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Analysis of a stochastic model for the spread of tuberculosis with regard to reproduction and seasonal immigration of individuals

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Abstract — A stochastic model for the spread of tuberculosis is proposed taking into account the reproduction and seasonal immigration of individuals. The system of difference equations majorating the system of equations for mathematical expectations of sizes of considered cohorts of individuals is studied. Conditions for the parameters of the model are obtained so that under those conditions the sizes of cohorts of afflicted individuals do not exceed the given mean level. The results of numerical experiments are presented for the study of dynamics of mean sizes of cohorts of individuals subject to parameters of immigration inflow.

Keywords: Stochastic recurrence equations, mathematical modelling, Monte-Carlo methods, epidemiology, tuberculosis.

Papers [6–8] present stochastic models and computation algorithms aimed to the study of the dynamics of tuberculosis spread and HIV infection in regions of Russia. The development of models and algorithms used the following techniques: (1) stochastic recurrence relations and integer variables reflecting the dynamics of the sizes of cohorts of individuals, (2) a parametric description distinguishing individuals relative to certain characteristics, (3) a family of random variables specifying the length of stay of individuals in different cohorts, (4) probabilistic schemes of contacts of individuals similar to those arising in chain-binomial models [1, 3, 4].

The Monte Carlo method is used in combination with the technology of distributed computing on personal and hybrid computers for computational experiments with the models. Results of selection of parameters of the stochastic models of spread and control of tuberculosis are presented in [7] on the base of comparison of mathematical expectations of cohorts of individuals with real data. It was shown in [6, 8] that an analytic study of stochastic models of spread and control of TB and HIV in the regions of Russia can be performed on the basis of systems of nonlinear difference equations with given initial data. Solutions to these systems serve as upper bounds for mathematical expectations of sizes of studied cohorts of individuals. The presence of such systems of difference equations essentially simplifies computational experiments with stochastic models and their application for analysis of real data. The integer nature of variables in stochastic models and proper

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use of mathematical expectations of those variables are particularly important for the study of the problem of total eradication of mentioned diseases.

The aim of the present paper is the development of the stochastic models proposed in [6] subject to processes of reproduction and seasonal immigration of individuals in the regions of Russia. Note that these two factors were not explicitly considered in previous deterministic and stochastic models. The objective of the work includes the construction of equations of the model, analytical and numerical study of the behaviour of mathematical expectations of model variables depending on parameters of immigration inflows of individuals.

1. Stochastic model equations

We construct the equations of the model on the basis of [6]. Let us consider a certain region where the adult population (individuals elder than 16 years) is divided into the following six basic cohorts: S for non-infected individuals, L for infected individuals, D for undiagnosed sick individuals without bacterial excretion, B for undiagnosed sick individuals with bacterial excretion, D_0 for detected sick individuals without bacterial excretion, B_0 for detected sick individuals with bacterial excretion. In addition, let us introduce two auxiliary cohorts, E for died individuals or those who left the considered region, N for individuals younger 16 years born and living in this region. By $C = \{S, L, D, B, D_0, B_0\}$ we denote the collection of basic cohorts. We assume that the time t is discrete in the model, i.e., $t = 0, 1, \ldots, T$, where $T \in \mathbb{N}$ is fixed. The unit of time is 24 hours. We introduce the following notations:

x_H is an individual x from the cohort $H \in C$ or the cohort $H = N$; $x_H(t)$ is the number of individuals x in the cohort $H \in C$ at the time moment t; $\widehat{x}_H(t-1)$ is the number of individuals x_H living from the time moment $t-1$ to t and not leaving the considered region, $H \in C$;

$u_{A,M}(t)$ is the number of individuals x_A passing to the cohort M in the time interval $(t-1, t]$, $A, M \in C$, $A \neq M$; $u_{A,A}(t)$ is the number of individuals x_A staying in the cohort A within the period $(t-1, t]$, $A \in C$; $u_{A,E}(t)$ is the number of individuals x_A leaving the region or died in the period $(t-1, t]$, $A \in C$;

$g_H(t)$ is the number of individuals elder than 16 years and passing to the cohort $H \in C$ from other regions in the period $(t-1, t]$; $f_S(t)$ is the number of non-infected individuals x_N reaching the age of 16 years to the time moment $t-1$ and entering the cohort S in the period $(t-1, t]$; $f_L(t)$ is the number of infected individuals x_N reaching the age of 16 years to the time moment $t-1$ and entering the cohort L in the period $(t-1, t]$.

The system of equations of the model has the form

$$x_S(t) = \widehat{x}_S(t-1) - u_{S,L\cup D}(t) + f_S(t) + g_S(t) \tag{1.1}$$

$$x_L(t) = \widehat{x}_L(t-1) + u_{S,L}(t) + u_{D,L}(t) + u_{D_0,L}(t) - u_{L,D}(t) + f_L(t) + g_L(t) \tag{1.2}$$

$$x_D(t) = \widehat{x}_D(t-1) + u_{S,D}(t) + u_{L,D}(t) + u_{B,D}(t) - u_{D,L}(t) - u_{D,B}(t) - u_{D,D_0}(t) + g_D(t) \tag{1.3}$$

$$x_B(t) = \widehat{x}_B(t-1) + u_{D,B}(t) - u_{B,D}(t) - u_{B,B_0}(t) + g_B(t) \tag{1.4}$$

$$x_{D_0}(t) = \widehat{x}_{D_0}(t-1) + u_{D,D_0}(t) + u_{B_0,D_0}(t) - u_{D_0,B_0}(t) - u_{D_0,L}(t) + g_{D_0}(t) \tag{1.5}$$

$$x_{B_0}(t) = \widehat{x}_{B_0}(t-1) + u_{B,B_0}(t) + u_{D_0,B_0}(t) - u_{B_0,D_0}(t) + g_{B_0}(t) \tag{1.6}$$

$$t = 1,2,3,\dots,T$$

$$x_S(0) = x_S^{(0)}, \quad x_L(0) = x_L^{(0)}, \quad x_D(0) = x_D^{(0)} \tag{1.7}$$

$$x_B(0) = x_B^{(0)}, \quad x_{D_0}(0) = x_{D_0}^{(0)}, \quad x_{B_0}(0) = x_{B_0}^{(0)}. \tag{1.8}$$

We fix $t = 1,2,3,\dots,T$ and assume that each variable $x_H(t-1)$, $H \in C$, takes a fixed value. We describe conditional distribution laws for the variables entering (1.1)–(1.6) under the assumption that in each time interval $(t-1,t]$ all individuals behave independently and their behaviour does not depend on events preceding the time moment $t-1$.

