S©MR

СИБИРСКИЕ ЭЛЕКТРОННЫЕ
МАТЕМАТИЧЕСКИЕ ИЗВЕСТИЯ
Siberian Electronic Mathematical Reports
http://semr.math.nsc.ru
ISSN 1813-3304

Vol. 21, No. 1, pp. 125–163 (2024)
https://doi.org/10.33048/semi.2024.21.010

УДК 519.174.7
MSC 05C50

CONCEPT CONTROLLING MODEL FOR ARRESTING EPIDEMICS, INCLUDING COVID-19

G.D. KAMINSKIY, YU. I. PROSTOV, D.A. SEMENOVA, M.YU. PROSTOV, N.N. PIMENOV, E.I. VESELOVA, A.S. VINOKUROV, E.V.KARAMOV, A.E. PANOVA, A.S. TURGIEV, V.V. CHERNETSOVA, A.E. LOMOVTSEV

Communicated by M.A. Shishlenin

Abstract: Concept controlling model for arresting epidemics (further on - the model) of emerging, new and re-emerging infections has been developed. Epidemic force parameters are defined: high values of contact rate of infection in acute (R_1) and chronic (R_2) forms of disease, high frequency of chronization γ_2 with pathogen excretion, high rate of loss of natural immunity k_1, high inflow of susceptible population μ. Control targets have been identified: infected persons (detection, isolation and treatment δ), transmission mechanism (regime-restrictive measures, sanitary and hygienic procedures r), the decrease in susceptibility (vaccination, pre- and post-exposure prophylaxis λ). Critical interdependencies between epidemic force parameters and control coefficients were studied. We obtained threshold conditions for "zero infection"asymptotic stability. In order to achieve the target result more quickly, the use of "supercritical"control levels is proposed, with the model determining the time to achieve the result. The need to affect both acute and chronic forms of

Kaminskiy, G.D. et. al., Concept controlling model for arresting epidemics, including COVID-19.

This work was carried out with the financial support of the Ministry of Education and Science of the Russian Federation: grant No. 075-11-2020-011 (13.1902.21.0040).

Received November, 29, 2022 , published February, 28, 2024.

infection has been proven. The model allows to solve direct and inverse problems.

Keywords: control of communicable diseases, threshold, intervention campaign, parameters of the epidemic process, mathematical model.

1 Introduction

1.1. Principles of the mathematical theory of epidemics. The mathematical theory of the spread of infectious diseases is the progressively developing branch of knowledge [6, 29]. It allows us to understand the mechanism of development of the epidemic process [32]. Attention to the mathematical theory of the spread of infectious diseases has increased in connection with the COVID-19 pandemic [21, 28, 38].

The effectiveness of both the simplest and most complex models has been proven. A classic example is the Kermack and McKendrick model [48].

Currently, there is no single model of epidemics and there are only few works to prove the comparability of some models to others. In addition, the question of the applicability areas of each of the models is not well understood: for example, which model is relevant to describe dynamics near the equilibrium, and which model describes outbreaks or drops in incidence far from the stationary state; how the shapes of epidemic curves differ in different models. In most cases, models have a large, in some cases redundant, number of parameters. The types of outbreak models are presented in Table 1.

Understanding that a general (integrative) model of epidemics in the future will certainly be created, the authors of the present work turned to a differential model to highlight general (mathematical) principles important in epidemic (medical) terms. As long as there is no integrative mathematical theory, agent models remain more imitative. Though in differential equations with delay, analytical study is difficult, the system of differential equations per se is much closer to mathematical theory.

1.2. Definitions. The force of epidemia - a set of parameters of the infectious and epidemic process, that determines a high level of stationary epidemic state, rapid movement towards it and struggling fluctuations.

The counter force - a set of epidemic management (control) parameters that are adequate to the force of epidemia that make the stationary epidemic state unstable and ensure a decrease in incidence until disease is eliminated ("epidemic arrest").

The intervention campaign - application of epidemic management (control) parameters in practice, characterized by preliminary computational mathematics, preparation and use of necessary and sufficient powers and means to achieve the goal of arresting epidemia.

TABLE 1. Types of epidemic models.

Model	Use and features of the model	Use and features of the model
1	Differential Model	This model contains differential equations for the classes of susceptible, exposed (individuals in the latent phase), infected, quarantined, immune, treated, vaccinated, and deceased. This type also includes structured models that describe epidemics in each city (territory) using separate systems of differential equations and contain a matrix established of connections between cities (territories) [16, 7, 27]. Parameter profiles are exponential in time.
2	Integral Model	This is the most accurate model computationally, as the infectiousness profile is documented by days of illness. Special profiles are used to show the loss of immunity and timely case detection with subsequent neutralization of infectiousness. The number of new cases of diseases in the Integral Model is determined by the formula: $$A(t) = R\left(\int_0^T A(t-\tau)e^{-\mu\tau}\rho(\tau)d\tau\right)X(t)$$ $A(t)$, disease incidence; $\rho(\tau)$, infectiousness profile (standardized), $\int_0^T \rho(\tau)d\tau = 1$; μ, inflow/outflow of susceptible individuals $X(t)$; R, the contact rate. The Integral Model is sometimes equivalent to the multiclass Differential Model or the Model of Delay Differential Equations [97, 9, 5].
3	Territorial Agent-Based Model	The Agent-Based Model properly describes the slow changes of transmission activity and incidence. There is no contact rate (R) in the Territorial Agent-Based Model. Instead, there is the likelihood of encounters of infected and susceptible individuals and the likelihood of being infected during a single exposure. It is matched to the area, infrastructure, and social categories and age groups of the population. Both the Territorial Agent-Based Model and the Integral Model enable distributed profiles (by day). This Model is more precise in describing some types of dynamics, specifically sites of chain-binomial infection transmission [39].
4	Randomized Model	This is a variant in Models 1-3, where at each step the contact rate R, the inflow of susceptible μ, and the number of newly infected are shown as randomly distributed. This Model provides expected means as well as upper and lower confidence limits [24, 36].
5	Models based on the Mean Field Game Theory	This Model is based on a coupled pair of partial differential equations: the Fokker-Planck (Kolmogorov) Equation that evolves forward in time and determines the distribution of interacting subjects over the state space; and the Hamilton-Jacobi-Bellman Equation that evolves back in time and defines if the chosen strategy is optimal [98, 20, 1].

2 Purpose, requirements and structure of the study.

2.1. Purpose. The purpose of this work is to create the concept controlling model to assess the force of the epidemia and to determine the counter force value to arrest the epidemia.

2.2. Requirements. Primary demand: counter force should be adequate to the applied force [18].

The model should describe at least two-member parasitic systems consisting of two interacting populations - the parasite and the host (models with vectors and microbe conservation in the environment are by definition more complex and should be considered separately).

The model represents a Procrustean bed for saturating the system with the set of parameters, in "simple"cases the model degenerates. This is necessary to include all the parameters that determine the strength of the epidemic process and the strength of the response.

The model should assimilate the occurrence of both acute and chronic, infectious conditions, taking into account possible fading of immune response.

The model must have the necessary and sufficient complexity to reproduce the epidemic process of acute and chronic infections, as well as the combination of acute infection and carriage in one infection. Since some dangerous infections (for example, HIV-infection) have high mortality rates (in certain groups), the model must work with a changing population size. Variables must be specified in absolute numbers.

The model should have the complete set of the control targets. Management should be implemented in relation to the sources of the causative agent of the infection, the mechanism of its transmission and the susceptible organism. The model should provide an assessment of combined infectious disease control measures.

2.3. Structure. - Solving the direct problem of building the concept controlling model ("epidemic arrest").

- Study of stationary solutions of the model and their stability (instability) in the aspect of control.

- Solving the inverse problem to determine the parameters of the epidemic process based on comparison of model data with real ones.

- Pre calculation and implementation of intervention campaigns.

3 Model construction

3.1. Selection and characterization of infection and epidemic process parameters. Contact rate of infection R is the main parameter of the epidemic process [30]. It shows how many susceptible are infected from a single infected subject in case of complete susceptibility of the population. The more R is, the greater the rate of increase in incidence and the overall diseased number in the epidemic. Despite the pronounced selection pressure, which contributes to the reproduction of more virulent parasites, the R parameter does not grow indefinitely. To explain this pattern, the concept of compromise was drawn out [12], however causation of this phenomenon is not yet well understood.

The contact rate of infection is a complex (multi-faceted) parameter that reflects biological (virulence of the pathogen), environmental (crowding of the population, wastewater level, sewerage defects) and social factors (regime-restrictive measures, including lockdown).

There are estimates of the contact rate R depending on nosology, significant variability of R within nosology is shown [6, 10].

The contact rate R should be considered variate depending on territories, population groups, time periods (depending on sanitary conditions).

The infection intensity parameter α characterizes the duration of the infectious process and is expressed as the inverse time of its duration (1/day, week, month, etc.) [42]. It is during this time the number of successful events,

designated by parameter R, will take place. Next, the patient can recover, die or become chronically infected. Recovery intensity β represents the intensity of transition to the class of resistant $R(t)$. In infections without mortality and chronization, $\alpha = \beta$. In general, $\alpha = \beta + \epsilon + \gamma_2$, where β – is the recovery rate, ϵ – is the disease dependent death rate, γ_2 – is the chronization rate. This approach is very important, for example, in chronic viral hepatitis C, where there is a recovery, chronization and significant mortality associated with the effect on humans of the virus [87].

The natural movement of the population (inflow and outflow) is indicated by the parameter μ. It characterizes the born and arrived μ_1, as well as the dead and departed μ_2. For most problems of mathematical modeling of epidemics $\mu_1 = \mu_2 = \mu$, however, the model provides for the ability to analyze growing, decreasing populations and populations with substitution of removed. The absolute number of births and arrivals is $\mu_1 N$, where N is the total population in which the epidemic process develops.

Important parameters are the coefficient of loss of natural immunity k_1 and artificial (vaccine) immunity k_2. In some infections, the loss of natural immunity is absent $k_1 = 0$, in others (COVID-19) there may be a significant loss of immunity [23]. A high value loss of natural immunity coefficient causes a greater value of incidence and prevalence.

Estimation of parameters, taken from scientific papers, are given in Appendix A.

3.2. Selection and characterization of control parameters. In physical and technical systems, there is a clear understanding of control, and effective control always implies achieving a target and right trajectory, obtaining a result. In epidemiological systems, difficulties arise. Globally, the management of the epidemic process is a system of directed impacts, the result of which is a systematic reduction in the incidence of the population, up to the interruption of the epidemic process and its elimination. The main control parameter is the intensity of vaccination (and pre-exposure prophylaxis) of susceptible λ_1 and those who have been ill λ_2. The λ_2 parameter is used for infections with loss of immunity. Control through isolation, detection and treatment is divided into two parts: δ_1 - for persons with acute infection, δ_2 - for carriers. The identification and treatment of carriers is of great importance, since without this the elimination of epidemics is impossible. The parameter δ_3 characterizes the time of stay of infectious patients in a state of isolation (quarantine). The effect on the transmission mechanism is determined by the control factor r, which reduces the probability of effective contact $r \cdot R$. Measures of influence on the transmission mechanism include all ways to reduce effective contacts, that is, lockdown, intergroup isolation, safe behavior, sanitary measures. Thanks to them, it is possible to achieve containment in the range of $r \in [0.2; 0.6]$.

The epidemic process is managed through an intervention campaign mechanism. At the preliminary stage, it includes a calculation of the necessary levels of

control, time to start, duration, time to result, monitoring application and reaching goal.

Note 1. *Identification of infected is carried out using clinical, epidemiological and laboratory methods. Clinical methods involve the identification of vivid symptoms of the disease (fever, intoxication, loss of smell and taste). Epidemiological methods - narrowing the scope of search among individuals in direct contact or potential contact (risk group). Laboratory methods include testing for DNA/RNA and/or antigen of the causative agent of the infection. In order to more identify the sources of pathogens of infection, including in the early stages of the disease, tracing and testing of contacts is strongly recommended as well as repeated (screening, saturation) testing, including using non-invasive tests.*

Note 2. *Treatment of identified cases leads to a decrease in the concentration of the pathogen in the human body, a decrease in infectious activity and a decrease in the spread of the disease. In some infections, isolation of the identified patient at home or in a hospital is possible. In this case, the person goes to the Q (t) class - quarantined.*

Note 3. *Prevention of infection of susceptible individuals includes vaccination and preventive treatment (before and after contact). Vaccination involves revaccination, which ensures the preservation of immunity.*

Note 4. *The impact on the mechanism of transmission of infection includes sanitary measures in relation to the human habitat, as well as regime-restrictive measures (for example, the introduction of a self-isolation regime). Susceptible people are not allowed into the infected area.*

3.3. Differential equations. The system of differential equations – **concept controlling model of arresting epidemics** - comprises 7 independent differential equations, depicting 7 major variables:

$$\begin{cases} S(t)' = -\dfrac{rS(t)(R_1\alpha_1 A(t) + R_2\alpha 2C(t))}{S(t)+E(t)+A(t)+C(t)+R(t)+V(t)} + \\ + \mu_1 N - \mu_2 S(t) + k_1 R(t) + k_2 V(t) - \lambda_1 S(t) \\ E(t)' = \dfrac{rS(t)(R_1\alpha_1 A(t) + R_2\alpha_2 C(t))}{S(t)+E(t)+A(t)+C(t)+R(t)+V(t)} - (\gamma_1+\mu_2)E(t) \\ A(t)' = \gamma_1 E(t) - (\beta_1+\gamma_2+\epsilon_1+\delta_1+\mu_2)A(t) \\ C(t)' = \gamma_2 A(t) - (\beta_2+\epsilon_2+\delta_2+\mu_2)C(t) \\ R(t)' = \beta_1 A(t) + \beta_2 C(t) + \delta_3 Q(t) - (\lambda_2+k_1+\mu_2)R(t) \\ V(t)' = \lambda_1 S(t) + \lambda_2 R(t) - (k_2+\mu_2)V(t) \\ Q(t)' = \delta_1 A(t) + \delta_2 C(t) - (\delta_3+\mu_2)Q(t) \end{cases} \tag{1}$$

The flow chart of the model is given on Figure 1. One class is hidden and includes people who left the population and died due to infection and

natural causes (class *DW - Dead and Withdrawn*). Before treatment patients are identified and isolated, forming class *Q (t)* - quarantined. The *Q (t)* class and the *DW* class are not presented for interaction as contacts. To calculate the proportion of susceptible, the absolute number of susceptible *S (t)* is divided by the sum of

S (t) + E (t) + A (t) + C (t) + R (t) + V (t)

to show the probability of contacts of infected and susceptible. Thus, the model represents mass action well in case that the total population changes, either grows, remains stable, or decreases.

