Multiple imputation methods for incomplete longitudinal ordinal data: a simulation study

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14 September 2012

Outline of the presentation

- Introduction
- Methods for (incomplete) Non-Gaussian longitudinal data
  - Generalized Estimating Equations (GEE)
  - Multiple imputation based GEE (MI-GEE)
- Simulation plan
- Results
- Conclusions

Analysis of ordinal longitudinal data

Units: Subjects, objects ($i = 1, \cdots, N$)

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Missing data mechanism (Little and Rubin, 1987)

MCAR - Missing completely at random

- independent of (both observed and unobserved) measurements

MAR - Missing at random

- conditional on observed measurements, independent of unobserved measurements

MNAR - Missing not at random

- dependent on unobserved and (also possibly) observed measurements

GEE

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- Define of a $(K-1)$ expanded vector of binary responses $\mathbf{Y}_{ij}^{*} = (Y_{ij1}^{*}, \ldots, Y_{ij,(K-1)}^{*})'$ where $Y_{ijk}^{*} = 1$ if $Y_{ij} = k$ and 0 otherwise
- $logit[Pr(Y_{ij} \leq k)] = logit[Pr(Y_{ijk}^{*} = 1)] = \boldsymbol{\beta}_{0k} + \mathbf{x}_{ij}'\boldsymbol{\beta}$

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$$\sum_{i=1}^{N} \frac{\partial \boldsymbol{\pi}_\mathbf{i}'}{\partial \boldsymbol{\beta}} \mathbf{W}_\mathbf{i}^{-1} (\mathbf{Y}_\mathbf{i}^* - \boldsymbol{\pi}_\mathbf{i}) = 0$$

where $\mathbf{Y}_i^* = (\mathbf{Y}_{i1}^*, ..., \mathbf{Y}_{iT}^*)'$, $\boldsymbol{\pi}_\mathbf{i} = E(\mathbf{Y}_i^*)$ and $\mathbf{W_i = V_i^{1/2} R_i V_i^{1/2}}$ with $\mathbf{V}_i$ the diagonal matrix of the variance of the element of $\mathbf{Y}_i^*$. The matrix $\mathbf{R}_i$ is the 'working' correlation matrix that expresses the dependence among repeated observations over the subjects.

GEE - Large sample properties

$$\sqrt{N}(\hat{\beta} - \beta)\ N(0, I_0^{-1} I_1 I_0^{-1})$$

- $\hat{\beta}$ are consistent even if working correlation matrix is incorrect
- uncorrected specification of the correlation structure affects efficiency of $\hat{\beta}$
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- Solution: Use Multiple Imputation (MI) as a preliminary step

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1. Imputation stage - $Y_{ij}^{missing} \Rightarrow Y_{ij}^{1}, \cdots, Y_{ij}^{M}$
2. Analysis stage - Analyze the M completed datasets using GEE

$$\left(\hat{\beta^m}, \hat{var}(\hat{\beta^m})\right), m = 1, \cdots, M$$

3. Pooling stage - Combination of the M results

$$\hat{\beta}^* = \frac{1}{M} \sum_{m=1}^{M} \hat{\beta}_m \quad \mathbf{T} = \mathbf{W} + \left(1 + \frac{1}{M}\right) \mathbf{B}$$

where $\mathbf{W} = \frac{1}{M} \sum_{m=1}^{M} \hat{var}(\hat{\beta^m})$ and $\mathbf{B} = \frac{1}{M-1} \sum_{m=1}^{M} (\hat{\beta}_m - \hat{\beta}^*)(\hat{\beta}_m - \hat{\beta}^*)'$

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Imputation mechanism

Any monotone response pattern can be written as $\mathbf{Y} = (\mathbf{Y}^o, \mathbf{Y}^{missing})$.
Let $\boldsymbol{\theta}$ represents the parameter vector of the distribution of the response $\mathbf{Y}$. The idea is to impute missing data using $f(\mathbf{Y}^{missing}|\mathbf{Y}^o, \boldsymbol{\theta})$.

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Imputation mechanisms based on :

- Markov chain Monte Carlo (MCMC)

- Stochastic regression (ordinal logistic regression (OIM))

Imputation methods - MCMC

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2. **P-step** New value for $\boldsymbol{\theta}$, $\boldsymbol{\theta}_{(j)}$, is drawn from a transition distribution, considering the previous value $\boldsymbol{\theta}_{(j)} \approx h_s(\boldsymbol{\theta}_{(j-1)})$.

Both steps are iterated long enough to provide a stationary Markov chain $(\mathbf{Y}^{missing}_{(1)}, \boldsymbol{\theta}_{(1)}), (\mathbf{Y}^{missing}_{(2)}, \boldsymbol{\theta}_{(2)}), \cdots$ and last iteration is used to impute $\mathbf{Y}^{missing}$ in the dataset.

Repeat to obtain M sets of imputed values.

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Problem when applied to ordinal data

- Normality assumption fails
- Imputed values are no longer integers between 1 and K $\rightarrow$ rounding

Imputation methods - OIM

Ordinal imputation model:

$$logit[Pr(Y_{ij} \leq k)|\mathbf{x}^*_{ij}] \quad = \quad \gamma_{0k} + \mathbf{x'}^*_{ij}\gamma \tag{1}$$

where the covariates typically include $\mathbf{X}_{ij}$, possible auxiliary covariates $\mathbf{A}_{ij}$, and the previous outcomes $\tilde{\mathbf{Y}}_{ij} = (Y_{i1}, ..., Y_{i,j-1})$.

