Subsample ignorable likelihood methods for regression with missing values of covariates
(throwing data away can actually pay!)

Roderick J. Little

University of Michigan

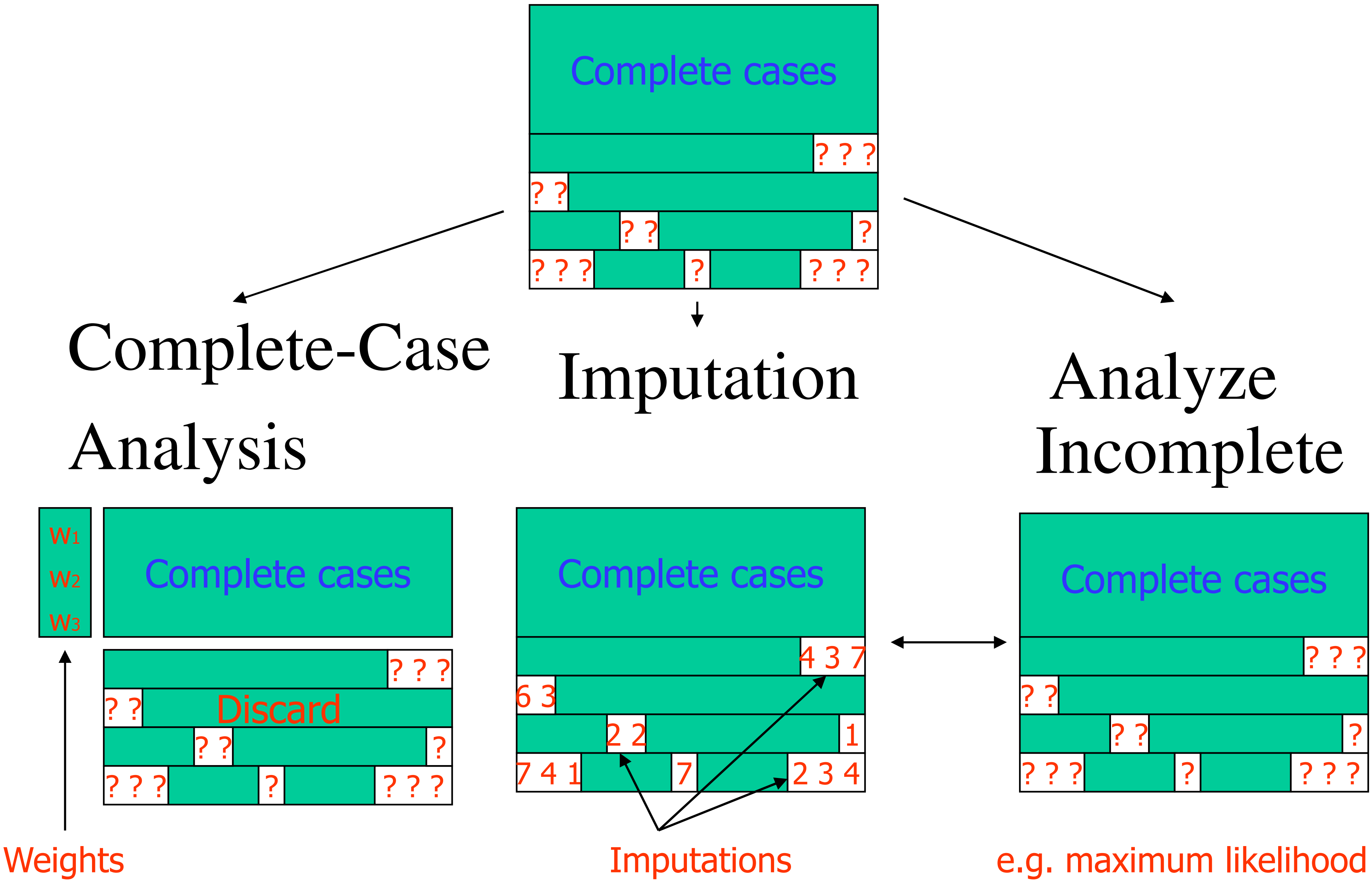
Outline

- Likelihood methods for repeated-measures with missing data
  - Missing data for outcomes and predictors
- Tools: Ignorable likelihood methods, selective discarding of incomplete cases
  - Positive feature: no model required for missing-data mechanism, even though some models are not MAR
- Also apply ideas to missing covariates in survival analysis
- Little & Zhang (in press)

Key Idea

- Rubin's (1976) MAR theory does not distinguish between missing outcomes and predictors
  - Here adopt a "divide and conquer" strategy
- An alternative to MNAR modeling the missing data mechanism is to drop cases with missing values of predictors from the analysis
  - Valid when missingness does not depend on outcomes

Missing Data: General Strategies



Likelihood approaches

- Maximum Likelihood (ML, REML) for large samples
- Bayes for small samples
- Multiple imputation (MI) of missing values based on predictive distribution for a Bayesian model, with Bayesian MI combining rules (SAS PROC MI, IVEWARE, MICE, etc.)
- "Ignorable likelihood" – no model for missing-data mechanism
- Assumes data are missing at random (MAR): "missingness does not depend on missing data, given observed data"
- When not MAR, ML generally requires a model for the mechanism, which is often weakly identified and vulnerable to misspecification
- Here, discuss methods that avoid modeling the mechanism

Unweighted CC analysis

•Drops incomplete cases
• Hence inefficient if there is substantial information in these cases
•Loss of information depends on pattern and estimand
•E.g. Figure 1: for mean of *Y* the incomplete cases have substantial information, when *X*'s are predictive
•For regression of *Y* on *X*, incomplete cases have no information, under MAR
•But there is info under NMAR

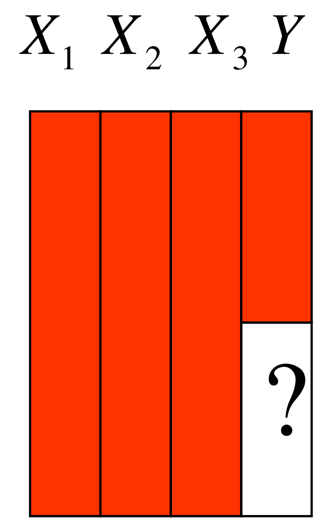


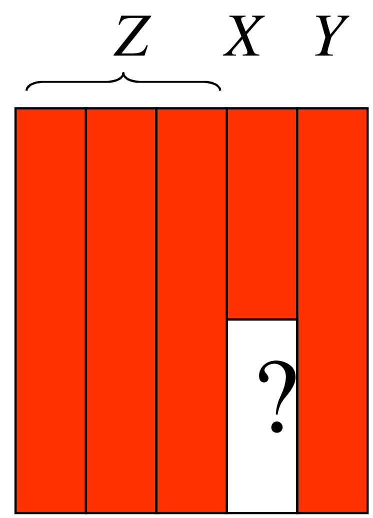
Figure 1

Missing data in X

Target: regression of Y on X, Z; missing data on X

IL methods include information for the regression in the incomplete cases (particularly intercept and coefficients of Z) and are valid assuming MAR:

Pr(X missing)= $g(Z, Y)$



BUT: if Pr(X missing)= $g(Z, X)$

CC analysis is consistent, but IL methods (or weighted CC) are inconsistent since mechanism is not MAR

Simulations favoring IL often generate data under MAR, <u>hence are biased against CC</u>

(A) Missing data in X

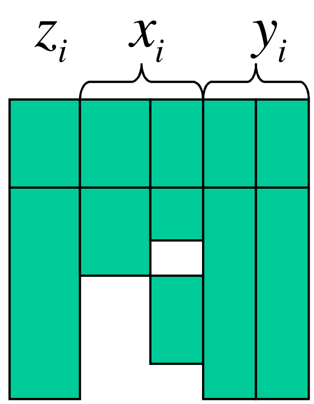
Could be vector

Pattern	Observation, i	z_i	x_i	y_i	R_{x_i}
P1	$i = 1,\ldots,m$	√	√	√	$u_x = (1,\ldots,1)$
P2	$i = m+1,\ldots,n$	√	?	√	$\bar{u}_x$