Let $H \in C$ be a certain cohort. By $\rho_H \in (0,1)$ we denote the probability that the individual x_H residing in the considered region live from the moment $t-1$ to the moment t. The variable $\widehat{x}_H(t-1)$ has the binomial distribution with the parameters $(x_H(t-1);\rho_H)$, i.e.,

$$\widehat{x}_H(t-1) \sim \mathrm{B}\big(x_H(t-1);\rho_H\big), \quad H \in C. \tag{1.9}$$

We assume that in the time period $(t-1,t]$ the individuals x_B, x_{B_0} visit $\xi_t^{(B)}$ and $\xi_t^{(B_0)}$ places where they may have contacts with the individuals x_S, x_L, x_N. We assume

$$\xi_t^{(B)} = \sum_{n=1}^{\widehat{x}_B(t-1)} \psi_{nt}^{(B)}, \qquad \xi_t^{(B_0)} = \sum_{n=1}^{\widehat{x}_{B_0}(t-1)} \psi_{nt}^{(B_0)} \tag{1.10}$$

where each variable $\psi_{nt}^{(B)}$ and $\psi_{nt}^{(B_0)}$ denotes the number of places visited by particular individuals from x_B, x_{B_0} living from the time moment $t-1$ to the moment t. The variables $\{\psi_{nt}^{(B)}\}$ are identically distributed, mutually independent, and do not depend on $\widehat{x}_B(t-1)$; the variables $\{\psi_{nt}^{(B_0)}\}$ are identically distributed, mutually independent, and do not depend on $\widehat{x}_{B_0}(t-1)$; $\{\psi_{1t}^{(B)}\}$, $\{\psi_{1t}^{(B_0)}\}$ are nonnegative integer-valued random variables with given distribution laws. In particular, we assume that for any fixed T the following equality holds: $\mathrm{E}\psi_{1t}^{(B)} = r_B$, $\mathrm{E}\psi_{1t}^{(B_0)} = \gamma_{B_0} r_B$, $t = 1,\dots,T$, where $r_B > 0$, $\gamma_{B_0} \in [0,1]$ are some constants.

We consider individuals from the cohorts S and L living from the time moment $t-1$ to the moment t. We introduce the following parameters: $\lambda_S, \lambda_L \in (0,1)$ are the probabilities to visit the place of probable contact with the individuals x_B, x_{B_0} for the individuals x_S, x_L in the time interval $(t-1,t]$; $\delta_S, \delta_L \in (0,1)$ are the probabilities of infection for the individuals x_S, x_L after their contacts with the individuals x_B, x_{B_0}; $p_{S,D} \in (0,1)$ is the probability of disease development for the individual x_S infected after the contact with the individuals x_B, x_{B_0}; $\vartheta_L \in (0,1)$ is the probability of spontaneous activation of disease for the individual x_L during the time interval $(t-1,t]$. Fix $\xi_t^{(B)}$, $\xi_t^{(B_0)}$, $\widehat{x}_S(t-1)$, $\widehat{x}_L(t-1)$. The probability of infection for the individual x_S within the time interval $(t-1,t]$ is equal to

$$\mu_t^{(S)} = 1-(1-\lambda_S\delta_S)^{\xi_t^{(B)}+\xi_t^{(B_0)}}. \tag{1.11}$$

The distribution of the variable $u_{S,L\cup D}(t)$ is given under the fixed $\mu_t^{(S)}$ by the binomial law

$$u_{S,L\cup D}(t) \sim \mathrm{B}\big(\widehat{x}_S(t-1);\mu_t^{(S)}\big). \tag{1.12}$$

For fixed $u_{S,L\cup D}(t)$ we assume that

$$u_{S,D}(t) \sim \mathrm{B}\big(u_{S,L\cup D}(t);p_{S,D}\big) \tag{1.13}$$

and $u_{S,L}(t) = u_{S,L\cup D}(t) - u_{S,D}(t)$. The probability of disease development for the individual x_L in the time interval $(t-1,t]$ equals

$$\mu_t^{(L)} = 1-(1-\vartheta_L)(1-\lambda_L\delta_L)^{\xi_t^{(B)}+\xi_t^{(B_0)}}. \tag{1.14}$$

For the fixed $\mu_t^{(L)}$ we assume

$$u_{L,D}(t) \sim \mathrm{B}\big(\widehat{x}_L(t-1);\mu_t^{(L)}\big). \tag{1.15}$$

By $p_{K,M}\in(0,1)$ we denote the probability of passing individual x_K, $K,M\in C$, $K\neq M$, to the cohort M in the time interval $(t-1,t]$. We assume that for each $K\in C$ the relation $\sum_{M\in C, M\neq K} p_{K,M} < 1$ is valid. We assume $p_{D,D} = 1-p_{D,L}-p_{D,B}-p_{D,D_0}$, $p_{B,B} = 1-p_{B,D}-p_{B,B_0}$, $p_{B_0,B_0} = 1-p_{B_0,D_0}$, $p_{D_0,D_0} = 1-p_{D_0,B_0}-p_{D_0,L}$. We introduce the following groups of variables:

$$u_D(t) = (u_{D,L}(t),u_{D,B}(t),u_{D,D_0}(t),u_{D,D}(t))$$

$$u_B(t) = (u_{B,D}(t),u_{B,B_0}(t),u_{B,B}(t)), \quad u_{B_0}(t) = (u_{B_0,D_0}(t),u_{B_0,B_0}(t))$$

$$u_{D_0}(t) = (u_{D_0,B_0}(t),u_{D_0,L}(t),u_{D_0,D_0}(t))$$

representing the individuals passing from the cohorts D, B, B_0, D_0 to other cohorts in the time interval $(t-1,t]$ and also the remaining individuals. Under the fixed $\widehat{x}_D(t),\widehat{x}_B(t),\widehat{x}_{B_0}(t),\widehat{x}_{D_0}(t)$ we deal with the following multinomial distribution law:

$$u_D(t) \sim \mathrm{M}\big(\widehat{x}_D(t);\, p_{D,L};\, p_{D,B};\, p_{D,D_0};\, p_{D,D}\big) \tag{1.16}$$

$$u_B(t) \sim \mathrm{M}\big(\widehat{x}_B(t);\, p_{B,D};\, p_{B,B_0};\, p_{B,B}\big) \tag{1.17}$$

$$u_{B_0}(t) \sim \mathrm{M}\big(\widehat{x}_{B_0}(t);\, p_{B_0,D_0};\, p_{B_0,B_0}\big) \tag{1.18}$$

$$u_{D_0}(t) \sim \mathrm{M}\big(\widehat{x}_{D_0}(t);\, p_{D_0,B_0};\, p_{D_0,L};\, p_{D_0,D_0}\big). \tag{1.19}$$

