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Workshop on Composite Likelihood Methods

Composite Likelihood Analysis of Mixed Autoregressive Probit Models with Application to Pain Severity Diaries

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joint with Claudia Czado, Munich

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Outline

- Pain severity diaries;
- data from some migraine sufferers living in Toronto;
- mixed autoregressive probit models for ordinal responses;
- composite likelihood inference and model selection;
- simulations and analysis of the migraine data.

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Pain severity diaries

- Longitudinal study of chronic and recurrent pain conditions, as migraine, back pain, ...
- patients record pain severity in a diary over a time period;
- rating scale of symptoms severity;
- electronic data collection (palmtop computers): data frequency can be very high;
- poor statistical analysis in medical journals...
- need for statistical methods to adequately deal with "large" longitudinal ordinal data.

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Headache and weather in Toronto?

- Longitudinal study conduced by psychologist Kostecki-Dillon during years 1993-1996;
- four daily ratings of the headache intensity recorded from 133 Canadian (Toronto) patients;
- weather conditions collected from the closest weather station;
- measurement periods varied in length from one day up to seven months.

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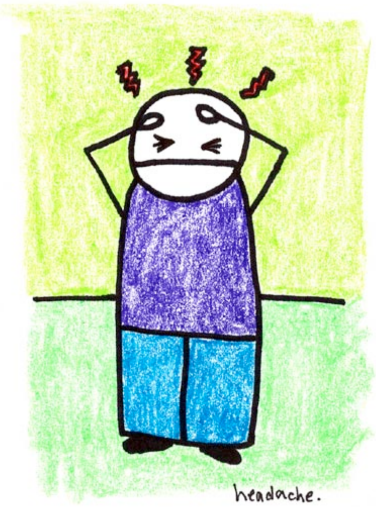
Headache and weather?

(Prince et al., *Headache* 2004)

- Forty-five million Americans seek medical attention for headaches yearly causing an estimated labor cost of $13 billions;
- Prince et al. found that about half (!?) of their migraine patients are sensitive to weather;
- other studies investigating the relationship between weather conditions and headache have been negative or inconclusive, e.g. Cooke et al. (*Headache*, 2000).



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Headache data

- Headache sufferers classified in three categories:

  a) migraine without aura,

  b) migraine with aura,

  c) mixed migraine/tension headache;
- omitted patients with very large number of missing observations in subsequent measurements or less than one day of measurements;
- final data set comprises 119 patients with a total of 16,366 measurements, 1,157 of which are missing.

Headache data

- 119 patients;
- number of observations per patients range from 16 (four days) to 1,352 (338 days), mean value 137.53 (34.38 days)
- number of observations per measurement period range from 4 (one day) to 852 (213 days), mean value 61.53 (15.38 days)
- unfortunately, all the weather conditions covariates are missing when responses are missing...

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Headache scale

intensity	freq.	condition
0	9210	no headache
1	2455	mild headache: aware of it only when attending.
2	1685	moderate headache: could be ignored at times.
3	1156	painful headache: continuously aware of it, but able to start or continue daily activities as usual.
4	526	severe headache: continuously aware of it, able to perform only undemanding tasks.
5	177	intense headache: continuously aware of it, incapacitating. Unable to start or continue activity.

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Covariates

- Personal: age, sex, education, work, marital status, smoke, ...
- clinical: assumption of analgesics, years suffering, comorbid illness, neuroticism, ...
- calendar: day, week, month, season;
- weather conditions from the closest weather station: sunshine, humidity, wind direction and speed, windchill, pressure, air quality, ...
- total number of covariates: 54!

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Modelling the migraine data

Components of a candidate model:

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Modelling the migraine data

Components of a candidate model:

- response on ordinal scale;

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Modelling the migraine data

Components of a candidate model:

- response on ordinal scale;
- regression term;

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Modelling the migraine data

Components of a candidate model:

- response on ordinal scale;
- regression term;
- allow for patients' heterogeneity;

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Modelling the migraine data

Components of a candidate model:

- response on ordinal scale;
- regression term;
- allow for patients' heterogeneity;
- allow for different pain-memory patterns in distinct groups of patients, e.g. females vs males, patients taking medicaments or not, patients with different kind of headache;

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Latent modelling of migraine data

Ordinal rate for t-th records in the j-th measurement period of the i-th subject seen as censored continuous observation

$$Y_{ijt} = k \leftrightarrow c_{k-1} < Y^*_{ijt} \le c_k, \quad k = 1, \ldots, 6,$$

for suitable cut-points, $-\infty = c_0 < c_1 < \ldots < c_6 = \infty$.

