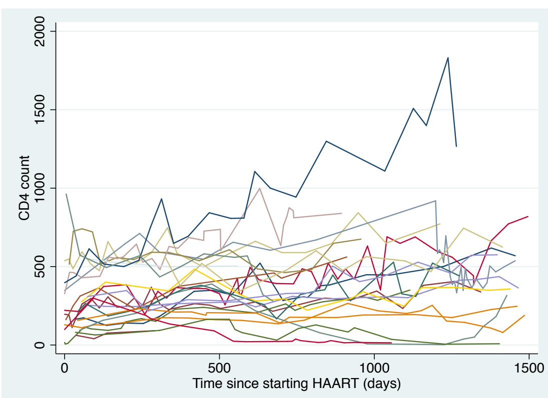
Longitudinal Data
Fall 2014

Naïve Analysis of Longitudinal Data
(Major Themes)



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Major Themes

1. Dependent data – impact on estimation and inference. Why can't I just use the tools I already know? MT1

2. Using longitudinal history in regression.
   – Avoiding, by default, treating the data like cross-sectional data. What am I missing by using the tools I already know? MT2

3. Estimating contribution of variance from different units. Can I better understand where my variation comes from?
4. MT3
5. Efficiency. Can I make my estimators more precise? MT4

1. Dependent data

- If one takes more than one measurement on a subject $\longrightarrow$ can no longer assume all observations are statistically independent.

- Statistical inference is easier if the data consists of independent measures.

- e.g., $var(Y_{i1}+Y_{i2})=var(Y_{i1})+var(Y_{i2})+2*cov(Y_{i1},Y_{i2})$

Treating longitudinal data like cross-sectional data: inference

- Consider a simple, random (mixed?) effects model.

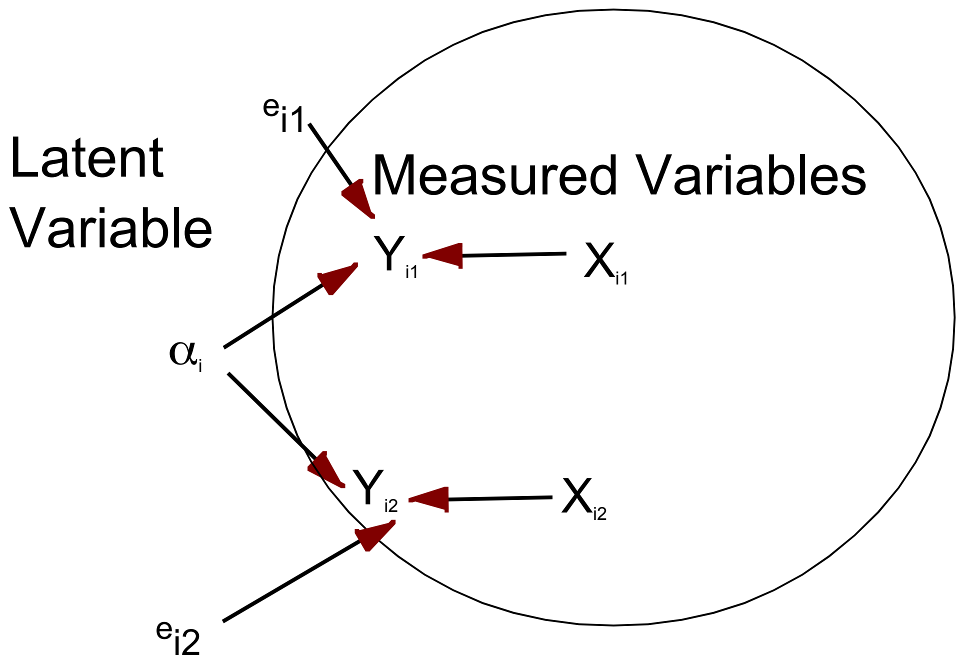
- The experiment is cd4 count measured twice on each of m randomly selected individuals.