We consider (1.1), (1.2) and the summands $f_S(t)$ and $f_L(t)$ representing the supplement of the cohorts S and L due to the growing young generation of the region. By $\tau = 5840$ days (16 years) we denote the boundary of the age group of individuals x_N. For $t = 1,\dots,\tau$ assume that $f_S(t)$, $f_L(t)$ are given deterministic functions $f_S^{(0)}(t)$, $f_L^{(0)}(t)$ taking nonnegative integer values. Further, let $t = \tau+1,\dots,T$. We assume that $G(t-\tau-1)$ describes the number of individuals born in this region in the time interval $I_t = [t-\tau-1, t-\tau)$ and supplying the cohort N ($I_t = (0,1)$ for $t = \tau+1$). The function $G(t-\tau-1)$ takes nonnegative integer values and is a random process with given probability characteristics. We introduce the parameter $\sigma(\tau+1) \in (0,1)$ as the probability that a newborn individual x_N lives up to the age of $\tau+1$ and does not leave the region due to migration. We assume that the individuals x_N behave independently. We define the random variable $v(t,\tau+1)$ describing the number of individuals from $G(t-\tau-1)$ living up to the age of $\tau+1$ and not leaving the region. Assuming that t and $G(t-\tau-1)$ are fixed, we obtain

$$v(t,\tau+1) \sim \mathrm{B}\big(G(t-\tau-1);\sigma(\tau+1)\big). \tag{1.20}$$

Fix the values $\xi^{(B)}_{t-\tau-1+j}$, $\xi^{(B_0)}_{t-\tau-1+j}$, $j = 1,\dots,\tau+1$, given by formulas (1.10). By the analogy with (1.11), we assume that the probability of infection for the individual x_N born in the time interval $(t-\tau-1, t-\tau]$ and reaching the age $\tau+1$ to the time moment t in the region is equal to

$$\nu_t^{(N)} = 1 - \prod_{j=1}^{\tau+1} (1-\lambda_j\delta_j)^{\xi^{(B)}_{t-\tau-1+j}+\xi^{(B_0)}_{t-\tau-1+j}} \tag{1.21}$$

where $\lambda_j \in (0,1)$ is the probability that the individual x_N of age $a \in (j-1, j]$ visits the place of probable contact with the individuals x_B, x_{B_0} in the time interval $(t-1,t]$, $\delta_j \in (0,1)$ is the probability of infection for the individual x_N of age $a \in (j-1, j]$ after his contact with the individuals x_B, x_{B_0}, $j = 1,\dots,\tau+1$. We fix $v(t,\tau+1)$, $\nu_t^{(N)}$ and assume

$$f_L(t) \sim \mathrm{B}\big(v(t,\tau+1);\nu_t^{(N)}\big), \quad f_S(t) = v(t,\tau+1) - f_L(t). \tag{1.22}$$

In the equations of system (1.1)–(1.6) the summands $g_H(t)$ represent the immigration inflows of individuals into the cohort $H \in C$, take nonnegative integer values, and are random processes with the given probability characteristics. Without loss of generality, assume that $x_S^{(0)}$, $x_L^{(0)}$, $x_D^{(0)}$, $x_B^{(0)}$, $x_{D_0}^{(0)}$, $x_{B_0}^{(0)}$ entering (1.7), (1.8) are given integer nonnegative constants.

Completing the description of the model, we assume that all random variables entering (1.1)–(1.22) are independent in common except for the variables which interconnections are given in a specially stipulated form. System (1.1)–(1.8) of model equations determines the random process

$$X(t) = (x_S(t), x_L(t), x_D(t), x_B(t), x_{D_0}(t), x_{B_0}(t)), \quad t = 0,1,\dots,T$$

with integer-valued nonnegative components. The description of this process for $t > \tau$ requires both preceding values of $X(t-1)$ and a 'prehistory' of the process $X(t-2)$, $X(t-3), \ldots, X(t-\tau-1)$. The nonnegativity of the components of $X(t)$ follows from the structure of the equations of the model. The variant of the model where the summands $g_H(t)$, $H \in C$, are absent is of certain importance. In this case the system of model equations can have the solution in the form of a random process $X(t) = X_0(t)$ so that

$$X_0(t) = (x_S(t), 0, 0, 0, 0, 0), \quad t = t_0, t_0+1, \ldots, T$$

where $t_0 > 0$ is some time moment. The process $X_0(t)$ reflects the dynamics of the population size in the considered region under the absence of tuberculosis.

2. Upper estimates of mathematical expectations of the components of the random process *X(t)* and the indicator R_0

Let $\mathrm{E}\eta$ denote the mathematical expectation of a certain random variable η. Assume that $\mathrm{E}g_H(t) = \varphi_H(t) \geqslant 0$, $H \in C$, $\mathrm{E}G(t) = \varphi_N(t) \geqslant 0$, $t = 1, \ldots, T$, are finite for any fixed T and, in addition, there exists a constant $\varphi_N^* > 0$ such that

$$\varphi_N(t) \leqslant \varphi_N^*, \quad t = 0, 1, 2, \ldots. \tag{2.1}$$

We denote $r_{N,j} = -\ln(1-\lambda_j\delta_j)$, $j = 1, \ldots, \tau+1$, $r_N = \sum_{j=1}^{\tau+1} r_{N,j}$, $r_S = -\ln(1-\lambda_S\delta_S)$, $r_L = -\ln(1-\lambda_L\delta_L)$, $d_L = 1-\vartheta_L$, and

$$h_1(x,y) = 1 - \exp(-r_S r_B(\rho_B x + \gamma_{B_0}\rho_{B_0} y))$$
$$h_2(x,y) = 1 - d_L \exp(-r_L r_B(\rho_B x + \gamma_{B_0}\rho_{B_0} y)), \quad x \geqslant 0, \quad y \geqslant 0.$$

We fix $t = 0, 1, \ldots, T$ and introduce the following numeric characteristics:

$$c_1(t) = \mathrm{E}x_S(t), \quad c_2(t) = \mathrm{E}x_L(t), \quad c_3(t) = \mathrm{E}x_D(t)$$
$$c_4(t) = \mathrm{E}x_B(t), \quad c_5(t) = \mathrm{E}x_{D_0}(t), \quad c_6(t) = \mathrm{E}x_{B_0}(t).$$

