to appear in "Deterministic and Stochastic Models for AIDS Epidemics and HIV Infection with Interventions"

A Class of Methods for HIV Contact Tracing in Cuba: Implications for Intervention and Treatment.

Y. H. HSIEH¹ H. de Arazoza² R. Lounes ³ J. Joanes⁴

Abstract

A class of four linear and nonlinear differential equations models is given to describe the detection of HIV-positive individuals in Cuba through random screening and contact tracing. The basic reproduction number is obtained for each of the four models. Cuban HIV data from 1986 to 2002 are used to fit the models for the purpose of comparison. We also use the models to gauge the difference in detection time through random screening and contact tracing. Remarks on the implications for intervention measures and treatment of people living with HIV in Cuba are also given.

Key words: HIV, AIDS, Cuba, contact tracing, mathematical model, basic reproduction number, intervention measures, HAART.

1 Introduction

The first Acquired Immunodeficiency Syndrome (AIDS) case was diagnosed in Cuba in April of 1986. This signaled the starting point of the Human Immunodeficiency virus (HIV/AIDS) epidemic in the country, although some HIV-positive persons had been detected at the end of 1985. At the early stages the Cuban Government had initiated several preventive measures to try to contain the possible outbreak of the epidemic (Granich et al., 1995; Pèrez Avila et al., 1996; Swanson et al., 1995). Among these measures was a total ban on the import of blood, and blood byproducts. Once the first cases were confirmed, a program based on the experience with other sexually transmitted diseases was started. In 1983, the Ministry of Health in Cuba set up a national committee on AIDS and had screened eight million people by June 1990, with all provinces in Cuba started building AIDS sanatoriums. By 1993, day care hospitals started treating patients replacing the sanatorium system (Koike, 2002). The AIDS program also had, among other measures, the tracing of sexual contacts of known HIV-positive (HIV+) persons, to prevent the spreading HIV. When a person is detected as living with HIV, an epidemiological interview is carried out by the Epidemiology Department

¹Department of Applied Mathematics, National Chung-Hsing University, Taichung, Taiwan, hsieh@amath.nchu.edu.tw

²Dpto Ecuaciones Diferenciales, Facultad Matemtica y Computacin, Universidad de la Habana, San Lázaro y L Habana 4 Cuba, arazoza@comuh.uh.cu

³Université Paris V, Ufr de Mathématique et Informatique, équipe MAP5, FRE CNRS 2428, 45 rue des Saints-Pères 75270 Paris cedex 06, France, lounes@math-info.univ-paris5.fr

⁴Dpt. of Epidemiology, Ministry of Public Health, Habana, Cuba

of his municipality or by his family doctor as part of the Partner Notification Program. After this interview the Epidemiology Department tries to locate the sexual partners of the person through the network of the Health System. The person living with HIV usually does not participate in this process, though they normally help in notifying their present partners. Trying to locate the sexual partners is a very complex job and one that in some cases takes a lot of time. This task is one of high level of priority for the Health System, and it is something that is under constant supervision to try to determine how effective it is in the prevention of the spread of HIV. All data used in this work is from the time period of 1986-2002.

The number of AIDS cases in Cuba at the end of 2002 is 2090 with 448 females and 1642 males. Of the males 83.5% are homo-bisexuals (we consider the group of homo-bisexuals to be formed by homosexuals and bisexuals). There have been 1057 deaths due to AIDS. Through the Health System HIV/AIDS program a total of 4517 HIV-positive individuals have been found, including 942 females and 3575 males. Of the HIV-positive males, 85.7% are homo-bisexuals. As of December of 2003, number of people in Cuba receiving HAART treatment is 1287 which constitutes all those in need according to CDC AIDS definition case of patients with cd4 of less than 200 cels/mm3. However in the near future it is planned that those with cd4 around 350 or less (or high viral load) will also be treated. In fact currently some cases (around 5%) are already being treated with cd4 over 200 or only for having a high viral load but the authors have not received the exact numbers from the sources (Ministry of Public health, 2003).

