Modelling the dynamics of biomarkers during primary HIV infection taking into account the uncertainty of infection date

Julia Drylewicz [1,2], Jérémie Guedj [1,2], Rodolphe Thiébaut [1,2] and Daniel Commenges [1,2] on behalf of the CASCADE Collaboration

[1] INSERM, U897 Epidemiology and Biostatistics Research Center, Bordeaux, F-33076 France
[2] University of Bordeaux 2, Bordeaux, F-33076 France

During primary HIV infection, plasma virus concentrations and CD4+ cells count present a very complex dynamics with a peak of HIV RNA at 2-3 weeks after infection and a dramatic decrease of CD4 followed by a rebound. Parametric and non parametric models have been suggested for fitting reapeated measurements of these markers. Alternatively, mechanistic approaches based on ordinary differential equations have been also proposed [3, 1]. These models are based on biological knowledge and take into account the complex non-linear interactions between virus and cells (prey-predator models). The estimation of the parameters of these models is difficult and different methods have been recently proposed. A main difficulty in the context of primary HIV infection is that the date of infection is generally unknown. For some patients, the date of last negative HIV test is available in addition to the date of first positive HIV test (seroconverters). Therefore, the date of infection, which defines the baseline time of the model, is interval-censored. We extended a recently developped method for estimating the parameters of dynamical models using a population approach [2] for taking into account the uncertainty of the date of infection. We applied this method to a sample of 82 HIV-infected patients from a large collaboration of observational cohorts of seroconverters : the Concerted Action on Seroconversion to AIDS and Death in Europe (CASCADE).

References

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