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Reply to Lawn and Wood

To the Editor—Lawn and Wood [1] raise an important issue concerning the relationship between CD4 cell counts and mortality in people infected with HIV and note that there is substantial variation in CD4 cell counts at death. As CD4 cell counts decline, the incidence of opportunistic infections increases monotonically [2]; if such infections are left untreated, then people may die when their CD4 cell counts are still relatively high, just as an HIV-negative person might. For example, in a comparison of 8 studies, the mean CD4 cell count in HIV-positive patients presenting with tuberculosis was 202 cells/ μ L (range, 136–269 cells/ μ L) [3]. If better data on the time course of CD4 cell counts in a sufficiently large sample of HIV-positive patients were available, more-sophisticated models of the relationship between CD4 cell count decline, the incidence of opportunistic infections, and mortality could be developed. Our model, which draws on the limited data that are currently available, is a step in this direction.

It is nevertheless worth noting that

evidence from industrialized as well as low- and middle-income countries suggests that the majority of AIDS-related deaths occur at very low CD4 cell counts. For example, in a study in South Africa in the early 1990s, the median CD4 cell count at the onset of AIDS was 98 cells/ μ L for heterosexual patients and 40 cells/ μ L for homosexual patients, after which the median survival time was 17 and 7 months, respectively [4]. In an Australian cohort followed between 1986 and 1991, the median CD4 cell count at death was 10 cells/ μ L [5]. In Uganda, a recent study showed that the median CD4 cell count at death was 24 cells/ μ L [6]. In the United Kingdom, a study reported mean CD4 cell counts at death of 19 cells/ μ L in 1988, 44 cells/ μ L in 1997, and 58 cells/ μ L in 1998 [7].

For the purpose of our model, the variation in CD4 cell counts at death is less important than the variation in and level of CD4 cell counts before HIV seroconversion, which appear to affect the rate of CD4 cell count decline and, hence, the survival time after infection. A recent study compared CD4 cell counts in HIV-negative persons from 7 countries, and the medians varied from 599 cells/ μ L in Botswana to 968 cells/ μ L in Tanzania [8]; the authors suggested that CD4 cell count reference ranges should be established for local populations, given the pivotal role played by CD4 cell counts in decision making on the initiation and monitoring of highly active antiretroviral therapy.

The most important prediction of our model is that the distribution of survival times is independent of the initial CD4 cell count, and this prediction is not substantively altered if we assume a somewhat higher CD4 cell count at death. To the extent that the prediction is true, it suggests that, for a given person or group of people, survival from a given CD4 cell count will be longer for those whose initial CD4 cell count is low than for those in whom it is high. More-extensive data and more-sophisticated models could provide important insights into the relationship among CD4 cell count, the progression of

HIV infection, and mortality, as Lawn and Wood suggest.

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