*КРАТКИЕ СООБЩЕНИЯ*

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# MATHEMATICAL MODELLING OF SPREAD COVID-19 EPIDEMIC FOR PREVENTIVE MEASURES TO PROTECT LIFE AND HEALTH OF ELDERLY

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Quantitative approaches based on mathematical modelling are used to justify a set of measures aimed at justifying a set of preventive measures to protect the life and health of older people in the context of COVID-19 pandemic. Analysis of the state of development of actuarial mathematical models of mortality in the COVID-19 epidemic shows the need to construct models that reflect the dynamics of the studied ratios of infection rates, morbidity, recovery and mortality in the dynamics of the pandemic, taking into account the influence of external factors on this process. Most of the known mathematical models for predicting the spread and consequences of COVID-19 are compartmental models that implement sequential transitions between states with the allocation of groups of individuals with different affiliation to the progression/decline of the spread of infection. To compensate for the shortcomings of the compartmental models due to the assumption of population homogeneity and the lack of adequate approaches to the scalability of the simulation results, models based on the Monte Carlo method and the concept of multi-agent systems are used. The development of modelling methods is associated with the need to expand information support for healthcare professionals and health care organizers with the possibility of online configuration of parameters of mathematical models and the use of data from «cloud services» with visualization of the results of modelling.

*Keywords: mathematical models of COVID-19 spread; compartment model; actuarial model; SIR-model; mathematical modelling of epidemics; multi-agent systems.*

## Introduction

In the context of the implementation of a set of measures to counteract the COVID-19 pandemic, it is noted that the greatest risk of infection is characteristic of the population whose age exceeds 65 years. This leads to an interest in the objective quantitative characterization of the negative consequences of COVID-19 for the elderly, both in terms of mortality and quality of life indicators, using mathematical modelling [1].

The priorities of protecting human interests in the light of the threats to life and health under study require operating with reliable data sources and well-developed methods of statistical analysis, which allow a doctor to choose one of the alternative options for action.

A convincing example of popular work in this direction is provided by a statistical model of the dependence of mortality on age (on a semi-logarithmic scale) based on comparative data for three European countries with different scenarios of population isolation [2]. It is shown that:

– in the range of 30–90 years, the dependencies of the logarithms of mortality on age fall on straight lines, strictly parallel to the lines of the dependence of total mortality on age in accordance with the Gompertz law;

– regardless of the stage of the epidemic and the country of observation, the periods of doubling of mortality in this age range are close to 7,5 years;

– the probability of infection with a new coronavirus infection and its symptomatic manifestation do not depend much on age.

The dependencies presented in [2] confirm the validity of applying actuarial models in the context of loss analysis under conditions of the COVID-19 pandemic. The third position is also expected, since it is the most difficult to obtain reliable statistical data in the studied time periods. In fact, this is another evidence that it is important to have adequate tools for mathematical modelling when analyzing life and health risks.

Currently, thanks to the wide access to the Internet, interested users have the opportunity to work with stochastic models of this kind that are customized for research purposes, using both their own and freely distributed data. Further, in this context, a brief overview of the work in the field of constructing models of morbidity, mortality and spread of COVID-19 is given.

## 1. State of Development of Actuarial Mathematical Models of Mortality in COVID-19 Epidemic

The problem of identifying differences in mortality due to COVID-19 in different age groups remains relevant, which is confirmed by the presence of a large number of publications. In the literature, there are results of a study of age differences in COVID-19 cases based on sample observations of losses for different countries. For example, [3] provides such estimates for cities in Northern Italy, which, according to the authors, indicate that age and sex indicators differ significantly: for men aged 65–74 years, this estimate is 2,10%, which is 3,5 times higher than for men 55–64 years, and 2,7 times higher than for women 65–74 years. Note that when using the results of the performed meta-analysis procedures, it is necessary to pay attention to the original terminology base (which may differ in different sources) and the factor of variability in the number of cases from time to time. Thus, based on the provisions presented in [2], it can be stated that the use of analytical methods to describe mortality in subpopulations is quite legitimate.

Regarding the impact of preventive measures on the spread of COVID-19, there are studies in which, based on observational data, attempts are made to find combinations of different indices to quantify the impact of social distancing on reducing the number of confirmed cases of infection.