YEAR	HIV+	AIDS	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	33
1993	102	82	59
1994	122	102	62
1995	124	116	82
1996	234	99	93
1997	363	129	99
1998	362	150	99
1999	493	176	123
2000	545	258	143
2001	642	392	117
2002	644	407	90
Total	4517	2090	1057

 ${\it Table~1.}$ NEW HIV+, AIDS CASES AND DEATHS DUE TO AIDS BY YEAR CUBA:1986-2002

From the table we can see the epidemic is very low-prevalent. Indeed, with a population of around 11 millions Cuba have a cumulative incidence rate for AIDS of 190 per million (11.2)

per million per year). One of the characteristics of the Cuban Program for the HIV/AIDS epidemic is that there is an active search of HIV-positive persons through the sexual contacts of known HIV infected persons. As a result, 29.1% of all HIV-positive persons detected have been found through contact tracing. The rest of the infected persons are found through a "blind" screening, a search of HIV-positive individuals by serotesting of blood donors, pregnant women, persons with other sexually transmitted diseases, etc. at clinics. Non-parametric estimation of the mean time for the health authority to find a sexual partner notified by a detected HIV-positive person through the Contact Tracing Program has been found to be 54.3 months, with a standard deviation of 0.631 (Figure 1).

Contact tracing has been used as a method to control endemic contagious diseases (Hethcote et al., 1982, 1984). While there is still a debate about contact tracing for the HIV infection (April et al., 1995; Rutherford et al., 1988) the resurgence of infectious tuberculosis and outbreaks of drug-resistant tuberculosis secondary to HIV-induced immunodepression is forcing many public health departments to reexamine this policy (Altman, 1997; CDC-MMWR, 1991). A model of the HIV epidemic allowing for contact tracing would help evaluate the effect of this method of control on the size of the HIV epidemic, and give some idea as to the effectiveness of the Health System in finding them.

Our objective is to model the contact tracing aspect of the HIV detection system, to try to obtain some information that could be useful to the Health System in Cuba in evaluating the way the program is working, and to ascertain its usefulness in terms of intervention and treatment of HIV. Other models have been used to study the effect of contact tracing with this objective in mind (Lounes et al., 1999; Arazoza et al., 2000). However, these were essentially linear models. We will now introduce non-linearity to model contact tracing. We will also discuss the implications of our results for the purpose of intervention and treatment of HIV/AIDS in Cuba.

2 The models

As we noted, the Cuban Program to control the HIV/AIDS epidemic is based on the active search of persons infected with HIV, long before they show any signs of AIDS. Our objective is not to model how new infections by HIV are generated, but how the HIV infected persons are detected. We will consider the following variables:

- 1. X(t) is of HIV-infected persons that do not know they are infected at time t,
- 2. Y(t) is the number of HIV-infected persons that know they are infected at time t,
- 3. Z(t) is the number of persons with AIDS at time t.

As the detection system has several search methods, we will separate the individuals in Y(t) into two classes

- $Y_1(t)$ is the number of HIV-infected persons that know they are infected at time t and were detected in a random type search,
- $Y_2(t)$ the number of HIV-infected persons that know they are infected at time t and were detected through contact tracing.

Evidently, $Y(t) = Y_1(t) + Y_2(t)$ for all t. With the following constant coefficients:

- 1. N sexually active population,
- 2. α the rate of recruitment of new HIV infected persons infected by X,
- 3. α' the rate of recruitment of new HIV infected persons infected by Y,
- 4. k_1 the rate at which the unknown HIV infected persons are detected by the system, independently of other HIV-positive persons (through "random" screening),
- 5. k_2 the rate at which unknown HIV-infected persons are detected by the system through contact tracing,
- 6. β the rate at which the undetected HIV-positive persons develop AIDS, reciprocal of the mean incubation
- 7. β' the rate at which the detected HIV-positive persons develop AIDS, the reciprocal of the mean time it takes to go from Y to Z,
- 8. μ the mortality rate of the sexually active population,
- 9. μ' the mortality rate of the population with AIDS.

The model dynamics is described by the following system:

$$\frac{dX}{dt} = \alpha NX + \alpha' NY - (k_1 + \mu + \beta) X - f(k_2, X, Y),$$

$$\frac{dY_1}{dt} = k_1 X - (\mu + \beta') Y_1,$$

$$\frac{dY_2}{dt} = f(k_2, X, Y) - (\mu + \beta') Y_2,$$

$$\frac{dZ}{dt} = \beta X + \beta' Y - \mu' Z.$$
(1)

We consider the system only in the region $\mathcal{D} = \{X \geq 0, Y \geq 0, Z \geq 0\}$. It is clear that \mathcal{D} is positively invariant under the flow induced by (1). First, we make following three remarks regarding the system in (1):

1. In (1) there are two ways individuals can move from the unknown HIV infected class (X) to the known HIV infected class (Y). One way is through the term $f(k_2, X, Y)$. This is the term we utilize to model contact tracing. In other words, the individual is found through his contacts with persons that are known to live with HIV. The other way they can be detected is through the screening term k_1X which models all the other "random" ways of searching for HIV-positives. (For other HIV models using constant and nonlinear screening terms, see (Hsieh, 1991; Velasco-Hernandez et al., 1994; de Arazoza et al., 2003).) It is important to note that $1/k_1$ can be viewed as the mean time from infection to detection for the persons found through means other than contact tracing.

- 2. The term $f(k_2, X, Y)$ models contact tracing, the way it is given in the model indicates that the process is one that goes on for a long time, because it involves all the individuals in the class Y and this is confirmed numerically by the result that the mean time to finding a contact is 54.3 months (Figure 1). If we consider the numerical result that the mean time from detection to AIDS is 86.8 months (Figure 2) we can see that, in the mean, infected contacts of an HIV-positive person are found for more than 32 months before that person who is living with HIV develops AIDS. To consider more than one class of known HIV-positive persons (before onset of AIDS) in the model, i.e., one class where contact are found and another where contacts are no longer found, would complicate the model unnecessarily for it is not clear that this complication would give more information on the dynamics of the epidemic. Of course variations are high, some persons have very few contacts and are easy to locate, while others may have a large number of contacts, of which some may be impossible to locate. Furthermore, some persons have a lot of "casual" contacts and they do not remember enough information on these contacts to make it possible to find them. Others may have fewer contacts and possess a better knowledge of the contact's full name and/or addresses that make it more likely for the Health System to find them. Some contacts would refuse being tested for HIV, even if they are found. In general, of the more than 15000 contacts 80% have been found and tested. We will attempt, as a first approximation, to find the value of k_2 and to ascertain the general effect of this contact tracing on the time it takes for a person living with HIV to be detected.
- 3. We assume that the known HIV infected persons are infectious, but at a much lower rate than those that do not know they are infected. In this sense α' will be taken as a fraction of α .
- 4. The passage to AIDS is modeled in a linear way. This could be modeled in a more general way, but for the Cuban case the best fit to an incubation curve is still an exponential. This can be seen in Figure 3 which gives us the cumulative hazard function for the time to AIDS which is a straight line and this corresponds to an exponential model.

Several possibilities arise for the contact tracing term $f(k_2, X, Y)$. In this work, we will consider the following four models:

- 1. k_2X
- $2. k_2Y$
- 3. k_2XY
- 4. $k_2 \frac{XY}{X+Y}$

The first two models are linear models, while the last two are non-linear. In order to make full comparison, we will give some analytical results for each of the models and compute the basic reproduction number for each one. Furthermore, we will fit the models to the Cuban contact tracing data to see which model explains the data most satisfactorily.

Let
$$k = k_1 + k_2$$
, $\lambda = \alpha N$ and $\lambda' = \alpha' N$.

2.1 The k_2X model

In this case the system is:

$$\frac{dX}{dt} = (\lambda - k - \mu - \beta)X + \lambda'Y,$$

$$\frac{dY}{dt} = kX - (\mu + \beta')Y,$$

$$\frac{dZ}{dt} = \beta X + \beta'Y - \mu'Z.$$
(2)

It is a linear model and the basic reproduction number is:

$$\mathcal{R}_0 = \frac{\lambda}{k + \mu + \beta} + \frac{\lambda'}{\mu + \beta'} \frac{k}{k + \mu + \beta}.$$

If $\mathcal{R}_0 > 1$, then all trajectories go to infinity, otherwise the Disease-free Equilibrium (DFE) at (0,0) is the only equilibrium and is globally asymptotically stable.

2.2 The k_2Y model

In this case the system is:

$$\frac{dX}{dt} = \lambda X + \lambda' Y - (k_1 + \mu + \beta) X - k_2 Y,$$

$$\frac{dY}{dt} = k_1 X + k_2 Y - (\mu + \beta') Y,$$

$$\frac{dZ}{dt} = \beta X + \beta' Y - \mu' Z.$$
(3)

It is also a linear model and the basic reproduction number is:

$$\mathcal{R}_{0} = \frac{\lambda}{k_{1} + \mu + \beta} + \frac{k_{1}\lambda'}{(k_{1} + \mu + \beta)(\mu + \beta')} \frac{k_{2}}{k_{2} + \mu + \beta} \frac{\mu + \beta - \lambda}{\mu + \beta'}.$$

Again, if $\mathcal{R}_0 > 1$, then all trajectories go to infinity, otherwise (0,0) is unique and globally asymptotically stable

2.3 The k_2XY model

This model is similar to one studied by de Arazoza and Lounes (2002), but considering only the variable Y. The system is

$$\frac{dX}{dt} = \lambda X + \lambda' Y - (k_1 + \mu + \beta) X - k_2 XY,$$

$$\frac{dY}{dt} = k_1 X + k_2 XY - (\mu + \beta') Y,$$

$$\frac{dZ}{dt} = \beta X + \beta' Y - \mu' Z.$$
(4)

Where $\lambda = \alpha N$ and $\lambda' = \alpha' N$.

In the region $\mathcal{D} = \{X \geq 0, Y \geq 0, Z \geq 0\}$, the system has two equilibria, one is the DFE at $P_0 = (0, 0, 0)$, and the other is a unique endemic $P^* = (X^*, Y^*, Z^*)$ at

$$X^* = \frac{\sigma \gamma + \lambda' k_1}{k_2(\sigma + k_1)}, \quad Y^* = \frac{\sigma \gamma + \lambda k_1}{k_2(\gamma - \lambda')}, \quad Z^* = \frac{\beta X^* + \beta' Y^*}{\mu'}, \tag{5}$$

with $\sigma = \lambda - k_1 - \beta - \mu$, $\gamma = \beta' + \mu$.

The basic reproduction number for the system is

$$\mathcal{R}_0 = \frac{\lambda}{k_1 + \mu + \beta} + \frac{\lambda'}{\mu + \beta'} \frac{k_1}{k_1 + \mu + \beta}.$$

If $\mathcal{R}_0 < 1$ and the endemic equilibrium P^* is feasible (i.e. $\gamma > \lambda'$), then the DFE P_0 is stable and its basin of attraction consists of a triangle formed by the axes and the line of slope

$$\frac{\sigma + k_1}{\sigma(\lambda' - \gamma)} \left\{ \frac{\lambda' k_1}{\gamma - \lambda'} + \lambda_1 \right\}.$$

that passes through P^* , where λ_1 is the negative eigenvalue of the Jacobian matrix at P^* .

If $\mathcal{R}_0 > 1$, then P_0 is unstable and P^* is globally asymptotically stable in the region \mathcal{D} .

If $\mathcal{R}_0 = 1$, P^* and P_0 coincide, 0 is a simple eigenvalue for the Jacobian at P_0 and the other eigenvalue is $\sigma - \gamma$ which is negative. Therefore P_0 is globally asymptotically stable in the region \mathcal{D} .

2.4 The $k_2 \frac{XY}{X+Y}$ model

The system considered here is:

$$\frac{dX}{dt} = \lambda X + \lambda' Y - (k_1 + \mu + \beta) X - k_2 \frac{XY}{X + Y},$$

$$\frac{dY}{dt} = k_1 X + k_2 \frac{XY}{X + Y} - (\mu + \beta') Y,$$

$$\frac{dZ}{dt} = \beta X + \beta' Y - \mu' Z.$$
(6)

As before we will consider the system formed by the first two equations in (1). Let $x=\frac{X}{X+Y},\ y=\frac{Y}{X+Y}$ be the respective proportions of unknown and known HIV-positives in the HIV-positive population. Since x+y=1, we have

$$x' = \lambda x + \lambda' y - (\beta + \mu + k_1) x - k_2 x y - x \left(\lambda x + \lambda' y - (\beta + \mu) x - (\beta' + \mu) y \right)$$

$$= (1 - x) \left(\lambda x + \lambda' y - (\beta + \mu) x \right) - k_1 x - k_2 x y + (\beta' + \mu) x y$$

$$= (\lambda' - \lambda + k_2 + \beta - \beta') x^2 + (\lambda - 2\lambda' - k_1 - k_2 + \beta' - \beta) x + \lambda',$$

$$y' = k_1 x + k_2 x y - (\beta + \mu) y - y \left(\lambda x + \lambda' y - (\beta + \mu) x - (\beta' + \mu) y \right)$$

$$= k_1 x + k_2 x y - (\beta' + \mu) y (1 - y) - y \left(\lambda x - \lambda' y - (\beta + \mu) x \right).$$

Here $x'=0 \Rightarrow -(\lambda x+\lambda'(1-x)-(\beta+\mu)x)\,(1-x)+k_1x+k_2x(1-x)-(\beta+\mu)x(1-x)=0$. Equivalently $(\lambda-\gamma\lambda-k_2)x^2-(\lambda-2\gamma\lambda-k_1-k_2)x-\gamma\lambda=0$ has unique positive solution x^* between 0 and 1. Also let y^* be the corresponding solution for y'=0. x^* is globally asymptotically stable on the one-dimensional line between 0 and 1, which means that the straight line $\frac{X(t)}{Y(t)}=\frac{x^*}{y^*}$ on the positive XY-quadrant is an asymptotic line for all trajectories, either going to (0,0) or infinity.

Let $\sigma = k_2 y^* (1 + x^*)$. Then, the basic reproduction number of the system is:

$$\mathcal{R}_0 = \frac{\lambda}{\mu + \beta + k_1 + \sigma} \frac{k_1}{\mu + \beta + k_1 + \sigma} \frac{\lambda}{\mu + \beta'} - \sigma \frac{\lambda + k_1 - (\beta + \mu)}{(\mu + \beta')(\mu + \beta + k_1 + \sigma)}.$$

3 Fitting the models to Cuban data

We fit the models to the data for the known HIV-positives and AIDS cases in Cuba. We will use the following values for the parameters which were estimated from the HIV data in Cuba:

 $X(0) \in [200, 230]$, the number of unknown HIV-positives in 1986 estimated from the number of HIV-positives who were detected after 1986 but were found to be already infected in 1986,

Y(0) = 94, number of HIV positives who were known to be alive at the end of 1986,

Z(0) = 3, number of AIDS cases who were alive at the end of 1986,

 $\mu = 0.0053$, yearly mortality rate for the HIV-positive cases for 1991 – 2000, (S.D. = 0.0030), computed from the number of death for HIV infected persons not related to AIDS,

 $\mu' \in [0.66, 0.85]$, obtained from the 95% confidence interval for the median of the survival time to AIDS (1987 – 2000),

 $\lambda = \alpha N = 0.5744$, the infection rate of the undetected HIV-positives obtained from the value of the parameter λ in the model developed in (Lounes et al., 1999), (S.D.=0.0096),

 $\beta = 0.1135$, from the incubation period $(1/\beta)$ estimated from 1218 persons whose probable date of infection has been determined during the observation period 1987 – 2000, (S.D.=0.0031),

 $\beta' = 0.1350$, from the mean time from detection to AIDS $(1/\beta')$ (1987 – 2000), (S.D. = 0.0026),

We take λ' the infection rate of the known HIV-positives, to be a fraction of λ ; $\lambda' = r\lambda$ and consider $r \in (0, 0.1)$.

We fit the models to the data to obtain values for k_1 and k_2 by minimizing a relative error function. As traditional optimization methods failed to work properly we used a genetic algorithm approach and a random search for local minima (Arazoza et al., 2000). To compute standard errors for the parameters, 300 fitting runs were made using different values for the known parameters taken randomly form their confidence interval.

The following table gives the mean values found for k_1 and k_2 .

Model	mean k_1	$\operatorname{sd} k_1$	mean k_2	$\operatorname{sd} k_2$	mean error	sd error
k_2X	0.2423	0.0229	0.1232	0.0110	16.6823	1.2322
k_2Y	0.2786	0.0280	0.0984	0.0036	18.5417	1.0827
$k_2 \frac{XY}{X+Y}$	0.2547	0.0242	0.2457	0.0133	17.1199	1.1790
k_2XY	0.3031	0.0254	0.00024	0.000038	20.3743	0.9922

Table 2.
Parameters

4 Discussion and concluding remarks

The question now is which model is the best one in the sense of best fit for the data. In other words, which of the four models offers the best model for contact tracing? By comparing the mean errors of the four models in Table 1, the order of suitability of the four models in the sense of the smallest mean errors is:

- 1. $k_2 X$
- 2. $k_2 \frac{XY}{X+Y}$
- $3. k_2Y$
- $4. k_2 XY$

However, we note that the contact tracing term $k_2 \frac{XY}{X+Y}$ in Model 4 can be approximated by Model 1 (i.e. k_2X) when Y >> X and by Model 2 (i.e., k_2Y) when X >> Y. In other words, Model 4 approximates whichever that is the smaller of the two linear models whenever one contact tracing term is much larger than the other. Moreover, $k_2 \frac{XY}{X+Y}$ is smaller than the corresponding contact tracing terms in either Model k_2X or Model k_2Y . Hence Model 4 $(k_2 \frac{XY}{X+Y})$, as a model for the contact tracing, offers a conservative compromise between the two extremes of contact tracing in the linear models and should be the best from the theoretical point of view. Estimates of the unknown HIV-positive population in Cuba (de Arazoza et al., 2003; Hsieh et al., 2002, 2001), though not a negligible number, have shown that, in recently years, approximately two thirds of the HIV-positive persons in Cuba have been detected. Hence realistically Model 4 is probably more appropriate than either Models 1 or 2. The simple "mass mass action" contact tracing term in Model 3 (k_2XY) gives the "worst" fit and should be discarded

We also made an ANOVA test on the error for the 4 models, yielding the following result:

SOURCE	SS	df	MS	F	Prob;F
COLUMNS	2493	3	831.255	656.45	0
ERROR	1514.49	11960	1.266	-	-
TOTAL	4008.25	1199	-	-	-

Table 3. ANOVA analysis for fitting errors for the 4 models

That is, the errors for the 4 groups of models are different and testing one against the other gives the order that we have given in Table 2.

To further utilize our result, we compute the mean detection time for random screening to detect an HIV-positive, $(1-p)/k_1$, for Models 1,2 and 4, and the mean detection time for contact tracing to detect one HIV-positive person, p/k_2 , for Model 1 only. Here p=0.291 is the proportion of known HIV-positive persons detected through contact tracing. The results are given in Table 4 below.

Model	mean detection time	mean detection time	difference
	by random screening (A)	by contact tracing (B)	(A-B)
k_2X	35.1 months	28.3 months	6.8 months
$k_2 \frac{XY}{X+Y}$	33.4 months	NA	NA
k_2Y	30.1 months	NA	NA

Table 4.

The result indicates that using Model 1, the contacting tracing program shortens the time of detection for an HIV-positive person by 6.8 months. The other models cannot be used to draw any similar conclusions.

Finally, we consider the implications of contact tracing for the intervention measures and treatment of HIV in Cuba. The intervention program in Cuba has gone through several phases, the most recent being the establishment of anonymous testing sites for HIV. Currently there are three anonymous testing sites functioning in Havana (which reports more than 50% of HIV-positive people nationwide) and there are immediate plans to have at least one in each of the Central and Eastern regions in addition to the ones in Havana. The long-term plan is to have at least one site in every province. These sites also have pre- and post-counseling services to report contacts and reduce future contacts. Around 80% of people testing positive in anonymous sites eventually decide to adhere to Confidential HIV reporting system (normal system). Typically once a person knows his or her HIV sero-positive status, change in sexual behavior occurs even without having a good educational background. Only a minority of people keep on having risky behaviors after knowing his/her positive serological status. Hence early diagnosis through random screening, contact tracing, and, more recently, anonymous testing has been instrumental in keeping the HIV prevalence in Cuba at a low level. (Joanes Fiol, 2003)

The detection of HIV-positive persons subsequently made their treatment possible. The first therapeutic methods employed in Cuba, appearing first in 1986, consisted of the use of domestically produced immune-modulators. Treatments making use of transfer factor and the recombinant interferon alpha were conducted with satisfactory results. In 1987, AZT therapy was introduced into Cuba's healthcare system. Donations made by individuals and international organizations made it possible in 1996 to offer triple AIDS therapy to 100 Cubans afflicted with the disease. Though more substantial donations were made in the years to follow, due the recent increase in the HIV-infected population size (Hsieh et al., 2001) the need of the populations were, of yet, not entirely met. (Lantero Abreu, 2003)

In 1997, when the domestic production of these pharmaceuticals entered its research phase, the Cuban government paid the international prices to acquire all of the medication needed to offer triple therapy (HAART) to mothers and children who were HIV positive. From 2001 onward, a wider variety of domestically manufactured anti-retroviral agents became

increasingly available in Cuba, resulting in a 100% level of coverage by the end of 2002. With the advances in therapeutic treatment, the early detection and diagnosis of HIV-positive persons through contact tracing, as evident from our modeling, has taken an increasingly important role in improving the quality of life for those living with HIV/AIDS. Acknowledgments:

The authors would like to thank Drs. Jose Joanes Fiol and Maria Isela Lantero Abreu of National Aids Programme, Ministry of Public Health of Cuba, for providing the up-to-date information on the intervention and treatment of HIV in Cuba. YHH is supported by National Science Council (Taiwan) under grant NSC92-2115-M-005-002. H. de Arazoza received support from Equipe Probabilits, Statistique et Modlisation Laboratoire de Mathmatique University Paris-Sud, France and from University Ren Descartes, Laboratoire de Statistique Mdicale, quipe MAP5 FRE CNRS 2428. Part of the work was carried while H. de Arazoza was a guest researcher at the Dpt. Tecnologa Electrnica, E.T.S. Ingeniera Telecomunicacin, Universidad de Mlaga, Spain.

References

- [1] L. Altman. Sex, Privacy and Tracking the HIV Infection. New York Times. 11/4/1997.
- [2] K. April, F. Thévoz. Le Contrôle de l'entourage ("Contact Tracing") a été négligé dans le cas des infections par le VIH. Revue Médicale de la Suisse Romande. 115 (1995) 337-340.
- [3] H. Arazoza, R. Lounes, T. Hoang, Y. Interian. Modeling HIV Epidemic Under Contact Tracing - The Cuban Case. Journal of Theoritical Medicine. Vol 2 (2000) 267-274.
- [4] Center for Disease Control and Prevention. Transmission of multidrug resistant tuberculosis from an HIV positive client in a residential substance-abuse treatment facility – Michigan. MMWR, 40 (8) (1991) 129.
- [5] H. de Arazoza and R. Lounes. A non linear model for a sexually transmitted disease with contact tracing. IMA. J. Math. Appl. Med. Biol. Vol 19(3) (2002) 30-37.
- [6] H. de Arazoza, R. Lounes, J. Pérez and T. Hoang. What percentage of the Cuban HIV-AIDS Epidemic is known?. Revista del Instituto de Medicina Tropical de Cuba. Vol 55(1)2003; 55(1).
- [7] R. Granich R, B. Jacobs, J. Mermin and A. Pont A. Cuba's national AIDS program The first decade. West J Med. Vol 163 (1995) 139-144.
- [8] H.W. Hethcote, J.A. Yorke. Gonorrhea Transmission Dynamics and Control. Lecture Notes in Biomathematics 56. Springer Verlag. 1984.
- [9] H.W. Hethcote, J.A. Yorke, A. Nold. Gonorrhea Modeling: Comparison of Control Methods. Math. Biosci. 58 (1982) 93-109.
- [10] Y. H. Hsieh. Modeling the effect of screening in HIV transmission dynamics. In: Busenberg S and Martelli M. (eds) Proceedings of International Conference on Differential Equations and its Applications to Mathematical Biology, Claremont, 1990. (Lect. Notes Biomath., V.92, pp. 99-120) 1991, Berlin Heidelberg New York, Springer.

