The Use of Score Tests for Inference on Variance Components

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Overview

- *Linear mixed model: marginal* versus *hierarchical view*
- *Implications for likelihood ratio test*
- *Results for the score test case*
- *Results for scalar and vector case*
- *Application:* The rat data

A Simple Linear Mixed Model

$$y_{ij} = \boldsymbol{x_{ij}}'\boldsymbol{\beta} + b_i + \varepsilon_{ij}$$

$$\begin{cases} b_i \sim N(0, \tau^2) \\ \\ \varepsilon_{ij} \sim N(0, \sigma^2) \end{cases} \text{ind.}$$

$\Longrightarrow$

$$\boldsymbol{y_i} = \begin{pmatrix} y_{i1} \\ \vdots \\ y_{in_i} \end{pmatrix} \sim N\left[X_i\boldsymbol{\beta}, \begin{pmatrix} \sigma^2+\tau^2 & \cdots & \tau^2 \\ \vdots & \ddots & \vdots \\ \tau^2 & \cdots & \sigma^2+\tau^2 \end{pmatrix}\right]$$

Hierarchical:

$$\begin{cases} \sigma^2 > 0 \\ \tau^2 \geq 0 \end{cases}$$

$\Longrightarrow$

Marginal: $V_i = \tau^2 J_{n_i} + \sigma^2 I_{n_i}$ PD

The General Linear Mixed Model

$$\boldsymbol{y_i} = X_i\boldsymbol{\beta} + Z_i\boldsymbol{b}_i + \boldsymbol{\varepsilon}_i$$

$$\left\{\begin{array}{l}\boldsymbol{b}_i \sim N(\mathbf{0}, D) \\ \\ \boldsymbol{\varepsilon}_i \sim N(\mathbf{0}, \Sigma_i)\end{array}\right. \quad \text{ind.}$$

$\Longrightarrow$

$$\boldsymbol{y_i} = \begin{pmatrix} y_{i1} \\ \vdots \\ y_{in_i} \end{pmatrix} \sim N\left[X_i\boldsymbol{\beta} \ , \ V_i = Z_iDZ_i' + \Sigma_i \right]$$

Hierarchical:

$$\left\{\begin{array}{ll}\Sigma_i & \text{PD} \\ D & \text{PD}\end{array}\right.$$

$\Longrightarrow$

Marginal: $V_i = Z_iDZ_i' + \Sigma_i$ PD

Marginal $\neq$ Hierarchical

- Balanced data, two measurements per subject ($n_i = 2$)

- **Model 1** can follow from a hierarchical model:

$$\begin{pmatrix} Y_{i1} \\ Y_{i2} \end{pmatrix} = N \left[\begin{pmatrix} \mu_1 \\ \mu_2 \end{pmatrix}, \begin{pmatrix} 2 & 1 \\ 1 & 3 \end{pmatrix} \right]$$

- **Model 2** does not follow from a hierarchical model:

$$\begin{pmatrix} Y_{i1} \\ Y_{i2} \end{pmatrix} = N \left[\begin{pmatrix} \mu_1 \\ \mu_2 \end{pmatrix}, \begin{pmatrix} 2 & -1 \\ -1 & 3 \end{pmatrix} \right]$$

Marginal $\neq$ Hierarchical

- Balanced data, two measurements per subject ($n_i = 2$)

- **Model 1:** *Random intercepts + heterogeneous errors*

$$V = \begin{pmatrix} 1 \\ 1 \end{pmatrix} (d) \begin{pmatrix} 1 & 1 \end{pmatrix} + \begin{pmatrix} \sigma_1^2 & 0 \\ 0 & \sigma_2^2 \end{pmatrix} = \begin{pmatrix} d + \sigma_1^2 & d \\ d & d + \sigma_2^2 \end{pmatrix}$$

- **Model 2:** *Uncorrelated intercepts and slopes + measurement error*

$$V = \begin{pmatrix} 1 & 0 \\ 1 & 1 \end{pmatrix} \begin{pmatrix} d_1 & 0 \\ 0 & d_2 \end{pmatrix} \begin{pmatrix} 1 & 1 \\ 0 & 1 \end{pmatrix} + \begin{pmatrix} \sigma^2 & 0 \\ 0 & \sigma^2 \end{pmatrix} = \begin{pmatrix} d_1 + \sigma^2 & d_1 \\ d_1 & d_1 + d_2 + \sigma^2 \end{pmatrix}$$

