The partial proportional odds model in the analysis of longitudinal ordinal data

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Notation

Problem: Analysis of ordinal longitudinal data
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Time, gender, age ...
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Domains: Medicine, psychology, social science,...
Motivating example - Quality of life

Dataset

- 247 patients with malignant brain cancer treated by RT+CT or RT
- Assessment of the quality of life at 8 occasions
  - Baseline, End RT, End RT + (3,6,9)months, End RT + (1, 1.5, 2)years
- EORTC QLQC30 questionnaire - Appetite loss scale
  - Have you lacked appetite? ('Not at all', 'A little', 'Quite a bit', 'Very much')
- Covariates: Time, Treatment (RT+CT vs RT), Tumor cell (pure vs mixed)
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Summary of the data

$N=247$, $T=8$, $K=4$
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Questions of interest

- Treatment effect
- Tumor cell effect
Proportional odds model

Aim is to find a model that takes into account

- the ordinal nature of the outcome under study
- the correlation between repeated observations
- the unavoidable presence of missing data
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**Proportional odds model**

\[
\text{logit}[\Pr(Y_{ij} \leq k)] = \theta_k + x_{ij}'\beta, \quad i = 1, \ldots, N; \quad j = 1, \ldots, T
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, \quad k = 1, \ldots, K - 1
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Properties: invariant when reversing the order of categories
deleting/collapsing some categories
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Assumption: relationship between \( Y \) and \( X \) is the same for all categories of \( Y \)
Testing the proportional odds model

Tests for assessing proportionality when the outcomes are uncorrelated were extended to longitudinal data (Stiger, 1999).

What if the proportional odds assumption is violated?

- Fitting a more general model
- Dichotomize the ordinal variable and fit separate binary logistic regression models (Bender, 1998).

Our solution

- Fitting a model that allows relaxing the proportional odds assumption when necessary
The partial proportional odds model (Peterson and Harrel, 1990) allows non-proportional odds for all or a subset $q$ of the $p$ explanatory covariates.

In univariate case,

$$\text{logit}[Pr(Y \leq k)] = \theta_k + x'\beta + z'\gamma_k, \quad k = 1, \cdots, K - 1$$

where $z$ is a $q$-dimensional vector ($q \leq p$) of the explanatory variables for which the proportional odds assumption does not hold and $\gamma_k$ is the ($q \times 1$) corresponding vector of coefficients and $\gamma_1 = 0$. When $\gamma_k = 0$ for all $k$, the model reduces to the proportional odds model.
Extension of the partial proportional odds model to longitudinal data (Donneau et al., 2010)

In a longitudinal setting,

$$\text{logit}[\Pr(Y_{ij} \leq k)] = \theta_k + x_{ij}'\beta + z_{ij}'\gamma_k , \quad i = 1, \cdots, N; \quad j = 1, \cdots, T; \quad k = 1, \cdots, K - 1$$

where $$(z_{i1}, \cdots, z_{iT})'$$ is a $$(T \times q)$$ matrix, $q \leq p$, of a subset of $q$-explanatory variables for which the proportional odds assumption does not apply and $\gamma_k$ is the $$(q \times 1)$$ corresponding vector of regression parameters with $\gamma_1 = 0$.

As an example ($p=2$ and $q=1$), assume that the proportional odds assumption holds for $X_1$ and not for $X_2$, then

$$\text{logit}[\Pr(Y_{ij} \leq k)] = \theta_k + \beta_1 X_1 + (\beta_2 + \gamma_{k,2})X_2$$
Estimation of the regression parameters

