* Subject $i \in$ Group 1

$$E[Y_{ij}] = \beta_1 + \beta_2 \cdot t_{ij} + \beta_3 t_{ij}^2$$

* Subject $k \in$ Group 2

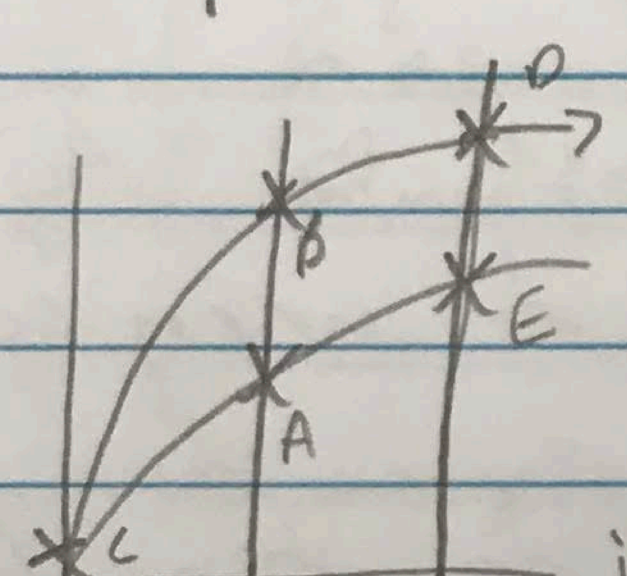
$$E[Y_{kj}] = \alpha_1 + \alpha_2 t_{ij} + \alpha_3 t_{ij}^2$$

* Same mean for ref group: $t_{i1} = 0$,

$$E[Y_{i1}] = E[Y_{k1}]$$

restriction on a theoretical mean, not observed $\beta_1 = \alpha_1$ $\leftarrow$ restrictions

t_{ij}	0	6	12	20	24
1	β_1				
2	β_1				



Are the curves identical?
(changes over the time are the same?)

if the same

$A - C = B - C$

$D - C = E - C$

$\beta_2 = \alpha_2$

$\beta_3 = \alpha_3$

$$\eta_{12} = \beta_1 + 6\beta_2 + 36\beta_3$$
$$\eta_{22} = \beta_1 + 6\alpha_2 + 36\alpha_3$$

Change: Group 1: $6\beta_2 + 36\beta_3$

Group 2: $6\alpha_2 + 36\beta_3$

Difference: $6[(\alpha_2 + 6\alpha_3) - (\beta_2 + 6\beta_3)]$

contrast that represents treatment effect

$\eta_{13} = \beta_1 + 12\beta_2 + 144\beta_3$

- $12[(\alpha_2 + 12\alpha_3) - (\beta_2 + 12\beta_3)]$

Other contrasts

Will find out that contrasts are linear combinations of each other. Only 2 are unique → those 2 make the others

Things to do
- Write down cell means
- contrasts
- linear combinations

Hyp test: Put all 4 contrasts in SAS, SAS will figure out only 2 unique

Fitting this → can put the two equations together

create var t_{ij} that is 1 for group 1, 0 for group 2, etc
- 5 covariates → 5 columns in design matrix

- another way: fit model where the rows are a factor (class) with 2 levels
→ model statement : t_{ij} t_{ij}^2 t_{ij} * group t_{ij}^2 * group (but there won't be a group main effects variable)

t_{ij}: slope for group 2, α_2 , t_{ij}^2: slope for group 2, α_3

$\underbrace{t_{ij} * \text{group} : \beta_2 - \alpha_2 \qquad t_{ij}^2 * \text{group} : \beta_3 - \alpha_3}_{\text{contrast, treatment effect}}$

make sure that t_{ij} and group are quantitative variables

group is 0 or 1

-> not class

don't say "class group"

REML: biased for β

$Y_1 \ldots Y_n$ iid $N(\mu, \sigma^2)$

$L_{REML}(\sigma^2, \underset{\sim}{K}) \Rightarrow \hat{\sigma}^2_{REML} = \frac{RSS}{n-1}$

$E[\hat{\sigma}^2_{REML}] = \sigma^2$

$E[\hat{\sigma}^2_{MLE}] = \frac{n-1}{n}\sigma^2 \quad \leftarrow \frac{RSS}{n}$

In more complicated models, not unbiased

If interested in $\frac{1}{\sigma^2} \rightarrow \frac{1}{\hat{\sigma}^2_{REML}}$

