A mathematical model for the impact of PrEP use and its increase in coverage on the transmission of HIV/AIDS: Study in Brazil

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Abstract

In this work, we present a mathematical model for the study of HIV/AIDS considering the implementation of Pre-Exposure Prophylaxis (PrEP). A method to study the effect of increasing the use of PrEP and the incidence of HIV in a population is proposed in the model. We perform computational simulations, using demographic and HIV/AIDS data from Brazil, and utilize the Markov Chain Monte Carlo method with a Bayesian approach to estimate model parameters. We compare different increases in the coverage of the PrEP program and verify the positive effect of reducing the incidence of HIV and the number of cases avoided by an increase in PrEP coverage in the population.

Model

For the construction of the model, we considered the following compartments: Susceptibles (S), exposed to HIV/AIDS (E), people using PrEP (P), HIV cases (H), AIDS cases (A), and HIV/AIDS positive cases with undetectable viral load in blood (V). The model that studies the behavior of HIV/AIDS with the presence of PrEP in a population is described as:

$$\frac{dS}{dt} = \Lambda + \epsilon_f P + \epsilon_{s2} E - (\mu + \lambda + \alpha_s + \epsilon_p) S, \tag{1}$$

$$\frac{dE}{dt} = \lambda S - (\epsilon_{s1} + \mu + \epsilon_{s2}) E, \tag{2}$$

$$\frac{dP}{dt} = \epsilon_p S - (\mu + \epsilon_f + \epsilon_D) P, \tag{3}$$

$$\frac{dH}{dt} = \phi(\epsilon_{s1} E + \epsilon_D P) + \sigma_H V + \alpha_s S - (\mu + d_H + \tau + \sigma_{HI}) H, \tag{4}$$

$$\frac{dA}{dt} = (1 - \phi)(\epsilon_{s1} E + \epsilon_D P) + \omega V + \tau H - (\mu + d_H + \nu) A, \tag{5}$$

$$\frac{dV}{dt} = \sigma_{HI} H + \nu A - (\mu + d_H + \sigma_H + \omega) V. \tag{6}$$

with initial conditions:
$S(t_0) > 0, E(t_0) > 0, P(t_0) \geq 0, H(t_0) > 0, A(t_0) > 0$ and $V(t_0) > 0$.
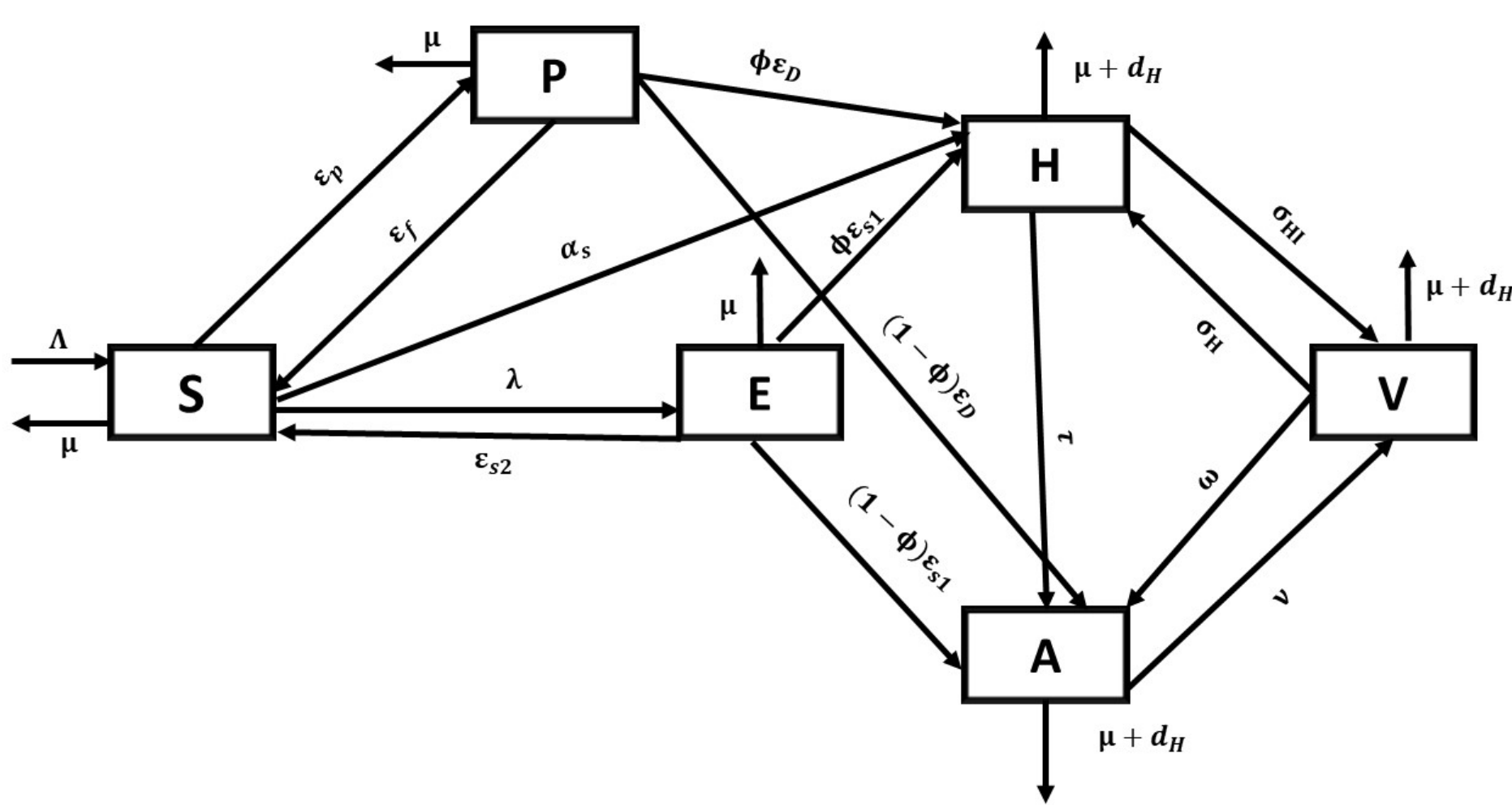

