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

Backdrop

- 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

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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 $\boldsymbol{\vartheta}_t$
- Experience and tractability drive model choices for $R_{1t}, \ldots, R_{It} \mid \boldsymbol{\vartheta}_t$
  - joint modelling of heterogeneous variables is not viable
  - conditioning facilitates the model structuring process
  - reliance on (arguable) Normal approximations is not required

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ATLAS: a Test-Bed

- 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 $\Longrightarrow$ N, Poi, HPoi, NBin, HNBin, ZINBin
  - continuous variable R_3 is strongly asymmetric – and negatively (!) log-skewed $\Longrightarrow$ N, LN, G, LSN, LST

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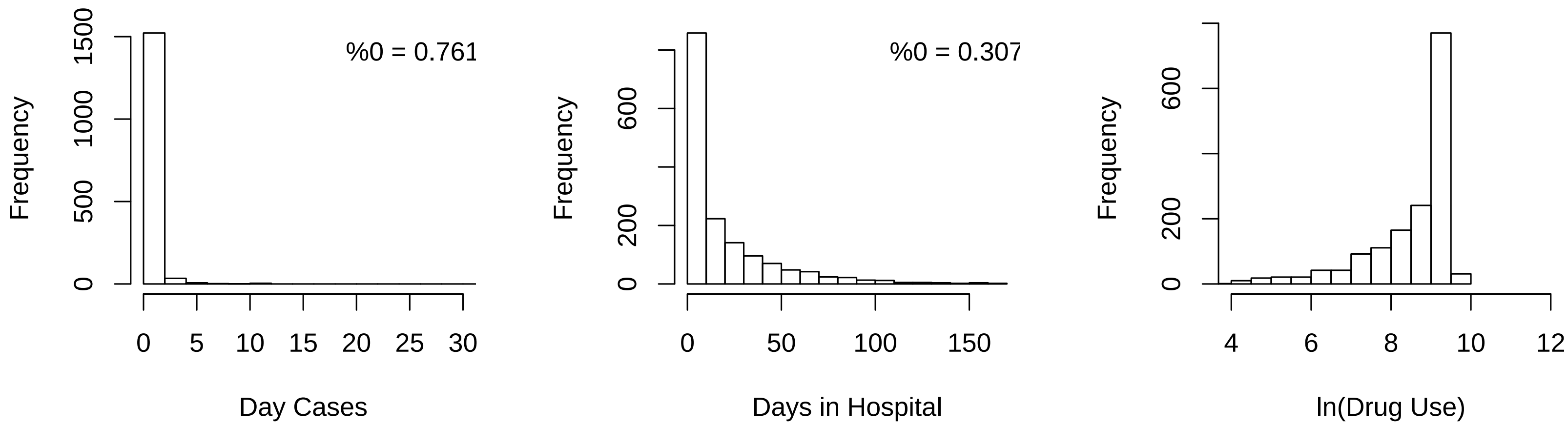
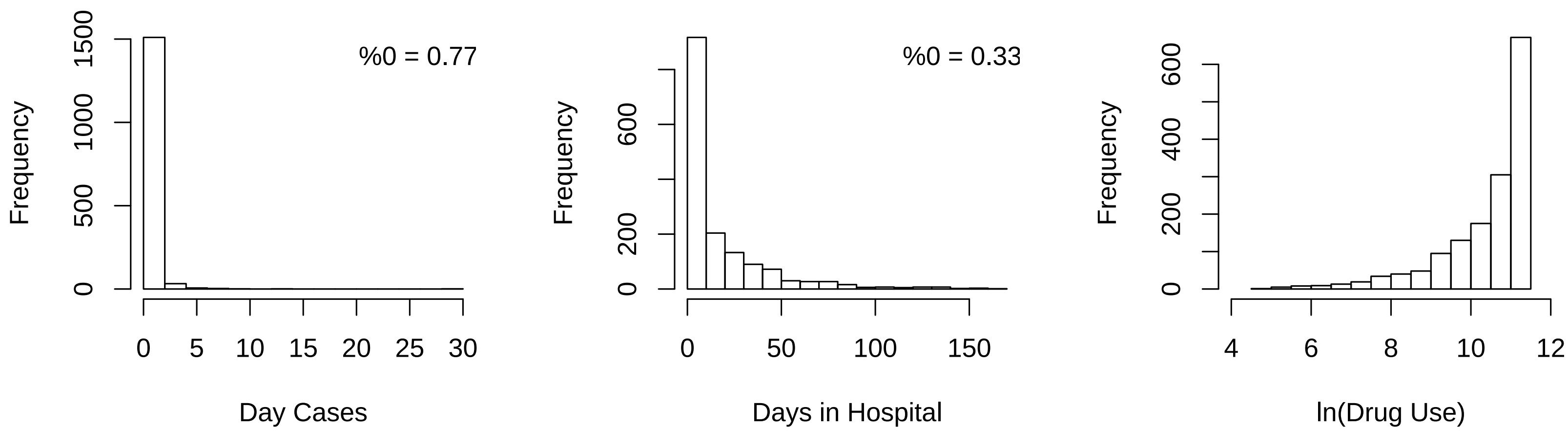
Control arm



