

## **A random-effects functional-regression approach for assessing control in the management of renal anaemia**

Robert M. West<sup>1</sup>, Bo Wang<sup>2</sup>, Eric J. Will<sup>3</sup>, and Jian Q. Shi<sup>4</sup>

<sup>1</sup>Bisostatistics Unit, University of Leeds, UK;

<sup>2</sup>Department of Mathematics, University of York, UK;

<sup>3</sup>St James's Hospital, Leeds, UK;

<sup>4</sup>Department of Statistics, University of Newcastle, UK;

The construction of Gaussian Process Functional Regressions developed by [1] is extended to include random effects. This focus of this presentation is to demonstrate an application of random effects GPFR models to the management of renal anaemia. [2] provides background for the application and an initial functional data analysis.

Measurement of patient haemoglobin (Hb) levels are taken at monthly intervals over a period of a year and their Hb response is considered as a Gaussian process function. Dose of an agent that stimulates production of red blood cells and so increases Hb is modelled as a functional covariate.

Inspection of Hb response curves reveals a variety of patterns and the strongest relationship of current Hb is with the dose level delivered two-months earlier – that is there is a lag between the injection of the stimulating agent and increased production of red blood cells.

The dose-response relationship has been shown to be nonlinear and is made more complex by intercurrent events. By fitting a random-effects functional regression, individual variability can be accommodated whilst revealing the general dose-response relationship.

Results reveal a common quadratic dose–response mean relationship among different patients. Further, using a nonlinear covariance model reveals a tendency for patient Hb response to vary over time for each individual patient. A consequence of this last is that individual monitoring and control of patients is seen to be necessary: the dose–response relationship is found for the general dialysis population but management of individuals is still required.

The original trial was to compare the two agents using the same management system. The random effects GPFR was shown to provide a useful tool for predicting Hb response in individual dialysis patients. The accuracy of prediction was seen to be similar under the two agents and thus management was equally as effective under the two agents.

In conclusion, random-effects GPFRs have provided useful understanding of several aspects of a clinical application.

## **References**

- [1] J. Q. Shi, B. Wang, R. Murray-Smith, D. M. Titterington (2007) Gaussian process functional regression modeling for batch data. *Biometrics* 63: 714-723.
- [2] West RM, Harris K, Gilthorpe MS, Tolman C, and Will EJ (2007) A description of the variability of patient responses in the control of renal anemia – functional data analysis applied to a randomized controlled clinical trial in hemodialysis patients. *Journal of the American Society of Nephrology* 18: 2371–2376.