Supplementary material for: Evaluating the cost-effectiveness of pre-exposure prophylaxis (PrEP) and its impact on HIV-1 transmission in South Africa
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Mathematical model

The mathematical model underlying this analysis is a simple extension of the model developed and parameterized in [1]. Parameter descriptions for this model are given in table S1, while parameter values are listed in Tab. 1 [1]. Parameter description and values related to inclusion of PrEP in the model descriptions are given in table S2.

It consists of only a few compartments which are all structured by age. Throughout the index $k$ refers either to females ($k = f$) or to males ($k = m$). Let:

- $S_k(t,x)$ be the susceptible population of sex $k$ aged $x$ ($x \geq 1$, age $x$ corresponding to those people whose exact age is between $x - 1$ and $x$) at time $t$ ($t \geq t_0$).
- $P_k(t,x,y)$ be the HIV− population of sex $k$ aged $x$ at time $t$ that have received PrEP for $y$ years.
- $I'_k(t,x,y)$ be the population of sex $k$ aged $x$ at time $t$ that has been HIV+ for $y$ years ($1 \leq y \leq x$) who are infected and receiving PrEP.
- $I_k(t,x,y)$ be the population of sex $k$ aged $x$ at time $t$ that has been HIV+ for $y$ years ($1 \leq y \leq x$) who are not receiving ART or PrEP.
- $A_k(t,x,y)$ is the HIV+ population of sex $k$ aged $x$ at time $t$ that is receiving ART and that spent $y$ years ($1 \leq y < x$) infected but without treatment.
- $N_k(t,x) = S_k(t,x) + P_k(t,x) + I'_k(t,x) + I_k(t,x) + A_k(t,x)$ where, with a slight abuse of notation,

$$
\begin{align*}
    P_k(t,x) &= \sum_{y \leq x} P_k(t,x,y), \quad I'_k(t,x) = \sum_{y \leq x} I'_k(t,x,y) \\
    I_k(t,x) &= \sum_{y \leq x} I_k(t,x,y), \quad A_k(t,x) = \sum_{y < x} A_k(t,x,y)
\end{align*}
$$

Keeping the notations of [1], set $J_k(t,x) = I_k(t,x) + \varepsilon \left( I'_k(t,x) + A_k(t,x) \right)$. The force of infection is assumed to be

$$
\begin{align*}
    \lambda_f(t,x) &= 1 - \exp \left( -p_f(1-c(t,x))r(x)\sum_z s(x,z)J_m(t,z)/N_m(t,z) \right) \\
    \lambda_m(t,x) &= 1 - \exp \left( -p_m\sum_z (1-c(t,z))r(z)s(z,x)J_f(t,z)/N_m(t,x) \right)
\end{align*}
$$
for non PrEP users and
\[
\lambda'_f(t,x) = 1 - \exp \left( -p_f(1-\phi)(1-c'(t,x)) r(x) \sum_z s(x,z) J_m(t,z)/N_m(t,z) \right)
\]
\[
\lambda'_m(t,x) = 1 - \exp \left( -p_m \sum_z (1-\phi)(1-c'(t,z)) r(z) s(z,x) J_f(t,z)/N_m(t,x) \right)
\]
for PrEP users. Let $\theta'_k$ be the PrEP starting rate for people whose age is between $x-1$ and $x$. The ART starting rate is assumed to be
\[
\theta(t,x,y) = h_2(t) \rho(x,y) \psi/(1-\psi) + h_3(t) \tau
\]
Notice that under the current ART program ($h_2 = 1$ and $h_3 = 0$), HIV+ people are subject to two competing risks: the risk of dying at a rate $\rho(x,y)$, and the risk (the chance) of starting ART at a rate $\rho(x,y) \psi/(1-\psi)$. Thus a fraction $\psi$ starts ART.

The rate at which PrEP individuals start ART is assumed to be higher:
\[
\theta^*(t,x,y) = \nu \theta(t,x,y) \nu > 1
\]
to account for the likelihood that PrEP users will undergo regular screening and thus be more likely to enroll for ART.

Our assumptions regarding the initial condition $t = t_0$ are as follows. For all $1 \leq x \leq \omega$, we assume that $S_k(t_0,x) = N_k(t_0,x)$ except that $S_m(t_0,x_0) = N_m(t_0,x_0) - 1$. For all $1 \leq y \leq x \leq \omega$, we assume that $I_k(t_0,x,y) = 0$ except that $I_m(t_0,x_0,1) = 1$. Finally, $A_k(t_0,x,y) = 0$ for all $1 \leq y < x \leq \omega$.