Using the results of [6, 8], for any fixed T we obtain the estimates

$$0 \leqslant c_i(t) \leqslant z_i(t), \quad i = 1, \ldots, 6, \quad t = 0, 1, \ldots, T \tag{2.2}$$

where the variables $z_1(t), \ldots, z_6(t)$ satisfy the following system of nonlinear difference equations with the given initial data:

$$z_1(0) = z_1^{(0)} = x_S^{(0)}, \qquad z_2(0) = z_2^{(0)} = x_L^{(0)}, \qquad z_3(0) = z_3^{(0)} = x_D^{(0)}$$

$$z_4(0) = z_4^{(0)} = x_B^{(0)}, \qquad z_5(0) = z_5^{(0)} = x_{D_0}^{(0)}, \qquad z_6(0) = z_6^{(0)} = x_{B_0}^{(0)} \tag{2.3}$$

$$
\begin{aligned}
z_1(t) &= \rho_S z_1(t-1) + f_S^{(0)}(t) + \varphi_S(t)\\
z_2(t) &= (1-p_{S,D})\rho_S z_1(t-1)h_1(z_4(t-1), z_6(t-1)) + \rho_L d_L z_2(t-1)\\
&\quad + p_{D,L}\rho_D z_3(t-1) + p_{D_0,L}\rho_{D_0} z_5(t-1) + f_L^{(0)}(t) + \varphi_L(t)\\
z_3(t) &= p_{D,D}\rho_D z_3(t-1) + p_{S,D}\rho_S z_1(t-1)h_1(z_4(t-1), z_6(t-1))\\
&\quad + \rho_L z_2(t-1)h_3(z_4(t-1), z_6(t-1)) + p_{B,D}\rho_B z_4(t-1) + \varphi_D(t)\\
z_4(t) &= p_{B,B}\rho_B z_4(t-1) + p_{D,B}\rho_D z_3(t-1) + \varphi_B(t)\\
z_5(t) &= p_{D_0,D_0}\rho_{D_0} z_5(t-1) + p_{D,D_0}\rho_D z_3(t-1) + p_{B_0,D_0}\rho_{B_0} z_6(t-1) + \varphi_{D_0}(t)\\
z_6(t) &= p_{B_0,B_0}\rho_{B_0} z_6(t-1) + p_{B,B_0}\rho_B z_4(t-1)\\
&\quad + p_{D_0,B_0}\rho_{D_0} z_5(t-1) + \varphi_{B_0}(t), \quad t = 1,\dots,\tau
\end{aligned}
\tag{2.4}
$$

$$
\begin{aligned}
z_1(t) &= \rho_S z_1(t-1) + \varphi_N^* \sigma(\tau+1) + \varphi_S(t)\\
z_2(t) &= (1-p_{S,D})\rho_S z_1(t-1)h_1(z_4(t-1), z_6(t-1)) + \rho_L d_L z_2(t-1) + \varphi_N^* \sigma(\tau+1)\\
&\quad \times \left(1 - \exp\Big(-\sum_{j=1}^{\tau+1} r_{N,j} r_B(\rho_B z_4(t-\tau-2+j) + \gamma_{B_0}\rho_{B_0} z_6(t-\tau-2+j))\Big)\right)\\
&\quad + p_{D,L}\rho_D z_3(t-1) + p_{D_0,L}\rho_{D_0} z_5(t-1) + \varphi_L(t)\\
z_3(t) &= p_{D,D}\rho_D z_3(t-1) + p_{S,D}\rho_S z_1(t-1)h_1(z_4(t-1), z_6(t-1))\\
&\quad + \rho_L z_2(t-1)h_2(z_4(t-1), z_6(t-1)) + p_{B,D}\rho_B z_4(t-1) + \varphi_D(t)\\
z_4(t) &= p_{B,B}\rho_B z_4(t-1) + p_{D,B}\rho_D z_3(t-1) + \varphi_B(t)\\
z_5(t) &= p_{D_0,D_0}\rho_{D_0} z_5(t-1) + p_{D,D_0}\rho_D z_3(t-1)\\
&\quad + p_{B_0,D_0}\rho_{B_0} z_6(t-1) + \varphi_{D_0}(t)\\
z_6(t) &= p_{B_0,B_0}\rho_{B_0} z_6(t-1) + p_{B,B_0}\rho_B z_4(t-1) + p_{D_0,B_0}\rho_{D_0} z_5(t-1) + \varphi_{B_0}(t)\\
&\qquad t = \tau+1,\dots,T.
\end{aligned}
\tag{2.5}
$$

Rewrite system (2.4), (2.5) in a more compact form. Let

$$u^{(j)} = \mathrm{col}(u_1^{(j)}, u_2^{(j)}, u_3^{(j)}, u_4^{(j)}, u_5^{(j)}, u_6^{(j)}) \in R_+^6, \quad j = 1,\dots,\tau+1$$

$$u = (u^{(1)}, u^{(2)}, \dots, u^{(\tau+1)})$$

$$
\begin{aligned}
f_1(u) &= \rho_S u_1^{(1)} + \varphi_N^* \sigma(\tau+1)\\
f_2(u) &= (1-p_{S,D})\rho_S u_1^{(1)} h_1(u_4^{(1)}, u_6^{(1)}) + \rho_L d_L u_2^{(1)}\\
&\quad + \varphi_N^* \sigma(\tau+1)\big(1 - e^{-\sum_{j=1}^{\tau+1} r_{N,j} r_B(\rho_B u_4^{(\tau+2-j)} + \gamma_{B_0}\rho_{B_0} u_6^{(\tau+2-j)})}\big) + p_{D,L}\rho_D u_3^{(1)} + p_{D_0,L}\rho_{D_0} u_5^{(1)}\\
f_3(u) &= p_{D,D}\rho_D u_3^{(1)} + p_{S,D}\rho_S u_1^{(1)} h_1(u_4^{(1)}, u_6^{(1)}) + \rho_L u_2^{(1)} h_2(u_4^{(1)}, u_6^{(1)}) + p_{B,D}\rho_B u_4^{(1)}\\
f_4(u) &= p_{B,B}\rho_B u_4^{(1)} + p_{D,B}\rho_D u_3^{(1)}
\end{aligned}
$$

$$f_5(u) = p_{D_0,D_0}\rho_{D_0}u_5^{(1)} + p_{D,D_0}\rho_D u_3^{(1)} + p_{B_0,D_0}\rho_{B_0}u_6^{(1)}$$
$$f_6(u) = p_{B_0,B_0}\rho_{B_0}u_6^{(1)} + p_{B,B_0}\rho_B u_4^{(1)} + p_{D_0,B_0}\rho_{D_0}u_5^{(1)}$$
$$f(u) = \mathrm{col}(f_1(u),\dots,f_6(u)).$$

In all calculations below we assume that the inequality $w^{(1)} \leqslant w^{(2)}$ is considered component-wise for the vectors $w^{(1)}, w^{(2)} \in R^m$. It is not difficult to show that $f(u)$ is a nonnegative and nondecreasing function of its arguments, namely, for any $w^{(1)}, w^{(2)}$ from the domain of definition of $f(u)$ and such that $w^{(1)} \leqslant w^{(2)}$ we have the inequality $0 \leqslant f(w^{(1)}) \leqslant f(w^{(2)})$.