- Model is, for the jth measurement on individual i,

$$Y_{ij} = \mu + \alpha_i + e_{ij}$$

where, $E(\alpha_i)=0$, $E(e_{ij})=0$, α_i indep. of e_{ij} and e_{i1} independent of e_{i2}.

A simple random effects model for correlation



Consequences of Ignoring Correlation

- σ_α^2 = variance between individuals (variance of α_i). *inter-individual*

- σ_e^2 = variance within an individual (variance of e_{ij}). *intra-individual*

- The correlation between measurements within an individual is:

$$\rho = \frac{\sigma_\alpha^2}{\sigma_\alpha^2 + \sigma_e^2}$$

Correlation induced by repeated measures, cont.

- Estimate the mean as:

$$\overline{Y} = \frac{1}{2m}\sum_{i=1}^{m}\sum_{j=1}^{2} Y_{ij}$$

- Naively estimate the variance (simple sample variance) of the average (ignoring correlation) as:

$$\hat{\mathrm{var}}(\overline{Y}) = \frac{s^2}{N} = \frac{\left[\frac{1}{N-1}\right]\sum_{i=1}^{m}\sum_{j=1}^{2}(Y_{ij}-\overline{Y})^2}{N}$$

cont.

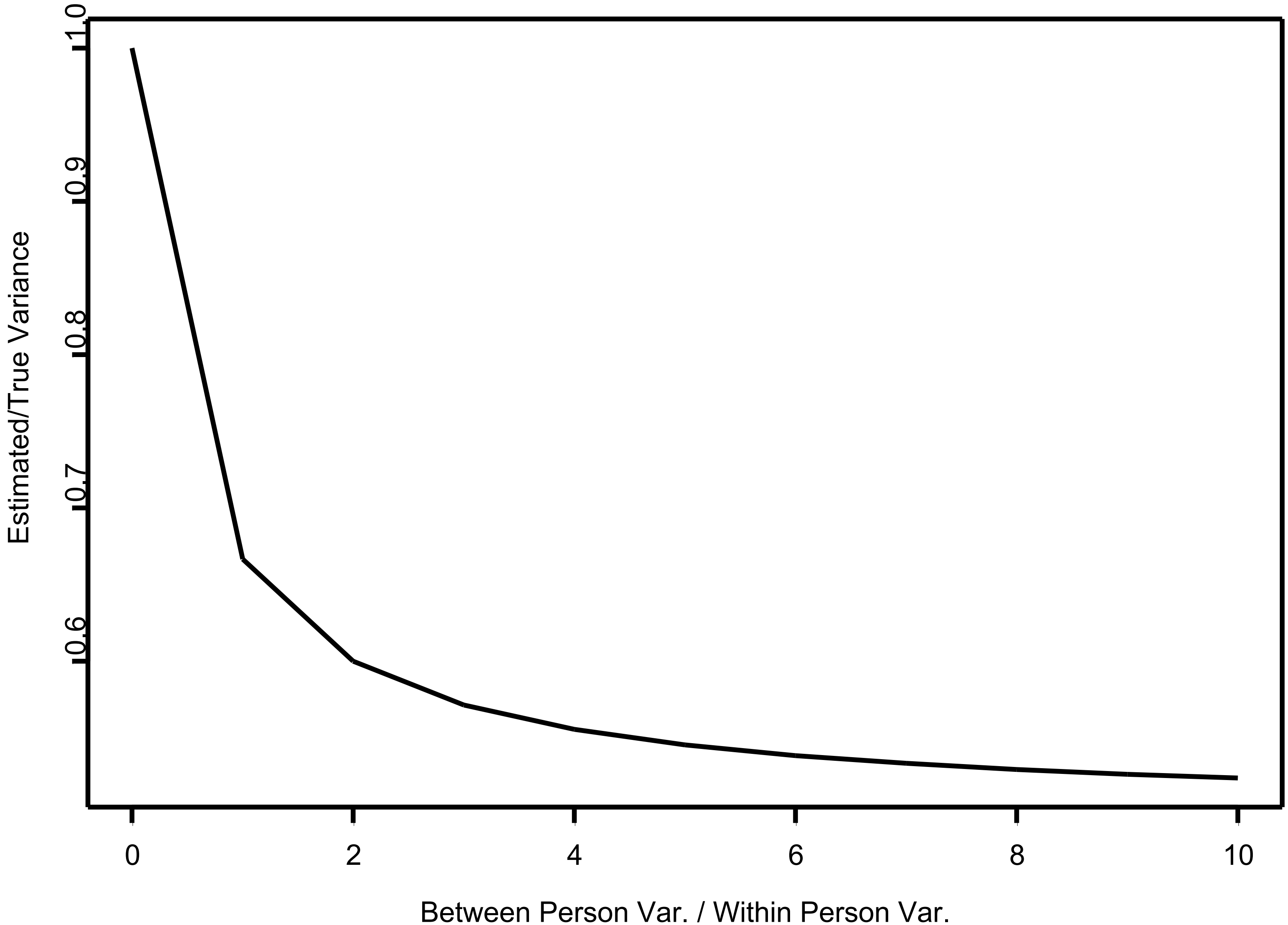
- Expected value of this variance estimate is:

$$\frac{\sigma_\alpha^2 + \sigma_e^2}{2m}$$

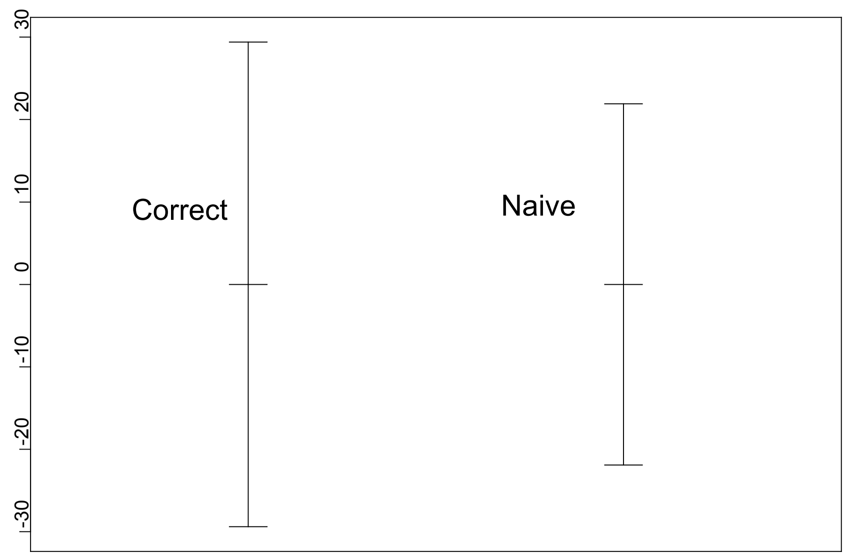
- However, because of the correlation induced by repeated measurements on the same individual, the true variance of the sample average is:

$$\frac{2\sigma_\alpha^2 + \sigma_e^2}{2m}$$

Ignoring Correlation and Inference on Mean



95% CI resulting from correct and naïve estimates of variance



2. Using longitudinal history in regression

- Make the covariates included in regression address the question of interest.
- In many cases, a cross-sectional study can be confounded in a way the longitudinal study is not.
- One way this can happen is how subjects are recruited over time.
- A hypothetical example: CD4 count and time since diagnosis of AIDS.