- GEE - extension of GLM to longitudinal data (Liang and Zegger, 1986)
- Define of a $(K - 1)$ expanded vector of binary responses
  \[ Y_{ij} = (Y_{ij,1}, \ldots, Y_{ij,(K-1)})' \] where $Y_{ijk} = 1$ if $Y_{ij} \leq k$ and 0 otherwise
- $\text{logit}[Pr(Y_{ij} \leq k)] = \text{logit}[Pr(Y_{ijk} = 1)] \rightarrow$ member of GLM family

\[
\sum_{i=1}^{N} \frac{\partial \pi_i'}{\partial \beta} W_i^{-1}(Y_i - \pi_i) = 0
\]

where $Y_i = (Y_{i1}, \ldots, Y_{iT})'$, $\pi_i = E(Y_i)$ and $W_i = V_i^{1/2} R_i V_i^{1/2}$ with $V_i$ the diagonal matrix of the variance of the element of $Y_i$. The matrix $R_i$ is the 'working' correlation matrix that expresses the dependence among repeated observations over the subjects.
Missing data

Missing data patterns

- Drop out / attrition
- Non-monotone missingness

Missing data mechanism (Little and Rubin, 1987)

- MCAR: Missing completely at random
- MAR: Missing at random
- MNAR: Missing not at random
Example : Appetite loss - (1) Treatment effect

Model

- Consider the model:

\[
\text{logit}[\Pr(Y_{ij} \leq k)] = \theta_k + (\beta_1 + \gamma_{k1})t_{ij} + (\beta_2 + \gamma_{k2})\text{Treat}_i + (\beta_3 + \gamma_{k3})t_{ij} \times \text{Treat}_i
\]

- \( k = 1, 2, 3 \)
- \( t_{ij} \): \( j^{th} \) time of measurement on subject \( i \)
- \( \text{Treat}_i \): treatment group (1 = RT+CT vs 0 = RT)

Assumption

- Missing data mechanism is MCAR (GEE)
- Proportional odds assumption is verified for \( t, \text{Treat} \) and \( t \times \text{Treat} \).
  - \( \gamma_{k,t} = 0 \) \( (p = 0.86) \)
  - \( \gamma_{k,Treat} = 0 \) \( (p = 0.21) \)
  - \( \gamma_{k,t \times Treat} = 0 \) \( (p = 0.17) \)
Example : Appetite loss - (1) Treatment effect

Model becomes

\[
\text{logit}[Pr(Y_{ij} \leq k)] = \theta_k + \beta_1 t_{ij} + \beta_2 \text{Treat}_i + \beta_3 (t_{ij} \times \text{Treat}_i), \quad k = 1, 2, 3
\]

Estimation

<table>
<thead>
<tr>
<th>Covariates</th>
<th>Estimate</th>
<th>SE</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\theta_1$</td>
<td>1.21</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>$\theta_2$</td>
<td>2.48</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>$\theta_3$</td>
<td>3.81</td>
<td>0.21</td>
<td></td>
</tr>
<tr>
<td>$t_{ij}$</td>
<td>0.08</td>
<td>0.04</td>
<td>0.033</td>
</tr>
<tr>
<td>$\text{Treat}_i$</td>
<td>-0.39</td>
<td>0.19</td>
<td>0.034</td>
</tr>
<tr>
<td>$t_{ij} \times \text{Treat}_i$</td>
<td>-0.12</td>
<td>0.05</td>
<td>0.009</td>
</tr>
</tbody>
</table>

A significant difference between treatment arms was found in favor of the RT alone treatment.
Example : Appetite loss - (2) Tumor cell effect

Model

- Consider the model:

\[
\logit[Pr(Y_{ij} \leq k)] = \theta_k + (\beta_1 + \gamma_{k1})t_{ij} + (\beta_2 + \gamma_{k2})Tumor_i + (\beta_3 + \gamma_{k3})t_{ij} \times Tumor_i
\]

- \( k = 1, 2, 3 \)
- \( t_{ij} \): \( j^{th} \) time of measurement on subject \( i \)
- \( Tumor_i \): type of diagnosed tumor (1=pure vs 0=mixed)

