Bayesian variable selection for identifying subgroups in cost-effectiveness analysis

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Outline

Analysis of subgroups

- Policy–makers interest cost–effectiveness for patient subgroups (NICE Decision Support Unit, 2007)

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- Moreno et al. (2012) proposed an analysis of subgroups based on an optimal Bayesian variable selector.

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- Moreno et al. (2012) proposed an analysis of subgroups based on an optimal Bayesian variable selector.
- In this work we show a simulation study to compare both methods.

Nixon and Thompson (2005) model

Differences betweeen subgroups

Modelization for a patient *j* in arm *i*.

$$E_{ij} \sim Dist(\phi_{Eij}, \sigma_{Ei})$$
$$C_{ij} \sim Dist(\phi_{Cij}, \sigma_{Ci})$$
$$\phi_{Eij} = \mu_{Ei} + \beta_i(C_{ij} - \phi_{Cij}) + \sum \gamma_E x_{ij} + \sum \delta_E I_i x_{ij}$$
$$\phi_{Cij} = \mu_{Ci} + \sum \gamma_C x_{ij} + \sum \delta_C I_i x_{ij}$$

Comments

- Covariates have the same influence for both treatments, except subgroups.
- Detecting subgroups is reduced to an hypothesis test about the statistical relevance of parameters δ.
- Its modelization is appropriate for Normal and Gamma models.

Model proposed by Moreno *et al. (2012)*

Differences betweeen subgroups

Modelization for a patient j in arm i.

$$(E_{ij}, C_{ij}) \sim MVN((\phi_{Eij}, \phi_{Cij}), \Sigma_i)$$
$$\phi_{Eij} = \beta_{0i} + \sum \beta_i x_{ij}$$
$$\phi_{Cij} = \gamma_{0i} + \sum \gamma_i x_{ij}$$

Comments

- Objective Bayesian variable selection is carried out to detect the covariates with influence. Selecting covariates define a subgroup over the effectiveness and (or) cost.
- Normal and Log–normal distributions can be considered.

Bivariate Objective Bayesian Variable Selection

Posterior probability for each model

$$P(M_j|\mathbf{Y},\mathbf{X}_j) = \frac{B_{j1}(\mathbf{Y},\mathbf{X}_j)}{1 + \sum_{k=2}^{2^{p-1}} B_{k1}(\mathbf{Y},\mathbf{X}_k)}$$

Intrinsic prior (Torres et al., 2011)

$$\pi_1^I(\mathbf{B}_1, \sigma_1) = c\frac{1}{\sigma_1},\ \pi_j^I(\mathbf{B}_j, \sigma_j|\mathbf{B}_1, \sigma_1) =$$

$$N_{j\times 2}\left[\mathbf{B}_j|\Delta_j, \frac{n}{j+1}(\sigma_j^2 + \sigma_1^2)\left((\mathbf{X}_j^t\mathbf{X}_j)^{-1} \otimes \mathbf{V}\right)\right] \times \frac{2\sigma_j}{\sigma_1^2(1 + \sigma_j^2/\sigma_1^2)},$$

where $\Delta = \left(\mathbf{0}_{(j-1)\times 2}\mathbf{B}_1\right)$.

Bivariate Objective Bayesian Variable Selection

Bayes factor for intrinsic priors

$$B_{k1}(\mathbf{Y},\mathbf{X}_k) =$$
$$2(k+1)^{(k-1)} \int_0^{\pi/2} \frac{\sin(\varphi)^{2(k-1)+1}(n+(k+1)\sin^2\varphi)^{(n-k)}}{\cos(\varphi)^{-1}[(k+1)\sin^2\varphi + n\mathcal{B}_{k1}]^{(n-1)}} d\varphi.$$

where

$$\mathcal{B}_{k1} = \frac{tr[\mathbf{H}_{\mathbf{X}_k}\mathbf{Y}\mathbf{V}^{-1}\mathbf{Y}^t]}{tr[\mathbf{H}_{\mathbf{X}_1}\mathbf{Y}\mathbf{V}^{-1}\mathbf{Y}^t]},$$

and $\mathbf{H}_{\mathbf{X}} = \mathbf{I}_n - \mathbf{X}(\mathbf{X}^t\mathbf{X})^{-1}\mathbf{X}^t$.