Key: √ denotes observed, ? denotes observed or missing

P1: complete cases

P2: incomplete X



XMAR $\Rightarrow$ Ignorable Likelihood

Target: Parameters ϕ of regression of Y on X, Z

Full Model: $p(x_i, y_i \mid z_i, \theta) \times p(R_{x_i} \mid z_i, x_i, y_i, \psi); \phi = \phi(\theta)$

If we assume XMAR:

$p(R_{x_i} \mid z_i, x_i, y_i, \psi) = p(R_{x_i} \mid z_i, x_{\text{obs},i}, y_i, \psi)$ for all $x_{\text{mis},i}$

Then $L_{\text{full}}(\theta, \psi) = L_{\text{ign}}(\theta) \times L_{\text{md}}(\psi)$, can base inference on

$$L_{\text{ign}}(\theta) = \text{const.} \times \prod_{i=1}^{n} p(x_{\text{obs},i}, y_i \mid z_i, \theta)$$

XMAR $\Rightarrow$ Ignorable Likelihood

Target: $\phi = \phi(\theta)$ = parameters of regression of Y on X, Z

ML: $\hat{\phi} = \phi(\hat{\theta})$

Bayes: draw $\phi^{(d)} = \phi(\theta^{(d)})$

Multiple imputation: draw $X_{\text{mis}}^{(d)} \sim P(X_{\text{mis}} \mid \text{data})$,
apply MI combining rules to estimates of ϕ

XCOV $\Rightarrow$ Complete-Case Analysis

Assume XCOV:completeness of X depends on covariates, not outcomes:

$$p\left(R_{x_i}=u_x \mid z_i, x_i, y_i, \psi\right)\right) = p\left(R_{x_i}=u_x \mid z_i, x_i, \psi\right)\right) \text{ for all } y_i \text{ (MNAR)}$$

$$L_{\text{full}}(\theta,\psi)=\prod_{i=1}^{m} p(R_{x_i}=u_x, x_i, y_i \mid z_i, \theta, \psi) \prod_{i=m+1}^{n} p(R_{x_i}, x_{\text{obs},i}, y_i \mid z_i, \theta, \psi)$$

$$=\prod_{i=1}^{m} p(y_i \mid x_i, R_{x_i}=u_x, z_i, \theta, \psi)\, p(R_{x_i}=u_x, x_i \mid z_i, \theta, \psi)$$

By XCOV

$$\times \prod_{i=m+1}^{n} p(R_{x_i}, x_{\text{obs},i}, y_i \mid z_i, \theta, \psi)$$

$$=\prod_{i=1}^{m} p(y_i \mid x_i, z_i, \phi) \times p(R_{x_i}=u_x, x_i \mid z_i, \theta, \psi) \prod_{i=m+1}^{n} p(R_{x_i}, x_{\text{obs},i}, y_i \mid z_i, \theta, \psi)$$

$$= L_{cc}(\phi) \times L_{\text{rest}}(\theta,\psi)$$

Maximizing $L_{cc}(\phi)$ is valid, but info in $L_{\text{rest}}(\theta,\psi)$ except in special cases

(B) Missing data on X and Y

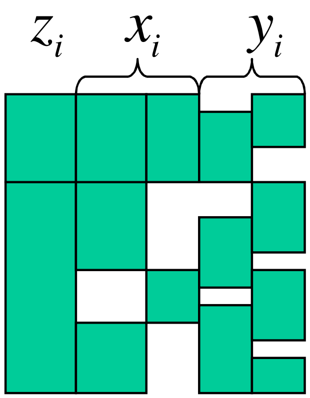
Could be vector

Pattern	Observation, i	z_i	x_i	y_i	R_{x_i}
P1	$i = 1,\ldots,m$	√	√	?	$u_x = (1,\ldots,1)$
P2	$i = m+1,\ldots,n$	√	?	?	$\bar{u}_x$