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The hidden process has baseline

$$Y^*_{ij1} = u_i + x'_{ij1}\beta + \epsilon_{ij1}$$

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$$Y^*_{ij1} = u_i + x'_{ij1}\beta + \epsilon_{ij1}$$

and subsequent (hidden) observations evolving as $(t \ge 2)$

$$Y^*_{ijt} = u_i + x'_{ijt}\beta + \eta_{ijt},$$

$$\eta_{ijt} = \gamma_{z_i}\eta_{ijt-1} + \epsilon_{ijt}.$$

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different autocorrelations for distinct groups of patients

Mixed autoregressive probit models

- Latent model:

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- Probabilistic assumptions:

a) Gaussian random effects, $u_i \stackrel{i.i.d.}{\sim} \mathcal{N}(0, \sigma^2)$

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b) Gaussian (hidden) innovations, $\epsilon_{ijt} \overset{i.i.d.}{\sim} \mathcal{N}(0, \sigma_\epsilon)$

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$\Downarrow$

mixed autoregressive probit model

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$\Downarrow$

mixed autoregressive probit model

- Identifiability: fix scale and position of Y^*_{ijt}, e.g.

a) first cut-point, $c_1 = 0$,

b) variance innovation, $\sigma^2_\epsilon = 1$.

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Likelihood inference?

- Likelihood function involves 119 (= number of patients) intractable integrals;
- each of the integrals has dimension equal to the number of obs per patients, here ranging from 16 (four days) to 1,352 (338 days)!
- Model obtained by categorizing a Gaussian state space model;
- ...but Kalman filter is not directly applicable!
- Monte Carlo methods as in Durbin and Koopman (2001) appear too costly, at least with actual technologies.
- Robustness issue (?) inference based on high-dimensional distributional assumptions...

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Pairwise likelihood of order m

Pseudolikelihood constructed from pairs apart not more than m units

$$c\ell^{(m)}(\theta; y) = \sum_{i=1}^{N} \sum_{j=1}^{n_i} w_{ij}\, p\ell_{ij}^{(m)}(\theta; y_{ij})$$

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$$\sum_{t=m+1}^{n_{ij}} \sum_{l=1}^{m \wedge (t-1)} \log \mathrm{P}_\theta \left(Y_{ijt} = y_{ijt}, Y_{ijt-l} = y_{ijt-l}\right) k_{ijt} k_{ijt-l}$$

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$$c\ell^{(m)}(\theta; y) = \sum_{i=1}^{N} \sum_{j=1}^{n_i} w_{ij} \boxed{p\ell_{ij}^{(m)}(\theta; y_{ij})}$$

obs per period

$$\sum_{t=m+1}^{n_{ij}} \sum_{l=1}^{m \wedge (t-1)} \log \mathrm{P}_\theta \left(Y_{ijt} = y_{ijt}, Y_{ijt-l} = y_{ijt-l} \right) k_{ijt} k_{ijt-l}$$

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w_{ij} period-specific weights,

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Pairwise likelihood of order m

Pseudolikelihood constructed from pairs apart not more than m units

$$c\ell^{(m)}(\theta; y) = \sum_{i=1}^{\overset{\text{patients}}{N}} \sum_{j=1}^{\overset{\text{measurement periods}}{n_i}} w_{ij}\, \boxed{p\ell_{ij}^{(m)}(\theta; y_{ij})}$$

$$\sum_{t=m+1}^{\overset{\text{obs per period}}{n_{ij}}} \sum_{l=1}^{m\wedge(t-1)} \log \mathrm{P}_\theta \left(Y_{ijt} = y_{ijt}, Y_{ijt-l} = y_{ijt-l}\right) k_{ijt} k_{ijt-l}$$

w_{ij} period-specific weights,
k_{ijt} missing value indicator.