Hierarchical versus Marginal: Testing

- **Marginal:**
  - ▷ Typically two-sided
  - ▷ Hypotheses in compound-symmetric case: $\boxed{\tau^2 = 0 \quad \textit{vs.} \quad \tau^2 \neq 0}$
  - ▷ Null distribution for likelihood ratio and score test: $\boxed{\chi^2_1}$

- **Hierarchical:**
  - ▷ Must be one-sided
  - ▷ Hypotheses in compound-symmetric case: $\boxed{\tau^2 = 0 \quad \textit{vs.} \quad \tau^2 > 0}$
  - ▷ Null distribution for likelihood ratio and . . .: $\boxed{\frac{1}{2}\chi^2_0 + \frac{1}{2}\chi^2_1}$

Two Questions

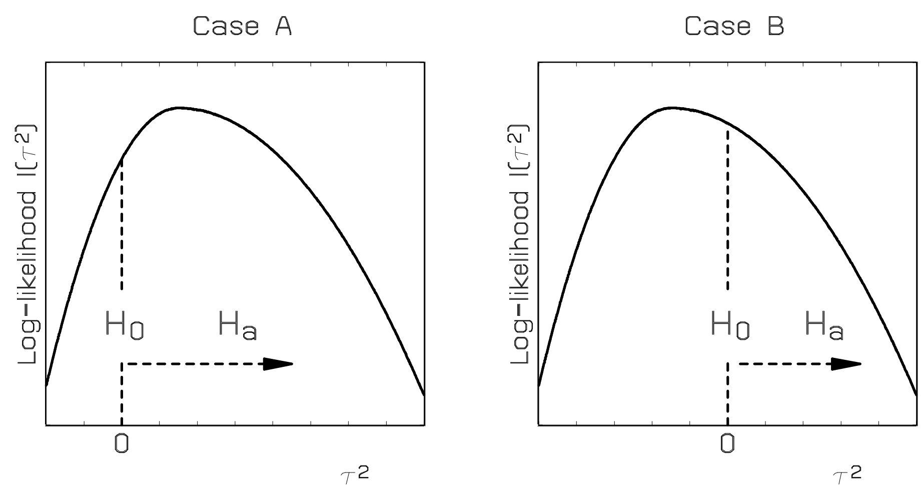
Vector parameter situation ?

and/or

Score test situation ?

One-sided, Scalar, Likelihood Ratio Test

$$T_{LR} = 2 \ln \left[\frac{\max_{H_0} \ell(\tau^2)}{\max_{H_a} \ell(\tau^2)} \right].$$



Case A	Case B
$P(T_{LR} > c \mid H_0, \hat{\tau}^2 \geq 0) P(\hat{\tau}^2 \geq 0 \mid H_0) = 0.5 P(\chi^2_1 > c)$	$P(T_{LR} > c \mid H_0, \hat{\tau}^2 < 0) P(\hat{\tau}^2 < 0 \mid H_0) = 0.5 P(\chi^2_0 > c)$
$P(T_{LR} > c \mid H_0) = \frac{1}{2} P(\chi^2_1 > c) + \frac{1}{2} P(\chi^2_0 > c)$	

More general: Nelder (1954), Chernoff (1954),
Self & Liang (1987), Stram & Lee (1994, 1995),
Shapiro (1988), Raubertas, Lee & Nordheim (1986)

Confusion About the Score Test

"No boundary problem since no fitting under H_a"

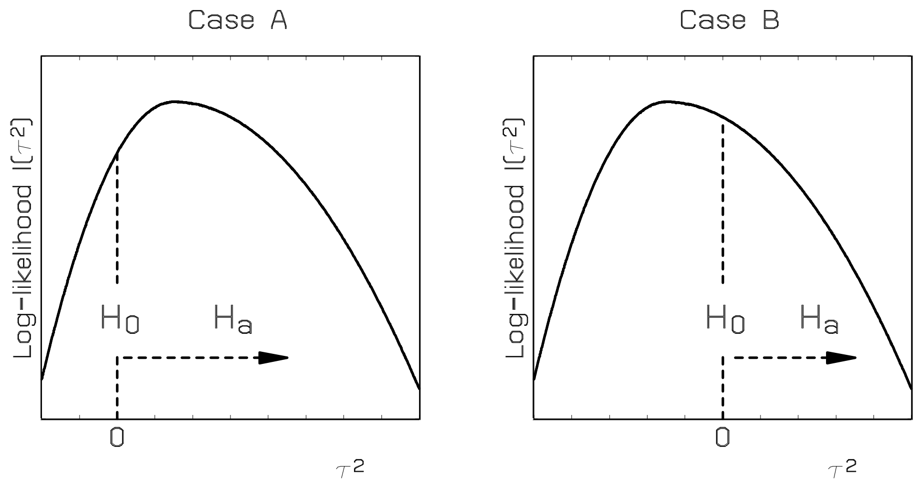
"LR and score not necessarily equivalent under non-standard conditions"

