Bayesian Hierarchical Approaches for Multiple Outcomes in Routinely Collected Healthcare Data

Raymond Carragher[1,2,4], Tanja Mueller[1] , Marion Bennie[1,3], Chris Robertson[2]

[1]Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, UK; [2]Department of Mathematics and Statistics, University of Strathclyde, Glasgow, UK; [3]Public Health and Intelligence Strategic Business Unit, NHS National Services Scotland, Edinburgh, UK; [4]Health Data Research (UK)

Use routinely collected healthcare data to assess outcomes and risks for patients

Data Sources
- Practitioner
- Hospital
- Laboratory
- Prescribing
- Genetic

Data Issues
- Biased
- Outcome coding
- Low outcomes rates
- Treatments changes

Analysis approach
- Stratify patients into similar groups
- Group similar outcomes (ICD.10)

Advantages
- Balanced comparisons
- Leverage relationships

Choice of Method: Bayesian analysis
- Outcome occurrence rates
- Multiple outcomes
- Hierarchical models
- Sharing and shrinkage
- Scanning large numbers of outcomes
- Suitable for accumulating data
- Decision support

Models

$$X^c_{bj,h} \sim Poisson\left(\lambda^c_{bj,h} T^c_{bj,h}\right)$$

$$T^c_{bj,h} = \sum_{i \in R^c_{bj,h}} t_{ih}$$

$$\log \lambda^c_{bj,h} = \gamma^c_{bj,h} + x_c \vartheta^c_{bj,h}$$

$$\vartheta^c_{bj,h} \sim \pi^c_b I_{[\vartheta^c_{bj,h}=0]} + (1-\pi^c_b) N(\mu^c_{\vartheta b}, \sigma^c_{\vartheta b})$$

Results
- Posterior probabilities are used to assess the association of outcomes with treatments. e. g. $P(\vartheta^c_{bj,h} > 0)$
- Obtain estimates of rates for different patient stratifications
- Identify interesting outcomes
- Adjusting for multiple comparison issues.
- Provided the initial assumptions are correct.

Case study: Direct oral anticoagulant (DOAC) Scotland study (2011 – 2015)[1]

Data

- Scottish Morbidity Records (SMR0/SMR1)
- Prescribing Information (PIS)
- National Records of Scotland (NRS)

Direct Oral Anticoagulants

DOAC	Approval date
Dabigatran	5th August 2011
Rivaroxaban*	13th January 2012
Apixaban	11th January 2013

*Rivaroxaban is the baseline treatment

Patient stratification

Name	Sex	Age	Concomitant Medicines
M/0-64/0-4	M	0-64	0-4
M/0-64/5+	M	0-64	5+
M/65+/0-4	M	65+	0-4
M/65+/5+	M	65+	5+
F/0-64/0-4	F	0-64	0-4
F/0-64/5+	F	0-64	5+
F/65+/0-4	F	65+	0-4
F/65+/5+	F	65+	5+

Outcome groupings (ICD.10)

Outcome	Grouping	Group description
Ischemic stroke	I00-I99	Circulatory system
Haemorrhagic stroke	I00-I99	Circulatory system
Systemic embolism	I00-I99	Circulatory system
Pulmonary embolism	I00-I99	Circulatory system
Myocardial infarction	I00-I99	Circulatory system
Transient ischaemic attack	G00-G99	Nervous system
Gastrointestinal bleed	BLEED	Bleeds
Other bleed	BLEED	Bleeds
Other ADR	OTHERADR	Adverse Drug Reaction

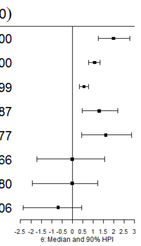
Results

Outcomes with increased/decreased rate compared to Rivaroxaban

Outcome	Grouping	Treatment	Increase/Decrease
Myocardial Infarction	Circulatory system	Apixaban	Increase
Other bleed	Bleeds	Apixaban	Decrease
Other bleed	Bleeds	Dabigatran	Decrease
Pulmonary embolism	Circulatory system	Dabigatran	Decrease

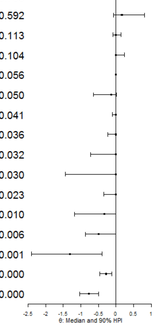
Myocardial infarction (Apixaban)

Cluster	$P(\theta<0)$	$P(\theta=0)$	$P(\theta>0)$
M/0-64/5+	0.000	0.000	1.000
F/65+/5+	0.000	0.000	1.000
M/65+/5+	0.000	0.001	0.999
F/0-64/5+	0.002	0.012	0.987
F/65+/0-4	0.005	0.018	0.977
F/0-64/0-4	0.408	0.226	0.366
M/0-64/0-4	0.502	0.218	0.280
M/65+/0-4	0.726	0.168	0.106



All outcomes

Treatment	Grouping	Outcome	$P(\theta<0)$	$P(\theta=0)$	$P(\theta>0)$
Apixiban	I00-I99	Myocardial infarction	0.000	0.000	1.000
Apixiban	I00-I99	Ischemic stroke	0.004	0.132	0.865
Apixiban	I00-I99	Haemorrhagic stroke	0.026	0.266	0.708
Apixiban	I00-I99	Systemic embolism	0.073	0.335	0.592
Apixiban	G00-G99	Transient ischaemic attack	0.086	0.801	0.113
Dabigatran	G00-G99	Transient ischaemic attack	0.056	0.840	0.104
Dabigatran	I00-I99	Ischemic stroke	0.046	0.899	0.056
Apixiban	I00-I99	Pulmonary embolism	0.582	0.367	0.050
Dabigatran	I00-I99	Myocardial infarction	0.088	0.872	0.041
Apixiban	BLEED	Gastrointestinal bleed	0.333	0.632	0.036
Dabigatran	OTHER_ADR	Other ADR	0.297	0.671	0.032
Dabigatran	I00-I99	Systemic embolism	0.420	0.550	0.030
Dabigatran	BLEED	Gastrointestinal bleed	0.296	0.680	0.023
Dabigatran	I00-I99	Haemorrhagic stroke	0.559	0.431	0.010
Apixiban	OTHER_ADR	Other ADR	0.821	0.173	0.006
Dabigatran	I00-I99	Pulmonary embolism	0.957	0.042	0.001
Apixiban	BLEED	Other bleed	0.954	0.045	0.000
Dabigatran	BLEED	Other bleed	1.000	0.000	0.000



[1]Mueller T, Alvarez-Madrazo S, Robertson C, Wu O, Bennie M. Comparative safety and effectiveness of direct oral anticoagulants in patients with atrial fibrillation in clinical practice in Scotland. *British Journal of Clinical Pharmacology* 2019; 85(2): 422–431. doi:10.1111/bcp.13814

Summary

The existence of large scale data sources containing the health records of thousands of patients provides an opportunity and a requirement to move beyond a single variable analysis to develop methods capable of analysing multiple outcomes, providing the possibility of moving towards a more precise approach to medicine delivery. Hierarchical Bayesian methods are a suitable approach for analysing this type of data. Hierarchies of outcomes may be easily incorporated in models and posterior probabilities provide a method for assessing outcome occurrence. Bayesian methods are also well suited to handling the analysis of constantly accumulating data, such as healthcare records.

Contact: raymond.carragher@strath.ac.uk