Not a linear function even though $\hat{\sigma}^2_{REML}$ is unbiased estimator of σ^2, $\frac{1}{\hat{\sigma}^2_{REML}}$ is not unbiased estimator of $\frac{1}{\sigma^2}$

WLS: $\hat{\mu} = \frac{1}{n}\sum_{i=1}^{n} Y_i = \frac{\sum Y_i / \hat{\sigma}^2_{REML}}{\sum 1 / \hat{\sigma}^2_{REML}}$

If OLS and WLS give you same $\hat{\beta}$, then that $\hat{\beta}$ will be unbiased

$E[\underset{\sim}{Y}] = X\underset{\sim}{\beta}$

$cov(\underset{\sim}{Y}) = \underbrace{\Sigma_{n\times n}(\underset{\sim}{\theta})}$ ← $q\times 1$

Σ is a function of θ, Σ depends on θ

$\hat{\beta}_{OLS} = (X^TX)^{-1}X^T\underset{\sim}{Y}$ ← can compute this w/out knowi

$E(\hat{\beta}_{OLS}) = (X^TX)^{-1}X^TE(\underset{\sim}{Y})$

$= (X^TX)^{-1}X^TX\beta$

$= \underset{\sim}{\beta}$

$\hat{\underset{\sim}{\eta}} = X\hat{\beta}_{OLS}$

$E(\hat{\underset{\sim}{\eta}}) = X\underset{\sim}{\beta} = \underset{\sim}{\eta}$

$\underset{\sim}{R} = \underset{\sim}{Y} - \hat{\underset{\sim}{\eta}}$ ← expected value is 0

$\hat{\beta}_{OLS}$ is unbiased. It might not be ideal b/c not using the appropriate weights, but unbiased

	ML	REML
$\underset{\sim}{\beta}$	generally biased	generally biased
determine $\underset{\sim}{\theta}$ cov matrix	generally biased	generally biased

$\underset{\sim}{\hat{\beta}} = (X^T\hat{\Sigma}^{-1}X)^{-1}(X^T\hat{\Sigma}^{-1}\underset{\sim}{Y})$ ← same for both ML and REML

Diff: $\hat{\Sigma}^{-1}$ plug in ML or REML when this happens

if $\hat{\underset{\sim}{\beta}} = (X^T \hat{\Sigma}^{-1} X)^{-1} (X^T \hat{\Sigma}^{-1} \underset{\sim}{Y}) = (X^T X)^{-1} X^T \underset{\sim}{Y}$

then $\hat{\underset{\sim}{\beta}}$ is unbiased

this happens when $Y_1, \ldots Y_n$ iid $N(\mu, \sigma^2)$

If you insist on unbiased estimators for variance, you might get negative estimator.

1. If unbiasedness is very important, use the OLS, but you <u>might</u> lose a lot of efficiency.

2. If you used $\hat{\beta}_{OLS}$, then to get the standard errors you still need to estimate Σ

$\mathrm{cov}(\hat{\beta}_{OLS}) = \mathrm{cov}(A\underset{\sim}{Y}) = A \Sigma A^T$ ← need to know sigma or estimate sigma

linear combination of Y $A: (X^T X)^{-1} X^T$

→ to compute standard errors

Lose efficiency: Less efficient, Less power, less precision

model-based (naive) Variance Estimator → h1 in GEE

If you trust in the structure of your covariance for standard errors

REML and MLE are consistent + asymptotically the same. Anything that is asymptotically normal number of independent objects

$$\sqrt{K}\,(\hat{\underset{\sim}{\beta}} - \underset{\sim}{\beta}) \xrightarrow{d} N(0, \Gamma')$$

$K^\delta \to \delta < 1$

HW K) ① No interaction → regressions on the baseline (4 of them)
- 4 slopes in control group same as 4 slopes in case group

② At baseline, 2 groups have same mean

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2 groups

randomization means these two are the same

$$\begin{bmatrix} \sigma_{11} & \sigma_{12} \\ \sigma_{21} & \sigma_{22} \end{bmatrix} \qquad \begin{bmatrix} \tau_{11} & \tau_{12} \\ \tau_{21} & \tau_{22} \end{bmatrix}$$

If the slopes are the same, then

same if lines are parallel

$$\frac{\sigma_{12}}{\sigma_{11}} \qquad \frac{\tau_{12}}{\tau_{11}}$$

same from randomization

HW 6 like the TLC analysis, just 1 more column

Exam: on material up to last week → but material today is similar