By $z(t) = \mathrm{col}(z_1(t),\dots,z_6(t))$ we denote the column vector given by relations (2.3)–(2.5). We assume

$$\varphi(t) = \mathrm{col}(\varphi_S(t), \varphi_L(t), \varphi_D(t), \varphi_B(t), \varphi_{D_0}(t), \varphi_{B_0}(t)).$$

We write the system of equations for $z(t)$ in a vector form. We have

$$z(t) = f(z(t-1),\dots,z(t-\tau-1)) + \varphi(t), \quad t = \tau+1,\dots,T \tag{2.6}$$

$$z(t) = z^{(0)}(t), \quad t = 0,1,\dots,\tau. \tag{2.7}$$

The initial conditions in (2.7) are taken from solutions to system (2.3), (2.4). One can see that $z^{(0)}(t) \geqslant 0$, $t = 0,1,\dots,\tau$. Relation (2.6) implies $z(t) \geqslant 0$ for each $t = \tau+1,\dots,T$. Note that the solution $z(t)$ to system (2.6), (2.7) is determined for any fixed $T > 0$. This allows us to study the behaviour of $z(t)$ for $t \to \infty$. We apply the approach based on the theory of monotone operators [2, 5]. We suppose there exists

$$w^{(0)} \in R^6, \quad 0 \leqslant f(w^{(0)},\dots,w^{(0)}) \leqslant w^{(0)} \tag{2.8}$$

and construct $w(t) \in R^6_+$ according to the rule

$$w(t) = f(w(t-1),\dots,w(t-\tau-1)), \quad t = \tau+1, \tau+2, \dots \tag{2.9}$$

$$w(t) = w^{(0)}, \quad t = 0,1,\dots,\tau. \tag{2.10}$$

Based on the properties of $f(u)$ and on formulas (2.8)–(2.10), we get

$$w^{(0)} \geqslant w(\tau+1) \geqslant w(\tau+2) \geqslant w(\tau+3) \geqslant \dots \geqslant 0. \tag{2.11}$$

Relation (2.11) implies that there exists $\lim_{t\to\infty} w(t) = w^{(*)} \in R^6_+$ and (2.9) implies that $w^{(*)}$ satisfies the relations

$$w \in R^6, \quad w = f(w,\dots,w), \quad 0 \leqslant w \leqslant w^{(0)}. \tag{2.12}$$

Note that one of the solutions to (2.12) is the vector

$$w^{(*)} = \mathrm{col}(w_1^{(*)}, 0,0,0,0,0), \quad w_1^{(*)} = \varphi_N^* \sigma(\tau+1)/(1-\rho_S). \tag{2.13}$$

We consider the solution $z(t)$ to problem (2.6), (2.7) in the case

$$\varphi(t) = 0, \quad t = 0, 1, \ldots, \tau, \tau+1, \tau+2, \ldots \tag{2.14}$$

Relations (2.14) mean that the immigration inflows $g_H(t)$ are absent, $H \in C$. Let the initial data for (2.7) be such that

$$z^{(0)}(t) \leqslant w^{(0)}, \quad t = 0, 1, 2, \ldots, \tau. \tag{2.15}$$

Using (2.6)–(2.15), we get the inequalities

$$0 \leqslant z(t) \leqslant w(t) \leqslant w^{(0)}, \quad t = \tau+1, \tau+2, \ldots \tag{2.16}$$

Relation (2.16) implies

$$0 \leqslant \liminf_{t\to+\infty} z(t) \leqslant \limsup_{t\to+\infty} z(t) \leqslant w^{(*)}. \tag{2.17}$$

Suppose $w^{(*)}$ is the unique solution to (2.12). Relation (2.17) implies

$$0 \leqslant \liminf_{t\to+\infty} z_1(t) \leqslant \limsup_{t\to+\infty} z_1(t) \leqslant w_1^{(*)}, \quad \lim_{t\to+\infty} z_i(t) = 0, \quad i = 2, \ldots, 6.$$

Below we use Chebyshev's inequality, i.e., if η is a nonnegative random variable with a finite mathematical expectation $\mathrm{E}\eta > 0$ and $\varepsilon > 0$ is a given number, then $\mathrm{P}\{\eta > \varepsilon\} \leqslant \mathrm{E}\eta/\varepsilon$. Based on (2.2), we apply Chebyshev's inequality to the components $x_L(t)$, $x_D(t)$, $x_B(t)$, $x_{D_0}(t)$, $x_{B_0}(t)$ of the process $X(t)$ substituting the estimates of $z_2(t)$–$z_6(t)$ instead of the second–sixth components of $\mathrm{E}X(t)$.

Assertion 2.1. We suppose inequality (2.1) holds, there exists $w^{(0)}$ satisfying (2.8), and relations (2.14), (2.15) are valid. In this case, we have
(1) $0 \leqslant \mathrm{E}x_H(t) \leqslant w^{(0)}, \quad H \in C, \quad t = 0, 1, \ldots, \tau, \tau+1, \tau+2, \ldots$;
(2) if, in addition, $w^{(*)}$ is the unique solution to system (2.12), then

$$0 \leqslant \liminf_{t\to+\infty} \mathrm{E}x_S(t) \leqslant \limsup_{t\to+\infty} \mathrm{E}x_S(t) \leqslant w_1^{(*)}$$

$$\lim_{t\to+\infty} \mathrm{E}x_H(t) = 0, \quad \lim_{t\to+\infty} P\{x_H(t) = 0\} = 1, \quad H = L, D, B, D_0, B_0.$$

Now we consider the behaviour of the solution $z(t)$ to problem (2.6), (2.7) for the case of seasonal migration. We use the following description of $\varphi(t)$ instead of (2.14). We define the following sequence of time moments:

$$0 = t_0 < t_1 < t_2 < \ldots < t_{k-1} < t_k < \ldots \tag{2.18}$$

so that $t_{n-1} \leqslant \tau < t_n$ for some $n = 1, 2, \ldots$. We assume

$$\varphi(t) = 0, \quad t \in (t_{k-1}, t_k), \quad \varphi(t_k) \geqslant 0, \quad \sum_{i=1}^{6} \varphi_i(t_k) > 0, \quad k = 1, 2, \ldots \tag{2.19}$$

