Antiretroviral Preexposure Prophylaxis for HIV Prevention

TO THE EDITOR: Thigpen et al. (Aug. 2 issue)[1] report that persons who are seronegative for the human immunodeficiency virus (HIV) and who are receiving tenofovir disoproxil fumarate and emtricitabine (TDF–FTC) for preexposure prophylaxis had decreased bone mineral density at 24 months, as compared with those receiving placebo. In HIV-infected cohorts, TDF causes an initial loss of bone density over a period of 6 to 12 months, but there is stable bone density subsequently.[2,3] These findings are consistent with other studies that have shown short-term loss of bone density in patients initiating antiretroviral treatment but stable bone density in those already receiving antiretroviral treatment.[4]

In contrast, Thigpen et al. found the opposite pattern: participants receiving TDF–FTC had relatively stable bone density for 12 months and then lost bone density between 12 and 24 months. The bone-density substudy had a high withdrawal rate, with only 40% of the participants having a bone-density measurement at 12 months and 26% at 24 months. This pattern could occur if participants with either normal bone density on the initial measurement or stable bone density on early serial measurements were more likely to withdraw. Can the authors report the baseline bone-density results and the changes over time among participants who withdrew, as compared with those who completed the study?

Mark J. Bolland, M.B., Ch.B., Ph.D.
Andrew Grey, M.D.
University of Auckland
Auckland, New Zealand
m.bolland@auckland.ac.nz

No potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: What would we think of a cholera-prevention trial in which a population was given doxycycline prophylaxis or placebo without attention being paid to the quality of their water supply? This analogy came to mind while reading the articles by Thigpen et al., Van Damme et al.,[1] and Baeten et al.[2] on the three trials evaluating the efficacy of antiretroviral therapy as preexposure prophylaxis. In dealing with a cholera outbreak, the key intervention is dealing with the upstream problem — contaminated water. Similarly, in the case of the African countries with generalized HIV epidemics, the key prevention intervention should be directed toward the underlying determinants of these epidemics. An accumulating amount of evidence now points to the high rates of sexual-partner concurrency in these countries as being key drivers of generalized HIV epidemics.[3] Unfortunately, although the three trials list what they regard as the available strategies for the prevention of HIV infection, these do not include the various programmatic interventions shown to reduce both concurrency and the incidence of HIV infection.[4] Preexposure prophylaxis, as advocated by these trials, seems destined to become another intervention that distracts from the crucial job of ensuring safer sexual networks.

Chris Kenyon, M.D.
Robert Colebunders, M.D.
Institute of Tropical Medicine
Antwerp, Belgium
chriskenyon0@gmail.com

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DR. THIGPEN AND COLLEAGUES REPLY: Bolland and Grey note that patients with HIV infection receiving TDF–FTC have a decline in bone min-

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