MATHEMATICAL EPIDEMIOLOGY OF HIV/AIDS IN CUBA DURING THE PERIOD 1986-2000

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Abstract. The dynamics of HIV/AIDS epidemics in a specific region is determined not only by virology and virus transmission mechanisms, but also by region's socioeconomic aspects. In this paper we study the HIV transmission dynamics for Cuba. We modify the model of de Arazoza and Lounes [1] according to the background about the virology and the socioeconomic factors that affect the epidemiology of the Cuban HIV outbreak. The two main methods for detection of HIV/AIDS cases in Cuba are "random" testing and contact tracing. As the detection equipment is costly and depends on biotechnological advances, the testing rate can be changed by many external factors. Therefore, our model includes time-dependent testing rates. By comparing our model to the 1986-2000 Cuban HIV/AIDS data and the de Arazoza and Lounes model, we show that socioeconomic aspects are an important factor in determining the dynamics of the epidemic.

1. **Introduction.** Human immunodeficiency virus (HIV) is a global problem with an estimated 40 million infected worldwide [2]. Population infectivity estimates range as high as 8.5% for sub-Saharan Africaand as low as less than 0.1% for East Asia and for Australia and New Zealand. Cuba, in this respect, is remarkable as its infectivity is estimated at less than 0.1% despite its status as a relatively resource-poor nation [3, 4]. The understanding of Cuban HIV/AIDS infectivity dynamics may assist the design of preventive and reactive measures to HIV in countries with

TABLE 1. New cases of HIV, AIDS, AIDS-related deaths in Cuba 1986-2000 [1].

Year	HIV cases	AIDS cases	Death due to AIDS
1986	99	5	2
1987	75	11	4
1988	93	14	6
1989	121	13	5
1990	140	28	23
1991	183	37	17
1992	175	71	32
1993	102	82	59
1994	122	102	62
1995	124	116	80
1996	234	99	92
1997	363	129	99
1998	362	150	98
1999	493	176	122
2000	545	251	142

high HIV prevalence. This hypothesis is supported by Cubas well-developed health care system, despite its resource limitations [3, 4].

The purpose of this paper is to develop a new model that explains the dynamics of the HIV/AIDS epidemic in Cuba, focusing on the period of 1986-2000. We built our model upon the work of de Arazoza and Lounes (2002), and we confront both models with the available data [1]. We begin in Section 2 with a review of the virology of HIV/AIDS within the socioeconomic framework of Cuba 1986-2000. The formulation and brief analysis of the mathematical model follows in Section 3, as well as the comparison of the model with data. We finish with a discussion in Section 4.

2. **Background.** With a total population of 11 million and less than 1000 infected, Cuba's HIV/AIDS epidemic is a small one. As part of the HIV/AIDS prevention program, Cuba has an active search of seropositives through the sexual contacts of known HIV-infected persons; this system is called contact tracing. Infected persons are also found through a "blind" search of blood donors, pregnant women, persons with other sexually transmitted diseases, etc. [1]. Both methods are very successful in locating HIV-positive persons [1]. The numbers of newly diagnosed HIV cases, AIDS cases, and AIDS-related deaths per year in Cuba are detailed in Table 1 and plotted in Figure 1 below [1]. However, fluctuations in these numbers are due both to the character of the HIV virus and to the manner in which the Cuban population has been monitored for its presence. A model which does not distinguish virology, the socioeconomic framework in which this virology exists (i.e., the epidemiology), and the way this framework has been observed, may generalize very poorly.