Thus, although the model is based on the equations of Kermack and McKendrick, it differs in the set of classes acutely and chronically infected, in the set of control parameters and classes created by this control, in the selection of interacting components in calculating the action of masses, in accounting for vaccination of susceptible, ill and time of loss of natural and artificial immunity, the possibility of application in populations of changing numbers. According to the combination and set of properties, the model is independent, adapted for medical (epidemiological) purposes of describing the main human infections and various ways to control them, including integrated management, being at the intersection of mathematics and medicine.

Model is closest to SEIR-HCD model [47].

Variables: $S(t)$ - number of susceptible, $E(t)$ - number of exposed but not yet infected, $A(t)$ - number of acutely infected, $C(t)$ - number of chronically infected, $R(t)$ - number of resistant, $V(t)$ - number of those who have post-vaccination immunity, $Q(t)$ - number of isolated for treatment (quarantined).

Parameters of the infectious process: $\alpha(\alpha_1, \alpha_2)$ - intensity of infection, $\beta(\beta_1, \beta_2)$ - intensity of recovery, k_1 - intensity of natural immunity loss, $\epsilon(\epsilon_1, \epsilon 2)$ - infectious disease-related mortality rate.

Parameters of the epidemic process: R - contact rate of infection, μ_2 - intensity of population outflow, $\mu_1 N$ - intensity of population inflow.

Control coefficients (control intensity coefficients): λ_1 - intensity of vaccination of susceptible and pre-exposure prophylaxis, λ_2 - intensity of vaccination of recovered (they may be prone to immunity loss and therefore need vaccination), δ_1 - intensity of detection, isolation and treatment of acutely infected, δ_2 - intensity of detection, isolation and treatment of chronically infected, r - impact on the contact rate of infection with the addition of a control component through the implementation of safety measures and sanitary and hygienic measures.

Parameter k_2 - intensity of vaccination immunity loss - holds an intermediate position between the parameters of the epidemic force and the parameters of counteraction.

Variables, parameters of infection and epidemic process, control parameters are given in Tables 2 and 3.

To model seasonality to contact rates R_1 and R_2 the seasonal forcing $(1+ \ +\iota \sin\left(\frac{2\pi t+\theta}{INT}\right))$, where ι – the intensity of seasonal fluctuations, θ –

TABLE 2. Variables and parameters of concept controlling model of the epidemic process (beginning)

Name	Description
Variables	
$S(t)$	susceptible
$E(t)$	exposed - persons in the latent period
$A(t)$	acute infection
$C(t)$	chronic infection (carriers)
$R(t)$	immune - resistant
$V(t)$	immune - vaccinated
$Q(t)$	isolated (quarantined)
Parameters of epidemic force	
α_1	intensity of infection of acutely infected
α_2	intensity of infection of chronically infected
β_1	intensity of recovery of acutely infected
β_2	intensity of recovery of chronically infected
γ_1	intensity of transition from latent period to acute infection
γ_2	intensity of transition from acute to chronic infection
k_1	intensity of natural immunity loss
k_2	intensity of vaccine immunity loss
ϵ_1	mortality from acute infection
ϵ_2	mortality from chronic infection
R_1	contact rate for acutely infected
R_2	contact rate for chronically infected
μ_2	general population mortality rate, population outflow
$\mu_1 N$	birth rate, population inflow

the duration of the phase shift indicating the seasonal maximum, INT – dimension (observation interval: 365.25 days, 12 months, 52.18 weeks).

The comparison of model data with real data is carried out according to the number of new cases given by the formula

$$\left\{ \frac{rS(t)(R_1\alpha_1 A(t) + R_2\alpha_2 C(t))}{S(t) + E(t) + A(t) + C(t) + R(t) + V(t)} \right. \tag{2}$$

The main control parameter is vaccination of susceptible $S(t)$ with intensity λ_1. Both vaccination and revaccination are necessary for the formation of lifelong immunity. The model for $k_1 \neq 0$ assumes the need to vaccinate recovered patients, for them tot to loose immunity. The vaccination intensity of recovered patients is indicated as λ_2. In some cases, people are vaccinated without clinical and serological data on the past disease. In this case, $\lambda_1 = \lambda_2 = \lambda$.

The model introduced the assumption that isolated (quarantined) persons recover from the disease and return with immunity. If the general intensity

TABLE 3. Variables and parameters of concept controlling model of the epidemic process (continuation)

Name	Description
Parameters of counter force	
λ_1	intensity of vaccination of susceptible and pre-exposure prophylaxis
λ_2	intensity of vaccination of recovered
δ_1	intensity of detection, isolation and treatment of acutely infected
δ_2	intensity of detection, isolation and treatment of chronically infected
δ_3	rate of return from isolation with immunity
r	added component of contact rate control through implementation of safe behavior measures and sanitary measures

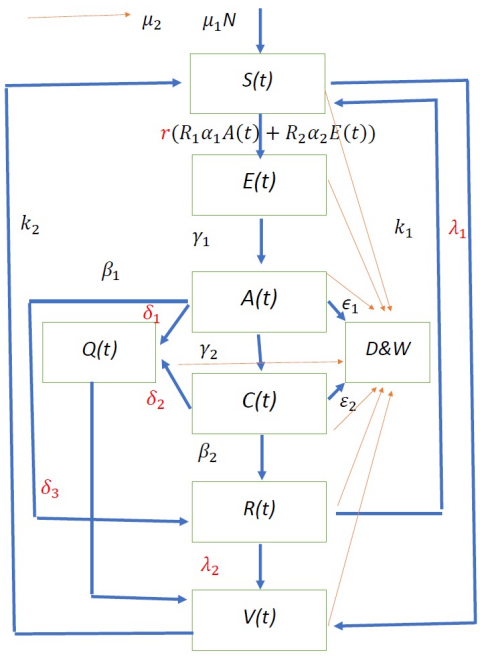


FIG. 1. Flow chart of the model. Variables in blocks, parameters of epidemic and infection are highlighted in black, control parameters are highlighted in red.

of detection and isolation of sources of the causative agent of infection is applied (without differentiation into acute and chronically infected), then $\delta_1 = \delta_2 = \delta$.

Model degradation procedures are discussed in paragraph 3.4 and Appendix B.

The model operates in absolutes.

3.4. The system properties. Next, we will assume that $\mu_1 = \mu_2 = \mu$. Trivial solution of differential equation system (1) - the state of "zero incidence":

$$\begin{cases} S = \dfrac{(k_2+\mu)N}{k_2+\lambda_1+\mu} \\ E = 0 \\ A = 0 \\ C = 0 \\ R = 0 \\ V = \dfrac{N\lambda_1}{k_2+\lambda_1+\mu} \\ Q = 0 \end{cases} \tag{3}$$

The following theorem gives the criterion of the trivial solution (3) stability.

Theorem. Trivial solution (3) of the system (1) is asymptotically stable in the first approximation if and only if

$$r < \frac{(\mu+\gamma_1)(\mu+\beta_1+\epsilon_1+\delta_1+\gamma_2)(\mu+\beta_2+\epsilon_2+\delta_2)(\mu+k_2+\lambda_1)}{(R_1\alpha_1(\mu+\beta_2+\epsilon_2+\delta_2)+R_2\alpha_2\gamma_2)(\mu+k_2)\gamma_1} \tag{4}$$

Proof. Rearrange the equations in the system (1) as follows

$$\begin{cases} S(t)' = -\dfrac{rS(t)(R_1\alpha_1A(t)+R_2\alpha 2C(t))}{S(t)+E(t)+A(t)+C(t)+R(t)+V(t)} + \\ \quad +\mu_1N-\mu_2S(t)+k_1R(t)+k_2V(t)-\lambda_1S(t) \\ V(t)' = \lambda_1S(t)+\lambda_2R(t)-(k_2+\mu_2)V(t) \\ R(t)' = \beta_1A(t)+\beta_2C(t)+\delta_3Q(t)-(\lambda_2+k_1+\mu_2)R(t) \\ A(t)' = \gamma_1E(t)-(\beta_1+\gamma_2+\epsilon_1+\delta_1+\mu_2)A(t) \\ E(t)' = \dfrac{rS(t)(R_1\alpha_1A(t)+R_2\alpha_2C(t))}{S(t)+E(t)+A(t)+C(t)+R(t)+V(t)} - (\gamma_1+\mu_2)E(t) \\ C(t)' = \gamma_2A(t)-(\beta_2+\epsilon_2+\delta_2+\mu_2)C(t) \\ Q(t)' = \delta_1A(t)+\delta_2C(t)-(\delta_3+\mu_2)Q(t) \end{cases} \tag{5}$$

The Jacobian of the trivial solution (3) of the system (5) is

$$Jac_{triv} = \begin{pmatrix} -\mu-\lambda_1 & k_2 & k_1 & -\frac{R_1\alpha_1(k_2+\mu)r}{k_2+\lambda_1+\mu} & 0 & -\frac{R_2\alpha_2(k_2+\mu)r}{k_2+\lambda_1+\mu} & 0 \\ \lambda_1 & -k_2-\mu & \lambda_2 & 0 & 0 & 0 & 0 \\ 0 & 0 & -k_1-\mu-\lambda_2 & \beta_1 & 0 & \beta_2 & \delta_3 \\ 0 & 0 & 0 & \beta_1-\gamma_2-\epsilon_1-\delta_1-\mu & \gamma_1 & 0 & 0 \\ 0 & 0 & 0 & -\frac{R_1\alpha_1(k_2+\mu)r}{k_2+\lambda_1+\mu} & -\gamma_1-\mu & \frac{R_2\alpha_2(k_2+\mu)r}{k_2+\lambda_1+\mu} & 0 \\ 0 & 0 & 0 & \gamma_2 & 0 & -\beta_2-\epsilon_2-\delta_2-\mu & 0 \\ 0 & 0 & 0 & \delta_1 & 0 & \delta_2 & -\delta_3-\mu \end{pmatrix} \tag{6}$$

The characteristic polynomial $p(t)$ of the matrix Jac_{triv} can be represented as

$$p(t) = (t+\mu)(t+\mu+\lambda_1+k_2)(t+\mu+\lambda_2+k_1)(t+\mu+\delta_3)q(t) \tag{7}$$

where $q(t)$ - characteristic polynomial of the matrix

$$M = \begin{pmatrix} -\mu-\beta_1-\epsilon_1-\delta_1-\gamma_2 & \gamma_1 & 0 \\ R_1\alpha_1 r\frac{\mu+k_2}{\mu+k_2+\lambda_1} & -\mu-\gamma_1 & R_2\alpha_2 r\frac{\mu+k_2}{\mu+k_2+\lambda_1} \\ \gamma_2 & 0 & -\mu-\beta_2-\epsilon_2-\delta_2 \end{pmatrix} \tag{8}$$

Since all the roots of the multiplier

$$(t+\mu)(t+\mu+\lambda_1+k_2)(t+\mu+\lambda_2+k_1)(t+\mu+\delta_3) \tag{9}$$

are negative, then the stability of the polynomial $p(t)$ is determined by the stability of the polynomial $q(t)$.
Let's enter the designations:

$$\begin{aligned} p_1 &= \beta_1+\epsilon_1+\delta_1 \\ p_2 &= \beta_2+\epsilon_2+\delta_2 \\ q_1 &= R_1\alpha_1\frac{\mu+k_2}{\mu+k_2+\lambda_1} \\ q_2 &= R_2\alpha_2\frac{\mu+k_2}{\mu+k_2+\lambda_1} \end{aligned} \tag{10}$$

Calculating the coefficients of the polynomial $q(t) = t^3 + a_1t^2 + a_2t + a_3$, we get

$$\begin{aligned} &a_1 = \gamma_1+\gamma_2+p_1+p_2+3\mu \\ &a_2 = (2\mu+p_1+p_2+\gamma_2-rq_1)\gamma_1+3\mu^2+2(p_1+p_2+\gamma_2)\mu+p_2(p_1+\gamma_2) \\ &a_3 = \mu^3+(p_1+p_2+\gamma_1+\gamma_2)\mu^2+((p_1+p_2-rq_1+\gamma_2)\gamma_1+p_2(p_1+\gamma_2))\mu+ \\ &+((p_1-rq_1+\gamma_2)p_2-\gamma_2rq_2)\gamma_1 \end{aligned} \tag{11}$$

From the Routh-Hurwitz criterion, we obtain that the trivial stationary solution is asymptotically stable in the first approximation if and only if

$$\begin{cases} a_1 > 0 \\ a_2 > 0 \\ a_3 > 0 \\ a_1 a_2 - a_3 > 0 \end{cases} \tag{12}$$

where a_1, a_2, a_3 are defined in formulas (10, 11). Note that the inequality $a_1 > 0$ is always valid. Let's consider the inequality $a_2 > 0$. Solving this with regard to the parameter r we get that

$$r < r_2 = \frac{(\gamma_2 + 2\mu + p_1 + p_2)\gamma_1 + 3\mu^2 + 2(p_1 + p_2 + \gamma_2)\mu + p_2(p_1 + \gamma_2)}{q_1\gamma_1} \tag{13}$$

Next, consider the inequality $a_3 > 0$. Solving it with regard to the parameter r we get that

$$r < r_3 = \frac{(\mu + \gamma_1)(\mu + p_2)(\mu + p_1 + \gamma_2)}{\gamma_1(q_2\gamma_2 + \mu q_1 + q_1 p_2)} \tag{14}$$

We calculate the difference $r_2 - r_3$. We get that

$$\begin{aligned} r_2 - r_3 = (q_1\gamma_1(q_2\gamma_2 + \mu q_1 + q_1 p_2))^{-1}(2q_1\mu^3 + ((p_1 + 4p_2\gamma_1 + \gamma_2)q_1 + 3q_2\gamma_2)\mu^2 + \\ + 2(q_2\gamma_2 + q_1 p_2)(p_1 + p_2 + \gamma_1 + \gamma_2)\mu + p_2^2(p_1 + \gamma_1 + \gamma_2)q_1 + \\ \gamma_2((p_2 + \gamma_1)\gamma_2 + p_2(p_1 + \gamma_1) + \gamma_1 p_1)q_2) > 0 \end{aligned} \tag{15}$$

From (15) we get that $r_3 < r_2$. Therefore, if inequality (14) is valid, then the inequality (13) is also valid.