Figure 1. Flow chart of Model (1)-(6).

Basic Properties of Model

We proved the existence and non-negativity of the solution of Model (1)-(6), and found the biologically feasible region.

- **Part I** (Theorem): Let initial data be $S(t_0) > 0, E(t_0) > 0, P(t_0) > 0, H(t_0) > 0, A(t_0) > 0$ and $V(t_0) > 0$. Then, the solutions $(S(t), E(t), P(t), H(t), A(t), V(t))$ of model (1)-(6) are positive for all $t > 0$. Furthermore,

$$\limsup_{t \to \infty} N(t) \leq \frac{\Lambda}{\mu}. \tag{7}$$

- **Part II** (Lemma): The closed set $\Omega = \left\{ (S, E, P, H, A, V) \in \mathbb{R}_+^6 : N(t) \leq \frac{\Lambda}{\mu} \right\}$ is positively-invariant and attracts all solutions of Model (1)-(6).

- **Part III** (Theorem): The solutions of the model (1)-(6) with non-negative initial conditions exist for all time.

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Incidence

Incidence is the number of newly diagnosed cases of a disease. The incidence rate is the number of new cases of a disease divided by the number of people at risk of contracting the disease [1]. New entries in the HIV compartment are incorporated into the model with the following differential equation respectively:

$$\frac{dI}{dt} = \phi(\epsilon_{s1} E + \epsilon_D P) + \alpha_s S. \tag{8}$$

The HIV incidence is defined as:

$$I^*(t) = I(t) - I(t-1), \tag{9}$$

where t is the current time and $t - 1$ is the moment of time immediately preceding.

Increase PrEP Coverage

The new PrEP coverage is based on the percentage increase of the current coverage, so the parameter ϵ_p (Use PrEP rate) in the period 2025-2035 will have the following structure:

$$\epsilon_p(t) = \epsilon_p(t-1) + p_s \epsilon_p(t-1), \tag{10}$$

where $\epsilon_p(t)$ is the current coverage in that year, $\epsilon_p(t-1)$ is the coverage in the previous year, and p_s is the percent increase in coverage.

Parameter Estimation

For the estimation of the model parameters, we used the MCMC (Markov Chains Monte Carlo) with a Bayesian approach [2, 3]. The algorithm was implemented in `R` through the `Rstan` package. To solve the deterministic system, we used a predictor-corrector method based on the Runge-Kutta predictor of order 4 and corrector of order 5.

