EPAD Deliverable 2.6

Disease Risk Modelling Report

Executive Summary

This deliverable 2.6 describes the disease modelling work done to date within Work Package 2 by the MRC Biostatistics Unit, University of Cambridge in preparation for when the longitudinal data from the EPAD Longitudinal Cohort Study (EPAD-LCS) become available.

Our work so far has focussed on using historical/existing data to develop appropriate methodology and explore issues that may be relevant for the modelling of the EPAD-LCS longitudinal data. We have identified relevant data sources, and the clinical outcomes, biomarkers and covariates/risk factors which should be considered when developing an Alzheimer's disease (AD) risk model that captures the four important dimensions contributing to participants with pre-clinical or prodromal disease (i.e. early stage disease) having differing rates of progression to Alzheimer's Dementia or cognitive decline. The four important dimensions comprise cognitive functioning levels, biomarker levels, risk factors and time. Our modelling investigations started off with the Delor Model, but then moved on to considering mixed effects models and latent class mixed models and ended with the consideration of multivariate models for cognitive outcomes and biomarkers over time, adjusting for risk factors. Specifically, we have considered the modelling of cognitive outcomes, such as the Mini Mental State Examination (MMSE), the Clinical Dementia Rating Sum of Boxes (CDRSOB) and the Alzheimer's Disease Assessment Scale Sub-Scores (ADAS-11) and biomarker processes, such as Hippocampal Volume (HV), and the cross-validation of latent class mixed models. We have further investigated the power to detect treatment effects using composite outcomes as opposed to the individual components; and the use of our models to inform selection into the EPAD-LCS. Moreover, we have interacted with Interuniversity MicroElectronics Center (IMEC) in order to deliver optimised software which can be used in EPAD; with the Edinburgh statistician; and through monthly teleconference calls with other EPAD partner organisations interested in the disease modelling.

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