

- rural Africa: is there a difference in median time to AIDS and survival compared with that in industrialized countries? *AIDS* **2002**; 16:597–603.
- Badri M, Lawn SD, Wood R. Short-term risk of AIDS or death in people infected with HIV-1 before antiretroviral therapy in South Africa: a longitudinal study. *Lancet* **2006**; 368:1254–9.
 - El-Sadr WM, Lundgren JD, Neaton JD, et al. CD4+ count-guided interruption of antiretroviral treatment. *N Engl J Med* **2006**; 355: 2283–96.
 - Whitworth J, Morgan D, Quigley M, et al. Effect of HIV-1 and increasing immunosuppression on malaria parasitaemia and clinical episodes in adults in rural Uganda: a cohort study. *Lancet* **2000**; 356:1051–6.

Potential conflicts of interest: none reported.

Financial support: Wellcome Trust (grant 074641 to S.D.L.); US National Institutes of Health (grant A1058736-01A1 to R.W.).

Reprints or correspondence: Dr. Stephen D. Lawn, Desmond Tutu HIV Centre, Institute of Infectious Disease and Molecular Medicine, Faculty of Health Sciences, University of Cape Town, Anzio Rd., Observatory 7925, Cape Town, South Africa (stevelawn@yahoo.co.uk).

The Journal of Infectious Diseases **2007**; 195:1078–9
© 2007 by the Infectious Diseases Society of America. All rights reserved. 0022-1899/2007/19507-0023\$15.00
DOI: 10.1086/512164

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.

**Brian G. Williams,¹ Eline L. Korenromp,^{3,5}
Eleanor Gouws,⁴ George P. Schmid,²
Bertran Auvert,^{6,7,8} and Christopher Dye¹**

¹Stop TB Department and ²HIV/AIDS Department, World Health Organization, ³The Global Fund to Fight AIDS, TB, and Malaria, and ⁴Policy, Evidence, and Partnerships Department, Joint United Nations Program on HIV/AIDS, Geneva, Switzerland; ⁵Department of Public Health, Erasmus Medical Center, University Medical Centre Rotterdam, Rotterdam, The Netherlands; ⁶Institut National de la Santé et de la Recherche Médicale, Unité 687, and ⁷University of Versailles–Saint Quentin, Faculté de Médecine Paris–Ile-de-France-Ouest, Saint Maurice, and ⁸AP-HP, Hôpital Ambroise Pare, Boulogne, France

References

- Lawn SD, Wood R. CD4 cell count distributions and HIV-associated mortality in Africa. *J Infect Dis* **2007**; 195:1078–9 (in this issue).
- Freedberg KA, Losina E, Weinstein MC, et al. The cost effectiveness of combination antiretroviral therapy for HIV disease. *N Engl J Med* **2001**; 344:824–31.
- Williams BG, Dye C. Antiretroviral drugs for tuberculosis control in the era of HIV/AIDS. *Science* **2003**; 301:1535–7.
- Maartens G, Wood R, O’Keefe E, Byrne C. Independent epidemics of heterosexual and homosexual HIV infection in South Africa—survival differences. *QJM* **1997**; 90:449–54.
- Mills GD, Jones PD. Relationship between CD4 lymphocyte count and AIDS mortality, 1986–1991. *AIDS* **1993**; 7:1383–6.
- Siika AM. Predictors of mortality in HIV-infected adult African patients receiving highly active antiretroviral therapy [abstract MoPdb04]. In: Program and abstracts of the 16th International AIDS Conference (Toronto). Geneva: International AIDS Society, **2006**.
- Porter K. Changes in mean CD4 cell count at death in persons with known duration of HIV infection [abstract TuPec3330]. In: Program and abstracts of the 13th International AIDS Conference (Durban, South Africa). Geneva: International AIDS Society, **2000**.
- Bussmann H, Wester CW, Masupu KV, et al. Low CD4+ T-lymphocyte values in human immunodeficiency virus-negative adults in Botswana. *Clin Diagn Lab Immunol* **2004**; 11:930–5.

Potential conflicts of interest: none reported.

Reprints or correspondence: Dr. Brian G. Williams, World Health Organization, WHO/CDS/HTM/STB/TME, 20 Ave. Appia, Geneva 1211, Switzerland (williamsbg@who.int).

The Journal of Infectious Diseases **2007**; 195:1079
© 2007 by the Infectious Diseases Society of America. All rights reserved. 0022-1899/2007/19507-0024\$15.00
DOI: 10.1086/512165