Treatment arm



Model Formulation

$$\begin{cases} R_{1t} \sim \text{Dist}_1\left(\vartheta_{1t}, \vartheta_{2t}\right) \\ R_{2t} \mid R_{1t} \sim \text{Dist}_{2|1}\Big(\vartheta_{3t} + \vartheta_{4t}\big[R_{1t} - \mathbb{E}(R_{1t})\big], \vartheta_{5t}\Big) \\ R_{3t} \mid R_{1t}, R_{2t} \sim \text{Dist}_{3|1,2}\Big(\vartheta_{6t} + \vartheta_{7t}\big[R_{1t} - \mathbb{E}(R_{1t})\big] \\ \qquad + \vartheta_{8t}\big[R_{2t} - \mathbb{E}(R_{2t} \mid R_{1t})\big], \vartheta_{9t}\Big) \end{cases}$$

– 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

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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

Control	HNBin-HNBin-LST	ZINBin-ZINBin-LST	HNBin-HNBin-LSN	ZINBin-ZINBin-LSN
RMSPE_1	1.964	1.951	1.957	1.96
RMSPE_2	1.001	1.001	0.999	0.999
RMSPE_3	0.001	0.001	1.149	1.151
SMD	4.857	4.806	6.141	6.157

Treatment	HNBin-HNBin-LST	ZINBin-ZINBin-LST	HNBin-HNBin-LSN	ZINBin-ZINBin-LSN
RMSPE_1	1.304	1.309	1.316	1.308
RMSPE_2	1.001	1.006	1.007	1.008
RMSPE_3	0.003	0.001	1.175	1.176
SMD	2.71	2.73	4.106	4.087