2.1. **Virology.** An average HIV-infected individual progresses through distinct stages of the disease. Infectiousness (i.e., the probability of transmission) varies greatly depending upon the stage of the disease. First comes a period of primary infection (lasting part of a year [5]). During the primary stage, infectiousness first
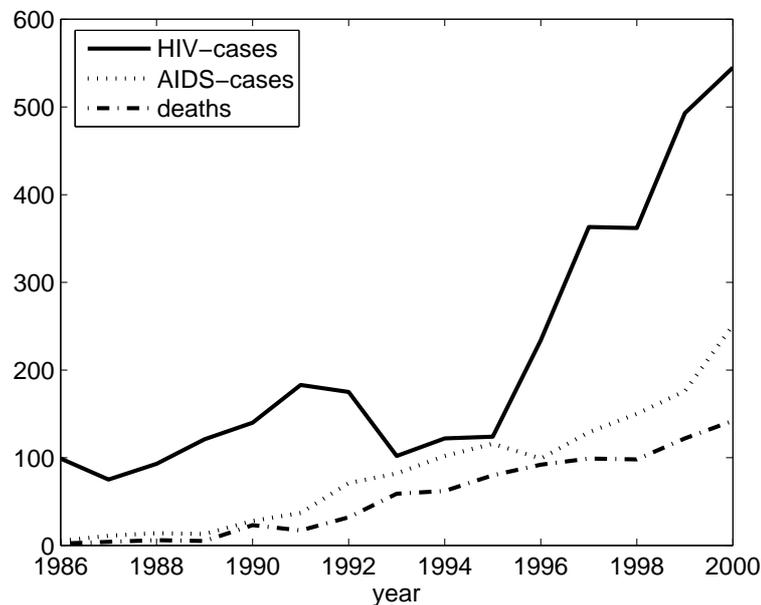
FIGURE 1. New cases of HIV, AIDS, AIDS-related deaths in Cuba 1986-2000 [1].

rises and then drops. Seroconversion usually occurs before the end of the first year. A person then enters an asymptomatic period (averaging seven years without treatment [5]) in which infectiousness is low. This is followed by a symptomatic stage (averaging three years until death, without treatment [5]) where infectiousness rises again. Although toward the end of the symptomatic stage individuals are experiencing severe AIDS and activity is decreased, the symptomatic stage begins while individuals are relatively healthy and still very active. The average stage infectivity rates for semen have a small peak shortly after initial infection followed, by a larger peak during the symptomatic phase [6]. This correlates with the changes in viral load observed as a person progresses through the disease [7, 8, 9, 10]. This pattern is due to the physiology of the disease, the way the infected persons' bodies interact with the virus [11, 12, 13, 14], and is largely independent of the sexual practices. In Cuba, most of the transmissions occur through sexual intercourse (about a 1:1 ratio of heterosexual to homosexual transmission) [15, 16, 17, 18].

2.2. **HIV in Cuba.** Cuba treated the introduction of HIV into the country in 1986 as a public health emergency, introducing control measures to contain the spread of the disease. As a result, Cuba has one of the lowest prevalence rates of HIV infection in the world. Cuba's HIV prevalence of 0.03% is nearly 11 times lower than that of the United States [19, 20]. In 1986, Cuba introduced a national screening program. Cuba had a well-developed health care system that assigned a primary care physician to all citizens and conducted routine surveillance for infectious disease [21, 22]. To reduce the risk of transmission Cuba instituted numerous measures, including contact tracing, isolation (quarantine) of HIV-infected individuals and a total ban on the import of blood and blood byproducts [15, 23]. Initially,

quarantined individuals lived in isolation in sanitariums. By 1993, patients could choose between living within a sanitarium or living at home. In the sanitariums, people are provided with good meals, a partial salary, free medications and care from physicians [24]. Most individuals can not provide the care necessary for themselves and therefore most choose to live in the sanitariums [15]. Once a person is quarantined, he or she is no longer a factor in the transmission of the disease. Contact tracing in Cuba involves searches for HIV-positive persons through the sexual contacts of known HIV-infected individuals. This practice has proven to be quite effective in Cuba [23]. Since a significant fraction of those found to be HIV-positive are identified through contact tracing, a model of HIV in Cuba must allow for contact tracing.