The research results show the need to construct models that reflect the dynamics of the studied ratios of infection rates, morbidity, recovery and mortality in the dynamics of the pandemic, taking into account the influence of external factors on this process (distancing, isolation, population density, migration, etc.), as well as mathematical models to support decision-making during sanitary and epidemiological investigations [4–6]. It is obvious that there is a need to search for new and improve existing mathematical models, as well as methods for setting their parameters in the context of practical problems.

## 2. State of Mathematical Models for Predicting Spread and Consequences of COVID-19

Active attempts to construct substantial and adequate models for the spread of COVID-19 in our country began immediately when the World Health Organization announced the beginning of COVID-19 pandemic. St. Petersburg (head of the working group – A.I. Borovkov) was one of the first to create a mathematical model of the spread of coronavirus. To do this, the developers used the Kermak–McKendrick compartmental model, which was previously effectively used to predict the spread of epidemics.

In the simplest variants of constructing such a model, rigid sequential transitions between cells (or states, classes, etc.) are set, and in the studied population, groups of individuals with different belonging to the "progression/decline" of the infection spread process are distinguished ($S$ denotes vulnerable, $I$ stands for infected and spreading the virus, $R$ means recovered and immune). The transition sequence looks like $S > I > R$, so the base model is called the *SIR*-model [7].

A large number of publications provide mathematical calculations that show how predictive indices showing the growth or decline of the epidemic are obtained from the initial ratios; calculation formulas are derived and classification of compartment models is given according to their level of complexity (the number of distinguished cells and the types of transitions between them). If the number of people in each cell is known at some point in time, then *SIR*-models can be used to predict the spread of the disease and the duration of the epidemic. By introducing new elements into the model, it is possible to analyze the impact of external factors to reduce the spread of the epidemic, such as quarantine and distance control, etc.

The interpretation of the main and additional factors that describe the characteristics of the epidemic within the framework of compartment models (the base number of reproduction, the effective number of reproduction, the growth coefficient or the time of infection of the patient, and others) are presented in [8].

The following models represent development of *SIR*-models:

*SIRS* – "susceptible-infected-recovered-susceptible": a model for describing the dynamics of diseases with temporary immunity (recovered individuals become susceptible again over time);

*SEIR* – "susceptible-contact-infected-recovered": a model for describing the spread of diseases with an incubation period;

*SIS* – "susceptible-infected-susceptible": a model for the spread of a disease to which no immunity is developed;

*MSEIR* – "immune from birth-susceptible-contact-infected-recovered": a model that takes into account the immunity of children acquired in utero.

Recently, many authors prefer the *SEIR* or *SEIRD* models ($D$ stands for designation of the mortality cell), and scientific simulators were developed to visualize calculations based on such models. Mathematical models with on-screen settings of an extended set of modelling parameters were developed, which allows to evaluate the directions for improving information support for health care organizers (the share of hospitalization, the share of mortality, the index of contagiousness, etc.). The availability of open databases on COVID-19 pandemic contributes to testing a large number of proposed software implementations of *SIR*-models.

The analysis of examples of the use of compartmental models based on data from domestic sources shows that the most difficult issues are the content justification of the choice of data sources, as well as the assumptions and limitations in the parametric identification of models. The quality of the model selection is affected by the presence of high uncertainty of the initial data, including such difficulties as determining the real number of people who are in the incubation period (experts find it difficult to fix the duration, the values are said to be from 5 to 28 days with a distribution mode of 14 days). Large interference is caused by the error in testing the infection rate of the population (especially at the early stages of the development of numerous tests), the presence of both false-positive and false-negative test results.

There is no consensus in the expert community about the risk of infection from asymptomatic (infected or already infected) cases: different understanding of this phenomenon requires the construction of several scenarios for the spread of the epidemic.

One of the critical stages to construct the model is setting the so-called contact intensity coefficient with subsequent infection. According to expert estimates, a person with COVID-19 can infect another 3,3–5,5 people in his or her environment. At the start of the pandemic, it was believed that this coefficient belongs to the range (2...3), although there are also estimates of this coefficient from the range (6...7). This means that additional research is needed to clarify the complex of interrelated issues.

In [9], four scenarios of the spread of COVID-19 coronavirus are considered, in which the authors applied a discrete logistic equation describing the increase in the number of cases, which comes from the Verhulst equation used to model the COVID-19 epidemic based on the basic *SIR*-model. This shows the relevance of the classical results of mathematical modelling of epidemics.