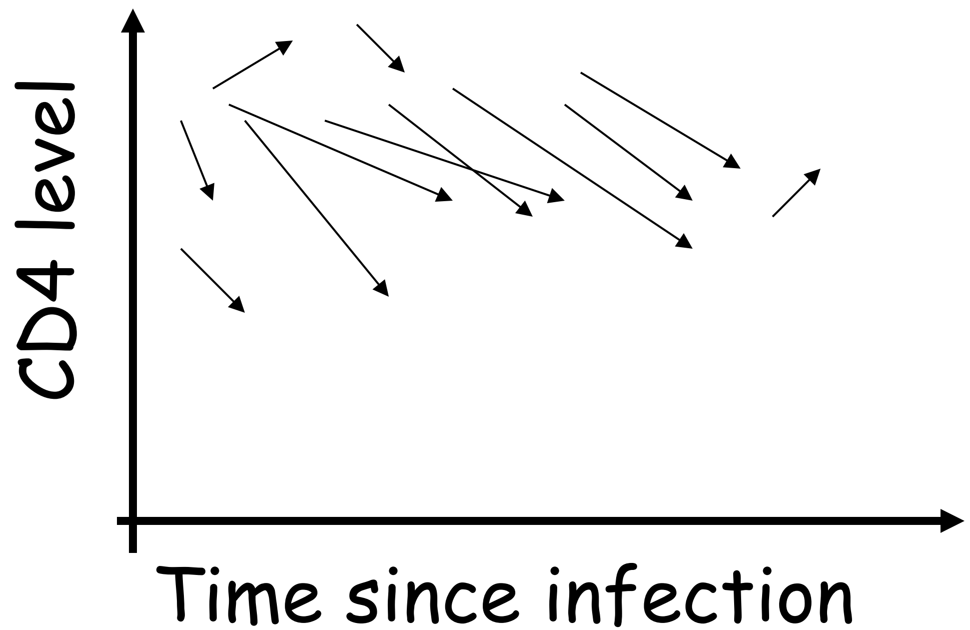
Longitudinal questions/parameters

- One might expect, particularly in an earlier era a true average decline in CD4 count with time since dx.

- However, if one recruits subjects and only measure once their CD4 counts and record the time since dx, a bias can result.

- Why?
  - (perhaps) subjects who live longer will have on average higher CD4 counts for their time since dx and,
  - because they live longer and they contribute more to the pool of people with longer times since diagnosis than subjects that have a steep decline, who tend to die earlier thus contributing less data.

Cross-sectional vs Longitudinal Information



(a) cross-sectional: CD4 doesn't change much in time

(b) longitudinally: CD4 decreases (on average) in time

Example from Diggle, et al.