Numerical Simulations

We used the data reported by the Brazilian Ministry of Public Health between 2003 and 2019 and the compartment of individuals who are in the PrEP program, we assume zero value until 2018.
We compare two possible increases in PrEP coverage between 2025 and 2035, Coverage I, which is an increase of 25% per year, and Coverage II, an increase of 35% per year, both following Formula (10), with respect to keeping the current rate of PrEP use fixed.
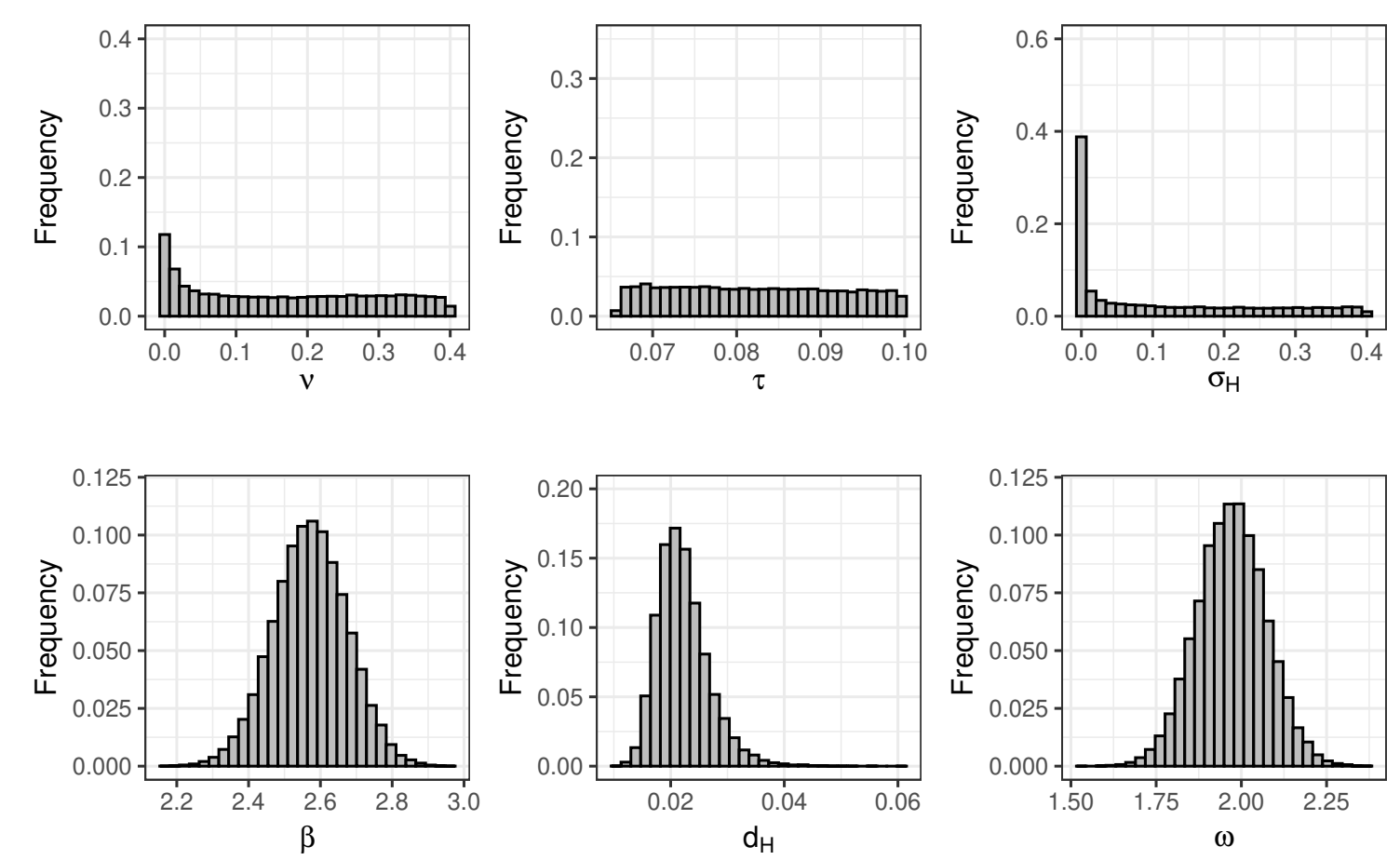