When modelling the COVID-19 epidemic based on the *SEIRD* model, the solution depends on two main parameters: the rate of infection and the rate of recovery. Complicating the model by introducing additional coefficients (quarantine and hospitalization) allowed to take into account restrictive anti-epidemic measures in the modelling, but did not allow to obtain results that fully meet the needs of the practice. The reason for this is that *SEIRDS* are based on the assumption of homogeneity, when the population in question is considered uniformly mixed, which does not allow for the different infection channels and foci of infection inherent in COVID-19. In addition, there are no adequate approaches to the scalability of the results of epidemic modelling based on the *SEIRD*-model.

To level out these features, COVID-19 epidemic models based on the Monte-Carlo mathematical method and the concept of multi-agent systems were developed [10–12]. A distinctive feature of these models was the personification of information about each "typical individual". The implemented model takes into account data on each representative of a certain social group of residents about their localization, social affiliation, and signs of infection.

This allows, first, to set the characteristics of behavior depending on social affiliation and role, daily activity, habitual places of stay outside the home, etc., and second, to take into account the features of places and time spent surrounded by other people with pre-defined restrictions on crowding. Taking into account this statement of the problem, at each step of the modelling, the probability of infection of a conditional individual of a particular social group is calculated, depending on the time of probable contact, the number of infected people in the room, the area of the room in accordance with the activity scenario assigned to it.

Based on the results of such calculations, taking into account the known statistics of hospitalization and disease outcomes, it is possible, among other things, to count deaths in individual cohorts, in particular, among the elderly. To do this, it is necessary to set up a multi-agent model by analogy in such a way as to take into account the peculiarities of behavioral activity and the social circle of an elderly person.

Despite the impressive results of constructing mathematical models of this kind, we should not lose sight of the paramount importance of building an ontology of the subject area, since without expert knowledge today it is not possible to operate with the input data necessary to solve predictive problems. It is obvious that expert views on such a complex topic are differ, and even significantly. From this point of view, in conditions of uncertainty, adequate mathematical methods are additionally needed to generalize rank preferences of experts about the duration of recovery, about the latent period of the disease, etc. at all stages of its development.

## Conclusion

Drawing attention to the issues of mathematical modelling of COVID-19 pandemic and the expected losses in the cohort of elderly people is of great importance today in light of the threats of repeated focal outbreaks due to insufficiently researched issues of immunity stability after the disease and the effectiveness of vaccination, the development of technologies for which is actively underway in the world.

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## МАТЕМАТИЧЕСКОЕ МОДЕЛИРОВАНИЕ РАСПРОСТРАНЕНИЯ ЭПИДЕМИИ COVID-19 ДЛЯ ПРЕВЕНТИВНЫХ МЕР ЗАЩИТЫ ЖИЗНИ И ЗДОРОВЬЯ ПОЖИЛЫХ ЛЮДЕЙ

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Для обоснования комплекса мероприятий, направленных на обоснование комплекса превентивных мер сохранения жизни и здоровья пожилых людей в условиях пандемии COVID-19, применяют количественные подходы, основанные на математическом моделировании. Анализ состояния разработки актуарных математических моделей смертности при эпидемии COVID-19 показывает необходимость построения моделей, которые отражают динамику изучаемых соотношений показателей инфицированности, заболеваемости, выздоровления и смертности в динамике пандемии с учетом влияния на этот процесс внешних факторов. Большинство известных математических моделей прогнозирования распространения и последствий COVID-19 являются компартментальными моделями, реализующими последовательные переходы между состояниями с выделением групп лиц с различной принадлежностью к прогрессированию/спаду распространения инфекции. Для нивелирования недостатков компартментальных моделей, обусловленных принятием допущения об однородности популяции населения и отсутствием адекватных подходов к масштабируемости результатов моделирования применяют модели, основанные на методе Монте – Карло и концепции многоагентных систем. Развитие методов моделирования связывается с необходимостью расширения информационной поддержки медицинского персонала и врачей – организаторов здравоохранения с обеспечением возможности онлайн-настройки параметров математических моделей и задействования данных из «облачных сервисов» с визуализацией результатов моделирования.

*Ключевые слова: математические модели распространения COVID-19; компартментальная модель; актуарная модель; SIR-модель; математическое моделирование эпидемий; многоагентная система.*

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