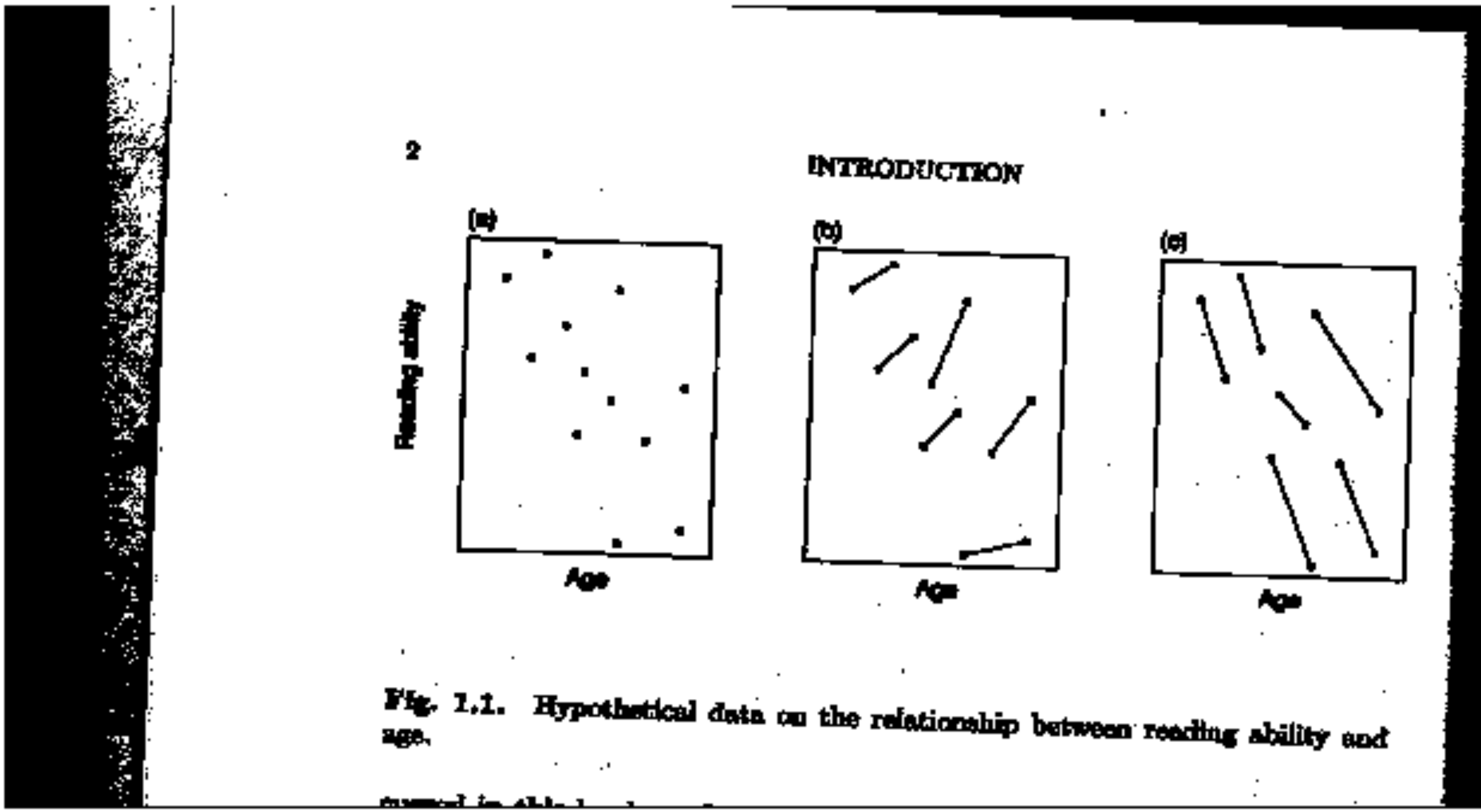

2 INTRODUCTION

Fig. 1.1. Hypothetical data on the relationship between reading ability and age.

Separating out longitudinal (interesting) from cross-sectional (maybe less interesting) effects

- Consider the model:

$$E[Y_{ij} \mid X_{i1} = x_{i1}, X_{ij} = x_{ij}] =$$

$$\beta_0 + \beta_C x_{i1} + \beta_L (x_{ij} - x_{i1})$$

- β_L represents the expected change in Y given a change in X_{ij} relative to the baseline value (X_{i1}) - longitudinal effect.

- β_C represents the expected difference in average Y across two sub-populations that differ by their baseline values, X_{i1} - cross-sectional effect.