2.2.1. *HIV Data.* To model the Cuban HIV epidemic, one has to acknowledge contact tracing and quarantines as well as any inconsistencies with the available data (Table 1, Figure 1). The second column in Table 1 represents those individuals who tested positive for HIV during that year; they may have acquired the disease some time before. The total number of HIV cases in column two includes both newly tested HIV-positives and people in the AIDS stage. Because of this combination along with the aggressive testing of Cuba, we believe the AIDS data (column 3) to be more reliable than the HIV data. From Table 1, it appears that from 1990-1992 there was an increase in the number of newly HIV-infected persons. This increase was due to the discovery and contact tracing, from approximately 1990 to 1992, of a highly sexually active group. [25]. Because of a 1992 United States embargo, new HIV testing equipment was no longer available to Cuba [15], leading to a decrease in the number of newly HIV infected individuals being discovered that year. These two events are highlighted in Figure 2. A model of the HIV epidemic in Cuba must account for these two significant events.

3. Mathematical models and analysis.

3.1. **Previous Model.** De Arazoza and Lounes have modeled Cuba's HIV/AIDS epidemic. They consider three divisions of the population, undiagnosed HIV positive (U), diagnosed HIV positive (D), and AIDS (A), with the following constant coefficients (values listed in Table 2):

1. N, total size of the sexually-active population,
2. α, the rate of recruitment of new HIV-infected persons, infected by U,
3. α', the rate of recruitment of new HIV-infected persons, infected by D,
4. k_1, the rate at which the unknown HIV-infected persons are detected by the system ("random"' search),
5. k_2, the rate at which the unknown HIV-infected persons are detected through contact tracing,
6. β, the rate at which the HIV positives develop AIDS,
7. μ, the mortality rate of the sexually active population,
8. μ', the mortality rate of the population with AIDS.

In this model there are two ways individuals can go from unknown HIV-infected to diagnosed HIV-infected, through contact tracing (k_2UD) and detection through all other random searching for seropositives (k_1U). Authors assume that the known HI-infected persons are infectious, but at a much lower rate than those who do not know they are infected.
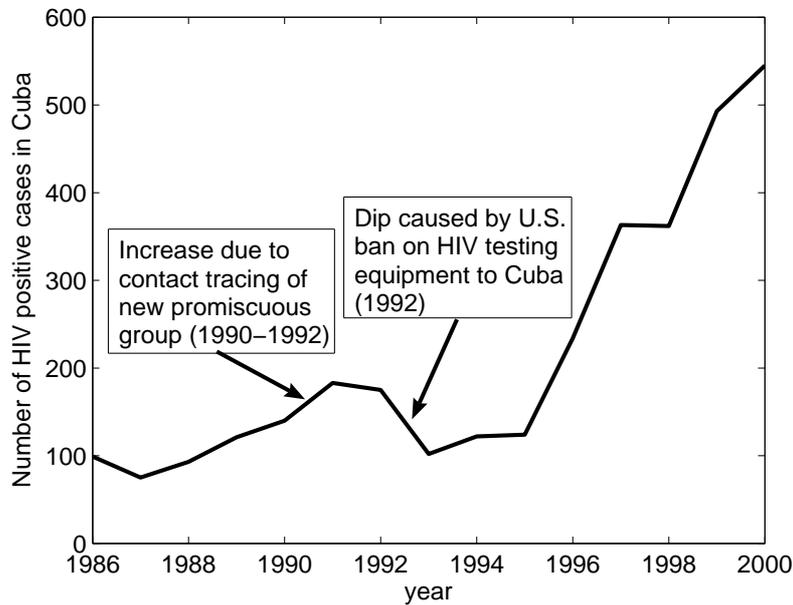
FIGURE 2. Socioeconomic factors that influenced diagnosis of HIV positive persons.

Their model equations are:

$$U' = \alpha NU + \alpha' ND - (k_1 + \mu + \beta)U - k_2 UD, \tag{1a}$$

$$D' = k_1 U + k_2 UD - (\mu + \beta)D, \tag{1b}$$

$$A' = \beta(U + D) - \mu' A. \tag{1c}$$

3.2. **Model Design.** To improve upon the previous model by de Arazoza and Lounes, we have made three major changes:

1. We consider four divisions of the population, susceptible (S), undiagnosed HIV positive (U), diagnosed HIV positive (D), and AIDS (A). We considered this to be a closed population and all births equal deaths.

