
Is “Dead” the same as “Missing”?

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NACC

National Alzheimer's Coordinating Center

Outline

- Introduce targets of inference in regression models
- Two examples of longitudinal data
 - Data missing due to dropout
 - Data recorded truncated by death
- Having the right covariates in a regression model doesn't guarantee having the right target of inference

Targets of Inference

$$E(Y_{ij}) = \beta_0 + \beta_1 \cdot X_{ij}$$

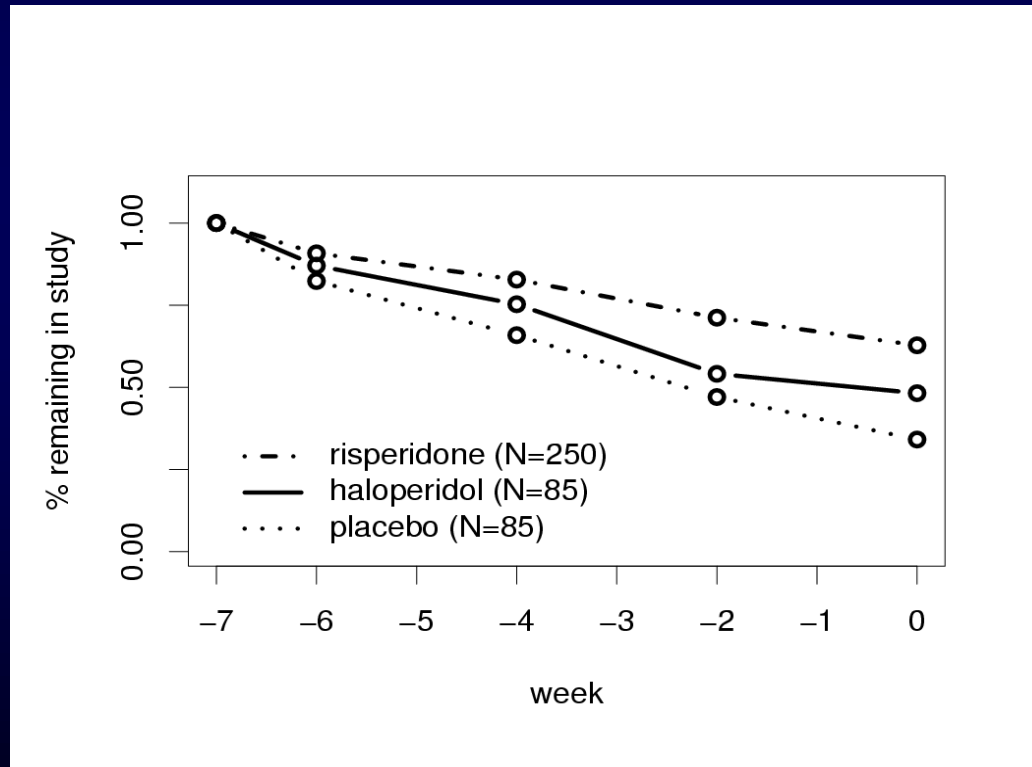
- Sampling influences interpretation
 - Cognitive functioning was maintained, *in the absence of disease*
 - Treatment was effective, *for those who followed the protocol*
 - Deterioration was faster in African Americans than in whites, *for ADC-registered patients*
- We report exclusions of enrolled subjects, but what conditioning is *implicit*?