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4. Repeat steps 1 to 3 to obtain M sets of imputed values.

Simulation plan

Longitudinal ordinal data model:

$$\text{logit}[\Pr(Y_{ij} \leq k | x_i, t_j)] = \beta_{0k} + \beta_x x_i + \beta_t t_j + \beta_{tx} x_i t_j \quad (k = 1, \cdots K-1)$$

with a binary group effect ($x = 0$ or 1), an assessment time (t) and an interaction term between group and time.

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MAR missingness generation:

$$\text{logit}[\Pr(D_i = j | x_i, Y_{i,(j-1)})] = \psi_0 + \psi_x x_i + \psi_{prev} Y_{i,(j-1)}$$

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Model simulation parameters (Well-balanced data):
$K = 2, 3, 4, 5$ and 7
$T = 3, 5$
$N = 100, 300, 500$
Missingness $= 10\%, 30\%, 50\%$
$\rightarrow$ 90 different combination patterns. For each pattern, 500 random samples were generated.

Simulation results

Relative bias (%)

Relative bias (Mean ± SD)

	MCMC	OIM	Difference
β_x	89.4 ± 13.1	99.5 ± 15.5	-10.1 ± 8.91
β_t	84.6 ± 10.4	100.9 ± 8.95	-16.4 ± 9.58
β_{tx}	90.6 ± 5.73	99.7 ± 5.37	-9.10 ± 4.60

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Simulation results - Relative bias β_{tx}

Number of levels K

K	MCMC	OIM	Difference
2	92.9 ± 5.18	101.2 ± 2.93	-8.35 ± 4.29
3	94.1 ± 2.98	103.4 ± 4.23	-9.35 ± 4.34
4	88.0 ± 6.71	99.1 ± 6.05	-11.1 ± 4.66
5	89.1 ± 5.36	99.5 ± 3.09	-10.4 ± 4.70
7	88.7 ± 5.56	95.0 ± 6.12	-6.34 ± 3.87
	< 0.0001	< 0.0001	0.034

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Number of time points T

T	MCMC	OIM	Difference
3	91.7 ± 5.82	100.9 ± 5.34	-9.26 ± 4.73
5	89.4 ± 5.47	98.4 ± 5.14	-8.94 ± 4.51
	0.007	0.009	0.61

Simulation results - Relative bias β_{tx}

Sample size

N	MCMC	OIM	Difference
100	90.5 $\pm$ 6.60	97.7 $\pm$ 6.73	-7.22 $\pm$ 4.18
300	90.9 $\pm$ 5.37	100.8 $\pm$ 4.77	-9.88 $\pm$ 4.48
500	90.2 $\pm$ 5.29	100.4 $\pm$ 3.85	-10.2 $\pm$ 4.67
	0.74	0.027	0.0002

Simulation results - Relative bias β_{tx}

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500	90.2 $\pm$ 5.29	100.4 $\pm$ 3.85	-10.2 $\pm$ 4.67
	0.74	0.027	0.0002

Rate of missingness

Missingness	MCMC	OIM	Difference
10%	95.4 $\pm$ 2.65	100.1 $\pm$ 2.47	-4.64 $\pm$ 0.94
30%	89.9 $\pm$ 3.23	99.9 $\pm$ 3.57	-9.94 $\pm$ 2.21
50%	86.3 $\pm$ 6.29	99.0 $\pm$ 8.31	-12.7 $\pm$ 4.92
	< 0.0001	0.37	< 0.0001

Conclusions

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- MCMC yields highly underestimated model parameters
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↑ Absolute bias increases

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MSE

- MCMC and OIM were similar

Conclusion - General

MCMC is not really recommended to impute longitudinal ordinal data.

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MCMC is not really recommended to impute longitudinal ordinal data.

Advisable to impute missing ordinal data using appropriate method.

Thank you.

Simulation results - Relative bias β_{tx} - Skewed

No relationship between the OIM relative bias and the modeling parameters
MCMC relative bias increased with K ($p = 0.0002$) and the rate of missingness ($p = 0.0005$)

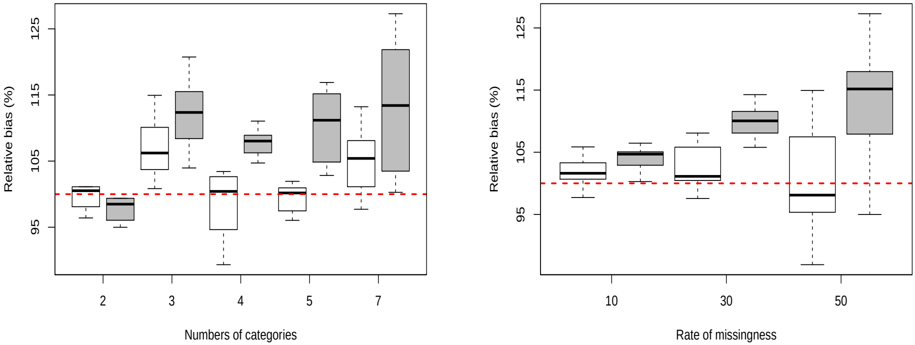

Figure: Relative bias (%) of β_{tx} according to the number of categories and the rate of missingness (MCMC= shaded boxplot - OIM=empty boxplot)