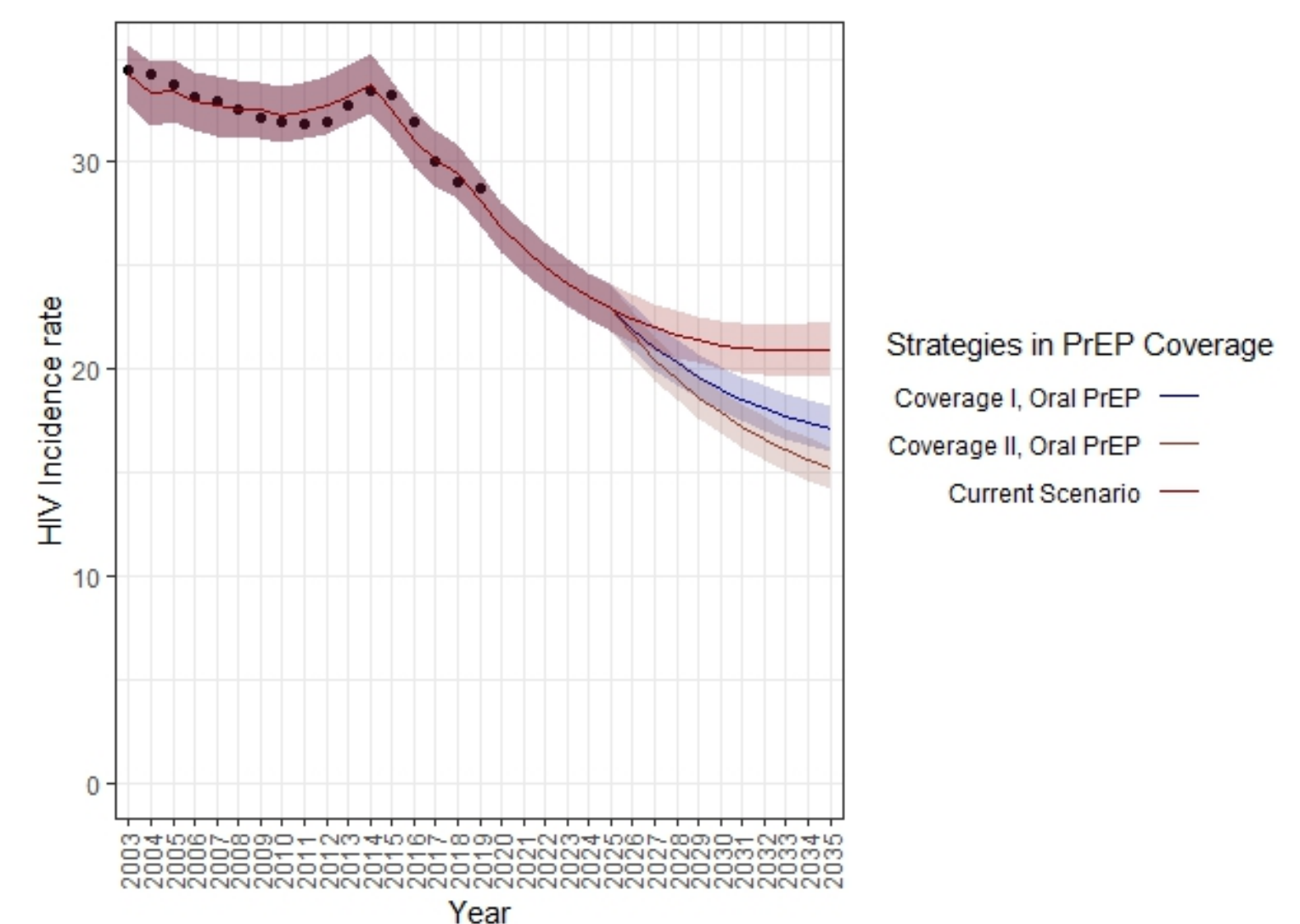Figure 2. Posterior probability density functions obtained using MCMC with Bayesian approach.

Figure 3. Behavior of the HIV incidence rate for the different increases in coverage starting in 2025 and when we maintain PrEP with the current coverage until 2035. The credibility intervals between 2.5% and 97.5% are shown and the black points are the real data reported.

	2.5%	50%	97.5%
Coverage I	15985	50879	85448
Coverage II	42774	77269	111868
Difference	26790	26390	26420

Table 1. Number of cases avoided in 2035 with the different coverage increases started in 2025, compared to maintaining the current coverage until 2035. Shows the difference in the number of cases avoided between Coverage I and Coverage II.

Conclusion

In this article, we present a mathematical model for HIV/AIDS transmission that incorporates current PrEP programs. We studied two possible increases in PrEP program coverage of 25% and 35%. With the results reported by the model. We compare the behavior after increasing coverage by 25% and 35% in 2025 compared to maintaining the current coverage with oral PrEP.
With the results reported by the model, we found that increasing PrEP coverage and maintaining antiretroviral therapy coverage for newly diagnosed patients is effective in reducing HIV cases.
The results of the model we present demonstrate the potential of PrEP to reduce the incidence of HIV in Brazil. This model, by adapting the initial conditions and parameters, can be studied in other regions, countries or localities.

References

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