Abstract:

BACKGROUND: Antiretroviral preexposure prophylaxis is a promising approach for preventing human immunodeficiency virus type 1 (HIV-1) infection in heterosexual populations. METHODS: We conducted a randomized trial of oral antiretroviral therapy for use as preexposure prophylaxis among HIV-1-serodiscordant heterosexual couples from Kenya and Uganda. The HIV-1-seronegative partner in each couple was randomly assigned to one of three study regimens--once-daily tenofovir (TDF), combination tenofovir-emtricitabine (TDF-FTC), or matching placebo--and followed monthly for up to 36 months. At enrollment, the HIV-1-seropositive partners were not eligible for antiretroviral therapy, according to national guidelines. All couples received standard HIV-1 treatment and prevention services. RESULTS: We enrolled 4758 couples, of whom 4747 were followed: 1584 randomly assigned to TDF, 1579 to TDF-FTC, and 1584 to placebo. For 62% of the couples followed, the HIV-1-seronegative partner was male. Among HIV-1-seropositive participants, the median CD4 count was 495 cells per cubic millimeter (interquartile range, 375 to 662). A total of 82 HIV-1 infections occurred in seronegative participants during the study, 17 in the TDF group (incidence, 0.65 per 100 person-years), 13 in the TDF-FTC group (incidence, 0.50 per 100 person-years), and 52 in the placebo group (incidence, 1.99 per 100 person-years), indicating a relative reduction of 67% in the incidence of HIV-1 with TDF (95% confidence interval [CI], 44 to 81; $P<0.001$) and of 75% with TDF-FTC (95% CI, 55 to 87; $P<0.001$). Protective effects of TDF-FTC and TDF alone against HIV-1 were not significantly different ($P=0.23$), and both study medications significantly reduced the HIV-1 incidence among both men and women. The rate of serious adverse events was similar across the study groups. Eight participants receiving active treatment were found to have been infected with HIV-1 at baseline, and among these eight, antiretroviral resistance developed in two during the study. CONCLUSIONS: Oral TDF and TDF-FTC both protect against HIV-1 infection in heterosexual men and women. (Funded by the Bill and Melinda Gates Foundation; Partners PrEP ClinicalTrials.gov number, NCT00557245.).