Key: √ denotes observed, ? denotes observed or missing

P1: covariates complete

P2: x incomplete



XYMAR $\Rightarrow$ Ignorable Likelihood

Target: Parameters ϕ of regression of Y on X, Z

Model: $p(x_i, y_i \mid z_i, \theta)$

Assume XYMAR:

$$p(R_{x_i}, R_{y_i} \mid z_i, x_i, y_i, \psi) = p(R_{x_i}, R_{y_i} \mid z_i, x_{\text{obs},i}, y_{\text{obs},i}, \psi)$$

for all $x_{\text{mis},i}, y_{\text{mis},i}$

Then $L_{\text{full}}(\theta, \psi) = L_{\text{ign}}(\theta) \times L_{\text{md}}(\psi),$ can base inference on

$$L_{\text{ign}}(\theta) = \text{const.} \times \prod_{i=1}^{n} p(x_{\text{obs},i}, y_{\text{obs},i} \mid z_i, \theta)$$

IL Inference about $\phi(\theta),$ as before

XCOV, YSMAR $\Rightarrow$ IL on cases with X observed

Target: Parameters ϕ of regression of Y on X, Z

Assume:

XCOV: completeness of X depends on covariates, not outcomes:

$$p\left(R_{x_i} = u_x \mid z_i, x_i, y_i, \psi)\right)$$

$$= p\left(R_{x_i} = u_x \mid z_i, x_i, \psi)\right) \text{ for all } y_i$$

YSMAR: Y is MAR in subsample with X observed:

$$p(R_{y_i} \mid R_{x_i} = u_x, z_i, x_i, y_i, \psi)$$

$$= p(R_{y_i} \mid R_{x_i} = u_x, z_i, x_i, y_{\text{obs},i}, \psi) \text{ for all } y_i$$

MNAR

SSIL: Apply IL to subsample with X fully observed (P1)

(B) Missing data on X and Y

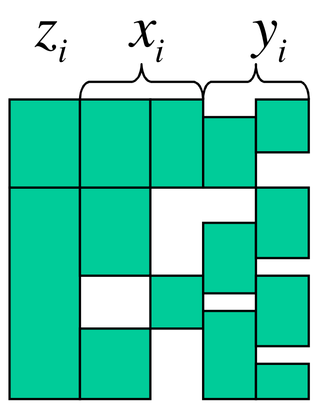
Could be vector

Pattern	Observation, i	z_i	x_i	y_i	R_{x_i}
P1	$i = 1,\ldots,m$	√	√	?	$u_x = (1,\ldots,1)$
P2	$i = m+1,\ldots,n$	√	?	?	$\overline{u}_x$

Key: √ denotes observed, ? denotes observed or missing

P1: covariates complete

P2: x incomplete



SSIL likelihood under XCOV,YSMAR

$$L_{\text{full}}(\theta,\psi)=\prod_{i=1}^{n} p(R_{x_i}, x_{\text{obs},i}, R_{y_i}, y_{\text{obs},i} \mid z_i,\theta,\psi)$$

$$=\prod_{i=1}^{m} p(R_{x_i}=u_x, x_i, R_{y_i}, y_{\text{obs}.i} \mid z_i,\theta,\psi)\times L_{\text{rest}}(\theta,\psi)$$

$$=L_{\text{rest}}(\theta,\psi)\times\prod_{i=1}^{m}\left(p(R_{x_i}=u_x, x_i \mid z_i,\theta,\psi)\right) \longleftarrow L^{*}_{\text{rest}}(\theta,\psi)$$

$$\times\prod_{i=1}^{m}\left(\int p(y_i \mid x_i, R_{x_i}=u_x, z_i,\theta,\psi)\, p(R_{y_i} \mid y_i, x_i, R_{x_i}=u_x, z_i,\theta,\psi)\,dy_{\text{mis}}\right)$$