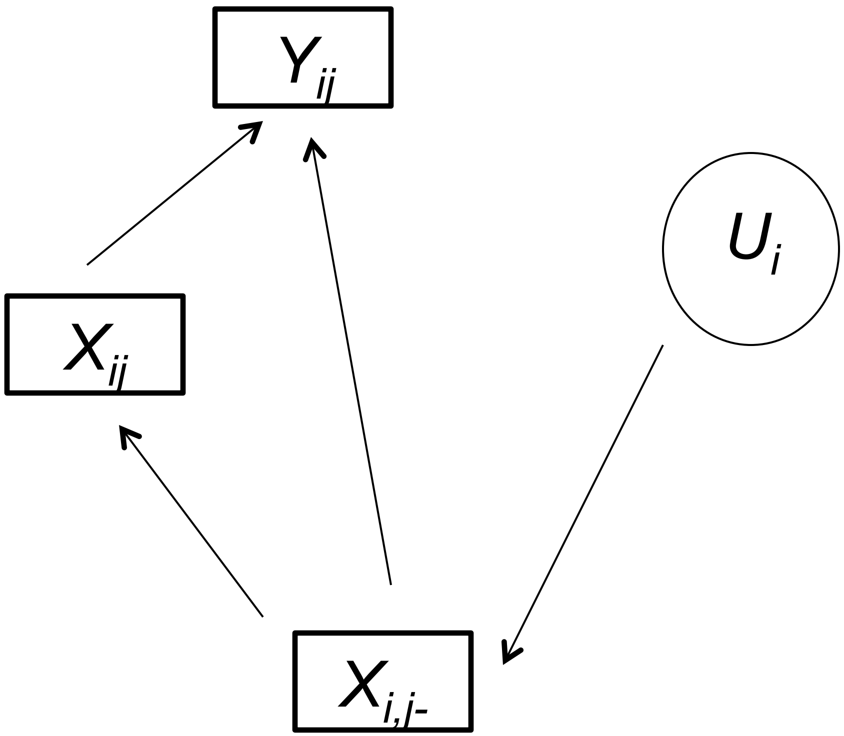
Only X-sectional Data

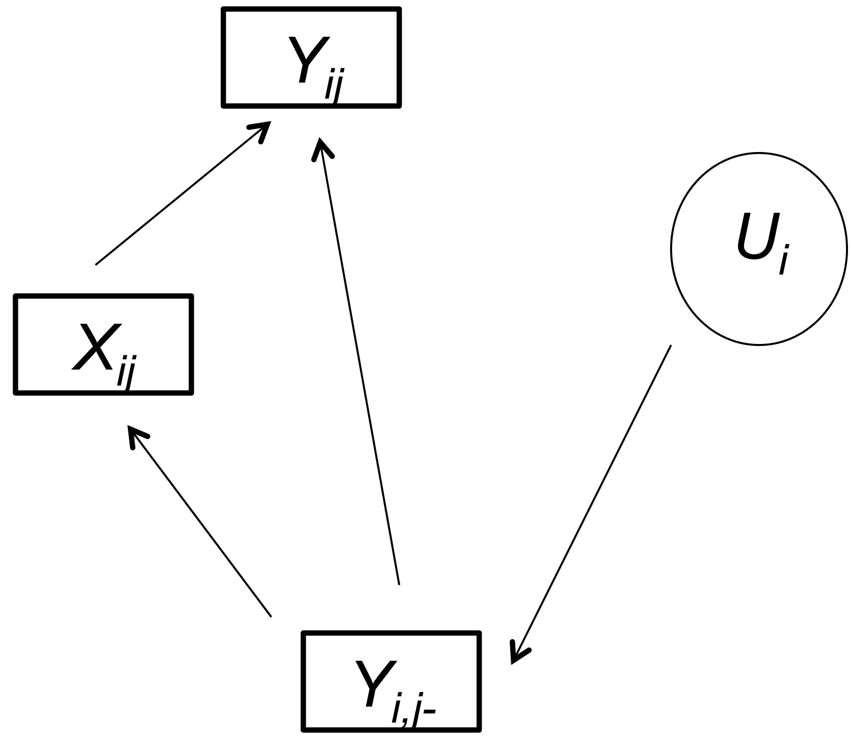
- In a x-sectional study, only can estimate:

$$E[Y_{i1} \mid X_{i1} = x_{i1}] = \beta_0 + \beta_C x_{i1}$$

- Can use cross-sectional data to estimate longitudinal effect only if $\beta_C = \beta_L$.