Various Views on Score Test Case

Unconstrained, two-sided view	Implicit	Jacqmin-Gadda & Commenges (1995) Lin (1997) le Cessie & van Houwelingen (1995)
	Explicit	Paul & Islam (1995)
Constrained, one-sided view		Silvapulle & Silvapulle (1995) Hall & Præstgaard (2001) Verbeke & Molenberghs (2003)

One-sided, Scalar, Score Test

$$T_S = \left[\left. \frac{\partial \ell(\tau^2)}{\partial \tau^2} \right|_{\tau^2=0} \right]^2 \left[- \left. \frac{\partial^2 \ell(\tau^2)}{\partial \tau^2 \partial \tau^2} \right|_{\tau^2=0} \right]^{-1}$$



Case A	**Case B**
$T_S = \left[\left. \frac{\partial \ell(\tau^2)}{\partial \tau^2} \right\|_{\tau^2=0} \right]^2 \left[- \left. \frac{\partial^2 \ell(\tau^2)}{\partial \tau^2 \partial \tau^2} \right\|_{\tau^2=0} \right]^{-1}$	$T_S = 0$
$P(T_S > c \| H_0, \hat{\tau}^2 \geq 0) P(\hat{\tau}^2 \geq 0 \| H_0) = 0.5 P(\chi^2_1 > c)$	$P(T_S > c \| H_0, \hat{\tau}^2 < 0) P(\hat{\tau}^2 < 0 \| H_0) = 0.5 P(\chi^2_0 > c)$
$P(T_S > c \| H_0) = \frac{1}{2} P(\chi^2_1 > c) + \frac{1}{2} P(\chi^2_0 > c)$	

Likelihood Ratio Test: General Results

- Historical: Nelder (1954)

  Chernoff (1954)

- Fundamental result: Self and Liang (1987)

- Variance components in mixed models: Stram and Lee (1994, 1995)

- Reparametrization (e.g., Cholesky decomposition) does not help

- Fairly general hypotheses: D_k *versus* D_{k+1}

- Null distribution for likelihood ratio test: $\frac{1}{2}\chi^2_k + \frac{1}{2}\chi^2_{k+1}$

- More general: Shapiro (1988)

  Raubertas, Lee, and Nordheim (1986)

Score Test: General Results

$$H_0 : \boldsymbol{\psi} = \mathbf{0} \qquad \textit{versus} \qquad H_a : \boldsymbol{\psi} \in \mathcal{C}$$

- $\mathcal{C}$: closed, convex cone in Euclidean space; vertex at origin

- Silvapulle & Silvapulle (1995)

- **A one-sided score test statistic:**

$$T_S := \boldsymbol{Z}'_N H^{-1}_{\psi\psi}(\widehat{\boldsymbol{\theta}}_H)\boldsymbol{Z}_N \;-\; \inf\big\{(\boldsymbol{Z}_N - \boldsymbol{b})' H^{-1}_{\psi\psi}(\widehat{\boldsymbol{\theta}}_H)(\boldsymbol{Z}_N - \boldsymbol{b}) | \boldsymbol{b} \in \mathcal{C}\big\}$$

One-sided Score Test

- Simplified notation:

$$T_S = \boldsymbol{Z}' H^{-1} \boldsymbol{Z} \ - \ \inf \left\{ (\boldsymbol{Z} - \boldsymbol{b})' H^{-1} (\boldsymbol{Z} - \boldsymbol{b}) | \boldsymbol{b} \in \mathcal{C} \right\}$$

- Special case: $\mathcal{C} = \mathbb{R}_+$

  Form of statistic:

$$\begin{cases} Z \geq 0 \ : \ T_S = \boldsymbol{Z} H^{-1} \boldsymbol{Z} \\ Z < 0 \ : \ T_S = 0 \end{cases}$$

