Bayesian Multivariate Modelling of Patient Level Healthcare Resource Use Data in RCTs

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Outline

♦ Backdrop

♦ Modelling Approach

♦ ATLAS: a Test-Bed
  – Model Formulation
  – Model Validation and Selection
  – Drawing Predictions

♦ Concluding Remarks
CEA informs allocation decisions in UK health policy

- RCTs typically offer (a wealth of) IPD on health-care resource use
- analyses often proceed from converting data into monetary figures

By direct modelling of health-care resources

1. a more efficient and transparent analytic perspective is enabled
2. features of the underlying distributions are explicitly addressed
3. relationships between the different cost drivers are accounted for

The Bayesian approach provides sound and powerful model building, criticism and selection tools
Modelling Approach

♦ Patients $r = 1, \ldots, n_t$ in arm $t \in \{C, T\}$ of a RCT consume resource items $i = 1, \ldots, I$
  
  – individual resource uses $R_{rit}$ are recorded
  – their distributions are characterised by unknown parameters $\vartheta_t$

♦ Experience and tractability drive model choices for $R_{1t}, \ldots, R_{It} | \vartheta_t$
  
  – joint modelling of heterogeneous variables is not viable
  – conditioning facilitates the model structuring process
  – reliance on (arguable) Normal approximations is not required
The ATLAS trial compared low- versus high-dose ACE-inhibitor lisinopril in the study of chronic heart failure.

Focus is upon “Day Cases”, “Days in Hospital” and “Drug Use”, with $n_C = 1571$ and $n_T = 1554$

- discrete variables $R_1, R_2$ are over-dispersed and strongly concentrated at zero $\Rightarrow$ N, Poi, HPoi, NBin, HNBin, ZINBin
- continuous variable $R_3$ is strongly asymmetric – and negatively (!) log-skewed $\Rightarrow$ N, LN, G, LSN, LST
Control arm

Day Cases

Days in Hospital

ln(Drug Use)

Frequency

%0 = 0.761

Frequency

%0 = 0.307

Treatment arm

Day Cases

Days in Hospital

ln(Drug Use)

Frequency

%0 = 0.77

Frequency

%0 = 0.33

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Model Formulation

\[
\begin{align*}
R_{1t} & \sim \text{Dist}_1(\varphi_{1t}, \varphi_{2t}) \\
R_{2t} \mid R_{1t} & \sim \text{Dist}_{2|1}(\varphi_{3t} + \varphi_{4t}[R_{1t} - \mathbb{E}(R_{1t})], \varphi_{5t}) \\
R_{3t} \mid R_{1t}, R_{2t} & \sim \text{Dist}_{3|1,2}(\varphi_{6t} + \varphi_{7t}[R_{1t} - \mathbb{E}(R_{1t})] \\
& \quad + \varphi_{8t}[R_{2t} - \mathbb{E}(R_{2t} \mid R_{1t})], \varphi_{9t})
\end{align*}
\]

– locations are linear in their conditioning variables (as in Normal case)

– reviewed distributions were fitted with ‘vague’ priors

– parametrisation meets constraints on variables (e.g. non-negativity)

– non-Normal distributions are fitted by means of MCMC simulation
Model Validation and Selection

♦ Conventional Bayesian diagnostics are based around residuals
  – RMSPEs measure the fit of marginal predictive distributions
  – SMDs account for how well the observed relationships are modelled

♦ Various statistical tools for model selection are available off-the-shelf
  – AIC, BIC and DIC offset model adequacy and complexity
  – consistent scores to be expected in non-hierarchical contexts
  – models should not just be ranked at their score’s face value
Table 1: Diagnostic checks from models with lowest AIC, BIC & DIC

<table>
<thead>
<tr>
<th>Control</th>
<th>HNBin-HNBin-LST</th>
<th>ZINBin-ZINBin-LST</th>
<th>HNBin-HNBin-LSN</th>
<th>ZINBin-ZINBin-LSN</th>
</tr>
</thead>
<tbody>
<tr>
<td>RMSPE$_1$</td>
<td>1.964</td>
<td>1.951</td>
<td>1.957</td>
<td>1.96</td>
</tr>
<tr>
<td>RMSPE$_2$</td>
<td>1.001</td>
<td>1.001</td>
<td>0.999</td>
<td>0.999</td>
</tr>
<tr>
<td>RMSPE$_3$</td>
<td>0.001</td>
<td>0.001</td>
<td>1.149</td>
<td>1.151</td>
</tr>
<tr>
<td>SMD</td>
<td>4.857</td>
<td>4.806</td>
<td>6.141</td>
<td>6.157</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment</th>
<th>HNBin-HNBin-LST</th>
<th>ZINBin-ZINBin-LST</th>
<th>HNBin-HNBin-LSN</th>
<th>ZINBin-ZINBin-LSN</th>
</tr>
</thead>
<tbody>
<tr>
<td>RMSPE$_1$</td>
<td>1.304</td>
<td>1.309</td>
<td>1.316</td>
<td>1.308</td>
</tr>
<tr>
<td>RMSPE$_2$</td>
<td>1.001</td>
<td>1.006</td>
<td>1.007</td>
<td>1.008</td>
</tr>
<tr>
<td>RMSPE$_3$</td>
<td>0.003</td>
<td>0.001</td>
<td>1.175</td>
<td>1.176</td>
</tr>
<tr>
<td>SMD</td>
<td>2.71</td>
<td>2.73</td>
<td>4.106</td>
<td>4.087</td>
</tr>
</tbody>
</table>
### Drawing Predictions

**Table 2: Predictive means (std. dev.) from preferred model**

<table>
<thead>
<tr>
<th>Arm</th>
<th>Resource Use</th>
<th>ATLAS</th>
<th>HNBin-HNBin-LSN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>$R_1$</td>
<td>0.434 (2.063)</td>
<td>0.436 (1.053)</td>
</tr>
<tr>
<td></td>
<td>$R_2$</td>
<td>19.022 (26.797)</td>
<td>19.022 (26.8)</td>
</tr>
<tr>
<td></td>
<td>$R_3$</td>
<td>7244.613 (4183.973)</td>
<td>5691.996 (3886.575)</td>
</tr>
<tr>
<td>Treatment</td>
<td>$R_1$</td>
<td>0.381 (1.185)</td>
<td>0.382 (0.902)</td>
</tr>
<tr>
<td></td>
<td>$R_2$</td>
<td>16.936 (25.569)</td>
<td>16.845 (25.44)</td>
</tr>
<tr>
<td></td>
<td>$R_3$</td>
<td>45893.03 (26216.35)</td>
<td>35838.7 (23913.19)</td>
</tr>
</tbody>
</table>
Concluding Remarks

♦ Estimated distributions appear to fit the data reasonably well
  – proposed models outperform more popular instances (e.g. Normal)
  – added complexity of multivariate structure is offset by its efficiency

♦ Promising start can be fruitfully followed by additional refining work
  – original distributions are still to some extent misrepresented
  – only fairly standard (and parametric) distributions were reviewed

♦ What comes next?
  – hierarchical models would naturally account for multi-centre scenarios
  – introduction of covariates would lead into a regression framework