Next, consider the function $\phi(r) = a_1 a_2 - a_3$. Note, that function $\phi(r)$ is linear and can be given by formula

$$\begin{aligned} \phi(r) = a_1 a_2 - a_3 = -((2\mu + p_1 + \gamma_1 + \gamma_2)q_1 - q_2\gamma_2)\gamma_1 r + \\ + (2\mu + p_2 + \gamma_1)(2\mu + p_1 + \gamma_1 + \gamma_2)(2\mu + \gamma_2 + p_1 + p_2) \end{aligned} \tag{16}$$

Note that

$$\phi(0) = (2\mu + p_2 + \gamma_1)(2\mu + p_1 + \gamma_1 + \gamma_2)(2\mu + \gamma_2 + p_1 + p_2) > 0 \tag{17}$$

and

$$\begin{aligned} \phi(r_3) = \frac{\gamma_1 + \gamma_2 + 3\mu + p_1 + p_2}{(\mu + p_2+)q_1 + \gamma_1 q_2}\Big(2q_1\mu^3 + \\ + ((q_1 + 3q_2)\gamma_2 + q_1(p_1 + 4p_2 + \gamma_1))\mu^2 + \\ + 2(q_2\gamma_2 + p_2 q_1)(p_1 + p_2 + \gamma_1 + \gamma_2)\mu + \\ + q_2(p_2 + \gamma_1)\gamma_2^2 + (p_2^2 q_1 + q_2(p_1 + \gamma_1)p_2 + p_1 q_2\gamma_1)\gamma_2 + p_2^2 q_1(p_1 + \gamma_1)\Big) > 0 \end{aligned} \tag{18}$$

As $\phi(r)$ - linear function and $\phi(0) > 0$ and $\phi(r_3) > 0$, then $\phi(r) > 0$ at $r \in [0, r_3]$. Thus,

$$a_1 a_2 - a_3 > 0, r \in [0, r_3] \tag{19}$$

From (13), (14), (19) and inequality $r_3 < r_2$ we get that system of inequalities (12) is equal to inequality (14). Substituting values (10) into the inequality (14) we obtain (4). Theorem is proved.

Now let's look at the following examples.

Example 1.

Current parameters of the new coronavirus infection COVID-19 are given: $\mu = 0.000157; R_1 = 4; R_2 = 4; \gamma_1 = 0.25; \gamma_2 = 0.001; \alpha_1 = 0.074; \alpha_2 = 0.050; \beta_1 = 0.074; \beta_2 = 0.050; k_1 = 0.0055; \epsilon_1 = 0; \epsilon_2 = 0, N = 100,000$. Let's set control parameters by vaccination: $\delta_1 = 0; \delta_2 = 0; \delta_3 = 0; \lambda_1 = 0.003; k_2 = 0.001; \lambda_2 = 0$. Determine by formula (4) the required critical level of limitation of the transmission mechanism. It turns out to be r =0.90.

Let us apply this control option. For the trivial solution (the solution of «zero infection»), we have the following coefficients of the characteristic polynomial:

$Coeffi = [4.32 \cdot 10^{-19}, 1.53 \cdot 10^{-14}, 1.47 \cdot 10^{-10}, 4.52 \cdot 10^{-7}, 1.79 \cdot 10^{-4}, 2.04 \cdot 10^{-2}, 3.86 \cdot 10^{-1}, 1]$

The following Routh-Hurwitz coefficients are obtained:

$CoeffHur = [3.86 \cdot 10^{-1}, 7.69 \cdot 10^{10-3}, 1.31 \cdot 10^{-6}, 5.68 \cdot 10^{-13}, 7.96 \cdot 10^{-23}, 1.11 \cdot 10^{-36}, 4.78 \cdot 10^{-55}]$

The following coefficients are obtained $a_2, a_3, a_1 a_2 - a_3 : a_2 = 1.66 \cdot 10^{-2}, a_3 = 7.45 \cdot 10^{-7}, a_1 a_2 - a_3 = 6.23 \cdot 10^{-3}$.

Now let's loose the restrictions of the transmission mechanism $r = 0.91$.

For trivial solution ("zero infection"state solution) we have the following coefficients of the characteristic polynomial:

$Coeffi = [-5.63 \cdot 10^{-18}, -6.47 \cdot 10^{-14}, -1.34 \cdot 10^{-10}, 3.40 \cdot 10^{-7}, 1.66 \cdot 10^{-4}, 2.02 \cdot 10^{-2}, 3.86 \cdot 10^{-1}, 1]$

The following Routh-Hurwitz coefficients are obtained:

$CoeffHur = [3.86 \cdot 10^{-1}, 7.62 \cdot 10^{-3}, 1.21 \cdot 10^{-6}, 4.34 \cdot 10^{-12}, -4.51 \cdot 10^{-23}, 3.76 \cdot 10^{-36}, -2.12 \cdot 10^{-53}]$

Negative coefficients appeared.

The following coefficients are obtained $a_2, a_3, a_1 a_2 - a_3 : a_2 = 1.64 \cdot 10^{-2}, a_3 = -9.72 \cdot 10^{-6}, a_1 a_2 - a_3 = 6.16 \cdot 10^{-3}$.

Coefficient $a_3 < 0$.

The trivial stationary solution ("zero infection"state solution) has become unstable. The epidemic is resuming. The following number of infected people is registered: in the latent phase of the disease E_0 - 21 people, in the acute phase of the disease A_0 - 70 people, in the chronic (prolonged) phase of the disease C_0 - 1 person.

Example 2.

Let's solve the problem in the space of all three control coefficients. The current parameters of the new coronavirus infection COVID-19 are given as in example 1. It is required to build a diagram of the countermeasures, namely the dependence of the impact on the contact rate r on the intensity of detection, isolation and quarantine of sources of infection $\delta_1 = \delta_2$ and the volume of vaccination λ_1. The result is shown in Figure 2. With a high intensity of δ and λ_1, a significant decrease in the contact rate of infection (for example, lockdown) is not required ($r = 0.7$, yellow). At low intensity δ and λ_1, a sharp decrease in the contact rate of infection is required ($r = 0.3$, blue color). Also, if there are opportunities for effective vaccination λ_1, then the intensity of detection and quarantine of infection sources δ can be less. The most effective impacts are in all basic areas of control.

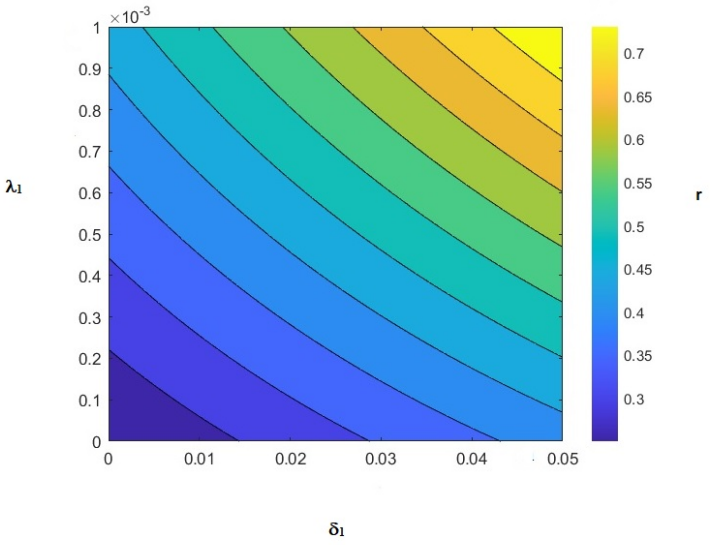


FIG. 2. Diagram counter forces. Parameters as in example 1. $\delta_3 = 0.048$ Observation interval - days.

Rule 1. *The greater the impact of vaccination and pre-exposure prophylaxis and the more intensive the detection and limitation of infectious agent sources, the less isolation is necessary. The higher the level of vaccination and pre-exposure prophylaxis, the lower the level of detection of sources of the causative agent of infection may be.*

Example 3.

Given are parameters of the strength of the epidemic process of viral hepatitis C. Viral hepatitis C has an acute and chronic phase of the disease. Let's answer the question: is it possible to identify and treat only the chronic

phase of the disease? In this very case can we reach a critical level of control ("epidemic arrest")? Let's build the dependence δ_2 on the contact rate of the acute phase of the disease R_1. It can be seen that the epidemic process control by identifying and treating the exclusively chronic phase of the disease is possible if and only if less than one susceptible person is infected from one patient during the acute phase Figure 3. After this level, "system collapse"occurs and management due to the impact on chronic patients becomes ineffective. In a drug (narcotic induced) epidemic, patients in the acute phase infect more than 1 person, therefore, measures should be carried out in relation to both acute and chronic patients.

Rule 2. *Measures to identify, isolate and treat the sources of the causative agent of infection should be aimed at both acute and chronic patients.*

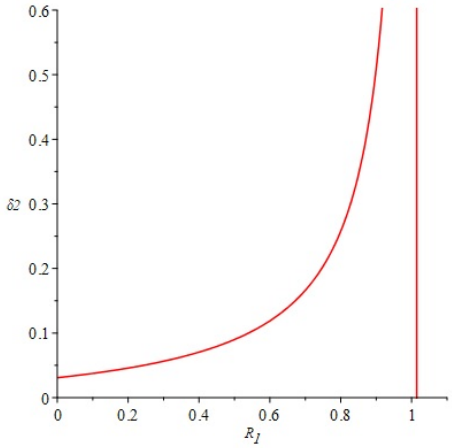


FIG. 3. Possibility to achieve critical level of control due to detection and treatment of chronic patients δ_2 depending on contact rate of acute phase of disease R_1: $\mu = 0.0022; R_2 = 4; \gamma_1 = 0.095; \gamma_2 = 0.0913; \alpha_1 = 0.164; \alpha_2 = 0.028; \beta_1 = 0.064; \beta_2 = 0; k_1 = 0.2667; \epsilon_1 = 0.006; \epsilon_2 = 0.028; \delta_1 = 0; \delta_3 = 0.167; r = 1; \lambda_1 = 0; \lambda_2 = 0$. Follow-up interval month.

Example 4.

The result of changing the stability of the epidemic process in formula (4) does not depend on the population size N, the intensity of loss of natural immunity k_1, the transition of the quarantined to general population δ_3. However, the time to reach "zero infection"("epidemic arrest") may depend on these parameters.

If the control conditions are close to the threshold, the extinction time of the infection is significant. This is especially manifested in chronic infections, carriage, temporary natural immunity, high contact rate R, high influx of

susceptible population μ (high epidemic strength), which makes it difficult to move towards trivial equilibrium. A particular time to reach a critically low concentration can be obtained by numerically solving differential equations. The target outcome is a condition with less than 1 infected person (quantum) over the period of maximum duration of infection. The corresponding diagram is shown in Figure 4. It means that when natural immunity fades, the time of «epidemic arrest» significantly lengthens.

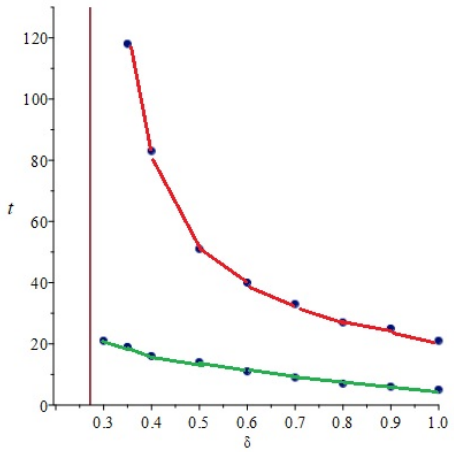


FIG. 4. The diagram of the dependence of the time of 'epidemic arrest' versus the rate of detection and treatment of sources of infection in two strains of hepatitis C virus: lifelong immunity $k_1 = 0$ - green line, immunity lasting 1 month $k_1 = 1$ - red line: $\delta_1 = \delta_2 = \delta, \mu = 0.0022; R_1 = 2.5; R_2 = 4; \gamma_1 = 0.095; \gamma_2 = 0.0913; \alpha_1 = 0.164; \alpha_2 = 0.028; \beta_1 = 0.064; \beta_2 = 0; \epsilon_1 = 0.006; \epsilon_2 = 0.028; \delta_1 = 0; \delta_3 = 0.167; r = 1; \lambda_1 = 0; \lambda_2 = 0$. Follow-up interval month. Vertical brown line represents critical level δ of stability loss

Rule 3. *The threshold condition of "epidemic arrest"determines the critical level of impact, the time of "epidemic arrest"at this very threshold level can be significant. Therefore, the mathematical model (1) makes it possible to calculate fare above the threshold (supercritical) levels of impact, which make it possible to achieve a result in a closer predictable time.*

Thus, management is active and aggressive. If all three control factors remain at a higher level, the interruption time of the epidemic process is reduced and the cessation of the epidemic process is achieved.

Analytical approximation of time to arrest the epidemia is given in Appendix B.