2. We incorporate the variation in infectivity as a person progresses through the disease, by considering the rate for a susceptible to be infected by an individual with AIDS, ω. With the aggressive "random" testing in Cuba, by the time individuals progress to the AIDS stage they have been diagnosed. Although individuals with AIDS are much more infectious than individuals with HIV [6], an AIDS individual would have fewer contacts with susceptible persons compared to the contacts made by undiagnosed individuals with susceptibles thus, ω is lower than the rate for a susceptible to be infected by an undiagnosed HIV person, denoted α'. When comparing persons in the the AIDS stage and diagnosed HIV persons, since AIDS stage is more infectious, we assume the rate for a susceptible to be infected by an individual with AIDS, ω, to be higher than the rate of a diagnosed HIV positive individual, α'.

3. Undiagnosed individuals are diagnosed by their doctors at a rate k_1, and through contact tracing at a rate k_2. We consider three phases for contact tracing, 1986-1989, 1990-1991 and 1992-2000, and two phases for "random" testing, 1986-1991 and 1992-2000. In each period, k_1 and k_2 are constant. We estimate that during 1990 and 1991 contact tracing increased 25% because of the detection of a highly sexually active group, and that after 1992 diagnosis by doctors was reduced to 75% of its former value due to the United States embargo. We obtain values of k_1 and k_2 by fitting the Cuban HIV/AIDS data.

The dynamics of the Cuban HIV/AIDS epidemic are described by the following model:

$$
\begin{aligned}
S' &= -(\omega A + \alpha U + \alpha' D)S + \mu' A + \mu(U + D), & \text{(2a)} \\
U' &= (\omega A + \alpha U + \alpha' D)S - (k_1 + \mu + \beta)U - k_2 UD, & \text{(2b)} \\
D' &= k_1 U + k_2 UD - (\mu + \beta)D, & \text{(2c)} \\
A' &= \beta(U + D) - \mu' A. & \text{(2d)}
\end{aligned}
$$

This model holds within each of the periods. The initial conditions for each period are taken to keep the overall solution continuous (i.e., initial conditions are the final conditions for the previous period). Solutions to (2) with positive initial conditions remain positive for all periods. System (2) has a unique solution with initial conditions $(S(0), U(0), D(0), A(0)) = (5.5 \text{ million}, 230, 94, 3)$.

3.3. **Numerical results.** Estimates of k_1 and k_2 are obtained by minimizing the following error function by fitting the data. For each of the fifteen years we compute the square of the difference between our model epidemic and the Cuban HIV data given in Table 1. Let RMS denote the square root of the average of those fifteen numbers.

$$
RMS\,Error = \left[\frac{1}{15} \sum_{1986-2000} [D_{model}(t) - D_{HIV\,Data}(t)]^2 \right]^{1/2}. \qquad (3)
$$

We select the values of k_1 and k_2 that minimize RMS, by taking the gradient of the $(RMS\,Error)^2$ and using Newton's method to find a zero of the vector field. The parameter values are given in Table 2. The initial values for U, D and A were chosen to be the same as those used in de Arazoza and Lounes [1] and $S(0)$ was estimated to be 5.5 million (assuming half of the 11 million population [26] are of a sexually active age). The resulting curves for both the diagnosed HIV cases and AIDS cases are shown in Figure 3. We compared our model results with the de Arazoza and Lounes model. As seen in Figure 3, our model is a better fit to the data.

3.4. **Basic reproduction ratio.** The basic reproduction ratio, $\mathcal{R}_0$, is a dimensionless parameter that gives the expected number of secondary cases per primary case of infection in an entirely susceptible population. As a result, $\mathcal{R}_0$ has a threshold value equal to one; i.e., infection will spread and result in epidemic if $\mathcal{R}_0 > 1$, whereas the infection will die out if $\mathcal{R}_0 < 1$.

Model (2) has a disease-free equilibrium (DFE), ε_0, given by

$$
\varepsilon_0 : (S, U, D, A) = (S_0, 0, 0, 0). \qquad (4)
$$

TABLE 2. Values of parameters used in simulations.