XCOV ↓ YSMAR ↓

$$=L^{*}_{\text{rest}}(\theta,\psi)\times\prod_{i=1}^{m}\int p(y_i \mid x_i, z_i,\phi)\, p(R_{y_i} \mid y_{\text{obs},i}, x_i, R_{x_i}=u_x, z_i,\psi)\,dy_{\text{mis}}$$

$$=L^{*}_{\text{rest}}(\theta,\psi)\times\prod_{i=1}^{m} p(y_{\text{obs},i} \mid x_i, z_i,\phi)\prod_{i=1}^{m} p(R_{y_i} \mid y_{\text{obs},i}, x_i, R_{x_i}=u_x, z_i,\psi)$$

SSIL maximizes this

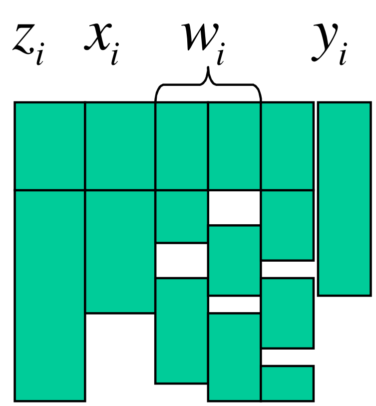
Two covariates *X*, *W* with different mechanisms

Pattern	Observation, i	z_i	x_i	w_i	y_i	R_{x_i}	R_{w_i}
P1	$i = 1,\ldots,m$	√	√	√	?	u_x	u_w
P2	$i = m+1,\ldots,m+r$	√	√	?	?	u_x	$\bar{u}_w$
P3	$i = m+r+1,\ldots,n$	√	?	?	?	$\bar{u}_x$	$\bar{u}_w$

P1: covariates complete

P2: *x* obs, *w*, *y* may be mis

P3: *x* mis, *w*, *y* may be mis



XCOV, WYSMAR $\Rightarrow$ IL on cases with X observed

- Target: regression of *Y* on *Z*, *X*, and *W*
- Assume:

(XCOV) Completeness of X can depend on covariates but not Y:

$$p\left(R_{x_i} = u_x \mid z_i, x_i, w_i, y_i, \psi_x)\right) = p\left(R_{x_i} = u_x \mid z_i, x_i, w_i, \psi_x)\right) \text{ for all } y_i$$

(WYMAR) Missingness of (W, Y) is MAR within subsample of cases with X observed:

$$p(R_{(w_i, y_i)} \mid z_i, x_i, w_i, y_i, R_{x_i} = u_x; \psi_{wy\cdot x}) =$$

$$p(R_{(w_i, y_i)} \mid z_i, x_i, w_{\text{obs},i}, y_{\text{obs},i}, R_{x_i} = u_x; \psi_{wy\cdot x}) \quad \text{for all } w_{\text{mis},i}, y_{\text{mis},i}$$

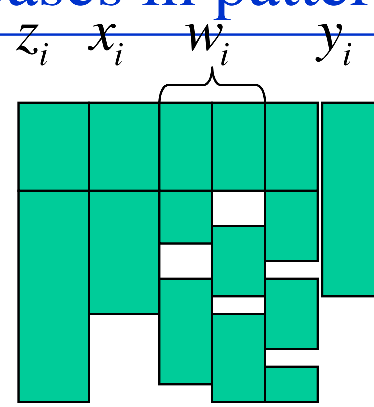
- SSIL: apply IL method (e.g. ML) to the subsample of cases for which *X* is observed
- Proof of consistency: similar to previous case, treating *W* and *Y* as block

Two covariates X, W with different mechanisms

Pattern	Observation, i	z_i	x_i	w_i	y_i	R_{x_i}	R_{w_i}
P1	$i = 1,\ldots,m$	√	√	√	?	u_x	u_w
P2	$i = m+1,\ldots,m+r$	√	√	?	?	u_x	$\bar{u}_w$
P3	$i = m+r+1,\ldots,n$	√	?	?	?	$\bar{u}_x$	$\bar{u}_w$

