HIV-1 Drug Resistance Resulting from Antiretroviral Therapy Far Exceeds That From Pre-exposure Prophylaxis

TO THE EDITOR—We challenge the conclusions drawn by Hurt et al in their Viewpoint article “Pre-exposure Prophylaxis and Antiretroviral Resistance: HIV Prevention at a Cost?” The authors cite the very few cases of human immunodeficiency virus (HIV) drug resistance that have occurred in seroconverters from trials of pre-exposure prophylaxis (PrEP) as evidence of the potential for PrEP to jeopardize the long-term utility of tenofovir (TFV) and emtricitabine (FTC) in first-line treatment regimens in resource-limited settings. They also speculate that the possible increase in resistance from PrEP could offset the enormous benefit of preventing HIV infection in at-risk populations [1].

To date, only 3 cases of resistance from PrEP have occurred in a total of 80 seroconverters on active antiretroviral (ARV) arms from 3 large HIV prevention trials: 0 of 35 sequenced in the TFV gel arm in the CAPRISA-004 clinical trial [2]; 2 of 36 in the oral TDF-FTC arm in the iPrEx study [3], and 1 of 9 in the TDF2 study [4]. All 3 cases had unrecognized acute HIV infection before being placed on TFV-containing PrEP. No cases of resistance have yet been identified in trial participants who became infected after starting ARV-containing gel or tablets. By contrast, first-line antiretroviral therapy (ART) fails to suppress viremia in 22% of persons on therapy [5] and up to 95% of those who fail ART have drug-resistant HIV-1 [6]. Given that >6.6 million persons worldwide have started ART [7], failure of ART to suppress viremia, rather than failure of PrEP to prevent HIV infection, is driving the spread of drug resistance in the developing world.

Indeed, recent surveys report an increase in transmitted drug resistance in resource-limited settings, from previous estimates of <5% using World Health Organization threshold surveys conducted before 2008 [8] to as high as 12.3% in various regions in sub-Saharan Africa, particularly in areas of treatment scale-up [9]. This increase has occurred as a consequence of ART roll-out without the influence of PrEP.

More than 681,000 lives have been saved from expanding treatment roll-out [10], and an effective PrEP agent has the potential for further impact by preventing HIV-1 infection in the first place. Drug resistance will always be a risk with the use of antiretrovirals, but exaggeration of risk serves no purpose other than to raise fear and impede progress toward ending the AIDS epidemic.

Notes

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