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Pairwise terms

Probability of a pair of obs separated by *l* lags

$$\mathrm{P}_\theta(Y_{ijt} = a, Y_{ijt-l} = b) = \int_{c_{a-1}}^{c_a} \int_{c_{b-1}}^{c_b} f_\theta(y^*_{ijt}, y^*_{ijt-l}) \mathrm{d}y^*_{ijt} \mathrm{d}y^*_{ijt-l}$$

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$$\phi_2\left(\frac{y^*_{ijt}-x'_{ijt}\beta}{\sqrt{\sigma^2+(1-\gamma^2_{z_i})^{-1}}}, \frac{y^*_{ijt-l}-x'_{ijt-l}\beta}{\sqrt{\sigma^2+(1-\gamma^2_{z_i})^{-1}}}; \frac{\sigma^2+\gamma^l_{z_i}(1-\gamma^2_{z_i})^{-1}}{\sigma^2+(1-\gamma^2_{z_i})^{-1}}\right)$$

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approximation based on stationary assumption

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Period-specific weights

- Optimal weights difficult to be derived;
- comparison between:

a) unweighed pairwise likelihood of order m, versus

b) weighted version constructed under the extreme scenario of perfect dependence, *i.e.*

$$w_{ij} = \underbrace{\left(\sum_{t=m+1}^{n_{ij}} \sum_{l=1}^{m \wedge (t-1)} k_{ijt} k_{ijt-l} \right)}_{\text{number of pairs per period}}^{-1}$$

with this choice, pairwise likelihood equals the ordinary likelihood in case of perfect dependence.

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with this choice, pairwise likelihood equals the ordinary likelihood in case of perfect dependence.

but after H. Joe's talk, I understood that this is not the best comparison...

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Godambe information

The maximum pairwise likelihood estimator solves the composite likelihood score

$$u^{(m)}(\theta; y) = \sum_{i=1}^{N} u_i^{(m)}(\theta; y) = \sum_{i=1}^{N} \left(\sum_{j=1}^{n_i} w_{ij} \nabla p\ell_{ij}^{(m)}(\theta; y) \right)$$

Standard errors may be estimated from the observed Godambe information

$$\hat{\Sigma}^{(m)}(y) = \left\{ \hat{\mathrm{H}}^{(m)}(y) \right\}^{-1} \hat{\mathrm{J}}^{(m)}(y) \left\{ \hat{\mathrm{H}}^{(m)}(y) \right\}^{-1}$$

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(but Hessians may be avoided)

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$$\mathrm{J}^{(m)}(\hat{\theta}; y) = \frac{1}{N} \sum_{i=1}^{N} u_i^{(m)}(\hat{\theta}; y) u_i^{(m)}(\hat{\theta}; y)'$$

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One-step jackknife

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One-step jackknife

- Maximum pairwise likelihood estimators for the variance components prone of severe downward bias;

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One-step jackknife

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- jackknife: simple, although rough, bias-correction;

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One-step jackknife

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- jackknife: simple, although rough, bias-correction;
- one-step jackknife for computational convenience:

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One-step jackknife

- Maximum pairwise likelihood estimators for the variance components prone of severe downward bias;
- jackknife: simple, although rough, bias-correction;
- one-step jackknife for computational convenience:

$$\hat{\theta}_{-i} = \hat{\theta} + \left[\mathrm{H}_{-i}(\hat{\theta}; y)\right]^{-1} u_{-i}(\hat{\theta}; y)$$

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$$\tilde{\theta}_i = N\theta - (N-1)\hat{\theta}_{-i} \qquad \text{Tukey's pseudovalues}$$

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$$\hat{\theta}_J = \frac{1}{N}\sum_{i=1}^{N}\tilde{\theta}_i$$ one-step jackknife estimator

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$$\hat{\theta}_J = \frac{1}{N}\sum_{i=1}^{N}\tilde{\theta}_i$$ one-step jackknife estimator

- Tukey's pseudovalues may be used to obtain standard errors estimates somehow more robust than the sandwich estimate.

Model selection

Two model selection problems...

a) identifying the pairwise likelihood order:

$$m = \underset{m \in \mathbb{N}_+}{\operatorname{argmin}} \left[\operatorname{tr} \left\{ \hat{\Sigma}^{(m)}(y) \right\} \right]$$

b) given the order, selecting the model by minimising the composite likelihood information criterion

$$\mathrm{CLIC}^{(m)} = -2\, c\ell^{(m)}(\hat{\theta}; y) + 2 \operatorname{tr} \left\{ \mathrm{H}^{(m)}(y) \hat{\Sigma}^{(m)}(y) \right\}$$

Need to iterate between order identification and model selection.

A single model selection procedure would be preferable...

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Code

- maop: R package for binary and ordinal probit models with or without random effects and autocorrelations;
- calls to C for more demanding operations;
- bivariate Gaussian integrals approximated by Fortran 77 routine written by A. Genz (1996, JCGS);
- starting values from MASS function polr (Venables and Ripley, 2002) assuming absence of the random effect and null autocorrelation;
- plan to make the package public available through CRAN.

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Simulation studies

- Data generated mimicking the migraine data structure in terms of patients, measurement periods and missing responses;
- assumed model:

  a) regression: 12 regressors most of them categorical, included also time-varying (weather) covariates. Total no. of mean parameters is 25 + 4 cut-points;

  b) association: random effect, different autocorrelation for patients who take prophylactic medication and those who do not;
- 500 simulated data sets with parameter values set at MPLE of order 4;
- data fitted by MPLE of order from 1 to 10.

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c_4	2.209	0.010	0.054	0.005	0.061	0.000	0.035
c_5	3.131	0.021	0.082	0.010	0.098	0.003	0.062
intercept	-0.991	-0.001	0.316	0.012	0.357	0.015	0.366
edlev2	-0.423	-0.001	0.277	0.010	0.297	0.010	0.308
edlev3	-0.236	-0.004	0.229	-0.010	0.261	0.006	0.236
edlev4	-0.322	-0.023	0.315	-0.014	0.400	0.005	0.358
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neo5	-0.036	-0.003	0.339	0.004	0.411	0.026	0.427
wdir.nwY	0.263	0.000	0.072	-0.004	0.080	-0.002	0.055
wc:neo2	0.000	0.001	0.020	0.000	0.022	-0.002	0.017
wc:neo3	0.033	0.001	0.016	0.000	0.017	0.000	0.020
wc:neo4	0.036	0.000	0.019	-0.001	0.021	0.001	0.021
wc:neo5	0.033	0.001	0.016	0.001	0.018	-0.001	0.019
γ_{no}	0.614	0.016	0.052	0.011	0.069	-0.009	0.047
γ_{yes}	0.243	-0.019	0.100	-0.002	0.137	0.080	0.144
σ	0.761	-0.139	0.089	0.013	0.107	0.034	0.097

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	true	WMCL bias	WMCL st.err.	jack-WMCL bias	jack-WMCL st.err.	jack-MCL bias	jack-MCL st.err
c_2	0.774	0.002	0.026	0.002	0.029	0.001	0.018
c_3	1.466	0.005	0.039	0.003	0.044	0.001	0.026
c_4	2.209	0.010	0.054	0.005	0.061	0.000	0.035
c_5	3.131	0.021	0.082	0.010	0.098	0.003	0.062
intercept	-0.991	-0.001	0.316	0.012	0.357	0.015	0.366
edlev2	-0.423	-0.001	0.277	0.010	0.297	0.010	0.308
edlev3	-0.236	-0.004	0.229	-0.010	0.261	0.006	0.236
edlev4	-0.322	-0.023	0.315	-0.014	0.400	0.005	0.358
working2	0.562	0.000	0.278	0.007	0.312	-0.041	0.316
working3	0.280	-0.005	0.222	-0.008	0.248	0.008	0.197
sexM	-0.207	-0.002	0.236	0.006	0.276	0.009	0.480
married2	0.458	-0.015	0.178	-0.013	0.203	-0.006	0.218
married3	0.531	0.009	0.250	0.016	0.281	0.009	0.333
hatype2	0.125	0.014	0.198	0.018	0.251	-0.013	0.221
hatype4	0.460	0.011	0.313	0.011	0.378	-0.015	0.311
medanalgY	1.030	0.009	0.228	0.004	0.273	-0.009	0.231
medprophY	0.511	0.001	0.191	0.006	0.213	-0.017	0.215
cophysY	-0.286	0.003	0.159	-0.003	0.175	0.015	0.221
bed	-0.101	-0.002	0.035	0.000	0.038	0.001	0.021
wc	-0.020	-0.001	0.012	-0.001	0.013	0.000	0.013
neo2	-0.353	0.006	0.264	0.009	0.290	0.002	0.377
neo3	-0.476	0.001	0.267	-0.001	0.299	0.022	0.278
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neo5	-0.036	-0.003	0.339	0.004	0.411	0.026	0.427
wdir.nwY	0.263	0.000	0.072	-0.004	0.080	-0.002	0.055
wc:neo2	0.000	0.001	0.020	0.000	0.022	-0.002	0.017
wc:neo3	0.033	0.001	0.016	0.000	0.017	0.000	0.020
wc:neo4	0.036	0.000	0.019	-0.001	0.021	0.001	0.021
wc:neo5	0.033	0.001	0.016	0.001	0.018	-0.001	0.019
γ_{no}	0.614	0.016	0.052	0.011	0.069	-0.009	0.047
γ_{yes}	0.243	-0.019	0.100	-0.002	0.137	0.080	0.144
σ	0.761	-0.139	0.089	0.013	0.107	0.034	0.097

