Single Nucleotide Polymorphisms Associated With Fasting Blood Glucose Trajectory And Type 2 Diabetes Incidence: A Joint Modelling Approach

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In observational cohorts, longitudinal data are collected with repeated measurements at predetermined time points for many biomarkers, along with other covariates measured at baseline. In these cohorts, time until a certain event of interest occurs is commonly reported and very often, a relationship will be observed between a biomarker repeatedly measured over time and that event. Joint models were designed to efficiently estimate statistical parameters by combining a mixed model for the longitudinal biomarker trajectory and a survival model for the event risk, using a set of random effects to account for the link between the two types of data.

First, using genotypes assayed with the MetaboChip DNA arrays (Illumina) from close to 4,500 subjects recruited in the French cohort D.E.S.I.R. (Données Épidémiologiques sur le Syndrome d’Insulino-Résistance), we assessed the feasibility of implementing the joint modelling approach in a real high-throughput genomic dataset. Second, we checked model consistency based on different simulation scenarios, varying sample size, minor allele frequency, number of repeated measurements and missing data patterns. In our study, the event of interest was onset of type 2 diabetes (T2D), and the longitudinal biomarker repeatedly measured over time was fasting plasma glucose level.

To the best of our knowledge, joint models have never been applied into a genetic epidemiology context and could help identify novel loci sharing effects on both glycaemic traits and T2D.