- Equivalence: $T_{LR} = T_S + o_p(1)$

p values

from weighted sums of χ^2 variables

Structure of D	**Hypotheses**	**Null distribution**
Unstructured	D_k *vs.* D_{k+1}	$\frac{1}{2}\chi^2_k + \frac{1}{2}\chi^2_{k+1}$
Variance components	D_k diagonal *vs.* $D_{k+k'}$ diagonal	$\sum_{m=0}^{k'} 2^{-k'} \binom{k'}{m} \chi^2_m$

Estimation versus Testing in Mixed-Models Setting

	Estimation	**Testing**
Hierarchical	In line with intuition	*Extended theory*
Marginal	*Confusion about negative variance*	Classical theory

Summary of Result for Score Test

▷ General:

$$H_0 : \boldsymbol{\psi} = \mathbf{0} \qquad \text{vs.} \qquad H_a : \boldsymbol{\psi} \in \mathcal{C}$$

$\mathcal{C}$: closed, convex cone in Euclidean space; vertex at origin

▷ One-sided score test:

$$T_S = \boldsymbol{Z}' H^{-1} \boldsymbol{Z} - \inf\left\{(\boldsymbol{Z} - \boldsymbol{b})' H^{-1} (\boldsymbol{Z} - \boldsymbol{b}) | \boldsymbol{b} \in \mathcal{C}\right\}$$

▷ Equivalence:

$$T_{LR} = T_S + o_p(1)$$

▷ **But:** Calculation of one-sided T_S less straightforward

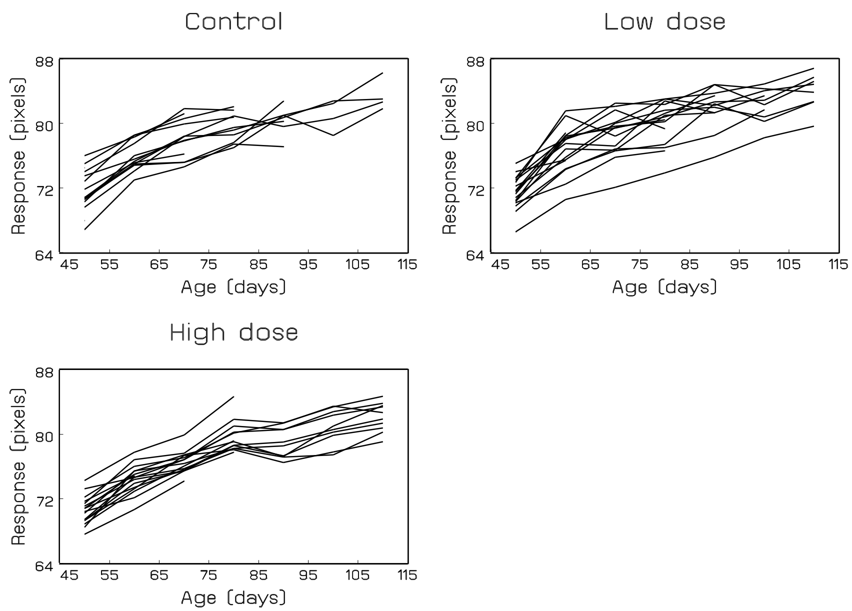
The Rat Data

- Department of Dentistry, K.U.Leuven

How does craniofacial growth depend on testosterone production ?

- Randomized experiment in which 50 male Wistar rats are randomized to:
  - ▷ Control (15 rats)
  - ▷ Low dose of Decapeptyl (18 rats)
  - ▷ High dose of Decapeptyl (17 rats)

The Rat Data



- Treatment starts at the age of 45 days.
- Measurements taken every 10 days, from day 50 on.
- The responses are distances (pixels) between well defined points on x-ray pictures of the skull of each rat, reflecting height of skull.

