

# Model explains why HIV prevention dosing differs by sex

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A mathematical model developed by NIH grantees predicts that women must take the antiretroviral medication Truvada daily to prevent HIV infection via vaginal sex, whereas just two doses per week can protect men from HIV infection via anal sex. This finding helps explain why two large clinical trials testing HIV pre-exposure prophylaxis, or PrEP, in women failed to show efficacy. Participants in the [VOICE](#) and [FEM-PrEP](#) trials of Truvada and tenofovir (another antiretroviral) for HIV prevention were counseled to take one of the medications daily. However, because they actually took the antiretroviral only about 29 percent of the time in VOICE and about 36 percent of the time in FEM-PrEP, the PrEP strategy did not work.

Angela D. M. Kashuba, Pharm.D., of the University of North Carolina, and colleagues determined what intracellular ratios of active [tenofovir](#) and emtricitabine, the drugs that compose Truvada, to the DNA molecules with which they compete are necessary to prevent HIV replication. Next, using data from an [early clinical trial in women](#), the researchers created a [mathematical model](#) that predicts these ratios in vaginal, cervical and rectal tissues given standard doses of medication taken 2 to 7 days per week. Then, the scientists calculated the percentage of a study [population](#) that would achieve the effective drug-to-DNA-molecule ratio by taking tenofovir or Truvada at each dosing frequency.

The model forecasts that two standard doses per week of Truvada or a daily standard dose of tenofovir would achieve the target ratio in rectal tissue across a study population. A daily standard dose of Truvada would

achieve the target ratio in vaginal tissue in more than 75 percent of a study population, according to the model, and in cervical tissue in half of the population. A daily standard dose of tenofovir would achieve the target ratio in cervical and vaginal tissues in less than half of a study population, the model predicts.

It is easier to achieve the target ratio in rectal tissue than in cervical and vaginal tissues, according to the scientists, because the concentration of DNA molecules is lower and of tenofovir is higher in rectal tissue than in the female genital tract.

Both men and women who are prescribed Truvada for PrEP should take the pill daily as directed, according to Centers for Disease Control and Prevention guidelines.

**More information:** ABSTRACT:ML Cottrell et al. Predicting effective Truvada® PrEP dosing strategies with a novel PK–PD model incorporating tissue active metabolites and endogenous nucleotides (EN). HIV Research for Prevention 2014. Cape Town, South Africa.

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