Modeled Effectiveness of Non-Daily PrEP Based on Sex Coverage Data from HPTN 067/ADAPT Study

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INTRODUCTION

Non-daily PrEP dosing is a strategy that may be effective if sufficient PrEP doses correspond with sexual exposure. HPTN 067 is a phase II, randomized, open-label, pharmacokinetic and behavioral study of the use of Intermittent oral PrEP. Its primary objective was to evaluate the feasibility of intermittent dosing of PrEP regimen among HIV-uninfected MSM/TGW and WSM at high risk of acquiring HIV infection (178 MSM/TGW in Bangkok, 179 MSM/TGW in New York and 179 women in Cape Town). Here we present analysis based on data from Cape Town.

PREP REGIMENS AND SEX ACTS COVERAGE

- Three PrEP regimens are compared – daily, time-driven and event-driven as defined in the table below
- Pill taking is informed by an electronic dispensing device (Wisepill ™) that recorded each opening
- Sexual activity is based on weekly interviews by phone or in person, i.e., entirely based on self-reported data
- Sex coverage was defined as follows:
  - Fully covered acts - pills taken within 2 days before and 1 day after an act. This definition is more restrictive than the definition used in the trial protocol.
  - Partially covered acts - only before or after pill is taken

Regimen (Description)[1]	% Acts Fully Covered[2]	% Acts Partially Covered[2]
Daily	72%	21%
Time-driven (two regular pills/week 3-4 days apart + one pill within 2h after sex)	36%	53%
Event-driven (pills taken within 2 days before + within 2h after sex)	42%	46%

[1] No more than 1 dose daily and 7 doses weekly
[2] Based on data from the site in Cape Town, South Africa

SCENARIOS AND EFFECTIVENESS METRICS

- PrEP protection: We explore wide range (50%-90%) efficacy in reducing the HIV acquisition risk per fully covered acts and explore scenarios with:
  - **Half of the PrEP protection** retained for partially covered acts
  - **No protection** retained for partially covered acts
- **Effectiveness** $= 1 - \frac{\text{HIV incidence with PrEP}}{\text{HIV incidence without PrEP}}$

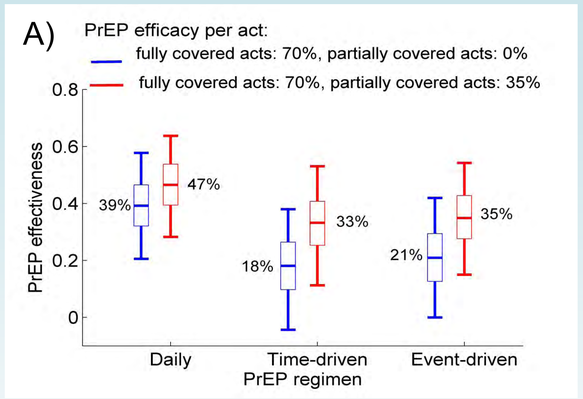
METHODS

We used a stochastic mathematical model informed by South African data to simulate one year of sexual behavior of a female cohort (average 1.2 sex-days/week) under three PrEP regimens from the trial. We modeled the reduction in HIV incidence and the number of pills that would be needed under different dosing regimens.
Regimen effectiveness was estimated as 1 minus the ratio of HIV incidence when PrEP is used vs. not used. As a proxy for costs saved, the number of pills required for each regimen was compared across different frequencies and distribution of sexual intercourse assuming perfect adherence.

MODEL DEVELOPMENT

- **Stochastic individual-based mathematical model simulates HIV acquisition among a cohort of uninfected females followed for 1 year.**
- **2000 women are assigned in 2 risk groups with number and type of current partnerships (short- or long-term) based on data from South Africa**
- **Exposure to HIV is simulated twice: assuming that PrEP is used or not.**
- **Existing partnerships are initialized with the following attributes:**
  - Starting day
  - Partner's risk level (high, low)
  - Frequency of sexual activity
  - Proportion of sex acts protected by condom
  - Practicing anal sex (yes, no). If yes, prevalence of anal sex is assigned.
  - HIV status of the partner
  - ART status of the partner
- **Daily each participant may :**
  - Initiate a new partnership (short-term) – rate varies by risk level
  - Have sex with some active partners based on the frequency of acts for each partnership. If the partner is HIV+ the probability of HIV acquisition depends on the type of the act (vaginal or anal), if the act is protected by condom, partner's HIV stage and ART status, PrEP protection (based on sex act coverage – full or partial)
  - Active partner(s) may acquire HIV outside the relationship depending on his (their) risk level
  - Short-term partnership convert into long-term after 9 months
  - Break up a partnership – vary by partnership type and concurrency status.
- **Rates of initiation and dissolution of partnerships, frequency, type, and protection of sexual acts are calibrated for South Africa (Cape Town).**

