Resume: Estimation of HIV infected individuals using a model with competing risks of diagnosis and illness onset

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Resume of forthcoming article
As an original study is expected to be printed elsewhere, herewith a Resume of the study is provided for this proceedings.

Background
Acquired immunodeficiency syndrome (AIDS) is a disease of immunocompromised host with a number of opportunistic infections, caused the human immunodeficienty virus (HIV). Following infection with HIV, it takes on average 10 years to develop AIDS. Once developing AIDS, its diagnosis is properly made by AIDS expert and certainly reported in industrialized countries including Japan where there are a number of AIDS specialized healthcare facilities. Nevertheless, unless infected individuals undertake voluntary blood testing, the infection status with HIV is unrecognized before developing AIDS.

Since the reported dataset of AIDS cases captures the transmission dynamics of some 10 years ago, we cannot objectively understand if the epidemic is downward or upward trend at present only by looking at AIDS cases. Backcalculation method is a well-known statistical method that has permitted us to estimate HIV incidence using the AIDS case data and the incubation period distribution. Namely, the incidence of AIDS cases is written as a convolution of the HIV incidence (i.e. new infections with HIV) and the probability density function of the incubation period of AIDS, and deconvolution procedure has helped us to estimate HIV incidence from such relationship.

While the backcalculation method has been useful and was widely applied to different settings, the AIDS incidence in Japan has not reflected the entire number of AIDS diagnoses from 1999, due to cessation of reporting previously diagnosed HIV infected individuals that progressed to AIDS. For this reason, all AIDS cases have not been counted in Japan, making it unrealistic to apply the simple convolution equation to

the observed AIDS case data. Moreover, in addition to AIDS cases, there have been reports of diagnosed HIV infection status among blood donors and a statistical method that could offer estimates of HIV incidence using both AIDS cases and HIV diagnoses has been called for.

A multistate model was proposed as ideal method to be applied to the Japan dataset. In addition to such a well parameterized model, the present study aimed to develop a model that captures the data generating process of HIV/AIDS in a simpler yet general manner using a competing risk model. Employing the competing risk model, the interplay between HIV diagnosis and onset of AIDS is captured.

Method

Basic model structure

A competing risk model that captures the data generating process of HIV diagnosis and onset of AIDS has been mathematically formulated (Figure). The rate of HIV diagnosis was modeled as a function of calendar time, while the illness onset of AIDS was assumed to be regulated by an independently and identically distributed incubation period distribution.
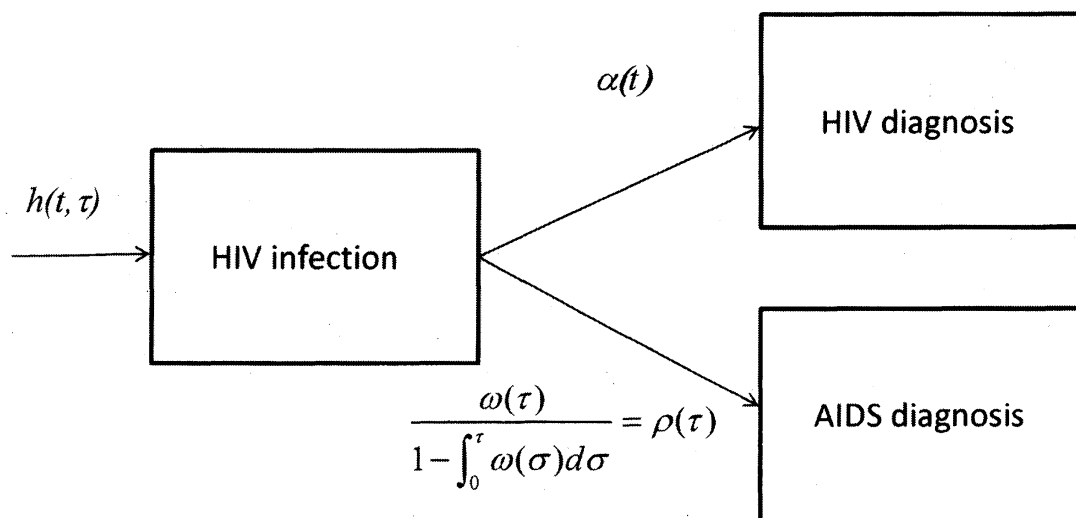

Figure. Competing risk model as applied to HIV/AIDS

Available data

HIV/AIDS surveillance record in Japan: Bimonthly (1984 -2000) or quarterly (2001-present) numbers of HIV infection and AIDS diagnosis are obtained. Among AIDS diagnosis, information with regard to previous HIV diagnosis is not available. Reporting interval in surveillance system is revised due to the different law (AIDS Prevention Law

1989-1999 and the National Epidemiological Surveillance of Infectious Diseases from Mar. 1999). Registration system of AIDS excluded those who were diagnosed as HIV-infected after the revision.

We obtained the maximum likelihood estimates of unknown parameters including the HIV incidence and the rate of diagnosis. Likelihood function was explicitly derived from McKendrick equation system. Assuming that the HIV incidence is characterized by a non-homogeneous Poisson process, both the resulting HIV diagnoses and AIDS incidence were assumed to follow Poisson distributions.

Results/Discussion

Estimated number of people living with HIV/AIDS (PLWHA) was on the order of 26000 as of the end of 2014. The estimates were comparable to those obtained using a three-stage multistate model that was employed in the past. As an advantage of the proposed model, it was shown that the forecast can be obtained in real-time accounting for both parameter uncertainty and demographic stochasticity. As a visual confirmation of the goodness-of-fit, observed and expected cumulative numbers of HIV infections and AIDS cases were compared.

A general representation of HIV/AIDS model in Japan was considered. The proposed competing risk model permits a simpler sensitivity analysis of the model estimates to different incubation periods.

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