Assertion 2.2. Let inequality (2.1) be valid and the following conditions hold: there exists $w^{(0)}$ satisfying (2.8); $w^{(*)}$ is the unique solution to (2.12); the initial data $z^{(0)}(t)$ satisfy (2.15); the function $\varphi(t)$ given by (2.18), (2.19) is such that $z(t_n)+\varphi(t_n)\leqslant w^{(0)}$, $z(t_{k+1})+\varphi(t_{k+1})\leqslant w^{(0)}$, $k=n,n+1,\dots$ In this case $0\leqslant \mathrm{E}x_H(t)\leqslant w^{(0)}$, $H\in C$, $t=\tau+1,\tau+2,\dots$

Completing this section, consider inequality (2.8) that plays a leading role in the construction of estimators for $z(t)$. Inequalities (2.8) have the following componentwise form:

$$w_1^{(0)}\geqslant 0,\dots,w_6^{(0)}\geqslant 0 \tag{2.20}$$

$$\rho_S w_1^{(0)}+\varphi_N^*\sigma(\tau+1)\leqslant w_1^{(0)} \tag{2.21}$$

$$\begin{aligned}(1-p_{S,D})\rho_S w_1^{(0)}h_1(w_4^{(0)},w_6^{(0)})+\rho_L d_L w_2^{(0)}+p_{D,L}\rho_D w_3^{(0)}+p_{D_0,L}\rho_{D_0}w_5^{(0)}\\ +\varphi_N^*\sigma(\tau+1)h_3(w_4^{(0)},w_6^{(0)})\leqslant w_2^{(0)}\end{aligned} \tag{2.22}$$

$$\begin{aligned}p_{D,D}\rho_D w_3^{(0)}+p_{S,D}\rho_S w_1^{(0)}h_1(w_4^{(0)},w_6^{(0)})+\rho_L w_2^{(0)}h_2(w_4^{(0)},w_6^{(0)})\\ +p_{B,D}\rho_B w_4^{(0)}\leqslant w_3^{(0)}\end{aligned} \tag{2.23}$$

$$p_{B,B}\rho_B w_4^{(0)}+p_{D,B}\rho_D w_3^{(0)}\leqslant w_4^{(0)} \tag{2.24}$$

$$p_{D_0,D_0}\rho_{D_0}w_5^{(0)}+p_{D,D_0}\rho_D w_3^{(0)}+p_{B_0,D_0}\rho_{B_0}w_6^{(0)}\leqslant w_5^{(0)} \tag{2.25}$$

$$p_{B_0,B_0}\rho_{B_0}w_6^{(0)}+p_{B,B_0}\rho_B w_4^{(0)}+p_{D_0,B_0}\rho_{D_0}w_5^{(0)}\leqslant w_6^{(0)} \tag{2.26}$$

where $h_3(x,y)=1-\exp(-r_N r_B(\rho_B x+\gamma_{B_0}\rho_{B_0}y))$, $x\geqslant 0, y\geqslant 0$. Take the solution to inequality (2.21) in the form $w_1^{(0)}=w_1^{(*)}+\Delta_1^{(0)}$, where $\Delta_1^{(0)}\geqslant 0$ is an arbitrary fixed number. We consider inequalities (2.24)–(2.26) in the form of equalities. Transforming (2.21)–(2.26), we obtain the following system for $w_2^{(0)}$ and $w_4^{(0)}$:

$$w_2^{(0)}\geqslant 0,\ w_4^{(0)}\geqslant 0 \tag{2.27}$$

$$w_2^{(0)}\geqslant \beta_1 w_4^{(0)}+\beta_2(1-\mathrm{e}^{-\beta_3 w_4^{(0)}})+\beta_4(1-\mathrm{e}^{-\beta_5 w_4^{(0)}}) \tag{2.28}$$

$$\beta_6(1-\mathrm{e}^{-\beta_7 w_4^{(0)}})+\rho_L w_2^{(0)}(1-d_L e^{-\beta_8 w_4^{(0)}})\leqslant \beta_9 w_4^{(0)} \tag{2.29}$$

where the coefficients $\beta_1>0,\dots,\beta_9>0$ are expressed through $w_1^{(0)}$ and the coefficient of system (2.21)–(2.26). It is seen from (2.27)–(2.29) that there exists $w^{(0)}$ satisfying (2.8) and $w^{(*)}$ is the unique solution to system (2.12) if

$$R_0=(\rho_L\vartheta_L(\beta_1+\beta_2\beta_3+\beta_4\beta_5)+\beta_6\beta_7)/\beta_9<1. \tag{2.30}$$

In order to obtain appropriate $w^{(0)}$ explicitly, we apply the following technique. For fixed $\gamma>0$ we have

$$1-\mathrm{e}^{-\gamma x}\leqslant \gamma x,\quad 1-d_L\mathrm{e}^{-\gamma x}\leqslant d_L\gamma x+\vartheta_L,\quad x\geqslant 0. \tag{2.31}$$

Taking into account (2.31), we estimate the nonlinear expressions in (2.28), (2.29) from above and consider the system of inequalities

$$w_2^{(0)} \geqslant (\beta_1 + \beta_2\beta_3 + \beta_4\beta_5)w_4^{(0)} \tag{2.32}$$

$$\beta_6\beta_7 w_4^{(0)} + \rho_L w_2^{(0)}(d_L\beta_8 w_4^{(0)} + \vartheta_L) \leqslant \beta_9 w_4^{(0)} \tag{2.33}$$

which we study in association with (2.27). We assume in (2.32) that

$$w_2^{(0)} = (\beta_1 + \beta_2\beta_3 + \beta_4\beta_5)w_4^{(0)} \tag{2.34}$$

and for (2.33) we take the maximal admissible solution, i.e.,

$$w_4^{(0)} = \hat{w}_4{}^{(0)} = \frac{\beta_9(1-R_0)}{\rho_L d_L(\beta_1 + \beta_2\beta_3 + \beta_4\beta_5)\beta_8}. \tag{2.35}$$

The other components of the vector $w^{(0)} = \hat{w}^{(0)}$ are obtained from formulas indicated above.

Remark 2.1. Let $R_0 < 1$ and $\hat{w}^{(0)}$ satisfy inequalities (2.15). For the required $w^{(0)}$ we can take $w^{(0)} = \tilde{w}^{(0)}$ so that $0 < \tilde{w}_4^{(0)} < \hat{w}_4{}^{(0)}$ and inequalities (2.15) hold for $\tilde{w}^{(0)}$.

