# 2/25/2010 36-402/608 ADA-II H. Seltman

## Handout #13: Repeated Measures (Part 1B)
## Extension of t-test and ANOVA to multivariate outcomes

1. Goals

   (a) Test whether there are treatment differences in a multivariate case where the dimension of $\boldsymbol{\mu}$ is, say, p>1, and $K$ is the number of treatments (including the control):

   $$H_0 : \boldsymbol{\mu}_1 = \cdots = \boldsymbol{\mu}_K$$

   (b) In a one-group case, simultaneously test whether there are differences in the means of the various measurements made on each experimental unit.

   $$H_0 : \mu_1 = \cdots = \mu_p$$

2. Multi-group case

   (a) Review: for $K = 2$ groups and $p = 1$ and $\bar{d} = \bar{x}_1 - \bar{x}_2$ and $\delta = \mu_1 - \mu_2$:

   $$T = \frac{\bar{d} - \delta_{\text{Hyp.}}}{\text{SE}(\bar{d})}$$

   $$T^2 = \text{F} = \text{MS}_B/\text{MS}_E = \bar{d}\,(\text{SE}^2)^{-1}\,\bar{d}$$

   - Constant variance assumption suggests: use $s_p^2$ from pooling
   - Estimate sampling variance $\text{SE}^2 = s_p^2/n_1 + s_p^2/n_2$.
   - $\text{SE}^2 = \frac{n_1+n_2}{n_1 n_2} s_p^2$

   (b) Extension for $K = 2$ $(n_1 + n_2), p$ measurements per subject

   - Let $\bar{\mathbf{d}}$ be the length $p$ column vector of the mean differences.
   - Let $\mathbf{S}$ be the pooled estimated variance-covariance matrix of the responses. (What is the size and what are in the diagonal and off-diagonal positions?)
   - Define
   $$T^2 = \frac{n_1 n_2}{n_1 + n_2}\,\bar{\mathbf{d}}'\,\mathbf{S}^{-1}\,\bar{\mathbf{d}}$$
   - Note that $T^2$ is a scalar.
   - If $\mathbf{S}$ is diagonal, then $T^2$ is just the sum of the individual t statistics, but if the multiple outcome measures are correlated, an appropriate correction is made.
   - Hotelling found that $\frac{n_1+n_2-p-1}{n_1+n_2-2}T^2$ is distributed as $F_{p,n_1+n_2-p-1}$ under $H_0 : \boldsymbol{\delta} = \mathbf{0}$.
   - What are the assumptions?

(c) Extension for $K \geq 2$ (MANOVA; M=multivariate)

- From the usual deviations, construct SSCP (sum of squares and cross products) matrices instead SS scalars.
- For just one treatment factor we have $\text{SSCP}_B$ for the treatment (between treatment groups) and $\text{SSCP}_W$ within treatment groups. Both are size $p$ by $p$.
- Construct MS matrices as SSCP/df.
- Calculate an F ratio matrix as $\text{MS}_B(\text{MS}_W)^{-1}$
- Need a scalar criterion to make a cut-off between null and alternative hypotheses: Hotelling's $T^2$, Wilks' lambda (equivalent to the likeilhood ratio test), Pillai's trace and Roy's greatest roots are alternatives using different combinations of the eigenvalues of the F matrix or $(\text{MS}_B + \text{MS}_W)(\text{MS}_W)^{-1}$

3. Single group case

   (a) Analogous to above, we'd be testing $\boldsymbol{\mu} = \mathbf{0}$, when we really want to simultaneously test whether pairs of means of the variables differ from each other.

   (b) We can construct $p - 1$ difference variables, then test $\boldsymbol{\mu} = \mathbf{0}$ for the *differences*. Then the test is $T^2 = n\ \mathbf{m}'\ \mathbf{S}^{-1}\mathbf{m}$ and $\frac{n-2}{2(n-1)}T^2$ follows the $F_{2,n-2}$ distribution when $\boldsymbol{\mu} = \mathbf{0}$.

4. Extra point: These methods have "general" variance covariance matrices, and do not make use of the ordering of the multiple values. As a supplement, classical repeated measures ANOVA looks at a set of orthogonal contrasts the focus on linear, quadratic, etc. trends (and assume equal spacings, and do not allow use of any data from any subject with at least one missing value).

5. Breakout and Discussion