Missing Data (Dropout) Example

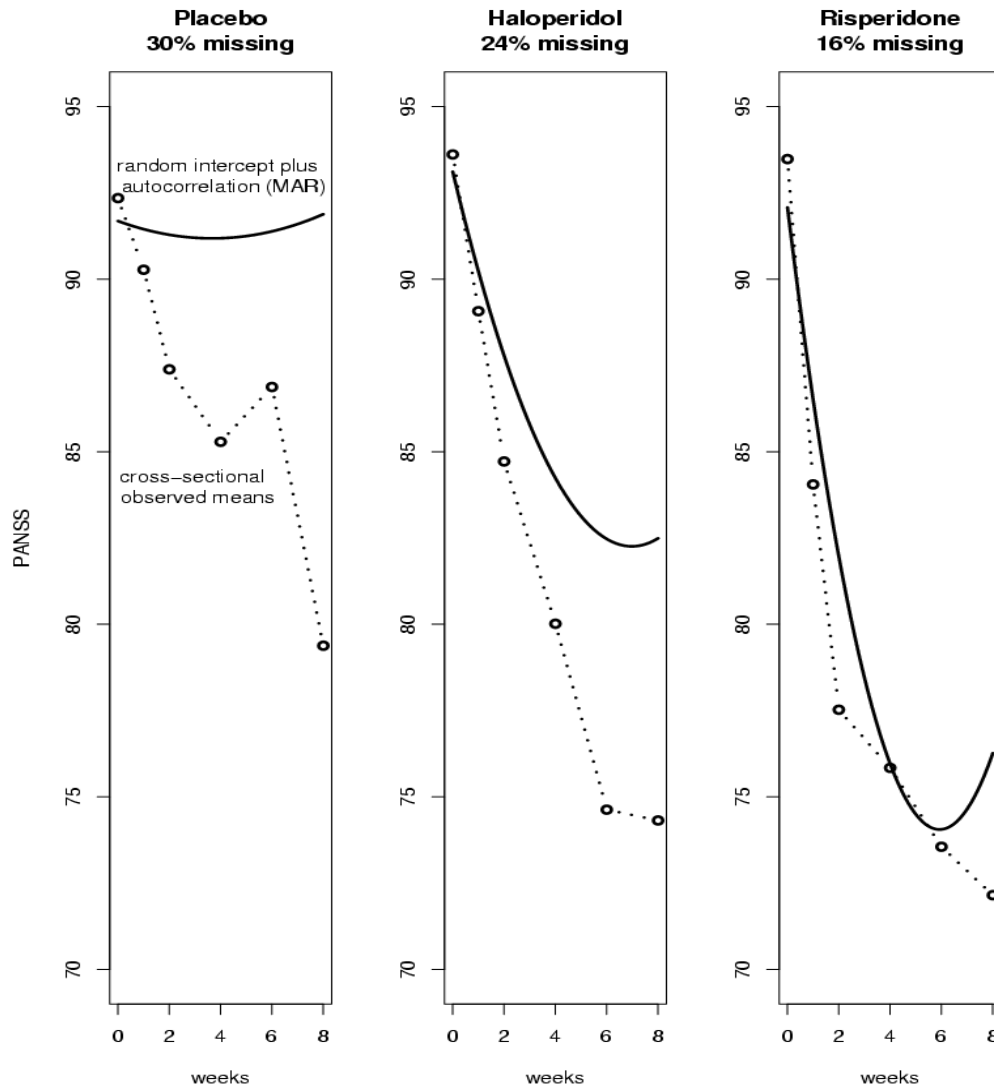
- Randomized Clinical Trial of 3 schizophrenia treatments
- Response variable – Positive and Negative Syndrome Scale (PANSS)
- 8 weeks of treatment (after washout), PANSS at 0,1,2,4,6,8 weeks

Missing Data (Dropout) Example

Considerable dropout in all three treatment groups



Missing Data (Dropout) Fitted Models



- Cross-sectional means
 - $E(\text{PANSS}|\text{observed})$
 - Have different people at each timepoint
- Linear mixed model
 - $E(\text{PANSS})$
 - No effect of placebo

Truncation Due to Death Example

- NACC Minimum Data Set (MDS)
- Mini-Mental State Examination (MMSE) for 500 living, 500 deceased
- Criteria
 - At least 3 MMSE (2 if deceased)
 - 30 days – 2 years between MMSE
 - MMSE within 1 year of death if deceased

