Modelling Physicians' Recommendations for Optimal Medical Care by Random Effects Stereotype Regression

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Program

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Motivation

36 physicians were asked to decide on the optimal rehabilitation setting for patients with traumatic brain injury (TBI).

Each one was given 10 typical TBI disease histories and the recommended rehabilitation setting (in-patient, day-clinic, out-patient) should be given.

Which factors (concerning physicians as well as disease histories) are influential on setting preferences?

Problems

1. Recommendations within one physician are expected to be correlated.

2. Is the response on an ordinal or on a multinomial scale?

3. Question (U. Hasenbein): 'Is the day-clinic setting more close to the in-patient or the out-patient setting?'

(Partial) Solutions

Solution Problem 1:

$\rightarrow$ Mixed models

Solution Problems 1+2:

$\rightarrow$ Mixed models for ordinal or multinomial responses
(Hedeker/Gibbons, 1994; Tutz/Hennevogl, 1996;
Hartzel/Caffo/Agresti, 2001)

Solution Problems 2+3:

$\rightarrow$ Stereotype regression model (Anderson, 1984)

But all three problems simultaneously???

The Model (Solution to Problems 1+2+3)

Interpret the Stereotype Modell as a non-linear regression model with random effects.

Concrete:

Given are $i = 1, \ldots, N$ clusters (physicians), each with T_i observations (disease histories).

Y_{ij} is the response value for observation j in cluster i, $j = 1, \ldots, T_i$ with response probability $\pi_{ijr} = P(Y_{ij} = r), r = 1, \ldots, R$.

x_{ij} is a vector of (fixed) covariates.

Model equation:

$$\log\left(\frac{\pi_{ijr}}{\pi_{ijR}}\right) = \theta_r + \phi_r \beta x'_{ij} + u_{ir}, \quad r = 1, \ldots, R-1,$$

with restrictions

$\theta_R = 0$, $\beta_R = 0$, $\phi_1 = 0$ and $\phi_R = 1$.

Assumption:

The random effects are normally distributed with an unstructured covariance matrix $\mathbf{\Sigma}$, e.g. for $u_i' = (u_{i1}, \ldots, u_{i,R-1})$ we have

$$u_i \sim N((0, \ldots, 0)', \mathbf{\Sigma}) \text{ with}$$

$$\mathbf{\Sigma} = \begin{pmatrix} \sigma^2_{11} & \sigma^2_{12} & \cdots & \sigma^2_{1,R-1} \\ & \sigma^2_{22} & \cdots & \sigma^2_{2,R-1} \\ & & \ddots & \vdots \\ & & & \sigma^2_{R-1,R-1} \end{pmatrix}$$

Features

- Derived from multinomial logistic RE model of Hartzel et al., 2001, by the non-linear parameter restriction $\beta_r = \phi_r \beta$.

- ML estimation is difficult: likelihood function is a product of N integrals which do not have closed form.

- More random effects (than just the intercepts) can be incorporated.

Estimation Methods

Adaptive Gauss-Hermite quadrature: Numerical integration, SAS PROC NLMIXED, yields 'exact' ML-estimates

Further: (work in progress) NPMLE, MCMC, Posterior mean estimation, Marginal models

Results

Response: Recommended rehabilitation setting (in-patient [reference], day-clinic [DC], out-patient [OP])

Covariates: all binary

- Is the physician a neurologist? (NEURO)
- Is the physician a specialist? (SPECIAL)
- Is time since TBI longer than 3 months (TIME)
- Is the patient severely handicapped after TBI (SEVERITY)

	RE Multinomial Model		RE Stereotype Model
	Fixed effects		
	DC	OP	
$\widehat{\beta}_{NEURO}$	-0.56 (0.74)	-0.36 (0.90)	1.36 (0.93)
$\widehat{\beta}_{SPECIAL}$	-0.63 (0.78)	-0.04 (0.94)	0.40 (0.88)
$\widehat{\beta}_{TIME}$	2.51 (0.41)	3.43 (0.50)	4.23 (0.58)
$\widehat{\beta}_{SEVERITY}$	-1.94 (0.43)	-3.29 (0.47)	-2.60 (0.53)
$\widehat{\phi}_2$	–	–	0.55 (0.09)
	Random effects		
$\widehat{\sigma}_1^2$	1.47 (0.35)	–	2.01 (0.96)
$\widehat{\sigma}_2^2$	–	1.87 (0.43)	2.62 (1.20)
$\widehat{\sigma}_{12}^2$	2.54 (1.11)		1.94 (0.93)
	Model selection criteria		
AIC	499.3		487.5
BIC	516.7		503.3

SAS PROC NLMIXED

```
proc nlmixed data=tbi;
     parms u2=-1.5 u3=-3 phi2=0.5
           b_special=1.5 ...
           sd2=2 sd3=2 cov23=2;

     eta  = b_special*special + b_neuro*neuro +
            b_time * time + b_severity*severity;

     p1=                   1 / (1+exp(u2 + phi2*eta)+exp(u3 + eta));
     p2= exp(u2 + phi2*eta)/ (1+exp(u2 + phi2*eta)+exp(u3 + eta));
     p3= exp(u3 +      eta)/ (1+exp(u2 + phi2*eta)+exp(u3 + eta));

     if resp1 then loglike=log(p1);  else
     if resp2 then loglike=log(p2);  else
                   loglike=log(p3);
     model setting ~ general(loglike);
     random u2 u3 ~ normal([a2,a3],[sd2,cov23,sd3])
                     subject=physician;
run;
```

Conclusion

- A random effects Stereotype regression model can easily be defined.

- Factors influencing physicians' recommendations for optimal medical care in TBI patients could be identified. Additional information about distances between response categories was gained.

- Estimation with standard software is possible.

- Still some things to do: simulation, different estimation methods.

Literature

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