Simulation

X_1, X_2 and X_3 covariates were simulated from a Uniform(0,10) distribution.

$$E_{ij} \sim N(\phi_{Eij}, 1)$$

$$C_{ij} \sim N \text{ or } Gamma(\phi_{Cij}, 1)$$

Bivariate normal distribution with $\rho = 0.5$ or FGM copula for Normal-Gamma simulation.

Treatment 1:

$$\phi_{E_{i1}} = 1 + 0.7X_{1i} + 0.2X_{2i}$$

$$\phi_{C_{i1}} = 5 + 1X_{1i} + 0.3X_{2i}$$

Treatment 2:

$$\phi_{E_{i2}} = 2 + 0.7X_{1i} + 0.1X_{2i}$$

$$\phi_{C_{i2}} = 8 + 2X_{1i} + 0.2X_{2i}$$

Simulation

$$E_{ij} \sim N(\phi_{Eij}, 1)$$

$$log - C_{ij} \sim N(\phi_{Cij}, 0.1)$$

Bivariate normal distribution with $\rho = 0.5$

Treatment 1:

$$\phi_{C_{i1}} = 1.74235 + 0.1X_{1i} + 0.03X_{2i}$$

Treatment 2:

$$\phi_{C_{i2}} = 1.79444 + 0.2X_{1i} + 0.02X_{2i}$$

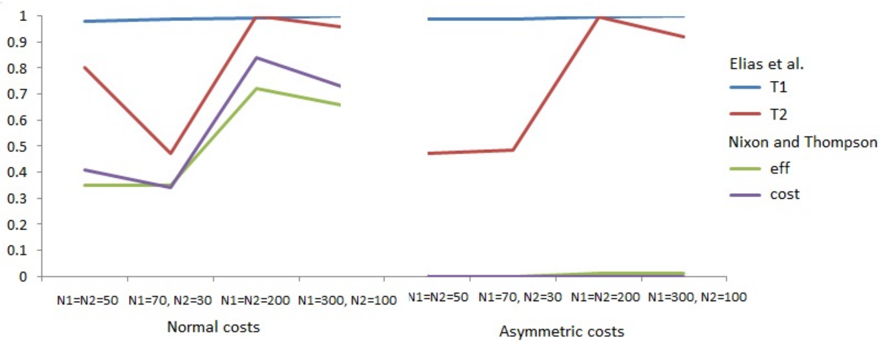
Simulation

Different frameworks for different sample–sizes were considered. We carry out 1.000 simulations and we define as an optimal selection when:

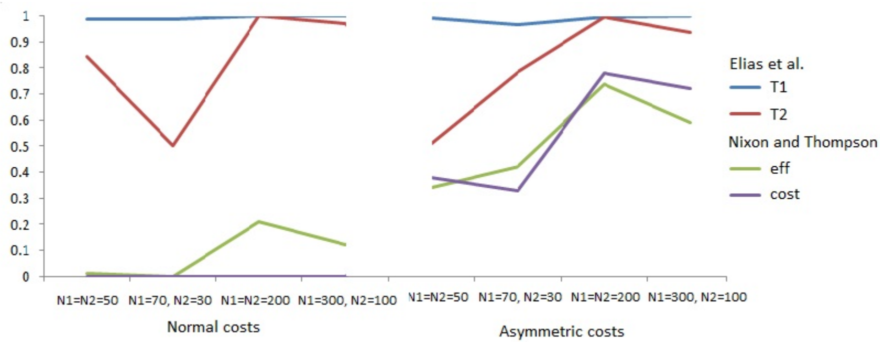
- Objective variable selection: The model with the highest posterior probability is intercept, X1 and X2. The selecction is carry out for the Treatment 1 and 2.
- Nixon and Thompson model: Only the variable X2 is detected as a subgroup for effectiveness and X1 and X2 are detected as subgroups for the cost model.