SSIL: analyze cases in patterns 1 and 2

P1: covariates complete
P2: x obs, w, y may be mis
P3: x mis, w, y may be mis



Simulation Study

- For each of 1000 replications, 5000 observations *Z*, *W*, *X* and *Y* generated as:

$$\left(y_i \mid z_i, w_i, x_i \right) \sim_{\text{ind}} N(1 + z_i + w_i + x_i, 1)$$

$$(z_i, w_i, x_i) \sim_{\text{ind}} N(0, \Sigma),\ \ \Sigma = \begin{pmatrix} 1 & \rho & \rho \\ \rho & 1 & \rho \\ \rho & \rho & 1 \end{pmatrix}$$

- 20-35% of missing values of *W* and *X* generated by four mechanisms

Simulation: missing data mechanisms

Mechanisms	$\alpha_0^{(w)}$	$\alpha_z^{(w)}$	$\alpha_w^{(w)}$	$\alpha_x^{(w)}$	$\alpha_y^{(w)}$	$\alpha_0^{(x)}$	$\alpha_z^{(x)}$	$\alpha_w^{(x)}$	$\alpha_x^{(x)}$	$\alpha_y^{(w)}$
I: All valid	-1	1	0	0	0	-1	1	0	0	0
II: CC valid	-1	1	1	1	0	-1	1	1	1	0
III: IML valid	-2	1	0	0	1	-2	1	1	0	1
IV: SSIML valid	-1	1	1	1	0	-2	1	1	0	1

$$\text{logit}\left(P(R_{w_i}=0 \mid z_i, w_i, x_i, y_i)\right) = \alpha_0^{(w)} + \alpha_z^{(w)} z_i + \alpha_w^{(w)} w_i + \alpha_x^{(w)} x_i + \alpha_y^{(w)} y_i$$

$$\text{logit}\left(P(R_{x_i}=0 \mid R_{w_i}=1, z_i, w_i, x_i, y_i)\right) = \alpha_0^{(x)} + \alpha_z^{(x)} z_i + \alpha_w^{(x)} w_i + \alpha_x^{(x)} x_i + \alpha_y^{(x)} y_i$$

RMSEs*1000 of Estimated Regression Coefficients for Before Deletion (BD), Complete Cases (CC), Ignorable Maximum Likelihood (IML) and Subsample Ignorable Maximum Likelihood (SSIML), under Four Missing Data Mechanisms.

	$\rho = 0$				$\rho = 0.8$			
	I*	II	III	IV	I	II	III	IV
BD	27	28	28	27	50	46	50	46
CC	45	44	553	322	86	71	426	246
IML	37	231	36	116	58	96	53	90
SSIML	42	133	360	49	70	80	319	69
Valid:	ALL	CC	IML	SSIML	ALL	CC	IML	SSIML

Missing Covariates in Survival Analysis

$\{t_1,...,t_k\}$ distinct survival times, j = unit that fails at time t_j (no ties);

$R_j =$ risk set at time t_j, $z_j, x_j, w_j =$ covariates, as before.

Complete data: contribution of data at time t_j to partial likelihood is

$$L_j = \frac{\lambda(y=t_j \mid z_j, x_j, w_j, \beta)}{\sum_{k \in R_j} \lambda(y=t_k \mid z_k, x_k, w_k, \beta)}, \lambda(y=t_j \mid z_j, x_j, w_j, \beta) = \text{ hazard}$$

With z_j, w_j fully observed, x_j covariate-dependent complete, i.e.:

$$\Pr(R_{x_j} = u_x \mid y_j, z_j, x_j, w_j) = \Pr(R_{x_j} = u_x \mid z_j, x_j, w_j)$$

then $\lambda(y=t_j \mid R_{x_j} = u_x, z_j, x_j, w_j, \beta) = \lambda(y=t_j \mid z_j, x_j, w_j, \beta)$

That is, conditioning on $R_{x_j} = u_x$ for each risk set

gives a valid partial likelihood

also OK for time-varying x_j

SSIL for Survival Analysis

SSIL for partial likelihood: Assume

XCOV: x_j is covariate-dependent missing:

$$\Pr(R_{x_j} = u_x \mid y_j, z_j, x_j, w_j) = \Pr(R_{x_j} = u_x \mid z_j, x_j, w_j)$$

WSMAR: missing values of w_j are MAR

in subsample with x_j observed:

$$\Pr(R_{w_j} \mid R_{x_j} = u_x, y_j, z_j, x_j, w_j) = \Pr(R_{w_j} \mid R_{x_j} = u_x, y_{\text{obs},j}, z_j, x_j, w_{\text{obs},j})$$

Then can apply SSIL methods to partial likelihood
in subsample with w_j observed.