Parameter	Description	de Arazoza	Ours[Source]	
$S(0)$	Initial condition for Susceptibles	N/A	5.5 million [26]	
$U(0)$	Initial condition for HIV Undiagnosed	230	230 [1]	
$D(0)$	Initial condition for HIV Diagnosed	94	94 [1]	
$A(0)$	Initial condition for AIDS	3	3 [1]	
ω	Rate for a susceptible individual to become infected by an individual with AIDS	N/A	$8.5 \cdot 10^{-8}$ [a]	
α	Rate for a susceptible individual to become infected by an undiagnosed HIV positive individual	$9.3267 \cdot 10^{-8}$	$9.3267 \cdot 10^{-8}$ [1]	
α'	Rate for a susceptible individual to become infected by a diagnosed HIV positive individual	$5.4 \cdot 10^{-9}$	$5.4 \cdot 10^{-9}$ [1]	
β	Rate at which HIV positive individuals develop AIDS	0.10788	0.14 [5]	
μ	Mortality rate for HIV positive individuals	0.75	0.75 [1]	
μ'	Mortality rate for individuals with AIDS	0.0053	0.0053 [1]	
k_1	"Random" testing rate performed by doctors	0.3743	1986-1991	0.3850 [b]
			1992-2000	0.2929 [b]
k_2	Testing rate due to contact tracing	$2.27 \cdot 10^{-5}$	1986-1989, 1992-2000	$3.26 \cdot 10^{-5}$ [b]
			1990-1991	$5.89 \cdot 10^{-4}$ [b]

(a) Estimate based on α and α'
(b) Estimate to fit data

$\mathcal{R}_0$ is calculated for constant values of k_1 and k_2, that is, there is an $\mathcal{R}_0$ for each time period. We are interested in looking at the stability of a simpler model of (2) with each k constant throughout. We are interested in the final period, with each k set to their final value.

From Dieckman et al. [27], $\mathcal{R}_0$ is the spectral radius (ρ) of the next generation matrix (see also [28]), $\mathbb{K}$,

$$\mathcal{R}_0 = \rho(\mathbb{K}), \tag{5}$$

where $\mathbb{K} = \mathbf{F}\mathbf{V}^{-1}$. $\mathbf{F}$ and $\mathbf{V}$ come from the Jacobian matrix of the linearization of (2) about the DFE. Here, non-negative matrix $\mathbf{F}$ shows new infections, and the inverse of the non-singular matrix $\mathbf{V}$ gives the expected times that individuals spend in each of the compartments. $\mathbf{F}$ and $\mathbf{V}$ are respectively given by
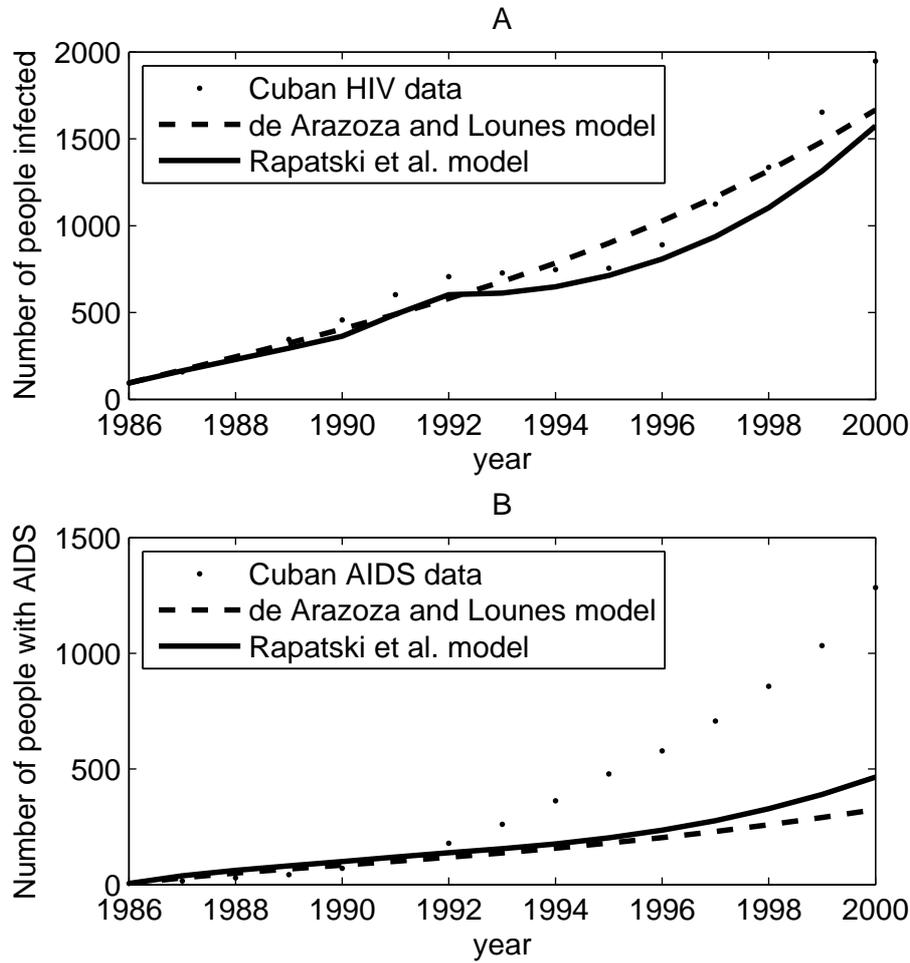
A