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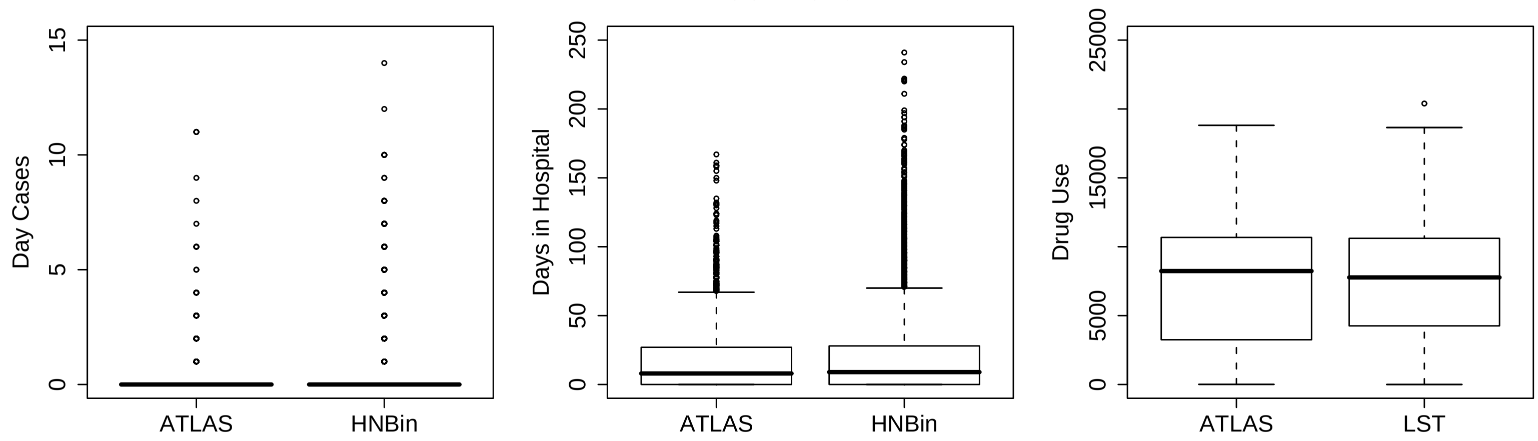
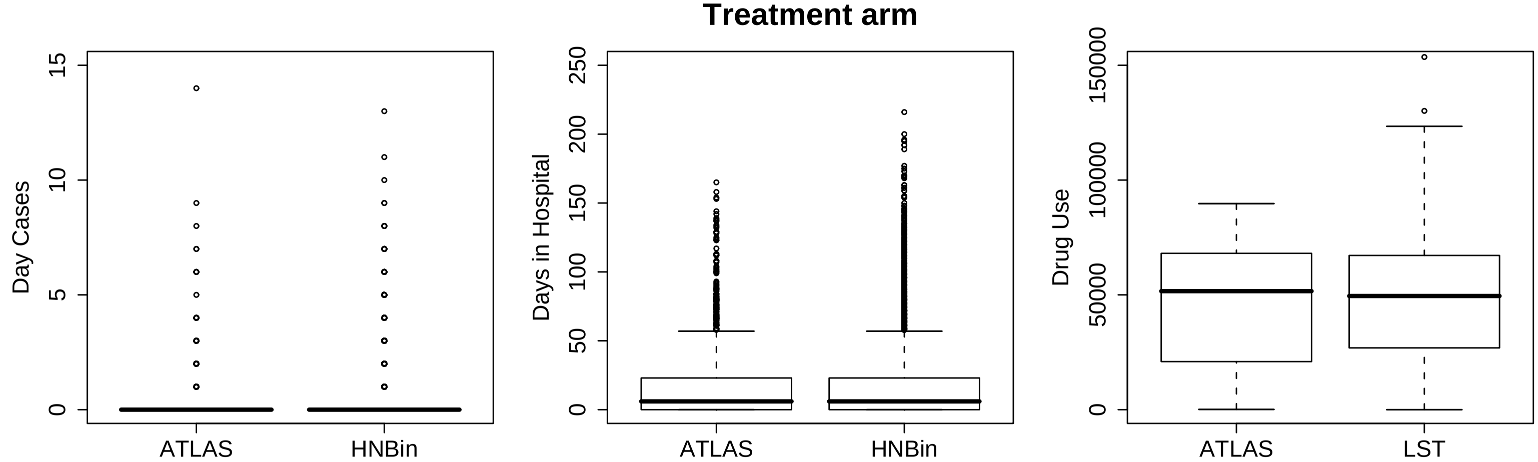
Control arm