How to choose *X*, *W*

- Choice requires understanding of the mechanism:
- Variables that are missing based on their underlying values belong in *X*
- Variables that are SMAR belong in *W*
- Collecting data about why variables are missing is obviously useful to get the model right
- But this applies to all missing data adjustments…

Other questions and points

- How much is lost from SSIL relative to full likelihood model of data and missing data mechanism?
  - In some special cases, SSIL is efficient for a pattern-mixture model
  - In other cases, trade-off between additional specification of mechanism and loss of efficiency from conditional likelihood
- MAR analysis applied to the subset does not have to be likelihood-based
  - E.g. weighted GEE, AIPWEE
- Assuming XCOV, MNAR analysis for Y can also be applied to subset with X observed

A longitudinal application of SMAR

- Zhou, Little and Kalbfleisch (2011) consider block-sequential missing-data models factored as

$$f(V_i, R_i \mid \theta, \psi)$$

$$= f(V_{i(1)}, R_{i(1)} \mid \theta^{(1)}, \psi^{(1)})$$

$$\times f(V_{i(2)}, R_{i(2)} \mid H_{i(1)}, \theta^{(2)}, \psi^{(2)})$$

$$\ldots \qquad \times f(V_{i(B)}, R_{i(B)} \mid H_{i(B-1)}, \theta^{(B)}, \psi^{(B)})$$

$H_{i(j)}$ = history up to j, including missing-data indicators

$f(V_{i(j)}, R_{i(j)} \mid H_{i(j-1)}, \theta^{(j)}, \psi^{(j)})$

could have selection or pattern-mixture factorization

Special case: Block-conditional MAR models

$$f(V_{i(j)}, R_{i(j)} \mid H_{i(j-1)}, \theta^{(j)}, \psi^{(j)})$$

$$= f(V_{i(j)} \mid H_{i(j-1)}, \theta^{(j)}) \times f(R_{i(j)} \mid H_{i(j-1)}, V_{i(j)}, \psi^{(j)})$$

$$= f(V_{i(j)} \mid V_{i(1)}, ..., V_{i(j-1)}, \theta^{(j)}) \times f(R_{i(j)} \mid H_{i(j-1)}, V_{\text{obs},i(j)}, \psi^{(j)})$$

$$L_{\text{full}}(\theta, \psi \mid Y_{\text{obs}}, M) = L_{\text{bm}}(\theta) \times L_{\text{rest}}(\theta, \psi)$$

Extends SMAR

$$L_{\text{bm}}(\theta) = \prod_{j=1}^{B} \prod_{i \in Q_j} f(V_{\text{obs},i(j)} \mid V_{i(1)}, ..., V_{i(j-1)}, \theta^{(j)})$$

$Q_j = \{$Set of cases with $V_{i(1)}, ..., V_{i(j-1)}$ observed$\}$

$L_{\text{bm}}(\theta)$ = Block-monotone reduced likelihood

Inference based on $L_{\text{bm}}(\theta)$ is simpler, since does not involve ψ

Conclusions

- Sometimes discarding data is useful!
- SSIL: selectively discards data based on assumed missing-data mechanism
- More efficient than CC
- Valid for mechanisms where IL, CC are inconsistent
- Little, R.J. & Zhang, N. (2011). Subsample Ignorable Likelihood for Regression Analysis with Missing Data. To appear in *JRSSC*.
- Zhou, Y., Kalbfleisch, J.D. & Little, R.J. (2010). Block-Conditional MAR Models for Missing Data. *Statistical Science*, 25, 4, 517-532.
- rlittle@umich.edu for copy of papers

and thanks to my recent students…

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