

**MODELING CORRELATED DATA FROM A STUDY OF BRAZILIAN FAMILIES**

Suely R. Giolo<sup>1</sup>, Júlia P. Soler<sup>2</sup>, Mariza de Andrade<sup>3</sup>, Alexandre Pereira<sup>4</sup>, Camila M. Oliveira<sup>4</sup>  
and José E. Krieger<sup>4</sup>

<sup>1</sup>*Department of Statistics, Federal University of Paraná, Brazil*

<sup>2</sup>*Department of Statistics, University of São Paulo, Brazil*

<sup>3</sup>*Division of Biostatistics, Mayo Clinic, Rochester, Minnesota*

<sup>4</sup>*Laboratory of Genetics and Molecular Cardiology, University of São Paulo, Brazil*

Quantitative genetic analysis of complex diseases that exhibit variation in age at onset involves a number of difficulties, given that there is an important family aggregation pattern that need to be modeled and also because the occurrence of the disease may fail to be observed in the study due to censoring. In this work, our objective is to evaluate the effect of genetic and environmental factors on the age of diagnosis of several cardiovascular risk factors (such as hypertension, diabetes and high cholesterol) and its corresponding quantitative variables (such as systolic and diastolic blood pressure, fasting blood glucose and total cholesterol). Since age at onset is difficult to access, we will use age of diagnosis as the surrogate for age at onset. We analyzed the data from 81 families, involving 1,666 individuals, from the village of Baependi in the state of Minas Gerais, Brazil. To obtain estimates of heritability for the quantitative variables we applied variance components approach. For the age at onset variables we adopted the model proposed by Pankratz et al. (2005), which combines the flexibility of genetic analysis via the variance components model with Cox proportional hazard model. The effect of genes is also considered through variance components models in which heritability of the quantitative variables is adjusted for the age at onset variables. To fit the models we used the Sequential Oligogenic Linkage Analysis Routine (Solar) program and the R library kinship.

References

- Almasy L., Blangero J (1998) Multipoint quantitative-trait linkage analysis in general pedigrees. *Am J Hum Genet* 62:1198-1211.
- Amos C (1994) Robust variance components approach for assessing genetic linkage in pedigrees. *Am J Hum Genet* 54:535-543.
- Pankratz VS, de Andrade M, Therneau, TM (2005) Random-effects Cox proportional hazard model: general variance components methods for time-to event data. *Genet Epidemiol* 28:97-109.
- Ripatti S, Palmgren J (2000) Estimation of multivariate frailty models using penalized partial likelihood. *Biometrics* 56:1016-1022.