## **Real-Time Monitoring of Progression Towards Renal Failure in Primary Care Patients**

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A widely used method of monitoring patient's kidney function is the estimated glomerular filtration rate (eGFR), measured over time. The eGFR tends to decrease naturally with increasing age, and to vary unpredictably for other reasons, for example in response to changes in a person's general level of fitness. Nevertheless, an unusually sharp decrease is considered to be a useful predictor of kidney failure; current guidelines suggest that a rate of change of 5% per year or more is indicative of a need for specialist treatment. Measurements of eGFR can be obtained from routine blood tests taken in primary care settings.

In this talk, we shall address the problem of using such routinely collected data for early detection of incipient kidney failure. Our data are obtained from two UK treatment centres. They consist of an irregularly spaced time series of eGFR measurements on each person together with a number of explanatory variables including each person's age, any relevant co-morbidity and medication. We shall formulate and fit a dynamic regression model for the data, in which the rate of change of eGFR over time is modelled as a continuous-time stochastic process B(t). Conditional on a subject-specific *i* and a time-specific rate of change  $B_i(t_{ij})$ , the model for the time-sequence  $Y_{ij} : j = 1, ..., n_i$  is that

$$Y_{ij} = \alpha_0 + \alpha_1 \times x_i + \alpha_2 \times \min(0, x_i - 65) + A_i + B_i(t_{ij}) \times t_{ij} + Z_{ij} \quad : \quad j = 1, ..., n_i; i = 1, ..., m_i + A_i + A_i$$

The  $Z_{ij}$  are mutually independent,  $Z_{ij} \sim N(0, \tau^2)$ , the pairs  $\{A_i, B_i(0)\}$  are distributed as  $A_i \sim N(0, \nu^2)$ ,  $B_i(0) \sim N(\beta, \omega^2)$  and  $\text{Cov} \{A_i, B_i(0)\} = \gamma$ , and the process  $B_i(t)$  evolves over time as Brownian motion, hence for any  $t \geq u$ ,

$$B_i(t)|B_i(u) \sim N(B_i(u), (t-u)\sigma^2).$$

We will also assume a integrated Brownian motion for the process  $B_i(t)$ , and compare the models through a simulation study. The parameter  $\alpha_2$  reflects the apparent change in the rate of pregression above age 65, as seen in preliminary analysis. Two different time metameters are also used, age and time since first measurement, to admit the possibility that the cross-sectional and longitudinal effects of age may be different, i.e.  $\beta \neq \alpha_1$ . We then use the model to make predictive inferences for the current rate of change in eGFR. Considering a subject *i* with initial age  $x_i$ , who provides measurements of eGFR at time  $t_{ij} : j = 1, ..., n_i$ . For any  $k \leq n_i$ , let  $Y_i^k = (Y_{i1}, ..., Y_{ik})$ . The main goal is to evaluate the conditional distribution of  $\beta + B_i(t_{ik})$  given  $Y_i^k$ .

## References

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