Longitudinal data gives more opportunity to adjust for unmeasured confounders

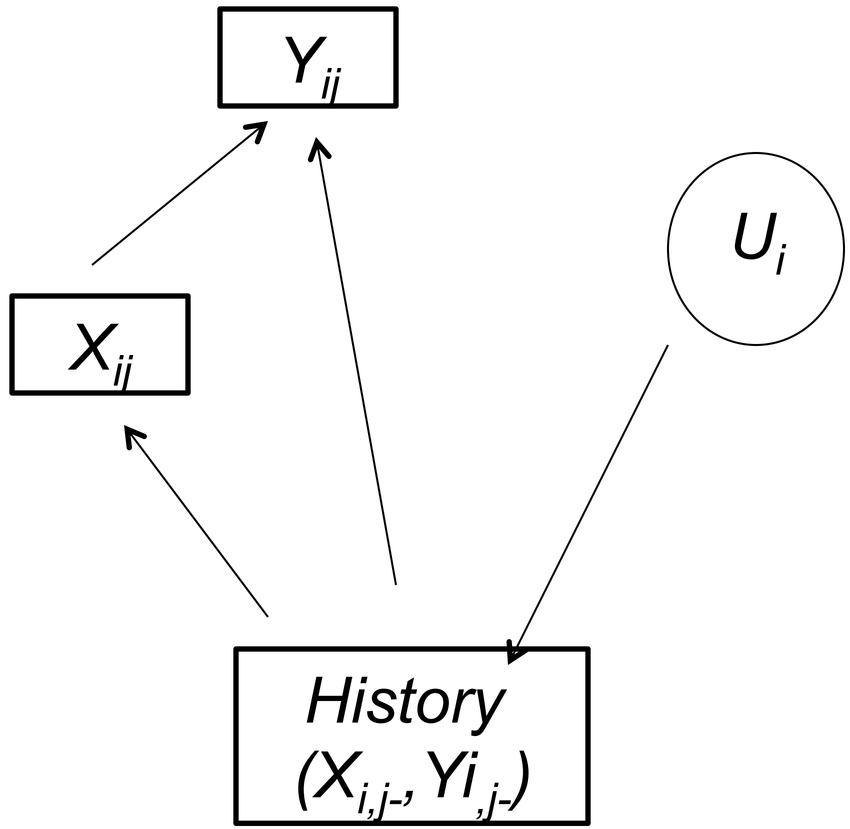




Unmeasured Confounder (U_i) blocked by past measure of covariates ($X_{i,j-}$).

Unmeasured Confounder (U_i) blocked by past measure of outcome ($Y_{i,j-}$).

Most Generally: Adjust for entire history



Still begs the question of how to adjust for history– we will discuss more later in the term, but in general…..

Regression using More complicated functions of past

- Parameterizing the model based on the measured past – i.e., whole past

$$E[Y_{ij} \mid \mathbf{X}_{i1}, \mathbf{X}_{i2}, \ldots, \mathbf{X}_{i(j-1)}, \mathbf{X}_{ij}, Y_{i1}, Y_{i2}, \ldots, Y_{i(j-1)}]$$

3. Partition of Variance

- One can use the repeated measures to distinguish the degree of variation in Y across time for one person from the variation in Y among persons.

- E.g., subject *j* within family *i*, measured at time *k*: $Y_{ijk} = b_0 + b_{0i} + b_{0ij} + e_{ijk}$

then under assumptions:

$$\mathrm{var}(Y_{ijk}) = \mathrm{var}(b_{0i}) + \mathrm{var}(b_{0ij}) + \mathrm{var}(e_{ijk})$$

4. Efficiency

- If the within subject variability is high, can gain a lot of efficiency by taking repeated measurements on the same subject.
  - Example - $Y_{ij} = \mu + \alpha_i + e_{ij}$

$$\bar{y}_{i.} \equiv \frac{1}{n_i} \sum_{j=1}^{n_i} y_{ij} \longrightarrow \mathrm{var}(\bar{y}_{i.}) = \sigma_\alpha^2 + \frac{\sigma_e^2}{n_i}$$

Re-Cap

- Is ignoring correlation of measurements on same individual (unit) OK?
  - For estimation – yes (usually) – although one can do better by not ignoring it.
  - For inference – NO!

- Advantages of Longitudinal Data
  - Can distinguish x-sectional from longitudinal effects (can eliminate some of the confounding due to individual-level differences by looking at change in outcome vs. change in explanatory variable).
  - Can model association of current outcome with entire history.
  - Partition Variance
  - Increased efficiency.