4 Using a model to solve the inverse problem to determine epidemic strength and strength of counter-action.

4.1. Epidemic data and parameter estimation. The materials used were data from medical organizations on the number of registered cases of 13 infections. 11 acute infections: measles, rubella, mumps, viral hepatitis A, influenza A, COVID-19, whooping cough, chicken pox, scarlet fever, Sonnei dysentery, gonorrhea; 2 chronic infections: viral hepatitis C, HIV infection. Transmission mechanism: aerosol - 8 infections, fecal-oral - 2 infections, hemo-contact and sexual - 2 infections, sexual - 1 infection. Etiological factor: viruses - 8 infections, bacteria - 5 infections.

The observation period covered: measles - 60 years (1961-2021), rubella - 46 years (1975-2021), mumps - 60 years (1961-2021), viral hepatitis A - 51 years (1970-2021), influenza A - 29 years (1992-2021), COVID-19 - 665 days (01.03.2020-25.12.2021), whooping cough - 30 years (1991-2021), chicken pox - 30 years (1991-2021), scarlet fever - 33 years (1961-1994), Sonnei dysentery - 30 years (1991-2021), gonorrhea - 30 years (1991-2021), viral hepatitis C - 30 years (1991-2021), HIV infection - 30 years (1991-2021).

In total, 413,887 cases were analyzed: measles - 17,485, rubella - 18,049, mumps - 19,350, viral hepatitis A - 4,826, influenza A - 196,890, COVID-19 - 85,997, whooping cough - 1,558, chicken pox - 26,633, scarlet fever - 15,838, Sonnei dysentery - 3 332, gonorrhea - 8,694, viral hepatitis C - 1,468, HIV infection - 13,767.

Data on measles, rubella, mumps, viral hepatitis A, chicken pox and scarlet fever were collected in the city of Novomoskovsk, Tula region; data on influenza A, whooping cough, Sonnei dysentery, gonorrhea collected in the city of Tula; viral hepatitis C and HIV infection - in the Tula region; COVID-19 - in the city of Khasavyurt of the Republic of Dagestan.

The follow-up interval for infections varied. For influenza A and COVID-19, daily data are collected; for measles, rubella, mumps, viral hepatitis A, pertussis, chicken pox, scarlet fever, Sonnei dysentery and gonorrhea - weekly data; viral hepatitis C and HIV infection - monthly data.

The inverse problem was solved by performing minimization of the convex functional. Euclidean distance D and normalized Euclidean distance D_{norm} between model and real data determined by the following formulas was used:

$$D = \sqrt{\frac{\Sigma_0^P (I_t - M_t)^2}{P}} \tag{20}$$

$$D_{norm} = \sqrt{\frac{\Sigma_0^P \frac{(I_t - M_t)^2}{(I_t - M_t)}}{P}} \tag{21}$$

where I_t is the actual value of the number of new cases per observation interval t, M_t is the model value of the number of new cases per observation interval t, P is duration of observation.

The detection (optimization) of parameters was carried out by universal gradient descent method; individual, pairwise and group selection of parameters within the specified limits was conducted using 3-5 iterations [91].

The criterion for stopping iterations was the absence of further change in the Euclidean distance.

Major parameters of the epidemic process, chosen for detection (optimization) was the contact rate R and the intensity of seasonal fluctuations ι of the contact rate R.

For the functional estimation we used the following number of measurement dots (according to time interval and dimension): measles - 1,588, rubella - 1,812, mumps - 2,024, viral hepatitis A - 2,476, influenza A - 10,200, COVID-19 - 665, whooping cough - 1,428, chicken pox - 1,425, scarlet fever - 1,605, Sonnei dysentery - 1,412, gonorrhea - 1,473, viral hepatitis C - 369, HIV infection - 369

The duration of the phase shift θ was determined by the day of maximum incidence on the seasonality curve.

Information about the parameters of the infectious process α (α_1, α_2), k and others are taken from [99, 73, 100] and literary sources (A).

Epidemic control parameters (counter measure) were calculated by numerically solving the system of differential equations (1), while comparing the family set of control parameters for various possible time intervals to achieve «epidemic arrest».

The criterion of «epidemic arrest» was taken as such a number of acute $A(t)$ and chronic $C(t)$ forms of infection, in which the probability of interruption $p = 0.5$. The probability of interruption was calculated by the formula

$$p = (1 - \frac{S(t)}{S(t) + E(t) + A(t) + C(t) + R(t) + V(t)})^{R_1 A(t) + R_2 C(t)} \tag{22}$$

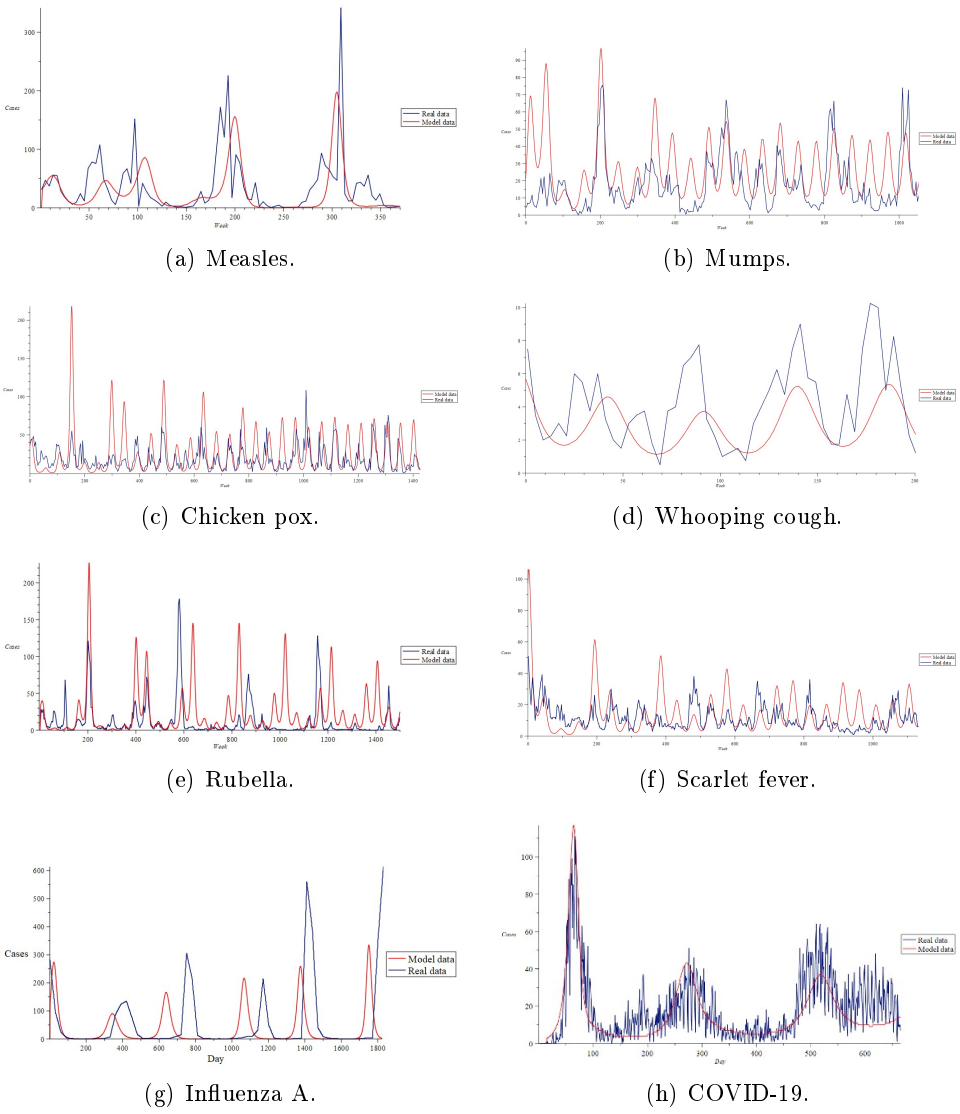
where

$1 - \frac{S(t)}{S(t)+E(t)+A(t)+C(t)+R(t)+V(t)}$

- probability of interruption per 1 contact, $R_1 A(t) + R_2 C(t)$ - the total number of independent potential contacts from existing sources of the causative agent of infection. On average, zero infection corresponded to a level of 0.5 people per population.

Intervention campaigns were carried out on the basis of countermeasures parameters established in computational experiments. Efficacy was assessed by achieving "zero infection"as no incidence during the maximum duration of infection.

4.2. Mathematical modeling of the epidemic process without control. The greatest contagiousness was observed in COVID-19 ($R = 5.7$) and measles ($R = 5.1$), the smallest - in scarlet fever ($R = 1.6$) and gonorrhea ($R = 1.2$). All the other diseases had $R \in [2.4; 4.4]$. The contact rate range



(a) Measles. (b) Mumps.

(c) Chicken pox. (d) Whooping cough.

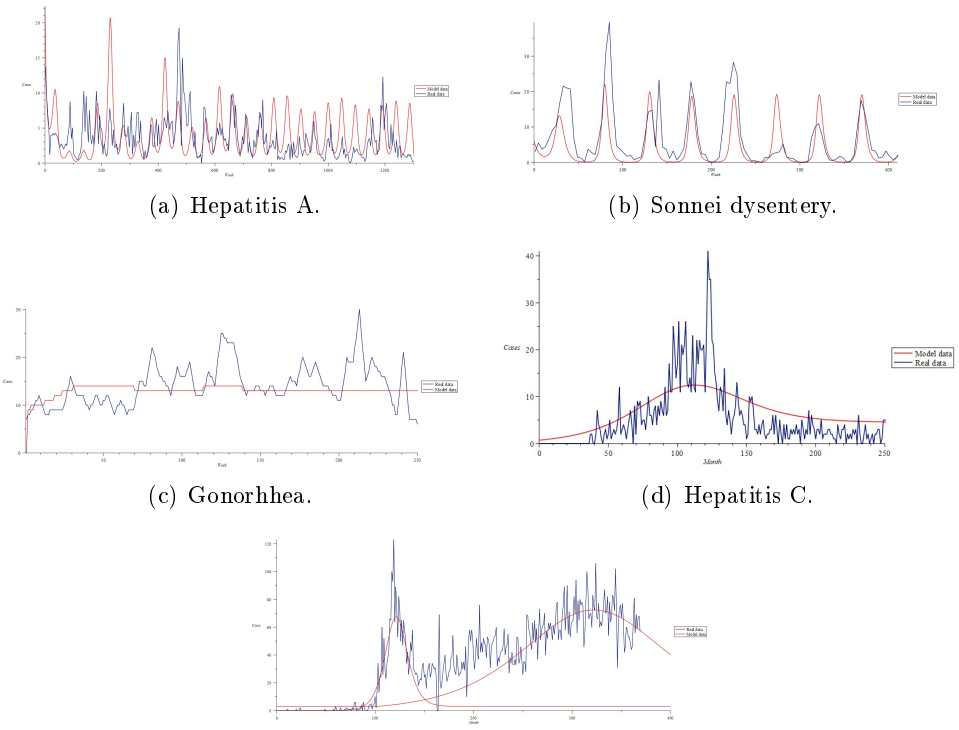
(e) Rubella. (f) Scarlet fever.

(g) Influenza A. (h) COVID-19.

FIG. 5. Real and model data of new infectious disease cases, beginning

shows that the causative agents of these diseases (with the exception of COVID-19) are in a state of compromise with the human population [86]. We did not receive the contact rates in the range of 6-11, as it is given in [14, 85] reviews, possibly due to more robust conditions of our study, concerning materials (long period of survey) and methods (optimization algorithms).

The value of the contact rate R appeared to depend on the route of transmission, as an excellent example provided HIV infection. We estimated at narcotic route of transmission the contact rate $R = 4.5$ and at sexual route $R = 1.5$, that is 3 times higher. In viral hepatitis C, only the narcotic



(a) Hepatitis A.

(b) Sonnei dysentery.

(c) Gonorhhea.

(d) Hepatitis C.

(e) HIV-infection.

FIG. 6. Real and model data of new cases of infectious diseases, continuation

transmission route was considered due to the low intensity of the sexual transmission [87].

Most acute infections are characterized by seasonality. Seasonal intensity ι ranged from 0.10 for scarlet fever and 0.13 for measles to 0.40 for viral hepatitis A and 0.45 for chicken pox.

The maximum activity of the seasonal factor for measles, mumps, chicken pox, rubella occurred in January, whooping cough, influenza A, COVID-19 - in September, scarlet fever - in October (aerosol infections). Maximum activity of seasonal factor of Sonnei dysentery, viral hepatitis A - September-October (fecal-oral infections). This suggests the possibility of using a model for infections with different transmission mechanisms.

Cyclic fluctuations in incidence are due to the superimposition of sinusoidal perturbations on the system's natural frequency of oscillation. In measles, there are rises every 2 years (biennial peaks), which was described in the classic works on epidemiology [88]. The mumps incidence model reproduced a 3-4 year periodicity, the varicella model - a 4-year periodicity. Over 31 years of observation, 7 rises in the incidence of rubella were recorded, the cycle duration was 4 years. The model reproduced the 4-year periodicity of

viral hepatitis A. The periodicity in Sonnei dysentery and gonorrhea was not detected, since in these infections the rate of loss of immunity is high, which dampens the fluctuations.

Our study showed that for all infections except COVID-19, the starting point was close to equilibrium. With COVID-19, fluctuations were carried out away from equilibrium, the epidemic began against the background of the susceptibility of the population.

Considering the reproducibility of the model (relatively small fluctuations of D_{norm} from infection to infection), we can talk about the possibility of measuring the epidemic strength. With fluctuations around the stationary state, the model allows you to determine the proportion of susceptible without taking additional measurements.

Infection disease modelling is shown in Figure 5,6.

Parameters of the infectious and epidemic process and initial conditions for its development are given in Table 4.

5 Mathematical modelling of the epidemic process with control.

13 intervention campaigns, 11 on acute infections and 2 on chronic infections (HIV infection and viral hepatitis C), are calculated. 10 intervention campaigns are realized. On 3 campaigns calculations of force of influence (counter-force) are prepared. In 2 cases (whooping cough and scarlet fever) it wasn't succeeded to reach the rated level of influence, and the result of the termination of incidence ("arrest of epidemic") wasn't achieved.