3. Numerical experiments

The aim of numerical experiments was to study the dynamics of mathematical expectations $\mathrm{E}X(t)$ of the components of the process $X(t)$ subject to immigration inflows of individuals. The simulation of implementations of the process $X(t)$ used the Monte Carlo method. The results of calculations are presented in the form of graphs and tables of the following numeric characteristics:

$$c_1(t) + c_2(t) = \mathrm{E}x_S(t) + \mathrm{E}x_L(t),\ c_3(t) + c_4(t) = \mathrm{E}x_D(t) + \mathrm{E}x_B(t),$$
$$c_5(t) + c_6(t) = \mathrm{E}x_{D_0}(t) + \mathrm{E}x_{B_0}(t). \tag{3.1}$$

The calculations were performed for the time intervals $t = 1, \dots, \tau$; $t = \tau+1, \dots, 2\tau$; $\dots, T$, where $T = 18250$ days. On each of these intervals, a simulation algorithm similar to that described in [6] was applied. The new elements in the simulation algorithm were auxiliary variables containing weighted sums of the random variables $\xi^{(B)}_{t-\tau-1+j}$ and $\xi^{(B_0)}_{t-\tau-1+j}$ entering (1.21). These variables reflect the 'prehistory' of development of the cohorts S and L. Numeric characteristics (3.1) were estimated by standard formulas of mathematical statistics. Statistical estimates for (3.1) and confidence intervals for them were obtained from 30 implementations of the process $X(t)$. The dynamics of statistical estimates of numeric characteristics (3.1) is presented in Fig. 1 (digits 1–4 denote the number of numerical experiment). For each fixed t (years) the rows of Table 1 contain the interval estimates of numeric characteristics (3.1), $P = 0.95$.

The initial data were the following: $x_S^{(0)} = 250000$, $x_L^{(0)} = 350000$, $x_D^{(0)} = 6800$, $x_B^{(0)} = 650$, $x_{D_0}^{(0)} = 2000$, $x_{B_0}^{(0)} = 2500$. The variable $G(1),\dots,G(t),\dots$ were mutually independent. For fixed t the variable $G(t)$ possesses the Poisson distribution, $\mathrm{E}G(t) = \varphi_N(t) = 50$. The other parameters were $\sigma(\tau+1) = 0.92$, $\rho_S = 0.99995$, $\rho_L = 0.99995$, $\rho_D = 0.999$, $\rho_B = 0.992$, $\rho_{D_0} = 0.9998$, $\rho_{B_0} = 0.9992$, $\lambda_S = 2\cdot 10^{-5}$, $\delta_S = 10^{-3}$, $\lambda_L = 2\cdot 10^{-5}$, $\delta_L = 10^{-4}$, $\vartheta_L = 0.00015$, $r_B = 2$, $\gamma_{B_0} = 0.2$, $p_{S,D} = 0.05$, $p_{D,L} = 0.001$, $p_{D,B} = 0.002$, $p_{D,D_0} = 0.004$, $p_{B,D} = 0.005$, $p_{B,B_0} = 0.009$, $p_{D_0,L} = 0.012$, $p_{D_0,B_0} = 0.008$, $p_{B_0,D_0} = 0.007$, $\lambda_j = 10^{-6}$, $\delta_j = 10^{-4}$, $j = 1,\dots,3000$, $\lambda_j = 10^{-5}$, $\delta_j = 10^{-4}$, $j = 3001,\dots,5841$, $f_S^{(0)}(t) = 40$, $f_L^{(0)}(t) = 5$, $t = 1,\dots,5840$. For these parameters, $R_0 = 0.834 < 1$. If we assume $\Delta_1^{(0)} = 5000$, then, using (2.34) and (2.35), we get $\hat{w}_1^{(0)} = 925000$, $\hat{w}_2^{(0)} = 2630477$, $\hat{w}_3^{(0)} = 62751$, $\hat{w}_4^{(0)} = 5728$, $\hat{w}_5^{(0)} = 15969$, $\hat{w}_6^{(0)} = 10261$. It is clear that the inequalities $\mathrm{E}X(0) \leqslant \hat{w}^{(0)}$ hold.

Experiment 1 assumes no immigration inflows, experiments 2–4 take into account such flows. Sequence (2.18) is simulated by the formula $t_0 = 0$, $t_k = t_{k-1} + v_k$, where $v_1,\dots,v_k,\dots$ is a set of mutually independent, identically distributed random variables; each v_k has the geometric distribution with the parameter $\mathrm{E}v_k = m_v$, $k = 1,2,\dots$, $m_v > 0$ is a given constant. We assume that $m_v = 90$, 30, 10 days for experiments 2, 3, 4, respectively. For fixed $t = t_k$ the random variables $g_H(t)$ have the Poisson distribution with the parameters $\mathrm{E}g_H(t) = \varphi_H(t)$: $\varphi_S(t) = 180$, $\varphi_L(t) = 230$, $\varphi_D(t) = 15$, $\varphi_B(t) = 10$, $\varphi_{D_0}(t) = 8$, $\varphi_{B_0}(t) = 12$. The values of the constant m_v and the parameters $\mathrm{E}g_H(t) = \varphi_H(t)$ are taken so that the mean annual immigration inflow of individuals V_{imm} does not exceed the mean annual number of born individuals lived up to the age of 16, i.e., $V_{\mathrm{sur}} = 365\,\varphi_N(t)\sigma(\tau+1) = 16790$ (people/year). We have $V_{\mathrm{imm}} = 1845.28; 5535.83; 16607.5$ people per year for experiments 2, 3, 4, respectively.

Figure 1 and Table 1 show that in Experiment 1 the numeric indicators $c_3(t) + c_4(t)$ and $c_5(t) + c_6(t)$ decrease in the course of time (see Assertion 2.1). For Experiments 2 and 3 the values of $c_3(t) + c_4(t)$ and $c_5(t) + c_6(t)$ first increase slightly and then decrease to a relatively low level. The behaviour of these numeric indicators is in accordance with Assertion 2.2. The results of Experiment 4 are principally different, a considerable intensification of immigration inflow causes an essential growth of all studied numeric indicators.

