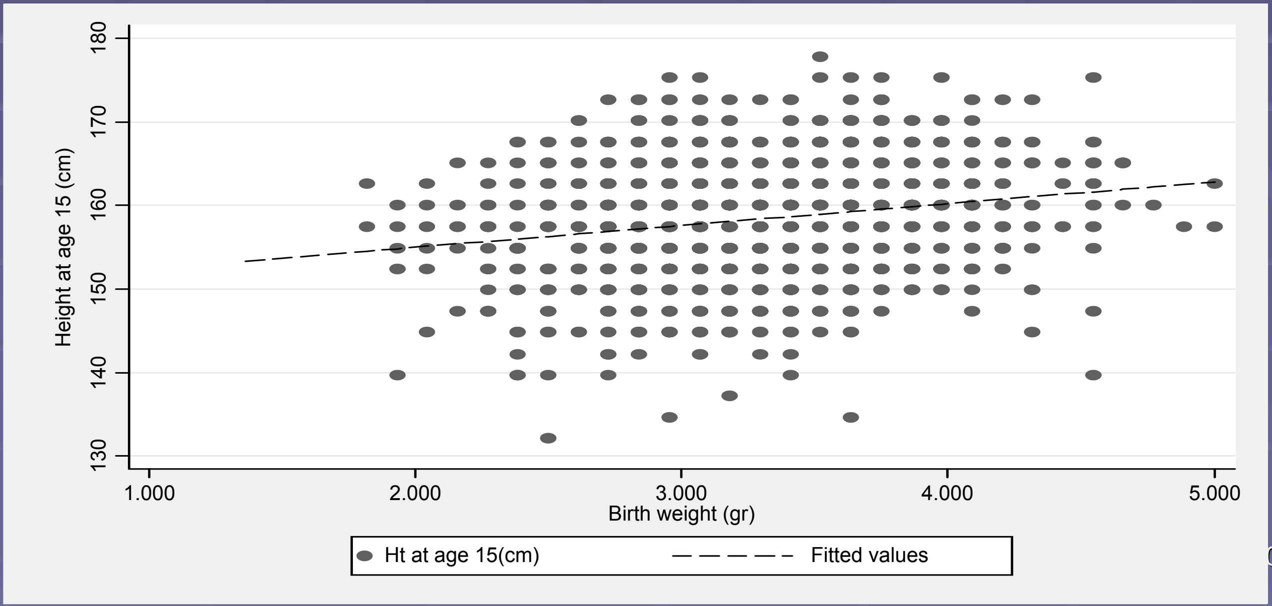
Example

MRC 1946 birth cohort: **2187** women

x_1: HT at 15 and breast cancer by age 53: **1689**

MI procedure:

- **HT15=** f(birth weight)
- **Prob(missing)=**f(birth weight, breast cancer)



MI programs:

A. mi_create_reg.ado

draws missing HT15 using results from regression of observed HT15 on (BW, BRCA) m times to create m imputed datasets

B. mi_logit.ado

runs logistic regression on each imputed dataset and saves the results

C. mi_summary.ado

summarises the results as in Shafer (1997)

Draws for ht at age 15 cond. on BW and BRCA:

Original estimates:

$\hat{\sigma}=6.19$, $\hat{\beta}_0=149.79$,

$\hat{\beta}_1=2.60$, $\hat{\beta}_2=1.48$

(N=1683)

(l)	$\sigma_{(l)}$	$\beta_{0\,(l)}$	$\beta_{1\,(l)}$	$\beta_{2\,(l)}$
1	6.20	149.75	2.60	1.54
2	6.34	149.91	2.60	1.40
3	6.26	149.43	2.59	1.62
4	6.20	149.74	2.60	1.41
5	6.03	149.83	2.61	1.52

```
         OBSERVED                          MI
---------------------------------------------------------
 OR     (95% CI)          |   OR           95% CI.
---------------------------------------------------------
1.045 (1.00,1.10)         |  1.044       (1.00,1.09)
```

iii) conditional draws from a random effects model

- **Using all childhood growth data** $\underline{y}_i$ (px1 vector):

p Observed values: $\underline{y}_i = Z\,\underline{\eta}_i + \; + \underline{\varepsilon}_i$

q Latent factors: $\underline{\eta}_i = \beta\,\underline{X}_i + \underline{u}_i$

$\underline{\varepsilon} \sim N(0, \Sigma)$, $\underline{u} \sim N(0, \Psi)$, **independence assumptions**

Explanatory variables: $\underline{X}_i$

Loading factors (fcn of observation times): Z

i.e. $y_i \sim N(\beta\,\underline{X}_i,\; Z_i \Psi Z_i' + \Sigma)$

Imputation procedure in similar steps

For imputation run $l = 1, \ldots, m$:

1. Draw $\Sigma_{(l)}$ from inverse Wishart based on $\hat{\Sigma}$
2. Draw $\Psi_{(l)}$ from inverse Wishart based on $\hat{\Psi}$
3. Draw $\underline{\eta}_{(l)}$ from $N(\underline{\eta}_{pred}, Z'\Psi_{(l)} Z)$
4. Draw missing values from $N(\underline{\eta}_{(l)}, \Sigma_{(l)})$
5. New dataset: observed plus imputed in step 3

MI program:

A. mi_create_growth.ado

Logistic regression with imputed growth variables

Use conditional draws, with several explanatory factors (including breast cancer)

		Observed data (N=904, D=33)		Observed and imputed data (N=2187, D=59)	
HEIGHT	Units	OR	95%CI	OR	95%CI
Intercept at 2yrs	*cm*	**1.08**	0.71,1.66	**1.18**	0.87,1.60
Velocity 2-4 yrs	*cm/yr*	**1.02**	0.67,1.56	**1.14**	0.88,1.51
Velocity 4-7 yrs	*cm/yr*	**1.53**	1.04,2.24	**1.41**	1.08,1.85
Velocity 7-11yrs	*cm/yr*	**1.44**	0.92,2.25	**1.15**	0.81,1.62
Velocity 11-15ys	*cm/yr*	**1.23**	0.78,1.93	**1.30**	0.99,1.70
Velocity 15-adulthood	*cm/yr*	**1.05**	0.70,1.58	**0.94**	0.71,1.24

Summary

- **MI requires great care in creating imputed values**
  A. mi_create_reg.ado & mi_create_growth.ado
  B. mi_logit.ado & mi_ologit.ado
  C. mi_summary.ado

- **Other Stata programs:**
  - impute.ado
  - regmsng.ado
  - hotdeck.ado

  - implogit.ado
  - Gary Kings' programs: clarify
  - Ken Scheve's programs