The intervention campaign against measles began since 1968. Due to high efficiency of vaccine at the first step the implementation only of a vaccination campaign, without special events for identification of sources of the causative agent of an infection and reduction of the mechanism of activity of transfer, was supposed. Calculation showed the critical level of vaccination λ_1 not less than 0.0082, time of the termination of epidemic process of measles T had to be 249 weeks. Vaccination started with smaller intensity, namely $\lambda_1 = 0.0079$, time of achievement of decrease in incidence was 310 weeks, however in 360 weeks from the beginning of a vaccination campaign incidence of measles renewed. In April, 1976 about 85 cases of diseases per week, May, 1982 – up to 48 cases, March, 1984, October, 1984, April, 1985, June, 1987, April, 1988 – till 10-14 cases were registered.

In 1994 the campaign was reconsidered: the intensity of vaccination increased to critical ($\lambda_1 = 0.0082$). Special attention was paid to immunization of the persons coming to kindergartens and schools. After 1994, only singular cases were registered: 4 in July 2003, 1 in August 2003, 1 in September 2003, 1 in October 2018, 7 in March, 2019. Now the priority attention is paid to a re-vaccination of senior citizens. The general period of observation was 60 years B– from 1961 to 2021.

TABLE 4. Epidemic force parameters for the infectious disease spectrum.

Parameter	Measles	Mumps	Chicken pox	Whooping cough	Rubella	Scarlet fever	Influenza A	COVID-19	Viral hepatitis A	Sonnei dysentery	Gonorrhea	Viral hepatitis C	HIV-infection:*
R_1	5.1	3.45	3.3	3.0	2.4	1.3	4.4	5.7	2.9	2.9	1.2	1.2	1.6/0.4
R_2	0	0	0	0	0	0.3	0	0	0	0	0	1.5	2.9/1.1
ι	0.13	0.24	0.45	0.20	0.33	0.10	0.12	0.12	0.40	0.20	0	0	0
θ	-40	-37	-37	-22	-40	-26	200	200	-25	-72	0	0	0
μ	0.002	0.002	0.002	0.003	0.002	0.002	0.000137	0.000137	0.002	0.002	0.000694	0.00216	0.00333/0.00167
k_1	0	0	0	0	0.000251	0.000383	0.00005	0.0055	0	0.02	0.07777	0.00833	0
γ_1	0	0.7	0.7	0.8	0.6	0.8	0.33	0.25	0.5	0	0.9	0.0954	0.166
α_1	0.636	0.318	0.33	0.368	0.368	1	0.2	0.074	0.25	0.70	0.5	0.01644	0.01644
β_1	0.636	0.318	0.33	0.368	0.368	0.99	0.199	0.072	0.25	0.70	0.5	0.006364	0
γ_2	0	0	0	0	0	0.01	0	0	0	0	0	0.0913	0.01644
α_2	0	0	0	0	0	0.125	0	0	0	0	0	0.02778	0.03/0.0138
β_2	0	0	0	0	0	0.125	0	0	0	0		0	0
ϵ_1	0	0	0	0	0	0	0.001	0.002	0	0	0	0.006	0.001
ϵ_2	0	0	0	0	0	0	0	0	0	0	0	0.02778	0.03/0.0138
N	18,000	18,000	18,000	3,000	18,000	18,000	60,000	2,500	3,000	500	1,200	1,200	2,000/14,000
S_0	3,600	6,210	4,500	990	6,300	11,880	19,800	2,225	1,020	250	996	1,080	1,960/13,720
E_0	45	20	90	8	80	90	450	8	70	20	19	40	40
Dimension	Week	Week	Week	Week	Week	Week	Day	Day	Week	Week	Week	Month	Month
D	42.04	25.69	24.91	2.64	40.38	16.22	88.20	12.46	3.27	6.34	4.32	5.16	9.21/14.32
D_{norm}	3.81	3.05	2.84	0.94	4.21	2.42	5.74	1.85	1.06	1.36	0.79	1.32	1.17/1.56

*On the left is a narcotic epidemic, on the right is a sex epidemic

The intervention campaign against mumps began since 1982. Calculations showed the following parameters of the intervention campaign: $\lambda = 0.0086; \delta =$

$0.03; r = 0.2; T = 155$ weeks (dimension – week). At these parameters the campaign was effective. The real term of achievement of result was 262 weeks. From January to April, 1999 the outbreak of mumps connected with an infection drift on the territory was noted.

The vaccine against chicken pox in the Russian Federation isn't included into the national vaccine schedule. In this regard calculation of the intervention company of chicken pox on the future is carried out. Taking into account the measured force of epidemic process of chicken pox the following intervention campaign is developed: $\lambda = 0.0036; \delta_1 = 0.02; r = 0.3; T = 165$ weeks. The realization is expected.

The intervention campaign concerning whooping cough began in 1995. By calculations the intensity of intervention $\lambda_1 = 0.0057, r = 0.2; \delta_1 = 0.03; \delta_3 = 0.33; T = 210$ weeks. However it wasn't succeeded to reach the specified intensity of parameters of management. The vaccine had not expecting full efficiency. The actual intensity of vaccination λ_1 taking into account the activity of vaccine was 0.0035, and this intensity of vaccination was lower than critical. The number of cases of diseases of whooping cough decreased by 5 times: from 6-10 cases up to 0-2 cases a week, the chains of infection proceeding. Though the incidence decreased, from arresting point of view it was the failure. The failure reason - counter-force insufficiency.

Due to gaining of availability of rubella vaccines, since 2007 (beginning of a campaign), the intervention campaign for prevention of incidence of a rubella was planned. According to the plan, the intensity of vaccination was $\lambda_1 = 0.0017$; intensity of identification, isolation of sources of infection was $\delta_1 = 0.05$. Sanitary and hygienic actions in organized collectives (increases in requirements to intragroup isolation and airing of rooms) were carried out with intensity of $r = 0.4$. Time of the termination of epidemic process had to be $T = 80$ weeks. The key planned targets when holding a campaign were reached. Time to achieve the result was 92 weeks.

Management of epidemic process of scarlet fever was carried out along with management of epidemic process of streptococcal pharyngitis. Influence force is determined: $\lambda_1 = 0.0008; \delta_1 = 0.07; \delta_2 = 0.07; r = 0.15; T = 90$. To reduce susceptibility it was supposed to use pre - and post-contact prophylaxis by antibiotics. However these actions had restrictions due to toxicities and refusals of treatment. The intervention campaign began in 1984. Parameters of the carried-out company $\lambda = 0.0006; \delta_1 = 0; r = 0$. The timeliness of identification of cases suffered as before detected patients managed to infect healthy, also significant contribution is made by chronic forms. The incidence of scarlet fever decreased by 4 times, but remains at the level of 10 cases a week during seasonal rise in October, a month later after formation of organized groups at schools and kindergartens.

To carry out an intervention campaign in relation to influenza A, the parameters for controlling the epidemic process of influenza are determined: $\lambda_1 = 0.0015; \lambda_2 = 0.0015; \delta_1 = 0.03; r = 0$ (dimension - day). The planned time to achieve the result was 400 days. Vaccination was carried out with

seasonal vaccines made on the basis of the last strain of the previous seasonal period. The campaign started in 2004. It was possible to almost completely follow the parameters laid down in the calculations. The actual time to achieve the result was 600 days. The company should be recognized as effective, vaccination and revaccination against influenza continue annually.

The intervention campaign against COVID-19 is based on the example of the city of Moscow. The COVID-19 epidemic began with the following initial conditions: $X_0 = 0.89; A_0 = 200$ (absolute number of patients). The contact rate R of the Wuhan variant in Moscow at the start appeared to be 2.7. Lockdown was announced on day 68 of the epidemic, the intensity of the lockdown was $r = 0.4$. On the 195 day of the epidemic, there was a partial lockout, which lasted up to 380 days ($r = 0.65$). From day 380, the lockout became full ($r = 1$). The intensity of detection, isolation and treatment of sources of infection was $\delta = 0.09$.

Lockdown saved time for the deployment of beds, including intensive care beds, which ensured a reduction in mortality associated with COVID-19.

Viral hepatitis A was a serious problem for the territory – the city of Novomoskovsk, Tula region in 1970 - ties – that was due to the unsatisfactory sanitary and hygienic state of the water supply in certain areas of the city, which launched a seasonal epidemic. Further, the epidemic was actively supported by contact and household transmission of the virus (person to person transmission) among younger schoolchildren and preschoolers (schools and pre-schools). An intervention campaign was planned with a focus on the mechanism of transmission, $r = 0.65$. Other parameters of the intervention campaign $\lambda_1 = 0.0011; \delta_1 = 0.05; T =$105 (dimension - week).

The campaign began in 1997. Reconstruction of the water supply system was carried out and measures were introduced for group isolation and disinfection in facilities of elementary schoolchildren and preschoolers (schools and pre-schools), as well as vaccination of children and adults. Actual parameters of the campaign: $\lambda_1 = 0.0005; \delta_1 = 0.26; r = 0.1$, that is, the emphasis was shifted to sanitary and hygienic measures and the identification and isolation of sources of the causative agent of infection. The time to achieve the result was 450 weeks. The campaign should be considered effective.

The epidemiological significance of Sonnei dysentery (causative agent - *Shigella sonnei*) was due to the intensive contact and household transmission in schools and preschool institutions in the period 1991-1999. An intervention campaign was planned with an emphasis on the reconstruction of preschool institutions with the introduction of intra-group isolation, as well as increasing the provision of kindergartens to the population. Regulations have been introduced for the work of medical personnel of schools and preschool institutions to identify symptoms and laboratory research. The campaign began in 1999. The targets were $\lambda_1 = 0$; $\delta_1 = 0.12$; $r = 0.6$; $T = 28$ (dimension - week). Identified and sick people are isolated, treated and returned to the population.

Actual campaign parameters were $\lambda_1 = 0$; $\delta_1 = 0.4$; $r = 0.6$. The result is achieved 40 weeks after the start of the intervention campaign. The campaign should be considered effective.

The intervention campaign against gonorrhea was performed in 2 stages: from 1996 to 2004, from 2004 to 2022. In 1996-2004, there was a decrease in transmission rate due to the use of condoms $r = 0.95$, detection and treatment with training in safe behavior with an intensity of $\delta = 0.1$. In 2004-2022, the intensity of these measures was $r = 0.90$; $\delta_1 = 0.118$.

To calculate the intervention campaign for viral hepatitis C, a population of injecting drug users was considered. The parameters of the intervention campaign are planned: $\lambda_1 = 0.02; \delta_1 = 0.06; \delta_2 = 0.06; r = 0.7; T = 99$ months. Indicator λ_1 - pre-exposure prophylaxis, δ - detection and treatment of acute and chronic forms, r - compliance with safe behavior measures. The campaign is planned after the availability of direct acting agents for treatment and prophylaxis [45].

A general population was considered to calculate the HIV intervention campaign. Critical levels of control in HIV infection were defined as $\lambda_1 = 0.015; \delta_1 = 0.06; \delta_2 = 0.06; r = 0.65; T = 150$ months. Parameter r - impact on the mechanism of transmission of infection (safe behavior), δ - identification of the sources of the causative agent of infection with taking for treatment. Parameter λ - pre-exposure prophylaxis with antiretroviral drugs (tenofovir and emtricitabine). COVID-19 has postponed the start of the program. To start an intervention campaign, it is necessary to accumulate the necessary resources and funds, namely non-invasive tests for HIV infection, outreach workers for testing, and low-threshold access points for the issuance of therapy and pre-exposure prophylaxis.

Infection disease modelling is shown in Figure 7,8.

Parameters of the infectious and epidemic process and initial conditions for its development are given in Table 5.

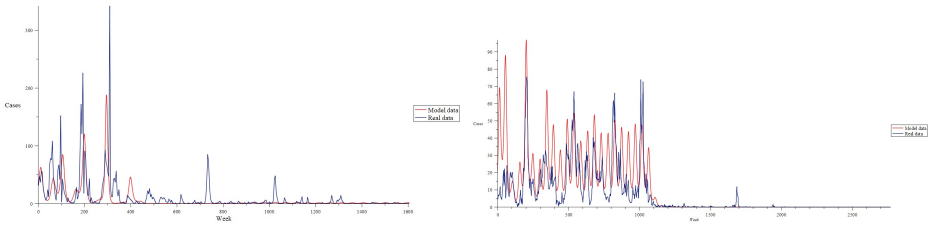
6 Conclusions and perspectives of the study.

Mathematical modeling of the epidemic process is an effective mean to diminish and eliminate the infectious disease incidence.

Determining the parameters of the epidemic process based on incidence data is an inverse problem, formulating concept controlling model is an ill-posed problem [46].

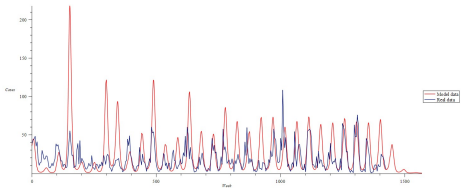
Traditional approach in quantitative epidemiology is to form the model according to unique qualities of infection disease [101]. In this paper we adhered to another paradigm of the general mechanisms of development of epidemic process, each infection serving as the special case. On the basis of this we formed the Procrustean bed of 7 differential equations, including epidemic force and counter force.