We consider Remark 2.1 and construct the vector $\tilde{w}^{(0)}$ which allows us to determine admissible parameters of inflow $\varphi(t)$ in Assertion 2.2. We require that the mean size of the cohort B does not exceed $\tilde{w}_4^{(0)} = 1500$ people. In this case

$$\tilde{w}^{(0)} = (925000, 688837, 16432, 1500, 4183, 2687).$$

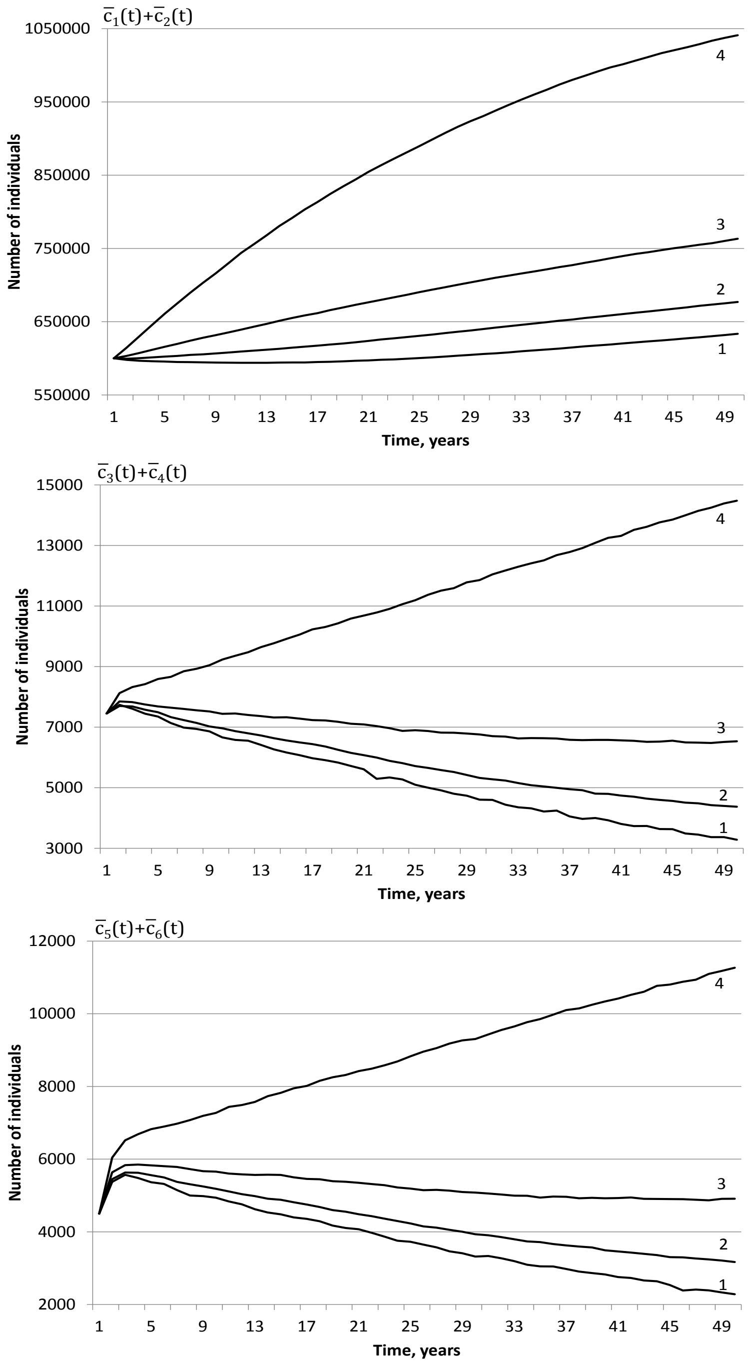

Figure 1. The dynamics of statistical estimates of numeric indicators (3.1). Digits indicate the numbers of numerical experiments.

Table 1. Confidence intervals for numeric indicators (3.1).

t	$c_1(t)+c_2(t)$	$c_3(t)+c_4(t)$	$c_5(t)+c_6(t)$
Experiment 1			
16	594391 ± 46.06	6075 ± 101.92	4397.5 ± 20.58
32	608113 ± 1211.28	4439 ± 39.21	3272 ± 23.52
48	630237 ± 617.39	3369 ± 19.61	2389.49 ± 10.78
Experiment 2			
16	615866 ± 884.34	6496.31 ± 26.03	4814.59 ± 31.71
32	643848 ± 989.04	5236.71 ± 32.86	3854.29 ± 29.37
48	673352 ± 1015.28	4425.73 ± 26.94	3242.37 ± 30.26
Experiment 3			
16	658633 ± 2041.04	7283.77 ± 50.72	5498.91 ± 44.28
32	712785 ± 2026.13	6688.69 ± 54.03	5026.41 ± 43.97
48	757183 ± 1576.93	6479.31 ± 50.08	4866.43 ± 48.06
Experiment 4			
16	803213 ± 2467.32	10057.31 ± 54.31	7949.13 ± 62.52
32	945886 ± 3026.69	12170.69 ± 74.94	9551.47 ± 81.43
48	1033610 ± 3566.93	14248.81 ± 110.14	11097.29 ± 91.01

Therefore, the expected upper bounds for the studied numeric indicators are

$$c_1(t)+c_2(t) \leqslant 1613837, \qquad c_3(t)+c_4(t) \leqslant 17932$$

$$c_5(t)+c_6(t) \leqslant 6870, \quad t = 1,\dots,T. \tag{3.2}$$

Note that inequalities (3.2) hold in experiments 1–3 and are violated for the indicator $c_5(t)+c_6(t)$ in experiment 4 for $t > 5$ years (see Fig. 1).

Varying the values of the parameters $\mathrm{E}g_H(t)$ and the constant m_v, one can estimate the admissible mean level of immigration inflows of individuals of the cohorts D and B which cannot cause the growth of the numeric indicator $c_5(t)+c_6(t)$. In particular, we assume that the immigration inflow consists only of non-detected patients (cohorts D and B), namely, $\varphi_D(t) = 355$, $\varphi_B(t) = 100$, $\varphi_S(t) = \varphi_L(t) = \varphi_{D_0}(t) = \varphi_{B_0}(t) = 0$. The calculations show that for $m_v = 90$ days we have $c_5(t)+c_6(t) \leqslant 4725$; if $m_v = 30$ days, then $c_5(t)+c_6(t) \leqslant 6075$ (on the whole simulation interval). In both these cases the maximal mathematical expectation of the total size of the cohorts D_0 and B_0 (detected afflicted individuals) does not exceed the level presented in (3.2). The dynamics of $c_5(t)+c_6(t)$ is practically the same as in Fig. 1 (experiments 2 and 3). For $m_v = 10$ days this result is not true, i.e., $c_5(t)+c_6(t)$ monotonically increases, $c_5(t)+c_6(t) > 10000$ for $t = 25$ years and $c_5(t)+c_6(t) > 14500$ for $t = 48$ years. We come to the conclusion that for sufficiently rare immigration inflows the particular portion of afflicted persons in the group of individuals coming to the region does not influence the dynamics of the mean sizes of the cohorts D_0 and B_0.

In conclusion, we consider inequality (2.30) that leads to the study of sufficiently complicated relations between the parameters of the model appearing in R_0. From the practical viewpoint, it is necessary to construct an indicator R_1 such that $R_0 < R_1$

and the inequality $R_1 < 1$ can be verified on the base of available official statistics. The problem of calculation of R_0 or construction of its estimator R_1 from real data is an important problem for verification of the model and its practical use.

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