B

FIGURE 3. Comparison of model (2) and Arazoza and de Lounes model [1]. A) Data for HIV positive cases in Cuba, B) Data for AIDS cases in Cuba

$$\mathbf{F} = \begin{pmatrix} \alpha S & \alpha' S & \omega S \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \quad \text{and} \quad \mathbf{V} = \begin{pmatrix} k_1 + \mu + \beta + k_2 D & 0 & 0 \\ -k_1 - k_2 D & \mu + \beta & 0 \\ -\beta & -\beta & \mu' \end{pmatrix}. \tag{6}$$

The basic reproduction ratio for model (2) is given by

$$\mathcal{R}_0 = \frac{S(0)}{\beta + \mu} \left(\frac{\alpha(\beta + \mu) + \alpha' k_1}{k_1 + \mu + \beta} + \frac{\beta \omega}{\mu'} \right). \tag{7}$$

An advantage of considering $\mathcal{R}_0$ on a generation basis, is that we obtain expression (7) for $\mathcal{R}_0$ in terms of the model's parameters, which provides implications for the control of the epidemic, which we discuss in Section 4.
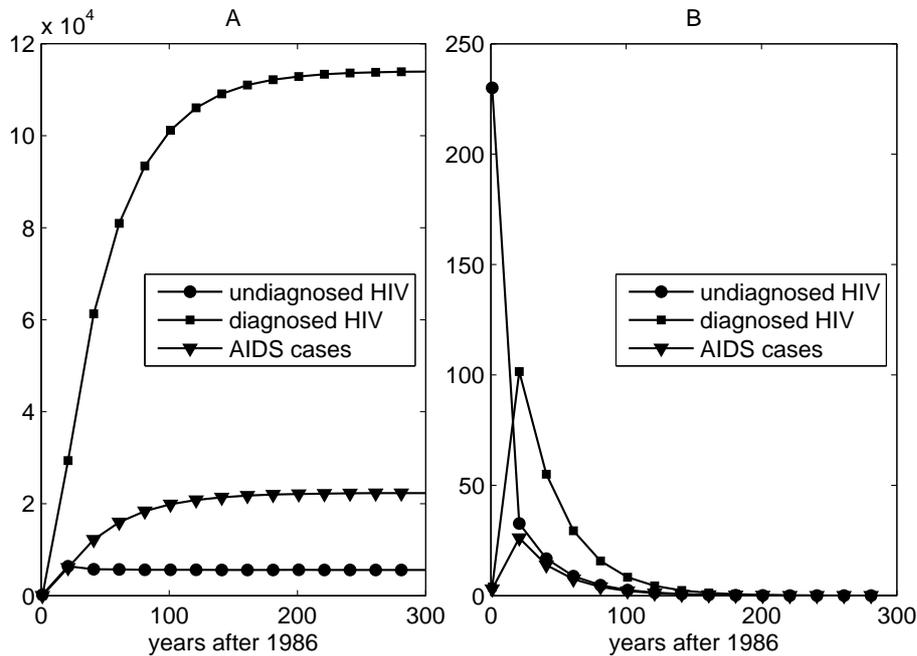
FIGURE 4. A) $\mathcal{R}_0 > 1$, the system reaches endemic equilibrium,
B) $\mathcal{R}_0 > 1$, disease free equilibrium.