We discovered that success – **epidemic arrest** – is achievable only if counter force is equal or stronger to the applied force, and proved the threshold

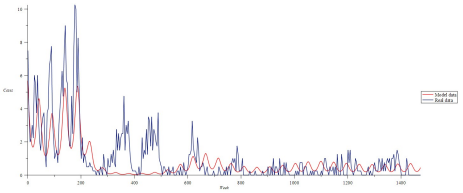


(a) Measles

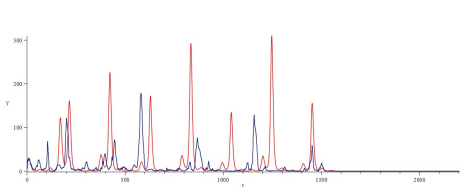
(b) Mumps



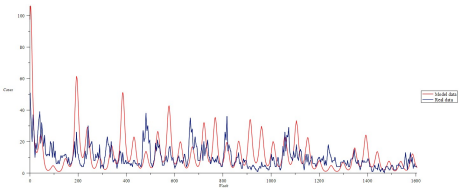
(c) Chicken pox



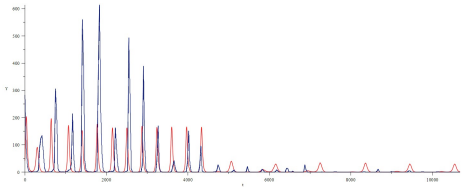
(d) Whooping cough



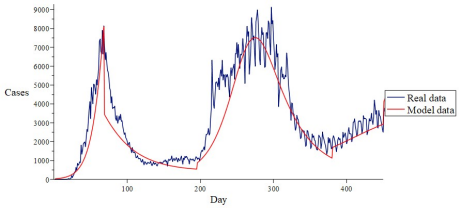
(e) Rubella



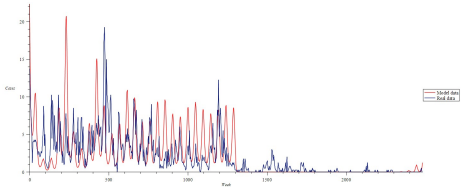
(f) Scarlet fever



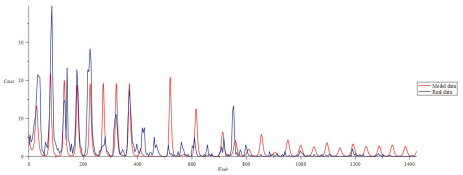
(g) Influenza A



(h) COVID-19

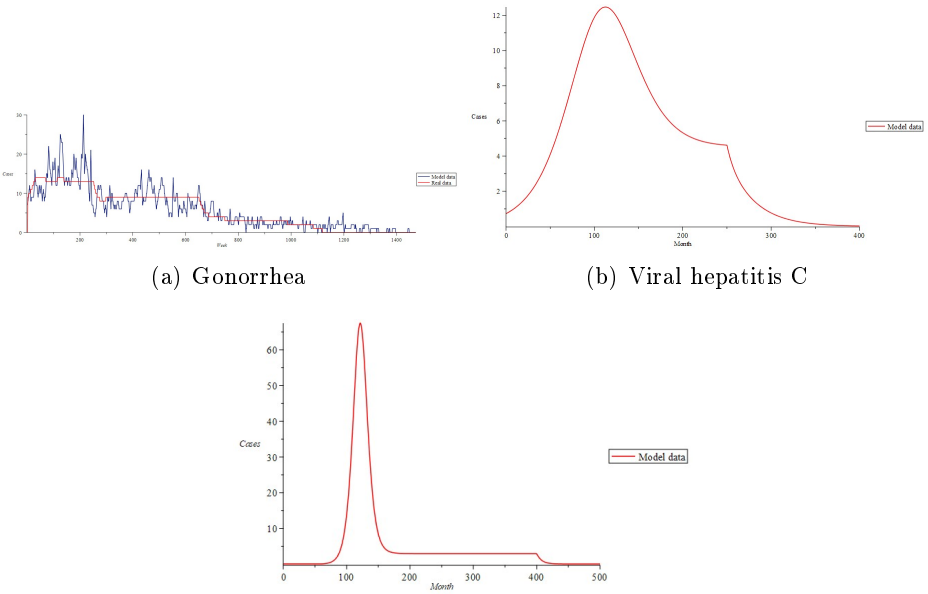


(i) Viral hepatitis A



(j) Sonnei dysentery

FIG. 7. New cases of infection diseases 1968 - 2021 during intervention campaigns: 1968 - 2021: model and real data (the beginning).



(a) Gonorrhea

(b) Viral hepatitis C

(c) HIV-infection

FIG. 8. New cases of infection diseases 1968 - 2021 during intervention campaigns: model and real data (the continuation).

control conditions for obtaining by the trivial ("zero incidence") solution asymptotic stability.

We used methodology of inverse problems to measure the main epidemic force parameters. Additional to estimations of the contact rate R we obtained the solutions for it's seasonal variation amplitude ι. Estimations of R showed evolutionary limitation on uncontrolled parameter elevation.

The main perspective is the study of the stability and uniqueness of the solution of the inverse problem to establish the parameters of epidemic process. Another perspective is the optimization of the algorithm for solving the inverse problem, id.est. finding the most optimal solutions in the event of several local minima of the Euclidean distance.

In general, the correctness of solving the inverse problem of restoring (calculation, identification) force parameters seems very responsible, because the planning of the countermeasure depends on it.

From fundamental recursion it is important to find general and interrelated stability criteria for both trivial and nontrivial stationary state solution in the first approximation.

The study made it possible to draw the following conclusions:

1. For the spectrum of infectious diseases, the concept controlling model allows to differentiate epidemic process parameters (epidemic force) and epidemic arrest parameters (the counter force).

TABLE 5. Control parameters for contagious diseases spectrum

Parameters	Measles	Mumps	Chicken pox	Whooping cough	Rubella	Scarlet fever	Influenza A	COVID-19	Viral hepatitis A	Dysentery Sonnei	Gonorrhea	Viral hepatitis C	HIV-infection
Estimated control parameters													
r	0	0.20	0.30	0.20	0.40	0.15	0	-	0.65	0.6	-	0.7	0.65
δ_1	0	0.03	0.02	0.03	0.05	0.07	0.03	-	0.05	0.12	-	0.06	0.06
δ_2	0	0	0	0	0	0.07	0	-	0	0	-	0	0
δ_3	0	0.3	0.5	0.33	0.5	0.5	0.14	-	0.33	0.5	-	0.33	0
λ_1	0.0082	0.0086	0.0036	0.0057	0.0017	0.0008	0.0015	-	0.0011	0	-	0.02	0.015
λ_2	0	0	0	0	0.0017	0	0.0015	-	0	0	-	0	0
T	310	155	165	210	80	90	400	-	105	28	-	110	150
Dimension	52.18	52.18	52.18	52.18	52.18	52.18	365.25	-	52.18	52.18	-	12	12
Real control parameters													
r	0	0.20	-	0	0.40	0	0	0.40/0.65*	0.1	0.6	0.95/0.90*	-	-
δ_1	0	0.03	-	0.03	0.05	0	0.03	0.09	0.26	0.4	0.1/0.118*	-	-
δ_2	0	0	-	0	0	0	0	-	0	0	-	-	-
δ_3	0	0.3	-	0.33	0.5	0.5	0.14	-	0.33	0.5	-	-	-
λ_1	0.0082	0.0040	-	0.0035	0.0017	0.0006	0.0015	0	0.0005	0	0	-	-
λ_2	0	0	-	0	0.0017	0	0	0	0	0	0	-	-
T	340	262	-	-	92	-	600	-	450	40	-	-	-
Dimension	52.18	52.18	-	-	52.18	52.18	365.25	365.25	52.18	52.18	52.18	-	-

*Piecewise control data

2. Epidemic force parameters make difficult the movement of the system to "zero infection". They are: high values of contact rate of infection in acute

(R_1) and chronic (R_2) forms of disease, high frequency of chronization γ_2 (with intensive pathogen excretion), high rate of loss of natural immunity k_1, high inflow of susceptible population and huge population size $\mu_1 N$.

3. In the course of solving the inverse problem the "strength"of 13 major infections, including contact rate R and its seasonal variation component ι, was determined. The value of the contact rate R appeared to depend on the route of transmission. Modelling of HIV-infection showed that at narcotic route the contact rate found to be 3 times higher then at sexual route.

4. Three control targets were identified: infected persons (detection, isolation and treatment δ), transmission mechanism (regime-restrictive measures (lockdown), sanitary and hygienic measures r), as well as a decrease in susceptibility (vaccination, pre- and post-exposure prophylaxis λ).

5. We have drawn out the condition of the system movement to "zero infection". This is phase transition of a trivial stationary solution from unstable to stable state, when the reaction force (counter force) is applied above the threshold level. Intervention measures below the threshold are ineffective.

6. Based on this condition, mutual potentiation of anti-epidemic measures of different directions is established. With successful detection, isolation and treatment of patients, as well as vaccination, the size of the lockdown (which is economically destructive) can be reduced.

7. The significance of influence on both acute and chronic forms of infection has been proved.

8. Time to "arrest of the epidemic"is determined. Freedom of choice suggests that the work may be less intense and the result will be obtained after a longer period of time, or the work may be more intense and the result will come faster. As in the case of bank loans, quick repayment is cheaper, but not always possible due to the limited annual budget. Concept controlling model for arresting epidemics serving as the powerful computational tool to achieve result and solve choice problems.

7 Funding

This work was carried out with the financial support of the Ministry of Education and Science of the Russian Federation: grant No. 075-11-2020-011 (13.1902.21.0040).

A Parameters of the infection process of acute and chronic infections

Chronic infections

N	Disease	Infection rate α	Recovery rate β (1/days)	Source	Immunity loss rate k (1/days)	Source
1	HIV infection	0.00046019	0	[77]	0	[76]
2	Viral hepatitis C	0.00055533	0.000055	[75]	0.00027767	[50]

Acute infections

N	Disease	Infection rate α and recovery rate β (1/days)	Source	Immunity loss rate k (1/days)	Source
3	Chicken pox	0.04714286	[74]	0	[51]
4	Viral hepatitis A	0.03571429	[73]	0	[72]
5	Influenza	0.2	[71]	0.00005	[70]
6	Gonorrhea	0.071429	[69]	0.01111	[68]
7	Sonne dysentery	0.1	[67]	0.00285714	[66]
11	Whooping cough	0.05262857	[65]	0	[64]
12	Measles	0.09	[63]	0	[62]
13	Rubella	0.05257	[61]	0.00003586	[60]
20	Respiratory streptococcal infection, scarlet fever	0.142857	[59]	0.00005476	[58]
24	Mumps	0.04542857	[57]	0	[56]
26	New coronavirus infection COVID-19	0.074	[55, 52]	0.0055	[54, 53]

For acute infections $\alpha = \beta$

B Time to arrest the epidemia in the degradation content

To examine analytically the timing of the arrest of epidemics, we perform two types of degradation procedures.

Type one, is summarizing of classes: assume $E(t) + A(t) = Y(t)$. So we do not form exposure class $E(t)$ - the infected patients go directly to the class of $Y(t), R(t) + Q(t) = Z(t)$. So we do not form a quarantine class $Q(t)$ - the identified patients are treated and go directly to the class $Z(t)$.

Type two we make several parameters equal to zero. We 1) neglect the mortality rate ($\epsilon_1 = \epsilon_2 = 0$), 2) we assume that inflow μ_1 is equal to outflow μ_2 and designated as μ, 3) vaccination is carried out without taking into account the history of the disease, both susceptible and recovered with equal intensity are vaccinated ($\lambda_1 = \lambda_2 = \lambda$), 4) vaccinated people are regularly re-vaccinated and maintain their vaccine immunity ($k_2 = 0$), 5) chronization intensity $\gamma_2 = 0$, which empties the chronic $C(t)$ class.

As a result the sum of all classes is 1 ($S(t) + Y(t) + Z(t) + V(t) = 1$). Each variable is maintained in proportions.

So the system contains 4 differential equations for 4 classes ($S(t), Y(t), Z(t), V(t)$), 3 equations are independent, one dependent:

$$\begin{cases} S(t)' = -Rr\alpha S(t)Y(t) + \mu - \mu S(t) + kR(t) - \lambda S(t) \\ Y(t)' = Rr\alpha S(t)Y(t) - (\beta + \mu + \delta)Y(t) \\ R(t)' = (\beta + \delta)Y(t) - (k + \mu + \lambda)R(t) \\ V(t)' = \lambda S(t) + \lambda R(t) - \mu V(t) \end{cases} \tag{23}$$

The system (23) has 3 control parameters, where λ is the intensity of vaccination, δ is the intesity of contact tracing and isolation/treatment, r - the limitation of mechanism of transmission. In most cases $Y(t) << S(t) + R(t) + V(t)$, that is why

$$S(t) + R(t) + V(t) \approx 1 \tag{24}$$

From this we draw that vaccination intensity $V(t)$ is proportionate to unvaccinated $1 - V(t)$:

$$\frac{\mathrm{d}}{\mathrm{d}t} V(t) = \lambda\,(1 - V(t)) - \mu\, V(t) \tag{25}$$

Solving this differential equation we get:

$$V(t) = -\frac{\lambda\,\left(\mathrm{e}^{-(\lambda+\mu)t} - 1\right)}{\lambda + \mu} \tag{26}$$

Taking into account expression (24) we substitute $R(t)$ by $1 - S(t) - V(t)$ and insert it into the differential equation for $S(t)$, neglecting the component of reducing $S(t)$ by the new cases:

$$\frac{\mathrm{d}}{\mathrm{d}t} S(t) = \mu - \mu\, S(t) + k\left(1 - S(t) + \frac{\lambda\,\left(\mathrm{e}^{-(\lambda+\mu)t} - 1\right)}{\lambda + \mu}\right) - \lambda\, S(t) \tag{27}$$

We solve this differential equation with initial condition for susceptible S_0:

$$S(t) = \frac{(\lambda + \mu)\,(-1 + S_0)\,\mathrm{e}^{-(\mu+k+\lambda)t} + \lambda\,\mathrm{e}^{-(\lambda+\mu)t} + \mu}{\lambda + \mu} \tag{28}$$

We insert the equation for $S(t)$ into the differential equation for $Y(t)$:

$$\frac{\mathrm{d}}{\mathrm{d}t} Y(t) = \left(\frac{rR\alpha\,\left((\lambda + \mu)\,(-1 + S_0)\,\mathrm{e}^{-(\mu+k+\lambda)t} + \lambda\,\mathrm{e}^{-(\lambda+\mu)t} + \mu\right)}{\lambda + \mu} - \beta - \delta - \mu\right) Y(t) \tag{29}$$