Truncation Due to Death Fitted Models

- GEE with indep. corr. (linear regression)

$$E(Y_{ij}) = \beta_0 + \beta_1 \cdot X_{ij}$$

- Random intercept

$$E(Y_{ij}) = \beta_0 + b_{i0} + \beta_1 \cdot X_{ij}$$

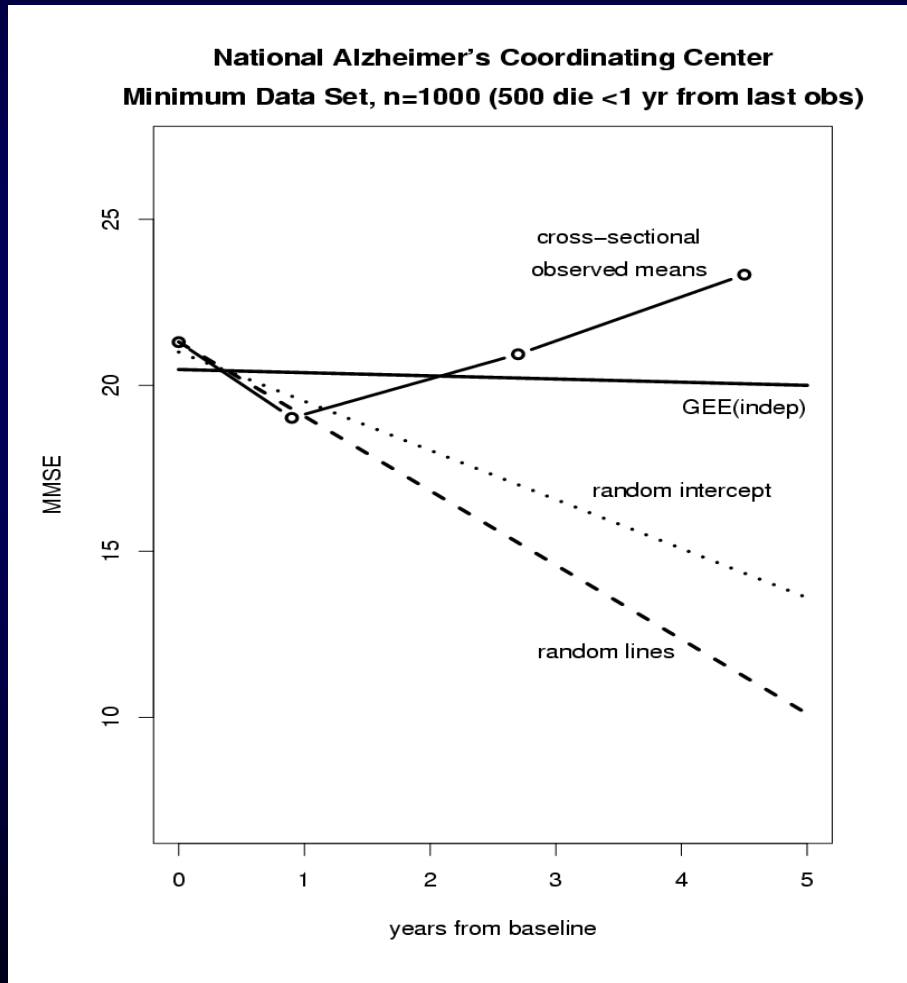
$$b_{i0} \sim N(0, \sigma^2)$$

- Random intercept and slope

$$E(Y_{ij}) = \beta_0 + b_{i0} + (\beta_1 + b_{i1}) \cdot X_{ij}$$

$$\underline{b_i} \sim N(0, D)$$

Truncation Due to Death Fitted Models



- GEE
 - $E(\text{MMSE}|\text{alive})$
 - Closest to observed means
- Linear Mixed Models
 - $E(\text{MMSE})$
 - Resurrect deceased subjects

Targets of Inference: Summary

- Sometimes you want to condition, sometimes you don't
- Can't always tell what you're conditioning on
- Slippery slope

Example: is there decline for “normal” elderly?

- AD, makes sense to exclude
- MCI, exclude?
- Preclinical MCI?...

Targets of Inference: Summary

- “Dead” is not the same as “Missing”
 - Think about desired target of inference
 - Look at models of longitudinal data that ignore correlation among responses
 - Check functional form (i.e., linearity) for the regression model you will interpret