

## When to Start ART in Africa

**TO THE EDITOR:** In their Perspective article, De Cock and El-Sadr (March 7 issue)<sup>1</sup> highlight the need for data on when to start antiretroviral therapy (ART) for HIV-infected people in Africa who have CD4+ counts above 350 cells per cubic millimeter. However, their proposed solution — a new randomized, controlled trial in Africa — is flawed.

First, before a new randomized, controlled trial could commence in Africa, data from the Strategic Timing of Antiretroviral Treatment (START) trial (ClinicalTrials.gov number, NCT00867048), the Early Antiretroviral Treatment and/or Early Isoniazid Prophylaxis Against Tuberculosis in HIV-Infected Adults (TEMPRANO) trial (NCT00495651), and the Evaluating Strategies to Reduce Mother-to-Child Transmission of HIV Infection in Resource-Limited Countries (PROMISE) trial (NCT01061151) will most likely disturb the equipoise that arguably exists today.

Second, although the authors argue that African populations have more coexisting conditions than other populations, patients with coexisting conditions may derive greater benefit from early treatment.<sup>2</sup> Therefore, a new trial in Africa might contribute little if other studies show a significant benefit from earlier ART.

Finally, the authors acknowledge that millions of people do not receive ART as recommended by guidelines based on current data. This lack of treatment may be due to fiscal constraints and lack of capacity in the health system; implementation research could better identify strategies for earlier linkage to treatment or for building such capacity. Most important, sustainable funding for treating people with HIV who we know require such treatment for their health is more urgently needed than an additional randomized, controlled trial on when to start ART in Africa.

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1. De Cock KM, El-Sadr WM. When to start ART in Africa — an urgent research priority. *N Engl J Med* 2013;368:886-9.
2. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med* 2011; 365:493-505.

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**THE AUTHORS REPLY:** Public health decisions and the commitment of billions of dollars for health programs must be based on the best possible scientific evidence. Yet recommendations concerning when to start ART in the millions of people living with HIV are based more on opinion than on conclusive evidence; this highlights the need for a definitive trial in sub-Saharan Africa, the most severely affected region globally. Other studies cited by Shah and Grady will provide useful information but not necessarily all the answers required. The START trial focuses predominantly on patients in industrialized countries, where the HIV-associated spectrum of disease is different from that which predominates in sub-Saharan Africa. The TEMPRANO trial is limited in size and geographic location, and the PROMISE trial involves pregnant women.

It is often hazardous in medicine to base therapeutic and policy guidance on results of single trials, exclusively observational studies, or studies designed with a different primary purpose. Implementation science to better guide the use of resources and enhance program quality is critically important but cannot replace evidence-based decision making. Decisions about the best use of resources are better informed when policy options are based on the strongest science.

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