Simulations

- Regressor parameters very similarly estimated with any choice of the pairwise likelihood order;
- association parameters instead quite badly estimated with pairwise likelihood of order 1;
- also one-step jaccknife estimators somehow numerically unstable with pairwise lik of order 1;
- difficulties fixed by using order 2 or more;
- very small differences from order 2 to 10...

order	1	2	3	...	10
$\mathrm{tr}(\hat{\Sigma}^{(m)})$	2.064	1.718	1.754	...	1.713

Migraine data analysis

- Models fitted by pairwise likelihood of order 4;
- one-step jackknife for bias-correction and standard errors estimate;
- models selected in a hierarchical way:

  a) person-specific covariates;

  b) measurement time covariates;

  c) weather covariates;

  d) iterations;
- all models include patient-specific random effects;
- different autocorrelation for distinct groups of patients.

Migraine data analysis

The “final model” includes:

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Migraine data analysis

The "final model" includes:

- working conditions

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Migraine data analysis

The "final model" includes:

- working conditions worse for part-time or not working

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- marital status

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The "final model" includes:

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- marital status worse for singles

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The "final model" includes:

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- assumption of analgesics

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- prophylactic headache medication

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- different autocorrelation for males and females
  more persistence of symptoms for females but...

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married2	0.467	0.158	2.952		0.457	0.158	2.891
married3	0.385	0.224	1.715		0.391	0.218	1.795
medanalgY	0.955	0.194	4.925		0.949	0.196	4.848
medprophY	0.507	0.202	2.510		0.513	0.204	2.518
bed	-0.102	0.053	1.935		-0.101	0.052	1.930
cophysY	-0.330	0.146	2.268		-0.328	0.145	2.265
neo2	0.061	0.134	0.458		0.060	0.132	0.456
wc	-0.019	0.008	2.262		-0.019	0.008	2.270
neo2:wc	0.034	0.011	3.072		0.033	0.011	2.973
γ	0.451	0.034	13.170	F	0.518	0.054	9.555
				M	0.256	0.145	1.766
σ	0.869	0.076	11.416		0.833	0.079	10.528

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Migraine data analysis

autocorr.	$c\ell(\hat{\theta}; y)$	CLIC
sex	-646.889	1309.688
constant	-647.129	1309.746
neuroticism	-646.953	1310.103
analgesic	-647.082	1310.218
prophylactic	-646.910	1310.505
hatype	-646.881	1310.773

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Sexual differences?

- The models with constant and sex-based autocorrelation have very similar estimates of the regressors and the random effect;
- CLIC suggests a slightly better fit for the "sex model";
- this is in contrasts with the Wald test:

$$\hat{\gamma}_{\mathrm{F}} - \hat{\gamma}_{\mathrm{M}} = 0.262 \text{ with standard error } 0.186;$$

- but Wald test may be quite inexact...
- either CLIC may be imprecise because of the numerical difficulties associated with the penalty...

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Parametric bootstrap

- Testing the hypothesis

$$\begin{cases} \mathrm{H}_0 : & \gamma_{\mathrm{F}} = \gamma_{\mathrm{M}} \\ \mathrm{H}_1 : & \gamma_{\mathrm{F}} \neq \gamma_{\mathrm{M}} \end{cases}$$

  by the composite likelihood ratio W(y).
- Overcome difficulties of the nonstandard asymptotic distribution of W(y) by simple parametric bootstrap:

$$\hat{p} = \frac{1 + \sum_{b=1}^{B} \mathrm{I}_{\{W(y_b^*) \geq W(y)\}}}{1 + B}$$

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- Migraine data: estimated p-value using 500 bootstrap samples equals to 0.243: no sexual differences.