Treatment arm



ATLAS vs. HNBin-HNBin-LST

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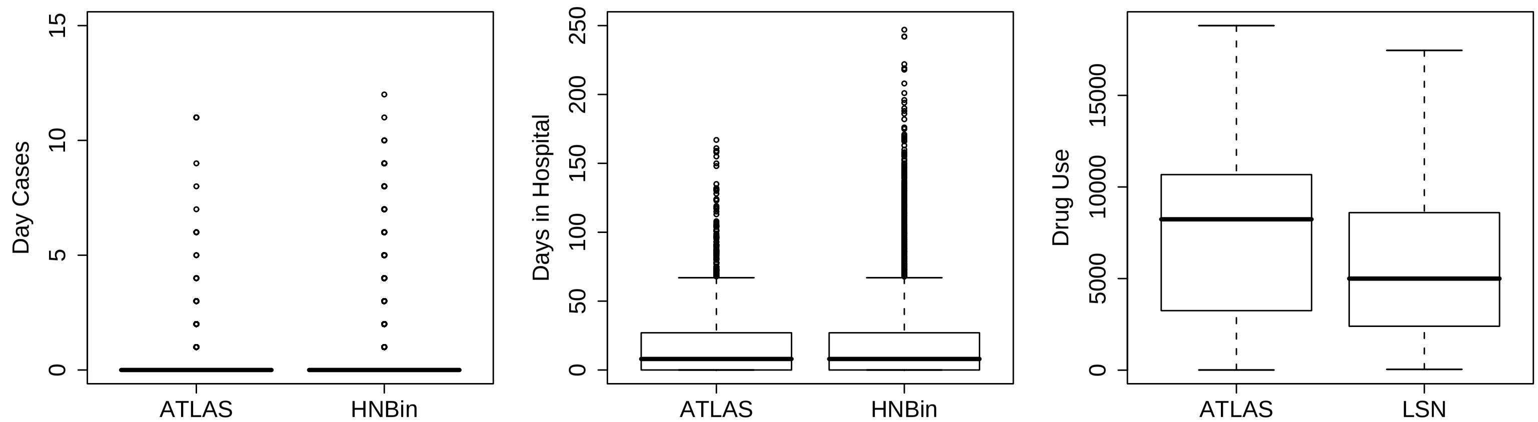
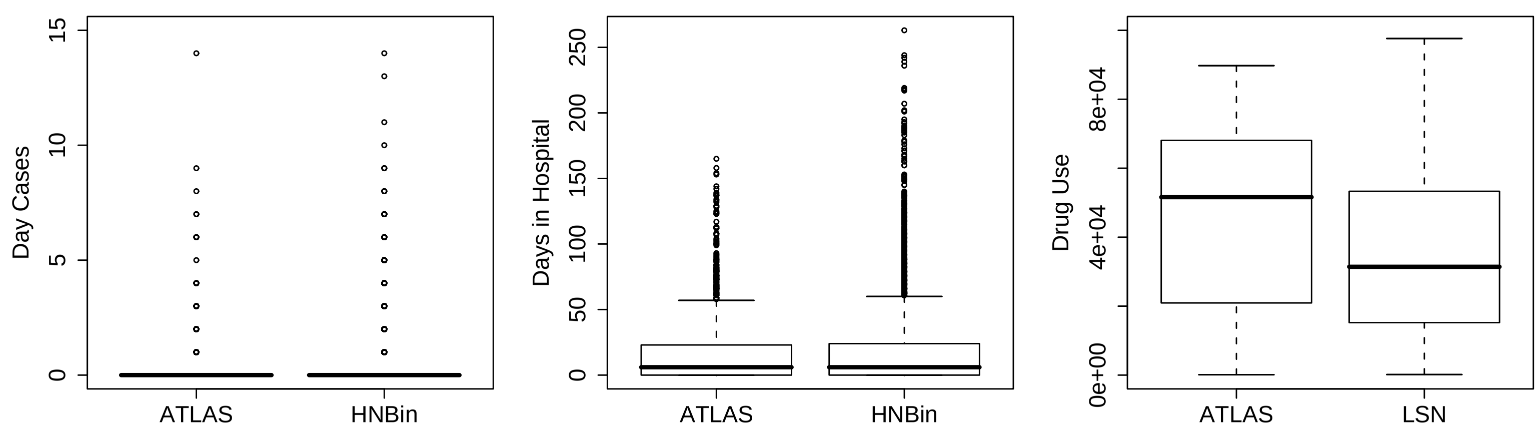
Control arm



Treatment arm



ATLAS vs. HNBin-HNBin-LSN

Drawing Predictions

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

Arm	Resource Use	ATLAS	HNBin-HNBin-LSN
	R_1	0.434 (2.063)	0.436 (1.053)
Control	R_2	19.022 (26.797)	19.022 (26.8)
	R_3	7244.613 (4183.973)	5691.996 (3886.575)
	R_1	0.381 (1.185)	0.382 (0.902)
Treatment	R_2	16.936 (25.569)	16.845 (25.44)
	R_3	45893.03 (26216.35)	35838.7 (23913.19)

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 <u>standard</u> (and <u>parametric</u>) distributions were reviewed
- What comes next?
  - hierarchical models would naturally account for multi-centre scenarios
  - introduction of covariates would lead into a regression framework