Assumption

- Missing data mechanism is MCAR (GEE)
- Proportional odds assumption is not met for \( t, Tumor \) and \( t \times Tumor \).
  \[
  \gamma_{k,t} = 0 \quad (p = 0.015)
  \]
  \[
  \gamma_{k,Tumor} = 0 \quad (p = 0.044)
  \]
  \[
  \gamma_{k,t \times Tumor} = 0 \quad (p = 0.008)
  \]
Example : Appetite loss - (2) Tumor cell effect

Estimations

Table 2: GEE parameter estimates for the appetite loss scale - Partial proportional odds model

<table>
<thead>
<tr>
<th>Covariates</th>
<th>k</th>
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<tbody>
<tr>
<td>$\theta_1$</td>
<td>1</td>
<td>-0.75</td>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td>$\theta_2$</td>
<td>2</td>
<td>1.58</td>
<td>0.41</td>
<td></td>
</tr>
<tr>
<td>$\theta_3$</td>
<td>3</td>
<td>1.93</td>
<td>0.78</td>
<td></td>
</tr>
<tr>
<td>$t_{ij}$</td>
<td>1</td>
<td>0.49</td>
<td>0.06</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>$t_{ij}$</td>
<td>2</td>
<td>-0.10</td>
<td>0.12</td>
<td>0.39</td>
</tr>
<tr>
<td>$t_{ij}$</td>
<td>3</td>
<td>0.53</td>
<td>0.22</td>
<td>0.015</td>
</tr>
<tr>
<td>$Tumor_j$</td>
<td>1</td>
<td>1.30</td>
<td>0.20</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>$Tumor_j$</td>
<td>2</td>
<td>0.45</td>
<td>0.33</td>
<td>0.18</td>
</tr>
<tr>
<td>$Tumor_j$</td>
<td>3</td>
<td>1.14</td>
<td>0.65</td>
<td>0.079</td>
</tr>
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<td>0.04</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>$t_{ij} \times Tumor_j$</td>
<td>2</td>
<td>0.092</td>
<td>0.097</td>
<td>0.34</td>
</tr>
<tr>
<td>$t_{ij} \times Tumor_j$</td>
<td>3</td>
<td>-0.32</td>
<td>0.16</td>
<td>0.04</td>
</tr>
</tbody>
</table>
Example: Appetite loss - (2) Tumor cell effect

\[ \text{logit} \left[ Pr(Y_{ij} \leq 1) \right] = -0.75 + 0.49t_{ij} + 1.30 \text{Tumor}_j - 0.34t_{ij} \times \text{Tumor}_j \]
\[ \text{logit} \left[ Pr(Y_{ij} \leq 2) \right] = 1.58 - 0.10t_{ij} + 0.45 \text{Tumor}_j + 0.092t_{ij} \times \text{Tumor}_j \]
\[ \text{logit} \left[ Pr(Y_{ij} \leq 3) \right] = 1.93 + 0.53t_{ij} + 1.14 \text{Tumor}_j - 0.32t_{ij} \times \text{Tumor}_j \]

where 1=’Not at all’, 2=’A little’, 3=’Quite a bit’, 4=’Very much’

Interpretation

▸ At baseline, pure cell tumor patients have \( e^{1.30} = 3.7 \) time higher odds of having no appetite loss than mixed cells tumor patients.

▸ At baseline, pure cell tumor patients have \( e^{0.45} = 1.6 \) time higher odds of having at most little appetite loss than mixed cells tumor patients.

▸ At baseline, pure cell tumor patients have \( e^{1.14} = 3.1 \) time higher odds of having at most quite a bite appetite loss than mixed cells tumor patients.
Conclusion

We have explored the extension of the partial proportional odds model to the case of longitudinal data

- Estimation mechanism (GEE)
- Testing for the proportional odds assumption for each covariate
- Final model that takes into account the ordinal nature of the variable under study
  takes into account the correlation between repeated observations
  allows relaxing the proportional odds assumption (when necessary)
- Missing data to be first investigated (GEE, WGEE, Mi-GEE)
Thank you for your attention