ESTIMATES OF PREP EFFECTIVENESS BASED ON SEX ACT COVERAGE



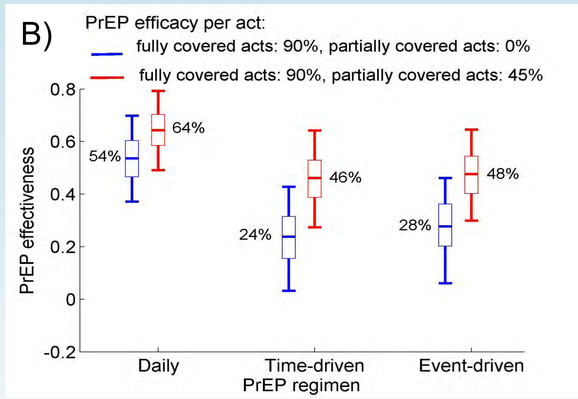


Figure 1. Reduction in HIV incidence due to PrEP use assuming A) 70% efficacy, B) 90% efficacy and C) 50% efficacy of PrEP per fully covered act. Presented results are based on 1000 simulations per scenario – interquartile range (box), 90% uncertainty interval (whiskers).

ESTIMATES OF WEEKLY PILL COUNT

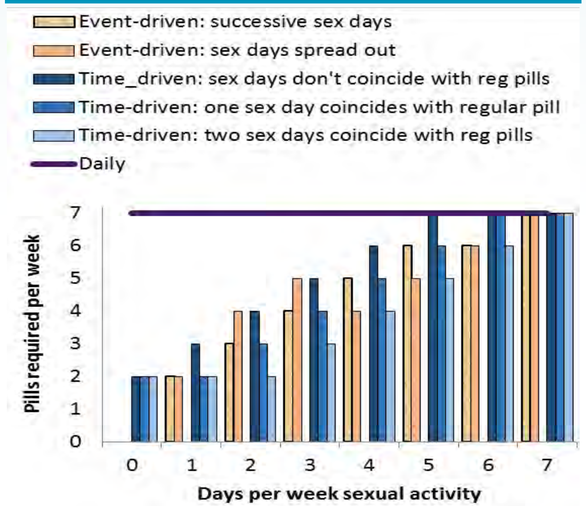
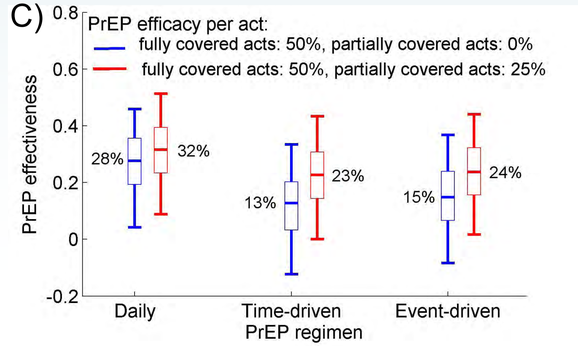


Figure 2. Pills needed by PrEP regimen for different frequency and distribution of sexual activity assuming that PrEP is taken as prescribed in the trial regimens



CONCLUSIONS

Non-daily PrEP may substantially reduce the number of pills required for the level of sexual activity observed in the HPTN 067 trial. However, non-daily PrEP is unlikely to be as effective as daily PrEP in reducing HIV incidence among women in South Africa due to higher sex act coverage observed in the daily use arm. The significant proportion of sex acts partially covered by PrEP implies that the effectiveness of non-daily PrEP depends on the protection provided with partial dosing.

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