We solve this differential equation with initial conditions Y_0, designating expression for $F(t)$:

$$F(t) = -Rr\alpha\,(\lambda+\mu)^2\,(-1+S_0)\,\mathrm{e}^{-(\mu+k+\lambda)t} - R\lambda\,r\alpha\,(\mu+k+\lambda)\,\mathrm{e}^{-(\lambda+\mu)t} - \\ - t\,(\mu+\beta+\delta)\,\lambda^3 + (Rr\,(\mu\,t+S_0)\,\alpha - t\,(\mu+\beta+\delta)\,(3\,\mu+k))\,\lambda^2 + \\ + (R\,(\mu\,(k+2\,\mu)\,t + k + (2\,S_0-1)\,\mu)\,r\alpha - 2\,t\,(\mu+\beta+\delta)\,(3\,\mu\cdot 1/2+k)\,\mu)\,\lambda + \\ + (Rr\,((\mu+k)\,t+S_0-1)\,\alpha - t\,(\mu+\beta+\delta)\,(\mu+k))\,\mu^2 \tag{30}$$

$$Y\,(t) = Y_0\,\mathrm{e}^{\frac{F(t)}{(\lambda+\mu)^2(\mu+k+\lambda)}} \tag{31}$$

Let us necessitate that after time T the prevalence of the disease should be $Y(T) = n$. We solve the equation for velocity of tracing cases and cases isolation and treatment δ:

$$\delta = \frac{1}{T(\lambda+\mu)^2(\mu+k+\lambda)}\Big(-Rr\alpha\,(\lambda+\mu)^2(-1+S_0)\,\mathrm{e}^{-(\mu+k+\lambda)T} - \\ - (\lambda+\mu)^2(\mu+k+\lambda)\ln\left(\frac{n}{Y_0}\right) - R\lambda\,r\alpha\,(\mu+k+\lambda)\mathrm{e}^{-(\lambda+\mu)T} - \mu^4 T + \\ + T\,(R\alpha\,r-\beta-k-3\,\lambda)\,\mu^3 + (-3\,\lambda^2 T + 2\,(R\alpha\,r-k-3/2\,\beta)T\lambda + Rr(Tk + \\ + S_0 - 1)\alpha - kT\beta)\mu^2 + \big(-\lambda^2 T + T(R\alpha\,r - 3\,\beta - k)\lambda + Rr(Tk + 2\,S_0 - 1)\alpha - \\ - 2\,kT\beta)\lambda\,\mu + \big(-T\beta\,\lambda^2 + (RS_0\,\alpha\,r - kT\beta)\lambda + R\alpha\,kr\big)\lambda\big) \tag{32}$$

This formula comprises major control parameters r, δ, λ, as well as critical level of case incidence n, time to achieving critical level of case incidence (time to arrest the epidemia) T, force parameters of the epidemic process.

Assuming parameters $R = 4; \mu = 0.000157; k = 0.0055; \alpha = 0.074; \beta = 0.074; S_0 = 0.25; Y_0 = 0.05; r = 1; n = 6.01\cdot 10^{-7}; \lambda := 0.001; \delta = 0.119$, with the formula (32) we get $T = 488.7$ days.

Let us study the impact of the epidemic force parameters on elongation of time to result T (enhance 1 %): $R - 9.9\%; k - 2.8\%; \mu - 0.1\%$.

Let us study the impact of the counter-force parameters on the shortening of time to result T (enhance 1 %): $r - 11.3\%; \delta - 7.8\%; \lambda - 2.6\%$. If we look at intervention campaigns, those where prioritizing diminishing mechanism of transmission was involved – were successful.

References

[1] H. Gao, W. Li, M. Pan, Z. Han, H.V. Poor, *Modeling COVID-19 with mean field evolutionary dynamics: Social distancing and seasonality*, J. Commun. Networks, **23**:5 (2021), 314–325.

[2] WHO, *International health regulations, (second ed.)*, World Health Organization, 2005.

[3] Zatsepin, O.V. et al, *A COVID-19 agent-based model*, Zababakhin scientific readings: a collection of materials of the XV International Conference, Snezhinsk (2021), 302.

[4] K.P. Hadeler, *Parameter identification in epidemic models*, Math. Biosci., **229**:2 (2011), 185–189. Zbl 1208.92067

[5] Z. Fodor, S.D. Katz, T.G. Kovacs, *Why integral equations should be used instead of differential equations to describe the dynamics of epidemics*, arXiv:2004.07208, 2020.

[6] R.M. Anderson, *Transmission dynamics and control of infectious disease agents*, In: Anderson, R.M., May, R.M. (eds), *Population Biology of Infectious Diseases*, Dahlem Workshop Reports, **25**, Springer, Berlin, Heidelberg, 1982, 149–176.

[7] Cano, C., *The SIR models, their applications, and approximations of their rates*, Louisiana Tech University, 2020.

[8] N. Ferguson, et al, *Report 9: Impact of non-pharmaceutical interventions (NPIs) to reduce COVID19 mortality and healthcare demand*, Imperial College London, 2020.

[9] R. Feßler, *A General Integral Equation Model for Epidemics*, Fraunhofer Institute for Industrial Mathematics ITWM, 2020.

[10] R.M. Anderson, *The population dynamics of infectious diseases: theory and applications*, Springer, 2013.

[11] D.L. Heymann, *Control of communicable diseases manual*, American Public Health Association, 2008.

[12] S. Alizon, M. van Baalen, *Emergence of a convex trade-off between transmission and virulence*, Am. Nat., **165**:6 (2005), E155–E167.

[13] R.M. Anderson, C. Fraser, A.C. Ghani, C.A. Donnelly, S. Riley, N.M. Ferguson, G.M. Leung, T.H. Lam, A.J. Hedley, *Epidemiology, transmission dynamics and control of SARS: the 2002–2003 epidemic*, Philos. Trans. R. Soc. Lond. B Biol. Sci., **359**:1447 (2004), 1091–1105.

[14] R.M. Anderson, R.M. May, *Infectious diseases of humans: dynamics and control*, Oxford University Press, Oxford, 1992.

[15] S.M.N. Arifin, C. Zimmer, C. Trotter, A. Colombini, E. Sidikou, F.M. LaForce, T. Cohen, R. Yaesoubi, *Cost-effectiveness of alternative uses of polyvalent meningococcal vaccines in Niger: An agent-based transmission modeling study*, Med. Decis. Making., **39**:5 (2019), 553–567.

[16] M.S. Aronna, R. Guglielmi, L.M. Moschen, *A model for COVID-19 with isolation, quarantine and testing as control measures*, Epidemics, **34** (2021), 100437.

[17] K.E. Atkins, A.F. Read, S.W. Walkden-Brown, N.J. Savill, M.E. Woolhouse, *The effectiveness of mass vaccination on Marek's disease virus (MDV) outbreaks and detection within a broiler barn: A modeling study*, Epidemics, **5**:4 (2013), 208–217.

[18] V.D. Beliakov, *Revoliutsiia v epidemiologii*, Zhurnal Mikrobiologii Epidemiologii i Immunobiologii, **12** (1974), 20–24.

[19] A.S. Benenson, *Control of communicable diseases in man thirteenth edition*, American Public Health Association, 1981.

[20] A. Bensoussan, J. Frehse, P. Yam, *Mean field games and mean field type control theory*, Springer, New York, 2013. Zbl 1287.93002

[21] M. Biggerstaff, et al, *Early insights from statistical and mathematical modeling of key epidemiologic parameters of COVID-19*, Emerg. Infect. Dis., **26**:11 (2020), e201074.

[22] S. Cauchemez, N.M. Ferguson, *Likelihood-based estimation of continuous-time epidemic models from time-series data: application to measles transmission in London*, J. R. Soc. Interface, **5**:25 (2008), 885–897.

[23] M. Cevik, M. Tate, O. Lloyd, A.E. Maraolo, J. Schafers, *SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis*, Lancet Microbe, **2**:1 (2021), e13–e22.

[24] B.M. Chen-Charpentier, D. Stanescu, *Epidemic models with random coefficients*, Math. Comput. Modelling, **52**:7-8 (2010), 1004–1010. Zbl 1205.60127

[25] F.T. Cutts el al, *Using models to shape measles control and elimination strategies in low- and middle-income countries: A review of recent applications*, Vaccine, **38**:5 (2020), 979–992.

[26] A. Datta, P. Winkelstein, S. Sen, *An agent-based model of spread of a pandemic with validation using COVID-19 data from New York State*, Physica A: Statistical Mechanics and its Applications, **585** (2022), 126401.

[27] J. Demongeot, Q. Griette, P. Magal, *SI epidemic model applied to COVID-19 data in mainland China*, Royal Society Open Science, **7**:12 (2020), 201878.

[28] L. Ferretti et al, *Quantifying SARS-CoV-2 transmission suggests epidemic control with digital contact tracing*, Science, **368**:6491 (2020), eabb6936.

[29] C. Fraser, S. Riley, R.M. Anderson, N.M. Ferguson, *Factors that make an infectious disease outbreak controllable*, Proc. Nat. Acad. Sci., **101**:16 (2004), 6146–6151.

[30] F.M. Guerra, S. Bolotin, G. Lim, et al., *The basic reproduction number (R_0) of measles: a systematic review*, Lancet Infectious Diseases, **17**:12 (2017), e420–e428.

[31] E.S. Knock et al, *Key epidemiological drivers and impact of interventions in the 2020 SARS-CoV-2 epidemic in England*, Sci. Transl. Med., **13**:602 (2021), eabg4262.

[32] M. Koivu-Jolma, A. Annila, *Epidemic as a natural process*, Math. Biosci., **299** (2018), 97–102. Zbl 1393.92048

[33] A. Matsuki, G. Tanaka, *Intervention threshold for epidemic control in susceptible-infected-recovered metapopulation models*, Phys. Rev. E, **100** (2019), Article ID 022302.

[34] D.M. Morens, G.K. Folkers, A.S. Fauci, *The challenge of emerging and re-emerging infectious diseases*, Nature, **430** (2004), 242–249.

[35] R. Padmanabhan, H.S. Abed, N. Meskin, T. Khattab, M. Shraim, M.A. Al-Hitmi, *A review of mathematical model-based scenario analysis and interventions for COVID-19*, Comput. Methods Programs Biomed., **209** (2021), Article ID 106301.

[36] Y.S. Popkov, Y.A. Dubnov, A.Y. Popkov, *Forecasting development of COVID-19 epidemic in European Union using entropy-randomized approach*, IA, **20**:5 (2021), 1010–1033.

[37] K. Shah, D. Saxena, D. Mavalankar , *Secondary attack rate of COVID-19 in household contacts: a systematic review*, QJM, **113**:12 (2020), 841–850.

[38] Y. Shao, J. Wo, *IDM editorial statement on the 2019-nCoV*, Infect. Dis. Model., **5** (2020), 233–234.

[39] P.C.L. Silva, P.V.C. Batista, H.S. Lima, M.A. Alves, F.G. Guimarães, R.C.P. Silva, *COVID-ABS: An agent-based model of COVID-19 epidemic to simulate health and economic effects of social distancing interventions*, Chaos Solitons Fractals, **139** (2020), Article ID 110088.

[40] S. Sturniolo, W. Waites, T. Colbourn, D. Manheim, J. Panovska-Griffiths, *Testing, tracing and isolation in compartmental models*, PLOS Comput. Biol., **17**:3 (2021), Article ID e1008633.

[41] K.M. Thompson, D.A. Kalkowska, *Review of poliovirus modeling performed from 2000 to 2019 to support global polio eradication*, Expert Rev. Vaccines, **19**:7 (2020), 661–686.

[42] L. Zhou, Y. Wang, Y. Xiao, M.Y. Li, *Global dynamics of a discrete age-structured SIR epidemic model with applications to measles vaccination strategies*, Math. Biosci., **308** (2019), 27–37. Zbl 1411.34072

[43] A. Zumla, G. Ippolito, B. McCloskey, M. Bates, R. Ansumana, D. Heymann, R. Kock, F. Ntoumi, *Enhancing preparedness for tackling new epidemic threats*, Lancet Respir. Med., **5**:8 (2017), 606–608.

[44] D. Wilson, J. Taaffe, *Tailoring the local HIV/AIDS response to local HIV/AIDS epidemics*, In K.K. Holmes (eds.) et. al., *Major infectious diseases. (3rd ed.)*, The International Bank for Reconstruction and Development / The World Bank., 2017, 157–178.

[45] M. Kretzschmar, L. Wiessing, *New challenges for mathematical and statistical modeling of HIV and hepatitis C virus in injecting drug users*, AIDS, **22**:13 (2008), 1527–1537.

[46] S.I. Kabanikhin, O.I. Krivorot'ko, *Mathematical modeling of the Wuhan COVID-2019 epidemic and inverse problems*, Comput. Math. Math. Phys., **60**:11 (2020), 1889–1899. Zbl 1455.92134

[47] O.I. Krivorot'ko, S.I. Kabanikhin, N.Yu. Zyat'kov, A.Yu. Prikhod'ko, N.M. Prokhoshin, M.A. Shishlenin, *Mathematical modeling and forecasting of COVID-19 in Moscow and Novosibirsk region*, Sib. Zh. Vychisl. Mat., **23**:4 (2020), 395–414. Zbl 1505.92202

[48] W.O. Kermack, A.G. McKendrick, *A contribution to the mathematical theory of epidemics*, Proc. R. Soc. Lond., Ser. A, **115** (1927), 700–721. JFM 53.0517.01

[49] A.L. Lloyd, *Estimating variability in models for recurrent epidemics: assessing the use of moment closure techniques*, Theor. Popul. Biol., **65**:1 (2004), 49–65. Zbl 1105.92031

[50] S.L. Currie, et al, *A prospective study to examine persistent HCV reinfection in injection drug users who have previously cleared the virus*, Drug Alcohol Depend., **93**:1–2 (2008), 148–154.