Since we are interested in the simpler model where k's are constant throughout, our system becomes an autonomous system. The equilibrium ε_0 is locally asymptotically stable if $\mathcal{R}_0 < 1$ [28], and the population is not vulnerable to disease outbreaks. In the case when $\mathcal{R}_0 > 1$, the DFE is unstable so the disease can invade the population, eventually leading to an endemic equilibrium. These two types of dynamics are illustrated by simulations of model (2) in Figure 4.

4. **Discussion.** In this paper we present a new model for studying HIV/AIDS epidemic in Cuba, based on the Arazoza and Lounes model [1]. We modified their model in three ways. First, we allow for "random" testing rate (k_1) and contact tracing rate (k_2) to vary in time to reflect the fluctuating socioeconomic situation in the country. Second, we assume that persons who developed AIDS can infect susceptible individuals. Even though the people in the AIDS class have fewer sexual contacts than the asymptomatic, HIV-positive individuals, symptomatic individuals are highly infectious. The viral load in the symptomatic (AIDS) stage can be up to 150 times higher than in the asymptomatic stage [6], so the probability of transmission of HIV remains substantial in the symptomatic stage and we include it in the model (parameter ω). Lastly, since total population in Cuba is much greater (more than four orders of magnitude) than the number of people affected by HIV and AIDS, Arazoza and Lounes [1] assume that the susceptible population is constant in time, and thereby reduce a dimension in their system. We, on the other hand, model the changes in the susceptible class as well.

To test our model, we have used the yearly HIV-positive cases, AIDS cases, and deaths due to AIDS in Cuba in the period from 1986 to 2000 (Table 1 from [1]).

Data include newly HIV-infected people, the number of people who developed AIDS symptoms, and the number of people who died from complications of AIDS. From the data we cannot infer the time of HIV infection.

The current state of the HIV/AIDS epidemic in Cuba is described with the parameter values given in Table 2. For these values, $\mathcal{R}_0 > 1$, so the number of new, diagnosed and undiagnosed, HIV infections in Cuba is increasing. However, compared with $\mathcal{R}_0$ values for sub-Saharan Africa (9.62 [29]) and India (31 [29]), $\mathcal{R}_0$ for the Cuban epidemic is very small.

As long as $\mathcal{R}_0$ remains greater than one, the HIV/AIDS epidemic will continue to spread in Cuba. Mechanisms that decrease the value of $\mathcal{R}_0$ in (7) below the threshold are the mechanisms that can put the epidemic under control. Equation (7) suggests two ways of controlling the epidemic: increasing the rate at which unknown HIV-infected persons are detected (k_1) and decreasing the rate of infection (α).

Let us look at the two possible mechanisms of control more closely. Increasing the testing rate requires more effective, precise and affordable HIV-detection tests and a thorough and systematic testing organized by the public health system. As increasing the detection rate depends on advances in biotechnology and the structure of the public health system, increasing the testing rate enough to bring $\mathcal{R}_0$ below the threshold is unlikely at the moment. On the other hand, there are widely available, affordable methods that decrease the infection rate, α. The proper use of condoms has been shown to reduce the risk of transmission of HIV in two ways. Condom use reduces the risk of transmission of HIV and it significantly reduces the spread of other sexually transmitted infections (STIs). Since many STIs can cause abrasion of the genital skin and membranes, STIs may facilitate both transmission and acquisition of HIV [30]. Given that less than a third of people use condoms with their non-regular partners [31], increased condom use is a promising measure against the future spread of HIV/AIDS epidemic in Cuba.

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