長庚大學醫學院臨床醫學研究所
畢業生研究成果

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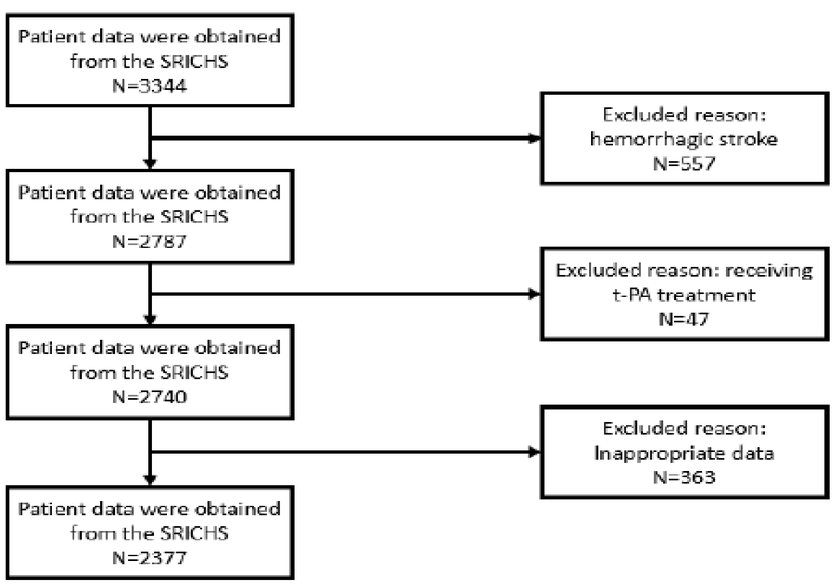
畢業論文題目（中文）：以混合模型討論腦中風病人功能性癒後之預測因子

畢業論文題目（英文）：Using mixture models for Predicting discharge functional outcome in acute ischemic stroke

BACKGROUND

- Stroke causes ischemic damage to the brain tissue, and the consequence varies from mild, transient loss of consciousness, disability, to sudden death.
- Developing means of assessing progress after stroke could be helpful and able to give clinicians tools to facilitate optimum patient management, and provide a tool for predicting the management costs after a stroke.
- Logistic regression model is wildly used at analyzing prognostic factors associative with outcome.
- For the purpose to deal the mixing population of first ever and recurrent stroke patients, finite mixture models might come to the rescue.

Figure 1. Flow diagram of the subjects selection for this study.



OBJECTIVE

- To analyze the data, which is not normal or cannot be approximated by a single distribution.
- To determine the number of unobserved or hidden components and to classify individual observations according to their predicted component probabilities using FMM.
- To deal with the problems of collinearity or multicollinearity among explanatory variables and generate meaningful results.
- To characterize each component group identified by FMM and uncover their differences.
- To compare differences of the predicting factors of post-stroke outcomes from logistic regression and FMM.
- To determine the relationship between discharge functional outcome and clinical variables in each component group using FMM.

METHOD

- Study Population: This study was based on the data from the Stroke Registry in Chang Gung Healthcare System, since July 2007 to December 2014, from patients who had been sent to Keelung Chang Gung hospital and were diagnosed as having stroke.
- Finite mixture models provide a parametric approach and flexible framework for analyzing and describing an unknown distribution in terms of mixtures of known distributions.
- Let $X_1, X_2, \ldots, X_n$ be independently, and identically distributed k-dimensional observations from a distribution with probability density function

$$f(x; p) = \sum_{i=1}^{k} p_i f_i(x),$$

where p_i is the i^{th} mixing proportion or the probability that the observation x_i pertains to the i^{th} component and $f_i(x)$ is the i^{th} component density.

- If the component distributions are of the same distributional form, the mixture is called homogeneous. The general model could be expressed to:

$$f(y) = \sum_{i=1}^{k} p_i f_i(y; x', \beta i, \Phi i).$$

RESULT

- The outcome has been transformed from mRS socre at discharge into three major categories: the score of mRS 0, 1, and 2 were classified as Discharge mRS Performance 1, the score 3 and 4 classified as Discharge mRS Performance 2, and the score 5 and 6 as Discharge mRS Performance 3.
- According to the results of FMM, a Two-component mixture model, there were only NIH stroke score at admission and heart disease associated with Discharge mRS Performance in the component 1, and in the component 2, NIH stroke score at admission, mRS score at admission, age, sex, heart disease, hypertension, hyperlipidemia, diabetes mellitus, and alcohol and cigarette use were associated with Discharge mRS Performance.
- The predictive responses were different among 3 categories. There were 100% accurateness that all cases correctly classified in Discharge mRS Performance 1, 93.6% of Discharge mRS Performance 2, and only 58.4% of Discharge mRS Performance 3.

Two-component Mixture Model Examining Influence of Clinical Variables on Discharge Functional Outcome, for Both Types of Stroke Patients (First-Ever and Recurrent)

Component	Variable	β	Standard Error	P
1	NIHSS(Ward)*	0.02	0.002	<.0001
1	mRS(Ward)	-0.02	0.01	0.087
1	Age	0.001	0.001	0.383
1	Sex†	0.05	0.03	0.085
1	Heart Disease*	-0.06	0.03	0.021
1	Hypertension	-0.03	0.04	0.471
1	Hyperlipidemia	0.01	0.03	0.734
1	Diabetes Mellitus	0.0004	0.03	0.988
1	Alcohol use	0.01	0.04	0.741
1	Smoking	-0.06	0.03	0.059
1	Obesity	0.06	0.03	0.063
2	NIHSS(Ward)*	9.1×10^{-6}	1.2×10^{-6}	<.0001
2	mRS(Ward)*	2.1×10^{-5}	2.7×10^{-6}	<.0001
2	Age*	-9.5×10^{-7}	3.1×10^{-7}	0.002
2	Sex†*	1.8×10^{-4}	8.7×10^{-6}	<.0001
2	Heart Disease*	2.6×10^{-5}	8.4×10^{-6}	0.002
2	Hypertension*	-9.0×10^{-5}	9.2×10^{-6}	<.0001
2	Hyperlipidemia*	-6.0×10^{-5}	7.2×10^{-6}	<.0001
2	Diabetes* Mellitus	6.2×10^{-5}	7.4×10^{-6}	<.0001
2	Alcohol use*	1.2×10^{-4}	9.4×10^{-6}	<.0001
2	Smoking*	-1.2×10^{-4}	8.5×10^{-6}	<.0001
2	Obesity*	-6.0×10^{-4}	7.5×10^{-6}	<.0001

*Significant at 5 percent level.
†: male as the reference

CONCLUSION

- In this study, an alternative approach for modeling stroke patient's predictor of functional outcome, alcohol and cigarette use, hypertension, and hyperlipidemia, are found to have significant effects, and these risk factors have not been identified using the single logistic regression model.
- Mixture models provide a general framework for combining all potentially relevant information, not to split the sample into two parts, and avoid resulting in a loss of power because of the sample size reduction.
- There was a trend of accuracy rate with the level change of Discharge mRS Performance, a decreased predictive accuracy was associated with a poor functional outcome in both the logistic regression and the mixture model, which a higher Discharge mRS Performance level was corresponding with a lesser accuracy rate.

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