[51] A.A. Gershon, M.D. Gershon, *Pathogenesis and current approaches to control of varicella-zoster virus infections*, Clin. Microbiol. Rev., **26**:4 (2013), 728–743.

[52] O. Puhach, et al, *Infectious viral load in unvaccinated and vaccinated individuals infected with ancestral, Delta or Omicron SARS-CoV-2*, Nat. Med., **28**:7 (2022), 1491–1500.

[53] F.A. Inthamoussou, F. Valenciaga, G. Núñez, *Extended SEIR model for health policies assessment against the COVID-19 pandemic: the case of argentina*, J. Healthc. Informa. Res., **6**:1 (2022), 91–111.

[54] I. Cherednik,, *Modeling the waves of covid-19*, Acta Biotheoretica, **70**:8 (2021).

[55] A. Singanayagam, et al, *Duration of infectiousness and correlation with RT-PCR cycle threshold values in cases of COVID-19, England, January to May 2020*, Eurosurveillance , **25**:32 (2020), 2001483.

[56] D. Greenhalgh, *Threshold and stability results for an epidemic model with an age-structured meeting rate*, IMA J. Math. Appl. Med. Biol., **5**:2 (1988), 81–100.

[57] R.M. Anderson, J.A. Crombie, B.T. Grenfell, *The epidemiology of mumps in the UK: A preliminary study of virus transmission, herd immunity and the potential impact of immunization*, Epidemiol. Infect., **99**:1 (1987), 65–84.

[58] H. Zhong, W. Wang, *Mathematical modelling for scarlet fever with direct and indirect infections*, J. Biol. Dyn., **14**:1 (2020), 767–787.

[59] S. Basetti, J. Hodgson, T.M. Rawson, A. Majeed, *Scarlet fever: a guide for general practitioners*, London J. Prim. Care, **9**:5 (2017), 77–79.

[60] H.M. Yang, A.S. Silveira, *The loss of immunity in directly transmitted infections modeling: Effects on the epidemiological parameters*, Bull. Math. Biol., **60**:2 (1998), 355–372. Zbl 1053.92512

[61] W.J. Edmunds, O.G. van de Heijden, M. Eerola, N.J. Gay, *Modelling rubella in Europe*, Epidemiol. Infect., **125**:3 (2000), 617–634.

[62] K.C. Corey, A. Noymer, *A "post-honeymoon" measles epidemic in Burundi: mathematical model-based analysis and implications for vaccination timing*, PeerJ, **4** (2016), e2476.

[63] B.F. Finkenstädt, O.N. Bjørnstad, B.T. Grenfell, *A stochastic model for extinction and recurrence of epidemics: estimation and inference for measles outbreaks*, Biostatistics, **3**:4 (2002), 493–510. Zbl 1138.62350

[64] G. Rozhnova, A. Nunes, *Modelling the long-term dynamics of pre-vaccination pertussis*, J. R. Soc. Interface, **9**:76 (2012), 2959–2970.

[65] P. Pesco, P. Bergero, G. Fabricius, D. Hozbor, *Modelling the effect of changes in vaccine effectiveness and transmission contact rates on pertussis epidemiology*, Epidemics, **7** (2014), 13–21.

[66] H. Allen, et al, *Evidence for re-infection and persistent carriage of Shigella species in adult males reporting domestically acquired infection in England*, Clin. Microbiol. Infecti., **27**:1 (2021), 126.e7–126.e13.

[67] A.A. Shad, W.A. Shad, *Shigella sonnei: virulence and antibiotic resistance*, Arch. Microbiol., **203**:1 (2021), 45–58.

[68] M.W. Russell, S.D. Gray-Owen, A.E. Jerse, *Editorial: Immunity to Neisseria gonorrhoeae*, Front. Immunol., **11** (2020), 1375.

[69] H.W. Hethcote, J.A. Yorke, A. Nold, *Gonorrhea modeling: a comparison of control methods*, Math. Biosci., **58**:1 (1982), 93–109. Zbl 0486.92024

[70] R.G. Woolthuis, J. Wallinga, M. van Boven, *Variation in loss of immunity shapes influenza epidemics and the impact of vaccination*, BMC Infect. Dis., **17** (2017), 632.

[71] A Cori, A.J. Valleron, F. Carrat, G.S. Tomba, G. Thomas, P.Y. Boëlle, *Estimating influenza latency and infectious period durations using viral excretion data*, Epidemics, **4**:3 (2012), 132–138.

[72] Z. Hussain, B.C. Das, S.A. Husain, N.S. Murthy, P. Kar, *Increasing trend of acute hepatitis A in north India: need for identification of high-risk population for vaccination*, J. Gastroenterol. Hepatol., **21**:4 (2006), 689–693.

[73] I. Czumbel, C. Quinten, P. Lopalco, J.C. Semenza, and ECDC expert panel working group, *Management and control of communicable diseases in schools and other child care settings: systematic review on the incubation period and period of infectiousness*, BMC Infect. Dis., **18**:1 (2018), 199.

[74] G. Freer, M. Pistello, *Varicella-zoster virus infection: natural history, clinical manifestations, immunity and current and future vaccination strategies*, New Microbiol., **41**:2 (2018), 95–105.

[75] C.K. Aitken, J. Lewis, S.L. Tracy, T. Spelman, D.S. Bowden, M. Bharadwaj, H. Drummer, M. Hellard, *High incidence of hepatitis C virus reinfection in a cohort of injecting drug users*, Hepatology, **48**:6 (2008), 1746–1752.

[76] P.K. Drain, et al, *Point-of-care HIV viral load testing: an essential tool for a sustainable global HIV/AIDS response*, Clin. Microbiol. Rev., **32**:3 (2008), e00097-18.

[77] B.G. Williams, V. Lima, E. Gouws, *Modelling the impact of antiretroviral therapy on the epidemic of HIV*, Curr. HIV Res., **9**:6 (2011), 367–382.

[78] N.K. Martin, P. Vickerman, M. Hickman, *Mathematical modelling of hepatitis C treatment for injecting drug users*, J. Theor. Biol., **274**:1 (2011), 58–66. Zbl 1331.92082

[79] M.M Cassell, R. Wilcher, R.A. Ramautarsing, N. Phanuphak, T.D. Mastro,, *Go where the virus is: An HIV micro-epidemic control approach to stop HIV transmission*, Glob. Health Sci. Pract., **8**:4 (2020), 614–625.

[80] N. Scott, et al, *Hepatitis C elimination in Myanmar: Modelling the impact, cost, cost-effectiveness and economic benefits*, Lancet Reg. Health West. Pac., **10**:100129 (2021), 100129.

[81] Revell, A. et al, *Computational models as predictors of HIV treatment outcomes for the Phidisa cohort in South Africa*, South. Afr. J. HIV Med., **17**:1 (2016), 450.

[82] Y. Zhou, Y. Shao, Y. Ruan, J. Xu, Z. Ma, C. Mei, J. Wu,, *Modeling and prediction of HIV in China: transmission rates structured by infection ages*, Math. Biosci. Eng., **5**:2 (2008), 403–418. Zbl 1158.92327

[83] T. Brown, W. Peerapatanapokin, *The Asian Epidemic Model: a process model for exploring HIV policy and programme alternatives in Asia*, Sexually Transmitted Infections, **80**:suppl 1 (2004), i19–i24.

[84] A. Blake, J.E. Smith, *Modeling hepatitis C elimination among people who inject drugs in new hampshire*, JAMA Network Open, **4**:8 (2021), Article ID e2119092.

[85] P. van den Driessche, *Reproduction numbers of infectious disease models*, Infect. Dis. Model., **2**:3 (2017), 288–303.

[86] S. Alizon, A. Hurford, N. Mideo, M. Van Baalen, *Virulence evolution and the trade-off hypothesis: history, current state of affairs and the future*, J. Evol. Biol., **22**:2 (2009), 245–259.

[87] V. Tahan, C. Karaca, B. Yildirim etc., *Sexual transmission of HCV between spouses*, Am. J. Gastroenterol., **100**:4 (2005), 821–824.

[88] R. Marguta, A. Parisi, *Periodicity, synchronization and persistence in pre-vaccination measles*, J. R. Soc. Interface, **13**:119 (2016), Article ID 20160258.

[89] D.P. Greenberg, C.H. von König, U. Heininger, *Health burden of pertussis in infants and children*, Pediatr. Infect. Dis. J., **24**:(5 Suppl.) (2005), S39–43.

[90] J.D. Cherry, *Pertussis: challenges today and for the future*, PLoS Pathog., **9**:7 (2013), Article ID e1003418.

[91] I.S. Fazakas-Anca, A. Modrea, S. Vlase, *Using the stochastic gradient descent optimization algorithm on estimating of reactivity ratios*, Materials (Basel), **14**:16 (2021), Article ID 4764.

[92] S. Bilal, B.K. Singh, A. Prasad, E. Michael, *Effects of quasiperiodic forcing in epidemic models*, Chaos, **26**:9 (2016), Article ID 093115. MR3549637

[93] D. Gromov, I. Bulla, O. Silvia Serea, E.O. Romero-Severson, *Numerical optimal control for HIV prevention with dynamic budget allocation*, Math. Med. Biol., **35**:4 (2018), 469–491. Zbl 1410.92121

[94] A.A. Aliyu, *Public health ethics and the COVID-19 pandemic*, Ann. Afr. Med., **20**:3 (2021), 157–163.

[95] G.V. Demidenko, *Systems of differential equations of higher dimension and delay equations*, Sib. Math.J., **53**:6 (2012), 1021–1028. Zbl 1264.34131

[96] W.C. Miller, *Infectious disease (in) epidemiology*, Epidemiology, **21**:5 (2010), 593–594.

[97] G.V. Demidenko, *Systems of differential equations of higher dimension and delay equations*, Sib. Math.J., **53**:6 (2012), 1021–1028. Zbl 1264.34131

[98] V. Petrakova, O. Krivorotko, *Mean field game for modeling of COVID-19 spread*, J. Math. Anal. Appl., **514**:1 (2022), Article ID 126271. Zbl 1492.91044

[99] F. Brauer, C. Castillo-Chavez, Z. Feng, *Control of communicable diseases in man*, Springer, 2019.

[100] A.S. Benenson, *"Red Book 2021 Report of the Committee of Infectious Diseases*, American Public Health Association, 1981.

[101] F. Brauer, C. Castillo-Chavez, Z. Feng, *Mathematical models in epidemiology*, Springer, New York, 2019. Zbl 1433.92001

Grigoriy Dmitrievich Kaminskiy
National Medical Research Center of Phthisiopulmonology and Infectious Diseases of the Ministry of Health of the Russian Federation,
Dostoevsky St., house 4, building 2
127473, Moscow, Russia
State Health Organization Tula Regional Center for Control and Prevention of AIDS and Infectious Diseases,
Drejera embankment, house 14,
300002, Tula, Russia
Email address: gregkaminski.gk@gmail.com

Prostov Yuri Ivanovich
National Medical Research Center of Phthisiopulmonology and Infectious Diseases of the Ministry of Health of the Russian Federation,
Dostoevsky St., house 4, building 2
127473, Moscow, Russia
Email address: ProstovPro@gmail.com

Semenova Diana Anzorovna
National Medical Research Center of Phthisiopulmonology and Infectious Diseases of the Ministry of Health of the Russian Federation,
Dostoevsky St., house 4, building 2
127473, Moscow, Russia
Email address: dianasoulmate@yandex.ru

Prostov Mikhail Yurievich
National Medical Research Center of Phthisiopulmonology and Infectious Diseases of the Ministry of Health of the Russian Federation,
Dostoevsky St., house 4, building 2
127473, Moscow, Russia
Email address: ProstoMi@gmail.com

Pimenov Nikolai Nikolaievich
National Medical Research Center of Phthisiopulmonology and Infectious Diseases of the Ministry of Health of the Russian Federation,
Dostoevsky St., house 4, building 2
127473, Moscow, Russia
Email address: n.pimenov@mail.ru

Veselova Elena Igorevna
National Medical Research Center of Phthisiopulmonology and Infectious Diseases of the Ministry of Health of the Russian Federation,
Dostoevsky St., house 4, building 2
127473, Moscow, Russia
Email address: drveselovae@mail.ru

Vinokurov Anatoliy Sergeyevich
National Medical Research Center of Phthisiopulmonology and Infectious Diseases of the Ministry of Health of the Russian Federation,
Dostoevsky St., house 4, building 2
127473, Moscow, Russia
Email address: vinok@mail.ru

Karamov Eduard Vladimirovich
National Medical Research Center of Phthisiopulmonology and Infectious Diseases of the Ministry of Health of the Russian Federation,
Dostoevsky St., house 4, building 2
127473, Moscow, Russia,
Federal State Budgetary Institution National Research Centre for Epidemiology and Microbiology named after the Honorary Academician N. F. Gamaleya of the Ministry of Health of the Russian Federation,
Gamalei str., house 18,
123098, Moscow, Russia
Email address: karamov2004@yandex.ru

Panova Anna Evgenyevna,
National Medical Research Center of Phthisiopulmonology and Infectious Diseases of the Ministry of Health of the Russian Federation,
Dostoevsky St., house 4, building 2
127473, Moscow, Russia
Email address: anna_panova@bk.ru

Turgiev Ali Saladinovich,
National Medical Research Center of Phthisiopulmonology and Infectious Diseases of the Ministry of Health of the Russian Federation,
Dostoevsky St., house 4, building 2
127473, Moscow, Russia,
Federal State Budgetary Institution National Research Centre for Epidemiology and Microbiology named after the Honorary Academician N. F. Gamaleya of the Ministry of Health of the Russian Federation,
Gamalei str., house 18,
123098, Moscow, Russia
Email address: turgiev@ld.ru

Chernetsova Valeriya Vladimirovna,
National Research University Moscow Power Engineering Institute,
Krasnokazarmennaya str., house 17, building 3
111250, Moscow, Russia
Email address: chernet@mail.ru

Lomovtsev Alexandr Eduardovich,
The Department of Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing for Tula Region,
Oboronnaya str., house 114,
300045, Tula, Russia
Email address: lom44@rambler.ru