For $t \geq t_0$ and $1 \leq x \leq \omega - 1$, the susceptible population is given by
\[
S_k(t+1,1) = b(t) (1-\pi(t)),
\]
\[
S_k(t+1,x+1) = (1-\mu_k(x))(1-\lambda_k(t,x))(1-\theta'_k(t,x))S_k(t,x)
+ (1-\mu_k(x))(1-\lambda'_k(t,x)) \phi' P_k(t,x)
\]
The PrEP receiving population is given for $t \geq t_0$ and $1 \leq y \leq x$ by
\[
P_k(t+1,x+1,1) = (1-\mu_k(x))(1-\lambda_k(t,x)) \theta'_k(t,x) S_k(t,x),
\]
\[
P_k(t+1,x+1,y+1) = (1-\mu_k(x))(1-\lambda'_k(t,x)) (1-\phi') P_k(t,x,y)
\]
The PrEP receiving population who are infected is given for $t \geq t_0$ and $1 \leq y \leq x \leq \omega - 1$ by
\[
I'_k(t+1,x+1,1) = (1-\mu_k(x)) \lambda'_k(t,x) (1-\phi') P_k(t,x)
+ (1-\mu_k(x)) \lambda_k(t,x) \theta'_k(t,x) S_k(t,x)
\]
\[
I'_k(t+1,x+1,y+1) = (1-\mu_k(x))(1-\rho(x,y))(1-\phi'_k(t,x,y)) I_k(t,x,y)
+ (1-\mu_k(x)) \phi (1-\sigma(t,y)) A_k(t,x,y)
+ (1-\mu_k(x))(1-\rho(x,y)) \phi'_k (1-\theta^*(t,x,y)) I'_k(t,x,y)
\]
Here $\phi'_k \geq \phi$ is the rate at which HIV+ PrEP users will discontinue PrEP use. The infected population without treatment is given for $t \geq t_0$ and $1 \leq y \leq x \leq \omega - 1$ by
\[
I_k(t+1,1,1) = b(t) \pi(t),
\]
\[
I_k(t+1,x+1,1) = (1-\mu_k(x)) \lambda_k(t,x) (1-\theta'_k(t)) S_k(t,x),
+ (1-\mu_k(x)) \lambda'_k(t,x) \phi' P_k(t,x,y)
\]
\[
I_k(t+1,x+1,y+1) = (1-\mu_k(x))(1-\rho(x,y))(1-\theta(t,x,y)) I_k(t,x,y)
+ (1-\mu_k(x)) \phi (1-\sigma(t,y)) A_k(t,x,y)
+ (1-\mu_k(x))(1-\rho(x,y)) \phi'_k (1-\theta^*(t,x,y)) I'_k(t,x,y)
\]
The ART-treated population is given for \( t \geq t_0 \) and \( 1 \leq y \leq x \leq \omega - 1 \) by

\[
A_k(t + 1, x + 1, y) = (1 - \mu_k(x))(1 - \phi)(1 - \sigma(y)) A_k(t, x, y) \\
+ (1 - \mu_k(x))(1 - \rho(x, y)) \theta(t, x, y) I_k(t, x, y) \\
+ (1 - \mu_k(x))(1 - \rho(x, y))(1 - \phi'_x) \theta^*(t, x, y) I'_k(t, x, y)
\]

setting \( A_k(t, 1, 1) = 0 \) for all \( t \) for convenience.

Acknowledgments

References

1. Bacaer N, Pretorius C, Auvert B (2010) An age-structured model for the potential impact of generalized access to antiretrovirals on the South African HIV epidemic. Bull Math Biol doi:10.1007/s11538-010-9535-2.

Tables
Table 1. Notations and parameter description. "M2C" stands for mother-to-child, "prob." for probability.

| Notation  | Description |
|-----------|-------------|
| $k$       | sex (female or male) |
| $t_0$     | year of introduction of HIV |
| $t$       | time, $t \geq t_0$ |
| $\omega$ | maximum age considered |
| $x$       | age, $1 \leq x \leq \omega$ |
| $y$       | time since infection without ART |
| $x_0$     | age of first infected woman |
| $b(t_0)$ | annual male (and female) births at $t = t_0$ |
| $p_f$     | HIV transmission prob. (man to woman) |
| $p_m$     | HIV transmission prob. (woman to man) |
| $q_0$     | M2C transmission prob. |
| $q_1$     | M2C transmission prob. with PMTCT |
| $\varepsilon$ | relative infectiousness of people on ART |
| $\phi$   | ART drop-out |
| $\tau$   | annual proportion tested for HIV |
| $N_k(t_0, x)$ | age pyramid at $t = t_0$ |
| $\mu_k(x)$ | death rate if HIV- |
| $b(t)/b(t_0)$ | changing birth rate |
| $\beta(x)$ | normalized female fertility |
| $u$       | under-reporting of male sexual partners |
| $u_r(x)$  | reported turnover of male sexual partners |
| $s(x, y)$ | choice of male sexual partner |
| $c(t, x)$ | condom use |
| $\rho(x, y)$ | AIDS mortality |
| $\rho_1(y)$ | adult AIDS mortality |
| $\sigma(y)$ | mortality under ART |
| $h_1(t)$ | access to PMTCT |
| $h_2(t)$ | access to current ART program |
| $h_3(t)$ | access to the “test and treat” strategy |
| $\psi$   | proportion starting ART in current program |
Table 2. Extension to notations and parameters used in [1]. PrEP parameters used in Section: “Universal PrEP and UTT: comparative impact”

| Notational parameters |   |
|-----------------------|---|
| $k$: sex (female or male) | $f$ or $m$ |
| $t_0$: year of introduction of HIV | $t \geq t_0$ |
| $t$: time |   |
| $\omega$: maximum age considered |   |
| $x$: age | $1 \leq x \leq \omega$ |
| $y$: disease duration | $1 \leq y \leq \omega$ |

| PrEP sub-model |   |
|---------------|---|
| $\theta_k$: access to PrEP | 20% per year |
| $\theta(t, x, y)$: access to ART for non-PrEP users | eq. 1 |
| $\theta^\ast = \nu \theta$: access to ART for PrEP users | $\nu = 1.5$ |
| $\varphi$: efficacy of PrEP | 90% |
| $\varphi'$: PrEP drop-out | 1.5% per year |
| $\varphi_{\prime}':$ PrEP discontinuation rate | 100% per year |
| $c_k'(t, x)$: condom substitution for those using PrEP | 0% |