HIV Disease Progression in South Africa using Multistate Markov Models

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An understanding of HIV progression and factors that influence disease progression can have great value in the development of new treatment strategies. Although Sub-Saharan Africa is noted for its high HIV prevalence there is an absence of research on HIV progression and factors affecting it. In patients who do not receive antiretroviral therapy, a decreasing CD4 count is strongly associated with an increasing risk of AIDS and death. There have been numerous statistical approaches to examine HIV progression in terms of CD4 count decline, the most popular of which include linear mixed models and multistate Markov models (1,2). The multistate approach can be considered superior due to the ability to estimate the length of stay in different CD4 count intervals and to investigate probabilities of transitions to lower CD4 counts.

A cohort of 336 ARV naive HIV positive individuals enrolled into the Sinikithemba study conducted in McCords hospital, Durban, South Africa was studied. Patients were followed for a median of 3.54 years (IQR 1.91 - 4.52 years) and had a median of 12 visits (IQR 4 - 17 visits). The median time between visits was 0.26 years.

HIV progression was investigated through the application of a five state Markov model with reversible transitions. The four transient states are based on CD4 count intervals with ARV initiation as an absorbing fifth state. The rate of CD4 count decline was examined and predictions of the HIV state trajectory are made through the use of transition probability matrices. The effect of age, gender and baseline CD4 count on individual state transition rates was examined using the Cox proportional hazards model.

A key finding, consistent with previous research, was that the rate of decline in CD4 count tends to decrease at lower levels. It was also noted that patients enrolling with a CD4 count less than 350 have a far lower chance of immune recovery, and a substantially higher chance of immune deterioration compared to patients with a higher CD4 count. This study found multistate models to be a powerful tool in HIV/AIDS research which can offer a deeper understanding of the natural progression of the disease.

The focus of this study was immune deterioration in ARV naive patients. It is of further interest to explore the rates of immune recovery in patients on antiretroviral therapy. The heterogeneity between individuals cannot always be completely explained by observed covariates. In such cases this residual heterogeneity should be modeled as a random effect. Furthermore, the CD4 count is a marker which is subject to great variability and measurement error. An area of further work would be to formulate a Bayesian model which models two processes: the disease process (as a Markov process) and the measurement process.

The work presented here is based on: Reddy T. The Application of Multistate Markov Models to HIV Disease Progression (Master's thesis). Durban: University of KwaZulu Natal; 2010.

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References: