

HIV/AIDS INFECTION SPREAD: SIMULATION AND CONTROL

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Abstract. The model of the HIV/AIDS infection spread is proposed and investigated. The paper deals with some specific features of the disease spread at the initial stage, i.e., when the infection extent is small enough. We propose a model characterizing any risk group by three differential equations. These equations describe the dynamics of active susceptible, active infected, and passive infected individuals. The evaluation of parameters from demographical and medical data is discussed. The package for the investigation of infection is presented, and possibilities to control the infection are shown. Two general directions of control may be distinguished: the HIV/AIDS blood tests and the publicity and availability of protective means. The investigations showed under what conditions the HIV/AIDS infection may be stopped.

Key words: infection control, HIV/AIDS infection, health care, simulation.

1. Introduction. Transmission models of the HIV/AIDS epidemic help to explore both the nature of disease spread in a population and the efficiency of control strategies, as well as to predict the extent of infection in the near future. A number of models allows to study the AIDS epidemic within specific risk groups and among them. The following risk groups have the greatest influence on the infection spread: homo/bisexual men (two levels of productivity), intravenous drug users, highly promiscuous heterosexual men and women.

This paper concerns some specific features of the disease spread at the initial stage, i.e., when the infection extent is small enough. This is especially important for some East Europe countries now. The evaluation of parameters from demographical and medical data is discussed. The software package for the investigation of infection is presented, and possibilities to control the infection are investigated.

The models and their parameters must take into account the growth of foreign relations, the national and economic specific character of the target country. All calculations are made on the data from Lithuania.

2. The models. Three main approaches are used in the recent scientific literature: extrapolation of observed data (Karon, Devine and Morgan, 1989), the models based on differential equations (DEM) (Kaplan, 1989, 1990; Van Druten and coworkers, 1990; Sattenspiel and Castillo-Chavez, 1990; Kault and McLeod, 1991; Jacquez and Simon, 1990), and stochastic models (SM) (Cairns, 1991; Mode, 1991).

The extrapolation is used when one has plentiful statistics on the number of infected and sick persons. These data may be approximated by a curve which can be extended to the future. We don't have plentiful statistics, so only two last approaches (DEM and SM) are suitable in our case. Both these models permit a simultaneous investigation of changes in the number of persons infected with HIV in all risk groups. We investigate the DEM model in this paper.

An important assumption of DEM models is that the choice of partners is independent of the former choices. Another assumption deals with sexual mixing in the population. We chose the model of random proportionate mixing within the group of risk, because this model is less complicated and, as shown by Kaplan (1989), it leads to useful conclusions. The partnership is assumed to be rather short. Also, we assume that the population may be divided into some risk groups, which differ in parameters of the sexual behavior. This leads to the model similar to that given by Van

Druten and coworkers (1990), but we added an equation, which describes the growth in number of infected individuals, who usually don't spread the infection (e.g., impotents and a part of persons indicated as infected). Such individuals make a significant part among the infected persons at low growth of infection. We propose a model describing any risk group by three differential equations, which simulate the dynamics of active susceptible, active infected, and passive infected individuals.

$$\frac{dx_i}{dt} = u_i^x + u_i \cdot (x_i^0 + y_i^0 + z_i^0) - (\mu^i + \mu_2^i) \cdot x_i - \frac{x_i}{x_i + y_i} \sum_{j=1}^n b_{ij} \cdot p_{ij} \cdot y_j \quad (1)$$

$$\frac{dy_i}{dt} = u_i^y + \frac{x_i}{x_i + y_i} \sum_{j=1}^n b_{ij} \cdot p_{ij} \cdot y_j - (\mu^i + \mu_1 + \mu_2^i + k_i) \cdot y_i \quad (2)$$

$$\frac{dz_i}{dt} = u_i^z + (k_i + \mu_2^i) \cdot y_i - (\mu^i + \mu_1) \cdot z_i, \quad (3)$$

$$i = 1, 2, \dots, n,$$

where

$x_i = x_i(t)$ is the number of susceptible individuals in the i -th group;
 $y_i = y_i(t)$ is the number of infected individuals, who take part in the infection spread;

$z_i = z_i(t)$ is the number of infected individuals, who do not spread the infection;

n is the number of groups;

x_i^0 , y_i^0 and z_i^0 are initial values of x_i , y_i and z_i ;

u_i^x is the number of susceptible individuals recruited into the group per time unit;

u_i^y is the number of infected individuals recruited into the group per time unit (these individuals take part in the infection spread);

u_i^z is the number of infected individuals recruited into the group per time unit (these individuals do not spread the infection);

u_i is the birth rate;

μ^i is the mortality rate not due to AIDS;

μ_1 is the mortality rate due to AIDS;

μ_2 is the rate at which an individual leaves the group because of any reasons other than death (e.g., old age, impotence and so on);

k_i is the rate of prophylaxis;

b_{ij} is the averaged number of contacts of an individual in group j with persons in group i per unit time;

p_{ij} is the probability of infection from an infective person in group j to a susceptible one in group i per contact.

The balance of contacts must be satisfied: $N_j b_{ij} = N_i b_{ji}$, where $N_j = x_j + y_j$.

The influence of relations with more infected foreign countries is important at the initial stage of the epidemic. We can simulate this influence by subtracting from equation (1) and adding to (2), correspondingly, the item $x_i \cdot \sum_{j=1}^n s_{ji} c_j p_{ij}$, where s_{ji} is the number of contacts of an individual from the i -th group with foreigners in the j -th group, c_j is the supposed portion of infected individuals among foreigners of the j -th group.

More sophisticated models were also investigated (e.g., including the possibility for individuals to move from group to group, permitting various transmission modes, and so on).

The model (1) - (3) like all other DEM models gives only averaged quantities x_i, y_i, z_i . It uses some averaged quantities (e.g., the number of contacts of an individual in group j made with persons in group i per unit time), too. Therefore, some specific traits of the infection spread in population cannot be evaluated by such a model. The mentioned above imperfections of DEM can be overcome in stochastic models, however a lot of problems arises in this case as well (e.g., the model requires more parameters, the computational expenditure grows significantly).

3. The parameters. All the models of HIV/AIDS transmission require to solve the problems of statistical estimation of the initial extent of infection, and of various rates: mortality, partner-changing, prophylaxis and other ones. The knowledge of transmission modes and probabilities is also necessary. The main prob-

lem encountered is the extent of compromise between a complexity of model and a possibility to estimate unknown parameters: the growth of complexity increases the number of parameters and decreases our possibilities of their good estimation.

The parameters of the model (1) - (3) may be evaluated directly or determined for any group i by such demographical and medical parameters:

- U_i^+ is the number of individuals recruited into the group per year;
- $U_i^?$ is the per cent of infected among U_i^+ ;
- U_i^- is the per cent of infected individuals, which do not spread the infection, recruited into the group per year;
- U_i is the per cent of birth per year;
- M^i is the per cent of mortality per year not because of AIDS;
- M_1 is the per cent of mortality because of AIDS per year;
- M_2^i is the per cent of individuals excluded out of the group per year for any reasons other than death;
- K^i is the per cent of persons examined on the AIDS tests per year;
- α^i is the per cent of individuals, using protective means during sexual contacts;
- v^i is the per cent of individuals, terminating the infection spreading after diagnoses of infection per year.

The calculation of parameters μ^i , μ_1 and μ_2^i from M^i , M_1 and M_2^i will be detailed below. These parameters influence the removal of infected individuals.

Let the dynamics of the number of individuals from the i -th group be determined by one of these parameters (e.g. M^i). In a year the number of active infected in (2) must be $y_i = y_i^0 \cdot (1 - M^i/100)$. It is a solution of the equation

$$\frac{dy}{dt} = -\ln(1 - M^i/100) \cdot y. \quad (4)$$

So, $\mu^i = -\ln(1 - M^i/100)$. Approximately $\mu^i = M^i/100$ for small $M^i/100$. The parameters μ_1^i and μ_2^i are determined analogously.

Equation (4) may be solved by iterative procedure dividing the year into a fixed number m of equal parts Δt . The numbers

of infected individuals at the fixed moments $y_i^0, y_i^1, \dots, y_i^m$ may be calculated by a recurrent formula:

$$y_i^k = y_i^{k-1} \cdot (1 - M^i/100)^{\Delta t}.$$

Analogously, if the dynamics of the number of infected individuals from the i -th group is determined only by the parameters of mortality (M^i and M_1), then

$$y_i^k = y_i^{k-1} \cdot (1 - M^i/100)^{\Delta t} \cdot (1 - M_1/100)^{\Delta t}.$$

The rate of prophylaxis k_i in (1) - (3) is a composite parameter:

$$k_i = v^i K^i / 10000,$$

if the individuals are selected randomly for AIDS tests and the same individual may be tested repeatedly.

The individuals from the same group can have various rates of contacts. It is shown by Jacquez and Simon (1990), that at the initial stage of infection the following averaged b_{ij} may be used:

$$b_{ij} = \frac{\sum_k (b_{ij}^k)^2 N_i^k}{\sum_k b_{ij}^k N_j^k},$$

where N_j^k is the per cent of individuals from the j -th group with the contact rate b_{ij}^k .

The probability p_{ij} of infection from an infective person in group j to a susceptible one in group i per contact depends on the probability of transmission per unprotected contact p_{ij}^* , the probability of failure of protection r_{ij} ($r_{ij} = 0.1$ using a condom), and the probability to use the protection in the i/j contact λ_{ij} :

$$p_{ij} = p_{ij}^* (1 + \lambda_{ij}(r_{ij} - 1)).$$

The prophylaxis has effect upon the use of protection (λ_{ij} varies from 0 to 1). Usually, a person from the j -th group gets into contact with other groups with the same protection parameter $\lambda_{ij} = \lambda_j = \alpha^j / 100$, $j = \overline{1, n}$.

The analysis of data selected in Lithuania in 1990 showed that with the probability 0.95 the number of infected persons is not greater than 194 (155 men and 39 women) and not less than 27 (26 men and 1 woman). Most probably there were 79 infected (71 men and 6 women). The examination showed 10 infected ones.

4. The software. The computer software, the Package for Investigation of HIV/AIDS Infection (PIHI), realizing DEM is developed.

The key goals in PIHI user-interface design were:

- speed of learning;
- speed of use;
- reduction of error rate;
- attractiveness of the interface.

A number of dialog forms can be used to seek our goals. Such forms are menus, command languages, natural-language dialogue and question-answer dialogue (see Falley and coworkers (1990)). Let us discuss the forms.

The fundamental advantage of menus is that the user can work with already familiar words and meanings. The usage of menus reduces the memory load for users and is especially attractive for new users. On the other hand, menus limit the size of the selection set of alternatives.

The use of a command language can accommodate large selection sets, is easy to be extended and is fast for experienced users. The learning time is relatively long, errors are more likely because of the possibility of typing errors.

The natural language dialogue is too complicated to realize and the typing of long sentences is rather tedious.

The question-answer dialogue is computer-initiated, and the user's response is constrained to a set of expected answers. The learning time and speed of use is low, the typing skill required is high.

Therefore, we may conclude that menus is the most suitable form for PIHI.

Turbo Pascal (version 6.0) and its object-oriented application

framework Turbo Vision, was used as a tool to write the PIHI. Turbo Vision is a complete object oriented library, including: windows, pull-down menus, mouse support, built-in color installation, buttons, scroll bars, input boxes and so on. We used these tools, because our application needed a high-performance, flexible and consistent interactive user interface.

Pull-down menus were used for:

- the selection of one of the possible models (single-group or multi-group);
- the selection of the parameters of the model for input;
- the selection of the graphical output of the modeling results;
- the choice of a suitable color palette for elements of graphical views.

A radio button construction was used for input of the model parameters in the cases, when the set of possible data values was limited (for example, the year of the end of modelling). In the cases of usual data input an input line construction was used. The most reliable values of the model parameters are set in the PIHI by default.

The Turbo Vision windows were used for:

- output of results;
- the help texts;
- the error messages.

A global context-sensitive help system is created. The help text depends on the place of the package program, where you press the F1 key.

First version of the PIHI package requires for the MS-DOS 3.3 version or the later one. The main *exe* file of the PIHI requires for 89 K bytes of memory. Some auxiliary files contain the information on the help texts, parameter values by default and so on.

The run time of the PIHI package is negligible for the user except for the time of modelling which in some cases may cause pauses of 10–15 seconds.

5. Control of the infection spread. The parameters k_i and p_{ij} may be controlled by means of prophylaxis. That may be done

by the efforts of varying the values of K^i , v^i and α^i , where

- K^i is the per cent of persons examined on the AIDS test per year;
- α^i is the per cent of individuals, using protective means during sexual contacts;
- v^i is the per cent of individuals, terminating per year the infection spread after the diagnosis of infection.

The number of contacts b_{ij} may vary too as a result of prophylaxis.

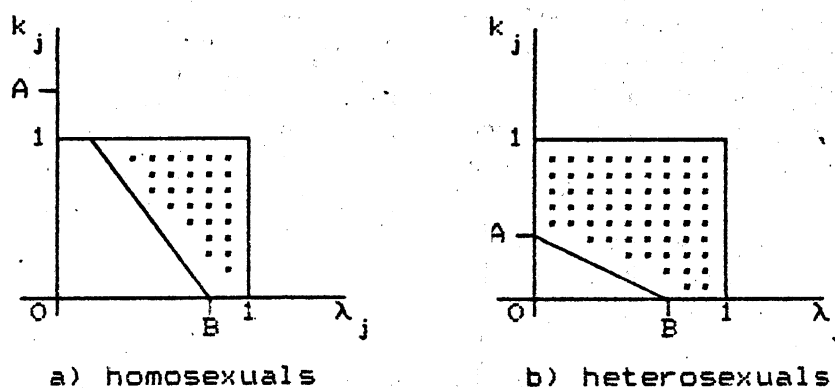


Fig. 1. The regions, where HIV decreases.

5.1. The conditions when an increase of infection stops.

Let $y = \sum_{i=1}^n y_i$, $u_i^y = 0$ and $\mu_s^y = \mu^y + \mu_1^y + \mu_2^y$. Recall $k_i = v^i K^i$, $\lambda_i = \alpha_i/100$. Then, by summing (2) over i and taking into account $x_i/(x_i + y_i) \leq 1$ we have, that $dy/dt \leq 0$ for any x_i and y_i , if and only if

$$\sum_{i=1}^n b_{ij} p_{ij}^* - \mu_s^j \leq k_j + \lambda_j \sum_{j=1}^n b_{ij} p_{ij}^* (1 - r_{ij}), \quad j = \overline{1, n}. \quad (5)$$

I.e., the spread of HIV decreases in this case. There is a natural rate of spread for infected persons of the j -th group on the left side of the inequality, and the prevention of spread on the right side. In Fig. 1 the region, where (5) is satisfied, is marked by

points (a) for homosexuals and b) for heterosexuals). Here $A = \sum_{i=1}^n b_{ij} p_{ij}^* - \mu_i^j$, $B = A / \sum_{i=1}^n b_{ij} p_{ij}^* (1 - r_{ij})$, $\sum_{i=1}^n b_{ij} = 200$ in all cases, $p_{ij}^* = 0.0075$ for homosexuals and $p_{ij}^* = 0.002$ for heterosexuals. A significant increase of k_j is too expensive. Also, it is doubtful that a major part of the indicated persons will not spread infection. On the other hand, we see that usage of protection means is very effective. Our further investigations deal with a minimization of expenses caused by HIV, varying the level of prophylaxis.

5.2. Investigations of control on the basis of real initial data. The following values of the parameters for (1) – (3) were chosen on the basis of the world experience and the data gathered in Lithuania during 1990: $n = 3$ (homosexual men, promiscuous heterosexual men and women); $x_1^0 = 93000$; $x_2^0 = 140000$; $x_3^0 = 140000$; $y_1^0 = 61$; $y_2^0 = 1$; $y_3^0 = 7$; $z_1^0 = 9$; $z_2^0 = 0$; $z_3^0 = 1$; $U_i^+ = 0$, $U_i^- = 0$, $U_i^y = 0$, $M_i^x = 0.5\%$, $M_i^z = 2.1\%$, $U_i = 2.6\%$; $i = \overline{1, n}$; $M_1 = 12.5\%$; $p_{11}^* = 0.0075$; $p_{13}^* = 0.004$; $p_{23}^* = 0.002$; $b_{11} = 70$; $b_{12} = 0$; $b_{13} = 2$; $b_{22} = 0$; $b_{23} = 50$; $b_{33} = 0$; $K^1 = 8.8\%$; $K^2 = 8.8\%$; $K^3 = 12.5\%$.

The values of α^i and v^i are known very approximately. The values of K^i are known in recent years and may be planned for the future. The spread of infection will be illustrated by varying the values of α^i and K^i . The values of v^i were set to be equal to 90%. $\alpha^i = \alpha$, $i = \overline{1, n}$. The period of simulation is from 01.01.1991 till 01.01.1998. $y = \sum_{i=1}^n y_i$ and $z = \sum_{i=1}^n z_i$ in Fig. 2–4.

The following experiments are performed:

1. The values $K^1 = 8.8\%$, $K^2 = 8.8\%$, $K^3 = 12.5\%$ are fixed; α takes the following values: 10%, 30%, 50%, 70%, 90%. The results are marked by 1, 2, 3, 4 and 5, correspondingly (see Fig. 2 a and b).

2. The values of K^i , $i = \overline{1, n}$, are made all equal and take the following values: 6%, 8%, 10%, 12%, 14%. The results are marked by 1, 2, 3, 4 and 5, correspondingly (see Fig. 3 a) for fixed $\alpha = 30\%$ and b) for $\alpha = 50\%$).

3. The values $K^1 = 8.8\%$, $K^2 = 8.8\%$, $K^3 = 12.5\%$ are fixed. An assumption is made, that the usage of protective means during sexual contacts grows and α converges to 100% at infinite time as an inverse exponent. α_1 is the initial value of α . α_2 is the forecasted

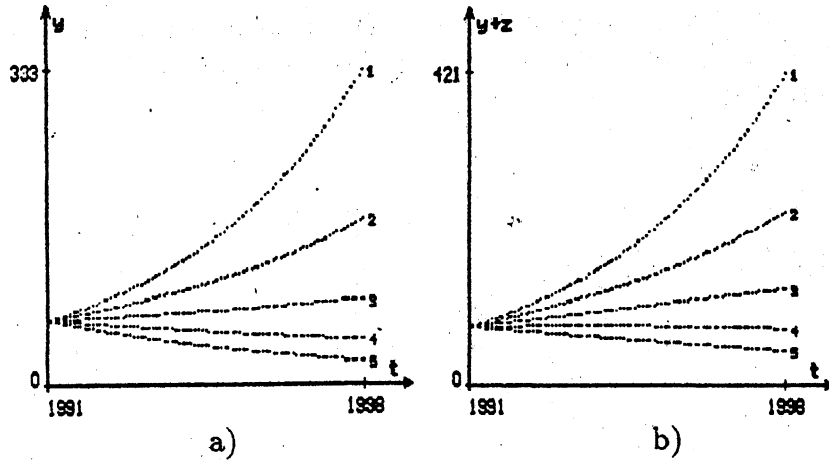


Fig. 2(a, b). The experiments varying α .

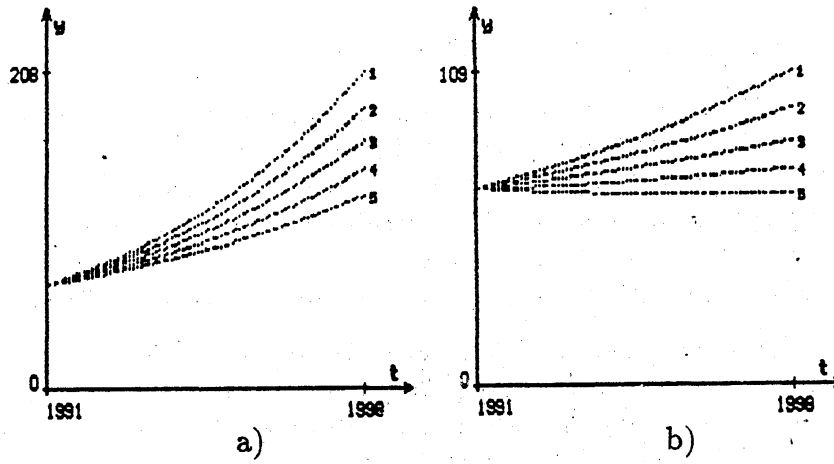


Fig. 3(a, b). The experiments varying K^i .

value of α at the end of simulation period. $\alpha_1 = 20\%$. α_2 takes the following values: 20%, 30%, 50%, 70%, 90%. The results are marked by 1, 2, 3, 4 and 5, correspondingly (see Fig. 4 a).

4. The indispensable blood test of people is performed only. $K^1 = K^2 = K^3 = 4\%$ in this case. Other conditions are like in 3 (see Fig. 4 b).

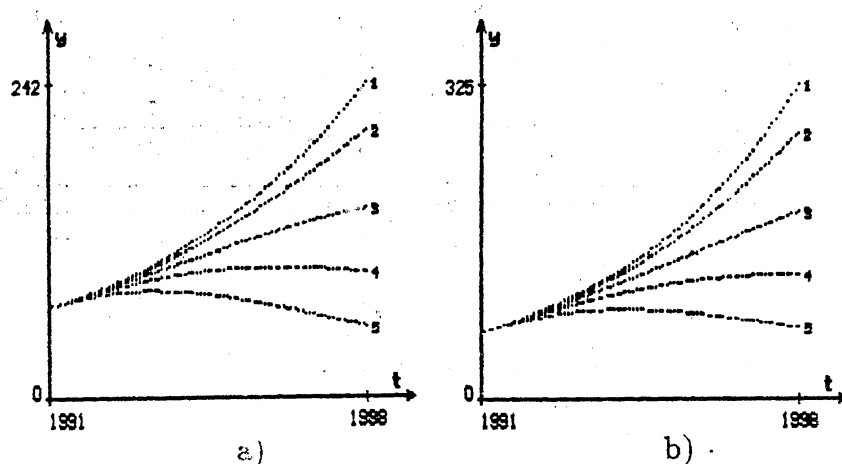


Fig. 4 (a, b). The experiments varying α_2 .

The experiments showed that the parameters α^i and K^i have a significant influence upon the infection spread. It is necessary to increase their real values. The means of increasing K^i are very expensive and it is impossible to reach high K^i due to social reasons. So the stress must be put on the increase of the usage of protection means – the infection spread stops when $\alpha^i = 70\%$ approximately.

6. Conclusions. This paper deals with the infection spread by means of sexual contacts only. The existence of infected intravenous drug users change the situation significantly. However, there are no such infection cases observed in Lithuania yet.

The investigations showed under what conditions the HIV/AIDS infection may be stopped. Two general directions may be dis-

tinguished: the HIV/AIDS blood tests and the publicity and availability of protective means. The last one is considerably cheaper and more effective. The infection spread stops when approximately 70% of individuals use preventive means and only indispensable HIV/AIDS blood test is performed (donors, venereal patients, complicated operations).

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