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Conclusions

- Numerical difficulties with approximating the variance of the gradient suggest care with Wald-type and CLIC-statistics;
- some kind of model-averaging? compromise estimators as in Hjort and Claeskens (2003, JASA)?
- optimal cluster-specific weights? Joe and Lee's work...
- improving the one-step jackknife? yes, but care to be paid on the computational complexity!
- extending the model to deal with time-irregular data by replacing the autoregressive residuals with variogram-type models.

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Reference

Varin, C. and Czado, C. (2008). A mixed probit model for the analysis of pain severity data. (submitted)

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www.dst.unive.it/~sammy

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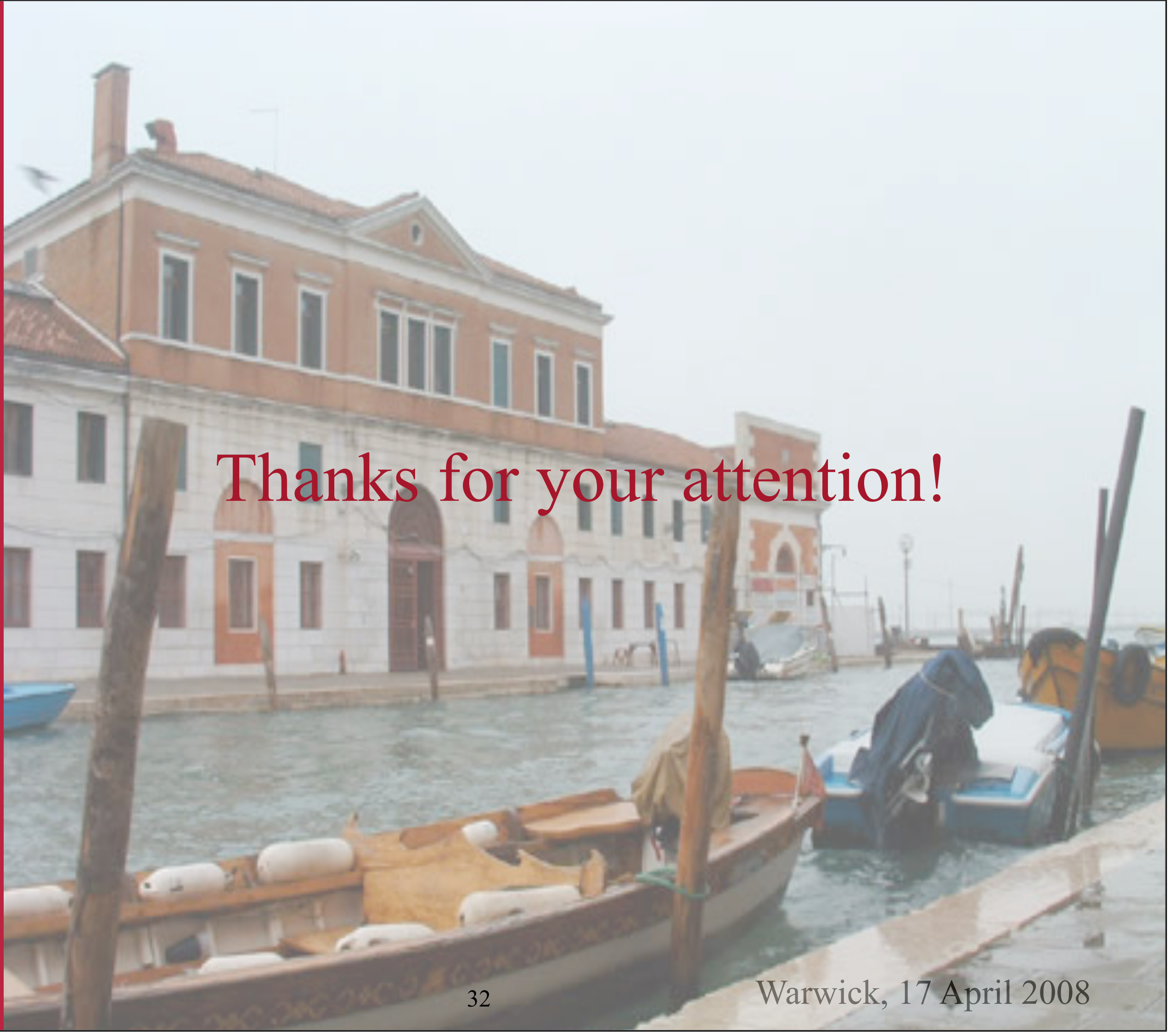

Thanks for your attention!