- [11] Y. H. Hsieh, H. Arazoza, S. M. Lee and C. W. S. Chen. Estimating the number of HIV-infected Cubans by sexual contact. Int. J. of Epidemiology. Vol 31 (2002) 679-683.
- [12] Y. H. Hsieh, S. M. Lee, C. W. S. Chen and H. Arazoza. On the recent sharp increase of HIV infections in Cuba. AIDS Vol 15(3) (2001) 426-428.
- [13] J. Joanes Fiol. National Aids Programme, Ministry of Public Health, Cuba. 2003. (personal communication).
- [14] S. Koike. Assessment of the Cuban approach to AIDS and HIV. Nippon Koshu Eisei Zasshi. Vol 49(12) (2002) 1268-77. (In Japanese)
- [15] 15. M. I. Lantero Abreu. Head of National Aids Programme. Ministry of Public Health, Cuba. 2003. (personal communication).
- [16] R. Lounes, H. de Arazoza. A two-type model for the Cuban national programme on HIV/AIDS. IMA. J. Math. Appl. Med. Biol. 16 (1999) 143-154.
- [17] Ministry of Public health. HIV/AIDS/STD Weekly report, National Department of Epidemiology, Ministry of Public health, Cuba. December 6th, 2003
- [18] J. Pérez, R. Torres, J. Joanes, M. Lantero, H. de Arazoza. HIV control in Cuba. Biomed. and Pharmacother. 50 (1996) 216-219.
- [19] G. Rutherford, J. Woo. Contact Tracing and the Control of Human Inmunodeficiency Virus. J. Amer. Med. Assoc. 259 (1988) 3609-3610.
- [20] J. M. Swanson , A. E. Gill, K. Wald and K. A. Swanson . Comprehensive care and the sanatorium: Cuba's response to HIV/AIDS. JANAC Vol 6(1) (1995) 33-41.
- [21] J. X. Velasco-Hernandez Y. H. Hsieh. Modeling the effect of treatment and behavioral change in HIV transmission dynamics. J Math Biol. Vol 32 (1994) 233-249.

KAPLAN-MEIER FOR CONTACT TRACING

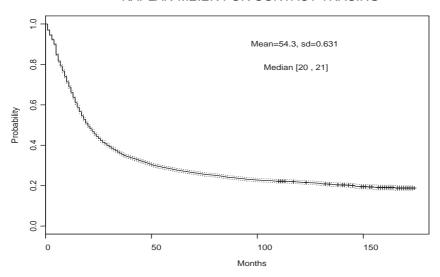


Figure 1: Estimated time for contact tracing using declared sexual partners from 1986-2001, using Kaplan-Meier method.

KAPLAN-MEIER FOR INCUBATION FROM DETECTION

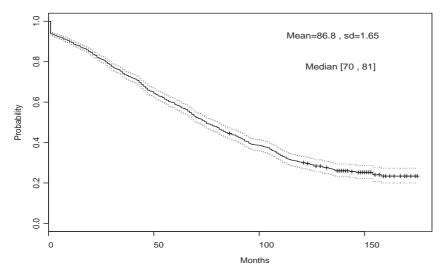


Figure 2: Estimated time from detection to AIDS-defined illness (ADI) for $4517~\mathrm{HIV/AIDS}$ patients in Cuba from 1986-2002 using Kaplan-Meier method

Cummulative hazard function for Incubation Period

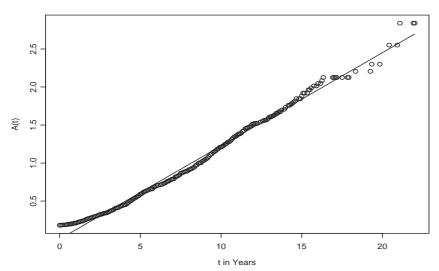


Figure 3. Cumulative hazard function for time to AIDS in Cuba, 1986-2002.