## ABSTRACT

### BACKGROUND:

Daily oral antiretroviral preexposure prophylaxis (PrEP) is a promising strategy for prevention of HIV-1 acquisition. Three clinical trials demonstrated PrEP efficacy; however, two PrEP trials among women did not find protection against HIV-1. One hypothesis proposed for these divergent results is that PrEP efficacy may be reduced in populations with higher HIV-1 incidence.

### METHODS:

Using data from the Partners PrEP Study, a randomized, placebo-controlled trial of daily oral tenofovir (TDF) and emtricitabine/tenofovir (FTC/TDF) PrEP among heterosexual HIV-1 serodiscordant couples from Kenya and Uganda, we assessed PrEP efficacy among subgroups at higher risk for HIV-1 acquisition, including subgroups of women with high HIV-1 incidence.

### RESULTS:

The overall placebo arm HIV-1 incidence was 2.0 per 100 person-years. Among higher risk subgroups, placebo arm HIV-1 incidence ranged from 3.9 to 6.6 per 100 person-years. In all subgroups, PrEP was protective against HIV-1 acquisition, with efficacy point estimates ranging from 64 to 84%. Among subgroups of women with placebo-arm HIV-1 incidence more than 5.0, efficacy estimates ranged from 64 to 84%. Monthly visit attendance for PrEP refills and tenofovir detection in plasma were high.

### CONCLUSION:

Among higher-risk subgroups in the Partners PrEP Study, including groups solely of higher-risk women, both TDF alone and combined FTC/TDF PrEP had consistently high efficacy for HIV-1 protection. PrEP, when used with high adherence, is a highly effective prevention strategy for higher risk heterosexuals. Prioritizing PrEP for persons at high risk of HIV-1 will maximize its prevention impact.