Model for Rat Data

$$Y_{ij} = \begin{cases} \beta_0 + b_{1i} + (\beta_1 + b_{2i})t_{ij} + \varepsilon_{ij}, & \text{if low dose,} \\ \beta_0 + b_{1i} + (\beta_2 + b_{2i})t_{ij} + \varepsilon_{ij}, & \text{if high dose,} \\ \beta_0 + b_{1i} + (\beta_3 + b_{2i})t_{ij} + \varepsilon_{ij}, & \text{if control.} \end{cases}$$

- $t = \ln(1 + (\text{Age} - 45)/10)$

- *Four sub-models:*
  - ▷ **Model 1:** no random effects
  - ▷ **Model 2:** random intercepts only ($\Rightarrow$ marginal: compound symmetry)
  - ▷ **Model 3:** random intercepts and random slopes; uncorrelated
  - ▷ **Model 4:** random intercepts and random slopes; correlated

Four Models

Model	Structure	One-sided	Two-sided
1	$D = \begin{pmatrix} 0 \end{pmatrix}$	$\widehat{D} = \begin{pmatrix} 0 \end{pmatrix}$	$\widehat{D} = \begin{pmatrix} 0 \end{pmatrix}$
2	$D = \begin{pmatrix} d_{11} \end{pmatrix}$	$\widehat{D} = \begin{pmatrix} 3.44 \end{pmatrix}$	$\widehat{D} = \begin{pmatrix} 3.44 \end{pmatrix}$
3	$D = \begin{pmatrix} d_{11} & 0 \\ 0 & d_{22} \end{pmatrix}$	$\widehat{D} = \begin{pmatrix} 3.44 & 0 \\ 0 & 0.00 \end{pmatrix}$	$\widehat{D} = \begin{pmatrix} 3.77 & 0 \\ 0 & -0.17 \end{pmatrix}$
4	$D = \begin{pmatrix} d_{11} & d_{12} \\ d_{12} & d_{22} \end{pmatrix}$	$\widehat{D} = \begin{pmatrix} 3.41 & 0.01 \\ 0.01 & 0.00 \end{pmatrix}$	$\widehat{D} = \begin{pmatrix} 2.83 & 0.48 \\ 0.48 & -0.33 \end{pmatrix}$

Results

Mod		Ref	LR test		Score test	
			One-sided	Two-sided	One-sided	Two-sided
1	$D = 0$					
2	$D = \left(d_{11} \right)$ $\widehat{D} = \left(3.44 \right)$	1	$1102.7 - 928.7 = 174$ $\frac{1}{2}\chi^2_0 + \frac{1}{2}\chi^2_1$ $p < 0.0001$	$1102.7 - 928.7 = 174$ χ^2_1 $p < 0.0001$	$27.15 - 0.0 = 27.15$ $\frac{1}{2}\chi^2_0 + \frac{1}{2}\chi^2_1$ $p < 0.0001$	27.15 χ^2_1 $p < 0.0001$
3	$D = \begin{pmatrix} d_{11} & 0 \\ 0 & d_{22} \end{pmatrix}$ $\widehat{D} = \begin{pmatrix} 3.77 & 0 \\ 0 & -0.17 \end{pmatrix}$	2	$928.7 - 928.7 = 0.0$ $\frac{1}{2}\chi^2_0 + \frac{1}{2}\chi^2_1$ $p = 1.0000$	$928.7 - 927.4 = 1.3$ χ^2_1 $p = 0.2542$	$1.67 - 1.67 = 0$ $\frac{1}{2}\chi^2_0 + \frac{1}{2}\chi^2_1$ $p = 1.0000$	1.67 χ^2_1 $p = 0.1963$
4	$D = \begin{pmatrix} d_{11} & d_{12} \\ d_{12} & d_{22} \end{pmatrix}$ $\widehat{D} = \begin{pmatrix} 2.83 & 0.48 \\ 0.48 & -0.33 \end{pmatrix}$	2	$928.7 - 928.6 = 0.1$ $\frac{1}{2}\chi^2_1 + \frac{1}{2}\chi^2_2$ $p = 0.8515$	$928.7 - 925.8 = 2.9$ χ^2_2 $p = 0.2346$	$2.03 - 1.93 = 0.1$ $\frac{1}{2}\chi^2_1 + \frac{1}{2}\chi^2_2$ $p = 0.8515$	2.03 χ^2_2 $p = 0.3624$

General Testing Result

- One-sided testing holds generally for vector (random-effects) case:

$$\boldsymbol{\psi} = \mathbf{0} \qquad \textit{versus} \qquad \boldsymbol{\psi} \in \mathcal{C}$$

- Covers important constrained cases in hierarchical models

- Likelihood ratio and score test statistic have same null distribution

- Critical level determined from mixtures of χ^2 variables

Unified Theory

- Same null distribution for:
  - ▷ Likelihood ratio test
  - ▷ Score test
  - ▷ *Wald test*
- Critical level determined from mixtures of χ^2 variables