Testing Differences in Glucose Profiles using AUC and Mixed Models

Presenter: Robbie A. Beyl, PhD
Problem Overview

Oral Glucose Tolerance test
• Subjects are given a glucose solution
• Glucose levels are measured at four time points

Goal
• Determine if treatment groups have different glucose profiles

Oral Glucose Tolerance Test

The pathologist will give you:
75 ml glucose drink

Then ask you to:
Wait 2 hours

Take blood and test glucose levels
$y_{itk}$ denotes the response for the $i^{th}$ treatment at the $t^{th}$ time for the $k^{th}$ subject

- $i = 1, 2$
- $t = 0, 60, 120, 180$

Adjust responses using baseline values for each subject

- $y_{itk} - y_{i0k}$
Area under the Curve

- Traditionally used to test differences in glucose profiles

Calculate AUC for each subject
- Trapezoid rule
  \[ z_{ik} \approx y_{i2k} + y_{i3k} + \frac{1}{2} y_{i4k} \]

Test \( \mu_{z_1} = \mu_{z_2} \)
- Two sample t-test
Consider only $t = 60, 120, 180$

Mixed effect linear model
- $Y = \beta_0 + \beta_1(t) + \beta_2(t_{rt} \times t) + \epsilon$
- Unstructured covariance matrix for each subject

Test $\beta_2 = 0$
- F-test
Simulation conducted under $H_0$: \[
\begin{pmatrix}
\mu_{160} \\
\mu_{1120} \\
\mu_{1180}
\end{pmatrix} = \begin{pmatrix}
\mu_{260} \\
\mu_{2120} \\
\mu_{2180}
\end{pmatrix}
\]

- 25 subjects for each treatment
- 1000 replications
- Values for population mean and standard deviation at each time point based on data obtained from Pennington Biomedical Research Center
Simulations

<table>
<thead>
<tr>
<th></th>
<th>AUC</th>
<th>Mixed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I error</td>
<td>0.058</td>
<td>0.0062</td>
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</tbody>
</table>

AUC

Mixed p-value

AUC p-value
## Crossing Profiles

<table>
<thead>
<tr>
<th>$t$</th>
<th>Treatment</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>60</td>
<td>104.4</td>
<td>110.3</td>
</tr>
<tr>
<td>120</td>
<td>90</td>
<td>105.6</td>
</tr>
<tr>
<td>180</td>
<td>70</td>
<td>30.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time</th>
<th>Glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>60</td>
<td>110.3</td>
</tr>
<tr>
<td>120</td>
<td>105.6</td>
</tr>
<tr>
<td>180</td>
<td>30.5</td>
</tr>
</tbody>
</table>

- **Treatment**
- **Control**

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**Graph:**
- Blue line: Treatment
- Red line: Control

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ASA Conference on Statistical Practice
Crossing Profiles

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<thead>
<tr>
<th></th>
<th>AUC</th>
<th>Mixed</th>
</tr>
</thead>
<tbody>
<tr>
<td>p-value</td>
<td>0.1978</td>
<td>0.0056</td>
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</tbody>
</table>

![Graph showing glucose levels over time for Treatment and Control groups.]

Time

Glucose
Both methods can give vastly different p-value
• No cases where mixed p-value is high and a AUC p-value is low

Crossing Profiles
• P-values from mixed procedure are generally lower than those from AUC procedure

Future plans include investigating the power of these tests when crossing profiles occur
Robbie A. Beyl  
Assistant Professor  
Biostatistics  
Pennington Biomedical Research Center  
6400 Perkins Rd.  
Baton Rouge, LA 70808  
USA  
Robbie.Beyl@pbrc.edu

Jeff H. Burton  
Assistant Professor  
Biostatistics  
Pennington Biomedical Research Center  
6400 Perkins Rd.  
Baton Rouge, LA 70808  
USA  
Jeffrey.Burton@pbrc.edu

William D. Johnson  
Professor  
Biostatistics  
Pennington Biomedical Research Center  
6400 Perkins Rd.  
Baton Rouge, LA 70808  
USA  
William.Johnson@pbrc.edu

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