Simulations were carried out with Mathematika and WinBUGS using the R2WinBUGS package.

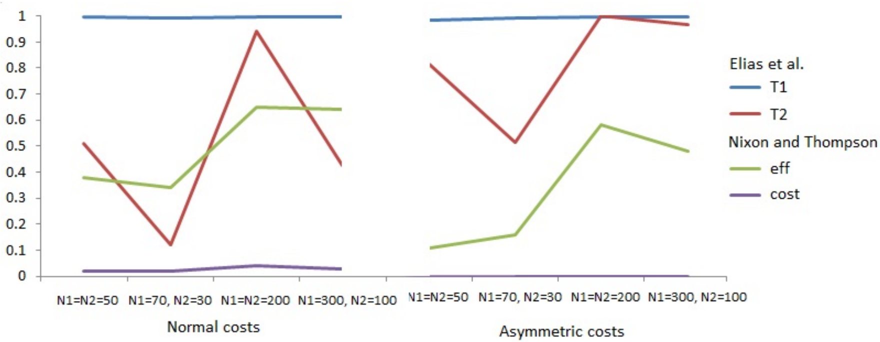
Results: Normal data



Results: Gamma data



Results: Log–normal data



Example with real data

- Data from a randomized clinical trial (Hérnandez et al., 2003) that compares two alternative treatments for exacerbated chronic obstructive pulmonary disease (COPD): home hospitalization or conventional
- Effectiveness: Difference between the score at the beginning and at the end of the study of the St. George's Respiratory Questionnaire (SGRQ).
- Potential covariates: Age, sex, smoking habit, forced expiratory volume in one second (FEV), exacerbations requiring in–hospital admission (HOSV) and the score at he beginning of the study (SGRQ1).

Example with real data: Variable Selection

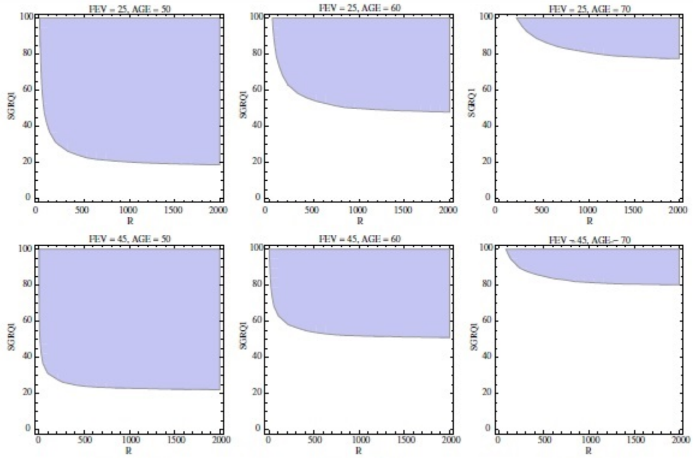
Treatment 1

SGRQ1, Age, FEV

Treatment 2

SGRQ1, FEV

Example with real data: Posterior analysis



Conclusions

- Cost–effectiveness analysis based on regression methods facilitates the analysis of subgroups with the inclusion of interactions terms in the model.
- The identification of subgroups is reduced to an hypothesis test about the relevance of these parameters.
- Bayesian Variable Selection is proposed as a natural way for the identification of subgroups.
- Simulation study shows the preference for the Bayesian Variable Selection.
- Bayesian Variable Selection obtains good results even with small sample sizes.
- Bayesian Variable Selection is less sensitive to the distribution assumption.